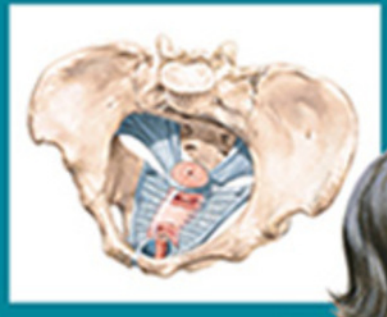
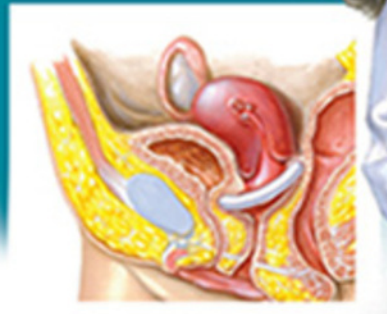




ROGER P. SMITH

NETTER'S OBSTETRICS & GYNECOLOGY

3rd EDITION

ELSEVIER

Expert CONSULT Built with inkling | E books

Any screen. Any time. Anywhere.

Activate the eBook version
of this title at no additional charge.

Expert Consult eBooks give you the power to browse and find content, view enhanced images, share notes and highlights—both online and offline.

Unlock your eBook today.

1. Visit **expertconsult.inkling.com/redeem**
2. Scratch off your code
3. Type code into "Enter Code" box
4. Click "Redeem"
5. Log in or Sign up
6. Go to "My Library"

It's that easy!

Scan this QR code to redeem your eBook through your mobile device:

Place Peel Off Sticker Here

For technical assistance:
email expertconsult.help@elsevier.com
call 1-800-401-9962 (inside the US)
call +1-314-447-8200 (outside the US)

ELSEVIER

2015v1.0

ELSEVIER

NETTER:

It's How You Know Anatomy.

Netter Collection of Medical Illustrations, 2nd Edition

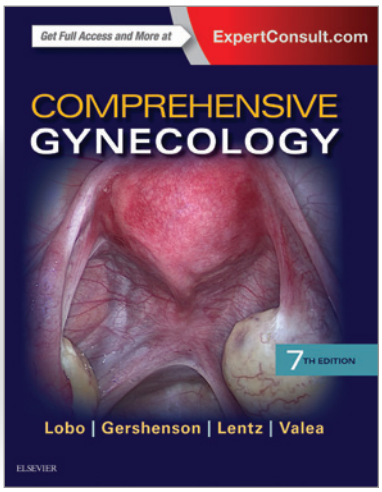
The Netter Collection of Medical Illustrations, Dr. Frank H. Netter's decades of work devoted to depicting each of the major body systems, has been updated and brought into modern context. The second edition of the legendary "**green books**" offers **Netter's timeless work**, now arranged and enhanced by **modern text and radiologic imaging**. **Contributions** by field-leading doctors and teachers from world-renowned medical institutions are supplemented with **new illustrations** created by **master artist-physician Carlos Machado** and other top medical illustrators working in the Netter tradition.

Netter's Correlative Imaging Series

The ***Netter's Correlative Imaging*** series pairs classic Netter and Netter-style illustrations with imaging studies and succinct descriptions to provide you with a richer understanding of human anatomy. These comprehensive, normal anatomy atlases cover all major sections of the body, featuring illustrated plates side-by-side with the most common imaging modalities for each region.

Shop online at **elsevierhealth.com**

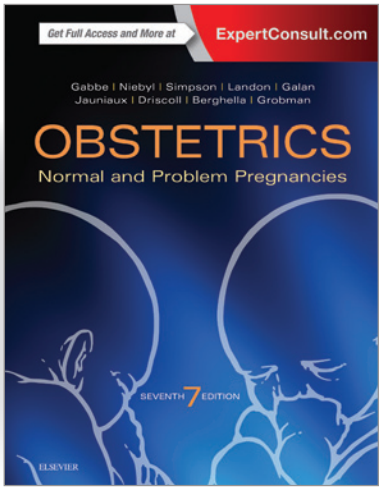
Stay current and connected in ObGyn with coverage of the latest hot topics.



Comprehensive Gynecology, 7th Edition

Rogerio A. Lobo, MD, David M. Gershenson, MD, Gretchen M. Lentz, MD, and Fidel A. Valea, MD

The primary gynecology text for over 25 years, ***Comprehensive Gynecology*** covers all of the **key issues** residents may encounter. This 7th edition has been **fully updated with a wealth of new content**, including current discussions of minimally invasive surgical approaches to gynecologic care, infertility issues and treatments, effectively managing menopausal patients, and more.



Obstetrics: Normal and Problem Pregnancies, 7th Edition

Steven G. Gabbe, MD, Jennifer R. Niebyl, MD, Joe Leigh Simpson, MD, Mark B. Landon, MD, Henry L. Galan, MD, Eric R.M. Jauniaux, MD, PhD, Deborah A. Driscoll, MD, Vincenzo Berghella, MD, and William A. Grobman, MD

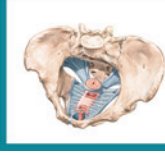
Obstetrics: Normal and Problem Pregnancies remains a go-to **choice for authoritative guidance** on managing today's obstetric patient. **International experts** put the latest knowledge in this specialty at your fingertips, with current and relevant information on everything from fetal origins of adult disease, to improving global maternal health, to important topics in day-to-day obstetrical practice. **Highly readable, well illustrated, and easy to understand**, this bestselling obstetrics reference is an ideal tool for residents.

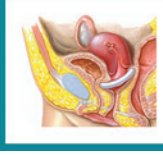
Shop online at **elsevierhealth.com!**

ELSEVIER

NETTER'S OBSTETRICS & GYNECOLOGY

3rd EDITION





Roger P. Smith, MD

Assistant Dean for Graduate Medical Education
Professor of Clinical Biologic Sciences
Charles E. Schmidt College of Medicine
Florida Atlantic University
Boca Raton, Florida

Illustrations by **Frank H. Netter,** MD

Contributing Illustrators
Carlos A.G. Machado, MD
John A. Craig, MD
Kristen Wienandt Marzejon, MS, MFA
Joe Chovan
James A. Perkins, MS, MFA
Tiffany S. DaVanzo, MA, CMI

ELSEVIER

ELSEVIER

1600 John F. Kennedy Blvd.
Ste 1800
Philadelphia, PA 19103-2899

NETTER'S OBSTETRICS AND GYNECOLOGY, THIRD EDITION ISBN: 978-0-7020-7036-5

Notices

Knowledge and best practice in this field are constantly changing. As new research and experience broaden our understanding, changes in research methods, professional practices, or medical treatment may become necessary.

Practitioners and researchers must always rely on their own experience and knowledge in evaluating and using any information, methods, compounds, or experiments described herein. In using such information or methods they should be mindful of their own safety and the safety of others, including parties for whom they have a professional responsibility.

With respect to any drug or pharmaceutical products identified, readers are advised to check the most current information provided (i) on procedures featured or (ii) by the manufacturer of each product to be administered, to verify the recommended dose or formula, the method and duration of administration, and contraindications. It is the responsibility of practitioners, relying on their own experience and knowledge of their patients, to make diagnoses, to determine dosages and the best treatment for each individual patient, and to take all appropriate safety precautions.

To the fullest extent of the law, neither the Publisher nor the authors, contributors, or editors, assume any liability for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein.

Library of Congress Cataloging-in-Publication Data

Names: Smith, Roger P. (Roger Perry), 1949- author. | Netter, Frank H. (Frank Henry), 1906-1991, illustrator.
Title: Netter's obstetrics and gynecology / Roger P. Smith ; illustrations by Frank H. Netter ; contributing illustrators, Carlos A.G. Machado, John A. Craig, Kristen Wienandt Marzejon, Joe Chovan, James A. Perkins, Tiffany S. DaVanzo.
Other titles: Obstetrics and gynecology
Description: Third edition. | Philadelphia, PA : Elsevier, [2017] | Includes bibliographical references and index.
Identifiers: LCCN 2016051375 | ISBN 9780702070365 (hardcover : alk. paper)
Subjects: | MESH: Genital Diseases, Female | Obstetric Surgical Procedures | Pregnancy Complications | Atlases
Classification: LCC RG110 | NLM WP 17 | DDC 618.1–dc23 LC record available at https://lccn.loc.gov/2016051375

Content Strategist and Content Development Specialist: Marybeth Thiel
Publishing Services Manager: Patricia Tannian
Project Manager: Ted Rodgers
Design Direction: Patrick Ferguson

Printed in China
Last digit is the print number: 9 8 7 6 5 4 3 2 1

PREFACE

No student of medicine, past or present, is unaware of the extraordinary series of medical illustrations created by Dr. Frank Netter. It is an incredible body of work that has been carried forward by the talented Carlos Machado, MD, and John Craig, MD, since Dr. Netter's passing. Older physicians have looked with envy at these images, wishing they had been available when they were learning; established physicians return to them as comfortable sources of information; young physicians seek them out for the wealth of information they contain and their ability to make clear difficult clinical concepts. This spirit of concise reference and resource is the premise of this text.

This third edition maintains the same consistent format in presenting topics to facilitate rapid access—the same information is in the same location—that was so well received in the first and second editions. Chapters have been organized to provide a quick, concise resource for the diagnosis and treatment of common conditions encountered by anyone who provides care for women. In producing this third edition, more than 25 new topics have been added, including sections on embryology and anatomy, a more intuitive organization has been developed, an expanded section on commonly encountered procedures is included, new artwork has been developed, and subtle enhancements (such as indications of the level of evidence provided for references) have been made throughout the work.

It is our hope that this work will be both a useful resource and a celebration of the artistic richness that is clinical medicine.

Roger P. Smith, MD

ABOUT THE ARTISTS

FRANK H. NETTER, MD

Frank H. Netter was born in 1906 in New York City. He studied art at the Art Students League and the National Academy of Design before entering medical school at New York University, where he received his MD degree in 1931. During his student years, Dr. Netter's notebook sketches attracted the attention of the medical faculty and other physicians, allowing him to augment his income by illustrating articles and textbooks. He continued illustrating as a sideline after establishing a surgical practice in 1933, but he ultimately opted to give up his practice in favor of a full-time commitment to art. After service in the United States Army during World War II, Dr. Netter began his long collaboration with the CIBA Pharmaceutical Company (now Novartis Pharmaceuticals). This 45-year partnership resulted in the production of the extraordinary collection of medical art so familiar to physicians and other medical professionals worldwide.

In 2005, Elsevier purchased the Netter Collection and all publications from Icon Learning Systems. There are now over 50 publications featuring the art of Dr. Netter available through Elsevier, Inc. (in the US: www.us.elsevierhealth.com/Netter; outside the US: www.elsevierhealth.com).

Dr. Netter's works are among the finest examples of the use of illustration in the teaching of medical concepts. The 13-book *Netter Collection of Medical Illustrations*, which includes the greater part of the more than 20,000 paintings created by Dr. Netter, became and remains one of the most famous medical works ever published. The Netter *Atlas of Human Anatomy*, first published in 1989, presents the anatomical paintings from the Netter Collection. Now translated into 16 languages, it is the anatomy atlas of choice among medical and health professions students the world over.

The Netter illustrations are appreciated not only for their aesthetic qualities, but, more important, for their intellectual content. As Dr. Netter wrote in 1949, ". . . clarification of a subject is the aim and goal of illustration. No matter how beautifully painted, how delicately and subtly rendered a subject may be, it is of little value as a *medical illustration* if it does not serve to make clear some medical point." Dr. Netter's planning, conception, point of view, and approach are what inform his paintings and what make them so intellectually valuable.

Frank H. Netter, MD, physician and artist, died in 1991.

Learn more about the physician-artist whose work has inspired the Netter Reference collection:

http://www.netterimages.com/artist/netter.htm.

CARLOS MACHADO, MD

Carlos Machado was chosen by Novartis to be Dr. Netter's successor. He continues to be the main artist who contributes to the Netter collection of medical illustrations.

Self-taught in medical illustration, cardiologist Carlos Machado has contributed meticulous updates to some of Dr. Netter's original plates and has created many paintings of his own in the style of Netter as an extension of the Netter collection. Dr. Machado's photorealistic expertise and his keen insight into the physician/patient relationship inform his vivid and unforgettable visual style. His dedication to researching each topic and subject he paints places him among the premier medical illustrators at work today.

Learn more about his background and see more of his art at:

http://www.netterimages.com/artist/machado.htm.

ONLINE CONTENTS

Visit www.ExpertConsult.com for the following:

Printable Patient Education Brochures from Ferri's Netter Patient Advisor, 3rd Edition

1. Managing Your Anorexia Nervosa
2. Breast Cancer: Screening and Prevention
3. Managing Your Bulimia
4. Managing Your Cervical Cancer
5. Managing Your Cervical Incompetence
6. Managing Your Cervical Polyps
7. Managing Your Dysmenorrhea
8. Managing Your Dysfunctional Uterine Bleeding
9. Managing Your Endometriosis
10. Managing Your Female Sexual Dysfunction
11. Managing Your Fibrocystic Breast Disease
12. Managing Your Hyperemesis Gravidarum
13. Managing Your Infertility
14. Kegel Exercises Strengthening Your Pelvic Floor Muscles
15. Managing Your Lactational Mastitis
16. Managing Your Menopause
17. Managing Your Menorrhagia
18. Managing Your Morning Sickness
19. Managing Your Ovarian Cancer
20. Managing Your Ovarian Cysts
21. Managing Your Pelvic Inflammatory Disease
22. Managing Your Uterine Fibroids
23. Managing Your Vaginal Dryness
24. Managing Your Bacterial Vaginal Infection
25. Managing Your Miscarriage
26. Weight Control For Women

CONTENTS

SECTION XIII
Obstetric Conditions and Concerns

PART IV: PROCEDURES

SECTION XIV
Procedures

SECTION

Embryology

This page intentionally left blank

SEXUAL DIFFERENTIATION

1

Genetic sex is determined by the complement and function of sex chromosomes (X and Y) that are present at the time of conception. A Y chromosome carrying specific genes is necessary for the development of testes. The testes are responsible for the organization of the sexual duct system into a male configuration and for the suppression of the paramesonephric (Müllerian) system responsible for female anatomic structures. In the absence of a Y chromosome, specifically required genes, or a functioning gonad, the development will be female. General phenotypic development of the female is viewed as a default event, although new evidence of a more complex process is emerging.

Sexual differentiation genes are located on the Y chromosome, the primary of which is the *SRY* gene, also called the testis-determining factor. The *SRY* gene is found on the short arm of the Y chromosome and influences Sertoli cell differentiation, mesonephric ridge cell development, and male architectural development of the gonad, including blood vessels and other structures of the testes. Several other genes, including those that express

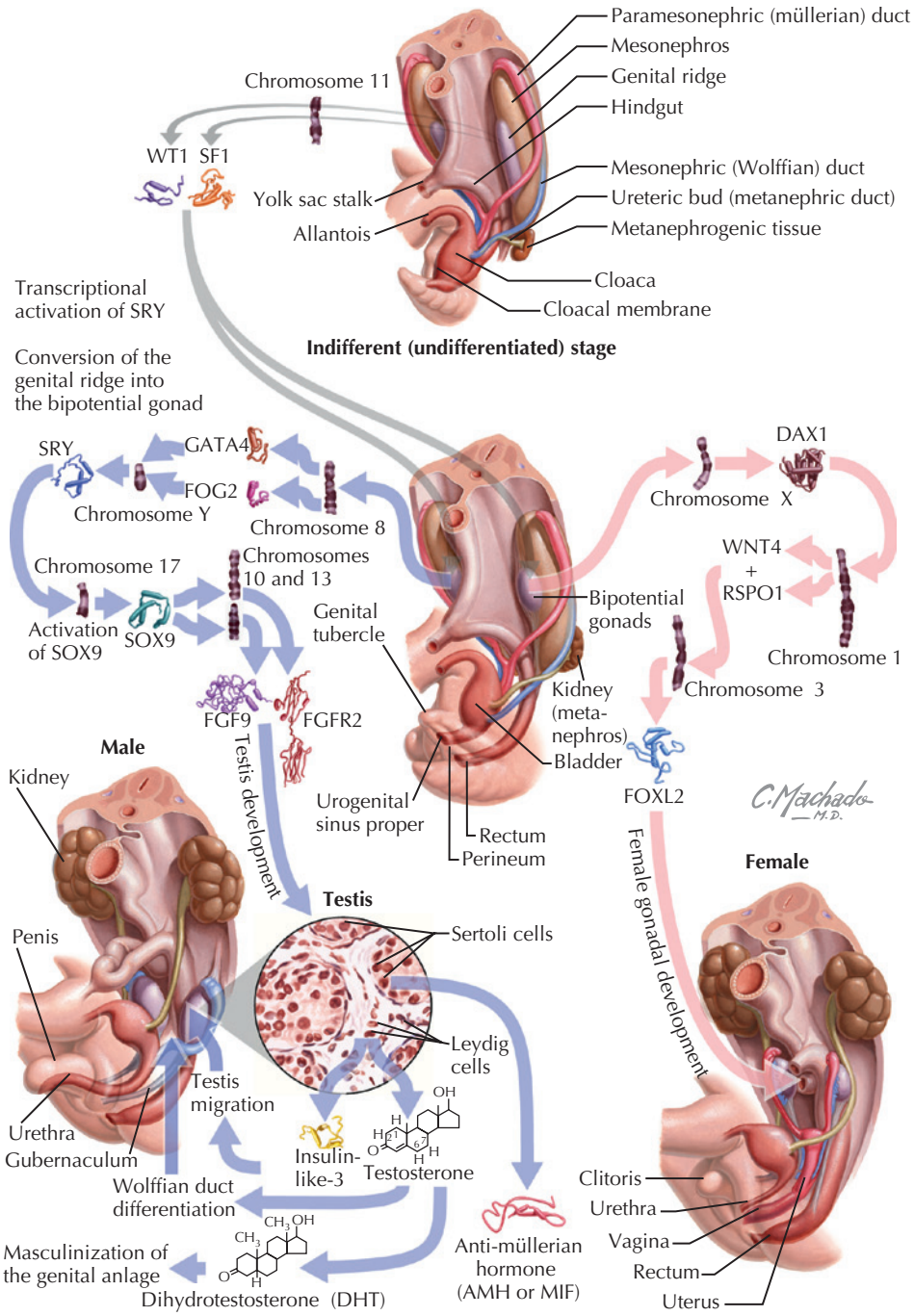


Figure 1.1 Genetics and biology of early reproductive tract development

steroidogenic factor-1, WT1, and DAX1, on other chromosomes, are also necessary for normal testicular development. To date, multiple mutations of the *SRY* gene have been reported and all are associated with sex reversals (female phenotype).

As discussed earlier, genes in other locations are also important for complete male sexual differentiation. DAX1, a nuclear hormone receptor, can alter *SRY* activity during development by suppressing genes downstream to *SRY* that would normally induce testicular differentiation. A second gene, *WNT4*, largely confined to the adult ovary, may also serve as an "antitestis" gene. In very rare male individuals a Y chromosome may be absent, but the *SRY* gene may be present on another chromosome, most commonly the X chromosome, resulting in a male phenotype. It is becoming apparent that genes, such as *WNT4* and *DAX1*, can proactively induce female gonadal development even in the presence of *SRY*, thereby further complicating the picture. This may account for individuals who are exceptions to the normal sexual dichotomy (eg, males with a uterus or females with an XY karyotype) or who exhibit biologic and/or behavioral characteristics of both sexes.

Male gonadal development precedes female development, and the early secretion of testosterone and anti-Müllerian hormone (AMH) steers the further development of the genital tracts away from the default female phenotype. At a critical point, AMH, produced by Sertoli cells, and testosterone, secreted by Leydig cells, must be produced in sufficient amounts. AMH acts locally, thus suppressing the Müllerian duct system. Testosterone acts systemically, thus causing the differentiation of the mesonephric duct system and male development of the urogenital tubercle, urogenital sinus, and urogenital folds. Enzymes involved in testosterone biosynthesis and conversion to dihydrotestosterones are regulated by genes located on autosomes. The ability to secrete AMH is a recessive trait coded on either an autosome or the X chromosome, and genes for the development of cytoplasmic receptors of androgens seem to be coded on the X chromosome.

The development of the ovary occurs at approximately the 11th or 12th week of gestation, although the primordial germ cells migrate several weeks earlier to the germinal ridge. Two functional X chromosomes are necessary for the optimal development of the ovary. Thus, in 45,X and 46,XY females the ovaries are almost invariably devoid of oocytes. In contrast, germ cells in the testes do best when only one X chromosome is present; rarely do they survive in the XX or XXY condition.

When non-Y-bearing oocytes enter the differentiating gonad, the primary sex cords break up and encircle the oocytes in the cortex of the gonad (in contrast to the structure of the XY gonad). This occurs at approximately 16 weeks of gestation, and the isolated cell clusters are called primordial follicles. No new oogonia form after birth and many of them degenerate well before birth. Those that remain grow and become primary follicles to be stimulated following puberty.

2 UPPER GENITAL TRACT DEVELOPMENT

Phenotypic gender is determined by a complex tissue differentiation process that begins in the medial genital thickening or ridges on the posterior surface of the embryonic body cavity. Once gonadal sexual differentiation has begun, several other events must occur for normal male or female phenotypic differentiation to occur. During the fifth week after conception, coelomic epithelium, later known as germinal epithelium, thickens in the area of the medial aspect of the mesonephros. As germinal epithelial cells proliferate, they invade the underlying mesenchyme, producing the gonadal ridge. In the sixth week after conception the primordial germ cells, which formed at approximately the fourth week after conception, in the wall of the yolk sac, migrate up the dorsal mesentery of the hindgut and enter the undifferentiated gonad. These cells will differentiate into testes or ovaries based on the gene functions noted in Chapter 1, Sexual Differentiation.

Signaled by the arrival of primordial germ cells in the fifth week after conception, two sets of paired genital ducts, the mesonephric or nephric (wolffian) ducts and the paramesonephric (müllerian) ducts, develop. The mesonephric system is the precursor to the male genital system and the paramesonephric to the female reproductive structures. The mesonephros is a prominent excretory structure that consists of a series of mesonephric tubules. The tubules connect with the elongating mesonephric (wolffian) ducts as the latter extend caudally, terminating in the urogenital sinus on each side of the midline. Derived from the evagination of the coelomic epithelium, the paramesonephric ducts develop lateral to each of the mesonephric ducts. The cephalward ends of these ducts open directly into the peritoneal cavity, whereas the distal ends grow caudally, fuse in the lower midline, and form the uterovaginal primordium. They join the urogenital sinus as an elevation, known as the müllerian tubercle, which separates the urogenital area from the more posterior gut. Under the influence of the *SRY* gene in the prototestis the mesonephric (wolffian) ducts are maintained during development. As the developing male Sertoli cells begin to differentiate in response to SRY, they secrete a glycoprotein hormone, müllerian-inhibiting substance (MIS) or antimüllerian hormone (AMH), which causes the paramesonephric (müllerian) ducts to regress rapidly between the 8th and 10th fetal weeks. Without testosterone and AMH the mesonephric ducts degenerate and disappear, and the paramesonephric ducts develop into a uterus, fallopian tubes, and upper vagina. Leydig cells synthesize insulin-like-3 (coded by the *INSL3* gene) to promote transabdominal testicular descent into the scrotum. Mutations in this gene may lead to cryptorchidism. In females a structure similar to the gubernaculum develops in the inguinal canal, giving rise to the round ligaments that suspend the uterus in the adult.

Primary sex cords condense and extend to the medullary portion of the developing testes. They branch and join to form the rete testis. The testis therefore is primarily a medullary organ. Eventually the rete testis connects with the tubules of the mesonephric system and joins the developing epididymal duct. Müllerian duct remnants in the male include the appendix testis (hydatid of Morgagni) and the prostatic utricle. In females, MIS is not present, so müllerian ducts remain and the mesonephric tubules and ducts degenerate in the absence of androgens. This often results in remnant epoöphoron and paroöphoron cystic structures within the ovarian mesentery and Gartner duct cysts within the anterolateral vaginal wall. These structures are clinically important because they may develop into sizable and symptomatic cysts (see Chapter 105, Vaginal Cysts).

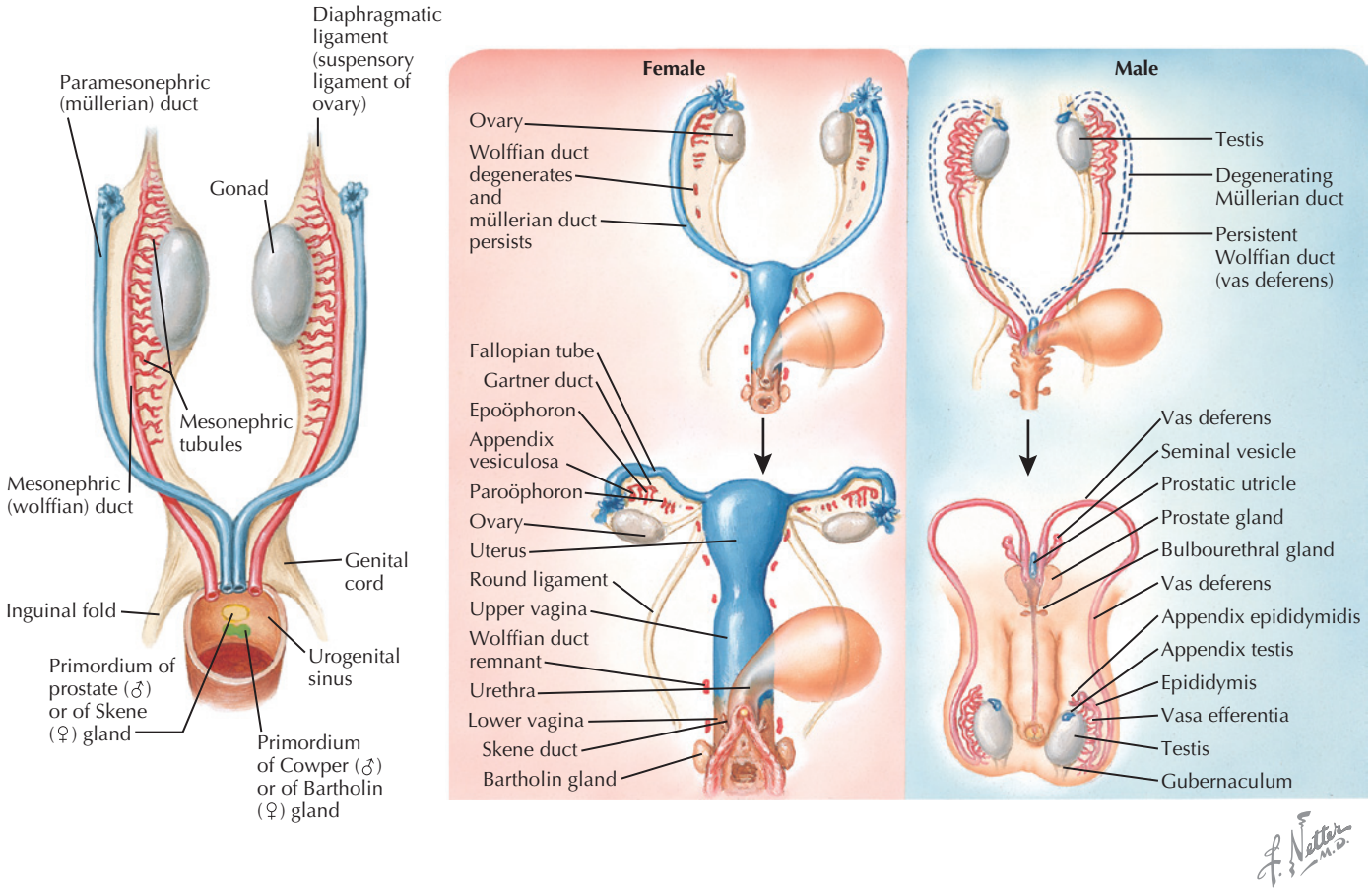


Figure 2.1 Homologs of the internal genitalia

The process of development and loss of the müllerian and wolffian systems begins at approximately the sixth week after conception and proceeds in a cephalad to caudal fashion. The more cephalad portions of the paramesonephric ducts, which open directly into the peritoneal cavity, form the fallopian tubes. The fused portion or uterovaginal primordium gives rise to the epithelium and glands of the uterus and cervix. Endometrial stroma and myometrium are derived from adjacent mesenchyme. Failure of the development of the paramesonephric ducts leads to agenesis of the cervix and uterus. Failure of fusion of the caudal portion of these ducts may lead to a variety of uterine anomalies, including complete duplication of the uterus and cervix or partial duplication of a variety of types (see Section VI, Chapter 136, Uterine Anomalies: Bicornuate, Septate, and Unicornuate Uterus). Peritoneal reflections in the area adjacent to the fusion of the two paramesonephric ducts give rise to the broad ligaments. Mesenchymal tissue here develops into the parametria.

The remnants of the mesonephric duct in the female include a small structure called the appendix vesiculosa, a few blind tubules in the broad ligaments (the epoöphoron), and a few blind tubules adjacent to the uterus (collectively called the paroöphoron). Remnants of the mesonephric duct system are often present in the broad ligaments or may be present adjacent to the uterus and/or vagina as Gartner duct cysts. The epoöphoron or paroöphoron may develop into cysts. Cysts of the epoöphoron are known as paraovarian cysts.

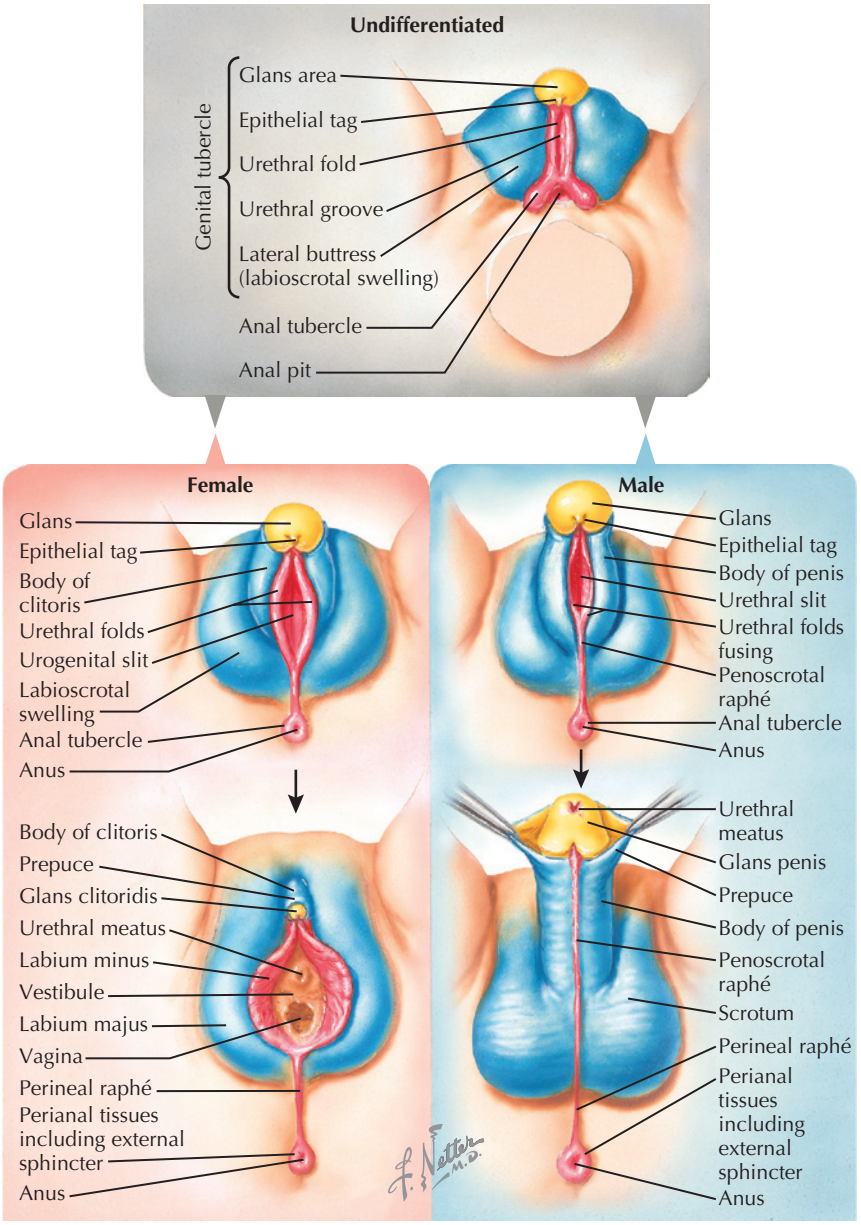


Figure 3.1 Homologs of external genitalia

imperforate until late in the embryonic life. However, occasionally, perforation does not completely occur (imperforate hymen). Failure of the sinovaginal bulbs to form leads to agenesis of the vagina. The precise boundary between the paramesonephric and urogenital sinus portions of the vagina has not been established.

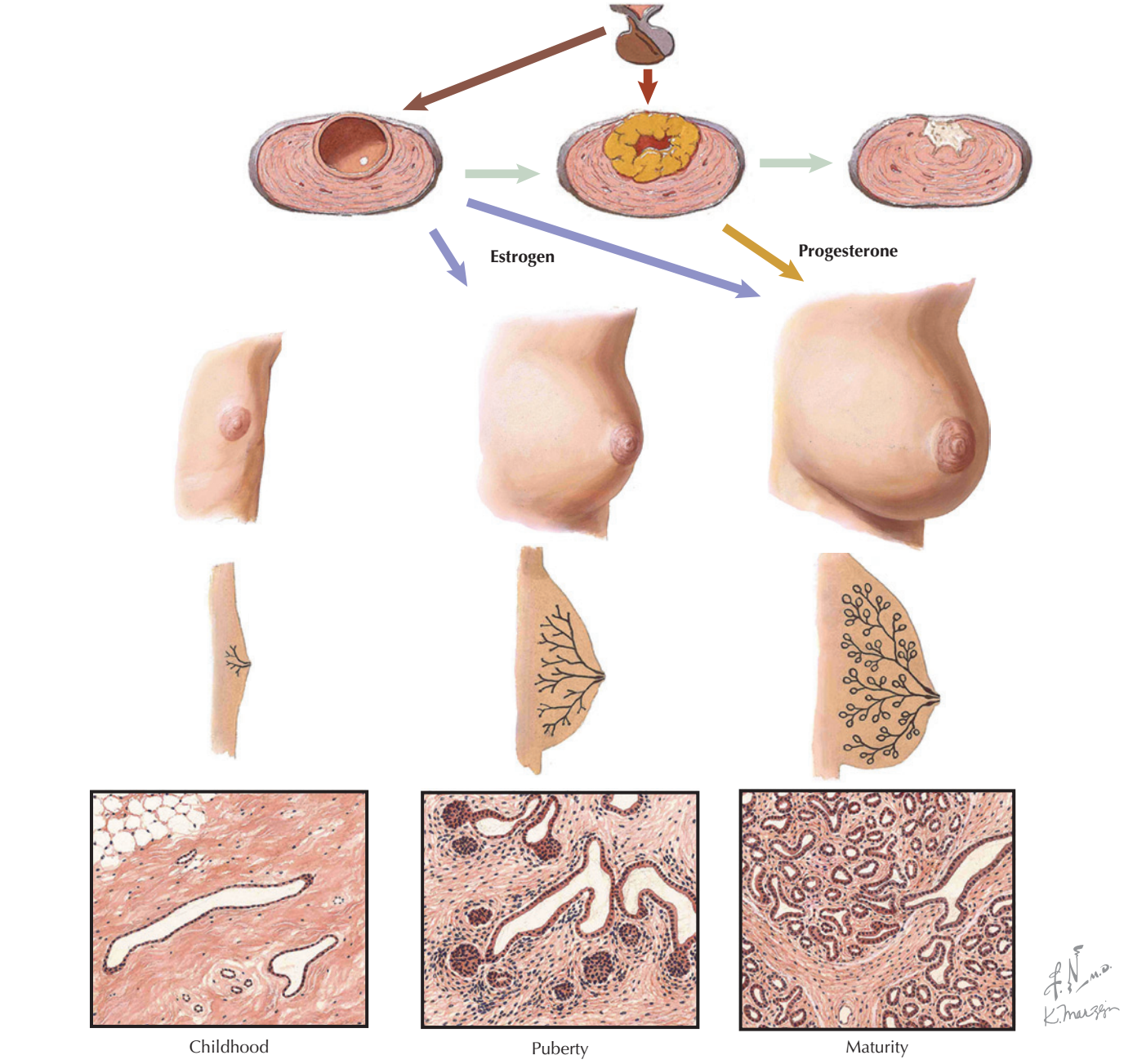
Beginning in the fourth week after conception, the genital tubercle develops at the ventral tip of the cloacal membrane, with the labioscrotal swellings and urogenital folds developing soon after on either side of the cloacal membrane. In both sexes the genital tubercle subsequently elongates to form a phallus. By the end of the sixth week, the cloacal membrane is joined by the urorectal septum. This septum separates the cloaca into the urogenital sinus ventrally and the anal canal and rectum dorsally. The point on the cloacal membrane where the urorectal septum fuses will become the site of the perineal body. The cloacal membrane, now in two parts, then ruptures, opening the vulva and anal canal. Failure of the anal membrane to rupture results in an imperforate anus. With the opening of the urogenital membrane a urethral groove forms on the undersurface of the phallus, completing the undifferentiated portion of external genital development. Differences between male and female embryos can be observed as early as the ninth week, but the distinct final forms are not found until 12 weeks of gestation.

Feminization of the undifferentiated external genitalia occurs in the absence of androgenic stimulation. The embryonic phallus remains quiescent and becomes the clitoris. The urogenital folds remain unfused except in front of the anus, forming the posterior fourchette. The unfused urogenital folds form the labia minora, while the labioscrotal folds remain as the labia majora. The labioscrotal folds fuse anteriorly to form the mons pubis. A portion of the urogenital sinus between the level of the hymen and the labia develops into the vestibule of the vagina, into which the urethra, the vagina, and the ducts of Bartholin glands enter. Beyond 12 weeks of gestation, the labioscrotal folds will no longer fuse when exposed to androgens, although other manifestations of masculinization may occur.

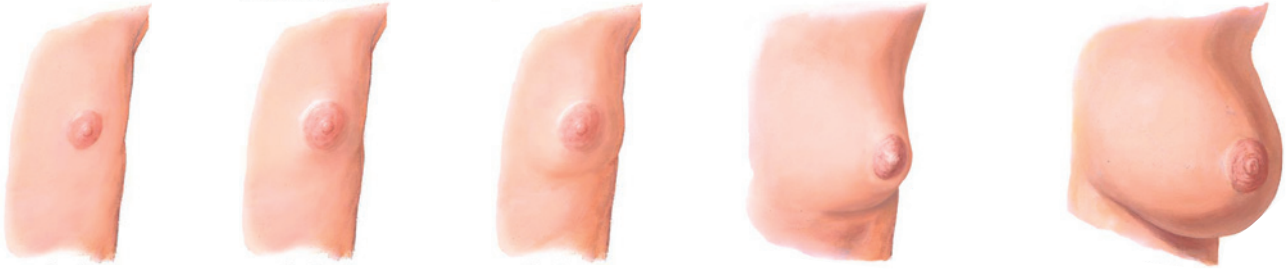
In contrast to the long-held belief that the development of the female genital was passive and occurred in the absence of androgens, the large number of estrogen receptors found in the genital tissues suggests that there is a role for maternal estrogens in the development of the female external genitalia. Female external

genital structures also contain androgen receptors. The distribution of androgen receptors resembles that of the male, which explains why the female genitalia can be masculinized if exposed to high androgen levels early in gestation.

The auxiliary genital glands of the female genitalia form from buds that grow out of the urethra. These buds come from the surrounding mesenchyme and form the urethral and paraurethral glands (Skene glands). These glands correspond to the prostate gland in males. Similar outgrowths of the urogenital sinus form the vestibular glands (Bartholin glands), which are homologous to the bulbourethral glands in the male.



Tanner Stages of Breast Development



Stage 1
Elevation of papilla only

Stage 2
Breast bud: elevation of breast and papilla as a small mound and enlargement of areolar diameter

Stage 3
Additional enlargement of breast and areola with no separation of their contours

Stage 4
Areola and papilla project from surface of breast to form secondary mound

Stage 5
Mature stage with projection of papilla only with recession of the areola to the general contour of the breast

Figure 4.1 Developmental stages of the breast

SECTION II

Anatomy

This page intentionally left blank

EXTERNAL GENITALIA

The perineum is bound in front by the mons veneris, behind by the buttocks, and laterally by the thighs. More deeply it is limited by the margins of the pelvic outlet; namely, the pubic symphysis and arcuate ligament, ischiopubic rami, ischial tuberosities, sacrotuberous ligaments, sacrum, and coccyx. The vulva includes the portions of the female genital tract that are externally visible in the perineal region.

The mons veneris is a fatty prominence that overlies the symphysis pubis. It is covered by curly sexual (pubic) hair that functions as a dry lubricant during intercourse. From the mons veneris the labia majora extend in elliptical fashion to enclose the vulval cleft. They contain an abundance of adipose tissue and sebaceous and sweat glands and are covered by hair on their upper outer surfaces. Posteriorly a slightly raised connecting ridge, the posterior commissure or fourchette, joins them. Between the fourchette and the vaginal orifice a shallow, boat-shaped depression, the fossa navicularis, is evident. The labia minora are thin, firm, pigmented, redundant folds of skin, which split anteriorly to enclose the clitoris. Laterally, they bound the vestibule and diminish gradually as they extend posteriorly. The skin of the small labia is devoid of hair follicles, poor in sweat glands, and rich in sebaceous glands.

The clitoris, a small, cylindrical, erectile organ situated at the lower border of the symphysis, is composed of two crura, a body and a glans. The crura lie deeply in close apposition with the periosteum of the ischiopubic rami. They join to form the body of the clitoris, which extends downward beneath a loose prepuce and is capped by the acorn-shaped glans. Generally, only the glans of the clitoris is externally visible between the two folds formed by the bifurcation of the labia minora.

The vestibule becomes apparent on separation of the labia. Within it are found the hymen, the vaginal orifice, the urethral meatus, and the opening of Skene and Bartholin ducts. The external

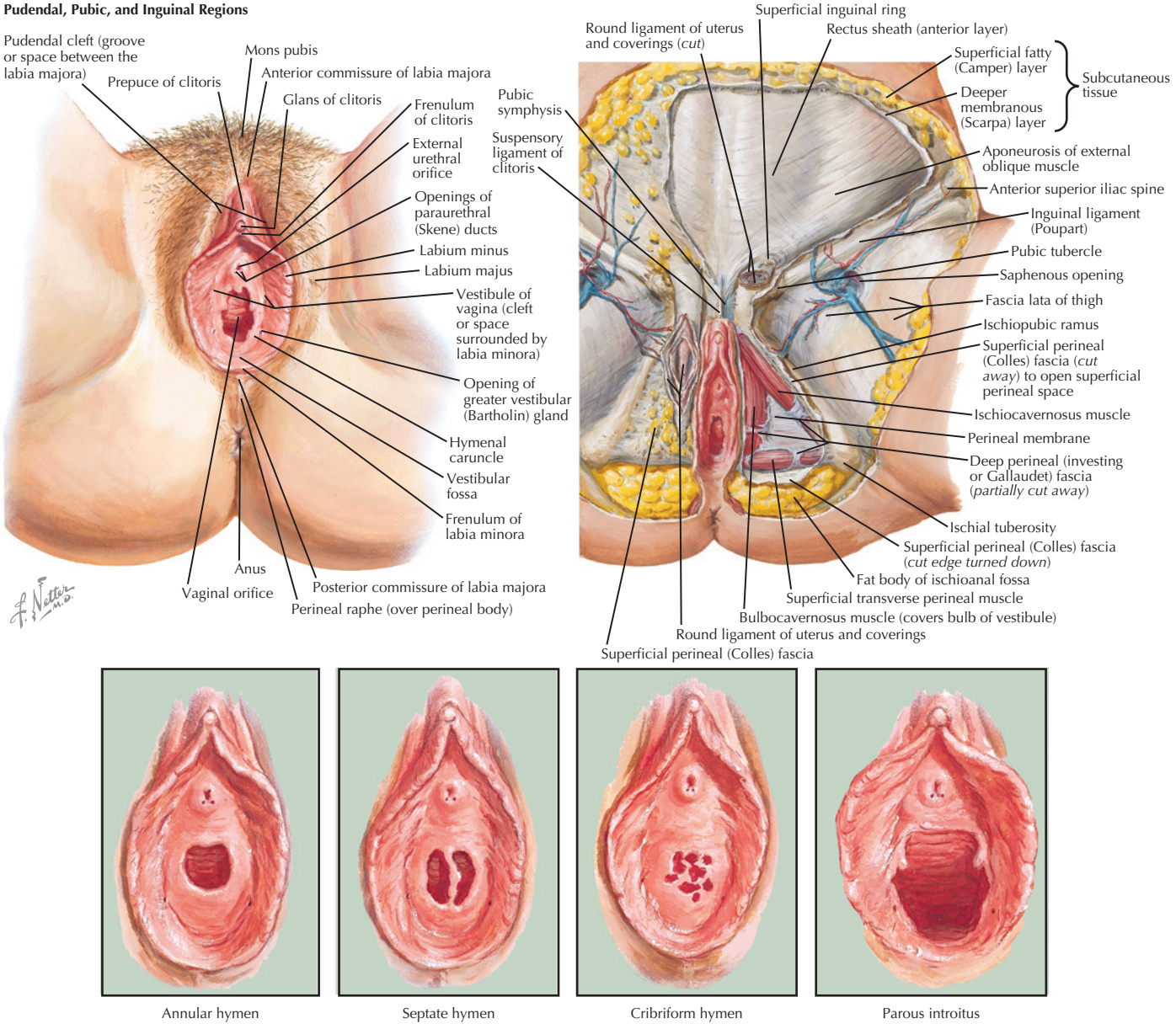


Figure 5.1 External genitalia

urethral meatus is situated on a slight papilla-like elevation, approximately 2 cm below the clitoris. In the posterolateral aspect of the urinary orifice lie the openings of Skene ducts. They run below and parallel to the urethra for a distance of 1–1.5 cm. Bartholin ducts are visible on each side of the vestibule, in the groove between the hymen and the labia minora, at about the junction of the middle and posterior thirds of the lateral boundary of the vaginal orifice. Each duct, approximately 1.5 cm in length, passes inward and lateral to the deeply situated vulvovaginal glands. The Bartholin glands are situated posterior to the 3 and 9 o'clock locations, which is important clinically when a Bartholin gland abscess is considered in patients with labial swelling.

The hymen is a thin, vascularized membrane or its remnants (the hymenal ring), which separates the vagina from the vestibule. It is covered on both sides by stratified squamous epithelium. As a rule, it shows great variation in thickness and in the size and shape of the hymenal openings (annular, septate, cribriform, crescentic, fimbriate, etc.). After tampon usage, coitus, and childbirth, the shrunken remnants of the hymen are known as carunculae hymenales or hymenal caruncles. The presence or absence of the hymen is insufficient to determine the presence or absence of past sexual activity.

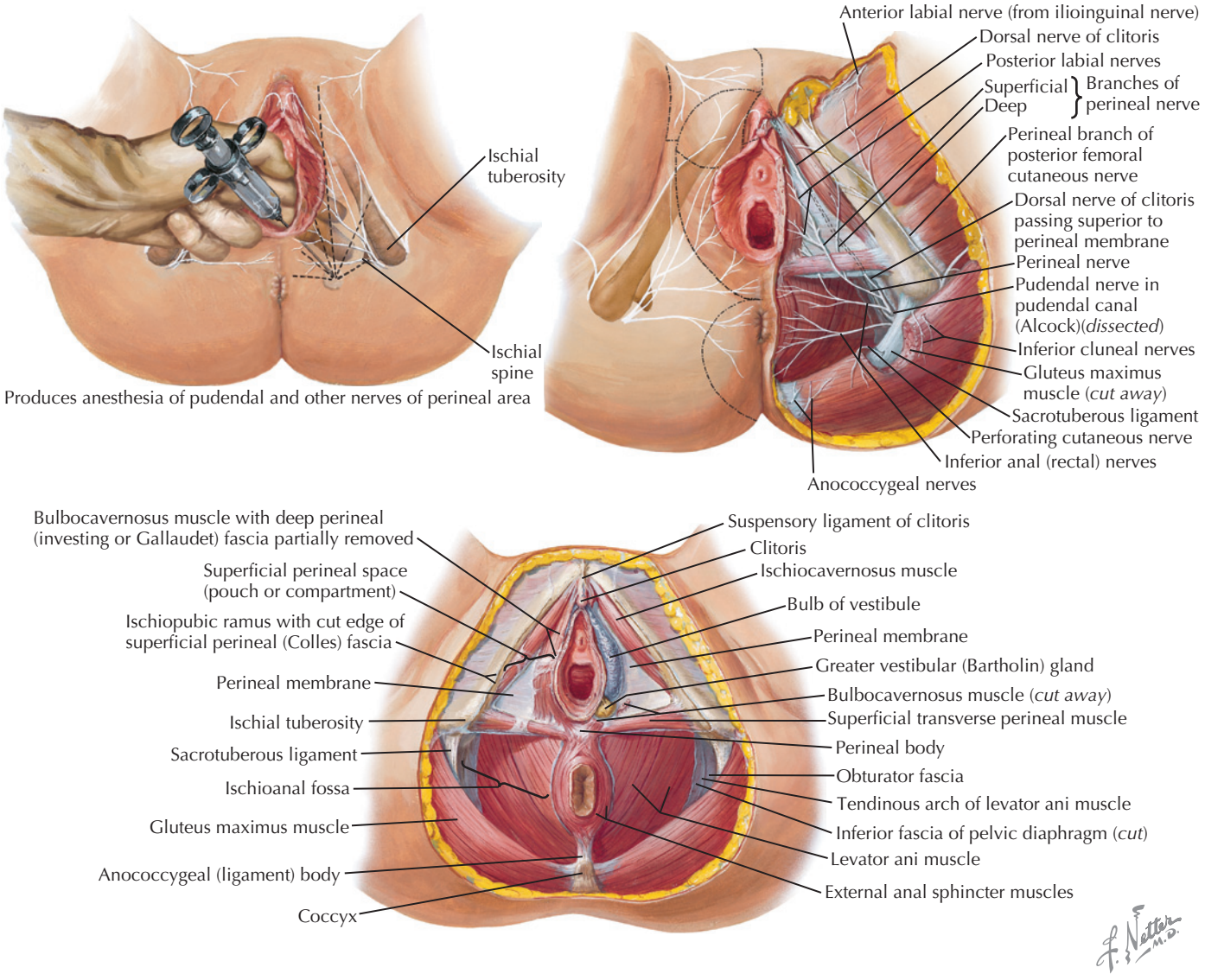


Figure 6.1 Innervation of external genitalia and perineum

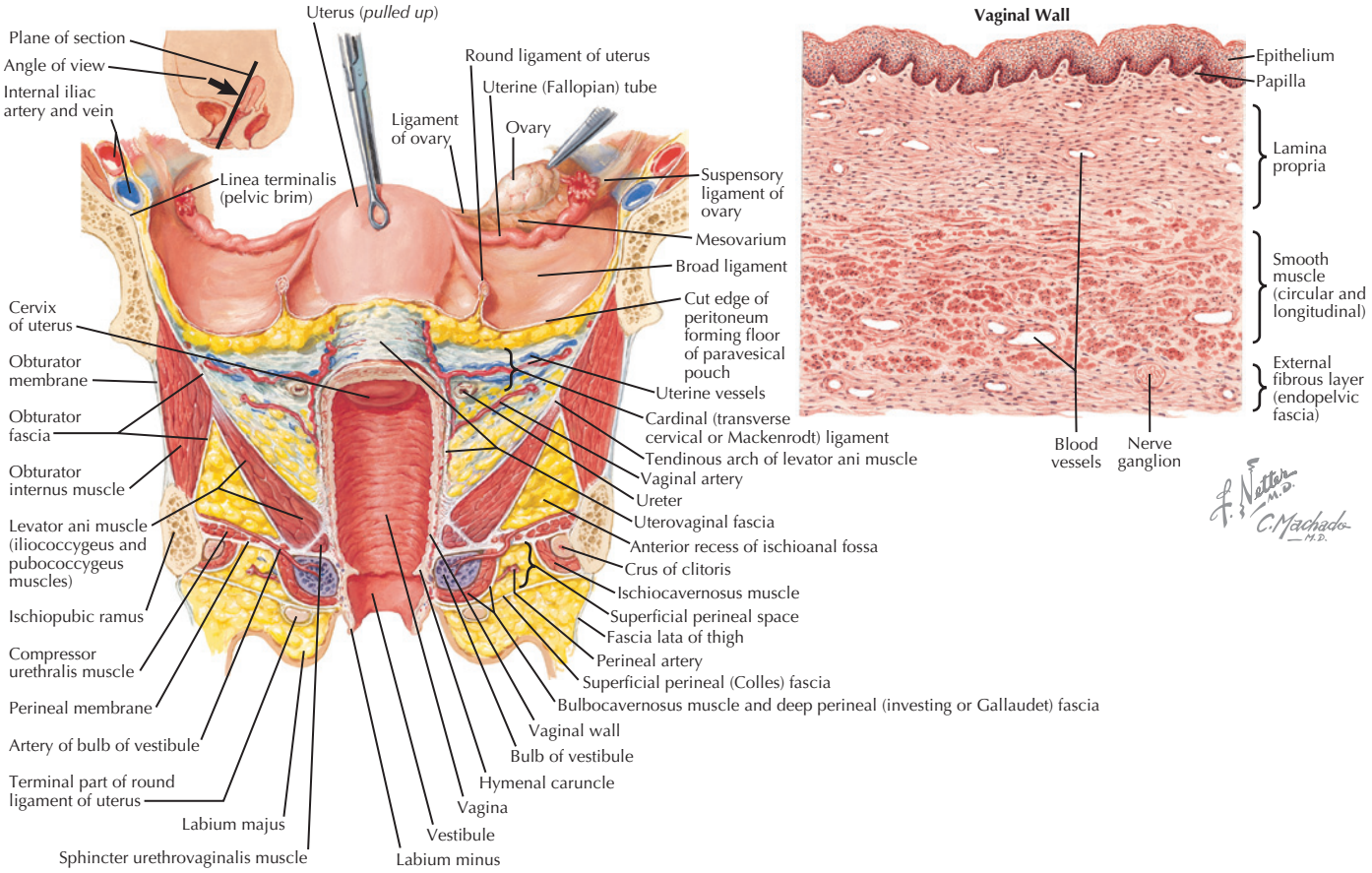


Figure 7.1 Support of pelvic viscera

sends more and larger papillae into the underlying connective tissue, giving the basement membrane an undulating outline. These papillae are more numerous on the posterior wall and near the vaginal orifice. Beneath the epithelium, which has a thickness of 150–200 μm, a dense connective tissue layer known as the lamina propria is supported by elastic fibers crossing from the epithelium to the underlying muscle. These elastic fibers, here and throughout the pelvis, are critical for pelvic support and function. The lamina propria becomes less dense as it approaches the muscle, and in this area, it contains a network of large, thin-walled veins, giving it the appearance of erectile tissues. The smooth muscle beneath this layer is divided into internal circular and external longitudinal groups, the latter being thicker, stronger, and continuous with superficial muscle bundles of the uterus. No dividing membrane or fascia separates these two interlacing muscle groups. The adventitial coat of the vagina is a thin, firm, fibrous layer arising from the visceral or endopelvic fascia. In this fascia and in the connective tissue between the fascia and the muscle runs another large network of veins and a rich nerve supply.

In its distal extreme the vagina opens to the vulva at the hymenal ring, opening at the caudal end of the vulva, behind the opening of the urethra. When upright the vaginal tube points in an upward–backward direction with the axis of the upper portion of the vagina close to the horizontal plane and curving toward the hollow of the sacrum. In most women an angle of at least 90 degrees is formed between the vagina and uterus. The cervix is directed downward and backward to rest against the posterior vaginal wall. The spaces between the cervix and attachment of the vagina are called fornices, with the posterior fornix considerably larger than the anterior fornix.

Although there is wide variation, the length of the vagina is approximately 6–9 cm (2.5–3.5 in.) along the anterior wall and 8–12 cm (3–4.5 in.) along the posterior wall. During sexual arousal, the upper portion of the vagina elongates and widens through a relative upward movement of the uterus and cervix. This is considered to facilitate capture and retention of sperm to improve the chance of conception.

Throughout most of its length the vagina lies directly on top of the descending rectum, separated by the rectovaginal septum. The upper one-fourth of the vagina is separated from the rectum by the rectouterine pouch (posterior cul-de-sac). The urethra and base of the urinary bladder lie above the anterior vaginal wall, separated by the thin layers of endopelvic fascia. As they enter the bladder, the ureters pass forward and medialward close to the lateral fornices.

The vagina is held in position by the surrounding endopelvic fascia and ligaments. The lower third of the vagina is surrounded and supported by the urogenital and pelvic diaphragms. The levator ani muscles and the lower portion of the cardinal ligaments support the middle third of the vagina, while the portions of the cardinal ligaments and parametria support the upper third.

The vagina is supplied with an extensive anastomotic network of vessels that surround its length. The vaginal artery originates either directly from the uterine artery or as a branch of the internal iliac artery arising posterior to the origin of the uterine and inferior vesical arteries. There is an anastomosis with the descending cervical branch of the uterine artery to form the azygos arteries. Branches of the internal pudendal, inferior vesical, and middle hemorrhoidal arteries also contribute to the interconnecting network from below. These can be a significant source of bleeding with obstetric lacerations. They are also important in the development of vaginal transudate during sexual arousal, when the vagina produces lubrication to aid in penetration.

While the muscular hammock of the levator plate provides the caudal (inferior) floor for the pelvic viscera, the organs of the pelvis have their own mechanisms of support. When either or both of these two support systems fail, it can result in clinical dysfunctions, including urinary incontinence, fecal retention, and dyspareunia. The viscera contained in the female pelvis minor include the pelvic colon, urinary bladder and urethra, uterus, uterine tubes, ovaries, and vagina.

The term endopelvic fascia (actually a pseudofascia) refers to the reflections of the superior fascia of the pelvic diaphragm on the pelvic viscera. At the points where these hollow organs pierce the pelvic floor, tubular fibrous investments are carried upward from the superior fascia as tightly fitting collars, which blend with and may even become inseparable from their outer muscle coat. Thus three tubes of fascia are present, encasing the urethra and bladder, the vagina and lower uterus, and the rectum. These fascial envelopes, with interwoven muscle fibers, are utilized in the repair of cystoceles and rectoceles anteriorly and posteriorly. It is also within this fibrous tube investing the lower uterine segment that the so-called intrafascial hysterectomy is performed in an effort to protect the support of the remaining vaginal cuff. The vesical, uterine, and rectal layers of endopelvic fascia are continuous with the superior fascia of the pelvic diaphragm, obturator fascia, iliac fascia, and transversalis fascia.

Uterine support is maintained directly and indirectly by a number of peritoneal, ligamentous, fibrous, and fibromuscular structures. Of these the most important are the cardinal ligaments and pelvic diaphragm with its endopelvic fascial extensions. The vesicouterine peritoneal reflection is sometimes referred to as the anterior ligament of the uterus and the rectouterine peritoneal reflection as the posterior ligament. These are not true ligaments, and they provide only limited additional support. The round ligaments are flattened bands of fibromuscular tissue invested with visceral peritoneum that extend from the angles of the uterus downward, laterally, and forward, through the inguinal canal to terminate in the labia majora. These are analogous to the gubernaculum in males.

The sacrouterine (uterosacral) ligaments are true ligaments of musculofascial consistency that run from the upper part of the cervix to the sides of the sacrum. At the uterine end, they merge with the adjacent posterior aspect of the cardinal ligaments and endopelvic fascial tube. The broad ligaments consist of wing-like double folds of peritoneum reflected from the lateral walls of the uterus to the lateral pelvic walls. Their superior margins encase the uterine tube and round ligaments. They then continue as the infundibulopelvic ligaments as they progress laterally and superiorly. Inferiorly the ensheathed uterine vessels and cardinal ligaments may be felt. Within the two peritoneal layers are found loose areolar tissue and fat, the fallopian tube, the round ligament, the ovarian ligament, the parametrium, the epoöphoron, paroöphoron and Gartner's duct, the uterine and ovarian vessels, lymphatics, and nerves.

The cardinal or transverse cervical ligaments (of Mackenrodt) are composed of condensed fibrous tissue and some smooth muscle fibers. They extend from the lateral aspect of the uterine isthmus in a tent-like fashion toward the pelvic wall, to become inserted, fan-shaped, into the obturator and superior fasciae of the pelvic diaphragm. This triangular septum of heavy fibrous tissue includes the thick connective tissue sheath, which invests the uterine vessels.

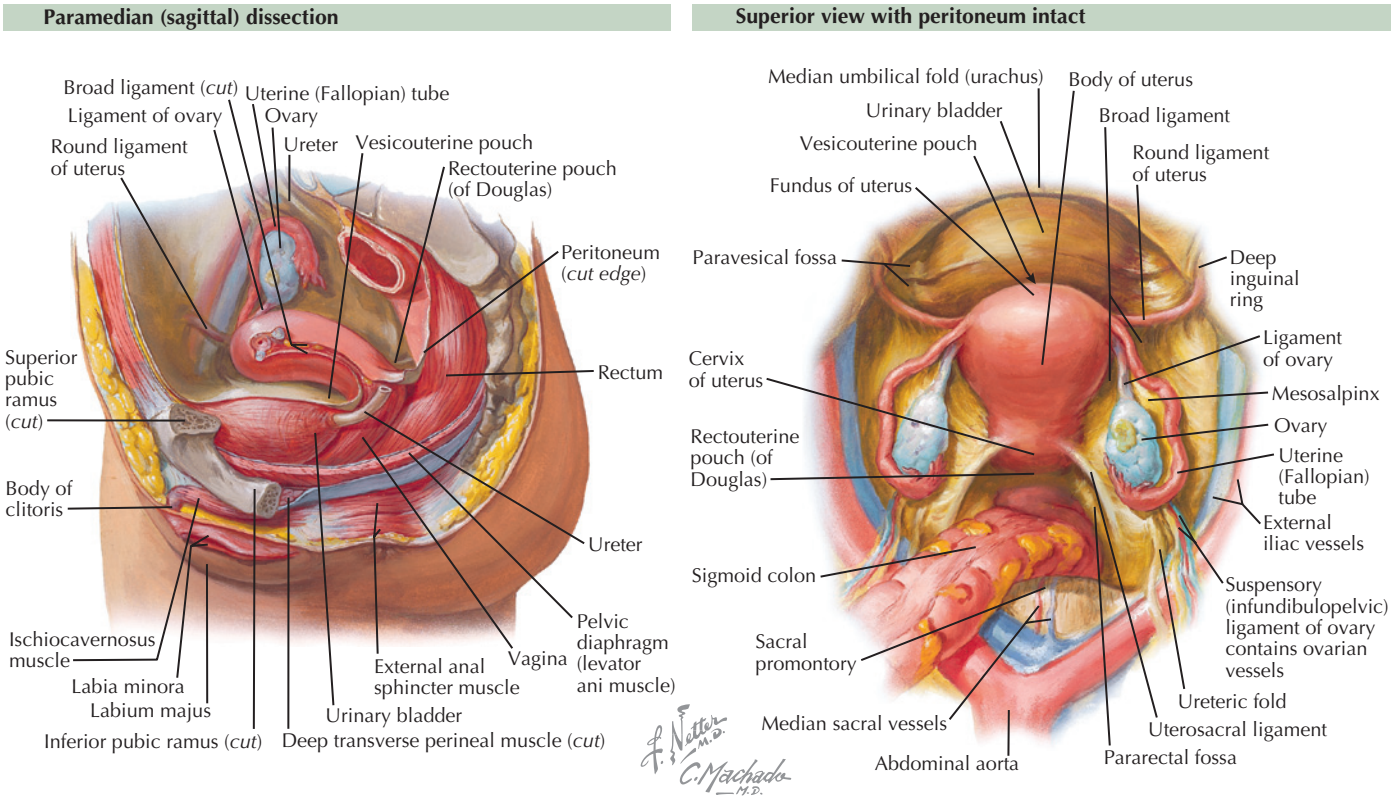


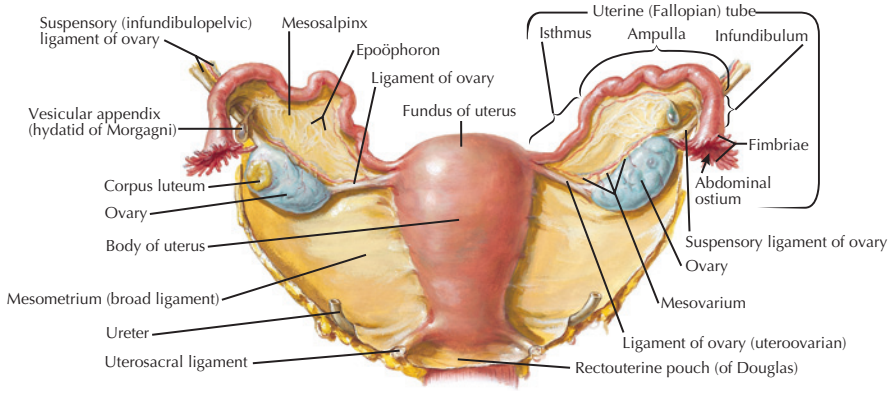
Figure 8.1 Paramedian dissection and super views of pelvic visera

Mesially and inferiorly the cardinal ligaments merge with the uterovaginal and vesical endopelvic fascial envelopes. Posteriorly, they are integrated with the uterosacral ligaments.

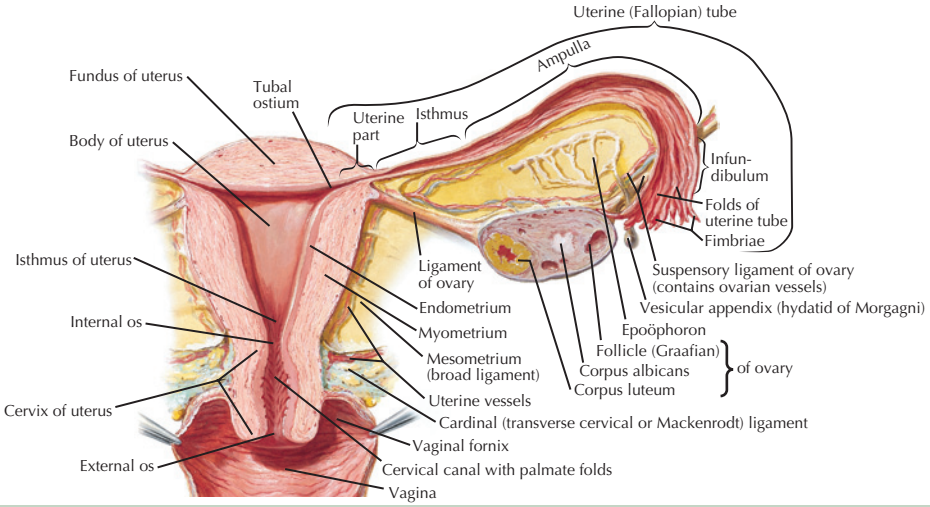
The vesical and rectal endopelvic fasciae maintain bladder and rectum support, respectively.

With the exception of the ovarian, superior hemorrhoidal, and middle sacral arteries the hypogastric divisions of the common iliac arteries supply the pelvic viscera. The uterine artery arises from the anterior division of the hypogastric artery close to or in common with the middle hemorrhoidal or vaginal artery. It courses slightly forward and medialward on the superior fascia of the levator ani muscle to the lower margin of the broad ligament. It arches over the ureter approximately 2 cm from the uterus. At the level of the isthmus, it gives off a descending cervical branch, which surrounds the cervix and anastomoses with the branches of the vaginal artery. The main uterine vessels follow a tortuous course upward along the lateral margin of the uterus, giving off spiral branches to the anterior and posterior surfaces of the uterus. The uterine artery terminates in a tubal branch within the mesosalpinx and an ovarian ramus, which anastomoses with the ovarian artery in the mesovarium.

Posterior view



Frontal section



Fallopian tubes

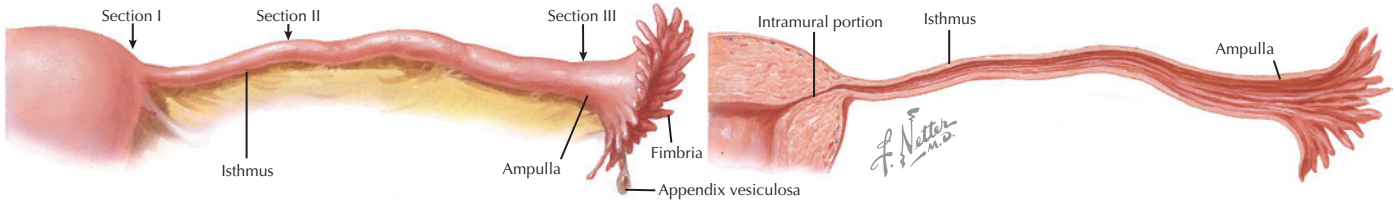


Figure 9.1 Uterus, ovaries, uterine, and Fallopian tubes

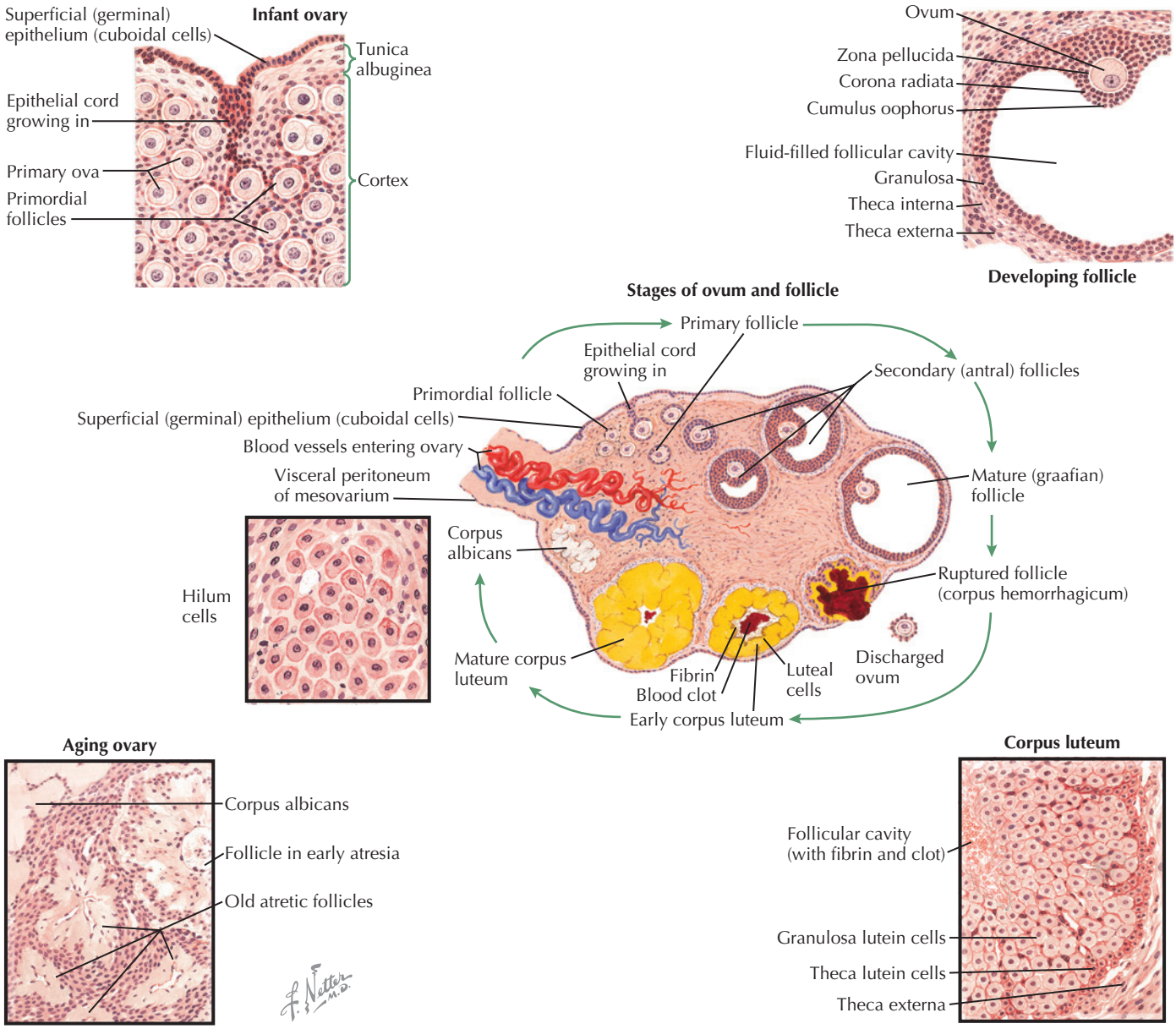


Figure 10.1 Ovarian Structures and development

occurs after menarche and during adolescence. Two layers, the germinal epithelium and the tunica albuginea, constitute the surface of the prepubertal ovary. They are crowded with primordial ova that are surrounded by dark-staining cells, the origin of the future granulosa cells.

As the primordial follicle develops, it sinks, with its single layer of epithelial cells, toward the center of the ovary. The attendant cells proliferate to form a layered coating of granulosa cells. A crescentic cavity forms eccentrically, in which follicular fluid accumulates. From the surrounding ovarian stroma a capsule of theca cells differentiates. The theca interna is rich in capillaries, on which the avascular theca granulosa must depend for nourishment. That stage of development is reached before menarche, while still little or no follicle-stimulating hormone is present. Before menarche, most, if not all, of these follicles develop no further but degenerate and become atretic.

The mature gonad is an approximately almond-shaped structure, pitted, and scarred by the stigmata of ovulation. Spiral arteries enter at the hilus and are involved in sequential changes during the cyclic ebb and sway of follicle growth and development of corpora lutea. In the hilus are also found cells with morphologic and histochemical properties, similar to the interstitial cells of the testis, vestiges from the fetal period, before sexual differentiation occurred. Proliferation of these cells or tumor formation may result in virilization.

In the ripening follicle, a dense layer of granulosa cells, the cumulus oophorus, closely protects the egg. A transparent membrane, the zona pellucida, encloses a fluid-filled perivitelline space in which the egg floats freely. The cumulus cells immediately next to the zona arrange themselves outward to form the corona radiata. The egg itself is a spherical body composed of clear protoplasm. It contains a round, dark-staining nucleus, with a definite surrounding membrane and an eccentric nucleolus.

The two-layered theca envelope coats the follicle. The theca interna is composed of large epithelioid cells interspersed in connective tissue and rich in blood and lymph vessels. The theca externa

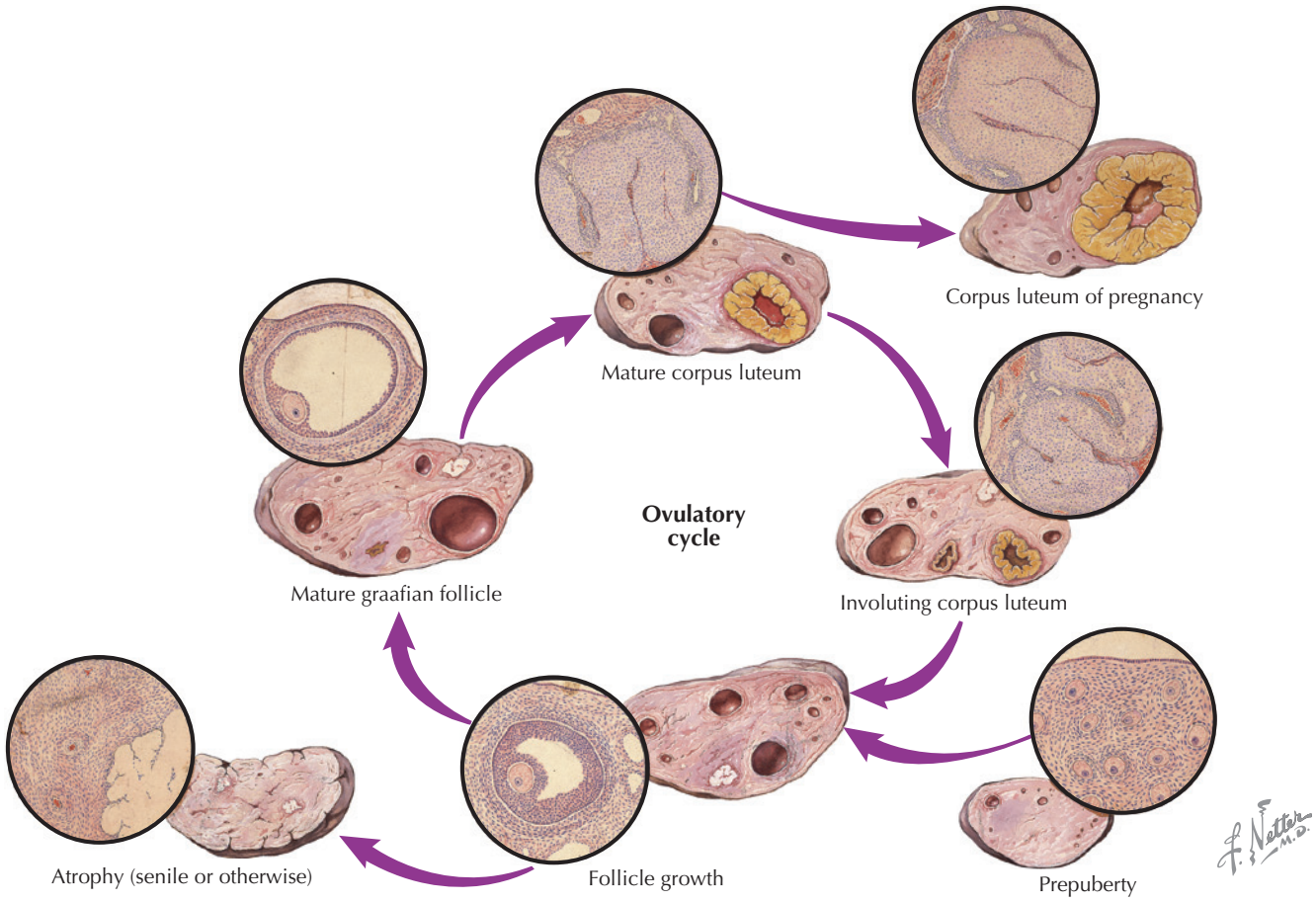


Figure 10.2 Ovarian cycle

is thick and dense, consisting of circularly arranged connective tissue fibers.

In the follicles that do not mature but degenerate the granulosa layer first becomes disorganized. The corona loses its radial arrangement. Thereafter, the follicular cavity shrinks, and soon the egg itself loses its characteristic features. Hyaline is deposited in a wavy, concentric band. Up to this point the theca interna has continued to be a prominent layer of large, vesicular, nucleated cells. Degenerative changes rapidly progress until nothing is left except an amorphous hyaline scar.

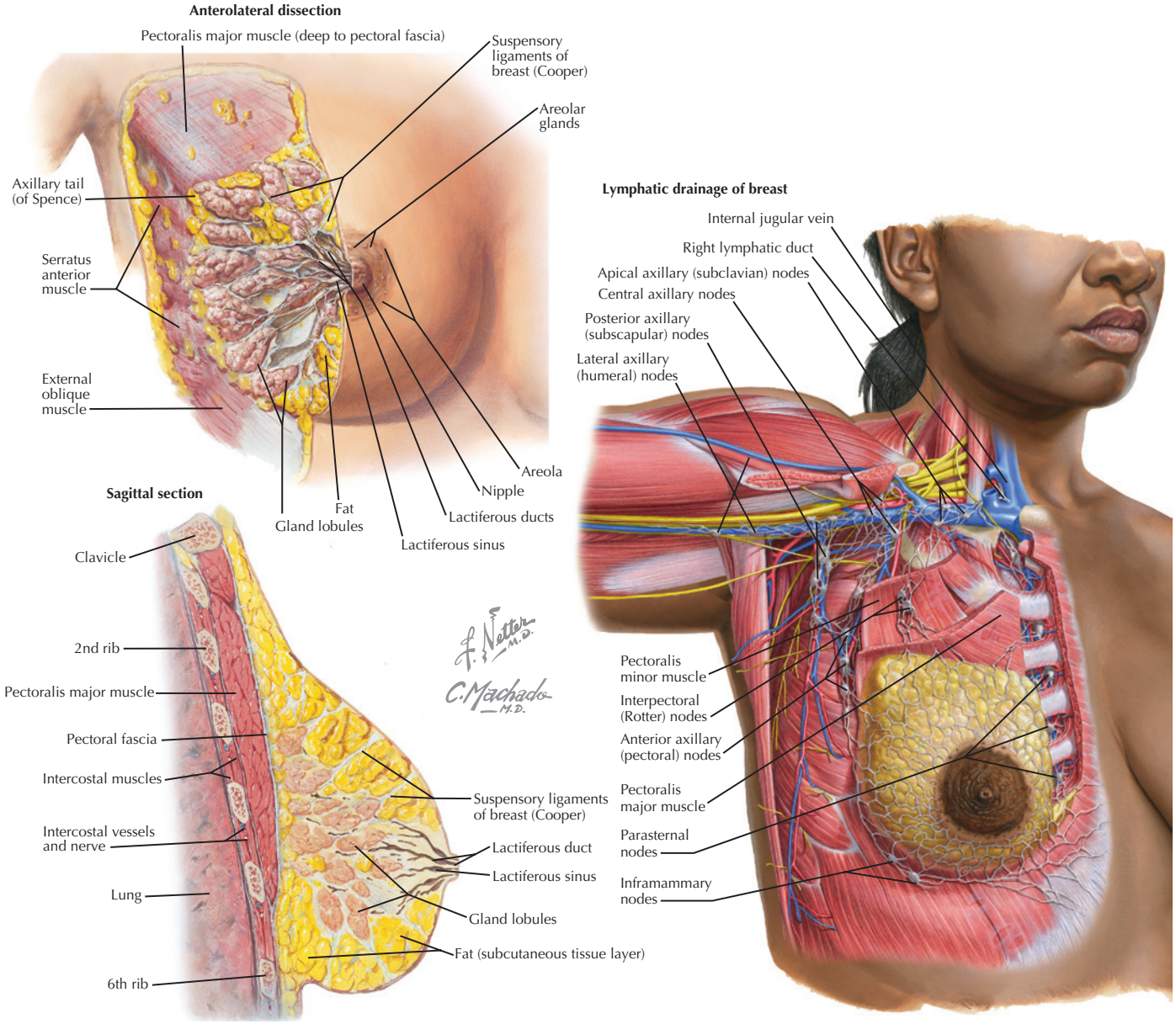


Figure 11.1 Position, structure, and lymphatic drainage of the breast

chest wall. From them sprout variable numbers of secondary tubules. These end in epithelial masses forming the lobules or acinar structures of the breast. The number of tubules and the size of the acinar structures vary greatly in different individuals and at different stages of life. In general, the terminal tubules and acinar structures are most numerous during the childbearing period and reach their full physiologic development only during pregnancy and lactation. These epithelial structures constitute collectively the parenchyma of the gland. The stroma is composed of a mixture of fibrous and fatty tissue, and in the absence of pregnancy and lactation the relative amounts of fatty and fibrous tissue determine the size and consistency of the breast.

Fatty deposits surround and intermix with the glandular elements and make up a significant portion of the breast structure, providing much of its bulk and shape. The ratio of fatty to glandular tissue varies among individuals and with the stage of life. During menopause, the relative amount of fatty tissue increases as the glandular tissue decreases. A rich vascular and lymphatic network supplies the breasts.

The sources of the abundant vascular supply of the mammary gland are the descending thoracic aorta, from which the posterior intercostal arteries branch off; the subclavian artery, from which the internal mammary artery arises; and the axillary artery, serving the mammary gland through the lateral thoracic artery and sometimes through another branch, the external mammary artery. Additional blood may be supplied by branches from the thoracodorsal artery and thoracoacromial artery, which is a short trunk that arises from the forepart of the axillary artery, its origin being generally overlapped by the upper edge of the pectoralis minor.

The lymphatic distribution of the breast is complex. The mammary gland has a very rich network of lymph vessels, which is separated into two planes, the superficial or subareolar plexus of lymphatics and the deep or fascial plexus. Both originate in the interlobular spaces and in the walls of the lactiferous ducts. The

lymph nodes that drain the breast are not linked in a straight line; instead, they are staggered, variable, and fixed within fat pads. This arrangement complicates lymph node removal during breast cancer surgery.

The sensory innervation of the breast follows the normal distribution of the dermatomes and is mainly derived from the anterolateral and anteromedial branches of the thoracic intercostal nerves T_3–T_5. Supraclavicular nerves from the lower fibers of the cervical plexus also provide innervation to the upper and lateral portions of the breast. Sensory enervation of the nipple is from the lateral cutaneous branch of T_4.

Support for the breast comes from both the skin envelope and fibrous suspensory ligaments of Astley Cooper that anchor the breast to the pectoralis major fascia. The enveloping fascia of the breast is continuous with the pectoral fascia. It subdivides the glands into lobules and sends strands into the overlying skin, which in the upper hemisphere, are known as the suspensory ligaments of Cooper. Because these strands are not taut, they enable the natural motion of the breast, but result in breast ptosis as these ligaments relax with age.

This page intentionally left blank

SECTION III

General Health Considerations and Counseling

This page intentionally left blank

PUBERTY: NORMAL SEQUENCE

12

THE CHALLENGE

The onset of puberty in adolescents is a time of great emotional and physical change. By understanding the normal sequence of events and being sensitive to the presence of abnormalities, the caregiver may be able to make the most of opportunities to improve health and well-being.

Scope of the Problem

The variety of decisions, concerns, and changes confronting an adolescent are formidable, not the least of which are health issues that result from rapid growth, sexual maturation, and emerging sexuality. Puberty involves physical, emotional, and sexual changes that mark the transition from childhood to adulthood. Despite the potential need for medical education and care, teenagers have the lowest rate of physician office visits of any group. Embarrassment, an inability to pay, a lack of familiarity with healthcare delivery options, and legal obstructions to access contribute to the lack of care.

Objectives of Management

Understanding the normal sequence of events involved in sexual maturation is important for counseling young women who may be concerned about "being normal." Identifying adolescents in whom the progression of sexual maturation is not normal is important so that timely evaluation and intervention may be achieved.

TACTICS

Relevant Pathophysiology

Hormonally, puberty involves a change from negative gonadal feedback to the establishment of the circadian and ultradian gonadal rhythms and the positive feedback controls that result in monthly cycles and fertility. It appears that three elements must be present for puberty to progress normally: adequate body mass, adequate sleep, and exposure to light. These factors appear to facilitate or allow the complex hypothalamic, pituitary, and ovarian changes that must occur. As the hypothalamus matures, there is a decrease in its sensitivity to estrogen, resulting in an increase in the production and release of gonadotropin-releasing hormone (GnRH). Consequently, follicle-stimulating hormone (FSH) levels begin to increase at approximately the 8th–10th year of life, accompanied by an increase in estrogen levels. As the sensitivity of the hypothalamus to negative feedback further decreases, FSH and luteinizing hormone (LH) levels continue to increase and acquire the rhythmic patterns necessary for normal cycling. Eventually, these hormones reach a sufficient level that the follicles can respond, initiating cyclic ovulation and menstruation.

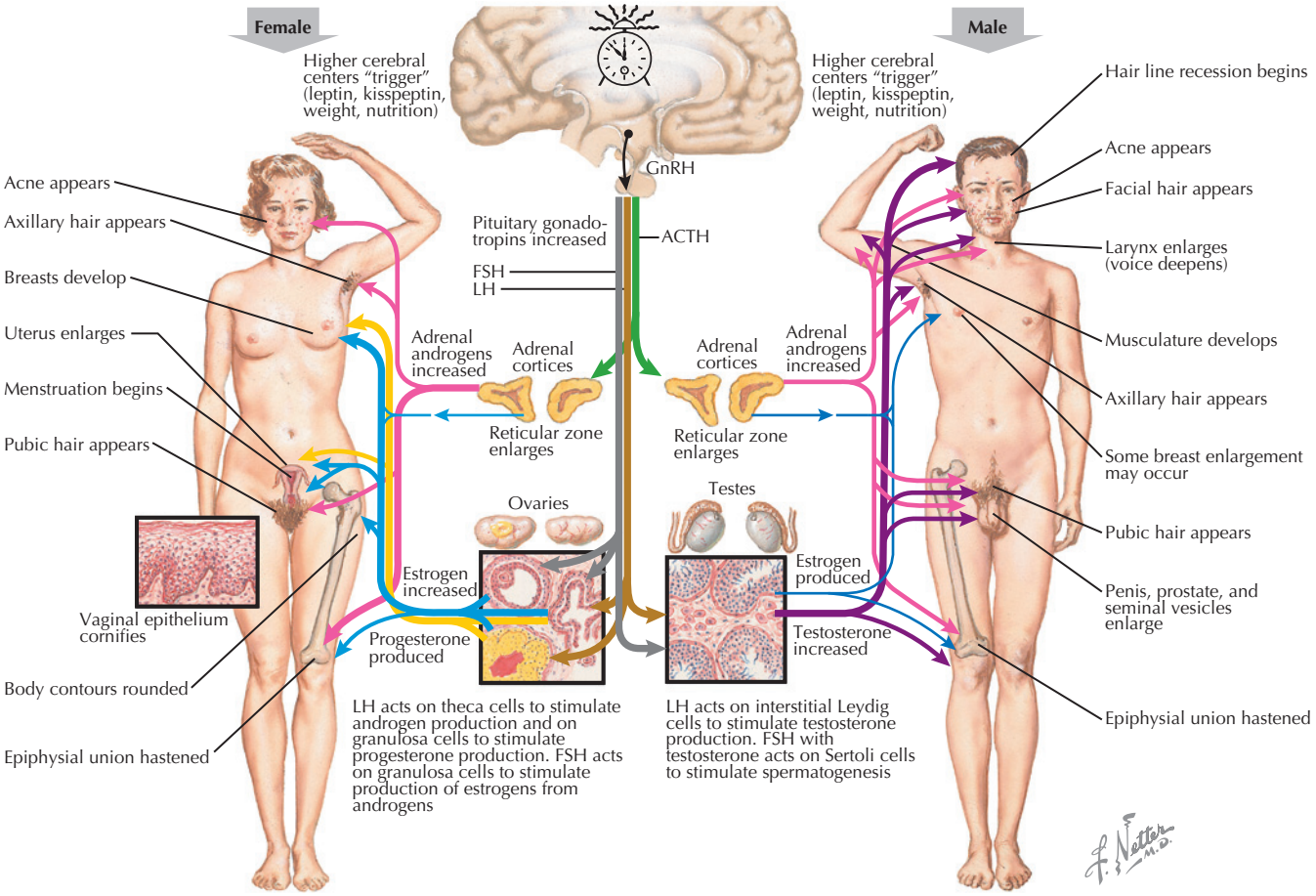


Figure 12.1 Hormonal events in female and male pubescence

Strategies

The changes of puberty generally follow a predictable pattern. A growth spurt and the rounding of body curves generally herald puberty. Breast tissue begins to develop, the nipples darken, and fat is laid down in the shoulders, hips, buttocks, and in front of the pubic bone (the mons). Body hair begins to appear because of the influence of androgens made in small amounts by the ovary and adrenal glands. Height increases because of accelerated growth in the long bones of the body, capped off by the closure of the growth centers near the end of puberty. Generally, this growth spurt begins approximately 2 years before the start of menstruation itself, with growth slowing about the same time menstruation begins.

Patient Education

American College of Obstetricians and Gynecologists Patient Education Pamphlet AP041 (Your Changing Body - Especially for Teens), 2012.

American College of Obstetricians and Gynecologists Patient Education Pamphlet AP042 (You and Your Sexuality - Especially for Teens), 2012.

American College of Obstetricians and Gynecologists Patient Education Pamphlet AP049 (Your First Period - Especially for Teens), 2012.

IMPLEMENTATION

Special Considerations

The average age of first menstruation (menarche) is approximately 11.6 years, with a normal age range of 8–16 years. These age ranges have gradually declined over the past few years and are as much as 2 years earlier for girls of African-American descent. Menarche generally occurs after the growth spurt and beginning of breast development, while changes in the pubic hair and labia are still under way. Although there is some variation in the normal progression of events, thelarche is the indication of pubertal change for most, followed by adrenarche, peak growth velocity, and ending with the onset of menstruation. This sequence generally takes 4.5 years to run its course, with a range of 1.5–6 years.

REFERENCES

LEVEL II

McDowell MA, Brody DJ, Hughes JP. Has age at menarche changed? Results from the National Health and Nutrition Examination Survey (NHANES) 1999–2004. *J Adolesc Health*. 2007;40:227-231. [Epub 2007 Jan 24].

Sanchez-Garrido MA, Tena-Sempere M. Metabolic control of puberty: roles of leptin and kisspeptins. *Horm Behav*. 2013;64(2):187-194.

LEVEL III

American College of Obstetricians and Gynecologists. *Menstruation in girls and adolescents: Using the menstrual cycle as a vital sign*. Washington, DC: ACOG; 2009 ACOG Committee Opinion 349.

American College of Obstetricians and Gynecologists. *Guidelines for adolescent health care*. 2nd ed. Washington, DC: ACOG; 2011.

Chulani VL, Gordon LP. Adolescent growth and development. *Prim Care*. 2014;41(3):465-487.

Neely EK, Crossen SS. Precocious puberty. *Curr Opin Obstet Gynecol*. 2014;26(5):332-338.

Reindollar RH, McDonough PG. Pubertal aberrancy: etiology and clinical approach. *J Reprod Med*. 1984;29:391.

Figure 13.1 The ages of 12–18 years represent a time of extreme changes in the body, body image, personality, and personal interactions. The physician must be aware of these changes, initiate a frank and open dialogue, and assure confidentiality except in those cases where safety or bodily harm are involved.

- Tobacco, alcohol, other drugs (including complementary and alternative medicines; data from the 2003 Youth Risk Behavior Surveillance Report indicate that many adolescents will begin engaging in risk-taking behaviors by the age of 13 years: 27.8% of adolescents report alcohol use before the age of 13 years)
- Abuse/neglect (20%–40% of adults report abuse or sexual victimization before 18 years of age)
- Sexual practices

Physical

- Height
- Weight (body mass index)
- Blood pressure
- Secondary sexual characteristics (Tanner staging)
- Pelvic examination (annually after 21 years of age)
- Skin

Laboratory (Only as Dictated by the Patient's History)

- Periodic
  - Pap test with high-risk human papillomavirus (HPV) cotesting (at or after 21 years of age, annually thereafter until at least three negative tests, then the interval may be increased). Note: Many patients are unaware of the difference between a Pap test and a pelvic examination for any other reason and this can be a good opportunity to discuss the difference.)
  - Cholesterol, high-density lipoprotein cholesterol (every 5 years)
- As indicated by risk factors
  - Hemoglobin
  - Bacteriuria testing
  - Sexually transmitted disease testing—chlamydia and gonorrhea (if the patient has had sexual contact, screening for STIs is important but urine-based STI testing can be an efficient means for doing so without a speculum examination)
  - Human immunodeficiency virus (HIV) testing
  - Genetic testing/counseling
  - Rubella titer
  - Tuberculosis skin test
  - Lipid profile
  - Fasting glucose

Imaging

None indicated as routine care

COUNSELING

It is important to discuss issues of confidentiality with both the patient and her parent or guardian: concerns over confidentiality often are a barrier to the delivery of healthcare services, especially reproductive healthcare, for adolescents. To overcome this obstacle, a discussion of this topic at the initial visit is important along with advice about relevant state and local statutes. For example, if the patient discloses any evidence or risk of bodily harm to herself or others, confidentiality must be breached. Furthermore, state laws may mandate the reporting of physical or sexual abuse of minors. Physicians should be familiar with state and local statutes regarding the rights of minors to healthcare services and the federal and state laws that affect confidentiality.

The main purpose of the initial reproductive health visit is preventive health, including educational information, rather than problem-focused care. Preventive counseling for parents or other supportive adults can include discussions about physical, sexual, and emotional development; signs and symptoms of common conditions affecting adolescents; and encouragement of lifelong healthy behaviors.

- Sexuality (including topics such as prevention of pregnancy and STIs) is important because more than 85% of adolescent females will have had some form of sexual contact (vaginal, anal, oral, or same sex) by the age of 19 years; nearly one-third of all ninth graders report having had sexual intercourse, and more than 60% of all 12th graders report having had sexual intercourse.
- Development
- High-risk behaviors
- Preventing unwanted/unintended pregnancy
  - Postponing sexual involvement
  - Contraceptive options (should also include emergency contraceptive options)
  - STIs
  - Partner selection
  - Barrier protection
- Date rape prevention
- Fitness
- Hygiene (including dental); fluoride supplementation/treatment
- Dietary/nutritional assessment (including eating disorders, calcium intake, and folic acid supplementation of 0.4 mg/day)
- Exercise program
- Psychosocial evaluation
- Interpersonal/family relationships
- Sexual identity
- Personal goal development
- Behavioral/learning disorders
- Abuse/neglect
- Cardiovascular risk factors
  - Family history
  - Hypertension
  - Dyslipidemia
  - Obesity
  - Diabetes mellitus

- Health/risk behaviors
- Injury prevention
  - Safety belts and sports or bicycle helmets
  - Recreational hazards
  - Firearms
  - Hearing damage
  - Sports
  - Skin exposure to ultraviolet rays
  - Suicide/depressive symptoms
  - Tobacco, alcohol, and other drugs

COUNSELING RESOURCES

American College of Obstetricians and Gynecologists Patient Education Pamphlet AP041 *(Your Changing Body - Especially for Teens)*, 2012.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP042 (*You and Your Sexuality - Especially for Teens)*, 2015.

American College of Obstetricians and Gynecologists Patient Education Pamphlet AP049 (*Your First Period - Especially for Teens)*, 2012.

American College of Obstetricians and Gynecologists. *Birth control (Especially for teens). ACOG Patient Education Pamphlet AP112*. Washington, DC: ACOG; 2013.

American College of Obstetricians and Gynecologists. *(Your first ob-gyn visit Especially for teens). ACOG Patient Education Pamphlet AP150*. Washington, DC: ACOG; 2015.

INTERVENTIONS: IMMUNIZATIONS

If not already accomplished, HPV and hepatitis B vaccine series.

Meningococcal conjugate vaccine (MCV4) is now recommended. For adolescents who have not received MCV4, the CDC now recommends vaccination before entry into high school, at approximately 15 years of age.

Periodic

- Tetanus-diphtheria booster (once between the ages of 14 and 16 years)

High-Risk Groups

- Measles, mumps, rubella (MMR) vaccine
- Hepatitis B vaccine

REFERENCES

LEVEL II

Grunbaum JA, Kann L, Kinchen S, et al. Youth risk behavior surveillance - United States, 2003 [published errata appear in MMWR Morb Mortal Wkly Rep 2004;53:536. *MMWR Morb Mortal Wkly Rep*. 2005;54:608]. *MMWR Surveill Summ*. 2004;53:1-96.

Mosher WD, Chandra A, Jones J. Sexual behavior and selected health measures: men and women 15–44 years of age, United States, 2002. *Adv Data*. 2005;362:1-55.

LEVEL III

American College of Obstetricians and Gynecologists. *Primary and Preventive Care*. Clinical Updates in Women's Health Care, 2007;VI(2): 1-106.

American College of Obstetricians and Gynecologists. *Adolescent Confidentiality and Electronic Health Records. Committee Opinion #599*. Washington, DC: ACOG; 2014.

American College of Obstetricians and Gynecologists. *Human Papillomavirus Vaccination. Committee Opinion #641*. Washington, DC: ACOG; 2015.

American College of Obstetricians and Gynecologists. *Guidelines for adolescent health care*. 2nd ed. Washington, DC: ACOG; 2011.

American College of Obstetricians and Gynecologists. Primary and preventive health care for female adolescents. In: *Health Care for Adolescents*. Washington, DC: ACOG; 2003:1-24.

American College of Obstetricians and Gynecologists. Screening for cervical cancer. Practice Bulletin No. 131. *Obstet Gynecol*. 2012;120: 1222-1238.

Ornstein RM, Fisher MM. Hormonal contraception in adolescents: special considerations. *Paediatr Drugs*. 2006;8:25-45.

Zuckerbrot RA, Maxon L, Pagar D, et al. Adolescent depression screening in primary care: feasibility and acceptability. *Pediatrics*. 2007;119: 101-108.

Figure 14.1 During the early reproductive years, girlhood gives way to careers, motherhood, and family responsibilities with all the attendant physical and emotional changes.

SCREENING

History

- Reason for visit
- Health status: medical, surgical, family
- Dietary/nutritional assessment
- Physical activity
- Tobacco, alcohol, and other drugs (including complementary and alternative medicines)
- Abuse/neglect
- Sexual practices

Physical

- Height
- Weight (body mass index, BMI)
- Blood pressure
- Neck: adenopathy, thyroid
- Breasts
- Abdomen
- Pelvic examination
- Skin

Laboratory

- Periodic
  - Pap test with high-risk human papillomavirus (HPV) cotesting (physician and patient discretion after three consecutive normal tests or negative viral cotesting)
  - Cholesterol, high-density lipoprotein cholesterol (every five years)
- As indicated by risk factors
  - Bacteriuria testing
  - Fasting glucose test or hemoglobin A1c
  - Genetic testing/counseling
  - Hemoglobin
  - Human immunodeficiency virus (HIV) testing
  - Mammography
  - Rubella titer
  - STI testing
  - Thyroid-stimulating hormone
  - Tuberculosis skin test

Imaging

Screening mammography may be started before the age of 40 years for patients with a strong family history of early onset breast cancer or heritable cancer syndromes.

COUNSELING

For those considering or at risk for pregnancy, counseling regarding preconception testing, immunization, and nutrition is always appropriate. Healthcare encounters during this period are also an excellent opportunity to discuss long-term health improvement strategies such as weight control, exercise, and nutrition.

Sexuality

- High-risk behaviors
- Contraceptive options
  - Genetic counseling
  - Prevention of unwanted pregnancy (including emergency contraceptive options)
- STIs
  - Partner selection
  - Barrier protection
- Sexual function

Fitness

- Hygiene (including dental)
- Dietary/nutritional assessment (folic acid supplementation for those at risk for or considering pregnancy; 0.4 mg/day has been shown to reduce the risk of neural tube defects)
- Exercise program

Psychosocial Evaluation

- Interpersonal/family relationships
- Domestic violence (there are more than 1.5 million cases of domestic violence each year; 20%–40% of adults report abuse or sexual victimization before the age of 18 years, and 10%–25% of wives)
- Job satisfaction
- Lifestyle/stress
- Sleep disorders

Cardiovascular Risk Factors

- Family history
- Hypertension
- Dyslipidemia
- Obesity/diabetes mellitus
- Lifestyle

Health/Risk Behaviors

Injury Prevention

- Safety belts and sports and bicycle helmets
- Recreational hazards
- Firearms
- Hearing
- Breast self-examination (while data on the efficacy of breast self-examination is lacking, and some organizations actually discourage the practice, the possibility of detecting breast disease make this recommendation reasonable)
- Breast cancer chemoprophylaxis (selective estrogen receptor modulator therapy for high-risk women over the age of 35 years)
- Skin exposure to ultraviolet rays
- Suicide/depressive symptoms
- Tobacco, alcohol, and other drugs

COUNSELING RESOURCES

American College of Obstetricians and Gynecologists. Mammography and Other Screening Tests for Breast Problems. ACOG Patient Education Pamphlet AP178. Washington, DC: ACOG; 2015.

American College of Obstetricians and Gynecologists. Cholesterol and Women's Cardiovascular Health. ACOG Patient Education Pamphlet AP101. Washington, DC: ACOG; 2014.

American College of Obstetricians and Gynecologists. Healthy Eating. ACOG Patient Education Pamphlet BP130. Washington, DC: ACOG; 2013.

American College of Obstetricians and Gynecologists. Good Health Before Pregnancy. ACOG Patient Education Pamphlet AP056. Washington, DC: ACOG; 2015.

National Cancer Institute. Breast cancer screening. Available at: <http://www.cancer.gov/types/breast/patient/breast-screening-pdq>; accessed 12.12.2015.

INTERVENTIONS: IMMUNIZATIONS

If not already accomplished, HPV and hepatitis B vaccine series

Periodic

- Tetanus–diphtheria booster (every 10 years)

High-Risk Groups

- Measles, mumps, rubella (MMR) vaccine
- Hepatitis B vaccine
- Influenza vaccine
- Pneumococcal vaccine

REFERENCES

LEVEL II

Hahn KA, Strickland PA, Hamilton JL, et al. Hyperlipidemia guideline adherence and association with patient gender. *J Womens Health (Larchmt)*. 2006;15(9):1009-1013.

Mosher WD, Chandra A, Jones J. Sexual behavior and selected health measures: men and women 15–44 years of age, United States, 2002. *Adv Data*. 2005;362:1-55.

LEVEL III

American College of Obstetricians and Gynecologists. Breast cancer screening. Practice Bulletin No. 122. *Obstet Gynecol*. 2011;118:372-382.

American College of Obstetricians and Gynecologists. *Primary and Preventive Care*. Clinical Updates in Women's Health Care, 2007;VI(2):1-106.

American College of Obstetricians and Gynecologists. *Guidelines for women's health care*. 2nd ed. Washington, DC: ACOG; 2002.

American College of Obstetricians and Gynecologists. Management of gynecologic issues in women with breast cancer. Practice Bulletin No. 126. *Obstet Gyencol*. 2012;119:666-682.

American College of Obstetricians and Gynecologists. Screening for cervical cancer. Practice Bulletin No. 131. *Obstet Gynecol*. 2012;120:1222-1238.

TACTICS

Relevant Pathophysiology

Currently available contraceptive methods seek to prevent pregnancy by preventing the sperm and egg from uniting or by preventing implantation and growth. These goals are accomplished by preventing the development and release of the egg (oral and nonoral hormonal contraceptives and long-acting hormonal methods), preventing the union of sperm and egg by imposing a mechanical, chemical, or temporal barrier between sperm and egg (condom, diaphragm, foam, intrauterine contraceptive devices, rhythm method, withdrawal, and postcoital oral contraception), or altering the likelihood of implantation or growth (RU-486). Relative efficacy (first year failure, both real and theoretical) is shown in the accompanying table.

Strategies

For a couple to use a method, it must be accessible, immediately available (especially in coitally dependent or "use oriented" methods), and of reasonable cost. The impact of a method on spontaneity or the modes of sexual expression preferred by the patient and his/her partner may also be important considerations. A decision tree based on these concepts is presented in Fig. 15.1.

Patient Education

American College of Obstetricians and Gynecologists Patient Education Booklets:

- #AB020 (Birth Control, 2015)
- #AP112 (Birth Control - Especially for Teens, 2013),
- #AP011 (Sterilization for Women and Men, 2015)
- #AP022 (Barrier Methods of Birth Control: Diaphragm, Sponge, Cervical Cap, and Condom, 2013)
- #AP185 (Combined Hormonal Birth Control: Pill, Patch, and Ring, 2014)
- #AP024 (Fertility Awareness-Based Methods of Family Planning, 2014)
- #AP035 (Sterilization by Laparoscopy, 2013)
- #AP052 (Postpartum Sterilization, 2013)
- #AP114 (Emergency Contraception, 2015)
- #AP180 (Hysteroscopic Sterilization, 2012)
- #AP184 (Long-Acting Reversible Contraception, 2014)
- #AP186 (Progestin-Only Hormonal Birth Control Methods: Pills and Injections, 2014)

IMPLEMENTATION

Special Considerations

Adolescent patients require reliable contraception but often have problems with adherence. Careful counseling about options (including abstinence), the risks of pregnancy and sexually transmitted infections, and the need for both contraception and disease protection must be provided. These patients may be better served by methods that rely less on the user for reliability [intrauterine contraceptive devices (IUCDs) or long-acting hormonal agents such as injections, ring, patches, and implants] than those that depend on consistent use (use-oriented methods and those that are very time-sensitive such as progestin-only oral contraceptives).

Contraception for breastfeeding mothers may include oral contraceptives if milk flow is well established. Long-acting progesterone contraceptives may actually result in a slight increase in breast milk production. Barrier contraceptives are not contraindicated in these patients. IUCDs, copper- or hormone-containing, may also be placed once the uterus has returned to normal or immediately postpartum following delivery of the placenta.

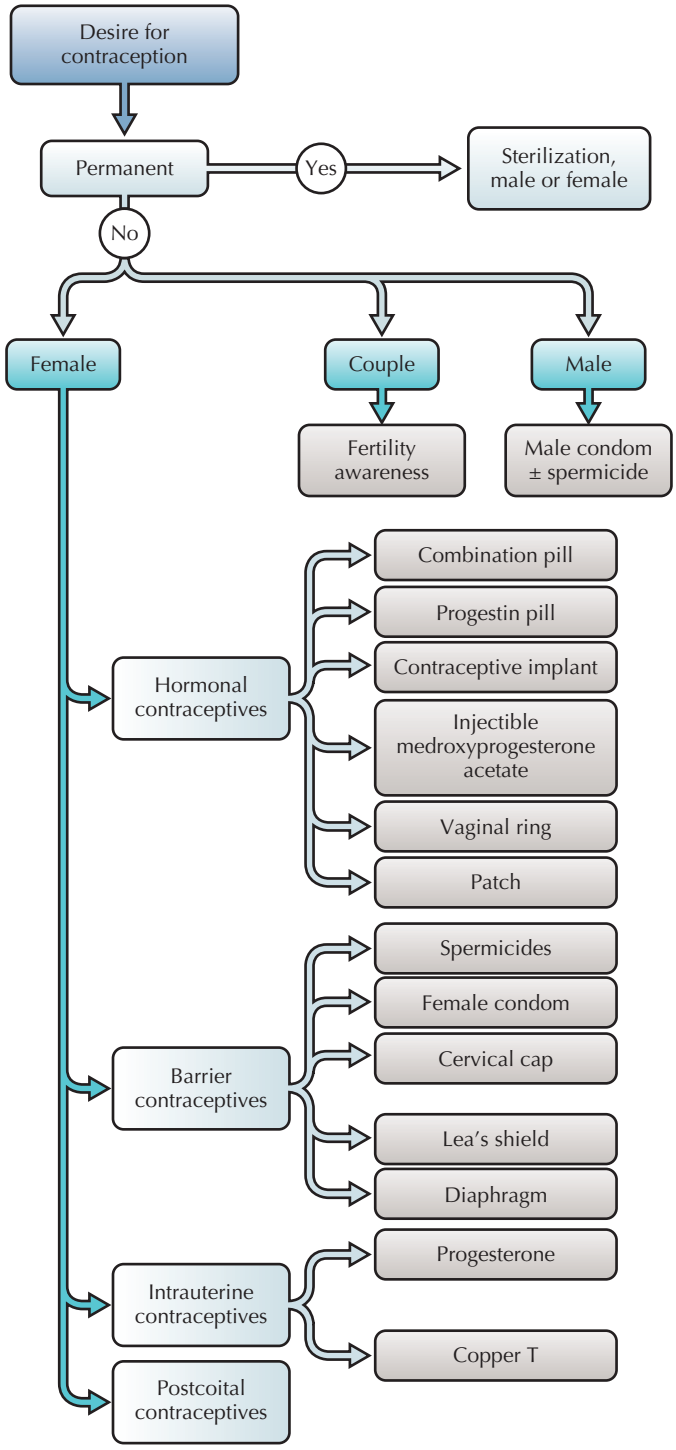


Figure 15.1 One of many possible decision tree approaches to the choice of contraceptive methods. Methods shown in gray have a relatively higher failure rate and should not be used if pregnancy prevention is a high priority. (Reused with permission from Beckman RB, Ling FW, Herbert WN, et al. *Obstetrics and Gynecology*, 7th ed. Baltimore: Williams & Wilkins; 2013.)

Patients over the age of 35 years may continue to use low-dose oral contraceptives if they have no other risk factors and do not smoke. Adherence concerns are generally less in these patients, making use-oriented methods more acceptable and reliable. Long-term methods (IUCDs, long-acting progesterone contraception,

or sterilization) may also be appropriate. Until menopause is confirmed by clinical or laboratory methods, contraception must be continued.

Following abortion (spontaneous or induced), ovulation may occur as soon as after 2 weeks. If oral contraceptives are selected, they should be started immediately after the abortion.

Contraceptive Use Among Women in the United States, 2012

Method	Percent of Users	Perfect Use Failure[a]	Actual Use Failure[a]
Oral contraceptives	23.3	0.3	8.0
Sterilization (female)	22.6	0.5	0.5
Condom (male)	13.7	2.0	15.0
Intrauterine contraceptive device	9.3	0.1–0.6	0.1–0.8
Sterilization (male)	7.4	0.1	0.15
Withdrawal	4.4	4.0	27.0
Injectable	4.1	0.05	3.0
Vaginal ring	1.8	1.8	2.0
Periodic abstinence (calendar)	1.2	9.0	25.0
Implant	1.2	0.05	0.05
Transdermal patch	0.5	0.3	8.0
Emergency contraception	0.2	0.2	0.2
Other (sponge, cervical cap, female condom, etc.)	0.3	5–26	16–32

[a]Percentage of women experiencing unintended pregnancy within first year of use

Data from: The Alan Guttmacher Institute. Contraceptive Use in the United States, October 2015. Available at http://www.guttmacher.org/pubs/fb_contr_use.html accessed on November 12, 2015.

REFERENCES

LEVEL III

American College of Obstetricians and Gynecologists. *Emergency contraception. ACOG Practice Bulletin 152*. Washington, DC: ACOG; 2015.

American College of Obstetricians and Gynecologists. *Long-Acting Reversible Contraception: Implants and Intrauterine Devices. ACOG Practice Bulletin 121*. Washington, DC: ACOG; 2011.

American College of Obstetricians and Gynecologists. *Noncontraceptive Uses of Hormonal Contraceptives. ACOG Practice Bulletin 110*. Washington, DC: ACOG; 2010.

American College of Obstetricians and Gynecologists. *Use of hormonal contraception in women with coexisting medical conditions. ACOG Practice Bulletin 73*. Washington, DC: ACOG; 2013.

Benagiano G, Bastianelli C, Farris M. Contraception today. *Ann N Y Acad Sci*. 2006;1092:1-32.

Deligeoroglou E, Christopoulos P, Creatsas G. Contraception in adolescence. *Ann N Y Acad Sci*. 2006;1092:7-90.

Draper BH, Morroni C, Hoffman M, et al. Depot medroxyprogesterone versus norethisterone oenanthate for long-acting progestogenic contraception. *Cochrane Database Syst Rev*. 2006;(3):CD005214.

Evans G, Sutton EL. Oral contraception. *Med Clin North Am*. 2015;99(3):479-503.

Glasier A, Gulmezoglu AM, Schmid GP, et al. Sexual and reproductive health: a matter of life and death. *Lancet*. 2006;368(9547):1595-1607.

Hansen LB, Saseen JJ, Teal SB. Levonorgestrel-only dosing strategies for emergency contraception. *Pharmacotherapy*. 2007;27:278-284.

Krashin J, Tang JH, Mody S, et al. Hormonal and intrauterine methods for contraception for women aged 25 years and younger. *Cochrane Database Syst Rev*. 2015;(8):CD009805.

Kulier R, Helmerhorst FM, O'Brien P, et al. Copper containing, framed intra-uterine devices for contraception. *Cochrane Database Syst Rev*. 2006;(3):CD005347.

McNamee K. The vaginal ring and transdermal patch: new methods of contraception. *Sex Health*. 2006;3:135-142.

Phillips SJ, Tepper NK, Kapp N, et al. Progestogen-only contraceptive use among breastfeeding women: a systematic review. *Contraception*. 2015;pii: S0010-7824(15)00585-5.

Practice Committee of the American Society for Reproductive Medicine. Hormonal contraception: recent advances and controversies. *Fertil Steril*. 2006;86(5 suppl):S229-S235.

- Dietary/nutritional assessment
- Physical activity
- Tobacco, alcohol, and other drugs (including complementary and alternative medicines)
- Abuse/neglect
- Sexual practices
- Urinary and fecal incontinence (These issues become more common with childbearing and age, but patients seldom volunteer these complaints.)

Physical

- Height
- Weight (body mass index [BMI])
- Blood pressure
- Oral cavity
- Neck: adenopathy, thyroid
- Breasts
- Abdomen
- Pelvic and rectovaginal examination
- Skin

Laboratory

- Periodic
  - Pap test (physician and patient discretion after three consecutive normal tests if low risk)
  - Cholesterol, high-density lipoprotein cholesterol (every 5 years, starting at the age of 45 years)
  - Fecal occult blood test (Testing requires the collection of two to three samples of stool collected by the patient at home to be valid. A single stool sample collected at the time of digital rectal examination is not sufficient to adequately screen for colon cancer.)
  - Sigmoidoscopy (every 3–5 years after the age of 50 years; double-contrast barium enema study may be substituted or a complete colonoscopy may be performed every 10 years)
- As indicated by risk factors
  - Bacteriuria testing
  - Colonoscopy
  - Fasting glucose test
  - Hemoglobin
  - Human immunodeficiency virus (HIV) testing
  - Lipid profile
  - Mammography
  - Sexually transmitted disease testing
  - Thyroid-stimulating hormone test
  - Tuberculosis skin test

Imaging

- Mammography (every 1–2 years until the age of 50 years; annually beginning at 50 years of age)
- Bone density assessment (Testing should be performed on the basis of an individual woman's risk profile and is not indicated unless the results will influence a treatment or management decision. Testing may be recommended to postmenopausal women younger than 65 years who have risk factors for osteoporosis.)

COUNSELING

Healthcare encounters during this period are an excellent opportunity to discuss long-term health improvement strategies such as weight control, exercise, and nutrition. As women approach the transition from reproduction to maturity, there are often increased opportunities to rededicate to healthy lifestyles and prevention. The increasing importance of surveillance as one ages is also an important message for patients in this age group.

Sexuality

- High-risk behaviors
- Contraceptive options
  - Genetic counseling (for selected women in this age range)
  - Prevention of unwanted pregnancy (including emergency contraceptive options)
- Sexually transmitted disease
  - Partner selection
  - Barrier protection
- Sexual function (including sexual pain)

Fitness

- Hygiene (including dental)
- Dietary/nutritional assessment (1000–1200 mg of calcium by diet and/or supplements; folic acid supplementation of 0.4 mg/day up to the age of 50 years)
- Discussion of exercise program and the importance of remaining physically active

Psychosocial Evaluation

- Interpersonal/family relationships
- Domestic violence
- Job/work satisfaction
- Lifestyle/stress
- Retirement planning
- Sleep disorders

Cardiovascular Risk Factors

- Family history
- Hypertension
- Dyslipidemia
- Obesity/diabetes mellitus
- Lifestyle

Health/Risk Behaviors

- Hormone replacement therapy (Data suggests that when hormone replacement is initiated within 10 years of menopause, it is not associated with some of the adverse effects reported in the Women's Health Initiative [WHI] study and may even be associated with reductions in such things as cardiovascular disease.)
- Breast cancer chemoprophylaxis (selective estrogen receptor modulator therapy for high-risk women over the age of 35 years)
- Injury prevention
  - Safety belts
  - Recreational hazards
  - Sports involvement
  - Vision and hearing
- Breast self-awareness
- Skin exposure to ultraviolet rays
- Suicide/depressive symptoms
- Tobacco, alcohol, and other drugs

COUNSELING RESOURCES

American College of Obstetricians and Gynecologists. Cholesterol and your health. ACOG Patient Education Pamphlet AP101. Washington, DC: ACOG; 2014.

American College of Obstetricians and Gynecologists. Healthy eating. ACOG Patient Education Pamphlet BP130. Washington, DC: ACOG; 2013.

American College of Obstetricians and Gynecologists. Keeping Your Heart Healthy. ACOG Patient Education Pamphlet BP122. Washington, DC: ACOG; 2004.

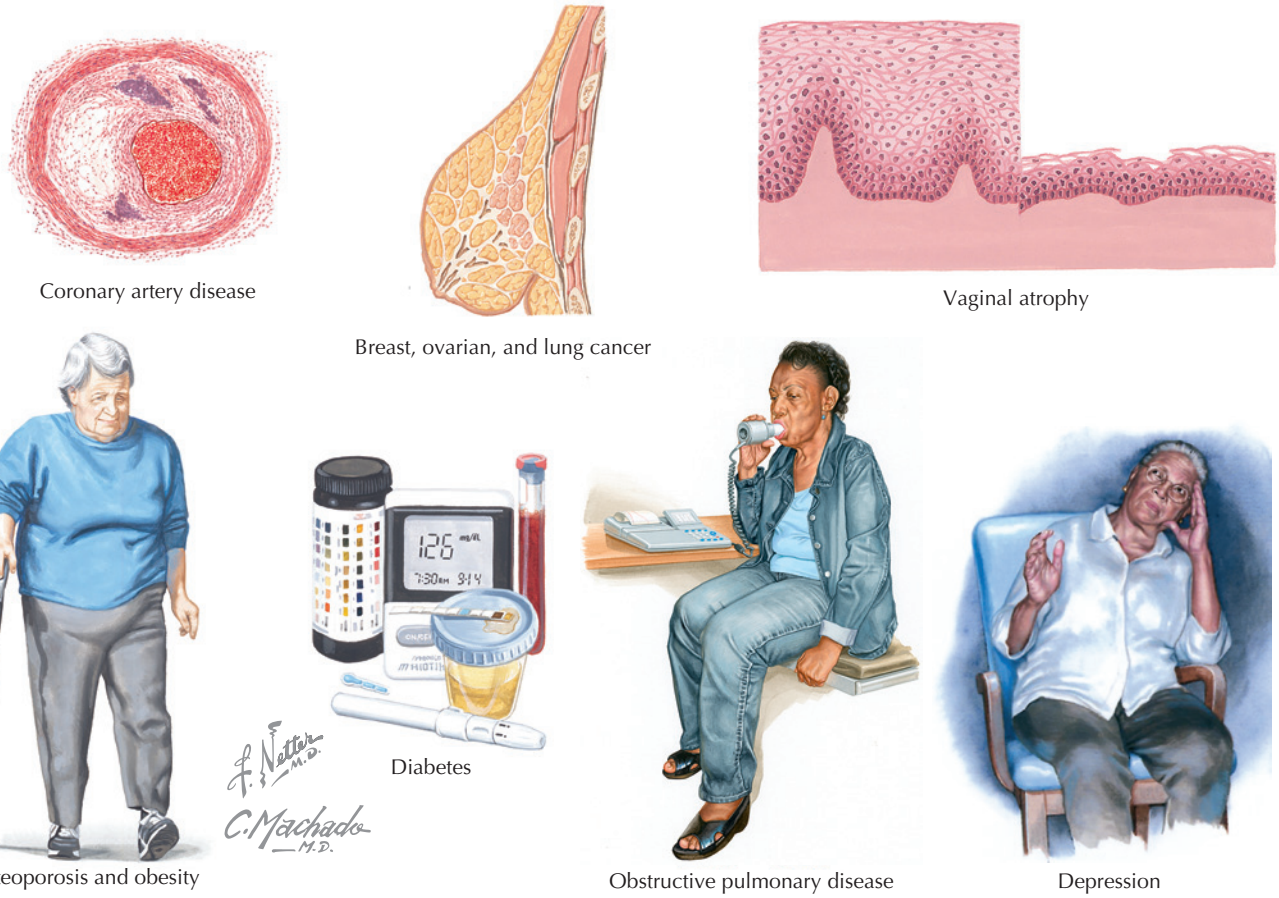


Figure 16.1 Leading causes of death and morbidity in women aged 40–64 years

American College of Obstetricians and Gynecologists. Midlife Transitions: Perimenopause to Menopause. ACOG Patient Education Pamphlet AP013. Washington, DC: ACOG; 2014.

American College of Obstetricians and Gynecologists. Perimenopausal Bleeding and Bleeding After Menopause. ACOG Patient Education Pamphlet AP162. Washington, DC: ACOG; 2010.

American College of Obstetricians and Gynecologists. The menopause years. ACOG Patient Education Pamphlet AP047. Washington, DC: ACOG; 2015.

INTERVENTIONS: IMMUNIZATIONS

Periodic

- Tetanus–diphtheria booster (every 10 years)
- Influenza vaccine (annually beginning at the age of 50 years)

High-Risk Groups

- Measles, mumps, rubella (MMR) vaccine
- Hepatitis A and/or B vaccine
- Influenza vaccine
- Pneumococcal vaccine
- Varicella vaccine

REFERENCES

LEVEL I

Rasgon NL, Geist CL, Kenna HA, et al. Prospective randomized trial to assess effects of continuing hormone therapy on cerebral function in postmenopausal women at risk for dementia. *PLoS ONE*. 2014;9(3):e89095.

LEVEL II

Avis NE, Crawford SL, Greendale G, et al. Duration of menopausal vasomotor symptoms over the menopause transition. *JAMA Intern Med*. 2015;175(4):531-539.

Grodstein F, Manson JE, Stampfer MJ. Hormone therapy and coronary heart disease: the role of time since menopause and age at hormone initiation. *J Womens Health*. 2006;15:35-44.

Manson JE, Chlebowski RT, Stefanick ML, et al. Menopausal hormone therapy and health outcomes during the intervention and extended poststopping phases of the Women's Health Initiative randomized trials. *JAMA*. 2013;310(13):1353-1368.

Rossouw JE, Prentice RL, Manson JE, et al. Postmenopausal hormone therapy and risk of cardiovascular disease by age and years since menopause. *JAMA*. 2007;297:1465-1477.

LEVEL III

American College of Obstetricians and Gynecologists. *Care of the aging woman*. Clinical Updates in Women's Health Care, Vol VIII, No 4, October 2009 (Reaffirmed 2015).

American College of Obstetricians and Gynecologists. *Colorectal Cancer Screening Strategies. Committee Opinion #609*. Washington, DC: ACOG; 2014.

American College of Obstetricians and Gynecologists. *Hormone Therapy and Alternative Therapies for Menopause*, Clinical Updates in Women's Health Care, Vol XIV, No 4, October 2015.

Giordano S, Hage FG, Xing D, et al. Estrogen and cardiovascular disease: is timing everything? *Am J Med Sci*. 2015;350(1):27-35.

Hahn KA, Strickland PA, Hamilton JL, et al. Hyperlipidemia guideline adherence and association with patient gender. *J Womens Health (Larchmt)*. 2006;15(9):1009-1013.

Manson JE, Hsia J, Johnson KC, et al. Estrogen plus progestin and the risk of coronary heart disease. *N Engl J Med*. 2003;349:523-534.

Nkonde-Price C, Bender JR. Menopause and the heart. *Endocrinol Metab Clin North Am*. 2015;44(3):559-564.

Figure 17.1 Fatigue and dyspnea on exertion with decreased exercise tolerance are common complaints.

Imaging

- Mammography
- Bone density assessment (Bone mineral density testing should be recommended to all postmenopausal women aged 65 years or older. In the absence of new risk factors, densitometry should not be performed more frequently than every 2 years.)

COUNSELING

As functions change due to aging, both the patient and provider should be vigilant for subtle losses of abilities and should be prepared to make accommodations as required.

Sexuality

- Sexual functioning
- Sexual behaviors
- Sexually transmitted diseases

Fitness

- Hygiene (general and dental)
- Dietary/nutritional assessment (women in this age group should take 1200 mg of calcium and 10 µg of vitamin D per day to prevent osteoporosis)
- Discussion of exercise program and the importance of remaining physically active

Psychosocial Evaluation

- Neglect/abuse
- Lifestyle/stress
- Depression/sleep disorders (These are particularly prevalent, but often overlooked, similar to patient's age.)
- Family relationships
- Job/work/retirement satisfaction

Cardiovascular Risk Factors

- Hypertension
- Dyslipidemia
- Obesity
- Diabetes mellitus
- Sedentary lifestyle

Health/Risk Behaviors

- Hormone replacement therapy
- Breast cancer chemoprophylaxis (selective estrogen receptor modulator therapy for high-risk women)
- Injury prevention
  - Safety belts and helmets
  - Occupational hazards
  - Recreational hazards
  - Fall prevention
  - Hearing and visual acuity/glaucoma screening
  - Breast self-examination
  - Skin exposure to ultraviolet rays
  - Suicide/depressive symptoms
  - Tobacco, alcohol, and other drugs

COUNSELING RESOURCES

American College of Obstetricians and Gynecologists. Healthy eating. ACOG Patient Education Pamphlet BP130. Washington, DC: ACOG; 2013.

American College of Obstetricians and Gynecologists. Cholesterol and your health. ACOG Patient Education Pamphlet AP101. Washington, DC: ACOG; 2014.

American College of Obstetricians and Gynecologists. Exercise and Fitness. ACOG Patient Education Pamphlet BP045. Washington, DC: ACOG; 2010.

American College of Obstetricians and Gynecologists. Keeping Your Heart Healthy. ACOG Patient Education Pamphlet BP122. Washington, DC: ACOG; 2004.

American College of Obstetricians and Gynecologists. Perimenopausal Bleeding and Bleeding After Menopause. ACOG Patient Education Pamphlet AP162. Washington, DC: ACOG; 2010.

American College of Obstetricians and Gynecologists. Osteoporosis. ACOG Patient Education Pamphlet AP048. Washington, DC: ACOG; 2013.

American College of Obstetricians and Gynecologists. The menopause years. ACOG Patient Education Pamphlet AP047. Washington, DC: ACOG; 2015.

INTERVENTIONS: IMMUNIZATIONS

Periodic

- Tetanus-diphtheria booster (every 10 years)
- Influenza vaccine (annually; should be given as the high-potency dose)
- Pneumococcal vaccine, including the tridecavalent vaccine containing 13 serotypes of pneumococcus (If the PVC13 vaccine is used, it should be followed in 1 year by the standard pneumococcal vaccine.)

High-Risk Groups

- Hepatitis B vaccine
- Varicella vaccine (if not already administered)

REFERENCES

LEVEL II

Huang A, Grady D, Blackwell T, et al. Hot flushes, bone mineral density, and fractures in older postmenopausal women. *Obstet Gynecol*. 2007; 109:841-847.

LEVEL III

American Cancer Society. *American Cancer Society Guidelines for the Early Detection of Cancer*. Available at: <http://www.cancer.org/healthy/findcancerearly/cancerscreeningguidelines/american-cancer-society-guidelines-for-the-early-detection-of-cancer>, Accessed 13.11.15.

American College of Obstetricians and Gynecologists. *Care of the aging woman*. Clinical Updates in Women's Health Care, Vol VIII, No 4, October 2009 [Reaffirmed 2015].

American College of Obstetricians and Gynecologists. *Colorectal Cancer Screening Strategies. Committee Opinion #609*. Washington, DC: ACOG; 2014.

Nowalk MP, Zimmerman RK, Cleary SM, et al. Missed opportunities to vaccinate older adults in primary care. *J Am Board Fam Pract*. 2005;18: 20-27.

This page intentionally left blank

SECTION IV

Diseases, Disorders, and Common Problems

This page intentionally left blank

ABORTION

18

INTRODUCTION

Description: Abortion is the loss or failure of early pregnancy in several forms: complete, incomplete, inevitable, missed, septic, and threatened. A complete abortion is the termination of a pregnancy before the age of viability, typically defined as occurring at less than 20 weeks from the first day of the last normal menstrual period or involving a fetus with a weight less than 500 g. Most complete abortions generally occur before 6 weeks or after 14 weeks of gestation. An incomplete abortion is the spontaneous passage of some, but not all, of the products of conception, associated with uniform pregnancy loss. A pregnancy wherein the rupture of the membranes and/or cervical dilation occurs during the first weeks of pregnancy is labeled as an inevitable abortion. Uterine contractions typically follow, ending in the spontaneous loss of the pregnancy for most patients. A missed abortion is the retention of a failed intrauterine pregnancy for an extended period; however, with ultrasound studies, this can often be detected significantly sooner than it could be on clinical grounds alone. A septic abortion is a variant of an incomplete abortion in which the uterus and its contents are infected. A threatened abortion is a pregnancy that is at a risk for some reason. Most often, this applies to any pregnancy wherein vaginal bleeding or uterine cramping occurs but no cervical changes have occurred.

Prevalence: Estimates for the frequency of complete abortions are as high as 50%–60% of all conceptions and between 10% and 15% of known pregnancies. Of pregnant women hospitalized for bleeding, 60% have an incomplete abortion. Less than 2% of fetal losses are missed abortions. Septic abortions occur in 0.4–0.6 of 100,000 spontaneous pregnancy losses. Threatened abortions occur in 30%–40% of pregnant women.

Predominant Age: Reproductive.

Genetics: Some chromosomal abnormalities are associated with reduced or absent fertility and increased risk of fetal loss (eg, translocations).

ETIOLOGY AND PATHOGENESIS

Causes: Endocrine abnormalities (25%–50%)—hyperandrogenism, in utero diethylstilbestrol (DES) exposure (rare now), luteal phase defect, and thyroid disease. Genetic factors (10%–70%)—balanced translocation/carrier state, nondisjunction, trisomy (40%–50%, trisomy 16 most common, any possible except trisomy 1), monosomy X (15%–25%), and triploidy (15%), tetraploidy (5%). Reproductive tract abnormalities (6%–12%)—abnormality of placentation, bicornuate or unicornuate uterus, incompetent cervix, intrauterine adhesions (Asherman syndrome), leiomyomata uteri (submucous), and septate uterus. Infection—*Mycoplasma hominis*, syphilis, toxoplasmosis, *Ureaplasma ureolyticus*, and possibly chlamydia and herpes. Systemic disease—chronic cardiovascular disease, chronic renal disease, diabetes mellitus, and systemic lupus erythematosus/lupus anticoagulant. Environmental factors—alcohol, anesthetic gases, drug use, radiation, smoking, and toxins. Other factors—advanced maternal age, delayed fertilization (old egg), and trauma.

Risk Factors: Increasing parity, increasing maternal age, increasing paternal age, a short interval between pregnancies, excessive caffeine consumption (≥6 cups of coffee per day). Retention of tissue after pregnancy loss increases the risk of a septic abortion.

SIGNS AND SYMPTOMS

- General—vaginal bleeding (may be bright red to dark in color)
  - Abdominal cramping (frequently rhythmic, accompanied by pelvic or low back pressure)
  - Passage of tissue (complete and incomplete abortion)
  - Cervical dilation (typical of all types of abortion except missed and threatened)
  - Cervical dilation with tissue visible at the cervical os (diagnostic of either incomplete or inevitable abortion)
- Missed abortion—decreased or minimal uterine growth early in pregnancy
  - Vaginal bleeding that changes to a dark brown discharge that continues
  - Loss of early symptoms of pregnancy, such as breast fullness or morning sickness
  - Disseminated intravascular coagulopathy (DIC) can occur when an intrauterine fetal demise in the second trimester has been retained beyond 6 weeks after the death of the fetus (rare)
- Septic abortion—severe hemorrhage (vaginal)
  - Midline lower abdominal pain
  - Uterine and perimetric tenderness
  - Bacteremia
  - Septic shock
  - Renal failure
- Threatened abortion—implantation bleeding

DIAGNOSTIC APPROACH

Differential Diagnosis

- Ectopic pregnancy
- Cervical polyps, cervicitis
- Molar pregnancy
- Possibility of trauma, including the perforation of the uterus or vagina, when sepsis is present
- Other causes of lower abdominal discomfort (eg, urinary tract infection, constipation)

Associated Conditions: 30% of patients treated by sharp curettage for missed abortion have intrauterine adhesions. Septic abortion is associated with septic shock, ascending infection (myometritis, pelvic inflammatory disease), disseminated intravascular coagulopathy, and renal failure.

Workup and Evaluation

Laboratory: Administer a pregnancy test (if pregnancy has not been confirmed). If serial determinations of quantitative β-human chorionic gonadotropin (β-hCG) do not reveal at least a 66% increase every 48 hours, the outlook for the pregnancy is poor. Perform complete blood count (if blood loss has been excessive). Serial determinations of serum β-hCG may be used to confirm pregnancy loss but are not required for diagnosis.

Imaging: Ultrasonography of the uterus may be used to confirm the loss of intrauterine contents, the absence of a fetal pole, or the failure to grow. While the presence of fetal cardiac activity is reassuring, it does not guarantee a favorable outcome.

Special Tests: None indicated.

Diagnostic Procedures: If significant cervical dilation is identified by speculum and bimanual examination or if tissue is seen at the cervix, the diagnosis of inevitable or incomplete abortion is established.

Pathologic Findings

Products of conception (including chorionic villi); in a missed abortion there is the absence of a fetal pole.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Support and evaluation are helpful. Analgesia if required. Rh-negative mothers should be treated with Rh immune globulin after completing the abortion. Because ovulation may occur as early as 2 weeks after an abortion, a discussion of contraception is warranted.

Specific Measures: When there is a complete abortion, immediate considerations include control of bleeding, prevention of infection, pain relief (if required), and emotional support. Ensuring that all the products of the conception have been expelled from the uterus controls bleeding. Although most patients with an incomplete or inevitable abortion spontaneously pass the remaining tissue (complete abortion), bleeding, cramping, and the risk of infection associated with expectant management generally support surgical evacuation. If retained tissue is present or cannot be ruled out, curettage must be promptly performed. When a missed abortion is diagnosed, evacuation of the uterus can be accomplished either through dilation and evacuation or through medical therapies such as prostaglandin therapies or mifepristone (RU-486), based on the stage of the pregnancy and other considerations. Septic abortion requires immediate and aggressive management. Broad-spectrum parenteral antibiotics, fluid therapy, and prompt evacuation of the uterus are indicated. Emergency evacuation of the uterine contents is mandatory because of the significant threat they represent. When the diagnosis of threatened abortion is made, intervention should be minimal, even when bleeding is accompanied by low abdominal pain and cramping. If there is no evidence of cervical change, the patient can be reassured and encouraged to continue normal activities. If significant pain or bleeding persists, especially bleeding leading to hemodynamic alterations, the evacuation of the uterus should be conducted.

Diet: No specific dietary changes are indicated unless immediate surgical therapy is being considered. In that case, nothing should be taken by mouth.

Activity: Generally there is no restriction. When sepsis is present, bed rest is initially required while therapy is instituted. After evacuation is accomplished and fever is reduced, the patient may return to normal activity. Although frequently recommended, a short period of bed rest has no documented benefit for patients with a threatened abortion.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP038 (Bleeding During Pregnancy), AP090 (Early Pregnancy Loss), AP100 (Repeated Miscarriage), AP062 (Dilation and Curettage [D&C]), and AB012 (Planning Your Pregnancy).

Drug(s) of Choice

- To hasten the expulsion of tissue and reduce bleeding—Incomplete abortion: Misoprostol, 600 mcg orally. Misoprostol, 400 mcg sublingually, is an alternative but supporting published research is limited.
  - Missed abortion: Misoprostol, 800 mcg vaginally or 600 mcg sublingually; may be repeated every 3 hours for two additional doses.
  - Oxytocin 10–20 units/L IV fluids or methylergonovine maleate (Methergine) 0.2 mg IM may be used, but has largely been replaced by misoprostol.
- Septic abortion—aggressive fluid therapy, antibiotic therapy (clindamycin 900 mg IV every 8 hours plus gentamicin 5 mg/kg IV once/day, with or without ampicillin 2 g IV every 4 hours. Alternatively, a combination of ampicillin, gentamicin, and metronidazole 500 mg IV every 8 hours can be used). If clinical improvement is evident by 48 hours, further antibiotics may not be necessary.

Contraindications: Undiagnosed vaginal bleeding.

Precautions: Methergine should be used with care in patients with hypertension.

Interactions: Vasoconstrictors and ergot alkaloids.

Alternative Drugs

Prostaglandin E_2, mifepristone (RU-486). For septic abortion, other broad-spectrum antibiotics, singly or in combination, are available.

FOLLOW-UP

Patient Monitoring: Anticipate the normal return of menstrual function in 4–6 weeks, and offer contraceptive counseling. Patients with septic abortions must be monitored for the possibility of septic shock during the early treatment period.

Prevention/Avoidance: None. Septic abortions may be prevented by the prompt evacuation of the uterus in patients with incomplete or inevitable abortions. Data on the risk of sepsis for patients with missed abortions is lacking; therefore, expectant, medical, or surgical managements are all acceptable.

Possible Complications: Infection (myometritis, pelvic inflammatory disease) may occur. Removal of the products of conception, combined with vaginal rest (no tampons, douches, or intercourse), provides adequate protection against infection for most patients.

Expected Outcome: The risk of pregnancy loss subsequent to a spontaneous abortion increases slightly, although much of this increase may be due to selection for those with factors that preclude successful pregnancy. For those with an inevitable abortion who do not spontaneously lose the pregnancy, infection or bleeding often ensues, requiring the evacuation of the uterus. Missed abortions may spontaneously abort, progressing through incomplete to complete stages, or they may be evacuated. After the pregnancy has terminated (spontaneous or medically induced abortion or surgical evacuation of products of conception), normal menses return in 4–6 weeks. With aggressive antibiotic treatment and prompt evacuation of the uterus the outcome should be good for patients with a septic abortion. Among patients with a threatened abortion, one half go on to lose the pregnancy in a spontaneous abortion. (The risk of failure is greater in those who bleed for 3 or more days.) For those who carry the fetus to viability, there is a greater risk for preterm delivery and low fetal birth weight and a higher incidence of perinatal mortality. There does not, however, appear to be a higher incidence of congenital malformations in these newborns.

MISCELLANEOUS

Other Notes: When losses are caused by aneuploidy or polyploidy, they tend to happen earlier in gestation (75% before 8 weeks) and are more likely to recur in subsequent pregnancies Abnormal development, including the zygote, embryo, fetus, or placenta, is common. Expulsion of the pregnancy is almost always preceded by the death of the embryo or fetus. For threatened abortion, intercourse is usually proscribed for 2–3 weeks, or longer, although this probably provides more psychologic support than medical effect. Progesterone therapy for threatened abortions is of no benefit and may result in virilization of a fetus or a missed abortion. It should not be used. Incomplete abortions are more common after the 10th week of gestation, when fetal and placental tissues tend to be separately passed.

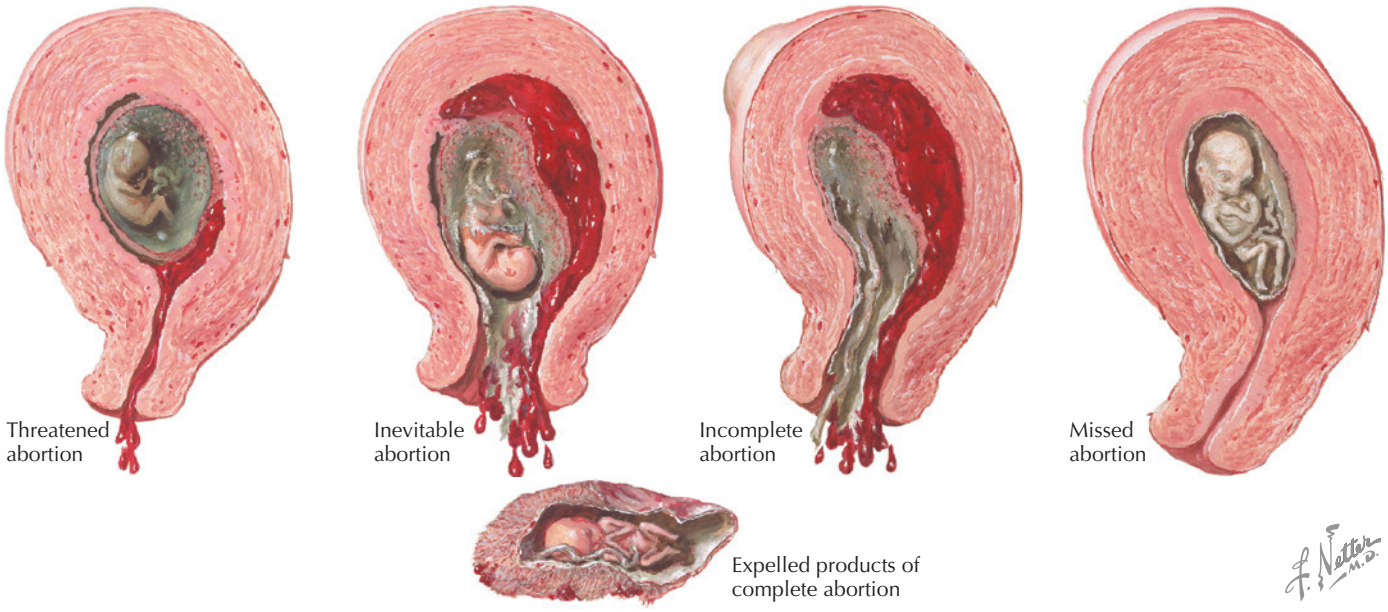


Figure 18.1 Abortion

ICD-10-CM Codes: O03.9 (Complete or unspecified spontaneous abortion without complication), O03.4 (Incomplete spontaneous abortion without complication), O03.39 (Inevitable abortion-Incomplete spontaneous abortion with other complications), O02.1 (Missed abortion), O03.37, O03.87 (Septic abortion-Spontaneous abortion, complicated by genital tract and pelvic infection, incomplete, Sepsis following incomplete spontaneous abortion), O20.0 (Threatened abortion, antepartum condition or complication).

REFERENCES

LEVEL I

Savaris RF, Moraes GS, Cristovam RA, et al. Are antibiotics necessary after 48 hours of improvement in infected/septic abortions? a randomized controlled trial followed by a cohort study. *Am J Obstet Gynecol*. 2011;204:301.e1-301.e5.

LEVEL II

Batzofin JH, Fielding WI, Friedman EA. Effect of vaginal bleeding in early pregnancy on outcome. *Obstet Gynecol*. 1984;63:515.

Boklage CE. Survival probability of human conceptions from fertilization to term. *Int J Fertil*. 1990;35:75.

Bromley B, Harlow BL, Laboda LA, et al. Small sac size in the first trimester: a predictor of poor fetal outcome. *Radiology*. 1991;178:375.

Chen LW, Wu Y, Neelakantan N, et al. Maternal caffeine intake during pregnancy and risk of pregnancy loss: a categorical and dose-response meta-analysis of prospective studies. *Public Health Nutr*. 2015;1.

Finkielman JD, De Feo FD, Heller PG, et al. The clinical course of patients with septic abortion admitted to an intensive care unit. *Intensive Care Med*. 2004;30:1097.

Funderburk SJ, Guthrie D, Meldrum D. Outcome of pregnancies complicated by early vaginal bleeding. *Br J Obstet Gynecol*. 1980;87:100.

Hakim-Elahie E, Tovell HM, Burnhill MS. Complications of first-trimester abortions: a report of 170,000 cases. *Obstet Gynecol*. 1990;76:129.

Lemmers M, Verschoor MA, Hooker AB, et al. Dilatation and curettage increases the risk of subsequent preterm birth: a systematic review and meta-analysis. *Hum Reprod*. 2015;pii: dev274.

Li J, Zhao H, Song JM, et al. A meta-analysis of risk of pregnancy loss and caffeine and coffee consumption during pregnancy. *Int J Gynaecol Obstet*. 2015;130:116.

Mackenzie WE, Holmes DS, Newton JR. Spontaneous abortion rate in ultrasonographically viable pregnancies. *Obstet Gynecol*. 1988;71:81.

Schaff EA, Stadalius LS, Eisinger SH, et al. Vaginal misoprostol administered at home after mifepristone (RU486) for abortion. *J Fam Pract*. 1997;44:353.

Swahn ML, Bygdeman M. The effect of the antiprogestin RU 486 on uterine contractility and sensitivity to prostaglandin and oxytocin. *Br J Obstet Gynaecol*. 1988;95:126.

Thom DH, Nelson LM, Vaughan TL. Spontaneous abortion and subsequent adverse birth outcomes. *Am J Obstet Gynecol*. 1992;166:111.

LEVEL III

American College of Obstetricians and Gynecologists. Medical management of first-trimester abortion. Practice Bulletin No. 143. *Obstet Gynecol*. 2014;123:676.

American College of Obstetricians and Gynecologists. Misoprostol for postabortion care. ACOG Committee Opinion No. 427. *Obstet Gynecol*. 2009;113:465-468.

Atim U, Effa EE, Olabisi O, et al. Antibiotics for treating septic abortion. *Cochrane Database Syst Rev*. 2015;(2):<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011528/abstract>.

Chen BA, Creinin MD. Contemporary management of early pregnancy failure. *Clin Obstet Gynecol*. 2007;50:67.

Eschenbach DA. Treating spontaneous and induced septic abortions. *Obstet Gynecol*. 2015;125:1042-1048.

Kripke C. Expectant management vs. surgical treatment for miscarriage. *Am Fam Physician*. 2006;74:1125.

Smith RP. *Gynecology in Primary Care*. Baltimore: Williams & Wilkins; 1997:99.

Stubblefield PG, Grimes DA. Septic abortion. *N Engl J Med*. 1994;331:310.

Tang OS, Ho PC. Clinical applications of mifepristone. *Gynecol Endocrinol*. 2006;22:655.

19 ABUSE: PHYSICAL AND SEXUAL

INTRODUCTION

Description: Abuse is a pattern of physical or emotional trauma that occurs in a continuing relationship (see Chapter 32, Domestic Violence). Although the definition of abuse requires only one episode of abuse, a pattern of escalating violence is more typical. (In at least one-fourth of cases, there have been three or more episodes of violence in the 6 months preceding the report of abuse.) In the United States, women are at a greater risk of injury or death at the hands of a domestic partner than from an unrelated attacker. Sexual abuse is a specific form of physical abuse that is related to trauma of a sexual nature or a pattern of coercive sexual activities. Sexual abuse includes, but is not limited to, disrobing, exposure, photography or posing, oral–genital contact, insertion of foreign bodies, and vaginal or rectal intercourse.

Prevalence: More than 1.5 million cases of domestic violence annually occur. It is estimated that between 5% and 25% of women who are treated for injuries in emergency rooms receive these injuries as a result of domestic violence. Of adults, 20%–40% report abuse or sexual victimization before the age of 18 years and 10%–25% of wives report one or more episodes of sexual abuse.

Predominant Age: Any, most common teens to 30s.

Genetics: Women are the primary victims of domestic violence, accounting for almost 95% of incidents.

ETIOLOGY AND PATHOGENESIS

Causes: Multiple factors. Alcohol or drugs are often involved, although they are not causative factors.

Risk Factors: Such abuse occurs at a slightly higher rate among those of lower educational or socioeconomic status.

SIGNS AND SYMPTOMS

Physical Abuse

Signs and symptoms are highly variable. In almost 85% of reported cases, the injuries sustained are sufficient to require medical treatment. Between 5% and 25% of women treated for injuries in emergency rooms receive these injuries as a result of domestic violence. The correct diagnosis is rendered in less than 5% of women. The most frequent locations for injuries are the head, neck, chest, abdomen, and breasts. Upper-extremity injuries result from defensive efforts.

Sexual Abuse

Signs and symptoms are nonspecific.

DIAGNOSTIC APPROACH

Differential Diagnosis

- Depression (may mimic the vague complaints that should raise the suspicion of abuse)
- Coagulopathy (leading to bruising)

Associated Conditions: More than one-half of men who abuse their wives also abuse their children. Between one-third and one-half of all murders of women occur at the hands of a male partner.

Workup and Evaluation

Laboratory: No evaluation is indicated.

Imaging: No imaging is indicated unless fracture or other injury is suspected.

Special Tests: The five-question Abuse Assessment Screen increases the likelihood of detecting abuse. The longer it has been since an assault or when abuse is ongoing, the more likely it is for the presenting complaints to be unrelated to the underlying acute concerns generated by the attack. Somatic complaints and subtle behavioral changes may suggest the possibility of domestic violence or abuse.

Diagnostic Procedures: History and suspicion. Because one of the pivotal aspects of sexual assault is the loss of control, every effort should be made to allow the patient control over even the most trivial aspects of the physical examination.

Pathologic Findings

In the typical battering relationship, three phases are usually present: a tension-building phase that gradually escalates; the battering incident, which may be triggered by almost any event; and a period of contrition, during which the batterer apologizes and asks for forgiveness. This cycle tends to repeat and escalate with greater physical harm and risk and less remorse.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Offer support, contact with social agencies, and assistance with developing means for independence (eg, money, transportation, destination, child care) should escape become necessary.

Specific Measures: Assess and manage any injuries present. The patient should be given the telephone number of and directions to a shelter or safe house.

Diet: No specific dietary changes are indicated.

Activity: No restriction.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP083 (Domestic Violence).

Drug(s) of Choice

None indicated. Great care must be used with any antidepressants or other mood-altering drugs given in these situations.

FOLLOW-UP

Patient Monitoring: In many locations, suspected sexual assault must be reported to law enforcement authorities. In all locations, suspected abuse, sexual or otherwise, occurring to a minor must be reported.

Prevention/Avoidance: None. Patients must be told they are not at fault and that their efforts to change the abuser are unlikely to have an effect in reducing the number of future episodes.

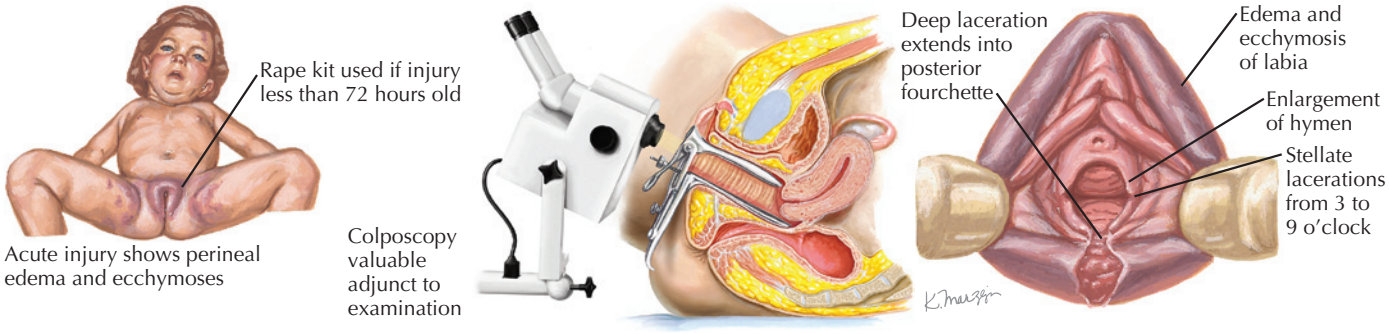
Possible Complications: Escalating violence with an increasing risk of severe injury or death.

Expected Outcome: The pattern of physical or sexual abuse is ongoing. Acute management of trauma is only a part of the larger problem and interpersonal dysfunction. If the abuser receives counseling and treatment, the outcome can be good; without it, there is a great risk of continued or worsening abuse. Abuse is associated with poorer general and sexual health for the victim. In one study, more than half of the women who were abused had experienced common physical complaints during the previous 12 months compared with one-third of the nonabused.

MISCELLANEOUS

Pregnancy Considerations: Of pregnant women, 10%–20% report physical abuse during pregnancy. For these women, injuries to the breast and abdomen are more frequent.

Acute injury



Chronic injury

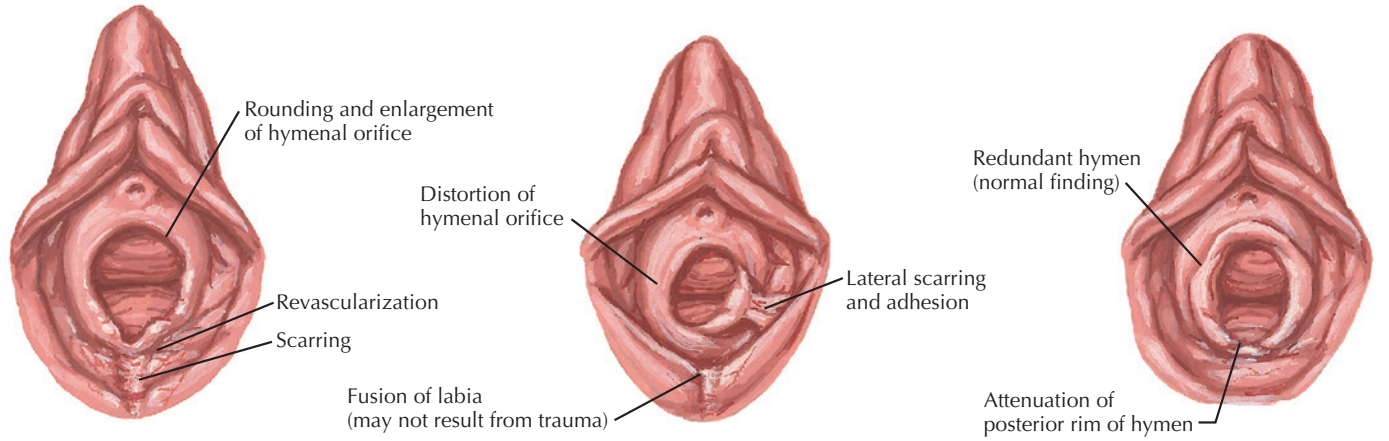


Figure 19.1 Sexual abuse in girls

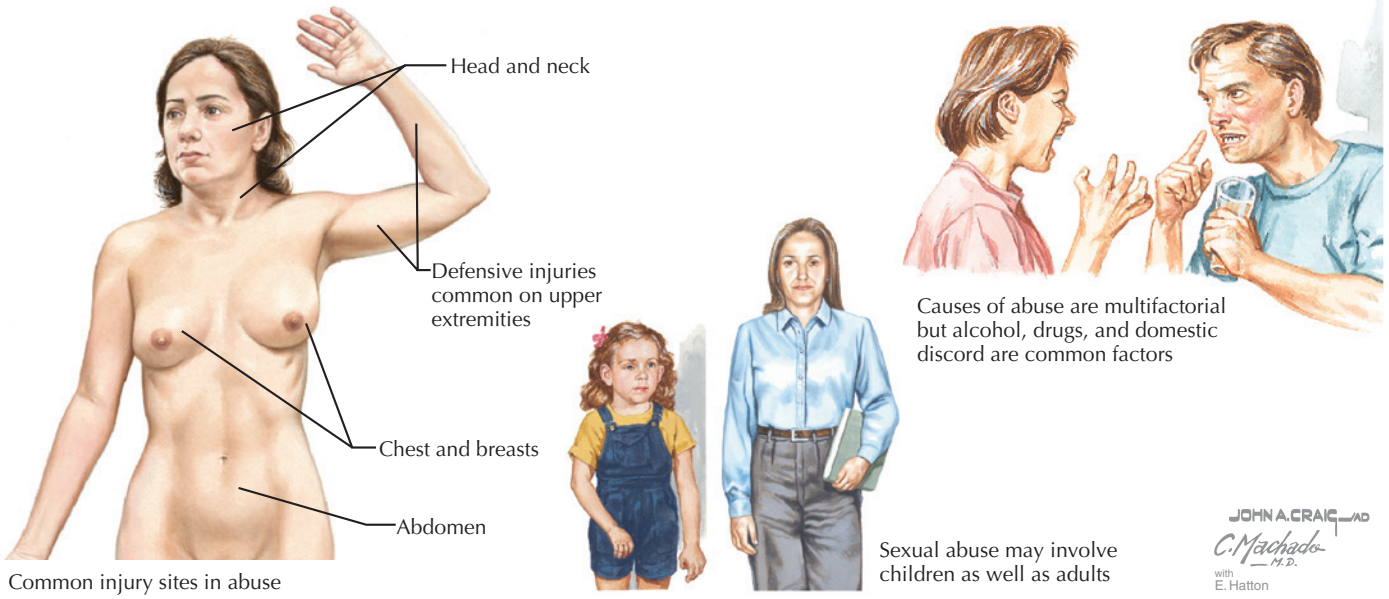


Figure 19.2 Physical and sexual abuse

ICD-10-CM Codes: T74.11XA, T76.11XA (Adult physical abuse, confirmed, initial encounter; Adult physical abuse, suspected, initial encounter), T74.91XA, T76.91XA (Unspecified adult maltreatment, confirmed, initial encounter; Unspecified adult maltreatment, suspected, initial encounter).

REFERENCES

LEVEL II

Elliott L, Nerney M, Jones T, et al. Barriers to screening for domestic violence. *J Gen Intern Med*. 2002;17:112.

Joseph B, Khalil M, Zangbar B, et al. Prevalence of domestic violence among trauma patients. *JAMA Surg*. 2015;1.

Leserman J. Sexual abuse history: prevalence, health effects, mediators, and psychological treatment. *Psychosom Med*. 2005;67:906.

O'Doherty L, Hegarty K, Ramsay J, et al. Screening women for intimate partner violence in healthcare settings. *Cochrane Database Syst Rev*. 2015;(7):CD007007.

Rodriquez MA, Bauer HM, McLoughlin E, et al. Screening and intervention for intimate partner abuse: practices and attitudes of primary care physicians. *JAMA*. 1999;282:468.

Ulla Pikarinen U, Saisto T, Schei B, et al. Experiences of physical and sexual abuse and their implications for current health. *Obstet Gynecol*. 2007; 109:1116.

LEVEL III

AMA Council on Scientific Affairs. Violence against women: relevance for medical practitioners. *JAMA*. 1992;267:3184.

American College of Obstetricians and Gynecologists. *Intimate Partner Violence ACOG Committee Opinion 518*. Washington, DC: ACOG; 2012.

American Medical Association Code of Medical Ethics: *Opinion 2.02 - Physicians' Obligations in Preventing, Identifying, and Treating Violence and Abuse*, Available at: <http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion202.page>. Accessed 25.11.15.

Black MC, Basile KC, Breiding MJ, et al. *Centers for Disease Control and Prevention. The National Intimate Partner and Sexual Violence Survey: 2010 Summary Report*. Available at: <http://www.cdc.gov/violenceprevention/pdf/nisvs_report2010-a.pdf>, Accessed 25.11.15.

Chez RA. Woman battering. *Am J Obstet Gynecol*. 1988;158:1.

Chrisler JC, Ferguson S. Violence against women as a public health issue. *Ann N Y Acad Sci*. 2006;1087:235.

García-Moreno C, Hegarty K, d'Oliveira AF, et al. The health-systems response to violence against women. *Lancet*. 2015;385(9977):1567.

Gerber GL, Cherneski L. Sexual aggression toward women: reducing the prevalence. *Ann N Y Acad Sci*. 2006;1087:35.

Hillard PJ. Physical abuse in pregnancy. *Obstet Gynecol*. 1985;66:185.

Iverson KM, Vogt D, Dichter ME, et al. Intimate partner violence and current mental health needs among female veterans. *J Am Board Fam Med*. 2015;28:772.

Sugg N. Intimate partner violence: prevalence, health consequences, and intervention. *Med Clin North Am*. 2015;99:629.

U.S. Preventive Services Task Force: *Intimate Partner Violence Screening: Fact Sheet and Resources*. Rockville, MD, Agency for Healthcare Research and Quality. Available at <http://www.ahrq.gov/professionals/prevention-chronic-care/healthier-pregnancy/preventive/partnerviolence.html>, Accessed 25.11.15.

Wathen CN, MacMillan HL. Prevention of violence against women: recommendation statement from the Canadian Task Force on Preventive Health Care. *CMAJ*. 2003;169:582.

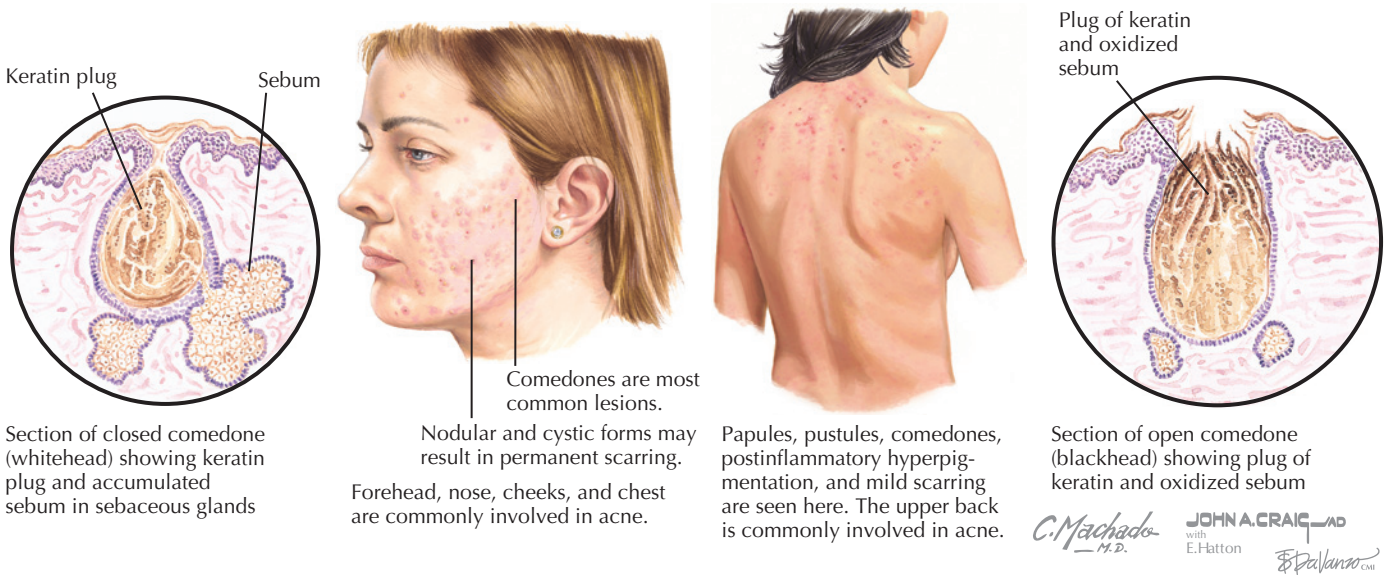


Figure 20.1 Acne vulgaris

- Virilizing conditions (such as polycystic ovary syndrome, congenital adrenal hyperplasia, and androgen-secreting tumors)

Concerns: Acne may serve as a surrogate for other issues with sexual development, menstruation, and contraception.
Associated Conditions: Social or emotional withdrawal.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated.
Special Tests: None indicated.
Diagnostic Procedures: History and physical examination. Several scales exist to grade severity, but none has been universally accepted.

Pathologic Findings

Increased oiliness of the skin, increased skin thickness with hypertrophic sebaceous glands, perifolliculitis, and scarring.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: General hygiene, nail clipping (to reduce secondary trauma and infections), twice-a-day cleansing with a mild soap, oil-free sunscreens.
Specific Measures: Comedone extraction (with extractor), topical medical therapy. Light-based treatment modalities have generally fallen out of use due to cost and low efficacy.
Diet: No specific dietary changes indicated. (None has been demonstrated to be effective, and diet is not considered to play a role in causation.)
Activity: No restriction.
Patient Education: General hygiene measures, need for long-term treatment. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP041 (Your Changing Body [Especially for Teens]), AP112 (Birth Control [Especially for Teens]), AB020 (Birth Control Pills).

Drug(s) of Choice

- Azelaic acid, 20% concentration gel, applied topically twice daily (more expensive than retinoids)
- Benzoyl peroxide 5% applied to skin every night (does not create bacterial resistance)
- Tretinoin (retinoic acid) 0.025% cream applied to skin every night (apply for 30 minutes after washing reduces side effects)
- Topical antibiotics: erythromycin, clindamycin (2%) in water base
- Systemic antibiotics: tetracycline 250 mg PO four times daily for 7–10 days then tapering to lowest effective dose, erythromycin 250 mg PO four times daily for 7–10 days then tapering to lowest effective dose
- Oral contraceptives (reduce androgen production by the ovaries)

Contraindications: Known or suspected allergy, hepatic dysfunction for oral agents, pregnancy (tetracycline and isotretinoin).
Precautions: Tetracycline and benzoyl peroxide may cause photosensitivity.
Interactions: Tetracycline should not be given with antacids, dairy products, or iron. Erythromycin should not be given with terfenadine (Seldane) and astemizole because it may cause cardiac abnormalities including arrhythmias and death. Broad-spectrum antibiotics may (theoretically) interfere with oral contraceptive efficacy.

Alternative Drugs

- Tretinoin (retinoic acid) 0.025% gel applied on chest or back every night.
- Isotretinoin (Accutane) 0.5–1 mg/kg/day in two doses for 12–16 weeks with a second course possible after an 8-week interval (associated with significant side effects including dry skin, dryness of the mucous membranes, and cheilitis).

FOLLOW-UP

Patient Monitoring: Periodic follow-up (monthly) until control is obtained. For patients receiving isotretinoin, liver function, lipid concentrations, and the possibility of pregnancy should be monitored.
Prevention/Avoidance: None.
Possible Complications: Scarring, hypopigmentation or hyperpigmentation, keloidal scarring on the sternum or shoulders.
Expected Outcome: Gradual improvement over time and with therapy.

MISCELLANEOUS

Pregnancy Considerations: Pregnancy may cause a flare-up or remission of acne. Isotretinoin, tetracycline, and erythromycin should not be used during pregnancy.

ICD-10-CM Codes: L70.0 (Acne Vulgaris).

REFERENCES

LEVEL I

Rafiei R, Yaghoobi R. Azithromycin versus tetracycline in the treatment of acne vulgaris. *J Dermatolog Treat*. 2006;17:217.

LEVEL II

Santos MA, Belo VG, Santos G. Effectiveness of photodynamic therapy with topical 5-aminolevulinic acid and intense pulsed light versus intense pulsed light alone in the treatment of acne vulgaris: comparative study. *Dermatol Surg*. 2005;31:910.

LEVEL III

Arowojolu AO, Gallo MF, Lopez LM, et al. Combined oral contraceptive pills for treatment of acne. *Cochrane Database Syst Rev*. 2007;(24): CD004425.

Bhate K, Williams HC. Epidemiology of acne vulgaris. *Br J Dermatol*. 2013;168:474.

Hay RJ, Johns NE, Williams HC, et al. The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions. *J Invest Dermatol*. 2013;134:1527.

Knutsen-Larson S, Dawson AL, Dunnick CA, et al. Acne vulgaris: pathogenesis, treatment, and needs assessment. *Dermatol Clin*. 2012;30:99.

Mariwalla K, Rohrer TE. Use of lasers and light-based therapies for treatment of acne vulgaris. *Lasers Surg Med*. 2005;37:333.

Purdy S, de Berker D. Acne. *BMJ*. 2006;333:949.

Strauss JS, Krowchuk DP, Leyden JJ, et al. American Academy of Dermatology/American Academy of Dermatology Association: Guidelines of care for acne vulgaris management. *J Am Acad Dermatol*. 2007;56:651.

Titus S, Hodge J. Diagnosis and treatment of acne. *Am Fam Physician*. 2012;86:734.

Williams C, Layton AM. Persistent acne in women: implications for the patient and for therapy. *Am J Clin Dermatol*. 2006;7:281.

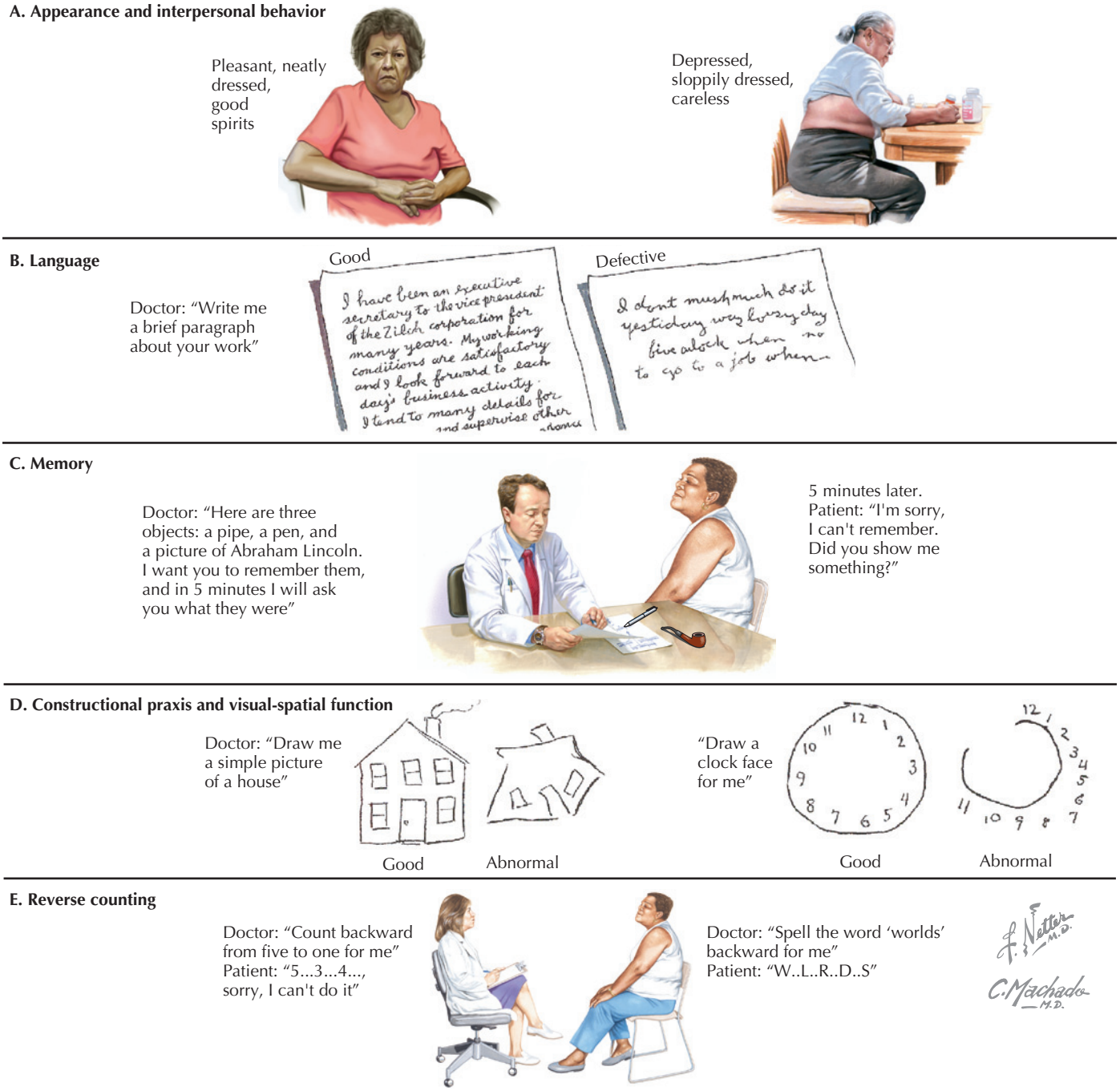


Figure 21.1 Testing for defects of higher cortical function

Pathologic Findings

β-Amyloid deposits in neuritic plaques and on arteriolar walls characterize the disease. Pyramidal cell loss, decreased cholinergic innervation, and neuritic senile plaques are also observed.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Support, exercise to reduce restlessness and improve sleep, continued cognitive challenge, and family support.

Specific Measures: Estrogen replacement is associated with a 50% reduction in risk and a delay in the onset of symptoms in some studies, although more recent studies do not confirm these findings. For those with Alzheimer changes, estrogen replacement near the time of menopause appears to improve function; late replacement (as in the Women's Health Initiative study) does not.

Diet: No specific dietary changes indicated.

Activity: No restriction except those imposed by ability.

Patient Education: Reassurance. Extensive educational materials are available from support groups, Internet sites, and the Alzheimer's Association (Chicago).

Drug(s) of Choice

Acetylcholinesterase inhibitors (tacrine, rivastigmine, galantamine, and donepezil) and NMDA receptor antagonist (memantine) are

used but benefits are small. Only donepezil is approved for treatment of advanced dementia. Drugs may be used to improve specific manifestations such as insomnia or depression.

Contraindications: Avoid anticholinergic drugs such as tricyclic antidepressants and antihistamines.

Precautions: Tacrine (Cognex) may cause liver toxicity. Benzodiazepines may produce paradoxical excitation. Triazolam (Halcion) can produce memory loss, confusion, or psychotic reactions. Care must be taken in the use of all drugs in these patients as they tend to tolerate them poorly and confusion may lead to dosing errors.

Alternate Therapies: Ginkgo biloba has shown some promise in clinical studies.

FOLLOW-UP

Patient Monitoring: Watch for problems with nutrition, further mental deterioration, and drug use. Provide continuing and aggressive family support. Periodically evaluate the need for nursing home placement or other assistance.

Prevention/Avoidance: None. Some data suggest that remaining intellectually active (games or puzzles), physical activity, and social interaction may reduce the risk or delay the onset.

Possible Complications: Progressive deterioration with metabolic changes, dehydration, drug overdose, falls, depression, and suicide.

Expected Outcome: Poor—progressive deterioration with 3- to 9-year average survival.

MISCELLANEOUS

ICD-10-CM Codes: G30.9 (Alzheimer disease, unspecified), F03.90 (Unspecified dementia without behavioral disturbance).

REFERENCES

LEVEL III

Ballard C, Gauthier S, Corbett A, et al. Alzheimer's disease. *Lancet*. 2011;377(9770):1019.

Birks J, Grimley E, Van Dongen M. Ginkgo biloba for cognitive impairment and dementia. *Cochrane Database Syst Rev*. 2002;(4):CD003120.

Birks J, Harvey RJ. Donepezil for dementia due to Alzheimer's disease. *Cochrane Database Syst Rev*. 2006;(1):CD001190.

Burns A, Iliffe S. Alzheimer's disease. *BMJ*. 2009;338:b158.

Geldmacher DS, Whitehouse PJ. Evaluation of dementia. *N Engl J Med*. 1996;335:330.

Progress Report on Alzheimer's Disease 1996. *Washington, DC, National Institute on Aging, US Dept of Health and Human Services, 1996*. NIH publication 96–4137.

Querfurth HW, LaFerla FM. Alzheimer's disease. *NEJM*. 2010;362:329.

Wenk GL. Neuropathologic changes in Alzheimer's disease. *J Clin Psychiatry*. 2003;64(suppl 9):7.

World Health Organization, *Dementia fact sheet, N°362, March 2015*. Available at; <http://www.who.int/mediacentre/factsheets/fs362/en/> Accessed 01.12.15.

Zamrini E. Emerging drug therapies for dementia. *Geriatr Aging*. 2006;9:107, 110.

22 ANEMIA

INTRODUCTION

Description: Anemia is the reduction, ie, below normal, in the oxygen-carrying capacity of the blood as reflected by the hemoglobin or hematocrit values. Women are at a higher risk because of menstrual blood loss.

Prevalence: More than 20% of women; 50%–60% of pregnant women.

Predominant Age: Reproductive age is the most common for women.

Genetics: Hemoglobinopathies, such as sickle cell disease and thalassemia, are associated with anemia.

ETIOLOGY AND PATHOGENESIS

Causes: Abnormalities of production (eg, iron deficiency, chronic disease, chemotherapy, radiation, and vitamin B_{12} deficiency). Abnormalities of destruction or loss (eg, hemorrhage, hemolysis, and sickle cell disease).

Risk Factors: Excessive blood loss (menorrhagia), poor diet, pica, malabsorption, chronic disease, endocrinopathy (thyroid). Smokers have slightly higher hemoglobin values (0.5–1.0 g/dL).

SIGNS AND SYMPTOMS

- Asymptomatic
- Fatigue, palpitations, dyspnea, exhaustion (late signs)
- Ice craving, spooning, or ridging of fingernails (iron deficiency anemia)
- Sore mouth or dysphagia (B_{12} or iron deficiency anemia)
- Joint and bone pain (sickle cell anemia)

DIAGNOSTIC APPROACH

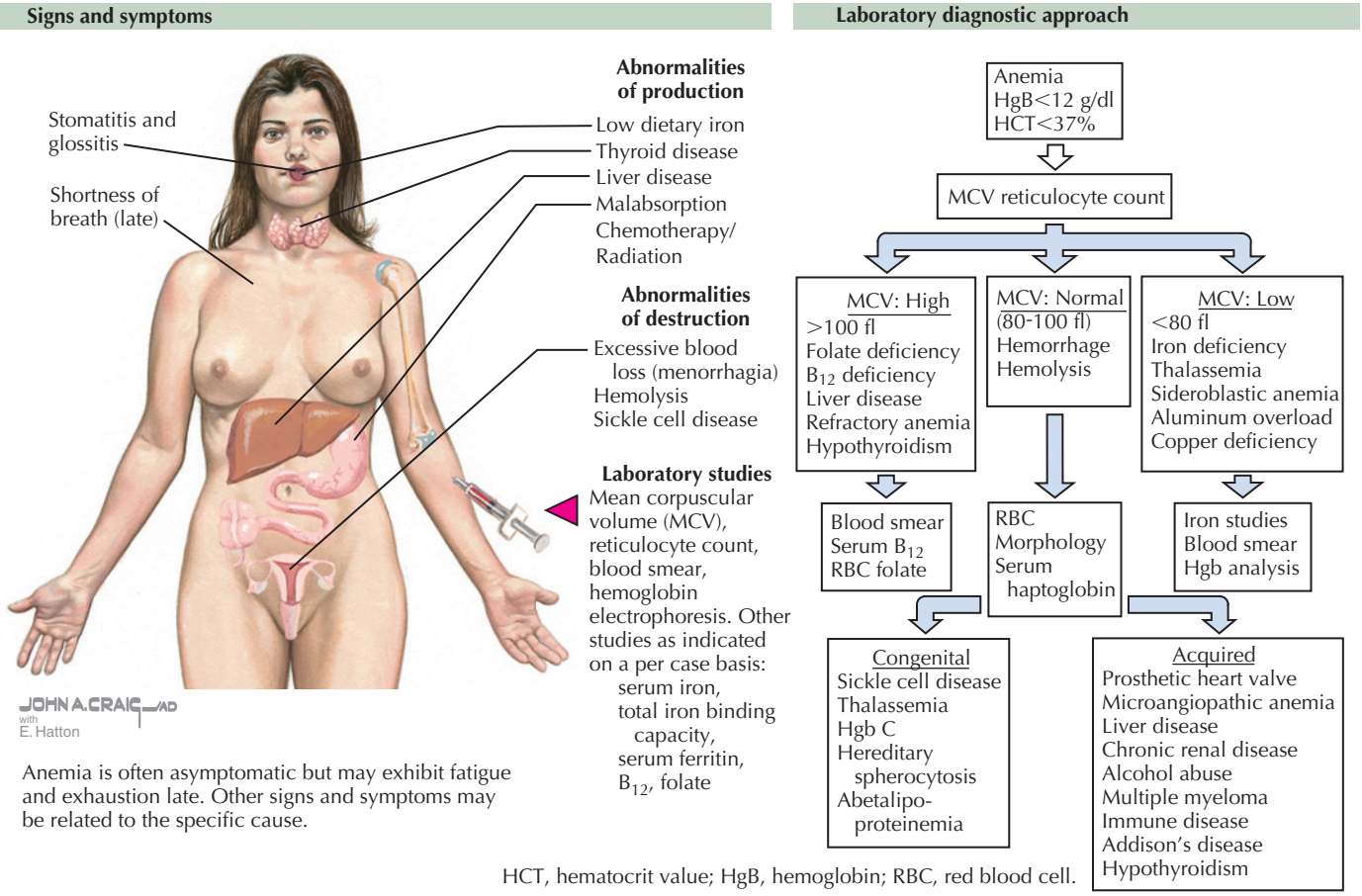
Differential Diagnosis

See Fig. 22.1.

Associated Conditions: Stomatitis, ridging or spooning of fingernails, hypersegmented polymorphonuclear neutrophils (megaloblastic anemia).

Workup and Evaluation

Laboratory: Mean corpuscular volume, reticulocyte count, blood smear, iron studies, hemoglobin electrophoresis; others based on individual patient—serum iron, total iron binding capacity, and serum ferritin.



Anemia is often asymptomatic but may exhibit fatigue and exhaustion late. Other signs and symptoms may be related to the specific cause.

HCT, hematocrit value; HgB, hemoglobin; RBC, red blood cell.

Figure 22.1 Anemia

Imaging: No imaging indicated.
Special Tests: Bone marrow analysis (not necessary for the majority of patients).
Diagnostic Procedures: Laboratory evaluation.

Pathologic Findings

Based on underlying cause.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, diet counseling, and control of menstrual abnormalities.
Specific Measures: Based on cause.
Diet: Adequate iron (7–12 mg/day) and folate (1–5 mg/day).
Activity: No restriction.
Patient Education: Diet counseling. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP001 (Nutrition During Pregnancy).

Drug(s) of Choice

- Iron supplements (ferrous sulfate 300–350 mg PO three times daily) for 6–12 months or longer. Parenteral iron may be given to patients with severe anemia or to those who do not comply with oral therapy.
- For pernicious anemia—vitamin B_{12} 100 mg intramuscularly (IM) monthly. Treatment of megaloblastic anemia resulting from B_{12} deficiency with folate will reverse anemia, but progressive and irreversible neurologic damage may result. B_{12} levels should always be checked if this is suspected.

Precautions: Anaphylaxis may occur with parenteral iron.
Interactions: Ascorbic acid increases iron absorption.

FOLLOW-UP

Patient Monitoring: Normal health maintenance, periodic evaluation of blood count.
Prevention/Avoidance: Good diet, control of excessive menstrual blood loss.
Possible Complications: Progressive and irreversible neurologic damage may result with untreated vitamin B_{12} deficiency.
Expected Outcome: Generally good response to iron therapy (iron deficiency type).

MISCELLANEOUS

Pregnancy Considerations: Anemia more common in pregnancy.
ICD-10-CM Codes: D64.9 (Anemia, unspecified - others based on cause).

REFERENCES

LEVEL III

Agency for Healthcare Research and Quality. *Screening for iron deficiency anemia in childhood and pregnancy: update of the 1996 U.S. Preventive Task Force review. AHRQ Publication No. 06-0590-EF-1*. Rockville (MD): AHRQ; 2006.

American College of Obstetricians and Gynecologists. Anemia in pregnancy. ACOG Practice Bulletin No. 95. *Obstet Gynecol*. 2008;112:201.

Centers for Disease Control and Prevention. Recommendations to prevent and control iron deficiency in the United States. *MMWR Recomm Rep*. 1998;47(RR–3):1.

Pena-Rosas JP, Viteri FE. Effects of routine oral iron supplementation with or without folic acid for women during pregnancy. *Cochrane Database Syst Rev*. 2006;(3):Art. No.: CD004736.

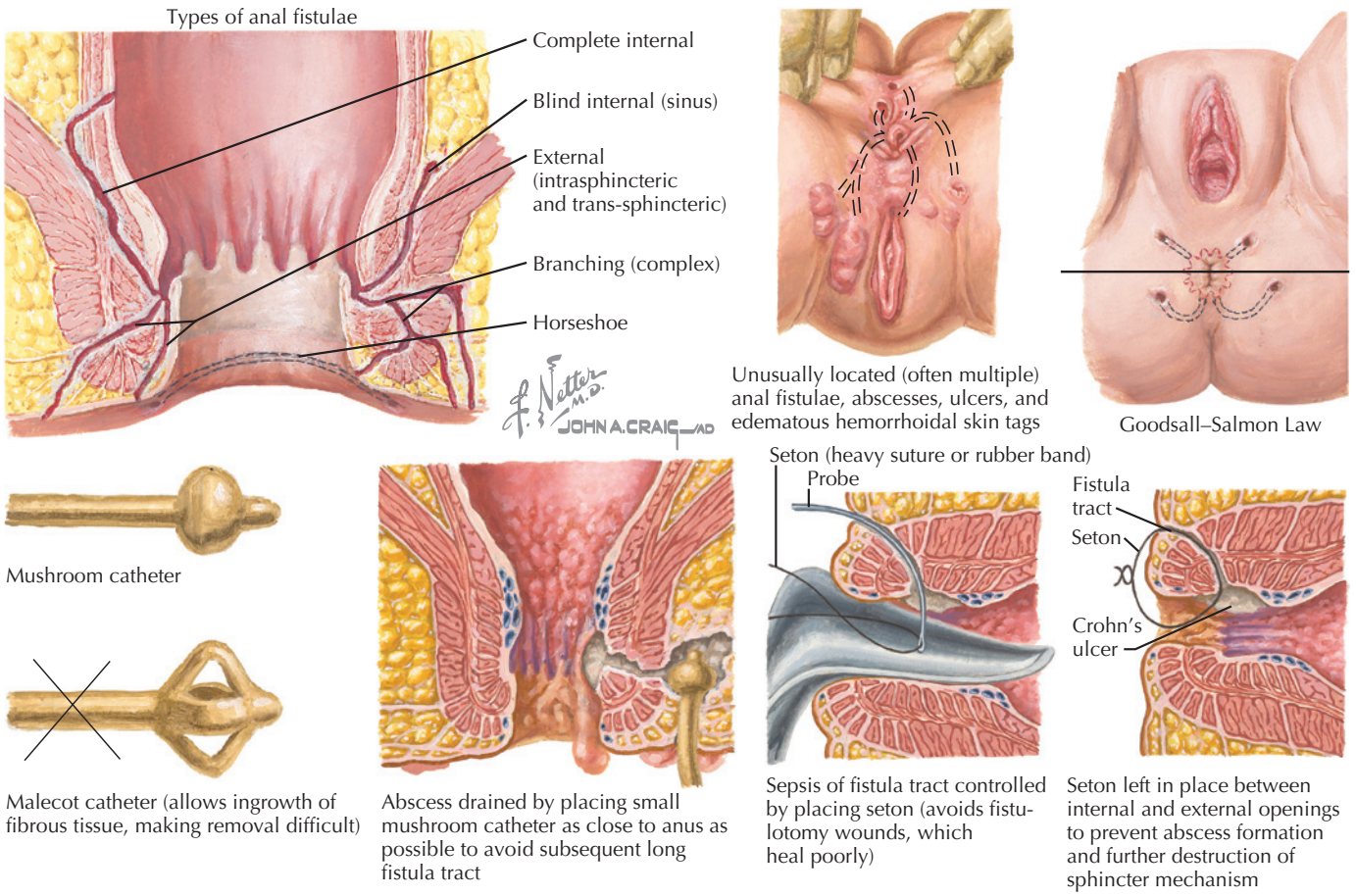


Figure 23.1 Appearance and management of anorectal Crohn's disese

MISCELLANEOUS

Other Notes: Goodsall–Salmon law states that fistulae with an external opening anterior to a plane passing transversely through the center of the anus will follow a straight radial course to the dentate line. Fistulae with their openings posterior to this line will follow a curved course to the posterior midline. Exceptions to this rule are external openings more than 3 cm from the anal verge, which almost always originate as a primary or secondary tract from the posterior midline, consistent with a previous horseshoe abscess.

Pregnancy Considerations: No effect on pregnancy, although may affect the choice of an episiotomy site, should one be used.

ICD-10-CM Codes: K60.3 (anal fistula), K60.4 (rectal fistula), K60.5 (anorectal fistula).

REFERENCES

LEVEL I

Pescatori M, Ayabaca SM, Cafaro D, et al. Marsupialization of fistulotomy and fistulectomy wounds improves healing and decreases bleeding: a randomized controlled trial. *Colorectal Dis*. 2006;8:11.

LEVEL II

Buchanan GN, Halligan S, Williams AB. Magnetic resonance imaging for primary fistula in ano. *Br J Surg*. 2003;90:877.

Ding JH, Bi LX, Zhao K, et al. Impact of three-dimensional endoanal ultrasound on the outcome of anal fistula surgery: a prospective cohort study. *Colorectal Dis*. 2015;17:1104.

Quah HM, Tang CL, Eu KW, et al. Meta-analysis of randomized clinical trials comparing drainage alone vs primary sphincter-cutting procedures for anorectal abscess-fistula. *Int J Colorectal Dis*. 2006;21:602. [Epub 2005 Nov 30].

LEVEL III

Gravante G, Giordano P. The role of three-dimensional endoluminal ultrasound imaging in the evaluation of anorectal diseases: a review. *Surg Endosc*. 2008;22:1570.

Halligan S, Stoker J. Imaging of fistula in ano. *Radiology*. 2006;239:18.

Jacob TJ, Perakath B, Keighley MR. Surgical intervention for anorectal fistula. *Cochrane Database Syst Rev*. 2010;(5):CD006319.

Jones J, Tremaine W. Evaluation of perianal fistulas in patients with Crohn's disease. *MedGenMed*. 2005;7:16.

Kim MJ. Transrectal ultrasonography of anorectal diseases: advantages and disadvantages. *Ultrasonography*. 2015;34:19.

Rizzo JA, Naig AL, Johnson EK. Anorectal abscess and fistula-in-ano: evidence-based management. *Surg Clin North Am*. 2010;90:45.

Sneider EB, Maykel JA. Anal abscess and fistula. *Gastroenterol Clin North Am*. 2013;42:773.

24 ANXIETY

INTRODUCTION

Description: Anxiety is a common acute or chronic emotion that is associated with physical symptoms. It is two to three times more common in women. Subtypes of anxiety include situational anxiety, adjustment disorders, panic disorders, phobias, and post-traumatic stress disorder. Moreover, obsessive–compulsive disorders are often classified in this group.
Prevalence: Eighteen percent of women; 40 million Americans.
Predominant Age: 20–45 years.
Genetics: Increased risk of panic disorders within monozygotic twins. Panic disorder, social phobia, and obsessive–compulsive disorders have a genetic base.

ETIOLOGY AND PATHOGENESIS

Causes: Psychosocial stressors (eg, pregnancy loss or breast cancer), abnormality of neurotransmitter systems (serotonin, norepinephrine, and γ-aminobutyric acid), involving the amygdala and hippocampus.
Risk Factors: Social, family, or financial stress; medical illness; family history; and a lack of social support network.

SIGNS AND SYMPTOMS (VARY WITH SUBTYPE)

- Unrealistic or excessive worry
- Sense of impending doom
- Nervousness or instability
- Palpitations or tachycardia
- Hyperventilation or sense of suffocation
- Systemic systems (nausea, abdominal pain, paresthesias, diaphoresis, chest tightness, dizziness, muscle tension, headaches, and backaches)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Cardiovascular (ischemic heart disease, valvular disease, cardiomyopathies, arrhythmias, mitral valve prolapse)
- Respiratory (asthma, emphysema, pulmonary embolism)
- Central nervous system (transient ischemia, psychomotor epilepsy, essential tremor)
- Metabolic (hyperthyroidism, adrenal insufficiency, pheochromocytoma, Cushing syndrome, hypoglycemia, hypokalemia, hyperparathyroidism, myasthenia gravis)
- Nutritional (thiamine, pyridoxine, or folate deficiency)
- Medication/drugs (caffeine, alcohol, cocaine, sympathomimetics, amphetamine)

Associated Conditions: Mitral valve prolapse, irritable bowel syndrome (IBS), depression, agoraphobia, substance abuse, and somatoform disorders.

Workup and Evaluation

Laboratory: No specific evaluation indicated. Tests should be based on the diagnoses being considered (eg, thyroid function studies).
Imaging: No imaging indicated.
Special Tests: None indicated.
Diagnostic Procedures: History and psychologic testing.

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and assessment of cause and subtype, screening for substance abuse, counseling, establishing ties to support systems, beginning exercise program, and maintaining frequent follow-up.
Specific Measures: Psychotherapy (cognitive-behavioral therapy), medications.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP106 (Depression), AP068 (Alcohol and Women), AP083 (Domestic Violence).

Drug(s) of Choice

- Acute anxiety or adjustment disorders—short-term benzodiazepines: alprazolam 0.25 mg 2–3 times daily, increase in 0.25-mg increments if required.
- Generalized anxiety—azapirones: buspirone [BuSpar] 5 mg PO 2–3 times daily, increased every 2–3 days to a maximum of 60 mg/day.
- Panic disorders and phobias—selective serotonin reuptake inhibitors (SSRIs; fluoxetine [Prozac] 4 mg PO, increased by 4 mg every 5 days to maximum of 40 mg; sertraline [Zoloft] 25 mg PO, increased by 25 mg every 5 days; paroxetine [Paxil] 10 mg PO increased by 10 mg every 5 days).
- Obsessive-compulsive disorders—SSRIs or clomipramine (Anafranil) 25 mg PO two times daily, increased to 250 mg/day.

Contraindications: Benzodiazepines are contraindicated in the first trimester of pregnancy, in patients with acute alcohol intoxication, and in patients with sleep apnea or open-angle glaucoma.
Precautions: Agents with short half-lives (eg, alprazolam) have a high potential for dependency and withdrawal symptoms. Acute withdrawal may precipitate panic attacks or seizures. Hepatic and renal function should be monitored in patients using benzodiazepines or buspirone. Breastfeeding should be discouraged in women taking chronic or high-dose benzodiazepines.
Interactions: Buspirone should not be used with monomine oxidase inhibitors (MAOIs).

Alternative Drugs

Panic disorders and phobias—imipramine (Tofranil) 10–25 mg PO every night, increased by 10–25 mg/day every 2 weeks to a maximum of 300 mg/day in adults and 100 mg/day in adolescents and elderly patients.

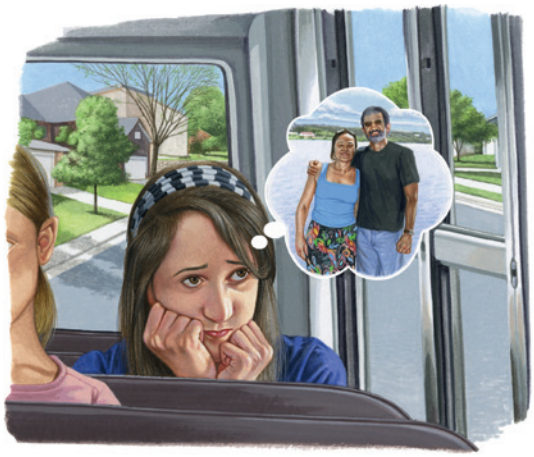
FOLLOW-UP

Patient Monitoring: Frequent follow-up, identification and treatment of associated depression, periodic assessment of renal and hepatic function (based on medical therapy chosen).
Prevention/Avoidance: Stress management, relaxation training.
Possible Complications: Social withdrawal or isolation, drug dependence or side effects.
Expected Outcome: Generally good outcome. (Obsessive–compulsive disorders and post-traumatic stress disorders are more difficult to treat.)

Five major types of anxiety disorders are:

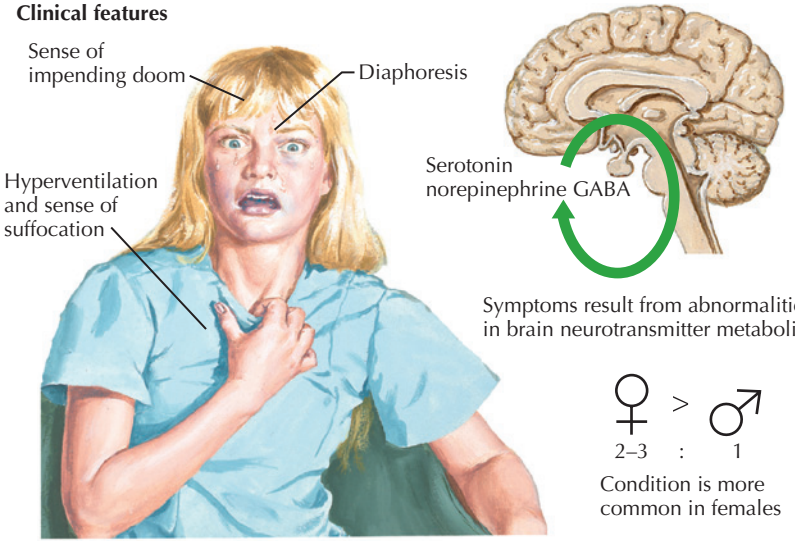
- Generalized anxiety disorder
- Obsessive-compulsive disorder (OCD)
- Panic disorder
- Post-traumatic stress disorder (PTSD)
- Social phobia (or social anxiety disorder)

Generalized anxiety disorder (many worries and fears)



Social anxiety disorder (afraid of social interactions)

Clinical features



Anxiety may be acute or chronic and the scope of the condition includes situation anxiety, panic disorders, phobias and adjustment, and post-traumatic disorders

Obsessive-Compulsive Disorder

"I am embarassed that my hands are so chapped. I never told you before about my fear of germs and constant washing because I was afraid you would think I was crazy."

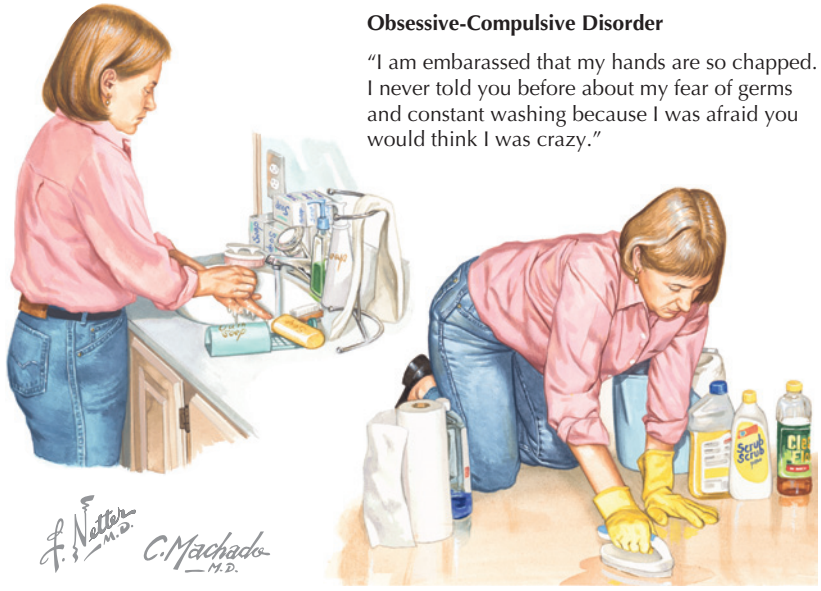


Figure 24.1 Clinical features and types of anxiety

MISCELLANEOUS

Pregnancy Considerations: Medical therapy must be adjusted based on the risk and requirement. Cognitive–behavioral therapy has been suggested as the first-line therapy during pregnancy.

ICD-10-CM Codes: F41.9 (Anxiety disorder, unspecified).

REFERENCES

LEVEL II

Hirai M, Clum GA. A meta-analytic study of self-help interventions for anxiety problems. *Behav Ther*. 2006;37:99. [Epub 2006 Mar 24].

Marchesi C, Ossola P, Amerio A, et al. Clinical management of perinatal anxiety disorders: a systematic review. *J Affect Disord*. 2015;190:543.

Spitzer R, Williams JBW, Kroenke K, et al. The PRIME-MD study: description, validation and clinical utility of a new procedure for diagnosing mental disorders in primary care. *JAMA*. 1994;272:1749.

LEVEL III

Altemus M, Sarvaiya N, Neill Epperson C. Sex differences in anxiety and depression clinical perspectives. *Front Neuroendocrinol*. 2014;35:320.

Brookman RR, Sood AA. Disorders of mood and anxiety in adolescents. *Adolesc Med Clin*. 2006;17:79.

Goodman JH, Chenausky KL, Freeman MP. Anxiety disorders during pregnancy: a systematic review. *J Clin Psychiatry*. 2014;75:e1153.

Maass SW, Roorda C, Berendsen AJ, et al. The prevalence of long-term symptoms of depression and anxiety after breast cancer treatment: a systematic review. *Maturitas*. 2015;82:100.

McHenry J, Carrier N, Hull E, et al. Sex differences in anxiety and depression: role of testosterone. *Front Neuroendocrinol*. 2014;35:42.

Ross LE, McLean LM. Anxiety disorders during pregnancy and the postpartum period: a systematic review. *J Clin Psychiatry*. 2006;67:1285.

Schneier FR. Clinical practice. Social anxiety disorder. *N Engl J Med*. 2006;355:1029.

Tyrer P, Baldwin D. Generalised anxiety disorder. *Lancet*. 2006;368:2156.

Yonkers KA, Blackwell KA, Glover J, et al. Antidepressant use in pregnant and postpartum women. *Annu Rev Clin Psychol*. 2014;10:369.

25 ASTHMA

INTRODUCTION

Description: Asthma (from the Greek for "panting") is an intermittent or chronic obstructive tracheobronchial condition that is characterized by wheezing or cough. Adult-onset asthma is more common in women and poses potential problems during pregnancy.
Prevalence: Seven percent of the United States population.
Predominant Age: Adults aged 16–40 years (50% of patients are younger than 10 years).
Genetics: Familial association with reactive airway disease, ectopic dermatitis, and allergic rhinitis.

ETIOLOGY AND PATHOGENESIS

Causes: Allergic factors (airborne pollens, molds, house dust, animal dander, feather pillows; a 2004 study showed that 71% had more than one allergy and 42% had more than three allergies), smoke or pollutants, viral upper-respiratory infections, aspirin or nonsteroidal antiinflammatory agents, exercise, gastrointestinal reflux.
Risk Factors: Family history and viral pneumonitis in infancy.

SIGNS AND SYMPTOMS

- Shortness of breath
- Wheezing and coughing (one or both)
- Prolonged exhalation
- Decreased breath sounds, hyperresonant chest
- Periodic (especially nocturnal) attacks
- Cyanosis and tachycardia
- Pulsus paradoxus, accessory muscle used for breathing, flattened diaphragm on chest radiograph or physical examination

Symptoms are usually worse at night and in the early morning. Up to 40% of asthmatic women of childbearing age may experience a cyclical exacerbation of asthmatic symptoms during the perimenstrual period.

DIAGNOSTIC APPROACH

Differential Diagnosis

- Recurrent pneumonia
- Chronic bronchitis
- Viral or fungal infection
- Aspiration (foreign body)
- Cystic fibrosis
- Tuberculosis
- Mitral valve prolapse
- Congestive heart failure
- Chronic obstructive pulmonary disease

Associated Conditions: Reflux esophagitis, sinusitis.

Workup and Evaluation

Laboratory: Complete blood count, arterial blood gases (severe cases).
Imaging: No imaging indicated. (Chest radiograph shows hyperinflation, atelectasis, or air leak, but it is nonspecific.)
Special Tests: Sweat chloride test (childhood), nasal eosinophils, pulmonary function testing (peak expiratory flow rate), allergy testing (selected patients).
Diagnostic Procedures: History, physical examination, pulmonary function testing (forced expiratory volume in 1 second, or FEV_1). An excellent office screening test is to ask the patient to blow out a lit match held at arm's length. Patients with reduced FEV_1 are unable to accomplish this task.

Pathologic Findings

Narrowing of large and small airways because of bronchial smooth muscle spasm, edema, and inflammation of the bronchial mucosa with increased mucus production characterize acute attacks. Chronic inflammatory changes are histologically observed. Biochemical factors related to inflammation mediators include chemical, eosinophil, and neutrophil chemotactic factors, bradykinins, and others.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, eliminate irritants, education, caffeine for mild symptoms.
Specific Measures: Mild—intermittent β-agonists via inhaler or cromolyn sodium four times daily plus low-dose inhaled steroids (beclomethasone dipropionate 400 mg/day) may add slow-release xanthines, leukotriene modifiers (montelukast, zafirlukast, pranlukast, and zileuton). Methylxanthines (theophylline and aminophylline), if sufficient control cannot be achieved with inhaled glucocorticoids and long-acting β-agonists alone. Severe—cromolyn sodium plus high-dose inhaled steroids plus theophylline (therapeutic level 10–20 mg/mL), inhaled β-agonist to reverse airflow obstruction. During asthma attacks, patients should avoid fluid loading, intermittent positive pressure breathing, or airway mist or humidification; these worsen symptoms.
Diet: No specific dietary changes indicated. Avoid known allergens (if any).
Activity: No restriction or restriction based on pulmonary function, except for those with exercise-induced asthma (eg, cold weather, excessive activity).
Patient Education: Understanding of disease and use of inhalers, education about triggering factors and allergens.

Drug(s) of Choice

- Cromoglycate and nedocromil
- Steroids (beclomethasone, prednisone)
- β-Agonists (albuterol, bitolterol, salmeterol, terbutaline)
- Methylxanthines (theophylline)
- Anticholinergics (atropine, ipratropium bromide)
- Leukotriene antagonists

Contraindications: Sedatives, mucolytics.
Precautions: β-Agonists should only be intermittently used.
Interactions: Erythromycin and ciprofloxacin slow theophylline clearance and can increase levels by 15%–20%.

Alternative Drugs

Histamine H_1-antagonists, methotrexate

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: Avoid known allergens, aspirin, nonsteroidal antiinflammatory and β-adrenergic blocking drugs. Have a prearranged action plan for acute attacks. Obtain annual influenza immunization. Avoid food additives known to precipitate attacks (sulfites and tartrazine).
Possible Complications: Respiratory failure, atelectasis, pneumothorax, death. Mortality increases with more than three emergency visits or more than two hospital admissions per year, nocturnal symptoms, history of intensive care unit admission or

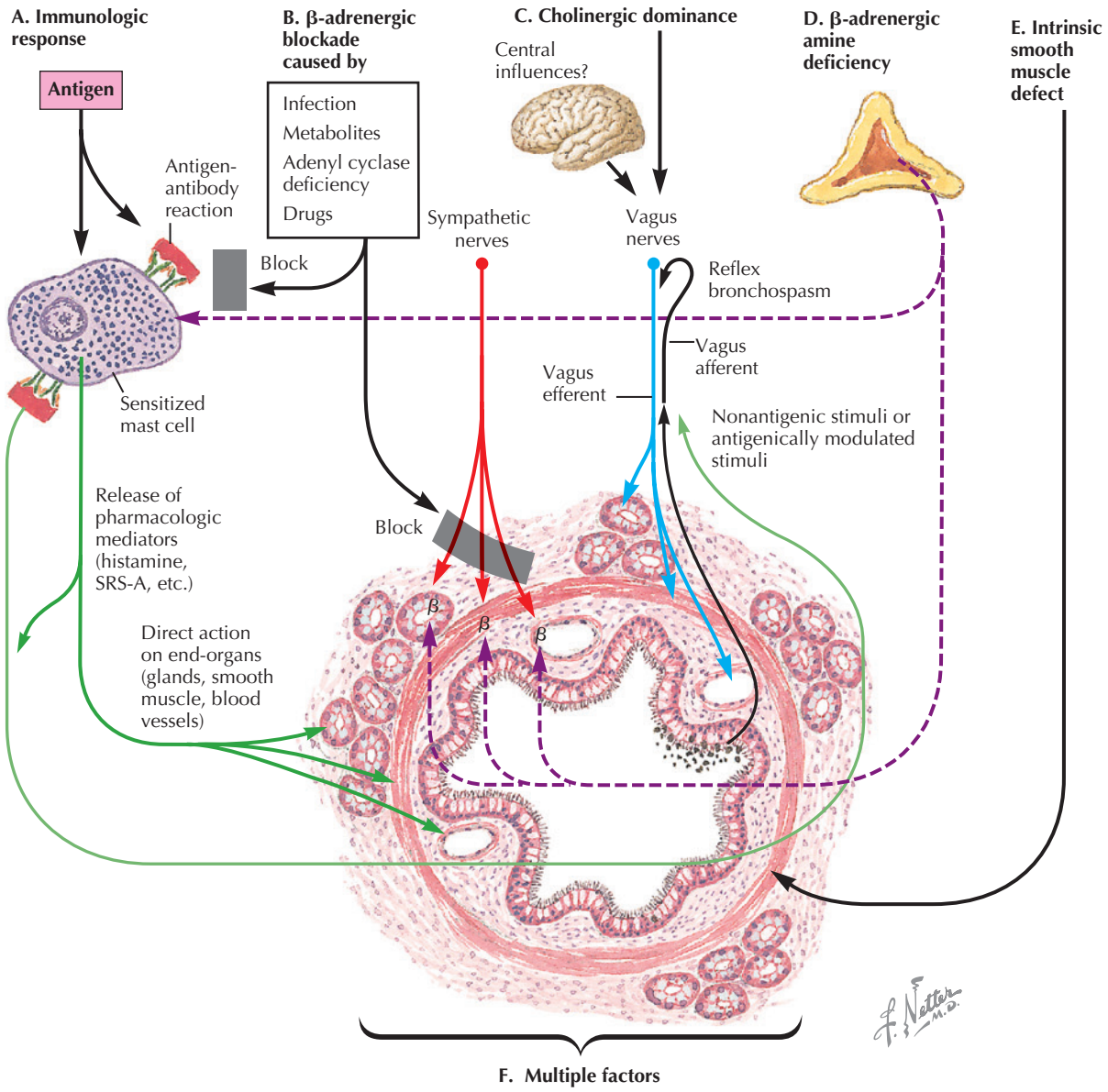


Figure 25.1 Postulated mechanisms of airway hyperactivity causing asthma

mechanical ventilation, steroid dependence, and history of syncope with attacks.

Expected Outcome: Excellent with careful management.

MISCELLANEOUS

Other Notes: For those with exercise-induced asthma, activities in which the patient breathes large amounts of cold air (eg, skiing or running) are more likely to provoke an attack, whereas swimming in an indoor, heated pool, with warm, humid air, is less likely to cause problems.

Pregnancy Considerations: Approximately 50% of patients have no change in symptoms, 25% improve, and 25% worsen. Asthma is found in 1% of pregnant patients, 15% of whom have one or more significant attacks during gestation. The effects are highly variable but may include chronic hypoxia, intrauterine growth restriction, and (rarely) fetal death.

ICD-10-CM Codes: J45.909 (Unspecified asthma, uncomplicated), J45.998 (Other asthma).

REFERENCES

LEVEL III

Ali Z, Hansen AV, Ulrik CS. Exacerbations of asthma during pregnancy: impact on pregnancy complications and outcome. *J Obstet Gynaecol*. 2015;14:1.

American College of Obstetricians and Gynecologists. Asthma in pregnancy. ACOG Practice Bulletin No. 90. *Obstet Gynecol*. 2008;111:457. (reaffirmed 2014).

Bain E, Pierides KL, Clifton VL, et al. Interventions for managing asthma in pregnancy. *Cochrane Database Syst Rev*. 2014;(10):CD010660.

British Thoracic Society, Scottish Intercollegiate Guidelines Network (SIGN). *British Guideline on the Management of Asthma. Guideline No. 63*. Edinburgh: SIGN; 2004.
Fanta CH. Asthma. *N Engl J Med*. 2009;360:1002.
Global Strategy for Asthma Management and Prevention. Available at: <http://www.ginasthma.org/uploads/users/files/GINA_Report2011_May4.pdf> Accessed 05.12.15.
Keselman A, Heller N. Estrogen Signaling Modulates Allergic Inflammation and Contributes to Sex Differences in Asthma. *Front Immunol*. 2015;6:568.
National Asthma Education and Prevention Program. *Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma*. Bethesda, Md: National Institutes of Health; 1997. pub no 97–4051.
Nolan TE. Upper respiratory and pulmonary problems. *Clin Obstet Gynecol*. 1995;38:147.
Pinnock H, Shah R. Asthma. *Br Med J*. 2007;334:847.
Rodrigo GJ, Rodrigo C, Hall JB. Acute asthma in adults: a review. *Chest*. 2004;125:1081.
Skoczyński S, Semik-Orzech A, Szanecki W, et al. Perimenstrual asthma as a gynecological and pulmonological clinical problem. *Adv Clin Exp Med*. 2014;23:665.
Van Zutphen AR, Bell EM, Browne ML, et al. Maternal asthma medication use during pregnancy and risk of congenital heart defects. *Birth Defects Res A Clin Mol Teratol*. 2015;103:951.
Zein JG, Erzurum SC. Asthma is Different in Women. *Curr Allergy Asthma Rep*. 2015;15:28.

26 CHOLELITHIASIS

INTRODUCTION

Description: Cholelithiasis is the formation of stones in the gallbladder or biliary collecting system. Most stones (80%) are the result of precipitation of supersaturated cholesterol. Women are three times more likely than men to form gallstones.
Prevalence: Ten percent of the population; 1 million cases per year.
Predominant Age: Seventy percent of patients are older than 40 years.
Genetics: Ratio of women to men is 3:1; some races at greater risk (eg, Pima Indians). Pigment gallstones affect men and women equally. A mutation in the gene ABCG8 significantly increases a person's risk of gallstones.

ETIOLOGY AND PATHOGENESIS

Causes: The metabolic alteration leading to cholesterol stones is thought to be a disruption in the balance between hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase and cholesterol 7α-hydroxylase. HMG-CoA controls cholesterol synthesis, whereas cholesterol 7α-hydroxylase controls the rate of bile acid formation. Patients who form cholesterol stones have elevated levels of HMG-CoA and depressed levels of cholesterol 7α-hydroxylase. This change in ratio increases the risk of precipitation of cholesterol as stones.
Risk Factors: Age, female gender, parity (75% of affected patients have had one or more pregnancies), obesity (15–20 pounds overweight is associated with a two-fold increase in risk; 50–75 pounds excess weight is associated with a six-fold increase in risk) and weight cycling, estrogen use (oral), cirrhosis, diabetes, and Crohn disease. A family history of cholelithiasis in siblings or children results in a two-fold increase in risk. Vegetarians are at a nine-fold lower risk.

SIGNS AND SYMPTOMS

- Asymptomatic (60%–70%; 50% become symptomatic; 20% develop complications)
- Fatty food intolerance
- Variable right upper quadrant pain with radiation to the back or scapula
- Nausea or vomiting (often mistaken for "indigestion")
- Fever usually associated with cholangitis

DIAGNOSTIC APPROACH

Differential Diagnosis

- Gastroenteritis
- Esophageal reflux
- Malabsorption
- Irritable bowel syndrome (IBS)
- Peptic ulcer disease
- Coronary artery disease
- Pneumonia
- Appendicitis

Associated Conditions: Cirrhosis, pancreatitis, and ileus.

Workup and Evaluation

Laboratory: Supportive, but often not diagnostic—complete blood count, serum bilirubin, amylase, alkaline phosphatase, and aminotransferase measurements.
Imaging: Ultrasonography of the gallbladder (96% accuracy for diagnosing sludge or a stone in the gallbladder).
Special Tests: Cholescintigraphy (also called gallbladder radionuclide scan or hepatobiliary [HIDA] scan).
Diagnostic Procedures: History, physical examination, ultrasonography, and laboratory investigation.

Pathologic Findings

Supersaturated bile, inflammation when accompanied by infection or obstruction.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Watchful waiting and dietary modifications.
Specific Measures: Oral therapy, surgical extirpation, lithotripsy.
Diet: Reduced fatty food and cholesterol intake.
Activity: No restriction.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP064 (Weight Control: Eating Right and Keeping Fit). Gallstones, available at: http://www.webmd.com/digestive-disorders/gallstones. Accessed 7.12.15.

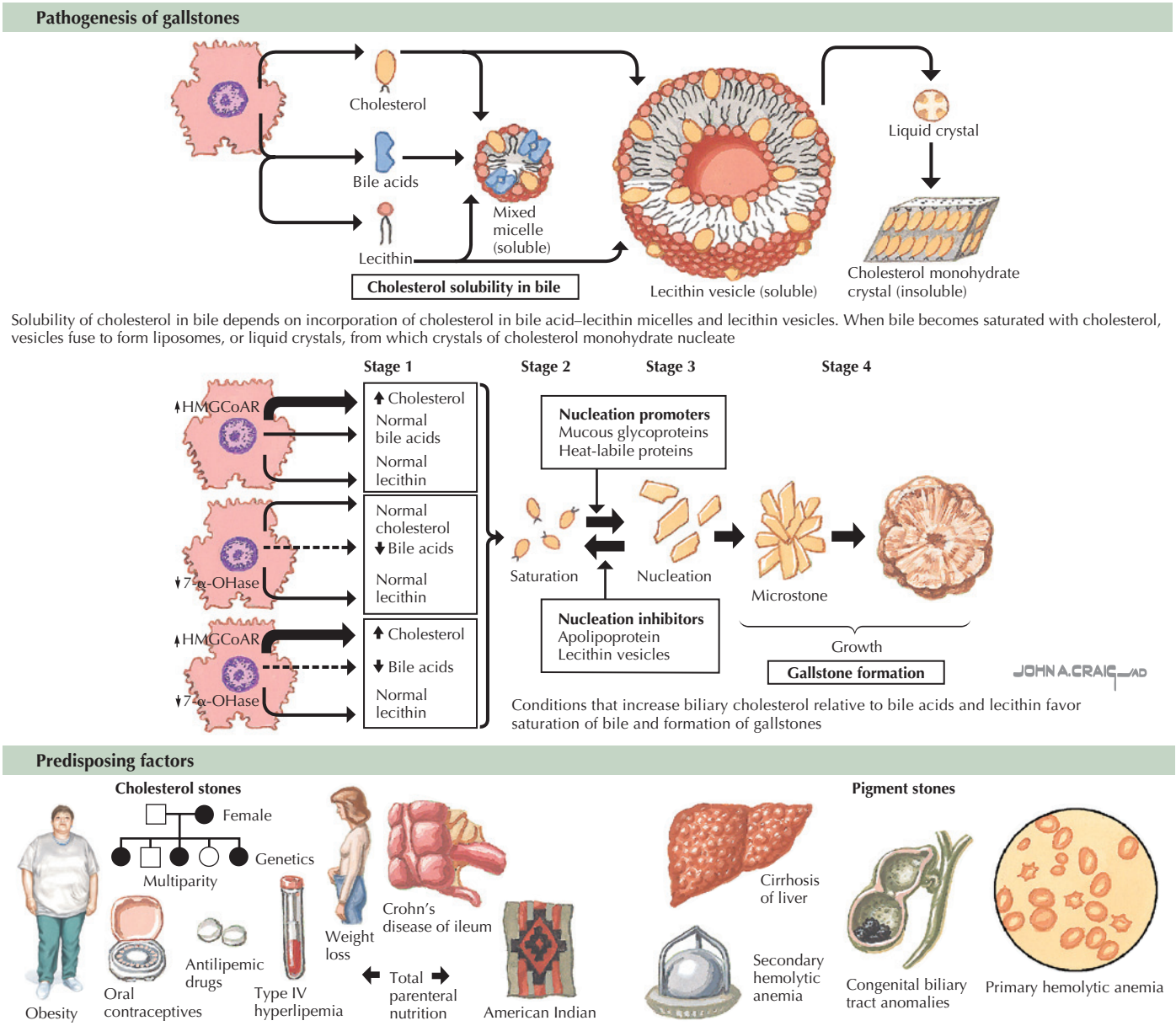


Figure 26.1 Pathogenesis and predisposing factors of cholelithiasis

Drug(s) of Choice

- Ursodeoxycholic acid (Actigall) 8–10 mg/kg/day as two to three doses.

Contraindications: Known allergy, acute cholecystitis, abnormal liver function, calcified stones (not cholesterol based).

Precautions: The rate of stone dissolution (approximately 1 mm/mo) limits applicability for stones greater than 1.5–2 cm in size.

Interactions: None.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.

Prevention/Avoidance: Low-fat and low-cholesterol diet may delay symptoms. Oral prophylaxis during rapid weight loss has been advocated for those otherwise at risk.

Possible Complications: Acute cholecystitis, pancreatitis, ascending cholangitis, peritonitis, internal fistulization. Stones re-form in approximately 50% of patients treated with oral therapy, although the majority (85%) remains asymptomatic. Those who have recurrent symptoms respond to additional courses of oral therapy.

Expected Outcome: Generally good with either oral or surgical therapy. Oral therapy results in resolution of symptoms in 2–3 months. Despite this, gallstone disease is responsible for about 10,000 deaths per year in the United States.

MISCELLANEOUS

Pregnancy Considerations: Of pregnant patients, 3%–4% experience gallstone symptoms. Women with increased parity and multifetal pregnancies are at greatest risk.

ICD-10-CM Codes: K80.20 (Calculus of gallbladder without cholecystitis without obstruction).

REFERENCES

LEVEL II

Ellington SR, Flowers L, Legardy-Williams JK, et al. Recent trends in hepatic diseases during pregnancy in the United States, 2002-2010. *Am J Obstet Gynecol*. 2015;212:524.

Wong AC, Ko CW. Carbohydrate intake as a risk factor for biliary sludge and stones during pregnancy. *J Clin Gastroenterol*. 2013;47:700.

LEVEL III

American College of Obstetricians and Gynecologists. Nausea and vomiting of pregnancy. Practice Bulletin No. 153. *Obstet Gynecol*. 2015;126:e12.

Bennett GL, Balthazar EJ. Ultrasound and CT evaluation of emergent gallbladder pathology. *Radiol Clin North Am*. 2003;41:1203.

Bhattacharya D, Ammori BJ. Contemporary minimally invasive approaches to the management of acute cholecystitis: a review and appraisal. *Surg Laparosc Endosc Percutan Tech*. 2005;15:1.

Date RS, Kaushal M, Ramesh A. A review of the management of gallstone disease and its complications in pregnancy. *Am J Surg*. 2008;196:599.

Ko CW, Beresford SA, Schulte SJ. Incidence, natural history, and risk factors for biliary sludge and stones during pregnancy. *Hepatology*. 2005;41:359.

Martin DJ, Vernon DR, Toouli J. Surgical versus endoscopic treatment of bile duct stones. *Cochrane Database Syst Rev*. 2006;(2):CD003327.

Portincasa P, Moschetta A, Palasciano G. Cholesterol gallstone disease. *Lancet*. 2006;368:230-239.

Shaffer EA. Epidemiology and risk factors for gallstone disease: has the paradigm changed in the 21st century? *Curr Gastroenterol Rep*. 2005;7:132.

Shaffer EA. Gallstone disease: epidemiology of gallbladder stone disease. *Best Pract Res Clin Gastroenterol*. 2006;20:981.

Tazuma S. Gallstone disease: epidemiology, pathogenesis, and classification of biliary stones (common bile duct and intrahepatic). *Best Pract Res Clin Gastroenterol*. 2006;20:1075.

van Erpecum KJ. Gallstone disease. Complications of bile-duct stones: acute cholangitis and pancreatitis. *Best Pract Res Clin Gastroenterol*. 2006;20:1139.

Wang HH, Liu M, Clegg DJ, et al. New insights into the molecular mechanisms underlying effects of estrogen on cholesterol gallstone formation. *Biochim Biophys Acta*. 2009;1791:1037.

Yusoff IF, Barkun JS, Barkun AN. Diagnosis and management of cholecystitis and cholangitis. *Gastroenterol Clin North Am*. 2003;32:1145.

Figure 27.1 Cramping in chronic pelvic pain

Diagnostic Procedures: History, physical examination, ultrasonography, and laboratory investigation. Single-digit palpation of the levator plate, piriformis, and obturator muscles can elicit the tenderness of pelvic floor tension myalgia.

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Diagnosis and treatment of any underlying pathophysiologic etiologies, analgesics, antidepressants (when indicated). The goal of the treatment is not necessarily complete eradication of pain, but rather finding effective strategies that allow functional living.

Specific Measures: The mainstay of treatment of muscular components of pelvic pain is physical therapy. Biofeedback or relaxation training may of help. Complementary strategies (eg, mindfulness-based medication, yoga, acupuncture), good sleep hygiene, exercise, smoking cessation, healthy eating, and social support. Presacral neurectomy (surgical interruption of the superior hypogastric plexus) is effective at treating central uterine pain, dysmenorrhea, and endometriosis but is associated with a high degree of complications.

Diet: No specific dietary changes indicated.

Activity: No restrictions.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP099 (Chronic Pelvic Pain).

Drug(s) of Choice

- Nonsteroidal antiinflammatory drugs and opioid narcotics (adverse outcomes and limited efficacy associated with long-term use).
- Neuromodulatory medications (eg, tricyclic antidepressants, neurotransmitter reuptake inhibitors, neuroleptics), psychologic adjuncts (eg, cognitive-behavioral therapy, pain psychotherapy, sexual counseling). Duloxetine and desvenlafaxine can be useful.
- Neuroleptics such as gabapentin, pregabalin, and lamotrigine are generally employed when symptoms are neuropathic in nature.

Contraindications: Based on the agent used.

Precautions: Opioid narcotics should be used with caution, if at all. The use of gonodatropin-releasing hormone agonists does not reliably differentiate gynecologic from other causes of pain.

Interactions: Based on the agent used.

Alternative Drugs

- Combined oral contraceptives are effective in reducing dysmenorrhea and cyclic symptoms associated with endometriosis.
- Tricylcic antidepressants such as amitriptyline, nortriptyline, and desipramine have a long record of being effective in treating chronic pain.
- Trigger point injection (1–5 mL of 1% lidocaine or 0.25%–0.5% bupivacaine) for entrapped segmental nerve (eg, ilioinguinal) or abdominal wall trigger point.

FOLLOW-UP

Patient Monitoring: Frequent follow-up, identification, and treatment of associated depression.

Prevention/Avoidance: Early and effective treatment of conditions associated with chronic pain states.

Possible Complications: Dysfunctional adaptive behaviors, social withdrawal or isolation, drug seeking, dependence or side effects, sexual or social dysfunction.

Expected Outcome: Persistent pain, initially met with anger and denial, leading to acceptance and functional adaptations.

MISCELLANEOUS

Other Notes: Whether mood disorder is a predisposing factor to, or a result of, chronic pain is not clear. Pain that first develops prior to menarche is unlikely to have a gynecologic etiology.

ICD-10-CM Codes: R10.2 (Pelvic and perineal pain), G89.29 (Other chronic pain).

REFERENCES

LEVEL I

Ling FW. Randomized controlled trial of depot leuprolide in patients with chronic pelvic pain and clinically suspected endometriosis. Pelvic Pain Study Group. *Obstet Gynecol*. 1999;93:51.

Petta CA, Ferriani RA, Abrao MS, et al. Randomized clinical trial of a levonorgestrel-releasing intrauterine system and a depot GnRH analogue for the treatment of chronic pelvic pain in women with endometriosis. *Hum Reprod*. 2005;20:1993.

Zullo F, Palomba S, Zupi E, et al. Effectiveness of presacral neurectomy in women with severe dysmenorrhea caused by endometriosis who were treated with laparoscopic conservative surgery: a 1-year prospective randomized double-blind controlled trial. *Am J Obstet Gynecol*. 2003; 189:5.

LEVEL II

Clemons JL, Arya A, Myers DL. Diagnosing Interstitial cystitis in women with chronic pelvic pain. *Obstet Gynecol*. 2002;100:337.

Deguara CS, Pepas L, Davis C. Does minimally invasive surgery for endometriosis improve pelvic symptoms and quality of life? *Curr Opin Obstet Gynecol*. 2012;24:241.

Ferrero S, Gillott DJ, Venturini PL, et al. Use of aromatase inhibitors to treat endometriosis-related pain symptoms: a systematic review. *Reprod Biol Endocrinol*. 2011;9:8.

Tirlapur SA, Daniels JP, Khan KS, et al. Chronic pelvic pain: how does noninvasive imaging compare with diagnostic laparoscopy? *Curr Opin Obstet Gynecol*. 2015;27:445.

Tu FF, Fitzgerald CM, Kuiken T, et al. Comparative measurement of pelvic floor pain sensitivity in chronic pelvic pain. *Obstet Gynecol*. 2007; 110:1244.

Vercellini P, Fedele L, Aimi G, et al. Association between endometriosis stage, lesion type, patient characteristics and severity of pelvic pain symptoms: a multivariate analysis of over 1000 patients. *Hum Reprod*. 2007;22:266.

LEVEL III

American College of Obstetricians and Gynecologists. Chronic pelvic pain. ACOG Practice Bulletin No. 51. *Obstet Gynecol*. 2004;103:589.

American College of Obstetricians and Gynecologists. Management of endometriosis. Practice Bulletin No. 113. *Obstet Gynecol*. 2010;116:223.

Cheong YC, Smotra G, Williams AC. Non-surgical interventions for the management of chronic pelvic pain. *Cochrane Database Syst Rev*. 2014; (3):CD008797.

Howard F. Chronic pelvic pain. *Obstet Gynecol*. 2003;101:594.

Howard FM. The role of laparoscopy in chronic pelvic pain: promise and pitfalls. *Obstet Gynecol Surv*. 1993;48:357.

Lamvu G. Role of hysterectomy in the treatment of chronic pelvic pain. *Obstet Gynecol*. 2011;117:1175.

Latthe P, Mignini L, Gray R, et al. Factors predisposing women to chronic pelvic pain: systematic review. *BMJ*. 2006;332:749.

Mathias SD, Kuppermann M, Liberman RF, et al. Chronic pelvic pain: prevalence, health-related quality of life, and economic correlates. *Obstet Gynecol*. 1996;87:321.

Reiter RC, Gambone JC. Demographic and historic variables in women with idiopathic chronic pelvic pain. *Obstet Gynecol*. 1990;75:428.

Steege JF, Siedhoff MT. Chronic pelvic pain. *Obstet Gynecol*. 2014;124:616.

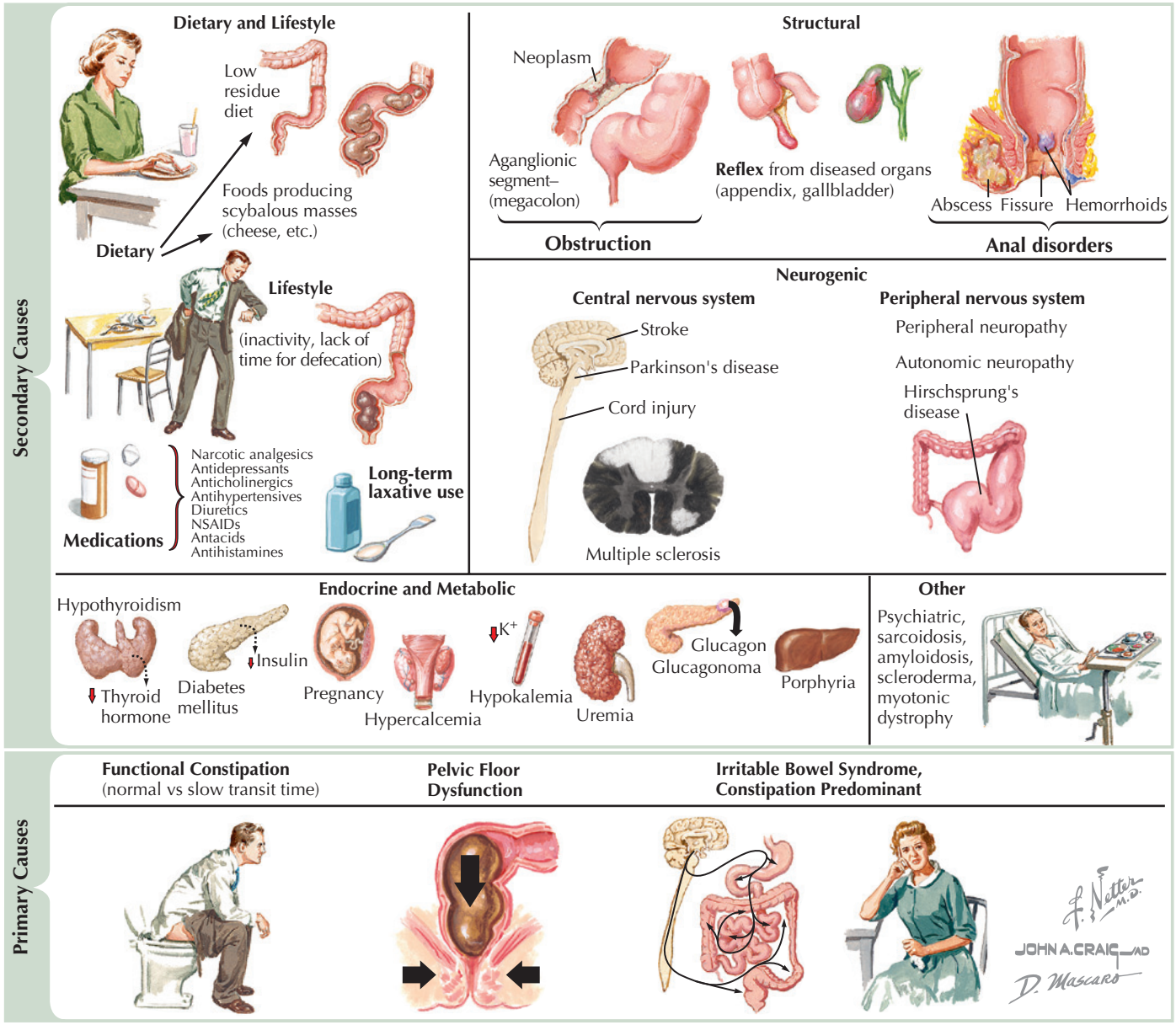


Figure 28.1 Overview of constipation

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Fluids, dietary fiber, fiber supplements, and physical activity.
Specific Measures: Mechanical assistance (enemas), mechanical disimpaction.
Diet: Increased dietary fiber, adequate fluids, and fiber supplements as needed.
Activity: No restriction, activity encouraged.
Patient Education: Reassurance, diet counseling.

Drug(s) of Choice

- Fiber supplements, stool softeners (docusate sodium 100 mg PO two times daily), laxatives (use with caution)

Contraindications: Bowel obstruction, peritonitis
Precautions: Laxative abuse and dependence are common. Patients should be warned about their appropriate use.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: Adequate fiber and fluid, physical activity
Possible Complications: Impaction, fluid or electrolyte imbalance with laxative abuse, possible increase in the risk of colon cancer (proposed, but unproved).
Expected Outcome: Good with adequate diet, fluid, and activity.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, although pregnancy (and associated iron supplementation) may make constipation worse.
ICD-10-CM Codes: K59.00 (Constipation, unspecified).

REFERENCES

LEVEL I

Dipalma JA, Cleveland MV, McGowan J, et al. A randomized, multicenter, placebo-controlled trial of polyethylene glycol laxative for chronic treatment of chronic constipation. *Am J Gastroenterol*. 2007;102:1436.

Dupont C, Campagne A, Constant F. Efficacy and safety of a magnesium sulfate-rich natural mineral water for patients with functional constipation. *Clin Gastroenterol Hepatol*. 2014;12:1280.

LEVEL III

American College of Obstetricians and Gynecologists. *Lower Gastrointestinal Tract Disorders*. Clinical Updates in Women's Health Care, 2015;XIV:1.

Bharucha AE, Pemberton JH, Locke GR 3rd. American Gastroenterological Association technical review on constipation. *Gastroenterology*. 2013;144:218.

Frizelle F, Barclay M. Constipation in adults. *Clin Evid*. 2005;14:557.

Lacy BE, Weiser K. Gastrointestinal motility disorders: an update. *Dig Dis*. 2006;24:228.

Leung FW. Etiologic factors of chronic constipation: review of the scientific evidence. *Dig Dis Sci*. 2007;52:313. [Epub 2007 Jan 12].

Longstreth GF, Thompson WG, Chey WD, et al. Functional bowel disorders. *Gastroenterology*. 2006;130:1480.

Thoua N, Emmanuel A. Treating functional lower gastrointestinal symptoms. *Clin Med*. 2006;6:449.

Wald A. Constipation in the primary care setting: current concepts and misconceptions. *Am J Med*. 2006;119:736.

Wald A. Chronic constipation: advances in management. *Neurogastroenterol Motil*. 2007;19:4.

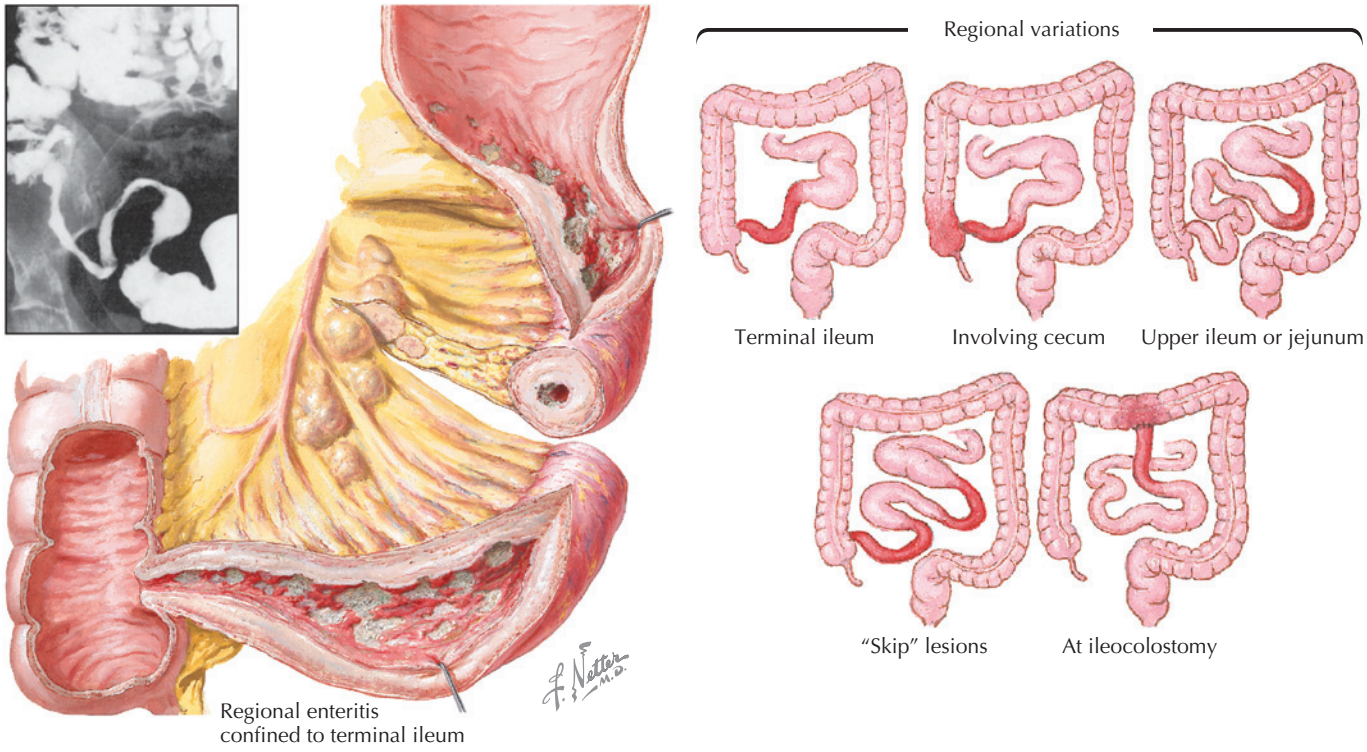


Figure 29.1 Crohn disease

Diet: No specific dietary changes indicated; increased dietary fiber sometimes recommended.
Activity: No restriction.

Drug(s) of Choice

- Mesalamine (5-aminosalicylic acid), methotrexate, or azathioprine (Imuran) for maintenance and suppression.
- Prednisone (20–40 mg PO daily, tapered after 4–6 weeks) or sulfasalazine or mesalamine at increased doses for acute exacerbations. Other immunosuppressives (6-mercaptopurine, azathioprine, infliximab [Remicade]) may also be used. Biologic therapies (e.g., infliximab, adalimumab) are gaining in use for refractory patients.
- For acute management, antibiotics, antidiarrheals, and fluid replacements may be needed.

Precautions: Folic acid supplements should be used with mesalamine.

FOLLOW-UP

Patient Monitoring: Weight and symptoms, periodic blood count, and sedimentation rate. Endoscopy to monitor disease (as needed)
Prevention/Avoidance: None.
Possible Complications: Bowel thickening, stenosis, and internal fistula formation are common. Short bowel syndromes and malabsorption are common after repeated surgery. One study found a 2.5-fold increase in the risk of colon cancer in patients with Crohn disease.
Expected Outcome: Need for eventual or repeated surgery very likely.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: K50.90 (Crohn disease, unspecified, without complications).

REFERENCES

LEVEL II

Chande N, Tsoulis DJ, MacDonald JK. Azathioprine or 6-mercaptopurine for induction of remission in Crohn's disease. *Cochrane Database Syst Rev*. 2013;(4):CD000545.

Ekbom A, Helmick C, Zack M. Increased risk of large-bowel cancer in Crohn's disease with colonic involvement. *Lancet*. 1990;336:357.

Khan KJ, Dubinsky MC, Ford AC, et al. Efficacy of immunosuppressive therapy for inflammatory bowel disease: a systematic review and meta-analysis. *Am J Gastroenterol*. 2011;106:630.

LEVEL III

American College of Obstetricians and Gynecologists. Lower Gastrointestinal Tract Disorders. *Clinical Updates in Women's Health Care*. 2015;XIV(5):1-138.

Kornbluth A, Sachar DB. Practice Parameters Committee of the American College of Gastroenterology: Ulcerative colitis practice guidelines in adults (update): American College of Gastroenterology, Practice Parameters Committee. *Am J Gastroenterol*. 2004;99:1371.

Podolsky DK. Inflammatory bowel disease. *N Engl J Med*. 2002;347:417.

30 DEPRESSION (UNIPOLAR)

INTRODUCTION

Description: Depression is a biochemically mediated state in which anger, frustration, loss of pleasure, and withdrawal predominate. This must be separated from normal stress reactions and grief. The term may be used to describe a mood state, syndrome, or mental disorder.

Prevalence: Twenty million American adults per year; one in six to eight lifetime risk; 6%–14% of primary care visits; 2:1 female to male ratio (1:1 after the age of 55 years) Depression is the fourth most common reason to seek medical care, yet may be missed in more than 50% of cases.

Predominant Age: Rare before puberty. Commonly begins in 20s–30s; average 40 years.

Genetics: Possible defect on chromosome 11 or X.

ETIOLOGY AND PATHOGENESIS

Causes: Proposed—alteration in norepinephrine or serotonin through impaired synthesis of neurotransmitters, increased breakdown or metabolism of neurotransmitters, increased uptake of neurotransmitters.

Risk Factors: Strong family history (depression, suicide, alcoholism, substance abuse). Women are at greatest risk during adolescence (up to 60% meet the criteria), the premenstrual period, pregnancy, the postpartum period, perimenopause, after pregnancy loss (three times increased risk), and with infertility (two times increased risk). Women are especially vulnerable to depression after giving birth.

SIGNS AND SYMPTOMS

- Depressed mood or anhedonia plus five or more other symptoms over a 2-week period:
  - Weight loss
  - Sleep changes
  - Psychomotor changes
  - Fatigue
  - Feeling of worthlessness or guilt
  - Inability to concentrate
  - Thoughts of death

  (Hallucinations and delusions may appear in profound cases.)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Endocrine disorders (diabetes, pituitary, adrenal, thyroid)
- Malignancies
- Infections
- Neurologic disorders (organic brain disease)
- Autoimmune disease
- Cardiovascular, hepatic, or renal disease
- Vitamin or mineral deficiency or excess
- Medication side effect (cardiovascular drugs, hormones, anticancer agents, antiinflammatory or antiinfective agents, amphetamines [withdrawal], L-dopa, cimetidine, ranitidine]

Associated Conditions: Chronic pain, sexual dysfunction, weight changes (up or down), bipolar disorders (manic depression), schizophrenia, and substance abuse

Workup and Evaluation

Laboratory: No evaluation indicated (clinical diagnosis only). Urine toxicology screen for drugs of abuse (when suspected).

Imaging: No imaging indicated unless organic brain syndrome is being considered.

Special Tests: Zung's Self-Rating Depression Scale, Beck's Depression Inventory, Criteria for Epidemiologic Studies Depression Scale, Children's Depression Inventory, or similar tests.

Diagnostic Procedures: Complete evaluation to rule out organic cause. Depression scales are helpful but are not required.

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, support, and evaluation of support systems available to the patient.

Specific Measures: Psychotherapy (patients with mild depression without psychosis), medical therapy (choose agent to optimize benefit, decrease risk, and avoid drug interactions), electroshock therapy in patients with refractory conditions (controversial).

Diet: No specific dietary changes indicated.

Activity: No restriction.

Patient Education: Reassurance, careful instruction on medication use. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP057 (Premenstrual Syndrome), AP091 (Postpartum Depression), AP106 (Depression).

Drug(s) of Choice

- Tricyclic agents—amitriptyline 50–300 mg/day; doxepin 5–300 mg/day; imipramine 50–300 mg/day; nortriptyline 50–200 mg/day.
- Monoamine oxidase inhibitors (MAOIs).
- Selective serotonin reuptake inhibitors (SSRIs)—fluoxetine 10–80 mg/day; fluvoxamine 100–300 mg/day; paroxetine 10–50 mg/day; sertraline 50–200 mg/day.
- Serotonin norepinephrine reuptake inhibitors (SNRIs)—venlafaxine 75–375 mg/day.
- Noradrenergic and specific serotonergic agents—mirtazapine 15–45 mg/day.
- Miscellaneous agents—nefazodone 200–600 mg/day; trazodone 150–400 mg/day; bupropion 300–400 mg/day.

Contraindications: See individual agents. Most agents are pregnancy category B. Many are contraindicated in patients with seizure disorders or cardiac arrhythmias (tricyclic agents).

Precautions: MAOIs are associated with both treatment and adverse reactions that appear as emergencies. Overdoses may be lethal. SSRIs are associated with nausea (20%–35%) and sexual dysfunction (10%–30%). Some agents can alter the dose or effectiveness of other drugs such as antihypertensive agents, digoxin, and antiseizure medications. Fluoxetine, sertraline, and paroxetine are best given in the morning.

Interactions: MAOIs and SSRIs or SNRIs may have lethal interactions and must not be used together. (Allow at least 2 weeks to elapse between therapies.) Avoid use of nonprescription drugs with pseudoephedrine, phenylephrine, or phenylpropanolamine.

Alternative Drugs

- Additional tricyclic agents include clomipramine 100–250 mg/day, desipramine 50–300 mg/day, protriptyline 14–60 mg/day, and trimipramine 75–300 mg/day.
- A large study conducted by the National Center for Complementary and Alternative Medicine has found that St. John's wort is

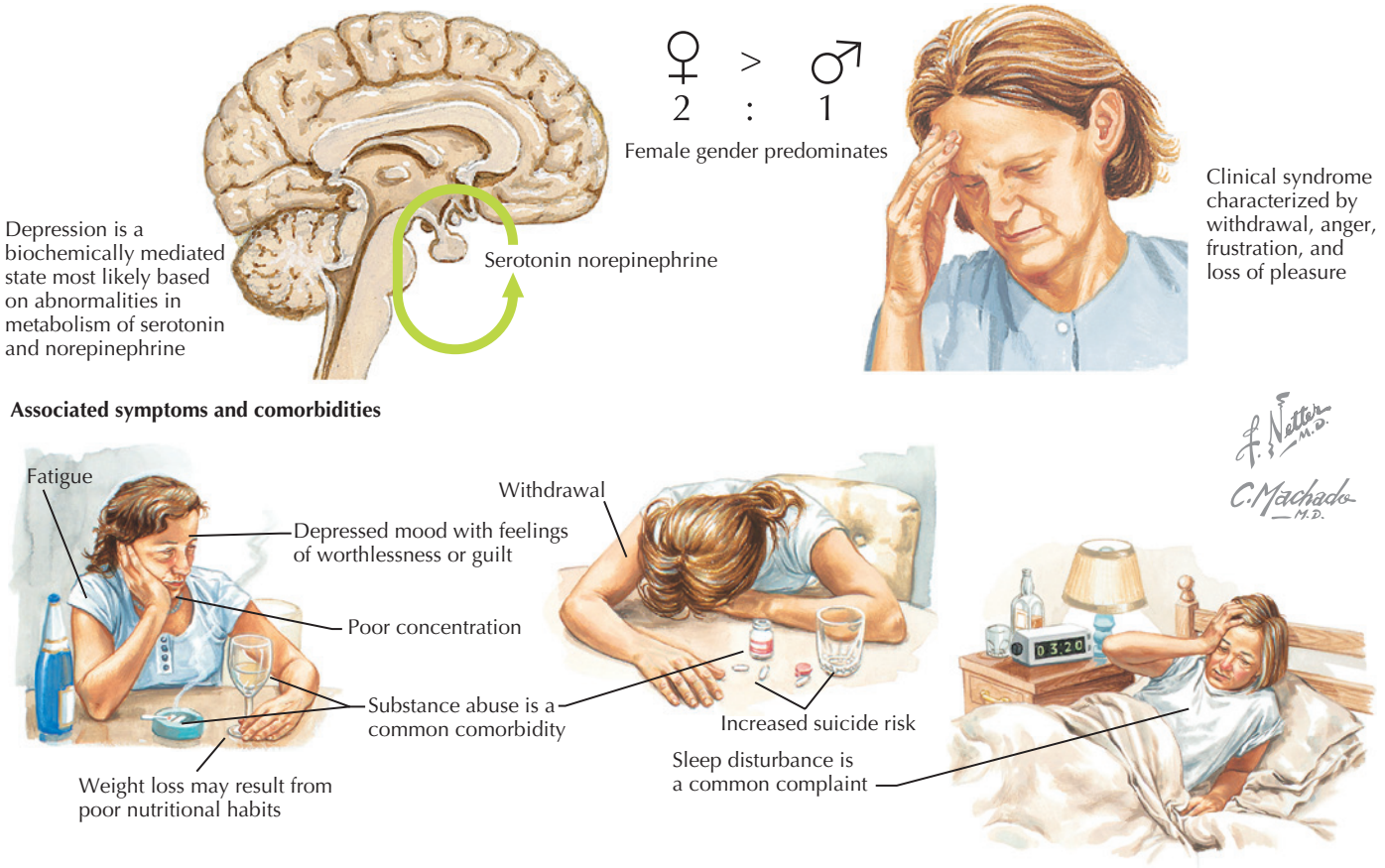


Figure 30.1 Depression

not effective for treating major depressive disorder Similarly, omega-3 fatty acids have not been demonstrated to be effective.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. Monitor for recurrence, substance abuse, or suicide. Patients must be monitored every 1–2 weeks after they start medication and reassessed at 6 weeks. Follow-up of treatment should continue every 3 months while therapy is maintained (6 months to 2 years). Initial treatment with a single antidepressant leads to remission in only 30%–50% of patients.

Prevention/Avoidance: None.

Possible Complications: Increased risk of general medical disorders and worsened prognosis, disability, impaired function (family, work, social, sexual), chronic pain, mortality (30,000 suicides per year in United States; adolescent girls are at the greatest risk).

Expected Outcome: Medical therapy is associated with 85%–90% success rates.

MISCELLANEOUS

Pregnancy Considerations: Up to 70% of pregnant patients have depressive symptoms and 10%–15% meet the diagnostic criteria for major depressive disorder during pregnancy. Symptoms often mimic those of pregnancy itself. Depression may result in poor nutrition, increased substance abuse, and poor fetal outcome. Drug therapy should be avoided or used sparingly in pregnancy unless benefits outweigh the risks. Postpartum depression is seen by many as a special form of depression.

ICD-10-CM Codes: F32.9 (Major depressive disorder, single episode, unspecified), N94.3 (Premenstrual tension syndrome).

REFERENCES

LEVEL II

Appleton KM, Sallis HM, Perry R, et al. Omega-3 fatty acids for depression in adults. *Cochrane Database Syst Rev*. 2015;(11):CD004692.

Fava GA, Ruini C, Belaise C. The concept of recovery in major depression. *Psychol Med*. 2007;37:307.

Lassen D, Ennis ZN, Damkier P. First-trimester pregnancy exposure to venlafaxine or duloxetine and risk of major congenital malformations: a systematic review. *Basic Clin Pharmacol Toxicol*. 2015.

Thachil AF, Mohan R, Bhugra D. The evidence base of complementary and alternative therapies in depression. *J Affect Disord*. 2007;97:23. [Epub 2006 Aug 22].

Thase ME, Haight BR, Richard N, et al. Remission rates following antidepressant therapy with bupropion or selective serotonin reuptake inhibitors: a meta-analysis of original data from 7 randomized controlled trials. *J Clin Psychiatry*. 2005;66:974.

LEVEL III

American College of Obstetricians and Gynecologists. Screening for perinatal depression. Committee Opinion No. 630. *Obstet Gynecol*. 2015;125:1268.

American College of Obstetricians and Gynecologists. Use of psychiatric medications during pregnancy and lactation. ACOG Practice Bulletin No. 92. *Obstet Gynecol*. 2008;111:1001.

Beck A. *Depression Inventory*. Philadelphia: Center for Cognitive Therapy; 1991.

Fancher T, Kravitz R. In the clinic. Depression. *Ann Intern Med*. 2007; 146:ITC5-1.

Norman TR, Burrows GD. Emerging treatments for major depression. *Expert Rev Neurother*. 2007;7:203.

31 DIVERTICULAR DISEASE

INTRODUCTION

Description: Diverticular disease involves the herniation of the colon mucosa through the muscular wall. These herniations are most common in the sigmoid and distal colon, increase in prevalence with age, and can lead to significant morbidity when rupture or abscess formation occurs. Diverticulosis is the presence of these herniations, whereas diverticulitis is the symptomatic state.
Prevalence: Twenty percent of patients, increasing with age to 40%–50% by the age of 60–80 years.
Predominant Age: Rare in patients younger than 40 years; most common in patients older than 50 years.
Genetics: Recent studies suggest a genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Speculative, not clearly established. Proposed—defect in colon motility with increased intraluminal pressure, exacerbated by a low-fiber diet or an intrinsic defect in the colon wall.
Risk Factors: Low-fiber diet, age older than 40 years, smoking, and previous diverticulitis. Obesity has been associated with an increase in risk of both diverticulitis and diverticular bleeding.

SIGNS AND SYMPTOMS

- Asymptomatic (75%–90%; diverticulosis)
- Left lower quadrant abdominal pain (worse after eating, better after bowel movement or flatus)
- Diarrhea or constipation
- Fever or chills
- Anorexia, nausea, vomiting
- Abdominal distention
- Peritonitis (rebound tenderness, guarding, rigidity, depressed bowel sounds)
- Rectal tenderness or mass on rectal examination

DIAGNOSTIC APPROACH

Differential Diagnosis

- Irritable bowel syndrome (IBS)
- Lactose intolerance
- Inflammatory bowel disease (ulcerative colitis, Crohn disease)
- Carcinoma of the colon
- Infectious colitis
- Appendicitis
- Ectopic pregnancy (in reproductive-age women)
- Tubo-ovarian abscess

Associated Conditions: Irritable bowel syndrome.

Workup and Evaluation

Laboratory: Complete blood count, sedimentation rate, urinalysis with culture.
Imaging: Barium enema generally demonstrates diverticulosis. Supine and upright abdominal radiograph may demonstrate free air in the peritoneal cavity if rupture has occurred.
Special Tests: Colonoscopy or flexible sigmoidoscopy.
Diagnostic Procedures: History and physical examination, imaging, or endoscopy.

Pathologic Findings

Herniation of colon mucosa through the muscularis, usually at the site of a perforating artery lying between two layers of serosa in the mesentery. Increased thickness of the muscular wall and narrowing of the gut lumen. With inflammation, necrosis and perforation occur.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: For diverticulosis—increased dietary fiber, stool softeners. Fiber supplements may be considered. For diverticulitis—evaluation, possible hospitalization (2%–5% of patients).
Specific Measures: Patients with diverticulitis may become acutely ill with sepsis, toxicity, and peritonitis. These patients require hospitalization, fluid support, and aggressive antibiotic treatment. Surgical resection may be considered in patients with multiple attacks, fistulae, or abscesses that do not respond to medical therapy.
Diet: Increased dietary fiber is desirable both as a preventive measure and to decrease the risk of complications in established disease. Patients who are acutely ill should receive nothing by mouth.
Activity: No restriction. Activity is encouraged to foster normal bowel function.
Patient Education: Reassurance, counseling regarding diet and the need for periodic flexible sigmoidoscopy or colonoscopy screening American College of Obstetricians and Gynecologists Patient Education Pamphlet AP130 (Healthy Eating), AP120 (Problems of the Digestive System).

Drug(s) of Choice

- Antispasmodics and adjuncts—hyoscyamine (Levsin) 0.125 mg PO one to two every 4 hours for 12/24 hours); buspirone (BuSpar) 15–30 mg PO daily.
- Antibiotics (ambulatory)—ciprofloxacin (500 mg orally twice daily) plus metronidazole (500 mg orally three times daily); amoxicillin-clavulanate (875/125 mg twice daily) is an acceptable alternative.
- Symptomatic control of diarrhea or constipation as needed.

Contraindications: See individual agents. Contraindications to flexible sigmoidoscopy: absolute—active diverticulitis, acute abdomen, blood dyscrasia, or coagulopathy, cardiopulmonary disease (acute or severe), inadequate bowel preparation, subacute bacterial endocarditis or prosthetic heart valve without adequate antibiotic prophylaxis, suspected bowel perforation; relative—active infection, peritonitis, pregnancy, recent abdominal surgery.
Precautions: If narcotic pain relievers are needed, meperidine (Demerol) is preferred; others should be avoided because they cause changes in bowel motility. Aminoglycosides may be associated with renal toxicity.
Interactions: See individual agents.

Alternative Drugs

Tobramycin may be used in combination with metronidazole.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. Monitor for development of symptoms; perform routine flexible sigmoidoscopy and fecal occult blood screening.
Prevention/Avoidance: High-fiber diet and good bowel habits.
Possible Complications: Diverticulitis develops in 5% of patients with diverticulosis each year; lifetime risk is 50%. Enterocutaneous, enterovaginal, and perirectal fistulae may occur. Acutely,

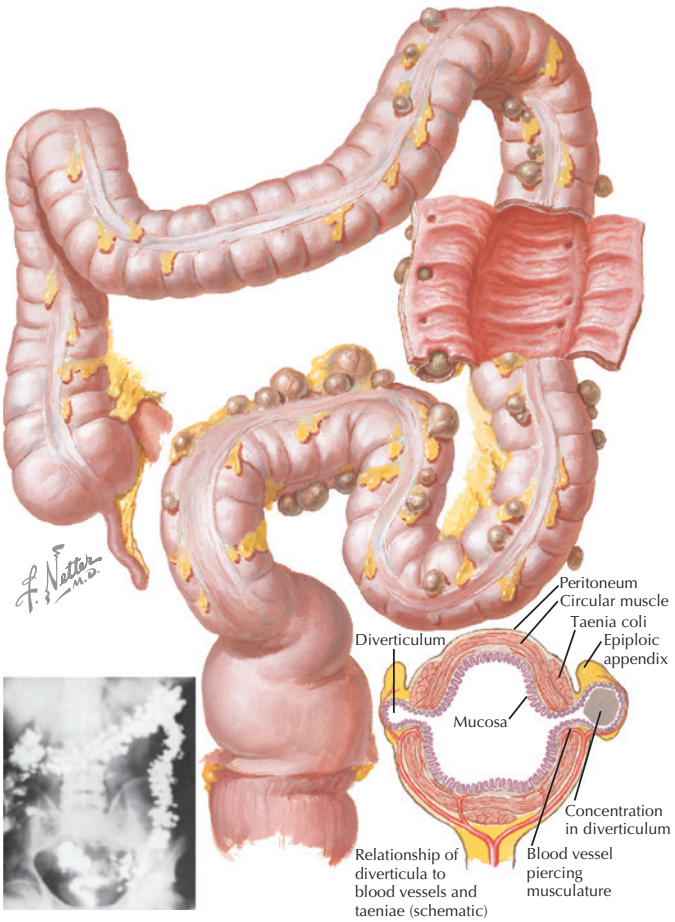


Figure 31.1 Diverticular disease

hemorrhage, perforation, abscess formation, peritonitis (with toxicity and collapse), and bowel obstruction may occur.

Expected Outcome: With early detection and dietary change, the prognosis is good. With aggressive management of the first episode of diverticulitis, two thirds of patients do not have a recurrence. Up to 20% of those with rectal bleeding caused by diverticular disease have a recurrence of bleeding.

MISCELLANEOUS

Pregnancy Considerations: No direct effect on pregnancy; uncommon in reproductive-age women.

ICD-10-CM Codes: K57.30 (Diverticulosis of large intestine without perforation or abscess without bleeding), K57.32 (Diverticulitis of large intestine without perforation or abscess without bleeding).

REFERENCES

LEVEL II

Cirocchi R, Arezzo A, Renzi C, et al. Is laparoscopic surgery the best treatment in fistulas complicating diverticular disease of the sigmoid colon? A systematic review. *Int J Surg*. 2015;24(Pt A):95.

Kaushik M, Bhullar JS, Bindroo S, et al. Minimally invasive management of complicated diverticular disease: current status and review of literature. *Dig Dis Sci*. 2016;61(3):663-72.

Purkayastha S, Constantinides VA, Tekkis PP, et al. Laparoscopic vs. open surgery for diverticular disease: a meta-analysis of nonrandomized studies. *Dis Colon Rectum*. 2006;49:446.

Zarling EJ, Bernsen MB. The effect of gender on the rates of hospitalization for gastrointestinal illnesses. *Am J Gastroenterol*. 1997;92:621.

LEVEL III

American College of Obstetricians and Gynecologists. Lower Gastrointestinal Tract Disorders. *Clinical Updates in Women's Health Care*. 2015;XIV(5):1-138.

Bugiantella W, Rondelli F, Longaroni M, et al. Left colon acute diverticulitis: an update on diagnosis, treatment and prevention. *Int J Surg*. 2015;13:157.

Di Mario F, Comparato G, Fanigliulo L, et al. Use of mesalazine in diverticular disease. *J Clin Gastroenterol*. 2006;40(7 suppl 3):S155.

D'Souza AL. Ageing and the gut. *Postgrad Med J*. 2007;83:44.

Frattini J, Longo WE. Diagnosis and treatment of chronic and recurrent diverticulitis. *J Clin Gastroenterol*. 2006;40(7 suppl 3):S145.

Frieri G, Pimpo MT, Scarpignato C. Management of colonic diverticular disease. *Digestion*. 2006;73(suppl 1):58. [Epub 2006 Feb 8].

Korzenik JR. Case closed? Diverticulitis: epidemiology and fiber. *J Clin Gastroenterol*. 2006;40(7 suppl 3):S112.

Lundy JB, Edwards KD, Parker DM, et al. Recurrent rectal diverticulitis. *Am Surg*. 2006;72:633.

Mosadeghi S, Bhuket T, Stollman N. Diverticular disease: evolving concepts in classification, presentation, and management. *Curr Opin Gastroenterol*. 2015;31:50.

Reichert MC, Lammert F. The genetic epidemiology of diverticulosis and diverticular disease: Emerging evidence. *United European Gastroenterol J*. 2015;3:409.

Sheth AA, Longo W, Floch MH. Diverticular disease and diverticulitis. *Am J Gastroenterol*. 2008;103:1550.

Templeton AW, Strate LL. Updates in diverticular disease. *Curr Gastroenterol Rep*. 2013;15:339.

Tursi A. The role of colonoscopy in managing diverticular disease of the colon. *J Gastrointestin Liver Dis*. 2015;24:85.

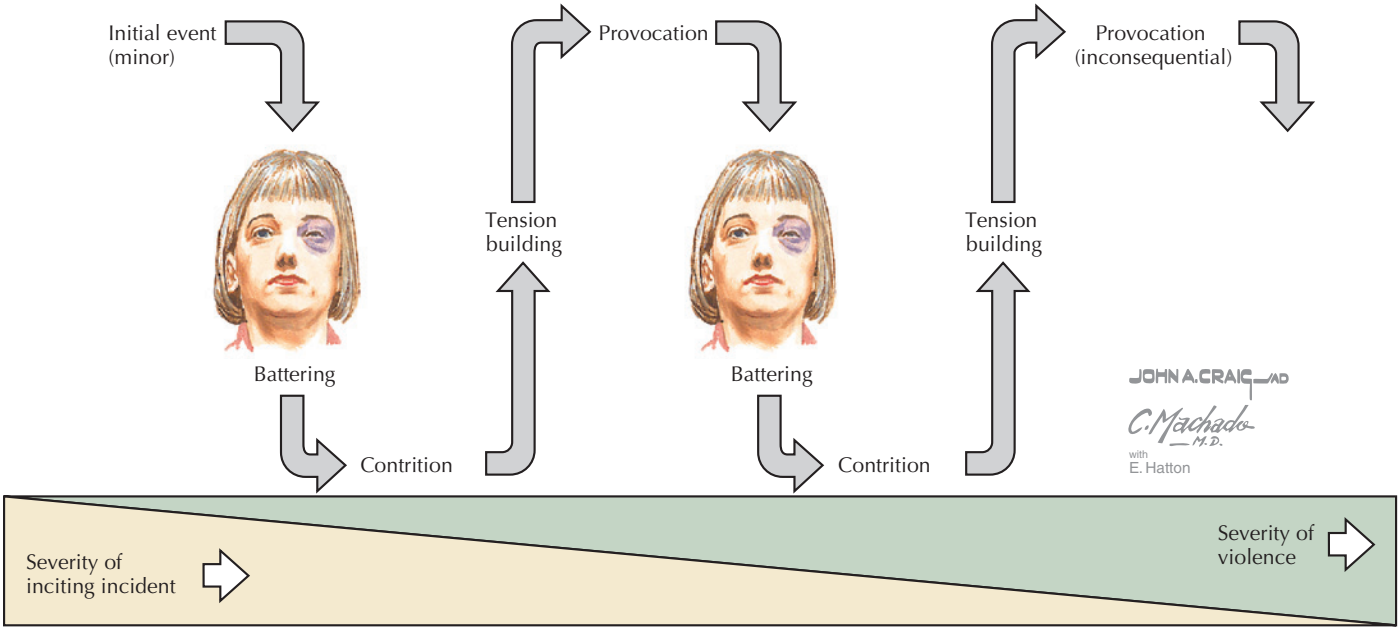
DOMESTIC VIOLENCE

32

INTRODUCTION

Description: Domestic violence (domestic abuse) is a pattern of behavior that involves violence or other abuse by one person against another in a home or family setting. It may include physical, verbal, emotional, economic, and sexual abuse, which can range from subtle, coercive forms, to overt acts (see Chapter 19, Abuse: Physical and Sexual).

Prevalence: More than 32 million Americans. Around the world, 10%–69% of women report physical assault by an intimate partner at some time in their life.



Cycle of abuse is characterized by progressively smaller incidents inciting progressively greater violence interspersed with periods of remorse.

Figure 32.1 Abuse cycle

Predominant Age: Most common during the early reproductive years, though elder abuse constitutes a special case.
Genetics: Male to female ratio is 1:5+. A wife or female partner is more commonly the victim of such violence.

ETIOLOGY AND PATHOGENESIS

Causes: Unknown
Risk Factors: Childhood physical or sexual victimization, prior history of intimate partner violence, alcohol or drug use, lower socioeconomic status, unemployment. Women with an unintended pregnancy have a higher risk (3-fold greater in one study)

SIGNS AND SYMPTOMS

- Direct signs of physical violence, often un- or inconsistently explained
- Delay in seeking treatment
- Frequent emergency room visits
- Vague somatic complaints ("hidden agenda")
- Inappropriate affect/poor eye contact
- Overly attentive or verbally abusive partner
- Social withdrawal
- Anxiety or depression

DIAGNOSTIC APPROACH

Differential Diagnosis

- Mood disorders (anxiety or depression independent of abuse)
- Poor health literacy
- Somatization

Associated Conditions: High-risk sexual behaviors, poor compliance (medical and contraceptive), substance abuse.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: Based upon injuries sustained only.
Special Tests: Screening for anxiety or depression is often warranted.
Diagnostic Procedures: History and physical examination. Several short questionnaires have been developed to assist screening: HITS (Hurt, Insult, Threaten, Scream), STaT (Slapped, Threatened, and Throw), HARK (Humiliation, Afraid, Rape, Kick), WAST (Woman Abuse Screen Tool), and SAFE (Stress/Safety, Afraid/Abused, Friend/Family, Emergency Plan).

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Support, survivor safety, survivor empowerment, perpetrator accountability. If significant risk factors are present, a safety plan should be implemented (an emergency kit with important documents, keys, money, and other essential items including cash, a place to go, signal to alert children or neighbors to call for help).
Specific Measures: Ensure that the patient has access to resources and escape plans.
Diet: No specific dietary recommendations.
Activity: No restriction, activity encouraged.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP083 (Domestic Violence)

Drug(s) of Choice

Only as needed for sequelae such as anxiety or depression. Analgesics for injuries as needed.
Contraindications: See individual agents.
Precautions: See individual agents.

FOLLOW-UP

Patient Monitoring: Normal health maintenance, frequent screening for abuse.
Prevention/Avoidance: None.

Possible Complications: Escalating violence with increasing frequency and severity of injury or possibility of death (in 2007, domestic violence accounted for 14% of all homicides in the United States). Headache, anxiety, depression, sleep disturbances, social isolation, eating disorders, and low self-esteem.

Expected Outcome: Violence tends to escalate with time unless the victim is removed from the setting.

MISCELLANEOUS

Pregnancy Considerations: Outside of any injuries sustained, no effect on pregnancy. Domestic violence often begins or increases during pregnancy and the postpartum period. Injuries to the abdomen increase during pregnancy.

ICD-10-CM Codes: Z91.410 (Personal history of adult physical and sexual abuse), T74.11 (current adult physical abuse, confirmed), Z91.419 (Personal history of unspecified adult abuse).

REFERENCES

LEVEL I

Kiely M, El-Mohandes AA, El-Khorazaty MN, et al. An integrated intervention to reduce intimate partner violence in pregnancy: a randomized controlled trial. *Obstet Gynecol*. 2010;115:273.

LEVEL II

Goodwin MM, Gazmararian JA, Johnson CH, et al. Pregnancy intendedness and physical abuse around the time of pregnancy: findings from the pregnancy risk assessment monitoring system, 1996-1997. PRAMS Working Group. Pregnancy Risk Assessment Monitoring System. *Matern Child Health J*. 2000;4:85.

Horan DL, Chapin J, Klein L, et al. Domestic Violence Screening Practices of Obstetrician-Gynecologists. *Obstet Gynecol*. 1998;92:785.

Jahanfar S, Howard LM, Medley N. Interventions for preventing or reducing domestic violence against pregnant women. *Cochrane Database Syst Rev*. 2014;(11):CD009414.

O'Doherty L, Hegarty K, Ramsay J, et al. Screening women for intimate partner violence in healthcare settings. *Cochrane Database Syst Rev*. 2015;(7):CD007007.

Rivas C, Ramsay J, Sadowski L, et al. Advocacy interventions to reduce or eliminate violence and promote the physical and psychosocial well-being of women who experience intimate partner abuse. *Cochrane Database Syst Rev*. 2015;(12):CD005043.

Taft A, O'Doherty L, Hegarty K, et al. Screening women for intimate partner violence in healthcare settings. *Cochrane Database Syst Rev*. 2013;(4):CD007007.

LEVEL III

American College of Obstetricians and Gynecologists. *Addressing Intimate Partner Violence, Reproductive and Sexual Coercion: A guide for Obstetric, Gynecologic and Reproductive Health Care Settings*, 2nd Edition. Available at: <http://www.acog.org/-/media/Departments/Violence-Against-Women/Reproguidelines.pdf?dmc=1&ts=20151206T0918553777>; Accessed 15.12.15.

American College of Obstetricians and Gynecologists. Elder abuse and women's health. Committee Opinion No. 568. *Obstet Gynecol*. 2013;122:187.

American College of Obstetricians and Gynecologists. Intimate partner violence. Committee Opinion No. 518. *Obstet Gynecol*. 2012;119:412.

American College of Obstetricians and Gynecologists. Reproductive and sexual coercion. Committee Opinion No. 554. *Obstet Gynecol*. 2013;121:411.

Ashur ML. Asking about domestic violence: SAFE questions. *JAMA*. 1993;269:2367.

McFarlane J, Parker B, Soeken K, et al. Assessing for abuse during pregnancy. Severity and frequency of injuries and associated entry into prenatal care. *JAMA*. 1992;267:3176.

Nelson HD, Bougatsos C, Blazina I. Screening women for intimate partner violence: a systematic review to update the U.S. Preventive Services Task Force recommendation. *Ann Intern Med*. 2012;156:796.

Sherin KM, Sinacore JM, Li XQ, et al. HITS: a short domestic violence screening tool for use in a family practice setting. *Fam Med*. 1998;30:508.

Sugg N. Intimate partner violence: prevalence, health consequences, and intervention. *Med Clin North Am*. 2015;99:629.

Tjaden P, Thoennes N. *Extent, nature, and consequences of intimate partner violence: findings from the National Violence Against Women Survey. Publication No. NCJ-181867*. Washington, DC: US Department of Justice; 2000.

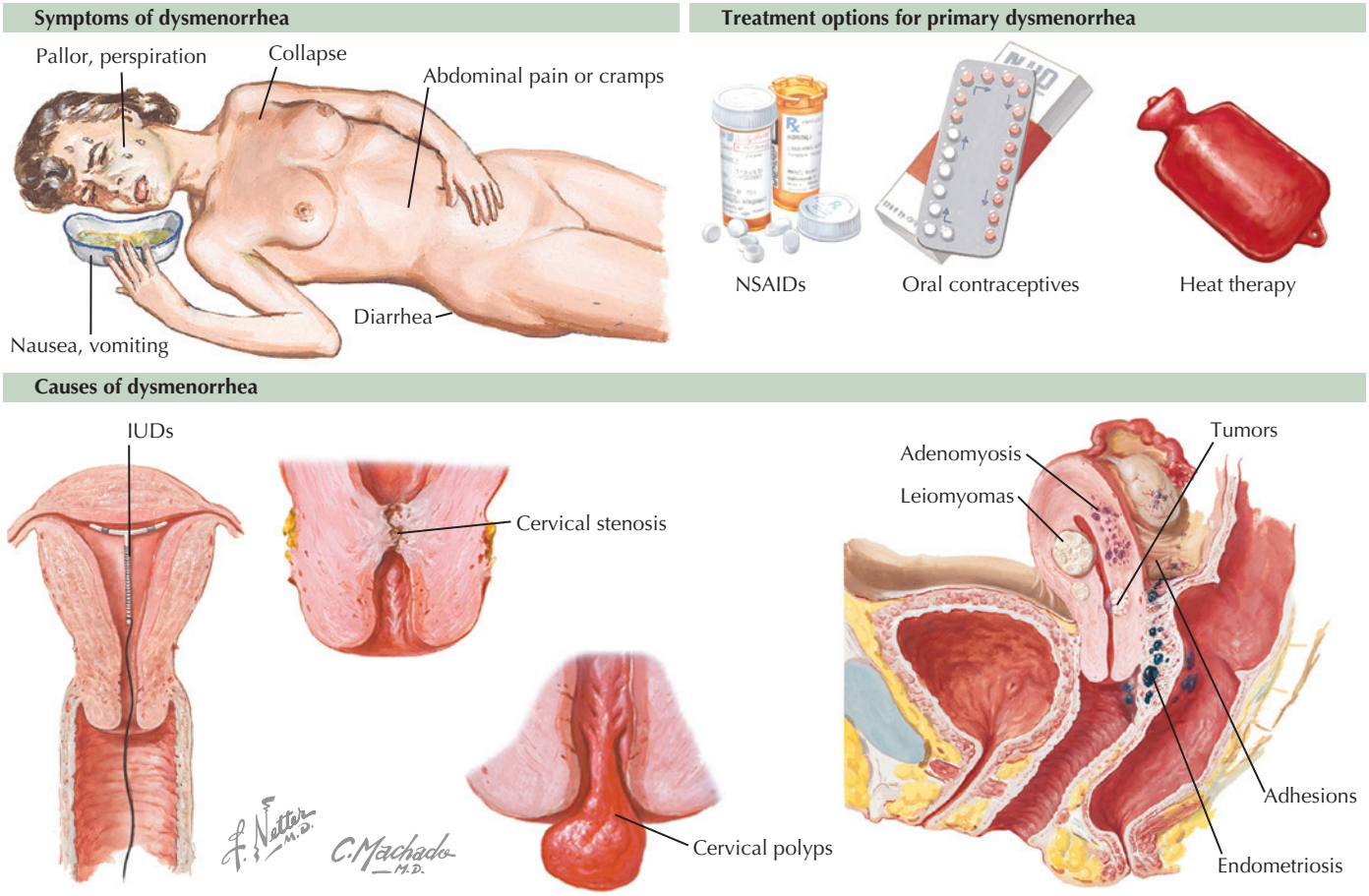


Figure 33.1 Symptoms and possible causes of dysmenorrhea

Risk Factors: None known.

SIGNS AND SYMPTOMS

- Primary—crampy, midline, lower abdominal pain (often demonstrated by a fist opening and closing)
- Nausea, vomiting, and diarrhea are common.
- Syncope
- Headache
- Secondary—midline lower abdominal or low back pain accompanying menstruation
- Pelvic heaviness or pressure
- Symptoms specifically associated with the underlying condition

DIAGNOSTIC APPROACH

Differential Diagnosis

- Endometriosis
- Irritable bowel syndrome
- Inflammatory bowel disease
- Somatization (rare)
- Abrupt onset of painful menstruation should suggest the possibility of a complication of pregnancy (abortion or ectopic pregnancy).

Associated Conditions: Menorrhagia is commonly associated.

Workup and Evaluation

Laboratory: Infrequently required, based on suspected or confirmed cause.

Imaging: For selected patients with secondary dysmenorrhea, ultrasonography of the pelvic organs may be indicated.

Special Tests: None indicated. Sigmoidoscopy may be helpful in selected patients with secondary dysmenorrhea.

Diagnostic Procedures: The absence of abnormality on pelvic examination, combined with historical characteristics, is diagnostic of primary dysmenorrhea. A pelvic examination that reveals a possible cause defines secondary dysmenorrhea.

Pathologic Findings

Based on the causative condition.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Rest, analgesics (nonsteroidal antiinflammatory agents or pain relievers), heat (heating pad, hot water bottle, self-heating pads [ThermaCare]).

Specific Measures: Primary—medical management most effective; heat (heating pad, hot water bottle, or self-heating pads (ThermaCare]) appears comparable to medical management for many; transcutaneous electrical nerve stimulation (TENS) is effective for selected patients; biofeedback has been suggested, but success has been poor or variable. Secondary—measures directed toward the underlying pathologic condition; modification of periods (oral contraceptives, menstrual suppression [depot medroxyprogesterone acetate, gonadotropic-releasing hormone, or GnRH, agonists]); surgery for specific pathologic conditions.

Diet: No specific dietary changes indicated.

Activity: No restriction; based on patient comfort.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP046 (Dysmenorrhea: Painful Periods), AP049 (Your First Period [Especially for Teens]), and others related to underlying causes: AP013 (Endometriosis), AP074 (Uterine Fibroids), AP077 (Pelvic Inflammatory Disease), and AP099 (Chronic Pelvic Pain).

Drug(s) of Choice

- Primary—nonsteroidal antiinflammatory drugs (NSAIDs): ibuprofen 800 mg, two at onset of flow and one every 4–6 hours prn pain; naproxen sodium 275 mg, two at onset of flow and one every 6–8 hours prn pain; meclofenamate 100 mg, one at onset of flow and one every 4–6 hours prn pain, mefenamic acid 250 mg, two at onset of flow and one every 4–6 hours prn pain.
- Secondary—based on pathophysiologic condition. NSAIDs or analgesics may be used.

Contraindications: Aspirin-sensitive asthma, ulcers, inflammatory bowel disease.

Precautions: Some patients experience increased stomach upset with NSAIDs, but this may be reduced by taking them with food.

Interactions: Other over-the-counter pain relievers containing NSAID compounds.

Alternative Drugs

Other rapidly acting NSAIDs may be used. Combination oral contraceptives generally provide milder periods (and contraception if necessary). Centrally acting analgesics may be added with care to avoid interaction with NSAIDs. Suppression of menstruation (depot medroxyprogesterone acetate, GnRH agonists) may be indicated for patients with severe pain. Levonorgesterol-containing intrauterine contraceptive devices generally provide lighter or absent menses.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.

Prevention/Avoidance: None.

Possible Complications: Most commonly side effects of medication. Anemia (if menorrhagia is present), others based on underlying cause.

Expected Outcome: Primary dysmenorrhea—significant relief of symptoms with medical therapy. If medical therapy does not produce pronounced improvement, the diagnosis should be reevaluated. The prevalence of primary dysmenorrhea declines with time. Secondary dysmenorrhea—based on cause and mode of therapy, resolution of symptoms is generally possible with NSAIDs, analgesics, or period modification.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.

ICD-10-CM Codes: N94.6 (Dysmenorrhea, unspecified), (others based on underlying cause).

REFERENCES

LEVEL I

Akin MD, Weingand KW, Hengehold DA, et al. Use of continuous low-level topical heat in the treatment of dysmenorrhea. *Obstet Gynecol*. 2001;97:343.

Sriprasert I, Suerungruang S, Athilarp P, et al. Efficacy of acupuncture versus combined oral contraceptive pill in treatment of moderate-to-severe dysmenorrhea: a randomized controlled trial. *Evid Based Complement Alternat Med*. 2015;2015:735690.

LEVEL III

American College of Obstetricians and Gynecologists. Noncontraceptive uses of hormonal contraceptives. Practice Bulletin No. 110. *Obstet Gynecol*. 2010;115:206.

Dawood MY. Primary dysmenorrhea: advances in pathogenesis and management. *Obstet Gynecol*. 2006;108:428.

Doty E, Attaran M. Managing primary dysmenorrhea. *J Pediatr Adolesc Gynecol*. 2006;19:341.

Harel Z. Dysmenorrhea in adolescents and young adults: etiology and management. *J Pediatr Adolesc Gynecol*. 2006;19:363.

Proctor M, Farquhar C. Diagnosis and management of dysmenorrhoea. *BMJ*. 2006;332:1134.

Proctor ML, Farquhar CM. Dysmenorrhoea. *Clin Evid*. 2006;15:2429.

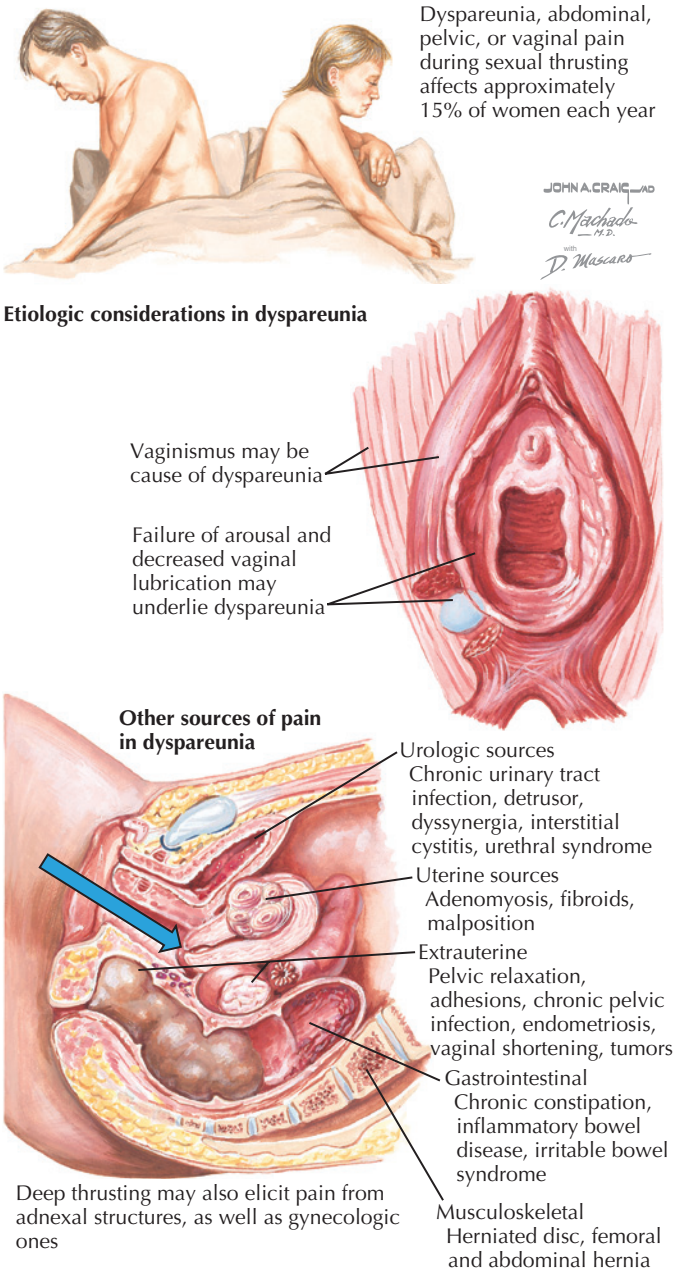


Figure 34.1 Etiologic considerations and others source of pain in dyspareunia

in origin. Most often a mixture of factors causes or contributes to the problem.

Risk Factors: Positions or practices that result in particularly deep or forceful penetration, such as male superior or rear-entry positions. Prior surgery, particularly following mesh placement for pelvic organ prolapse, or cosmetic procedures such as "vaginal rejuvenation."

SIGNS AND SYMPTOMS

Ache-like pain, crampy visceral pain, burning, a sense of fullness, or a feeling as if something is being bumped during deep sexual thrusting. Occasionally, the pain is sharp and abrupt in character. Pain often depends on the type of sexual activity involved or the positions used.

DIAGNOSTIC APPROACH

Differential Diagnosis

- Vulvitis
- Vestibulitis
- Vaginitis
- Bartholin gland infection, abscess, cyst
- Atrophic change
- Anxiety, depression, phobia
- Sexual or other abuse
- Pelvic mass (uterine leiomyomata, ovarian cyst)
- Shortening of the vagina after surgery or radiation

Associated Conditions: Vaginismus, orgasmic dysfunction.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated, pelvic (abdominal or transvaginal) ultrasonography for specific indications.
Special Tests: None indicated.
Diagnostic Procedures: History (general and sexual) and careful pelvic examination. (If discomfort is produced, it is important to be sure that the sensation matches that experienced during intercourse.)

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, reassurance, relaxation measures.
Specific Measures: Because dyspareunia is ultimately a symptom, the specific therapy for any form of sexual pain is focused on the underlying cause. Vaginal lubricants (water-soluble or long-acting agents such as Astroglide, Replens, Lubrin, and K-Y Jelly), local anesthetics (for vulvar lesions), or pelvic relaxation exercises may be appropriate while more specific therapy is under way.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance, relaxation training, alternate sexual positions and forms of expression. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP020 (When Sex is Painful), AP042 (You and Your Sexuality [Especially for Teens]).

Drug(s) of Choice

The judicious use of anxiolytics or antidepressant medications for selected patients may be appropriate but for short periods of time only.

ALTERNATIVE THERAPIES

Modifying sexual techniques used by the couple may reduce pain with intercourse. Delaying penetration until maximal arousal has been achieved improves vaginal lubrication, ensures vaginal apex expansion, and provides an element of control for the female partner. Sexual positions that allow women to control the direction and depth of penetration (such as woman astride) may also be helpful.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. Watch for signs of abuse, anxiety, or depression.
Prevention/Avoidance: None.
Possible Complications: Marital discord, orgasmic or libidinal dysfunction.

Expected Outcome: With diagnosis and treatment of the underlying cause, response should be good.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. Occasionally, the coital changes necessitated by the growing uterus may result in new-onset dyspareunia. Positional changes (as noted earlier) are generally sufficient to relieve these cases.

ICD-10-CM Codes: N94.1 (Dyspareunia).

REFERENCES

LEVEL III

American College of Obstetricians and Gynecologists. Adult manifestations of childhood sexual abuse. Committee Opinion No. 498. *Obstet Gynecol*. 2011;118:392.

American College of Obstetricians and Gynecologists. *Vulvodynia. ACOG Committee Opinion 345*. Washington, DC: ACOG; 2006.

American College of Obstetricians and Gynecologists. Vaginal placement of synthetic mesh for pelvic organ prolapse. Committee Opinion No. 513. *Obstet Gynecol*. 2011;118:1459.

American College of Obstetricians and Gynecologists. Vaginal "rejuvenation" and cosmetic vaginal procedures. ACOG Committee Opinion No. 378. *Obstet Gynecol*. 2007;110:737.

Fauconnier A, Chapron C. Endometriosis and pelvic pain: epidemiological evidence of the relationship and implications. *Hum Reprod Update*. 2005;11:595. [Epub 2005 Sep 19].

Fordney DS. Dyspareunia and vaginismus. *Clin Obstet Gynecol*. 1978;21:205.

Lamont JA. Female dyspareunia. *Am J Obstet Gynecol*. 1980;136:282.

Steege JF. Dyspareunia and vaginismus. *Clin Obstet Gynecol*. 1984;27:750.

Steege JF, Ling FW. Dyspareunia. A special type of chronic pelvic pain. *Obstet Gynecol Clin North Am*. 1993;20:779.

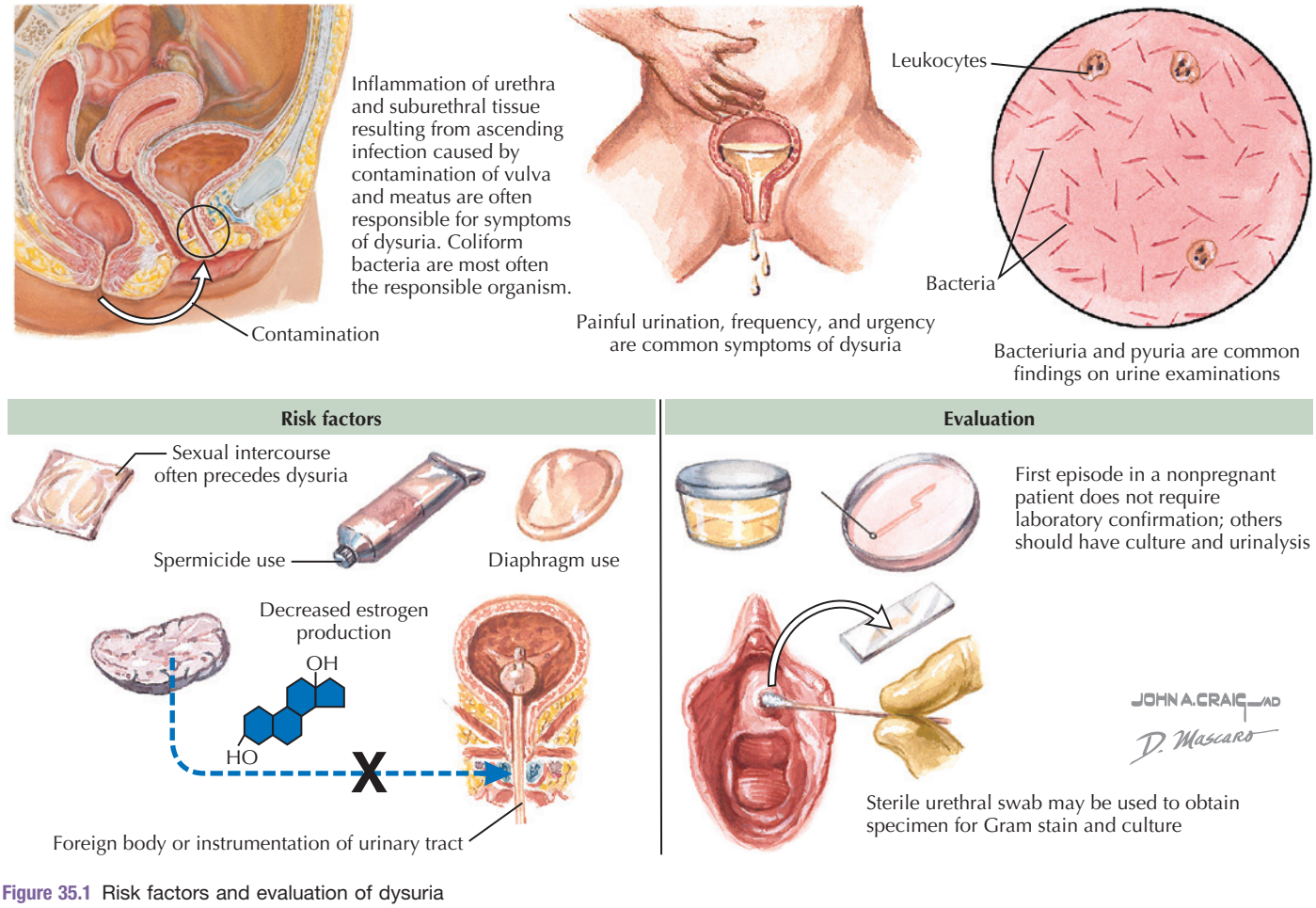


Figure 35.1 Risk factors and evaluation of dysuria

For others, urinalysis and culture should be performed. For uncentrifuged urine samples, the presence of more than one white blood cell per high-power field is 90% accurate for detecting infection. "Dipstick" point of care testing of a clean-voided sample demonstrating leukocyte esterase, nitrite, or bacteria is supportive of the clinical diagnosis, though not diagnostic. (False positive nitrite tests can occur with substances that turn the urine red, such as the bladder analgesic phenazopyridine or ingestion of beets.)

Imaging: No imaging indicated.

Special Tests: A sterile swab inserted into the urethra may also be used to obtain material for culture. Urine culture is helpful if there is reason to suspect antimicrobial resistance.

Diagnostic Procedures: History and physical examination, urinalysis. (Gentle pressure beneath the urethra or bladder trigone will often reproduce the patient's symptoms when significant urethritis is present.)

Pathologic Findings

Pyuria (hematuria may be present as well).

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Fluids, frequent voiding, and antipyretics. Urinary acidification (with ascorbic acid, ammonium chloride, or acidic fruit juices) and urinary analgesics (phenazopyridine [Pyridium]) may also be added based on the needs of the individual patient.

Specific Measures: Antibiotic therapy when infection is suspected.

Diet: Increased fluids and reduction of caffeine.

Activity: No restriction.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP050 (Urinary Tract Infections).

Drug(s) of Choice (Nonpregnant Patients)

- Single-dose therapy: amoxicillin 3 g; ampicillin 3.5 g; a first-generation cephalosporin 2 g; nitrofurantoin 200 mg; sulfisoxazole 2 g; trimethoprim 400 mg; trimethoprim/sulfamethoxazole (320/1600 mg); fosfomycin (3 g single dose).
- Three- to seven-day therapy: amoxicillin 500 mg every 8 hours; a first-generation cephalosporin 500 mg every 8 hours; ciprofloxacin 250 mg every 12 hours; nitrofurantoin 100 mg every 12 hours; norfloxacin 400 mg every 12 hours; ofloxacin 200 mg every 12 hours; sulfisoxazole 500 mg every 6 hours; tetracycline 500 mg every 6 hours; trimethoprim/sulfamethoxazole 160/800 mg every 12 hours; trimethoprim 100 (200) mg every 12 hours.

Contraindications: Known or suspected hypersensitivity.

Precautions: Urinary analgesics (phenazopyridine [Pyridium]) should be used for no longer than 48 hours and may stain some types of contact lenses.

Interactions: See individual medications.

Alternative Drugs (Pregnant Patients)

- Seven-day therapy—amoxicillin 500 mg every 8 hours; a first-generation cephalosporin 500 mg every 6 hours; nitrofurantoin 100 mg every 12 hours.

FOLLOW-UP

Patient Monitoring: No follow-up is necessary after single-dose treatment or after multiday treatment for nonpregnant women who experience resolution of their symptoms. Cure for all other patients should be confirmed by urinalysis and culture. Recurrent lower tract infections require prompt evaluation. Possible causes include incorrect or incomplete (eg, noncompliant) therapy, mechanical factors (such as obstruction or stone), or compromised host defenses.

Prevention/Avoidance: Frequent voiding, adequate fluid intake, voiding after intercourse.

Possible Complications: Urethral syndrome and interstitial cystitis. Bacteremia, septic shock, adult respiratory distress syndrome, and other serious sequelae are associated with pyelonephritis.

Expected Outcome: For most patients, symptoms (when resulting from infection) should resolve within 2–3 days after the initiation of therapy.

MISCELLANEOUS

Pregnancy Considerations: Those at high risk (eg, patients with diabetes) should be monitored carefully to avoid urethritis, cystitis, and ascending infection.

ICD-10-CM Codes: R30.0 (Dysuria), R30.9 (Painful micturition, unspecified), and O23.40 (Unspecified infection of urinary tract in pregnancy, unspecified trimester).

REFERENCES

LEVEL III

American College of Obstetricians and Gynecologists. Sulfonamides, nitrofurantoin, and risk of birth defects. Committee Opinion No. 494. *Obstet Gynecol*. 2011;117:1484.

Car J. Urinary tract infections in women: diagnosis and management in primary care. *BMJ*. 2006;332(7533):94.

Franco AV. Recurrent urinary tract infections. *Best Pract Res Clin Obstet Gynaecol*. 2005;19:861.

Gupta K, Trautner B. In the clinic. Urinary tract infection. *Ann Intern Med*. 2012;156:ITC3.

Hooton TM. Clinical practice. Uncomplicated urinary tract infection. *N Engl J Med*. 2012;366:1028.

Mittal P, Wing DA. Urinary tract infections in pregnancy. *Clin Perinatol*. 2005;32:749.

Nicolle L, Anderson PA, Conly J, et al. Uncomplicated urinary tract infection in women. Current practice and the effect of antibiotic resistance on empiric treatment. *Can Fam Physician*. 2006;52:612.

Scholes D, Hooton TM, Roberts PL, et al. Risk factors associated with acute pyelonephritis in healthy women. *Ann Intern Med*. 2005;142:20.

Sheffield JS, Cunningham FG. Urinary tract infection in women. *Obstet Gynecol*. 2005;106:1085.

Stamm W. Criteria for the diagnosis of urinary tract infection and for the assessment of therapeutic effectiveness. *Infection*. 1992;20(suppl 3):S151-S160.

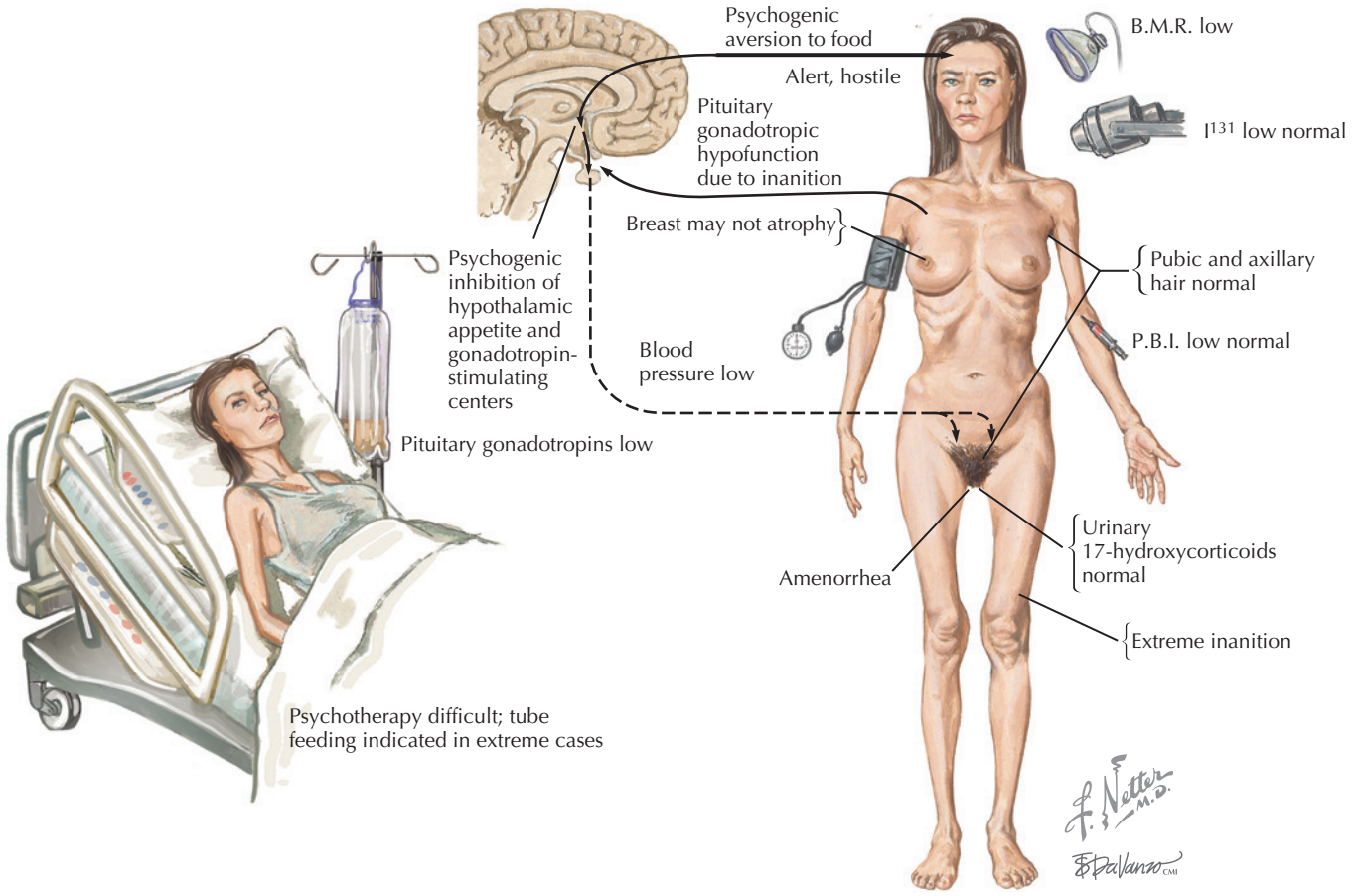


Figure 36.1 Anorexia nervosa

- Excessive exercise (marathon running)
- Bulimia—high-calorie binges followed by severe restriction
- Food collections or hoarding
- Medication abuse (laxatives, diuretics, ipecac, thyroid medication)
- Dental erosion and scarred knuckles (secondary to finger-induced vomiting)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Wasting disease (tumors)
- Depression
- Hypothalamic tumor
- Food phobia
- Gastrointestinal disease
- Other emotional disorders (conversion disorder, schizophrenia, body dysmorphic disorder)

Associated Conditions: Major depressive disorder (50%–75% of patients), obsessive–compulsive disorders (10%–13% of patients), bipolar disorder, sexual disinterest, growth arrest, hypotension and bradycardia, myocardial atrophy, mitral valve prolapse, hypothermia, and peripheral edema. Prolonged amenorrhea is associated with an increased risk of osteoporosis, which may not be reversible. Bulimia—social phobia and anxiety disorders, substance abuse, and shoplifting are common.

Workup and Evaluation

Laboratory: No evaluation specific for anorexia. For patients with bulimia there may be laboratory changes consistent with repeated vomiting (hypokalemia, hypomagnesemia, or hypochloremia).

Imaging: No imaging indicated.

Special Tests: Assessment of body fat. Several short screening questions have been validated to assist with the diagnosis.

Diagnostic Procedures: History and physical examination, Eating Attitudes Test.

Pathologic Findings

Anorexia nervosa—dry, cracked skin; sparse scalp hair; fine lanugo hair on extremities, face, and trunk; arrested maturation; pathologic fractures; cognitive defects. Bulimia—eroded dental enamel, esophagitis, Mallory–Weiss tears, parotid enlargement, gastric dilation.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Psychologic evaluation and support, supervised eating and exercise program, progressive increase in calories and activity as weight is regained (anorexia), limit access to bathroom for 2 hours after eating (bulimia).

Specific Measures: Hospitalization may be required, including intensive psychologic assessment and therapy. Tube feedings and intravenous fluids may be required for patients with anorexia.

Diet: Supervised program of re-education and behavior modification. For patients with anorexia, a gradual increase in caloric intake as part of a supervised program of re-education and behavior modification.

Activity: Stepwise increase based on weight change, avoiding goal-oriented activities.

Patient Education: Nutritional instruction, assistance with a food log. American College of Obstetricians and Gynecologists Patient

Education Pamphlet AP064 (Weight Control: Eating Right and Keeping Fit), AP045 (Exercise and Fitness), AP130 (Healthy Eating).

Drug(s) of Choice

- Olanzapine 2.5–10 mg/day
- Risperidone (mean dose, 2.5 mg/day)
- Fluoxetine (Prozac) 10–60 mg PO daily
- Oxazepam 15 mg or alprazolam 0.25 mg PO before meals to reduce anxiety about weight gain

Contraindications: See specific agents.

Precautions: Starved patients tend to be more sensitive to medications or have compromised renal, cardiac, or liver function.

Alternative Drugs

- Imipramine (Tofranil) 10 mg gradually increased to 200 mg or desipramine (Norpramin) 25 mg gradually increased to 150 mg PO daily.
- Lithium (Eskalith) 300 mg PO bid gradually increased until blood level of 0.6–1.2 mEq/L if bipolar disorder is present.
- Cisapride (Propulsid) 10–20 mg before meals to increase gastric emptying.
- Psyllium (Metamucil) 1 tablespoon every night to prevent constipation.

FOLLOW-UP

Patient Monitoring: Periodic weight measurements (weekly until stable, then monthly). Monitor for depression or suicidal ideation.

Prevention/Avoidance: Encourage healthy attitudes about weight, eating, and exercise; enhance self-esteem; and reduce stress.

Possible Complications: Drug and alcohol use/abuse, suicide, cardiac arrhythmia or arrest (potassium depletion), cardiomyopathy, suicide, necrotizing colitis, osteoporosis and osteoporotic fractures. Depression is common.

Expected Outcome: Highly variable with relapses common; better outcome with inpatient care. Bulimia may spontaneously remit.

MISCELLANEOUS

Pregnancy Considerations: Amenorrhea and infertility common in women with anorexia. For women with bulimia, the binge-purge cycle may affect fetal nutrition and growth when the behavior persists during pregnancy.

ICD-10-CM Codes: F50.00 (Anorexia nervosa, unspecified) and Z87.898 (Bulimia-Personal history of other specified conditions).

REFERENCES

LEVEL I

Attia E, Kaplan AS, Walsh BT, et al. Olanzapine versus placebo for outpatients with anorexia nervosa. *Psychol Med*. 2011;41:2177.

Hagman J, Gralla J, Sigel E, et al. A double-blind, placebo-controlled study of risperidone for the treatment of adolescents and young adults with anorexia nervosa: a pilot study. *J Am Acad Child Adolesc Psychiatry*. 2011;50:915.

LEVEL II

Centers for Disease Control and Prevention. Results from the National Adolescent Student Health Survey. *MMWR Morb Mortal Wkly Rep*. 1989;38:147.

Keski-Rahkonen A, Hoek HW, Susser ES, et al. Epidemiology and course of anorexia nervosa in the community. *Am J Psychiatry*. 2007;164:1259.

Legroux-Gerot I, Vignau J, Collier F, et al. Bone loss associated with anorexia nervosa. *Joint Bone Spine*. 2005;72:489.

Morgan JF, Reid F, Lacey JH. The SCOFF questionnaire: assessment of a new screening tool for eating disorders. *BMJ*. 1999;319:1467.

Signorini A, De Filippo E, Panico S, et al. Long-term mortality in anorexia nervosa: a report after an 8-year follow-up and a review of the most recent literature. *Eur J Clin Nutr*. 2007;61:119.

LEVEL III

Abrams SA, Silber TJ, Esteban NV, et al. Mineral balance and bone turnover in adolescents with anorexia nervosa. *J Pediatr*. 1993;123:326.

Brunet M 2nd. Female athlete triad. *Clin Sports Med*. 2005;24:623, ix.

Bruni V, Filicetti MF, Pontello V. Open issues in anorexia nervosa: prevention and therapy of bone loss. *Ann N Y Acad Sci*. 2006;1092:91.

Chamay-Weber C, Narring F, Michaud PA. Partial eating disorders among adolescents: a review. *J Adolesc Health*. 2005;37:417.

Cotton MA, Ball C, Robinson P. Four simple questions can help screen for eating disorders. *J Gen Intern Med*. 2003;18:53.

Hay PJ, Bacaltchuk J. Bulimia nervosa. *Clin Evid*. 2006;15:1315.

Hill LS, Reid F, Morgan JF, et al. SCOFF, the development of an eating disorder screening questionnaire. *Int J Eat Disord*. 2010;43:344.

Morris J, Twaddle S. Anorexia nervosa. *BMJ*. 2007;334(7599):894.

Nattiv A, Agostini R, Drinkwater B, et al. The female athlete triad. The inter-relatedness of disordered eating, amenorrhea, and osteoporosis. *Clin Sports Med*. 1994;13:405.

Phillipou A, Rossell SL, Castle DJ. The neurobiology of anorexia nervosa: a systematic review. *Aust N Z J Psychiatry*. 2014;48:128.

Yager J, Andersen AE. Clinical practice. Anorexia nervosa. *N Engl J Med*. 2005;353:1481.

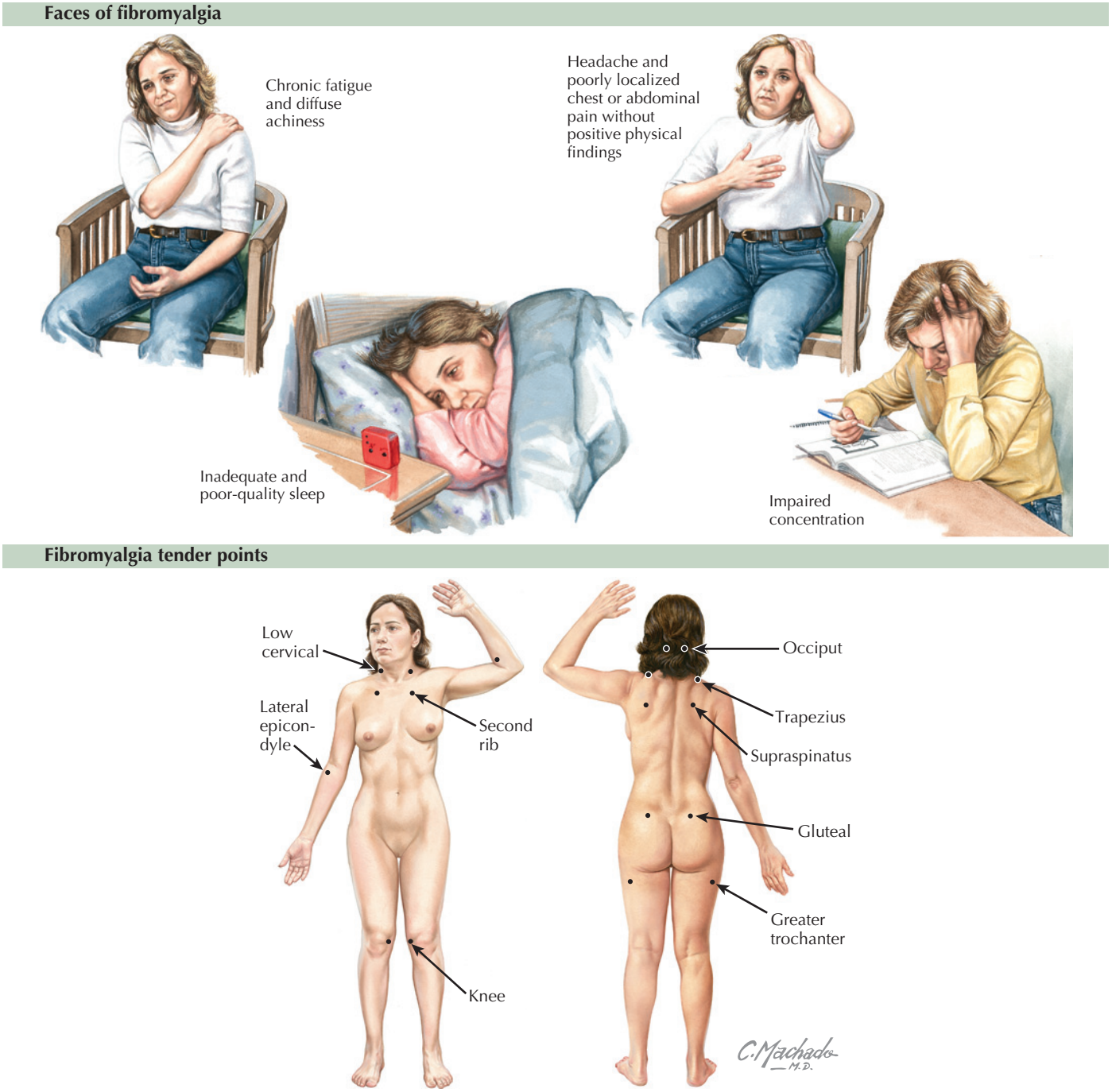


Figure 37.1 Fibromyalgia

ETIOLOGY AND PATHOGENESIS

Causes: Unknown, broadly considered to be a disorder of pain regulation.

Risk Factors: Sleep abnormalities, focal tissue abnormalities including myofascial trigger points, ligamentous trigger points, or osteoarthritis of the joints and spine.

SIGNS AND SYMPTOMS

- Widespread musculoskeletal pain and fatigue
- Tenderness in multiple soft tissue locations
- Fatigue
- Cognitive disturbances (problems with attention and difficulty with tasks that require rapid thought changes)
- Depression
- Headache
- Paresthesias

DIAGNOSTIC APPROACH

Differential Diagnosis

- Peripheral neuropathies, nerve entrapment
- Somatization
- Sleep disturbances

- Inflammatory and autoimmune rheumatologic disorders
- Ankylosing spondylitis
- Osteoarthritis
- Inflammatory myositis
- Tendinitis and bursitis
- Statin myopathy
- Infectious mononucleosis
- Hypothyroidism
- Chronic fatigue syndrome (systemic exertion intolerance disease)
- Obstructive sleep apnea and restless legs

Associated Conditions: Somatization, sleep disruptions, anxiety, depression, abdominal and chest wall pain, irritable bowel syndrome (IBS), migraine, palpitations, dyspnea, vulvodynia, dysmenorrhea, sexual dysfunction, weight fluctuations, night sweats, dysphagia, dysgeusia, and orthostatic intolerance.

Workup and Evaluation

Laboratory: No evaluation indicated except to rule out other possible causes.
Imaging: None indicated.
Special Tests: Screening for psychiatric conditions, including anxiety and depression, as indicated.
Diagnostic Procedures: History and physical examinations. Other than tenderness, no obvious abnormalities on physical examination. Diagnostic criteria require findings of at least 11 of 18 defined tender points.

Pathologic Findings

No specific findings. Despite symptoms of soft tissue pain, there is no tissue inflammation.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Reassurance, good sleep hygiene, an exercise program (including aerobic conditioning, stretching, and strengthening, and cardiovascular exercise), and cognitive behavioral therapy (CBT).
Specific Measures: Consultations as indicated.
Diet: No dietary restrictions.
Activity: No restriction, activity encouraged.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP099 (Chronic Pelvic Pain).

Drug(s) of Choice

- Tricyclic medications, such as amitriptyline, and several selective serotonin and norepinephrine reuptake inhibitors (SSRIs and SNRIs, respectively), including duloxetine and milnacipran, have shown efficacy.
- Gabapentin and pregabalin may also be useful in selected patients.
- In patients unresponsive to or intolerant of amitriptyline or who have severe fatigue or depression in addition to pain, treatment with duloxetine instead of amitriptyline may be effective.
- Data do not favor any one approach over another.

Contraindications: See specific agents.
Precautions: Only a minority of patients experience substantial improvement with drug therapy, and adverse side effects are common.

FOLLOW-UP

Patient Monitoring: Normal health maintenance; close follow-up of symptoms and therapeutic response.
Prevention/Avoidance: None known.
Possible Complications: Progression of symptoms and the emergence of psychiatric disease.
Expected Outcome: Fair to good with exercise and sleep therapy. There is a slight improvement with the addition of pharmacologic agents.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: M79.7 (Fibromyalgia).

REFERENCES

LEVEL II

Ángel García D, Martínez Nicolás I, Saturno Hernández PJ. Clinical approach to fibromyalgia: synthesis of evidence-based recommendations, a systematic review. *Reumatol Clin*. 2015;pii: S1699-258X(15)00110.

Halpern R, Shah SN, Cappelleri JC, et al. Evaluating guideline-recommended pain medication use among patients with newly diagnosed fibromyalgia. *Pain Pract*. 2015.

Moore RA, Derry S, Aldington D, et al. Amitriptyline for fibromyalgia in adults. *Cochrane Database Syst Rev*. 2015;(7):CD011824.

Sanada K, Díez MA, Valero MS, et al. Effects of non-pharmacological interventions on inflammatory biomarker expression in patients with fibromyalgia: a systematic review. *Arthritis Res Ther*. 2015;17:272.

Sanses TV, Chelimsky G, McCabe NP, et al. The pelvis and beyond: musculoskeletal tender points in women with chronic pelvic pain. *Clin J Pain*. 2015.

Walitt B, Nahin RL, Katz RS, et al. The prevalence and characteristics of fibromyalgia in the 2012 National Health Interview Survey. *PLoS ONE*. 2015;10:e0138024.

LEVEL III

Borchers AT, Gershwin ME, Fibromyalgia A. Critical and comprehensive review. *Clin Rev Allergy Immunol*. 2015;49:100.

Clauw DJ. Fibromyalgia: a clinical review. *JAMA*. 2014;311:1547.

Lauche R, Cramer H, Häuser W, et al. A systematic overview of reviews for complementary and alternative therapies in the treatment of the fibromyalgia syndrome. *Evid Based Complement Alternat Med*. 2015;2015:610615.

Ting TV, Barnett K, Lynch-Jordan A, et al. 2010 American college of rheumatology adult fibromyalgia criteria for use in an adolescent female population with juvenile fibromyalgia. *J Pediatr*. 2015;pii:S0022-3476(15)01170.

38 GALLBLADDER DISEASE

INTRODUCTION

Description: Any diseases that involves the gallbladder, most commonly because of the formation of cholesterol stones. Obstruction can result in either acute or chronic cholecystitis, leading to serious, sometimes life-threatening complications such as a gallbladder rupture. Approximately 20% of patients with acute cholecystitis develop infection. Acalculous gallbladder disease or biliary dyskinesia occurs without the presence of gallstones. Sclerosing cholangitis has an unknown etiology and is associated with an enlarged liver or spleen, decreased appetite, and weight loss. Gallbladder cancer is uncommon. Xanthogranulomatous cholecystitis is a rare form of gallbladder disease, which mimics gallbladder cancer, although it is not cancerous.

Prevalence: Ten percent of the population has some form of gallbladder disease. Cholangiocarcinomas and other bile duct tumors are rare (1–2/100,000 people; fewer than 5000 new cases per year in the United States).

Predominant Age: Greater than the age of 40 years.

Genetics: Ratio of women to men is 3 : 1 for gallstones. A mutation in the gene ABCG8 significantly increases the risk of gallstones in an individual.

ETIOLOGY AND PATHOGENESIS

Causes: The most common cause of gallbladder disease is the formation of cholesterol sludge or stones. These can lead to the obstruction of the common bile duct, resulting in inflammation, distention, and potential rupture (1%–3% of people with symptomatic gallstones develop acute cholecystitis). Ascending infection can also involve the gallbladder.

Risk Factors: Age, female gender, parity (75% of affected patients have had one or more pregnancies), obesity (15–20 lb overweight is associated with a 2-fold increase in risk; 50–75 lb excess weight is associated with a 6-fold increase in risk) and weight cycling, estrogen use (oral), cirrhosis, diabetes, and Crohn disease. A family history of cholelithiasis in siblings or children results in a 2-fold increase in risk. Approximately 10% of patients with cholelithiasis will have a stone pass into the common duct. Primary sclerosing cholangitis is associated with a lifetime risk of 7%–12% for gallbladder cancer.

SIGNS AND SYMPTOMS

- Asymptomatic (60%–70%)
- Variable right upper quadrant pain with radiation to the back or scapula
- Right upper quadrant tenderness
- Nausea or vomiting
- Fever
- Jaundice
- Pale stools
- Bloating and belching
- Heartburn and regurgitation
- Fever and chills (when cholecystitis is present)
- Chronic diarrhea (4–10 bowel movements every day for at least 3 months)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Gastroenteritis
- Esophageal reflux
- Malabsorption
- Irritable bowel syndrome (IBS)
- Peptic ulcer disease
- Coronary artery disease
- Pneumonia
- Appendicitis
- Fitz-Hugh–Curtis syndrome (perihepatitis caused by gonococcal infection)

Associated Conditions: Pancreatitis, ascending cholangitis, peritonitis, internal fistulization.

Workup and Evaluation

Laboratory: Bilirubin and alkaline phosphatase are usually elevated in acute cholecystitis, and especially in choledocholithiasis. Blood tests for pancreatitis (serum alanine aminotransferase, aspartate aminotransferase, bilirubin, alkaline phosphatase/gamma-glutamyl transpeptidase, amylase, and lipase) are appropriate when the diagnosis is entertained.

Imaging: Ultrasonography of the gallbladder (96% accuracy for diagnosing sludge or a stone in the gallbladder). Magnetic resonance cholangiopancreatography (MRCP) may be of help in selected cases.

Special Tests: Cholescintigraphy (also called gallbladder radionuclide scan or hepatobiliary [HIDA] scan).

Diagnostic Procedures: History and physical examination, ultrasonography, and laboratory investigation.

Pathologic Findings

Based on diagnosis. Gangrenous cholecystitis is the most common complication of cholecystitis, particularly in older patients, patients with diabetes, or those who delay seeking therapy. Emphysematous cholecystitis often heralds the development of gangrene, perforation, and other complications. Porcelain gallbladder is an uncommon manifestation of chronic cholecystitis that is characterized by intramural calcification of the gallbladder wall. Gallbladder polyps are usually found incidentally on ultrasonography and are benign.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Analgesics, fluids, and general support based upon the diagnosis.

Specific Measures: Single-incision laparoscopic cholecystectomy (SILC) is safe, and, although it requires more operating time, cosmetic satisfaction is higher than traditional (4-port) laparoscopic surgery. Endoscopic retrograde choliangiopancreatography (ECRP) with endoscopic sphincterotomy is the most common procedure for detecting and managing bile duct stones. A small number of patients may be candidates for extracorporeal shock wave lithotripsy (ESWL). The Natural Orifice Translumenal Endoscopic Surgery (NOTES) trial is exploring the possibility of removing the gallbladder through the mouth or vagina.

Diet: Reduced fatty food and cholesterol intake.

Activity: No restriction except as dictated by the patient's condition.

Patient Education: Gallstones, available at: http://www.webmd.com/digestive-disorders/gallstones, accessed on 7.12.15. Cholecystitis, available at: http://www.webmd.com/digestive-disorders/cholecystitis-10620, accessed on 7.12.15.

Drug(s) of Choice

- Ursodeoxycholic acid (Actigall) 8–10 mg/kg/day as two to three doses for cholesterol stones.

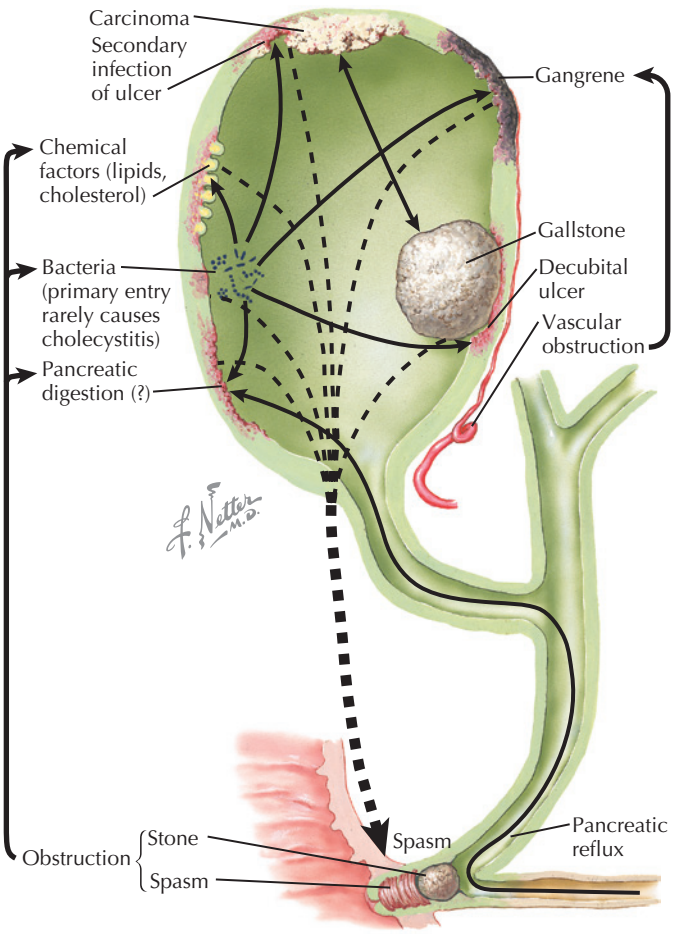


Figure 38.1 Interrelation of gallbladder diseases

- Admission to the hospital for supportive care, including intravenous fluids, correction of electrolyte disorders, and control of pain (nonsteroidal antiinflammatory drugs or opioids). Antibiotics may be indicated based on the clinical findings.

Contraindications: Known allergy, acute cholecystitis, abnormal liver function, calcified stones (not cholesterol based).

Precautions: The rate of stone dissolution (approximately 1 mm/mo) limits applicability for stones greater than 1.5–2 cm in size. In acute cases, surgical treatment is definitive and preferred.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.

Prevention/Avoidance: Some advocate a high-fiber, low-fat diet.

Possible Complications: Acute cholecystitis can progress to gangrene or perforation of the gallbladder if left untreated, resulting in fistula formation (10%), peritonitis (1%), or bowel obstruction (gallstone ileus). Infection develops in approximately 20% of patients with acute cholecystitis. Common bile duct stones are responsible for most cases of pancreatitis, which can be life threatening. There is a strong association between gallbladder cancer and cholelithiasis, chronic cholecystitis, and inflammation (gallstones are present in approximately 80% of patients with gallbladder cancer).

Expected Outcome: Good with appropriate medical or surgical therapy. Symptoms of gallbladder cancer usually do not appear until the disease has reached an advanced stage, but survival rates are rising with new therapeutic options.

MISCELLANEOUS

Pregnancy Considerations: Pregnancy increases the risk for gallstones, and pregnant women are more likely to develop symptoms. Surgery should be delayed until after delivery if possible.

ICD-10-CM Codes: K82.9 (Disease of gallbladder, unspecified), K82.8 (Other specified diseases of gallbladder), K80 (Cholelithiasis), K80.80 (Other cholelithiasis without obstruction), K80.8 (Other cholelithiasis), K80.20 (Calculus of gallbladder without cholecystitis without obstruction).

REFERENCES

LEVEL II

Chamberlain RS, Sakpal SV. A comprehensive review of single-incision laparoscopic surgery (SILS) and natural orifice transluminal endoscopic surgery (NOTES) techniques for cholecystectomy. *J Gastrointest Surg*. 2009.

Friedman GD. Natural history of asymptomatic and symptomatic gallstones. *Am J Surg*. 1993;165:399.

LEVEL III

Baron TH, Grimm IS, Swanstrom LL. Interventional approaches to gallbladder disease. *N Engl J Med*. 2015;373:357.

Bouyou J, Gaujoux S, Marcellin L, et al. Abdominal emergencies during pregnancy. *J Visc Surg*. 2015;152(suppl 6):S105.

Date RS, Kaushal M, Ramesh A. A review of the management of gallstone disease and its complications in pregnancy. *Am J Surg*. 2008;196:599.

Gore RM. Gallbladder imaging. *Gastroenterol Clin North Am*. 2010;39:265.

Knab LM, Boller AM, Mahvi DM. Cholecystitis. *Surg Clin North Am*. 2014;94:455.

Ko CW, Beresford SA, Schulte SJ. Incidence, natural history, and risk factors for biliary sludge and stones during pregnancy. *Hepatology*. 2005;41:359.

Konstantinidis IT, Deshpande V, Genevay M, et al. Trends in presentation and survival for gallbladder cancer during a period of more than four decades. *Arch Surg*. 2009;144:441.

Martin DJ, Vernon DR, Toouli J. Surgical versus endoscopic treatment of bile duct stones. *Cochrane Database Syst Rev*. 2006;(2):CD003327.

Portincasa P, Di Ciaula A, de Bari O, et al. Management of gallstones and its related complications. *Expert Rev Gastroenterol Hepatol*. 2015;1.

Yusoff IF, Barkun JS, Barkun AN. Diagnosis and management of cholecystitis and cholangitis. *Gastroenterol Clin North Am*. 2003;32:1145.

39 GASTRITIS

INTRODUCTION

Description: Gastritis is an inflammatory condition that affects the stomach lining and results in acute or chronic indigestion, bloating, "gas," and heartburn. Gastropathy (non-inflammatory) is usually caused by irritants such as drugs (eg, nonsteroidal antiinflammatory agents), alcohol, bile, circulatory failure, or chronic congestion.
Prevalence: Common.
Predominant Age: Any.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Generalized inflammation of the stomach lining, which in some cases, may be infectious (*Helicobacter pylori*).
Risk Factors: Cigarette smoking, alcohol abuse, some medications (nonsteroidal antiinflammatory drugs [NSAIDs]), bile reflux, radiation.

SIGNS AND SYMPTOMS

- Nausea, vomiting, dyspepsia, heartburn, and "gas" (symptoms are most common after eating large meals, consuming certain foods)
- Upper abdominal pain or tenderness
- Hiccups

DIAGNOSTIC APPROACH

Differential Diagnosis

- Gastrointestinal reflux
- Ulcer disease (gastric or duodenal)
- Esophageal cancer
- Linitis plastica

Associated Conditions: Bleeding, dysphagia, and gastric or duodenal ulcer.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated.
Special Tests: Gastroscopy (with or without biopsy) establishes the diagnosis but most often is unnecessary. A mucosal biopsy is required to distinguish between acute, chronic active, or chronic gastritis because endoscopic and radiologic features may be similar.
Diagnostic Procedures: History and physical examinations (suspicious), gastroscopy (diagnostic).

Pathologic Findings

Patchy erythema of the gastric mucosa (seldom full thickness) is most common in the pyloric antrum. Histologic findings can vary over a wide spectrum ranging from epithelial hyperplasia to extensive epithelial cell damage with infiltration by inflammatory cells.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Dietary changes, elevation of the head of the bed, smoking cessation, alcohol in moderation only, antacids. Antacids that coat (liquids) and those that tend to float on the surface of the stomach contents, such as Gaviscon, give better heartburn relief than other agents.
Specific Measures: Eliminate medications that contribute to reduced esophageal pressure, such as diazepam and calcium channel blockers, or that may damage the esophagus (NSAIDs). Use acid-blocking therapy.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance, diet counseling, behavior modification.

Drug(s) of Choice

- Antacids
- Histamine H_2 antagonists—cimetidine 800 mg two times daily; ranitidine 400 mg four times daily; famotidine 20 mg two times daily; nizatidine 150 mg two times daily.
- Hydrogen potassium pump blockers—omeprazole 20–40 mg daily for 4–8 weeks; esomeprazole 20–40 mg daily for 4–8 weeks; pantoprazole 40 mg daily for 8 weeks. Misoprostol (Cytotec) 100–200 mcg PO four times daily if mucosal injury is documented or suspected.

Contraindications: Known or suspected hypersensitivity. Misoprostol is contraindicated during pregnancy and lactation.
Precautions: If bismuth is prescribed, warn the patient about black stools. Because of a lack of long-term follow-up, hydrogen pump inhibitors may be taken for only 8–12 weeks.
Interactions: Multiple drug interactions are possible with agents such as cimetidine; check full prescribing information.

Alternative Drugs

- In patients with *H. pylori* infection, a combination of bismuth (Pepto-Bismol) and an antibiotic (metronidazole 250 mg every 6 hours; tetracycline 500 every 6 hours; or amoxicillin 500 mg every 8 hours) has been recommended for 2 weeks.
- A 4-week treatment with clarithromycin (Bixin) and either omeprazole (Prilosec) or ranitidine bismuth citrate (Tritec) may also be used.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. If significant gastric erosion is documented, repeat gastroscopy after 6 weeks is often recommended.
Prevention/Avoidance: Reduction of modifiable risk factors (eg, smoking).
Possible Complications: Chronic pain, ulcer formation, and perforation.
Expected Outcome: Generally good symptomatic relief, but long-term therapy is often required.

MISCELLANEOUS

Pregnancy Considerations: No direct effect on pregnancy, although severe gastritis may interfere with maternal nutrition.
ICD-10-CM Codes: K29.70 (Gastritis, unspecified, without bleeding), K29.90 (Gastroduodenitis, unspecified, without bleeding). Others based on a cause.

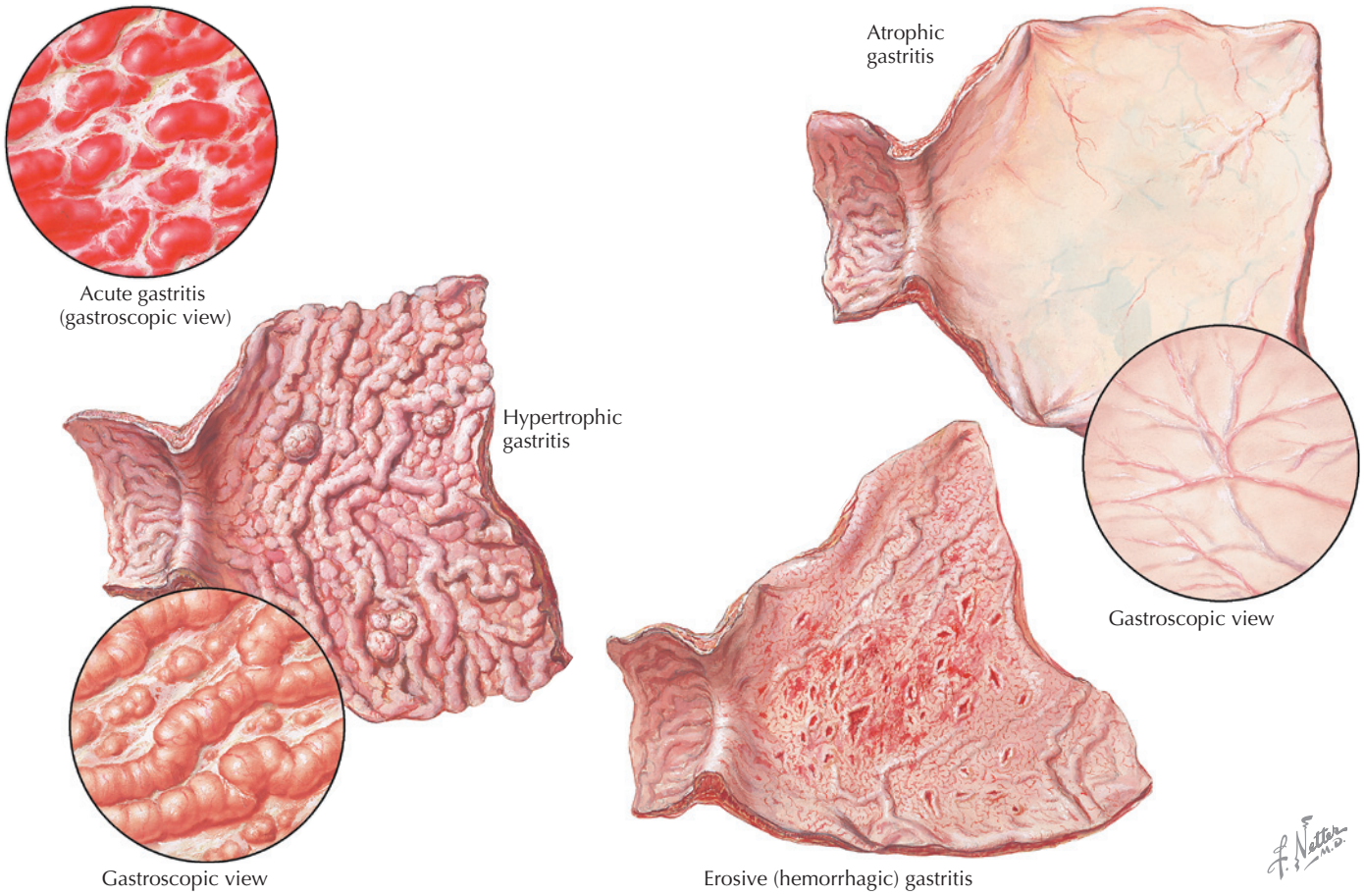


Figure 39.1 Gastritis

REFERENCES

LEVEL II

de Martel C, Parsonnet J. *Helicobacter pylori* infection and gender: a meta-analysis of population-based prevalence surveys. *Dig Dis Sci*. 2006;51: 2292. Epub 2006 Nov 7.

Israel DA, Peek RM Jr. The role of persistence in *Helicobacter pylori* pathogenesis. *Curr Opin Gastroenterol*. 2006;22:3.

LEVEL III

Feldman M, Burton ME. Drug therapy: histamine2-receptor antagonists—Standard therapy for acid-peptic disease. *N Engl J Med*. 1990;323(1672): 1749.

Moayyedi P, Talley NJ. Gastro-oesophageal reflux disease. *Lancet*. 2006;367(9528):2086.

Panteris V, Karamanolis DG. Different aspects in functional dyspepsia. *Hepatogastroenterology*. 2005;52:1782.

Rapkin AJ, Mayer EA. Gastroenterologic causes of chronic pelvic pain. *Obstet Gynecol Clin North Am*. 1993;20:663.

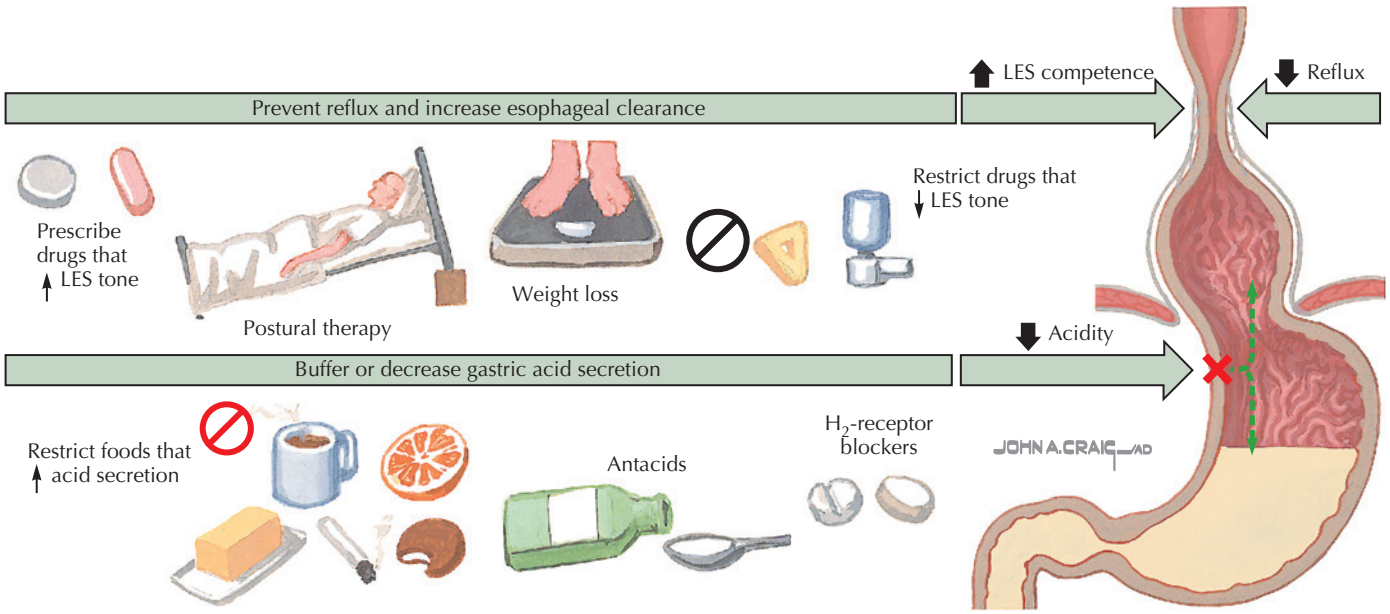


Figure 40.1 Principles of medical management in gastroesophageal reflux

SIGNS AND SYMPTOMS

- Upper abdominal pain, nausea, vomiting, dyspepsia, heartburn, chest pain, and "gas" (70%–85%; symptoms most common after large meals, consuming certain foods, and on assuming the recumbent position)
- Dysphagia (15%–20%, suggests stricture)
- Bronchospasm/asthma (15–20%)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Ulcer disease (gastric or duodenal)
- Chemical or infectious esophagitis
- Crohn disease of the esophagus
- Angina pectoris
- Achalasia
- Esophageal cancer

Associated Conditions: Dysphagia. Nocturnal aspiration may occur and be mistaken for asthma.

Workup and Evaluation

Laboratory: No evaluation indicated.

Imaging: Barium swallow may demonstrate hiatal hernia or esophageal narrowing. For patients who are pregnant, this should be reserved for after the completion of the pregnancy.

Special Tests: Upper gastrointestinal endoscopy eliminates other potential causes of gastroesophageal reflux disease that include esophageal motility disorders, erosive esophagitis, and peptic ulcer disease (gastric or duodenal), but its role is controversial.

Diagnostic Procedures: History (>80% accurate), physical examination, endoscopy, barium swallow.

Pathologic Findings

Acute inflammatory changes and hyperplasia of the basal layers of epithelium (85%). Squamous metaplasia of the lower esophagus may occur with chronic exposure to reflux acid (Barrett syndrome), which may undergo dysplasia or malignant change.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Dietary changes, elevation of the head of the bed, smoking cessation, alcohol in moderation only, weight loss, antacids. Antacids that coat (liquids), and those that tend to float on the surface of the stomach contents, such as Gaviscon, give better heartburn relief than other agents.

Specific Measures: Eliminate medications that contribute to reduced esophageal pressure, such as diazepam and calcium channel blockers, or that may damage the esophagus (nonsteroidal antiinflammatory drugs [NSAIDs]). Use acid-blocking therapy.

Diet: Avoid eating spicy or acidic meals, chocolate, onions, garlic, peppermint, and large meals before bedtime.

Activity: No restriction.

Patient Education: Reassurance, diet counseling, behavior modification. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP120 (Problems of the Digestive System).

Drug(s) of Choice

- Antacids
- Histamine H_2-antagonists—cimetidine 800 mg two times daily; ranitidine 400 mg four times daily; famotidine 20 mg two times daily; or nizatidine 150 mg two times daily.
- Hydrogen potassium pump blockers—omeprazole 20–40 mg daily for 4–8 weeks; esomeprazole 20–40 mg daily for 4–8 weeks; pantoprazole 40 mg daily for 8 weeks.
- Cisapride 10–20 mg four times daily, before meals and every night.
- Misoprostol (Cytotec) 100–200 mcg PO four times daily if mucosal injury is documented or suspected.

Contraindications: Known or suspected hypersensitivity. Misoprostol is contraindicated during pregnancy and lactation.

Precautions: A trial off of medications should be considered after 8–12 weeks.

Interactions: Multiple drug interactions are possible with agents such as cimetidine (check full Prescribing Information).

Alternative Drugs

Bethanechol, antiemetics, phenobarbital if necessary.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.

Prevention/Avoidance: Reduction of modifiable risk factors (eg, smoking, weight loss, diet).

Possible Complications: Esophageal stricture, bleeding. Prolonged exposure of acid to the esophagus may lead to stricture formation and dysphagia. Epithelial changes induced in the lower esophagus are also associated with an increased risk of esophageal cancer.

Expected Outcome: Generally good symptomatic relief, but long-term therapy is often required. Between 10%–40% of patients fail to respond symptomatically, either partially or completely, to proton pump inhibitor therapy.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, although it may worsen during pregnancy because of reduced esophageal tone and increased intraabdominal pressure caused by the expanding uterus. Sucralfate is considered safe during pregnancy and lactation because it is poorly absorbed. Proton pump inhibitors are not recommended in women who are breastfeeding due to the paucity of safety data.

ICD-10-CM Codes: K21.0 (Gastro-esophageal reflux disease with esophagitis).

REFERENCES

LEVEL II

Chang AB, Lasserson TJ, Kiljander TO, et al. Systematic review and meta-analysis of randomised controlled trials of gastro-oesophageal reflux interventions for chronic cough associated with gastro-oesophageal reflux. *BMJ*. 2006;332(7532):11. Epub 2005 Dec 5.

Dent J, El-Serag HB, Wallander MA, et al. Epidemiology of gastro-oesophageal reflux disease: a systematic review. *Gut*. 2005;54:710.

Gill SK, O'Brien L, Einarson TR, et al. The safety of proton pump inhibitors (PPIs) in pregnancy: a meta-analysis. *Am J Gastroenterol*. 2009; 104:1541.

Pasternak B, Hviid A. Use of proton-pump inhibitors in early pregnancy and the risk of birth defects. *N Engl J Med*. 2010;363:2114.

Peura DA, Freston JW, Haber MM, et al. Lansoprazole for long-term maintenance therapy of erosive esophagitis: double-blind comparison with ranitidine. *Dig Dis Sci*. 2009;54:955.

Ulualp SO, Roland PS, Toohill RJ, et al. Prevalence of gastro-esophagopharyngeal acid reflux events: an evidence-based systematic review. *Am J Otolaryngol*. 2005;26:239.

LEVEL III

DeVault KR, Castell DO. Guidelines for the diagnosis and treatment of gastroesophageal reflux disease. *Arch Intern Med*. 1995;155:2165.

Fass R. Proton-pump inhibitor therapy in patients with gastro-oesophageal reflux disease: putative mechanisms of failure. *Drugs*. 2007;67:1521.

Fennerty MB, Sampliner RE, Garewall HS. Barrett's oesophagus—cancer risk, biology and therapeutic management. *Aliment Pharmacol Ther*. 1993;7:339.

Kahrilas PJ, Lee TJ. Pathophysiology of gastroesophageal reflux disease. *Thorac Surg Clin*. 2005;15:323.

Locke GR 3rd. Current medical management of gastroesophageal reflux disease. *Thorac Surg Clin*. 2005;15:369.

Moayyedi P, Talley NJ. Gastro-oesophageal reflux disease. *Lancet*. 2006;367(9528):2086.

Nava-Ocampo AA, Velazquez-Armenta EY, Han JY, et al. Use of proton pump inhibitors during pregnancy and breastfeeding. *Can Fam Physician*. 2006;52:853.

Turcotte S, Duranceau A. Gastroesophageal reflux and cancer. *Thorac Surg Clin*. 2005;15:341.

Vakil N, van Zanten SV, Kahrilas P, et al. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol*. 2006;101:1900.

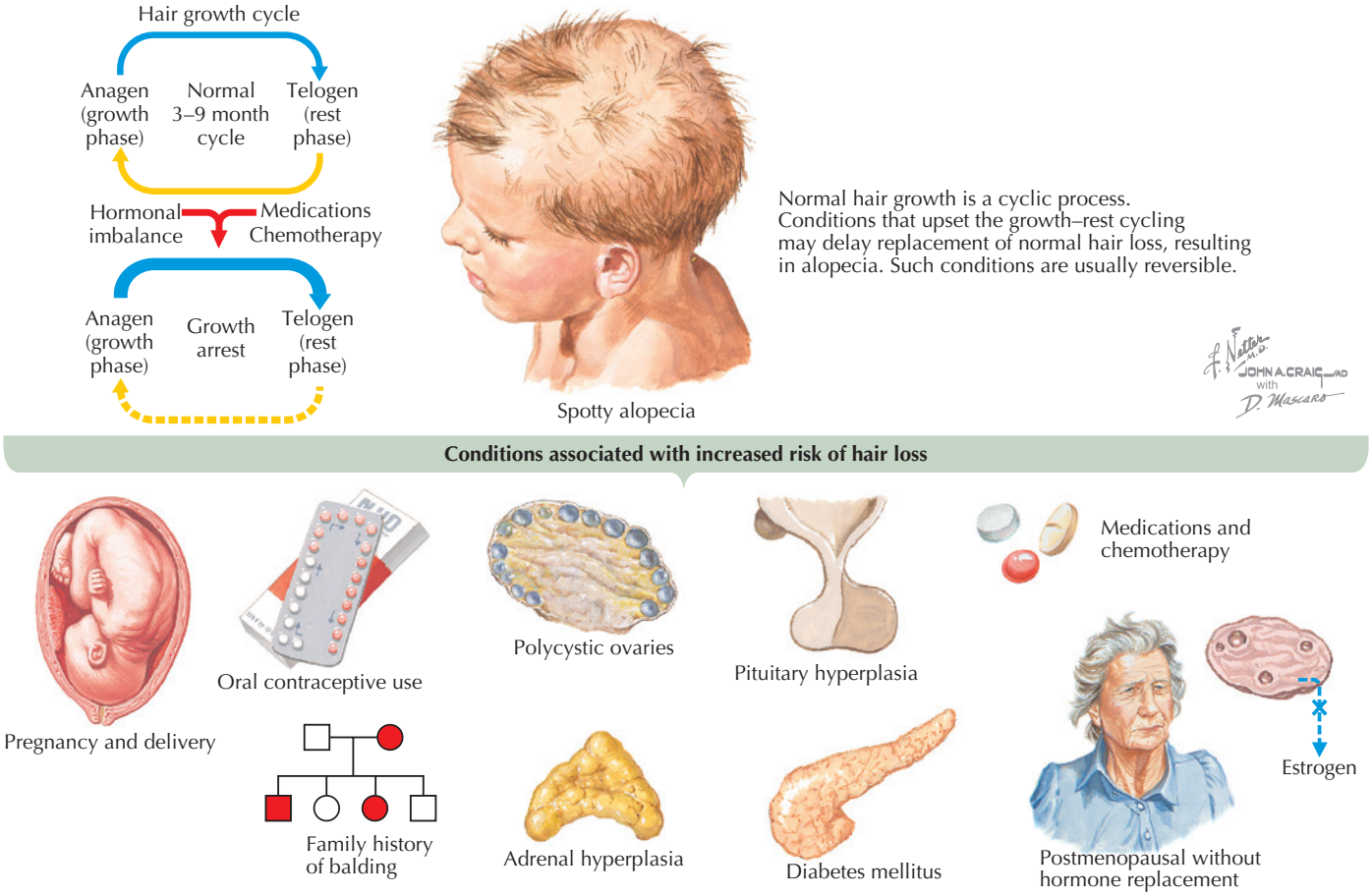


Figure 41.1 Hair loss and conditions associated with increased risk

also cause male-pattern hair loss (temporal balding, androgenic alopecia).

Risk Factors: Pregnancy, delivery, hormonal contraception, scalp disease, family history of baldness, nutritional deprivation, and drug or toxin exposure.

SIGNS AND SYMPTOMS

- Hair loss
- Pruritus, scaling, and broken hairs (tinea)
- Tapered, easily removed hair near the edge of patches (alopecia areata)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Telogen effluvium (as seen after pregnancy)
- Anagen effluvium (loss that includes growing hairs and may progress to complete baldness)
- Cicatricial alopecia (resulting from scarring)
- Androgenic alopecia (now called "female-pattern hair loss")
- Traction alopecia (trauma)
- Tinea capitis
- Drug, poison, or chemotherapy exposure
- Local infection or dermatitis
- Endocrinopathy (polycystic ovaries, adrenal hyperplasia, pituitary hyperplasia)
- Secondary syphilis

Associated Conditions: Alopecia areata, Down syndrome, vitiligo, diabetes, traction alopecia, and behavior aberrations.

Workup and Evaluation

Laboratory: No evaluation indicated except as dictated by specific differential diagnoses being considered.
Imaging: No imaging indicated.
Special Tests: Inspection of hair shafts, skin scraping for fungi.
Diagnostic Procedures: History, physical examination, inspection of hair shafts.

Pathologic Findings

If the base of the hair shaft is smooth, it came from natural (telogen) loss; if the base has the follicular bulb still attached (a white swelling at the end), the loss may be due to dermatologic or other disease conditions, and consultation is suggested.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, reassurance often is all that is required (telogen effluvium is self-limited).
Specific Measures: Based on cause, most are self-limited or reverse with correction of the underlying problem. For postmenopausal women, hormone replacement therapy often arrests or reverses hair loss.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance and information about hair growth.

Drug(s) of Choice

- For androgenic effluvium—topical minoxidil (Rogaine) 2% (approximately 40% response rate in 1 year).
- For alopecia areata—high-potency topical steroids.
- For tinea capitis—6- to 8-week therapy with either griseofulvin (ultramicrosize) 250–375 mg PO daily or ketoconazole 200 mg PO daily and careful hand washing.

Contraindications: Griseofulvin is contraindicated in pregnant patients and in those with porphyria and hepatocellular failure. Ketoconazole and itraconazole should not be used concomitantly with cisapride (Propulsid).

Precautions: Topical minoxidil can cause eye irritation. Griseofulvin use is associated with the possibility of photosensitivity, lupus-like syndromes, oral thrush, and granulocytopenia. Ketoconazole and itraconazole may be associated with hepatotoxicity.

Interactions: Minoxidil may potentiate the actions of other antihypertensive agents. Griseofulvin can interact with both barbiturates and warfarin. Ketoconazole and itraconazole may interact with warfarin, histamine H_2 blockers, digoxin, isoniazid, rifampin, and phenytoin.

Alternative Drugs

Finasteride (Propecia) has been used for male-pattern baldness in men, but it is ineffective for postmenopausal hair loss for women and is contraindicated during pregnancy.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. With ketoconazole and itraconazole periodic assessment of liver function is prudent.

Prevention/Avoidance: None.

Possible Complications: Social withdrawal.

Expected Outcome: Most hair loss is not permanent; a gradual return may be expected in 3–6 months after any causes have been eliminated. Only cicatricial alopecia is associated with permanent damage to the hair follicles.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, although delivery is often the trigger for increased hair loss.

ICD-10-CM Codes: L65.0 (Telogen effluvium), L65.9 (Nonscarring hair loss, unspecified), and L63.8 (Other alopecia areata).

REFERENCES

LEVEL II

Yip L, Zaloumis S, Irwin D, et al. Gene-wide association study between the aromatase gene (CYP19A1) and female pattern hair loss. *Br J Dermatol*. 2009;161:289.

LEVEL III

Atanaskova Mesinkovska N, Bergfeld WF. Hair: what is new in diagnosis and management? Female pattern hair loss update: diagnosis and treatment. *Dermatol Clin*. 2013;31:119.

Elewski BE. Clinical diagnosis of common scalp disorders. *J Investig Dermatol Symp Proc*. 2005;10:190.

Hordinsky MK. Medical treatment of noncicatricial alopecia. *Semin Cutan Med Surg*. 2006;25:51.

Hunt N, McHale S. The psychological impact of alopecia. *BMJ*. 2005; 331(7522):951.

Jackson AJ, Price VH. How to diagnose hair loss. *Dermatol Clin*. 2013;31: 21.

Roberts WE. Dermatologic problems of older women. *Dermatol Clin*. 2006;24:271, viii.

SIGNS AND SYMPTOMS

Tension Headache

- Dull, aching, and constant pain of mild to moderate intensity lasting from 30 minutes to 7 days, often located in the temples, around the head in a band, or up the back of the neck. It is rare, but some patients experience chronic tension-type headaches that are characterized by occurring 15 days/mo for 6 months or longer.
- Pressing or tightening quality (nonpulsating)
- Bilateral symmetry
- Not aggravated by physical activity
- No nausea or vomiting, photophobia or phonophobia (may have one but not both)
- Teeth grinding common

Cluster Headache

- Unilateral or orbital distribution (90% of headaches recur on the same side)
- Sharp, stabbing, or "ice pick" in character
- Symptoms of histamine release (nasal stuffiness and rhinorrhea, facial flushing, lacrimation, edema of eyelids)
- Symptoms are relieved when the patient is moving around
- Strong association with sleep
- Duration of less than 1 hour
- No aura or prodrome
- Annual recurrence common

DIAGNOSTIC APPROACH

Differential Diagnosis

- Depression
- Cervical spondylosis
- Temporomandibular joint syndrome
- Analgesic dependency
- Anemia
- Medication or toxin exposure
- Dental disease
- Temporal arteritis
- Trigeminal neuralgia
- Pheochromocytoma

Associated Conditions: Tension headache has been associated with an increased risk of epilepsy (4-fold). Cluster headaches are associated with seasonal allergy.

Workup and Evaluation

Laboratory: No evaluation indicated.

Imaging: No imaging indicated (computed tomography, electroencephalogram, and other evaluations are not indicated unless there is new onset of headaches after the age of 50 years) Some authors suggest neuroimaging (magnetic resonance imaging [MRI] scan) for patients being initially evaluated for cluster headaches.

Special Tests: None indicated.

Diagnostic Procedures: History.

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Tension headache—over-the-counter analgesics, rest, fluids, massage of shoulders, neck, or temples. Cluster headache—over-the-counter analgesics; rest; fluids; avoidance of

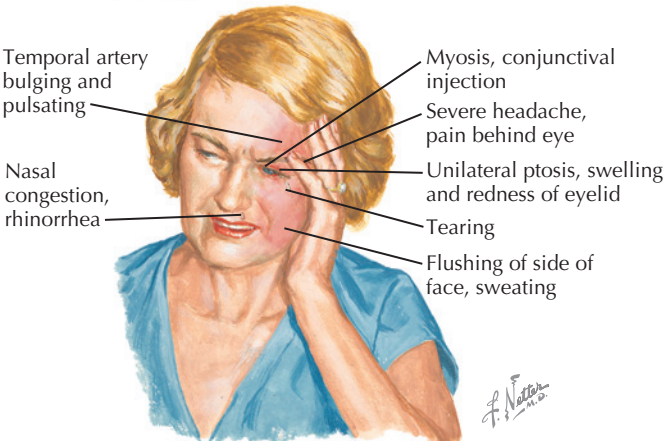
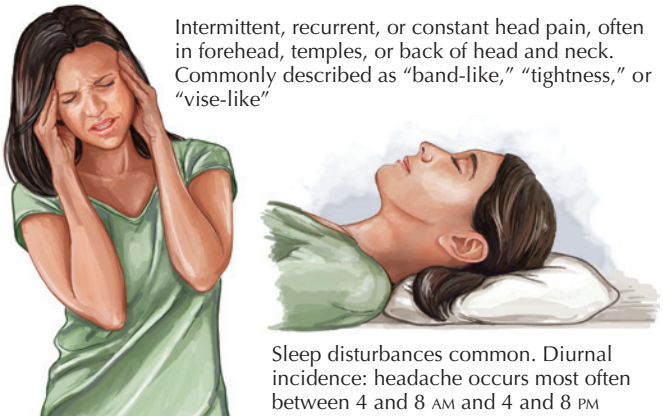


Figure 42.1 Cluster headache



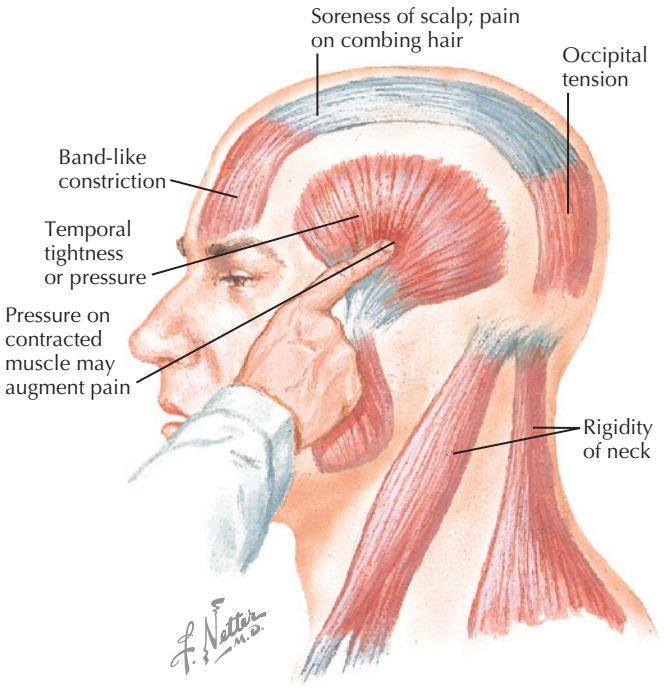


Figure 42.2 Muscle contraction headache

alcohol, bright lights, and noise. Some acute cluster headaches may require subcutaneous sumatriptan and oxygen inhalation.

Specific Measures: Nonsteroidal antiinflammatory drugs, stress reduction techniques, and biofeedback are indicated for tension headache. The effectiveness of analgesics tends to decrease with increasing headache frequency. Prophylaxis is most effective for cluster headaches.

Diet: No specific dietary changes indicated (caffeine restriction has been suggested). Patients should avoid alcohol or food known to hasten attacks.

Activity: No restriction, avoidance of known precipitating activities. Improved general fitness and strengthening may reduce incidence.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP124 (Headache).

Drug(s) of Choice

Tension headache—over-the-counter analgesics, nonsteroidal antiinflammatory drugs, antidepressants (when appropriate).

Cluster headache—prophylaxis: ergotamine 1–2 mg PO 2 hours before likely attack (eg, sleep); verapamil 80 mg PO four times daily; lithium carbonate (Eskalith) 300 mg PO two to four times daily; methysergide (Sansert) 2 mg three or four times daily; acute attacks: oxygen 100% 7–10 L/min via mask for 10–15 minutes; sumatriptan (Imitrex) 6 mg SC or 100 mg PO, may repeat dose once in 24 hours when separated by at least 1 hour; dihydroergotamine mesylate (DHE 45) 1 mg IM or IV. Octreotide 100 mcg is a somatostatin analog with a 90-minute half-life that may have advantages despite its increased cost and slower initial response rate. Although the symptoms of cluster headaches are consistent with histamine release, treatment with antihistamines is ineffective. Although data are limited, oxygen therapy may be effective for aborting cluster headache.

Contraindications: Aspirin-sensitive asthma, known or suspected sensitivity. See individual medications for others.

Precautions: Overuse of analgesics may lead to habituation and "analgesic rebound headaches" perpetuating the cycle of headache and analgesic use. Avoid the use of narcotic analgesics, especially oral agents in patients with cluster headaches; may convert attack to chronic form. The use of opioids or butalbital for tension headaches is not recommended.

Alternative Drugs

Cluster headache—indomethacin 25 mg PO four times daily; nifedipine 40–120 mg/day.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. Anticipate episodic recurrences for cluster headaches.

Prevention/Avoidance: Stress reduction, muscle strengthening and training, and biofeedback. For cluster headaches the prophylactic use of antihistamines should be considered during the times of year when the patient is most likely to have a recurrence. During the same period, alcoholic beverages and tobacco should be avoided because they may trigger an attack. These patients should also avoid sleep-cycle disruption.

Possible Complications: Headaches that are of sudden onset; begin after the age of 50 years; are dramatically different from past experience; have an accelerating pattern; are brought on by exertion, sexual activity, coughing, or sneezing; or are accompanied by focal neurologic signs are ominous and demand aggressive evaluation for possible intracranial or other pathologic cause. Patients with cluster headaches have an increased risk for peptic ulcers and gastrointestinal injury (from medications), caffeine dependence, coronary heart disease, and suicide.

Expected Outcome: Tension headaches generally resolve with rest and analgesics, although intermittent recurrence is common without lifestyle changes. Cluster headaches commonly have seasonal or annual recurrence patterns. Prolonged remission also is common.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. Pregnancy does not appear to affect the frequency of tension headaches. Cluster headaches are very rare in pregnancy. Pregnancy may alter medical therapy because of adverse effects of medications on the pregnant patient or fetus.

ICD-10-CM Codes: G44.209 (Tension-type headache, unspecified, not intractable) and G44.009 (Cluster headache syndrome, unspecified, not intractable).

REFERENCES

LEVEL II

Manzoni GC. Cluster headache and lifestyle: remarks on a population of 374 male patients. *Cephalalgia*. 1999;19:88.

Petersen AS, Barloese MC, Jensen RH. Oxygen treatment of cluster headache: a review. *Cephalalgia*. 2014;34:1079.

Russell MB, Andersson PG, Thomsen LL, et al. Cluster headache is an autosomal dominantly inherited disorder in some families: a complex segregation analysis. *J Med Genet*. 1995;32:954.

Ulrich V, Gervil M, Olesen J. The relative influence of environment and genes in episodic tension-type headache. *Neurology*. 2004;62:2065.

LEVEL III

American College of Obstetricians and Gynecologists. *Use of hormonal contraception in women with coexisting medical conditions. ACOG Practice Bulletin 73*. Washington, DC: ACOG; 2006.

APGO Educational Series on Women's Health Issues. *Strategies for the Management of Headache*. Washington, DC: APGO; 1998.

Cairns BE. The influence of gender and sex steroids on craniofacial nociception. *Headache*. 2007;47:319.

Francis GJ, Becker WJ, Pringsheim TM. Acute and preventive pharmacologic treatment of cluster headache. *Neurology*. 2010;75:463.

Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia*. 2013;33:629.

Jensen R. Peripheral and central mechanisms in tension-type headache: an update. *Cephalalgia*. 2003;23(suppl 1):49.

Russell MB. Epidemiology and genetics of cluster headache. *Lancet Neurol*. 2004;3:279.

Silberstein SD. The role of sex hormones in headache. *Neurology*. 1992; 42:37.

43 HEADACHE: MIGRAINE

INTRODUCTION

Description: Migraine headaches are recurrent severe headaches that last for 4–72 hours and are accompanied by neurologic, gastrointestinal, and autonomic changes. These may or may not be preceded by a characteristic aura.
Prevalence: Migraine headaches affect 15%–20% of women in the reproductive age. Approximately 10% of tension headache sufferers also have migraine headaches.
Predominant Age: Migraine headaches—ages 25–55 years (peak, 30–49 years), first attack generally between adolescence and 20 years.
Genetics: Migraines are three times more common in women than in men. Of migraine sufferers, 89% have a family history of headache.

ETIOLOGY AND PATHOGENESIS

Causes: Unknown; postulated: genetically linked vascular disruption secondary to neurochemical change, serotonin or norepinephrine metabolism, or tachykinin abnormality. These alterations may result in distention of and inflammation of cranial blood vessels. A strong relationship with female sex hormones is suspected.
Risk Factors: More common in upper-income patients (1.6 times); 60%–70% of women note a link with menstruation (14% of women have migraine headaches only during menses). Precipitating factors: some foods, stress or stress relief (let down), missed meals, excessive sleep.

SIGNS AND SYMPTOMS

- May be preceded by aura (20%)
- May begin with dull ache
- Unilateral pain (30%–40%, may switch sides from attack to attack)
- Pulsating quality (60%), rapid onset
- Moderate to severe intensity
- Made worse by activity
- Frequently accompanied by nausea (90%), vomiting (60%), photophobia (80%), blurred vision, scalp tenderness and neck stiffness, restlessness, irritability, nasal congestion, facial edema
- Menstrual migraine is characterized by onset between 1 day before and 4 days after menstruation (first day is most common). This pattern is observed in 15% of patients.

DIAGNOSTIC APPROACH

Differential Diagnosis

- Depression
- Cervical spondylosis
- Temporomandibular joint syndrome
- Analgesic dependency
- Anemia
- Medication or toxin exposure
- Dental disease
- Chronic sinusitis
- Temporal arteritis
- Trigeminal neuralgia
- Pheochromocytoma

Associated Conditions: Associated with increased risk of peptic ulcer and coronary heart disease. Epilepsy, depression, anxiety, Raynaud's phenomenon, mitral valve prolapse, stroke (debated), motion sickness, and panic disorders are more common in patients with migraine headaches.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated (computed tomography, electroencephalogram, and other evaluations are not indicated unless there is the new onset of headaches after the age of 50 years).
Special Tests: None indicated.
Diagnostic Procedures: History.

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Rest; fluids; analgesics; avoidance of alcohol, bright lights, and noise. Compression over the temporal artery may help. Biofeedback has been suggested but results vary.
Specific Measures: Nonsteroidal antiinflammatory drugs, stress reduction techniques, and biofeedback are indicated for tension headache. Migraine headaches should be treated with medical therapy for acute attacks and prophylaxis against recurrent headaches.
Diet: No specific dietary changes indicated (caffeine restriction has been suggested). Patients should avoid alcohol or food known to hasten attacks.
Activity: No restriction, avoidance of known precipitating activities. Improved general fitness and strengthening may reduce incidence. Bed rest for severe migraine attacks.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP124 (Headache).

Drug(s) of Choice

- Nonsteroidal antiinflammatory drugs—may provide relief for some or may abort the headache if taken early in the attack. Ergotamine preparations—ergotamine tartrate rectally at onset, may repeat in 1 hour or ergotamine tartrate 1 mg with caffeine 100 mg (Cafergot), two PO at onset, repeat every 30 minutes up to six per day; dihydroergotamine mesylate 1 mg IM or 2–3 mg intranasally at onset, 3 mg in 24 hours maximum. Serotonin agonists—sumatriptan 6 mg SC or 100 mg PO or 5–20 mg intranasally at onset, may repeat once in 24 hours with a minimum of 1 hour separation; naratriptan 1–2.5 mg PO, may repeat in 4 hours, 5 mg in 24 hours maximum; zolmitriptan 2.5 mg PO, may repeat in 2 hours, 10 mg in 24 hours maximum.

Contraindications: Aspirin-sensitive asthma, known or suspected sensitivity. Ergotamine is absolutely contraindicated during pregnancy. See individual medications for others.
Precautions: Overuse of analgesics may lead to habituation and "analgesic rebound headaches" perpetuating the cycle of headache and analgesic use. Significant side effects are possible with most migraine therapy—see individual agents. Use vasoactive agents with care in patients with cardiovascular disease.

Alternative Drugs

Antiemetics and phenothiazines may abort migraine headaches or help to relieve associated symptoms. Metoclopramide may be used to reduce nausea. Narcotic analgesics may be used for patients who do not achieve relief with other measures or cannot take other agents.

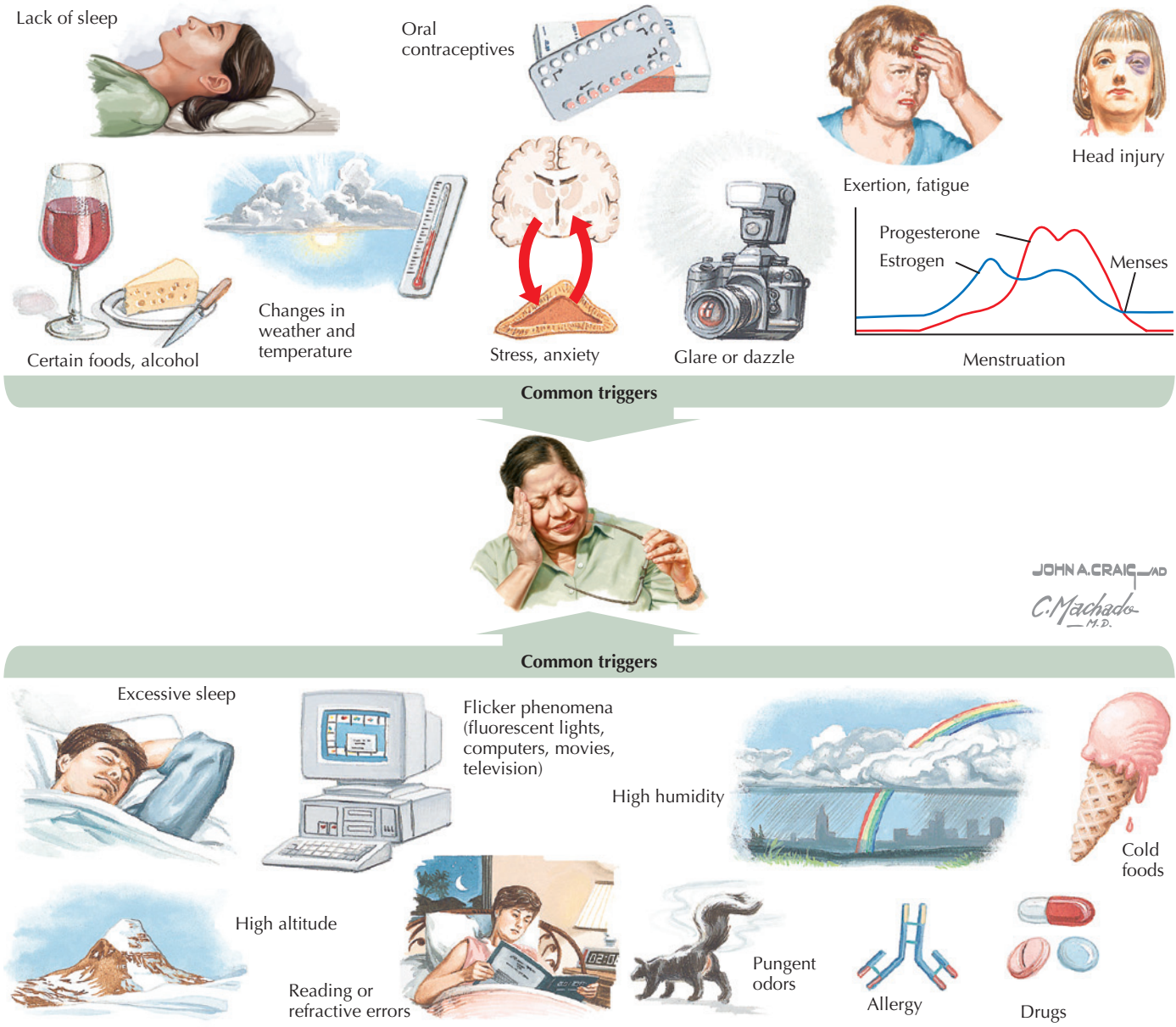


Figure 43.1 Triggers of migraine

FOLLOW-UP

Patient Monitoring: Normal health maintenance. Anticipate episodic recurrences.

Prevention/Avoidance: Patients who suffer from migraine headache should have adequate rest and fluids and avoid known triggers. Prophylactic medical therapy may be warranted for patients with two or more attacks per month. Prophylaxis may be attempted using β-blockers, divalproex, calcium antagonists, antidepressants, or serotonin antagonists.

Possible Complications: Headaches that are of sudden onset; begin after age 50; are dramatically different from past experience; have an accelerating pattern; are brought on by exertion, sexual activity, coughing, or sneezing; or are accompanied by focal neurologic signs are ominous and demand aggressive evaluation for possible intracranial or other pathologic cause. Patients with migraine headaches have an increased risk for peptic ulcers and gastrointestinal injury (from medications), caffeine dependence, coronary heart disease, and suicide. Some data suggest an increased risk for hypertensive disorders during pregnancy.

Expected Outcome: Migraines can generally be controlled, but recurrence is common. Severity and frequency tend to decline with age.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. Migraine headaches may worsen in the first trimester of pregnancy and generally become less severe in the second and third trimesters (60%–70%). Pregnancy may alter medical therapy because of adverse effects of medications on the pregnant patient or fetus. Acetaminophen (1000 mg) is first-line therapy during pregnancy.

ICD-10-CM Codes: G43.909 (Migraine, unspecified, not intractable, without status migrainosus) and G43.109 (Migraine with aura, not intractable, without status migrainosus).

REFERENCES

LEVEL I

Lipton RB, Baggish JS, Stewart WF, et al. Efficacy and safety of acetaminophen in the treatment of migraine: results of a randomized, double-blind, placebo-controlled, population-based study. *Arch Intern Med*. 2000;160:3486.

LEVEL II

Facchinetti F, Allais G, Nappi RE, et al. Migraine is a risk factor for hypertensive disorders in pregnancy: a prospective cohort study. *Cephalalgia*. 2009;29:286.

Granella F, Sances G, Zanferrari C, et al. Migraine without aura and reproductive life events. A clinical epidemiologic study in 1300 women. *Headache*. 1993;33:385.

Kudrow L. The relationship of headache frequency to hormone use in migraine. *Headache*. 1975;15:36.

Loder E, Rizzoli P, Golub J. Hormonal management of migraine associated with menses and the menopause: a clinical review. *Headache*. 2007;47:329.

LEVEL III

American College of Obstetricians and Gynecologists. *Use of hormonal contraception in women with coexisting medical conditions. ACOG Practice Bulletin 73*. Washington, DC: ACOG; 2006.

Brandes JL. The influence of estrogen on migraine: a systematic review. *JAMA*. 2006;295:1824.

Cairns BE. The influence of gender and sex steroids on craniofacial nociception. *Headache*. 2007;47:319.

Edelson RN. Menstrual migraine and other hormonal aspects of migraine. *Headache*. 1985;25:376.

Headache Classification Committee of the International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgia, and facial pain. *Cephalalgia*. 1988;8:1.

Loder EW. Menstrual migraine: pathophysiology, diagnosis, and impact. *Headache*. 2006;46(suppl 2):S55.

Silberstein SD. The role of sex hormones in headache. *Neurology*. 1992;42:37.

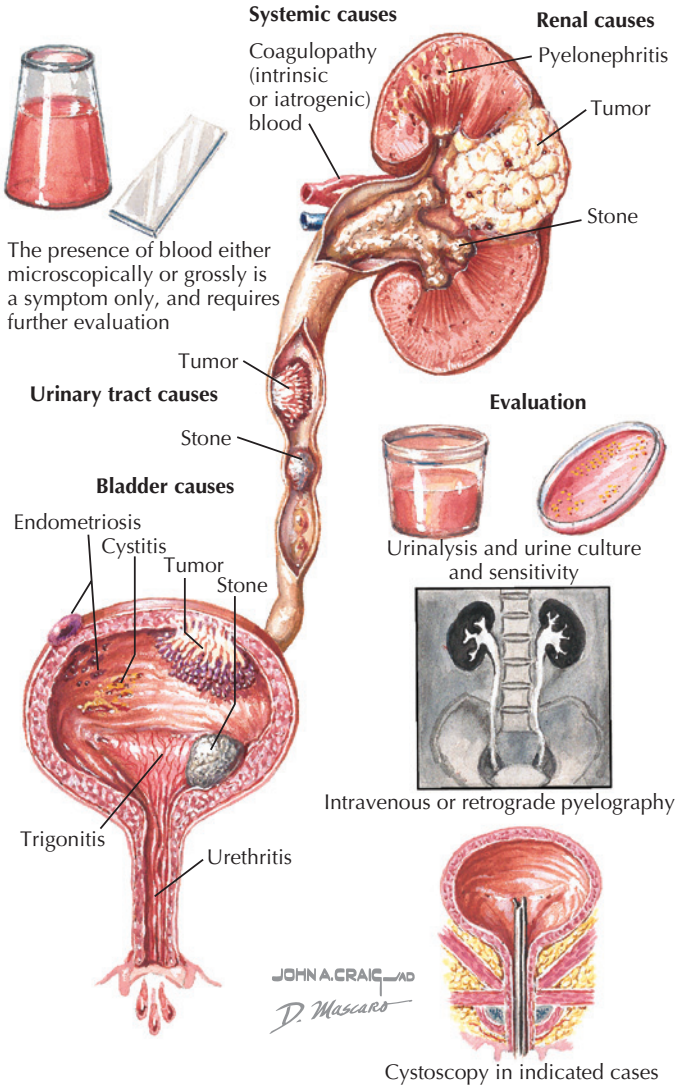


Figure 44.1 Causes and evaluation of hematuria

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP050 (Urinary Tract Infections).

Drug(s) of Choice

Drug choice is based on the cause.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: Failure to diagnose a malignancy in a timely manner. With large-volume bleeding, clotting with urethral obstruction is theoretically possible.
Expected Outcome: For most patients, the complete resolution of their symptoms occurs with appropriate treatment of the base problem.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy except that caused by the underlying condition. Computed tomographic urography should not be performed during pregnancy due to the higher radiation exposure involved versus conventional pyelography.
ICD-10-CM Codes: R31.9 (Hematuria, unspecified), R31.0 (Gross hematuria), and R31.2 (Other microscopic hematuria).

REFERENCES

LEVEL III

Cohen RA, Brown RS. Clinical practice. Microscopic hematuria. *N Engl J Med*. 2003;348:2330.
Feld LG, Waz WR, Perez LM, et al. Hematuria. An integrated medical and surgical approach. *Pediatr Clin North Am*. 1997;44:119.
Mahan JD, Turman MA, Mentser MI. Evaluation of hematuria, proteinuria, and hypertension in adolescents. *Pediatr Clin North Am*. 1997; 44:1573.
O'Connor OJ, McSweeney SE, Maher MM. Imaging of hematuria. *Radiol Clin North Am*. 2008;46:113.
Rodgers MA, Hempel S, Aho T, et al. Diagnostic tests used in the investigation of adult haemat [Epub 2006 Jul 28].
Silverman SG, Leyendecker JR, Amis ES Jr. What is the current role of CT urography and MR urography in the evaluation of the urinary tract? *Radiology*. 2009;250:309.
Tomson C, Porter T. Asymptomatic microscopic or dipstick haematuria in adults: which investigations or which patients? A review of the evidence. *BJU Int*. 2002;90:185.
Wai CY, Miller DS. Urinary bladder cancer. *Clin Obstet Gynecol*. 2002; 45:844.
Wollin T, Laroche B, Psooy K. Canadian guidelines for the management of asymptomatic microscopic hematuria in adults. *Can Urol Assoc J*. 2009;3:77.

45 HEMORRHOIDS

INTRODUCTION

Description: A hemorrhoid is a symptomatic dilation of the hemorrhoidal venous plexus that results in perianal swelling, itching, pain, hematochezia, and fecal soiling.
Prevalence: Present in 50%–80% of all Americans.
Predominant Age: Adult; more common after pregnancy.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Dilated rectal venous plexus with varying degrees of inflammation.
Risk Factors: Pregnancy, obesity, chronic cough, constipation, heavy lifting, sedentary work or lifestyle, hepatic disease, colon malignancy, portal hypertension, loss of muscle tone resulting from age, surgery, episiotomy, anal intercourse, or neurologic disease (multiple sclerosis).

SIGNS AND SYMPTOMS

- The development of symptoms prior to the age of 20 years is uncommon.
- Rectal bleeding
- Anal protrusion
- Anal itching and pain (especially with thrombosis or ulceration)
- Constipation and straining for bowel movement
- Rectal incontinence and soiling
- Hematochezia and stool mucus
- Anal fissure, infection, or ulceration
- Hemorrhoidal thrombosis

DIAGNOSTIC APPROACH

Differential Diagnosis

- Colon cancer
- Colon polyps
- Soiling caused by loss of anal tone (anal intercourse, multiple sclerosis, episiotomy)
- Pinworms
- Rectocele
- Fecal impaction
- Anal fissure or fistula

Associated Conditions: Liver disease, pregnancy, portal hypertension, and constipation.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated.
Special Tests: None indicated.
Diagnostic Procedures: History and physical examination.

Pathologic Findings

Enlarged hemorrhoidal veins with stasis and inflammation are common.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Stool softeners, bowel movement regulation, and topical medications.
Specific Measures: Surgical therapy is appropriate for those patients with debilitating symptoms or for whom medical therapy has failed (15%–20% of patients). Banding of internal hemorrhoids is better accepted by patients than traditional surgical therapy. Hemorrhoidal banding requires a minimum of equipment and is well suited to the office or outpatient surgical setting. Some aching is generally experienced for several days after hemorrhoid banding procedures. Sitz baths and topical analgesics such as witch hazel are generally sufficient. Injectable sclerosant solutions can also be used to treat symptomatic hemorrhoids.
Diet: Increased dietary fiber.
Activity: Avoid prolonged sitting, straining, or heavy lifting. Encourage physical fitness.
Patient Education: Reassurance, diet instruction.

Drug(s) of Choice

- Dietary fiber supplements.
- Stool softeners—docusate sodium (Colace, Dialose, Sof-Lax) 50–300 mg PO daily (larger doses are generally divided over the day).
- Topical analgesic sprays or ointments—benzocaine 20% spray or gel (Americaine, HurriCaine), dibucaine 1% ointment (Nupercainal).
- Antipruritics and antiinflammatory agents—hydrocortisone (Anusol-HC, Analpram-HC, Cortenema, Cortifoam, Epifoam, Proctofoam-HC), pramoxine 1% (Fleet rectal pads, Analpram HC), witch hazel 50% (Tucks pads or gel).
- Astringents—Preparation H.

Contraindications to Surgical Therapy: Acquired immunodeficiency syndrome (AIDS) or immunocompromise, anorectal fissures, bleeding diathesis or blood dyscrasia, inflammatory bowel disease, portal hypertension, rectal prolapse, undiagnosed anorectal tumor, undiagnosed rectal bleeding.
Precautions: See individual agents.
Interactions: Docusate sodium may potentiate the hepatotoxicity of other drugs; see individual agents.

Alternative Drugs

Flavanoids have been advocated, but a meta-analysis was unable to document efficacy. A small controlled trial suggested a benefit of topical nifedipine.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: Avoidance of constipation (bowel regularity); weight loss (if appropriate); physical fitness; avoidance of prolonged sitting, straining, or heavy lifting.
Possible Complications: Thrombosis, bleeding, secondary infection, ulceration, anemia, and rectal incontinence.
Expected Outcome: Resolution (spontaneous resolution or with medication), recurrence common.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. Hemorrhoids are extremely common as pregnancy progresses. Dietary prophylaxis and symptomatic therapy early reduce the severity of symptoms. At least partial resolution after delivery is expected.
ICD-10-CM Codes: K64.9 (Unspecified hemorrhoids), K64.4 (Residual hemorrhoidal skin tags), K64.8 (Other hemorrhoids), and K64.5 (Perianal venous thrombosis).

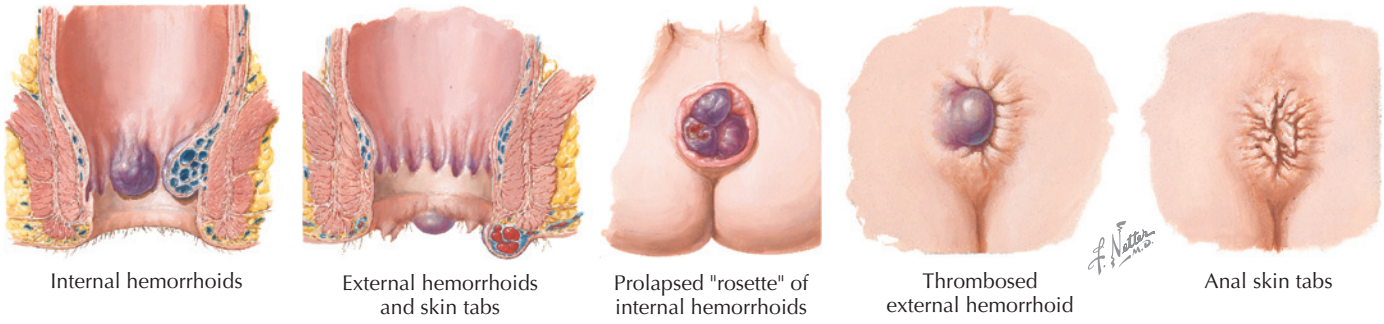


Figure 45.1 Types of hemorrhoids

REFERENCES

LEVEL II

Alonso-Coello P, Mills E, Heels-Ansdell D, et al. Fiber for the treatment of hemorrhoids complications: a systematic review and metaanalysis. *Am J Gastroenterol*. 2006;101:181.

Alonso-Coello P, Zhou Q, Martinez-Zapata MJ, et al. Meta-analysis of flavonoids for the treatment of haemorrhoids. *Br J Surg*. 2006;93:909.

Perrotti P, Antropoli C, Molino D, et al. Conservative treatment of acute thrombosed external hemorrhoids with topical nifedipine. *Dis Colon Rectum*. 2001;44:405.

Ripetti V, La Vaccara V, Greco S, et al. A randomized trial comparing stapled rectal mucosectomy versus open and semiclosed hemorrhoidectomy. *Dis Colon Rectum*. 2015;58:1083.

Simillis C, Thoukididou SN, Slesser AA, et al. Systematic review and network meta-analysis comparing clinical outcomes and effectiveness of surgical treatments for haemorrhoids. *Br J Surg*. 2015;102(13):1603–18.

Quijano CE, Abalos E. Conservative management of symptomatic and/or complicated haemorrhoids in pregnancy and the puerperium. *Cochrane Database Syst Rev*. 2005;(3):CD004077.

LEVEL III

Gearhart SL. Symptomatic hemorrhoids. *Adv Surg*. 2004;38:167.

Hollingshead JR, Phillips RK. Haemorrhoids: modern diagnosis and treatment. *Postgrad Med J*. 2015.

Nisar PJ, Scholefield JH. Managing haemorrhoids. *BMJ*. 2003;327(7419):847.

Parangi S, Levine D, Henry A, et al. Surgical gastrointestinal disorders during pregnancy. *Am J Surg*. 2007;193:223.

Riss S, Weiser FA, Schwameis K, et al. The prevalence of hemorrhoids in adults. *Int J Colorectal Dis*. 2012;27:215.

Rivadeneira DE, Steele SR, Ternent C, et al. Practice parameters for the management of hemorrhoids (revised 2010). *Dis Colon Rectum*. 2011;54:1059.

Wald A. Constipation, diarrhea, and symptomatic hemorrhoids during pregnancy. *Gastroenterol Clin North Am*. 2003;32:309, vii.

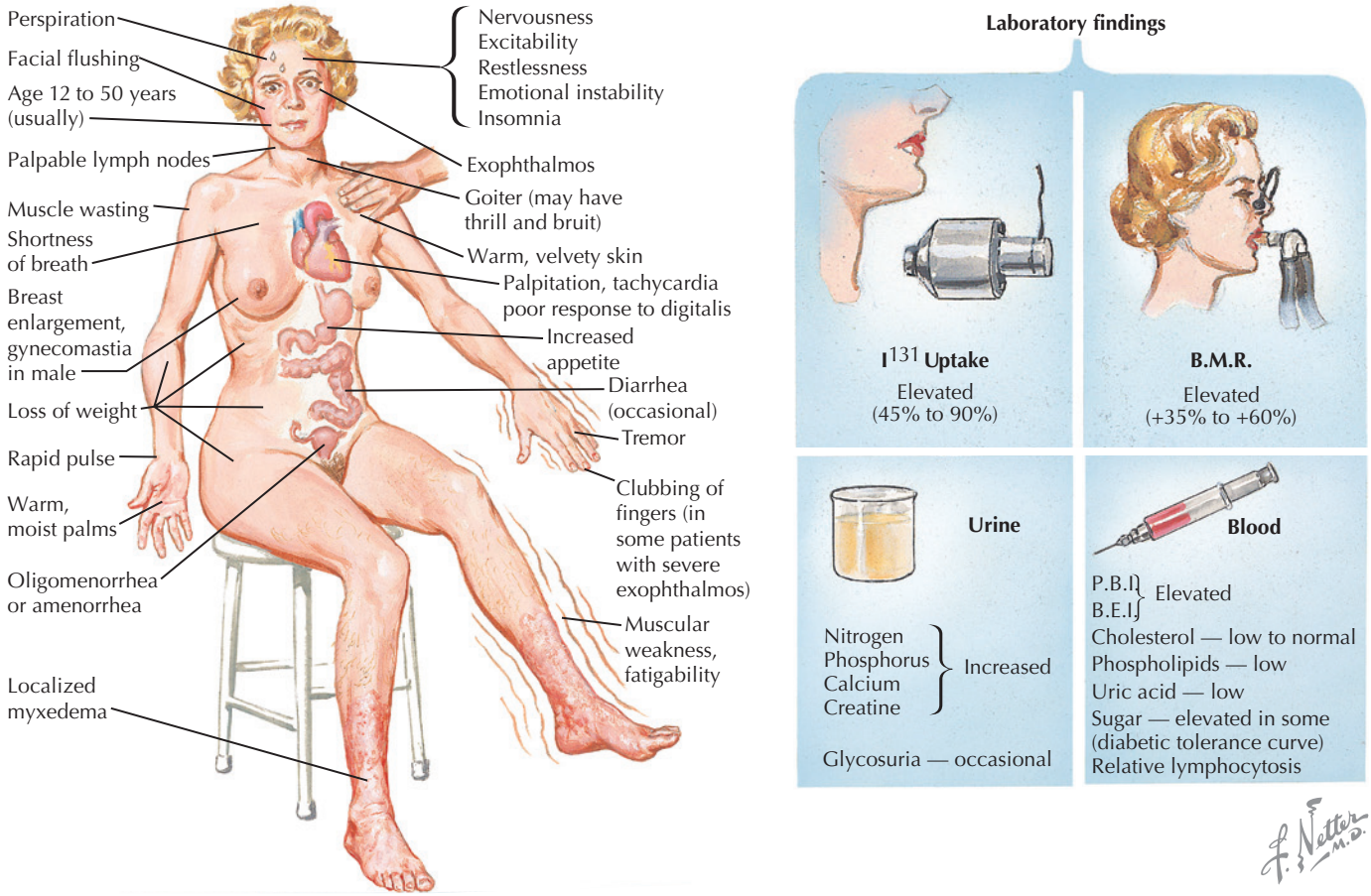


Figure 46.1 Symptoms and laboratory findings in hyperthyroidism

- Increased appetite (40%)
- Palpable goiter (90%)
- Tremor (65%)
- Exophthalmos (35%)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Physiologic changes of pregnancy
- Anxiety
- Malignancy
- Diabetes
- Pregnancy
- Hyperemesis gravidarum
- Menopause
- Pheochromocytoma
- Substance abuse (caffeine, diet preparations, cocaine)
- Struma ovarii

Associated Conditions: Other autoimmune diseases (Graves' disease).

Workup and Evaluation

Laboratory: Sensitive thyroid-stimulating hormone (below normal), T_3 radioimmunoassay (RIA; >200 ng/mL), T_4 radioimmunoassay (>160 nmol/L), free thyroxine index (>12).
Imaging: Radioiodine thyroid scan (diffuse uptake in Graves disease; focal uptake in nodular goiter).
Special Tests: None indicated.
Diagnostic Procedures: History, physical examination, and laboratory studies.

Pathologic Findings

Graves disease—diffuse hyperplasia; toxic nodules—discrete nodule formation.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and education about the need for continuing therapy, β-blockers for tachycardia symptoms or tremor.
Specific Measures: Antithyroid medication, therapeutic radioiodine, surgical reduction of thyroid, or excision of nodules.
Diet: No specific dietary changes indicated. Maintain adequate calories to avoid weight loss.
Activity: No restriction, as tolerated.
Patient Education: Education regarding the requirement for compliance with medication and follow-up. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP128 (Thyroid Disease).

Drug(s) of Choice

- For thyrotoxic crisis—propylthiouracil (PTU) 15–20 mg PO every 4 hours during the first day in addition to other therapies.
- Initial treatment—PTU 30–300 mg PO three times daily (no more than 300 mg/day during pregnancy), maintain at 25–300 mg PO two times daily; methimazole (Tapazole, MMI) 15–60 mg PO daily, maintain at 5–30 mg PO daily; radioiodine therapy: sodium iodine (I^{131}).
- Adjunctive therapy—propranolol (Inderal) 40–240 mg PO daily.

Contraindications: Radioiodine therapy is contraindicated in pregnancy (may cause fetal hypothyroidism or malformation). Propranolol is contraindicated in the presence of congestive heart failure, asthma, chronic bronchitis, hypoglycemia, and during pregnancy.
Precautions: Both PTU and methimazole may cause agranulocytosis, dermatitis, or hepatotoxicity.
Interactions: PTU may potentiate the actions of anticoagulants.

Alternative Drugs

Ipodate sodium (Oragrafin) 0.5 g PO four times daily (not used as primary therapy because of the possible induction of resistant hyperthyroidism).

FOLLOW-UP

Patient Monitoring: Normal health maintenance, undergo thyroid function test twice yearly. After radioiodine therapy, thyroid function should be checked at 6 and 12 weeks, 6 months, and then yearly.
Prevention/Avoidance: None.
Possible Complications: Hypothyroidism after medical therapy, vision change or loss caused by ophthalmopathy, pretibial myxedema or cardiac failure, muscle wasting and proximal muscle weakness. Surgical therapy—hypoparathyroidism, recurrent laryngeal nerve damage, hypothyroidism.
Expected Outcome: With early diagnosis and adequate treatment, a good outcome is expected.

MISCELLANEOUS

Pregnancy Considerations: Difficult to diagnose in pregnancy. Increased risk of spontaneous abortion, fetal growth restriction, preterm labor, and preeclampsia. Thyrotoxicosis often improves during pregnancy only to relapse postpartum—must be alert for this possibility. Any goiter is abnormal. Doses of PTU and methimazole must be reduced. Radioiodine therapy is contraindicated.
ICD-10-CM Codes: Based on cause, symptoms, and severity.

REFERENCES

LEVEL II

Luewan S, Chakkabut P, Tongsong T. Outcomes of pregnancy complicated with hyperthyroidism: a cohort study. *Arch Gynecol Obstet*. 2011;283:243.

LEVEL III

American College of Obstetricians and Gynecologists. Thyroid Disease in Pregnancy. ACOG Practice Bulletin 148. *Obstet Gynecol*. 2015;125:996.

Bahn Chair RS, Burch HB, Cooper DS, et al. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. *Thyroid*. 2011;21:593.

Casey BM, Leveno KJ. Thyroid disease in pregnancy. *Obstet Gynecol*. 2006;108:1283.

Cooper DS. Hyperthyroidism. *Lancet*. 2003;362(9382):459.

Cooper DS. Antithyroid drugs. *N Engl J Med*. 2005;352:905.

Fitzpatrick DL, Russell MA. Diagnosis and management of thyroid disease in pregnancy. *Obstet Gynecol Clin North Am*. 2010;37:173.

Krassas GE, Poppe K, Glinoer D. Thyroid function and human reproductive health. *Endocr Rev*. 2010;31:702.

Lazarus JH. Thyroid disorders associated with pregnancy: etiology, diagnosis, and management. *Treat Endocrinol*. 2005;4:31.

Mestman JH. Hyperthyroidism in pregnancy. *Best Pract Res Clin Endocrinol Metab*. 2004;18:267.

Nayak B, Burman K. Thyrotoxicosis and thyroid storm. *Endocrinol Metab Clin North Am*. 2006;35:663, vii.

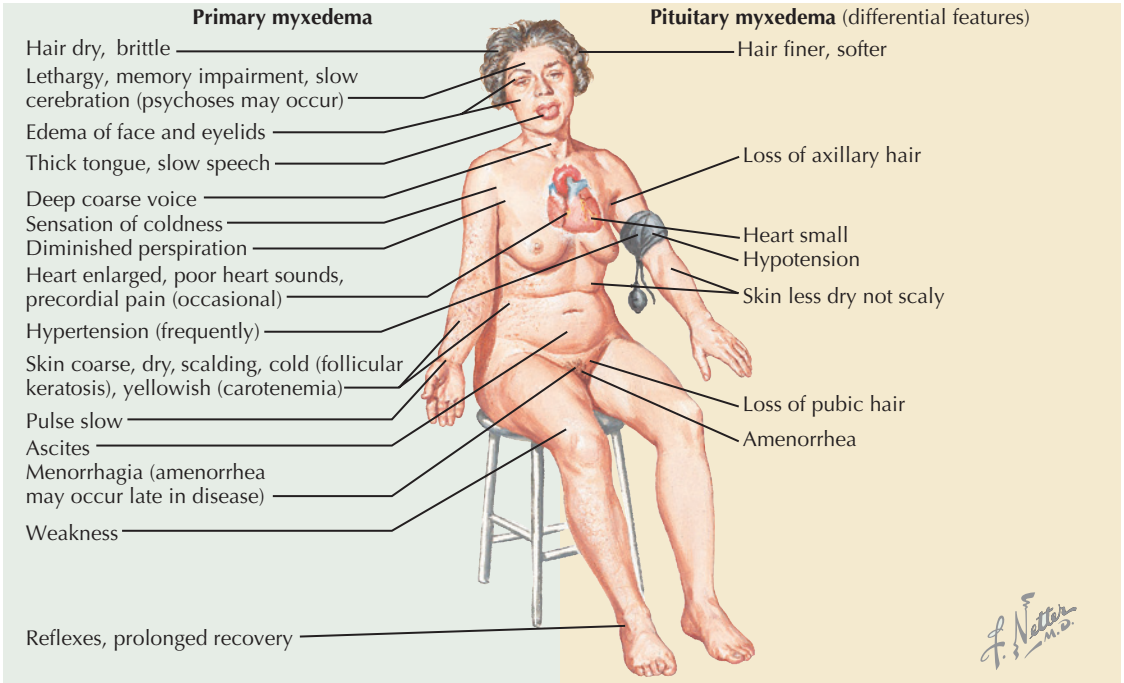
Redmond GP. Thyroid dysfunction and women's reproductive health. *Thyroid*. 2004;14(suppl 1):S5.

Ross DS. Radioiodine therapy for hyperthyroidism. *N Engl J Med*. 2011;364:542.

Schindler AE. Thyroid function and postmenopause. *Gynecol Endocrinol*. 2003;17:79.

Soldin OP. Thyroid function testing in pregnancy and thyroid disease: trimester-specific reference intervals. *Ther Drug Monit*. 2006;28:8.

Stagnaro-Green A, Abalovich M, Alexander E, et al. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. *Thyroid*. 2011;21:1081.



PBI and BEI; low – no rise after TSH	Low, but rise after TSH
I^{131}; 24-hour uptake low – no rise after TSH	Low, but rise after TSH
Cholesterol; elevated (usually)	Normal (usually)
Uric acid; elevated in males and postmenopausal females	Same
Urinary gonadotropins; positive	Absent
17-Ketosteroids; low	Lower

BEI, plasma butanol-extractable iodine; PBI, plasma protein-bound iodine; TSH, thyroid-stimulating hormone.

Figure 47.1 Signs and symptoms of hypothyroidism

- Menstrual disturbances (dysfunctional bleeding, amenorrhea, menorrhagia)
- Decreased memory, hearing loss
- Constipation
- Dry, coarse skin, brittle hair (hair loss is common)
- Periorbital puffiness, swelling of hands and feet
- Bradycardia, narrowed pulse pressure
- Anemia
- Cardiomegaly, pericardial effusion

DIAGNOSTIC APPROACH

Differential Diagnosis

- Depression
- Congestive heart failure
- Dementia
- Amyloidosis
- Nephrotic syndrome
- Chronic nephritis

Associated Conditions: Anemia, bipolar disorder, depression, diabetes mellitus, hypercholesterolemia, hyponatremia, idiopathic adrenocorticoid deficiency, mitral valve prolapse, myasthenia gravis, and vitiligo.

Workup and Evaluation

Laboratory: Sensitive TSH (>4 micro IU/mL), triiodothyronine (T_3) resin uptake (increased), thyroxine (T_4) radioimmunoassay (decreased), free thyroxine index (low). High serum human chorionic gonadotropin (hCG) levels during early pregnancy result in a reduction in the first trimester serum thyroid-stimulating hormone (TSH) concentrations.
Imaging: No imaging indicated.
Special Tests: None indicated.
Diagnostic Procedures: History, physical examination, and laboratory studies.

Pathologic Findings

The thyroid may be small and atrophic, normal, or enlarged.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, education about need for continuing therapy.
Specific Measures: Thyroid replacement mediation.
Diet: High-bulk diet to avoid constipation.
Activity: No restriction.
Patient Education: Education regarding need for compliance with medication and follow-up; American College of Obstetricians and Gynecologists Patient Education Pamphlet AP128 (Thyroid Disease).

Drug(s) of Choice

Levothyroxine (Synthroid, Levothroid) 50–100 mcg PO daily, increase by 25 mcg/day every 4–6 weeks until TSH is in normal range.
Contraindications: Adrenocorticoid insufficiency (uncorrected), thyrotoxic heart disease.

Precautions: The initial dose should be reduced in elderly patients.

Interactions: The dose of insulin, oral hypoglycemics, and anticoagulants may be required to be adjusted after thyroid therapy is initiated. Other possible interactions may be seen with oral contraceptives, estrogen, and cholestyramine. Ferrous sulfate may decrease the absorption of thyroid replacement medications.

FOLLOW-UP

Patient Monitoring: Thyroid status should be checked every 6 weeks until stable, then every 6 months. Because of the prevalence of hypothyroidism in older women, a baseline assessment should be obtained at the age of 45 years and periodic screening (biannually) is recommended in patients older than 60 years.

Prevention/Avoidance: None.

Possible Complications: Life threatening—coma (myxedema coma) and hypothermia. Treatment is with intravenous thyroid hormone replacement and steroid therapy. Supportive therapy (oxygen, assisted ventilation, fluid replacement) and intensive-care nursing may be indicated. Others—treatment-induced congestive heart failure, increased susceptibility to infection, megacolon, organic psychosis with paranoia, infertility and amenorrhea, or osteoporosis resulting from overtreatment.

Expected Outcome: With treatment, return to normal function. Relapse will occur if therapy is discontinued.

MISCELLANEOUS

Pregnancy Considerations: Medication may need to be adjusted. For those with hypothyroidism, TSH levels should be checked monthly during the first trimester, though evidence of altered outcomes is limited. TSH levels should be checked at 6 weeks postpartum. Women who develop postpartum thyroiditis have a 30% chance of developing hypothyroidism in the future. Any goiter during pregnancy is abnormal. During pregnancy, hypothyroidism is associated with an increased risk of preeclampsia and gestational hypertension, placental abruption, low birth weight and preterm delivery, and postpartum hemorrhage. The treatment of hypothyroidism in pregnancy is the same as in nonpregnant patient.

ICD-10-CM Codes: Based on cause, symptoms, and severity.

REFERENCES

LEVEL II

Breathnach FM, Donnelly J, Cooley SM, et al. Subclinical hypothyroidism as a risk factor for placental abruption: evidence from a low-risk primigravid population. *Aust N Z J Obstet Gynaecol*. 2013;53:553.

Cleary-Goldman J, Malone FD, Lambert-Messerlian G, et al. Maternal thyroid hypofunction and pregnancy outcome. *Obstet Gynecol*. 2008; 112:85.

Grozinsky-Glasberg S, Fraser A, Nahshoni E, et al. Thyroxine-triiodothyronine combination therapy versus thyroxine monotherapy for clinical hypothyroidism: meta-analysis of randomized controlled trials. *J Clin Endocrinol Metab*. 2006;91:2592.

Männistö T, Mendola P, Grewal J, et al. Thyroid diseases and adverse pregnancy outcomes in a contemporary US cohort. *J Clin Endocrinol Metab*. 2013;98:2725.

Schneuer FJ, Nassar N, Tasevski V, et al. Association and predictive accuracy of high TSH serum levels in first trimester and adverse pregnancy outcomes. *J Clin Endocrinol Metab*. 2012;97:3115.

LEVEL III

American College of Obstetricians and Gynecologists. Thyroid Disease in Pregnancy. ACOG Practice Bulletin 148. *Obstet Gynecol*. 2015;125:996.

Bach-Huynh TG, Jonklaas J. Thyroid medications during pregnancy. *Ther Drug Monit*. 2006;28:431.

Boelaert K, Franklyn JA. Thyroid hormone in health and disease. *J Endocrinol*. 2005;187:1.

Casey BM, Leveno KJ. Thyroid disease in pregnancy. *Obstet Gynecol*. 2006;108:1283.

Fitzpatrick DL, Russell MA. Diagnosis and management of thyroid disease in pregnancy. *Obstet Gynecol Clin North Am*. 2010;37:173.

Hypothyroidism in the pregnant woman. *Drug Ther Bull*. 2006;44:53.

Lao TT. Thyroid disorders in pregnancy. *Curr Opin Obstet Gynecol*. 2005; 17:123.

Lazarus JH. Thyroid disorders associated with pregnancy: etiology, diagnosis, and management. *Treat Endocrinol*. 2005;4:31.

Lazarus JH, Premawardhana LD. Screening for thyroid disease in pregnancy. *J Clin Pathol*. 2005;58:449.

Schindler AE. Thyroid function and postmenopause. *Gynecol Endocrinol*. 2003;17:79.

Soldin OP. Thyroid function testing in pregnancy and thyroid disease: trimester-specific reference intervals. *Ther Drug Monit*. 2006;28:8.

Stagnaro-Green A, Abalovich M, Alexander E, et al. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. *Thyroid*. 2011;21:1081.

Wartofsky L, Van Nostrand D, Burman KD. Overt and "subclinical" hypothyroidism in women. *Obstet Gynecol Surv*. 2006;61:535.

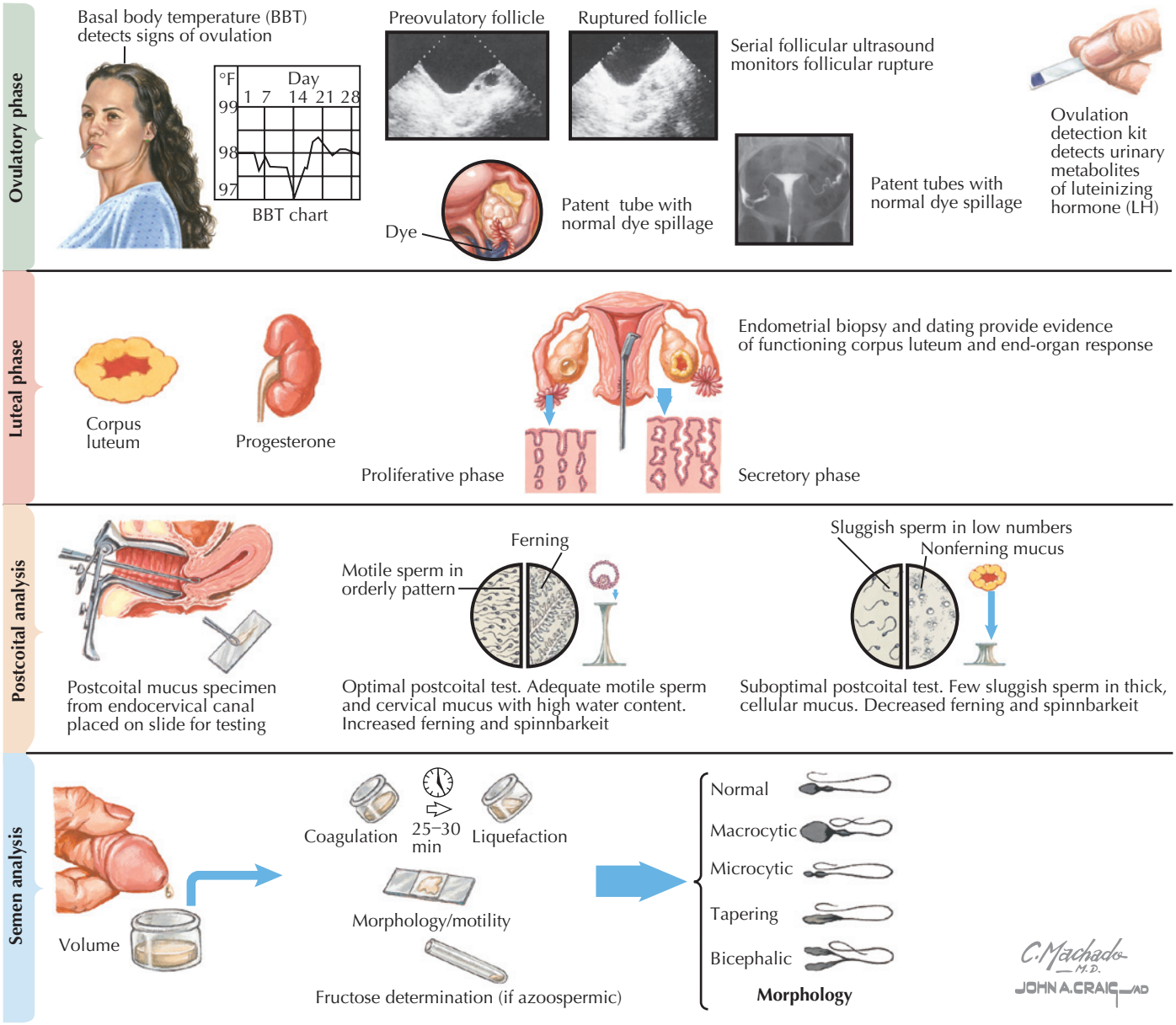


Figure 48.1 Infertility analysis

previously, regardless of the outcome of that pregnancy, are grouped in the secondary infertility group. Slightly more than one half of infertility patients fall into the primary group.

Objectives of Management: To establish the relevant cause or causes and develop strategies that result in conception and delivery. With improved understanding of the physiology of conception and a wide range of technologies that may be brought to bear to assist with procreation, 85% of "infertile" couples may be helped.

TACTICS

Relevant Pathophysiology: The male partner brings to the union sperm-laden semen, which is deposited in the vagina during intercourse. The average ejaculate has a volume of between 1 and 15 mL and contains more than 20 million spermatozoa. The survival of sperm in the female genital tract is considered to be at least 96 hours and may be as long as 8 days. However, it is probable that sperms are capable of fertilizing an egg for only the first 24–48 hours after ejaculation. The woman's gametic contribution, the oocyte, is released from the ovary during the mid-cycle process of ovulation, 14 days before the onset of menstruation, regardless of the total cycle length. Progesterone is produced by the luteinized follicle, producing a characteristic increase of between 0.5°F and 1°F in basal body temperature. The oocyte may be fertilized during the first 24 hours after ovulation only. Fertilization generally occurs in the distal portion of the fallopian tube. Pregnancy does not result unless the zygote passes into the uterine cavity at the correct time (3–5 days after fertilization), encounters a receptive endometrium, and can successfully implant and grow.

Strategies: To achieve pregnancy, three critical elements must be in place: (1) a sperm must be available, (2) an egg must be available, and (3) the sperm and egg must meet at a time and place conducive to fertilization. It is the investigation of these three elements that constitutes the evaluation of the infertile couple.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Booklet AP136 (Evaluating Infertility), AP137 (Treating Infertility).

IMPLEMENTATION

Special Considerations: While the evaluation of infertility proceeds, couples should be instructed to continue to attempt pregnancy through intercourse timed to the most fertile days of the cycle. Between one-third and one-half of all infertility problems may be diagnosed in the first phase of evaluation. The medical definition of infertility differs from that of fecundity, which refers to the physical ability of a woman to have children. Women with impaired fecundity include those who find it physically difficult or medically inadvisable to conceive and those who fail to conceive after 36 months of regular, unprotected intercourse. In short, fecundity deals with childbearing ability and fertility deals with childbearing performance. When dealing with infertility, establishing the diagnosis is not the problem; the problem is identifying the underlying pathophysiologic causes. Unlike most areas of medicine, the provider must deal with two patients at the same time because it is the couple that is infertile, not the man or woman. When the relative frequency of causes is considered, it is apparent that male and female factors are present in roughly equal proportion, with a small remainder that is idiopathic. This is important to consider during counseling. The distribution of causes is also helpful in designing a logical and efficient strategy for the evaluation of the infertile couple.

REFERENCES

LEVEL II

Declercq E, Luke B, Belanoff C, et al. Perinatal outcomes associated with assisted reproductive technology: the Massachusetts Outcomes Study of Assisted Reproductive Technologies (MOSART). *Fertil Steril*. 2015;103:888.

LEVEL III

Al-Inany H. Female infertility. *Clin Evid*. 2006;15:2465.

American College of Obstetricians and Gynecologists. Polycystic Ovary Syndrome. ACOG Practice Bulletin 41. *Obstet Gynecol*. 2009;114:936.

American College of Obstetricians and Gynecologists. *Perinatal Risks Associated with Assisted Reproductive Technology. ACOG Committee Opinion 324*. Washington, DC: ACOG; 2007.

Chandra A, Copen CE, Stephen EH. Infertility and impaired fecundity in the United States, 1982-2010: data from the National Survey of Family Growth. *Natl Health Stat Report*. 2013 Aug.

Dancet EA, D'Hooghe TM, van der Veen F, et al. "Patient-centered fertility treatment": what is required? *Fertil Steril*. 2014;101:924.

Grainger DA, Frazier LM, Rowland CA. Preconception care and treatment with assisted reproductive technologies. *Matern Child Health J*. 2006;10(suppl 5):S161.

Holzer H, Casper R, Tulandi T. A new era in ovulation induction. *Fertil Steril*. 2006;85:277.

Homburg R. Clomiphene citrate—End of an era? A mini-review. *Hum Reprod*. 2005;20:2043. [Epub 2005 May 5].

Keefe DL, Parry JP. New approaches to assisted reproductive technologies. *Semin Reprod Med*. 2005;23:301.

Messinis IE. Ovulation induction: a mini review. *Hum Reprod*. 2005;20:2688.

Practice Committee of American Society for Reproductive Medicine. Diagnostic evaluation of the infertile female: a committee opinion. *Fertil Steril*. 2012;98:302.

Practice Committee of the American Society for Reproductive Medicine. Aging and infertility in women. *Fertil Steril*. 2006;86(suppl 5):S248.

Practice Committee of the American Society for Reproductive Medicine. Optimal evaluation of the infertile female. *Fertil Steril*. 2006;86(suppl 5):S264.

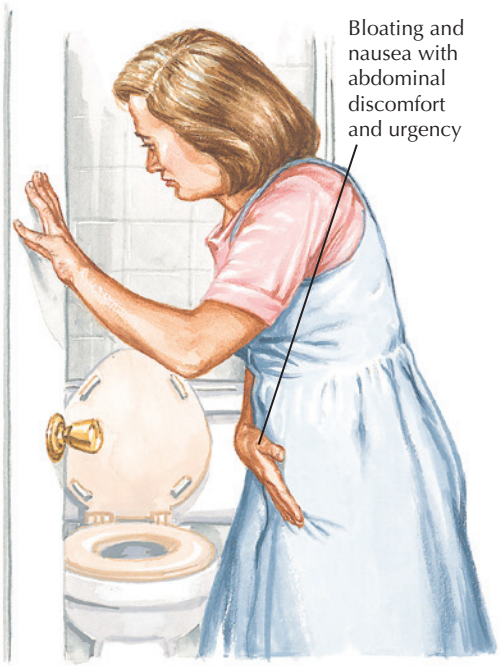
Rowe T. Fertility and a woman's age. *J Reprod Med*. 2006;51:157.

Slama R, Hansen OK, Ducot B, et al. Estimation of the frequency of involuntary infertility on a nation-wide basis. *Hum Reprod*. 2012;27:1489.

Urman B, Yakin K. Ovulatory disorders and infertility. *J Reprod Med*. 2006;51:267.

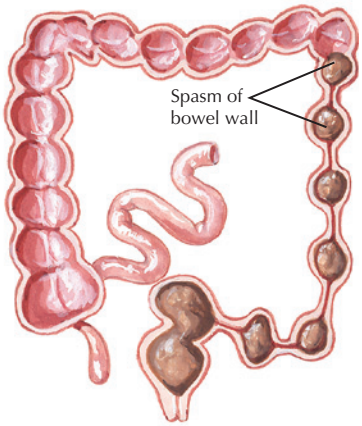
Van Voorhis BJ. Outcomes from assisted reproductive technology. *Obstet Gynecol*. 2006;107:183.

Van Voorhis BJ. Clinical practice. In vitro fertilization. *N Engl J Med*. 2007;356:379.

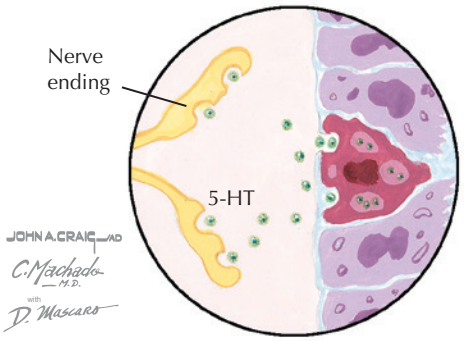


Irritable bowel syndrome is a syndrome of intermittent abdominal pain, diarrhea, and constipation related to hypermotility of the gut. Clinical variants include:

1) Spastic colitis characterized by chronic abdominal pain and constipation
2) Intermittent diarrhea that is usually painless
3) Combination of both with alternating diarrhea and constipation



Altered bowel wall sensitivity and motility result in IBS symptom complex



Actions of gut wall 5-hydroxytryptamine (5-HT) may underlie anomalies of motility

Rome III diagnostic criteria for irritable bowel syndrome	Alarm signs and symptoms that might suggest another diagnosis
Recurrent abdominal pain or discomfort** at least 3 days/month in the last 3 months associated with two or more of the following: 1. Improvement with defecation 2. Onset associated with a change in frequency of stool 3. Onset associated with a change in form (appearance) of stool	1) Anemia 2) Fever 3) Persistent diarrhea 4) Rectal bleeding 5) Severe constipation 6) Weight loss 7) Nocturnal GI symptoms 8) Family history of GI cancer, inflammatory bowel disease, or celiac disease 9) New onset of symptoms after age 50

*Criterion fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis
**"Discomfort" means an uncomfortable sensation not described as pain. In pathophysiology research and clinical trials, a pain/discomfort frequency of at least 2 days a week during screening evaluation is recommended for subject eligibility

Reprinted with permission from Rome Foundation

Figure 49.1 Irritable bowel syndrome

SIGNS AND SYMPTOMS

- Intermittent abdominal pain (often worse before menses)
- Bloating and nausea
- Alternating constipation and diarrhea

Symptoms are generally worse 1–1.5 hours after meals, with 50% of patients experiencing pain that lasts for hours or days; pain may last for weeks in up to 20% of patients. Pain is generally worse with high-fat meals, stress, depression, or menstruation and is better after bowel movements. There are four common clinical variants: (1) IBS with constipation characterized by chronic abdominal pain and constipation; (2) IBS with diarrhea, which is usually painless; (3) mixed IBS with alternating diarrhea and constipation (see box); and (4) unsubtyped IBS.

DIAGNOSTIC APPROACH

Differential Diagnosis

- Bacterial or parasitic infections
- Somatization
- Laxative abuse
- Iatrogenic diarrhea (dietary—eg, tea, coffee, food poisoning)
- Ulcerative colitis or Crohn disease
- Lactose intolerance
- Diverticular disease

Associated Conditions: High prevalence of psychopathologic conditions among IBS sufferers; a greater likelihood of somatization disorders, stress, anxiety disorders, depression, hysteria and hypochondriases, impaired sexual function, dysmenorrhea, dyspareunia, increased urinary frequency and urgency, and fibromyalgia symptoms.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated.
Special Tests: Flexible sigmoidoscopy or colonoscopy may be considered for selected patients.
Diagnostic Procedures: History and exclusion of other pathologic conditions.

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Because many of these patients have hysterical, depressive, and bipolar personality disorders, psychologic support is important. In some studies, placebo response rates are as high as 80%.
Specific Measures: Mild sedation with phenobarbital and tranquilizers may offer some relief, although long-term success is generally poor.
Diet: Bulk agents and increased dietary fiber; reduction in alcohol, fat, caffeine, sorbitol, and foods that increase flatulence. Both fasting and probiotic diets have been suggested with variable results.

Activity: No restriction.
Patient Education: Diet (increased fiber) and stress management. Biofeedback and relaxation techniques may be of some help.

Drug(s) of Choice

- Bulk-forming agents including guar gum; osmotic laxatives.
- 5-HT_3 receptor-blocking agents, (alosetron) may be used in patients with diarrhea. Melatonin has shown promise in some trials. Rifaximin 550 mg (Xifaxan) orally three times daily, a semisynthetic antibiotic based on rifamycin, has shown an 11% benefit over placebo.

Contraindications: Bowel obstruction or fecal impaction, known or suspected allergy to agent or any component.
Precautions: Empiric therapy may be initiated during the process of evaluation but should not be indefinitely continued without the establishment of a diagnosis. Bulk-forming agents must be taken with adequate fluid intake to prevent obstruction and provide optimal effects. Rectal bleeding, abdominal pain at night, or weight loss are not generally associated with IBS and should suggest further evaluation.

Alternative Drugs

- Linaclotide is a guanylate cyclase agonist that stimulates intestinal fluid secretion and transit and may be used for IBS with constipation when osmotic laxatives fail.
- Antispasmodics (eg, hyoscyamine 0.125–0.25 mg orally or sublingually three to four times daily) may be of help in selected patients.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: High-fiber diet, stress reduction.
Possible Complications: Continued dependency on others, adverse effects of work, school, or home functions. Relapses are common.
Expected Outcome: Transient response is often good with most therapies. Long-term relapse is common.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: K58.9 (Irritable bowel syndrome without diarrhea).

REFERENCES

LEVEL I

Chey WD, Lembo AJ, Lavins BJ, et al. Linaclotide for irritable bowel syndrome with constipation: a 26-week, randomized, double-blind, placebo-controlled trial to evaluate efficacy and safety. *Am J Gastroenterol*. 2012;107:1702.

Lu WZ, Gwee KA, Moochhalla S, et al. Melatonin improves bowel symptoms in female patients with irritable bowel syndrome: a double-blind placebo-controlled study. *Aliment Pharmacol Ther*. 2005;22:927.

Mulak A, Paradowski L. Effect of 5-HT1 agonist (sumatriptan) on anorectal function in irritable bowel syndrome patients. *World J Gastroenterol*. 2006;12:1591.

LEVEL II

American College of Obstetricians and Gynecologists. Lower Gastrointestinal Tract Disorders. *Clinical Updates in Women's Health Care*. 2015;XIV(5):1.

Blanchard EB, Lackner JM, Gusmano R, et al. Prediction of treatment outcome among patients with irritable bowel syndrome treated with group cognitive therapy. *Behav Res Ther*. 2006;44:317.

Chang L, Toner BB, Fukudo S, et al. Gender, age, society, culture, and the patient's perspective in the functional gastrointestinal disorders. *Gastroenterology*. 2006;130:1435.

Ford AC, Bercik P, Morgan DG, et al. Validation of the Rome III criteria for the diagnosis of irritable bowel syndrome in secondary care. *Gastroenterology*. 2013;145:1262.

Frissora CL, Koch KL. The role of gender and biological sex in irritable bowel syndrome. *Curr Gastroenterol Rep*. 2005;7(4):257.

Hershfield NB. Nongastrointestinal symptoms of irritable bowel syndrome: an office-based clinical survey. *Can J Gastroenterol*. 2005;19:231.

Kale-Pradhan PB, Wilhelm SM. Tegaserod for constipation-predominant irritable bowel syndrome. *Pharmacotherapy*. 2007;27:267.

LEVEL III

American College of Gastroenterology Task Force on Irritable Bowel Syndrome, Brandt LJ, Chey WD, et al. An evidence-based position statement on the management of irritable bowel syndrome. *Am J Gastroenterol*. 2009;104(suppl 1):S1.

Fukudo S. Sex and gender in irritable bowel syndrome. *J Gastroenterol*. 2006;41:608.

Longstreth GF, Thompson WG, Chey WD, et al. Functional bowel disorders. *Gastroenterology*. 2006;130:1480.

Saito YA, Camilleri M. Clinical application of pharmacogenetics in gastrointestinal diseases. *Expert Opin Pharmacother*. 2006;7:1857.

Spiller R. Clinical update: irritable bowel syndrome. *Lancet*. 2007;369 (9573):1586.

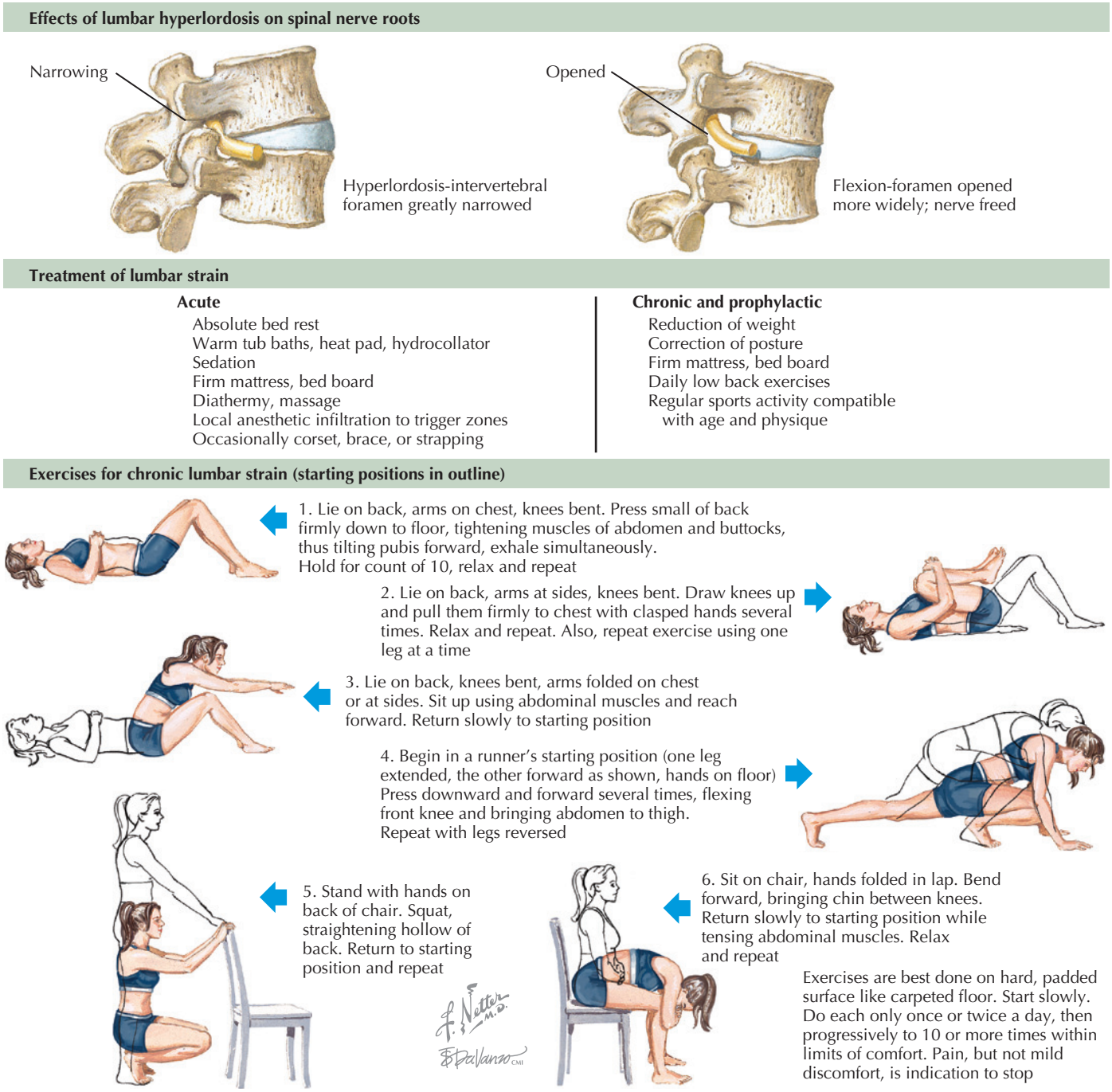


Figure 50.1 Lumbar strain in low back pain

Risk Factors: Obesity, poor posture, improper lifting, age, sedentary lifestyle, osteoporosis, psychosocial factors (secondary gain), and trauma. Smoking, low educational attainment, and female gender are also associated.

SIGNS AND SYMPTOMS

- Pain and discomfort between the level of the iliac spines and the lower ribs, generally sudden in onset after an injury or gradually over the subsequent 24 hours
- Radiation of pain to buttocks or posterior thighs (stopping at the knees); referred pain, not radicular; back pain greater than leg pain
- Pain aggravated by back motion, lifting, coughing, straining, bending, or twisting; relieved by rest
- Normal sensory, motor, and reflex findings; decreased range of motion

DIAGNOSTIC APPROACH

Differential Diagnosis

- Gynecologic disease (pregnancy, endometriosis, pelvic inflammatory disease)
- Gastrointestinal disease (duodenal ulcer, pancreatitis, irritable bowel syndrome, diverticulitis)
- Urinary tract disease (pyelonephritis, nephrolithiasis)

- Disc herniation or degenerative disease
- Osteoporotic fracture
- Fibromyalgia
- Spinal stenosis
- Spondylolisthesis
- Ankylosing spondylitis
- Arthritis (hip or back)
- Neoplasia (primary or metastatic)
- Fictitious complaint (somatization, secondary gain)

Associated Conditions: Chronic pain states (pelvic pain, headaches), radiculopathy, obesity, and psychosocial disease. Secondary gain often complicates both the diagnosis and treatment of low back pain. Warning signs of significant secondary gain include pending litigation or compensation, depression, hostility, and prolonged use of potent analgesics.

Workup and Evaluation

Laboratory: No evaluation indicated unless suggested by nonmechanical symptoms or atypical patterns of pain.

Imaging: Generally not required. When indicated (persistent pain, atypical symptoms)—magnetic resonance imaging (MRI) without contrast is generally considered the best initial test. Anteroposterior, lateral, and spot films of L_5–S_1 area may be of use in selected patients. Bone scan if tumor, trauma, or infection is suspected.

Special Tests: Computed tomography, magnetic resonance imaging, or myelography only for specific cause.

Diagnostic Procedures: History and physical examination (with special attention to the back and hips).

Pathologic Findings

Based on the cause

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Bed rest, short-term analgesics or anti-inflammatory agents, massage, or manipulation.

Specific Measures: Muscle relaxants, Williams' flexion exercises, physical therapy, topical low-level continuous heat therapy, transcutaneous electrical nerve stimulation (TENS).

Diet: No specific dietary changes indicated. Weight reduction, if appropriate.

Activity: Restricted activity for 3–6 weeks, then a gradual return to normal activity as tolerated. Patients should begin Williams flexion exercises as prevention for future injuries.

Patient Education: Posture and activity counseling, home back exercises. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP115 (Easing Back Pain During Pregnancy).

Drug(s) of Choice

- Nonsteroidal antiinflammatory drugs, muscle relaxants—cyclobenzaprine (Flexeril) 10 mg PO three times daily, diazepam (Valium) 5–10 mg PO two times daily.

Contraindications: See individual agents. Aspirin-sensitive asthma for most agents.

Precautions: See individual agents. Ulcer or renal disease for most agents.

Interactions: See individual agents.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.

Prevention/Avoidance: Muscle-strengthening exercises, care in lifting, maintenance of reasonable weight. Avoid tasks that aggravate (heavy lifting, bending, twisting, sudden movements). Weight reduction, if appropriate.

Possible Complications: Chronic low back pain, pain medication dependence, and dependency state resulting from secondary gain.

Expected Outcome: Gradual improvement with analgesics, muscle relaxants, massage, and exercise (1–6 weeks).

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, although pregnancy (and the postural changes brought about by it) may worsen existing low back pain. Some relief is gained when the fetus descends into the pelvis in the last days of the gestation, but the sudden return to upright and the constant bending to care for a newborn make this improvement short lived.

ICD-10-CM Codes: Based on the cause.

REFERENCES

LEVEL I

Delitto A, Piva SR, Moore CG, et al. Surgery versus nonsurgical treatment of lumbar spinal stenosis: a randomized trial. *Ann Intern Med*. 2015;162:465.

Friedman BW, Dym AA, Davitt M, et al. Naproxen with cyclobenzaprine, oxycodone/acetaminophen, or placebo for treating acute low back pain: a randomized clinical trial. *JAMA*. 2015;314:1572.

Gale GD, Rothbart PJ, Li Y. Infrared therapy for chronic low back pain: a randomized, controlled trial. *Pain Res Manag*. 2006;11:193.

Katz J, Pennella-Vaughan J, Hetzel RD, et al. A randomized, placebo-controlled trial of bupropion sustained release in chronic low back pain. *J Pain*. 2005;6:656.

Linde K, Witt CM, Streng A, et al. The impact of patient expectations on outcomes in four randomized controlled trials of acupuncture in patients with chronic pain. *Pain*. 2007;128:264.

Mayer JM, Ralph L, Look M, et al. Treating acute low back pain with continuous low-level heat wrap therapy and/or exercise: a randomized controlled trial. *Spine J*. 2005;5:395.

Tavafian SS, Jamshidi A, Mohammad K, et al. Low back pain education and short term quality of life: a randomized trial. *BMC Musculoskelet Disord*. 2007;8:21.

Warke K, Al-Smadi J, Baxter D, et al. Efficacy of transcutaneous electrical nerve stimulation (TENS) for chronic low-back pain in a multiple sclerosis population: a randomized, placebo-controlled clinical trial. *Clin J Pain*. 2006;22:812.

Ximenes A, Robles M, Sands G, et al. Valdecoxib is as efficacious as diclofenac in the treatment of acute low back pain. *Clin J Pain*. 2007;23:244.

LEVEL II

Centers for Disease Control and Prevention. *National Ambulatory Medical Care Survey: 2010 Summary Tables*. <http://www.cdc.gov/nchs/data/ahcd/namcs_summary/2010_namcs_web_tables.pdf> Accessed 14.12.15.

Demoulin C, Crielaard JM, Vanderthommen M. Spinal muscle evaluation in healthy individuals and low-back-pain patients: a literature review. *Joint Bone Spine*. 2007;74:9-13.

Farasyn A, Meeusen R. Validity of the new Backache Index (BAI) in patients with low back pain. *Spine J*. 2006;6:565.

Jarvik JG, Gold LS, Comstock BA, et al. Association of early imaging for back pain with clinical outcomes in older adults. *JAMA*. 2015;313:1143.

Katz JN. Lumbar disc disorders and low-back pain: socioeconomic factors and consequences. *J Bone Joint Surg Am*. 2006;88(suppl 2):21.

Rivero-Arias O, Gray A, Frost H, et al. Cost-utility analysis of physiotherapy treatment compared with physiotherapy advice in low back pain. *Spine*. 2006;31:1381.

LEVEL III

Chou R. In the clinic. Low back pain. *Ann Intern Med*. 2014;160:ITC6.

Chou R, Qaseem A, Owens DK, et al. Diagnostic imaging for low back pain: advice for high-value health care from the American College of Physicians. *Ann Intern Med*. 2011;154:181.

Deyo RA, Jarvik JG, Chou R. Low back pain in primary care. *BMJ*. 2014; 349:g4266.

Henschke N, Maher CG, Ostelo RW, et al. Red flags to screen for malignancy in patients with low-back pain. *Cochrane Database Syst Rev*. 2013;(2):CD008686.

Shelerud RA. Epidemiology of occupational low back pain. *Clin Occup Environ Med*. 2006;5:501, v.

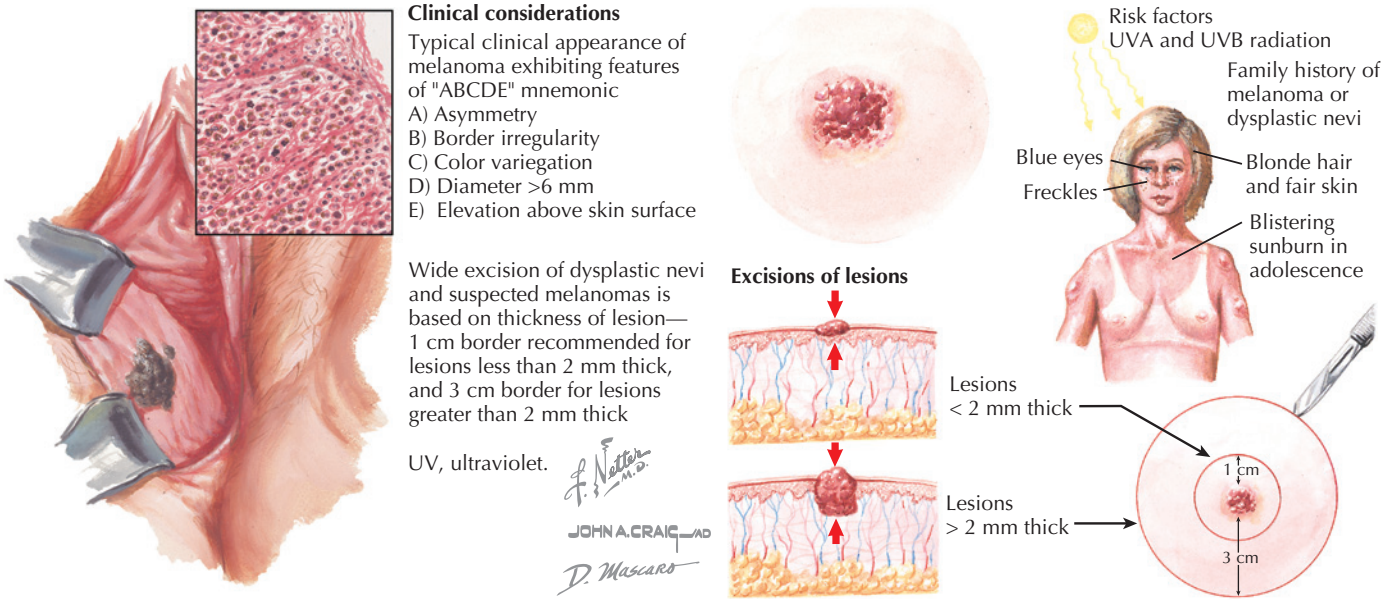


Figure 51.1 Clinical considerations and excisions of lesions in melanoma

FOLLOW-UP

Patient Monitoring: Frequent (every 3–6 months) total body inspection for abnormal or changing nevi. Annual chest radiograph (6% of recurrences diagnosed this way). Weekly self-examination.

Prevention/Avoidance: Avoidance of excessive sun exposure, especially blistering sunburn. Use of sunscreen.

Possible Complications: Disease progression or spread, cosmetic damage by excision.

Expected Outcome: Prognosis is based on staging—5-year survival if no local or distant spread (70%); less than 0.85-mm thick (95%–100%); lymphatic involvement (5%).

MISCELLANEOUS

Pregnancy Considerations: Although rarely observed in pregnancy, melanoma is considered to be exacerbated by this condition. Although any malignant metastasis to the fetus is rare, melanomas represent up to one-third of all malignancies found. Melanoma is one of the few malignancies that spreads to the placenta, and metastatic melanoma is a threat to both the fetus and mother. If a woman has had melanoma, it is recommended that she wait for 2 or more years before planning a pregnancy.

ICD-10-CM Codes: Based on location and severity of the disease.

REFERENCES

LEVEL I

Larkin J, Chiarion-Sileni V, Gonzalez R, et al. Combined nivolumab and ipilimumab or monotherapy in untreated melanoma. *N Engl J Med*. 2015;373:23.

LEVEL II

Ackerman A, Klein O, McDermott DF, et al. Outcomes of patients with metastatic melanoma treated with immunotherapy prior to or after BRAF inhibitors. *Cancer*. 2014;120:1695.

Byrom L, Olsen CM, Knight L, et al. Does pregnancy after a diagnosis of melanoma affect prognosis? Systematic review and meta-analysis. *Dermatol Surg*. 2015;41:875.

Giblin AV, Thomas JM. Incidence, mortality and survival in cutaneous melanoma. *J Plast Reconstr Aesthet Surg*. 2007;60:32.

Gokaslan H, Sismanoglu A, Pekin T, et al. Primary malignant melanoma of the vagina: a case report and review of the current treatment options. *Eur J Obstet Gynecol Reprod Biol*. 2005;121:243.

Lens M. Cutaneous melanoma: interferon alpha adjuvant therapy for patients at high risk for recurrent disease. *Dermatol Ther*. 2006;19:9.

LEVEL III

American Cancer Society. *What are the key statistics about melanoma skin cancer?* Available at: <http://www.cancer.org/cancer/skincancer-melanoma/detailedguide/melanoma-skin-cancer-key-statistics>, Accessed 14.12.15.

Bishop JN, Harland M, Bishop DT. The genetics of melanoma. *Br J Hosp Med (Lond)*. 2006;67:299.

Bishop JN, Harland M, Randerson-Moor J, et al. Management of familial melanoma. *Lancet Oncol*. 2007;8:46.

Driscoll MS, Grant-Kels JM. Nevi and melanoma in pregnancy. *Dermatol Clin*. 2006;24:199, vi.

Menzies SW. Cutaneous melanoma: making a clinical diagnosis, present and future. *Dermatol Ther*. 2006;19:32.

Niendorf KB, Tsao H. Cutaneous melanoma: family screening and genetic testing. *Dermatol Ther*. 2006;19:1.

Nobbenhuis MA, Lalondrelle S, Larkin J, et al. Management of melanomas of the gynaecological tract. *Curr Opin Oncol*. 2014;26:508.

Patrick RJ, Fenske NA, Messina JL. Primary mucosal melanoma. *J Am Acad Dermatol*. 2007;56:828.

Rouzier R, Haddad B, Atallah D, et al. Surgery for vulvar cancer. *Clin Obstet Gynecol*. 2005;48:869.

Siegel R, Ma J, Zou Z, et al. Cancer statistics, 2014. *CA Cancer J Clin*. 2014;64:9.

Tarhini AA, Agarwala SS. Cutaneous melanoma: available therapy for metastatic disease. *Dermatol Ther*. 2006;19:19.

U.S. Preventive Services Task Force. Screening for skin cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2009;150:188.

Wiggins CL, Berwick M, Bishop JA. Malignant melanoma in pregnancy. *Obstet Gynecol Clin North Am*. 2005;32:559.

52 MYOFASCIAL SYNDROMES

INTRODUCTION

Description: Myofascial syndrome is characterized by muscular and fascial pain and is associated with localized tenderness and pain referred to sites that are often remote. Myofascial pain syndromes and fibromyalgia frequently demonstrate trigger-point involvement. These syndromes may present as chronic lower abdominal or pelvic pain that is easily confused with gynecologic causes.
Prevalence: Three percent of the population.
Predominant Age: Sedentary middle-aged women.
Genetics: No genetic pattern. More common in women (80%–90%) than in men. Several studies indicate that women who have a family member with fibromyalgia are more likely to have fibromyalgia themselves.

ETIOLOGY AND PATHOGENESIS

Causes: Abnormal spasm of a small portion of a muscle resulting in an extremely taut, tender band of muscle (trigger point). Compression of this site elicits local tenderness and often reproduces the referred pain. Most trigger points are located at or near areas of moving or sliding muscle surfaces, although they are not limited to these locations. Genetics and physical and emotional stressors are possible contributory factors to the development of the illness.
Risk Factors: Stress, sleep deprivation, trauma, depression, and weather changes.

SIGNS AND SYMPTOMS

- Chronic pain referred to remote sites.
- "Trigger points" (hypersensitive areas overlying muscles that induce spasm and pain) that induce or reproduce the patient's symptoms. Trigger points may be found throughout the body but are most common in the abdominal wall, back, and pelvic floor when pelvic pain is the symptom. Most patients have 11 or more trigger points.
- Pain is worse in the morning, with stress or weather change, after nonrestorative sleep. Pain is better with activity, stress reduction, and rest.
- Two criteria established by the American College of Rheumatology: a history of widespread pain lasting more than 3 months and the presence of tender points.
- Urinary tract symptoms (frequency, urgency, incontinence, nocturia, dysuria, sensation of incomplete emptying, bladder pain)
- Vulvovaginal discomfort/dyspareunia

DIAGNOSTIC APPROACH

Differential Diagnosis

- Somatization
- Sympathetic dystrophy
- Muscle strain or sprain
- Polymyalgia rheumatica
- Temporal arteritis
- Irritable bowel syndrome (IBS)
- Low back strain or sprain
- Interstitial cystitis

Associated Conditions: Chronic pain syndromes, irritable bowel syndrome, depression, sleep abnormalities reduced physical endurance, and social withdrawal.

Workup and Evaluation

Laboratory: No evaluation indicated. Screening with an erythrocyte sedimentation rate (normal) may be helpful. Others based on diagnosis being considered.
Imaging: No imaging indicated.
Special Tests: None indicated.
Diagnostic Procedures: History and physical examination generally sufficient. Palpation of the anterior abdominal wall may demonstrate thickening or tenderness that is suggestive of the diagnosis.

Pathologic Findings

A trigger point is often felt as an extremely taut band of muscle (normal muscle should not be tender to firm compression and does not contain taut bands).

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, analgesics, heat (low-level continuous topical heat [ThermaCare], hot packs, ultrasound therapy), and general conditioning exercises.
Specific Measures: Transcutaneous electrical nerve stimulation (TENS), trigger-point injections. A 22-gauge needle is selected for trigger-point injections because of the amount of movement within the tissue that is often required to probe for and block the taut muscle bundle. Thinner needles may bend or break under these circumstances. The length of the needle should be sufficient to allow the entire trigger point to be reached without indenting the skin or having the hub at the skin surface. Superficial trigger points may also be treated with a "spray-and-stretch" technique (the area overlying the trigger point is sprayed with a coolant or freezing spray [eg, ethyl chloride] for several seconds, and the muscle is forcibly stretched by passive extension). Hypnosis and/or acupuncture may also be used.
Diet: No specific dietary changes indicated.
Activity: No restriction except that caused by pain. Directed pelvic floor physical therapy has shown good effect and for many represents first-line therapy.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP099 (Pelvic Pain).

Drug(s) of Choice

- Nonsteroidal antiinflammatory drugs (NSAIDs).
- Sleep aids—flurazepam (Dalmane) 15 mg PO every night, triazolam (Halcion) 0.125 mg PO every night, amitriptyline (Elavil) 20–25 mg PO every night.
- Muscle relaxants—cyclobenzaprine (Flexeril) 10 mg PO three times a day.
- Local anesthetic for injection (generally 1% lidocaine without epinephrine, limit injection to approximately 10 mL/site).
- Adjuvant therapy with gabapentin, pregabalin, and 5-HT_3 receptor-blocking agents gives good results for selected patients.

Contraindications: See individual agents. Trigger-point injections should not be attempted when infection is present near the planned site.
Precautions: Watch for side effects or dependence.

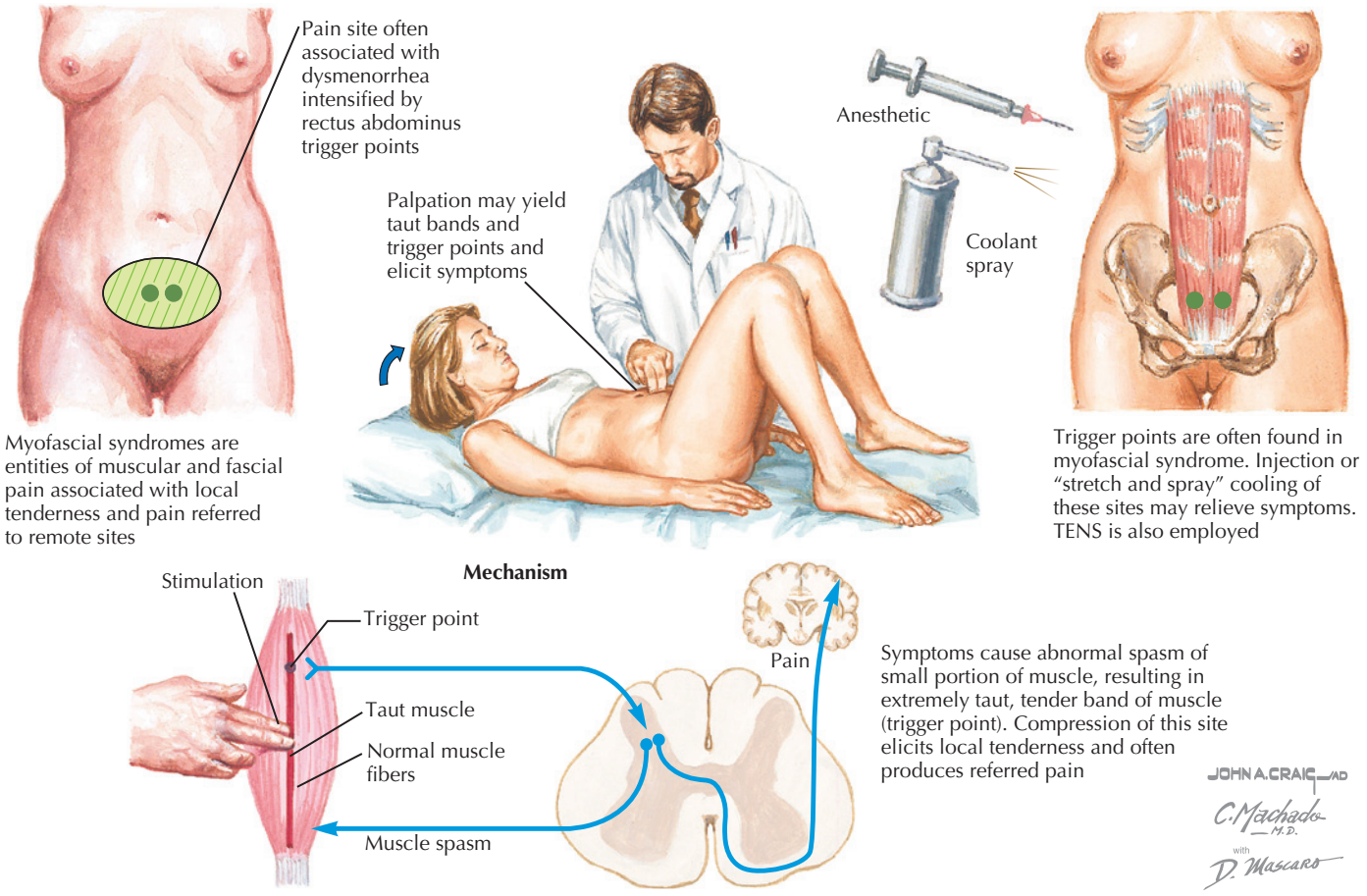


Figure 52.1 Myofascial syndromes

Alternative Drugs

- Trazodone (Desyrel) 50 mg PO every night.
- Botulinum toxin type A injections instead of local anesthetics.

FOLLOW-UP

Patient Monitoring: Normal health maintenance, monitor for medication side effects.

Prevention/Avoidance: Adequate restorative sleep, stress reduction, physical fitness, and activity.

Possible Complications: Depression, reduced physical endurance, social withdrawal, chronic pain, work compromise or absence. The most common complications of trigger-point injection are local ecchymoses and anesthetic agent toxicity. The latter is best avoided by strictly limiting the total dose given. Infection is rare if the skin is first disinfected and areas of frank infection are avoided.

Expected Outcome: Improvement with medical therapy is generally seen in 2–4 weeks. With the identification of a specific trigger point and the use of trigger-point injection, results should be good. Response to trigger-point injection routinely persists longer than the duration of action of the anesthetic agent used. This frequently extends to permanent relief after only one or two injections.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. Pregnancy may limit some therapies. Pregnancy is generally not a contraindication to trigger-point injections.

ICD-10-CM Codes: R10.2 (Pelvic and perineal pain), M79.1 (myofascial pain), M60.9 (myocitis), and G89.29 (Other chronic pain). Others based on type and location.

REFERENCES

LEVEL I

Gobel H, Heinze A, Reichel G, et al; Dysport Myofascial Pain Study Group. Efficacy and safety of a single botulinum type A toxin complex treatment (Dysport) for the relief of upper back myofascial pain syndrome: results from a randomized double-blind placebo-controlled multicentre study. *Pain*. 2006;125:82.

Graboski CL, Gray DS, Burnham RS. Botulinum toxin A versus bupivacaine trigger point injections for the treatment of myofascial pain syndrome: a randomised double blind crossover study. *Pain*. 2005;118:170.

Kamanli A, Kaya A, Ardicoglu O, et al. Comparison of lidocaine injection, botulinum toxin injection, and dry needling to trigger points in myofascial pain syndrome. *Rheumatol Int*. 2005;25:604.

LEVEL III

American College of Obstetricians and Gynecologists. Chronic pelvic pain. ACOG Practice Bulletin 51. *Obstet Gynecol*. 2004;103:589.

Bassaly R, Tidwell N, Bertolino S, et al. Myofascial pain and pelvic floor dysfunction in patients with interstitial cystitis. *Int Urogynecol J*. 2011;22:413.

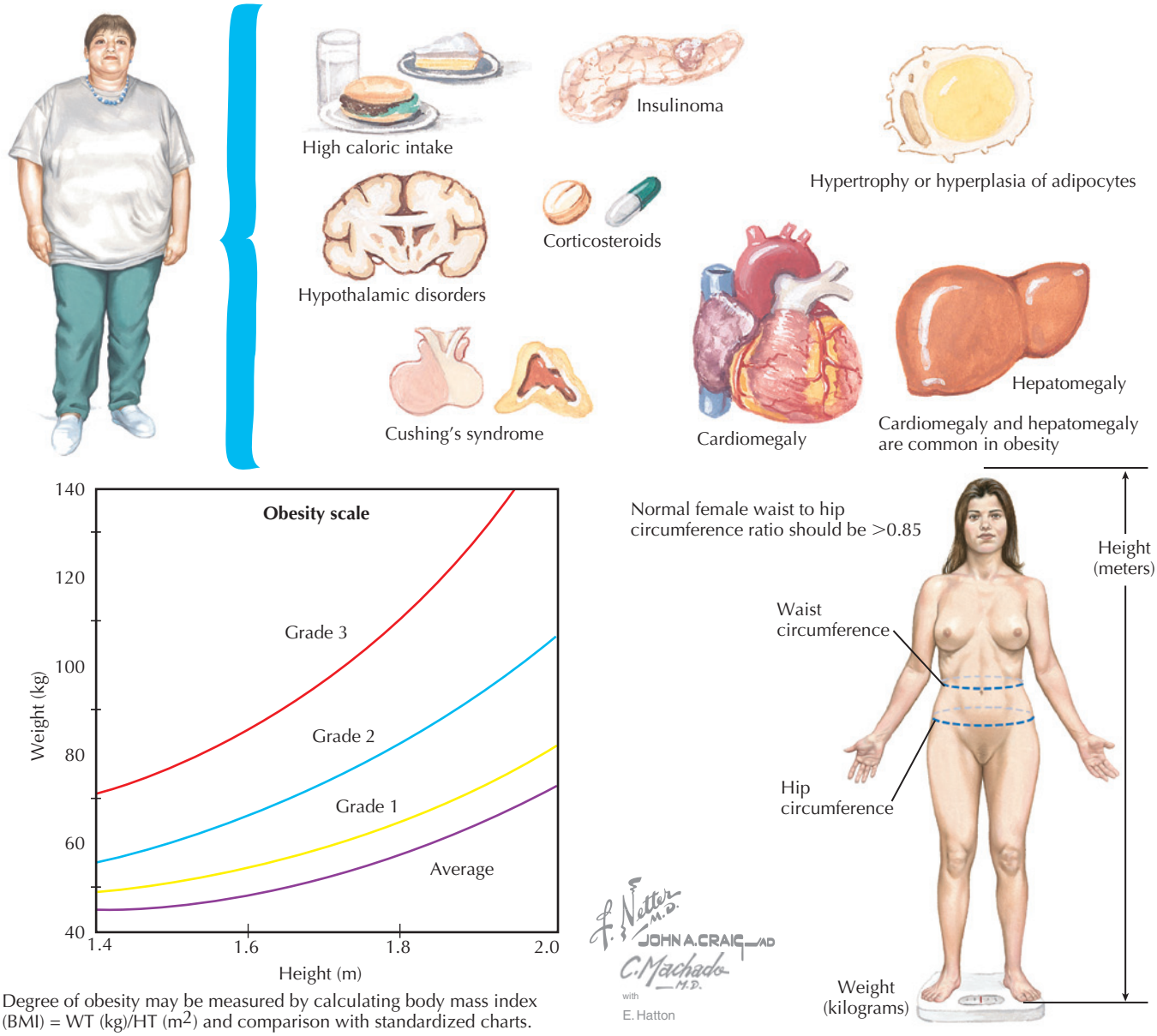
Borg-Stein J. Treatment of fibromyalgia, myofascial pain, and related disorders. *Phys Med Rehabil Clin N Am*. 2006;17:491, viii.

Cheong YC, Smotra G, Williams AC. Non-surgical interventions for the management of chronic pelvic pain. *Cochrane Database Syst Rev*. 2014;(3):CD008797.

Moldwin RM, Fariello JY. Myofascial trigger points of the pelvic floor: associations with urological pain syndromes and treatment strategies including injection therapy. *Curr Urol Rep*. 2013;14:409.

Soares A, Andriolo RB, Atallah AN, et al. Botulinum toxin for myofascial pain syndromes in adults. *Cochrane Database Syst Rev*. 2014;(7):CD007533.

Spitznagle TM, Robinson CM. Myofascial pelvic pain. *Obstet Gynecol Clin North Am*. 2014;41:409.



Degree of obesity may be measured by calculating body mass index (BMI) = WT (kg)/HT (m^2) and comparison with standardized charts.

Figure 53.1 Obesity

Alternative Drugs

Phenylpropanolamine (over-the-counter preparations)

FOLLOW-UP

Patient Monitoring: Long-term follow-up, screening for complications of drug therapy or obesity itself.

Prevention/Avoidance: Diet and exercise counseling (especially important for adolescents and children).

Possible Complications: Significant increase in risk for cardiovascular disease, diabetes mellitus, hypertension, hyperlipidemia, cholelithiasis, cholecystitis, osteoarthritis, gout, thromboembolism, and sleep apnea.

Expected Outcome: Long-term maintenance is difficult, and relapses are common. Individual motivation is the best predictor of success.

MISCELLANEOUS

Pregnancy Considerations: Obesity complicates pregnancy, and pregnancy is often the time of onset of obesity for many women. Weight gain should be monitored and adjusted downward for patients who are obese. Orlistat is a Category B medication (see others for specific pregnancy category).

ICD-10-CM Codes: E66.9 (Obesity, unspecified) and E66.01 [Morbid (severe) obesity due to excess calories].

REFERENCES

LEVEL I

Ebbeling CB, Leidig MM, Feldman HA, et al. Effects of a low-glycemic load vs low-fat diet in obese young adults: a randomized trial. *JAMA*. 2007;297:2092.

Gardner CD, Kiazand A, Alhassan S, et al. Comparison of the Atkins, Zone, Ornish, and LEARN diets for change in weight and related risk factors among overweight premenopausal women: the A TO Z Weight Loss Study: a randomized trial. *JAMA*. 2007;297:969.

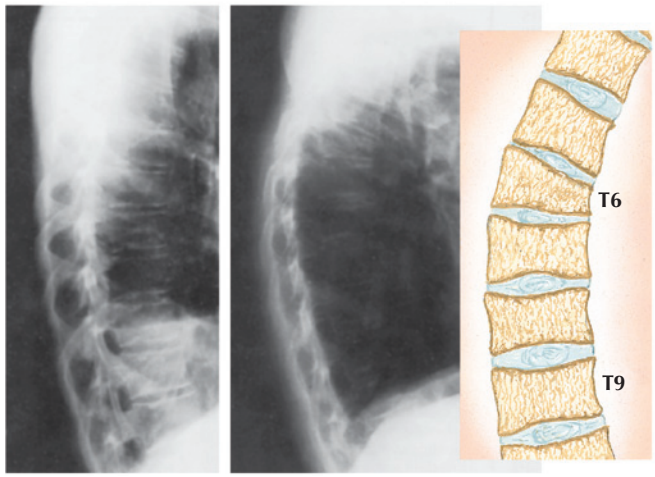
Mathus-Vliegen EM, de Wit LT. Health-related quality of life after gastric banding. *Br J Surg*. 2007;94:457.
Smith SR, Weissman NJ, Anderson CM, et al. Multicenter, placebo-controlled trial of lorcaserin for weight management. *N Engl J Med*. 2010;363:245.

LEVEL II

Alexander CI, Liston WA. Operating on the obese woman—A review. *BJOG*. 2006;113:1167.
Colquitt JL, Pickett K, Loveman E, et al. Surgery for weight loss in adults. *Cochrane Database Syst Rev*. 2014;(8):CD003641.
Gloy VL, Briel M, Bhatt DL, et al. Bariatric surgery versus non-surgical treatment for obesity: a systematic review and meta-analysis of randomised controlled trials. *BMJ*. 2013;347:f5934.
Janssen I, Mark AE. Elevated body mass index and mortality risk in the elderly. *Obes Rev*. 2007;8:41.
Olsen CM, Green AC, Whiteman DC, et al. Obesity and the risk of epithelial ovarian cancer: a systematic review and meta-analysis. *Eur J Cancer*. 2007;43:690.
Siebenhofer A, Jeitler K, Horvath K, et al. Long-term effects of weight-reducing drugs in hypertensive patients. *Cochrane Database Syst Rev*. 2013;(3):CD007654.
Yanovski SZ, Yanovski JA. Long-term drug treatment for obesity: a systematic and clinical review. *JAMA*. 2014;311:74.

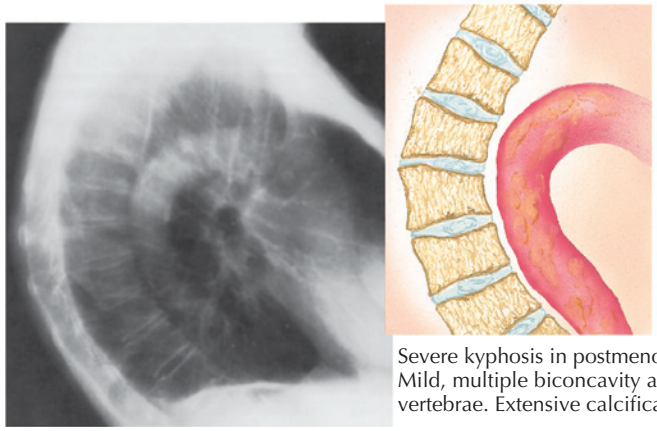
LEVEL III

Apovian CM, Aronne LJ, Bessesen DH, et al. Pharmacological management of obesity: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2015;100:342.
Bray GA, Ryan DH. Medical therapy for the patient with obesity. *Circulation*. 2012;125:1695.
Catalano PM. Management of obesity in pregnancy. *Obstet Gynecol*. 2007;109:419.
Centers for Disease control and Prevention. *Adult Obseity Facts*. <http://www.cdc.gov/obesity/data/adult.html>, Accessed 15.12.15.
ESHRE Capri Workshop Group. Nutrition and reproduction in women. *Hum Reprod Update*. 2006;12:193.
Flegal KM, Carroll MD, Kit BK, et al. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999-2010. *JAMA*. 2012;307:491.
Gray AD, Power ML, Zinberg S, et al. Assessment and management of obesity. *Obstet Gynecol Surv*. 2006;61:742.
Haslam D, Sattar N, Lean M. ABC of obesity. Obesity—Time to wake up. *BMJ*. 2006;333:640.
Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Circulation*. 2014;129:S102.
Lawlor DA, Lean M, Sattar N. ABC of obesity: obesity and vascular disease. *BMJ*. 2006;333:1060.
Milewicz A, Jedrzejuk D. Clinical aspects of obesity in the gynecological endocrinology practice. *Maturitas*. 2007;56:113.
Mitrakou A. Women's health and the metabolic syndrome. *Ann N Y Acad Sci*. 2006;1092:33.
Pasquali R. Obesity, fat distribution and infertility. *Maturitas*. 2006;54:363.
Pasquali R, Gambineri A, Pagotto U. The impact of obesity on reproduction in women with polycystic ovary syndrome. *BJOG*. 2006;113:1148.
Ramsay JE, Greer I, Sattar N. ABC of obesity. Obesity and reproduction. *BMJ*. 2006;333:1159.
Schneider JG, Tompkins C, Blumenthal RS, et al. The metabolic syndrome in women. *Cardiol Rev*. 2006;14:286.
Tsai AG, Wadden TA. In the clinic: obesity. *Ann Intern Med*. 2013;159:ITC3.
Wyatt SB, Winters KP, Dubbert PM. Overweight and obesity: prevalence, consequences, and causes of a growing public health problem. *Am J Med Sci*. 2006;331:166.
Yu CK, Teoh TG, Robinson S. Obesity in pregnancy. *BJOG*. 2006;113:1117.



Mild osteopenia in postmenopausal women. Vertebrae appear "washed-out"; no kyphosis or vertebral collapse

Anterior wedge compression at T6 in same patient 16 1/2 years later. Patient has lymphoma, with multiple biconcave ("codfish") vertebral bodies and kyphosis. Focal lesion at T6 suggests neoplasm



Severe kyphosis in postmenopausal woman. Mild, multiple biconcavity and wedging of vertebrae. Extensive calcification of aorta

Figure 54.1 Radiographic findings in osteoporosis

- Spinal, hip, or forearm fractures (with or without pain, fractures should be suspected in idiopathic back pain in at-risk patients)
- Loss of height (up to 4–8 inches)
- Development of kyphoscoliosis ("dowager's hump")

DIAGNOSTIC APPROACH

Differential Diagnosis

- Metastatic tumor (breast)
- Paget disease (osteitis deformans)
- Multiple myeloma
- Unreported trauma (abuse, elder abuse)
- Cushing syndrome

Associated Conditions: Dyspareunia, vulvodynia, atrophic vulvitis, increased risk of cardiovascular disease, hot flashes and flushes, sleep disturbances, urinary incontinence, and others associated with hypoestrogenic states.

Workup and Evaluation

Laboratory: No evaluation specifically indicated.

Imaging: Dual-energy X-ray absorptiometry (DEXA) or quantitative computed tomography. Routine radiographic studies (eg, chest radiograph) do not detect changes until almost 30% of bone has been lost (approximately equal to fracture threshold, 1 g/cm^2).

Special Tests: World Health Organization (WHO) Fracture Risk Assessment Tool (FRAX). Urinary tests for bone metabolites are investigational only.

Diagnostic Procedures: Radiographic assessment of bone mass.

Pathologic Findings

Loss of bone calcium, thinning of trabeculae, microfractures, macrofractures (spine, hips, forearms).

MANAGEMENT AND THERAPY

Nonpharmacologic

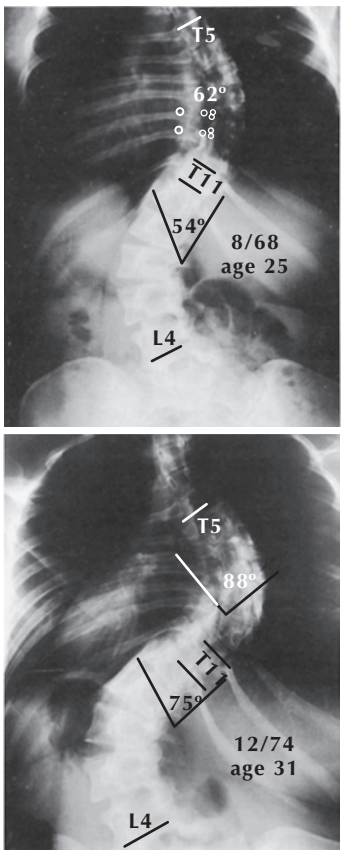
General Measures: Smoking cessation, alcohol and caffeine intake in moderation, weight-bearing exercise, adequate dietary calcium or supplementation.

Specific Measures: Bisphosphonates (oral preferred for cost and long-term safety data), calcitonin (infrequently used, reserved for selected patients as a therapeutic agent, not as prevention), selective estrogen receptor modulators (SERMs). Estrogen replacement therapy (when indicated for other reasons) will provide protection but is no longer considered sufficient to justify risks, based on the results of the Women's Health Initiative (WHI) study, although significant concerns about the methodologies of this study exist.

Diet: Adequate dietary intake of calcium (1000–1500 mg/day) and vitamin D (400–800 IU daily). Supplementation of vitamin D beyond this dose is generally not warranted.

Activity: Weight-bearing exercise or exercise against resistance. Low-impact activities for those with established bone loss.

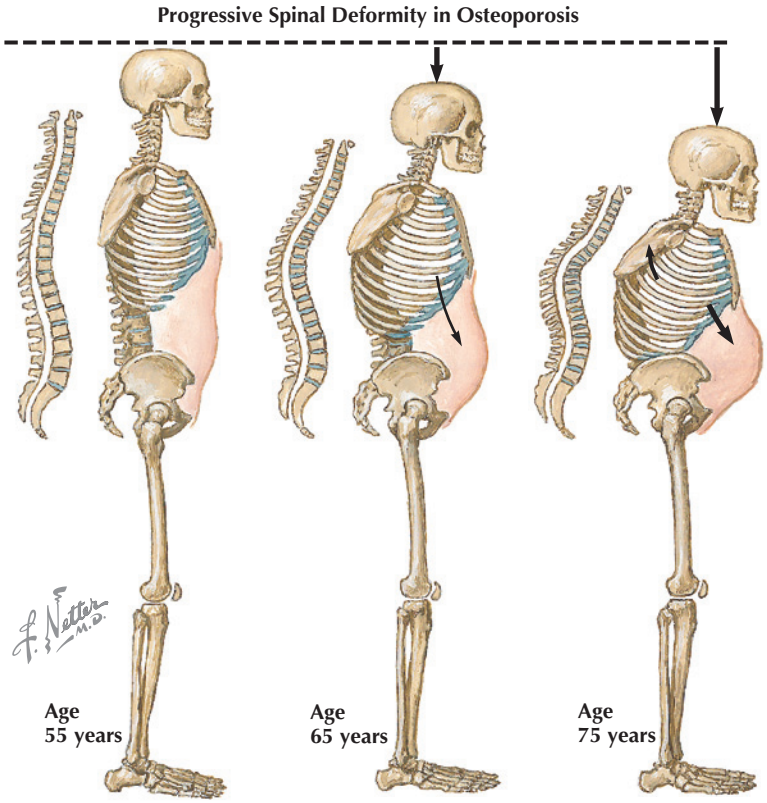
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP048 (Osteoporosis), AP047 (The Menopause Years), and AP045 (Exercise and Fitness).



Right thoracic curve of 62° and left lumbar curve of 54° in 25-year-old woman. Curve and grade II spondylolisthesis of L5 detected but not treated during adolescence. Curve increased slowly during adulthood

Increased curves in same woman at age 31 after two closely spaced pregnancies. Thoracic curve progressed to 88° and lumbar curve to 75°. Spondylolisthesis increased to grade III

Reproduced from Keim HA: The Adolescent Spine. New York, Grune & Stratton, 1976.



Compression fractures of thoracic vertebrae lead to loss of height and progressive thoracic kyphosis (dowager's hump). Lower ribs eventually rest on iliac crests, and downward pressure on viscera causes abdominal distention

Figure 54.2 Progression of scoliotic curve in adult

Drug(s) of Choice

- Bisphosphonates—alendronate sodium (Fosamax) 10 mg PO daily (must be taken on arising for the day with a full glass of water and nothing by mouth for 30 minutes); risedronate sodium (Actonel) 30 mg PO weekly; ibandronate sodium (Boniva) 150 mg PO monthly (must remain upright and with nothing by mouth for 60 minutes) or 3 mg IM every 3 months. Zoledronic acid once-yearly intravenous therapy. Denosumab is an alternative to intravenous zoledronic acid.
- Selective estrogen receptor modulators (also known as tissue selective estrogens). Many of these agents have bone activity and can protect or increase bone mass. For most, no current data reveal a reduction in the fracture rate, but this is expected to be the case when studies of longer-term use become available.
- Estrogen replacement therapy (with progesterone if indicated). See Chapter 188, Menopause, for dosage options. Estrogen's effect on bone protection appears to depend on obtaining a relatively normal (premenopausal) blood level (40–60 pg/mL) and is not affected by the route of therapy.

Contraindications: See Chapter 188, Menopause. Bisphosphonates are contraindicated in patients with esophageal stricture or difficulty swallowing, an inability to sit or stand for 30–60 minutes, in nursing mothers, and those with chronic kidney disease.

Precautions: See Chapter 188, Menopause. Patients must remain upright after the ingestion of bisphosphonates to avoid esophageal irritation. Long-term use may be associated with impaired mineralization; therefore, bisphosphonates should be cyclically administered (infrequent cases of osteonecrosis of the jaw have been reported in bisphosphonate users). Vitamin D should be judiciously used, if at all, because doses that increase calcium absorption are close to doses that result in bone resorption. If calcitonin is used, it must be administered with adequate calcium intake to avoid secondary hyperparathyroidism.

Interactions: See Chapter 188, Menopause. Calcium supplements and antacids may interfere with the absorption of some bisphosphonates and must be taken later in the day.

Alternative Drugs

Calcium supplements should be reserved for those with inadequate intake or a food intolerance that prevents achievement of sufficient dietary levels. Calcium carbonate provides the greatest percentage of elemental calcium, and calcium citrate is highly absorbable, making both acceptable supplements. When used, these should be taken in divided doses over the course of the day. Excessive intake of calcium supplements has been associated with an increased risk of stone formation and should be discouraged.

FOLLOW-UP

Patient Monitoring: Normal health maintenance and continued (lifelong) compliance with medical therapy must be encouraged. Periodic measurement of height may detect asymptomatic spinal fractures.

Prevention/Avoidance: Estrogen replacement therapy at menopause (when otherwise indicated), good diet (adequate calcium and vitamin D intake), and exercise (weight-bearing and

otherwise). Elimination or reduction of bone toxins (smoking and excess alcohol consumption)

Possible Complications: After hip fracture, half of patients require assistance walking and 15%–30% are institutionalized, often for the rest of their lives. Roughly, one in five patients with a hip fracture dies within 6 months of the fracture. Hip fracture is the 12th leading cause of death in women.

Expected Outcome: The rate of bone loss may be slowed by medical interventions, but these are most successful if instituted early. Estrogen replacement (when started early) is associated with a reduction by approximately 50% in the rate of hip and arm fractures in postmenopausal women. This value has been reported to increase to more than 90% when estrogen is used for more than 5 years. Vertebral fractures may be reduced by as much as 80% for these same women.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy (generally not a consideration). Most bisphosphonates are pregnancy category C medications.

ICD-10-CM Codes: M81.0 (Age-related osteoporosis without current pathological fracture).

REFERENCES

LEVEL I

Black DM, Delmas PD, Eastell R, et al; HORIZON Pivotal Fracture Trial. Once-yearly zoledronic acid for treatment of postmenopausal osteoporosis. *N Engl J Med*. 2007;356:1809.

Goss AN. Bisphosphonate-associated osteonecrosis of the jaws. *Climacteric*. 2007;10:5.

LEVEL II

Crandall CJ, Newberry SJ, Diamant A, et al. Comparative effectiveness of pharmacologic treatments to prevent fractures: an updated systematic review. *Ann Intern Med*. 2014;161:711.

Howe TE, Shea B, Dawson LJ, et al. Exercise for preventing and treating osteoporosis in postmenopausal women. *Cochrane Database Syst Rev*. 2011;(7):CD000333.

Kemmler W, Häberle L, von Stengel S. Effects of exercise on fracture reduction in older adults: a systematic review and meta-analysis. *Osteoporos Int*. 2013;24:1937.

LEVEL III

American College of Obstetricians and Gynecologists. Osteoporosis. Practice Bulletin No. 129. *Obstet Gynecol*. 2012;120:718.

Benhamou CL. Effects of osteoporosis medications on bone quality. *Joint Bone Spine*. 2007;74:39.

Cosman F, de Beur SJ, LeBoff MS, et al. Clinician's Guide to Prevention and Treatment of Osteoporosis. *Osteoporos Int*. 2014;25:2359.

Dennison E, Mohamed MA, Cooper C. Epidemiology of osteoporosis. *Rheum Dis Clin North Am*. 2006;32:617.

Gass M, Dawson-Hughes B. Preventing osteoporosis-related fractures: an overview. *Am J Med*. 2006;119:S3.

Hadjidakis DJ, Androulakis II. Bone remodeling. *Ann N Y Acad Sci*. 2006;1092:385.

Lambrinoudaki I, Christodoulakos G, Botsis D. Bisphosphonates. *Ann N Y Acad Sci*. 2006;1092:397.

Liberman UA. Long-term safety of bisphosphonate therapy for osteoporosis: a review of the evidence. *Drugs Aging*. 2006;23:289.

McCarus DC. Fracture prevention in postmenopausal osteoporosis: a review of treatment options. *Obstet Gynecol Surv*. 2006;61:39.

Poole KE, Compston JE. Osteoporosis and its management. *BMJ*. 2006; 333:1251.

Pyon EY. Once-monthly ibandronate for postmenopausal osteoporosis: review of a new dosing regimen. *Clin Ther*. 2006;28:475.

Raisz LG. Clinical practice. Screening for osteoporosis. *N Engl J Med*. 2005;353:164.

Rosen CJ. Clinical practice. Postmenopausal osteoporosis. *N Engl J Med*. 2005;353:595.

Sambrook P, Cooper C. Osteoporosis. *Lancet*. 2006;367:2010.

Silverman S, Christiansen C. Individualizing osteoporosis therapy. *Osteoporos Int*. 2012;23:797.

WHO Fracture Risk Assessment Tool. Available at: <http://www.shef.ac.uk/FRAX/>, Accessed 15.12.15.

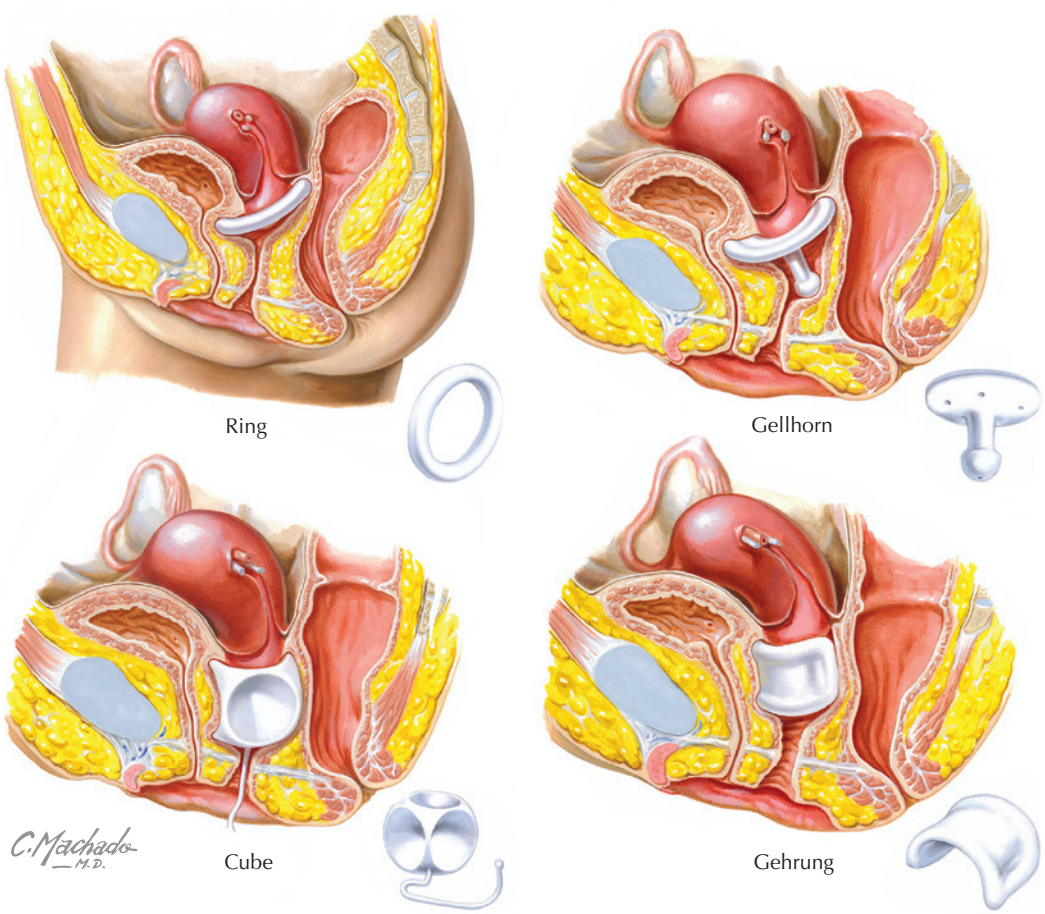


Figure 55.1 Types of pessaries

- **Strategies:** Pessaries are fitted and placed in the vagina similar to contraceptive diaphragm (see Chapter 262). The pessary is lubricated with a water-soluble lubricant, folded or compressed, and inserted into the vagina. The pessary is next adjusted so that it is in the proper position based on the type: ring and lever pessaries should sit behind the cervix (when present) and rest in the retropubic notch, the Gellhorn pessary should be entirely contained within the vagina with the plate resting above the levator plane, the Gehrung pessary must bridge the cervix to the limbs resting on the levator muscles on each side, and the ball or cube pessaries should occupy and occlude the upper vagina. All pessaries should allow the easy passage of an examining finger between the pessary and vaginal wall in all areas. Examination at 5–7 days after initial fitting is required to confirm proper placement, hygiene, and the absence of pressure-related problems (vaginal trauma or necrosis). Earlier evaluation (in 24–48 hours) may be advisable for patients who are debilitated or require additional assistance.
- **Patient Education:** Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP012 (Pelvic Support Problems), AP081 (Urinary Incontinence), AP166 (Surgery for Stress Urinary Incontinence), and AP183 (Surgery for Pelvic Organ Prolapse).

IMPLEMENTATION

- **Special Considerations:** Pessaries offer an excellent alternative to surgical repair, but the use of a pessary requires the cooperation and involvement of the patient. Patients who are unable or unwilling to manage the periodic insertion and removal of the device are poor candidates. Pessaries are not well tolerated and do not provide optimal support in patients who have low estrogen levels. For this reason, many suggest a minimum of 30 days of topical estrogen therapy (for those who are not already undergoing estrogen replacement) before a trial of pessary therapy. Patients who are going to use a pessary should be instructed on both proper insertion and removal techniques. Ring pessaries should be removed by hooking a finger into the opening of the pessary, gently compressing the device, and then withdrawing the pessary with gentle traction. Cube pessaries must also be compressed, but the suction created between the faces of the cube and the vaginal wall must be broken by gently separating the device from the vaginal sidewall. The locator string often attached to these pessaries should not be used for traction. Inflatable pessaries should be deflated before removal. The Gellhorn and Gehrung pessaries are removed by reversing their insertion steps.

REFERENCES

LEVEL I

Cundiff GW, Amundsen CL, Bent AE, et al. The PESSRI study: symptom relief outcomes of a randomized crossover trial of the ring and Gellhorn pessaries. *Am J Obstet Gynecol*. 2007;196:405.e1.

LEVEL II

Bugge C, Adams EJ, Gopinath D, et al. Pessaries (mechanical devices) for pelvic organ prolapse in women. *Cochrane Database Syst Rev*. 2013;(2): CD004010.

Collins S, Beigi R, Mellen C, et al. The effect of pessaries on the vaginal microenvironment. *Am J Obstet Gynecol*. 2015;212:60.e1.

Geoffrion R, Zhang T, Lee T, et al. Clinical characteristics associated with unsuccessful pessary fitting outcomes. *Female Pelvic Med Reconstr Surg*. 2013;19:339.

Lipp A, Shaw C, Glavind K. Mechanical devices for urinary incontinence in women. *Cochrane Database Syst Rev*. 2014;(12):CD001756.

Lone F, Thakar R, Sultan AH, et al. A 5-year prospective study of vaginal pessary use for pelvic organ prolapse. *Int J Gynaecol Obstet*. 2011;114:56.

Schaffer J, Nager CW, Xiang F, et al. Predictors of success and satisfaction of nonsurgical therapy for stress urinary incontinence. *Obstet Gynecol*. 2012;120:91.

Shaikh S, Ong EK, Glavind K, et al. Mechanical devices for urinary incontinence in women. *Cochrane Database Syst Rev*. 2006;(3):CD001756.

LEVEL III

American College of Obstetricians and Gynecologists. Urinary incontinence in women. ACOG Practice Bulletin 63. *Obstet Gynecol*. 2015; 126:e66.

Anders K. Devices for continence and prolapse. *BJOG*. 2004;111:61.

Culligan PJ. Nonsurgical management of pelvic organ prolapse. *Obstet Gynecol*. 2012;119:852.

Jelovsek JE, Maher C, Barber MD. Pelvic organ prolapse. *Lancet*. 2007; 369:1027.

Trowbridge ER, Fenner DE. Conservative management of pelvic organ prolapse. *Clin Obstet Gynecol*. 2005;48:668.

Waetjen LE, Subak LL, Shen H, et al. Stress urinary incontinence surgery in the United States. *Obstet Gynecol*. 2003;101:671.

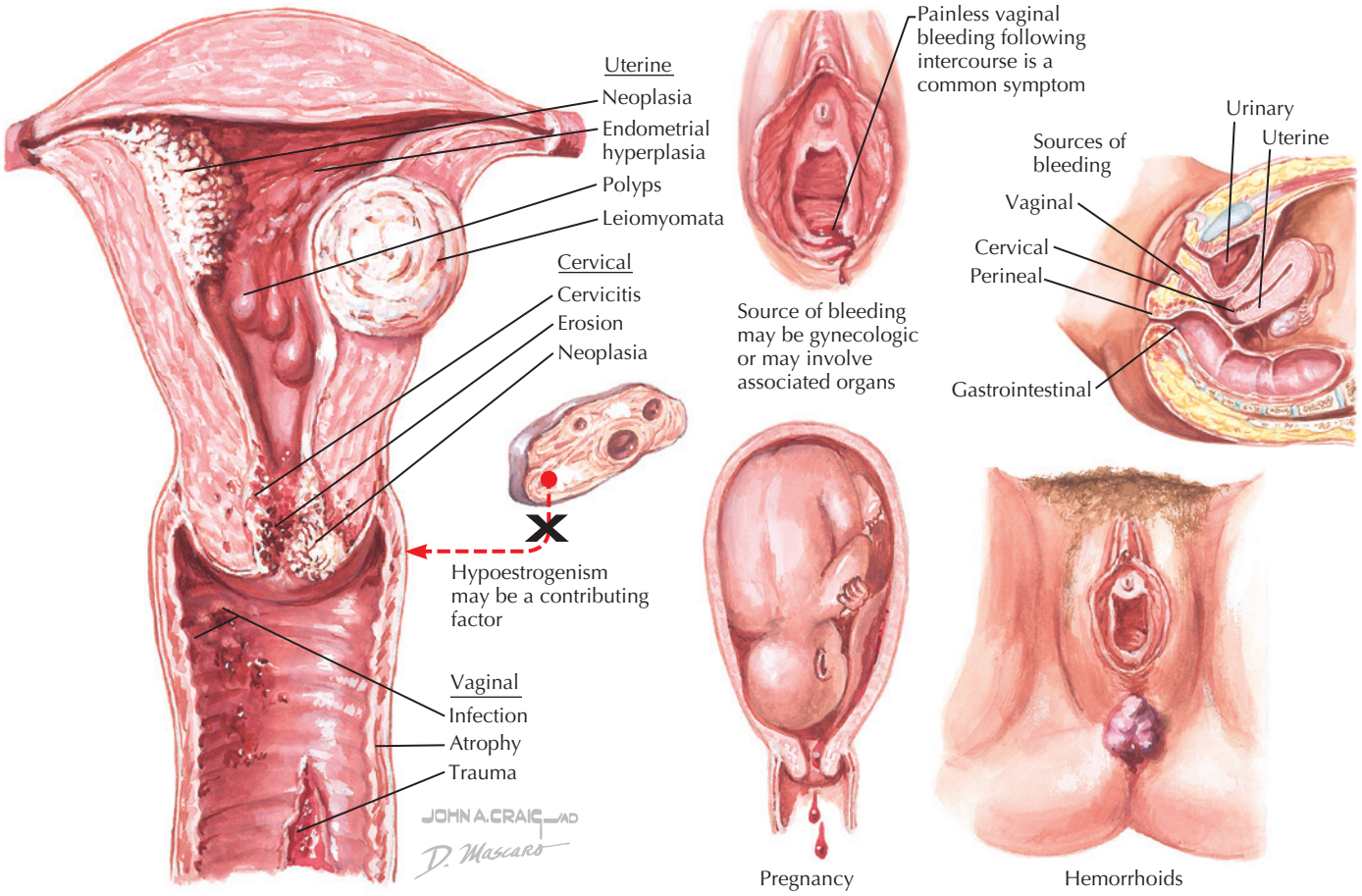


Figure 56.1 Clinical considerations in postcoital bleeding

Drug(s) of Choice

Based on the cause

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: Sexual dysfunction (rare).

Expected Outcome: Return to normal sexual function with reassurance and correction of the causative process.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. Slightly more common during pregnancy.
ICD-10-CM Codes: N93.0 (Postcoital and contact bleeding).

REFERENCES

LEVEL I

Bain C, Parkin DE, Cooper KG. Is outpatient diagnostic hysteroscopy more useful than endometrial biopsy alone for the investigation of abnormal uterine bleeding in unselected premenopausal women? A randomised comparison. *BJOG*. 2002;109:805.

LEVEL II

Davidson KG, Dubinsky TJ. Ultrasonographic evaluation of the endometrium in postmenopausal vaginal bleeding. *Radiol Clin North Am*. 2003;41:769.

Khattab AF, Ewies AA, Appleby D, et al. The outcome of referral with postcoital bleeding (PCB). *J Obstet Gynaecol*. 2005;25:279.

Kong GW, Yim SF, Cheung TH, et al. Cryotherapy as the treatment modality of postcoital bleeding: a randomised clinical trial of efficacy and safety. *Aust N Z J Obstet Gynaecol*. 2009;49:517.

Pretorius R, Semrad N, Watring W, et al. Presentation of cervical cancer. *Gynecol Oncol*. 1991;42:48.

Sahu B, Latheef R, Aboel Magd S. Prevalence of pathology in women attending colposcopy for postcoital bleeding with negative cytology. *Arch Gynecol Obstet*. 2007;276:471.

Selo-Ojeme DO, Dayoub N, Patel A, et al. A clinico-pathological study of postcoital bleeding. *Arch Gynecol Obstet*. 2004;270:34.

Shapley M, Blagojevic-Bucknall M, Jordan KP, et al. The epidemiology of self-reported intermenstrual and postcoital bleeding in the perimenopausal years. *BJOG*. 2013;120:1348.

Shapley M, Jordan J, Croft PR. A systematic review of postcoital bleeding and risk of cervical cancer. *Br J Gen Pract*. 2006;56:453.

Tehranian A, Rezaii N, Mohit M, et al. Evaluation of women presenting with postcoital bleeding by cytology and colposcopy. *Int J Gynaecol Obstet*. 2009;105:18.

PREMENSTRUAL SYNDROME

57

INTRODUCTION

Description: Premenstrual syndrome (PMS) and the more severe variant of premenstrual dysphoric disorder (PMDD) involve physical and emotional symptoms that are characterized by their relationship to menses. Symptoms are confined to a period of not more than 5 days before the onset of menstrual flow with complete resolution at or soon after the end of menstrual flow. Symptoms must persist over three or more consecutive menstrual cycles.

Prevalence: Reproductive age (25%–85%); lifestyle is affected in 5%–10% and 2%–5% meet strict criteria.

Predominant Age: Reproductive; most commonly 30s and 40s.

Genetics: Family tendency, preliminary evidence suggests that PMDD is associated with variations in *ESR1* (estrogen receptor alpha gene).

ETIOLOGY AND PATHOGENESIS

Causes: The physiologic foundations of PMS, PMDD, and premenstrual magnification (PMM) remain to be established. The most promising research into a cause of PMS has been in the areas of β-endorphins and serotonin.

Risk Factors: None known; some suggestion of a link to smoking and low educational attainment.

SIGNS AND SYMPTOMS

Physical or emotional symptoms confined to a period of not more than 5 days before the onset of menstrual flow with complete resolution at or soon after the end of menstrual flow. More than 150 different signs and symptoms have been described under the rubric of PMS (the character of the symptoms is not important, only the timing of their appearance). Symptoms that are present at all times but worsen before menses or those that appear at irregular intervals do not meet the criteria for PMS; they should be classified as PMM. The diagnosis of PMDD requires the presence of at least one affective symptom (mood swings, irritability, anger, difficulty concentrating, depression).

DIAGNOSTIC APPROACH

Differential Diagnosis

- Breast disorders
- Chronic fatigue states
- Drug and substance abuse
- Endocrinologic disorders
- Family, marital, and social stress
- Gastrointestinal conditions
- Gynecologic disorders
- Idiopathic edema
- Psychiatric and psychologic disorders

Associated Conditions: Bipolar disorders, sleep disorders, chronic pain states, and somatization.

Workup and Evaluation

Laboratory: Complete blood count, liver enzyme studies, endocrine studies (androgens, follicle-stimulating hormone [FSH]/luteinizing hormone [LH], glucose tolerance test, prolactin, thyroid function studies [highly sensitive thyroid-stimulating hormone, thyronine, thyrotropin-releasing hormone stimulation]), all to rule out other conditions.

Imaging: No imaging indicated.

Special Tests: Prospective menstrual calendar or other diary for a 3-month period to establish the diagnosis.

Diagnostic Procedures: History, physical examination, prospective menstrual calendar or diary. Research has shown that up to 80% of patients who present with self-diagnosed PMS fail to meet strict criteria for this diagnosis. Most are found to have other conditions ranging from mood disorders to irritable bowel syndrome or endometriosis. This observation makes it imperative that no therapy be instituted until the diagnosis can be firmly established.

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Lifestyle changes (20–45 minutes of aerobic exercise, three times weekly; smoking cessation; stress reduction), dietary changes and supplementation (adequate protein and complex carbohydrates; avoidance of alcohol, caffeine, and simple sugars; eating frequent small meals and plenty of fresh fruits and vegetables; reduction of dietary fat to <15%; salt restriction; increased dietary or supplemental fiber; calcium 1000 mg daily; magnesium 200 mg daily during luteal phase; vitamin B_6 50–200 mg daily; vitamin E 150–300 IU daily) all have been advocated but with few data to support the recommendations.

Specific Measures: Generally based on specific symptoms. A favorable response should be expected for 80% of patients with PMS and 50% of those with PMM.

Diet: See previous.

Activity: Aerobic exercise (20–45 minutes, three times weekly).

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlets AP057 (Premenstrual Syndrome), AP106 (Depression).

Drug(s) of Choice

- Hydrochlorothiazide 25–50 mg daily, luteal phase (for fluid retention).
- Selective serotonin reuptake inhibitors (SSRIs)—fluoxetine 20 mg daily; sertraline 50–150 mg daily; paroxetine 20–30 mg daily or controlled release 25 mg daily; citalopram 20–30 mg daily.
- Alprazolam 0.25 mg three to four times daily or atenolol 25 mg two to three times daily (for agitation and anxiety).
- Buspirone 5 mg three times daily or fluoxetine 20 mg daily (in the morning) for mood swings.
- Third-generation oral contraceptives (eg, desogestrel containing).
- Danazol sodium 200 mg daily (luteal phase) or continuous gonadotropin-releasing hormone (GnRH) agonists (depot leuprolide 3.75 mg IM monthly for a maximum of 6 months or nafarelin acetate nasal spray 200 mcg twice daily for a maximum of 6 months).

Contraindications: See individual agents.

Precautions: See individual agents.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.

Prevention/Avoidance: General stress reduction appears to blunt the cyclic symptoms experienced.

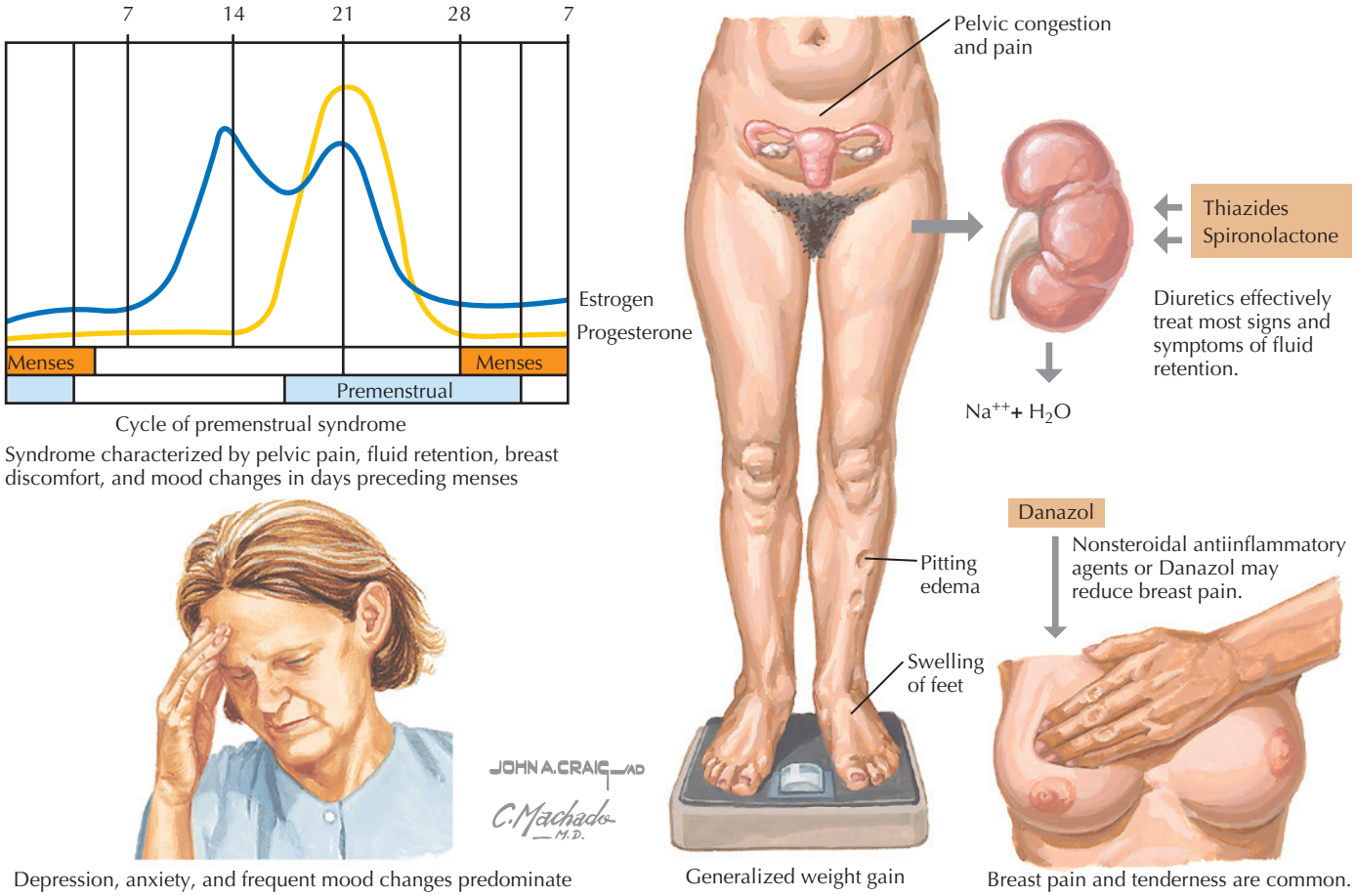


Figure 57.1 Signs and symptoms of premenstrual syndrome

Possible Complications: Social withdrawal or isolation, work or family disruption. The rate of suicide increases during the luteal phase.

Expected Outcome: Symptoms can generally be resolved through the process of diagnosis, providing insight and control to the patient, and pharmacologic intervention.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. Patients with a history of PMS may have exaggerated response to the hormonal changes associated with pregnancy.

ICD-10-CM Codes: N94.3 (Premenstrual tension syndrome).

REFERENCES

LEVEL I

Facchinetti F, Borella P, Sances G, et al. Oral magnesium successfully relieves premenstrual mood changes. *Obstet Gynecol*. 1991;78:177.

Goodale IL, Domar AD, Benson H. Alleviation of premenstrual syndrome symptoms with the relaxation response. *Obstet Gynecol*. 1990;75:649.

Schmidt PJ, Nieman LK, Danaceau MA, et al. Differential behavioral effects of gonadal steroids in women with and in those without premenstrual syndrome. *N Engl J Med*. 1998;338:209.

LEVEL II

Ford O, Lethaby A, Mol B, et al. Progesterone for premenstrual syndrome. *Cochrane Database Syst Rev*. 2006;(4):CD003415.

Garris PD, Sokol MS, Kelly K, et al. Leuprolide acetate treatment of catamenial pneumothorax. *Fertil Steril*. 1994;61:173.

Hartlage SA, Freels S, Gotman N, et al. Criteria for premenstrual dysphoric disorder: secondary analyses of relevant data sets. *Arch Gen Psychiatry*. 2012;69:300.

Huo L, Straub RE, Roca C, et al. Risk for premenstrual dysphoric disorder is associated with genetic variation in ESR1, the estrogen receptor alpha gene. *Biol Psychiatry*. 2007;62:925.

Kornstein SG, Pearlstein TB, Fayyad R, et al. Low-dose sertraline in the treatment of moderate-to-severe premenstrual syndrome: efficacy of 3 dosing strategies. *J Clin Psychiatry*. 2006;67:1624.

Krasnik C, Montori VM, Guyatt GH, et al. Medically Unexplained Syndromes Study Group. The effect of bright light therapy on depression associated with premenstrual dysphoric disorder. *Am J Obstet Gynecol*. 2005;193:658.

Lopez LM, Kaptein AA, Helmerhorst FM. Oral contraceptives containing drospirenone for premenstrual syndrome. *Cochrane Database Syst Rev*. 2012;(2):CD006586.

Marjoribanks J, Brown J, O'Brien PM, et al. Selective serotonin reuptake inhibitors for premenstrual syndrome. *Cochrane Database Syst Rev*. 2013;(6):CD001396.

Miller A, Vo H, Huo L, et al. Estrogen receptor alpha (ESR-1) associations with psychological traits in women with PMDD and controls. *J Psychiatr Res*. 2010;44:788.

Shah NR, Jones JB, Aperi J, et al. Selective serotonin reuptake inhibitors for premenstrual syndrome and premenstrual dysphoric disorder: a meta-analysis. *Obstet Gynecol*. 2008;111:1175.

LEVEL III

American College of Obstetricians and Gynecologists. Noncontraceptive uses of hormonal contraceptives. Practice Bulletin No. 110. *Obstet Gynecol*. 2010;115:206.

Braverman PK. Premenstrual syndrome and premenstrual dysphoric disorder. *J Pediatr Adolesc Gynecol*. 2007;20:3.

Futterman LA, Rapkin AJ. Diagnosis of premenstrual disorders. *J Reprod Med*. 2006;51:349.

Kroll R, Rapkin AJ. Treatment of premenstrual disorders. *J Reprod Med*. 2006;51:359.

O'Brien PM, Bäckström T, Brown C, et al. Towards a consensus on diagnostic criteria, measurement and trial design of the premenstrual disorders: the ISPMD Montreal consensus. *Arch Womens Ment Health*. 2011;14:13.

Rubinow DR. The premenstrual syndrome: new views. *JAMA*. 1992;268:1908.

Winer SA, Rapkin AJ. Premenstrual disorders: prevalence, etiology and impact. *J Reprod Med*. 2006;51:339.

Yonkers KA, O'Brien PM, Eriksson E. Premenstrual syndrome. *Lancet*. 2008;371:1200.

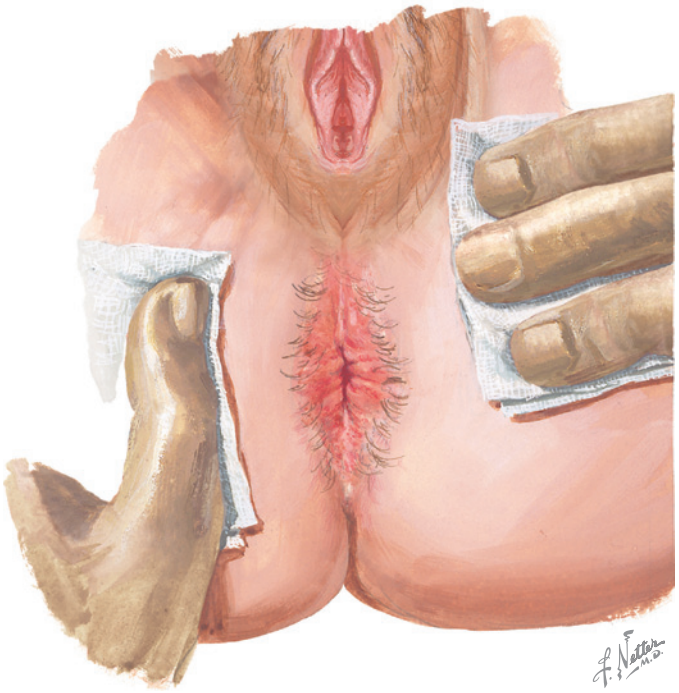


Figure 58.1 Perianal irritation resulting from pruritus ani

citrus, vitamin C, milk products, alcohol). When fecal soiling is a factor, increasing dietary fiber may be of help.

Activity: No restriction.

Patient Education: Reassurance, counseling about perineal hygiene, risk reduction.

Drug(s) of Choice

- Burow solution (Domeboro, aluminum acetate 5% aqueous solution, three to four times daily for 30–60 minutes).
- Crotamiton (Eurax) may be topically applied twice daily.
- Topical analgesic sprays or ointments—benzocaine (Americaine, Hurricaine) 20% spray or gel; dibucaine (Nupercainal) 1% ointment.
- Antipruritics and antiinflammatory agents—hydrocortisone (Anusol-HC, Analpram-HC, Cortenema, Cortifoam, Epifoam, Proctofoam-HC); pramoxine 1% (Fleet rectal pads, Analpram-HC); witch hazel 50% (Tucks pads or gel).
- Astringents—Preparation H.
- Topical capsaicin (0.006%) three times daily for 4 weeks.
- Intradermal injection of methylene blue has been used for refractory cases, but no randomized trials have been performed to support its use.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.

Prevention/Avoidance: Perineal hygiene, hormone replacement therapy, and avoidance of local irritants and laxatives.

Possible Complications: Secondary infection caused by excoriation, lichenification.

Expected Outcome: Good, with identification of underlying causation.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.

ICD-10-CM Codes: L29.0 (Pruritus ani).

REFERENCES

LEVEL I

Lysy J, Sistiery-Ittah M, Israelit Y, et al. Topical capsaicin—A novel and effective treatment for idiopathic intractable pruritus ani: a randomised, placebo controlled, crossover study. *Gut*. 2003;52:1323.

LEVEL II

Hicks CW, Wick EC, Leeds IL, et al. Patient symptomatology in anal dysplasia. *JAMA Surg*. 2015;150:563.

Suys E. Randomized study of topical tacrolimus ointment as possible treatment for resistant idiopathic pruritus ani. *J Am Acad Dermatol*. 2012;66:327.

Sutherland AD, Faragher IG, Frizelle FA. Intradermal injection of methylene blue for the treatment of refractory pruritus ani. *Colorectal Dis*. 2009;11:282.

LEVEL III

Daniel GL, Longo WE, Vernava AM 3rd. Pruritus ani. Causes and concerns. *Dis Colon Rectum*. 1994;37:670.

Henderson PK, Cash BD. Common anorectal conditions: evaluation and treatment. *Curr Gastroenterol Rep*. 2014;16:408.

Jones DJ. ABC of colorectal diseases. Pruritus ani. *BMJ*. 1992;305:575.

Nasseri YY, Osborne MC. Pruritus ani: diagnosis and treatment. *Gastroenterol Clin North Am*. 2013;42:801.

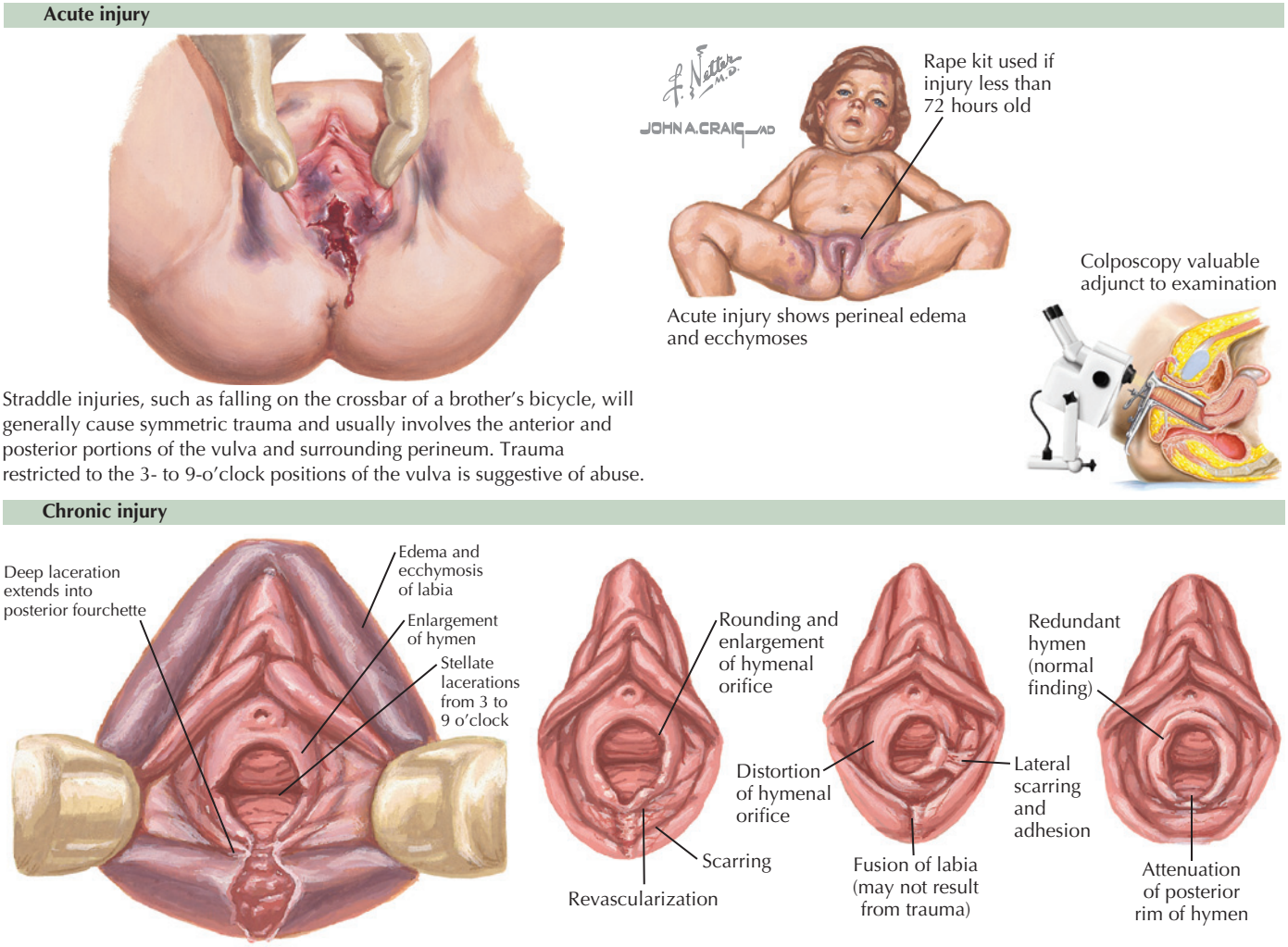


Figure 59.1 Rape injury in a child

deemed incapable of giving consent for any otherwise-consensual sexual activity, resulting in "statutory rape." Rape trauma syndrome is a well-recognized set of behaviors that occurs after a sexual assault. These responses are organized into three phases: the acute phase, lasting from hours to days; a middle or readjustment phase, lasting from days to weeks; and a final reorganization or resolution phase that involves lifelong changes.

Prevalence: Rape constitutes 5%–10% of violent crime and affects 601 of 100,000 women. It is the most underreported crime in the United States. Rape trauma syndrome occurs in virtually every case.

Predominant Age: Any age; highest risk is at the age of 16–24 years.

ETIOLOGY AND PATHOGENESIS

Causes: One-fourth to one-half of all rapes occur at home (either the victim's or the attacker's), but only one-third of these involve a male intruder. Most attackers are known to the victims. Of recurrent victims, approximately 25% have been raped by someone well known to them, such as an ex-lover, employer, coworker, neighbor, or relative, and two-thirds are vulnerable because of mental impairment, substance abuse, or a psychiatric disorder. Weapons are used in 30%–50% of sexual assaults (handguns are most common). Approximately 50% of campus rapes occur during dates. Estimates of sexual violence occurring in the setting of a dating relationship indicate that 10%–25% of high school students and 20%–50% of college students have experienced some form of sexual violence. Rape trauma syndrome can follow rape or other forms of intense physical or emotional trauma.

Risk Factors: Past history of victimization, youth, greater number of dating, or sexual partners. Studies indicate that alcohol use is involved in more than one-half of all rapes of college students. Use of illicit drugs, including flunitrazepam (Rohypnol), 3,4-met hylendioxymethamphetamine (MDMA or ecstasy), ketamine, and gamma hydroxybutyrate (GHB), increase the risk of rape. Rape trauma syndrome is more common in those older than 40 years, those assaulted in their homes by a stranger, and those with a history of previous mental illness.

SIGNS AND SYMPTOMS

- **Rape**—history of nonconsensual sexual activity
  - Physical signs of sexual activity (not limited to vaginal intercourse)
  - Physical signs of trauma or coercion (including impairment resulting from drugs, alcohol, or mental abilities)
- **Rape trauma syndrome—acute** (decompensation, inability to cope, volatile emotions, fear, guilt, anger, depression, and

problems concentrating are common; flashbacks are frequent; ideation is often disturbed)
- Middle or readjustment [resolution of many issues (may not be functional), flashbacks, nightmares, and phobias may develop]
- Reorganization (recognizes that event was an assault over which she could have no control)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Consensual intercourse
- Nonsexual trauma
- Rape trauma syndrome—depression
  - Mania
  - Psychosis

Associated Conditions: Pregnancy, sexually transmitted infections, and depression. Trauma in other areas of the body is more common than genital trauma (70.4% vs. 26.8%) with bruises, abrasions, or erythema on the thigh, upper arm, face, or neck.

Workup and Evaluation

Laboratory: As outlined in Special Tests, as well as in serum pregnancy test, cervical cultures, or DNA-based tests for sexually transmitted infections, a screening serologic test for syphilis and human immunodeficiency virus (HIV), hepatitis antigens, urinalysis (often with culture).

Imaging: No imaging indicated unless the possibility of internal injuries is suspected.

Special Tests: Special rape evaluation kits are available in many jurisdictions and should be used if available. Wood's light (ultraviolet light) causes semen stains to fluoresce.

Diagnostic Procedures: Examination under general anesthesia is also indicated any time the patient is unable to urinate or there is hematuria, lower abdominal tenderness, or signs of occult blood loss such as hypovolemia.

Pathologic Findings

The physical examination is normal in one-half of rape victims. Common sites of lacerations are the vaginal wall, lateral fornices, and cul-de-sac.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Major trauma must always be evaluated and treated first. Support should be provided with compassion, care, and sensitivity. The primary goal is to provide reassurance and a return of control. Support and assistance should be provided to move through the stages of resolution. Because one of the pivotal aspects of sexual assault is the loss of control, every effort should be made to allow the patient control over even the most trivial aspect of the physical examination.

Specific Measures: There are three basic responsibilities while caring for someone who may have been raped or abused: The detection and treatment of serious injuries, preservation of evidence, and protection against sequelae. All women deserve intensive follow-up and counseling. Assist in recognizing and adapting to changes that make up the rape trauma syndrome.

Diet: No specific dietary changes indicated.

Activity: No restriction.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP114 (Emergency Contraception), AP068 (Alcohol and Women), and AP083 (Domestic Violence).

Drug(s) of Choice

- Pregnancy interdiction—levonorgestrel 0.75 mg (Plan B) PO every 12 hours for two doses or ethinyl estradiol 0.05 mg plus norgestrel 0.5 mg (Ovral) two tablets PO twice a day for 2–5 days.
- Sexually transmitted infection prophylaxis—ceftriaxone 250 mg IM or spectinomycin 2 g IM, both followed by tetracycline 500 mg PO four times a day for 7 days or doxycycline 100 mg PO twice a day for 7 days.
- Prophylaxis—tetanus toxoid should be administered if indicated.

Contraindications: Known or suspected allergy, preexisting pregnancy.

Precautions: Nausea is common with high-dose estrogen pregnancy interdiction.

Alternative Drugs

- Pregnancy interdiction—ethinyl estradiol 5 mg PO daily for 5 days or conjugated estrogen 10 mg PO four times a day for 5 days. An intrauterine contraceptive device (copper) may be placed as an alternative to drug therapy for pregnancy interdiction.
- Sexually transmitted infection prophylaxis—amoxicillin 3 g PO or ampicillin 3.5 g PO plus probenecid 1 g PO as initial therapy, then follow as previous. The Centers for Disease Control and Prevention (CDC) recommends postexposure hepatitis B vaccination without hepatitis B immune globulin (HBIG).
- Erythromycin esterase 500 mg PO four times a day for 7 days may be substituted for tetracycline or doxycycline.

FOLLOW-UP

Patient Monitoring: Follow-up contacts by the health care provider, social service agencies, or support groups should be made early and often. Contacts at 1–2 weeks, a month, and periodically thereafter provide support and identify evolving problems. Physical reevaluation should be performed at 1 and 6 weeks to check for delayed symptoms or signs of pelvic infection, bleeding abnormalities, delayed menses, suicidal ideation, or other possible sequelae of the attack. Retesting for HIV and hepatitis B status should be done at 12–18 weeks. Healthcare providers should watch for a failure to move to resolution and the emergence of dysfunctional adaptations.

Prevention/Avoidance: Avoidance of high-risk situations, especially those involving alcohol or drugs.

Possible Complications: The risk of acquiring a sexually transmitted infection is uncertain but is estimated to be 3%–5% or less. The risk of becoming infected with HIV is unknown. When pregnancy interdiction is undertaken within 72 hours, efficacy approaches 90%. Efficacy is greater the earlier the interdiction is instituted; therapy may still be undertaken beyond 72 hours with declining results. Roughly one-third of rape victims suffer long-term psychiatric problems.

Expected Outcome: If both physical and mental traumas are addressed in a proactive manner, results should be good. This must include risk avoidance to reduce the chance of recurrence (up to one-fifth of rape victims have been victims previously). Even with care and support, the last phase of the rape trauma syndrome is often accompanied with painful transitions, frequently involving significant changes in lifestyle, work, or friends. Insomnia, depression, somatic complaints, and poor self-esteem are common during this phase. For some, this phase can be extremely disruptive and prolonged. Roughly one-third of rape victims suffer long-term psychiatric problems. The risk of this is greatest for those older than 40 years, those assaulted in their homes by a stranger, and those with a history of previous mental illness.

MISCELLANEOUS

Pregnancy Considerations: No effect on preexisting pregnancy. If pregnancy interdiction fails, some agents used may be teratogenic and a therapeutic abortion is recommended.

ICD-10-CM Codes: Z04.41 (Encounter for examination and observation following alleged adult rape) and F43.0 (Acute stress reaction).

REFERENCES

LEVEL II

Carey KB, Durney SE, Shepardson RL, et al. Incapacitated and forcible rape of college women: prevalence across the first year. *J Adolesc Health*. 2015;56:678.

Larsen ML, Hilden M, Lidegaard Ø. Sexual assault: a descriptive study of 2500 female victims over a 10-year period. *BJOG*. 2015;122:577.

Ranney ML, Gee EM, Merchant RC. Nonprescription availability of emergency contraception in the United States: current status, controversies, and impact on emergency medicine practice. *Ann Emerg Med*. 2006;47:461.

Rocca CH, Schwarz EB, Stewart FH, et al. Beyond access: acceptability, use and nonuse of emergency contraception among young women. *Am J Obstet Gynecol*. 2007;196:29.e1, discussion 90.e1.

LEVEL III

Abrahams N, Devries K, Watts C, et al. Worldwide prevalence of non-partner sexual violence: a systematic review. *Lancet*. 2014;383:1648.

American College of Obstetricians and Gynecologists. Access to emergency contraception. ACOG Committee Opinion 542. *Obstet Gynecol*. 2012;120:1250.

American College of Obstetricians and Gynecologists. Reproductive and sexual coercion. Committee Opinion No. 554. *Obstet Gynecol*. 2013; 121:411.

American College of Obstetricians and Gynecologists. Emergency contraception. ACOG Practice Bulletin 152. *Obstet Gynecol*. 2015;126:e1.

Burgess WA, Holmstrom LL. Rape trauma syndrome. *Am J Psychiatry*. 1974;131:981.

Cantu M, Coppola M, Lindner AJ. Evaluation and management of the sexually assaulted woman. *Emerg Med Clin North Am*. 2003;21:737.

Chrisler JC, Ferguson S. Violence against women as a public health issue. *Ann N Y Acad Sci*. 2006;1087:235.

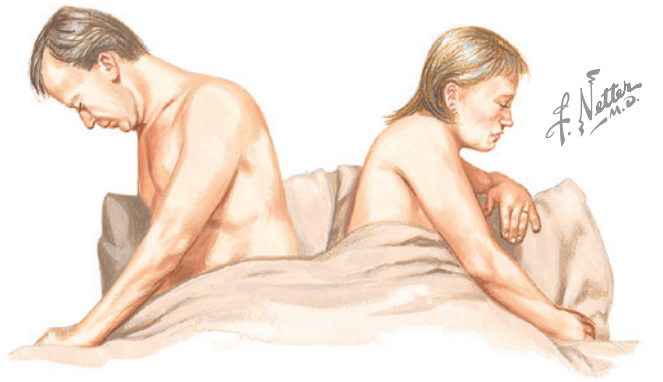
Emergency Contraception Website, operated by the Office of Population Research at Princeton University and by the Association of Reproductive Health Professionals, Available at: <http://ec.princeton.edu>, Accessed 16.12.15.

Hampton HL. Care of the woman who has been raped. *N Engl J Med*. 1995;332:234.

Kaufman M, American Academy of Pediatrics Committee on Adolescence. Care of the adolescent sexual assault victim. *Pediatrics*. 2008;122: 462.

Linden JA. Clinical practice. Care of the adult patient after sexual assault. *N Engl J Med*. 2011;365:834.

Workowski KA, Bolan GA, Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015;64:1.



Sex is more than intercourse Look at larger picture of sensuality
Leave each encounter feeling good Feel good—don't ask for orgasm
Give and receive pleasure Enjoy giving and accepting pleasure
Open good communications Listen without feeling criticized, provide cooperative communications
Learn to say "yes" instead of "no" (or at least "maybe") Learn to suggest alternatives, break rejection cycle
Improve the quality, not necessarily the quantity Better sex is better than more sex
Have fun, not work Sex shouldn't be work—requires interesting and interested partners
Allow "space" for each other Allow distance without abandonment
Go slowly, provide reassurance Take your time

Figure 60.1 Goals of sexual counseling or therapy. (Reused with permission from Smith RP, Gynecology in Primary Care. Baltimore: Williams and Wilkins; 1997:527.)

and desire that begins progress toward physical sexual expression) and arousal have occurred, orgasmic success requires effective stimulation, of a sufficient quality over a sufficient time, provided in a supportive environment. Failures in any of these areas may present as orgasmic problems.

- **Risk factors:** Abuse, restrictive rearing, depression, fatigue, sleep disorders.

DIAGNOSTIC APPROACH

Differential Diagnosis

- Depression and affective disorders
- Relational stress
- Physical or sexual abuse (current or past)
- Alcohol or drug use or abuse
- Conditioning (repeated orgasmic failure, restrictive rearing)
- Inappropriate expectations (inaccurate perception of "normal," "correct," or "expected")
- Multiple sclerosis or other neurologic processes
- Other sexual dysfunction (arousal, lubrication, dyspareunia, etc.) presenting as orgasmic failure

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated.
Special Tests: None indicated.
Diagnostic Procedures: History.

Pathologic Findings

None

MANAGEMENT AND THERAPY

General Measures: Reassurance, evaluation, stress reduction, relaxation training, encourage communication, sensate focusing (pleasuring). One of the simplest models for sexual therapy is the PLISSIT model. This model is made up of four levels of intervention: **P**ermission, **L**imited **I**nformation, **S**pecific **S**uggestions, and **I**ntensive **T**herapy. These steps are applied in order. At each step a large number of dysfunctions will be resolved, leaving few patients who require referral for intensive or specialized therapy.

- **Permission:** Many patients only need permission for what they are doing or want to do.
- **Limited Information:** When permission is not enough, providing limited information often will be the solution to the problem.
- **Specific Suggestion:** These do not have to be exotic, complex, or imaginative. In most cases, they will be obvious and suggested by the situation.
- **Intensive Therapy:** When the problem is more complex or deep seated, the intensive, specialized therapy of a trained sexual therapist, psychiatrist, psychologist, or other specialist should be considered.

Specific Measures: Specific suggestions for scheduled time together (including nonsexual time), sexual counseling as needed. Many patients who do not achieve orgasm during intercourse are fully orgasmic with additional manual stimulation, oral–genital stimulation, a vibrator, or masturbation (approximately 30%–40% of women require concurrent clitoral stimulation to achieve orgasm). This is common enough that it should be viewed as a problem only if it is a source of concern for the patient or her partner.

Diet: No specific dietary changes indicated (there is no true aphrodisiacs, but if the patient believes a food will enhance sexuality, it should not be denied).

Activity: No restriction.

Patient Education:

- American College of Obstetricians and Gynecologists Patient Education Booklet AP042 (Your and Your Sexuality), AP072 (Your Sexual Health), AP020 (When Sex Is Painful).
- Bacos CS, The Sex Bible: The Complete Guide to Sexual Love. Beverly, MA, Quiver, 2006.
- Comfort A, The New Joy of Sex. New York, Crown Publishers, Inc, 2002.
- Keeling B, Sexual Healing: The Complete Guide to Overcoming Common Sexual Problems. Alameda, CA, Hunter House Publishing, 2006.

Drug(s) of Choice

None. Hormone replacement therapy for postmenopausal women may improve sexual function, especially if vaginal dryness or atrophy play a role in the dysfunction. Testosterone treatment improves libido but does not result in improved sexual functioning and is generally not indicated as a treatment for sexual dysfunction except in women who are surgically menopausal. Flibanserin (Addyi) has been recently approved by the Food and Drug Administration (FDA) for hypoactive sexual desire disorder (HSDD). Side effects are common (hypotension), the efficacy is

limited (increased satisfying sexual events by 0.51 additional event per month over placebo) and because of potentially serious interactions with alcohol, fluconazole, and antidepressants treatment with Addyi will only be available through certified health care professionals and certified pharmacies.

Alternative Therapies

Biofeedback, relaxation therapy, marital or psychologic counseling as needed

Patient Monitoring: Normal health maintenance.

Prevention/Avoidance: Communication, maintenance of general health, adequate rest and exercise. Many patients who do not achieve orgasm during intercourse are fully orgasmic with additional manual stimulation, oral–genital stimulation, a vibrator, or masturbation (approximately 30%–40% of women require concurrent clitoral stimulation to achieve orgasm). This is common enough that it should be viewed as a problem only if it is a source of concern for the patient or her partner. Nicotine and selective serotonin receptor inhibitors (SSRIs) can cause low desire and difficulty with orgasm in women.

Possible Complications: Social withdrawal, depression, marital discord.

Expected Outcome: Generally good with a mixture of reassurance, sexual counseling, stress reduction, and graded exercises as appropriate.

Associated Conditions: Orgasmic dysfunction, dyspareunia, depression.

Pregnancy Considerations: No effect on pregnancy.

Synonyms: Inhibited desire.

ICD-910-CM Codes: F52.0 (Hypoactive sexual desire disorder) and F52.31 (Female orgasmic disorder).

REFERENCES

LEVEL I

Davis SR, Moreau M, Kroll R, et al. Testosterone for low libido in postmenopausal women not taking estrogen. *N Engl J Med*. 2008;359:2005.

Derogatis LR, Komer L, Katz M, et al. Treatment of hypoactive sexual desire disorder in premenopausal women: efficacy of flibanserin in the VIOLET Study. *J Sex Med*. 2012;9:1074.

LEVEL II

Shifren JL, Monz BU, Russo PA, et al. Sexual problems and distress in United States women: prevalence and correlates. *Obstet Gynecol*. 2008;112:970.

Simon JA, Kingsberg SA, Shumel B, et al. Efficacy and safety of flibanserin in postmenopausal women with hypoactive sexual desire disorder: results of the SNOWDROP trial. *Menopause*. 2014;21:633.

LEVEL III

American College of Obstetricians and Gynecologists. Female sexual dysfunction. Practice Bulletin No. 119. *Obstet Gynecol*. 2011;117:996.

Amato P. Categories of female sexual dysfunction. *Obstet Gynecol Clin North Am*. 2006;33:527.

Carey JC. Disorders of sexual desire and arousal. *Obstet Gynecol Clin North Am*. 2006;33:549.

Gracia CR, Freeman EW, Sammel MD, et al. Hormones and sexuality during transition to menopause. *Obstet Gynecol*. 2007;109:831.

Hatzimouratidis K, Hatzichristou D. Sexual dysfunctions: classifications and definitions. *J Sex Med*. 2007;4:241.

Kingsberg S. Testosterone treatment for hypoactive sexual desire disorder in postmenopausal women. *J Sex Med*. 2007;4:227.

McGloin L, Carey JC. Orgasmic dysfunction. *Obstet Gynecol Clin North Am*. 2006;33:579.

Stimmel GL, Gutierrez MA. Counseling patients about sexual issues. *Pharmacotherapy*. 2006;26:1608.

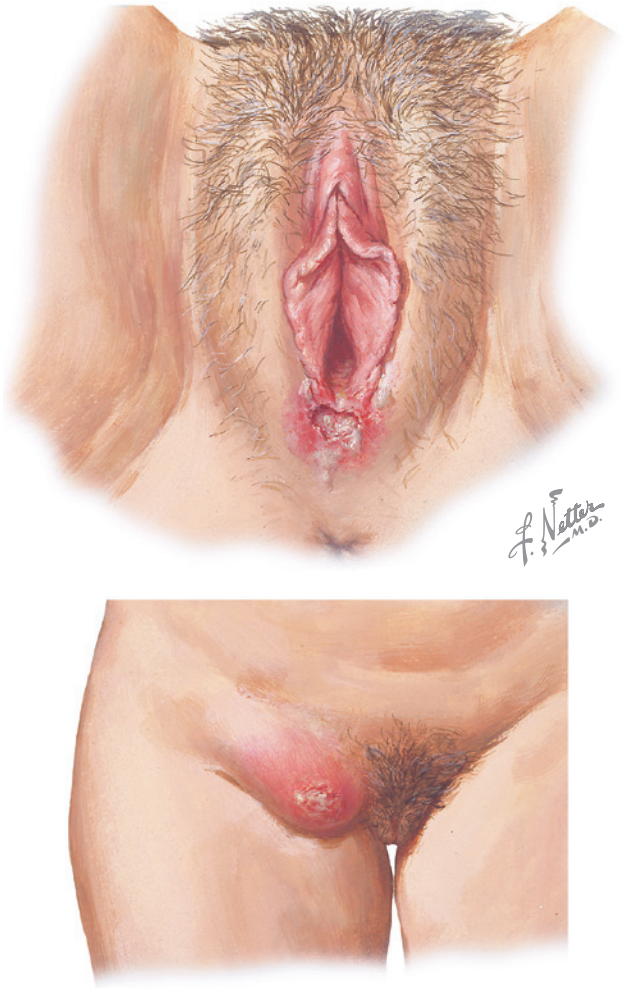


Figure 61.1 Appearance of chancroid

- Granuloma inguinale
- Lymphogranuloma venereum

Associated Conditions: Other STIs, HIV (approximately 10% of persons who have acquired chancroid in the United States are coinfected with *Treponema pallidum* or herpes simplex virus [HSV]. This percentage is higher in persons acquiring chancroid outside the United States.).

Workup and Evaluation

Laboratory: Gram stain and culture of materials from open ulcers. Because of the association with HIV and syphilis, serum testing is highly recommended.
Imaging: No imaging indicated.
Special Tests: None indicated.
Diagnostic Procedures: Diagnosis is established on the basis of clinical findings, finding the gram-negative coccobacillus on smears from the primary lesion or (rarely) on culture of aspirates of the bubo. Biopsy is also diagnostic, although not often performed.

Pathologic Findings

The *H. ducreyi* bacillus is a gram-positive, nonmotile, facultative anaerobe that can be seen in chains on Gram stain or in culture. Superficial and deep ulcers with granulomatous inflammation are found on biopsy.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, culture or Gram stain, topical cleansing, and care.
Specific Measures: Antibiotic treatment for patient and her sexual partner(s). Fluctuant nodes may be drained by aspiration through adjacent normal tissue, but incision and drainage delay healing and should not be attempted.
Diet: No specific dietary changes indicated.
Activity: No sexual activity, until lesions have healed.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP009 (How to Prevent Sexually Transmitted Diseases). Patients should be advised to have all sexual partners examined for diagnosis and treatment.

Drug(s) of Choice

- Azithromycin 1 g PO single dose; ceftriaxone 250 mg IM single dose; ciprofloxacin 500 mg PO twice a day for 3 days; erythromycin 500 mg PO four times a day. Treatment must continue for no less than 10 days or until the lesions heal, whichever is longer.

Contraindications: Erythromycin estolate and ciprofloxacin are contraindicated in pregnancy and should not be used. Ciprofloxacin is contraindicated in patients younger than 18 years.
Precautions: See individual agents. The safety of azithromycin in pregnancy has not been established.
Interactions: See individual agents.

Alternative Drugs

- Trimethoprim 160 mg plus sulfamethoxazole 800 mg PO twice a day. Treatment must continue for no less than 10 days or until the lesions heal, whichever is longer.
- Amoxicillin 500 mg plus clavulanic acid 125 mg (Augmentin) PO every 8 hours for 7 days.

FOLLOW-UP

Patient Monitoring: Follow-up evaluation for cure (improvement in 3–7 days), culture or other tests should be conducted, as well as screening for other STIs. As with all STIs, all sexual partners who have had sexual contact with the patient within the preceding 10 days should be screened and treated for probable infections.
Prevention/Avoidance: Use of barrier contraception (condoms, diaphragm), limitation or elimination of risky behavior (sexual promiscuity).
Possible Complications: Buboes may rupture and drain, causing extensive soft-tissue and skin damage. Chronic draining sinus tracts and abscesses may occur. Scarring is common.
Expected Outcome: If detected early, successful treatment with minimal sequelae may be expected. Buboes, if present, may take several weeks to resolve. Up to 10% of patients have a recurrence at the site of old ulcers.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, although the possibility of vertical transmission of other associated conditions (such as HIV infection) should be considered.
ICD-10-CM Codes: A57 (Chancroid).

REFERENCES

LEVEL I

Al-Tawfiq JA, Palmer KL, Chen CY, et al. Experimental infection of human volunteers with *Haemophilus ducreyi* does not confer protection against subsequent challenge. *J Infect Dis*. 1999;179:1283.

Kaul R, Kimani J, Nagelkerke NJ, Kibera HIV Study Group, et al. Monthly antibiotic chemoprophylaxis and incidence of sexually transmitted infections and HIV-1 infection in Kenyan sex workers: a randomized controlled trial. *JAMA*. 2004;291:2555.

Malonza IM, Tyndall MW, Ndinya-Achola JO, et al. A randomized, double-blind, placebo-controlled trial of single-dose ciprofloxacin versus erythromycin for the treatment of chancroid in Nairobi, Kenya. *J Infect Dis*. 1999;180:1886.

LEVEL II

Chen CY, Mertz KJ, Spinola SM, et al. Comparison of enzyme immunoassays for antibodies to *Haemophilus ducreyi* in a community outbreak of chancroid in the United States. *J Infect Dis*. 1997;175:1390.

Dillon SM, Cummings M, Rajagopalan S, et al. Prospective analysis of genital ulcer disease in Brooklyn, New York. *Clin Infect Dis*. 1997;24:945.

LEVEL III

Abeck D, Freinkel AL, Korting HC, et al. Immunohistochemical investigations of genital ulcers caused by *Haemophilus ducreyi*. *Int J STD AIDS*. 1997;8:585.

Eichmann A. Chancroid. *Curr Probl Dermatol*. 1996;4:20.

Workowski KA, Bolan GA, Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015;64:1.

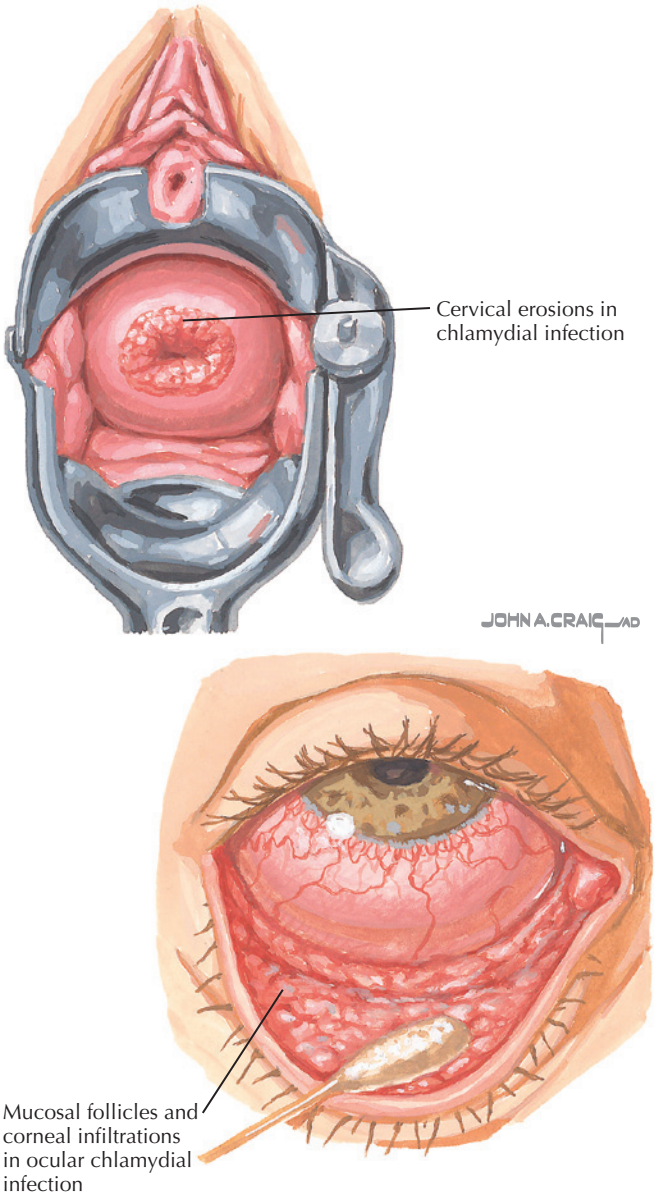


Figure 62.1 Chlamydial infections

Diagnostic Procedures: Physical examination, suspicion, and cervical culture

Pathologic Findings

This infection tends to involve the mucosal layers and not the entire structure. As a result, extensive damage may occur without dramatic symptoms if the fallopian tubes become infected.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and diagnosis.

Specific Measures: Aggressive antibiotic therapy should be instituted in those suspected of infection. Approximately 45% of patients with chlamydial infection have coexisting gonorrhea and this should be considered when choosing a therapy.

Diet: No specific dietary changes indicated.

Activity: No restriction (sexual continence required until infection is resolved).

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP009 (How to Prevent Sexually Transmitted Diseases). Patients should be advised to have all sexual partners seen for diagnosis and treatment.

Drug(s) of Choice

- Azithromycin 1 g PO, single dose.
- Doxycycline 100 mg PO twice a day for 7 days may also be used.

Contraindications: Quinolones (Ofloxacin), tetracyclines (including doxycycline), and erythromycin estolate are contraindicated in pregnancy and should not be used.

Precautions: Pregnant patients with chlamydial infections should be treated with azithromycin, amoxicillin 500 mg PO three times a day for 7–10 days, erythromycin base, or erythromycin ethylsuccinate.

Alternative Drugs

- Erythromycin—erythromycin base 500 mg PO four times a day for 7 days or erythromycin ethylsuccinate 800 mg PO four times a day for 7 days may be substituted for tetracycline in patients who are tetracycline sensitive or pregnant.
- Ofloxacin 300 mg PO twice a day for 7 days.
- Levofloxacin 500 mg orally once daily for 7 days.

FOLLOW-UP

Patient Monitoring: Follow-up evaluation for cure with culture or other tests (3–4 weeks after therapy) and screening for other STIs should be performed. As with all STIs, all sexual partners within the preceding 30 days should be screened and treated for probable infections.

Prevention/Avoidance: Use of barrier contraception (condoms, diaphragm), limitation or elimination of risky behavior (sexual promiscuity).

Possible Complications: Infertility, chronic pelvic pain. If PID occurs the risk of infertility roughly doubles with each subsequent episode, resulting in a 40% rate of infertility after only three episodes. Women with documented salpingitis have a 4-fold increase in their rate of ectopic pregnancy and 5%–15% of women require surgery because of damage caused by PID.

Expected Outcome: If detected early, successful treatment with minimal sequelae may be expected. Significant permanent damage is common despite treatment because of the indolent course of most infections, and thus, the late institution of therapy. Immunity to infection is not long lived; reinfection or persistent infection is common (up to 26% in 1 year).

MISCELLANEOUS

Pregnancy Considerations: There is an increased risk of premature rupture of the membranes and preterm delivery. Neonatal conjunctivitis and ophthalmia neonatorum may result if an infant does not receive adequate prophylaxis. Even with standard protection (1% $AgNO_3$ or 0.5% erythromycin ointment), complete protection is not assured.

ICD-10-CM Codes: A56.00 (Chlamydial infection of lower genitourinary tract, unspecified).

REFERENCES

LEVEL II

Hoover KW, Leichliter JS, Torrone EA, et al. Chlamydia screening among females aged 15-21 years—multiple data sources, United States, 1999-2010. *MMWR Surveill Summ*. 2014;63(suppl 2):80.

Lau C-Y, Qureshi AK. Azithromycin versus doxycycline for genital chlamydial infections: a meta-analysis of randomized clinical trials. *Sex Transm Dis*. 2002;29:497.

Lyss SB, Kamb ML, Peterman TA, et al. *Chlamydia trachomatis* among patients infected with and treated for *Neisseria gonorrhoeae* in sexually transmitted disease clinics in the United States. *Ann Intern Med*. 2003;139:178.

Ness RB, Trautmann G, Richter HE, et al. Effectiveness of treatment strategies of some women with pelvic inflammatory disease: a randomized trial. *Obstet Gynecol*. 2005;106:573.

Rours GI, Duijts L, Moll HA, et al. *Chlamydia trachomatis* infection during pregnancy associated with preterm delivery: a population-based prospective cohort study. *Eur J Epidemiol*. 2011;26:493.

Tanaka M, Nakayama H, Sagiyama K, et al. Evaluation of a new amplified enzyme immunoassay (EIA) for the detection of *Chlamydia trachomatis* in male urine, female endocervical swab, and patient-obtained vaginal swab specimens. *J Clin Pathol*. 2000;53:350.

LEVEL III

American College of Obstetricians and Gynecologists. Expedited partner therapy in the management of gonorrhea and chlamydial infection. Committee Opinion No. 632. *Obstet Gynecol*. 2015;125:1526.

Centers for Disease Control and Prevention. Recommendations for the Laboratory-Based Detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae*—2014. *MMWR Recomm Rep*. 2014;63(RR–2).

Crossman SH. The challenge of pelvic inflammatory disease. *Am Fam Physician*. 2006;73:859.

Gottlieb SL, Xu F, Brunham RC. Screening and treating *Chlamydia trachomatis* genital infection to prevent pelvic inflammatory disease: interpretation of findings from randomized controlled trials. *Sex Transm Dis*. 2013;40:97.

LeFevre ML, U.S. Preventive Services Task Force. Screening for *chlamydia* and gonorrhea: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2014;161:902.

Lee HH, Chernesky MA, Schachter J, et al. Diagnosis of *Chlamydia trachomatis* genitourinary infection in women by ligase chain reaction assay of urine. *Lancet*. 1995;345:213.

Low N. Screening programmes for chlamydial infection: when will we ever learn? *BMJ*. 2007;334:725.

Peipert JF. Clinical practice. Genital chlamydial infections. *N Engl J Med*. 2003;349:2424.

Torrone E, Papp J, Weinstock H. Prevalence of *Chlamydia trachomatis* genital infection among persons aged 14–39 years—United States, 2007–2012. *MMWR Morb Mortal Wkly Rep*. 2014;63:834.

Workowski KA, Bolan GA, Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015;64:1.

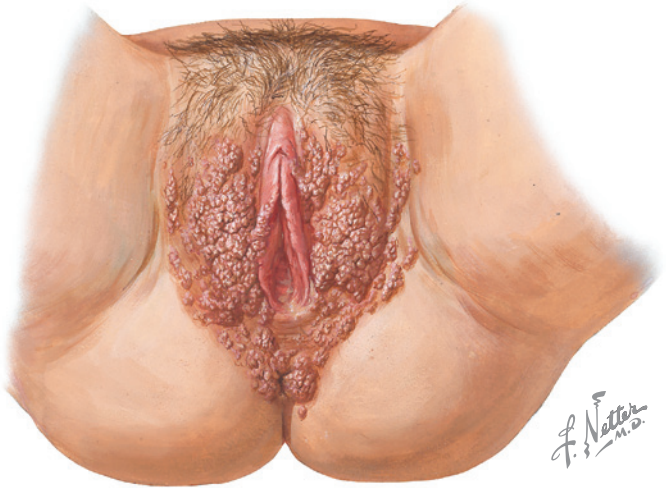


Figure 63.1 Condylomata acuminata

these sites are involved with the infection. Patients are at an increased risk for anogenital and head and neck cancers for more than 10 years following the diagnosis.

Workup and Evaluation

Laboratory: No evaluation indicated; tests for syphilis when indicated.
Imaging: No imaging indicated.
Special Tests: Colposcopic examination; Pap test; or the application of 3%–5% acetic acid to make apparent the raised, white, shiny plaques. Serotyping is not currently indicated when condylomata are the only issue. Biopsy is indicated if the warts are pigmented, indurated, fixed, bleeding, ulcerated, or if the diagnosis is unclear.
Diagnostic Procedures: Physical examination, colposcopy, and biopsy.

Pathologic Findings

Sessile (keratotic) lesions

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Local hygiene.
Specific Measures: The treatment of small, uncomplicated venereal warts is generally by cytolytic topical agents, such as podophyllin (Podophyllum resin), bichloracetic or trichloroacetic acid (TCA), or physical ablative methods such as laser, cryotherapy, or electrodesiccation. In rare selected patients, surgical excision or tangential shaving may be used.
Diet: No specific dietary changes indicated.
Activity: Sexual continence until partner(s) are examined and treated.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP009 (How to Prevent Sexually Transmitted Infections), AP191 (Human Papillomavirus Vaccination). Patients should be advised to have all sexual partners seen for diagnosis and treatment.

Drug(s) of Choice

- Podophyllin (20%–50% in tincture of benzoin, 25% ointment); podophyllotoxin (0.5% solution, Condylox); or bichloracetic or trichloroacetic acid (80%–100% solution, first-line therapy during pregnancy) carefully applied to the warts, protecting the adjacent skin, and allowed to remain for between 30 minutes and 4 hours before being washed off the lesions.
- With most topical therapy, slough of the treated lesions occurs in 2–4 days.
- Treatment may be repeated every 7–14 days as required.
- Patients may self-apply podofilox (0.5% solution or gel, twice a day for 3 days) or imiquimod (5% cream, Aldara, every night three times per week for up to 16 weeks or 3.75% cream once per day for up to 8 weeks).

Contraindications: Podophyllin may not be used during pregnancy because of absorption, potentially resulting in neural or myelotoxicity.
Precautions: To limit toxicity with podophyllin, treatments should be limited to less than 0.5 mL total volume and less than 10 cm^2 in area. Imiquimod should be washed from the vulva in the morning (after 6–10 hours).

Alternative Drugs

- Treatment with 5-fluorouracil 1% or 5% cream is often used as primary therapy or as an adjunct for cervical or vaginal lesions (applied daily until edema, erythema, or vesiculation occurs).
- Therapy with autologous vaccine, dinitrochlorobenzene, sinecatechins (a defined green tea extract) and interferon have been advocated but have yet to gain a significant place in clinical practice.

FOLLOW-UP

Patient Monitoring: Use of sitz baths, mild analgesics, and loose clothing can relieve discomfort and aid healing. The patient should be weekly examined until no further lesions are found. Because these patients are at a higher risk for cervical neoplasia, close follow-up with Pap tests, colposcopy, or both, at 6- to 12-month intervals is recommended. Follow-up serologic testing for syphilis and human immunodeficiency virus (HIV) infection as indicated. The sexual partners of patients with HPV should also be screened for genital warts.
Prevention/Avoidance: Limitation or elimination of risky behavior (sexual promiscuity). The use of condoms has not been shown to reduce the spread of HPV but should still be encouraged to reduce the spread of other STIs. Quadrivalent and 9-valent HPV vaccine (Gardasil: types 6, 11, 16, and 18; Gardasil 9: additional types 31, 33, 45, 52, and 58) should provide some measure of protection, although its primary indication is to reduce the risk of cervical cancer. Immunization is recommended for female adolescents and adults aged 9–26 years. Immunization programs using currently available vaccines have resulted in a drop in the incidence of infection in many studies.
Possible Complications: Those who are immunocompromised, such as patients who have received a transplant, patients with acquired immune deficiency syndrome (AIDS), or pregnant patients may experience rapid and exuberant growth of condyloma. External factors that suppress the immune system (steroids, cigarette smoking, metabolic deficiencies, and infections with other viruses such as herpes) may have similar effects. Several subtypes (16, 18, 31, 33, 35, and others) are associated with the development of cervical neoplasia. Approximately 90% of patients with cervical squamous cell carcinoma have evidence of HPV DNA present in their cervical tissues. It is currently considered that a cocarcinogen, such as smoking, other viruses, or nutritional factors, are required before malignant transformation may occur.
Expected Outcome: The success rate for resolution of overt warts is approximately 75%, with a recurrence rate of 65%–80%. If lesions persist or continually recur, cryosurgery, electrodesiccation, surgical excision, or laser vaporization may be required. If cryotherapy is chosen, three to six treatments are often required,

but cure rates are higher than those for podophyllin and comparable with those for laser ablation (60%–80%). Even with laser ablation, recurrence rates are reported to vary from 25% to 100%. Scarring is rare. HPV types 16, 18, 31, 33, and 35 are occasionally found in visible genital warts and have been associated with external genital (ie, vulvar, penile, and anal) squamous intraepithelial neoplasia (ie, squamous cell carcinoma in situ, bowenoid papulosis, erythroplasia of Queyrat, or Bowen disease of the genitalia). For this reason, recurrent lesions or those that do not respond as expected should be further investigated.

MISCELLANEOUS

Pregnancy Considerations: Pregnant patients may experience rapid and exuberant growth of condyloma, and lesions are more resistant to therapy. Extensive vaginal or vulvar lesions may require cesarean delivery to avoid extensive lacerations and suturing problems.

ICD-10-CM Codes: A63.0 [Anogenital (venereal) warts].

REFERENCES

LEVEL I

Georgala S, Katoulis AC, Befon A, et al. Oral inosiplex in the treatment of cervical condylomata acuminata: a randomized placebo-controlled trial. *BJOG*. 2006;113:1088.

Tatti S, Swinehart JM, Thielert C, et al. Sinecatechins, a defined green tea extract, in the treatment of external anogenital warts: a randomized controlled trial. *Obstet Gynecol*. 2008;111:1371.

LEVEL II

Bonnez W, Elswick RK Jr, Bailey-Farchione A, et al. Efficacy and safety of 0.5% podofilox solution in the treatment and suppression of anogenital warts. *Am J Med*. 1994;96:420.

Conley LJ, Ellenbrock TV, Bush TJ, et al. HIV-1 infection and risk of vulvovaginal and perianal condylomata acuminata and intraepithelial neoplasia: a prospective cohort study. *Lancet*. 2002;359:108.

Leval A, Herweijer E, Arnheim-Dahlström L, et al. Incidence of genital warts in Sweden before and after quadrivalent human papillomavirus vaccine availability. *J Infect Dis*. 2012;206:860.

Smith MA, Liu B, McIntyre P, et al. Fall in genital warts diagnoses in the general and indigenous Australian population following implementation of a national human papillomavirus vaccination program: analysis of routinely collected national hospital data. *J Infect Dis*. 2015;211:91.

Smith LM, Strumpf EC, Kaufman JS, et al. The early benefits of human papillomavirus vaccination on cervical dysplasia and anogenital warts. *Pediatrics*. 2015;135:e1131.

LEVEL III

American College of Obstetricians and Gynecologists. Cervical cancer screening and prevention. Practice Bulletin No. 157. American College of Obstetricians and Gynecologists. *Obstet Gynecol*. 2016;127:e1.

American College of Obstetricians and Gynecologists. Human papillomavirus vaccination. Committee Opinion No. 641. *Obstet Gynecol*. 2015;126:e38-e43.

Herrero R, González P, Markowitz LE. Present status of human papillomavirus vaccine development and implementation. *Lancet Oncol*. 2015;16:e206.

Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015;64:1.

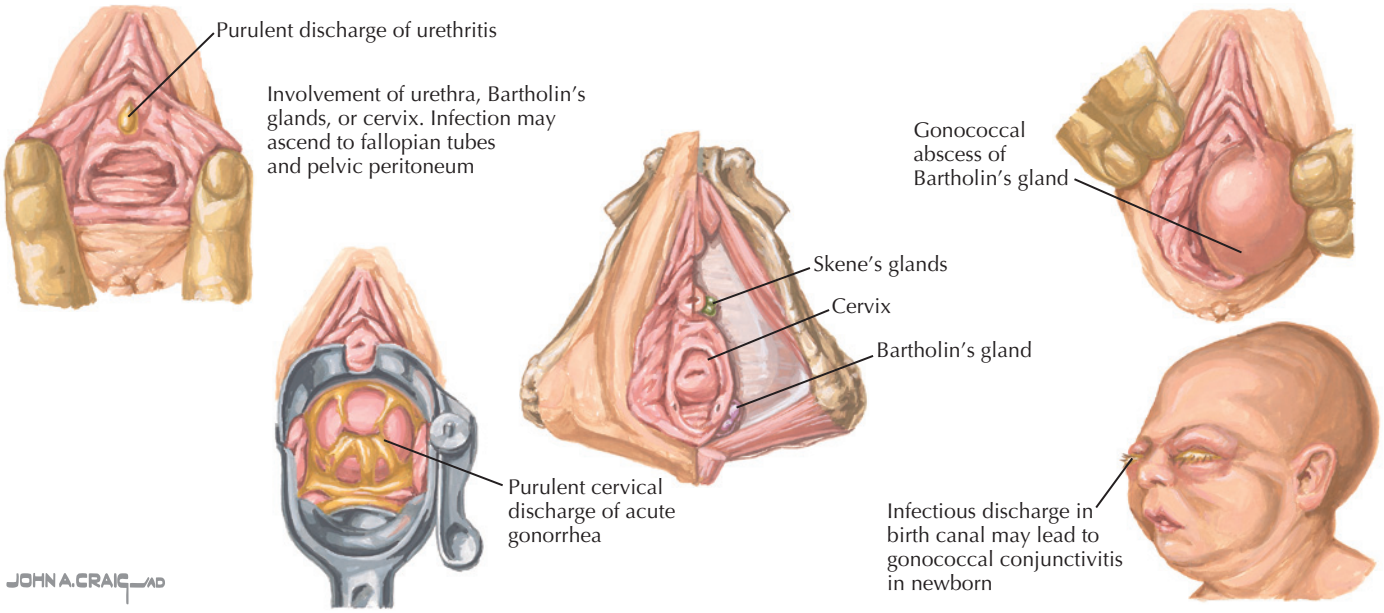


Figure 64.1 Gonorrhea

Workup and Evaluation

Laboratory: Traditional culturing on Thayer-Martin agar plates maintained in a CO_2-rich environment has been replaced by nucleic acid amplification testing (NAAT) as the preferred method. Cervical tests provide 80%–95% diagnostic sensitivity. Specimens should also be obtained from the urethra and anus, although these additional samples do not significantly increase the sensitivity of testing. A Gram stain of any cervical discharge for the presence of gram-negative intracellular diplococcus supports the presumptive diagnosis but does not establish it (sensitivity, 50%–70%; specificity, 97%). Even when the diagnosis is established by other methods, all cases of gonorrhea should have cultures obtained to assess antibiotic susceptibility, although therapy should not be delayed pending the results.
Imaging: No imaging indicated. Ultrasonography may demonstrate free fluid in the cul-de-sac when pelvic inflammation is present.
Special Tests: None indicated.
Diagnostic Procedures: Physical examination, suspicion, and cervical culture.

Pathologic Findings

Gram-negative intracellular diplococcus associated with diffuse inflammatory reaction (transluminal in the fallopian tube).

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and diagnosis.
Specific Measures: Aggressive antibiotic therapy should be instituted in patients suspected of having an infection.
Diet: No specific dietary changes indicated.
Activity: No restriction. Sexual continence is required until the infection has resolved.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP009 (How to Prevent Sexually Transmitted Diseases). Patients should be advised to have all sexual partners examined for diagnosis and treatment.

Drug(s) of Choice

- Ceftriaxone 250 mg IM in a single dose plus azithromycin 1 g orally in a single dose.

Contraindications: The use of ceftriaxone or cefixime is contraindicated in those patients with a history of an IgE-mediated β-lactam allergy, such as anaphylaxis, Stevens-Johnson syndrome, or toxic epidermal necrolysis.
Precautions: See individual agents.
Interactions: See individual agents.

Alternative Drugs

- Cefixime 400 mg orally in a single dose plus azithromycin 1 g orally in a single dose. Recent clinical trials showed that dual treatment with a single 320-mg dose of oral gemifloxacin plus a 2-g dose of oral azithromycin, or dual treatment with a single 240-mg dose of IM gentamicin plus a 2-g dose of oral azithromycin, were effective for uncomplicated urogenital gonorrhea.

FOLLOW-UP

Patient Monitoring: When patients are treated with the currently recommended ceftriaxone–azithromycin, therapy failure is rare and a follow-up culture is not necessary. Reexamination of the patient in 1–2 months for the possibility of reinfection may be warranted in patients at high risk. As with all sexually transmitted infections (STIs), all sexual partners within the preceding 30 days should be screened and treated for probable infections.
Prevention/Avoidance: Use barrier contraception (condoms, diaphragm), limitation or elimination of risky behavior (sexual promiscuity).
Possible Complications: Damage caused by *N. gonorrhoeae* infection causes an increased risk of recurrent pelvic infection, chronic pelvic pain, or infertility resulting from tubal damage or hydrosalpinx formation. The impact of a gonorrheal infection is much greater for women than for men. For every three men infected, two women are hospitalized for 1 or more days. For every 18 men infected, 1 woman undergoes surgery. It is estimated that one

episode of gonorrhea is associated with a 15% infertility rate and this increases to 75% for three or more infections. The risk of an ectopic pregnancy is increased 7–10 times in women with a history of salpingitis. Neonatal infections acquired from a mother with gonorrhea may result in conjunctivitis or pneumonia. Pregnant patients are more likely to experience disseminated gonococcal infection. They account for 7%–40% of all cases.

Expected Outcome: If detected early, successful treatment with minimal sequelae may be expected. Significant permanent damage is common despite treatment because of the indolent course of many infections and the late institution of therapy.

MISCELLANEOUS

Pregnancy Considerations: Pregnant patients should be treated with combined therapy as above. Patients with severe penicillin or cephalosporin allergy can be administered dual therapy with a 240-mg dose of IM gentamicin and 2-g oral azithromycin. Neonatal conjunctivitis and ophthalmia neonatorum may result if the infant does not receive adequate prophylaxis.

ICD-10-CM Codes: A54.00 (Gonococcal infection of lower genitourinary tract, unspecified), A54.29 (Other gonococcal genitourinary infections); others based on chronicity and organ involved.

REFERENCES

LEVEL II

Golden MR, Whittington WL, Handsfield HH, et al. Effect of expedited treatment of sex partners on recurrent or persistent gonorrhea or chlamydial infection. *N Engl J Med*. 2005;352:676.

Kirkcaldy RD, Bolan GA, Wasserheit JN. Cephalosporin-resistant gonorrhea in North America. *JAMA*. 2013;309:185.

Kirkcaldy RD, Hook EW 3rd, Soge OO, et al. Trends in *Neisseria gonorrhoeae* susceptibility to cephalosporins in the United States, 2006-2014. *JAMA*. 2015;314:1869.

Martin I, Sawatzky P, Liu G, et al. Decline in decreased cephalosporin susceptibility and increase in azithromycin resistance in *Neisseria gonorrhoeae*, Canada. *Emerg Infect Dis*. 2016;22:65.

LEVEL III

American College of Obstetricians and Gynecologists. Gynecologic care for women with human immunodeficiency virus. Practice Bulletin No. 117. *Obstet Gynecol*. 2010;117:1492.

American College of Obstetricians and Gynecologists. Expedited partner therapy in the management of gonorrhea and chlamydial infection. Committee Opinion No. 632. *Obstet Gynecol*. 2015;125:1526.

American College of Obstetricians and Gynecologists. Dual therapy for gonococcal infections. Committee Opinion No. 645. *Obstet Gynecol*. 2015;126:e95.

Centers for Disease Control and Prevention. 2014 *Sexually Transmitted Diseases Surveillance*. Available at: <http://www.cdc.gov/std/stats14/gonorrhea.htm> Accessed 16.01.16.

Centers for Disease Control and Prevention. Recommendations for the Laboratory-Based Detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* — 2014. *MMWR Recomm Rep*. 2014;63:(RR-02):1-19.

Kidd S, Workowski KA. Management of gonorrhea in adolescents and adults in the United States. *Clin Infect Dis*. 2015;61(suppl 8):S785.

LeFevre ML, U.S. Preventive Services Task Force. Screening for *chlamydia* and gonorrhea: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2014;161:902.

Low N, Unemo M. Molecular tests for the detection of antimicrobial resistant *Neisseria gonorrhoeae*: when, where, and how to use? *Curr Opin Infect Dis*. 2016;29:45.

Workowski KA, Bolan GA, Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015;64:1.

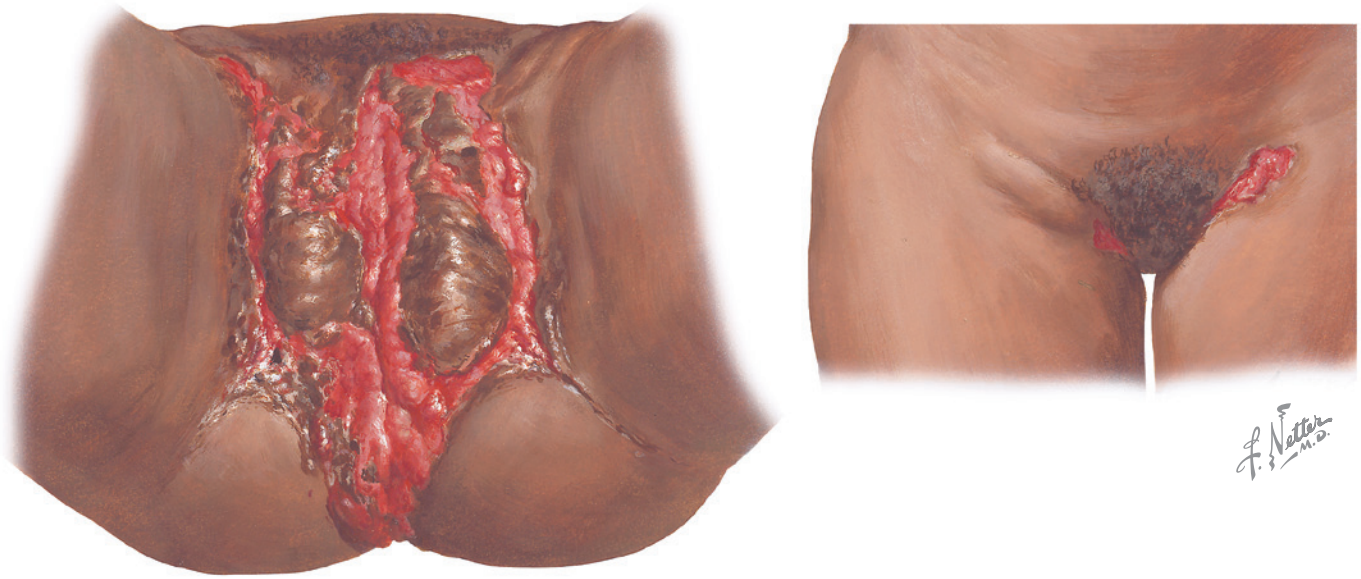


Figure 65.1 Granuloma inguinale

Workup and Evaluation

Laboratory: Gram stain and culture of material from open ulcers. Screening for other sexually transmitted infections (STIs) should also be considered.
Imaging: No imaging indicated.
Special Tests: Samples for biopsy may be taken from the edge of the ulcer to confirm the diagnosis. A crushed tissue smear may be examined for Donovan bodies.
Diagnostic Procedures: Diagnosis is clinically established through the identification of intracytoplasmic bacteria (Donovan bodies) in mononuclear cells.

Pathologic Findings

Granulation tissue associated with an extensive chronic inflammatory cell infiltrate and endarteritis. The ulcer is filled with fibrinous exudate and necrosis; plasma cells and mononuclear cells predominate. Donovan bodies (large vacuolated histiocytes with encapsulated bacilli) are diagnostic. Granuloma inguinale extends by local infiltration and by lymphatic permeation in later stages.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, culture or Gram stain, topical cleansing and care.
Specific Measures: Antibiotic therapy.
Diet: No specific dietary changes indicated.
Activity: No restriction. Sexual continence required until infection is resolved.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP009 (How to Prevent Sexually Transmitted Diseases). Patients should be advised to have all sexual partners examined for diagnosis and treatment.

Drug(s) of Choice

- Azithromycin 1 g PO once per week for at least 3 weeks and until all lesions have completely healed or
- Doxycycline 100 mg PO twice a day for a minimum of 3 weeks or
- Ciprofloxacin 750 mg PO twice a day for at least 3 weeks and until all lesions have completely healed or
- Erythromycin base 500 mg PO four times a day for at least 3 weeks and until all lesions have completely healed or
- Trimethoprim-sulfamethoxazole, one double-strength tablet PO twice a day for a minimum of 3 weeks.

Contraindications: Known or suspected allergy,
Precautions: Tetracyclines should not be used during pregnancy if at all possible because staining of teeth and inhibition of bone growth are both possible. Sulfonamides should not be used during pregnancy.
Interactions: See individual agents.

Alternative Drugs

- Ciprofloxacin 750 mg PO twice a day for a minimum of 3 weeks.
- Erythromycin 500 mg PO four times a day for a minimum of 3 weeks.
- If lesions fail to show improvement after the first week of treatment, chloramphenicol (500 mg PO three times a day) or gentamicin (1 mg/kg twice a day) should be considered.

FOLLOW-UP

Patient Monitoring: Because of relapse and late scarring, these patients should be followed carefully for several weeks. Follow-up evaluation for cure with culture or other tests should be carried out, as should screening for other STIs. As with all STIs, all sexual partners within the preceding 30 days should be screened and treated for probable infections as well.
Prevention/Avoidance: None.
Possible Complications: Secondary infection or significant scarring may occur in patients with untreated disease.
Expected Outcome: Gradual healing with antibiotic treatment, but scarring and vulvar stenosis are common and may require surgical treatment.

MISCELLANEOUS

Pregnancy Considerations: No direct effect on pregnancy. Women who are pregnant or lactating should be treated with macrolides

(erythromycin or azithromycin). However, because erythromycin estolate has been associated with hepatotoxicity in up to 10% of pregnancies, erythromycin base or erythromycin ethylsuccinate should be used.

ICD-9-CM Codes: A58 (Granuloma inguinale).

REFERENCES

LEVEL III

Basta-Juzbašić A, Čeović R. Chancroid, lymphogranuloma venereum, granuloma inguinale, genital herpes simplex infection, and molluscum contagiosum. *Clin Dermatol*. 2014;32:290.

Keck JW. Ulcerative lesions. *Clin Fam Pract*. 2005;7:13-30.

Krieger JN. Biology of sexually transmitted diseases. *Urol Clin North Am*. 1984;11:15-25.

Kuberski T. Granuloma inguinale (donovanosis). *Sex Transm Dis*. 1980;7:29.

Richens J. Donovanosis (granuloma inguinale). *Sex Transm Infect*. 2006;82 (suppl 4):iv21.

Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015;64:1.

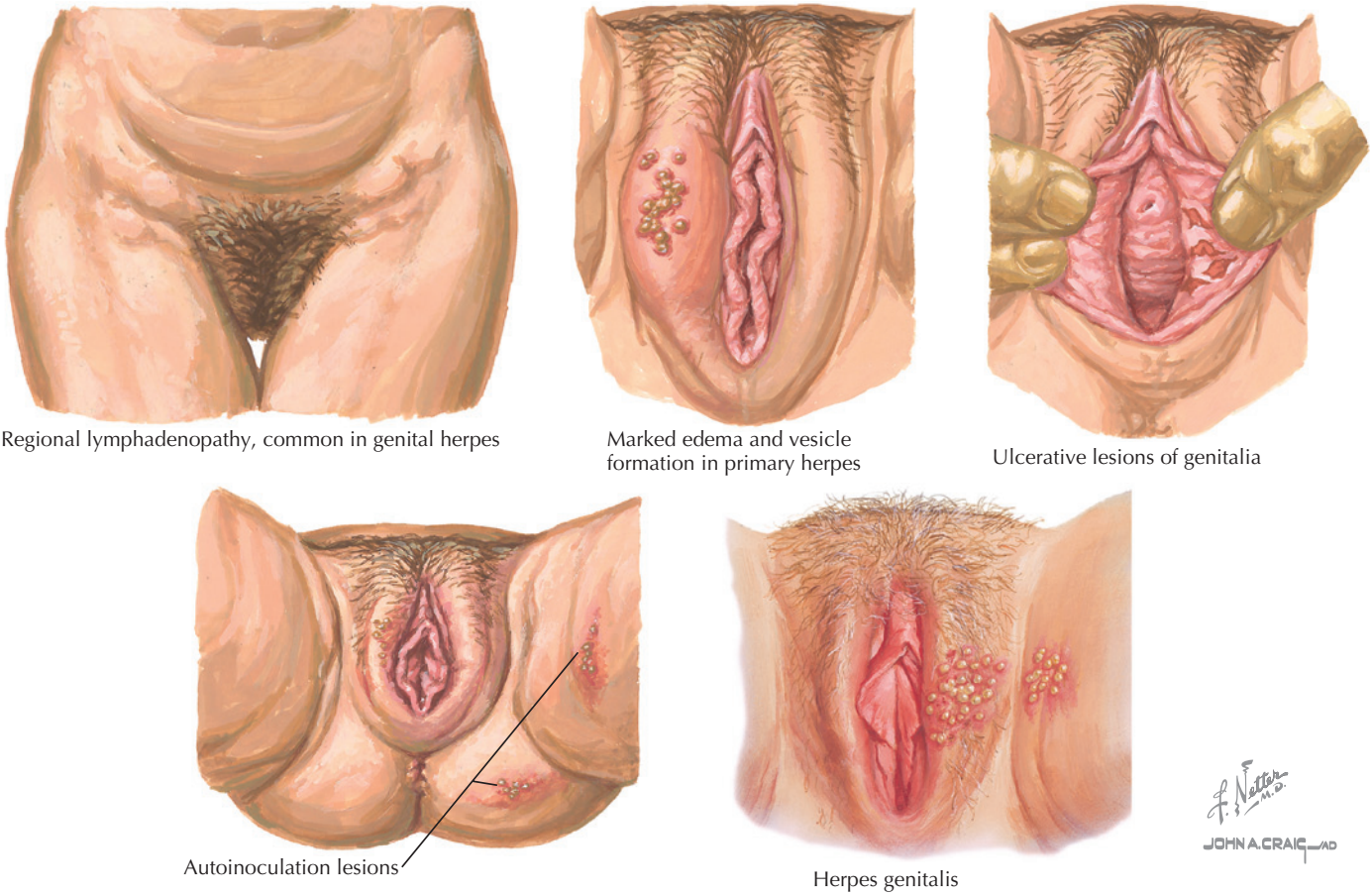


Figure 66.1 Lesions of herpes simplex

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Topical cleansing, sitz baths followed by drying with a heat lamp or hair dryer, analgesics.

Specific Measures: Topical analgesics (lidocaine (Xylocaine) 2% jelly, nonprescription throat spray with phenol), antiviral agents. If secondary infections occur, therapy with a local antibacterial cream, such as Neosporin, is appropriate.

Diet: No specific dietary changes indicated.

Activity: Pelvic rest until lesions have healed.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP009 (How to Prevent Sexually Transmitted Diseases). Patients should be advised to have all sexual partners examined for diagnosis and treatment. Counseling regarding the natural history of genital herpes, sexual and perinatal transmission, and methods to reduce transmission is integral to clinical management.

Drug(s) of Choice

- Acute (begun within 48 hours of onset)—acyclovir ointment (Zovirax or generic) 5% applied locally every 3 hours; acyclovir 400 mg PO three times a day or 200 mg PO five times a day while lesions are present; famciclovir (Famvir) 250 mg PO three times a day for 7–10 days); or valacyclovir (Valtrex) 1 g PO twice a day for 5 days will decrease the duration of symptoms and viral shedding.
- For frequent recurrences or suppression—acyclovir 400 mg PO three times a day or 800 mg PO twice a day, increased to five times a day with lesions; famciclovir (Famvir) 500 mg PO twice a day; or valacyclovir (Valtrex) 500 mg twice a day is effective in decreasing frequency and severity of flare-ups but use is generally limited to less than 6 months.

Contraindications: Known or suspected hypersensitivity. Acyclovir is pregnancy category C; famciclovir and valacyclovir are pregnancy category B. Suppressive therapy should not be used for pregnant patients.

Precautions: Thrombotic thrombocytopenic purpura/hemolytic uremic syndrome has been reported in some patients with HIV taking valacyclovir. It has not been encountered in patients who are immunocompetent. Antiviral agents should be used with caution in patients with compromised renal function.

Interactions: Antiviral agents may interact with or enhance the effects of nephrotoxic agents.

Alternative Drugs

In severe infections, acyclovir 5–10 mg/kg IV every 8 hours for 5–7 days may be required.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. Watch for possible recurrence.

Prevention/Avoidance: Sexual continence during prodrome to full healing, use of condoms to reduce risk, sexual monogamy. Prior HSV-1 infection does not affect the rate of HSV-2 acquisition, but increases the likelihood of asymptomatic infection by three-fold.

Possible Complications: Between 60% and 90% of patients have recurrences of the herpetic lesions in the first 6 months after initial infection. Although generally shorter and milder, these recurrent attacks are no less virulent. Having HSV-2 infection increases the risk of HIV acquisition.

Expected Outcome: Healing of the lesions is generally complete. Inguinal adenopathy may persist for several weeks after the resolution of the vulvar lesions. Suppuration is uncommon. Complete resolution of all symptoms occurs in 2–4 weeks.

MISCELLANEOUS

Pregnancy Considerations: Significant risk to neonate if acute infection or viral shedding occurs at the time of delivery or rupture of the membranes. Infection is also associated with an increased risk of early fetal loss. The risk for transmission to the neonate from an infected mother is high (30%–50%) among women who acquire genital herpes near the time of delivery and is low (<1%) among women with histories of recurrent herpes at term or who acquire genital HSV during the first half of pregnancy. Women with recurrent genital herpetic lesions at the onset of labor should give birth by cesarean delivery to prevent neonatal herpes; however, this does not completely eliminate the risk. Acyclovir may be orally administered to pregnant women with first-episode genital herpes or severe recurrent herpes and should be intravenously administered to pregnant women with severe HSV infection. Acyclovir treatment late in pregnancy (acyclovir 400 mg PO three times daily from 36 weeks of gestation) reduces the frequency of cesarean deliveries among women who have recurrent genital herpes by diminishing the frequency of recurrences at term. Recurrent HSV has not been associated with miscarriage or embryopathy.

ICD-10-CM Codes: A60.04 (Herpesviral vulvovaginitis).

REFERENCES

LEVEL I

Aoki FY, Tyring S, Diaz-Mitoma F, et al. Single-day patient initiated famciclovir therapy for recurrent genital herpes: a randomized, double-blind, placebo-controlled trial. *Clin Infect Dis*. 2006;42:8.

Sheffield JS, Hill JB, Hollier LM, et al. Valacyclovir prophylaxis to prevent recurrent herpes at delivery: a randomized clinical trial. *Obstet Gynecol*. 2006;108:141.

Watts DH, Brown ZA, Money D, et al. A double-blind, randomized, placebo-controlled trial of acyclovir in late pregnancy for the reduction of herpes simplex virus shedding and cesarean delivery. *Am J Obstet Gynecol*. 2003;188:836.

LEVEL II

Andrews WW, Kimberlin DF, Whitley R, et al. Valacyclovir therapy to reduce recurrent genital herpes in pregnant women. *Am J Obstet Gynecol*. 2006;194:774.

Corey L, Wald A, Patel R, et al. Once-daily valacyclovir to reduce the risk of transmission of genital herpes. *N Engl J Med*. 2004;350:11.

Gupta R, Wald A, Krantz E, et al. Valacyclovir and acyclovir for suppression of shedding of herpes simplex virus in the genital tract. *J Infect Dis*. 2004;190:1374.

Hollier LM, Wendel GD. Third trimester antiviral prophylaxis for preventing maternal genital herpes simplex virus (HSV) recurrences and neonatal infection. *Cochrane Database Syst Rev*. 2008;CD004946.

Nagot N, Ouedraogo A, Foulongne V, et al.; ANRS 1285 Study Group. Reduction of HIV-1 RNA levels with therapy to suppress herpes simplex virus. *N Engl J Med*. 2007;356:790.

Roberts CM, Pfister JR, Spear SJ. Increasing proportion of herpes simplex virus type 1 as a cause of genital herpes infection in college students. *Sex Transm Dis*. 2003;30:797.

Sheffield JS, Hollier LM, Hill JB, et al. Acyclovir prophylaxis to prevent herpes simplex virus recurrence at delivery: a systematic review. *Obstet Gynecol*. 2003;102:1396.

Wald A, Krantz E, Selke S, et al. Knowledge of partners' genital herpes protects against herpes simplex virus type 2 acquisition. *J Infect Dis*. 2006;194:42.

LEVEL III

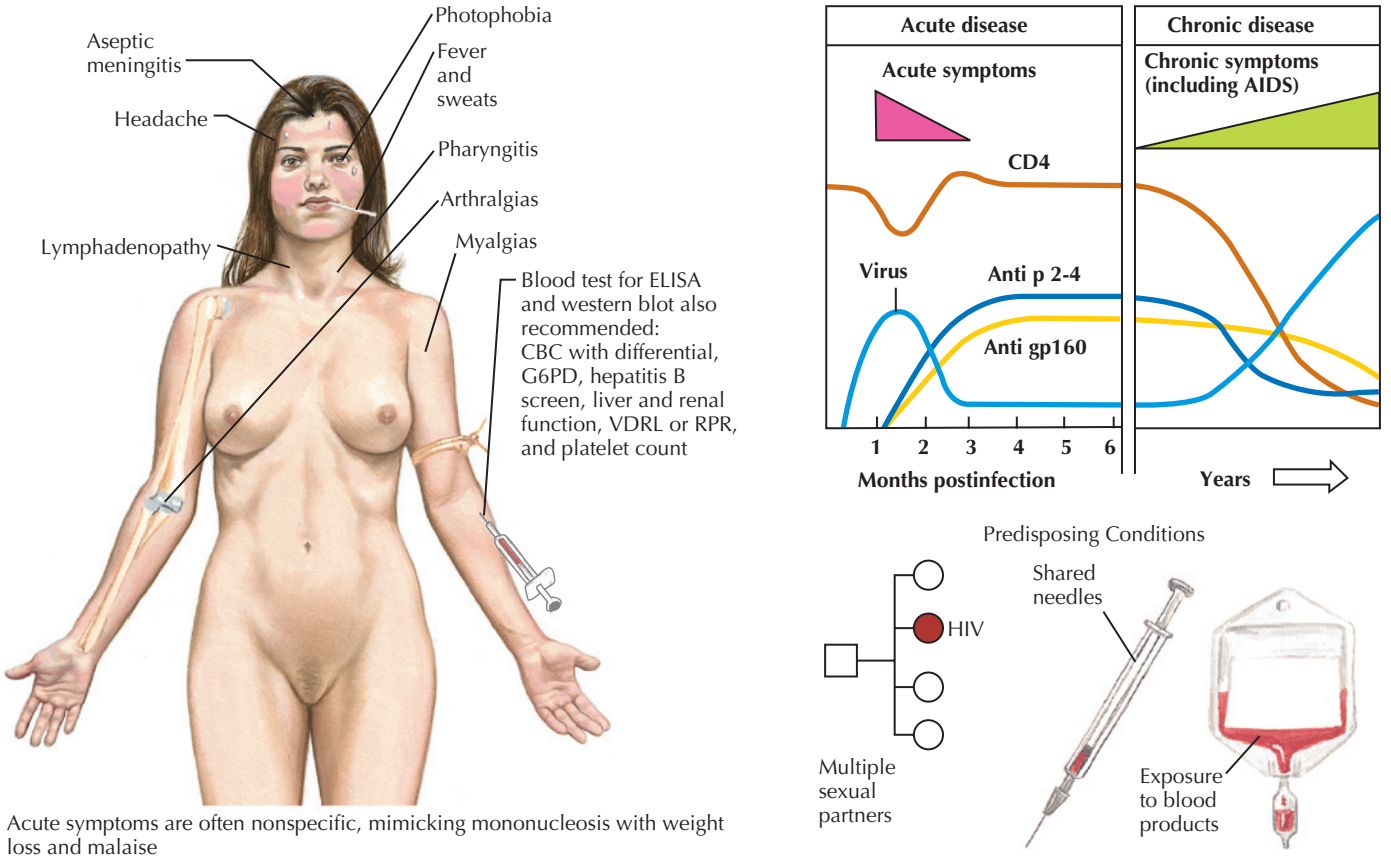
American College of Obstetricians and Gynecologists. Management of herpes in pregnancy. ACOG Practice Bulletin No. 82. *Obstet Gynecol*. 2007;109:1489.

Sen P, Barton SE. Genital herpes and its management. *BMJ*. 2007;334:1048.

Tita AT, Grobman WA, Rouse DJ. Antenatal herpes serologic screening: an appraisal of the evidence. *Obstet Gynecol*. 2006;108:1247.

Westhoff GL, Little SE, Caughey AB. Herpes simplex virus and pregnancy: a review of the management of antenatal and peripartum herpes infections. *Obstet Gynecol Surv*. 2011;66:629.

Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015;64:1.



AIDS, acquired immunodeficiency syndrome; CBC, complete blood count; ELISA, enzyme-linked immunosorbent assay; G6PD, glucose 6-phosphate dehydrogenase, RPR, rapid plasma reagin; VDRL, Venereal Disease Research Laboratory.

Figure 67.1 Clinical course and signs of HIV

women have a five-fold greater risk than other women of contracting HIV.

Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Infection with HIV, a retrovirus that preferentially infects helper lymphocytes but may infect macrophages, cells of the central nervous system, and possibly the placenta. Incubation from infection to clinical symptoms ranges from 5 days to 3 months, with an average of 2–4 weeks.

Risk Factors: Sexual activity (multiple partners or infected partner, 37% of all infections), parenteral exposure to blood (sharing needles, inadvertent needle stick), perinatal exposure of infants. There is no evidence that HIV infection may be transmitted by casual contact, immune globulin preparations, hepatitis B vaccine, or contact with biting insects. HIV infection following donor insemination has been reported.

SIGNS AND SYMPTOMS

- Nonspecific symptoms, often mimicking mononucleosis with aseptic meningitis (90%). Febrile pharyngitis is the most common, with fever, sweats, lethargy, arthralgia, myalgia, headache, photophobia, and lymphadenopathy lasting up to 2 weeks.

- Signs of loss of immune function—fever, weight loss, malaise, lymphadenopathy, central nervous system dysfunction, abnormal Pap test result, recurrent cervical intraepithelial neoplasia (CIN), oral or vaginal candidiasis. *Pneumocystis jirovecii* pneumonia is the most common AIDS-defining infection.
- Patients are often diagnosed late in the progression of the disease (up to 40% within 1 year of developing AIDS).

DIAGNOSTIC APPROACH

Differential Diagnosis

- Mononucleosis
- Systemic lupus erythematosus (SLE)

Associated Conditions: Associated with cardiac disease and abnormalities of bone marrow, kidney, and liver function. Psychiatric conditions and neurocognitive problems are common. Gynecologic—abnormal Pap test results, cervical intraepithelial neoplasia and cervical or anal cancer, condylomata acuminata, increased risk of pregnancy loss.

Workup and Evaluation

Laboratory: Enzyme-linked immunosorbent assay (ELISA) with positive results confirmed by Western blot analysis and virologic testing (HIV RNA levels; sensitivity and specificity >99%). Informed consent is recommended before testing. False-positive Western blot test results are uncommon and are found on the order of less than 1 in 130,000. Antibodies may not be detectable until 6–12 weeks after infection. Other tests include complete blood count, with differential white count, electrolytes, glucose 6-phosphate dehydrogenase, hepatitis B screen, liver and renal function tests, platelet count, Venereal Disease Research Laboratory (VDRL), or rapid plasma reagent (RPR) test.

Imaging: No imaging indicated.

Special Tests: Tests for tuberculosis (tuberculin skin test with control [*Candida*, mumps, tetanus]) and other infections should be considered in individuals with HIV, Pap test.

Diagnostic Procedures: ELISA and Western blot analysis.

Pathologic Findings

Reduced CD4 counts and diffuse evidence of immunocompromise.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Health maintenance, avoidance of stress and infection.

Specific Measures: Management is focused on stabilization of HIV disease, prevention of opportunistic infections, and prevention of perinatal transmission. When CD4 counts are less than 200, antibiotic prophylaxis should be initiated.

Diet: No specific dietary changes indicated.

Activity: No restriction.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP009 (How to Prevent Sexually Transmitted Diseases). Patient counseling should include the risk of infections associated with sexual behavior, intravenous drug use, the risk of transmission to an infant, the availability of treatment to reduce that risk, and the risk and benefits of treatment for the patient.

Drug(s) of Choice

- Antiretroviral therapy is used to reduce vertical transmission during pregnancy. Multiple drug therapy is common for individuals with HIV, but the best combination remains to be determined and guidelines are rapidly changing. Referral to a specialist is recommended.
- Prophylactic drugs—trimethoprim 160 mg, sulfamethoxazole 800 mg daily as prophylaxis for those at risk (CD4 counts, <200). Significant infections must be specifically and aggressively treated.

FOLLOW-UP

Patient Monitoring: Increased frequency of monitoring, including periodic assessment of blood and CD4 counts. The frequency depends on the stage of HIV infection, use of antiretroviral therapy, and presence of other medical or social comorbidities and complications.

Prevention/Avoidance: Avoidance of risky behaviors such as intravenous drug use or multiple sexual partners, universal precautions for healthcare workers, consistent use of condoms, substance abuse prevention and treatment programs, and counseling programs. Prophylaxis after acute exposure (eg, needle stick) with zidovudine singly or in combination with other agents has been shown to reduce the risk of infection.

Possible Complications: Opportunistic infections (bacterial, mycotic, and viral), increased risk of malignancy (cervical, Kaposi sarcoma, lymphoma), central nervous system dysfunction. Hormonal contraceptive can interfere with the efficacy of some antiretroviral agents and other medications commonly used.

Expected Outcome: After recovery from the initial infection, the patient enters a carrier state during which symptoms are absent, but viral shedding occurs. Immune dysfunction generally becomes apparent approximately 10 years after the initial infection. The development of immunocompromise is rare before 3 years after infection and less than 35% develop symptoms of AIDS before 5 years. Continuing progress in treatment of HIV infection and AIDS has resulted in a state of remission or quiescence for most patients who are treated early, appropriately, and who maintain treatment.

MISCELLANEOUS

Pregnancy Considerations: Significant risk of vertical transmission and worsening of maternal disease. Prenatal screening and suppressive strategies have reduced the risk of vertical transmission to approximately 2%. There is potential fetal risk associated with efavirenz.

ICD-10-CM Codes: Z21 [Asymptomatic human immunodeficiency virus (HIV) infection status], B20 [Human immunodeficiency virus (HIV) disease].

REFERENCES

LEVEL I

Gallant JE, DeJesus E, Arribas JR, et al.; Study 934 Group. Tenofovir DF, emtricitabine, and efavirenz vs. zidovudine, lamivudine, and efavirenz for HIV. *N Engl J Med*. 2006;354:251.

Gulick RM, Ribaudo HJ, Shikuma CM, et al.; AIDS Clinical Trials Group (ACTG) A5095 Study Team. Three- vs four-drug antiretroviral regimens for the initial treatment of HIV-1 infection: a randomized controlled trial. *JAMA*. 2006;296:769.

Lockman S, Shapiro RL, Smeaton LM, et al. Response to antiretroviral therapy after a single, peripartum dose of nevirapine. *N Engl J Med*. 2007;356:135.

LEVEL II

Chéret A, Nembot G, Mélard A, et al. Intensive five-drug antiretroviral therapy regimen versus standard triple-drug therapy during primary HIV-1 infection (OPTIPRIM-ANRS 147): a randomised, open-label, phase 3 trial. *Lancet Infect Dis*. 2015;15:387.

HIV-CAUSAL Collaboration, Ray M, Logan R, et al. The effect of combined antiretroviral therapy on the overall mortality of HIV-infected individuals. *AIDS*. 2010;24:123.

Martínez-Bonet M, Puertas MC, Fortuny C, et al. Establishment and replenishment of the viral reservoir in perinatally HIV-1-infected children initiating very early antiretroviral therapy. *Clin Infect Dis*. 2015; 61:1169.

Morrison CS, Chen PL, Kwok C, et al. Hormonal contraception and the risk of HIV acquisition: an individual participant data meta-analysis. *PLoS Med*. 2015;12:e1001778.

Nagot N, Ouedraogo A, Foulongne V, et al.; ANRS 1285 Study Group. Reduction of HIV-1 RNA levels with therapy to suppress herpes simplex virus. *N Engl J Med*. 2007;356:790.

Phillips SJ, Polis CB, Curtis KM. The safety of hormonal contraceptives for women living with HIV and their sexual partners. *Contraception*. 2016;93:11.

Pilcher CD, Eron JJ Jr, Vemazza PL, et al. Sexual transmission during the incubation period of primary HIV infection. *JAMA*. 2001;286:1713.

Polis CB, Phillips SJ, Curtis KM, et al. Hormonal contraceptive methods and risk of HIV acquisition in women: a systematic review of epidemiological evidence. *Contraception*. 2014;90:360.

Ralph LJ, McCoy SI, Shiu K, et al. Hormonal contraceptive use and women's risk of HIV acquisition: a meta-analysis of observational studies. *Lancet Infect Dis*. 2015;15:181.

LEVEL III

American College of Obstetricians and Gynecologists, Scheduled Cesarean Delivery and the Prevention of Vertical Transmission of HIV Infection, Committee Opinion 234, Washington, DC, ACOG, 2000.

Günthard HF, Aberg JA, Eron JJ, et al. Antiretroviral treatment of adult HIV infection: 2014 recommendations of the International Antiviral Society-USA Panel. *JAMA*. 2014;312:410.

Jourjy J, Dahl K, Huesgen E. Antiretroviral treatment efficacy and safety in older HIV-infected adults. *Pharmacotherapy*. 2015;35:1140.

Rubens M, Ramamoorthy V, Saxena A, et al. HIV vaccine: recent advances, current roadblocks, and future directions. *J Immunol Res*. 2015;2015: 560347.

Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015;64:1.

DIAGNOSTIC APPROACH

Differential Diagnosis

- Secondary syphilis (condyloma lata), other viral infections.

Associated Conditions: Other STIs.

Workup and Evaluation

Laboratory: No evaluation indicated (see special tests).
Imaging: No imaging indicated.
Special Tests: HPV serotyping for those with abnormal cervical cytology (Pap tests), colposcopy for those with persistently abnormal cytology or for surveillance of those with high-risk serotypes.
Diagnostic Procedures: Serotyping of HPV obtained from cervical cells. This testing is important for those with abnormal cervical cytology (atypical squamous cells of undetermined significance (ASCUS) or above Pap tests) or may be a part of cotesting to allow a reduced frequency of cervical cytologic screening. These tests will identify 13 high-risk serotypes. Because most young patients will clear even high-risk serotypes with no sequela, recommendations for serotyping and aggressive follow-up of abnormal Pap test results have changed to more conservative management schemes.

Pathologic Findings

Cellular atypia (koilocytotic changes) may be found in infected cells. Research suggests the degree of atypia to be a function of the serotype involved.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: There is no specific therapy available or indicated for HPV infection—most (>90%) infections are cleared by the body with little or no symptoms or sequela.
Specific Measures: Only those directed at the specific symptoms generated by persistent infection; condyloma or cervical epithelial change.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Booklet AP163 (Cancer of the Cervix), AP187 (Abnormal Cervical Cancer Screening Test Results), and AP191 (Human Papillomavirus Vaccination).

Drug(s) of Choice

None.
Contraindications: The HPV vaccines are currently contraindicated in patients with known allergies to any of its components and those who are currently pregnant.
Precautions: None.
Interactions: HPV vaccine can be administered at the same visit as other age-appropriate vaccines, such as the tetanus, diphtheria, and pertussis (Tdap) and quadrivalent meningococcal conjugate (MCV4) vaccines.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. Frequent cervical monitoring (cytology and/or colposcopy) for those found to have persistent high-risk serotypes.
Prevention/Avoidance: Abstinence. Condom use is thought to reduce the risk of transmission (a study among newly sexually active college women demonstrated a 70% reduction in HPV infection when their partners used condoms consistently and correctly). Vaccines that provide immunity against high-risk types 16 and 18 (considered to account for 70% of cervical cancers) and low-risk types 6 and 11 (associated with condylomata acuminata). Quadrivalent and 9-valent HPV vaccines (Gardasil: types 6, 11, 16, and 18; Gardasil 9: additional types 31, 33, 45, 52, and 58) are recommended for female adolescents and adults aged 9–26 years. The currently available vaccines are administered as a series of three injections over 6 months (0, 2, and 6 months) and may be associated with local pain, swelling, itching and redness, fever, nausea, or dizziness.
Possible Complications: Both high- and low-risk types of HPV can cause the growth of abnormal cells, but generally only the high-risk types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 69, and possibly a few others) are associated with cervical cancer. These high-risk types may cause flat condyloma that are often difficult to see compared with the more exuberant warts caused by low-risk types such as types 6 and 11. HPV 16 is the most common high-risk type, found in almost half of all cervical cancers (HPV 18 accounts for 10%–12% of cervical cancers). HPV 16 is also one of the most common types found in women without cancer. High-risk types can be detected in 99% of cervical cancers. It is important to note that most infections by both high- and low-risk types are spontaneously cleared and do not cause clinical problems.
Expected Outcome: Most infections spontaneously clear. For those with persistent infections, warty growths, dysplastic cellular changes, and epithelial cancers may emerge over time.

MISCELLANEOUS

Pregnancy Considerations: No direct effect on pregnancy. Vertical transmission to the infant during delivery may occur. Although vaccination during pregnancy is contraindicated, lactating women may receive the vaccine.
Other Notes: All warts are caused by papillomaviruses, but each type of HPV grows only in specific areas of the body. Those types associated with common warts found on the hands and feet are not sexually transmitted.

Table 68.1 HPV Serotypes and Common Clinical Conditions

Disease	HPV Strain
Anogenital warts	6 and 11 (90% of cases), 42, 43, 44, 55, and others
Cervical cancer, vulvar squamous cancer	16 and 18 (70% of cases), 31, 33, 35, 39, 45, 51
Bowen disease	16, 18, 31, 32, 34, and others
Common warts	2, 1, 7
Epidermodysplasia verruciformis	More than 15 strains
Flat cutaneous warts	3, 10
Focal epithelial hyperplasia	12, 32
Oral papillomas	6, 7, 11, 16, 32
Oropharyngeal squamous cell carcinoma	16 and others
Plantar warts	1, 2, 4
Respiratory papillomatosis	6 and 11

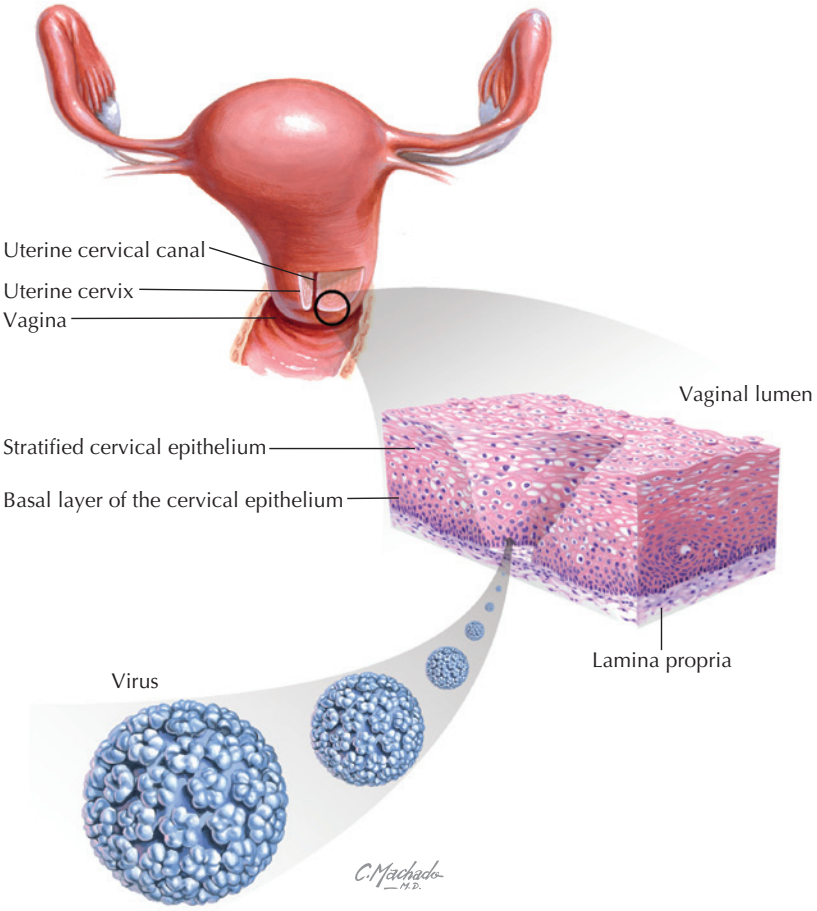


Figure 68.1 Human papillomavirus

Patients with low-grade squamous intraepithelial lesions (LSIL) or high-grade squamous intraepithelial lesions (HSIL) on Pap test results almost always have high-risk HPV on serotyping; thus, typing for these patients does not add anything to their management and is usually not indicated for these individuals. Between 5% and 30% of individuals infected with HPV are infected with multiple serotypes.

ICD-10-CM Codes: B97.7 (Papillomavirus as the cause of diseases classified elsewhere), R87.810 (Cervical high risk human papillomavirus [HPV] DNA test positive), A63.0 (Anogenital [venereal] warts).

REFERENCES

LEVEL I

FUTURE I/II Study Group, Dillner J, Kjaer SK, et al. Four year efficacy of prophylactic human papillomavirus quadrivalent vaccine against low grade cervical, vulvar, and vaginal intraepithelial neoplasia and anogenital warts: randomised controlled trial. *BMJ*. 2010;341:c3493.

LEVEL II

de Sanjose S, Quint WG, Alemany L, et al. Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. *Lancet Oncol*. 2010;11:1048.

Houlihan CF, Larke NL, Watson-Jones D, et al. Human papillomavirus infection and increased risk of HIV acquisition. A systematic review and meta-analysis. *AIDS*. 2012;26:2211.

Leval A, Herweijer E, Arnheim-Dahlström L, et al. Incidence of genital warts in Sweden before and after quadrivalent human papillomavirus vaccine availability. *J Infect Dis*. 2012;206:860.

Markowitz LE, Hariri S, Lin C, et al. Reduction in human papillomavirus (HPV) prevalence among young women following HPV vaccine introduction in the United States, National Health and Nutrition Examination Surveys, 2003-2010. *J Infect Dis*. 2013;208:385.

Munoz N, Bosch FX, de Sanjosé S, et al. Epidemiologic classification of human papillomavirus types associated with cervical cancer. *N Engl J Med*. 2003;348:518.

Smith LM, Strumpf EC, Kaufman JS, et al. The early benefits of human papillomavirus vaccination on cervical dysplasia and anogenital warts. *Pediatrics*. 2015;135:e1131.

Srodon M, Stoler MH, Baber GB, et al. The distribution of low and high-risk HPV types in vulvar and vaginal intraepithelial neoplasia (VIN and VaIN). *Am J Surg Pathol*. 2006;30:1513.

Steinau M, Hariri S, Gillison ML, et al. Prevalence of cervical and oral human papillomavirus infections among US women. *J Infect Dis*. 2014;209:1739.

Winer RL, Hughes JP, Feng Q, et al. Condom use and the risk of genital human papillomavirus infection in young women. *N Engl J Med*. 2006;354:2645.

LEVEL III

American College of Obstetricians and Gynecologists. Human papillomavirus vaccination. Committee Opinion No. 641. *Obstet Gynecol*. 2015;126:e38-e43.

American College of Obstetricians and Gynecologists. Cervical cancer screening and prevention. Practice Bulletin No. 157. American

College of Obstetricians and Gynecologists. *Obstet Gynecol*. 2016; 127:e1.
Clifford GM, Goncalves MA, Franceschi S; HPV and HIV Study Group. Human papillomavirus types among women infected with HIV: a meta-analysis. *AIDS*. 2006;20:2337.
Dunne EF, Markowitz LE. Genital human papillomavirus infection. *Clin Infect Dis*. 2006;43:624.
Herrero R, González P, Markowitz LE. Present status of human papillomavirus vaccine development and implementation. *Lancet Oncol*. 2015; 16:e206.
Trottier H, Franco EL. The epidemiology of genital human papillomavirus infection. *Vaccine*. 2006;24:S1.
Wiley D, Masongsong E. Human papillomavirus: the burden of infection. *Obstet Gynecol Surv*. 2006;61:S3.
Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015;64:1.

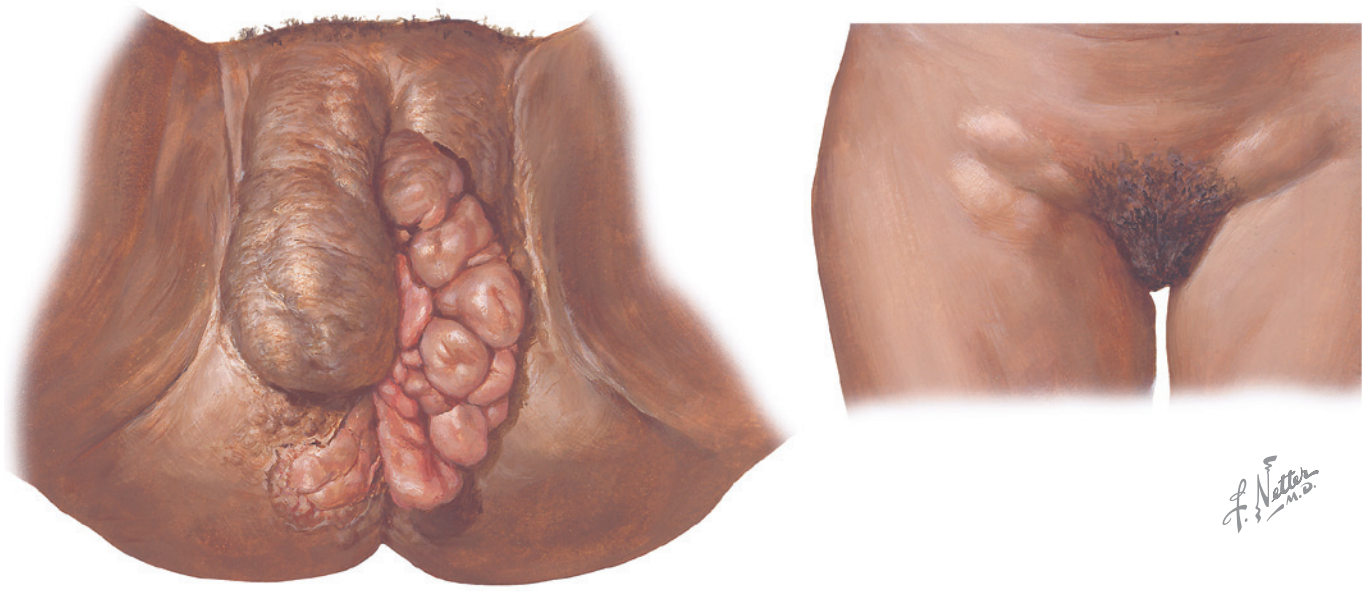


Figure 69.1 Lymphogranuloma venereum

Contraindications: Erythromycin estolate and tetracyclines are contraindicated in pregnancy and should not be used.
Precautions: Doxycycline is contraindicated in pregnant women.
Interactions: See individual agents.

Alternative Drugs

Erythromycin 500 mg PO four times a day for 3 weeks or sulfadiazine 2 g PO loading dose, 1 g PO four times a day for 14–21 days may be substituted. Azithromycin 1.0 g PO once weekly for 3 weeks has been suggested, but clinical data are lacking.

FOLLOW-UP

Patient Monitoring: Follow-up evaluation for cure with culture or other tests should be carried out, as should screening for other STIs. As with all STIs, all sexual partners within the preceding 30 days should be screened and treated for probable infections as well.
Prevention/Avoidance: Use of barrier contraception (condoms, diaphragm), limitation or elimination of risky behavior (sexual promiscuity).
Possible Complications: In one-third of patients, abscess formation, rupture, and fistula formation occur. Chronic progressive lymphangitis with chronic edema and sclerosing fibrosis may occur, causing extensive destruction of the vulva. Rectal stenosis also may occur and may be life threatening.
Expected Outcome: If detected early, successful treatment with minimal sequelae may be expected. Long-term scarring and disfigurement are common.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, although the possibility of vertical transmission of other associated conditions (such as HIV infection) should be considered. Pregnant and lactating women should be treated with erythromycin (doxycycline use is contraindicated in pregnant women).
ICD-10-CM Codes: A55 (Chlamydial lymphogranuloma [venereum]).

REFERENCES

LEVEL II

Chen CY, Chi KH, Alexander S, et al. A real-time quadriplex PCR assay for the diagnosis of rectal lymphogranuloma venereum and non-lymphogranuloma venereum *Chlamydia trachomatis* infections. *Sex Transm Infect*. 2008;84:273.

Pearlman MD, McNeeley SG. A review of the microbiology, immunology and clinical implications of *Chlamydia trachomatis* infections. *Obstet Gynecol Surv*. 1992;47:448.

LEVEL III

Ballard RC, Ye H, Matta A, et al. Treatment of chancroid with azithromycin. *Int J STD AIDS*. 1996;7:9.

Basta-Juzbašić A, Čeović R. Chancroid, lymphogranuloma venereum, granuloma inguinale, genital herpes simplex infection, and molluscum contagiosum. *Clin Dermatol*. 2014;32:290.

Campbell WF, Dodson MG. Clindamycin therapy for *Chlamydia trachomatis* in women. *Am J Obstet Gynecol*. 1990;162:343.

de Vries HJ, Morré SA, White JA, et al. European guideline for the management of lymphogranuloma venereum, 2010. *Int J STD AIDS*. 2010;21:533.

Goens JL, Schwartz RA, De Wolf K. Mucocutaneous manifestations of chancroid, lymphogranuloma venereum and granuloma inguinale. *Am Fam Physician*. 1994;49:415, 423.

Sevinsky LD, Lambierto A, Casco R, et al. Lymphogranuloma venereum: tertiary stage. *Int J Dermatol*. 1997;36:47.

Stoner BP, Cohen SE. Lymphogranuloma Venereum 2015: Clinical Presentation, Diagnosis, and Treatment. *Clin Infect Dis*. 2015;61(suppl 8):S865.

Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015;64:1.

SEXUALLY TRANSMITTED INFECTIONS: MOLLUSCUM CONTAGIOSUM

70

INTRODUCTION

Description: Molluscum contagiosum is a papillary lesion caused by viral infection (poxvirus) that is spread by skin-to-skin contact, first described in 1817.

Prevalence: 2/100,000; 1 of 40–60 patients with gonorrhea; approximately 1% of all skin disorders in the United States.

Predominant Age: Early reproductive age.

Genetics: No genetic pattern. The virus shares one-half of the genes found in variola and vaccinia viruses.

ETIOLOGY AND PATHOGENESIS

Causes: Molluscum contagiosum is caused by the largest member of the poxvirus group. This mildly contagious DNA virus infects epithelial tissues, and autoinoculation to other sites is common. The appearance of lesions ranges from 1 week to 6 months, with an average incubation period of 6 weeks. The virus can also infect other primates and kangaroos.

Risk Factors: Sexual activity and direct exposure to the infective agent.

SIGNS AND SYMPTOMS

- Asymptomatic
- After several weeks of incubation, a round, umbilicated papule, 1–5 mm in size, with a yellow, waxy core of cheesy material (these lesions may grow slowly for months; they may be solitary or occur in clusters) that may occur anywhere on the body except the palms and soles
- Eczema (10%)

The lesions of molluscum are highly contagious, and appropriate precautions should be used when examining the lesions or material from the lesions to avoid infection or spread.

DIAGNOSTIC APPROACH

Differential Diagnosis

- Sebaceous cysts
- Folliculitis
- Herpes simplex
- Dermal papilloma
- Nevus

Associated Conditions: Other sexually transmitted infections (STIs).

Workup and Evaluation

Laboratory: No evaluation indicated. Because patients who are immunosuppressed are at higher risk for molluscum, testing for

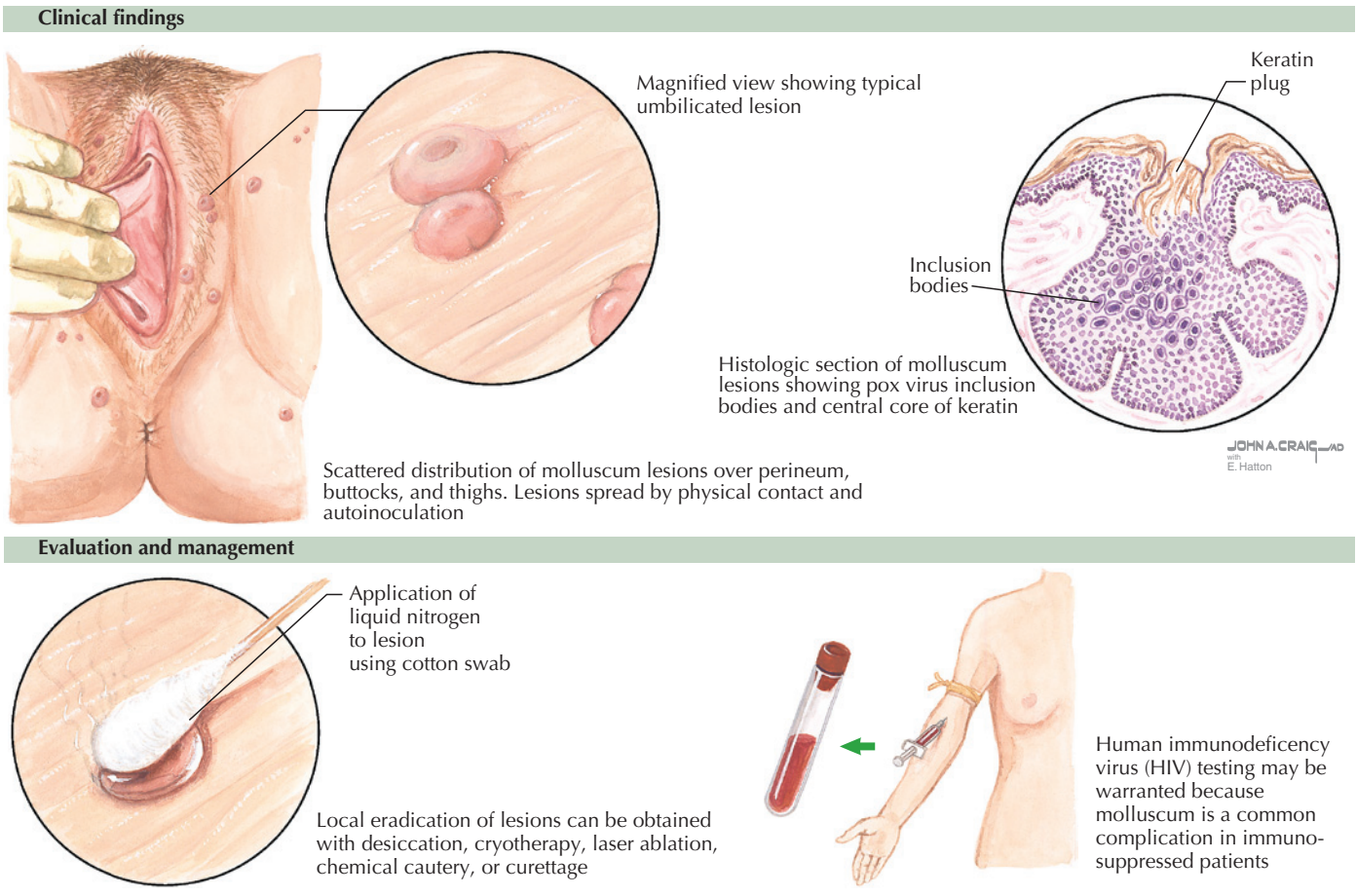


Figure 70.1 Clinical findings and evaluation and management of molluscum contagiosum

human immunodeficiency virus (HIV) infection should be considered.

Imaging: No imaging indicated.

Special Tests: Material from the lesions is microscopically examined; inclusion bodies are seen in the material from the core of the lesion (molluscum bodies or Henderson-Paterson bodies).

Diagnostic Procedures: Clinical picture and examination of material from lesion.

Pathologic Findings

Eosinophilic inclusion bodies (intracytoplasmic) in material from the core of the lesion

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Local care.

Specific Measures: Molluscum lesions may go away on their own in 6–9 months but can persist, via autoinoculation, for up to 4–5 years. Treatment is based on obliterating the lesion. This is done by desiccation, cryotherapy, curettage, laser ablation, or chemical cautery ($AgNO_3$; may cause hyperpigmentation and scarring, cantharidin, trichloroacetic acid, or 10% potassium hydroxide solution). Immune modulators (imiquimod 5% cream) have also been used for selected cases. Curettage of the base of the lesion (with the tip of an 18-gauge needle or curette) is also curative. Bleeding may be controlled with Monsel's solution (ferric subsulfate solution 20%).

Diet: No specific dietary changes indicated.

Activity: No restriction. Sexual continence required until infection is resolved.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP009 (How to Prevent Sexually Transmitted Diseases). Patients should be advised to have all sexual partners examined for diagnosis and treatment.

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Follow-up should occur in 1 month to look for new lesions.

Prevention/Avoidance: Limitation or elimination of risky behavior (sexual promiscuity).

Possible Complications: Local secondary infection.

Expected Outcome: Good response to lesion destruction (generally heals with little or no scarring).

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. Rare vertical transmission has been reported.

ICD-10-CM Codes: B08.1 (Molluscum contagiosum).

REFERENCES

LEVEL I

Hanna D, Hatami A, Powell J, et al. A prospective randomized trial comparing the efficacy and adverse effects of four recognized treatments of molluscum contagiosum in children. *Pediatr Dermatol*. 2006;23:574.

LEVEL II

Handjani F, Behazin E, Sadati MS. Comparison of 10% potassium hydroxide solution versus cryotherapy in the treatment of molluscum contagiosum: an open randomized clinical trial. *J Dermatolog Treat*. 2014;25:249.

Hughes P. Treatment of molluscum contagiosum with the 585-nm pulsed dye laser. *Dermatol Surg*. 1998;24:229.

Senkevich TG, Koonin EV, Bugert JJ, et al. The genome of molluscum contagiosum virus: analysis and comparison with other poxviruses. *Virology*. 1997;233:19.

Tyring SK. Molluscum contagiosum: the importance of early diagnosis and treatment. *Am J Obstet Gynecol*. 2003;189:S12.

Weller R, O'Callaghan CJ, MacSween RM, et al. Scarring in Molluscum contagiosum: comparison of physical expression and phenol ablation. *BMJ*. 1999;319:1540.

LEVEL III

Bard S, Shiman MI, Bellman B, et al. Treatment of facial molluscum contagiosum with trichloroacetic acid. *Pediatr Dermatol*. 2009;26:425.

Chen X, Anstey AV, Bugert JJ. Molluscum contagiosum virus infection. *Lancet Infect Dis*. 2013;13:877.

Gardner LS, Ormond PJ. Treatment of multiple giant molluscum contagiosum in a renal transplant patient with imiquimod 5% cream. *Clin Exp Dermatol*. 2006;31:452.

Tyring SK. Molluscum contagiosum: the importance of early diagnosis and treatment. *Am J Obstet Gynecol*. 2003;189:S12.

van der Wouden JC, van der Sande R, van Suijlekom-Smit LW, et al. Interventions for cutaneous molluscum contagiosum. *Cochrane Database Syst Rev*. 2009;CD004767.

Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015;64:1.

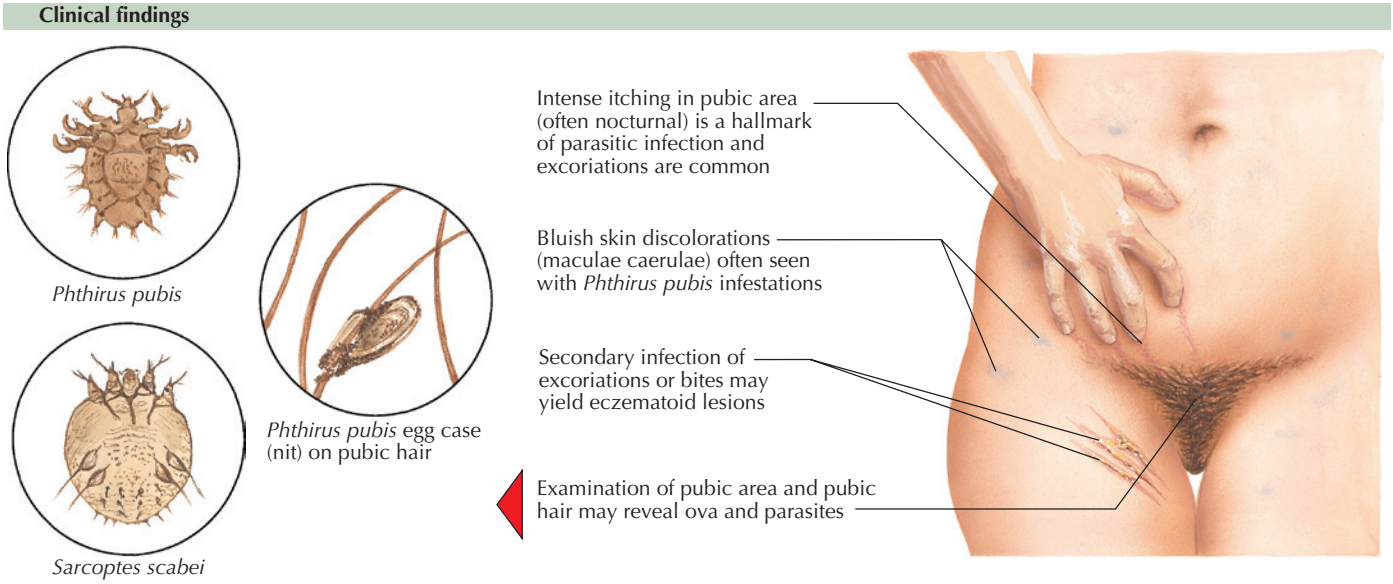


Figure 71.1 Clinical and management in parasites

SIGNS AND SYMPTOMS

- Intense itching (greatest at night), most frequently in the area of the pubic hair
- Infestations most frequently occur in the area of the pubic hair. Spread to other hairy areas can and does occur. Scabies infections are not confined to hairy area but may be found in any area of the body.

DIAGNOSTIC APPROACH

Differential Diagnosis

- Dermatoses
- Contact dermatitis
- Norwegian (crusted) scabies

Associated Conditions: Other sexually transmitted infections (STIs).

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated.
Special Tests: Close inspection of the affected area generally reveals nits, feces, burrows, or the insects themselves.
Diagnostic Procedures: History and physical examinations, microscopic examination of nits.

Pathologic Findings

Inflammatory reaction to the bite, burrow, and feces of the insect

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Local cleansing, soothing creams, or lotions may be used.
Specific Measures: Topical applications of insecticide. Other family members should be treated and the home disinfected at the same time. Scabies—bedding and clothing should be decontaminated (ie, either machine washed, machine dried using the hot cycle, or dry cleaned) or removed from body contact for at least 72 hours. Fumigation of living areas is unnecessary.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP009 (How to Prevent Sexually Transmitted Diseases). Patients should be advised to have all sexual partners examined for diagnosis and treatment.

Drug(s) of Choice

- Permethrin cream 5% applied to all areas of the body from neck down and washed off 8–14 hours later.
- Topical applications of lindane 1% (Kwell) lotion and shampoo applied for 4 minutes and then washed off.
- Malathion 0.5% lotion applied for 8–12 hours and washed off or ivermectin 250 mcg/kg repeated in 2 weeks

Contraindications: Lindane is contraindicated in premature neonates, pregnant or lactating patients, children younger than 2 years, or patients with Norwegian (crusted) scabies. Patients with

seizure disorders or known or suspected hypersensitivity should not use the product.

Precautions: Care must be taken to avoid the eyes. The dose of lindane should be reduced in elderly patients because of increased skin absorption. Lindane should not be used immediately after a bath or shower or by people who have extensive dermatitis (seizures have occurred when lindane was applied after a bath or used by patients who had extensive dermatitis). Aplastic anemia after lindane use has also been reported. Lindane is not recommended as a first-line therapy because of toxicity. It should only be used as an alternative if the patient cannot tolerate other therapies or if other therapies have failed.

Interactions: Oils and ointments may increase the rate of absorption and should not be used.

Alternative Drugs

Crotamiton (Eurax) 10% applied to all areas of the body from neck down for two nights; on the third night, wash off the medication. Repeat the cycle beginning the fourth night.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. Patients should be warned that the rash and pruritus of scabies might persist for up to 2 weeks after treatment.

Prevention/Avoidance: Sexual monogamy.

Possible Complications: Secondary skin infection from scratching.

Expected Outcome: Generally good response to insecticide therapy. Reinfection is possible if each partner, family members, and fomites are not all simultaneously treated.

MISCELLANEOUS

Pregnancy Considerations: No direct effect on pregnancy. Lindane is contraindicated during pregnancy.

ICD-10-CM Codes: B85.3 (*Phthirus pubis*) and 1B86 (Scabies).

REFERENCES

LEVEL II

Burkhart CG. Relationship of treatment-resistant head lice to the safety and efficacy of pediculicides. *Mayo Clin Proc*. 2004;79:661.

Pearlman DL. A simple treatment for head lice: dry-on, suffocation-based pediculicide. *Pediatrics*. 2004;114:e275.

LEVEL III

Chosidow O. Clinical practices. Scabies. *N Engl J Med*. 2006;354:1718.

Galiczynski EM Jr, Elston DM. What's eating you? Pubic lice (Pthirus pubis). *Cutis*. 2008;81:109.

Heukelbach J, Feldmeier H. Ectoparasites—The underestimated realm. *Lancet*. 2004;363:889.

Heukelbach J, Feldmeier H. Scabies. *Lancet*. 2006;367:1767.

Hosidow O. Scabies and pediculosis. *Lancet*. 2000;355:819.

Johnston G, Sladden M. Scabies: diagnosis and treatment. *BMJ*. 2005; 331:619.

Leone PA. Scabies and pediculosis pubis: an update of treatment regimens and general review. *Clin Infect Dis*. 2007;44(suppl 3):S153.

Nash B. Treating head lice. *BMJ*. 2003;326:1256.

Roberts RJ. Clinical practice. Head lice. *N Engl J Med*. 2002;346:1645.

Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015;64:1.

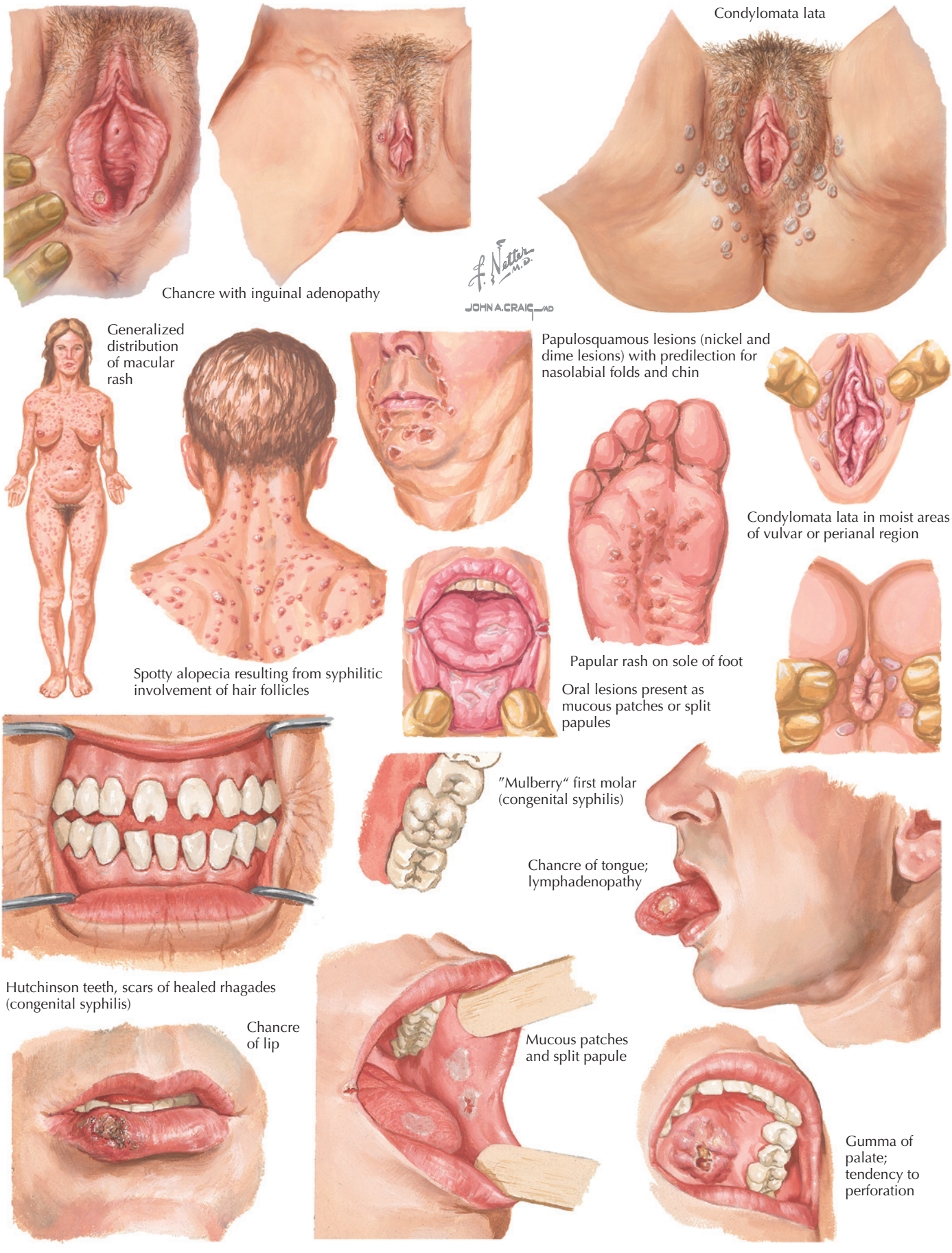


Figure 72.1 Syphilis

Workup and Evaluation

Laboratory: The Venereal Disease Research Laboratory (VDRL) and rapid plasma reagin (RPR) tests are nonspecific and good screening tests because they are rapid and inexpensive. The fluorescent treponemal antibody absorption or microhemagglutination *T. pallidum* tests are specific treponemal antibody tests that are confirmatory or diagnostic; they are not used for routine screening but are useful to rule out a false-positive screening test result. If neurosyphilis is suspected, a lumbar puncture with a VDRL test performed on the spinal fluid is required (unless clinical signs or symptoms of neurologic or ophthalmic involvement are present, cerebrospinal fluid analysis is not recommended for routine evaluation of patients who have primary or secondary syphilis). Screening for HIV infection should also be strongly considered. False-positive screening results may occur in patients with lupus, hepatitis, sarcoidosis, recent immunization, or drug abuse or during pregnancy. These test results may be falsely negative in the second stage of the disease as a result of high levels of anticardiolipin antibody that interfere with the test (prozone phenomenon). Up to 30% of patients with a primary lesion have negative test results (approximately 15%–25% of patients treated during the primary stage revert to being serologically nonreactive after 2–3 years).

Imaging: No imaging indicated.

Special Tests: The diagnosis may be made by identifying motile spirochetes on dark-field microscopic examination of materials from primary or secondary lesions or lymph node aspirates or through direct fluorescent antibody (DFA) testing.

Diagnostic Procedures: Physical examination, suspicion, serologic testing.

Pathologic Findings

Based on the stage of the disease.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and diagnosis.

Specific Measures: Antibiotic therapy based on the stage of the disease.

Diet: No specific dietary changes indicated.

Activity: No restriction. Sexual continence required until infection is resolved.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP009 (How to Prevent Sexually Transmitted Infections), AP071 (Gonorrhea, Chlamydia, and Syphilis). Patients should be advised to have all sexual partners (within 90 days of diagnosis) examined for diagnosis and treatment.

Drug(s) of Choice

- Benzathine penicillin G 2.4 million units IM in a single dose.
- Tertiary stage—benzathine penicillin G 7.2 million units total, administered as three doses of 2.4 million units IM each at 1-week intervals.
- Penicillin G, parenterally administered, is the preferred drug for treatment of all stages of syphilis. Dosage is based on the stage of the disease.
- **Contraindications:** Known or suspected allergy.

Alternative Drugs

- Doxycycline 100 mg PO twice a day or tetracycline 500 mg PO four times a day, both for 28 days. Pregnant patients who are allergic to penicillin should be desensitized and then treated with penicillin.
- A single 2-g oral dose of azithromycin has been evaluated in limited clinical trials, but increasing reports of macrolide resistance have tempered enthusiasm.

FOLLOW-UP

Patient Monitoring: Screening for other STIs. As with all STIs, all sexual partners, within the preceding 90 days, should be screened and treated for probable infections as well.

Prevention/Avoidance: Limitation or elimination of risky behavior (sexual promiscuity).

Possible Complications: If untreated, crippling damage to the central nervous or skeletal systems, heart, or great vessels often ensues in the form of destructive, necrotic, granulomatous lesions (gummas), which develop from 1 to 10 years after the initial infection. Serious cardiovascular or neurologic complications occur in 5%–20% of patients.

Expected Outcome: Early treatment is associated with resolution; permanent damage may occur if the disease is treated at a later stage. The Jarisch-Herxheimer reaction is an acute febrile reaction frequently accompanied by headache, myalgia, and other symptoms that usually occurs within the first 24 hours after any therapy for syphilis.

MISCELLANEOUS

Pregnancy Considerations: Parenteral penicillin G is the only therapy with documented efficacy for syphilis during pregnancy. Transplacental spread of syphilis occurs at any time during pregnancy and can result in congenital syphilis. Transplacental infection occurs in approximately 50% of patients with untreated primary or secondary disease. Half of these patients have premature deliveries, growth restriction, or stillbirths. Pregnant women with syphilis in any stage who report penicillin allergy should be desensitized and then treated with penicillin.

ICD-10-CM Codes: A51.0 (Primary genital syphilis), A51.31 (Condyloma latum), A51.39 (Other secondary syphilis of skin); others based on organ system and extent of disease.

REFERENCES

LEVEL I

Riedner G, Rusizoka M, Todd J, et al. Single-dose azithromycin versus penicillin G benzathine for the treatment of early syphilis. *N Engl J Med*. 2005;353:1236.

LEVEL II

Albright CM, Emerson JB, Werner EF, et al. Third-trimester prenatal syphilis screening: a cost-effectiveness analysis. *Obstet Gynecol*. 2015;126:479.

Alexander JM, Sheffield JS, Sanchez PJ, et al. Efficacy of treatment for syphilis in pregnancy. *Obstet Gynecol*. 1999;93:5.

Ballard RC, Berman SM, Fenton KA. Azithromycin versus penicillin for early syphilis. *N Engl J Med*. 2006;354:203.

Bowen V, Su J, Torrone E, et al. Increase in incidence of congenital syphilis—United States, 2012-2014. *MMWR Morb Mortal Wkly Rep*. 2015;64:1241.

Hollier LM, Harstad TW, Sanchez PJ, et al. Fetal syphilis: clinical and laboratory characteristics. *Obstet Gynecol*. 2001;97:947.

Hook EW 3rd, Behets F, Van Damme K, et al. A phase III equivalence trial of azithromycin versus benzathine penicillin for treatment of early syphilis. *J Infect Dis*. 2010;201:1729.

Newman L, Kamb M, Hawkes S, et al. Global estimates of syphilis in pregnancy and associated adverse outcomes: analysis of multinational antenatal surveillance data. *PLoS Med*. 2013;10:e1001396.

Walker GJ. Antibiotics for syphilis diagnosed during pregnancy. *Cochrane Database Syst Rev*. 2001;(3):CD001143.

LEVEL III

Doherty L, Fenton KA, Jones J, et al. Syphilis: old problem, new strategy. *BMJ*. 2002;325:153.

Patton ME, Su JR, Nelson R, et al. Primary and secondary syphilis–United States, 2005-2013. *MMWR Morb Mortal Wkly Rep*. 2014;63:402.

Pope V. Use of treponemal tests to screen for syphilis. *Infect Med*. 2004;21:399.

Riedner G, Rusizoka M, Todd J, et al. Single-dose azithromycin versus penicillin G benzathine for the treatment of early syphilis. *N Engl J Med*. 2005;353:1236.

U.S. Preventive Services Task Force. Screening for syphilis infection in pregnancy: U.S. Preventive Services Task Force reaffirmation recommendation statement. *Ann Intern Med*. 2009;150:705.

Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015;64:1.

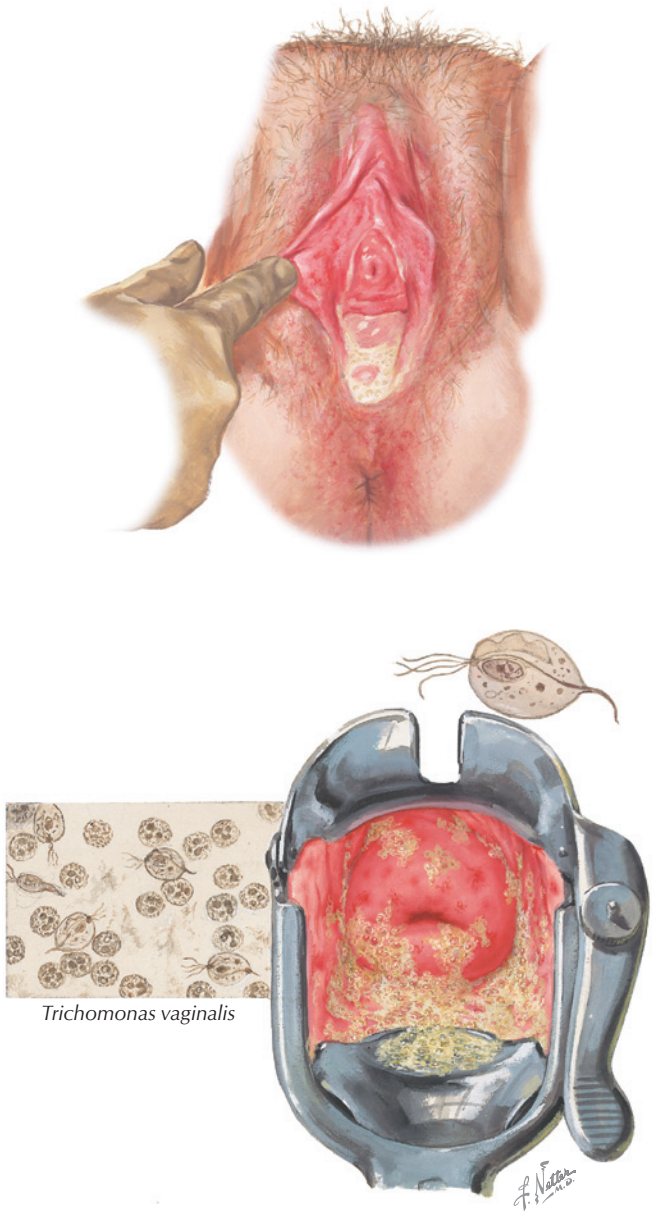


Figure 73.1 Trichomoniasis

Contraindications: Metronidazole is relatively contraindicated in the first trimester of pregnancy (pregnancy category B). Multiple studies and meta-analyses have not demonstrated a consistent association between metronidazole and teratogenic or mutagenic effects. Tinidazole is pregnancy category C.

Precautions: Metronidazole or tinidazole may produce a disulfiram-like reaction, resulting in nausea, vomiting, headaches, or other symptoms if the patient ingests alcohol. Patients should not use these agents if they have taken disulfiram in the preceding 2 weeks. Metronidazole must be used with care, or the dose should be reduced in patients with hepatic disease.

Interactions: Metronidazole may potentiate the effects of warfarin or coumarin and alcohol (as noted earlier).

Alternative Drugs

- Tinidazole 2 g PO in a single dose.
- Topical clotrimazole, povidone iodine (topical), hypertonic 20% saline douches.
- Metronidazole gel is considerably less efficacious for the treatment of trichomoniasis (<50%) than oral preparations of metronidazole and should not be used.
- Hypertonic saline douches may also be offered, which lyse the parasites through osmotic pressure.

FOLLOW-UP

Patient Monitoring: Follow-up serologic testing for syphilis and HIV infection as indicated.

Prevention/Avoidance: Sexual monogamy; use condoms during intercourse.

Possible Complications: Cystitis, infections of the Skene's or Bartholin's glands, increased risk of pelvic inflammatory disease (PID), pelvic pain, infertility, and other sequelae of STIs.

Expected Outcome: Resistance to metronidazole is uncommon (<5% with low-dose therapy, high-level resistance is rare). Most treatment failures are actually caused by reinfection or failure to comply with treatment.

MISCELLANEOUS

Pregnancy Considerations: Vaginal infections are associated with an increased risk of premature rupture of membranes, preterm delivery (increased by >40%), and low birthweight. Data do not suggest that metronidazole treatment results in reducing perinatal morbidity. Discontinue breastfeeding during metronidazole treatment and for 12–24 hours after the last dose. While using tinidazole, discontinue breastfeeding during treatment and for 3 days after the last dose.

ICD-10-CM Codes: A59.00 (Urogenital trichomoniasis, unspecified) and A59.01 (Trichomonal vulvovaginitis).

REFERENCES

LEVEL II

Burtin P, Taddio A, Ariburnu O, et al. Safety of metronidazole in pregnancy: a meta-analysis. *Obstet Gynecol*. 1995;172:525.

Forna F, Gulmezoglu AM. Interventions for treating trichomoniasis in women. *Cochrane Database Syst Rev*. 2003;(2):CD000218.

Klebanoff MA, Carey JC, Hauth JC, et al. National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units. Failure of metronidazole to prevent preterm delivery among pregnant women with asymptomatic *Trichomonas vaginalis* infection. *N Engl J Med*. 2001;345:487.

Okun N, Gronau KA, Hannah ME. Antibiotics for bacterial vaginosis or *Trichomonas vaginalis* in pregnancy: a systematic review. *Obstet Gynecol*. 2005;105:857.

Silver BJ, Guy RJ, Kaldor JM, et al. *Trichomonas vaginalis* as a cause of perinatal morbidity: a systematic review and meta-analysis. *Sex Transm Dis*. 2014;41:369.

Wiese W, Patel SR, Patel SC, et al. A meta-analysis of the Papanicolaou smear and wet mount for the diagnosis of vaginal trichomoniasis. *Am J Med*. 2000;108:301.

LEVEL III

American College of Obstetricians and Gynecologists. Vaginitis. ACOG Practice Bulletin No. 72. *Obstet Gynecol*. 2006;107:1195.

Anderson MR, Klink K, Cohrssen A. Evaluation of vaginal complaints. *JAMA*. 2004;291:1368.

Eckert LO. Clinical practice. Acute vulvovaginitis. *N Engl J Med*. 2006;355:1244.

Gülmezoglu AM, Azhar M. Interventions for trichomoniasis in pregnancy. *Cochrane Database Syst Rev*. 2011;(5):CD000220.

Kissinger P. Epidemiology and treatment of trichomoniasis. *Curr Infect Dis Rep*. 2015;17:484.

Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015;64:1.

THROMBOPHLEBITIS

74

INTRODUCTION

Description: Thrombophlebitis is an inflammatory condition of the veins with secondary thrombosis. This may occur in two forms: aseptic or suppurative (septic). The vessels may be either superficial or deep. Risk factors may be present, or the onset may be idiopathic. Risk varies with the location and cause.

Prevalence: Two million cases per year in the United States; 10% of nosocomial infections, intravascular (venous or arterial) catheter-related—88 of 100,000, 1 in 1600 during pregnancy. Pulmonary embolism is the seventh leading cause of maternal mortality, accounting for 9% of maternal deaths.

Predominant Age: Septic—childhood; aseptic—ages 20–30 years; superficial—older than 40 years.

Genetics: Uncommon—antithrombin III, proteins C and S, and factor XII deficiencies (autosomal dominant with variable penetrance), factor V Leiden or prothrombin C-20210-a genes.

ETIOLOGY AND PATHOGENESIS

Causes: Sepsis (*Staphylococcus aureus* [65%–75%], multiple organisms [14%]), hypercoagulable states (congenital deficiencies, malignancy, pregnancy, high-dose oral contraceptives, Behçet syndrome, Buerger disease, factor V Leiden deficiency), venous stasis (varicose veins), injury to vessel wall. Septic thrombophlebitis may be caused by *Candida albicans* in unusual cases. (Virchow triad: intimal damage [trauma, infection, or inflammation], stasis, or changes in the blood constituents [changes in coagulability].)

Risk Factors: Trauma (general or vascular), prolonged immobility (hospitalization, prolonged air travel), advanced age, obesity, pregnancy or puerperium (higher in multiple gestations), recent surgery, intravascular catheters or drug abuse, steroid or high-dose estrogen therapy (high-dose oral contraceptives), high altitude, hemoglobinopathies, malignancy, nephrotic syndrome, homocystinuria, congenital abnormality.

SIGNS AND SYMPTOMS

- Asymptomatic
- Generalized limb pain or swelling
- Swelling, tenderness, redness along the course of the vein
- Fever (70% of patients with septic thrombophlebitis)
- Warmth, erythema, tenderness, or lymphangitis (32%)
- Systemic sepsis (84% in suppurative cases)
- Red, tender cord
- Swelling of collateral veins

DIAGNOSTIC APPROACH

Differential Diagnosis

- Cellulitis
- Erythema nodosa
- Cutaneous polyarteritis nodosa
- Sarcoid
- Kaposi's sarcoma
- Ruptured synovial cyst (Baker cyst)
- Lymphedema
- Muscle tear, sprain, strain
- Venous obstruction (secondary to tumor, lymph node enlargement)

Associated Conditions: Budd-Chiari syndrome (hepatic vein thrombosis), renal vein thrombosis, homocystinuria, hypercoagulability states (antiphospholipid antibody syndrome), Behçet syndrome, and varicose veins.

Workup and Evaluation

Laboratory: Complete blood count, blood culture (positive in 80%–90% of superficial cases), D-dimer assay, coagulation profiles (antithrombin III levels are suppressed during the acute event—evaluations for abnormal levels should await the completion of therapy), activated partial thromboplastin time (APTT) and prothrombin time (PT) to monitor anticoagulant therapy. For patients with septic thrombosis—periodic white blood cell counts.

Imaging: Contrast venography is the "gold standard" for diagnosis. Doppler studies of vascular flow may be effective for some deep vessels. Chest radiography or spiral computed tomography if embolism is suspected.

Special Tests: Impedance plethysmography, I125-fibrinogen scans (not widely available and requires 41 hours), bone or gallium scans for associated periosteal sepsis, ventilation/perfusion scans of the lungs if an embolism is suspected. Duplex ultrasound evaluation is becoming the diagnostic study of choice to determine venous thrombosis. Magnetic resonance venography can detect both thigh and pelvic vein thrombosis with sensitivity of nearly 100% in nonpregnant patients.

Diagnostic Procedures: History, physical examination, imaging, or other diagnostic studies (impedance plethysmography, I125-fibrinogen scans).

Pathologic Findings

Clot is attached to the vessel wall with variable degrees of inflammation present in the vessel wall. Enlargement of the vessel with thickening is common. Perivascular suppuration or hemorrhage may be seen.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: For superficial aseptic conditions—heat, elevation, observation. For deep or septic thrombophlebitis—hospitalization, anticoagulation, bed rest for 1–5 days with progressive return to normal activity. Patients with deep vein thrombosis confined to the calf (distal to the popliteal system) may be managed as outpatients.

Specific Measures: Initially heparin anticoagulation, followed by oral maintenance therapy (warfarin) for 3–6 months for first episodes or 12 months for recurrent episodes. Filtering devices ("umbrellas") should be considered for those who cannot undergo anticoagulation therapy or those with evidence of emboli. Surgical excision of involved superficial veins (and tributaries) may be required.

Diet: No specific dietary changes indicated.

Activity: Initially bed rest for deep or extensive thrombosis with gradual return to activity in 1–5 days. No restriction once acute episode is resolved.

Patient Education: Patients who have had an episode of thrombosis should be instructed in risk reduction and warning signs that require reevaluation.

Drug(s) of Choice

- Heparin 5000–10,000 U IV bolus, followed by 1000 U/h IV (may also use bolus of 80 U/kg, followed by 18 U/kg/h). Dosage must be titrated on the basis of APTT: target >two times control. Low molecular weight heparin (LMWH) may also be used.
- Maintenance with warfarin (Coumadin) starting at 1–5 days. Initial dosage of 5–10 mg PO daily, adjusted on the basis of PT: target >1.3–1.5 times control (international normalized ratio

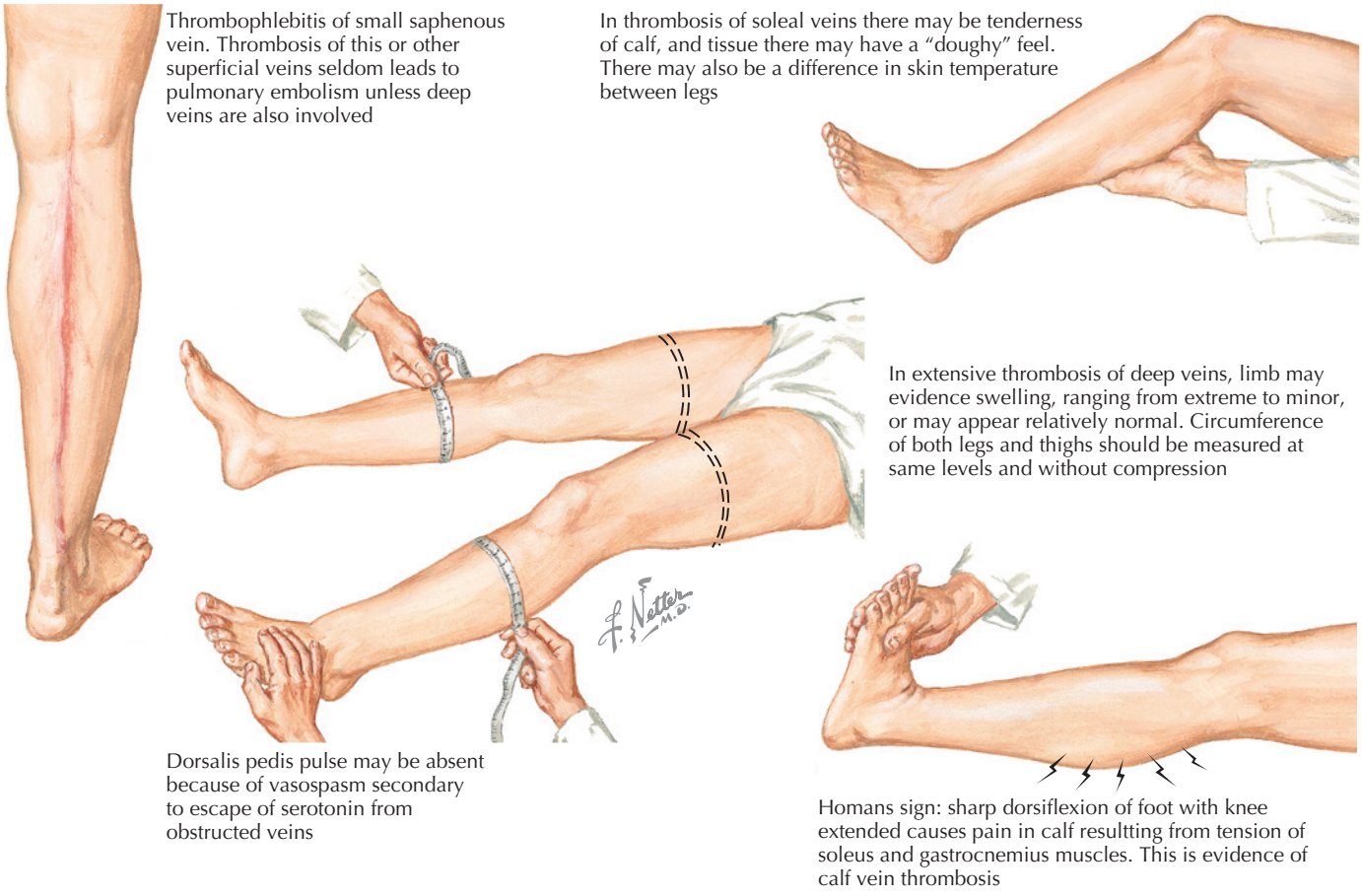


Figure 74.1 Clinical manifestations of leg vein thrombophlebitis

[INR] of 2.0–3.0). Intermittent subcutaneous heparin therapy with 15,000 U twice a day may also be used. The role of newer anticoagulants that do not require the level of monitoring of warfarin remains to be determined.

- Antibiotic therapy should be added for any patient suspected of sepsis (nafcillin 2 g IV every 6 hours; gentamicin 1–1.7 mg/kg IV).

Contraindications: Acute bleeding, recent neurosurgical procedure, known adverse reaction. Warfarin is contraindicated in pregnancy—these patients must continue heparin therapy. Relative contraindications—recent hemorrhage or surgery, peptic ulcer disease (severe), recent nonembolic stroke.

Precautions: Patients should continue to receive heparin until the target PT level is achieved. Heparin therapy may cause thrombocytopenia. Intramuscular injections should be avoided while patients are undergoing anticoagulant therapy. Warfarin therapy may be associated with necrotic skin lesions in a small number of patients (warfarin necrosis). Desogestrel-containing oral contraceptives are associated with a higher incidence of thromboembolism than other oral contraceptive formulations. This difference is small (20–30 of 100,000 vs. 10–15 of 100,000 for levonorgestrel and 4 of 100,000 for nonpregnant women).

Interactions: Agents that prolong or intensify the action of anticoagulants—alcohol, allopurinol, amiodarone, steroids, androgens, many antimicrobials, cimetidine, chloral hydrate, disulfiram, all nonsteroidal antiinflammatory agents, sulfinpyrazone, tamoxifen, thyroid hormone, vitamin E, ranitidine, salicylates. Agents, such as aminoglutethimide, antacids, barbiturates, carbamazepine, cholestyramine, diuretics, griseofulvin, rifampin, and oral contraceptives, reduce the efficacy of oral anticoagulants.

Alternative Drugs

- Thrombolytic agents (urokinase, streptokinase, tissue plasminogen activator) are effective in dissolving clots but remain investigational for the treatment of thrombosis.
- For mild superficial clots, nonsteroidal antiinflammatory agents may be used.

FOLLOW-UP

Patient Monitoring: Patients must be carefully monitored for embolization or further thrombosis. At the start of heparin therapy, the APTT must be monitored several times daily until the dose has been stabilized. The dose of warfarin must be monitored with periodic evaluation of the PT. Monitoring should be done daily until the target has been achieved, weekly for several weeks, and then monthly during maintenance therapy. Periodic checks should be made for hematuria and fecal occult blood.

Prevention/Avoidance: Avoid prolonged immobilization. Active prophylaxis (eg, for patients after surgery) using low-dose subcutaneous heparin, LMWH (enoxaparin), mechanical leg compression, and early ambulation. Changing intravenous sites every 48 hours reduces the risk of infection and inflammation.

Possible Complications: Pulmonary embolism (fatal in up to 20% of patients), phlegmasia cerulea dolens (rare). Hematuria or gastrointestinal bleeding may occur while patients are receiving

anticoagulants. Any bleeding must be investigated and not presumed to be related to therapy; therapy may unmask an underlying condition such as cancer or ulcer disease. After thrombophlebitis, persistent pain and swelling of the limb may occur. Septic thrombophlebitis is associated with bacteremia (85%), septic emboli (45%), or abscess formation or pneumonia (45%).

Expected Outcome: Superficial thrombophlebitis and distal deep disease generally respond to prompt therapy with eventual resolution of symptoms. Up to 20% of proximal thrombosis may lead to embolization.

MISCELLANEOUS

Pregnancy Considerations: The use of warfarin is contraindicated. Patients who must undergo anticoagulant therapy should be administered heparin or LMWH (intermittent subcutaneous therapy). Pregnancy causes a 49-fold increase in the incidence of phlebitis. Risk is increased with increased maternal age, multiparity, multiple pregnancy, hypertension, and preeclampsia. The utility of D-dimer testing is limited by the natural increase during pregnancy and slow return to normal following delivery.

ICD-10-CM Codes: Based on the location and type.

REFERENCES

LEVEL I

Prandoni P, Tormene D, Pesavento R, et al. High vs. low doses of low-molecular-weight heparin for the treatment of superficial vein thrombosis of the legs: a double-blind, randomized trial. *J Thromb Haemost*. 2005;3:1152.

Scurr JH, Machin SJ, Bailey-King S, et al. Frequency and prevention of symptomless deep-vein thrombosis in long-haul flights: a randomised trial. *Lancet*. 2001;357:1485.

Superficial Thrombophlebitis Treated by Enoxaparin Study Group. A pilot randomized double-blind comparison of a low-molecular-weight heparin, a nonsteroidal anti-inflammatory agent, and placebo in the treatment of superficial vein thrombosis. *Arch Intern Med*. 2003;163:1657.

LEVEL II

Cannegieter SC, Horváth-Puhó E, Schmidt M, et al. Risk of venous and arterial thrombotic events in patients diagnosed with superficial vein thrombosis: a nationwide cohort study. *Blood*. 2015;125:229.

Daniel KR, Jackson RE, Kline JA. Utility of lower extremity venous ultrasound scanning in the diagnosis and exclusion of pulmonary embolism in outpatients. *Ann Emerg Med*. 2000;35:547.

Di Nisio M, Wichers IM, Middeldorp S. Treatment for superficial thrombophlebitis of the leg. *Cochrane Database Syst Rev*. 2013;(4):CD004982.

James AH, Jamison MG, Brancazio LR, et al. Venous thromboembolism during pregnancy and the postpartum period: incidence, risk factors, and mortality. *Am J Obstet Gynecol*. 2006;194:1311.

Lepercq J, Conard J, Borel-Derlon A, et al. Venous thromboembolism during pregnancy: a retrospective study of enoxaparin safety in 624 pregnancies. *BJOG*. 2001;108:1134.

Morris JM, Algert CS, Roberts CL. Incidence and risk factors for pulmonary embolism in the postpartum period. *J Thromb Haemost*. 2010;8:998.

Tagalakis V, Kahn SR, Libman M, et al. The epidemiology of peripheral vein infusion thrombophlebitis: a critical review. *Am J Med*. 2002;113:146.

Tepper NK, Boulet SL, Whiteman MK, et al. Postpartum venous thromboembolism: incidence and risk factors. *Obstet Gynecol*. 2014;123:987.

LEVEL III

Bourjeily G, Paidas M, Khalil H, et al. Pulmonary embolism in pregnancy. *Lancet*. 2010;375:500.

Brown HL, Hiett AK. Deep vein thrombosis and pulmonary embolism in pregnancy: diagnosis, complications, and management. *Clin Obstet Gynecol*. 2010;53:345.

Marik PE, Plante LA. Venous thromboembolic disease and pregnancy. *N Engl J Med*. 2008;359:2025.

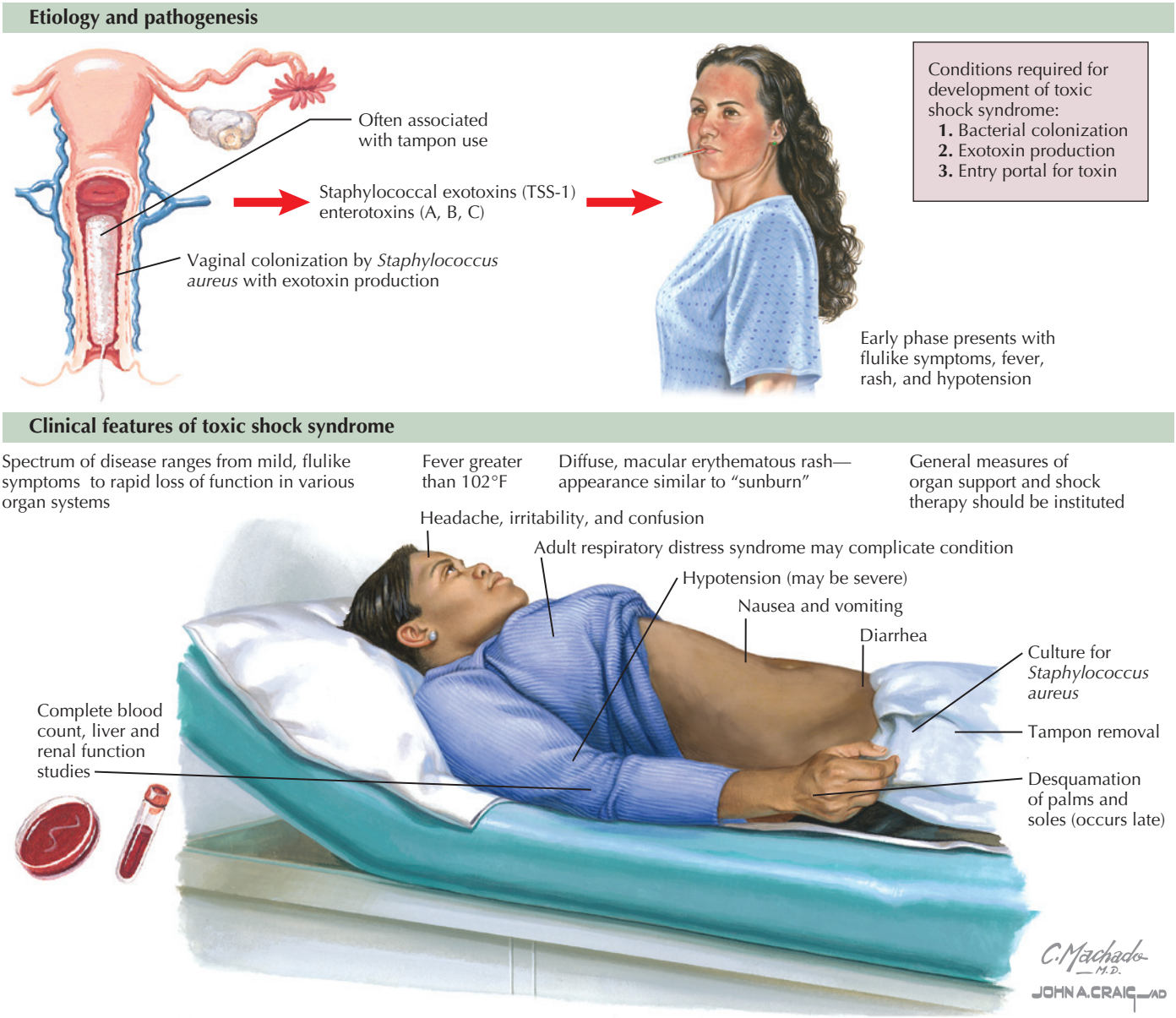


Figure 75.1 Etiology, pathogenesis, and clinical features of toxic shock syndrome

- Desquamation, particularly on palms and soles, can occur 1–2 weeks after the onset of the illness.

DIAGNOSTIC APPROACH

Differential Diagnosis

- Other exanthems (acute rheumatic fever, bullous impetigo, drug reaction, erythema multiforme, Kawasaki disease, leptospirosis, meningococcemia, Rocky Mountain spotted fever, rubella, rubeola, scarlet fever, viral disease)
- Gastrointestinal illness (appendicitis, dysentery, gastroenteritis, pancreatitis, staphylococcal food poisoning)
- Acute pyelonephritis
- Hemolytic uremic syndrome
- Legionnaires disease
- Meningococcemia
- Pelvic inflammatory disease (PID)
- Reyes syndrome
- Rhabdomyolysis
- Septic shock
- Stevens-Johnson syndrome
- Systemic lupus erythematosus
- Tick typhus

Associated Conditions: Other sources—surgical wounds (including dilation and curettage), nonsurgical focal infections, cellulitis, subcutaneous abscesses, mastitis, infected insect bites, postpartum (including transmission to the neonate), nonmenstrual vaginal conditions, vaginal infection, PID, steroid cream use. Even the use of laminaria to dilate the cervix has been reported to be associated with rare cases.

Workup and Evaluation

Laboratory: Cultures for *S. aureus*, complete blood count, liver and renal function studies. Leukocytosis may not be present; thrombocytopenia and anemia are present early.

Box 75.1 CHARACTERISTICS THAT DEFINE TOXIC SHOCK SYNDROME

- Fever > 38.9°C (102°F)
- Diffuse, macular, erythematous rash
- Desquamation of palms and soles 1–2 weeks after onset
- Hypotension (<90 torr systolic or orthostatic change)
- Negative blood, pharyngeal, and cerebrospinal fluid culture
- Negative serologic tests for measles, leptospirosis, Rocky Mountain spotted fever
- Three or more of the following organ systems:
  - Cardiopulmonary (respiratory distress, pulmonary edema, heart block, myocarditis)
  - Central nervous (disorientation or altered sensorium)
  - Gastrointestinal (vomiting, diarrhea)
  - Hematologic (thrombocytopenia of ≤100,000/mm^3)
  - Hepatic (>2-fold elevation of total bilirubin or liver enzymes, serum albumin > 2 g/dL)
- Mucous membrane inflammation (vaginal, oropharyngeal, conjunctival)
- Musculoskeletal (myalgia, >2-fold elevation of creatine phosphokinase)
- Renal (pyuria, >2-fold elevation of blood urea nitrogen or creatinine)

Imaging: No imaging indicated.
Special Tests: None indicated.
Diagnostic Procedures: History and physical findings.

Pathologic Findings

Lymphocyte depletion, subepidermic cleavage planes, cervical or vaginal ulcers.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Rapid evaluation and supportive intervention. Aggressive support and treatment of the attendant shock are paramount (frank shock is common by the time the patient is first seen for care).
Specific Measures: The site of infection must be identified and drained, most commonly by removing the contaminated tampon, vaginal sponges, or nasal packing. Antibiotic therapy with a β-lactamase-resistant antistaphylococcal agent should be initiated, but it should not alter the initial course of the illness. Other supportive measures (eg, mechanical ventilation, pressor agents) as required.
Diet: As tolerated and dictated by the patient's clinical status during the acute phase.
Activity: Bed rest during initial diagnosis and therapy.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP049 (Your First Period - Especially for Teens), AP042 (Barrier Methods of Birth Control: Diaphragm, Sponge, Cervical Cap, and Condom), and AP041 (Your Changing Body - Especially for Teens).

Drug(s) of Choice

Clindamycin 900 mg IV every 8 hours plus vancomycin 15–20 mg/kg/dose every 8–12 hours (not to exceed 2 g per dose).
Contraindications: Known or suspected allergy.
Precautions: The dose of oxacillin must be reduced if renal failure is present.
Interactions: See individual agents.

Alternative Drugs

Oxacillin or nafcillin 100 mg/kg per day given in divided doses every 6 hours.

FOLLOW-UP

Patient Monitoring: Intense monitoring is required during the initial phase of treatment. After resolution, normal health should be maintained.
Prevention/Avoidance: Frequent change of tampons. Use of sanitary pads at night. Although the risk of recurrence is low (10%–15%), patients who have had TSS should refrain from the use of tampons in the future.
Possible Complications: Adult respiratory distress syndrome is a common sequela of TSS, and patients must be monitored for the development of this complication. Acute renal failure, alopecia, and nail loss may also occur.
Expected Outcome: Although the prognosis for patients with TSS is generally good, mortality rates of 5%–10% are common.

MISCELLANEOUS

Pregnancy Considerations: Uncommon during pregnancy. May occur postpartum as a complication of operative delivery, endometritis, episiotomy infection, or nursing.
ICD-10-CM Codes: A48.8 (Other specified bacterial diseases).

REFERENCES

LEVEL II

Broome CV. Epidemiology of toxic shock syndrome in the United States. *Rev Infect Dis*. 1989;11:S14.

DeVries AS, Lesher L, Schlievert PM, et al. Staphylococcal toxic shock syndrome 2000-2006: epidemiology, clinical features, and molecular characteristics. *PLoS ONE*. 2011;6:e22997.

Hajjeh RA, Reingold A, Weil A, et al. Toxic shock syndrome in the United States: surveillance update, 1979–1996. *Emerg Infect Dis*. 1999;5(6).

Kain KC, Schulzer M, Chow AW. Clinical spectrum of nonmenstrual toxic shock syndrome (TSS): comparison with menstrual TSS by multivariate discriminant analyses. *Clin Infect Dis*. 1993;16:100.

Martin SR, Foley MR. Intensive care in obstetrics: an evidence-based review. *Am J Obstet Gynecol*. 2006;195:673.

Smit MA, Nyquist AC, Todd JK. Infectious shock and toxic shock syndrome diagnoses in hospitals, Colorado, USA. *Emerg Infect Dis*. 2013;19:1855.

Sutkin G, Capelle SD, Schlievert PM, et al. Toxic shock syndrome after laminaria insertion. *Obstet Gynecol*. 2001;98:959.

LEVEL III

American College of Obstetricians and Gynecologists. Medical management of first-trimester abortion. Practice Bulletin No. 143. *Obstet Gynecol*. 2014;123:676.

Centers for Disease Control and Prevention. Toxic-shock syndrome—United States. 1980. *MMWR*. 1997;46:492.

Reingold AL. Toxic shock syndrome: an update. *Am J Obstet Gynecol*. 1991;165:1236.

Schuchat A, Broome CV. Toxic shock syndrome and tampons. *Epidemiol Rev*. 1991;13:99.

Spaulding AR, Salgado-Pabón W, Kohler PL, et al. Staphylococcal and streptococcal superantigen exotoxins. *Clin Microbiol Rev*. 2013;26:422.

76 ULCERATIVE COLITIS

INTRODUCTION

Description: Ulcerative colitis is an inflammatory bowel disease that is characterized by inflammation limited to the mucosa of the large bowel and is primarily found in the descending colon and rectum (although the entire colon may be involved). The disease is also characterized by intermittent bouts of symptoms interspersed by periods of quiescence.
Prevalence: 70–150 in 100,000.
Predominant Age: 20–50 years; 20% of patients are younger than 21 years. The disease usually starts between the ages of 15 and 30 years and less frequently between the ages of 50 and 70 years.
Genetics: Family history presents in up to 20% (ulcerative colitis or Crohn disease). More common in some ethnic groups (eg, Jews).

ETIOLOGY AND PATHOGENESIS

Causes: An inflammatory process limited to the mucosa of the large bowel and primarily found in the descending colon and rectum, although the entire colon may be involved. Genetic, infectious, immunologic, and psychologic factors have been postulated to underlie the process.
Risk Factors: Family history. Negatively related to smoking.

SIGNS AND SYMPTOMS

- Abdominal pain (generally mild to moderate; the pain is frequently relieved by a bowel movement, but many report the sensation of incomplete evacuation)
- Diarrhea (voluminous, watery, with occasional blood)
- Fever and weight loss
- Arthralgias and arthritis (15%–20%)
- Aphthous ulcers of the mouth (5%–10%)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Irritable bowel syndrome (IBS; ulcerative colitis may be differentiated from IBS by the frequent presence of fever or bloody stools in ulcerative colitis)
- Crohn disease
- Hemorrhoids
- Colon carcinoma
- Diverticulitis
- Infectious diarrhea (*Escherichia coli, Salmonella, Shigella, Entamoeba histolytica)*
- Iatrogenic (antibiotic associated, laxative abuse, excessive sucralose ingestion)
- Radiation proctitis/colitis

Associated Conditions: Ocular complications (uveitis, cataracts, keratopathy, corneal ulceration, retinopathy; 4%–10% of patients), liver and biliary complications (cirrhosis, 1%–5%; sclerosing cholangitis, 1%–4%; bile-duct carcinoma), ankylosing spondylitis, and osteoporosis

Workup and Evaluation

Laboratory: No specific evaluation indicated. Complete blood count to evaluate blood loss or inflammation. Stool studies: *Clostridium difficile* toxin, stool cultures (*Salmonella*, *Shigella*, *Campylobacter*, *Yersinia*), and specific testing for *E. coli* O157:H7, microscopy for ova and parasites, *Giardia* stool antigen test if the patient has recently traveled to endemic areas. Albumin and potassium levels may be reduced, or liver function test results may be elevated.
Imaging: Barium enema (air contrast)—not required for the diagnosis.
Special Tests: Sigmoidoscopy, colonoscopy, or rectal biopsy.
Diagnostic Procedures: History, sigmoidoscopy, barium enema, or rectal biopsy.

Pathologic Findings

Superficial inflammation with ulceration is common. Hyperemia and hemorrhage are also common. The rectum is involved in 95% of cases, but the inflammation proximally extends in a continuous manner, at times even involving the terminal ileum.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and control of inflammation, prevention of complications, maintenance of nutrition (including adequate iron intake).
Specific Measures: Severe exacerbations may require hospitalization. Patients whose disease is refractory to medical therapy may require surgical resection (between 25% and 40% of patients with ulcerative colitis eventually undergo colectomy because of massive bleeding, severe illness, rupture of the colon, or risk of cancer).
Diet: No specific dietary changes indicated except for those based on other indications (eg, lactose intolerance).
Activity: No restriction.

Drug(s) of Choice

- Sulfasalazine 1–4 g PO daily (useful for both mild flare-ups and chronic suppression; approximately 10% of patients require chronic suppressive therapy).
- Steroid enemas or mesalamine (5-aminosalicylic acid [5-ASA]) enemas or suppositories).
- Prednisone 40–60 mg PO daily for flare-ups (tapered off over 2 months).

Contraindications: Known or suspected allergy or intolerance.
Precautions: Antidiarrheal agents may precipitate toxic megacolon.
Interactions: See individual agents.

Alternative Drugs

- Azathioprine and 6-mercaptopurine (6-MP) may be administered to patients who have not responded to 5-ASAs or corticosteroids or who are dependent on corticosteroids.
- Other oral 5-ASA derivatives are being studied. Antidiarrheal agents (diphenoxylate-atropine and loperamide) may be used but may precipitate toxic megacolon.

FOLLOW-UP

Patient Monitoring: Normal health maintenance, periodic follow-up to monitor status of the disease and possible complications. Colonoscopy should be performed every 1–2 years beginning at 7–8 years after the onset of the disease to observe for the possible development of cancer. Annual testing of liver function is desirable.
Prevention/Avoidance: None (prevention of complications as previously mentioned).
Possible Complications: Perforation, toxic megacolon, hepatic disease, bowel stricture and obstruction, colon cancer (30% after 25 years, less for left-sided disease). Mortality for initial attack is approximately 5%.

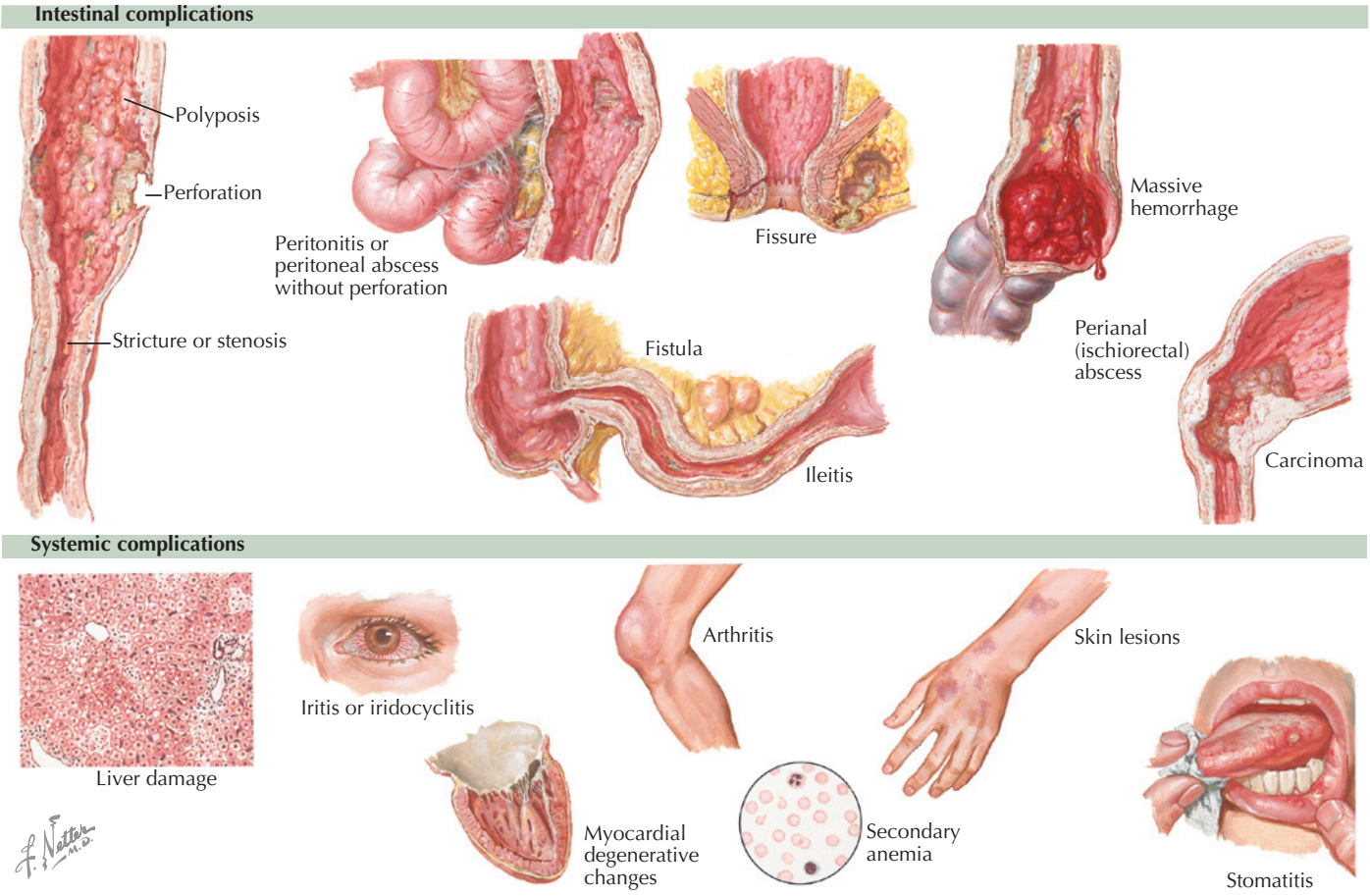


Figure 76.1 Intestinal and systemic complications in ulcerative colitis

Expected Outcome: Highly variable; 75%–85% of patients experience relapse, 20%–30% require colectomy, and extension of disease is observed in up to 20% within 5 years. The risk for colon cancer is the greatest factor that affects long-term prognosis and management.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. Of patients with inactive disease, 30% have relapses during pregnancy, with 15% having them in the first trimester. Treatment with sulfasalazine does not affect pregnancy outcome. It is recommended that pregnancy be delayed until the disease is in remission.

ICD-10-CM Codes: K51.90 (Ulcerative colitis, unspecified, without complications).

REFERENCES

LEVEL I

Ardizzone S, Maconi G, Russo A, et al. Randomised controlled trial of azathioprine and 5-aminosalicylic acid for treatment of steroid dependent ulcerative colitis. *Gut*. 2006;55:47.

Travis SP, Danese S, Kupcinskas L, et al. Once-daily budesonide MMX in active, mild-to-moderate ulcerative colitis: results from the randomised CORE II study. *Gut*. 2014;63:433.

LEVEL II

Bewtra M, Kaiser LM, TenHave T, et al. Crohn's disease and ulcerative colitis are associated with elevated standardized mortality ratios: a meta-analysis. *Inflamm Bowel Dis*. 2013;19:599.

Colombel JF, Rutgeerts P, Reinisch W, et al. Early mucosal healing with infliximab is associated with improved long-term clinical outcomes in ulcerative colitis. *Gastroenterology*. 2011;141:1194.

Feagan BG, Macdonald JK. Oral 5-aminosalicylic acid for induction of remission in ulcerative colitis. *Cochrane Database Syst Rev*. 2012;(10):CD000543.

Feagan BG, Macdonald JK. Oral 5-aminosalicylic acid for maintenance of remission in ulcerative colitis. *Cochrane Database Syst Rev*. 2012;(10):CD000544.

Jess T, Frisch M, Simonsen J. Trends in overall and cause-specific mortality among patients with inflammatory bowel disease from 1982 to 2010. *Clin Gastroenterol Hepatol*. 2013;11:43.

Marshall JK, Thabane M, Steinhart AH, et al. Rectal 5-aminosalicylic acid for maintenance of remission in ulcerative colitis. *Cochrane Database Syst Rev*. 2012;(11):CD004118.

Rutgeerts P, Sandborn WJ, Feagan BG, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. *N Engl J Med*. 2005;353:2462.

van Staa TP, Card T, Logan RF, et al. 5-Aminosalicylate use and colorectal cancer risk in inflammatory bowel disease: a large epidemiological study. *Gut*. 2005;54:1573.

LEVEL III

American College of Obstetricians and Gynecologists. Lower gastrointestinal tract disorders. *Clinical Updates in Women's Health Care*. 2015;XIV(5):1-138.

Cima RR, Pemberton JH. Medical and surgical management of chronic ulcerative colitis. *Arch Surg*. 2005;140:300.

Kornbluth A, Sachar DB. Practice Parameters Committee of the American College of Gastroenterology. Ulcerative colitis practice guidelines in adults: American College Of Gastroenterology, Practice Parameters Committee. *Am J Gastroenterol*. 2010;105:501.

Mowat C, Cole A, Windsor A, et al. Guidelines for the management of inflammatory bowel disease in adults. *Gut*. 2011;60:571.

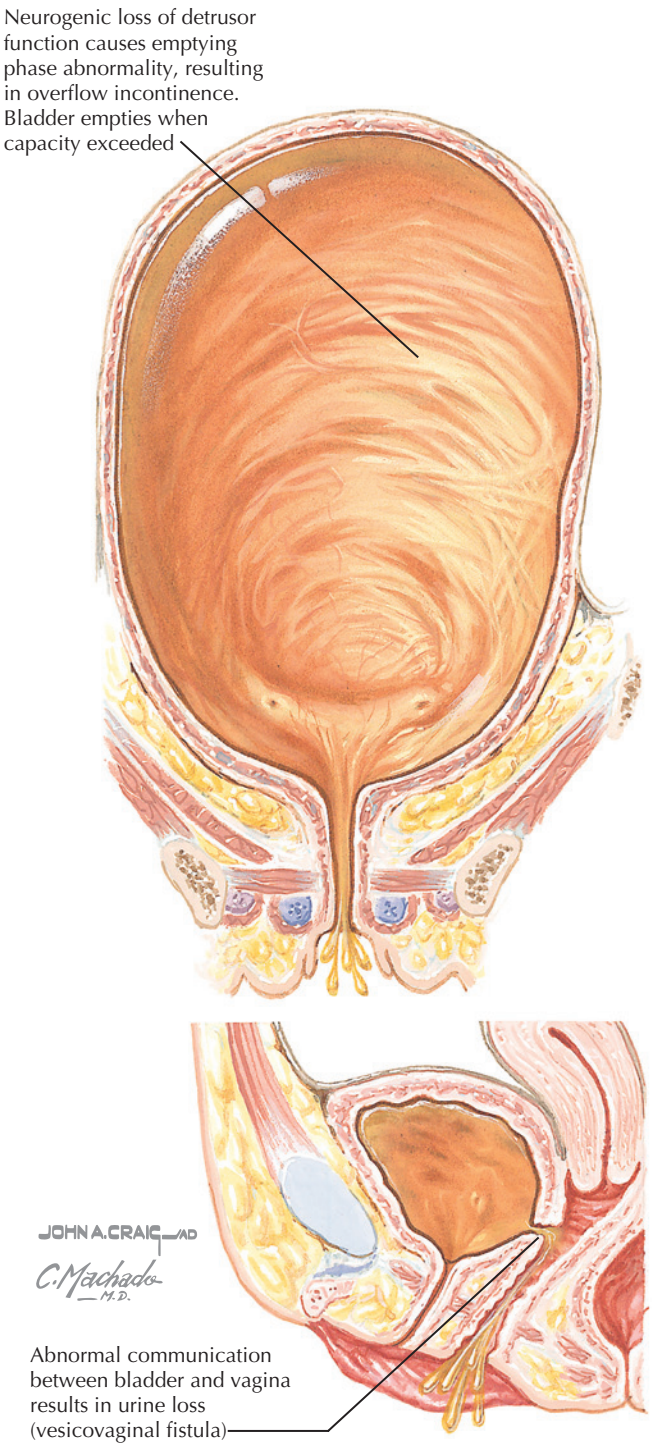


Figure 77.1 Bypass and overflow in urinary incontinence

[MRI] may be more sensitive than IVP or computed tomography [CT]). Retrograde urography, with the passage of ureteral stents, may also be required. Ultrasonography demonstrates a distended bladder in patients with overflow incontinence.

Special Tests: If a vesicovaginal fistula is found, cystoscopy is required to determine the location of the fistula in relation to the ureteral opening and bladder trigone. For those with overflow incontinence that is either recurrent or unrelated to an obvious cause, urodynamics testing (including a cystometrogram) should be considered.

Diagnostic Procedures: When a fistula is suspected, the installation of a dilute solution of methylene blue (or sterile milk) into the bladder while a tampon is in place in the vagina documents a vesicovaginal fistula. A ureterovaginal fistula may be documented in a similar fashion using intravenous indigo carmine. For patients with overflow incontinence, physical examination and catheter drainage of the bladder are diagnostic. Urodynamics testing (cystometrogram) generally confirms the diagnosis.

Pathologic Findings

Based on the cause. A distended, often hypotonic bladder is typical of patients with overflow incontinence.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Bypass incontinence—urinary diversion, protection of the vulva from continuous moisture (zinc oxide, diaper rash preparations). Overflow incontinence—treatment of urinary tract infection (if present)

Specific Measures: Bypass incontinence—vesicovaginal fistulae that occur in the immediate postoperative period should be treated by large-caliber transurethral catheter drainage. Spontaneous healing is evident within 2–4 weeks. Similarly, in patients with a ureterovaginal fistula, prompt placement of a ureteral stent, left in place for 2 weeks, enables spontaneous healing for approximately 25% of patients. Surgical repair of genitourinary fistulae is generally delayed by 2–4 months to allow complete healing of the original insult. In all cases, successful surgical repair comprises meticulous dissection of the fistulous tract and careful reapproximation of tissues. Overflow incontinence—prompt and continuous drainage if retention is present, timed voiding to reduce bladder volume, suprapubic pressure or Credé maneuver to reduce residual volume.

Diet: No specific dietary changes indicated.

Activity: No restriction.

Patient Education: Reassurance; American College of Obstetricians and Gynecologists Patient Education Pamphlet AP081 (Urinary Incontinence).

Drug(s) of Choice

- Bypass incontinence—none
- Overflow incontinence—pharmacologic therapy for these patients is often unsatisfactory, and many require long-term catheter drainage or intermittent self-catheterization to manage their problem.
- Urinary tract antibiotics if infection is present
- Acetylcholine-like drugs—bethanechol chloride (Urecholine) 10–50 mg three to four times per day; may also be given as 2.5–5 mg SC

Contraindications: Overflow incontinence—Hyperthyroidism, peptic ulcer, latent or active bronchial asthma, pronounced bradycardia or hypotension, vasomotor instability, coronary artery disease, epilepsy, or parkinsonism.

Precautions: Overflow incontinence—it is preferred that bethanechol be administered when the stomach is empty (1 hour before or 2 hours after meals). The sterile solution must not be administered IM or IV. Bethanechol should not be administered if the integrity of either the bladder wall or gastrointestinal tract is in question or may be mechanically obstructed.

Interactions: Overflow incontinence—bethanechol should be used with extreme care in patients receiving ganglion-blocking compounds.

Alternate Therapies: Overflow incontinence—intermittent self-catheterization, electrical stimulation, reduction cystoplasty, urinary diversion.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. Patients are at increased risk for urinary tract infections, vaginitis, and vulvitis. Patients who have experienced overflow incontinence have an increased risk of recurrence.

Prevention/Avoidance: Careful surgical technique should be used to reduce the risk of fistula formation. Surveillance in situations that predispose patients to retention (eg, after regional anesthesia, childbirth).

Possible Complications: Social isolation and vulvar and perineal irritation are common complications of any type of urinary incontinence. Ascending urinary tract infection (including pyelonephritis) may occur if a fistula or bladder distention is present.

Expected Outcome: Recurrence after surgical repair of a fistula is common, especially in patients who have undergone radiotherapy for malignancies. For patients with time-limited causes for overflow incontinence, a complete resolution with drainage should be expected. For patients with idiopathic retention or retention caused by chronic causation, frequent recurrence, possible dependence on self-catheterization, urinary diversion, and electrical stimulation are possible.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, although pregnancy (and vaginal delivery) increases the risk of urinary retention and overflow incontinence. Obstructed labor is a major cause of vesicovaginal fistula in developing countries.

ICD-10-CM Codes: Bypass incontinence—R32 (Unspecified urinary incontinence) and N39.45 (Continuous leakage). Overflow incontinence—N39.498 (Other specified urinary incontinence) and R39.14 (Feeling of incomplete bladder emptying), R39.42 (Without sensory awareness).

REFERENCES

LEVEL I

Barone MA, Widmer M, Arrowsmith S, et al. Breakdown of simple female genital fistula repair after 7 day versus 14 day postoperative bladder catheterisation: a randomised, controlled, open-label, non-inferiority trial. *Lancet*. 2015;386:56.

LEVEL II

Abou-El-Ghar ME, El-Assmy AM, Refaie HF, et al. Radiological diagnosis of vesicouterine fistula: role of magnetic resonance imaging. *J Magn Reson Imaging*. 2012;36:438.

Hilton P, Cromwell DA. The risk of vesicovaginal and urethrovaginal fistula after hysterectomy performed in the English National Health Service—a retrospective cohort study examining patterns of care between 2000 and 2008. *BJOG*. 2012;119:1447.

LEVEL III

American College of Obstetricians and Gynecologists. Urinary incontinence in women. Practice Bulletin No. 155. *Obstet Gynecol*. 2015; 126:e66-e81.

Dubeau CE. The aging lower urinary tract. *J Urol*. 2006;175:S11.

Norton P, Brubaker L. Urinary incontinence in women. *Lancet*. 2006; 367:57.

Sims JM. On the treatment of vesico-vaginal fistula. *Am J Med Sci*. 1852;23:59.

Wall LL. Obstetric vesicovaginal fistula as an international public-health problem. *Lancet*. 2006;368:1201.

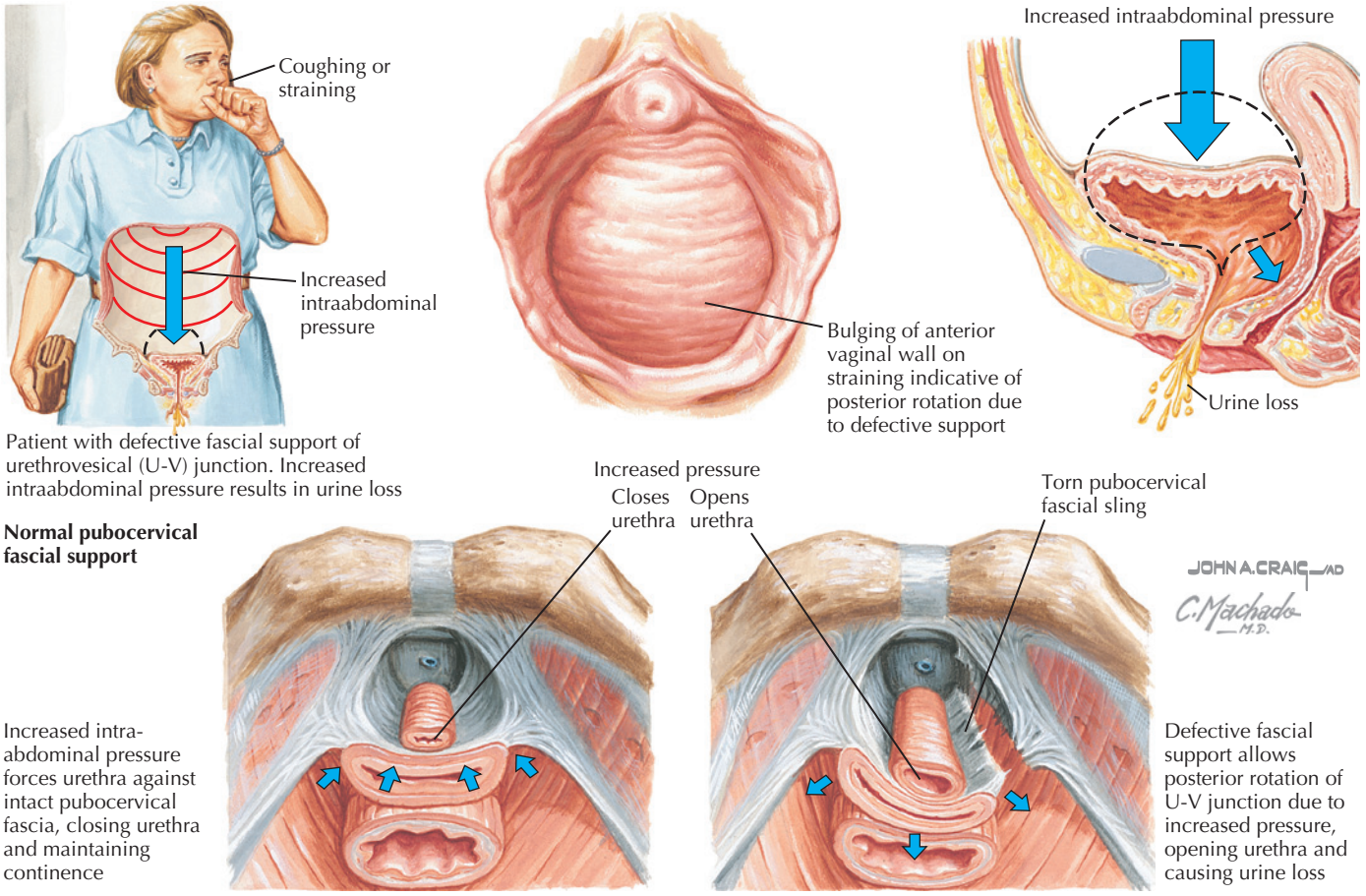


Figure 78.1 Stress incontinence in women

Associated Conditions: Vulvitis, vaginitis, pelvic relaxation, uterine prolapse, other hernias, recurrent urinary tract infection.

Workup and Evaluation

Laboratory: No evaluation indicated. Urinalysis is generally recommended, although results are nonspecific. Abrupt-onset incontinence in older patients should suggest infection, which may be confirmed through urinalysis or culture.

Imaging: Radiographic studies are sometimes performed as a part of complex urodynamics studies but are generally of limited utility.

Special Tests: A "Q-tip test" is generally recommended, although it as a poor predictive value—a cotton-tipped applicator dipped in 2% lidocaine (Xylocaine) is placed in the urethra, and anterior rotation with straining is measured. Greater than 30 degrees is abnormal. An evaluation of urinary function is advisable, especially if surgical therapy is being considered. In the past, the functional significance of a cystourethrocele was gauged by elevating the bladder neck (using fingers or an instrument) and asking the patient to strain (referred to as a Bonney or Marshall-Marchetti test). This test has fallen out of favor as it is nonspecific and unreliable.

Diagnostic Procedures: The best method to confirm stress incontinence is by pelvic examination—loss is best demonstrated by having the patient strain or cough while the vaginal opening is observed (preferably while the patient is standing). Urodynamics testing (simple or complex) may be used to evaluate other possible causes of incontinence.

Pathologic Findings

Based on the cause. Evidence of a loss of support for the urethra and/or bladder is generally apparent on physical examination in patients with stress urinary incontinence.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Weight reduction, treatment of chronic cough (if present), smoking cessation, timed voiding, topical or systemic estrogen replacement or therapy as indicated (rendered controversial by the Women's Health Initiative [WHI] study).

Specific Measures: Pessary therapy, pelvic muscle exercises (Kegel exercises; can be supplemented by the use of weighted vaginal cones), collagen injections (for ISD), surgical repair. Limited role for medical therapy. Chronic exposure to urine-soaked pads can result in contact dermatitis and skin breakdown.

Diet: No specific dietary changes indicated.

Activity: No restriction, although some reduction in heavy lifting may be prudent.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP081 (Urinary Incontinence), AP012 (Pelvic Support Problems), and AP166 (Surgery for Urinary Incontinence).

Drug(s) of Choice

- Imipramine hydrochloride (Tofranil) 50–150 mg PO daily is good for mixed incontinence and enuresis. Use with care in elderly patients.

- Duloxetine, a potent and relatively balanced serotonin and noradrenaline reuptake inhibitor, has been evaluated in phase II and III clinical trials and was found to be efficacious and safe in treating women with moderate to severe stress urinary incontinence symptoms. Approval for use in the United States has been delayed.
- Estrogen, either topically or systemically, is often prescribed to improve tissue tone, reduce irritation, and prepare tissues for surgical or pessary therapy.

Contraindications: Known or suspected sensitivity to medication, undiagnosed vaginal bleeding, breast cancer.

Precautions: α-Blocking agents used to treat hypertension may reduce urethral tone sufficiently to result in stress incontinence in patients with reduced pelvic support. Patients treated with angiotensin-converting enzyme inhibitors may develop a cough as a side effect of the medication, worsening incontinence symptoms and accelerating the appearance or worsening of a cystourethrocele.

Interactions: See individual agents.

Alternate Therapies: None at this time.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. Patients are at an increased risk for urinary tract infections, vaginitis, and vulvitis.

Prevention/Avoidance: The role of elective cesarean delivery in reducing pelvic floor trauma has been debated, but there are data to suggest that nerve damage in the pelvic floor may occur late in pregnancy without the trauma of vaginal delivery, resulting in an increased risk of eventual stress incontinence even with cesarean delivery.

Possible Complications: Social isolation and vulvar and perineal irritation are common complications of any type of urinary incontinence.

Expected Outcome: Generally favorable results may be obtained for patients with symptoms of stress incontinence through the use of a carefully selected and fitted pessary. Surgical therapy is associated with 40%–95% success in long-term correction of the anatomic defect and the associated symptoms (success rates vary on the basis of the type of procedure performed and duration of follow-up).

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, although pregnancy (and vaginal delivery) may contribute to a worsening of pelvic support problems.

ICD-10-CM Codes: N39.3 (Stress incontinence [female]).

REFERENCES

LEVEL I

Kitchener HC, Dunn G, Lawton V, et al.; COLPO Study Group. Laparoscopic versus open colposuspension—Results of a prospective randomized controlled trial. *BJOG*. 2006;113:1007.

Laurikainen E, Valpas A, Kivela A, et al. Retropubic compared with transobturator tape placement in treatment of urinary incontinence: a randomized controlled trial. *Obstet Gynecol*. 2007;109:4.

Oelke M, Roovers JP, Michel MC. Safety and tolerability of duloxetine in women with stress urinary incontinence. *BJOG*. 2006;113:22.

LEVEL II

Albo ME, Richter HE, Brubaker L, et al.; Urinary Incontinence Treatment Network. Burch colposuspension versus fascial sling to reduce urinary stress incontinence. *N Engl J Med*. 2007;356:2143.

Brubaker L, Cundiff GW, Fine P, et al.; Pelvic Floor Disorders Network. Abdominal sacrocolpopexy with Burch colposuspension to reduce urinary stress incontinence. *N Engl J Med*. 2006;354:1557.

Dean N, Herbison P, Ellis G, et al. Laparoscopic colposuspension and tension-free vaginal tape: a systematic review. *BJOG*. 2006;113:1345.

Freeman RM. The role of pelvic floor muscle training in urinary incontinence. *BJOG*. 2004;111:37.

Lipp A, Shaw C, Glavind K. Mechanical devices for urinary incontinence in women. *Cochrane Database Syst Rev*. 2014;(12):CD001756.

Matthews CA, Whitehead WE, Townsend MK, et al. Risk factors for urinary, fecal, or dual incontinence in the Nurses' Health Study. *Obstet Gynecol*. 2013;122:539.

Wu JM, Vaughan CP, Goode PS, et al. Prevalence and trends of symptomatic pelvic floor disorders in U.S. women. *Obstet Gynecol*. 2014;123:141.

LEVEL III

American College of Obstetricians and Gynecologists. Urinary incontinence in women. Practice Bulletin No. 155. *Obstet Gynecol*. 2015;126:e66.

Drutz H. Duloxetine in women awaiting surgery. *BJOG*. 2006;113:17.

Freeman RM. Initial management of stress urinary incontinence: pelvic floor muscle training and duloxetine. *BJOG*. 2006;113:10.

Mariappan P, Ballantyne Z, N'Dow JM, et al. Serotonin and noradrenaline reuptake inhibitors (SNRI) for stress urinary incontinence in adults. *Cochrane Database Syst Rev*. 2005;(3):CD004742.

Myers DL. Female mixed urinary incontinence: a clinical review. *JAMA*. 2014;311:2007.

Rogers RG. Clinical practice. Urinary stress incontinence in women. *N Engl J Med*. 2008;358:1029.

The American College of Obstetricians and Gynecologists. Evaluation of uncomplicated stress urinary incontinence in women before surgical treatment. Committee Opinion No. 603. *Obstet Gynecol*. 2014;123:1403.

Winters JC, Dmochowski RR, Goldman HB, et al. Urodynamic studies in adults: AUA/SUFU guideline. *J Urol*. 2012;188:2464.

Wood LN, Anger JT. Urinary incontinence in women. *BMJ*. 2014;349:g4531.

URINARY INCONTINENCE: URGE

79

INTRODUCTION

Description: Urinary incontinence is a sign, symptom, and disease all at the same time. Urge incontinence is the involuntary loss of urine accompanied by a sense of urgency or impending loss and is associated with increased bladder activity.
Prevalence: Urge incontinence accounts for 35% of patients with incontinence.
Predominant Age: Mid-reproductive age and older. Urge incontinence becomes more common during the 40s and beyond and is most common after menopause.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Allergy, bladder stone, bladder tumor, caffeinism, central nervous system tumors, detrusor muscle instability, interstitial cystitis, multiple sclerosis, Parkinson's disease, radiation cystitis, radical pelvic surgery, spinal cord injury, urinary tract infections (urinary tract infections [UTIs]; acute or chronic).
Risk Factors: Frequent UTIs.

SIGNS AND SYMPTOMS

- Reduced bladder capacity and early, intense sensations of bladder fullness
- Spontaneous and uninhibitable contractions of the bladder muscles, resulting in large-volume, uncontrolled urine loss
- Loss possibly provoked by activities such as hand washing or a change in position or posture or after (not during) changes in intraabdominal pressure such as a cough or sneeze

DIAGNOSTIC APPROACH

Differential Diagnosis

- Mixed incontinence (stress and urge)
- Stress incontinence
- UTIs
- Urinary tract fistula
- Interstitial cystitis
- Urethritis

Associated Conditions: Vulvitis, vaginitis, nocturia, enuresis (bed wetting).

Workup and Evaluation

Laboratory: No evaluation indicated. Urinalysis is generally recommended, although results are nonspecific. Abrupt onset of incontinence in older patients should suggest infection, which may be confirmed through urinalysis or culture.
Imaging: Radiographic studies are sometimes performed as a part of complex urodynamics studies but are generally of limited utility.
Special Tests: Measurement of postvoid urinary residual volume.
Diagnostic Procedures: History and physical examinations, urodynamics testing (simple or complex), and evaluation of sphincter tone and function (as an indication of neurologic function) are the best methods to establish the diagnosis of urge incontinence.

Pathologic Findings

Based on the cause. Patients with urge incontinence have a reduced bladder capacity, early first sensation, and uninhibited bladder contractions.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Treatment of any UTI present, timed voiding, smoking cessation.
Specific Measures: Medical therapy. Limited role for surgical repair.
Diet: No specific dietary changes indicated. Reduction in caffeine consumption and other bladder irritants may help some patients with symptoms of urgency incontinence.
Activity: No restriction.
Patient Education: Reassurance; American College of Obstetricians and Gynecologists Patient Education Pamphlet AP081 (Urinary Incontinence).

Drug(s) of Choice

- Flavoxate hydrochloride (Urispas) 100–200 mg PO three to four times a day (fewer side effects, more expensive than some).
- Imipramine hydrochloride (Tofranil) 25–50 mg PO twice to thrice a day (good for mixed incontinence and enuresis, 60%–75% effective).
- Oxybutynin hydrochloride (Ditropan) 5–10 mg PO three to four times a day. Side effects are common (75%), although the patch tends to have fewer side effects (60%–80% effective).
- Propantheline bromide (Pro-Banthine) 15–30 mg PO three to four times a day (few side effects, variable absorption, 60%–80% effective).
- Darifenacin (Enablex) 7.5 mg PO daily (blocks the M3 muscarinic acetylcholine receptor, which is primarily responsible for bladder muscle contractions).
- Solifenacin (Vesicare) 5 mg PO daily (urinary antispasmodic of the anticholinergic class).

Contraindications: Most agents are contraindicated in patients with urinary retention, narrow-angle glaucoma, or known or suspected hypersensitivity.
Precautions: Anticholinergic drugs must be used with caution in patients with obstructive gastrointestinal disease or tachycardia. Dry mouth is experienced by 40%–50% of patients. Darifenacin and solifenacin are contraindicated in urinary retention, gastric retention, or uncontrolled narrow-angle glaucoma and are pregnancy category C. Antimuscarinics have also been associated with dementia. Patients with severe or uncontrolled hypertension should not be prescribed mirabegron.
Interactions: Patients taking cytochrome P450 3A4 inhibitors (macrolide antibiotics or antifungal agents) must reduce their doses of tolterodine tartrate.
Alternate Therapies: Tolterodine tartrate (Detrol) 1–2 mg PO twice a day; dicyclomine hydrochloride (Bentyl) 20 mg IM four times a day (requires parenteral use); fesoterodine extended-release (ER) 4 mg PO daily; mirabegron (Myrbetriq, a β_3-adrenoceptor agonist) 25 mg PO daily (efficacy is evaluated by 8 weeks; may increase dose to 50 mg); terodiline hydrochloride (Micturin) 12.5–25 mg PO twice a day (available outside of the United States; carries some risk of esophageal and gastric erosions). A role for sacral neuromodulation (placement of a wire lead into the S3 foramen that is connected to a stimulation device) has been suggested but adverse events, including the need for subsequent surgeries means that the procedure should be reserved for selected patients with a failure of less invasive options.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. Patients are at an increased risk for UTIs, vaginitis, and vulvitis.

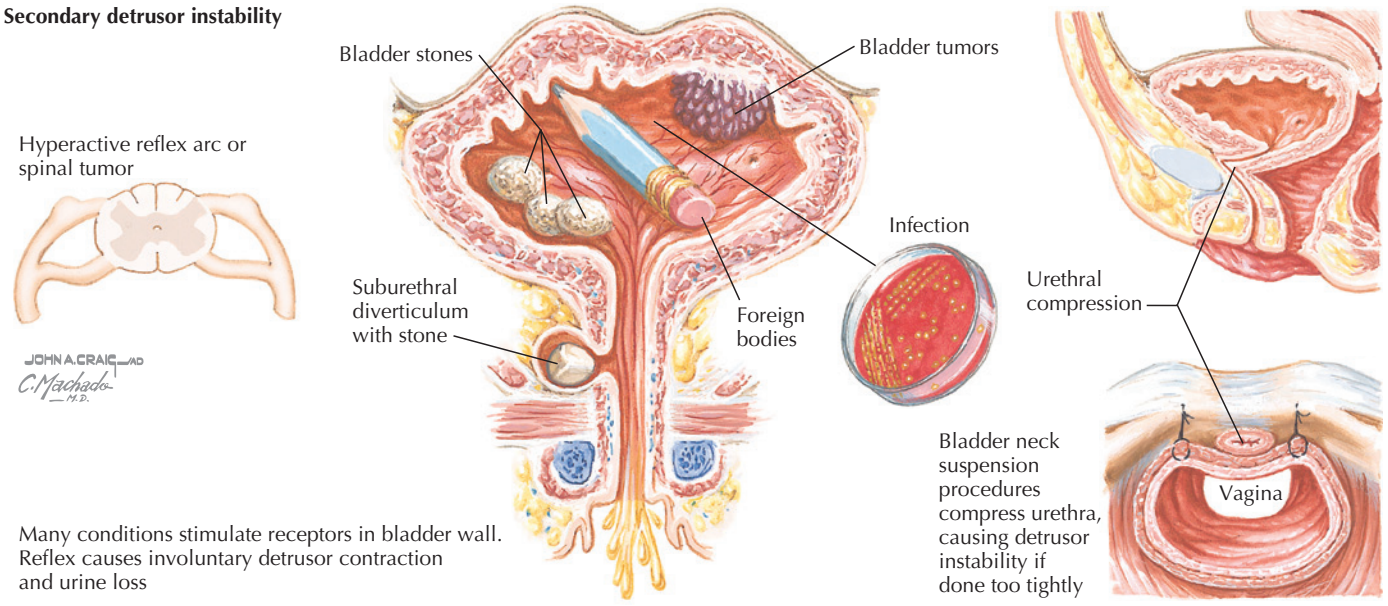


Figure 79.1 Other causes of incontinence

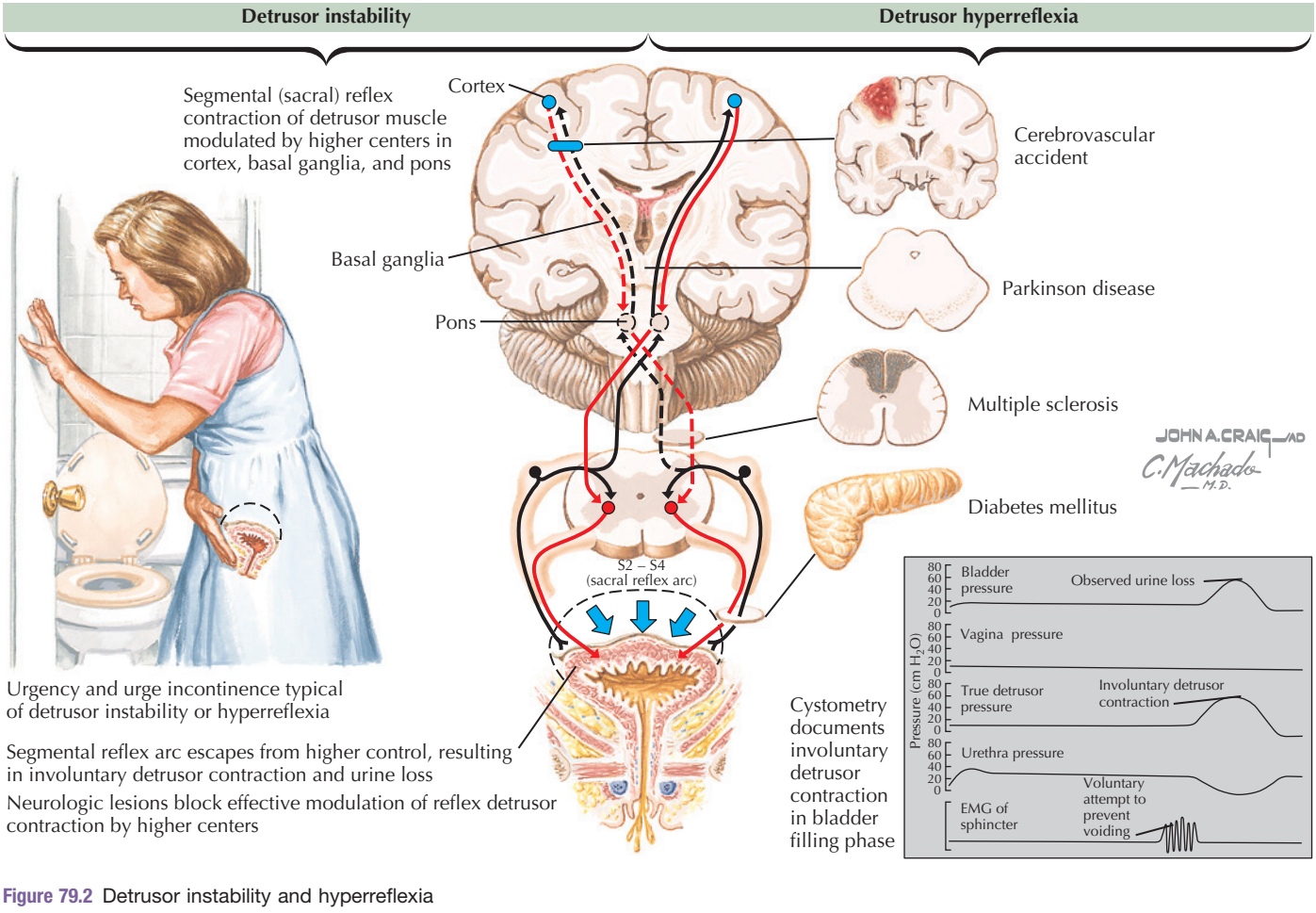


Figure 79.2 Detrusor instability and hyperreflexia

Prevention/Avoidance: Avoidance of and prompt treatment for UTIs are considered to reduce the risk for developing urge incontinence in the future.

Possible Complications: Social isolation and vulvar and perineal irritation are common complications of any type of urinary incontinence.

Expected Outcome: Patients with urge incontinence can expect generally good results with medical therapy and timed voiding.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. Pregnancy often induces frequency and urgency because of bladder compression by the fetal presenting part near term. Bethanechol, darifenacin, and solifenacin are pregnancy category C drugs.

ICD-10-CM Codes: R39.41 (Urge incontinence).

REFERENCES

LEVEL I

Green SA, Alon A, Ianus J, et al. Efficacy and safety of a neurokinin-1 receptor antagonist in postmenopausal women with overactive bladder with urge urinary incontinence. *J Urol*. 2006;176:2535, discussion 2540.

Richter HE, Burgio KL, Brubaker L, et al. Continence pessary compared with behavioral therapy or combined therapy for stress incontinence: a randomized controlled trial. *Obstet Gynecol*. 2010;115:609.

LEVEL II

Cody JD, Jacobs ML, Richardson K, et al. Oestrogen therapy for urinary incontinence in post-menopausal women. *Cochrane Database Syst Rev*. 2012;(10):CD001405.

Dumoulin C, Hay-Smith EJ, Mac Habée-Séguin G. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women. *Cochrane Database Syst Rev*. 2014;(5):CD005654.

Freeman RM. The role of pelvic floor muscle training in urinary incontinence. *BJOG*. 2004;111:37.

Hay-Smith EJ, Herderschee R, Dumoulin C, et al. Comparisons of approaches to pelvic floor muscle training for urinary incontinence in women. *Cochrane Database Syst Rev*. 2011;(12):CD009508.

Herbison GP, Dean N. Weighted vaginal cones for urinary incontinence. *Cochrane Database Syst Rev*. 2013;(7):CD002114.

Siegel S, Noblett K, Mangel J, et al. Results of a prospective, randomized, multicenter study evaluating sacral neuromodulation with InterStim therapy compared to standard medical therapy at 6-months in subjects with mild symptoms of overactive bladder. *Neurourol Urodyn*. 2015;34:224.

LEVEL III

American College of Obstetricians and Gynecologists. Urinary incontinence in women. Practice Bulletin No. 155. *Obstet Gynecol*. 2015;126:e66-e81.

Gibbs CF, Johnson TM 2nd, Ouslander JG. Office management of geriatric urinary incontinence. *Am J Med*. 2007;120:211.

Gormley EA, Lightner DJ, Faraday M, et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline amendment. *J Urol*. 2015;193:1572.

Myers DL. Female mixed urinary incontinence: a clinical review. *JAMA*. 2014;311:2007.

Noblett KL, Cadish LA. Sacral nerve stimulation for the treatment of refractory voiding and bowel dysfunction. *Am J Obstet Gynecol*. 2014;210:99.

Nygaard I. Clinical practice. Idiopathic urgency urinary incontinence. *N Engl J Med*. 2010;363:1156.

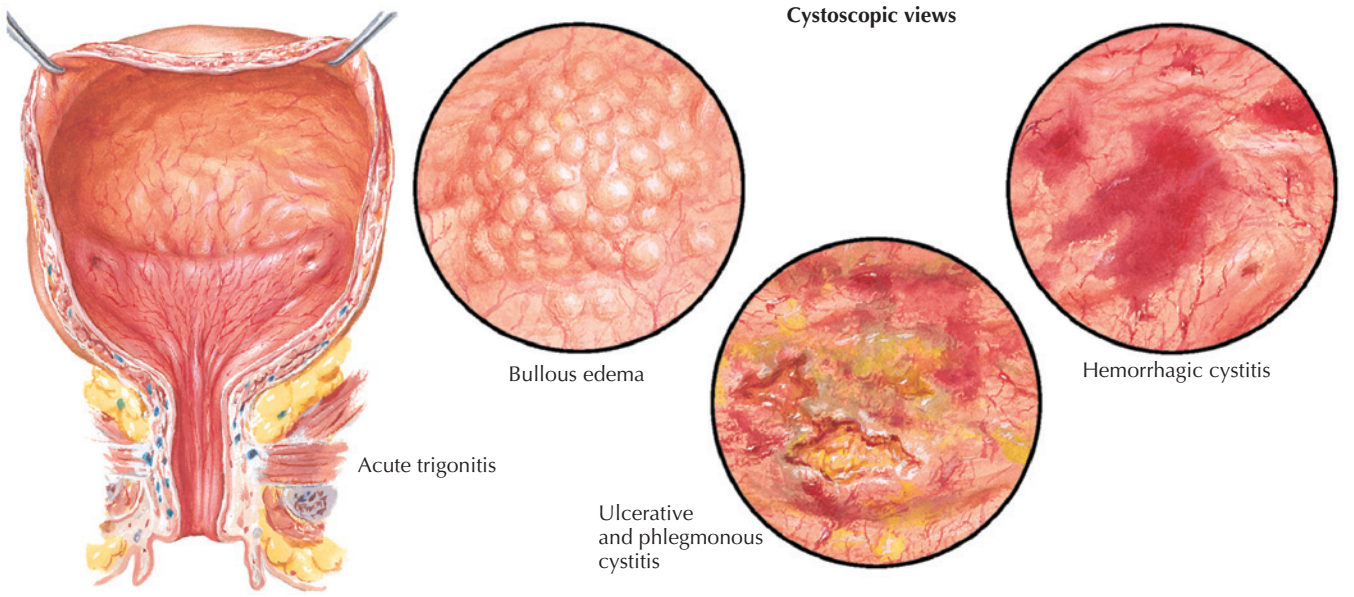
Qaseem A, Dallas P, Forciea MA, et al. Nonsurgical management of urinary incontinence in women: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2014;161:429.

The American College of Obstetricians and Gynecologists. OnabotulinumtoxinA and the bladder. Committee Opinion No. 604. *Obstet Gynecol*. 2014;123:1408.

Wein AJ, Rackley RR. Overactive bladder: a better understanding of pathophysiology, diagnosis and management. *J Urol*. 2006;175:S5.

Winters JC, Dmochowski RR, Goldman HB, et al. Urodynamic studies in adults: AUA/SUFU guideline. *J Urol*. 2012;188:2464.

Wood LN, Anger JT. Urinary incontinence in women. *BMJ*. 2014;349:g4531.



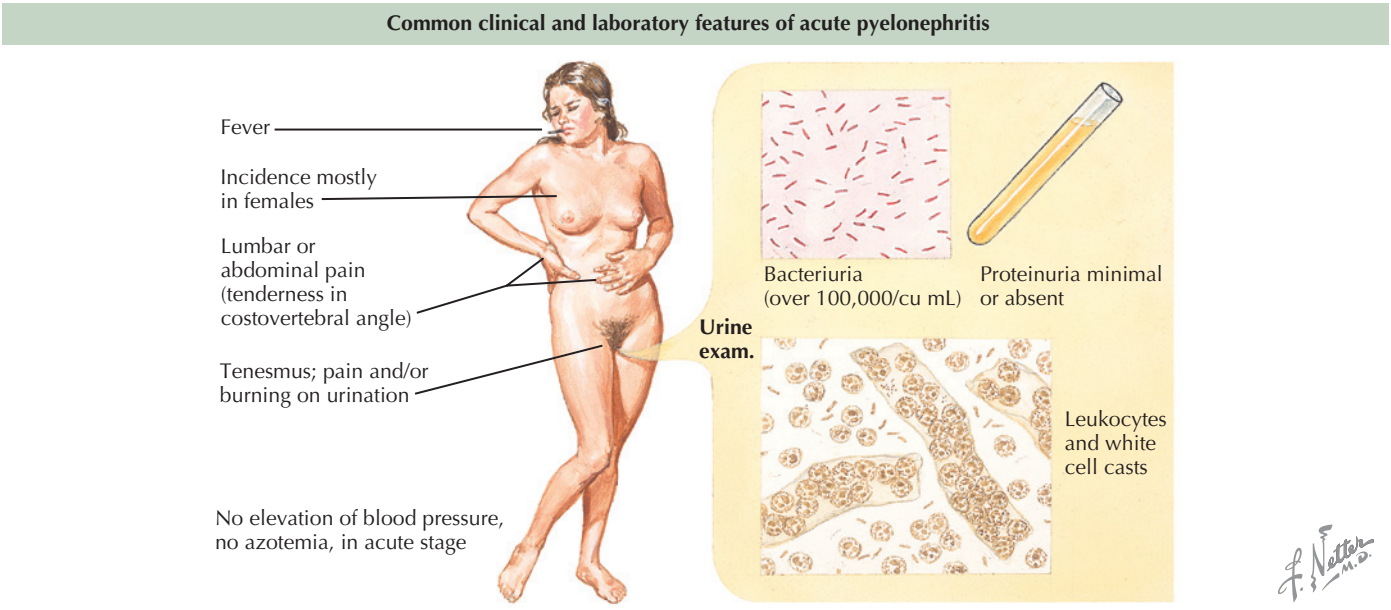


Figure 80.1 Urinary tract infections

Trichomonas, and yeasts are rare sources of infections, except in patients with diabetes, those who are immunosuppressed, or those requiring chronic catheterization. Infection with *Neisseria gonorrhoeae, Chlamydia trachomatis, Mycoplasma*, and *Ureaplasma* should all be considered when urethritis is suspected.

Risk Factors: Sexual activity, instrumentation, more virulent pathogens, altered host defenses, infrequent or incomplete voiding, foreign body or stone, obstruction, or biochemical changes in the urine (diabetes, hemoglobinopathies, pregnancy), estrogen deficiency, diaphragm use, and spermicides.

SIGNS AND SYMPTOMS

- Asymptomatic (5%)
- Frequency, urgency, nocturia, or dysuria
- Pelvic pressure or suprapubic pain (cystitis)
- Fever and chills (pyelonephritis)
- Pyuria (more than five white cells per high power field in a centrifuged specimen)
- Hematuria (infrequent)
- Costovertebral angle tenderness (pyelonephritis)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Traumatic trigonitis
- Urethral syndrome
- Interstitial cystitis
- Bladder tumors or stones
- Vulvitis and vaginitis (may give rise to external dysuria)
- Urethral diverticulum
- Infection in the Skene's glands
- Detrusor instability

Associated Conditions: Dyspareunia

Workup and Evaluation

Laboratory: Nonpregnant women with a first episode of classic symptoms suggestive of UTI do not need laboratory confirmation of the diagnosis; they may be empirically treated (data suggest that this is an acceptable strategy for women with fewer than three episodes per year, those who lack fever or flank pain, and those who have not been treated recently for the same symptoms). Others should have a urinalysis and culture performed. For uncentrifuged urine samples the presence of more than one white blood cell per high power field gives 90% accuracy in detecting infection. "Dipstick" point of care testing of a clean-voided sample that demonstrates leukocyte esterase, nitrite, or bacteria is supportive of the clinical diagnosis, although not diagnostic (false-positive nitrite tests can occur with substances that turn the urine red, such as the bladder analgesic phenazopyridine or ingestion of beets).

Imaging: No imaging indicated.

Special Tests: When urethritis is suspected, a swab inserted into the urethra may be used to obtain material for culture. Urine culture is helpful if there is reason to suspect antimicrobial resistance.

Diagnostic Procedures: History and physical examinations, urinalysis.

Pathologic Findings

Pyuria with white blood cell casts common.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Fluids, frequent voiding, and antipyretics. Urinary acidification (with ascorbic acid, ammonium chloride, or acidic fruit juices) and urinary analgesics (phenazopyridine [Pyridium)] may also be added based on the needs of the individual patient.

Specific Measures: Antibiotic therapy.

Diet: Increased fluids and reduction of caffeine consumption.

Activity: No restriction.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP050 (Urinary Tract Infections).

Drug(s) of Choice

- **Nonpregnant patients—single-dose therapy:** Amoxicillin 3 g, ampicillin 3.5 g, cephalosporin (first generation) 2 g, nitrofurantoin 200 mg, sulfisoxazole 2 g, trimethoprim (TMP) 400 mg, TMP/sulfamethoxazole 320/1600 mg, fosfomycin tromethamine (Monurol) 3 gm PO, fosfomycin (3-g single dose).
- **Three- to seven-day therapy:** Amoxicillin 500 mg every 8 hours, cephalosporin (first generation) 500 mg every 8 hours, ciprofloxacin 250 mg every 12 hours, nitrofurantoin 100 mg every 12 hours, norfloxacin 400 mg every 12 hours, ofloxacin 200 mg every 12 hours, sulfisoxazole 500 mg every 6 hours, tetracycline 500 mg every 6 hours, TMP/sulfamethoxazole 160/800 mg every 12 hours, TMP 200 mg every 12 hours.

Contraindications: Known or suspected hypersensitivity.

Precautions: Urinary analgesics (phenazopyridine [Pyridium]) should be taken for no longer than 48 hours and may stain some types of contact lenses.

Interactions: See individual medications.

Alternative Drugs

Pregnant patients: Seven-day therapy—amoxicillin 500 mg every 8 hours, cephalosporin (first generation) 500 mg every 6 hours, nitrofurantoin 100 mg every 12 hours.

FOLLOW-UP

Patient Monitoring: No follow-up is necessary after a single-dose treatment or multiday treatment for nonpregnant women who experience resolution of their symptoms. Confirmation of cure for all other patients should be conducted with urinalysis and culture. Those with recurrent infections should be evaluated for possible causes, and a program of patient-initiated single-dose therapy should be started as required for prophylaxis (after intercourse, daily, or three times weekly based on patient need). Possible causes of recurrent infection include incorrect or incomplete (eg, noncompliant) therapy, mechanical factors (such as obstruction or stone), or compromised host defenses.

Prevention/Avoidance: Frequent voiding, adequate fluid intake, and voiding after intercourse.

Possible Complications: Urethral syndrome and interstitial cystitis. Bacteremia, septic shock, adult respiratory distress syndrome, and other serious sequelae are associated with pyelonephritis. Recurrence rates may be as high as 20% (90% represent reinfection). Up to one-third of patients may develop pyelonephritis.

Expected Outcome: For most patients, symptoms should resolve within 2–3 days of the initiation of therapy. Some authors estimate that up to 50% of infections resolve without intervention.

MISCELLANEOUS

Pregnancy Considerations: Asymptomatic bacteriuria is more common during pregnancy (5%). Those at high risk (eg, patients with diabetes) should be carefully monitored.

ICD-10-CM Codes: N93.0 (Urinary tract infection, site not specified) and O23.40 (Unspecified infection of urinary tract in pregnancy, unspecified trimester).

REFERENCES

LEVEL II

Ambulatory Care Visits to Physician Offices, Hospital Outpatient Departments, and Emergency Departments: United States, 1999–2000. *Vital and Health Statistics*. Series 13, No. 157. Hyattsville, MD, National Center for Health Statistics, Centers for Disease Control and Prevention, U.S. Dept. of Health and Human Services, 2004.

LEVEL III

American College of Obstetricians and Gynecologists. Sulfonamides, nitrofurantoin, and risk of birth defects. Committee Opinion No. 494. *Obstet Gynecol*. 2011;117:1484.

American College of Obstetricians and Gynecologists. Urinary incontinence in women. ACOG Practice Bulletin 63. *Obstet Gynecol*. 2005;105:1533.

Car J. Urinary tract infections in women: diagnosis and management in primary care. *BMJ*. 2006;332:94.

Colgan R, Nicolle LE, McGlone A, et al. Asymptomatic bacteriuria in adults. *Am Fam Physician*. 2006;74:985.

Franco AV. Recurrent urinary tract infections. *Best Pract Res Clin Obstet Gynaecol*. 2005;19:861.

Gupta K, Trautner B. In the clinic. Urinary tract infection. *Ann Intern Med*. 2012;156:ITC3.

Hooton TM. Clinical practice. Uncomplicated urinary tract infection. *N Engl J Med*. 2012;366:1028.

Kunin CM. Urinary tract infections in females. *Clin Infect Dis*. 1994;18:1.

Lentz GM. Urogynecology. In: Katz VL, Lentz GM, Lobo RA, et al., eds. *Comprehensive Gynecology*. 5th ed. Philadelphia: Mosby/Elsevier; 2007: 545.

Macejko AM, Schaeffer AJ. Asymptomatic bacteriuria and symptomatic urinary tract infections during pregnancy. *Urol Clin North Am*. 2007;34:35.
Mittal P, Wing DA. Urinary tract infections in pregnancy. *Clin Perinatol*. 2005;32:749.
Nicolle L, Anderson PA, Conly J, et al. Uncomplicated urinary tract infection in women. Current practice and the effect of antibiotic resistance on empiric treatment. *Can Fam Physician*. 2006;52:612.
Scholes D, Hooton TM, Roberts PL, et al. Risk factors associated with acute pyelonephritis in healthy women. *Ann Intern Med*. 2005;142:20.
Sheffield JS, Cunningham FG. Urinary tract infection in women. *Obstet Gynecol*. 2005;106:1085.
Stamm W. Criteria for the diagnosis of urinary tract infection and for the assessment of therapeutic effectiveness. *Infection*. 1992;20(S151): S160.

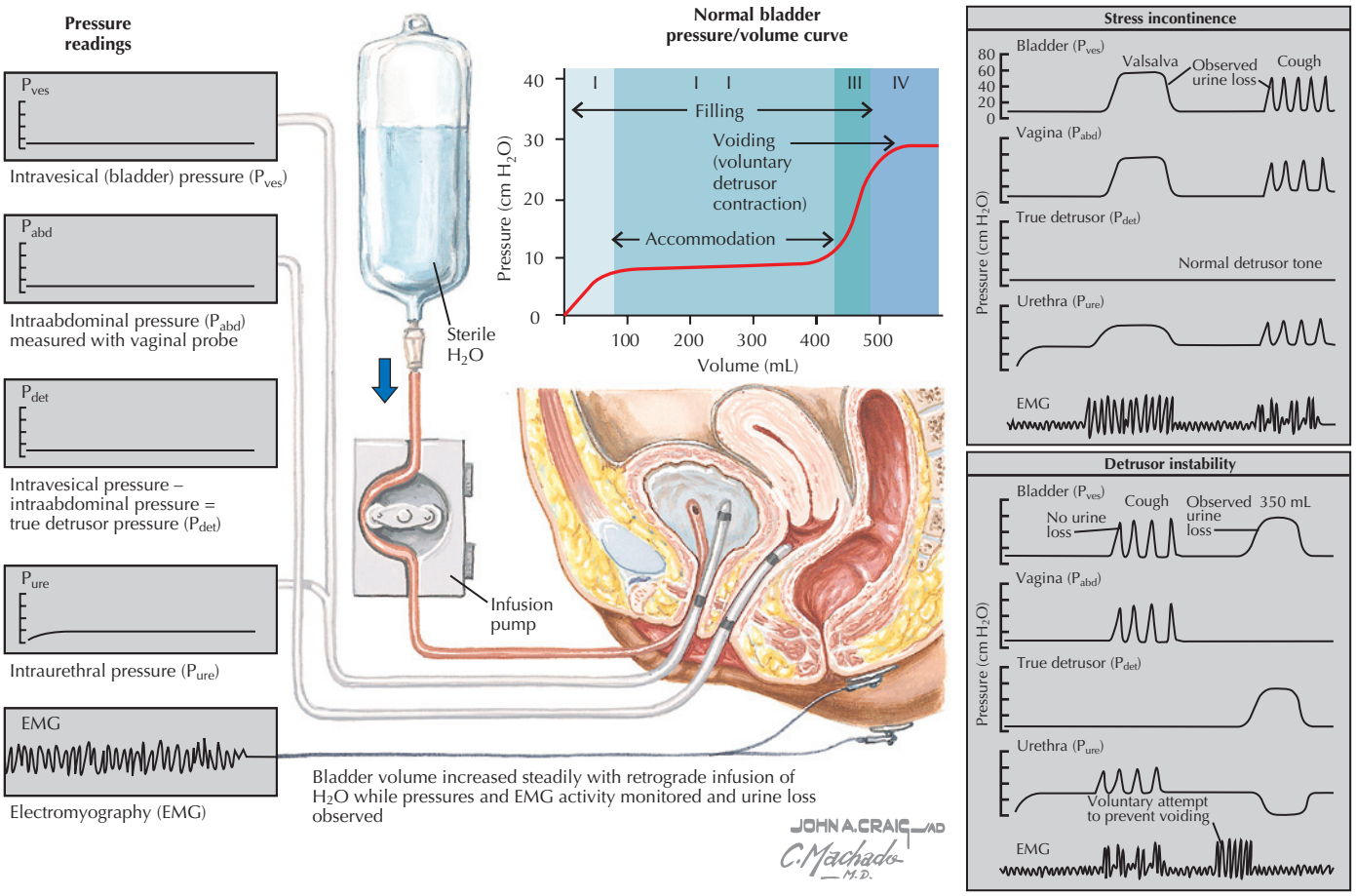


Figure 81.2 Complex cystometry

compliance). When bladder volume reaches a certain point (generally 150–200 mL) the first sensation of bladder fullness occurs. Additional increases in volume can be accomplished with an increasing sense of urgency but without uninhibited bladder contraction or incontinence. When bladder emptying is allowed, it should happen in an expeditious and efficient manner. Although the specific content of urodynamics testing varies, at a minimum, it includes cystometrics and provocative tests (such as coughing or straining while the bladder is full). Most centers include sophisticated evaluation of bladder compliance and contractility, cystoscopy, and evaluations of the voiding process itself. Pressure profiles of the bladder and urethra, electromyography, and fluoroscopic examinations may also be included.

Strategies: Simple Office Cystometrics—the patient should be in a relaxed, supine position with the bladder emptied. The patient is catheterized with a sterile technique using a straight catheter. Any residual urine is collected, measured for volume, and sent for culture to detect occult infection. The bladder is slowly filled (with sterile, warmed saline) by gravity at a rate of less than 3 mL/s. The patient is asked to report her first sensation of bladder fullness, and the volume infused at that point is noted. Filling continues in 25-mL aliquots until the patient is unable to tolerate more—this volume is recorded as the maximal bladder capacity. Any upward movement of the fluid column, intense sensation of urgency, or leakage around the catheter is abnormal. It suggests detrusor instability and should be noted. [More exact measurements of bladder function may be made by assembling intravenous tubing, a spinal manometer (or limb of extra tubing), and a three-way connector. The pressure inside the fluid column may be monitored, and the presence of bladder contractions can be more easily detected and documented. When this greater degree of accuracy is required, many prefer to proceed to formal urodynamics testing.] The catheter is removed, and the patient is asked to cough several times while leakage is noted. Leakage that occurs immediately after removal, is prolonged, or is of large volume suggests detrusor instability. These maneuvers may be repeated in the standing position.

Complex Urodynamic Testing—the procedures used in multichannel urodynamic test vary somewhat with the specifics of the equipment being used and local custom. Instead of using a simple straight catheter (as previous), bladder filling is accomplished by a catheter system equipped with sensors that can monitor bladder and urethral pressure (referenced pressures from the rectum or vagina may also be recorded). Following filling of the bladder, the catheter may be slowly pulled through the length of the urethra to measure both pressure and functional urethral length. After provocative tests are performed, the patient is asked to empty the bladder on a special commode that can measure flow rate and volume. Some centers augment these studies with radiographic evaluations of the bladder and urethra.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP081 (Urinary Incontinence), AP050 (Urinary Tract Infections), AP012 (Pelvic Support Problems), and AP166 (Surgery for Stress Urinary Incontinence).

IMPLEMENTATION

Special Considerations: "Urinary incontinence" may be a sign, symptom, or condition. It is defined as a condition in which

involuntary loss of urine may be objectively demonstrated, and the loss presents a social or hygienic problem. The volume of the loss is not as important as the impact it has on the patients and their life.

An assessment of voiding may be conducted by filling the bladder with 200 mL of fluid and listening to the patient's voiding from outside a bathroom door or while the patient voids behind a screen. The volume of flow (rate) may be estimated by the sound; the duration of flow may be timed with a stopwatch. Sophisticated measures of voiding parameters are typically included in formal urodynamics testing.

Residual bladder volume may also be measured by specialized ultrasonographic techniques.

REFERENCES

LEVEL II

Rachaneni S, Latthe P. Does preoperative urodynamics improve outcomes for women undergoing surgery for stress urinary incontinence? A systematic review and meta-analysis. *BJOG*. 2015;122:8.

Yalcin I, Versi E, Benson JT, et al. Validation of a clinical algorithm to diagnose stress urinary incontinence for large studies. *J Urol*. 2004; 171:2321.

LEVEL III

American College of Obstetricians and Gynecologists. Urinary incontinence in women. Practice Bulletin No. 155. *Obstet Gynecol*. 2015; 126:e66.

MacLachlan LS, Rovner ES. Good urodynamic practice: keys to performing a quality UDS study. *Urol Clin North Am*. 2014;41:363.

Nygaard IE, Heit M. Stress urinary incontinence. *Obstet Gynecol*. 2004; 104:607.

Raz O, Tse V, Chan L. Urodynamic testing: physiological background, setting-up, calibration and artefacts. *BJU Int*. 2014;114(suppl 1): 22.

Sutherst JR, Brown MC. Comparison of single and multichannel cystometry in diagnosing bladder instability. *BMJ*. 1984;288:1720.

Yared JE, Gormley EA. The role of urodynamics in elderly patients. *Clin Geriatr Med*. 2015;31:567.

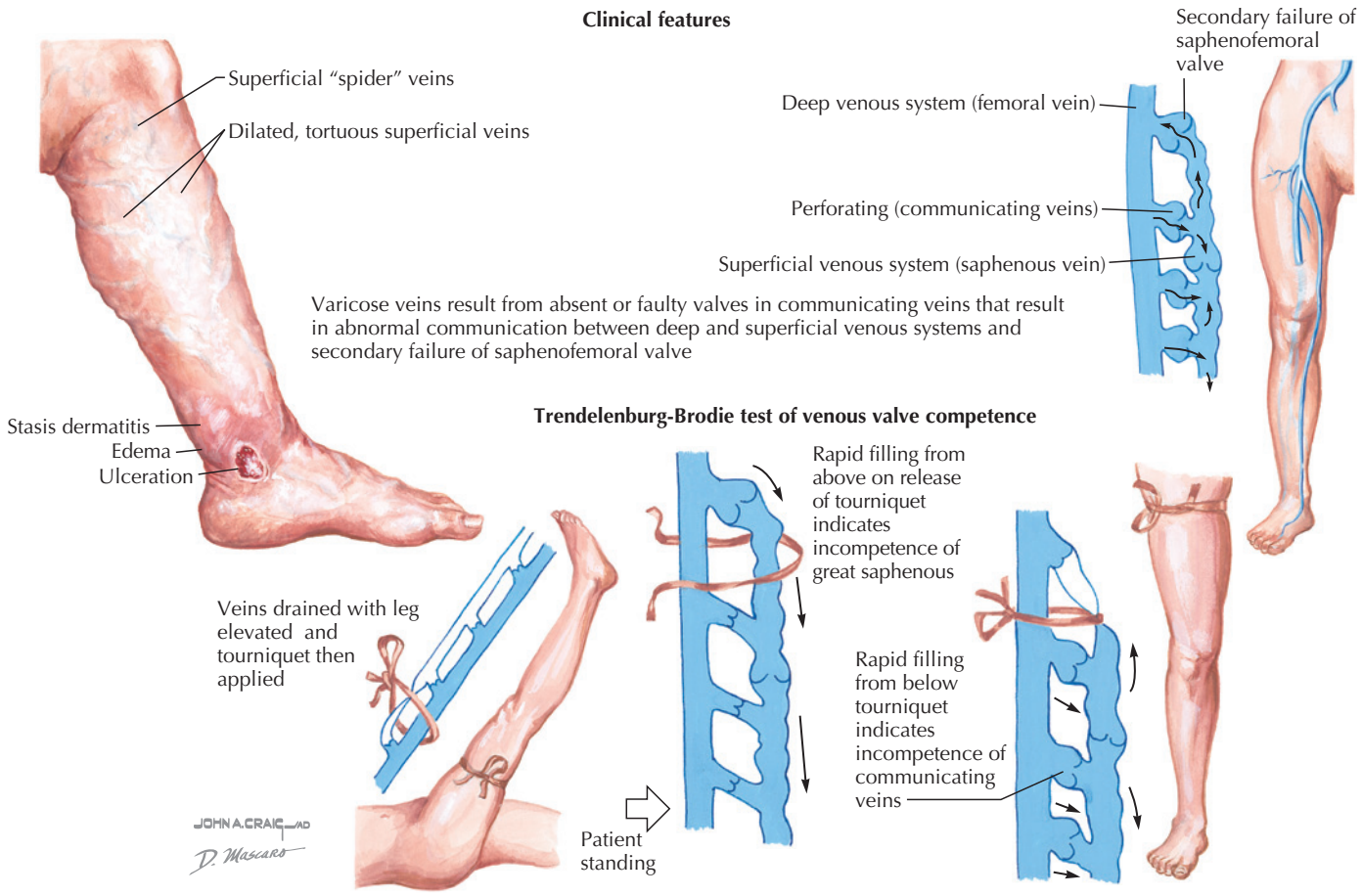


Figure 82.1 Clinical features and testing of varicose veins.

Specific Measures: Superficial veins may be eliminated with intracapillary injection of hypertonic saline (20%–25%) or 1%–3% solution of sodium tetradecyl sulfate (must be followed by compression for up to 3 weeks). Ligation or stripping of the saphenous veins should be considered in patients with pain, ulcers, recurrent phlebitis, or significant cosmetic problems.

Diet: No specific dietary changes indicated. Weight loss when appropriate.

Activity: Active exercise routines, including walking, using elastic stockings (applied before arising), avoiding prolonged standing or inactivity.

Patient Education: Education about risk factors and avoidance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP174 (Preventing Deep Vein Thrombosis), and AP169 (Skin Conditions During Pregnancy).

Drug(s) of Choice

None

Precautions: Some authors suggest that oral contraceptives should not be used within 6 weeks of sclerotherapy.

Alternative Drugs

Antibiotic therapy for infected ulcers.

FOLLOW-UP

Patient Monitoring: Normal health maintenance, evaluation for progression of disease or emergence of complications (skin ulcers).

Prevention/Avoidance: Avoidance of prolonged standing or inactivity, use of compression stockings, exercise, weight loss, leg elevation when at rest.

Possible Complications: Petechial hemorrhages, chronic edema, superficial ulceration and infection, chronic pigment change, eczema.

Expected Outcome: Generally a chronic condition with control possible through treatment.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. Pregnancy often worsens existing disease and increases the risk of future occurrence. Use of compression stockings should be encouraged for those at an increased risk.

ICD-10-CM Codes: I83 (Varicose veins of lower extremity).

REFERENCES

LEVEL I

Brittenden J, Cotton SC, Elders A, et al. A randomized trial comparing treatments for varicose veins. *N Engl J Med*. 2014;371:1218.

van Gent WB, Catarinella FS, Lam YL, et al. Conservative versus surgical treatment of venous leg ulcers: 10-year follow up of a randomized, multicenter trial. *Phlebology*. 2015;30:35.

LEVEL II

Alden PB, Lips EM, Zimmerman KP, et al. Chronic venous ulcer: minimally invasive treatment of superficial axial and perforator vein reflux speeds healing and reduces recurrence. *Ann Vasc Surg*. 2013;27:75.

Anwar MA, Georgiadis KA, Shalhoub J, et al. A review of familial, genetic, and congenital aspects of primary varicose vein disease. *Circ Cardiovasc Genet*. 2012;5:460.

Carroll C, Hummel S, Leaviss J, et al. Systematic review, network meta-analysis and exploratory cost-effectiveness model of randomized trials of minimally invasive techniques versus surgery for varicose veins. *Br J Surg*. 2014;101:1040.

Nesbitt C, Bedenis R, Bhattacharya V, et al. Endovenous ablation (radiofrequency and laser) and foam sclerotherapy versus open surgery for great saphenous vein varices. *Cochrane Database Syst Rev*. 2014;(7):CD005624.

Tisi PV, Beverley CA. Injection sclerotherapy for varicose veins. *Cochrane Database Syst Rev*. 2002;(1):CD001732.

LEVEL III

American College of Obstetricians and Gynecologists. Prevention of deep vein thrombosis and pulmonary embolism. ACOG Practice Bulletin No. 84. *Obstet Gynecol*. 2007;110:429.

Eberhardt RT, Raffetto JD. Chronic venous insufficiency. *Circulation*. 2005;111:2398.

SECTION V

Vulvar Disease

This page intentionally left blank

ACNE INVERSA (HIDRADENITIS SUPPURATIVA)

INTRODUCTION

Description: Acne inversa (formerly hidradenitis suppurativa) is a chronic, unrelenting, refractory infection of the skin and subcutaneous tissue that is initiated by the obstruction and subsequent inflammation of follicles and apocrine glands, with resultant sinus and abscess formation. This process may involve the axilla, vulva, and perineum.

Prevalence: Uncommon. Four to five times more common in females than in males. It is reported to occur in as many as 4% of women in some studies.

Predominant Age: Reproductive age (not observed before puberty).

Genetics: Suggestions of a family pattern, but a strong genetic link for most cases remains unproved. (In some studies, as many as 38% of patients have a similarly affected relative and a locus at chromosome 1p21.1-1q25.3 along with mutations in the secretase genes NCSTN, PSENEN, and PSEN1 and others have been reported. Pyogenic arthritis, pyoderma gangrenosum, acne, and hidradenitis suppurativa [PAPASH] have been associated with a novel mutation of the PSTPIP1 gene.)

ETIOLOGY AND PATHOGENESIS

Causes: Recurrent infections that arise in subcutaneous nodules. Proposed—hypersensitivity to androgens and follicular occlusion with rupture.

Risk Factors: None known. Proposed—excessive heat, perspiration, tight clothing, smoking, and obesity.

SIGNS AND SYMPTOMS

- Recurrent and chronic inflammatory and ulcerated portions of labia associated with pain and foul-smelling discharge
- Multiple draining sinuses and abscesses

DIAGNOSTIC APPROACH

Differential Diagnosis

- Sexually transmitted infection (granuloma inguinale, lymphogranuloma venereum)
- Crohn disease
- Fox-Fordyce disease
- Bacterial folliculitis and furunculosis

Associated Conditions: Dyspareunia, vulvodynia. Associations with metabolic syndrome and Crohn disease have been reported.

Workup and Evaluation

Laboratory: No evaluation indicated.

Imaging: No imaging indicated.

Special Tests: Biopsy of the affected area may be necessary to establish the diagnosis.

Diagnostic Procedures: History, physical, and biopsy of affected area.

Pathologic Findings

Inflammation of the apocrine glands with the occlusion of ducts, cystic dilation, and inspissation of keratin material. Multiple draining sinuses and abscesses are common.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Perineal hygiene, sitz baths, loose-fitting clothing, smoking cessation, weight reduction, avoidance of trauma.

Specific Measures: Most effective therapy is based on early, aggressive, wide excision of affected area. Topical therapy with antibiotics, topical steroids, oral contraceptives, antiandrogens, and isotretinoin may be used in early or mild cases.

Diet: No specific dietary changes indicated.

Activity: No restriction. Patients frequently abandon intercourse because of pain, discharge, odor, or embarrassment.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP088 (Disorders of the Vulva).

Drug(s) of Choice

Antibiotics—tetracycline 2 g PO daily, clindamycin topical daily; topical steroids; oral contraceptives; antiandrogens—finasteride (Proscar, Propecia, etc.), isotretinoin (Accutane) 0.5–2.0 mg/kg in two divided doses for 15–20 weeks. A second course may be considered after a 2-month hiatus.

Contraindications: Isotretinoin must not be taken during pregnancy. Therefore, isotretinoin should not be administered to women who are or may become pregnant.

Precautions: Isotretinoin should be given with food. Isotretinoin has been associated with the development of pseudotumor cerebri. Periodic assessment of liver function, cholesterol and triglyceride levels, and white blood counts should be conducted for patients undergoing isotretinoin therapy.

Interactions: See individual agents.

Alternative Drugs

- Dexamethasone or gonadotropin-releasing hormone agonists have been proposed, but costs and side effects limit their use.

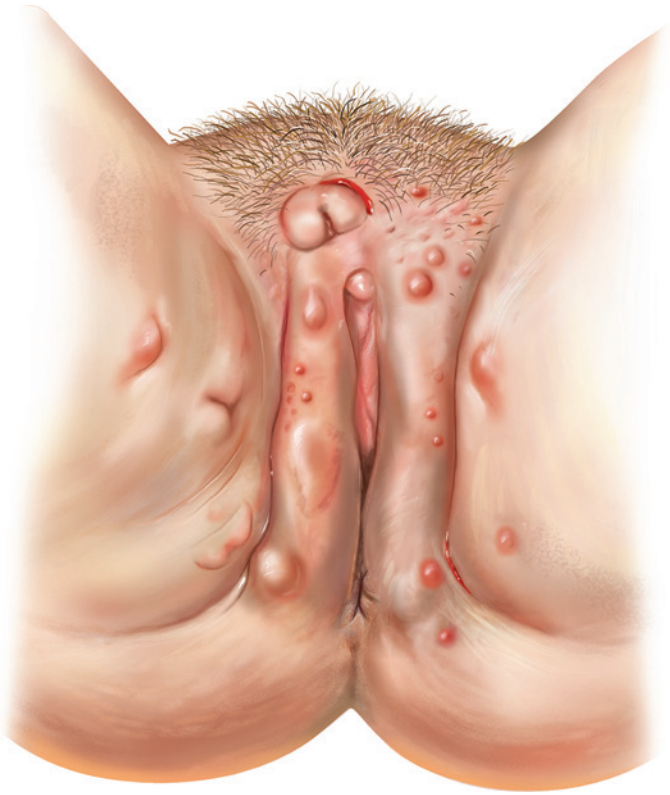


Figure 83.1 Appearance of acne inversa (hidradenitis suppurativa)

- Infliximab (Remicade) and other immunosuppressant agents have shown promise but are second-line therapies reserved for resistant cases.

FOLLOW-UP

Patient Monitoring: Normal health maintenance, watch for periodic worsening or secondary infection.

Prevention/Avoidance: Meticulous perineal hygiene; keep the affected area dry.

Possible Complications: Secondary infection, abscess formation, scarring, sexual dysfunction.

Expected Outcome: Relapses and chronic infections are common. With surgical excision, results are generally good, but scarring and dyspareunia may persist or result.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. Isotretinoin should not be administered to women who are or may become pregnant.

ICD-10-CM Codes: L73.2 (Hidradenitis suppurativa).

REFERENCES

LEVEL I

Sullivan TP, Welsh E, Kerdel FA, et al. Infliximab for acne inversa. *Br J Dermatol*. 2003;149:1046.

Al-Ali FM, Ratnamala U, Mehta TY, et al. Hidradenitis suppurativa (or acne inversa) with autosomal dominant inheritance is not linked to chromosome 1p21.1-1q25.3 region. *Exp Dermatol*. 2010;19:851.

LEVEL II

Crowley JJ, Mekkes JR, Zouboulis CC, et al. Association of hidradenitis suppurativa disease severity with increased risk for systemic comorbidities. *Br J Dermatol*. 2014;171:1561.

Gao M, Wang PG, Cui Y, et al. Inversa acne (hidradenitis suppurativa): a case report and identification of the locus at chromosome 1p21.1-1q25.3. *J Invest Dermatol*. 2006;126:1302.

Joseph MA, Jayaseelan E, Ganapathi B, et al. Acne inversa treated with finasteride. *J Dermatolog Treat*. 2005;16:75.

Kagan RJ, Yakuboff KP, Warner P, et al. Surgical treatment of acne inversa: a 10-year experience. *Surgery*. 2005;138:734, discussion 740.

Marzano AV, Trevisan V, Gattorno M, et al. Pyogenic arthritis, pyoderma gangrenosum, acne, and hidradenitis suppurativa (PAPASH): a new autoinflammatory syndrome associated with a novel mutation of the PSTPIP1 gene. *JAMA Dermatol*. 2013;149:762.

Mendonca CO, Griffiths CE. Clindamycin and rifampicin combination therapy for acne inversa. *Br J Dermatol*. 2006;154:977.

Miller IM, Ellervik C, Vinding GR, et al. Association of metabolic syndrome and hidradenitis suppurativa. *JAMA Dermatol*. 2014;150:1273.

Moul DK, Korman NJ. The cutting edge. Severe acne inversa treated with adalimumab. *Arch Dermatol*. 2006;142:1110.

Pink AE, Simpson MA, Desai N, et al. Mutations in the γ-secretase genes NCSTN, PSENEN, and PSEN1 underlie rare forms of hidradenitis suppurativa (acne inversa). *J Invest Dermatol*. 2012;132:2459.

Thielen AM, Barde C, Saurat JH. Long-term infliximab for severe acne inversa. *Br J Dermatol*. 2006;155:1105.

LEVEL III

Alikhan A, Lynch PJ, Eisen DB. Hidradenitis suppurativa: a comprehensive review. *J Am Acad Dermatol*. 2009;60:539.

Jemec GB. Clinical practice. Hidradenitis suppurativa. *N Engl J Med*. 2012;366:158.

Kelly AM, Cronin P. MRI features of acne inversa and review of the literature. *AJR Am J Roentgenol*. 2005;185:1201.

Slade DE, Powell BW, Mortimer PS. Acne inversa: pathogenesis and management. *Br J Plast Surg*. 2003;56:451.

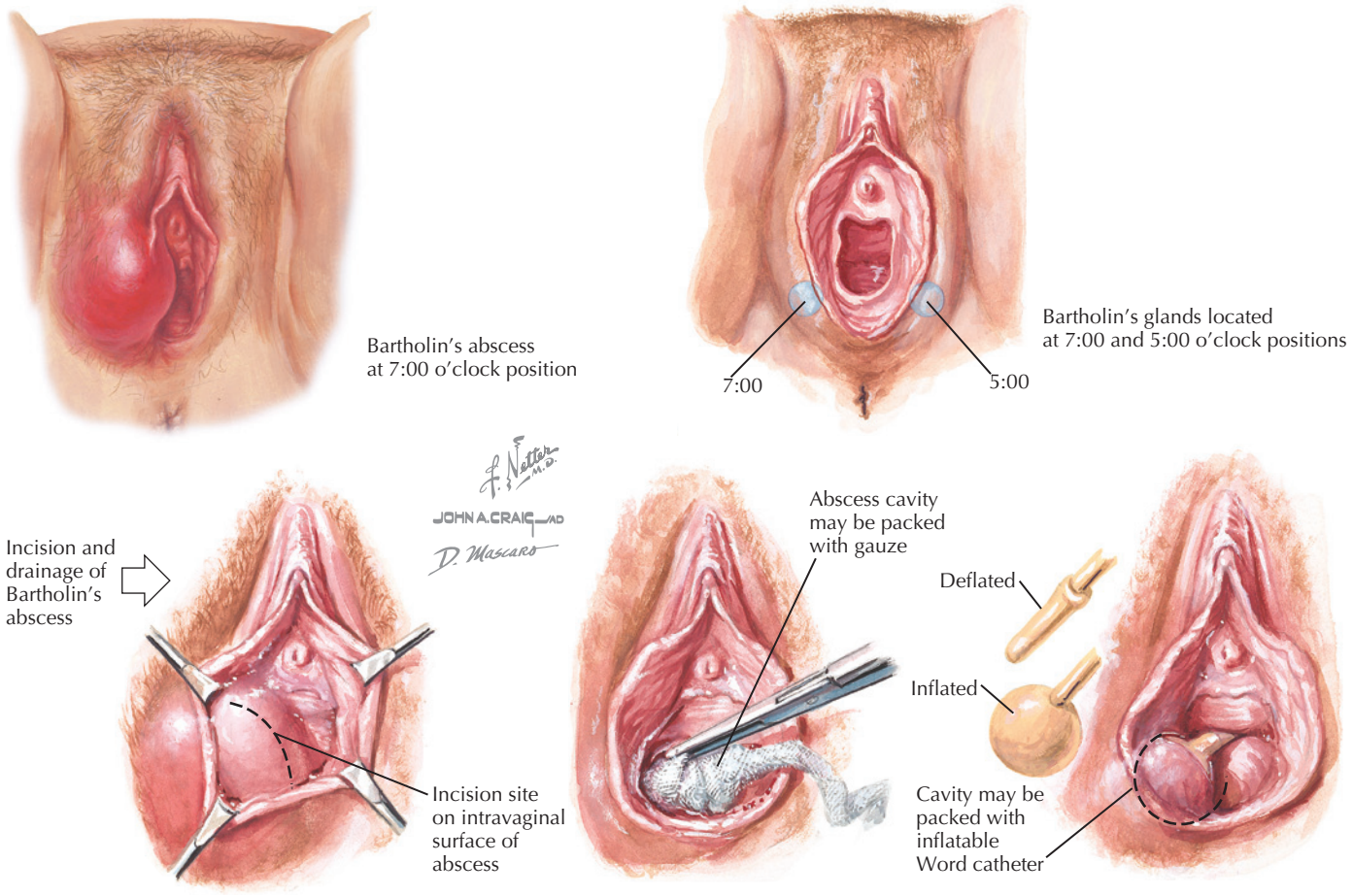


Figure 84.1 Bartholin gland abscess/infection

- Mesonephric cysts of the vagina
- Lipomas
- Fibromas
- Hernias
- Hydrocele
- Epidermal inclusion or sebaceous cyst
- Bartholin gland malignancy (rare)
- Neurofibroma
- Kaposi sarcoma (generally associated with immunocompromise)

Associated Conditions: Dyspareunia.

Workup and Evaluation

Laboratory: Because bartholinitis or Bartholin gland abscess may be gonococcal in origin, further evaluation for other sexually transmitted infection is prudent. Most often, culture-positive cysts are secondarily infected by coliform organisms or are polymicrobial, limiting the value of routine culture from the cyst.
Imaging: No imaging indicated.
Special Tests: None indicated.
Diagnostic Procedures: Inspection.

Pathologic Findings

Inflammation, dilation of the Bartholin gland duct, abscess formation

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, perineal hygiene.
Specific Measures: Mild infections may respond to antibiotic or topical therapies. Warm to hot sitz baths provide relief and promote drainage. Spontaneous drainage typically occurs in 1–4 days. Simple drainage is associated with recurrence; therefore, placement of a Word catheter, packing with iodoform gauze, or surgical marsupialization of the gland is desirable.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlets AP088 (Disorders of the Vulva) and AP190 (Vulvovaginal Health).

Drug(s) of Choice

- Trimethoprim-sulfamethoxazole one double-strength tablet PO twice daily for 7 days.
- Ampicillin 500 mg PO four times a day or other broad-spectrum antibiotic if cellulitis is present.
- For gonorrhea—ceftriaxone 125 mg IM, cefixime 400 mg PO single dose, or ciprofloxacin 500 mg PO single dose.

Contraindications: Known hypersensitivity or allergy to agent.

Alternative Therapies

Excision of the gland is often difficult and is associated with significant risk of morbidity, including intraoperative hemorrhage, hematoma formation, secondary infection, scar formation, and dyspareunia. For these reasons, excision is not generally recommended.

FOLLOW-UP

Patient Monitoring: Follow up to monitor for spontaneous drainage or the need for surgical intervention.
Prevention/Avoidance: Reduced exposure to sexually transmitted infection and vulvar trauma.
Possible Complications: Chronic cyst formation.
Expected Outcome: Recurrences occur in 5%–10% of patients after marsupialization.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: N75.1 (Abscess of Bartholin gland).

REFERENCES

LEVEL II

Eilber KS, Raz S. Benign cystic lesions of the vagina: a literature review. *J Urol*. 2003;170:717.

Kessous R, Aricha-Tamir B, Sheizaf B, et al. Clinical and microbiological characteristics of Bartholin gland abscesses. *Obstet Gynecol*. 2013;122:794.

Laartz BW, Cooper C, Degryse A, et al. Wolf in sheep's clothing: advanced Kaposi sarcoma mimicking vulvar abscess. *South Med J*. 2005;98:475.

Lee MY, Dalpiaz A, Schwamb R, et al. Clinical pathology of Bartholin's glands: a review of the literature. *Curr Urol*. 2015;8:22.

Wechter ME, Wu JM, Marzano D, et al. Management of Bartholin duct cysts and abscesses: a systematic review. *Obstet Gynecol Surv*. 2009;64:395.

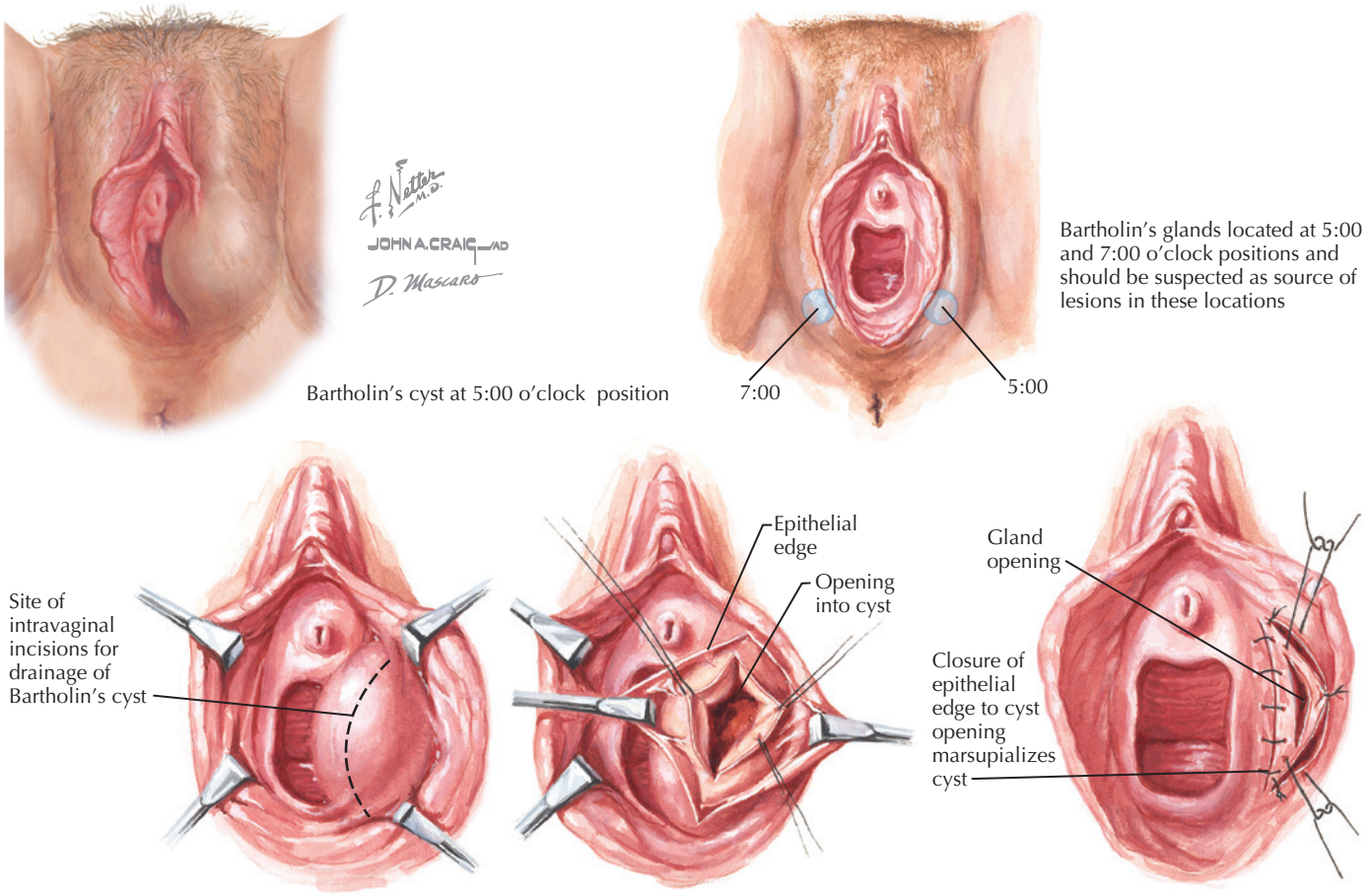


Figure 85.1 Bartholin gland cyst

Drug(s) of Choice

None indicated

Alternative Therapies

Excision of the gland is often difficult and is associated with significant risk of morbidity, including intraoperative hemorrhage, hematoma formation, secondary infection, scar formation, and dyspareunia. For these reasons, excision is not generally recommended.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: Reduced exposure to sexually transmitted infection and vulvar trauma.
Possible Complications: Dyspareunia, recurrent inflammation.
Expected Outcome: Recurrences occur in 5%–10% of patients following marsupialization.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: N75.0 (Cyst of Bartholin gland).

REFERENCES

LEVEL II

Eilber KS, Raz S. Benign cystic lesions of the vagina: a literature review. *J Urol*. 2003;170:717.

Laartz BW, Cooper C, Degryse A, et al. Wolf in sheep's clothing: advanced Kaposi sarcoma mimicking vulvar abscess. *South Med J*. 2005;98:475.

Lee MY, Dalpiaz A, Schwamb R, et al. Clinical pathology of Bartholin's glands: a review of the literature. *Curr Urol*. 2015;8:22.

Reif P, Ulrich D, Bjelic-Radisic V, et al. Management of Bartholin's cyst and abscess using the Word catheter: implementation, recurrence rates and costs. *Eur J Obstet Gynecol Reprod Biol*. 2015;190:81.

Wechter ME, Wu JM, Marzano D, et al. Management of Bartholin duct cysts and abscesses: a systematic review. *Obstet Gynecol Surv*. 2009; 64:395.

LEVEL III

Omole F, Simmons BJ, Hacker Y. Management of Bartholin's duct cyst and gland abscess. *Am Fam Physician*. 2003;68:135.

86 CONTACT VULVITIS

INTRODUCTION

Description: Contact vulvitis is characterized by vulvar irritation caused by contact with an irritant or allergen.
Prevalence: Relatively common.
Predominant Age: Any, but most common in reproductive and menopausal years.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Irritants may be primary or immunologic in character. The list of potential irritants can be extensive, including excessive hygiene ("feminine hygiene" sprays, deodorants and deodorant soaps, tampons, or pads—especially those with deodorants or perfumes), tight-fitting undergarments or those made of synthetic fabric, colored or scented toilet paper, and laundry soap or fabric softener residues. Even topical contraceptives, latex condoms, lubricants, "sexual aids," or semen may be the source of irritation. Soiling of the vulva by urine or feces can also create significant symptoms. Severe dermatitis of the vulva resulting from contact with poison ivy or poison oak is occasionally observed.
Risk Factors: Exposure to allergen (most often cosmetic or local therapeutic agents), immunosuppression, or diabetes.

SIGNS AND SYMPTOMS

- Diffuse reddening of the vulvar skin accompanied by itching or burning
- Symmetric, red, edematous change in the tissues
- Ulceration with weeping sores and secondary infection possible

DIAGNOSTIC APPROACH

Differential Diagnosis

- Vaginal infection
- Local *Candida* infection
- Vulvar dermatoses
- Atrophic vulvitis
- Vulvar dystrophy
- Pinworms
- Psoriasis
- Seborrheic dermatitis
- Neurodermatitis
- Impetigo
- Acne inversa

Associated Conditions: Dyspareunia, dysuria.

Workup and Evaluation

Laboratory: Examination of vaginal secretions under saline and 10% KOH (potassium hydroxide) to rule out possible vaginal infection.
Imaging: No imaging indicated.
Special Tests: Vulvar biopsy rarely required, although it may be diagnostic.
Diagnostic Procedures: A careful history, combined with the withdrawal of the suspected cause, usually both confirms the diagnosis and constitutes the needed therapy.

Pathologic Findings

Vulvar biopsy shows chronic inflammatory change and infiltration by histiocytes.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Perineal hygiene (keep the perineal area clean and dry, avoid tight undergarments or those made of synthetic fabric), education regarding prevention, encouragement to complete the prescribed course of therapy.
Specific Measures: Removal of identified (or possible) allergens, topical therapy.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance, education about avoidance or risk reduction. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP088 (Disorders of the Vulva) and AP190 (Vulvovaginal Health).

Drug(s) of Choice

- Wet compresses or soaks using Burow solution (aluminum acetate 2.5%–5% solution, three to four times daily for 30–60 minutes), followed by air drying or drying with a hair dryer on cool setting (loose-fitting clothing and the sparing use of a nonmedicated baby powder may facilitate the drying process).
- Steroid creams (hydrocortisone 0.5%–1%) or fluorinated corticosteroids (Valisone 0.1%, Synalar 0.01%) applied two to three times a day if needed.

Precautions: Further evaluation is warranted (including biopsy) if initial therapy does not produce significant improvement.

Alternative Drugs

Eucerin cream may be used to rehydrate the skin and reduce itching.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: Avoidance of possible allergens.
Possible Complications: Excoriation, chronic vulvar change (thickening).
Expected Outcome: With removal of the causative agent, complete resolution should be expected.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: N76.2 (Acute vulvitis) and N76.3 (Subacute and chronic vulvitis).

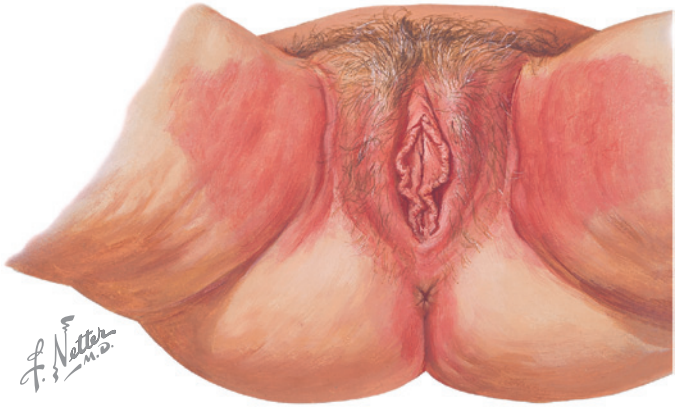


Figure 86.1 Contact vulvitis appearance

REFERENCES

LEVEL II

Chang TW. Familial allergic seminal vulvovaginitis. *Am J Obstet Gynecol*. 1976;126:442.

Fisher AA. Allergic reaction to feminine hygiene sprays. *Arch Dermatol*. 1973;108:801.

Moraes PS. Allergic vulvovaginitis induced by house dust mites: a case report. *J Allergy Clin Immunol*. 1998;101:557.

Nyirjesy P, Peyton C, Weitz MV, et al. Causes of chronic vaginitis: analysis of a prospective database of affected women. *Obstet Gynecol*. 2006;108: 1185.

LEVEL III

American College of Obstetricians and Gynecologists. Vaginitis. ACOG Practice Bulletin 72. *Obstet Gynecol*. 2006;107:1195.

American College of Obstetricians and Gynecologists. Diagnosis and management of vulvar skin disorders. ACOG Practice Bulletin No. 93. *Obstet Gynecol*. 2008;111:1243.

Nanda VS. Common dermatoses. *Am J Obstet Gynecol*. 1995;173:488.

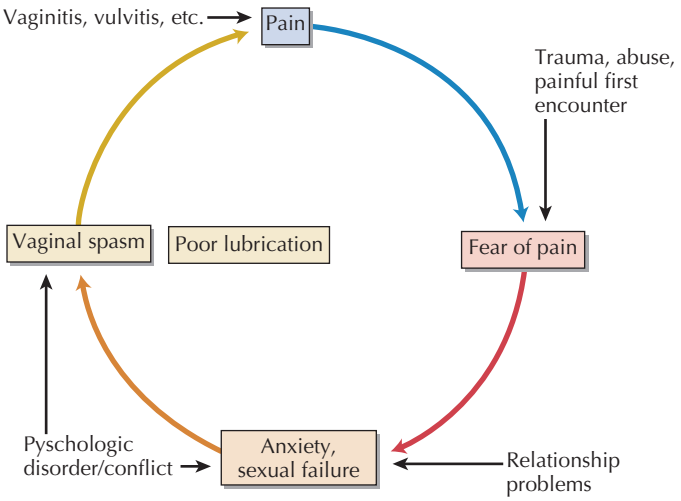


Figure 87.1 Self-perpetuating sexual pain

Patient Education: Reassurance, relaxation training, progressive desensitization. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP020 (When Sex Is Painful), AP042 (You and Your Sexuality-Especially for Teens), and AP088 (Disorders of the Vulva).

Drug(s) of Choice

The judicious use of anxiolytics or antidepressant medications for select patients may be appropriate but for short periods of time only.

Alternative Therapies

Modifying the sexual techniques used by the couple may reduce pain with intercourse. Delaying penetration until maximal arousal has been achieved improves vaginal lubrication, ensures vaginal apex expansion, and provides an element of control for the female partner. Sexual positions that allow the woman to control the direction and depth of penetration (such as woman astride) may also be of help.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. Watch for signs of abuse, anxiety, or depression.
Prevention/Avoidance: None.
Possible Complications: Marital discord, orgasmic or libidinal dysfunction.
Expected Outcome: With diagnosis and treatment of the underlying cause, the response should be good.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: N94.1 (Dyspareunia).

REFERENCES

LEVEL I

Abbott JA, Jarvis SK, Lyons SD, et al. Botulinum toxin type A for chronic pain and pelvic floor spasm in women: a randomized controlled trial. *Obstet Gynecol*. 2006;108:915.

LEVEL II

Munday P, Green J, Randall C, et al. Vulval vestibulitis: a common cause of dyspareunia? *BJOG*. 2005;112:500.

Shifren JL, Monz BU, Russo PA, et al. Sexual problems and distress in United States women: prevalence and correlates. *Obstet Gynecol*. 2008;112:970.

Zolnoun DA, Hartmann KE, Steege JF. Overnight 5% lidocaine ointment for treatment of vulvar vestibulitis. *Obstet Gynecol*. 2003;102:84.

LEVEL III

American College of Obstetricians and Gynecologists. Vulvodynia. ACOG Committee Opinion 345. *Obstet Gynecol*. 2006;108:1049.

American College of Obstetricians and Gynecologists. Vaginitis. ACOG Practice Bulletin No. 72. *Obstet Gynecol*. 2006;107:1195.

Basson R, Schultz WW. Sexual sequelae of general medical disorders. *Lancet*. 2007;369:409.

Edwards L. New concepts in vulvodynia. *Am J Obstet Gynecol*. 2003;189:S24.

National Institutes of Health. National Institutes of Health State-of-the-Science Conference statement: Management of menopause-related symptoms. *Ann Intern Med*. 2005;142:1003.

Ryan L, Hawton K. Female dyspareunia. *BMJ*. 2004;328:1357.

Steege JF, Zolnoun DA. Evaluation and treatment of dyspareunia. *Obstet Gynecol*. 2009;113:1124.

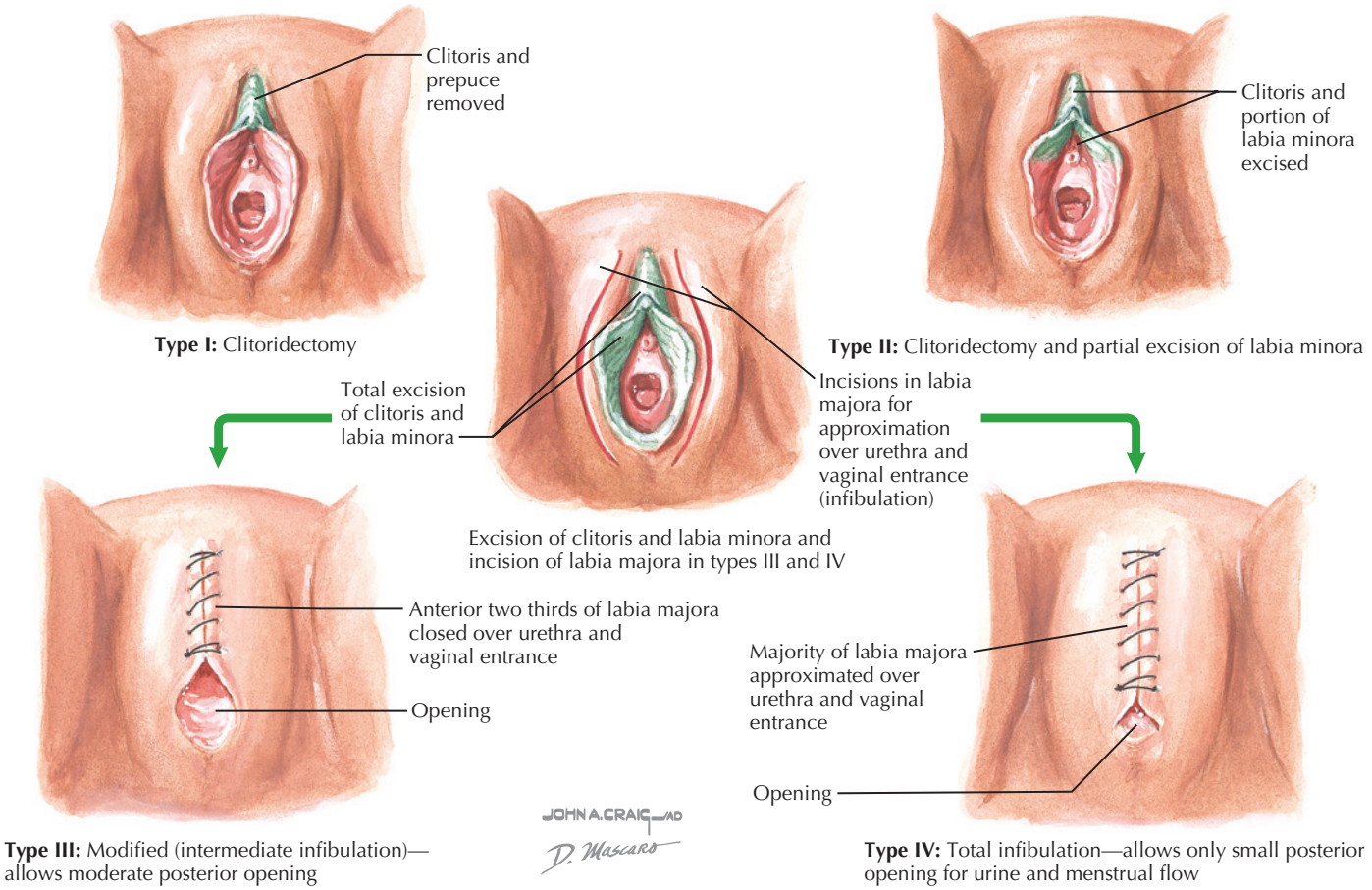


Figure 88.1 Female circumcision

- Type IV—pricking, piercing, or incising of the clitoris, labia, or both; stretching of the clitoris, labia, or both; cauterization by burning of the clitoris and surrounding tissue

Other forms of female genital mutilation include the following:

- Scraping of the tissue surrounding the vaginal orifice (angurya cuts) or cutting of the vagina (gishiri cuts)
- Introduction of corrosive substances or herbs into the vagina to cause bleeding or for the purpose of tightening or narrowing it
- Any other procedure that falls under the definition given previously

Prevalence: Approximately 168,000 women in the United States; approximately 96% of women in some African countries (eg, Somalia). Amnesty International estimates that it is performed on more than 130 million women worldwide.
Predominant Age: Majority performed during early teens.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Performed as part of ritual or religious beliefs, generally without the permission and often without the cooperation of the young girl herself.
Risk Factors: Most common in some African and Southeast Asian cultures.

SIGNS AND SYMPTOMS

- Significant scarring and deformity of the external genital structures, often to the point of complete obliteration of vaginal introitus (varies with the type and extent of the procedure performed)
- Obstruction may be sufficient to result in amenorrhea or dysmenorrhea
- Dyspareunia
- Orgasmic dysfunction
- Libidinal dysfunction
- Obstruction or hindrance to vaginal delivery

DIAGNOSTIC APPROACH

Differential Diagnosis

- Childhood burn injuries
- Intersex condition
- Imperforate hymen

Associated Conditions: Dyspareunia, libidinal dysfunction, and orgasmic dysfunction.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated.
Special Tests: None indicated.
Diagnostic Procedures: History and physical examinations.

Pathologic Findings

Absent or grossly scarred and deformed external genital tissues.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, support, and culturally sensitive education.

Specific Measures: Surgical opening of fused or scarred genital tissue may be necessary to allow for menstrual hygiene and sexual function. An anterior episiotomy, with or without subsequent repair, may be required at the time of childbirth (see the following).

Diet: No specific dietary changes indicated.

Activity: No restriction.

Patient Education: Culturally sensitive discussion of female anatomy, sexuality, and menstrual hygiene.

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Normal health maintenance. Cervical samples for cytologic examination may be difficult to obtain in patients with extensive scarring until or unless surgical revision is performed.

Prevention/Avoidance: Education of parents of young girls in cultures at risk for the procedure.

Possible Complications: Acutely (at the time of the procedure)—bleeding and infection (including tetanus), urinary retention, pain. Long-term—sexual dysfunction, difficulty with menstrual hygiene, recurrent vaginal or urinary tract infections, retrograde menstruation, hematocolpos, chronic pelvic inflammatory disease.

Expected Outcome: Sexual sequelae are often lifelong despite surgical revision (especially when clitoridectomy has been performed).

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, but presence may complicate conception and delivery. Delivery may require an anterior episiotomy with attendant increased risk of bleeding. Subsequent repair of the episiotomy is illegal in some locations, such as the United Kingdom and others, because this amounts to reinfibulation.

ICD-10-CM Codes: N90.81 (Female genital mutilation status), N90.811 (Female genital mutilation Type I status), N90.812 (Female genital mutilation Type II status), N90.813 (Female genital mutilation Type III status), and N90.814 (Female genital mutilation Type IV status).

REFERENCES

LEVEL II

Elmusharaf S, Elhadi N, Almroth L. Reliability of self reported form of female genital mutilation and WHO classification: cross sectional study. *BMJ*. 2006;333:124.

WHO study group on female genital mutilation and obstetric outcome, Banks E, Meirik O, et al. Female genital mutilation and obstetric outcome: WHO collaborative prospective study in six African countries. *Lancet*. 2006;367:1835.

LEVEL III

Adams KM, Gardiner LD, Assefi N. Healthcare challenges from the developing world: post-immigration refugee medicine. *BMJ*. 2004;328:1548.

Cappa C, Moneti F, Wardlaw T, et al. Elimination of female genital mutilation/cutting. *Lancet*. 2013;382:1080.

Council on Scientific Affairs, American Medical Association. Female genital mutilation. *JAMA*. 1995;274:1714.

Lentz GM. Rape, incest, and domestic violence. In: Katz VL, Lentz GM, Lobo RA, et al., eds. *Comprehensive Gynecology*. 5th ed. Philadelphia: Mosby/Elsevier; 2007:207.

Morgan J. Working towards an end to FGM. *Lancet*. 2015;385:843.

Rouzi AA, Alturki F. Female genital mutilation/cutting: an update. *Clin Exp Obstet Gynecol*. 2015;42:300.

Toubia N. Female circumcision as a public health issue. *N Engl J Med*. 1994;331:712.

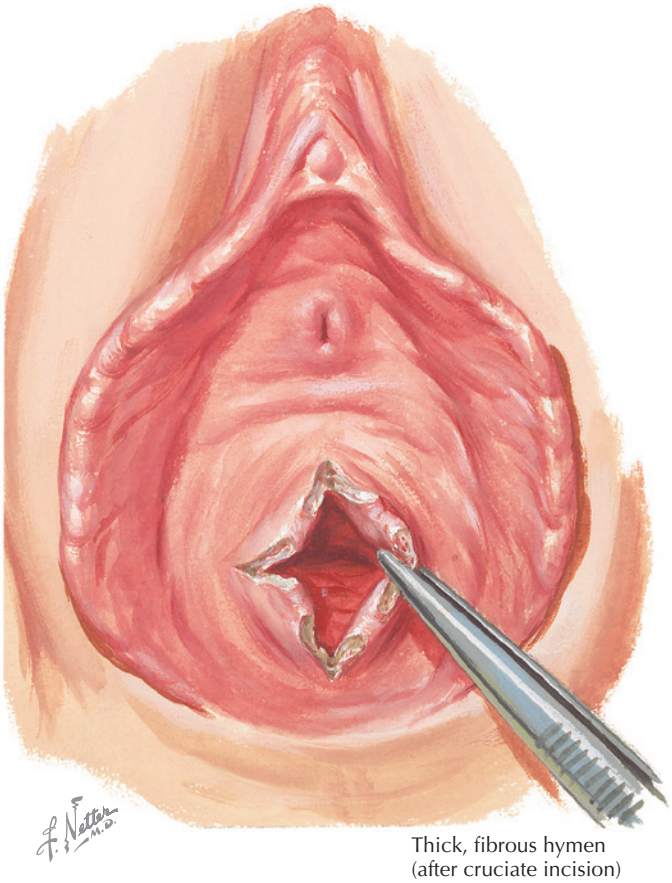


Figure 89.1 Hymenal stenosis

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated.
Special Tests: None indicated.
Diagnostic Procedures: History and physical examinations.

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, reassurance.
Specific Measures: Gentle digital dilation, surgical excision.
Diet: No specific dietary changes indicated.
Activity: No restriction.

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None
Possible Complications: Sexual dysfunction.
Expected Outcome: Generally good, but secondary problems (such as sexual dysfunction) may often persist.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy once achieved. Generally no effect on the route of delivery. Delivery (with or without an episiotomy) often results in improvement or resolution of symptoms.
ICD-10-CM Codes: N89.6 (Tight hymenal ring).

REFERENCES

LEVEL II

Berenson AB, Chacko MR, Wiemann CM, et al. A case-control study of anatomic changes resulting from sexual abuse. *Am J Obstet Gynecol*. 2000;182:820.

Berenson AB, Grady JJ. A longitudinal study of hymenal development from 3 to 9 years of age. *J Pediatr*. 2002;140:600.

McCann J, Miyamoto S, Boyle C, et al. Healing of hymenal injuries in prepubertal and adolescent girls: a descriptive study. *Pediatrics*. 2007; 119:e1094.

Segal TR, Fried WB, Krim EY, et al. Treatment of microperforate hymen with serial dilation: a novel approach. *J Pediatr Adolesc Gynecol*. 2015; 28:e21.

LEVEL III

American College of Obstetricians and Gynecologists. Müllerian agenesis: diagnosis, management, and treatment. Committee Opinion No. 562. *Obstet Gynecol*. 2013;121:1134.

Dietrich JE, Millar DM, Quint EH. Obstructive reproductive tract anomalies. *J Pediatr Adolesc Gynecol*. 2014;27:396.

Posner JC, Spandorfer PR. Early detection of imperforate hymen prevents morbidity from delays in diagnosis. *Pediatrics*. 2005;115:1008.

Quint EH, McCarthy JD, Smith YR. Vaginal surgery for congenital anomalies. *Clin Obstet Gynecol*. 2010;53:115.

90 HYPERPLASTIC VULVAR DYSTROPHY (SQUAMOUS CELL HYPERPLASIA, LICHEN SIMPLEX CHRONICUS)

INTRODUCTION

Description: Hypertrophic vulvar dystrophy (lichen simplex chronicus) causes a thickening of the vulvar skin over the labia majora, outer aspects of the labia minora, and clitoral areas. Eczematous inflammation or hyperkeratosis may be present.
Prevalence: Common, 40%–45% of non-neoplastic epithelial disorders.
Predominant Age: Middle to late reproductive age and older.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Unknown. Dermal reaction to chronic itch-scratch cycle. Often associated with or worsened by stress and can be seen as a localized variant of atopic dermatitis. It represents an end-stage response to a wide variety of possible initiating processes, including environmental factors and dermatologic disease.
Risk Factors: Genital atrophy (postmenopausal), recurrent vulvitis.

SIGNS AND SYMPTOMS

- Vulvar itching (almost always present)
- Dusky-red to thickened-white appearance of the vulva
- Fissuring and excoriations (common)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Vulvar cancer (premalignant or malignant changes)
- Chronic mycotic vulvitis
- Contact vulvitis
- Psoriasis
- Lichen sclerosus

Associated Conditions: Vulvodynia, vulvar pruritus, and dyspareunia.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated.
Special Tests: Biopsy may be required to confirm the diagnosis. Cultures for *Candida* or other dermatophytes should be considered.
Diagnostic Procedures: History, physical examination, colposcopy, or biopsy of lesions.

Pathologic Findings

Thickening of the epithelium with acanthosis, elongation of the epithelial folds, and chronic inflammatory changes (lymphocytes and plasma cells) occur. Hyperkeratosis may be present.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Perineal hygiene, sitz baths, stress reduction. Reduce or eliminate sources of irritation such as candidiasis or contact allergy. Wearing white cotton gloves (especially at night) reduces the tissue damage caused by scratching.
Specific Measures: Treatment is focused on interrupting the itch-scratch-rash-itch cycle. Topical steroids, perineal soothing agents, and agents to reduce itching are most effective. If significant improvement is not achieved in 3 months, biopsy is indicated.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP088 (Disorders of the Vulva).

Drug(s) of Choice

- Fluocinolone acetonide 0.025% or 0.01%, triamcinolone acetonide 0.01% or betamethasone valerate (Valisone) 0.1%, or a similar corticosteroid applied two to three times daily may give relief.
- Once relief is achieved, treatment should switch to hydrocortisone 2.5% cream or ointment.
- For itching: diphenhydramine hydrochloride (Benadryl) or hydroxyzine hydrochloride (Atrax) used at night.

Contraindications: See individual agents.

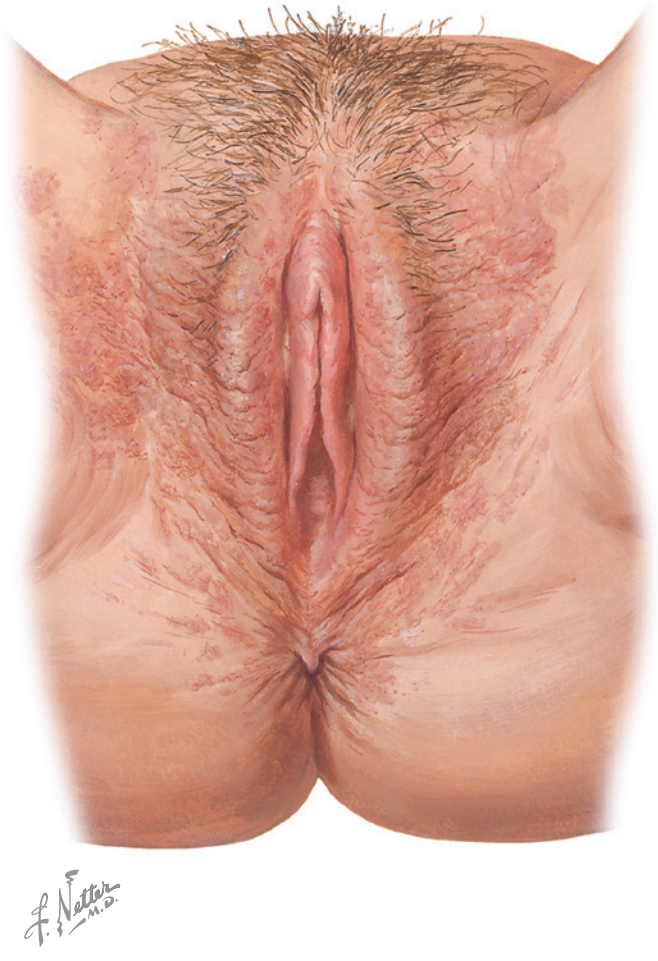


Figure 90.1 Hyperplastic vulvar dystrophy

Precautions: Fluorinated steroids should be used for short periods only and replaced with hydrocortisone or nonsteroidal therapies when possible.
Interactions: See individual agents.

Alternative Drugs

- Topical clobetasol propionate (0.05%) may be used if relief of pruritus is not achieved with less potent agents.
- Subcutaneous injections of triamcinolone (5 mg suspension mixed with 2 mL of saline) or alcohol (0.1–0.2 mL of absolute alcohol) have been reported but should be reserved for the most intractable disease.
- Topical progestins and androgens have been advocated as alternative therapies.

FOLLOW-UP

Patient Monitoring: Constant vigilance is required to watch for possible premalignant or malignant changes that can often mimic these lesions and those of lichen sclerosus.
Prevention/Avoidance: Avoidance of local irritants.
Possible Complications: Vulvar cancer may be overlooked; excoriation is common with secondary infection possible.
Expected Outcome: Generally good if itch-scratch cycle is broken.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: N90.6 (Hypertrophy of vulva).

REFERENCES

LEVEL I

Bousema MT, Romppanen U, Geiger JM, et al. Acitretin in the treatment of severe lichen sclerosus et atrophicus of the vulva: a double-blind, placebo-controlled study. *J Am Acad Dermatol*. 1994;30:225.

Li C, Bian D, Chen W, et al. Focused ultrasound therapy of vulvar dystrophies: a feasibility study. *Obstet Gynecol*. 2004;104:915.

LEVEL II

Cattaneo A, Bracco GL, Maestrini G, et al. Lichen sclerosis and squamous hyperplasia of the vulva. A clinical study of medical treatment. *J Reprod Med*. 1991;36:301.

LEVEL III

American College of Obstetricians and Gynecologists. Vulvodynia. ACOG Committee Opinion 345. *Obstet Gynecol*. 2006;108:1049.

American College of Obstetricians and Gynecologists. Diagnosis and management of vulvar skin disorders. ACOG Practice Bulletin No. 93. *Obstet Gynecol*. 2008;111:1243.

Jasionowski EA, Jasionowski PA. Further observations on the effect of topical progesterone on vulvar disease. *Am J Obstet Gynecol*. 1979;134:565.

McKay M. Vulvar dermatoses. *Clin Obstet Gynecol*. 1991;34:614.

Nanda VS. Common dermatoses. *Am J Obstet Gynecol*. 1995;173:488.

Stewart KM. Clinical care of vulvar pruritus, with emphasis on one common cause, lichen simplex chronicus. *Dermatol Clin*. 2010;28:669.

Virgili A, Bacilieri S, Corazza M. Managing vulvar lichen simplex chronicus. *J Reprod Med*. 2001;46:343.

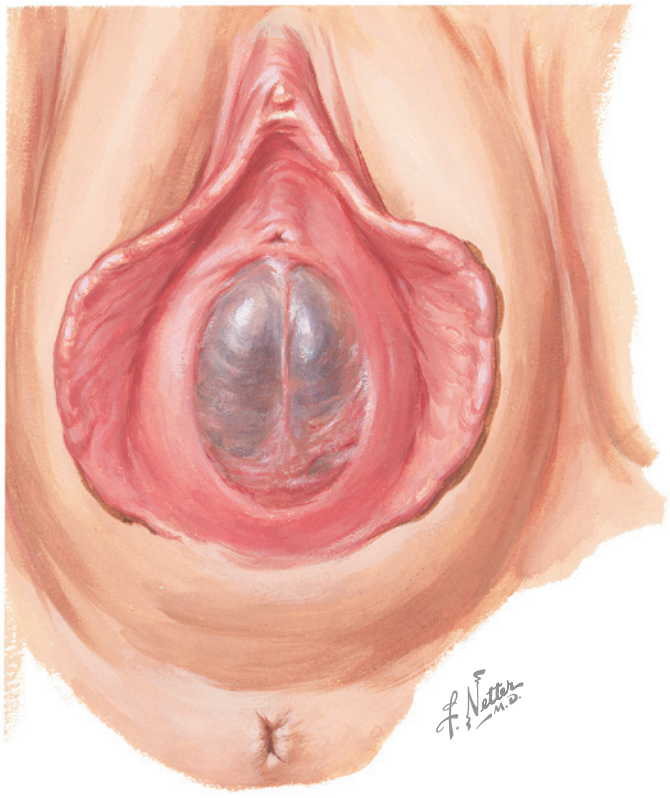


Figure 91.1 Imperforate hymen

Diet: No specific dietary changes indicated.
Activity: No restriction.

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: Hematocolpos, endometriosis, hymenal scarring and narrowing after surgical excision.
Expected Outcome: Generally good with early resection. Delayed diagnosis is associated with reduced fertility caused by secondary damage (endometriosis).

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, although often associated with conditions that do affect fertility, such as endometriosis. Reproductive outlook is best when diagnosis and treatment occur early.
ICD-10-CM Codes: Q52.3 (Imperforate hymen).

REFERENCES

LEVEL III

American College of Obstetricians and Gynecologists. Müllerian agenesis: diagnosis, management, and treatment. Committee Opinion No. 562. *Obstet Gynecol*. 2013;121:1134.

Dietrich JE, Millar DM, Quint EH. Obstructive reproductive tract anomalies. *J Pediatr Adolesc Gynecol*. 2014;27:396.

Posner JC, Spandorfer PR. Early detection of imperforate hymen prevents morbidity from delays in diagnosis. *Pediatrics*. 2005;115:1008.

Quint EH, McCarthy JD, Smith YR. Vaginal surgery for congenital anomalies. *Clin Obstet Gynecol*. 2010;53:115.

Winderl LM, Silverman RK. Prenatal diagnosis of congenital imperforate hymen. *Obstet Gynecol*. 1995;85:857.

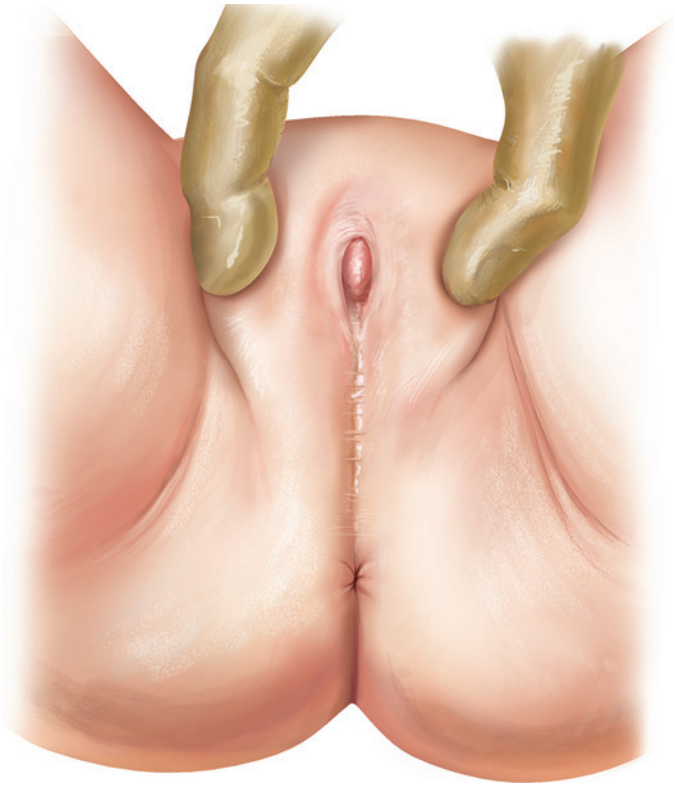


Figure 92.1 Labial adhesion

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated.
Special Tests: None indicated.
Diagnostic Procedures: History and physical examinations.

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, reassurance, perineal hygiene, and sitz baths.
Specific Measures: Treatment indicated only if urination is adversely affected, or if they are associated with recurrent infections or pain, otherwise they will spontaneously regress at puberty with the onset of increased estrogen production. Topical estrogen cream, gentle traction to separate the labia (only after estrogen pretreatment; generally not necessary and strongly discouraged). Surgical treatment is almost never required.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP041 (Your Changing Body-Especially for Teens).

Drug(s) of Choice

- Topical estrogen cream (Premarin vaginal cream, Dienestrol cream)—small portion applied to the vulva twice a day for 7–10 days. May be continued one to three times a week if desired, although generally not necessary.
- Topical betamethasone 0.05% twice daily for 4–6 weeks has been suggested as an alternative or adjunct to topical hormone therapy.

Contraindications: Undiagnosed vaginal bleeding.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: Good perineal hygiene.
Possible Complications: Vaginitis, urinary tract infection, urinary retention, or vaginal cyst formation.
Expected Outcome: Excellent.

MISCELLANEOUS

ICD-10-CM Codes: N90.9 (Noninflammatory disorder of vulva and perineum, unspecified).

REFERENCES

LEVEL II

Aribarg A. Topical oestrogen therapy for labial adhesions in children. *Br J Obstet Gynaecol*. 1975;82:424.

Bacon JL. Prepubertal labial adhesions: evaluation of a referral population. *Am J Obstet Gynecol*. 2002;187:327.

Ertürk N. Comparison of estrogen and betamethasone in the topical treatment of labial adhesions in prepubertal girls. *Turk J Med Sci*. 2014;44:1103.

Schober J, Dulabon L, Martin-Alguacil N, et al. Significance of topical estrogens to labial fusion and vaginal introital integrity. *J Pediatr Adolesc Gynecol*. 2006;19:337.

Stovall TG, Murman D. Urinary retention secondary to labial adhesions. *Adolesc Pediatr Gynecol*. 1988;1:203.

Tebruegge M, Misra I, Nerminathan V. Is the topical application of oestrogen cream an effective intervention in girls suffering from labial adhesions? *Arch Dis Child*. 2007;92:268.

LEVEL III

American College of Obstetricians and Gynecologists. Vaginal "rejuvenation" and cosmetic vaginal procedures. ACOG Committee Opinion No. 378. *Obstet Gynecol*. 2007;110:737.

Bacon JL, Romano ME, Quint EH. Clinical recommendation: labial adhesions. *J Pediatr Adolesc Gynecol*. 2015;28:405.

93 LICHEN PLANUS

INTRODUCTION

Description: Lichen planus is a non-neoplastic epithelial disorder that affects glabrous skin, hair-bearing skin and scalp, nails, mucous membranes, or the oral cavity and vulva.
Prevalence: Unknown, but relatively common. Estimated to affect 0.5%–2% of the population.
Predominant Age: 30–60 years; peak age 50–60 years.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Unknown. Proposed—autoimmune disorder, possibly initiated by certain drugs such as β-blockers and angiotensin-converting enzyme (ACE) inhibitors. Considered to arise from a T-cell-mediated autoimmune response against basal keratinocytes.
Risk Factors: None known.

SIGNS AND SYMPTOMS

- Red erosion and ulceration of the vulva and inner aspects of the labia minora (may precede oral lesions by years; 33% of patients)
- Loss of the labia minora with scarring, adhesions, and narrowing common (complete obliteration of the vagina possible)
- Dyspareunia and postcoital bleeding are common
- Oral lesions—reticulated gray, lacy pattern (Wickham striae) with gingivitis (vulvar involvement in 50% of patients with oral lesions)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Amebiasis
- Behçet syndrome
- Candidiasis
- Dermatophyte infection
- Desquamative inflammatory vaginitis (DIV)
- Lichen sclerosus
- Neurodermatitis
- Pemphigus and pemphigoid (cicatricial or bullous type)
- Plasma cell vulvitis
- Psoriasis
- Squamous cell hyperplasia
- Systemic lupus erythematosus
- Vulvar intraepithelial neoplasia (VIN III)

Associated Conditions: Hair loss and a history of papular lesions on the skin (ankle, dorsal surface of the hands, and flexor surfaces of the wrists and forearms). The disorder is often associated with other autoimmune diseases.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated.
Special Tests: Skin biopsy (taken from the nearby intact skin or mucous membranes rather than the ulcer). Direct immunofluorescence testing on fresh tissue. The vaginal pH is increased, usually to approximately 5–6.
Diagnostic Procedures: History, physical examination, and biopsy.

Pathologic Findings

Chronic inflammatory cell infiltrate (lymphocytes and plasma cells) involving the superficial dermis and the basal and parabasal epithelium. Liquefaction necrosis with colloid bodies may be present. Prominent acanthosis with a prominent granular layer and hyperkeratosis. Ulceration and bullae may be present. Hyperkeratosis is absent in the vulvar tissues. Sometimes labeled as DIV when vaginal discharge predominantly contains inflammatory cells and immature parabasal and basal epithelial cells.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, local cleansing, antipruritics.
Specific Measures: Therapy is often difficult, chronic, and prone to failure or relapse. Therapies include steroids, retinoids, griseofulvin, dapsone, cyclosporine, and surgery. Vaginal dilators may be necessary to maintain vaginal caliber.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP088 (Disorders of the Vulva).

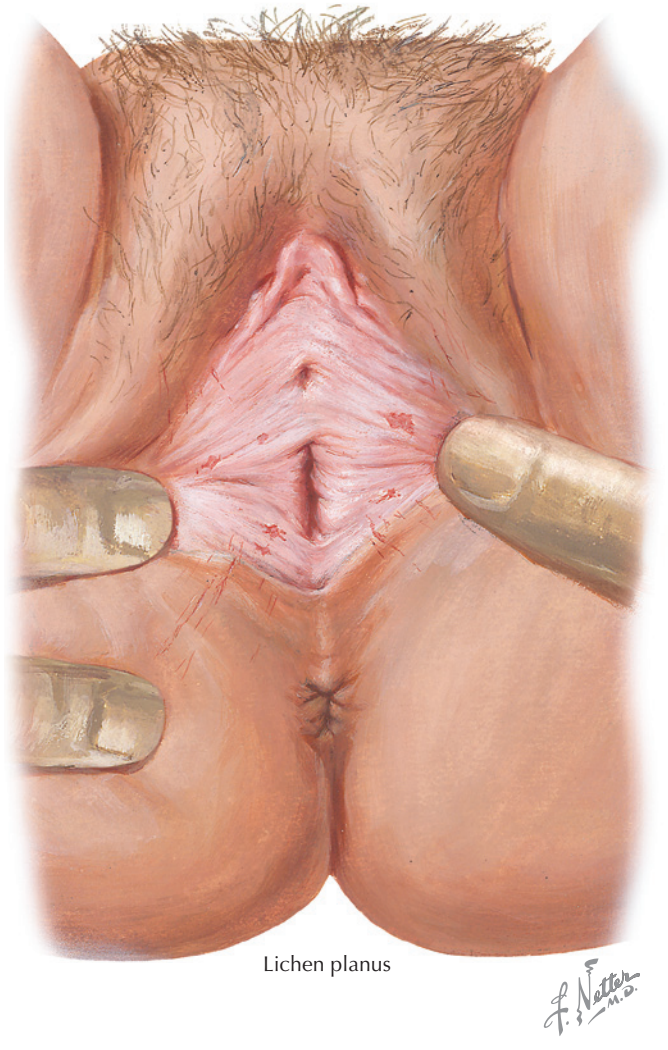


Figure 93.1 Lichen planus

Drug(s) of Choice

- Topical steroids—clobetasol 0.05% ointment, betamethasone valerate 0.1% ointment, or hydrocortisone 25 mg vaginal suppository daily
- Griseofulvin 250 mg PO twice a day.
- Dapsone 50–100 mg PO daily after negative results of screening for glucose-6-phosphate dehydrogenase.
- Isotretinoin (Accutane) 0.5–1 mg/kg/day in divided doses or etretinate (Tegison) 0.75–1 mg/kg/day in two doses
- Cyclosporine 1 mg/kg/day, increased weekly by 0.5 mg/kg/day up to 3–5 mg/kg/day.

Contraindications: Vulvar cancer. Isotretinoin and etretinate are teratogenic and must not be given during pregnancy or if there is a potential for pregnancy.

Precautions: Continued or prolonged use of topical steroids may result in thinning of the skin outside the area of lichen sclerosus with subsequent atrophy and traumatic injury (splitting and cracking). The use of dapsone, isotretinoin, etretinate, or cyclosporine requires careful monitoring of complete blood counts, liver function tests, cholesterol, triglycerides, electrolytes, urea nitrogen, creatinine, and creatinine clearance. Reliable contraception must be maintained if isotretinoin or etretinate is used.

Interactions: See individual agents.

FOLLOW-UP

Patient Monitoring: Because malignant change is possible, long-term follow-up is required.

Prevention/Avoidance: None.

Possible Complications: Vulvar lesions are often chronic and may undergo malignant change.

Expected Outcome: Chronic therapy required with relapses common.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.

ICD-10-CM Codes: L43.8 (Other lichen planus) and L66.1 (Lichen planopilaris).

REFERENCES

LEVEL II

Anderson M, Kutzner S, Kaufman RH. Treatment of vulvovaginal lichen planus with vaginal hydrocortisone suppositories. *Obstet Gynecol*. 2002;100:359.

Cooper SM, Ali I, Baldo M, et al. The association of lichen sclerosus and erosive lichen planus of the vulva with autoimmune disease: a case-control study. *Arch Dermatol*. 2008;144:1432.

Cooper SM, Wojnarowska F. Influence of treatment of erosive lichen planus of the vulva on its prognosis. *Arch Dermatol*. 2006;142:289.

Eisen D. The vulvovaginal-gingival syndrome of lichen planus. The clinical characteristics of 22 patients. *Arch Dermatol*. 1994;130:1379.

Jensen JT, Bird M, Leclair CM. Patient satisfaction after the treatment of vulvovaginal erosive lichen planus with topical clobetasol and tacrolimus: a survey study. *Am J Obstet Gynecol*. 2004;190:1759.

Kennedy CM, Galask RP. Erosive vulvar lichen planus: retrospective review of characteristics and outcomes in 113 patients seen in a vulvar specialty clinic. *J Reprod Med*. 2007;52:43.

Simpson RC, Littlewood SM, Cooper SM, et al. Real-life experience of managing vulval erosive lichen planus: a case-based review and U.K. multicentre case note audit. *Br J Dermatol*. 2012;167:85.

LEVEL III

American College of Obstetricians and Gynecologists. Diagnosis and management of vulvar skin disorders. ACOG Practice Bulletin No. 93. *Obstet Gynecol*. 2008;111:1243.

Bradford J, Fischer G. Management of vulvovaginal lichen planus: a new approach. *J Low Genit Tract Dis*. 2013;17:28.

Edwards L, Friedrich EG Jr. Desquamative vaginitis: lichen planus in disguise. *Obstet Gynecol*. 1988;71:832.

Kennedy CM, Galask RP. Erosive vulvar lichen planus: retrospective review of characteristics and outcomes in 113 patients seen in a vulvar specialty clinic. *J Reprod Med*. 2007;52:43.

Lotery HE, Galask RP. Erosive lichen planus of the vulva and vagina. *Obstet Gynecol*. 2003;101:1121.

McPherson T, Cooper S. Vulval lichen sclerosus and lichen planus. *Dermatol Ther*. 2010;23:523.

Pelisse M. Erosive vulvar lichen planus and desquamative vaginitis. *Semin Dermatol*. 1996;15:47.

Valdatta L, Tuinder S, Thione A, et al. Lichen planus cutis and squamous cell carcinoma. *Plast Reconstr Surg*. 2004;113:1085.

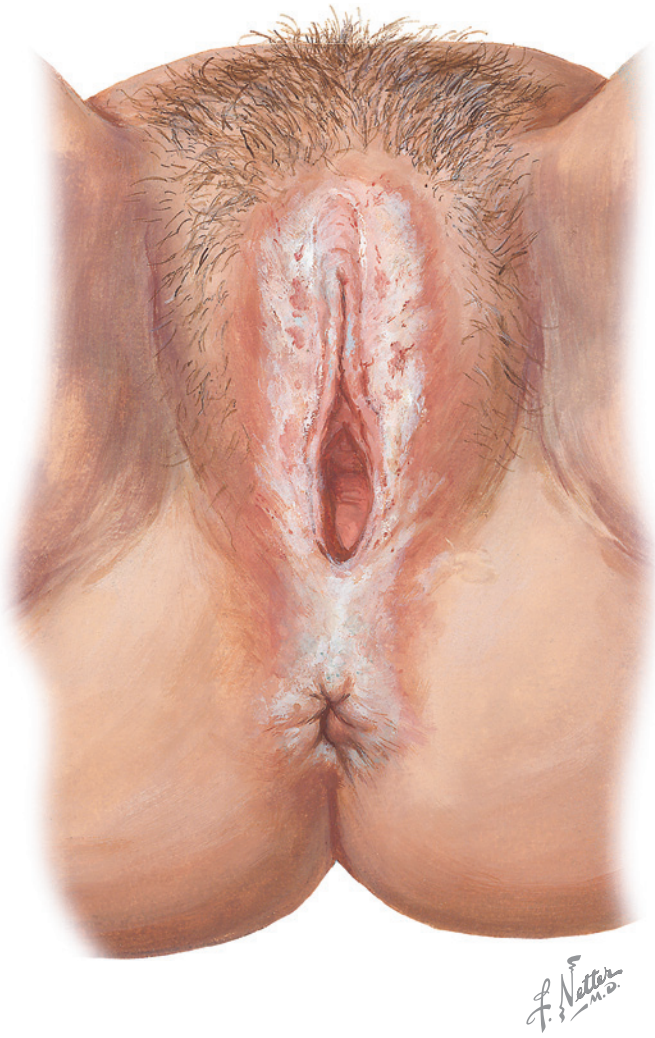


Figure 94.1 Lichen sclerosus

SIGNS AND SYMPTOMS

- Intense itching common (99%)
- Thinned, atrophic-appearing skin, with linear scratch marks or fissures (the skin often has a "cigarette-paper" or parchment-like appearance). These changes frequently extend around the anus in a figure-eight configuration.
- Perianal involvement can create the classic figure-eight or hourglass shape.
- Atrophic changes result in thinning or even loss of the labia minora and significant narrowing of the introitus
- Fissures, scarring, and synechiae cause marked pain for some patients
- Extragenital lesions reported in up to 13% of women with vulvar disease

DIAGNOSTIC APPROACH

Differential Diagnosis

- Lichen simplex chronicus (hyperplastic vulvar dystrophy)
- Scleroderma
- Vitiligo
- Paget's disease
- Vulvar candidiasis
- Squamous cell hyperplasia or carcinoma (when thickening is present)

Associated Conditions: Dyspareunia, vulvodynia, vulvar pruritus, hypothyroidism, vulvar squamous cancer (5% lifetime risk).

Workup and Evaluation

Laboratory: Thyroid function studies should be considered because up to one-third of patients have coexisting hypothyroidism.
Imaging: No imaging indicated.
Special Tests: Culture or KOH (potassium hydroxide) wet preparations of skin scrapings may help to evaluate the possibility of candidiasis. Punch biopsy of the skin will establish the diagnosis, but may not be required in many cases.
Diagnostic Procedures: History, physical examination, and biopsy of affected area.

Pathologic Findings

Loss of normal vulvar architecture with loss of rete pegs; a homogeneous dermis with edema, fibrin, and loss of vascularity; elastic fibers; and dermal collagen. Chronic inflammation is common, and spongiosis of the basilar epithelial cells is often present. Ulceration or hypertrophy may be present as a result of rubbing or scratching.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, perineal hygiene, cool sitz baths, moist soaks, or the application of soothing solutions such as Burow solution. Patients should be advised to wear loose-fitting clothing and keep the area dry and well ventilated. Emollients, such as petroleum jelly, may help in reducing local drying.
Specific Measures: Topical steroid therapy is preferred over the traditional testosterone cream. Surgical excision is occasionally required if medical therapy fails. This is associated with a high rate of recurrence and the risk of postsurgical scarring.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP088 (Disorders of the Vulva), AP028 (Vaginitis), and AP020 (When Sex Is Painful).

Drug(s) of Choice

- Burow solution (Domeboro) aluminum acetate 5% aqueous solution, three to four times daily for 30–60 minutes.
- Crotamiton 10% (Eurax) may be topically applied twice daily. High-potency prednisolone analogs (clobetasol propionate, Cormax, Temovate) 0.05% twice a day for 30 days, every night for 30 days, and then daily.
- Fluorinated corticosteroids (Valisone 0.1%, Synalar 0.01%) applied two to three times a day for 2 weeks. Lower-potency steroids (hydrocortisone) may be used after initial therapy or in children.
- Testosterone propionate in petrolatum (2%) applied two to three times daily for up to 6 months.

Contraindications: Vulvar cancer.
Precautions: Continued or prolonged use of topical steroids may result in thinning of the skin outside the area of lichen sclerosus with subsequent atrophy and traumatic injury (splitting and cracking). Prolonged testosterone propionate therapy may be associated with clitoral enlargement or pain, local burning, or erythema. Hirsutism may rarely result.

Alternative Drugs

- In select patients, intralesional steroids (Kenalog-10) may be used.

- Topical progesterone 400 mg in oil with 4 oz of Aquaphor applied twice a day may be substituted for testosterone cream in children.
- Topical tacrolimus has been studied in a limited number of patients, but it does not work as fast or as effectively as potent topical corticosteroids.
- UVA1 phototherapy may be an additional treatment option.

FOLLOW-UP

Patient Monitoring: Frequent follow-up (3–6 months) is required to watch for recurrence or worsening of symptoms.

Prevention/Avoidance: None.

Possible Complications: Scarring and narrowing of the introitus may be sufficient to preclude intercourse. Excoriation with secondary infections may occur. Areas that become hyperplastic as a result of scratching are thought to be at increased risk for premalignant or malignant changes (lifetime risk of squamous cell carcinoma is 3%–5%).

Expected Outcome: Initial response is generally good, but recurrence is common, often necessitating lifelong therapy.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy (generally not a consideration).

ICD-10-CM Codes: Based on the location and severity of disease.

REFERENCES

LEVEL I

Funaro D, Lovett A, Leroux N, et al. A double-blind, randomized prospective study evaluating topical clobetasol propionate 0.05% versus topical tacrolimus 0.1% in patients with vulvar lichen sclerosus. *J Am Acad Dermatol*. 2014;71:84.

LEVEL II

Bohm M, Frieling U, Luger TA, et al. Successful treatment of anogenital lichen sclerosus with topical tacrolimus. *Arch Dermatol*. 2003;139:922.

Bornstein J, Heifetz S, Kellner Y, et al. Clobetasol dipropionate 0.05% versus testosterone propionate 2% topical application for severe vulvar lichen sclerosus. *Am J Obstet Gynecol*. 1998;178:80.

Chi CC, Kirtschig G, Baldo M, et al. Topical interventions for genital lichen sclerosus. *Cochrane Database Syst Rev*. 2011;CD008240.

Cooper SM, Ali I, Baldo M, et al. The association of lichen sclerosus and erosive lichen planus of the vulva with autoimmune disease: a case-control study. *Arch Dermatol*. 2008;144:1432.

Kunstfeld R, Kirnbauer R, Stingl G, et al. Successful treatment of vulvar lichen sclerosus with topical tacrolimus. *Arch Dermatol*. 2003;139:850.

Lee A, Bradford J, Fischer G. Long-term management of adult vulvar lichen sclerosus: a prospective cohort study of 507 women. *JAMA Dermatol*. 2015;151:1061.

Luesley DM, Downey GP. Topical tacrolimus in the management of lichen sclerosus. *BJOG*. 2006;113:832.

Renaud-Vilmer C, Cavelier-Balloy B, Porcher R, et al. Vulvar lichen sclerosus: effect of long-term topical application of a potent steroid on the course of the disease. *Arch Dermatol*. 2004;140:709.

Terras S, Gambichler T, Moritz RK, et al. UV-A1 phototherapy vs clobetasol propionate, 0.05%, in the treatment of vulvar lichen sclerosus: a randomized clinical trial. *JAMA Dermatol*. 2014;150:621.

Zendell K, Edwards L. Lichen sclerosus with vaginal involvement: report of 2 cases and review of the literature. *JAMA Dermatol*. 2013;149:1199.

LEVEL III

American College of Obstetricians and Gynecologists. Diagnosis and management of vulvar skin disorders. ACOG Practice Bulletin No. 93. *Obstet Gynecol*. 2008;111:1243.

Goldstein AT, Burrows LJ. Surgical treatment of clitoral phimosis caused by lichen sclerosus. *Am J Obstet Gynecol*. 2007;196:126.

McPherson T, Cooper S. Vulval lichen sclerosus and lichen planus. *Dermatol Ther*. 2010;23:523.

Powell JJ, Wojnarowska F. Lichen sclerosus. *Lancet*. 1999;353:1777.

Scrimin F, Rustja S, Radillo O, et al. Vulvar lichen sclerosus: an immunologic study. *Obstet Gynecol*. 2000;95:147.

Smith YR, Haefner HK. Vulvar lichen sclerosus: pathophysiology and treatment. *Am J Clin Dermatol*. 2004;5:105.

Val I, Almeida G. An overview of lichen sclerosus. *Clin Obstet Gynecol*. 2005;48:808.

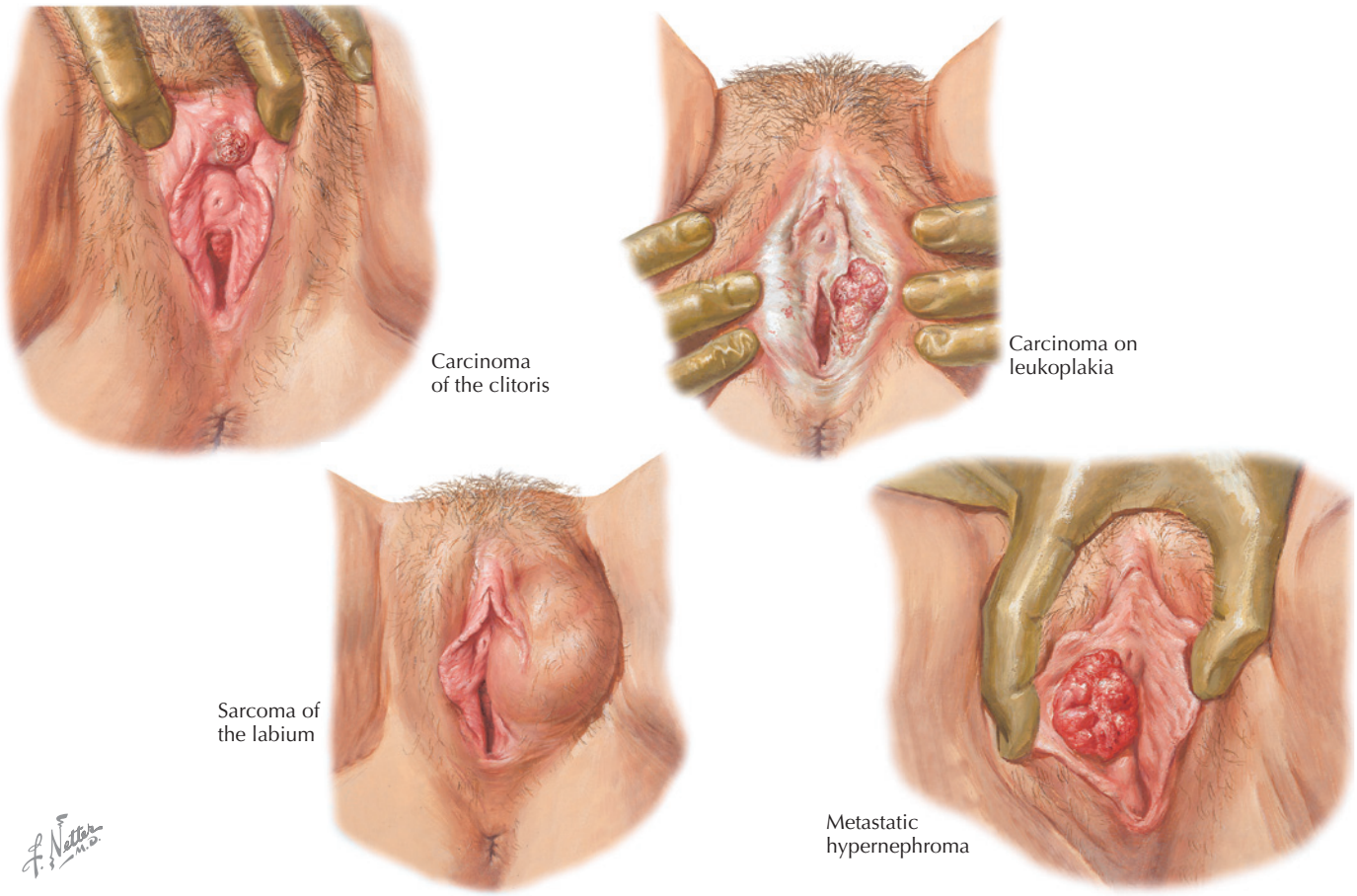


Figure 95.1 Types of vulvar cancer

- Ulcerated exophytic lesion or hyperkeratotic plaque (late in disease)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Hypertrophic vulvar dystrophy
- Lichen sclerosus

Associated Conditions: Hyperplastic vulvar dystrophy. A synchronous second malignancy, most commonly cervical neoplasia, is found in up to 22% of patients with a vulvar malignancy.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated, although positron emission tomography (PET) with computed tomography (CT) can identify regional lymph node metastases when spread is suspected. Magnetic resonance imaging (MRI) may assist in defining the extent of disease prior to surgery.
Special Tests: Biopsy of any suspicious lesion. A 5% acetic acid solution may be applied, and the vulva is examined by colposcopy.
Diagnostic Procedures: History, physical examination, and vulvar biopsy.

Pathologic Findings

Histologic types include squamous cell (90%), melanoma (5%), basaloid, warty, verrucous, giant cell, spindle cell, acantholytic squamous cell (adenoid squamous), lymphoepithelioma-like, basal cell, and Merkel cell. Sarcoma accounts for approximately 2% of vulvar cancers. Metastatic tumors from other sources are rare, but they do occur.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Early evaluation (generally by biopsy). The majority of women have had symptoms for more than 6 months before a diagnosis is made.
Specific Measures: Initial treatment consists of wide local excision (1-cm margins). Subsequent therapy, including node dissections and adjunctive therapy (radiation), is determined by the stage of disease, cell type, and surgical margins.
Diet: No specific dietary changes indicated.
Activity: No restriction, except as dictated by surgical therapy.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP088 (Disorders of the Vulva).

Drug(s) of Choice

None. Some reviews have suggested that imiquimod is an alternative to surgical management in select patients.

FOLLOW-UP

Patient Monitoring: Careful follow-up for recurrence or additional new lesions. Any patient who has had HPV-related dysplasia should avoid the vulvar use of topical steroids because this may increase the risk of recurrence.
Prevention/Avoidance: None.

Possible Complications: Distant spread and disease progression, secondary infection. Wound breakdown after surgical excision is common.

Expected Outcome: If tumor invasion is less than 1 mm, the risk of lymph node involvement is essentially 0, and high success rates may be expected. Five-year survival rates decline with advancing stage: 20% with deep node involvement. Overall, the 5-year survival rate is 70%.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, although the presence of a pregnancy may affect surgical therapeutic options.

ICD-10-CM Codes: Specific to cell type and location.

REFERENCES

LEVEL II

de Koning MN, Quint WG, Pirog EC. Prevalence of mucosal and cutaneous human papillomaviruses in different histologic subtypes of vulvar carcinoma. *Mod Pathol*. 2008;21:334.

de Witte CJ, van de Sande AJ, van Beekhuizen HJ, et al. Imiquimod in cervical, vaginal and vulvar intraepithelial neoplasia: a review. *Gynecol Oncol*. 2015;139:377.

Trietsch MD, Nooij LS, Gaarenstroom KN, et al. Genetic and epigenetic changes in vulvar squamous cell carcinoma and its precursor lesions: a review of the current literature. *Gynecol Oncol*. 2015;136:143.

LEVEL III

American College of Obstetricians and Gynecologists. Diagnosis and management of vulvar skin disorders. ACOG Practice Bulletin No. 93. *Obstet Gynecol*. 2008;111:1243.

American College of Obstetricians and Gynecologists. Management of vulvar intraepithelial neoplasia. Committee Opinion No. 509. *Obstet Gynecol*. 2011;118:1192.

American College of Obstetricians and Gynecologists. Human papillomavirus vaccination. Committee Opinion No. 641. *Obstet Gynecol*. 2015;126:e38.

Han SN, Verheecke M, Vandenbroucke T, et al. Management of gynecological cancers during pregnancy. *Curr Oncol Rep*. 2014;16:415.

Tan J, Chetty N, Kondalsamy-Chennakesavan S, et al. Validation of the FIGO 2009 staging system for carcinoma of the vulva. *Int J Gynecol Cancer*. 2012;22:498.

Tyring SK. Vulvar squamous cell carcinoma: guidelines for early diagnosis and treatment. *Am J Obstet Gynecol*. 2003;189:S17.

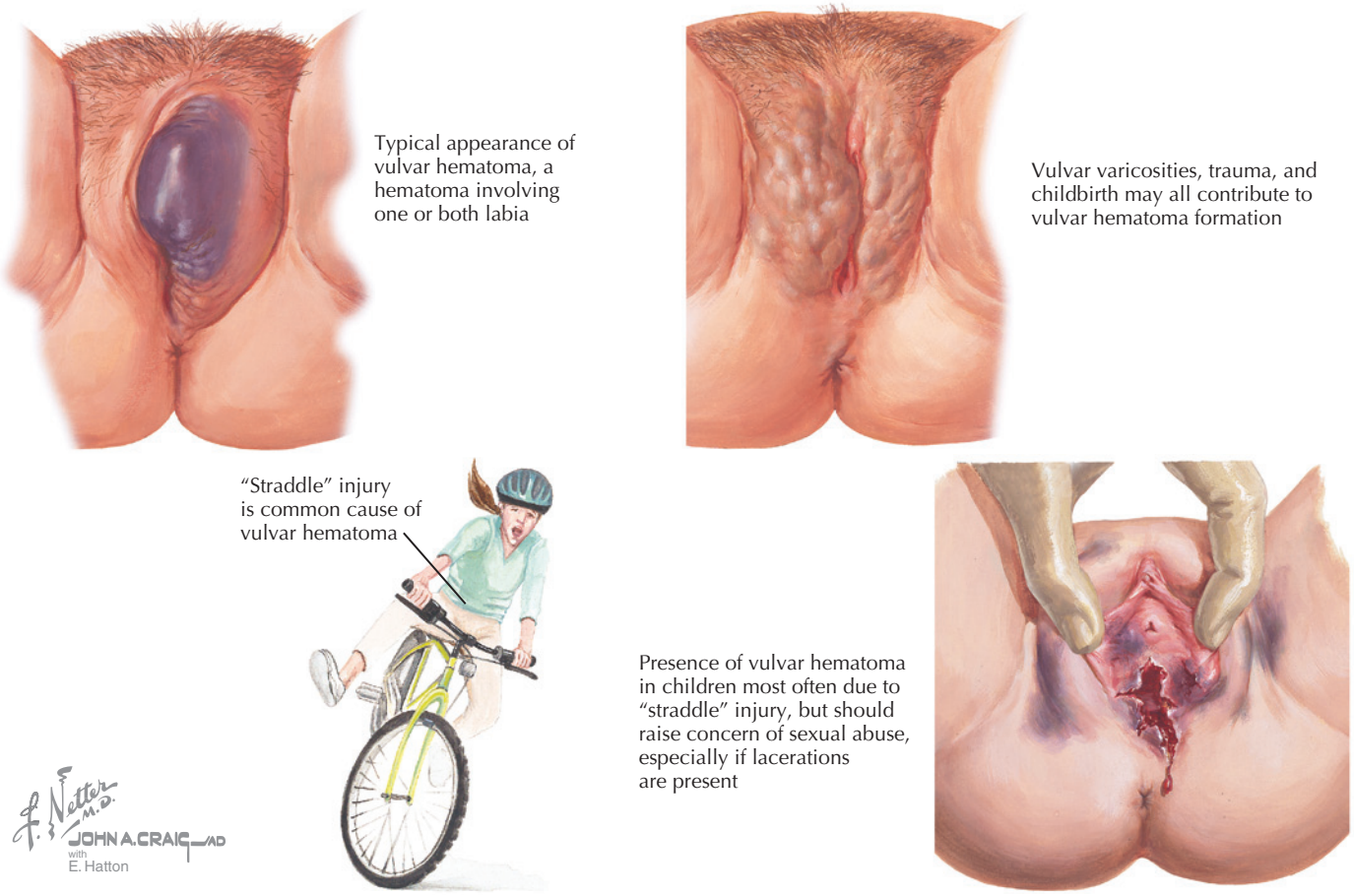


Figure 96.1 Vulvar hematoma

Drug(s) of Choice

Nonaspirin analgesics

FOLLOW-UP

Patient Monitoring: Observation for expanding hematoma, hemodynamic monitoring if blood loss severe. Ensure that voiding is not compromised.
Prevention/Avoidance: Proper footwear during sports.
Possible Complications: Chronic expanding hematoma with fibrosis and pain.
Expected Outcome: Most hematomas gradually resolve with conservative management only.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. May rarely complicate delivery if present before or during labor. More often, delivery precedes hematoma formation.
ICD-10-CM Codes: N90.89 (Other specified noninflammatory disorders of vulva and perineum) and O71.7 (Obstetric hematoma of pelvis).

REFERENCES

LEVEL II

Hoefgen HR, Merritt DF. Rope swing injuries resulting in vulvar trauma. *J Pediatr Adolesc Gynecol*. 2015;28:e13.

Iqbal CW, Jrebi NY, Zielinski MD, et al. Patterns of accidental genital trauma in young girls and indications for operative management. *J Pediatr Surg*. 2010;45:930.

Jones JG, Worthington T. Genital and anal injuries requiring surgical repair in females less than 21 years of age. *J Pediatr Adolesc Gynecol*. 2008;21:207.

Scheidler MG, Schultz BL, Schall L, et al. Mechanisms of blunt perineal injury in female pediatric patients. *J Pediatr Surg*. 2000;35:1317.

Spitzer RF, Kives S, Caccia N, et al. Retrospective review of unintentional female genital trauma at a pediatric referral center. *Pediatr Emerg Care*. 2008;24:831.

LEVEL III

Muram D, Levitt CJ, Frasier LD, et al. Genital injuries. *J Pediatr Adolesc Gynecol*. 2003;16:149.

Propst AM, Thorp JM Jr. Traumatic vulvar hematomas: conservative versus surgical management. *South Med J*. 1998;91:144.

Ridgeway LE. Puerperal emergency: vaginal and vulvar hematomas. *Obstet Gynecol Clin North Am*. 1995;22:275.

VULVAR LESIONS

97

THE CHALLENGE

The skin of the vulva is subject to all the changes that affect skin elsewhere in the body. In addition, the tissues of the vulva represent a rich ecosystem, with interactions between tissues, fluids, hormones, and microbes.

Scope of the Problem: In gynecologic practices, it is normal to see two or more patients a day with these concerns.

Objectives of Management: To establish a timely diagnosis and management plan for those patients with vulvar lesions.

TACTICS

Relevant Pathophysiology: The skin of the vulva is like that of other areas of the body with stratified squamous epithelium; hair follicles; and sebaceous, sweat, and apocrine glands. Just as in other areas of the body, the vulva is susceptible to inflammatory and dermatologic diseases. Intertrigo, acne inversa, psoriasis, seborrheic dermatitis, Fox-Fordyce disease, fifth disease, changes caused by Behçet or Crohn diseases, viral infections, and parasites may all affect the skin of the vulva. The skin of the vulva is also vulnerable to irritation from vaginal secretions, recurrent urinary loss, or contact with external irritants (such as soap residue, perfumes, fabric softeners, or infestation by pinworms). Changes may occur because of the effects of diabetes or hormonal alterations and dermatoses such as hypertrophic dystrophy, lichen sclerosus, and psoriasis.

Strategies: The character of the lesion or vulvar findings may be used to establish a working diagnosis for a patient with a vulvar lesion. Processes that result in lesions that occupy a superficial

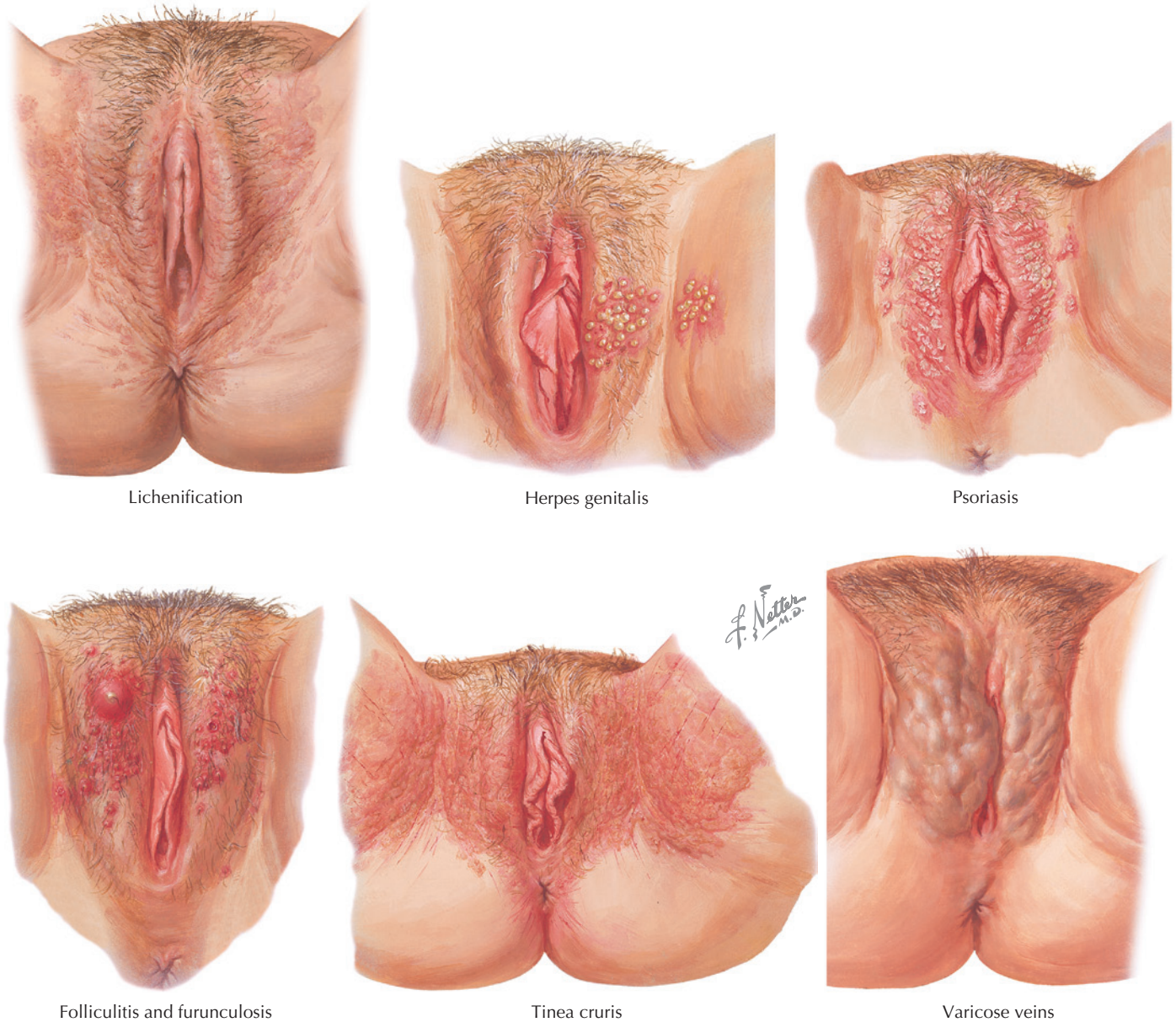


Figure 97.1 Vulvar lesions: Lichenification, herpes genitalis, psoriasis, folliculitis, furunculosis, tinea cruris, variocse veins

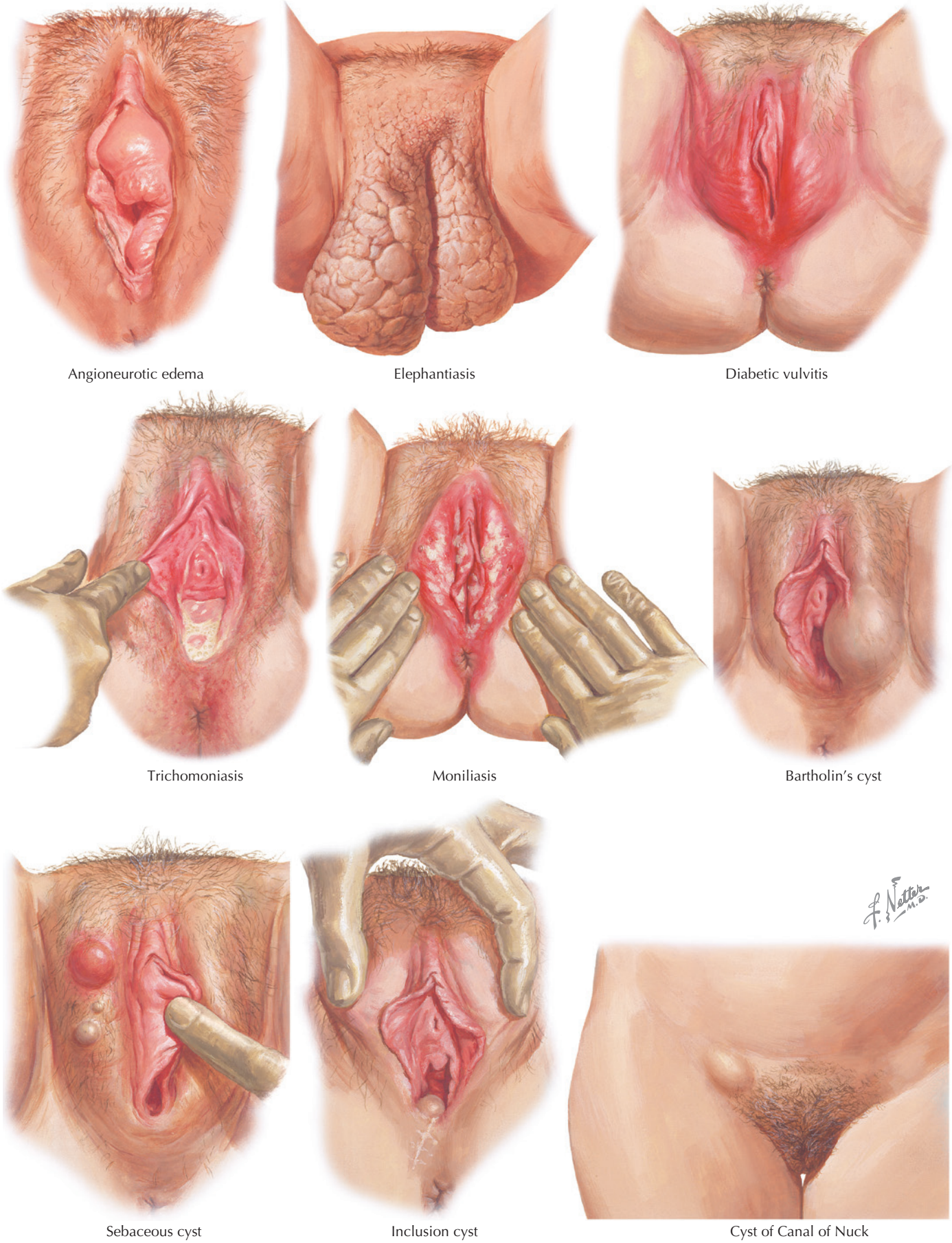
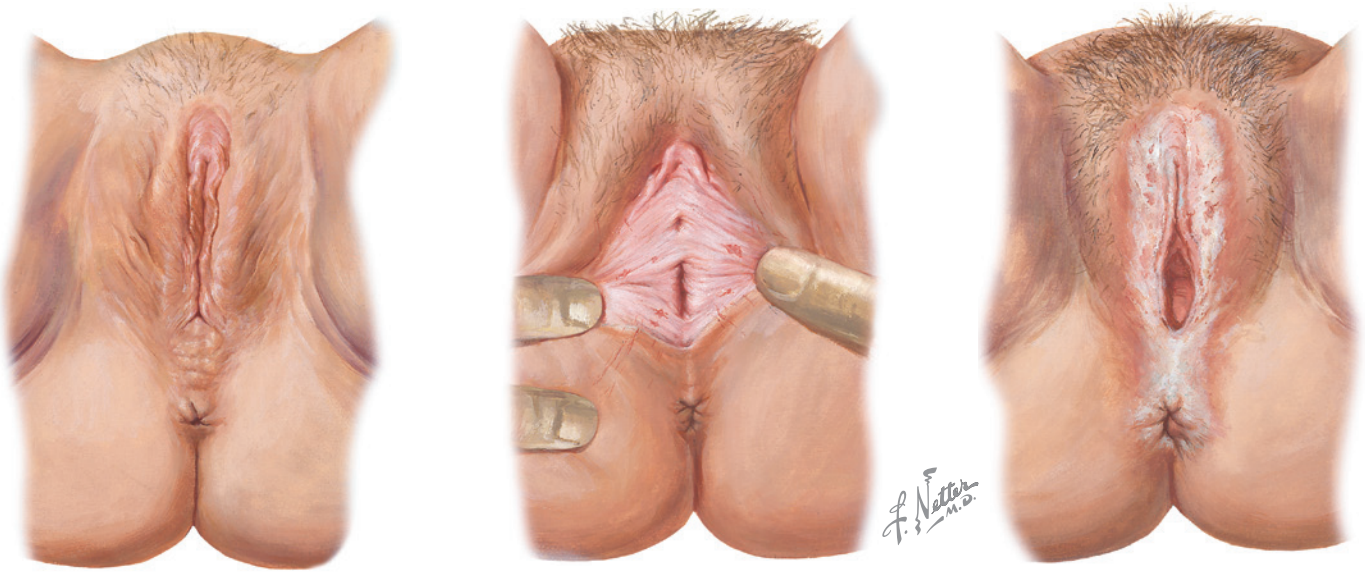


Figure 97.2 Vulvar lesions: angioneurotic edema, elephantiasis, diabetic vulvitis, trichomoniasiss, monilasis, Bartholin cyst, sebaceous cyst, inclusion cyst, Canal of Nuck cyst



Senile atrophy Kraurosis vulvae Leukoplakia

Figure 97.3 Vulvar lesions: Semile atrophy, krauosis vulvae, leukoplakia

location are different from those that cause processes deep within the tissues of the vulva. It is important to consider that many conditions that cause vulvar lesions may present in several forms. Consequently, in any decision tree based on lesion morphology, some diagnoses may be represented at the end of more than one branch (eg, seborrheic keratosis or nevus).

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP088 (Disorders of the Vulva).

IMPLEMENTATION

Special Considerations: In addition to the diagnoses discussed in the preceding, several other significant possibilities should always be considered when diffuse symptoms and findings are present: atopic dermatitis, contact dermatitis, fixed drug reaction, and factitial vulvitis. When cystic structures are encountered, the possibility of congenital remnants such as mesothelial cysts (cysts of the Canal of Nuck), Wolffian duct remnants, and periurethral cysts must be considered. Lipomas, neurofibromas, rhabdomyomas, schwannomas, and leiomyomas may present as fleshy tumors of the vulva. Of special importance are lesions that involve significant necrosis: necrotizing fasciitis and pyoderma gangrenosum. Both of these processes represent a significant threat to the life and health of the patient and require prompt and aggressive treatment.

REFERENCES

LEVEL III

American College of Obstetricians and Gynecologists. Diagnosis and management of vulvar skin disorders. ACOG Practice Bulletin No. 93. *Obstet Gynecol*. 2008;111:1243.

Heller DS. Benign tumors and tumor-like lesions of the vulva. *Clin Obstet Gynecol*. 2015;58:526.

McKay M. Vulvar dermatoses. *Clin Obstet Gynecol*. 1991;34:614.

Nanda VS. Common dermatoses. *Am J Obstet Gynecol*. 1995;173:488.

Peckham EM, Maki DG, Patterson JJ, et al. Focal vulvitis: a characteristic syndrome and cause of dyspareunia. Features, natural history, and management. *Am J Obstet Gynecol*. 1986;154:855.

98 VULVAR VESTIBULITIS (PROVOKED VULVODYNIA)

INTRODUCTION

Description: Vulvar vestibulitis (provoked vulvodynia) is an uncommon syndrome of intense sensitivity of the skin of the posterior vaginal introitus and vulvar vestibule, with progressive worsening, leading to loss of function. Provoked pain in other areas of the vulva is possible, but much less common.

Prevalence: Some estimates place it at 15% of all women, but significant, disabling symptoms are much less common.

Predominant Age: 19–81 years (median age, 36 years).

Genetics: No genetic pattern, although some studies suggest these women are more likely to carry immune-related gene polymorphisms.

ETIOLOGY AND PATHOGENESIS

Causes: Unknown. High degree of association with human papillomavirus (HPV) but no causal link established. Despite the implication of the term, true inflammation is not a characteristic of this process.

Risk Factors: None known. It has been postulated that the use of oral contraceptives increases the risk or severity of vulvar vestibulitis and that users who experience symptoms should switch to other methods of contraception. Strong evidence for either causation or significant improvement is lacking.

SIGNS AND SYMPTOMS

- Intense pain and tenderness at the posterior introitus and vestibule, most often present for 2–5 years (some authors suggest that symptoms should be present for more than 6 months before the diagnosis is made)
- Unable to use tampons (33%) or have intercourse (entry dyspareunia, 100%)
- Focal inflammation, punctation, and ulceration of the perineal and vaginal epithelium
- Punctate areas (1–10) of inflammation 3–10 mm in size may be seen between the Bartholin's glands (75%), hymenal ring, and middle perineum

DIAGNOSTIC APPROACH

Differential Diagnosis

- Vaginismus
- Chronic vulvitis
- Atrophic vaginitis
- Hypertrophic vulvar dystrophy
- Recurrent vaginal infections
- Herpes vulvitis
- Vulvar dermatoses
- Contact (allergic) vulvitis

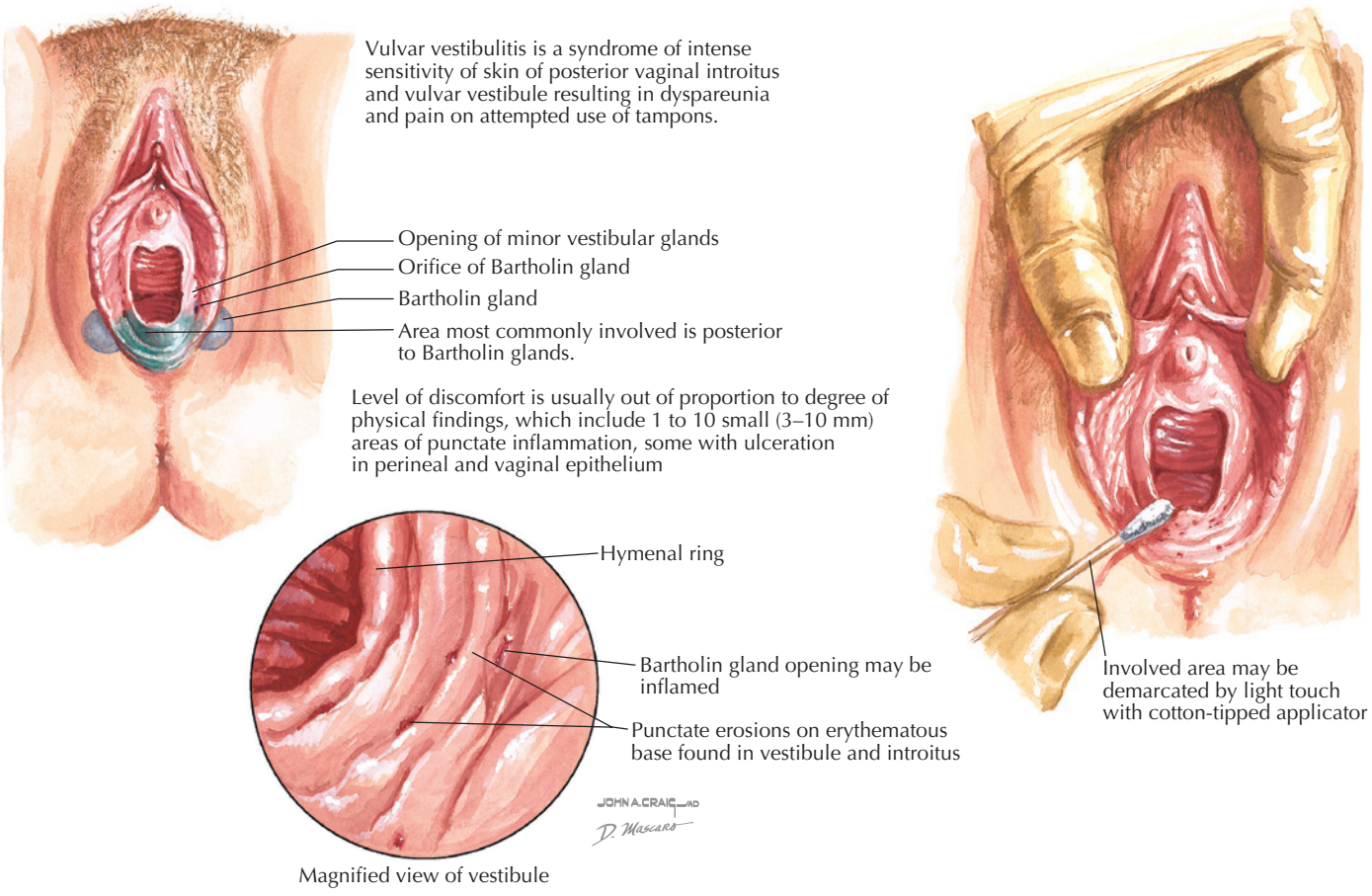


Figure 98.1 Vulvar vestibulitis

Associated Conditions: Sexual dysfunction, dyspareunia, and vulvodynia.

Workup and Evaluation

Laboratory: No evaluation indicated except to rule out other causes.
Imaging: No imaging indicated.
Special Tests: Colposcopy of the vulva (using 5% acetic acid) may reveal the characteristic punctate and acetowhite areas.
Diagnostic Procedures: History, physical examination, mapping of sensitive areas, and colposcopy.

Pathologic Findings

Small inflammatory punctate lesions vary in size from 3 to 10 mm, often with superficial ulceration. The Bartholin gland openings may also be inflamed. The area involved may be demarcated by light touching with a cotton-tipped applicator, although the level of discomfort is often out of proportion to the physical findings. Microscopic inflammation of minor vestibular glands may be seen but is not always present.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, perineal hygiene, cool sitz baths, moist soaks, or the application of soothing solutions such as Burow solution. Patients should be advised to wear loose-fitting clothing and keep the area dry and well ventilated.
Specific Measures: Topical anesthetics and antidepressants (amitriptyline hydrochloride) may reduce pain and itch. Interferon injections may provide relief in up to 60% of patients. Refractory disease may require surgical resection or laser ablation.
Diet: No specific dietary changes indicated. Reducing urinary oxalate through dietary means has been suggested but remains unproved.
Activity: No restriction (pelvic rest often recommended when symptoms are maximal).
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP127 (Vulvodynia), AP088 (Disorders of the Vulva), and AP020 (When Sex Is Painful).

Drug(s) of Choice

- Lidocaine (Xylocaine) 2% jelly (or 5% cream) topically as needed.
- Antidepressants—amitriptyline hydrochloride (Elavil) 25 mg PO every night or 10 mg PO three times a day.
- Interferon injections three times weekly for 4 weeks, introducing 1 million units at each of 12 areas (clock face) by the completion of the course.
- Gabapentin 100 mg at bedtime, increasing by 100 mg every 2–7 days to 3600 mg in divided doses three times per day, depending on tolerance.

Contraindications: Interferon injections cannot be administered during pregnancy.
Precautions: Patients should be warned that interferon injections are associated with flu-like symptoms and that a clinical response may not be seen for up to 3 months. Patients should abstain from intercourse during the series of injections.

FOLLOW-UP

Patient Monitoring: Frequent follow-up and monitoring are required. Frustration for both the patient and provider is common.
Prevention/Avoidance: None.
Possible Complications: Secondary infection, sexual dysfunction.
Expected Outcome: Spontaneous remission in one-third of patients over the course of 6 months. Chronic, continuing pain most common. Surgical therapy is associated with 50%–60% success.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: N76.1 or N76.3 (Subacute and chronic vulvitis).

REFERENCES

LEVEL I

Farajun Y, Zarfati D, Abramov L, et al. Enoxaparin treatment for vulvodynia: a randomized controlled trial. *Obstet Gynecol*. 2012;120:565.
Foster DC, Kotok MB, Huang LS, et al. Oral desipramine and topical lidocaine for vulvodynia: a randomized controlled trial. *Obstet Gynecol*. 2010;116:583.

LEVEL II

Harlow BL, Abenhaim HA, Vitonis AF, et al. Influence of dietary oxalates on the risk of adult-onset vulvodynia. *J Reprod Med*. 2008;53:171.
Harlow BL, Vitonis AF, Stewart EG. Influence of oral contraceptive use on the risk of adult-onset vulvodynia. *J Reprod Med*. 2008;53:102.
Reed BD, Legocki LJ, Plegue MA, et al. Factors associated with vulvodynia incidence. *Obstet Gynecol*. 2014;123:225.
Tommola P, Unkila-Kallio L, Paavonen J. Surgical treatment of vulvar vestibulitis: a review. *Acta Obstet Gynecol Scand*. 2010;89:1385.
Zolnoun DA, Hartmann KE, Steege JF. Overnight 5% lidocaine ointment for treatment of vulvar vestibulitis. *Obstet Gynecol*. 2003;102:84.

LEVEL III

American College of Obstetricians and Gynecologists. Vulvodynia. ACOG Committee Opinion 345. *Obstet Gynecol*. 2006;108:1049.
Bohm-Starke N. Medical and physical predictors of localized provoked vulvodynia. *Acta Obstet Gynecol Scand*. 2010;89:1504.
Danielsson I, Eisemann M, Sjoberg I, et al. Vulvar vestibulitis: a multifactorial condition. *BJOG*. 2001;108:456.
Edwards L. New concepts in vulvodynia. *Am J Obstet Gynecol*. 2003;189:S24.
Nunns D, Mandal D, Byrne M, et al. Guidelines for the management of vulvodynia. *Br J Dermatol*. 2010;162:1180.
Reed BD, Haefner HK, Edwards L. A survey on diagnosis and treatment of vulvodynia among vulvodynia researchers and members of the International Society for the Study of Vulvovaginal Disease. *J Reprod Med*. 2008;53:921.

This page intentionally left blank

SECTION VI

Vaginal Disease

This page intentionally left blank

CYSTOCELE/URETHROCELE

99

INTRODUCTION

Description: Loss of support for the anterior vagina, through the rupture or attenuation of the pubovesicocervical fascia, is manifested by the descent or prolapse of the urethra (urethrocele) or bladder (cystocele).
Prevalence: 10%–15% of women; 30%–40% after menopause.
Predominant Age: 40 years and older, increasing with age.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Loss of normal tissue integrity or tissue disruption as a result of trauma (childbirth, obstetric injury, surgery).
Risk Factors: Multiparity, obesity, chronic cough, heavy lifting, intrinsic tissue weakness or atrophic changes caused by estrogen loss. Many authors include smoking as a risk factor.

SIGNS AND SYMPTOMS

- Asymptomatic
- Pelvic pressure or "heaviness"
- Stress urinary incontinence, frequency, hesitancy, incomplete voiding, or recurrent infections
- Bulging of tissue at the vaginal opening
- Descent of the anterior vaginal wall during straining
- Positive results on "Q-tip test"

DIAGNOSTIC APPROACH

Differential Diagnosis

- Urethral diverticulum
- Skene's gland cyst, tumor, or abscess
- Anterior enterocele
- Gartner's duct cyst
- Urgency incontinence

Associated Conditions: Stress urinary incontinence, pelvic relaxation, uterine prolapse, and other hernias.

Workup and Evaluation

Laboratory: No evaluation indicated; perform urinalysis if urinary tract infection is suspected.
Imaging: No imaging indicated.
Special Tests: A "Q-tip test" is sometimes recommended, although it has a poor predictive value—a cotton-tipped applicator dipped in 2% lidocaine (Xylocaine) is placed in the urethra and anterior rotation with straining is measured. Greater than 30 degrees is abnormal. Either the Baden–Walker Halfway Scoring or the POPQ evaluation systems may be used to quantify the degree of prolapse present. An evaluation of urinary function is advisable, especially if surgical therapy is being considered. In the past, the functional significance of a cystourethrocele was gauged by elevating the bladder neck (using fingers or an instrument) and asking the patient to strain (referred to as a Bonney or Marshall-Marchetti test). This test has fallen out of favor as it is nonspecific and unreliable.
Diagnostic Procedures: Pelvic examination—best demonstrated by having the patient strain or cough and observing the vaginal opening through the separated labia. When an urethrocele or cystocele is present, a downward movement and forward rotation of the vaginal wall toward the introitus are demonstrated. A Sims speculum or the lower half of a Graves, Peterson, or other vaginal speculum may be used to retract the posterior vaginal wall, facilitating the identification of the support defect. The bladder should be partially filled (100–250 mL) during this examination.

Pathologic Findings

No characteristic histologic change. Chronic irritation or keratinization secondary to mechanical trauma may be found with complete prolapse.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Weight reduction, treatment of chronic cough (if present), topical or systemic estrogen replacement or therapy as indicated.
Specific Measures: Pessary therapy (the intermittent use of a large or super tampon may suffice for some patients), pelvic muscle exercises, surgical repair; limited role for medical therapy.
Diet: No specific dietary changes indicated.
Activity: Avoiding heavy lifting and straining may slow the rate of progression or risk of recurrence.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP0012 (Pelvic Support Problems), AP081 (Urinary Incontinence), AP166 (Surgery for Stress Urinary Incontinence), and AP183 (Surgery for Pelvic Organ Prolapse).

Drug(s) of Choice

None. Estrogen, either topically or systemically, is often prescribed to improve tissue tone, reduce irritation, and prepare tissues for surgical or pessary therapy.
Contraindications: Undiagnosed vaginal bleeding, breast cancer.
Precautions: α-Adrenergic blocking agents used to treat hypertension may reduce urethral tone sufficiently to result in stress urinary incontinence in patients with reduced pelvic support. Patients treated with angiotensin-converting enzyme (ACE) inhibitors may develop a cough as a side effect of medication, worsening incontinence symptoms, and accelerated appearance or worsening of a cystourethrocele.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: Compromised ureteral drainage may be found in patients with significant downward displacement of the trigone. Recurrent urinary tract infections may occur if the support defect leads to significant residual urine. Vaginal ulceration, bleeding, infection, or pain frequently accompanies complete prolapse. When surgical mesh is used as a part of the repair, the possibility of both acute and delayed complications must be recognized.
Expected Outcome: Generally favorable reduction in symptoms may be obtained with a carefully chosen and fitted pessary. Surgical therapy is associated with 95% success in long-term correction of the anatomic defect and associated symptoms.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, although pregnancy (and vaginal delivery) may cause or contribute to a worsening of pelvic support problems.
ICD-10-CM Codes: N81.9 (Female genital prolapse, unspecified), N81.10 (Cystocele, unspecified) or N81.11 (midline), and N81.0 (Urethrocele).

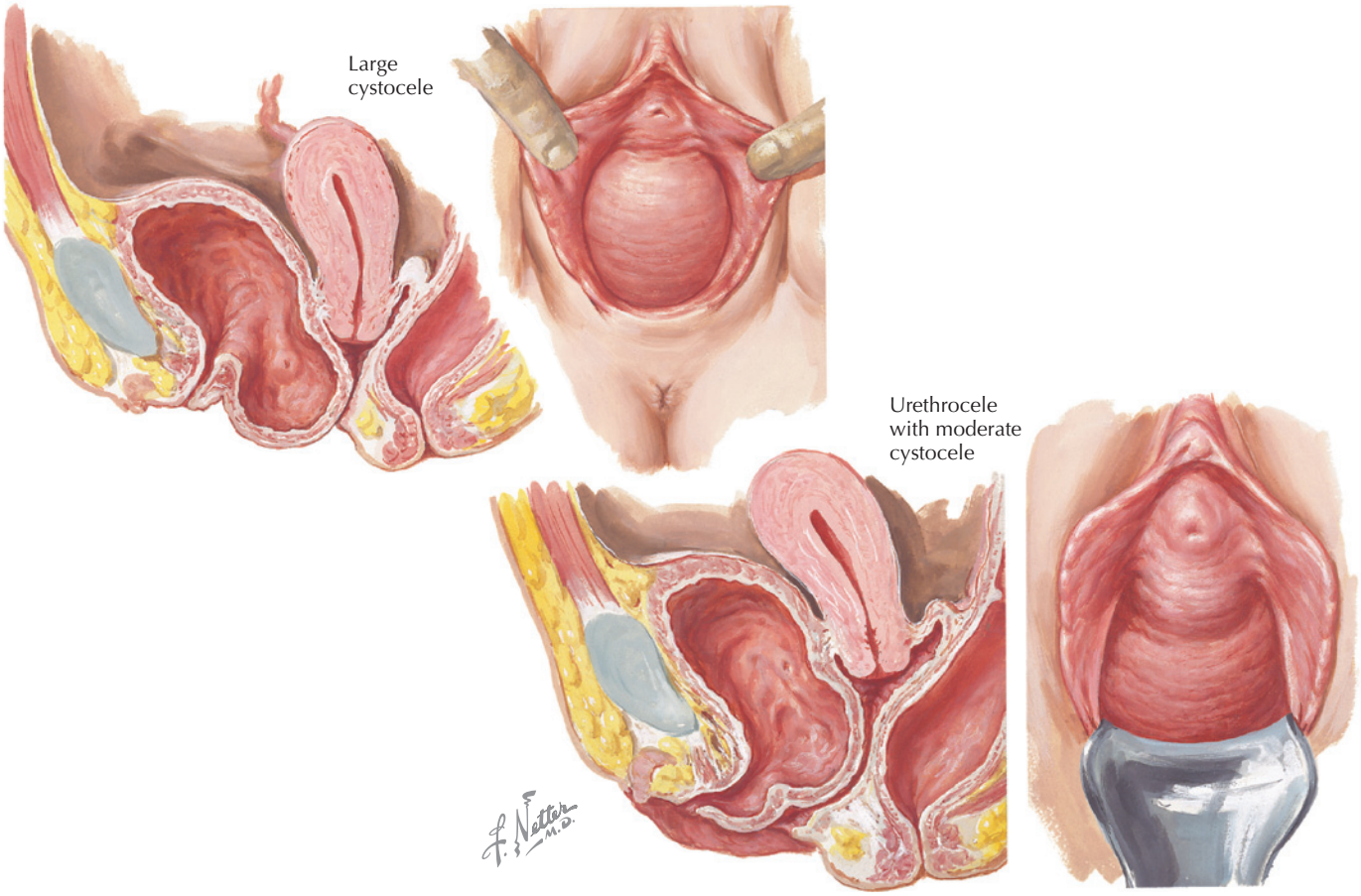


Figure 99.1 Cystocele and urethrocele

REFERENCES

LEVEL II

Barber MD, Maher C. Epidemiology and outcome assessment of pelvic organ prolapse. *Int Urogynecol J*. 2013;24:1783.

Colombo M, Vitobello D, Proietti F, et al. Randomised comparison of Burch colposuspension versus anterior colporrhaphy in women with stress urinary incontinence and anterior vaginal wall prolapse. *BJOG*. 2000;107:544.

Federkiw DM, Sand PK, Retzky SS, et al. The cotton swab test. Receiver-operating characteristic curves. *J Reprod Med*. 1995;40:42.

Maher C, Feiner B, Baessler K, et al. Surgical management of pelvic organ prolapse in women. *Cochrane Database Syst Rev*. 2013;(4):CD004014.

Vergeldt TF, Weemhoff M, IntHout J, et al. Risk factors for pelvic organ prolapse and its recurrence: a systematic review. *Int Urogynecol J*. 2015;26:1559.

LEVEL III

American College of Obstetricians and Gynecologists. Urinary incontinence in women. Practice Bulletin No. 155. *Obstet Gynecol*. 2015;126:e66.

Marinkovic SP, Stanton SL. Incontinence and voiding difficulties associated with prolapse. *J Urol*. 2004;171:1021.

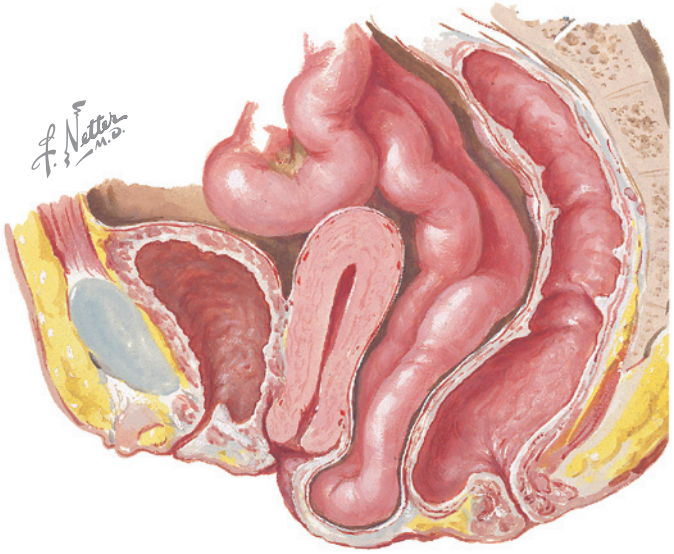


Figure 100.1 Enterocele with retrocele and prolapse of uterus

ETIOLOGY AND PATHOGENESIS

Causes: Loss or rupture of the normal support mechanisms in the pouch of Douglas. There is true herniation of the peritoneal cavity between the uterosacral ligaments and into the rectovaginal septum. Unlike a cystocele, urethrocele, or rectocele, the herniated tissue contains a true sac lined by parietal peritoneum.

Risk Factors: Multiparity, obesity, chronic cough, heavy lifting, intrinsic tissue weakness, or atrophic changes resulting from estrogen loss. Some authors include smoking as a risk factor.

SIGNS AND SYMPTOMS

- Asymptomatic
- Pelvic pressure or "heaviness"
- Bulging of tissue at the vaginal opening
- Descent of the apical vaginal wall during straining

DIAGNOSTIC APPROACH

Differential Diagnosis

- Urethral diverticulum
- Cystocele
- Rectocele
- Vaginal prolapse (generally includes an enterocele)
- Gartner's duct cyst

Associated Conditions: Pelvic relaxation, vaginal prolapse, other hernias, and bowel obstruction (rare).

Workup and Evaluation

Laboratory: No evaluation indicated.

Imaging: No imaging indicated.

Special Tests: When the enterocele prolapses to beyond the introitus, transillumination may reveal loops of small bowel or omentum within the sac.

Diagnostic Procedures: Pelvic examination—best demonstrated by having the patient strain or cough and observing the vaginal opening through the separated labia. Rectovaginal examination differentiates this condition from a rectocele.

Pathologic Findings

No characteristic histologic change. Chronic irritation or keratinization of the vaginal epithelium secondary to mechanical trauma may be found when the enterocele descends to the level of the vulva or beyond.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Weight reduction, treatment of chronic cough (if present), topical or systemic estrogen replacement or therapy as indicated.

Specific Measures: Pessary therapy (generally when the uterus is absent), surgical repair (abdominal or vaginal approach—McCall or Halban repair).

Diet: No specific dietary changes indicated.

Activity: No restriction.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP0012 (Pelvic Support Problems) and AP183 (Surgery for Pelvic Organ Prolapse).

Drug(s) of Choice

None. Estrogen, either topically or systemically, is often prescribed to improve tissue tone, reduce irritation, and prepare tissues for surgical or pessary therapy.

Contraindications: Undiagnosed vaginal bleeding, breast cancer.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.

Prevention/Avoidance: Maintenance of normal weight, use of surgical techniques at the time of hysterectomy that minimize the risk of enterocele formation (most commonly, this is plication of the uterosacral and cardinal ligaments).

Possible Complications: Bowel obstruction (rare).

Expected Outcome: Generally, favorable reduction of symptoms may be obtained with a carefully chosen and fitted pessary. Surgical therapy is associated with 95% success in long-term correction of the anatomic defect and the associated symptoms.

MISCELLANEOUS

Pregnancy Considerations: Generally not a consideration.

ICD-10-CM Codes: N81.5 (Vaginal enterocele).

REFERENCES

LEVEL II

Kelvin FM, Maglinte DD. Dynamic evaluation of female pelvic organ prolapse by extended proctography. *Radiol Clin North Am*. 2003;41:395.

Maher C, Feiner B, Baessler K, et al. Surgical management of pelvic organ prolapse in women. *Cochrane Database Syst Rev*. 2010;(4):CD004014.

Nasr AO, Tormey S, Aziz MA, et al. Vaginal herniation: case report and review of the literature. *Am J Obstet Gynecol*. 2005;193:95.

LEVEL III

American College of Obstetricians and Gynecologists. Urinary incontinence in women. Practice Bulletin No. 155. *Obstet Gynecol*. 2015;126:e66.

Chou Q, Weber AM, Piedmonte MR. Clinical presentation of enterocele. *Obstet Gynecol*. 2000;96:599.

Kobashi KC, Leach GE. Pelvic prolapse. *J Urol*. 2000;164:1879.

101 FISTULAE: GASTROINTESTINAL AND URINARY TRACT

INTRODUCTION

Description: A fistula is an abnormal communication between two cavities or organs. In gynecology, this usually refers to a communication between the gastrointestinal or urinary tract and the genital tract. Connections directly to the skin are not discussed here.

Prevalence: Gastrointestinal fistulae are uncommon, Urinary tract fistulae are estimated to occur in 1 of 200 abdominal hysterectomies.

Predominant Age: Reproductive age and older.

Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Urinary tract fistulae may result from surgical or obstetric trauma, irradiation, or malignancy, although the most common cause by far is unrecognized surgical trauma. Approximately 75% of urinary tract fistulae occur after abdominal hysterectomy. Signs of a urinary fistula (watery discharge) usually occur from 5 to 30 days after surgery (average, 8–12 days), although they may be present in the immediate postoperative period. Fistulae between the gastrointestinal tract and vagina may be precipitated by the same injuries that cause genitourinary fistulae; the most common are obstetric injuries and complications of episiotomies (lower one-third of the vagina). Fistulae may also follow hysterectomy or enterocele repair (upper one-third of vagina). Inflammatory bowel disease or pelvic radiation therapy may hasten or precipitate fistula formation.

Risk Factors: Gastrointestinal fistulae—obstetric tears, puncture wounds, inflammatory bowel disease, intra-abdominal surgery, carcinoma, radiation therapy, perirectal abscess. Although Crohn disease, lymphogranuloma venereum, or tuberculosis are recognized risk factors, these are uncommon. Urinary tract fistulae—surgery or radiation treatment. Urinary tract fistulae are most common after uncomplicated hysterectomy, although pelvic adhesive disease, endometriosis, or pelvic tumors increase the individual risk.

SIGNS AND SYMPTOMS

Gastrointestinal Fistulae

- Foul vaginal discharge
- Marked vaginal and vulvar irritation
- Fecal incontinence and soiling and the passage of fecal matter or gas from the vagina, pathognomonic
- Dyspareunia common
- Dark-red rectal mucosa or granulation tissue apparent in the vaginal canal at the site of the fistula

Urinary Tract Fistulae

- Continuous incontinence (occasionally made worse by position change or an increase in intra-abdominal pressure as with a cough or laugh)
- Vaginal and perineal wetness and irritation
- Granulation tissue at site of fistula

DIAGNOSTIC APPROACH

Differential Diagnosis

Gastrointestinal Fistulae

- Inflammatory bowel disease (Crohn disease)
- Pilonidal sinus
- Perianal or other abscess
- Rectal carcinoma

Urinary Tract Fistulae

- Overflow incontinence
- Urge incontinence

Associated Conditions: Inflammatory bowel disease, bacterial vaginitis, dyspareunia, vaginitis, vulvitis, and urinary tract infection.

Workup and Evaluation

Laboratory: No evaluation indicated. Evaluation of renal function (serum creatinine) is prudent but not diagnostic.

Imaging: If inflammatory bowel disease is suspected, lower gastrointestinal series. Intravenous or retrograde pyelography may be useful.

Special Tests: Gastrointestinal fistulae—methylene blue may be instilled in the rectum with a tampon in the vagina; staining indicates a communication. Sigmoidoscopy should be considered. Urinary tract fistulae—a tampon placed in the vagina with dye instilled into the bladder or dye given, usually intravenously, to be excreted by the kidney may be used to help find a fistula. Cystoscopy may help identify vesicovaginal fistulae.

Diagnostic Procedures: History, physical examination, probe of fistulous tract. Anoscopy, proctoscopy, sigmoidoscopy, or intravenous or retrograde pyelography may be helpful. Cystoscopy may be required to evaluate the location of a urinary tract fistula in relation to the ureteral opening and bladder trigone and to exclude the possibility of multiple fistulae.

Pathologic Findings

Inflammation and granulation changes from chronic infection. Tract may be single or multiple. Chronic bacterial vaginitis is generally present. Fistulae may be from the vagina to the bladder (vesicovaginal), to the urethra (urethrovaginal), or to the ureter (ureterovaginal). Communication between the bladder and uterus (vesicouterine) may also rarely occur.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Gastrointestinal fistulae—evaluation, stool softening, treatment of vaginitis. Urinary tract fistulae—urinary diversion (see the following text), protection of the vulva from continuous moisture (zinc oxide cream or diaper rash preparations).

Specific Measures: Gastrointestinal fistulae—for those that do not heal spontaneously (75% of fistulae), the only effective treatment is surgical. When the fistula is small, this is often carried out with the patient under general or spinal anesthesia in an ambulatory surgery unit. Fistulectomy or fistulotomy should not be performed in the presence of tissue edema or inflammation, diarrhea, or active inflammatory bowel disease. Urinary tract fistulae—vesicovaginal fistulae that occur in the immediate postoperative period should be treated by large-caliber transurethral catheter drainage. Spontaneous healing is evident within 2–4 weeks (20% of patients). Similarly, in patients with an ureterovaginal fistula, prompt placement of a ureteral stent, left in place for 2 weeks, allows spontaneous healing for approximately 30% of patients. When these conservative therapies fail, full surgical correction is required.

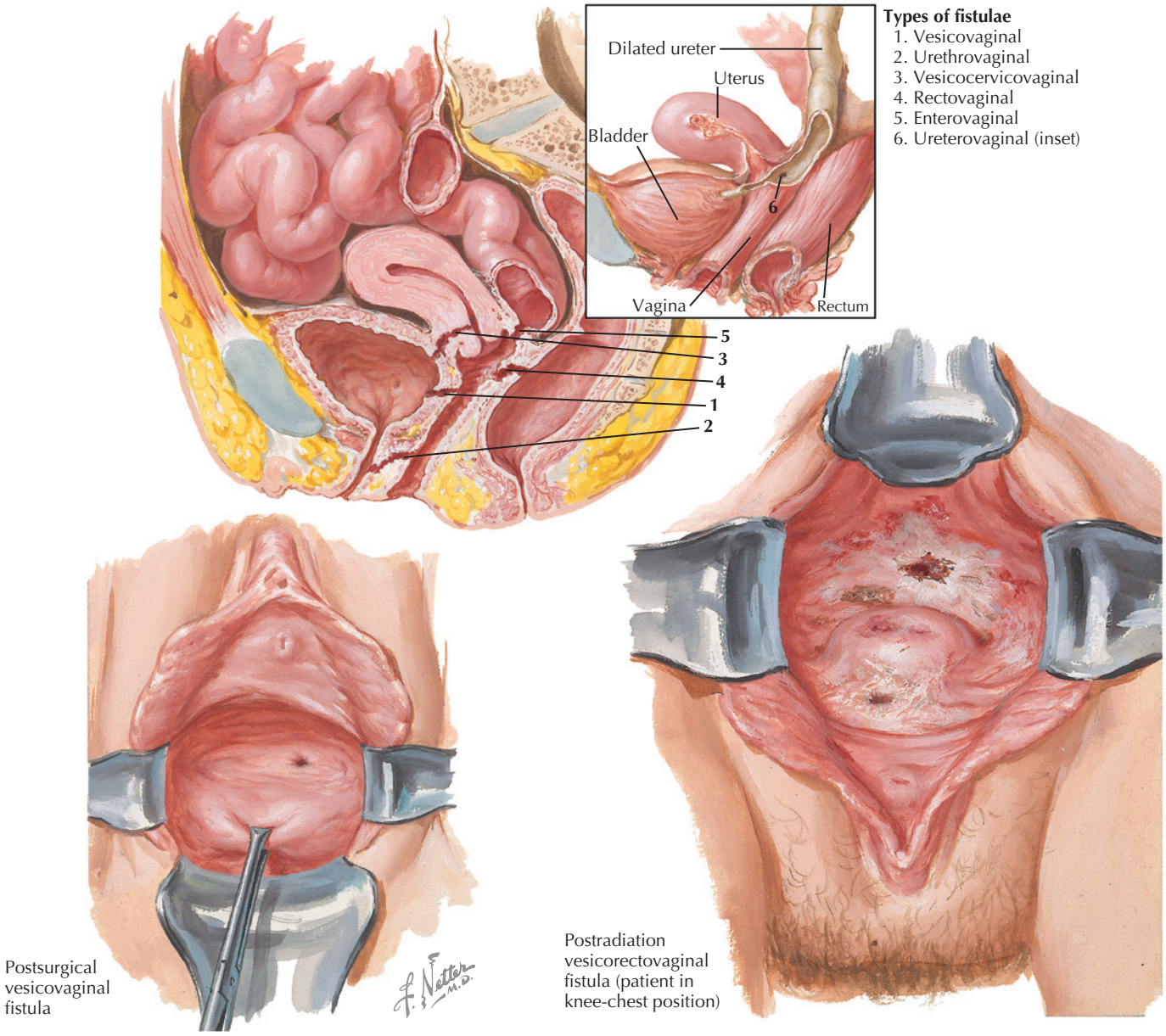


Figure 101.1 Types of fistulae and post-treatment appearance

Diet: Low-residue diet advisable for patients with a gastrointestinal fistula.

Activity: No restriction. Pelvic rest after surgical repair, until healing is completed.

Patient Education: Perianal care, sitz baths. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP081 (Urinary Incontinence).

Drug(s) of Choice

- Although the only effective treatment is surgical, the use of stool softeners may often be beneficial.
- If diarrhea is present, diphenoxylate hydrochloride (Lomotil) or a similar drug should be used to control symptoms.
- Treatment of coexisting vaginitis should be instituted.
- Urinary antisepsis should be considered when necessary.

FOLLOW-UP

Patient Monitoring: Patients with a gastrointestinal fistula should be closely followed during the postoperative period (hospital discharge is generally delayed until after the first bowel movement). Maintain routine healthcare. When a ureteral fistula has been repaired, follow-up intravenous pyelography should be planned for 3, 6, and 12 months to check for delayed stricture.

Prevention/Avoidance: Careful surgical and obstetric techniques including preoperative and perioperative bladder drainage, good visualization, careful dissection, and care in the placement of hemostatic sutures.

Possible Complications: Upper genital tract infection, recurrence, ascending urinary tract infection (including pyelonephritis).

Expected Outcome: Healing is generally good after surgical excision, although recurrence, when the original fistulae were caused by underlying disease or radiation therapy, is common.

MISCELLANEOUS

Pregnancy Considerations: No direct effect on pregnancy, although some causal processes may result in lower fertility or other effects on reproduction.

ICD-10-CM Codes: N82.4 (Other female intestinal-genital tract fistulae), N82.0 (Vesicovaginal fistula), and N82.1 (Other female urinary-genital tract fistulae).

REFERENCES

LEVEL II

Barone MA, Widmer M, Arrowsmith S, et al. Breakdown of simple female genital fistula repair after 7 day versus 14 day postoperative bladder catheterisation: a randomised, controlled, open-label, non-inferiority trial. *Lancet*. 2015;386:56.

Demirci U, Fall M, Göthe S, et al. Urovaginal fistula formation after gynaecological and obstetric surgical procedures: clinical experiences in a Scandinavian series. *Scand J Urol.* 2013;47:140.

Duong TH, Taylor DP, Meeks GR. A multicenter study of vesicovaginal fistula following incidental cystotomy during benign hysterectomies. *Int Urogynecol. J*. 2011;22:975.

Hilton P, Cromwell DA. The risk of vesicovaginal and urethrovaginal fistula after hysterectomy performed in the English National Health Service—a retrospective cohort study examining patterns of care between 2000 and 2008. *BJOG*. 2012;119:1447.

LEVEL III

American College of Obstetricians and Gynecologists. Episiotomy. ACOG Practice Bulletin No. 71. *Obstet Gynecol*. 2006;107:957.

American College of Obstetricians and Gynecologists. The role of cystourethroscopy in the generalist obstetrician–gynecologist practice. ACOG Committee Opinion No. 372. *Obstet Gynecol*. 2007;110:221.

American College of Obstetricians and Gynecologists. Urinary incontinence in women. Practice Bulletin No. 155. *Obstet Gynecol*. 2015;126:e66.

American College of Obstetricians and Gynecologists. Vaginal placement of synthetic mesh for pelvic organ prolapse. Committee Opinion No. 513. *Obstet Gynecol*. 2011;118:1459.

Michelassi F, Melis M, Rubin M, et al. Surgical treatment of anorectal complications in Crohn's disease. *Surgery*. 2000;128:597.

Saclarides TJ. Rectovaginal fistula. *Surg Clin North Am*. 2002;82:1261.

Wall LL. Obstetric vesicovaginal fistula as an international public-health problem. *Lancet*. 2006;368:1201.

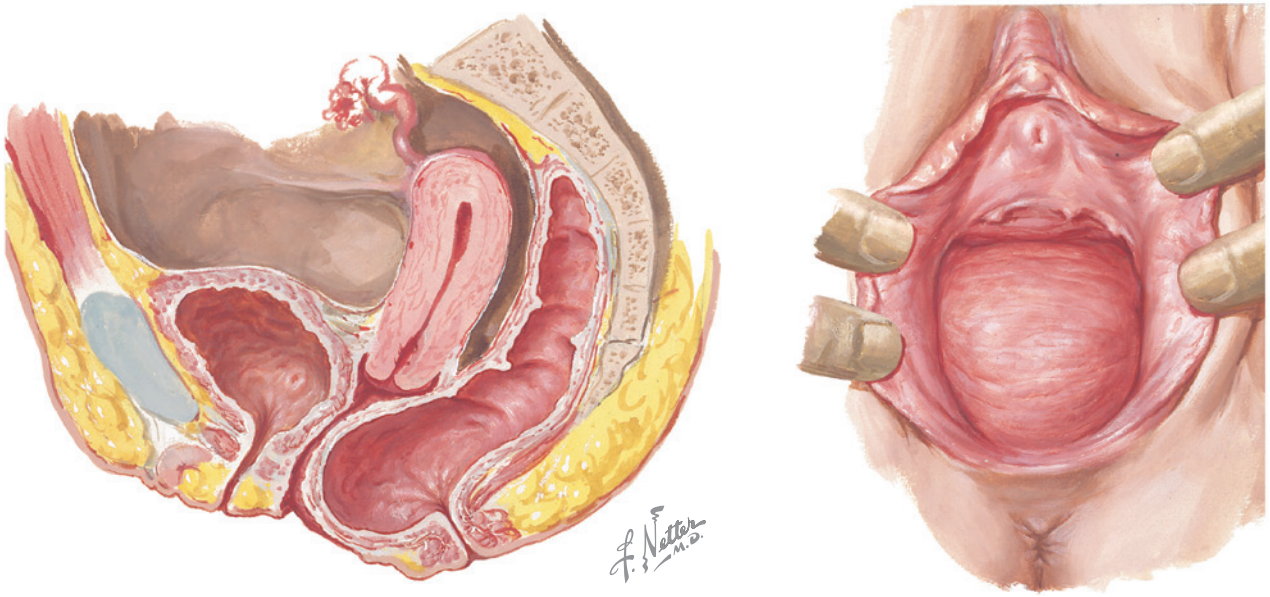


Figure 102.1 Large rectocele

Specific Measures: Pessary therapy, pelvic muscle exercises, surgical repair; limited role for medical therapy.
Diet: No specific dietary changes indicated.
Activity: Avoiding heavy lifting and straining may slow the rate of progression or risk of recurrence.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP012 (Pelvic Support Problems) and AP183 (Surgery for Pelvic Organ Prolapse).

Drug(s) of Choice

None. Estrogen, either topically or systemically, is often prescribed to improve tissue tone, reduce irritation, and prepare tissues for surgical or pessary therapy.
Contraindications: Undiagnosed vaginal bleeding, breast cancer.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: Laxative abuse/dependence. Vaginal ulceration, bleeding, infection, or pain frequently accompanies complete prolapse.
Expected Outcome: Generally favorable reduction of symptoms may be obtained with a carefully selected and fitted pessary. Surgical therapy is associated with 95% success in long-term correction of the anatomic defect and the associated symptoms.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, although pregnancy (and vaginal delivery) may cause or contribute to a worsening of pelvic support problems.
ICD-10-CM Codes: N81.9 (Female genital prolapse, unspecified), N81.6 (Rectocele), and N81.4 (Uterovaginal prolapse, unspecified).

REFERENCES

LEVEL I

Paraiso MF, Barber MD, Muir TW, et al. Rectocele repair: a randomized trial of three surgical techniques including graft augmentation. *Am J Obstet Gynecol*. 2006;195:1762.

LEVEL II

Cundiff GW, Fenner D. Evaluation and treatment of women with rectocele: focus on associated defecatory and sexual dysfunction. *Obstet Gynecol*. 2004;104:1403.

Maher C, Feiner B, Baessler K, et al. Surgical management of pelvic organ prolapse in women. *Cochrane Database Syst Rev*. 2013;(4):CD004014.

LEVEL III

American College of Obstetricians and Gynecologists. Urinary incontinence in women. Practice Bulletin No. 155. *Obstet Gynecol*. 2015;126:e66.

Bump RC, Mattiasson A, Bø K, et al. The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction. *Am J Obstet Gynecol*. 1996;175:10.

Kobashi KC, Leach GE. Pelvic prolapse. *J Urol*. 2000;164:1879.

103 SARCOMA BOTRYOIDES

INTRODUCTION

Description: Sarcoma botryoides is a rare form of sarcoma (embryonal rhabdomyosarcoma) that is generally found in the vagina of young girls. These tumors may rarely arise from the cervix. Although the cervical form of the sarcoma is histologically similar to the vaginal form, the prognosis for the cervical form is better.
Prevalence: Rare.
Predominant Age: Generally younger than 8 years and two-thirds younger than 2 years; most common neoplasm of the lower genital tract in premenarchal girls.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Unknown. Arises in the subepithelial layers of the vagina, often multicentric.
Risk Factors: None known.

SIGNS AND SYMPTOMS

- Vaginal bleeding
- Vaginal mass (resembles a cluster of grapes, may be hemorrhagic, myxoid, or both)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Urethral prolapse
- Vaginal polyp (pseudosarcoma botryoides)
- Endodermal sinus tumor (yolk sac tumor)
- Precocious puberty

Associated Conditions: None.

Workup and Evaluation

Laboratory: No specific evaluation indicated.
Imaging: No specific imaging indicated and only when necessary to evaluate tumor location and spread.
Special Tests: Biopsy of the mass.
Diagnostic Procedures: Physical examination, histologic tests.

Pathologic Findings

Tumor is often multicentric with loose myxomatous stroma containing malignant pleomorphic cells and eosinophilic rhabdomyoblasts that have characteristic cross striations (strap cells). Subepithelial aggregates of rhabdomyoblasts ("cambrium" layer) are characteristic.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation.
Specific Measures: Surgical excision combined with multiagent chemotherapy. Adjunctive radiotherapy has also been advocated but is generally reserved for patients with residual disease. Some recent studies have suggested that surgery can be delayed until after chemotherapy has been given, although long-term data are lacking.
Diet: No specific dietary changes indicated.
Activity: No restriction.

Drug(s) of Choice

Adjunctive multiagent chemotherapy only.

FOLLOW-UP

Patient Monitoring: Once surgery and chemotherapy have been completed, monitor for recurrence and general health maintenance.
Prevention/Avoidance: None.
Possible Complications: These are aggressive tumors; dissemination and recurrence are common. Spread is through direct invasion and metastasis to lymph nodes and distant sites (by

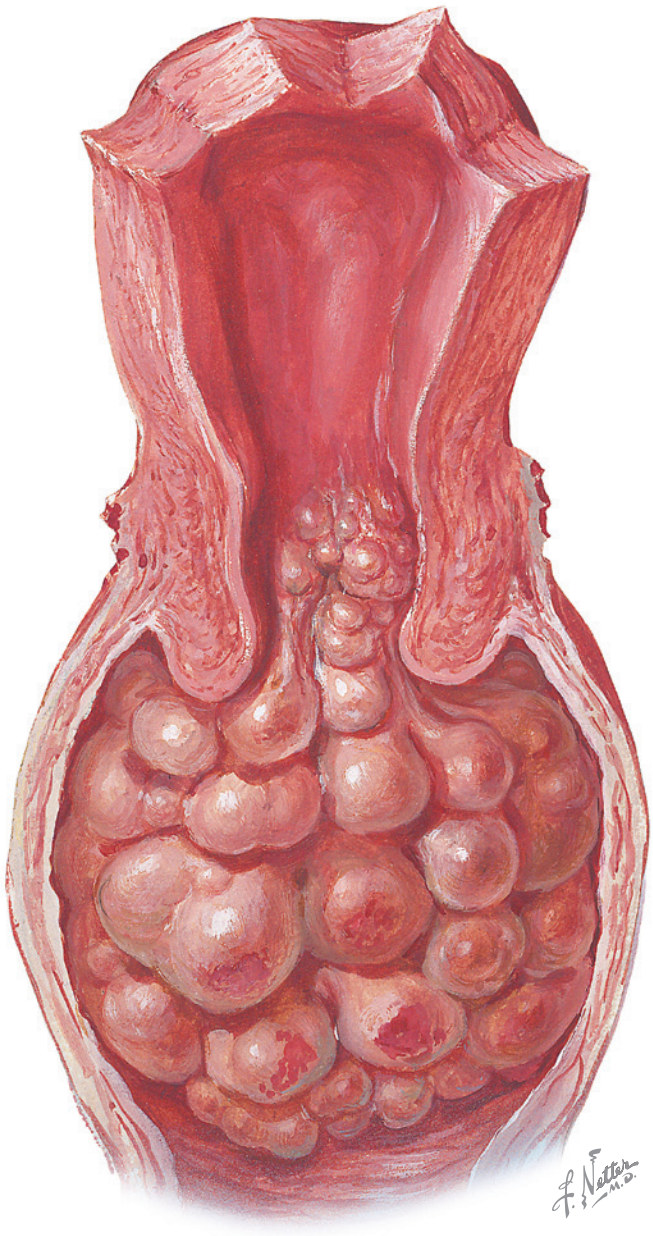


Figure 103.1 Sarcoma botryoides

hematogenous routes). The cause of death is generally by direct local extension.

Expected Outcome: Overall the prognosis is poor. Small series suggest that with the combination of surgical resection and combination chemotherapy, survival in more than 80% can be expected. Among those who survive, normal (eventual) pubertal changes and pregnancy have been reported.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy for those who survive and conceive.

ICD-10-CM Codes: C49.5 (Malignant neoplasm of connective and soft tissue of pelvis).

REFERENCES

LEVEL II

Behtash N, Mousavi A, Tehranian A, et al. Embryonal rhabdomyosarcoma of the uterine cervix: case report and review of the literature. *Gynecol Oncol*. 2003;91:452.

Hilgers RD. Pelvic exenteration for vaginal embryonal rhabdomyosarcoma: a review. *Obstet Gynecol*. 1975;45:175.

LEVEL III

Copeland LJ, Gershenson DM, Saul PB, et al. Sarcoma botryoides of the female genital tract. *Obstet Gynecol*. 1985;66:262.

Golbang P, Khan A, Scurry J, et al. Cervical sarcoma botryoides and ovarian Sertoli-Leydig cell tumor. *Gynecol Oncol*. 1997;67:102.

Gruessner SE, Omwandho CO, Dreyer T, et al. Management of stage I cervical sarcoma botryoides in childhood and adolescence. *Eur J Pediatr*. 2004;163:452. Epub 2004 Jun 2.

Tscherne G. Female genital tract malignancies during puberty. Uterine and cervical malignancies. *Ann N Y Acad Sci*. 1997;816:331.

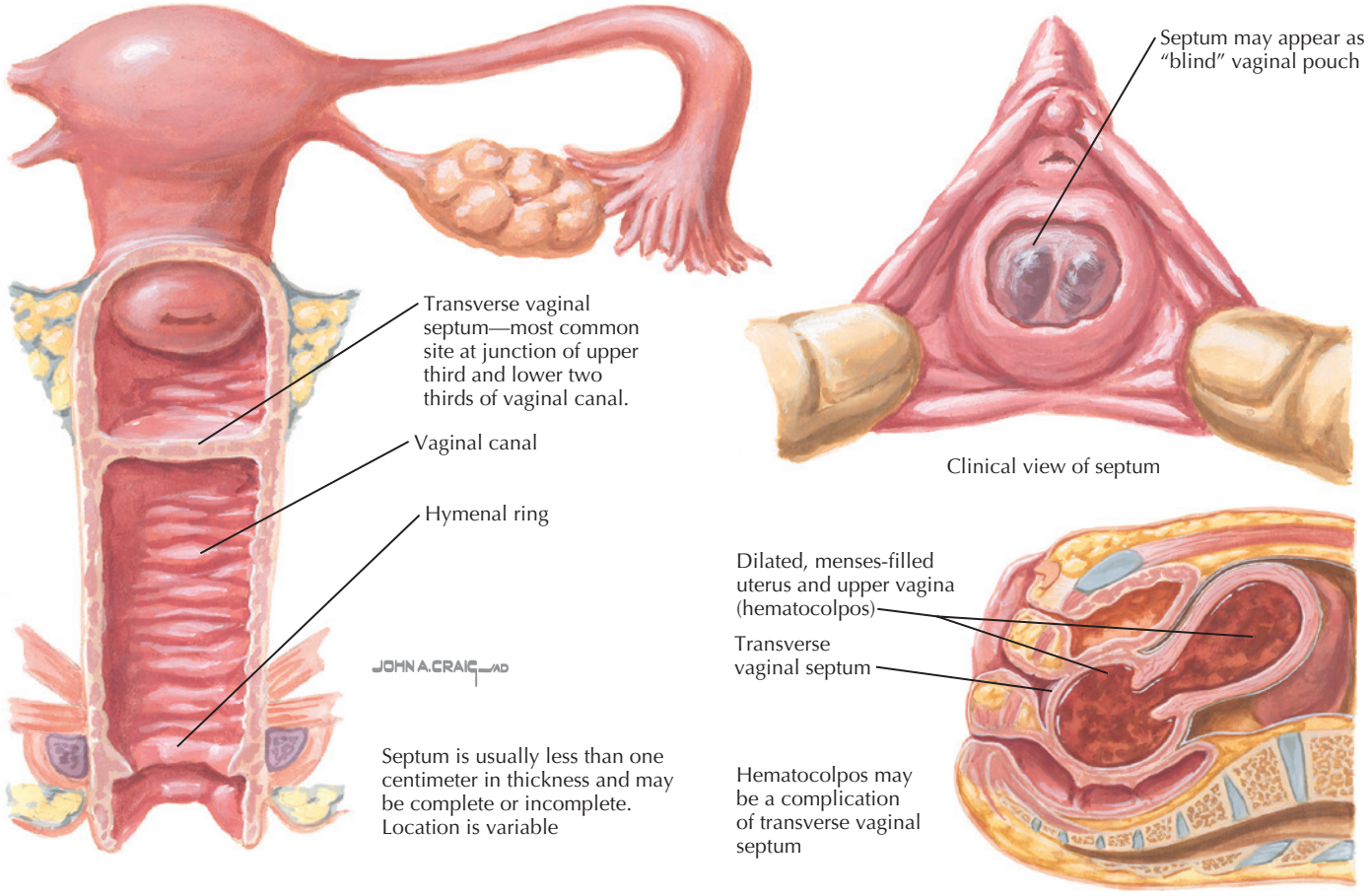


Figure 104.1 Transverse vaginal septum

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Once a normal vaginal canal has been restored, normal health maintenance. Patients must be monitored for narrowing of the vagina at the level of the removed septum or vaginal reanastomosis.

Prevention/Avoidance: None.

Possible Complications: It is rare, but a mucocolpos can cause serious and life-threatening compression of surrounding organs, leading to hydroureter, hydronephrosis, rectal compression and obstruction, restricted diaphragmatic excursion, compression of the vena cava, and cardiorespiratory failure. Fistulae to the urinary tract may occur. Prolonged obstruction of menstrual outflow is associated with the development of endometriosis and pelvic scarring (often extensive); chronic pelvic pain, dyspareunia, and infertility may result. Pregnancy rates for patients with corrected transverse septa range from 25% to 50% based on location of the septum and series report.

Expected Outcome: With timely diagnosis and treatment, prognosis is good.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy once pregnancy is achieved. Pregnancy success is greatest with septa that are lower in the vagina and repaired early. Based on the extent of vaginal reconstruction performed and the degree of subsequent scarring, cesarean delivery may be elected (approximately 50% of reported cases).

ICD-10-CM Codes: Q52.11 (Transverse vaginal septum).

REFERENCES

LEVEL II

Blanton EN, Rouse DJ. Trial of labor in women with transverse vaginal septa. *Obstet Gynecol*. 2003;101:1110.

McKusick VA, Weiboecher RG, Gragg GW. Recessive inheritance of a congenital malformation syndrome. *JAMA*. 1968;204:113.

Rock JA, Zacur HA, Dlugi AM, et al. Pregnancy success following surgical correction of imperforate hymen and complete transverse vaginal septum. *Obstet Gynecol*. 1982;59:448.

LEVEL III

American College of Obstetricians and Gynecologists. Müllerian agenesis: diagnosis, management, and treatment. Committee Opinion No. 562. *Obstet Gynecol*. 2013;121:1134.

Brenner P, Sedlis A, Cooperman H. Complete imperforate transverse vaginal septum. *Obstet Gynecol*. 1965;25:135.

Lilford RJ, Morton K, Dewhurst J. The diagnosis and management of the imperforate vaginal membrane in the pre-pubertal child. *Pediatr Adolesc Gynecol*. 1983;1:115.

Lopez C, Balogun M, Ganesan R, et al. MRI of vaginal conditions. *Clin Radiol*. 2005;60:648.

McKusick VA. Transverse vaginal septum (hydrometrocolpos). *Birth Defects Orig Artic Ser*. 1971;7:326.

VAGINAL CYSTS

105

INTRODUCTION

Description: Cystic masses in the vaginal wall are uncommon and may arise from either congenital (Gartner duct cysts) or acquired (epithelial inclusion cysts) processes.
Prevalence: 1 of 200 women.
Predominant Age: Generally from adolescence to middle reproductive years.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Congenital (Gartner duct cyst or remnant, generally found in the anterior lateral vaginal wall), structural (urethral diverticulum, loss of vaginal wall support), acquired (inclusion cyst; >50% of cysts).
Risk Factors: Episiotomy or obstetric laceration, gynecologic surgery.

SIGNS AND SYMPTOMS

- Asymptomatic
- May be associated with a sense of fullness
- Dyspareunia (uncommon)
- Difficulty with tampon insertion or retention
- Cystic mass lesion (1–5 cm) generally found in the lateral vaginal wall (congenital) or in midline posteriorly (acquired)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Urethral diverticulum
- Cystocele
- Urethrocele
- Rectocele
- Bartholin gland cyst
- Vaginal adenosis
- Vaginal endometriosis
- Perirectal abscess
- Vaginal fibromyoma

Associated Conditions: Slightly higher rate of upper genital tract malformations when embryonic remnants persist.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated.
Special Tests: Vaginal adenosis may be excluded by staining with Lugol solution (adenosis will not stain).
Diagnostic Procedures: History and physical examination.

Pathologic Findings

Most embryonic cysts are lined with cuboidal epithelium. Stratified epithelium suggests an inclusion (acquired) cyst.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and reassurance.
Specific Measures: Surgical excision if the mass is symptomatic or its cause is uncertain; otherwise, no therapy is required.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP088 (Disorders of the Vulva).

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: Mechanical irritation or interference with intercourse or childbirth (rare), infection (rare).
Expected Outcome: Some care must be used in the excision of large cysts so that vaginal scarring and stenosis do not occur; otherwise, surgical therapy should be successful.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: N89.8 (Other specified noninflammatory disorders of vagina) and Q52.4 (Other congenital malformations of vagina, Embryonal).

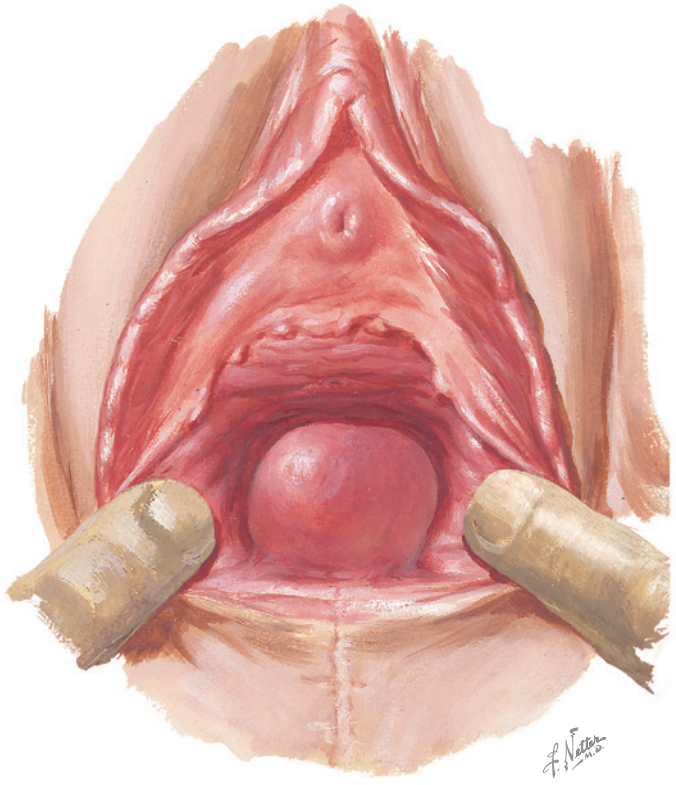


Figure 105.1 Inclusion cyst

REFERENCES

LEVEL II

Dwyer PL, Rosamilia A. Congenital urogenital anomalies that are associated with the persistence of Gartner's duct: a review. *Am J Obstet Gynecol*. 2006;195:354.

Eilber KS, Raz S. Benign cystic lesions of the vagina: a literature review. *J Urol*. 2003;170:717.

Pradhan S, Tobon H. Vaginal cysts: a clinicopathological study of 41 cases. *Int J Gynecol Pathol*. 1986;5:35.

Wai CY, Corton MM, Miller M, et al. Multiple vaginal wall cysts: diagnosis and surgical management. *Obstet Gynecol*. 2004;103:1099.

LEVEL III

Dmochowski RR, Ganabathi K, Zimmern PE, et al. Benign female periurethral masses. *J Urol*. 1994;152:1943.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP047 (The Menopause Years), AP028 (Vaginitis), AP020 (When Sex Is Painful), AP190 (Vulvovaginal Health), AP072 (Your Sexual Health), and AP088 (Disorders of the Vulva).

Drug(s) of Choice

- Estrogen replacement therapy when appropriate (see "Menopause")
- Water-soluble lubricants for intercourse
- Long-acting emollients (Replens, etc.)

Contraindications: Known or suspected allergy or intolerance to any agent.

Precautions: Petroleum-based products (eg, Vaseline) are difficult to remove and may lead to additional irritation.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.

Prevention/Avoidance: Estrogen replacement after menopause (for select patients).

Possible Complications: Vaginal lacerations and secondary infection, vulvar excoriations, sexual dysfunction.

Expected Outcome: Generally good results with topical or systemic therapy for estrogen loss. Good response to therapy for vaginitis.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy (generally not an issue).

ICD-10-CM Codes: Based on the cause.

REFERENCES

LEVEL I

Barnabei VM, Cochrane BB, Aragaki AK, et al. Women's Health Initiative Investigators. Menopausal symptoms and treatment-related effects of estrogen and progestin in the Women's Health Initiative. *Obstet Gynecol*. 2005;105:1063.

Loprinzi CL, Abu-Ghazaleh S, Sloan JA, et al. Phase III randomized double-blind study to evaluate the efficacy of a polycarbophil-based vaginal moisturizer in women with breast cancer. *J Clin Oncol*. 1997;15:969.

LEVEL II

Barnabei VM, Grady D, Stovall DW, et al. Menopausal symptoms in older women and the effects of treatment with hormone therapy. *Obstet Gynecol*. 2002;100:1209.

Brown JS, Vittinghoff E, Kanaya AM, et al.; Heart and Estrogen/Progestin Replacement Study Research Group. Urinary tract infections in postmenopausal women: effect of hormone therapy and risk factors. *Obstet Gynecol*. 2001;98:1045.

Bygdeman M, Swahn ML. Replens versus dienoestrol cream in the symptomatic treatment of vaginal atrophy in postmenopausal women. *Maturitas*. 1996;23:259.

Woods NF, Mitchell ES. Symptoms during the perimenopause: prevalence, severity, trajectory, and significance in women's lives. *Am J Med*. 2005;118:14.

LEVEL III

American College of Obstetricians and Gynecologists. Vaginitis. ACOG Practice Bulletin 72. *Obstet Gynecol*. 2006;107:1195.

American College of Obstetricians and Gynecologists. Female sexual dysfunction. Practice Bulletin No. 119. *Obstet Gynecol*. 2011;117:996.

American College of Obstetricians and Gynecologists. Management of menopausal symptoms. Practice Bulletin No. 141. *Obstet Gynecol*. 2014;123:202.

Avis NE, Brockwell S, Colvin A. A universal menopausal syndrome? *Am J Med*. 2005;118:37.

Hickey M, Davis SR, Sturdee DW. Treatment of menopausal symptoms: what shall we do now? *Lancet*. 2005;366:409.

Van Voorhis BJ. Genitourinary symptoms in the menopausal transition. *Am J Med*. 2005;118:47.

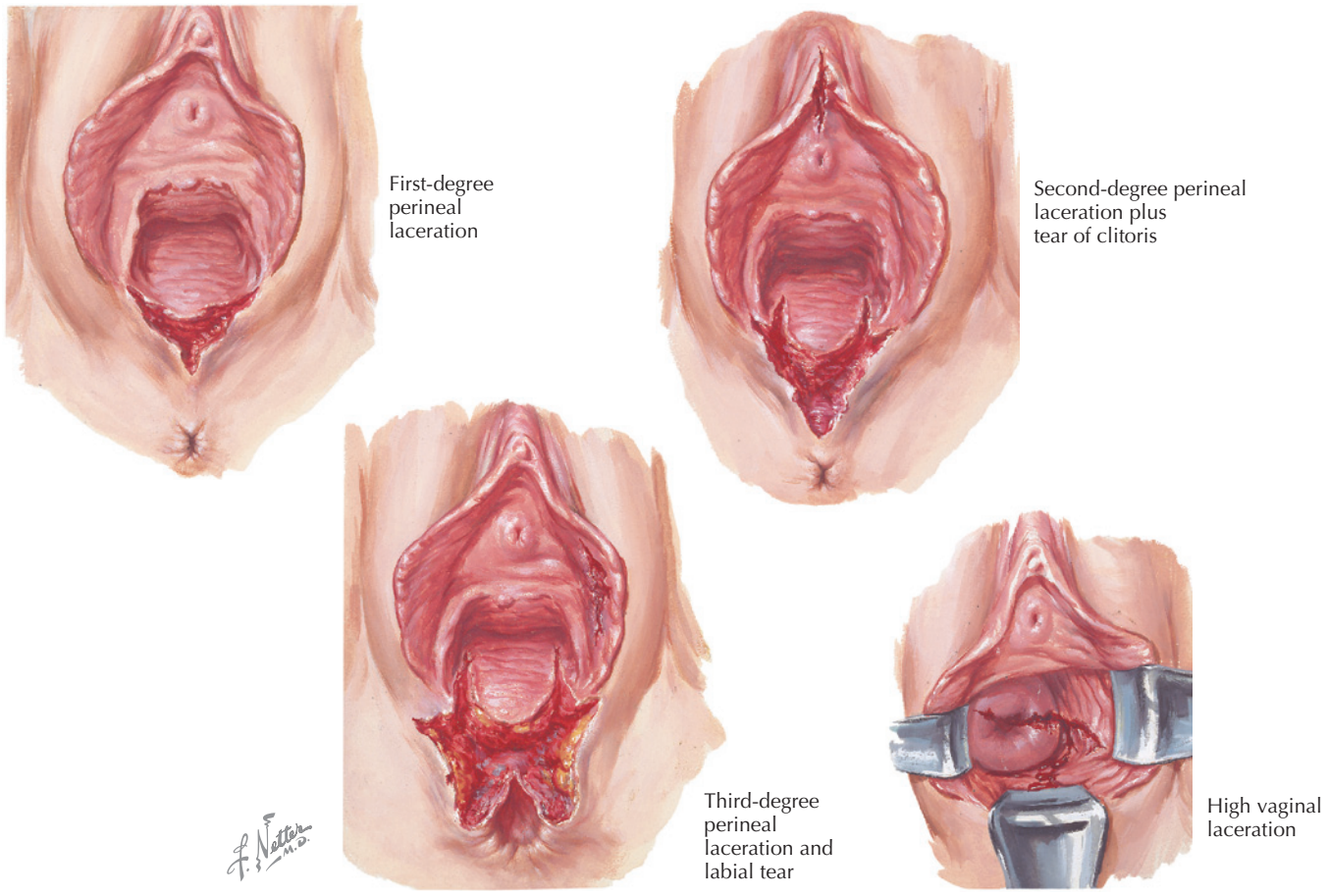


Figure 107.1 Vaginal lacerations (first, second, and third degrees)

- Sexual abuse/rape

Associated Conditions: Vaginal atrophy, sexual dysfunction, alcohol or drug use/abuse.

Workup and Evaluation

Laboratory: Complete blood count.
Imaging: No imaging indicated.
Special Tests: None indicated.
Diagnostic Procedures: History and physical examination (history is often misleading or false).

Pathologic Findings

The most common site of coital laceration is the posterior fornix, followed by the right and left fornices.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Rapid assessment and hemodynamic stabilization (when appropriate).
Specific Measures: Surgical closure of the laceration, evaluation of the integrity of the urinary and gastrointestinal tracts; may include exploratory laparotomy or laparoscopy in cases of evisceration or peritoneal breach.
Diet: No specific dietary changes indicated.
Activity: Pelvic rest (no tampons, douches, or intercourse) until healing has occurred.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP083 (Domestic Violence), and AP020 (When Sex Is Painful).

Drug(s) of Choice

- Local or general anesthesia for surgical repair.
- Treatment with an antibiotic is generally not required, except if a peritoneal breach is present.

FOLLOW-UP

Patient Monitoring: Normal health maintenance after healing has been completed.
Prevention/Avoidance: Avoidance of alcohol or drug use, careful consensual intercourse, adequate vaginal lubrication.
Possible Complications: Vaginal evisceration, excessive blood loss. In rare cases, death has been reported.
Expected Outcome: Generally good healing; the risk of recurrence is based on cause.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy unless the health or safety of the mother is compromised.
ICD-10-CM Codes: Based on the location and cause.

REFERENCES

LEVEL I

Garcia V, Rogers RG, Kim SS, et al. Primary repair of obstetric anal sphincter laceration: a randomized trial of two surgical techniques. *Am J Obstet Gynecol*. 2005;192:1697.

LEVEL II

Haefner HK, Andersen F, Johnson MP. Vaginal laceration following a jet-ski accident. *Obstet Gynecol*. 1991;78:986.

Hartmann K, Viswanathan M, Palmieri R, et al. Outcomes of routine episiotomy: a systematic review. *JAMA*. 2005;293:2141.

McCann J, Miyamoto S, Boyle C, et al. Healing of hymenal injuries in prepubertal and adolescent girls: a descriptive study. *Pediatrics*. 2007; 119:e1094. [Epub 2007 Apr 9].

Niv J, Lessing JB, Hartuv J, et al. Vaginal injury resulting from sliding down a water chute. *Am J Obstet Gynecol*. 1992;166:930.

Smith NC, Van Coeverden de Groot HA, Gunston KD. Coital injuries of the vagina in nonvirginal patients. *S Afr Med J*. 1983;64:746.

LEVEL III

Ahnaimugan S, Asuen MI. Coital laceration of the vagina. *Aust N Z J Obstet Gynaecol*. 1980;20:180.

American College of Obstetricians and Gynecologists. Limitations of perineal lacerations as an obstetric quality measure. Committee Opinion No. 647. *Obstet Gynecol*. 2015;126:e108.

American College of Obstetricians and Gynecologists. Operative vaginal delivery. Practice Bulletin No. 154. *Obstet Gynecol*. 2015;126:e56.

American College of Obstetricians and Gynecologists: Episiotomy. ACOG Practice Bulletin 71. *Obstet Gynecol*. 2006;107:957.

Friedel W, Kaiser IH. Vaginal evisceration. *Obstet Gynecol*. 1975;45:315.

Rafla N. Vaginismus and vaginal tears. *Am J Obstet Gynecol*. 1988;158: 1043.

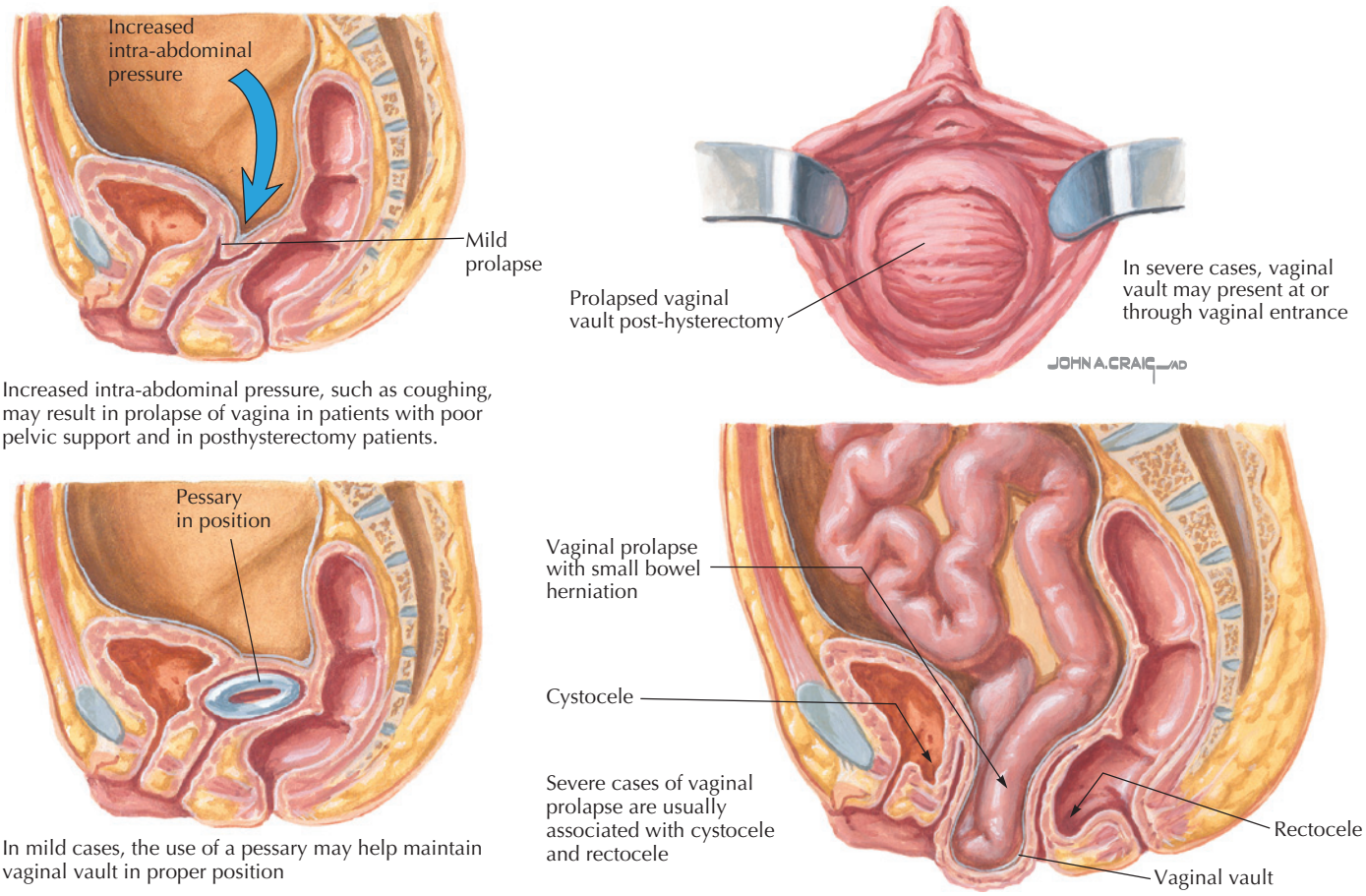


Figure 108.1 Vaginal prolapse

Activity: No restriction, although heavy lifting or strenuous activities may predispose to the development or recurrence of prolapse.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP012 (Pelvic Support Problems), AP081 (Urinary Incontinence), and AP183 (Surgery for Pelvic Organ Prolapse).

Drug(s) of Choice

Estrogen replacement therapy (for postmenopausal patients) improves tissue tone and healing and is often prescribed before surgical repair or as an adjunct to pessary therapy.

Contraindications: Estrogen therapy should not be used if undiagnosed vaginal bleeding is present.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. If a pessary is used, frequent follow-up (both initially and long term) is required.

Prevention/Avoidance: Maintenance of normal weight, avoidance of known (modifiable) risk factors.

Possible Complications: Thickening or ulceration of vaginal tissues, urinary incontinence, kinking of the ureters, and obstipation. Complications of surgical repair include intraoperative hemorrhage, nerve damage (sciatic), damage to the rectum or uterus, postoperative infection, and complications of anesthesia. The placement of a surgical mesh carries the risk for both acute and delayed complications and should be reserved for selected patients.

Expected Outcome: Vaginal prolapse tends to worsen with time. If uncorrected, complete prolapse is associated with vaginal skin changes, ulceration, and bleeding.

MISCELLANEOUS

ICD-10-CM Codes: N81.9 (Female genital prolapse, unspecified) and N99.3 (Prolapse of vaginal vault after hysterectomy).

REFERENCES

LEVEL I

Cundiff GW, Amundsen CL, Bent AE, et al. The PESSRI study: symptom relief outcomes of a randomized crossover trial of the ring and Gellhorn pessaries. *Am J Obstet Gynecol*. 2007;196:405.e1.

Meschia M, Pifarotti P, Bernasconi F, et al. Porcine skin collagen implants to prevent anterior vaginal wall prolapse recurrence: a multicenter, randomized study. *J Urol*. 2007;177:192.

LEVEL II

Kahn MA, Breitkopf CR, Valley MT, et al. Pelvic Organ Support Study (POSST) and bowel symptoms: straining at stool is associated with perineal and anterior vaginal descent in a general gynecologic population. *Am J Obstet Gynecol*. 2005;192:1516.

Maher C, Feiner B, Baessler K, et al. Surgical management of pelvic organ prolapse in women. *Cochrane Database Syst Rev*. 2013;(4):CD004014.

Morley GW, Delancey JOL. Sacrospinous ligament fixation for eversion of vagina. *Am J Obstet Gynecol*. 1988;158:872.

Sung VW, Washington B, Raker CA. Costs of ambulatory care related to female pelvic floor disorders in the United States. *Am J Obstet Gynecol*. 2010;202:483.e1.

Swift S, Woodman P, O'Boyle A, et al. Pelvic Organ Support Study (POSST): the distribution, clinical definition, and epidemiologic condition of pelvic organ support defects. *Am J Obstet Gynecol*. 2005;192:795.

Vergeldt TF, Weemhoff M, IntHout J, et al. Risk factors for pelvic organ prolapse and its recurrence: a systematic review. *Int Urogynecol J*. 2015;26:1559.

LEVEL III

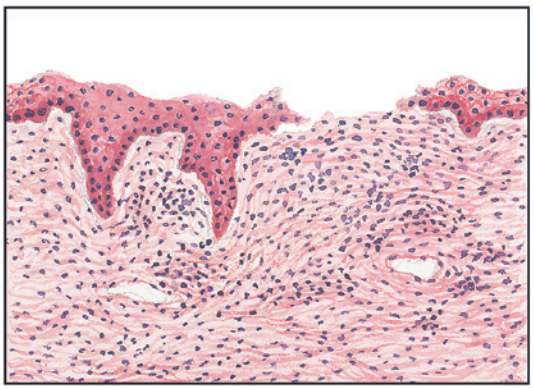
American College of Obstetricians and Gynecologists. Pelvic organ prolapse. ACOG Practice Bulletin 79. *Obstet Gynecol*. 2007;109:461.

American College of Obstetricians and Gynecologists. Choosing the route of hysterectomy for benign disease. ACOG Committee Opinion No. 444. *Obstet Gynecol*. 2009;114:1156.

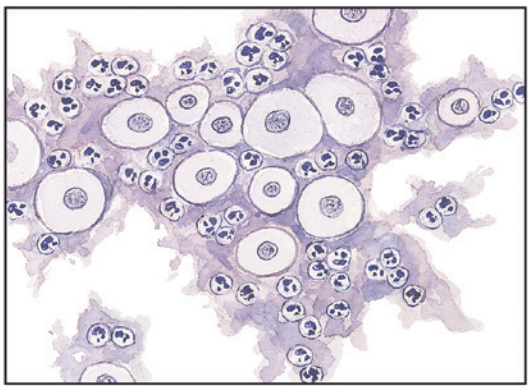
American College of Obstetricians and Gynecologists. Vaginal placement of synthetic mesh for pelvic organ prolapse. Committee Opinion No. 513. *Obstet Gynecol*. 2011;118:1459.

American College of Obstetricians and Gynecologists. Urinary incontinence in women. Practice Bulletin No. 155. *Obstet Gynecol*. 2015;126:e66.

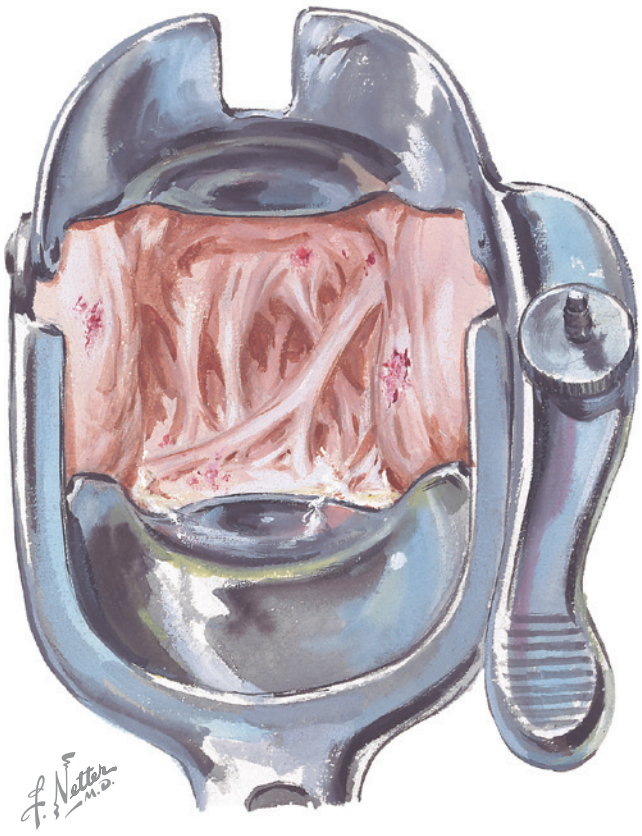
Cutner AS, Elneil S. The vaginal vault. *BJOG*. 2004;111:79.



Histology of vagina after menopause



Smear from postmenopausal vagina



Advanced stage with extensive adhesions

Figure 109.1 Vaginitis

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP047 (The Menopause Years), AP028 (Vaginitis), AP020 (When Sex Is Painful), AP190 (Vulvovaginal Health), AP072 (Your Sexual Health), and AP088 (Disorders of the Vulva).

Drug(s) of Choice

- Most common drug dosages are shown. Note: Because of concerns raised by the Women's Health Initiative (WHI) study, non-hormonal and topical estrogen therapies are preferred over oral estrogen therapy unless otherwise indicated. This does not avoid systemic estrogen absorption, which may actually be increased in the presence of significant atrophy (see below).
- Topical—17β-estradiol (transdermal) 0.05–0.10 mcg/day, conjugated equine estrogens 0.625 mg/g, estradiol 0.1 mg/g, estropipate 1.5 mg/g.
- Oral estrogens—conjugated equine estrogens 0.625–1.25 mg/day, diethylstilbestrol, esterified estrogens 0.625–1.25 mg/day, ethinyl estradiol 0.05 mg/day, micronized estradiol 0.5–1 mg/day, piperazine estrone sulfate, estropipate, quinestrol.
- Injectable estrogens—conjugated equine estrogens, estradiol benzoate, estradiol cypionate, estradiol valerate (oil), estrone (aqueous), ethinyl estradiol, polyestradiol phosphate.

Contraindications (Systemic Therapy): Active liver disease, carcinoma of the breast (current), chronic liver damage (impaired function), known sensitivity to topical vehicles, endometrial carcinoma (current), recent thrombosis (with or without emboli), unexplained vaginal bleeding.

Precautions: Up to 25% of estrogen placed in the vagina may be absorbed into the circulation. This amount may be even greater for patients with atrophic changes. Continuous estrogen exposure without periodic or concomitant progestins increases the risk of endometrial carcinoma by 6–8-fold when the uterus is present.

Interactions: See individual agents.

Alternative Drugs

Ospemifene (a selective estrogen receptor modulator [SERM]) acts as an estrogen agonist in the vagina but has no clinically significant estrogenic effect on the endometrium or breast. It was approved in 2013 for treating vaginal atrophy. Systemic side effects (hot flashes, increased risk of thromboembolism) and the need for daily dosing limit use of this therapy to selected patients.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. Patients may be at slightly greater risk for vaginal infections or trauma.

Prevention/Avoidance: Estrogen replacement therapy at menopause.

Possible Complications: Reduced resistance to infection, dyspareunia, and traumatic injury during intercourse.

Expected Outcome: Reversal of symptoms, reestablishment of normal physiology.

MISCELLANEOUS

Pregnancy Considerations: Menopause is associated with the loss of fertility.

ICD-10-CM Codes: N95.2 (Postmenopausal atrophic vaginitis).

REFERENCES

LEVEL I

Bachmann G, Lobo RA, Gut R, et al. Efficacy of low-dose estradiol vaginal tablets in the treatment of atrophic vaginitis: a randomized controlled trial. *Obstet Gynecol*. 2008;111:67.

Barnabei VM, Cochrane BB, Aragaki AK, et al. Women's Health Initiative Investigators. Menopausal symptoms and treatment-related effects of estrogen and progestin in the Women's Health Initiative. *Obstet Gynecol*. 2005;105:1063.

Lee YK, Chung HH, Kim JW, et al. Vaginal pH-balanced gel for the control of atrophic vaginitis among breast cancer survivors: a randomized controlled trial. *Obstet Gynecol*. 2011;117:922.

Simon JA, Bouchard C, Waldbaum A, et al. Low dose of transdermal estradiol gel for treatment of symptomatic postmenopausal women: a randomized controlled trial. *Obstet Gynecol*. 2007;109:588.

Speroff L. Efficacy and tolerability of a novel estradiol vaginal ring for relief of menopausal symptoms. *Obstet Gynecol*. 2003;102:823.

LEVEL II

Barnabei VM, Grady D, Stovall DW, et al. Menopausal symptoms in older women and the effects of treatment with hormone therapy. *Obstet Gynecol*. 2002;100:1209.

Suckling J, Lethaby A, Kennedy R. Local oestrogen for vaginal atrophy in postmenopausal women. *Cochrane Database Syst Rev*. 2006;(4):CD001500.

Woods NF, Mitchell ES. Symptoms during the perimenopause: prevalence, severity, trajectory, and significance in women's lives. *Am J Med*. 2005;118:14.

LEVEL III

American College of Obstetricians and Gynecologists. Vaginitis. ACOG Practice Bulletin 72. *Obstet Gynecol*. 2006;107:1195.

American College of Obstetricians and Gynecologists. Management of menopausal symptoms. Practice Bulletin No. 141. *Obstet Gynecol*. 2014;123:202.

Avis NE, Brockwell S, Colvin A. A universal menopausal syndrome? *Am J Med*. 2005;118:37.

Hickey M, Davis SR, Sturdee DW. Treatment of menopausal symptoms: what shall we do now? *Lancet*. 2005;366:409.

Van Voorhis BJ. Genitourinary symptoms in the menopausal transition. *Am J Med*. 2005;118:47.

- Dyspareunia
- Edema or erythema of the vulva

Bacterial Vaginosis

- Asymptomatic (20%–50% of patients)
- Increased discharge
- Vaginal odor (often more pronounced after intercourse)
- Vulvar burning or irritation

Uncommon

- Dysuria
- Dyspareunia
- Edema or erythema of the vulva

DIAGNOSTIC APPROACH

Differential Diagnosis

- Chlamydial cervicitis
- Gonococcal cervicitis
- *Trichomonas vaginalis* infection
- Vaginal candidiasis

Associated Conditions: Other vaginal or sexually transmitted infections, cervicitis, and vulvitis. Ascending infections including endometritis, pelvic inflammatory disease, human immunodeficiency virus (HIV) transmission, postoperative vaginal cuff cellulitis, preterm rupture of the membranes and endomyometritis, increased early pregnancy loss, and decreased success with in vitro fertilization.

Workup and Evaluation

Laboratory: Culture or monoclonal antibody staining may be obtained to evaluate other causes but are seldom necessary. Evaluation for concomitant sexually transmitted infections should be considered.

Imaging: No imaging indicated.

Special Tests: Vaginal pH 5–5.5, "whiff" test—the addition of 10% KOH to vaginal secretions to liberate volatile amines, causing a "fishy" odor (bacterial vaginosis).

Diagnostic Procedures: Physical examination, microscopic examination of vaginal secretions in normal saline. For bacterial vaginosis, the diagnosis requires three of the following (Amsel criteria): homogeneous discharge, pH 5–5.5, clue cells (>20%), positive "whiff" test. Commercial tests (such as for proline iminopeptidase activity, automated DNA probe assays, or chromogenic diagnostic tests) exist but are generally not necessary to establish the diagnosis. Gram staining of vaginal discharge is the gold standard.

Pathologic Findings

Increased white blood cells and number of bacteria when vaginal secretions are viewed under normal saline suggest vaginitis. Clue cells may be present but are often absent in vaginitis. For bacterial vaginosis, clue cells must represent 20% or more of epithelial cells seen.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Perineal hygiene, education regarding sexually transmitted infections.

Specific Measures: Medical therapy, vaginal acidification, cessation of douching.

Diet: No specific dietary changes indicated.

Activity: No restriction.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP028 (Vaginitis), AP009 (How to Prevent Sexually Transmitted Infections), and AP190 (Vulvovaginal Health).

Drug(s) of Choice

- Oral—metronidazole (Flagyl, Protostat) 500 mg twice daily for 7 days (90%–100% cure), oral ampicillin 500 mg every 6 hours for 7 days.
- Topical—clindamycin (5 g of cream, 100 mg of clindamycin) every night at bedtime for 7 days, metronidazole (5 g of cream, 37.5 mg of metronidazole) twice a day for 5 days.

Contraindications: Metronidazole is relatively contraindicated in the first trimester of pregnancy.

Precautions: Oral metronidazole is associated with the potential for systemic side effects, including a metallic taste in the mouth and stomach upset. Topical metronidazole is currently available in two forms: one for dermatologic use and one for intravaginal use. The pH of these two preparations is quite different, making it important to specify the form on the prescription to avoid significant chemical irritation. Some concerns have been raised about the risk of inducing antibiotic resistance through the use of topical clindamycin, although the clinical significance is uncertain.

Interactions: Because of a disulfiram-like reaction, patients must be warned to avoid alcohol intake during metronidazole therapy.

Alternative Drugs

- Oral—tetracycline 250–500 mg twice a day for 7 days, clindamycin 300–450 mg every 6 hours for 7 days. Tinidazole is a second-generation nitroimidazole that is considered as an alternative regimen.
- Topical—topical triple sulfa (cream or suppositories) twice a day for 7–10 days, vaginal acidification (Aci-Jel, Amino-Cerv, boric acid), povidone iodine as a douche or gel.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.

Prevention/Avoidance: Bacterial vaginosis is considered to develop 5–10 days after exposure to the involved bacteria. *Gardnerella* may be found in 90% of male partners of women with bacterial vaginosis. Hence, sexual transmission is postulated, although

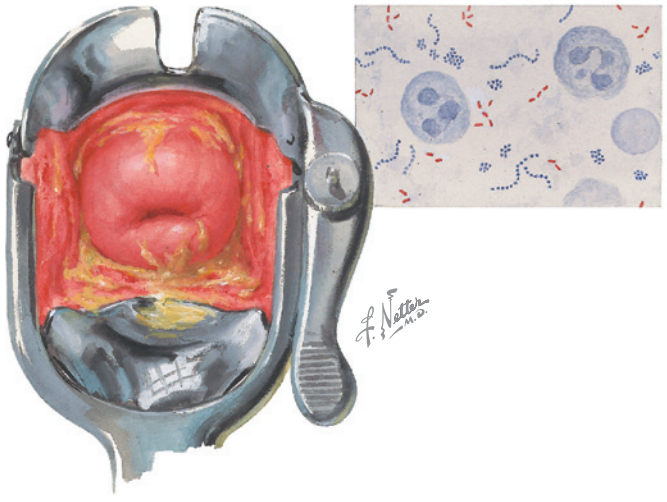


Figure 110.1 Bacterial vaginosis

bacterial vaginosis can occur in virginal women. The role of condoms in prevention is debated.

Possible Complications: Cystitis, cervicitis, infections of Skene's or Bartholin's glands, increased risk of pelvic inflammatory disease, pelvic pain, and infertility. Increased risk of upper genital tract infections and postoperative infections if surgery is performed while bacterial vaginosis is present. Increased risk of premature delivery, premature rupture of the membranes, and chorioamnionitis when bacterial vaginosis is present during pregnancy.

Expected Outcome: Most treatment failures are actually caused by reinfection or failure to comply with treatment.

MISCELLANEOUS

Pregnancy Considerations: Vaginal infections are associated with an increased risk of prematurity and premature rupture of the membranes.

ICD-10-CM Codes: N76.0 (Acute vaginitis) and N76.1 (Subacute and chronic vaginitis).

REFERENCES

LEVEL I

Sanchez S, Garcia PJ, Thomas KK, et al. Intravaginal metronidazole gel versus metronidazole plus nystatin ovules for bacterial vaginosis: a randomized controlled trial. *Am J Obstet Gynecol*. 2004;191:1898.

LEVEL II

Allsworth JE, Peipert JF. Prevalence of bacterial vaginosis: 2001-2004 National Health and Nutrition Examination Survey data. *Obstet Gynecol*. 2007;109:114.

Beigi RH, Austin MN, Meyn LA, et al. Antimicrobial resistance associated with the treatment of bacterial vaginosis. *Am J Obstet Gynecol*. 2004; 191:1124.

Brocklehurst P, Gordon A, Heatley E, et al. Antibiotics for treating bacterial vaginosis in pregnancy. *Cochrane Database Syst Rev*. 2013;(1): CD000262.

Kenyon C, Colebunders R, Crucitti T. The global epidemiology of bacterial vaginosis: a systematic review. *Am J Obstet Gynecol*. 2013;209:505.

Ness RB, Hillier SL, Kip KE, et al. Bacterial vaginosis and risk of pelvic inflammatory disease. *Obstet Gynecol*. 2004;104:761.

Oduyebo OO, Anorlu RI, Ogunsola FT. The effects of antimicrobial therapy on bacterial vaginosis in non-pregnant women. *Cochrane Database Syst Rev*. 2009;(3):CD006055.

Okun N, Gronau KA, Hannah ME. Antibiotics for bacterial vaginosis or *Trichomonas vaginalis* in pregnancy: a systematic review. *Obstet Gynecol*. 2005;105:857.

Ugwumadu A, Reid F, Hay P, et al. Natural history of bacterial vaginosis and intermediate flora in pregnancy and effect of oral clindamycin. *Obstet Gynecol*. 2004;104:114.

LEVEL III

American College of Obstetricians and Gynecologists. Vaginitis. ACOG Practice Bulletin 72. *Obstet Gynecol*. 2006;107:1195.

Anderson MR, Klink K, Cohrssen A. Evaluation of vaginal complaints. *JAMA*. 2004;291:1368.

Friese K. The role of infection in preterm labour. *BJOG*. 2003;110:52.

Ledger WJ. Historical review of the treatment of bacterial vaginosis. *Am J Obstet Gynecol*. 1993;169:474.

Mitchell H. Vaginal discharge—Causes, diagnosis, and treatment. *BMJ*. 2004;328:1306.

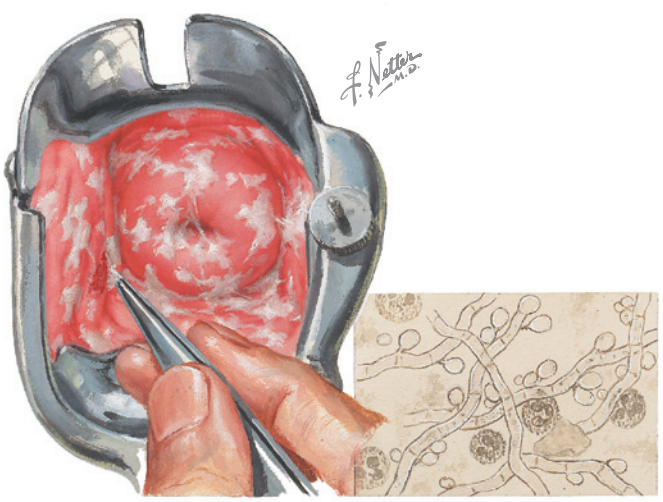


Figure 111.1 *Candida albicans*

Associated Conditions: Diabetes, immunosuppression or compromise (as risk factors for infection), chronic vulvitis.

Workup and Evaluation

Laboratory: Culture (Nickerson's or Sabouraud media) or monoclonal antibody staining may be obtained but are seldom necessary.
Imaging: No imaging indicated.
Special Tests: Vaginal pH 4–4.5.
Diagnostic Procedures: Physical examination, microscopic examination of vaginal secretions in normal saline and 10% KOH (potassium hydroxide).

Pathologic Findings

Branching and budding of vaginal monilia distinguish monilial vaginitis from lint or other foreign material. The use of 10% KOH lyses white blood cells and renders epithelial cells "ghost like," enabling easier identification.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Perineal hygiene (keep the perineal area clean and dry, avoid tight undergarments or those made of synthetic fabric), education regarding prevention, encouragement in completing the prescribed course of therapy.
Specific Measures: Medical therapy.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP028 (Vaginitis) and AP190 (Vulvovaginal Health).

Drug(s) of Choice

- Imidazoles—miconazole (Monistat) 200-mg suppositories every night at bedtime for 3 days or 2% cream 5 g every night at bedtime for 7 days; clotrimazole (Femcare, Gyne-Lotrimin, Mycelex) 100-mg inserts every night at bedtime for 7 days or 1% cream 5 g every night at bedtime for 7 days; butoconazole (Femstat) 2% cream 5 g every night at bedtime for 3 days; tioconazole (Vagistat) 6.5% ointment 4.6 g every night at bedtime.
- Triazoles—terconazole (Terazol) 80-mg suppositories every night at bedtime for 3 days or 0.8% cream 5 g every night at bedtime for 3 days or 0.4% cream 5 g every night at bedtime for 7 days; fluconazole (Diflucan) 150 mg PO single dose.

Contraindications: Known or suspected hypersensitivity or allergy. Imidazoles are contraindicated during the first trimester of pregnancy. Fluconazole is a pregnancy category C drug.
Precautions: Topical steroid preparations should be avoided. Use of oral ketoconazole requires baseline and follow-up liver function studies. Gastrointestinal side effects are common with oral therapies.
Interactions: Oral fluconazole should be used with caution in patients taking oral hypoglycemics, coumarin-type anticoagulants, phenytoin, cyclosporine, rifampin, or theophylline.

Alternative Drugs

Povidone iodine (topical), gentian violet (1%), and boric acid (600-mg capsules placed high in the vagina twice daily; can be fatal if swallowed).

FOLLOW-UP

Patient Monitoring: Normal health maintenance, frequent recurrences should suggest host compromise (eg, diabetes, human immunodeficiency virus, anemia).
Prevention/Avoidance: Good perineal hygiene, clothing and activities that allow perineal ventilation (cotton underwear, loose clothing).
Possible Complications: Vulvar excoriation caused by scratching, chronic vulvitis, secondary vaginal or vulvar infections.
Expected Outcome: A small number (<5%) of fungal infections are resistant to imidazole therapy and an increasing number of cases of fluconazole resistance have been reported. Organisms causing these infections are generally susceptible to triazoles. Approximately 30% of patients experience a recurrence of symptoms within a month (related to a continuing exposure, a change in host defenses [such as altered cellular immunity], or the ability of the fungus to burrow beneath the epithelium of the vagina).

MISCELLANEOUS

Pregnancy Considerations: Vaginal infections are associated with an increased risk of premature delivery and premature rupture of the membranes. The use of fluconazole has been associated with an increased risk of early pregnancy loss.
ICD-10-CM Codes: B37.3 (Candidiasis of vulva and vagina).

REFERENCES

LEVEL II

Javanovic R, Congema E, Nguyen H. Antifungal agents vs. boric acid for treating chronic mycotic vulvovaginitis. *J Reprod Med*. 1991;36:593.
Marchaim D, Lemanek L, Bheemreddy S, et al. Fluconazole-resistant *Candida albicans* vulvovaginitis. *Obstet Gynecol*. 2012;120:1407.
Molgaard-Nielsen D. Association between use of oral fluconazole during pregnancy and risk of spontaneous abortion and stillbirth. *JAMA*. 2016; 315:58.
Watson MC, Grimshaw JM, Bond CM, et al. Oral versus intra-vaginal imidazole and triazole anti-fungal treatment of uncomplicated vulvovaginal candidiasis (thrush). *Cochrane Database Syst Rev*. 2001;(4): CD002845.

LEVEL III

American College of Obstetricians and Gynecologists. Vaginitis. ACOG Practice Bulletin 72. *Obstet Gynecol*. 2006;107:1195.

Anderson MR, Klink K, Cohrssen A. Evaluation of vaginal complaints. *JAMA*. 2004;291:1368.

Eckert LO. Clinical practice. Acute vulvovaginitis. *N Engl J Med*. 2006;355:1244.

Marrazzo J. Vulvovaginal candidiasis. *BMJ*. 2002;325:586.

Mitchell H. Vaginal discharge—Causes, diagnosis, and treatment. *BMJ*. 2004;328:1306.

Pappas PG, Kauffman CA, Andes D, et al. Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2009;48:503.

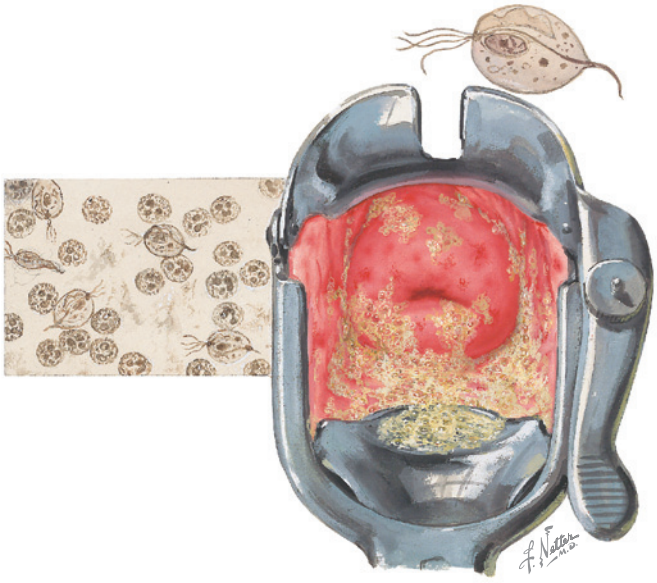


Figure 112.1 *Trichomonas vaginalis*

therapeutic levels in the urethra or perivaginal glands; therefore, the use of the gel is not recommended.

FOLLOW-UP

Patient Monitoring: Follow-up serologic testing for syphilis and human immunodeficiency virus (HIV) infection as indicated. The Centers for Disease Control and Prevention (CDC) recommends annual screening for asymptomatic colonization in HIV-infected women.

Prevention/Avoidance: Sexual monogamy, condom use for intercourse.

Possible Complications: Cystitis, urethritis, infections of Skene's or Bartholin's glands, increased risk of pelvic inflammatory disease, pelvic pain, infertility, and other sequelae of STIs.

Expected Outcome: Resistance to metronidazole is uncommon. Most treatment failures are actually caused by reinfection or failure to comply with treatment.

MISCELLANEOUS

Pregnancy Considerations: Vaginal infections are associated with an increased risk of prematurity and premature rupture of the membranes.

ICD-10-CM Codes: A59.01 (Trichomonal vulvovaginitis).

REFERENCES

LEVEL II

Forna F, Gulmezoglu AM. Interventions for treating trichomoniasis in women. *Cochrane Database Syst Rev*. 2003;(2):CD000218.

Gülmezoglu AM, Azhar M. Interventions for trichomoniasis in pregnancy. *Cochrane Database Syst Rev*. 2011;(5):CD000220.

Okun N, Gronau KA, Hannah ME. Antibiotics for bacterial vaginosis or *Trichomonas vaginalis* in pregnancy: a systematic review. *Obstet Gynecol*. 2005;105:857.

LEVEL III

American College of Obstetricians and Gynecologists. Vaginitis. ACOG Practice Bulletin 72. *Obstet Gynecol*. 2006;107:1195.

Anderson MR, Klink K, Cohrssen A. Evaluation of vaginal complaints. *JAMA*. 2004;291:1368.

Eckert LO. Clinical practice. Acute vulvovaginitis. *N Engl J Med*. 2006; 355:1244.

Kissinger P. Epidemiology and treatment of trichomoniasis. *Curr Infect Dis Rep*. 2015;17:484.

Mitchell H. Vaginal discharge—Causes, diagnosis, and treatment. *BMJ*. 2004;328:1306.

Workowski KA, Bolan GA. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015;64:1.

SECTION VII

Cervical Disease

This page intentionally left blank

ABNORMAL PAP SMEAR: ATYPICAL SQUAMOUS OR GLANDULAR CELLS OF UNDETERMINED ORIGIN

113

INTRODUCTION

Description: One of the most perplexing aspects of management under the Bethesda reporting system is how to interpret smears reported as showing atypical squamous or glandular cells (ASCUS, ASCH, or AGC). The atypical squamous cell (ASC) diagnosis has been developed to describe squamous cell changes that are more severe than reactive changes but not as marked as those found in squamous intraepithelial lesions (SIL, high and low grade). The ACS designation has been subdivided into "atypical squamous cells of undetermined significance" (ASCUS) and "atypical squamous cells cannot exclude HSIL" (ASCH). The latter includes the cytologic changes suggestive of HSIL but insufficient for a definitive diagnosis. The category of atypical glandular cells (AGC) includes a range of findings from benign reactive changes in endocervical or endometrial cells to adenocarcinoma.

Prevalence: ASC—approximately 3%–5% of all Pap tests; AGC—0.2%–0.4% of all Pap tests.

Predominant Age: Reproductive age.

Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: If not all, most of the changes seen result from infection by the human papillomavirus (HPV). The AGC diagnosis reflects benign reactive changes in endocervical or endometrial cells, endometrial hyperplasia, or adenocarcinoma.

Risk Factors: ASC—exposure to HPV. AGC—none known, except for those affecting possible pathologic causes (eg, unopposed estrogen therapy as a risk factor for endometrial carcinoma).

SIGNS AND SYMPTOMS

- Asymptomatic

DIAGNOSTIC APPROACH

Differential Diagnosis

- ASC—inflammatory change (cervicitis)
  - Low-grade squamous intraepithelial lesion (LGSIL) change
- AGC—benign reactive changes in endocervical or endometrial cells
  - Endometrial hyperplasia or adenocarcinoma
  - Endometritis secondary to an intrauterine contraceptive device
  - Tuberculous endometritis
  - Tubal carcinoma

Associated Conditions: ASC—HPV infection, vaginitis, cervicitis. AGC—dysfunctional uterine bleeding (may be present but is most often absent).

Workup and Evaluation

Laboratory: No evaluation indicated.

Imaging: No imaging indicated.

Special Tests: HPV serotyping followed by colposcopy if high-risk subtypes are found. In adolescents with high-risk subtypes, a repeat Pap test in 12 months or high-risk HPV test alone in 12 months is an acceptable alternative. If low-risk serotypes are the only finding, a repeat cervical cytology (Pap test) should be performed in 12 months. Ultrasonography (including sonohysterography using saline infusion into the uterine cavity) may be considered for the evaluation of Pap test results classified as AGC.

Diagnostic Procedures: Colposcopy, with or without cervical biopsy and endocervical curettage, should be considered if high-risk HPV serotypes are identified, high-risk factors are present, or the abnormality is persistent or recurrent. Endocervical or endometrial biopsy and/or hysteroscopy may be indicated for AGC results because between 9% and 38% of patients will have significant neoplasia eventually found (varying with age).

Pathologic Findings

Minimal gross findings, mildly elevated numbers of nucleated squamous cells with varying degrees of maturation when ASC is present.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation of comments made by the cytopathologist. Increased frequency of Pap tests until the abnormality is resolved or further diagnosis is established (for a follow-up Pap test result to be "negative," it must have normal or benign findings, but it also must be "satisfactory for interpretation").

Specific Measures: Treatment of infection or inflammation (if present). Treatment of atrophic change (if present). If the cytology report accompanying the AGC test indicates a probability of carcinoma, the endocervical canal and endometrial cavity should be evaluated. Cone biopsy, hysteroscopy, or both may be required to adequately evaluate these patients.

Diet: No specific dietary changes indicated.

Activity: No restriction.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP085 (Cervical Cancer Screening), AP135 (Colposcopy), AP163 (Cervical Cancer), and AP187 (Abnormal Cervical Cancer Screening Test Results).

Drug(s) of Choice

Based on specific indications.

FOLLOW-UP

Patient Monitoring: Normal health maintenance, increased frequency of Pap tests. If only low-risk serotypes are found, normal schedules for cervical cytology may be followed.

Prevention/Avoidance: Avoidance of HPV infection (ASC).

Possible Complications: Progression to more severe squamous abnormalities or occult disease unless a diagnosis is established and treatment is instituted. Data suggest that for adolescents, virtually all ASC- and low-grade HPV-mediated changes are transitory and that regression to normal is to be expected without intervention.

Expected Outcome: Most patients with ASC experience a spontaneous return to normal, as seen if their Pap tests are closely followed (the average length of detectable HPV is 13 months; >90% will clear the infection within 24 months). When a treatable condition is identified, this response rate is even better.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. The likelihood of significant pathologic changes with ASC abnormalities is small

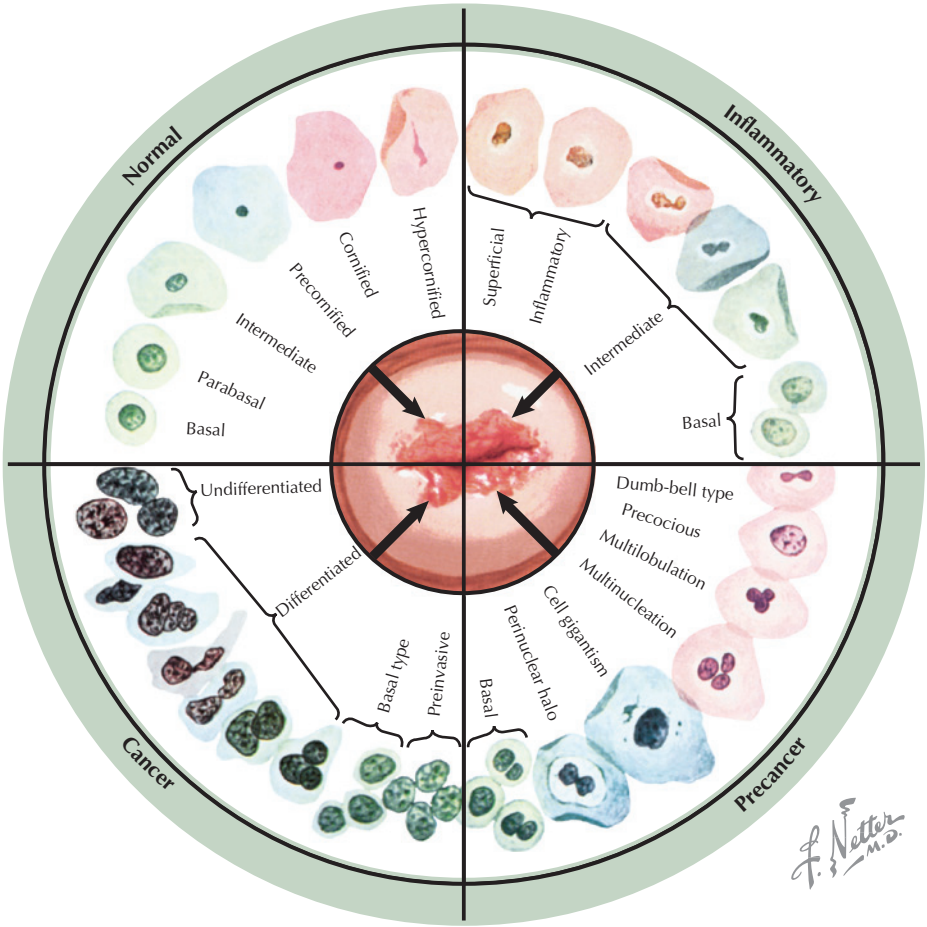


Figure 113.1 Cervical cell pathology in squamous tissue

enough that no proscription against pregnancy during the evaluation process is necessary. Although the possibility of significant complications is small in AGC, the underlying causes may be of sufficient concern to delay pregnancy until a diagnosis is established.

ICD-10-CM Codes: R87.610 (Atypical squamous cells of undetermined significance on cytologic smear of cervix), ASC-US, N87.9 (Dysplasia of cervix uteri, unspecified), and N87.619 (Unspecified abnormal cytological findings in specimens from cervix uteri [ACGUS]).

REFERENCES

LEVEL I

ASCUS-LSIL Triage Study (ALTS) Group. Results of a randomized trial on the management of cytology interpretations of atypical squamous cells of undetermined significance. *Am J Obstet Gynecol*. 2003;188:1383.

ASCUS-LSIL Triage Study (ALTS) Group. A randomized trial on the management of low-grade squamous intraepithelial lesion cytology interpretations. *Am J Obstet Gynecol*. 2003;188:1393.

LEVEL II

Castle PE, Fetterman B, Poitras N, et al. Relationship of atypical glandular cell cytology, age, and human papillomavirus detection to cervical and endometrial cancer risks. *Obstet Gynecol*. 2010;115:243.

Khan MJ, Castle PE, Lorincz AT, et al. The elevated 10-year risk of cervical precancer and cancer in women with human papillomavirus (HPV) type 16 or 18 and the possible utility of type-specific HPV testing in clinical practice. *J Natl Cancer Inst*. 2005;97:1072.

Levi AW, Kelly DP, Rosenthal DL, et al. Atypical squamous cells of undetermined significance in liquid-based cytologic specimens: results of reflex human papillomavirus testing and histologic follow-up in routine practice with comparison of interpretive and probabilistic reporting methods. *Cancer*. 2003;99:191.

Stoler MH, Wright TC Jr, Sharma A, et al. High-risk human papillomavirus testing in women with ASC-US cytology: results from the ATHENA HPV study. ATHENA (Addressing THE Need for Advanced HPV Diagnostics) HPV Study Group. *Am J Clin Pathol*. 2011;135:468.

LEVEL III

American College of Obstetricians and Gynecologists. Cervical cancer screening and prevention. Practice Bulletin No. 157. *Obstet Gynecol*. 2016;127:e1.

American College of Obstetricians and Gynecologists. Management of abnormal cervical cancer screening test results and cervical cancer precursors. Practice Bulletin No. 140. *Obstet Gynecol*. 2013;122:1338.

American College of Obstetricians and Gynecologists. Reproductive health care for adolescents with human immunodeficiency virus. Committee Opinion No. 572. *Obstet Gynecol*. 2013;122:721.

Dehn D, Torkko KC, Shroyer KR. Human papillomavirus testing and molecular markers of cervical dysplasia and carcinoma. *Cancer*. 2007;111:1.

Klinkhamer PJ, Meerding WJ, Rosier PF, et al. Liquid-based cervical cytology. *Cancer*. 2003;99:263.

Safaeian M, Solomon D, Wacholder S, et al. Risk of precancer and follow-up management strategies for women with human papillomavirus-negative atypical squamous cells of undetermined significance. *Obstet Gynecol*. 2007;109:1325.

ABNORMAL PAP SMEAR: LOW-GRADE SQUAMOUS INTRAEPITHELIAL LESIONS AND HIGH-GRADE SQUAMOUS INTRAEPITHELIAL LESIONS

114

INTRODUCTION

Description: Low-grade squamous intraepithelial lesions (LGSILs) encompass changes associated with human papillomavirus (HPV), mild dysplasia, and cervical intraepithelial neoplasia (CIN) I. High-grade squamous intraepithelial lesions (HGSILs) include CIN II and III and carcinoma in situ (CIS).
Prevalence: Less than 5% of Pap tests for low-grade abnormalities and 2% for high-grade abnormalities.
Predominant Age: Reproductive age.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: HPV appears to be responsible for the development of cervical dysplasia. Although as many as 70% of invasive cervical cancers have HPV serotypes 16 or 18 present, these types may also be detected in patients with LGSILs. Normal patients have HPV prevalence rates that vary from 10% to 50%, depending on the study technique and population evaluated.
Risk Factors: Exposure to HPV and other sexually transmitted infections (STIs); smoking is associated with a higher risk.

SIGNS AND SYMPTOMS

- Asymptomatic

DIAGNOSTIC APPROACH

Differential Diagnosis

- LGSILs—inflammatory change (cervicitis)
  - Cervical carcinoma
- HGSILs—cervical CIS
  - Invasive cervical carcinoma

Associated Conditions: HPV infection, vaginitis, cervicitis, cervical dysplasia, carcinoma in situ, invasive carcinoma of the cervix, endocervical adenocarcinoma.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated.
Special Tests: Cotesting, combining traditional cytology with HPV detection and reflex serotyping, has become widely accepted for women in the early to mid-reproductive years.
Diagnostic Procedures: For many patients with LGSILs, colposcopy, colposcopically directed biopsy, and endocervical curettage are appropriate to establish the source of the cytologic abnormality. For compliant adolescents, a repeat Pap test in 12 months or high-risk HPV test alone in 12 months is an acceptable alternative. If colposcopy is inadequate to delineate lesions present or the entire transformation zone cannot be seen, diagnostic conization may be needed. Colposcopy, colposcopically directed biopsy, and endocervical curettage should be used to evaluate all patients with HGSILs.

Pathologic Findings

Acetowhite areas on colposcopy, early vascular changes leading to mosaicism and punctation. Microscopic—loss of normal maturation, increased nuclear/cytoplasmic ratio, nuclear atypia (mild). Vascular changes leading to mosaicism and punctation (severe) are more typical of HGSILs. Nuclear atypia (moderate to severe) is also a feature of HGSILs.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation of comments made by the cytopathologist. Increased frequency of Pap tests until the abnormality is resolved or further diagnosis is established (for a follow-up Pap test to be "negative," it must have normal or benign findings, but it also must be "satisfactory for interpretation").
Specific Measures: Compliant patients with LGSILs and who have low-risk HPV serotypes may be followed by serial Pap tests. For those with no serotyping or high-risk types, colposcopy is indicated. If colposcopy is adequate and the histologic abnormality found is mild, obtaining follow-up Pap tests at 6-month intervals for 2 years or three normal tests is suitable. When HGSILs are present, the evaluation determines therapy: cryotherapy, electrocautery, electrosurgical loop excision, laser ablation, or conization. Treatment must be based on an accurate diagnosis and the extent of the lesion involved. Treatment of CIN 1 in women younger than 21 years is not recommended, even if the lesion persists. Virtually all are manifestations of a transient HPV infection and will resolve, although complete resolution may take up to 36 months.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP085 (Cervical Cancer Screening), AP135 (Colposcopy), AP163 (Cervical Cancer), and AP187 (Abnormal Cervical Cancer Screening Test Results).

Drug(s) of Choice

Based on specific indications, most therapy is surgical or ablative in nature.

FOLLOW-UP

Patient Monitoring: Normal health maintenance, increased frequency of Pap tests.
Prevention/Avoidance: Avoidance of HPV infection.
Possible Complications: Progression to more severe squamous abnormalities. Data suggest that for adolescents, virtually all atypical squamous cells of undetermined significance (ASCUS) and low-grade HPV-mediated changes are transitory and that regression to normal is to be expected without intervention.
Expected Outcome: Of patients with these findings, 60% or more undergo spontaneous regression of the underlying process, resulting in a return to normal Pap test results. Only 15% of patients with LGSILs progress to HGSILs. HGSIL abnormalities are more likely to progress and warrant more aggressive evaluation and treatment.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. Because of the potential significance of the HGSIL abnormality and pathologic conditions that cause it, a delay in pregnancy while evaluation is ongoing may be advisable.

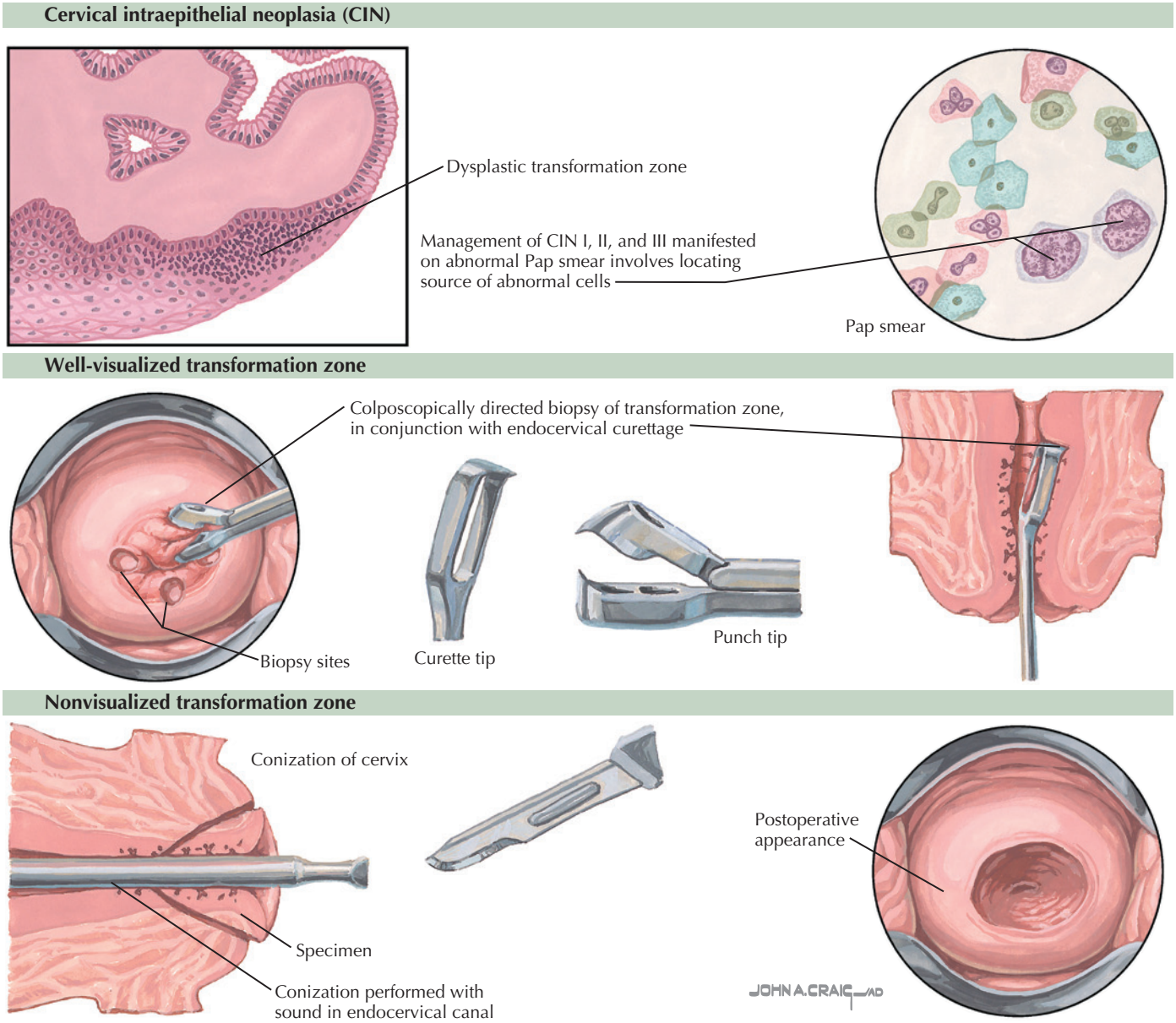


Figure 114.1 Abmormal pap smear: cervical intraepithelial neoplasia and transformation zones

ICD-10-CM Codes: N87.0 (Mild cervical dysplasia), N87.9 (Dysplasia of cervix uteri, unspecified, D06.9 (Carcinoma in situ of cervix, unspecified).

REFERENCES

LEVEL I

Brewster WR, Hubbell FA, Largent J, et al. Feasibility of management of high-grade cervical lesions in a single visit: a randomized controlled trial. *JAMA*. 2005;294:2182.

LEVEL II

Dehn D, Torkko KC, Shroyer KR. Human papillomavirus testing and molecular markers of cervical dysplasia and carcinoma. *Cancer*. 2007; 111:1.

Khan MJ, Castle PE, Lorincz AT, et al. The elevated 10-year risk of cervical precancer and cancer in women with human papillomavirus (HPV) type 16 or 18 and the possible utility of type-specific HPV testing in clinical practice. *J Natl Cancer Inst*. 2005;97:1072.

LEVEL III

American College of Obstetricians and Gynecologists. Cervical cancer screening and prevention. Practice Bulletin No. 157. *Obstet Gynecol*. 2016;127:e1.

American College of Obstetricians and Gynecologists. Management of abnormal cervical cancer screening test results and cervical cancer precursors. Practice Bulletin No. 140. *Obstet Gynecol*. 2013;122:1338.

American College of Obstetricians and Gynecologists. Reproductive health care for adolescents with human immunodeficiency virus. Committee Opinion No. 572. *Obstet Gynecol*. 2013;122:721.

Dehn D, Torkko KC, Shroyer KR. Human papillomavirus testing and molecular markers of cervical dysplasia and carcinoma. *Cancer*. 2007;111:1.

Massad LS, Einstein MH, Huh WK, et al. 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. 2012 ASCCP Consensus Guidelines Conference. *J Low Genit Tract Dis*. 2013;17:S1.

CARCINOMA IN SITU (CERVIX)

115

INTRODUCTION

Description: Carcinoma in situ of the cervix is characterized by morphologic alteration of the cervical epithelium in which the full thickness of the epithelium is replaced with dysplastic cells (cervical intraepithelial neoplasia [CIN] III). This change is generally associated either spatially or temporally with invasive carcinoma.
Prevalence: Less than 2% of Pap tests.
Predominant Age: Early 30s (approximate peak age, 32 years).
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Linked to some serotypes of human papillomavirus (HPV; 99.7% of cancers contain high-risk HPV serotypes).
Risk Factors: Infection by HPV, herpes virus, or cytomegalovirus; early sexual activity; multiple sexual partners; cigarette smoking (1.5 times risk); oral contraceptive use (two to four times risk); early childbearing; intrauterine diethylstilbestrol exposure; immunosuppression.

SIGNS AND SYMPTOMS

- Asymptomatic
- Abnormal cervical cytology
- Abnormal colposcopy

DIAGNOSTIC APPROACH

Differential Diagnosis

- Moderate dysplasia
- Microinvasive and invasive carcinoma

Associated Conditions: HPV infection, condyloma acuminata.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated.
Special Tests: Colposcopy, colposcopically directed biopsy, and endocervical curettage.
Diagnostic Procedures: Cervical cytologic examination, colposcopy, and biopsy.

Pathologic Findings

The entire thickness of the epithelium is replaced with abnormal (dysplastic) cells, but there is no invasion of the underlying stroma.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation of comments made by the cytopathologist.
Specific Measures: Cervical conization and endocervical curettage to confirm the absence of invasion or a more extensive lesion. In those wishing to preserve fertility, this may be curative; in others, standard hysterectomy may be considered. Ablative therapy can be considered only when the entire lesion is visible and invasion has been ruled out.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP085 (Cervical Cancer Screening), AP135 (Colposcopy), AP163 (Cervical Cancer), AP187 (Abnormal Cervical Cancer Screening Test Results), and AP110 (Loop Electrosurgical Excision Procedure).

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Follow-up cervical cytologic examination at 6 and 12 months or high-risk HPV test at 12 months, colposcopy for any abnormality.
Prevention/Avoidance: Reduction or avoidance of known risk factors.
Possible Complications: Advancement of disease or recurrence. Untreated disease is anticipated to progress to invasive carcinoma over the course of 12–86 months in 15%–40% of patients.
Expected Outcome: Low recurrence rates (<10%) for most therapies. When recurrence is found, 75% occur in 21 months.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. The presence of pregnancy complicates both the diagnosis and treatment:

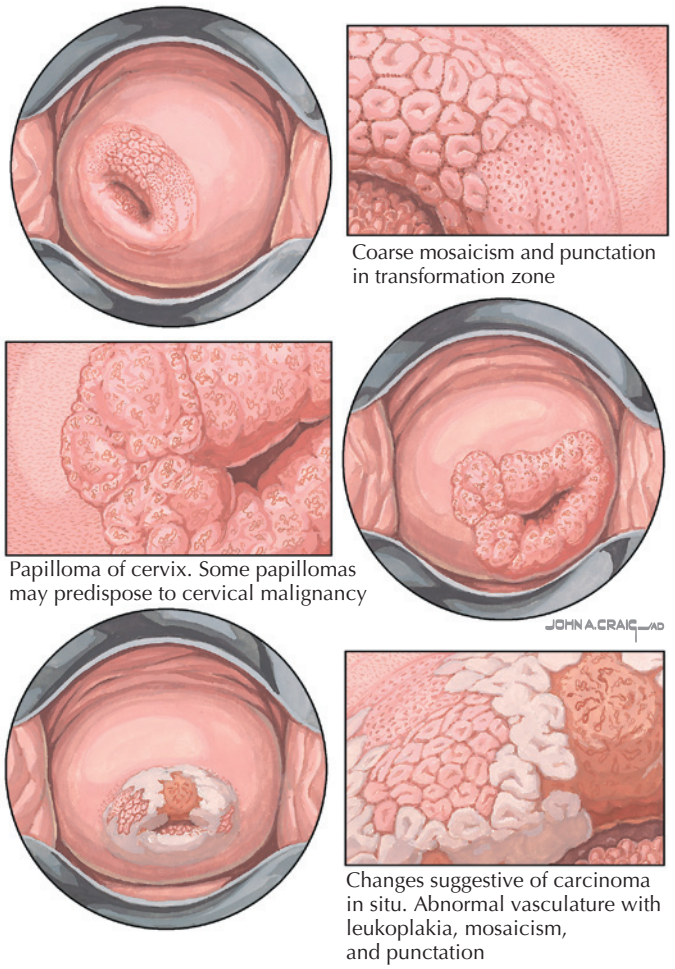


Figure 115.1 Colposcopic views of abnormal cervical changes

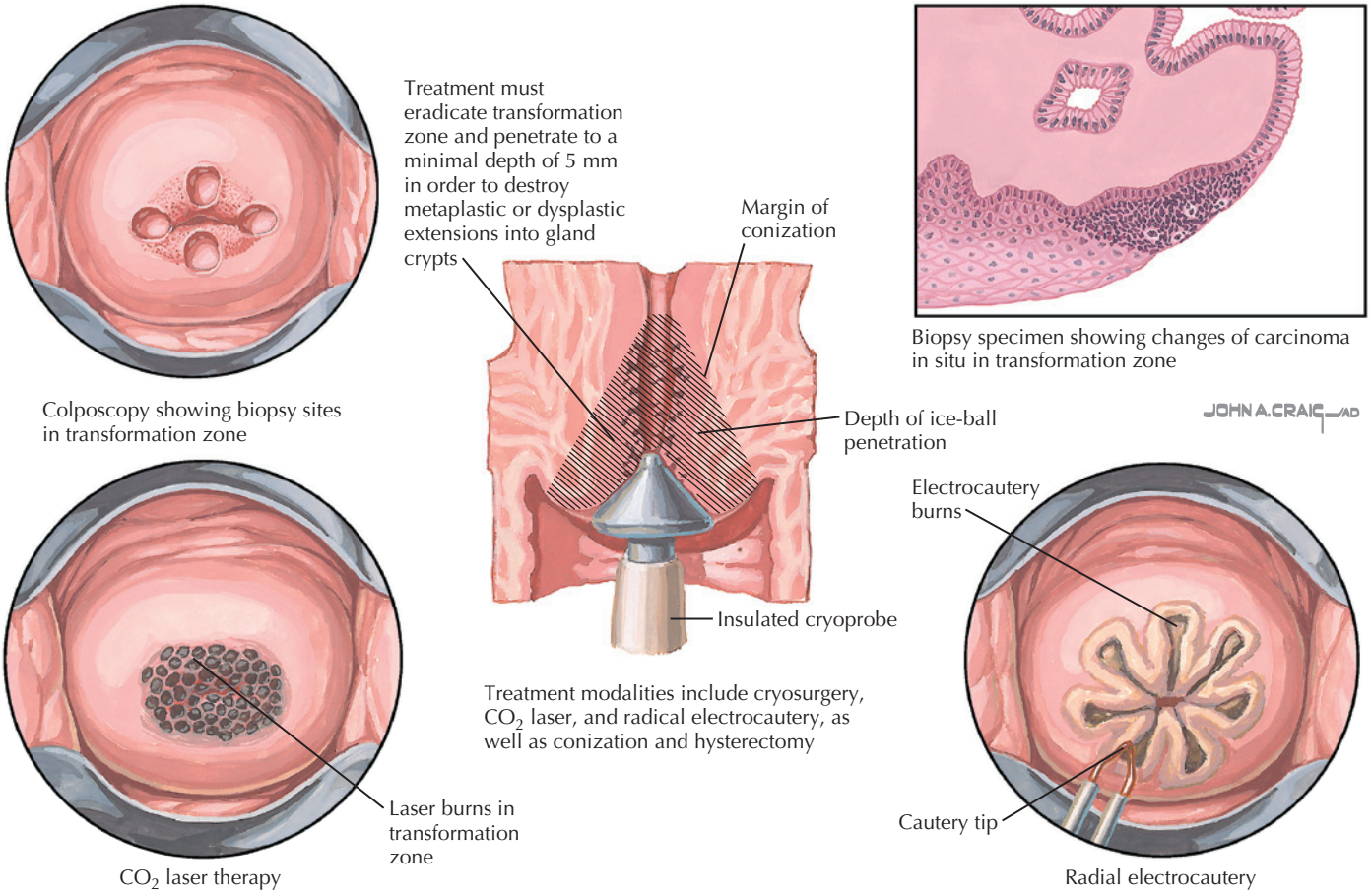


Figure 115.2 Management of carcinoma in situ (CIN III)

endocervical curettage is generally omitted and definitive therapy is delayed until after delivery; colposcopy is usually repeated every 6–10 weeks until term. In the absence of invasion, vaginal delivery is appropriate.

ICD-10-CM Codes: D06.9 (Carcinoma in situ of cervix, unspecified).

REFERENCES

LEVEL II

An HJ, Cho NH, Lee SY, et al. Correlation of cervical carcinoma and precancerous lesions with human papillomavirus (HPV) genotypes detected with the HPV DNA chip microarray method. *Cancer*. 2003; 97:1672.

Coupe VM, Berkhof J, Verheijen RH, et al. Cost-effectiveness of human papillomavirus testing after treatment for cervical intraepithelial neoplasia. *BJOG*. 2007;114:416.

de Sanjose S, Quint WG, Alemany L, et al. Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. Retrospective International Survey and HPV Time Trends Study Group. *Lancet Oncol*. 2010;11:1048.

LEVEL III

Massad LS, Einstein MH, Huh WK, et al. 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. 2012 ASCCP Consensus Guidelines Conference. *J Low Genit Tract Dis*. 2013;17:S1.

Walboomers JM, Jacobs MV, Manos MM, et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. *J Pathol*. 1999; 189:12.

CERVICAL CANCER

116

INTRODUCTION

Description: Almost all cancers of the cervix are carcinomas—85%–90% are squamous carcinoma and 10%–15% are adenocarcinoma.
Prevalence: 12,042 cases and 4074 deaths annually (2012 data). Lifetime risk: 1 in 135.
Predominant Age: 40s–60s; median age is 52 years.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Strongly linked to some serotypes of human papillomavirus (HPV; 99.7% of all cancers have oncogenic HPV DNA detectable) and is associated with early sexual activity and multiple partners.
Risk Factors: Early sexual activity, multiple sexual partners, HPV, African-American race, smoking, immunocompromised, minimal or neglected medical care (Pap test screening) associated with advanced disease.

SIGNS AND SYMPTOMS

- None until late in the disease
- Abnormal Pap test result
- Late: vaginal bleeding, dark vaginal discharge, postcoital bleeding, ureteral obstruction, back pain, loss of appetite, weight loss
- Exophytic, friable, bleeding lesion
- Late: supraclavicular or inguinal lymph nodes, leg swelling, ascites, pleural effusion, hepatomegaly

DIAGNOSTIC APPROACH

Differential Diagnosis

- Cervical eversion
- Cervical erosion
- Cervical polyp
- Condyloma acuminata
- Nabothian cyst

Associated Conditions: HPV, condyloma acuminata, abnormal vaginal bleeding.

Workup and Evaluation

Laboratory: An assessment of renal function is appropriate if ureteral compromise is suspected (advanced disease).
Imaging: Chest radiograph, intravenous pyelogram, and computed tomography (CT) or magnetic resonance imaging (MRI) are used to assess the extent of disease and to assist in staging. MRI has displaced other imaging modalities because of its ability to assess lymph nodes (72%–93% accuracy) and possible tumor spread. Staging is clinical and primarily relies on clinical examination and the status of the ureters.
Special Tests: Colposcopy and cervical biopsy (conization preferred), biopsy of vaginal or paracervical tissues may be required to assess extent of disease.
Diagnostic Procedures: History, physical examination, and histologic diagnosis. Barium enema, flexible sigmoidoscopy or cystoscopy (or both) may be performed in the cases of large tumors or for those who may undergo radiotherapy.

Pathologic Findings

Squamous cell carcinomas (large cell [keratinizing or nonkeratinizing], small cell, verrucous), adenocarcinoma (endocervical, endometrioid, clear cell, adenoid cystic, adenoma malignum), mixed carcinomas (adenosquamous, glassy cell).

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Timely evaluation and treatment.
Specific Measures: Therapy is based on the stage of the disease. Radical surgery is used for select patients with stages I and II disease. Radiotherapy (brachytherapy, teletherapy) is used for stages IB and IIA disease or greater. Postoperative radiotherapy reduces the risk of recurrence by almost 50%.
Diet: No specific dietary changes indicated.
Activity: No restriction except those imposed by therapies.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP163 (Cervical Cancer Screening), AP135 (Colposcopy), AP187 (Abnormal Cervical Cancer Screening Test Results), and AP110 (Loop Electrosurgical Excision Procedure), AP080 (Preparing for Surgery).

Drug(s) of Choice

Chemotherapy does not produce long-term cures, but response rates of up to 50% have been obtained with multiagent combinations (cisplatin, doxorubicin, and etoposide; other combinations have also been successful).

FOLLOW-UP

Patient Monitoring: Normal health maintenance, 90% of recurrences occur in the first 5 years.
Prevention/Avoidance: None. Adherence to screening guidelines enables diagnosis and treatment of premalignant changes.
Possible Complications: Risk of nodal involvement is based on the stage of the disease—pelvic nodes: stage I, 15%; stage II, 29%; stage III, 47%; para-aortic nodes: stage I, 6%; stage II, 19%; stage III, 33%.
Expected Outcome: Survival is based on the stage of the disease—stage IA, 99% at 5 years; stage IB, 85%–90%; stage IIA, 73%–80%; stage IIB, 68%; stage IIIA, 45%; stage IIIB, 36%; stage IVA, 15%; stage IVB, 2%. One-third of patients develop recurrences, half within 3 years after primary therapy (best prognosis for later recurrences). Short-term serious complications will occur in 1%–5% of surgical cases.

MISCELLANEOUS

Pregnancy Considerations: Rare in pregnancy. Pregnancy and vaginal delivery do not appear to alter the course of disease, although delivery is associated with hemorrhage. Early stages diagnosed late in pregnancy may be watched until after delivery. Advanced disease may require early delivery or interruption of pregnancy to allow aggressive therapy to begin.
ICD-10-CM Codes: C53.9 (Malignant neoplasm of cervix uteri, unspecified).

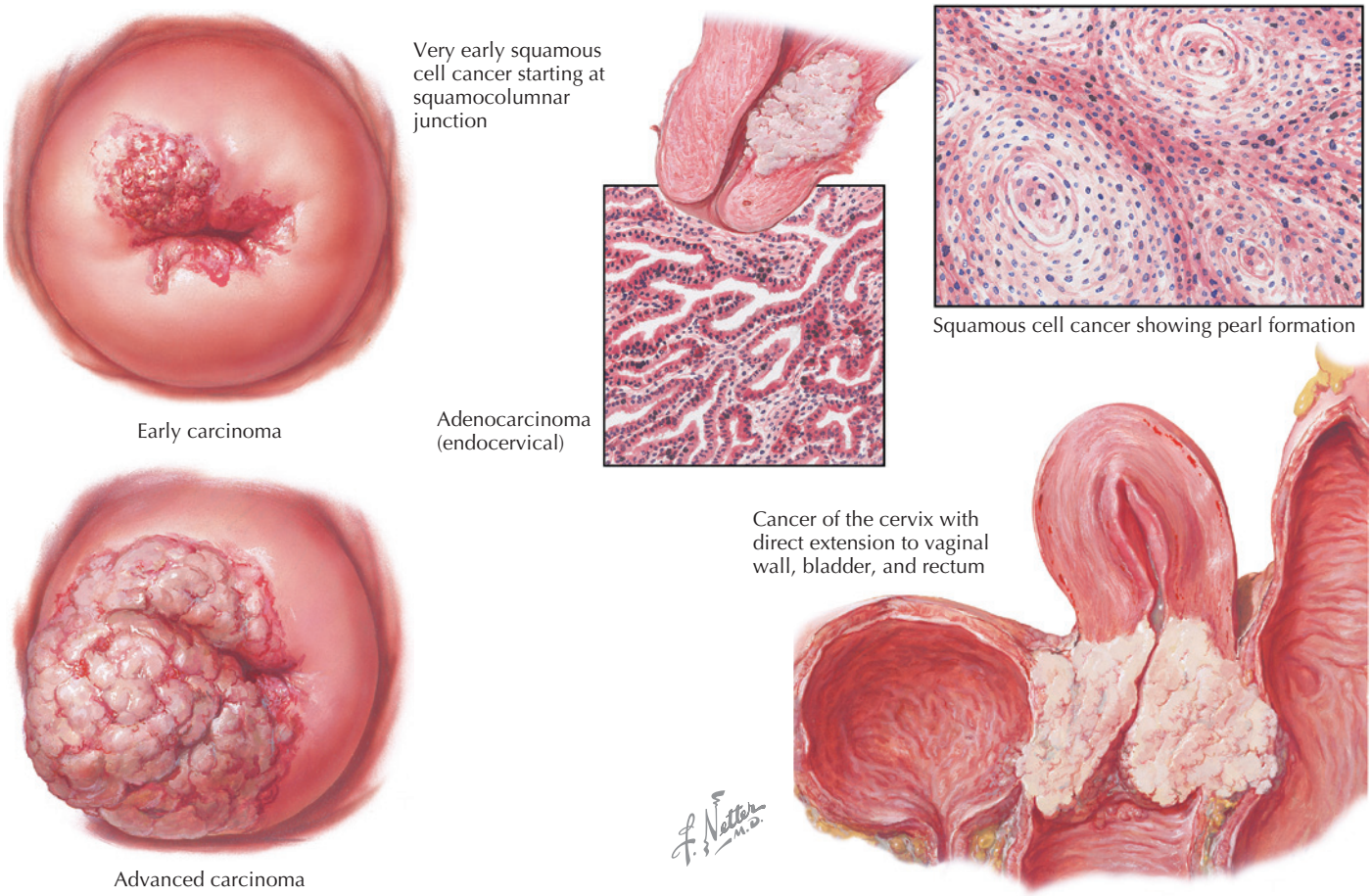


Figure 116.1 Early and advanced carcinoma

REFERENCES

LEVEL II

Bansal N, Herzog TJ, Shaw RE, et al. Primary therapy for early-stage cervical cancer: radical hysterectomy vs radiation. *Am J Obstet Gynecol*. 2009; 201:485.e1.

Dayes IS, Abuzallouf S. Local tumour control in women with carcinoma of the cervix treated with the addition of nitroimidazole agents to radiotherapy: a meta-analysis. *Br J Radiol*. 2005;78:777.

Katki HA, Gage JC, Schiffman M, et al. Follow-up testing after colposcopy: five-year risk of CIN 2+ after a colposcopic diagnosis of CIN 1 or less. *J Low Genit Tract Dis*. 2013;17:S69.

Khan MJ, Castle PE, Lorincz AT, et al. The elevated 10-year risk of cervical precancer and cancer in women with human papillomavirus (HPV) type 16 or 18 and the possible utility of type-specific HPV testing in clinical practice. *J Natl Cancer Inst*. 2005;97:1072.

Rogers L, Siu SS, Luesley D, et al. Radiotherapy and chemoradiation after surgery for early cervical cancer. *Cochrane Database Syst Rev*. 2012; (5):CD007583.

Westermann AM, Jones EL, Schem BC, et al. First results of triple-modality treatment combining radiotherapy, chemotherapy, and hyperthermia for the treatment of patients with stage IIB, III, and IVA cervical carcinoma. *Cancer*. 2005;104:763.

LEVEL III

Akin O, Mironov S, Pandit-Taskar N, et al. Imaging of uterine cancer. *Radiol Clin North Am*. 2007;45:167.

American College of Obstetricians and Gynecologists. Management of abnormal cervical cancer screening test results and cervical cancer precursors. Practice Bulletin No. 140. *Obstet Gynecol*. 2013;122:1338.

Basen-Engquist K, Paskett ED, Buzaglo J, et al. Cervical cancer. *Cancer*. 2003;98:2009.

Farthing A. Conserving fertility in the management of gynaecological cancers. *BJOG*. 2006;113:129.

Fielding JR. MR imaging of the female pelvis. *Radiol Clin North Am*. 2003;41:179.

Kumar R, Alavi A. PET imaging in gynecologic malignancies. *Radiol Clin North Am*. 2004;42:1155, ix.

Moore DH. Cervical cancer. *Obstet Gynecol*. 2006;107:1152.

Pannu HK, Fishman EK. Evaluation of cervical cancer by computed tomography: current status. *Cancer*. 2003;98:2039.

Schiffman M, Castle PE. The promise of global cervical-cancer prevention. *N Engl J Med*. 2005;353:2101.

Schiffman M, Castle PE. When to test women for human papillomavirus. *BMJ*. 2006;332:61.

Stewart AJ, Viswanathan AN. Current controversies in high-dose-rate versus low-dose-rate brachytherapy for cervical cancer. *Cancer*. 2006;107: 908.

Waggoner SE. Cervical cancer. *Lancet*. 2003;361:2217.

Wolf JK, Franco EL, Arbeit JM, et al. Innovations in understanding the biology of cervical cancer. *Cancer*. 2003;98:2064.

CERVICAL EROSION

INTRODUCTION

Description: Cervical erosion is the loss of the epithelial surface on the vaginal portion of the cervix, resulting in the exposure of the underlying cervical stroma. Cervical eversion (exposing the dark-red columnar epithelium of the endocervix, ectropion) is often mistaken for or incorrectly labeled as cervical erosion.
Prevalence: Uncommon. Ectropion is common in adolescents, pregnant patients, and those using combination oral contraceptives.
Predominant Age: Reproductive age.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Generally traumatic. May occur through sexual trauma (fingernail, sexual appliances), iatrogenic process (diaphragm, pessary, biopsy, or other instrumentation), tampon use, or pelvic organ prolapse, resulting in the exposure of the cervix outside the introitus.
Risk Factors: None known.

SIGNS AND SYMPTOMS

- Irregularly shaped, depressed lesion with a red base and sharp borders
- Bleeding generally absent, although tissues may bleed when touched, resulting in postcoital spotting
- Increased mucoid (clear) discharge may be present

DIAGNOSTIC APPROACH

Differential Diagnosis

- Cervical eversion (ectopy)
- Herpes simplex cervicitis
- Carcinoma under the surface of the epithelium (barrel lesion)
- Syphilis (primary lesion)
- Chronic cervicitis
- Cervical polyp
- *Chlamydia trachomatis* infection

Associated Conditions: Chronic cervicitis.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated.
Special Tests: Colposcopy can be used to confirm the diagnosis but is seldom indicated.
Diagnostic Procedures: Inspection of the cervix.

Pathologic Findings

Loss of surface epithelium. Evidence of inflammation is often present during the healing phase.

MANAGEMENT AND THERAPY

Nonpharmacologic

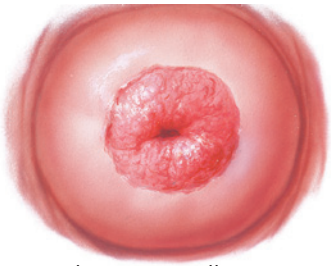
General Measures: Evaluation and reassurance.
Specific Measures: The use of acidifying agents and topical antibiotics is controversial and generally not necessary. Ablative or other measures aimed at reversing an ectropion carry the risk of cervical stenosis and should be avoided.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance.

Drug(s) of Choice

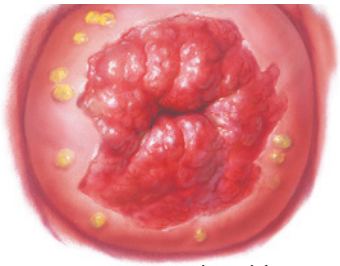
None

FOLLOW-UP

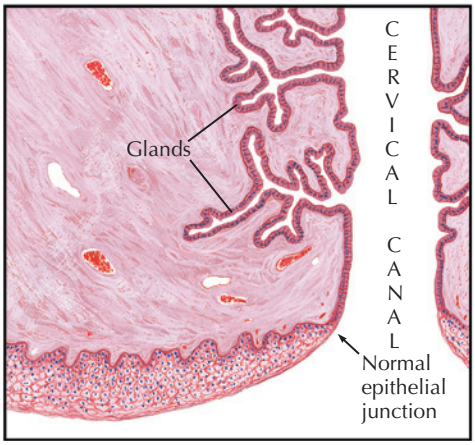
Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.



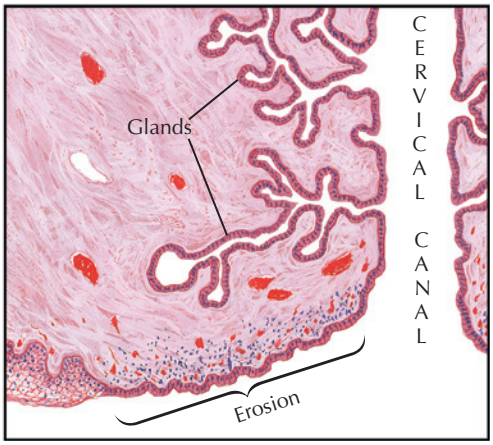
Congenital erosion in nulliparous cervix



Extensive erosion with proliferation (papillary erosion); also nabothian cysts



Section through normal portio vaginalis (schematic)



Section through portio vaginalis showing erosion (schematic)

F. Netter M.D.

Figure 117.1 Congenital and extensive cervical erosion

Possible Complications: Both overdiagnosis and underdiagnosis; treatment and intervention are generally not warranted and may create additional problems; failure to recognize a more sinister process (cancer) may lead to a delay in treatment.
Expected Outcome: Spontaneous and complete healing is the rule.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: N86 (Erosion and ectropion of cervix uteri) and N72 (Inflammatory disease of cervix uteri).

REFERENCES

LEVEL III

American College of Obstetricians and Gynecologists. Management of abnormal cervical cancer screening test results and cervical cancer precursors. Practice Bulletin No. 140. *Obstet Gynecol*. 2013;122:1338.

Barrett KF, Bledsoe S, Greer BE, et al. Tampon-induced vaginal or cervical ulceration. *Am J Obstet Gynecol*. 1977;127:332.

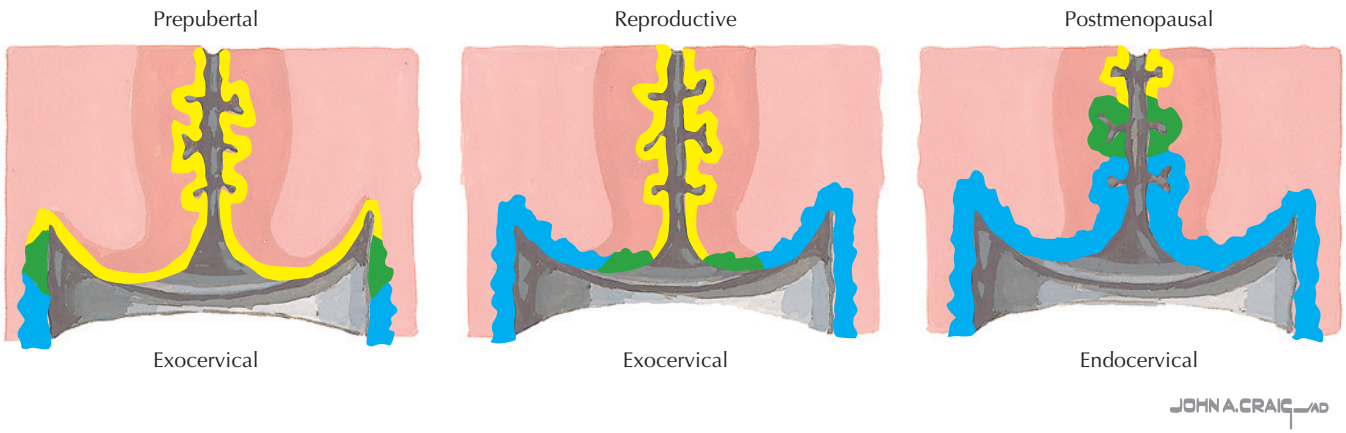


Figure 118.1 Cervical eversion: variations in location of transformation zone

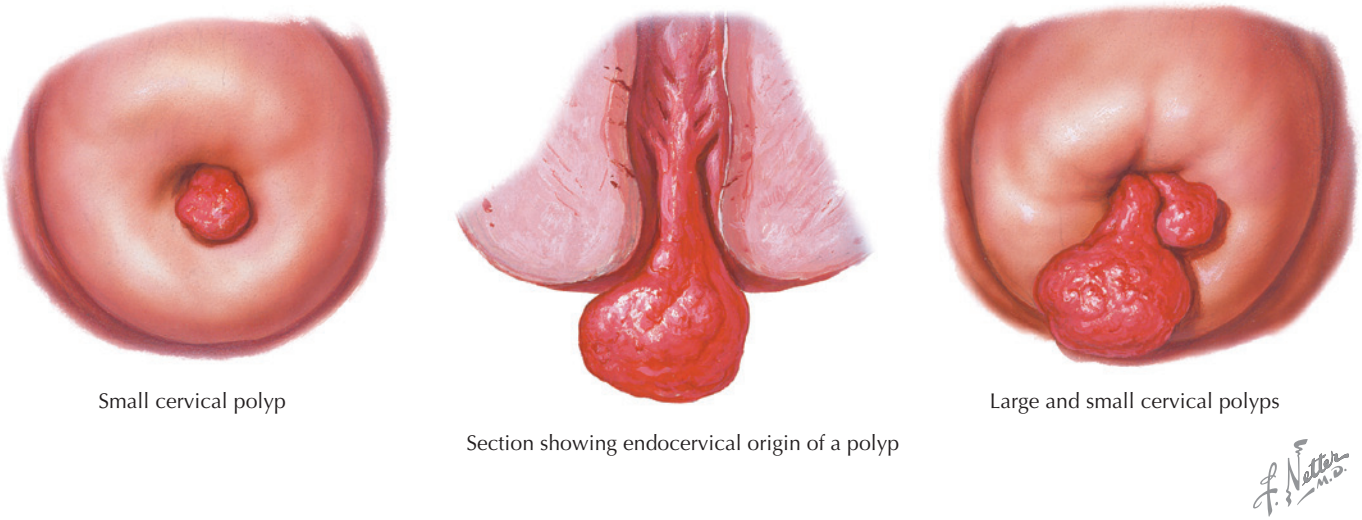


Figure 119.1 Cervical polyps

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP095 (Abnormal Uterine Bleeding).

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Normal health maintenance, no change in Pap test recommendations.
Prevention/Avoidance: None.
Possible Complications: Malignant change is extremely rare.
Expected Outcome: Excision or cautery is curative.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: N84.1 (Polyp of cervix uteri).

REFERENCES

LEVEL II

Duckman S, Suarez JR, Sese LQ. Giant cervical polyp. *Am J Obstet Gynecol*. 1988;159:852.

Kerner H, Lichtig C. Müllerian adenosarcoma presenting as cervical polyps: a report of seven cases and review of the literature. *Obstet Gynecol*. 1993;81:655.

Pradhan S, Chenoy R, O'Brien PMS. Dilatation and curettage in patients with cervical polyps: a retrospective analysis. *Br J Obstet Gynaecol*. 1995;102:415.

LEVEL III

American College of Obstetricians and Gynecologists. Diagnosis of abnormal uterine bleeding in reproductive-aged women. Practice Bulletin No. 128. *Obstet Gynecol*. 2012;120:197.

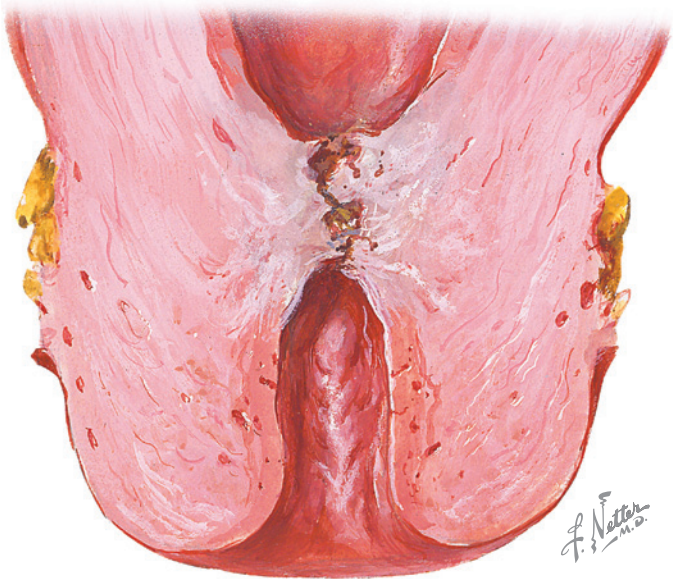


Figure 120.1 Stricture

DIAGNOSTIC APPROACH

Differential Diagnosis

- Endocervical cancer
- Endometrial cancer
- Uterine leiomyomata

Associated Conditions: Endometriosis, dysmenorrhea, chronic pelvic pain, and infertility.

Workup and Evaluation

Laboratory: Ultrasonography may demonstrate uterine enlargement or hematometra.
Imaging: No imaging indicated.
Special Tests: Inability to pass a 1- to 2-mm probe beyond the inner cervical os.
Diagnostic Procedures: History, physical examination, sounding of the endocervical canal with a small probe.

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, analgesics (nonsteroidal anti-inflammatory drugs) for dysmenorrhea.
Specific Measures: Dilation of the cervix with progressive dilators under ultrasound guidance. Placement of a cervical stent for several days after dilation has been advocated but is not universally accepted.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP062 (Dilation and Curettage [D&C]) and AP046 (Dysmenorrhea: Painful Periods).

Drug(s) of Choice

Symptomatic therapy until definitive surgical dilation.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: Care with surgical technique when cone biopsy or cautery of the cervix is used.
Possible Complications: Retrograde menstruation with the subsequent development of endometriosis, infertility, and chronic pelvic pain. In older patients, the development of hematometra or pyometra.
Expected Outcome: The risk of recurrence is small after dilation (based on causation).

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: N88.2 (Stricture and stenosis of cervix uteri) and Q51.828 (Other congenital malformations of cervix).

REFERENCES

LEVEL II

Baggish MS, Baltoyannis P. Carbon dioxide laser treatment of cervical stenosis. *Fertil Steril*. 1987;48:24.

Barbierie RL, Callery M, Perez SE. Directionality of menstrual flow: cervical os diameter as a determinant of retrograde menstruation. *Fertil Steril*. 1992;57:727.

Lin YH, Hwang JL, Huang LW, et al. Efficacy of hysteroscopic cervical resection for cervical stenosis. *J Minim Invasive Gynecol*. 2013;20:836.

Pradhan S, Chenoy R, O'Brien PMS. Dilatation and curettage in patients with cervical polyps: a retrospective analysis. *Br J Obstet Gynaecol*. 1995;102:415.

LEVEL III

Pinsonneault O, Goldstein DP. Obstructing malformations of the uterus and vagina. *Fertil Steril*. 1985;44:241.

121 CERVICITIS

INTRODUCTION

Description: Cervicitis is the inflammation (acute or chronic) of the endocervical glands or the ectocervix.
Prevalence: 10%–40% of women.
Predominant Age: Reproductive age; highest rate in adolescents to early 20s.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Endocervical—*Chlamydia trachomatis* (up to 60% of cases in some studies), *Neisseria gonorrhoeae*. Almost 50% of patients will not have an identifiable infection. Ectocervical—herpes simplex, human papillomavirus (HPV), *Mycoplasma* species (*Mycoplasma hominis, Ureaplasma urealyticum*), *Trichomonas vaginalis*.
Risk Factors: Exposure to sexually transmitted infections (STIs; multiple sexual partners), postpartum period.

SIGNS AND SYMPTOMS

- May be asymptomatic (60%)
- Mucopurulent discharge (yellow discharge with 10 or more white blood cells at magnification ×1000)
- Cervical erythema or edema, ulceration, and friability
- Deep-thrust dyspareunia

DIAGNOSTIC APPROACH

Differential Diagnosis

- Vaginitis
- Cervical neoplasia
- Cervical metaplasia
- Cervical erosion
- Cervical eversion

Associated Conditions: Cervical neoplasia, dyspareunia, postcoital bleeding, pelvic inflammatory disease, premature rupture of the membranes in pregnancy, premature labor, and prematurity.

Workup and Evaluation

Laboratory: Cervical culture, Gram stain of cervical material, enzyme-linked immunosorbent assay (ELISA), or fluorescent monoclonal antibody testing for *Chlamydia*. Consider serum testing for other STIs.
Imaging: No imaging indicated.
Special Tests: None indicated.
Diagnostic Procedures: Inspection, Gram stain, culture, ELISA, or fluorescent monoclonal antibody testing. Colposcopy may be of assistance in selected cases. Nucleic acid activation tests are the method of choice for detecting *C. trachomatis* or *N. gonorrhoeae*.

Pathologic Findings

Diffuse inflammatory changes, koilocytic changes with human papillomavirus infection. Chronic inflammatory changes are extremely common during the reproductive years and by themselves are not indicative of a pathologic state.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Diagnosis and management of causal agent.
Specific Measures: In rare patients with consistently negative cultures, cryosurgery of the cervix has been advocated, although this could result in cervical stricture or other postsurgical complications.
Diet: No specific dietary changes indicated.
Activity: No restriction. Sexual continence for 7 days after a single-day therapy or the completion of 7 days of treatments.
Patient Education: Infectious nature of the problem, need for partner evaluation, avoidance of STI; American College of Obstetricians and Gynecologists Patient Education Pamphlet AP009 (How to Prevent Sexually Transmitted Diseases), AP071 (Gonorrhea, Chlamydia, and Syphilis), and AP028 (Vaginitis: Causes and Treatments).

Drug(s) of Choice

- Without gonorrhea—azithromycin 1 g PO (single dose) or doxycycline 100 mg PO twice a day for 7 days
- With gonorrhea—ceftriaxone 250 mg IM in a single dose plus azithromycin 1g orally in a single dose.

Contraindications: Known or suspected allergy to medication. Doxycycline should not be used during pregnancy or nursing.
Precautions: Doxycycline should not be taken with milk, antacids, or iron-containing preparations.
Interactions: Doxycycline may interact with warfarin or oral contraceptives to reduce their effectiveness.

Alternative Drugs

Without gonorrhea—ofloxacin 300 mg PO twice a day for 7 days or erythromycin ethylsuccinate 800 mg PO four times a day for 7 days.

FOLLOW-UP

Patient Monitoring: Repeat cultures for test of cure, annual Pap tests.
Prevention/Avoidance: Use of condoms to reduce the risk of infection.
Possible Complications: Cervical atypia and neoplasia.
Expected Outcome: With treatment, good.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: N72 (Inflammatory disease of cervix uteri), A54.03 (Gonococcal cervicitis, unspecified), and A74.89 (Other chlamydial diseases).

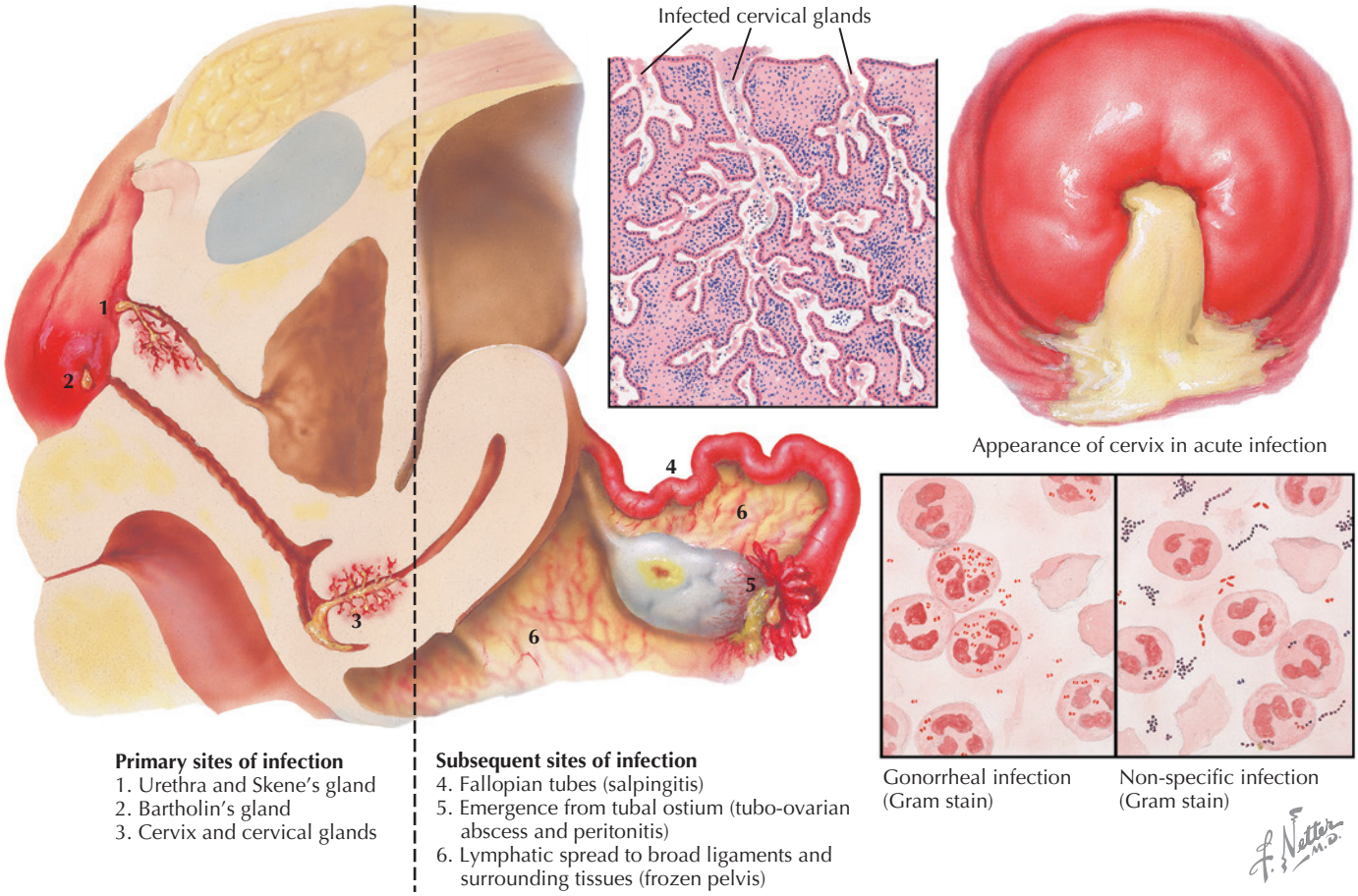


Figure 121.1 Cervicitis

REFERENCES

LEVEL I

Adair CD, Gunter M, Stovall TG, et al. Chlamydia in pregnancy: a randomized trial of azithromycin and erythromycin. *Obstet Gynecol*. 1998;91:165.

Paavonen J, Roberts PL, Stevens CE, et al. Randomized treatment of mucopurulent cervicitis with doxycycline or amoxicillin. *Am J Obstet Gynecol*. 1989;161:128.

LEVEL II

Bush MR, Rosa C. Azithromycin and erythromycin in the treatment of cervical chlamydial infection during pregnancy. *Obstet Gynecol*. 1994;84:61.

Manhart LE, Critchlow CW, Holmes KK, et al. Mucopurulent cervicitis and Mycoplasma genitalium. *J Infect Dis*. 2004;187:650.

Marrazzo JM, Handsfield HH, Whittington WLH. Predicting chlamydial and gonococcal cervical infection: implications for management of cervicitis. *Obstet Gynecol*. 2002;100:579.

Marrazzo JM, Wiesenfeld HC, Murray PJ, et al. Risk factors for cervicitis among women with bacterial vaginosis. *J Infect Dis*. 2006;193:617.

McClelland RS, Wang CC, Mandaliya K, et al. Treatment of cervicitis is associated with decreased cervical shedding of HIV-1. *AIDS*. 2001;15:105.

Schwebke JR, Weiss HL. Interrelationships of bacterial vaginosis and cervical inflammation. *Sex Transmit Dis*. 2002;29:59.

LEVEL III

American College of Obstetricians and Gynecologists. Expedited partner therapy in the management of gonorrhea and chlamydial infection. Committee Opinion No. 632. *Obstet Gynecol*. 2015;125:1526.

Brunham RC, Kuo CC, Stevens CE, et al. Therapy of cervical chlamydial infection. *Ann Intern Med*. 1982;97:216.

Centers for Disease Control and Prevention. Recommendations for the Laboratory-Based Detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae*—2014. *MMWR*. 2014;63(RR–2).

LeFevre ML, U.S. Preventive Services Task Force. Screening for Chlamydia and Gonorrhea: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2014;161:902.

Rosenfeld WD, Clark J. Vulvovaginitis and cervicitis. *Pediatr Clin North Am*. 1989;36:489.

122 NABOTHIAN CYSTS

INTRODUCTION

Description: Nabothian cysts are retention cysts of the cervix that are made up of endocervical columnar cells and that result from the closure of a gland opening, tunnel, or cleft by the process of squamous metaplasia.
Prevalence: Normal feature of the adult cervix.
Predominant Age: Reproductive age.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: A cervical gland opening, tunnel, or cleft that is covered by the process of squamous metaplasia.
Risk Factors: Chronic inflammation of the cervix.

SIGNS AND SYMPTOMS

- Asymptomatic
- Translucent or opaque, white to blue to yellow, raised bumps on the ectocervix (3 mm to 3 cm in diameter)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Cervical cancer (barrel or undermining type) uncommon

Associated Conditions: None.

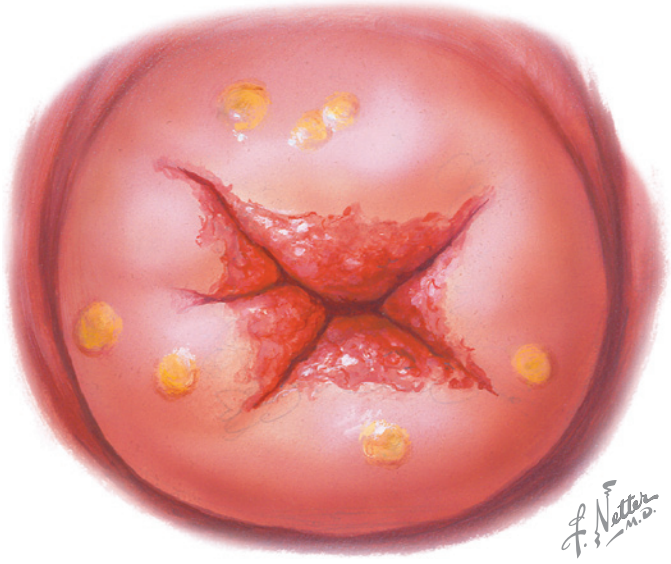


Figure 122.1 Stellate laceration with nabothian cysts

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated.
Special Tests: None indicated.
Diagnostic Procedures: Pelvic (speculum) examination.

Pathologic Findings

Mucus-filled cysts lined with columnar epithelium.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and reassurance.
Specific Measures: None necessary.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance.

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: Distortion or enlargement of the cervix is possible but unlikely.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: N72 (Inflammatory disease of cervix uteri).

REFERENCES

LEVEL III

Farrar HK, Nedoss BR. Benign tumors of the uterine cervix. *Am J Obstet Gynecol.* 1961;81:124.
Stepto RC. Treatment of the Nabothian cyst. *Am Fam Physician.* 1971;4:82.

SECTION VIII

Uterine Pathology

This page intentionally left blank

ADENOMYOSIS

123

INTRODUCTION

Description: Adenomyosis is characterized by endometrial glands and stroma found in the uterine wall (myometrium).
Prevalence: 10%–15% of women; may be present in 60% of aged women 40–50 years.
Predominant Age: 35–50 years.
Genetics: Familial predisposition (polygenic or multifactorial inheritance pattern).

ETIOLOGY AND PATHOGENESIS

Causes: Adenomyosis is derived from aberrant glands of the basalis layer of the endometrium. These grow by direct extension into the myometrium. A metaplastic process may also account for glandular growth.
Risk Factors: High levels of estrogen (postulated), parity, postpartum endometritis (postulated). Local endometrial invasion may be seen following cesarean delivery, myomectomy, or curettage.

SIGNS AND SYMPTOMS

- Asymptomatic (40%)
- Menorrhagia (40%–50%) often increasing in severity
- Dysmenorrhea
- Symmetric "woody" enlargement of the uterus (up to two to three times normal)
- Uterine tenderness that varies with the cycle (worst just before menstruation)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Uterine leiomyomata (most often resulting in asymmetric uterine changes)
- Endometrial polyp
- Endometrial hyperplasia
- Endometrial cancer
- Endometriosis (when pain is predominant symptom)
- Early pregnancy

Associated Conditions: Coexistent endometriosis (15%), uterine leiomyomata, dyspareunia, salpingitis isthmica nodosa.

Workup and Evaluation

Laboratory: No evaluation indicated, complete blood count if anemia is suspected.
Imaging: No imaging indicated except to rule out other possible pathologic conditions. Either transvaginal ultrasonography or magnetic resonance imaging (MRI) may demonstrate abnormalities (during ultrasonography, the uterus will have a heterogeneous texture, without focal abnormalities). MRI (T2 weighted or contrast-enhanced T1 weighted) will be more specific than ultrasonography.

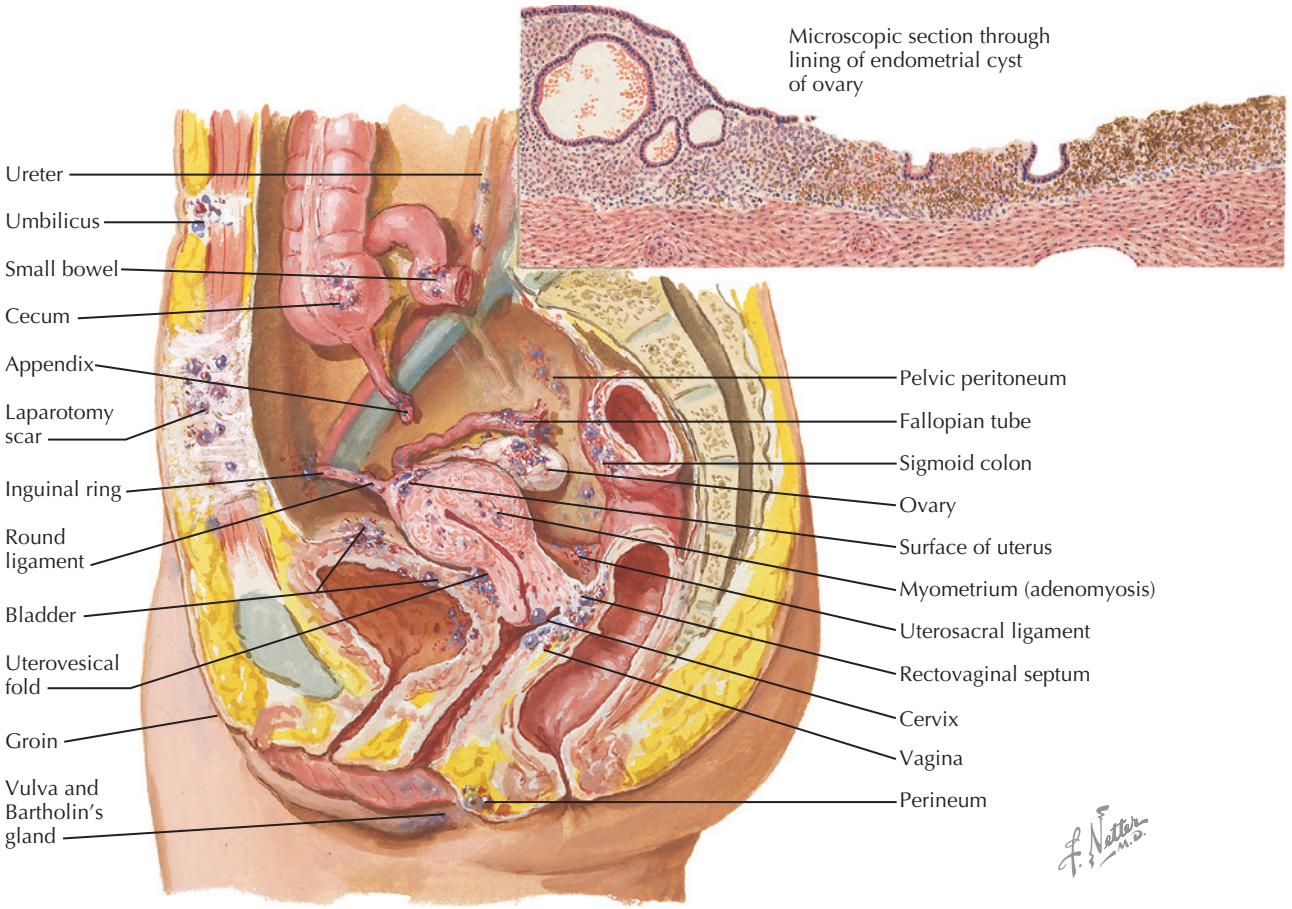


Figure 123.1 Possible locations of endometrial implants

Special Tests: Endometrial biopsy is seldom of help in establishing the diagnosis of adenomyosis, although it may be useful to rule out a possible endometrial cancer when that is a consideration.

Diagnostic Procedures: The characteristic history of painful, heavy periods, accompanied by a generous, symmetric, firm or "woody" uterus suggests, but does not confirm, the diagnosis. Only histologic examination can confirm the diagnosis.

Pathologic Findings

In adenomyosis, endometrial implants (glands and stroma) develop deep within the myometrial wall. Adenomyosis is, therefore, the intramural equivalent of extrauterine endometriosis. Diagnostic criteria require glands to be identified more than 2.5 mm below the basalis layer of the endometrium.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Analgesics (nonsteroidal antiinflammatory drugs), cyclic hormone therapy, gonadotropin-releasing hormone (GnRH) agonists.

Specific Measures: Hysterectomy is the definitive treatment for adenomyosis. Uterine artery embolization has been suggested but success is variable and not assured.

Diet: No specific dietary changes indicated.

Activity: No restriction.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP046 (Dysmenorrhea: Painful Periods) and AP008 (Hysterectomy).

Drug(s) of Choice

There is no satisfactory medical treatment for adenomyosis. All medical therapy is aimed at ameliorating the symptoms or delaying the progression of the condition. Symptoms generally resolve with the loss of ovarian function. Hormonal and other treatments for endometriosis have been attempted with variable success.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.

Prevention/Avoidance: None.

Possible Complications: Progressive menorrhagia, anemia, chronic pelvic pain. Some studies have suggested that these patients have a higher level of antiphospholipid autoantibodies, but the clinical significance of this is unknown. A link to infertility has been postulated but remains controversial.

Expected Outcome: Unless associated with endometriosis, surgical therapy (hysterectomy) is curative. Symptoms resolve with the loss of menstrual function at menopause.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, although an increased risk of preterm labor and rupture of the membranes has been reported.

ICD-10-CM Codes: N80.0 (Endometriosis of uterus).

REFERENCES

LEVEL II

Byun JY, Kim SE, Choi BG, et al. Diffuse and focal adenomyosis: MR imaging findings. *Radiographics*. 1999;19:S161.

Fedele L, Bianchi S, Dorta M, et al. Transvaginal ultrasonography in the diagnosis of diffuse adenomyosis. *Fertil Steril*. 1992;58:94.

Juang CM, Chou P, Yen MS, et al. Adenomyosis and risk of preterm delivery. *BJOG*. 2007;114:165.

Maheshwari A, Gurunath S, Fatima F, et al. Adenomyosis and subfertility: a systematic review of prevalence, diagnosis, treatment and fertility outcomes. *Hum Reprod Update*. 2012;18:374.

Reinhold C, Tafazoli F, Mehio A, et al. Uterine adenomyosis: endovaginal US and MR imaging features with histopathologic correlation. *Radiographics*. 1999;19:S147.

LEVEL III

American College of Obstetricians and Gynecologists. Diagnosis of abnormal uterine bleeding in reproductive-aged women. Practice Bulletin No. 128. *Obstet Gynecol*. 2012;120:197.

American College of Obstetricians and Gynecologists. Noncontraceptive uses of hormonal contraceptives. Practice Bulletin No. 110. *Obstet Gynecol*. 2010;115:206.

Arnold LL, Ascher SM, Schruefer JJ, et al. The nonsurgical diagnosis of adenomyosis. *Obstet Gynecol*. 1995;86:461.

Levgur M. Diagnosis of adenomyosis: a review. *J Reprod Med*. 2007;52:177.

Outwater EK, Siegelman ES, Van Deerlin V. Adenomyosis: current concepts and imaging considerations. *AJR Am J Roentgenol*. 1998;170:437.

Siegler AM, Camilien L. Adenomyosis. *J Reprod Med*. 1994;39:841.

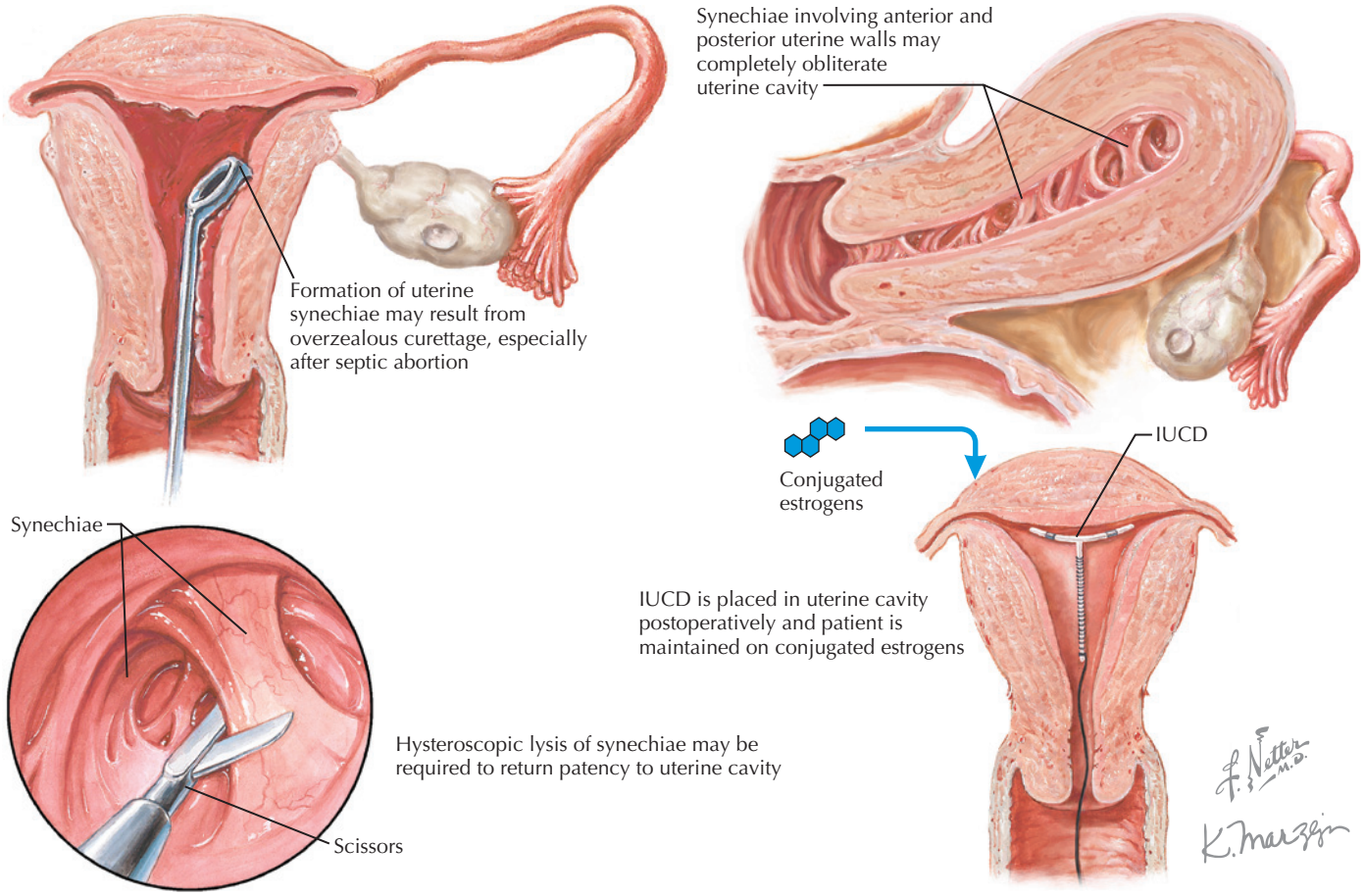


Figure 124.1 Asherman syndrome (uterine synechia)

period—some intrauterine adhesions form in 30% of patients treated by curettage for missed abortion), endometrial infection (tuberculosis or schistosomiasis), scarring after myomectomy or metroplasty. A severe pelvic infection unrelated to surgery may also lead to Asherman syndrome. Uterine compression sutures used in severe postpartum hemorrhage have been associated with intrauterine adhesions.

Risk Factors: Instrumentation of the uterine cavity complicated by infection. Endometrial infection unrelated to instrumentation, such as tuberculosis or schistosomiasis.

SIGNS AND SYMPTOMS

- Amenorrhea or hypomenorrhea

DIAGNOSTIC APPROACH

Differential Diagnosis

- Amenorrhea (primary or secondary)
- Cervical stenosis

Associated Conditions: Amenorrhea, infertility.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: Sonohysterography or hysterosalpingography.
Special Tests: None indicated.
Diagnostic Procedures: Hysteroscopy.

Pathologic Findings

Intrauterine scarring.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and support.
Specific Measures: Resection of intrauterine scars under hysteroscopic control, followed by intrauterine contraceptive device (IUCD) insertion and estrogen therapy.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP062 (Dilation and Curettage [D&C]).

Drug(s) of Choice

- Estrogen therapy for 1–2 months.
  - Oral—conjugated estrogen 1.25 mg daily, diethylstilbestrol 1 mg daily, esterified estrogens 1.25 mg daily, ethinyl estradiol 0.05 mg daily, micronized estradiol 1 mg daily, piperazine estrone sulfate, estropipate 1.25 mg daily.
  - Topical—17β-estradiol 0.1 mg/day.

Contraindications: Undiagnosed vaginal bleeding.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: Avoidance of excessive curettage, prompt treatment of endometritis after dilation and curettage.
Possible Complications: Hematocolpos, infertility.
Expected Outcome: Return to normal fertility and menstrual function after treatment.

MISCELLANEOUS

Pregnancy Considerations: Once treated, no effect on future pregnancy, though a case of placenta accreta has been reported.
ICD-10-CM Codes: N85.6 (Intrauterine synechiae).

REFERENCES

LEVEL I

Roy KK, Negi N, Subbaiah M, et al. Effectiveness of estrogen in the prevention of intrauterine adhesions after hysteroscopic septal resection: a prospective, randomized study. *J Obstet Gynaecol Res*. 2014;40:1085.

LEVEL II

Hare AA, Olah KS. Pregnancy following endometrial ablation: a review article. *J Obstet Gynaecol*. 2005;25:108.

Hooker AB, Lemmers M, Thurkow AL, et al. Systematic review and meta-analysis of intrauterine adhesions after miscarriage: prevalence, risk factors and long-term reproductive outcome. *Hum Reprod Update*. 2014;20:262.

Kjer JJ. Asherman syndrome in a Danish population. *Acta Obstet Gynecol Scand*. 2014;93:425.

Lin X, Wei M, Li TC, et al. A comparison of intrauterine balloon, intrauterine contraceptive device and hyaluronic acid gel in the prevention of adhesion reformation following hysteroscopic surgery for Asherman syndrome: a cohort study. *Eur J Obstet Gynecol Reprod Biol*. 2013;170:512.

Poujade O, Grossetti A, Mougel L, et al. Risk of synechiae following uterine compression sutures in the management of major postpartum haemorrhage. *BJOG*. 2011;118:433.

LEVEL III

AAGL Advancing Minimally Invasive Gynecology Worldwide. AAGL practice report: practice guidelines for management of intrauterine synechiae. *J Minim Invasive Gynecol*. 2010;17:1.

Al-Inany H. Intrauterine adhesions. An update. *Acta Obstet Gynecol Scand*. 2001;80:986.

Deans R, Abbott J. Review of intrauterine adhesions. *J Minim Invasive Gynecol*. 2010;17:555.

125 DYSFUNCTIONAL (ABNORMAL) UTERINE BLEEDING

INTRODUCTION

Description: Dysfunctional (abnormal) uterine bleeding is irregular or is intermenstrual bleeding with no clinically identifiable underlying cause.
Prevalence: 10%–15% of all gynecologic visits involve menstrual disturbances.
Predominant Age: Reproductive age; highest in adolescents and patients experiencing climacteric changes.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: The causes of abnormal uterine bleeding have been summarized by the PALM-COEIN system (see Figure 125.1). Anovulatory patients—chemotherapy, chronic illness, climacteric changes, endometrial carcinoma, endometrial hyperplasia, hormonal contraception (oral, injectable, intrauterine), iatrogenic (anticoagulation, hormone replacement), idiopathic, medications (anticholinergic agents, monamine oxidase inhibitors, morphine, phenothiazines, reserpine), nutritional disruption (anorexia, bulimia, excess physical activity), obesity, pituitary–hypothalamic–ovarian axis immaturity, pituitary tumor, polycystic ovary syndrome, stress, systemic disease (hepatic, renal, thyroid). Ovulatory patients—anatomic lesions (adenomyosis, cervical neoplasia, cervical polyps, endometrial carcinoma, endometrial polyps, leiomyomata, sarcoma), bleeding at ovulation, coagulopathies (natural or iatrogenic), endometritis, fallopian tube disease (infection, tumor), foreign body (intrauterine contraceptive device [IUCD], pessary, tampon), idiopathic, ingested substances (estrogens, ginseng), leukemia, luteal phase dysfunction, pelvic inflammatory disease (including tuberculosis), pregnancy related (abortion, ectopic, hydatidiform mole, retained products of conception), repeated trauma, systemic disease (hepatic, renal, thyroid).
Risk Factors: Prolonged anovulation.

SIGNS AND SYMPTOMS

- Intermenstrual bleeding (painless)
- Irregular menstrual cycles (typically prolonged interval)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Pregnancy
- Climacteric changes
- Anovulation
- Endometrial polyps
- Uterine leiomyomata
- Endometrial cancer
- Endometriosis
- Nonuterine sources of bleeding (eg, cervical, vaginal, vulvar, or perineal)
- Iatrogenic causes (hormones, oral contraceptives)

PALM - Structural

- ***P***olyp (AUB-P)
- ***A***denomyosis (AUB-A)
- ***L***eiomyomata (AUB-L)
  - Submucosal (AUB-L_{sm})
  - Other (AUB-L_o)
- ***M***alignancy/Hyperplasia (AUB-M)

COEIN - Nonstructural

- ***C***oagulopathy (AUB-C)
- ***O***vulatory dysfunction (AUB-O)
- ***E***ndometrial (AUB-E)
- ***I***atrogenic (AUB-I)
- ***N***ot yet classified (AUB-N)

Figure 125.1 PALM-COEIN classification of abnormal uterine bleeding. (Modified from Munro MG, Critchley HO, Broder MS, Fraser IS. FIGO classification system [PALM-COEIN] for causes of abnormal uterine bleeding in nongravid women of reproductive age. FIGO Working Group on Menstrual Disorders. *Int J Gynaecol Obstet*. 2011;113:3)

Associated Conditions: Anovulation, infertility, endometrial cancer, endometrial polyps or carcinoma, uterine leiomyomata, obesity.

Workup and Evaluation

Laboratory: Testing should be selected on the basis of the differential diagnoses under consideration.
Imaging: Pelvic ultrasonography or sonohysterography may be useful in select patients.
Special Tests: A menstrual calendar helps document the timing and character of the patient's bleeding. Endometrial biopsy, curettage, or hysteroscopy may be indicated.
Diagnostic Procedures: The diagnosis of dysfunctional uterine bleeding is one of exclusion. History and physical examination often point to possible causes for further evaluation.

Pathologic Findings

Proliferation of the endometrial tissues with irregular shedding evident in some patients; in other patients the endometrium is thin and atrophic.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation.
Specific Measures: Focused on underlying causation and desires of patient. If anovulation is the cause and fertility is not desired, periodic progestin therapy may be used to stabilize menstrual cycles and suppress intermenstrual bleeding. Suppression of menstrual cycling (gonadotropin-releasing hormone agonists, long-acting progestin, long-cycle combination oral contraceptives), endometrial ablation, or hysterectomy may be required for a small number of patients.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP095 (Abnormal Uterine Bleeding), AP049 (Your First Period-Especially for Teens, AP147 (Endometrial Hyperplasia), and AP162 (Perimenopausal Bleeding and Bleeding After Menopause).

Drug(s) of Choice

Medroxyprogesterone acetate 5–10 mg for 1–14 days each month. In approximately 85% of patients who have ovulated in the past, a single cycle provides adequate response.
Contraindications: Undiagnosed amenorrhea or bleeding.
Precautions: Progestins should not be used until pregnancy has been ruled out.

Alternative Drugs

Norethindrone acetate 5–10 mg for 10–14 days each month. The levonorgestrel intrauterine system (a polydimethylsiloxane sleeve containing 52 mg of levonorgestrel on the stem that releases 20 μg of levonorgestrel daily) may be inserted or combination oral contraceptives may be used.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: Anemia, endometrial hyperplasia or carcinoma if anovulation or simple hypertrophy is left untreated.
Expected Outcome: Return to normal menstrual pattern with the correction of underlying pathologic condition or periodic progestin therapy.

Miscellaneous

Pregnancy Considerations: No effect on pregnancy once established, aside from that resulting from causative conditions.
ICD-9-CM Codes: 626.8 and 626.4 (Irregular menstrual cycle).

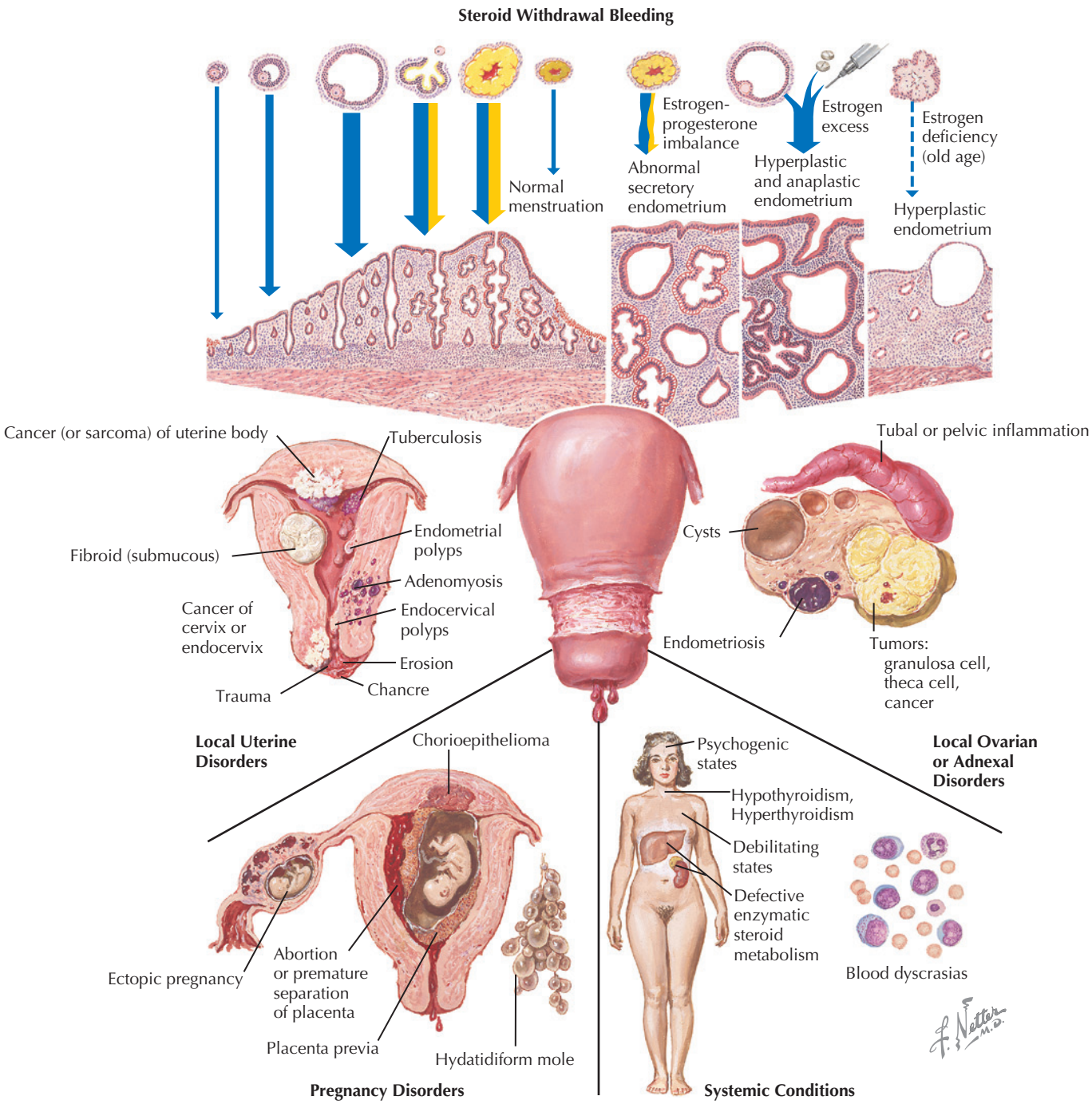


Figure 125.2 Functional and pathologic causes of uterine bleeding

REFERENCES

LEVEL I

Aberdeen Endometrial Ablation Trials Group. A randomized trial of endometrial ablation versus hysterectomy for the treatment of dysfunctional uterine bleeding: outcome at four years. *Br J Obstet Gynaecol*. 1999;106:360.

Pinion SB, Parkin DE, Abramovich DR, et al. Randomised trial of hysterectomy, endometrial laser ablation, and transcervical endometrial resection for dysfunctional uterine bleeding. *BMJ*. 1994;309:979.

LEVEL II

Falcone T, Desjardins C, Bourque J, et al. Dysfunctional uterine bleeding in adolescents. *J Reprod Med*. 1994;39:761.

La Sala GB, Blasi I, Gallinelli A, et al. Diagnostic accuracy of sonohysterography and transvaginal sonography as compared with hysteroscopy and endometrial biopsy: a prospective study. *Minerva Ginecol*. 2011;63:421.

LEVEL III

Albers JR, Hull SK, Wesley RM. Abnormal uterine bleeding. *Am Fam Physician*. 2004;69:1915.

American College of Obstetricians and Gynecologists. Diagnosis of abnormal uterine bleeding in reproductive-aged women. Practice Bulletin No. 128. *Obstet Gynecol*. 2012;120:197.

American College of Obstetricians and Gynecologists. Endometrial ablation. ACOG Practice Bulletin No. 81. *Obstet Gynecol*. 2007;109:1233.

American College of Obstetricians and Gynecologists. Management of abnormal uterine bleeding associated with ovulatory dysfunction. Practice Bulletin No. 136. *Obstet Gynecol*. 2013;122:176.

Pitkin J. Dysfunctional uterine bleeding. *BMJ*. 2007;334:1110.

ENDOMETRIAL CANCER

126

INTRODUCTION

Description: Endometrial cancer is characterized by malignant changes of the endometrial tissues. These are generally of the adenocarcinoma, adenosquamous, clear cell, or papillary serous cell types.

Prevalence: 2%–3% lifetime risk. The most frequent malignancy of the female reproductive tract, approximately 54,870 cases per year in the United States; 10,170 deaths each year (2015 estimate), eighth leading site of cancer-related death among American women.

Predominant Age: 55–65 years; less common below the age of 45 years (<20% of cases).

Genetics: No genetic pattern known except for conditions such as hereditary nonpolyposis colorectal cancer (HNPCC; Lynch syndrome). Cancers found in younger women are associated with mutations in the K-*ras*, PTEN, or MLH1 genes.

ETIOLOGY AND PATHOGENESIS

Causes: Unopposed (without progestins) estrogen stimulation (polycystic ovary syndrome, obesity, chronic anovulation, and estrogen replacement therapy without concomitant progestin) in 90% of cases. Selective estrogen receptor modulators with uterine activity (tamoxifen).

Risk Factors: Unopposed estrogen stimulation of the uterus (chronic anovulation, estrogen therapy, and obesity), tamoxifen use, early menarche, late menopause, nulliparity, breast or colon cancer, diabetes.

SIGNS AND SYMPTOMS

- Postmenopausal bleeding (90%)
- Abnormal glandular cells on Pap test (cervical cytologic tests detect only approximately 20% of known endometrial carcinomas)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Endometrial hyperplasia (complex, atypical)
- Cervical cancer
- Endometrial or cervical polyp
- Ovarian cancer metastatic to the endometrium
- Metachronous müllerian tumor
- Endometriosis
- Early pregnancy (younger women)
- Granulosa cell tumors

Associated Conditions: Obesity, irregular menstrual bleeding, infertility, breast or colon cancer.

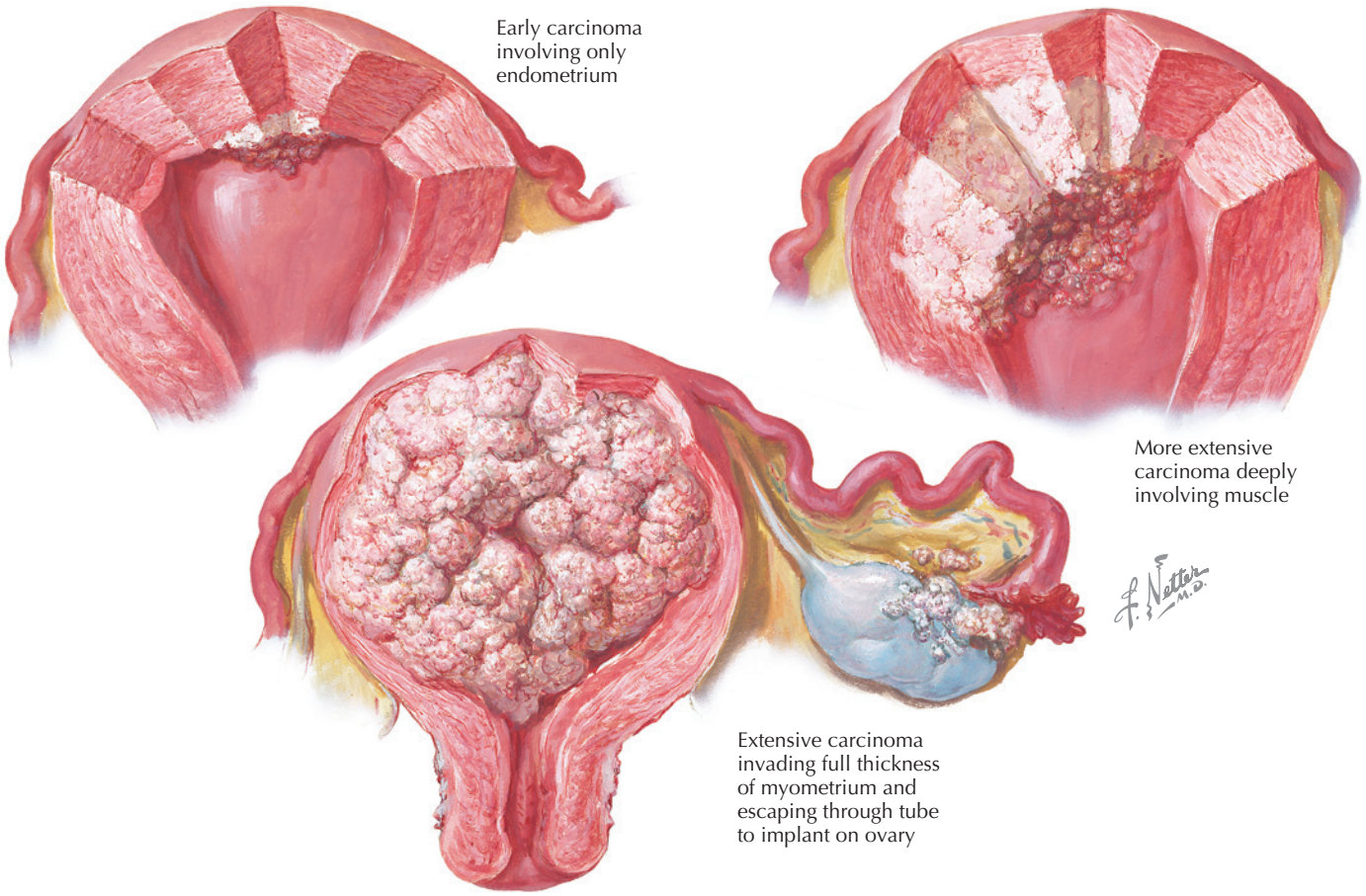


Figure 126.1 Uterine endometrial carcinoma stages and types

Workup and Evaluation

Laboratory: No evaluation indicated, except for preoperative screening, or others based on the differential diagnosis being considered.
Imaging: Chest radiograph (for metastases), transvaginal ultrasonography or sonohysterography may be useful (although concerns have been raised regarding the possibility of extrauterine spread induced by tubal spill of fluid during sonohysterography).
Special Tests: Endometrial biopsy (>90% accurate).
Diagnostic Procedures: History, physical examination, and endometrial biopsy.

Pathologic Findings

Atypical, hyperplastic glands with little or no stroma. Mitosis common.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and staging.
Specific Measures: Surgical exploration (staging) with hysterectomy, bilateral salpingo-oophorectomy, cytologic examination of the abdomen and diaphragm, para-aortic node sampling. Radiation to the vaginal cuff reduces local recurrence. Distant metastatic disease is treated with high-dose progestins, cisplatin, and doxorubicin (Adriamycin). The use of adjuvant radiotherapy in women with disease limited to the uterus based on systematic surgical staging is controversial.
Diet: No specific dietary changes indicated except as dictated by surgical therapy.
Activity: No restriction except as dictated by surgical therapy.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP097 (Cancer of the Uterus), AP008 (Hysterectomy), AP080 (Preparing for Surgery), AP095 (Abnormal Uterine Bleeding), AP134 (Endometrial Ablation), AP147 (Endometrial Hyperplasia), and AP007 (Reducing Your Risk of Cancer).

Drug(s) of Choice

- Hyperplasia and distant metastatic disease: megestrol (Megace) 160 mg PO daily for 3 months. This is generally followed by curettage or other evaluation to assess response.
- Doxorubicin (Adriamycin) or cisplatin chemotherapy.

Contraindications: See individual agents.
Precautions: High-dose progestins should be used with caution in patients with congestive heart failure because they may cause fluid retention.
Interactions: See individual agents.

FOLLOW-UP

Patient Monitoring: Follow-up Pap tests from vaginal cuff every 3 months for 2 years, then every 6 months for 3 years, then yearly. Chest radiograph annually.
Prevention/Avoidance: Correction of unopposed estrogen states or the addition of progestin.
Possible Complications: Distant spread with progression to death.
Expected Outcome: 5-year survival based on the stage and grade—stage I, 85%; stage II, 60%; stage III, 30%; stage IV, 10%.

MISCELLANEOUS

Pregnancy Considerations: Generally not considered because they are unlikely to coexist.
ICD-10-CM Codes: Specific to cell type and location.

REFERENCES

LEVEL I

Malur S, Possover M, Michels W, et al. Laparoscopic-assisted vaginal versus abdominal surgery in patients with endometrial cancer—A prospective randomized trial. *Gynecol Oncol*. 2001;80:239.

LEVEL II

Creasman WT, Odicino F, Maisonneuve P, et al. Carcinoma of the corpus uteri. *Int J Gynaecol Obstet*. 2003;83:79.

Cushing KL, Weiss NS, Voigt LF, et al. Risk of endometrial cancer in relation to use of low-dose, unopposed estrogens. *Obstet Gynecol*. 1998;91:35.

Kalogiannidis I, Lambrechts S, Amant F, et al. Laparoscopy-assisted vaginal hysterectomy compared with abdominal hysterectomy in clinical stage I endometrial cancer: safety, recurrence, and long-term outcome. *Am J Obstet Gynecol*. 2007;196:248.e1.

Lewin SN, Herzog TJ, Barrena Medel NI, et al. Comparative performance of the 2009 international Federation of gynecology and obstetrics' staging system for uterine corpus cancer. *Obstet Gynecol*. 2010;116:1141.

LEVEL III

Akin O, Mironov S, Pandit-Taskar N, et al. Imaging of uterine cancer. *Radiol Clin North Am*. 2007;45:167.

Amant F, Moerman P, Neven P, et al. Endometrial cancer. *Lancet*. 2005;366:491.

American College of Obstetricians and Gynecologists. Diagnosis of abnormal uterine bleeding in reproductive-aged women. Practice Bulletin No. 128. *Obstet Gynecol*. 2012;120:197.

American College of Obstetricians and Gynecologists. Endometrial ablation. ACOG Practice Bulletin No. 81. *Obstet Gynecol*. 2007;109:1233.

American College of Obstetricians and Gynecologists. Endometrial cancer. Practice Bulletin No. 149. *Obstet Gynecol*. 2015;125:1006.

American College of Obstetricians and Gynecologists. Endometrial intraepithelial neoplasia. Committee Opinion No. 631. *Obstet Gynecol*. 2015;125:1272.

American College of Obstetricians and Gynecologists. Tamoxifen and uterine cancer. Committee Opinion No. 601. *Obstet Gynecol*. 2014;123:1394.

Montgomery BE, Daum GS, Dunton CJ. Endometrial hyperplasia: a review. *Obstet Gynecol Surv*. 2004;59:368.

ENDOMETRIAL HYPERPLASIA: SIMPLE AND COMPLEX

127

INTRODUCTION

Description: Endometrial hyperplasia is caused by the abnormal proliferation of both the glandular and stromal elements of the endometrium with characteristic alteration in the histologic architecture of the tissues. It is this architectural change that differentiates hyperplasia from normal endometrial proliferation. Simple hyperplasia represents the least significant form of alteration. Complex hyperplasia represents the most significant form of alteration. The World Health Organization (WHO) classification of endometrial hyperplasia classifies hyperplasia into four groups: simple or complex, with or without atypia.

Prevalence: Five percent of patients with postmenopausal bleeding have endometrial hyperplasia.

Predominant Age: Late reproductive and early menopausal age; peak age 50–54 years.

Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Unknown.

Risk Factors: Unopposed estrogen stimulation of the uterus (chronic anovulation, estrogen therapy [four- to eight-fold risk], obesity [three-fold risk]), nulliparity (two- to three-fold risk), diabetes (two- to three-fold risk), polycystic ovarian syndrome, tamoxifen use.

SIGNS AND SYMPTOMS

- Asymptomatic
- Intermenstrual bleeding
- Menorrhagia
- Postmenopausal bleeding

DIAGNOSTIC APPROACH

Differential Diagnosis

- Endometrial adenocarcinoma
- Endocervical or endometrial polyps
- Endocervical carcinoma

Associated Conditions: Endocervical or endometrial polyps, squamous metaplasia, endometrial carcinoma. When nuclear atypia is present, more than 30% of patients will have a coexisting endometrial cancer.

Workup and Evaluation

Laboratory: No evaluation indicated.

Imaging: Ultrasonography may detect thickening of the endometrial stripe (no standard has emerged for a threshold of endometrial thickness that carries ideal positive and negative predictive values. It does not take the place of histologic evaluation.). Magnetic resonance imaging (MRI) may also diagnose endometrial thickening, but cost and low specificity argue against its use as a diagnostic tool.

Special Tests: Endometrial biopsy, hysteroscopy, or dilation and curettage.

Diagnostic Procedures: Endometrial biopsy. The diagnosis is histologic.

Pathologic Findings

- **Simple hyperplasia**—proliferation of both glandular and stromal elements with no atypia. The glands form simple tubules with wide variations in size from small to large cysts. There is little or no outpouching of the epithelium lining the cysts.
- **Complex hyperplasia**—proliferation of both glandular and stromal elements. Cellular atypia (characterized by disordered maturation, high nuclear/cytoplasmic ratio, nuclear pleomorphism, mitoses) may be present or absent. Glands are crowded with a "back-to-back" appearance. May be found with coexisting adenocarcinoma (17%–52% in various studies). Outpouching in glands is common. It should be noted that the reliability of histologic diagnosis of these two conditions has been questioned, with concordance between reviewers generally below 50%.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Prompt evaluation.

Specific Measures: Simple hyperplasia—medical therapy (progestin) is generally adequate. Many use dilation and curettage by itself or in combination with progestin therapy. Complex hyperplasia—for patients with hyperplasia without atypia or for selected patients who wish to preserve fertility, high-dose prolonged progestin therapy may be used. All others are treated by hysterectomy (with bilateral salpingo-oophorectomy).

Diet: No specific dietary changes indicated.

Activity: No restriction.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP147 (Endometrial Hyperplasia), AP095 (Abnormal Uterine Bleeding), AP097 (Cancer of the Uterus), and AP062 (Dilation and Curettage [D&C]).

Drug(s) of Choice

- **Simple Hyperplasia**—Medroxyprogesterone acetate (Provera, Cycrin) 10 mg PO daily for 10 days each month, norethindrone acetate (Aygestin) 10 mg PO daily for 10 days each month. The levonorgestrel-releasing intrauterine device 20 mcg/day (LNg20; Mirena) offers a good response and compliance rates.
- **Complex Hyperplasia**—Depot medroxyprogesterone acetate (Depo-Provera) up to 200–1000 mg IM weekly for 5 weeks, followed by 100–400 mg IM monthly, megestrol acetate (Megace) 40–160 mg PO daily for 6–12 weeks (some authors have advocated therapy for up to 48 months). Estrogen replacement therapy may be safely administered to those treated by hysterectomy.

Contraindications: Undiagnosed vaginal bleeding, thrombophlebitis, markedly impaired liver function, known or suspected breast cancer.

Precautions: Progestins should not be used during the first trimester of pregnancy.

Alternative Drugs

Combination oral contraceptives also may be used for simple hyperplasia.

FOLLOW-UP

Patient Monitoring: With simple hyperplasia or for complex hyperplasia medically managed, a follow-up endometrial sampling must be performed after 3 months, then every 6–12 months thereafter.

Prevention/Avoidance: None.

Possible Complications: Progression is uncommon with simple hyperplasia (1% to cancer, 3% to complex hyperplasia). A slight

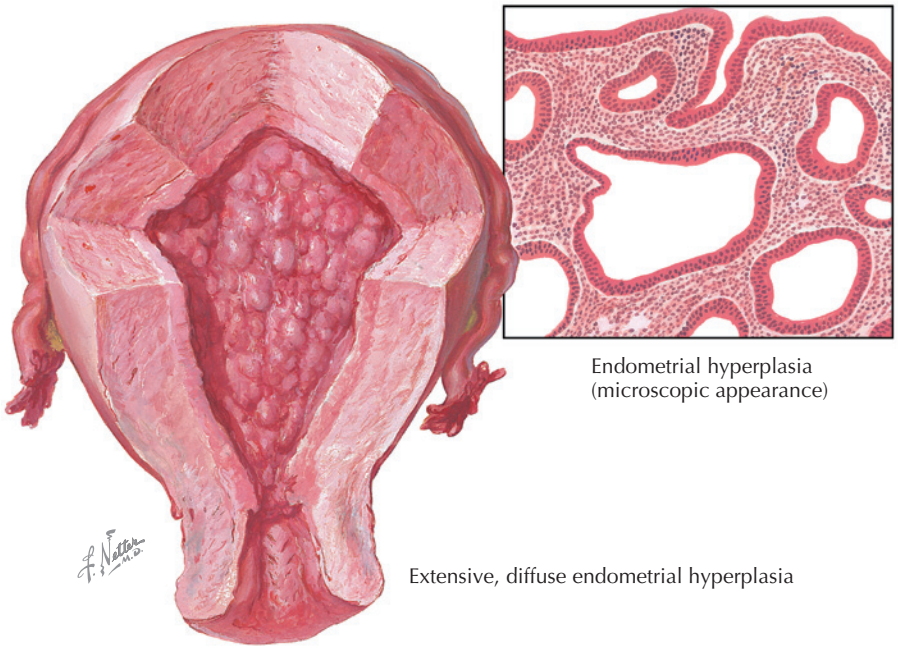


Figure 127.1 Endometrial hyperplasia

risk is associated with endometrial sampling (infection, perforation). Complex hyperplasia, especially with atypia, is associated with coexistent malignancy or the risk of progression to malignant changes (75% of patients) when untreated. The more atypical the cellular architecture, the greater the risk of malignancy; without atypia, 25% of hyperplasia will progress and 50% will persist.

Expected Outcome: Good response to medical therapy can be anticipated for patients with hyperplasia. Progression and recurrence are uncommon.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.

ICD-10-CM Codes: N85.00 (Endometrial hyperplasia, unspecified), N85.01 (Benign endometrial hyperplasia), and N85.02 (Endometrial intraepithelial neoplasia [EIN]).

REFERENCES

LEVEL I

Orbo A, Vereide A, Arnes M, et al. Levonorgestrel-impregnated intrauterine device as treatment for endometrial hyperplasia: a national multicentre randomised trial. *BJOG*. 2014;121:477.

Steiner AZ, Xiang M, Mack WJ, et al. Unopposed estradiol therapy in postmenopausal women: results from two randomized trials. *Obstet Gynecol*. 2007;109:581.

LEVEL II

Abu Hashim H, Ghayaty E, El Rakhawy M. Levonorgestrel-releasing intrauterine system vs oral progestins for non-atypical endometrial hyperplasia: a systematic review and metaanalysis of randomized trials. *Am J Obstet Gynecol*. 2015;213:469.

Clark TJ, Voit D, Gupta JK, et al. Accuracy of hysteroscopy in the diagnosis of endometrial cancer and hyperplasia: a systematic quantitative review. *JAMA*. 2002;288:1610.

Grady D, Ettinger B, Moscarelli E, et al. Multiple Outcomes of Raloxifene Evaluation Investigators. Safety and adverse effects associated with raloxifene: multiple outcomes of raloxifene evaluation. *Obstet Gynecol*. 2004;104:837.

Gunderson CC, Fader AN, Carson KA, et al. Oncologic and reproductive outcomes with progestin therapy in women with endometrial hyperplasia and grade 1 adenocarcinoma: a systematic review. *Gynecol Oncol*. 2012;125:477.

Kendall BS, Ronnett BM, Isacson C, et al. Reproducibility of the diagnosis of endometrial hyperplasia, atypical hyperplasia, and well-differentiated carcinoma. *Am J Surg Pathol*. 1998;22:1012.

Trimble CL, Kauderer J, Zaino R, et al. Concurrent endometrial carcinoma in women with a biopsy diagnosis of atypical endometrial hyperplasia: a Gynecologic Oncology Group study. *Cancer*. 2006;106:812.

Wang J, Wieslander C, Hansen G, et al. Thin endometrial echo complex on ultrasound does not reliably exclude type 2 endometrial cancers. *Gynecol Oncol*. 2006;101:120.

LEVEL III

American College of Obstetricians and Gynecologists. Diagnosis of abnormal uterine bleeding in reproductive-aged women. Practice Bulletin No. 128. *Obstet Gynecol*. 2012;120:197.

American College of Obstetricians and Gynecologists. Endometrial ablation. ACOG Practice Bulletin No. 81. *Obstet Gynecol*. 2007;109:1233.

American College of Obstetricians and Gynecologists. Endometrial cancer. Practice Bulletin No. 149. *Obstet Gynecol*. 2015;125:1006.

American College of Obstetricians and Gynecologists. Endometrial intraepithelial neoplasia. Committee Opinion No. 631. *Obstet Gynecol*. 2015;125:1272.

American College of Obstetricians and Gynecologists. Management of abnormal uterine bleeding associated with ovulatory dysfunction. Practice Bulletin No. 136. *Obstet Gynecol*. 2013;122:176.

American College of Obstetricians and Gynecologists. Tamoxifen and uterine cancer. Committee Opinion No. 601. *Obstet Gynecol*. 2014;123:1394.

ENDOMETRIAL POLYPS

128

INTRODUCTION

Description: Endometrial polyps are fleshy tumors that arise as local overgrowths of the endometrial glands and stroma and project beyond the surface of the endometrium. They are most common in the fundus of the uterus but may occur anywhere in the endometrial cavity. They are generally small (a few millimeters) but may enlarge to fill the entire cavity.
Prevalence: Up to 10% of women (from autopsy studies); 20% of uteruses removed because of cancer.
Predominant Age: 40–50 years; infrequent after menopause.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Unknown. A role for unopposed estrogen is hypothesized.
Risk Factors: Unopposed estrogen use, obesity, tamoxifen therapy (up to 36% of tamoxifen users).

SIGNS AND SYMPTOMS

- Asymptomatic (most)
- Abnormal bleeding (most common intermenstrual bleeding and menorrhagia, perimenopausal bleeding). One-fourth of women with abnormal bleeding patterns have an endometrial polyp.
- Polyps with long pedicles may protrude from the cervix.

DIAGNOSTIC APPROACH

Differential Diagnosis

- Endocervical polyp
- Endometrial cancer
- Prolapsed leiomyomata
- Retained products of conception
- Retained (and forgotten) intrauterine contraceptive device

Associated Conditions: Endometrial cancer (two-fold increase).

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: Sonohysterography generally identifies the polyp. Special attention should be directed to the fundus, where most polyps arise.
Special Tests: None indicated.
Diagnostic Procedures: History, physical examination, endometrial sampling, hysteroscopy, or curettage. Often not diagnosed until the uterus is removed for other reasons.

Pathologic Findings

Velvety surface with a rich central vascular core. Endometrial glands, stroma, and vascular channels are present with the epithelium identified on three sides to establish the pedunculated nature. Smooth muscle is occasionally present. The endometrial glands are often immature in appearance with a "Swiss cheese" cystic character that is independent of the phase of the cycle. Infection or metaplasia may be present.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation.
Specific Measures: Removal by curettage or operative hysteroscopy. All polyps removed should be histologically examined, although <5% contain malignancy.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP095 (Abnormal Uterine Bleeding) and AP062 (Dilation and Curettage [D&C]).

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: Evaluation and treatment of prolonged amenorrhea, treatment of unopposed estrogen states. Some have advocated prophylaxis for those taking tamoxifen by the placement of an intrauterine progesterone delivery system.
Possible Complications: Up to 0.5% of polyps undergo malignant transformation (low grade and stage).
Expected Outcome: Removal is generally curative even when malignant transformation is present.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: N84.0 (Polyp of corpus uteri).

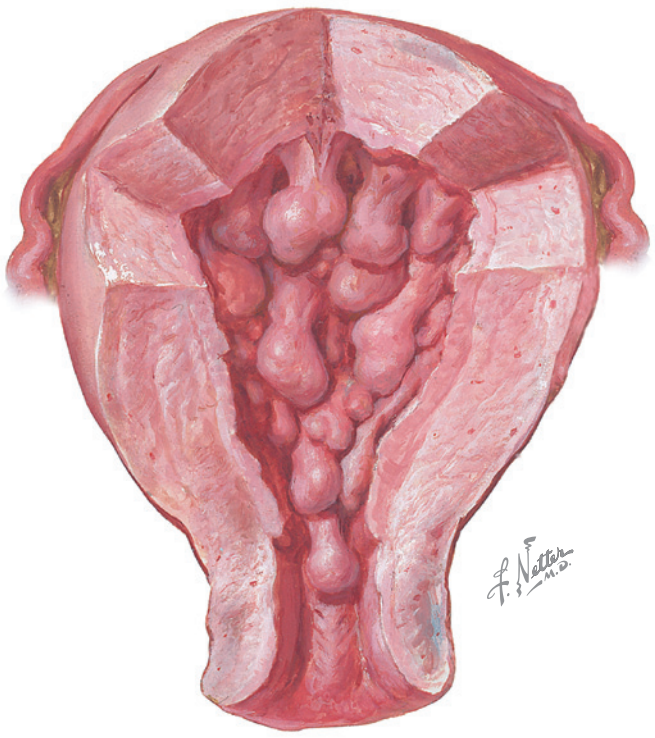


Figure 128.1 Multiple endometrial polyps

REFERENCES

LEVEL I

Marsh FA, Rogerson LJ, Duffy SR. A randomised controlled trial comparing outpatient versus daycase endometrial polypectomy. *BJOG*. 2006;113:896.

LEVEL II

Chan SS, Tam WH, Yeo W, et al. A randomised controlled trial of prophylactic levonorgestrel intrauterine system in tamoxifen-treated women. *BJOG*. 2007;114:1510.

Lee SC, Kaunitz AM, Sanchez-Ramos L, et al. The oncogenic potential of endometrial polyps: a systematic review and meta-analysis. *Obstet Gynecol*. 2010;116:1197.

Lieng M, Istre O, Qvigstad E. Treatment of endometrial polyps: a systematic review. *Acta Obstet Gynecol Scand*. 2010;89:992.

Maia H Jr, Maltez A, Studart E, et al. Ki-67, Bcl-2 and p53 expression in endometrial polyps and in the normal endometrium during the menstrual cycle. *BJOG*. 2004;111:1242.

Runowicz CD, Costantino JP, Wickerham DL, et al. Gynecologic conditions in participants in the NSABP breast cancer prevention study of tamoxifen and raloxifene (STAR). *Am J Obstet Gynecol*. 2011;205:535.e1.

Wong AW, Chan SS, Yeo W, et al. Prophylactic use of levonorgestrel-releasing intrauterine system in women with breast cancer treated with tamoxifen: a randomized controlled trial. *Obstet Gynecol*. 2013;121:943.

LEVEL III

American College of Obstetricians and Gynecologists. Diagnosis of abnormal uterine bleeding in reproductive-aged women. Practice Bulletin No. 128. *Obstet Gynecol*. 2012;120:197.

American College of Obstetricians and Gynecologists. Management of abnormal uterine bleeding associated with ovulatory dysfunction. Practice Bulletin No. 136. *Obstet Gynecol*. 2013;122:176.

American College of Obstetricians and Gynecologists. Tamoxifen and uterine cancer. Committee Opinion No. 601. *Obstet Gynecol*. 2014;123:1394.

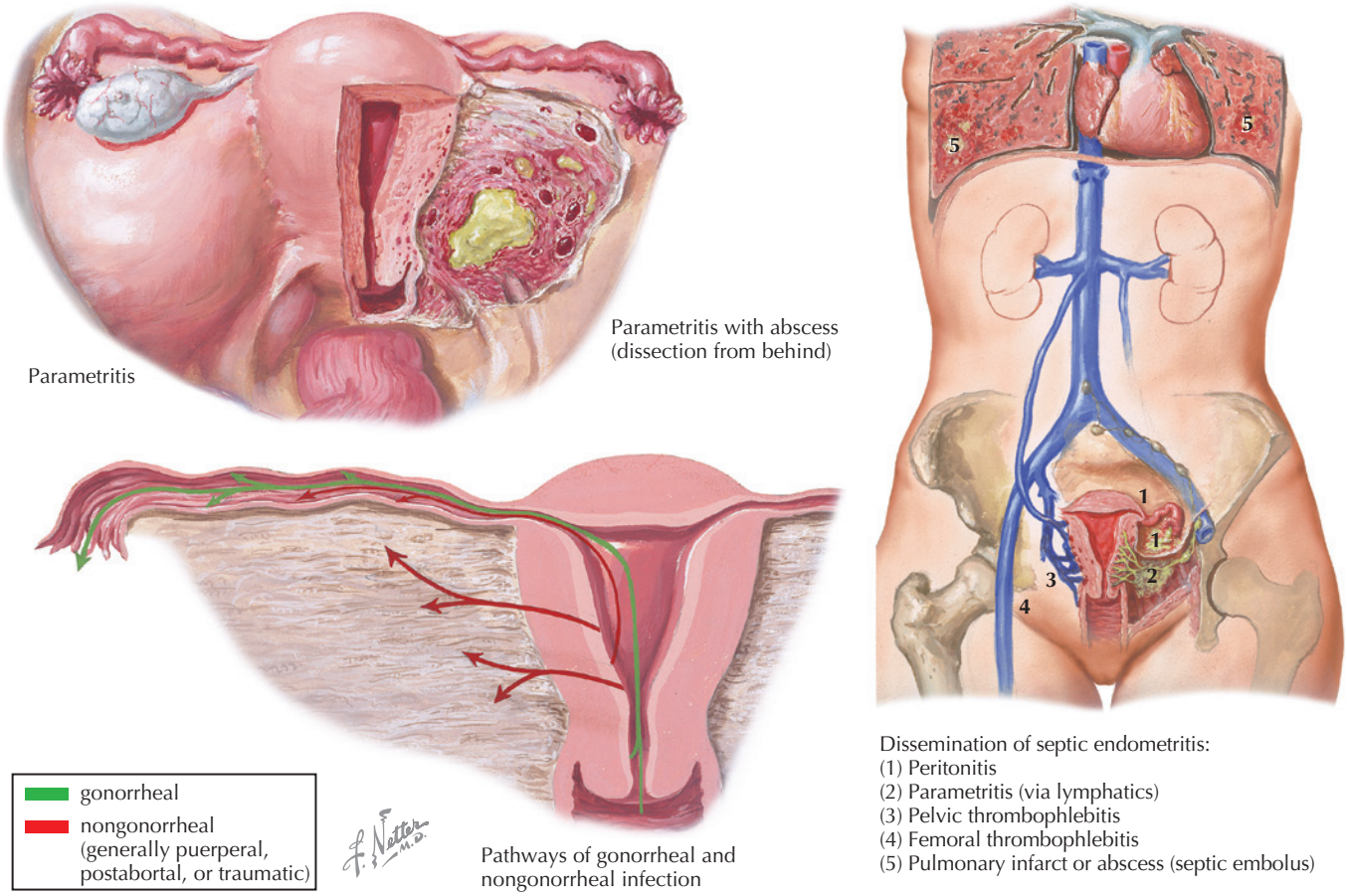


Figure 129.1 Endometritis: parametritis and septic endometritis

endometrial stroma. Sulfur granules may be present in *Actinomyces* infections.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, counseling about STIs (cervicitis).
Specific Measures: Antibiotic therapy (see later), removal of IUCD (if present).
Diet: No specific dietary changes indicated.
Activity: Pelvic rest (no tampons, douches, or intercourse) until therapy has been completed.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP095 (Abnormal Uterine Bleeding), AP099 (Chronic Pelvic Pain), and AP077 (Pelvic Inflammatory Disease).

Drug(s) of Choice

Doxycycline (Vibramycin) 200 mg PO initially, 100 mg PO daily for 10 days. If *Actinomyces* is found in a tubo-ovarian abscess, oral penicillin therapy should be continued for 12 weeks.
Contraindications: Known or suspected allergy to tetracycline.
Precautions: Photosensitivity may occur in patients taking doxycycline.
Interactions: Doxycycline may enhance the effect of warfarin. Doxycycline absorption is inhibited by most antacids and bismuth subsalicylate (Pepto-Bismol).

Alternative Drugs

Metronidazole or erythromycin may be substituted for doxycycline.

FOLLOW-UP

Patient Monitoring: Normal health maintenance, screening for STIs as needed.
Prevention/Avoidance: Reduce risk of cervicitis or STIs, asepsis during intrauterine procedures.
Possible Complications: Ascending infection resulting in salpingitis, tubo-ovarian abscesses, hydrosalpinx, peritonitis, and chronic pelvic pain.
Expected Outcome: Good with treatment.

MISCELLANEOUS

Pregnancy Considerations: Generally not applicable. *U. urealyticum* infection has been implicated as a rare cause of early pregnancy loss.
ICD-10-CM Codes: N71.0 (Acute inflammatory disease of uterus) and N71.1 (Chronic inflammatory disease of uterus). Codes for infections following pregnancy are specific to trimester and other factors.

REFERENCES

LEVEL I

Starr RV, Zurawski J, Ismail M. Preoperative vaginal preparation with povidone-iodine and the risk of postcesarean endometritis. *Obstet Gynecol*. 2005;105:1024.

Sullivan SA, Smith T, Chang E, et al. Administration of cefazolin prior to skin incision is superior to cefazolin at cord clamping in preventing postcesarean infectious morbidity: a randomized, controlled trial. *Am J Obstet Gynecol*. 2007;196:455.e1.

LEVEL II

Ness RB, Hillier SL, Kip KE, et al. Bacterial vaginosis and risk of pelvic inflammatory disease. *Obstet Gynecol*. 2004;104:761.

LEVEL III

American College of Obstetricians and Gynecologists. Antibiotic prophylaxis for gynecologic procedures. ACOG Practice Bulletin No. 104. *Obstet Gynecol*. 2009;113:1180.

American College of Obstetricians and Gynecologists. Use of prophylactic antibiotics in labor and delivery. Practice Bulletin No. 120. *Obstet Gynecol*. 2011;117:1472.

Crossman SH. The challenge of pelvic inflammatory disease. *Am Fam Physician*. 2006;73:859.

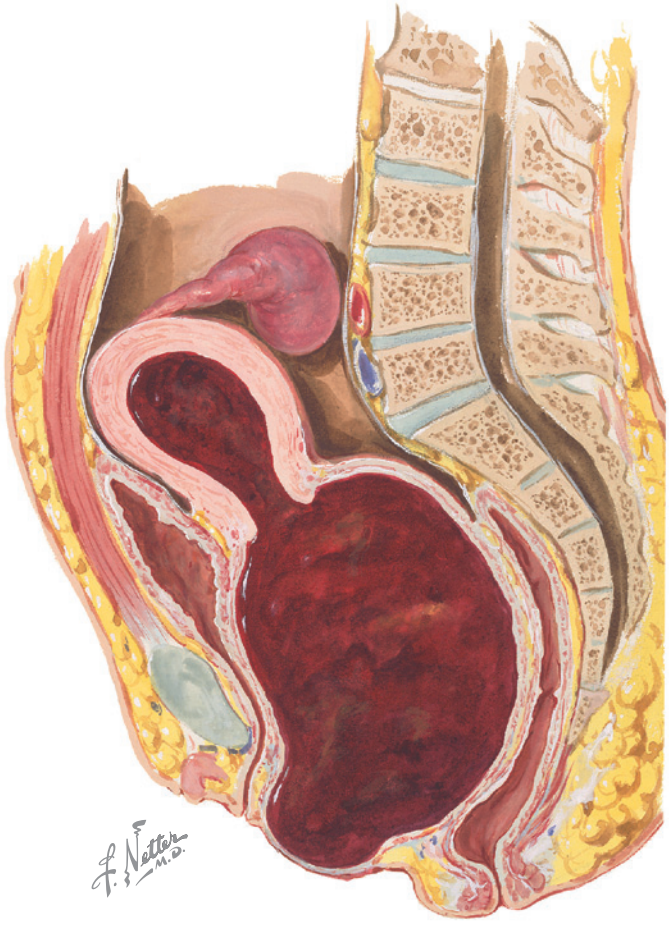


Figure 130.1 Hematocolpos with hematometra and hematosalpinx

Drug(s) of Choice

None. Therapy is based on the cause and clinical situation. Antibiotic treatment if infection is suspected (the antibiotic chosen should provide protection against possible colonization by *Bacteroides*, anaerobic *Staphylococcus* and *Streptococcus*, and aerobic coliform bacteria).

Contraindications: See individual agents.
Precautions: See individual agents.
Interactions: See individual agents.

FOLLOW-UP

Patient Monitoring: Normal health maintenance and periodic reassessment of the cervix and uterus.
Prevention/Avoidance: Avoid unnecessary cervical procedures and limit the scope of therapy when such procedures are necessary. Some authors suggest cervical sounding after such procedures to assess patency, although this has not been shown to reduce the incidence of stenosis.
Possible Complications: Infection (leading to pyometra), progression of underlying disease.
Expected Outcome: Based on the cause.

MISCELLANEOUS

Pregnancy Considerations: Incompatible with pregnancy.
ICD-10-CM Codes: N85.7 (Hematometra).

REFERENCES

LEVEL II

Gurtcheff SE, Sharp HT. Complications associated with global endometrial ablation: the utility of the MAUDE database. *Obstet Gynecol*. 2003;102:1278.

Sheih CP, Liao YJ, Liang WW, et al. Sonographic presentation of unilateral hematometra: report of two cases. *J Ultrasound Med*. 1995;14:695.

Vernooij CB, Kruitwagen RF, Rodrigus P, et al. Hematometra after radiotherapy for cervical carcinoma. *Gynecol Oncol*. 1997;67:325.

LEVEL III

American College of Obstetricians and Gynecologists. Endometrial ablation. ACOG Practice Bulletin 81. *Obstet Gynecol*. 2007;109:1233.

Jayasinghe Y, Rane A, Stalewski H, et al. The presentation and early diagnosis of the rudimentary uterine horn. *Obstet Gynecol*. 2005;105:1456.

McCausland AM, McCausland VM. Long-term complications of endometrial ablation: cause, diagnosis, treatment, and prevention. *J Minim Invasive Gynecol*. 2007;14:399.

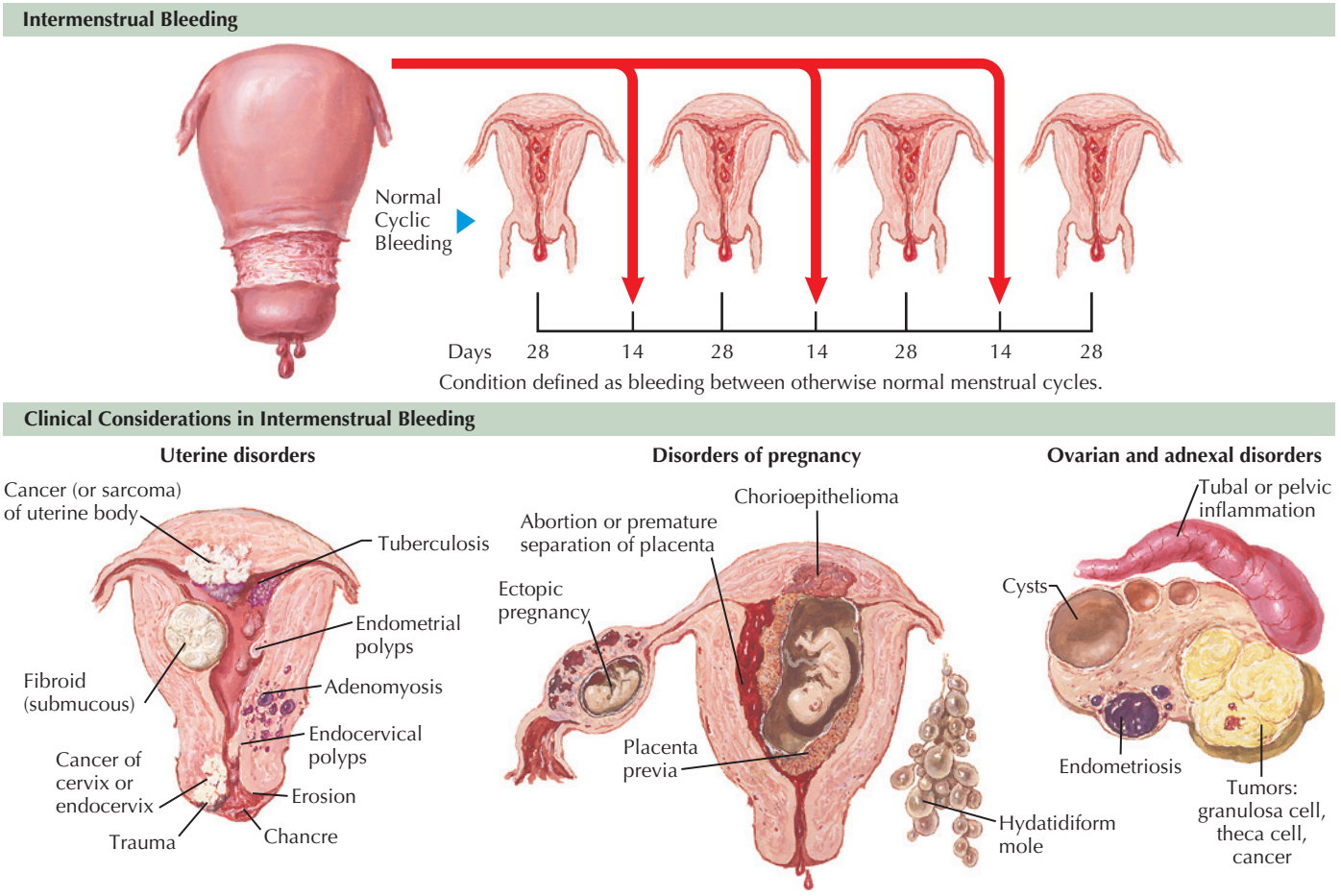


Figure 131.1 Clinical considerations and management of intermenstrual bleeding

Risk Factors: None known. The purported relationship to surgical sterilization has been disproved.

SIGNS AND SYMPTOMS

- Intermenstrual bleeding (painless)
- Bleeding after intercourse (common)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Pregnancy
- Climacteric changes
- Anovulation
- Endometrial polyps
- Uterine leiomyomata
- Cervical polyps, lesions, or cervicitis
- Endometrial cancer
- Endometriosis
- Nonuterine sources of bleeding (eg, vaginal, vulvar, or perineal)
- Coagulopathy (congenital or acquired)
- Iatrogenic (intrauterine device use, medications)

Associated Conditions: Endometrial hyperplasia, endometrial cancer, endometrial polyps, endocervical polyps or carcinoma, uterine leiomyomata.

Workup and Evaluation

Laboratory: Testing should be selected on the basis of diagnoses being considered.
Imaging: No imaging indicated.
Special Tests: A menstrual calendar helps to document the timing and character of the patient's bleeding. Endometrial biopsy, curettage, or hysteroscopy may be indicated.
Diagnostic Procedures: History and physical examinations often point to possible causes for further evaluation.

Pathologic Findings

Based on the underlying pathologic conditions.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation.
Specific Measures: Focused on underlying causation, age of the patient, and contraceptive needs.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP095 (Abnormal Uterine Bleeding), AP162 (Perimenopausal Bleeding and Bleeding After Menopause), and AP163 (Cancer of the Cervix).

Drug(s) of Choice

Based on the cause. Hormonal agents that produce endometrial thinning (such as combination contraceptives or long-acting progestins) can be useful in select patients when conception is not desired.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: Anemia.
Expected Outcome: Return to normal menstrual pattern with the correction of the underlying pathologic condition or periodic progestin therapy.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy aside from that resulting from causative conditions.
ICD-10-CM Codes: N92.1 (Excessive and frequent menstruation with irregular cycle) and N93.0 (Postcoital and contact bleeding).

REFERENCES

LEVEL II

Peterson HB, Jeng G, Folger SG, et al; U.S. Collaborative Review of Sterilization Working Group. The risk of menstrual abnormalities after tubal sterilization. U.S. Collaborative Review of Sterilization Working Group. *N Engl J Med*. 2000;343:1681.

LEVEL III

American College of Obstetricians and Gynecologists. Diagnosis of abnormal uterine bleeding in reproductive-aged women. Practice Bulletin No. 128. *Obstet Gynecol*. 2012;120:197.

American College of Obstetricians and Gynecologists. Management of abnormal uterine bleeding associated with ovulatory dysfunction. Practice Bulletin No. 136. *Obstet Gynecol*. 2013;122:176.

Bayer RL, DeCherney AH. Clinical manifestations and treatment of dysfunctional uterine bleeding. *JAMA*. 1993;269:1823.

Pitkin J. Dysfunctional uterine bleeding. *BMJ*. 2007;334:1110.

Thorneycroft IH. Cycle control with oral contraceptives: a review of the literature. *Am J Obstet Gynecol*. 1999;180:280.

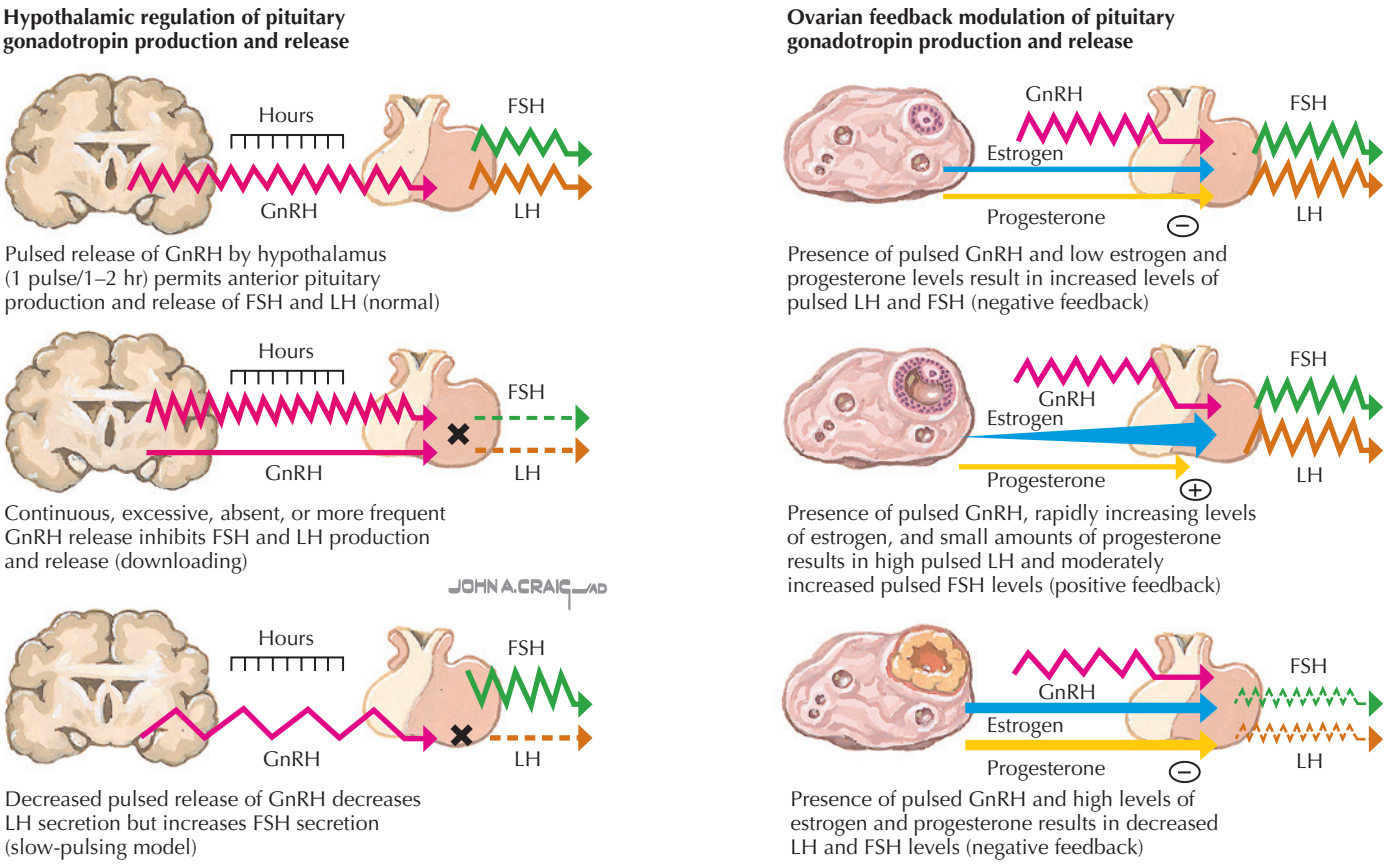


Figure 132.1 Neuroendocrine regulation of menstrual cycle

- Ovarian tumors (rare)

Associated Conditions: Anovulation, infertility, and obesity.

Workup and Evaluation

Laboratory: Testing should be selected on the basis of the different diagnoses under consideration.
Imaging: No imaging indicated.
Special Tests: A menstrual calendar helps to document the timing and character of the patient's bleeding to differentiate cyclic and non-cyclic causes. Endometrial biopsy, curettage, or hysteroscopy may be indicated in selected patients.
Diagnostic Procedures: History and physical examinations often indicate possible causes for further evaluation.

Pathologic Findings

Endometrial biopsy may indicate anovulation.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation.
Specific Measures: Focused on the underlying cause and desires of the patient. If anovulation is the cause and fertility is not desired, periodic progestin therapy may be used to stabilize the cycles and suppress intermenstrual bleeding.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP095 (Abnormal Uterine Bleeding), AP049 (Your First Period - Especially for Teens), and AP162 (Perimenopausal Bleeding and Bleeding After Menopause).

Drug(s) of Choice

Medroxyprogesterone acetate 5–10 mg for 10–14 days each month.
Contraindications: Undiagnosed amenorrhea or bleeding.
Precautions: Progestins should not be used until pregnancy has been ruled out.

Alternative Drugs

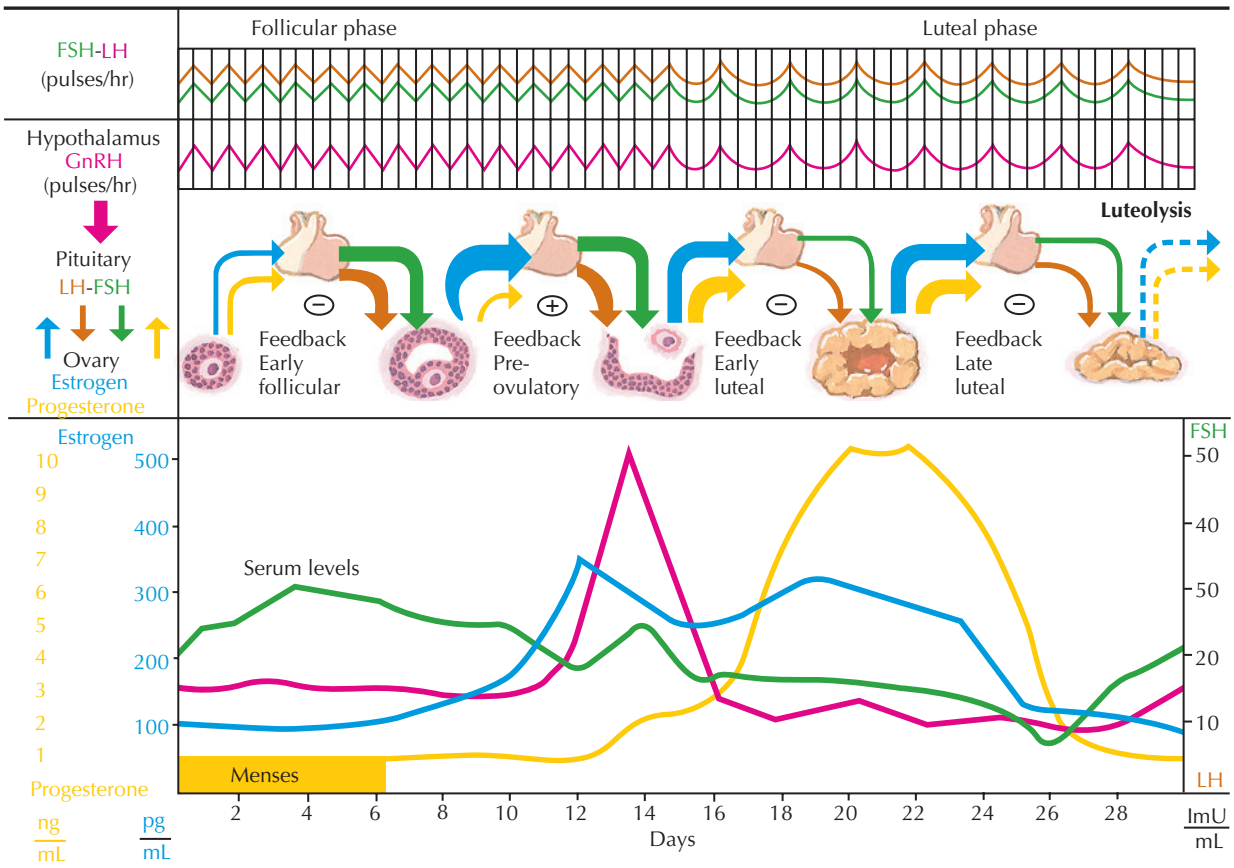
- Norethindrone acetate 5–10 mg for 10–14 days each month.
- Combination oral contraceptives or long-acting progestational agents, including intrauterine systems, may also be used.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: Endometrial hyperplasia or carcinoma if anovulation is left untreated.
Expected Outcome: Return to normal menstrual pattern with correction of underlying pathologic condition or periodic progestin therapy.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy once pregnancy is achieved.
ICD-10-CM Codes: N92.6 (Irregular menstruation, unspecified) and N92.5 (Other specified irregular menstruation).



FSH, follicle-stimulating hormore; GnRH, gonadotropin-releasing hormone; LH, luteinizing hormone.

Figure 132.2 Correlation of serum gonadotropic and ovarian hormone levels and feedback mechanisms

REFERENCES

LEVEL II

Adams Hillard PJ, Deitch HR. Menstrual disorders in the college age female. *Pediatr Clin North Am*. 2005;52:179, ix.

Fraiser IS. Treatment of ovulatory and anovulatory dysfunctional uterine bleeding with oral progestogens. *Aust N Z J Obstet Gynaecol*. 1990;30:353.

Hannoun AB, Nassar AH, Usta IM, et al. Effect of war on the menstrual cycle. *Obstet Gynecol*. 2007;109:929.

LEVEL III

American College of Obstetricians and Gynecologists. Practice bulletin No. 128: diagnosis of abnormal uterine bleeding in reproductive-aged women. *Obstet Gynecol*. 2012;120:197.

American College of Obstetricians and Gynecologists. Practice bulletin No. 136: management of abnormal uterine bleeding associated with ovulatory dysfunction. *Obstet Gynecol*. 2013;122:176.

Cowan BD, Morrison JC. Management of abnormal genital bleeding in girls and women. *N Engl J Med*. 1991;324:1710.

Thorneycroft IH. Cycle control with oral contraceptives: a review of the literature. *Am J Obstet Gynecol*. 1999;180:280.

Van Voorhis BJ. Genitourinary symptoms in the menopausal transition. *Am J Med*. 2005;118:47.

133 MENORRHAGIA

INTRODUCTION

Description: Menorrhagia—heavy menstrual flow—is generally divided into primary and secondary. Secondary is caused by (secondary to) some clinically identifiable cause; primary is caused by a disturbance in prostaglandin production. Menorrhagia is generally distinguished from acute vaginal bleeding (most often associated with pregnancy and pregnancy complications).
Prevalence: 10%–15% of women experience excessive menstrual flow.
Predominant Age: Reproductive age.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Secondary—see Differential Diagnosis in the following section. Primary—overproduction or an imbalance in the relative ratios of uterine prostaglandins (prostaglandin E_2, prostaglandin I_2, and thromboxane A_2). Some evidence suggests that patients with primary menorrhagia also have increased fibrinolysis, further enhancing a tendency to bleed.
Risk Factors: Diabetes, obesity, or chronic anovulation (which places the patient at a higher risk for endometrial hyperplasia or malignancy), systemic disease, or metabolic disturbances associated with bleeding dyscrasias.

SIGNS AND SYMPTOMS

- Menstrual loss of greater than 80 mL, which may result in anemia
- Excessive soiling or numbers of menstrual hygiene products used (objective studies have shown a poor correlation with the actual measured blood loss)
- Anemia (in the absence of other causes of anemia, anemia is diagnostic for menstrual volumes of greater than 80 mL per cycle)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Uterine leiomyomata (one-third of patients will have menorrhagia)
- Adenomyosis (40%–50% have menorrhagia)
- Endometrial or cervical polyp(s)
- Endometrial hypertrophy or hyperplasia
- Endometrial cancer
- Cervical lesions (including cancer)
- Infection (cervicitis, chronic endometritis)
- Intrauterine contraceptive device use
- Chronic anovulation
- Nongynecologic causes include blood dyscrasia or coagulopathy, hypothyroidism, leukemia, hepatic or renal disease, systemic lupus erythematosus, thyroid disease
- Benign or malignant hormone producing tumors of ovary (rare)

Associated Conditions: Anemia, toxic shock syndrome (prolonged tampon use).

Workup and Evaluation

Laboratory: Complete blood count, pregnancy test, clotting profile (as indicated).
Imaging: Pelvic ultrasonography (based on the diagnosis being considered—limited to the detection of secondary sources).
Special Tests: None indicated.
Diagnostic Procedures: History, physical, and laboratory evaluations.

Pathologic Findings

Based on the cause.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, nutritional support.
Specific Measures: Based on the cause. Nonsteroidal antiinflammatory drugs have been shown to reduce menstrual loss in primary menorrhagia. When taken for this indication, they must be taken continuously for the duration of flow. In patients with intractable menorrhagia or patients being prepared for extirpative surgery or endometrial ablation, therapy with gonadotropin-releasing hormone (GnRH) agonists may be considered. Uterine artery embolization has been advocated for select patients.
Diet: No specific dietary changes indicated. Iron supplementation if indicated (either ferrous sulfate or gluconate, 300 mg PO two to three times a day).
Activity: No restriction.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP095 (Abnormal Uterine Bleeding) and AP046 (Dysmenorrhea).

Drug(s) of Choice

- Conjugated estrogen 20–25 mg IV or intramuscular progestins have been widely advocated for acute bleeding.
- Oral estrogen (conjugated estrogen 2.5 mg, micronized estradiol 3–6 mg) may be acutely administered every 2 hours until the bleeding slows or stops. Estrogen therapy is then maintained for 20–25 additional days, with a progestin added for the last 10 days of treatment.
- Combination oral contraceptives containing estradiol and norgestrel (Ovral) four tablets a day for 3–5 days or until bleeding stops, followed by one daily for the duration of the pack or four tablets the first day, followed by three for 1 day, two the next day, and then one daily for the remainder of the package.
- For long-term therapy, levonorgestrel-releasing intrauterine systems have been shown to be effective in reducing menstrual blood loss.

Contraindications: Therapy should not be instituted until the possibility of pregnancy has been evaluated and a working diagnosis has been established.
Precautions: See individual agents.
Interactions: See individual agents.

Alternative Drugs

- When the endometrium is reasonably intact, high-dose progestin may be used to stop acute uterine bleeding (medroxyprogesterone acetate 10 mg PO three times a day or medroxyprogesterone acetate 150–300 mg IM depot).
- Nonsteroidal antiinflammatory agents have been shown to reduce menstrual loss by 30–50% when taken for the duration of flow (eg, meclofenamate sodium 100 mg PO three times a day during flow, mefenamic acid [Ponstel] 250 mg PO three times a day during flow).
- Levonorgestrel-releasing intrauterine systems have been shown to provide a comparable reduction in menstrual blood loss.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. Watch for anemia. Patients who are at a risk for endometrial hyperplasia

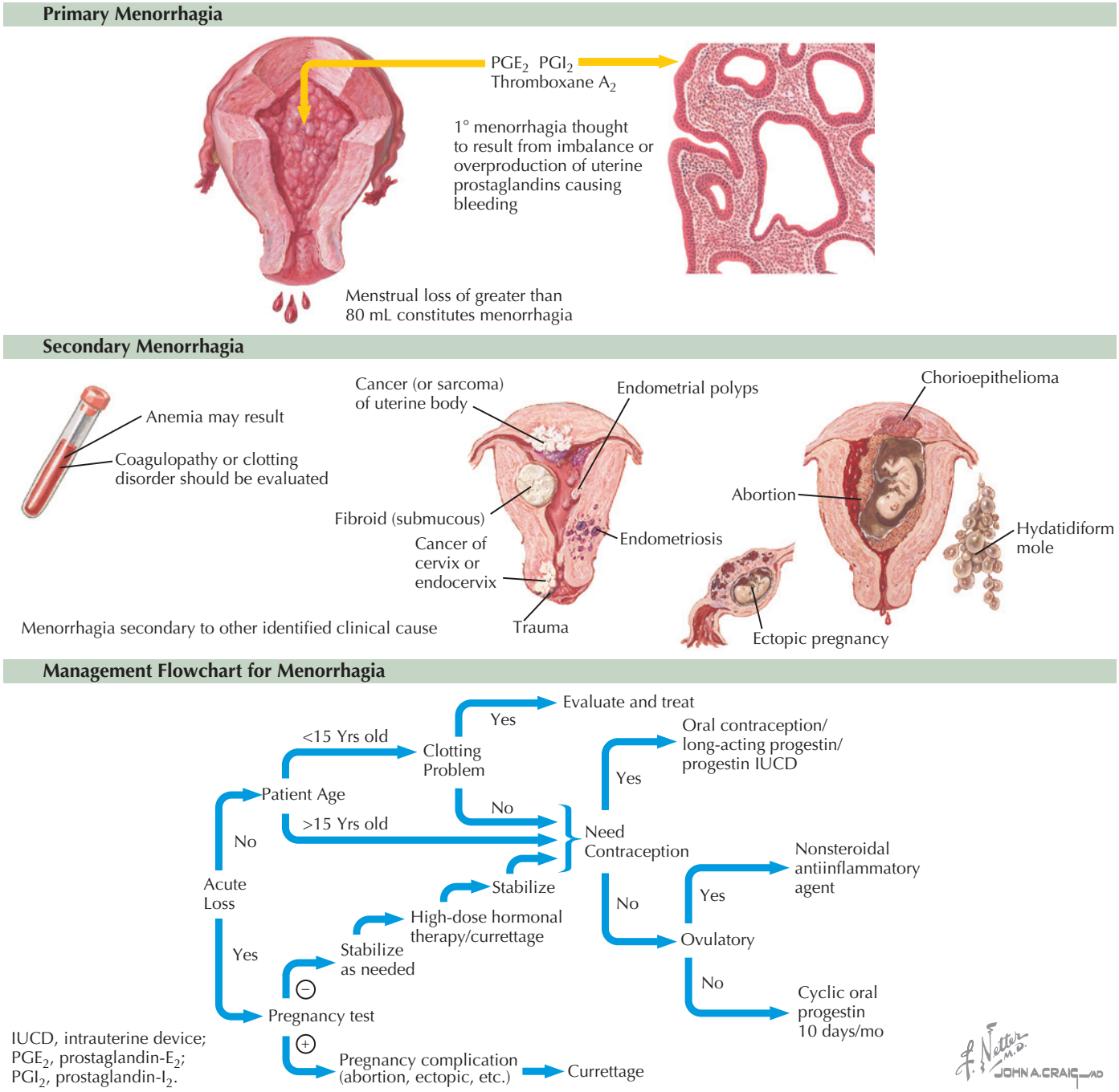


Figure 133.1 Primary and secondary menorrhagia and management

or neoplasia or those who do not respond to initial therapy may require endometrial biopsy, hysteroscopy, or diagnostic curettage.

Prevention/Avoidance: Based on the cause. If contraception is desired, oral combination contraceptives, continuously dosed progestins (orally, by injection, or as a medicated intrauterine device), or oral contraceptives (either monophasic or polyphasic) are reasonable options. In patients with intractable menorrhagia or those being prepared for extirpative surgery or endometrial ablation, therapy with gonadotropin-releasing hormone agonists may be considered for a maximum of 6 months. Cost and side effects limit this approach.

Possible Complications: Anemia, hypovolemia (acute loss).

Expected Outcome: Based on the cause; most patients respond to conservative therapy. The most successful therapy is directed at the underlying cause. Once acute control has been gained, cyclic estrogen/progestin therapy should be continued for an additional 3 months. During this interval, additional diagnostic studies may be considered and plans may be laid for long-term management, should it be necessary.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.

ICD-10-CM Codes: N92.0 (Excessive and frequent menstruation with regular cycle), N92.2 (Excessive menstruation at puberty), and N92.4 (Excessive bleeding in the premenopausal period).

REFERENCES

LEVEL I

Showstack J, Lin F, Learman LA, Ms Research Group, et al. Randomized trial of medical treatment versus hysterectomy for abnormal uterine bleeding: resource use in the Medicine or Surgery (Ms) trial. *Am J Obstet Gynecol*. 2006;194:332.

LEVEL II

Brown PM, Farquhar CM, Lethaby A, et al. Cost-effectiveness analysis of levonorgestrel intrauterine system and thermal balloon ablation for heavy menstrual bleeding. *BJOG*. 2006;113:797.

Busfield RA, Farquhar CM, Sowter MC, et al. A randomised trial comparing the levonorgestrel intrauterine system and thermal balloon ablation for heavy menstrual bleeding. *BJOG*. 2006;113:257.

Garside R, Stein K, Wyatt K, et al. Microwave and thermal balloon ablation for heavy menstrual bleeding: a systematic review. *BJOG*. 2005;112:12.

Hald K, Klow NE, Qvigstad E, et al. Laparoscopic occlusion compared with embolization of uterine vessels: a randomized controlled trial. *Obstet Gynecol*. 2007;109:20.

Reid PC, Virtanen-Kari S. Randomised comparative trial of the levonorgestrel intrauterine system and mefenamic acid for the treatment of idiopathic menorrhagia: a multiple analysis using total menstrual fluid loss, menstrual blood loss and pictorial blood loss assessment charts. *BJOG*. 2005;112:1121.

LEVEL III

American College of Obstetricians and Gynecologists. Alternatives to hysterectomy in the management of leiomyomas. ACOG Practice Bulletin No. 96. *Obstet Gynecol*. 2008;112:201.

American College of Obstetricians and Gynecologists. Diagnosis of abnormal uterine bleeding in reproductive-aged women. Practice Bulletin No. 128. *Obstet Gynecol*. 2012;120:197.

American College of Obstetricians and Gynecologists. Endometrial ablation. ACOG Practice Bulletin No. 81. *Obstet Gynecol*. 2007;109:1233.

American College of Obstetricians and Gynecologists. Management of abnormal uterine bleeding associated with ovulatory dysfunction. Practice Bulletin No. 136. *Obstet Gynecol*. 2013;122:176.

American College of Obstetricians and Gynecologists. Noncontraceptive uses of hormonal contraceptives. Practice Bulletin No. 110. *Obstet Gynecol*. 2010;115:206.

Duncan KM, Hart LL. Nonsteroidal antiinflammatory drugs in menorrhagia. *Ann Pharmacother*. 1993;27:1353.

Sharp HT. Assessment of new technology in the treatment of idiopathic menorrhagia and uterine leiomyomata. *Obstet Gynecol*. 2006;108:990.

Sowter MC. New surgical treatments for menorrhagia. *Lancet*. 2003;361:1456.

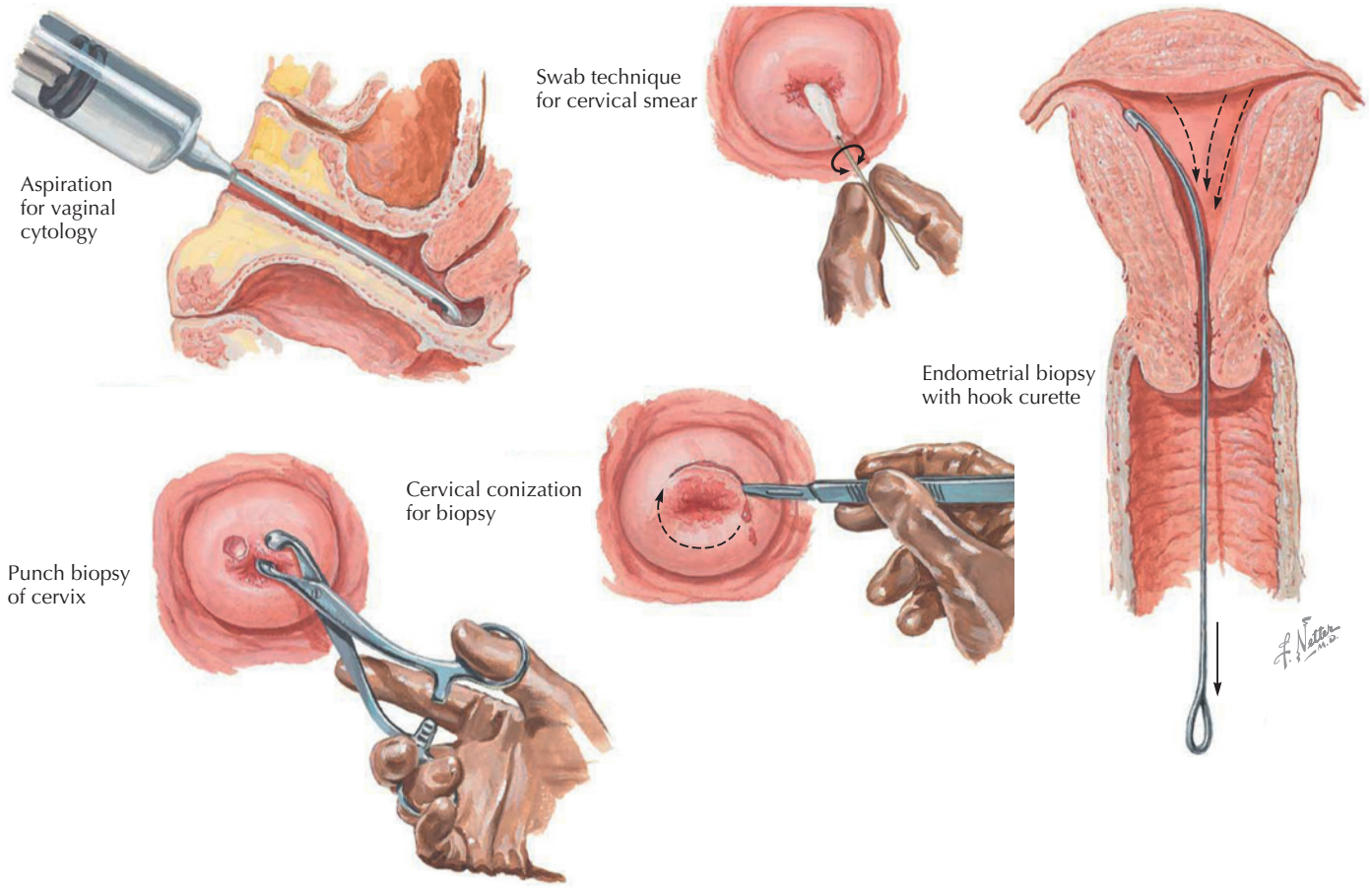


Figure 134.1 Evaluation of postmenopausal bleeding

Special Tests: Endometrial biopsy should be strongly considered to evaluate the cause and to check for the possibility of a malignancy.
Diagnostic Procedures: History and physical examinations, cervical cytologic examination, endometrial sampling.

Pathologic Findings

Varies with the cause.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation.
Specific Measures: Based on the cause identified.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP162 (Perimenopausal Bleeding and Bleeding After Menopause), AP025 (Ultrasound Exams), AP047 (The Menopause Years), and AP013 (Midlife Transitions: Perimenopause to Menopause).

Drug(s) of Choice (Based on the Pathophysiologic Condition Present)

In many cases of postmenopausal bleeding, the endometrium is thin and atrophic. This endometrium is prone to irregular slough, resulting in erratic, although generally light, bleeding. Because the endometrial tissue is so denuded, it does not respond well to progestational agents. Estrogen, alone initially or in combination with progestin therapy, is required to induce initial growth and the development of progestin receptors to effect endometrial stabilization.

FOLLOW-UP

Patient Monitoring: Postmenopausal bleeding should be presumed to indicate the presence of a malignancy, until proved otherwise. The only exception to this is the withdrawal bleeding that occurs as a part of cyclic estrogen–progesterone hormone therapy.
Prevention/Avoidance: None.
Possible Complications: Progression of undiagnosed malignancy.
Expected Outcome: If diagnosis is prompt and appropriate therapy is instituted, the outcome should be excellent.

MISCELLANEOUS

Pregnancy Considerations: Not applicable.
ICD-10-CM Codes: N95.0 (Postmenopausal bleeding).

REFERENCES

LEVEL I

Steiner AZ, Xiang M, Mack WJ, et al. Unopposed estradiol therapy in postmenopausal women: results from two randomized trials. *Obstet Gynecol*. 2007;109:581.

LEVEL II

Burbos N, Musonda P, Giarenis I, et al. Age-related differential diagnosis of vaginal bleeding in postmenopausal women: a series of 3047 symptomatic postmenopausal women. *Menopause Int*. 2010;16:5.

Clark TJ, Voit D, Gupta JK, et al. Accuracy of hysteroscopy in the diagnosis of endometrial cancer and hyperplasia: a systematic quantitative review. *JAMA*. 2002;288:1610.

de Kroon CD, de Bock GH, Dieben SW, et al. Saline contrast hysterosonography in abnormal uterine bleeding: a systematic review and meta-analysis. *BJOG*. 2003;110:938.

Prendergast EN, Misch E, Chou YA, et al. Insufficient endometrial biopsy results in women with abnormal uterine bleeding. *Obstet Gynecol*. 2014;123(suppl 1):180S.

van Dongen H, de Kroon CD, Jacobi CE, et al. Diagnostic hysteroscopy in abnormal uterine bleeding: a systematic review and metaanalysis. *BJOG*. 2007;114:664.

LEVEL III

American College of Obstetricians and Gynecologists. Diagnosis of abnormal uterine bleeding in reproductive-aged women. Practice Bulletin No. 128. *Obstet Gynecol*. 2012;120:197.

American College of Obstetricians and Gynecologists. Management of abnormal uterine bleeding associated with ovulatory dysfunction. Practice Bulletin No. 136. *Obstet Gynecol*. 2013;122:176.

Davidson KG, Dubinsky TJ. Ultrasonographic evaluation of the endometrium in postmenopausal vaginal bleeding. *Radiol Clin North Am*. 2003;41:769.

Opmeer BC, van Doorn HC, Heintz AP, et al. Improving the existing diagnostic strategy by accounting for characteristics of the women in the diagnostic work up for postmenopausal bleeding. *BJOG*. 2007;114:51.

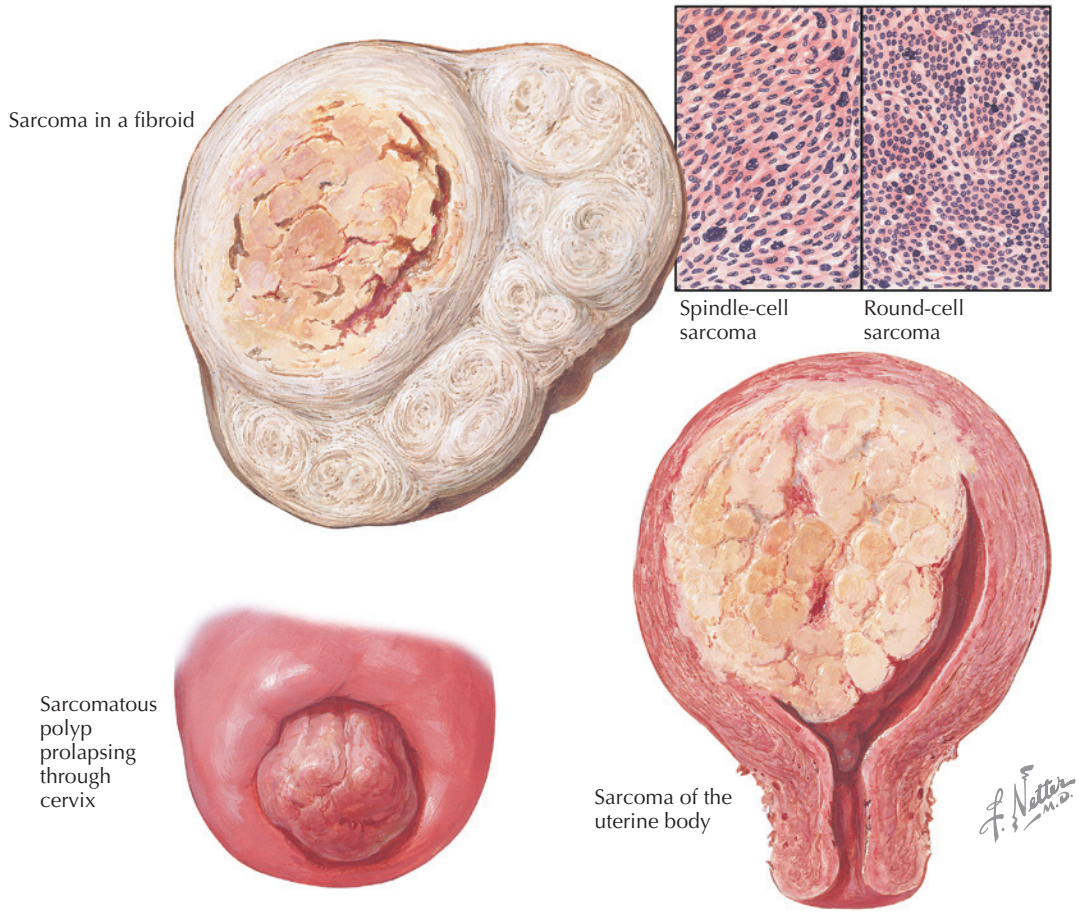


Figure 135.1 Types of sarcomas

Diet: No specific dietary changes indicated except as dictated by surgical therapy.
Activity: No restriction except as dictated by surgical therapy.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP097 (Cancer of the Uterus), AP008 (Hysterectomy), AP080 (Preparing for Surgery), AP095 (Abnormal Uterine Bleeding), and AP074 (Uterine Fibroids).

Drug(s) of Choice

None. Adjuvant chemotherapy (vincristine, actinomycin D, docetaxel and gemcitabine, and cyclophosphamide or doxorubicin [Adriamycin]) has been advocated but an improvement in prognosis has not been demonstrated. Temozolomide (an imidazotetrazine derivative) has been explored as an additional option.

FOLLOW-UP

Patient Monitoring: Follow-up Pap tests from vaginal cuff every 3 months for 2 years, then every 6 months for 3 years, then yearly. Chest, abdomen, and pelvic imaging every 3–4 months for 2–3 years, then every 6–12 months.
Prevention/Avoidance: None.
Possible Complications: Distant spread.
Expected Outcome: Depends on stage of tumor and number of mitotic figures present. Overall survival is approximately 20% at 5 years. Patients with stage I and II disease have better survival rates (75% and 60%, respectively).

MISCELLANEOUS

Pregnancy Considerations: Generally not a consideration because they are unlikely to coexist.
ICD-10-CM Codes: Specific to cell type and location.

REFERENCES

LEVEL II

Bodner K, Bodner-Adler B, Kimberger O, et al. Estrogen and progesterone receptor expression in patients with uterine leiomyosarcoma and correlation with different clinicopathological parameters. *Anticancer Res*. 2003;23:729.

Brooks SE, Zhan M, Cote T, et al. Surveillance, epidemiology, and end results analysis of 2677 cases of uterine sarcoma 1989-1999. *Gynecol Oncol*. 2004;93:204.

Einstein MH, Barakat RR, Chi DS, et al. Management of uterine malignancy found incidentally after supracervical hysterectomy or uterine morcellation for presumed benign disease. *Int J Gynecol Cancer*. 2008;18:1065.

Oduyebo T, Rauh-Hain AJ, Meserve EE, et al. The value of re-exploration in patients with inadvertently morcellated uterine sarcoma. *Gynecol Oncol*. 2014;132:360.

Sherman ME, Devesa SS. Analysis of racial differences in incidence, survival, and mortality for malignant tumors of the uterine corpus. *Cancer*. 2003;98:176.

Theben JU, Schellong AR, Altgassen C, et al. Unexpected malignancies after laparoscopic-assisted supracervical hysterectomies (LASH): an analysis of 1,584 LASH cases. *Arch Gynecol Obstet*. 2013;287:455.

Yildirim Y, Inal MM, Sanci M, et al. Development of uterine sarcoma after tamoxifen treatment for breast cancer: report of four cases. *Int J Gynecol Cancer*. 2005;15:1239.

LEVEL III

American College of Obstetricians and Gynecologists. Tamoxifen and uterine cancer. Committee Opinion No. 601. *Obstet Gynecol*. 2014;123:1394.

D'Angelo E, Prat J. Uterine sarcomas: a review. *Gynecol Oncol*. 2010;116:131.

Moinfar F, Azodi M, Tavassoli FA. Uterine sarcomas. *Pathology*. 2007;39:55.

Tropé CG, Abeler VM, Kristensen GB. Diagnosis and treatment of sarcoma of the uterus. A review. *Acta Oncol*. 2012;51:694.

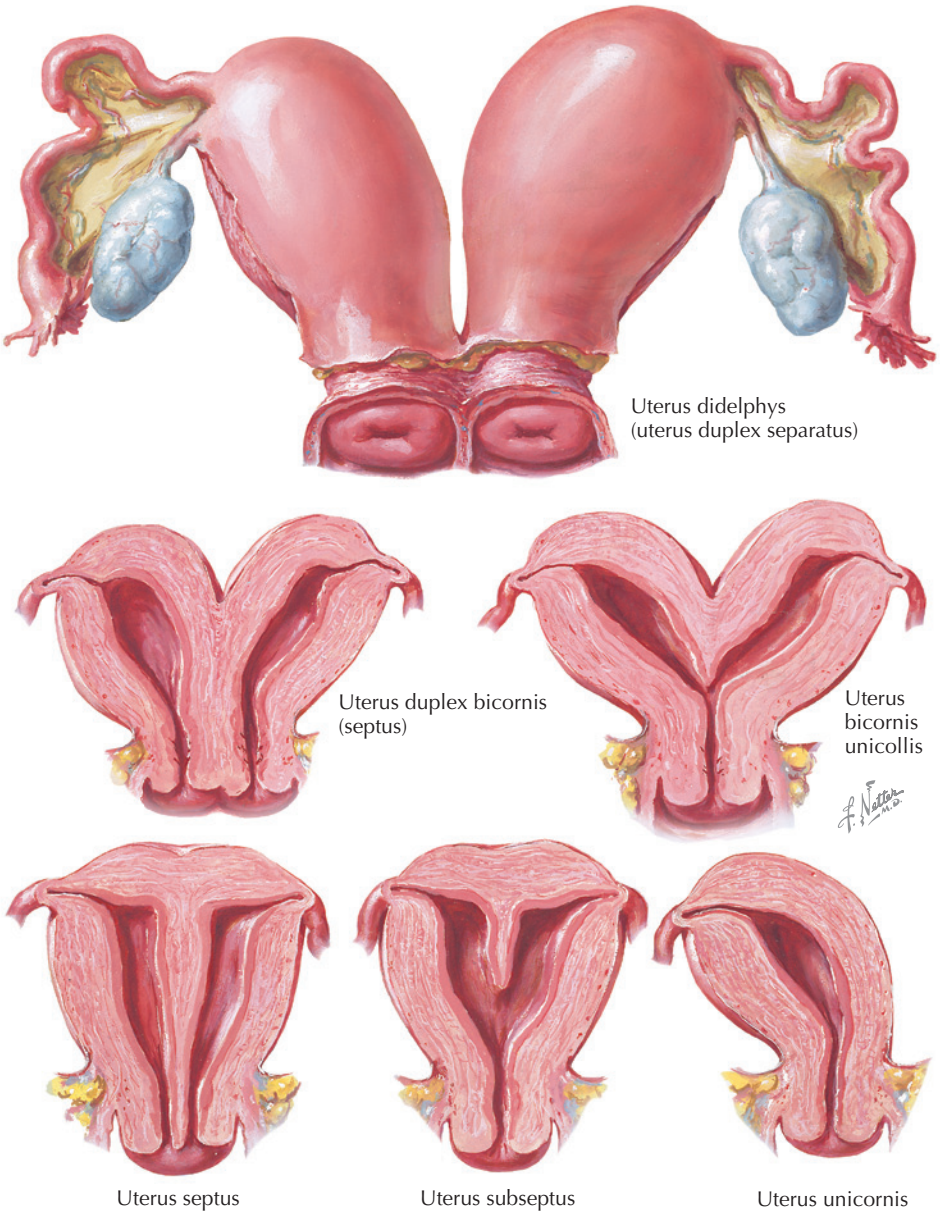


Figure 136.1 Uterine anomalies: bicornuate, septate, and unicornuate uterus

- When outflow is obstructed—hematometra
- Dysmenorrhea, abdominal pain, pelvic mass, abrupt blood discharge

DIAGNOSTIC APPROACH

Differential Diagnosis

- Leiomyomata
- Adnexal mass
- Endometriosis
- Chromosomal abnormality resulting in recurrent abortion

Associated Conditions: Endometriosis (75% when outflow obstruction is present), pelvic adhesions, recurrent abortion, infertility, dysmenorrhea, dyspareunia, hematocolpos, and renal anomalies (contralateral pelvic, horseshoe, or absent kidney).

Workup and Evaluation

Laboratory: No evaluation indicated.

Imaging: Hysterosalpingography, ultrasonography, or sonohysterography. Magnetic resonance imaging may be used, but expense and availability limit its utility.

Special Tests: Hysteroscopy or laparoscopy may be required to complete the evaluation.

Diagnostic Procedures: Physical examination, imaging, and direct observation by hysteroscopy, laparoscopy, or both. Differentiation between septate and bicornuate uterine anomalies requires visualization of the uterine fundus.

Pathologic Findings

In patients with a unicornuate uterus, a normal ovary and tube are generally present. A normal ovary may be present on the opposite side as well. The septate uterus is characterized by the presence of a fibrous septum of variable length with poor vascularization.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and education.

Specific Measures: Patients with nonobstructive abnormalities require no therapy. Patients with recurrent fetal wastage may be considered for uterine reunification (metroplasty) procedures or the excision of any septum, usually by operative hysteroscopy. Patients with a unicornuate deformity and recurrent fetal wastage should be counseled about adoption or the possibilities of in vitro fertilization with implantation into a host uterus.

Diet: No specific dietary changes indicated.

Activity: No restriction.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP079 (If Your Baby Is Breech), AP100 (Repeated Miscarriage), AP090 (Early Pregnancy Loss), and AP143 (Hysterosalpingography).

Drug(s) of Choice

None. Estrogen therapy is often administered for 1–2 months after the resection of a uterine septum, although the need for this is still debated.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.

Prevention/Avoidance: None.

Possible Complications: Obstruction of the outflow of menstrual blood is associated with a 75% chance of endometriosis with resultant pelvic scarring and infertility. There is an increased risk of ectopic pregnancy and early pregnancy loss (33%–35%).

Expected Outcome: Normal reproduction is frequently possible without intervention (25% of cases) for patients with a bicornuate uterus; metroplasty is associated with an increased likelihood of success when pregnancy failures have occurred (80%–90%). When the only abnormality is a uterine septum, normal reproduction is generally possible without intervention (85% success). For patients with a unicornuate uterus, a live birth rate of 40% may be expected; outcomes are not statistically different from those experienced by women with didelphic uteri.

MISCELLANEOUS

Pregnancy Considerations: Increased risk of pregnancy loss, premature delivery, or fetal malpresentation. The risk of ectopic pregnancy is increased for patients with a unicornuate uterus.

ICD-10-CM Codes: Q51.10 (Doubling of uterus with doubling of cervix and vagina without obstruction), Q51.2 (Other doubling of uterus), Q51.3 (Bicornate uterus), and Q51.4 (Unicornate uterus).

REFERENCES

LEVEL II

Lin PC. Reproductive outcomes in women with uterine anomalies. *J Womens Health (Larchmt)*. 2004;13:33.

Moutos DM, Damewood MD, Schlaff WD, et al. A comparison of the reproductive outcome between women with a unicornuate uterus and women with a didelphic uterus. *Fertil Steril*. 1992;58:88.

Reinhold C, Hricak H, Forstner R, et al. Primary amenorrhea: evaluation with MR imaging. *Radiology*. 1997;203:383.

Reichman D, Laufer MR, Robinson BK. Pregnancy outcomes in unicornuate uteri: a review. *Fertil Steril*. 2009;91:1886.

LEVEL III

Doyle MB. Magnetic resonance imaging in mullerian fusion defects. *J Reprod Med*. 1992;37:33.

Grimbizis GF, Camus M, Tarlatzis BC, et al. Clinical implications of uterine malformations and hysteroscopic treatment results. *Hum Reprod Update*. 2001;7:161.

Grimbizis GF, Gordts S, Di Spiezio Sardo A, et al. The ESHRE/ESGE consensus on the classification of female genital tract congenital anomalies. *Hum Reprod*. 2013;28:2032.

Jayasinghe Y, Rane A, Stalewski H, et al. The presentation and early diagnosis of the rudimentary uterine horn. *Obstet Gynecol*. 2005;105:1456.

Mayo-Smith WW, Lee MJ. MR imaging of the female pelvis. *Clin Radiol*. 1995;50:667.

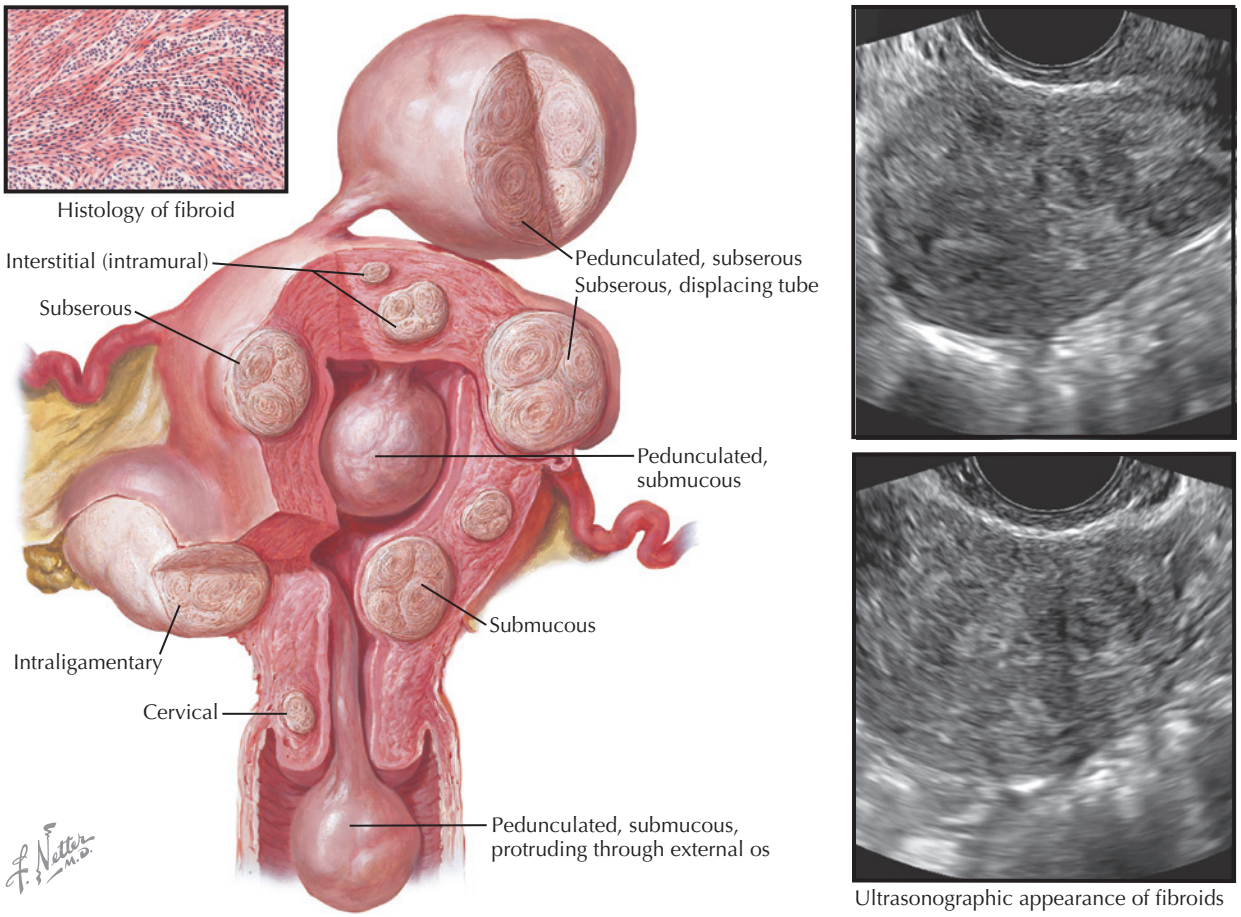


Figure 137.1 Uterine leiomyomata (fibroids, myoma) locations

reduced vitamin D levels, high-fat or high-protein diet (proposed). Smoking reduces the risk.

CLINICAL CHARACTERISTICS

Signs and Symptoms

- 30%–50% symptomatic
- Uterine enlargement and distortion
- Pelvic or abdominal heaviness, low back pain
- Pressure on bowel or bladder (ie, frequency, infrequently causing urinary retention or rarely hydroureter to develop)
- Dysmenorrhea, menorrhagia, intermenstrual bleeding (30%–40% of patients)
- Acute pain (with torsion or degeneration)
- Submucous fibroids may prolapse through the cervix
- Recurrent pregnancy loss

DIAGNOSTIC APPROACH

Differential Diagnosis

- Pregnancy
- Adnexal mass
- Other pelvic or abdominal tumor
- Pelvic kidney
- Urachal cyst
- Urinary retention

Associated Conditions: Dysmenorrhea, menorrhagia, miscarriage, and infertility (rare).

Workup and Evaluation

Laboratory: No evaluation indicated, hemoglobin or hematocrit if anemia suspected.
Imaging: Ultrasonography only when the diagnosis is uncertain.
Special Tests: None indicated.
Diagnostic Procedures: Pelvic examination is generally sufficient and may be augmented by ultrasonography but generally is not required.

Pathologic Findings

Localized proliferation of smooth muscle cells surrounded by a pseudocapsule of compressed muscle fibers. Of uterine fibroids, 70%–80% are found within the wall of the uterus, with 5%–10% lying below the endometrium and less than 5% arising in or near the cervix. Multiple fibroids are found in up to 85% of patients. Myomas may weigh up to 100 pounds.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Reassurance, observation.
Specific Measures: Surgical therapy (hysterectomy or myomectomy) for uncontrollable symptoms, rapid growth, or uncertain diagnosis. Medical therapy with gonadotropin-releasing hormone (GnRH) agonists may be temporarily used to prepare for surgery, pregnancy, or menopause. Uterine artery embolization may be

used for patients who are not surgical candidates or those who wish to preserve fertility. Successful pregnancy is possible, but uterine embolization has been associated with a number of both short- and long-term complications, making its role limited.

Diet: No specific dietary changes indicated.

Activity: No restriction.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP074 (Uterine Fibroids) or AP008 (Hysterectomy).

Drug(s) of Choice

Gonadotropin-releasing hormone agonists (therapy limited to 6 months)—buserelin (Depo-Lupron 3.75 mg IM monthly or 22.5 mg IM every 3 months); goserelin (Zoladex 3.6 mg implant SC monthly or 3-month implant SC every 3 months).

Contraindications: Pregnancy or possible pregnancy.

Precautions: Must exclude possibility of pregnancy before medical therapy. Gonadotropin-releasing hormone agonists may produce significant symptoms of estrogen withdrawal (menopause).

Interactions: None known.

Alternative Drugs

- Synarel nasal solution 2 mg/mL one spray in alternate nostril in the morning and evening (not labeled for the treatment of leiomyomata).
- Nonsteroidal antiinflammatory drugs may be used to reduce menorrhagia.
- Medroxyprogesterone acetate (depot) 100–300 mg IM every 1–3 months may be used to suppress menstruation.
- The antiprogestin mifepristone (RU-486) is effective but not approved for this indication in the United States.

FOLLOW-UP

Patient Monitoring: Watch for the development of symptoms. Monitor uterine size.

Prevention/Avoidance: None.

Possible Complications: Possibility of bone loss with prolonged gonadotropin-releasing hormone or progestin therapy. Leiomyomata may undergo degeneration (hyaline, 65%; myxomatous, 15%; calcific, 10%), rarely causing acute symptoms of pain.

Expected Outcome: Leiomyomata generally stop growing after menopause (even with estrogen replacement). Recurrence after myomectomy is common (25%).

MISCELLANEOUS

Pregnancy Considerations: May (rarely) interfere with early pregnancy or obstruct delivery. Fibroids may grow rapidly or undergo hemorrhage or necrosis and may occasionally even be a cause for disseminated intravascular coagulopathy. Cesarean delivery should be considered for subsequent deliveries if the endometrial cavity is entered during myomectomy.

ICD-10-CM Codes: D25.0 (Submucous leiomyoma of uterus), D25.1 (Intramural leiomyoma of uterus), D25.2 (Subserosal leiomyoma of uterus), and D25.9 (Leiomyoma of uterus, unspecified).

REFERENCES

LEVEL I

Fiscella K, Eisinger SH, Meldrum S, et al. Effect of mifepristone for symptomatic leiomyomata on quality of life and uterine size: a randomized controlled trial. *Obstet Gynecol*. 2006;108:1381.

LEVEL II

Aungst M, Wilson M, Vournas K, et al. Necrotic leiomyoma and gram-negative sepsis eight weeks after uterine artery embolization. *Obstet Gynecol*. 2004;104:1161.

Baird DD, Hill MC, Schectman JM, et al. Vitamin D and the risk of uterine fibroids. *Epidemiology*. 2013;24:447.

Marsh EE, Ekpo GE, Cardozo ER, et al. Racial differences in fibroid prevalence and ultrasound findings in asymptomatic young women (18-30 years old): a pilot study. *Fertil Steril*. 2013;99:1951.

Mehine M, Kaasinen E, Mäkinen N, et al. Characterization of uterine leiomyomas by whole-genome sequencing. *N Engl J Med*. 2013;369:43.

Steinauer J, Pritts EA, Jackson R, et al. Systematic review of mifepristone for the treatment of uterine leiomyomata. *Obstet Gynecol*. 2004;103:1331.

LEVEL III

American College of Obstetricians and Gynecologists. Alternatives to hysterectomy in the management of leiomyomas. ACOG Practice Bulletin No. 96. *Obstet Gynecol*. 2008;112:201.

American College of Obstetricians and Gynecologists. Endometrial ablation. ACOG Practice Bulletin No. 81. *Obstet Gynecol*. 2007;109:1233.

American College of Obstetricians and Gynecologists. Robotic surgery in gynecology. Committee Opinion No. 628. *Obstet Gynecol*. 2015;125:760.

Laughlin SK, Stewart EA. Uterine leiomyomas: individualizing the approach to a heterogeneous condition. *Obstet Gynecol*. 2011;117:396.

Stewart EA. Clinical practice. Uterine fibroids. *N Engl J Med*. 2015;372:1646.

Stewart EA, Morton CC. The genetics of uterine leiomyomata: what clinicians need to know. *Obstet Gynecol*. 2006;107:917.

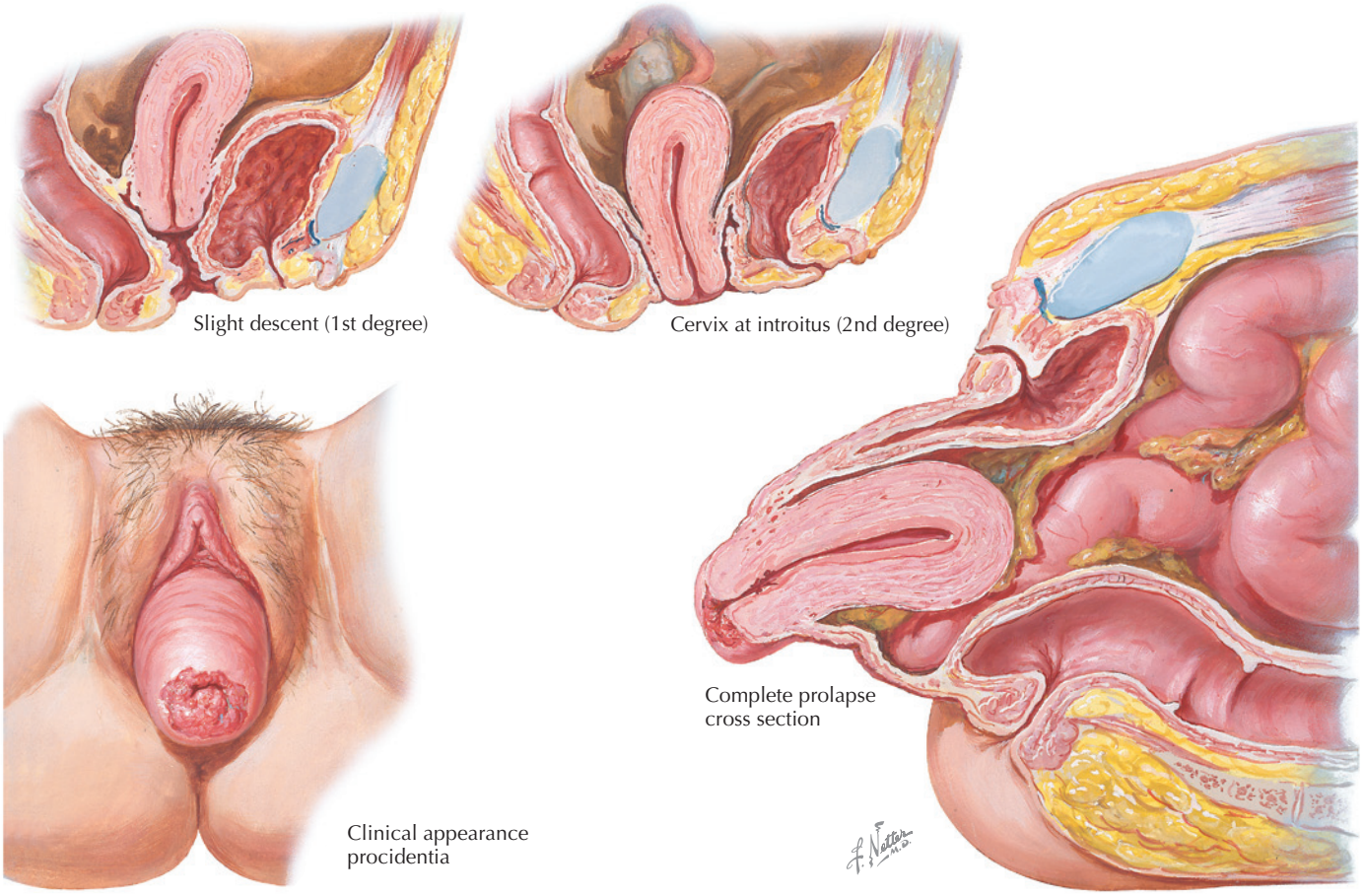


Figure 138.1 Types of uterine prolapses

ETIOLOGY AND PATHOGENESIS

Causes: Loss of normal structural support as a result of trauma (childbirth), surgery, chronic intraabdominal pressure elevation (such as obesity, chronic cough, or heavy lifting), or intrinsic weakness. Most common sites of injury are the cardinal and uterosacral ligaments and the levator ani muscles that form the pelvic floor, which may relax or rupture. Increased intraabdominal pressure from a pelvic mass or ascites may rarely weaken the pelvic support and result in prolapse. Injury to or neuropathy of the S_1–S_4 nerve roots may also result in decreased muscle tone and pelvic relaxation.

Risk Factors: Birth trauma, chronic intraabdominal pressure elevation (such as obesity, chronic cough, or heavy lifting), intrinsic tissue weakness, or atrophic changes, resulting from estrogen loss.

SIGNS AND SYMPTOMS

- Pelvic pressure or heaviness (a sense of "falling out")
- Mass or protrusion at or beyond the vaginal entrance
- New onset or paradoxical resolution of urinary incontinence
- Drying, thickening, chronic inflammation, and ulceration of the exposed tissues, which may result in bleeding, discharge, or odor

DIAGNOSTIC APPROACH

Differential Diagnosis

- Cystocele
- Urethrocele
- Rectocele
- Enterocele
- Prolapsed uterine leiomyomata
- Bartholin's cyst
- Vaginal cyst or tumor
- Cervical hypertrophy (with normal uterine support)

Associated Conditions: Urinary incontinence, pelvic pain, dyspareunia, intermenstrual or postmenopausal bleeding. Almost always associated with a cystocele, rectocele, and enterocele.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated.
Special Tests: Urodynamics testing may be considered if voiding or continence is altered. Either the Baden-Walker Halfway Scoring evaluation system or the Pelvic Organ Prolapse Quantification System (POP-Q) may be used to quantify the degree of prolapse present.
Diagnostic Procedures: History and physical examinations.

Pathologic Findings

Tissue change is common because of mechanical trauma and desiccation.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Weight reduction, modification of activity (lifting), addressing factors such as chronic cough.

Specific Measures: Minimal prolapse does not require therapy. For those with more severe prolapse or symptoms, pessary therapy (Smith-Hodge, doughnut, cube, or inflatable ball), surgical repair, or hysterectomy (with colporrhaphy) should be considered. Postmenopausal women should receive estrogen and progesterone replacement therapy for at least 30 days before pessary fitting or surgical repair. Colpocleisis may be required for selected patients.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP012 (Pelvic Support Problems), AP081 (Urinary Incontinence), AP166 (Surgery for Stress Urinary Incontinence), and AP183 (Surgery for Pelvic Organ Prolapse).

Drug(s) of Choice

Estrogen and progesterone therapy (for postmenopausal patients) improves tissue tone and healing and is often prescribed before surgical repair or as an adjunct to pessary therapy.
Contraindications: Estrogen therapy should not be used if undiagnosed vaginal bleeding is present.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. If a pessary is used, frequent follow-up (both initially and long term) is required. Most recommend monthly checks of the vaginal epithelium for lesions and to reassess pessary placement and fit.
Prevention/Avoidance: Maintenance of normal weight, avoidance of known (modifiable) risk factors.
Possible Complications: Thickening or ulceration of the vaginal tissues and cervix, urinary incontinence, kinking of the ureters, obstipation, sexual dysfunction.
Expected Outcome: Uterine descent tends to worsen with time. If uncorrected, complete prolapse is associated with vaginal and cervical skin changes, ulceration, and bleeding.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, though these conditions rarely coexist.

ICD-10-CM Codes: N81.2 (Incomplete uterovaginal prolapse), N81.3 (Complete uterovaginal prolapse), N81.9 (Female genital prolapse, unspecified), N81.4 (Uterovaginal prolapse, unspecified), and N81.9 (Female genital prolapse, unspecified).

REFERENCES

LEVEL I

Cundiff GW, Amundsen CL, Bent AE, et al. The PESSRI study: symptom relief outcomes of a randomized crossover trial of the ring and Gellhorn pessaries. *Am J Obstet Gynecol*. 2007;196:405.e1.

LEVEL II

Hagen S, Stark D. Conservative prevention and management of pelvic organ prolapse in women. *Cochrane Database Syst Rev*. 2011;(12):CD003882.

Ismail SI, Bain C, Hagen S. Oestrogens for treatment or prevention of pelvic organ prolapse in postmenopausal women. *Cochrane Database Syst Rev*. 2010;(9):CD007063.

Maher C, Feiner B, Baessler K, et al. Surgical management of pelvic organ prolapse in women. *Cochrane Database Syst Rev*. 2013;(4):CD004014.

Swift S, Woodman P, O'Boyle A, et al. Pelvic Organ Support Study (POSST): The distribution, clinical definition, and epidemiologic condition of pelvic organ support defects. *Am J Obstet Gynecol*. 2005;192:795.

Vergeldt TF, Weemhoff M, IntHout J, et al. Risk factors for pelvic organ prolapse and its recurrence: a systematic review. *Int Urogynecol J*. 2015;26:1559.

LEVEL III

American College of Obstetricians and Gynecologists. Urinary incontinence in women. Practice Bulletin No. 155. *Obstet Gynecol*. 2015;126:e66.

Culligan PJ. Nonsurgical management of pelvic organ prolapse. *Obstet Gynecol*. 2012;119:852.

Jelovsek JE, Maher C, Barber MD. Pelvic organ prolapse. *Lancet*. 2007;369:1027.

SECTION IX

Adnexal Disease

This page intentionally left blank

ADENOFIBROMA

139

INTRODUCTION

Description: An adenofibroma is an epithelial tumor that consists of glandular elements and large amounts of stromal (fibrous) elements. Adenofibromas are most commonly found as ovarian masses. They may also occur in the cervix or uterine body. Adenofibromas are closely related to cystadenofibromas, which have cystic areas but still contain more than 25% fibrous connective tissue.
Prevalence: Uncommon.
Predominant Age: Perimenopausal and postmenopausal.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Unknown.
Risk Factors: None known.

SIGNS AND SYMPTOMS

- Asymptomatic (often an incidental finding after oophorectomy)
- Adnexal mass (adenofibromas are bilateral in 25% of cases)
- Fibrous cervical or endometrial polyp
- Acute abdominal pain if torsion occurs (rare)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Thecoma (fibroma)
- Stromal and germ cell tumors
- Brenner tumor
- Endometrioma
- Benign cystic teratoma
- Serous or mucinous cystadenoma
- Metastatic tumors
- Pedunculated leiomyomata
- Endocervical polyp

Associated Conditions: None.

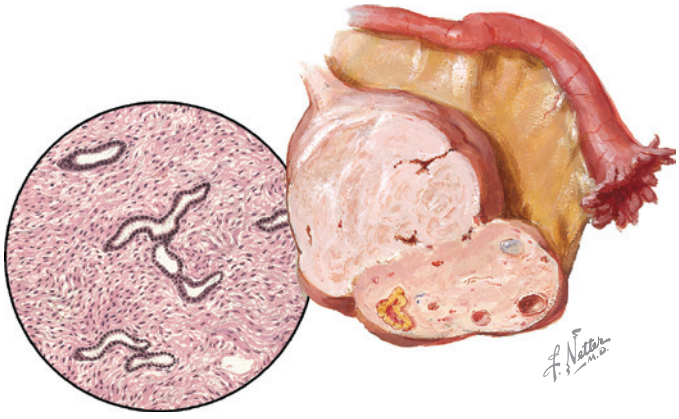


Figure 139.1 Serous adenofibroma

WORKUP AND EVALUATION

Laboratory: No specific evaluation indicated. Evaluate as with other adnexal or cervical masses.
Imaging: Ultrasonography suggests a solid tumor.
Special Tests: None indicated.
Diagnostic Procedures: Histopathology.

Pathologic Findings

Fibrous and epithelial elements make up this tumor. The epithelial components may be serous, mucinous, clear cell, or endometrioid. Epithelial or fibrous elements may predominate, changing the gross character of the tumor. Size is generally 1–15 cm in diameter.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and diagnosis.
Specific Measures: Simple surgical excision. Adenofibromas that are borderline or of low malignant potential do exist. These tumors must be treated on the basis of their size, location, and histologic evaluation, but they may require more extensive surgical therapy.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP075 (Ovarian Cysts) and AP096 (Cancer of the Ovary).

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: Torsion of solid ovarian tumors. Adenofibromas that are borderline or of low malignant potential may spread or recur.
Expected Outcome: Surgical excision is generally curative.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: Based on location and predominant cell type.

REFERENCES

LEVEL III

Fleischer AC. Transabdominal and transvaginal sonography of ovarian masses. *Clin Obstet Gynecol*. 1991;34:433.

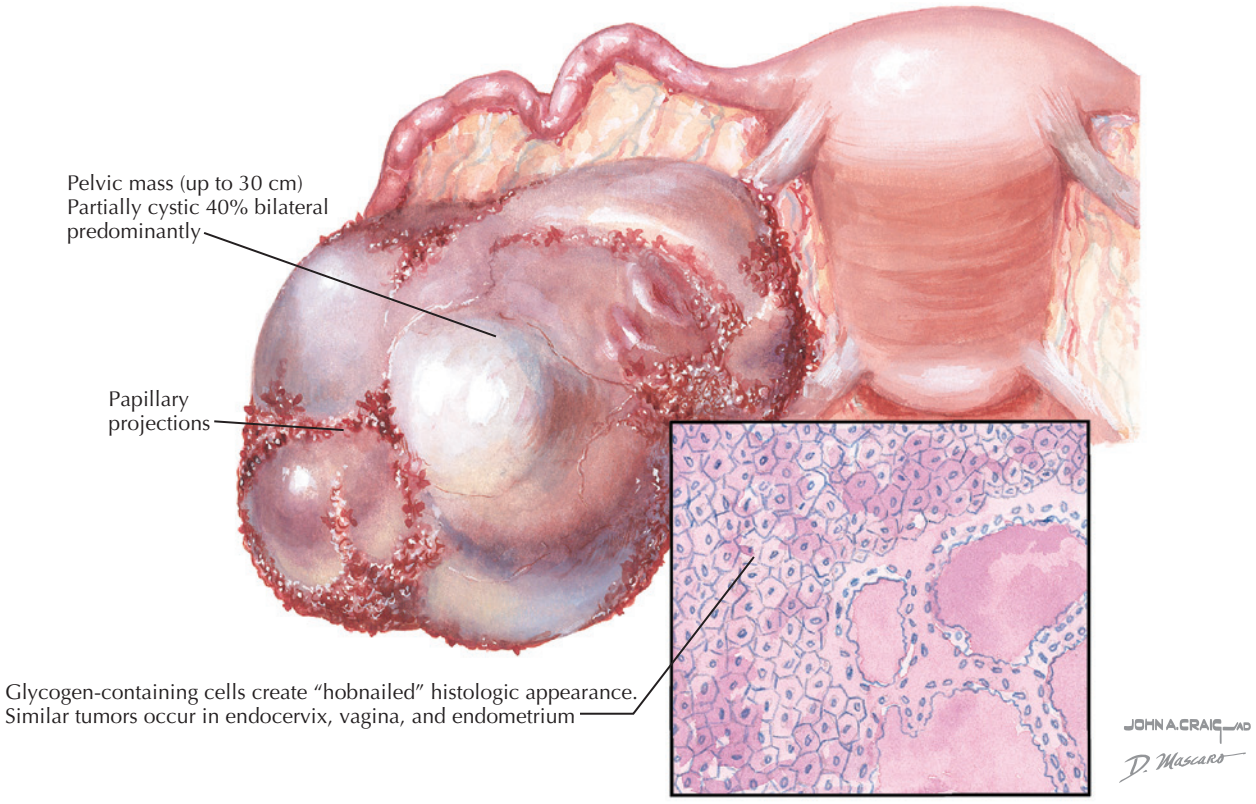
Herman JR, Locher GW, Goldhirsch A. Sonographic patterns of ovarian tumors: prediction of malignancy. *Obstet Gynecol*. 1987;69:777.

Montoriol PF, Mons A, Da Ines D, et al. Fibrous tumours of the ovary: aetiologies and MRI features. *Clin Radiol*. 2013;68:1276.

140 CLEAR CELL CARCINOMA

INTRODUCTION

Description: A clear cell carcinoma is an ovarian epithelial tumor made up of cells containing large amounts of glycogen, giving them a clear or "hobnailed" appearance. These tumors may also arise in the endocervix, endometrium, and vagina. Cervical and vaginal tumors have been linked to in utero exposure to diethylstilbestrol (DES).
Prevalence: 5%–11% of ovarian cancers.
Predominant Age: 40–78 years.
Genetics: No genetic pattern.



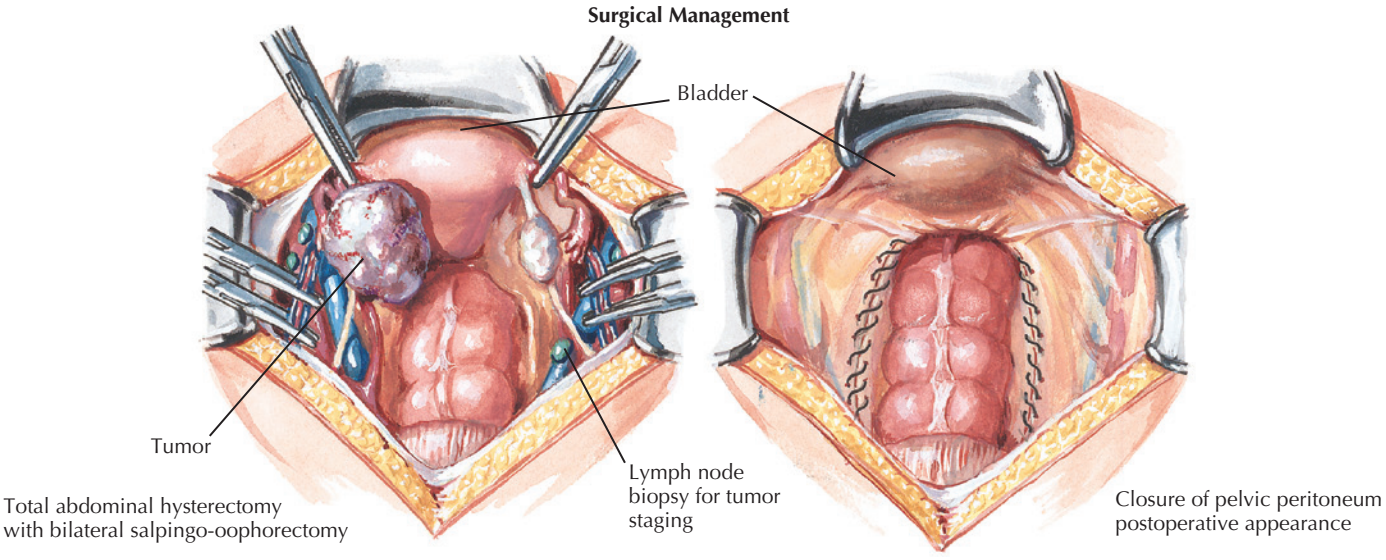


Figure 140.1 Clear cell carcinoma of ovary appearance and surgical management

ETIOLOGY AND PATHOGENESIS

Causes: Unknown. May arise from mesonephric or Müllerian elements.
Risk Factors: None known. Endometriosis has been postulated.

SIGNS AND SYMPTOMS

- Asymptomatic
- Pelvic mass (up to 30 cm)—partially cystic with yellow, gray, and hemorrhagic areas
- Papillary projections generally present, giving the mass a velvety appearance; 40% of tumors are bilateral

DIAGNOSTIC APPROACH

Differential Diagnosis

- Benign adnexal masses (corpus luteum, follicular cyst)
- Nongynecologic pelvic masses
- Hepatic, renal, or cardiac disease resulting in weight loss and ascites
- Endometriosis
- Hydrosalpinx
- Ectopic pregnancy (reproductive-age women)
- Pedunculated leiomyomata
- Pelvic or horseshoe kidney
- Gastrointestinal malignancy

Associated Conditions: Increased risk of vascular thrombotic events and paraneoplastic hypercalcemia.

Workup and Evaluation

Laboratory: As indicated before surgery. Serum testing for tumor markers, such as CA-125, lipid-associated sialic acid, carcinoembryonic antigen, and α-fetoprotein, should be reserved for following the progress of patients with known malignancies and not for prognostic evaluation.
Imaging: No imaging indicated.
Special Tests: A frozen-section histologic evaluation should be considered for any ovarian mass that appears suspicious for malignancy.
Diagnostic Procedures: History, physical examination, and imaging. Final diagnosis is established by histologic evaluation.

Pathologic Findings

Usually found as a malignant tumor. Despite the presence of hobnail cells that are similar to those observed in the endometrium, cervix, and vagina of women exposed to diethylstilbestrol in utero, there is no evidence that diethylstilbestrol has a role in clear cell ovarian tumors.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, supportive therapy based on symptoms.
Specific Measures: Requires surgical exploration and extirpation, including the uterus and contralateral ovary. Adjunctive chemotherapy (platinum-based and paclitaxel [Taxol]) or radiation therapy is often included, based on the location and stage of the disease. However, clear cell carcinoma is not as sensitive to platinum-based chemotherapy as the other histologic subtypes of ovarian cancers.
Diet: No specific dietary changes indicated, except those imposed by advanced disease.
Activity: No restriction except that imposed by advanced disease.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP096 (Cancer of the Ovary) and AP075 (Ovarian Cysts).

Drug(s) of Choice

None, except as adjunctive or symptomatic therapy.
Contraindications: See individual agents.
Precautions: Alkylating agents are associated with an increased risk for future leukemia (10% by 8 years after therapy).
Interactions: See individual agents.

FOLLOW-UP

Patient Monitoring: Careful follow-up for recurrent pelvic disease or enlargement of the remaining ovary (if any). This is generally performed by pelvic examination, augmented with ultrasonography in selected patients. In those suspected of having recurrent disease and other selected patients, second-look surgery may be desirable to assess progress and discover occult disease.
Prevention/Avoidance: None. Tubal ligation appears to reduce risk (by reducing the risk of endometriosis).
Possible Complications: Rapid spread and progressive deterioration of the patient's condition.
Expected Outcome: Typically aggressive course with rapid disease progression and spread. Clear cell ovarian carcinoma has the worst prognosis of all ovarian malignancies, with a 5-year survival rate of <40%. The 5-year survival rate is modified by stage of disease at diagnosis: limited to one ovary, 80%; higher stage disease, 11%.

MISCELLANEOUS

Pregnancy Considerations: No direct effect on pregnancy (generally not an issue).
ICD-10-CM Codes: C56 (Malignant neoplasm of ovary).

REFERENCES

LEVEL II

Chan JK, Teoh D, Hu JM, et al. Do clear cell ovarian carcinomas have poorer prognosis compared to other epithelial cell types? A study of 1411 clear cell ovarian cancers. *Gynecol Oncol*. 2008;109:370.

Sugiyama T, Kamura T, Kigawa J, et al. Clinical characteristics of clear cell carcinoma of the ovary: a distinct histologic type with poor prognosis and resistance to platinum-based chemotherapy. *Cancer*. 2000;88:2584.

LEVEL III

American College of Obstetricians and Gynecologists. The role of the obstetrician–gynecologist in the early detection of epithelial ovarian cancer. Committee Opinion No. 477. *Obstet Gynecol*. 2011;117:742.

del Carmen MG, Birrer M, Schorge JO. Clear cell carcinoma of the ovary: a review of the literature. *Gynecol Oncol*. 2012;126:481.

Hameed K, Burslem MRG, Tupper WRC. Clear cell carcinoma of the ovary. *Cancer*. 1969;24:452.

Sugiyama T, Kamura T, Kigawa J, et al. Clinical characteristics of clear cell carcinoma of the ovary: a distinct histologic type with poor prognosis and resistance to platinum-based chemotherapy. *Cancer*. 2000;88:2584.

Tan DS, Kaye S. Ovarian clear cell adenocarcinoma: a continuing enigma. *J Clin Pathol*. 2007;60:355.

141 DERMOID CYST

INTRODUCTION

Description: The most common ovarian tumor in young, reproductive-aged women is the cystic teratoma or dermoid, which originates from a germ cell and contains elements from all three germ cell layers. These tumors may be benign or malignant (1%–2% malignant, usually in women older than 40 years). Dermatoid cysts account for 20%–25% of all ovarian tumors, one-third of all benign tumors, and 70% of tumors in young women aged 10–30 years.
Prevalence: 15%–25% of ovarian tumors.
Predominant Age: 20s–30s (75%); most patients are younger than 40 years.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Unknown. Considered to arise from a single germ cell during the first meiotic division at approximately 13 weeks of fetal life. They routinely have a chromosomal makeup of 46,XX.
Risk Factors: None known.

SIGNS AND SYMPTOMS

- Asymptomatic (50%–60%)
- Adnexal mass (<10 cm in diameter in 80% of patients; bilateral in 10%–15% of patients)—the contents of cystic teratomas are of low density; they are often found "floating" anterior to the uterus or broad ligament, displacing the uterus posteriorly
- May present with pain secondary to torsion (approximately 10%) or bleeding into the cyst, a sense of pelvic heaviness, or dysmenorrhea
- Thyroid storm (when thyroid tissue predominates: struma ovarii) or carcinoid syndrome (rare)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Functional cysts (follicle, corpus luteum)
- Epithelial tumors (cystic or solid)
- Ectopic pregnancy
- Tubo-ovarian abscess
- Endometrioma
- Hydrosalpinx
- Paratubal cyst
- Appendiceal abscess

Associated Conditions: None.

WORKUP AND EVALUATION

Laboratory: No evaluation indicated. Some serum markers (hCG, AFT, LDH) may be elevated but are of little use in diagnosis.
Imaging: Ultrasonography (abdominal or transvaginal may be of assistance but usually is not required; when used, it has a 95%

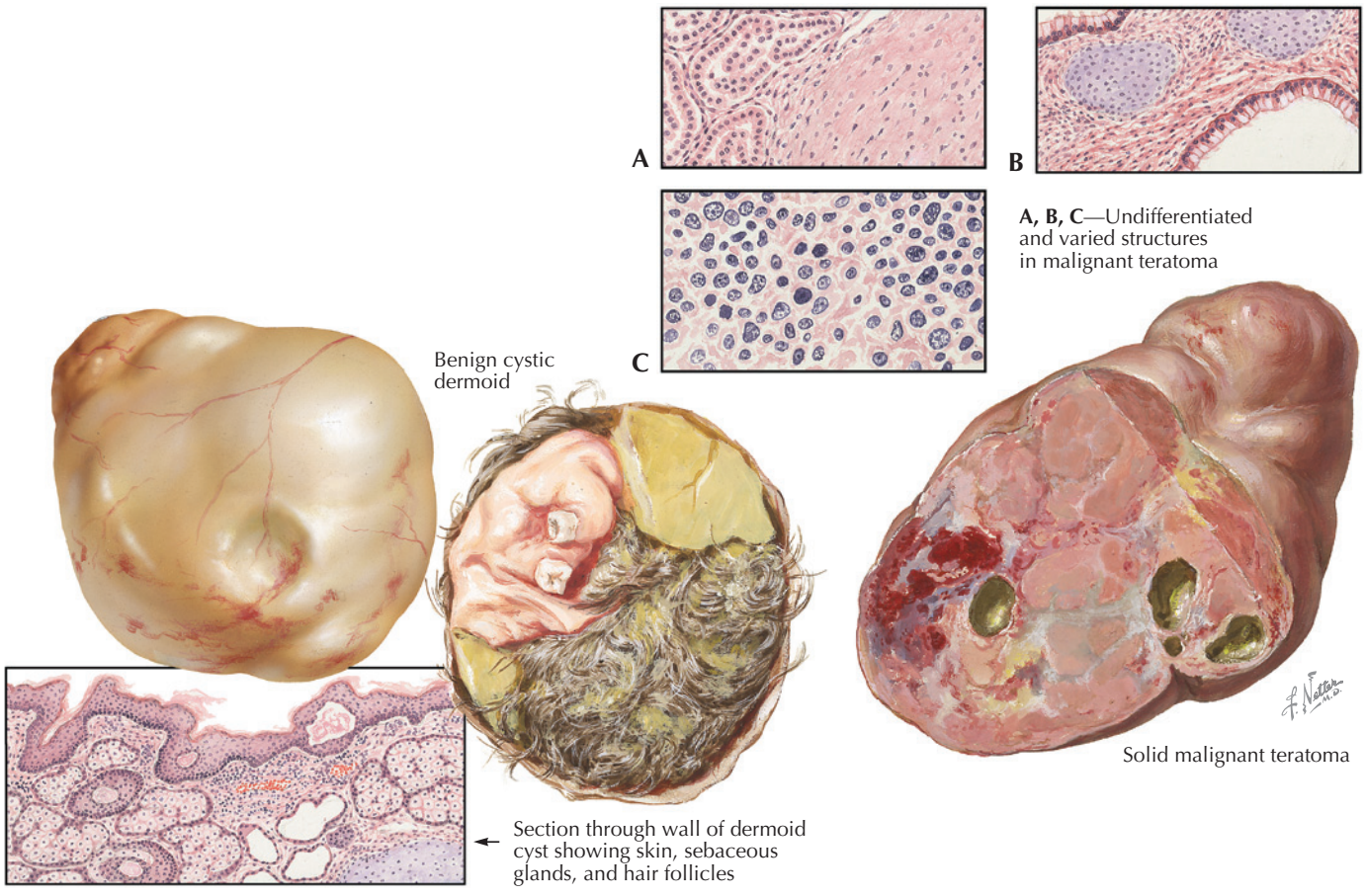


Figure 141.1 Dermoid cyst

positive predictive value). Of teratomas, 30%–50% have calcifications and may be detected by radiographic examination.

Special Tests: None indicated.

Diagnostic Procedures: History, physical examination, imaging. May be found incidentally at laparotomy or laparoscopy.

Pathologic Findings

These tumors are derived from primary germ cells and include tissues from all three embryonic germ layers (ectoderm, mesoderm, and endoderm). Consequently, they often contain hair, sebaceous material, cartilage, bone, teeth, or neural tissue. On some occasions, functional thyroid tissue may be present (up to 12% of cases). Cystic teratomas contain malignant elements in only approximately 1%–2% of cases.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, support for acute symptoms.

Specific Measures: Surgical exploration and resection.

Diet: No specific dietary changes indicated.

Activity: No restriction.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP075 (Ovarian Cysts).

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Normal health maintenance.

Prevention/Avoidance: None.

Possible Complications: Most common—torsion (3%–12%). Possible—infection, rupture, and malignant transformation (squamous carcinoma, 1%–2%). The risk of malignant transformation is greatest when these tumors are found in postmenopausal women. Recurrence of teratomas is as high as 3.4% in some studies. Rupture of a dermoid cyst can result in an intense chemical peritonitis and is a surgical emergency. Slow leakage may mimic disseminated carcinoma. Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis has been reported to be associated with teratomas.

Expected Outcome: Based on the size and location of the tumor, it is often possible to conserve some or most of the ovary while the tumor itself is resected.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. Of teratomas, 10% are diagnosed during pregnancy and account for 20%–40% of ovarian tumors found during pregnancy. Rupture of the cyst, although rare, is more common during pregnancy.

ICD-10-CM Codes: D27.9 (Benign neoplasm of unspecified ovary).

REFERENCES

LEVEL I

Wang PH, Lee WL, Juang CM, et al. Excision of mature teratoma using culdotomy, with and without laparoscopy: a prospective randomized trial. *BJOG*. 2001;108:91.

LEVEL II

Emoto M, Obama H, Horiuchi S, et al. Transvaginal color Doppler ultrasonic characterization of benign and malignant ovarian cystic teratomas and comparison with serum squamous cell carcinoma antigen. *Cancer*. 2000;88:2298.

Koonings PP, Campbell K, Mishell DR Jr, et al. Relative frequency of primary ovarian neoplasms: a 10-year review. *Obstet Gynecol*. 1989;74:921.

Mais V, Guerriero S, Ajossa S, et al. Transvaginal ultrasonography in the diagnosis of cystic teratoma. *Obstet Gynecol*. 1995;85:48.

Pantoja E, Noy MA, Axtmayer RW, et al. Ovarian dermoids and their complications: comprehensive historical review. *Obstet Gynecol Surv*. 1975;30:1.

Park CH, Jung MH, Ji YI. Risk factors for malignant transformation of mature cystic teratoma. *Obstet Gynecol Sci*. 2015;58:475.

LEVEL III

American College of Obstetricians and Gynecologists. Management of adnexal masses. ACOG Practice Bulletin No. 83. *Obstet Gynecol*. 2007;110:201.

Gallion H, van Nagell JR Jr, Donaldson ES, et al. Immature teratoma of the ovary. *Am J Obstet Gynecol*. 1983;146:361.

Linder D, McCau BK, Hecht F. Parthenogenic origin of benign ovarian teratomas. *N Engl J Med*. 1975;292:63.

Petersen WF, Prevost EC, Edmunds FT, et al. Benign cystic teratomas of the ovary. *Am J Obstet Gynecol*. 1955;70:368.

Smith AD 3rd, Samkoff L. Non-N-methyl-D-aspartate receptor antibody encephalitis with cerebellitis with associated ovarian teratoma. *JAMA Neurol*. 2015;72:1375.

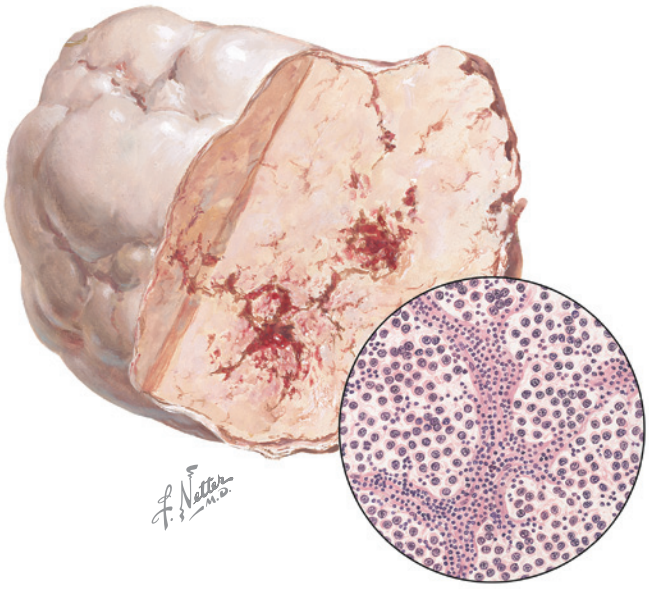


Figure 142.1 Dysgerminoma

SIGNS AND SYMPTOMS

- Asymptomatic
- Adnexal mass (bilateral in 5%–10%), lobulated, solid and soft or firm, with a gray-white or cream-colored cut surface, often with rapid growth
- These tumors may produce either testosterone or estrogens

DIAGNOSTIC APPROACH

Differential Diagnosis

- Benign adnexal masses (corpus luteum, follicular cyst)
- Endometriosis
- Hydrosalpinx
- Paratubal cyst
- Appendiceal abscess
- Ectopic pregnancy
- Pedunculated leiomyomata
- Pelvic or horseshoe kidney
- Nongynecologic pelvic masses

Associated Conditions: None.

WORKUP AND EVALUATION

Laboratory: As indicated before surgery. β-Human chorionic gonadotropin is often elevated (several thousand units), as is lactic dehydrogenase. Serum testing for tumor markers, such as CA-125, lipid-associated sialic acid, carcinoembryonic antigen, and α-fetoprotein, should be reserved for following the progress of patients with known malignancies and not for prognostic evaluation.

Imaging: Preoperative evaluation (computed tomography [CT] or ultrasonography) for possible lymph node enlargement or intra-abdominal spread is indicated for patients in whom malignancy is a significant possibility.

Special Tests: None indicated.

Diagnostic Procedures: History, physical examination, and imaging. Final diagnosis is established by histologic evaluation.

Pathologic Findings

Primitive germ cells with stroma infiltrated by lymphocytes (analogous to seminomas in the testes). Areas of malignant cells are found in 10%–15% of tumors, though the degree of histologic atypia is variable and only approximately one-third behave aggressively.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and supportive therapy based on symptoms.

Specific Measures: Surgical exploration and resection. When the tumor is confined to one ovary, preservation of the uterus and other ovary is possible to preserve fertility. These tumors are very sensitive to radiotherapy, which may be used as an adjunct or to treat recurrent disease. Multiagent chemotherapy has fewer side effects and is often the preferred adjunct.

Diet: No specific dietary changes indicated, except those imposed by advanced disease.

Activity: No restriction except that imposed by advanced disease.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP096 (Cancer of the Ovary) and AP075 (Ovarian Cysts).

Drug(s) of Choice

Adjunctive or symptomatic therapy. Combination chemotherapy in selected patients (vincristine, actinomycin D, and cyclophosphamide or bleomycin, etoposide, and cisplatin).

FOLLOW-UP

Patient Monitoring: Careful follow-up for recurrent pelvic disease or enlargement of the remaining ovary (if any). This is generally performed by pelvic examination, augmented with ultrasonography in selected patients. In patients suspected of having recurrent disease and other selected patients, second-look surgery may be desirable to assess progress and discover occult disease.

Prevention/Avoidance: None.

Possible Complications: Tumor progression or growth. These tumors tend to spread by lymphatic channels. Recurrence of tumor is found in 20% of patients, but recurrent disease generally responds well to additional surgery, chemotherapy, or radiation.

Expected Outcome: The prognosis is good for patients with pure dysgerminomas less than 15 cm in size. With limited disease and no indication of spread at the time of surgery (stage I), the 5-year survival rate is a greater than 90%.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. May be discovered during pregnancy because of age distribution.

ICD-10-CM Codes: Specific to cell type and location.

REFERENCES

LEVEL II

Gallion HH, van Nagell JR Jr, Donaldson ES, et al. Ovarian dysgerminoma: report of seven cases and review of the literature. *Am J Obstet Gynecol*. 1988;158:591.

Pectasides D, Pectasides E, Kassanos D. Germ cell tumors of the ovary. *Cancer Treat Rev*. 2008;34:427.

Smith HO, Berwick M, Verschraegen CF, et al. Incidence and survival rates for female malignant germ cell tumors. *Obstet Gynecol*. 2006;107:1075.

LEVEL III

American College of Obstetricians and Gynecologists. Management of adnexal masses. ACOG Practice Bulletin No. 83. *Obstet Gynecol*. 2007; 110:201.

Fleischer AC. Transabdominal and transvaginal sonography of ovarian masses. *Clin Obstet Gynecol*. 1991;34:433.

Tewari K, Cappuccini F, Disaia PJ, et al. Malignant germ cell tumors of the ovary. *Obstet Gynecol*. 2000;95:128.

ECTOPIC PREGNANCY

143

INTRODUCTION

Description: An ectopic pregnancy is one in which the fertilized egg is implanted outside of the endometrial cavity (fallopian tube [98%], ovary, abdominal cavity, or cervix). This is the leading cause of pregnancy-related maternal death in the first trimester (4%–10% of all pregnancy-related deaths).
Prevalence: 10–15 of 1000 pregnancies; varies with age, race, and location (highest in Jamaica and Vietnam).
Predominant Age: 25–34 years (>50%).
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Tubal damage or altered motility that causes the fertilized egg to be improperly transported, resulting in implantation outside the uterine cavity. The most common cause is acute salpingitis (50%). In the majority of the remaining patients (40%), no risk factor is apparent. Abnormal embryonic development may play a role.
Risk Factors: Tubal damage (pelvic infections; six-fold increased risk), prior ectopic pregnancy (10-fold increased risk), prior female sterilization, age 35–44 years (three-fold greater rate of extrauterine gestations than for women aged 15–24 years), nonwhite race (1.5-fold increased risk), assisted reproduction (twofold increased risk), cigarette smoking (30+/day: three- to five-fold increased risk), intrauterine contraceptive device (IUCD) use, and endometriosis. More than half of cases occur in women who have been pregnant three or more times.

SIGNS AND SYMPTOMS

- Normal signs and symptoms of pregnancy (amenorrhea, uterine softening)
- Acute abdominal pain (dull, crampy, or colicky)
- Evidence of intra-abdominal bleeding, including hypotension and collapse
- Adnexal mass (with or without tenderness)
- Vaginal bleeding
- Signs of peritoneal irritation
- Absence of a gestational sac on ultrasonography with β-human chorionic gonadotropin (β-hCG) level >2000 mIU/mL
- Abdominal pregnancy may be asymptomatic until near term

DIAGNOSTIC APPROACH

Differential Diagnosis

- Appendicitis
- Degenerating fibroid
- Dysfunctional uterine bleeding
- Endometriosis
- Gastroenteritis
- Mesenteric thrombosis
- Ovulation

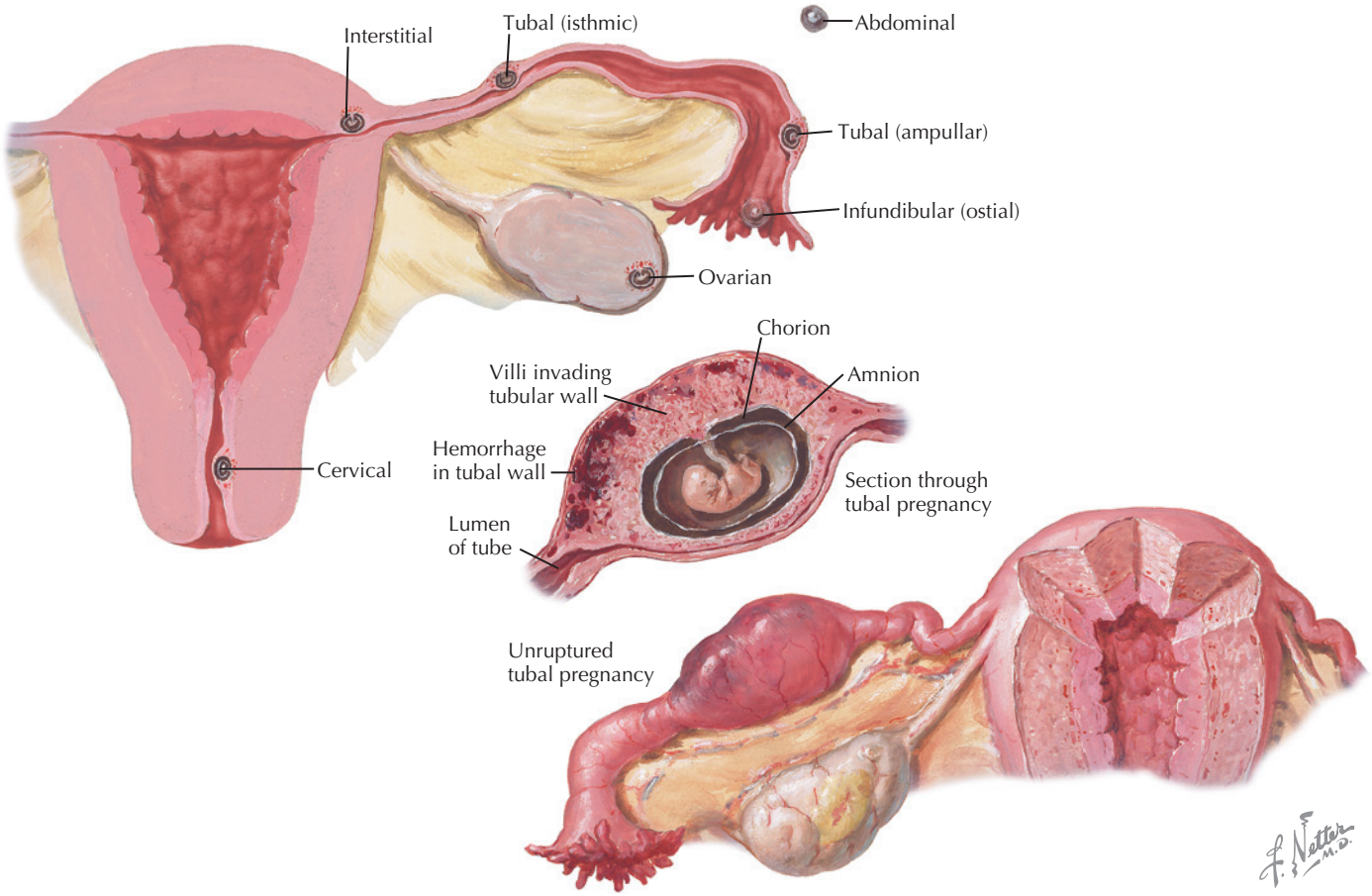
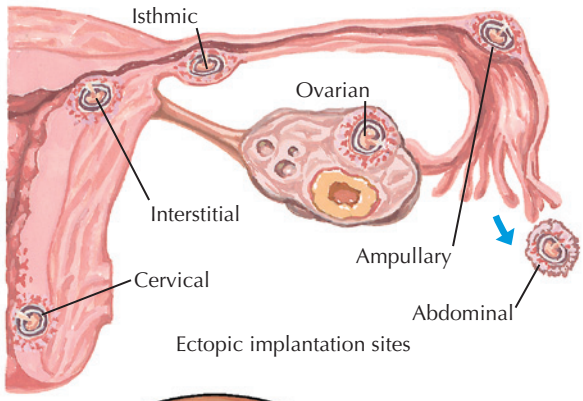
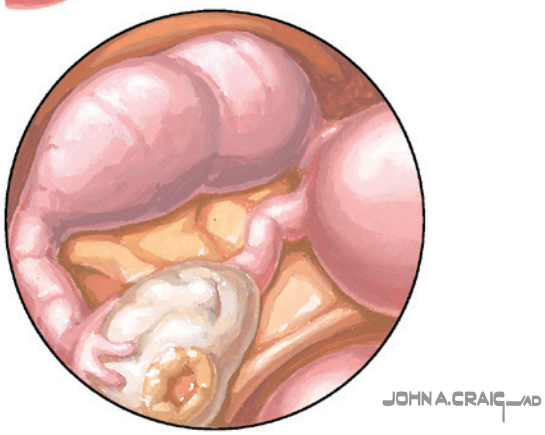


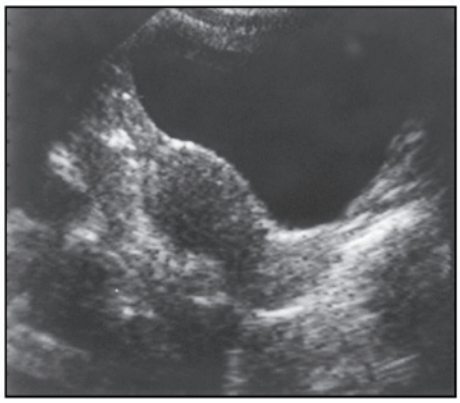
Figure 143.1 Site of ectopic implantation



Ectopic implantation sites



Laparoscopy may be used to confirm diagnosis of ectopic pregnancy


Sonogram of empty uterine cavity

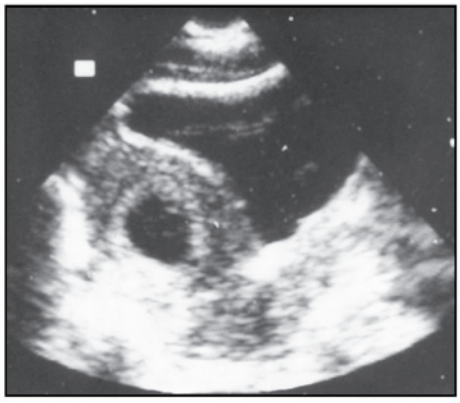

Sonogram of gestational sac

Figure 143.2 Diagnosis of ectopic pregnancy

- Ruptured corpus luteum cyst
- Salpingitis
- Septic abortion (fever > 38°C or a white blood count of >20,000 WBC/dL is rare in patients with ectopic pregnancies; the presence of either should suggest a pelvic infection, including septic abortion)
- Threatened or incomplete abortion
- Torsion of an adnexal mass

Associated Conditions: Pelvic inflammatory disease, infertility, and recurrent abortion.

Workup and Evaluation

Laboratory: Serial quantitative β-hCG levels (if patient's condition permits; 85% of viable pregnancies, demonstrate a rise of at least 66% every 48 hours during the first 40 days of pregnancy). Levels are lower than 3000 mIU/mL in approximately half of ectopic pregnancies. Serum progesterone (low) may be of diagnostic help if less than 6 weeks gestation (almost 90% of patients with an ectopic pregnancy have levels less than 30 nM/L [10 ng/mL]). A hematocrit level of less than 30% is found in approximately one-fourth of women with ruptured ectopic pregnancy.

Imaging: Ultrasonography (transvaginal preferred) may be augmented by color-flow Doppler studies.

Special Tests: Culdocentesis has largely been replaced by ultrasonography.

Diagnostic Procedures: History and physical examination, serum β-hCG level and ultrasonography. When laparoscopy is used as a diagnostic tool, there is a 2%–5% chance of a false-positive or false-negative diagnosis.

Pathologic Findings

Placental villi invading tissue other than the endometrium. Most ectopic pregnancies are tubal, with the ampulla (approximately 80%) and isthmus (12%) being the most common locations and 5% in the fimbrial region.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Rapid assessment and general support when intraabdominal bleeding is present.

Specific Measures: Expeditious diagnosis (diagnostic delay is a factor in approximately half of all deaths associated with ectopic pregnancy; 50% of patients have had one or more visits to a healthcare provider before the diagnosis is made, even in nonfatal cases). Surgical intervention generally is required for symptomatic patients (salpingostomy, salpingectomy). Medical therapy may be considered for asymptomatic or mildly symptomatic patients.

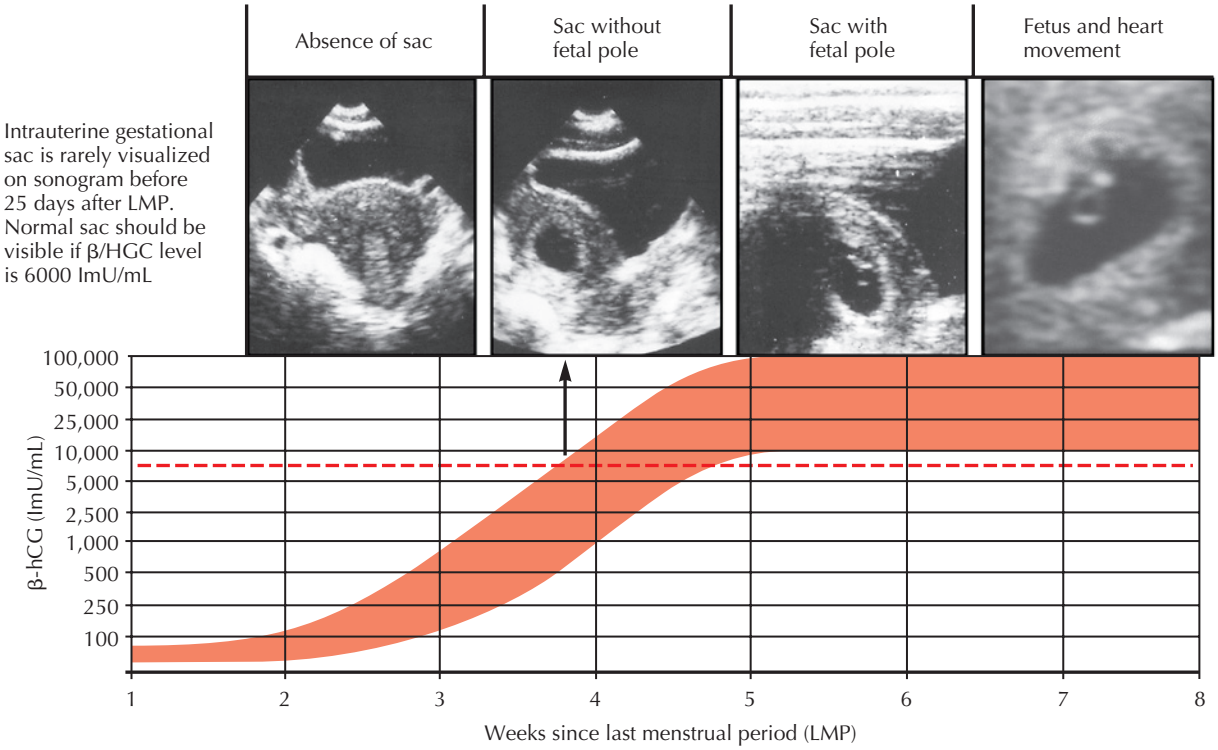
Diet: In acute rupture, nothing by mouth in anticipation of possible surgical intervention. If medical therapy is used, avoid folate supplements and folate-containing preparations (eg, multivitamins, prenatal vitamins).

Activity: No restriction except those dictated by the patient's status.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP077 (Pelvic Inflammatory Disease).

Drug(s) of Choice

Methotrexate IM 50 mg/m^2 surface area with a maximum of 80 mg.



hCG, human chorionic gonadotropin.

Figure 143.3 Pregnancy monitoring with serial sonograms and β-hCG determinations

Contraindications: Methotrexate should not be used if the β-hCG level is greater than 5000 mIU/mL, the adnexal mass is greater than 3–4 cm, or the patient's hemodynamic status is unstable. Patients with a history of active hepatic or renal disease, fetal cardiac activity demonstrated in the ectopic gestation, active ulcer disease, or significant alterations in blood count (white blood cell count <3000, platelet count of <100,000) are generally not candidates for this therapy.

All women with ectopic pregnancies who are Rh-negative and unsensitized should receive Rh immunoglobulin at a dose of 50 µg if the gestation is of less than 12 weeks duration and 300 µg if it is beyond 12 weeks.

Precautions: A transient increase in abdominal symptoms is often encountered 48–72 hours after methotrexate therapy. Approximately 5%–10% of medically managed patients experience complications before medical therapy can be effective, necessitating surgical intervention.

Interactions: If patients are receiving methotrexate therapy, they should not take multivitamins with folic acid (eg, prenatal vitamins) because this counteracts the effects of the methotrexate.

FOLLOW-UP

Patient Monitoring: Follow-up assessment of serum β-hCG level to confirm a decline toward normal.

Prevention/Avoidance: Reduce modifiable risk factors, such as pelvic infections.

Possible Complications: Rupture of an ectopic pregnancy dooms the pregnancy and may result in catastrophic intraabdominal bleeding that jeopardizes the life of the mother. It is the most common cause of maternal death in the first half of pregnancy. Maternal mortality from ectopic pregnancy has declined with earlier detection made possible by laboratory and ultrasonography diagnosis. Current statistics suggest a rate of 3.8 of 10,000 patients (varies with age and race—African Americans have a five-fold greater risk). Maternal death is most often associated with blood loss and delay in diagnosis.

Expected Outcome: With prompt diagnosis, the prognosis for the patient is good, although infertility rates are high (40%) and the likelihood of a successful pregnancy is reduced (50%). The prognosis for the current pregnancy is uniformly bad. Methotrexate therapy is associated with an approximately 90% efficacy rate.

MISCELLANEOUS

Pregnancy Considerations: Poor outcomes for future pregnancy including increased risk of subsequent ectopic implantation and spontaneous pregnancy loss.

ICD-10-CM Codes: O00.1 (Tubal pregnancy), O00.0 (Abdominal pregnancy), O00.2 (Ovarian pregnancy), and O00.8 (Other ectopic pregnancy).

REFERENCES

LEVEL I

Stovall TG, Ling FW, Buster JE. Outpatient chemotherapy of unruptured ectopic pregnancy. *Fertil Steril*. 1989;51:435.

LEVEL II

Barnhart KT, Gosman G, Ashby R, et al. The medical management of ectopic pregnancy: a meta-analysis comparing "single dose" and "multidose" regimens. *Obstet Gynecol*. 2003;101:778.

Creanga AA, Shapiro-Mendoza CK, Bish CL, et al. Trends in ectopic pregnancy mortality in the United States: 1980-2007. *Obstet Gynecol*. 2011;117:837.

Hajenius PJ, Mol F, Mol BW, et al. Interventions for tubal ectopic pregnancy. *Cochrane Database Syst Rev*. 2007;CD000324.

Khan KS, Wojdyla D, Say L, et al. WHO analysis of causes of maternal death: a systematic review. *Lancet*. 2006;367:1066.

Perkins KM, Boulet SL, Kissin DM, et al. Risk of ectopic pregnancy associated with assisted reproductive technology in the United States, 2001-2011. *Obstet Gynecol*. 2015;125:70.

Silva C, Sammel MD, Zhou L, et al. Human chorionic gonadotropin profile for women with ectopic pregnancy. *Obstet Gynecol*. 2006;107:605.

LEVEL III

Van Den Eeden SK, Shan J, Bruce C, et al. Ectopic pregnancy rate and treatment utilization in a large managed care organization. *Obstet Gynecol*. 2005;105:1052.

Alkatout I, Honemeyer U, Strauss A, et al. Clinical diagnosis and treatment of ectopic pregnancy. *Obstet Gynecol Surv*. 2013;68:571.

American College of Obstetricians and Gynecologists. Medical Management of Ectopic Pregnancy. ACOG Practice Bulletin No. 94. *Obstet Gynecol*. 2008;111:1479.

American College of Obstetricians and Gynecologists. Avoiding inappropriate clinical decisions based on false-positive human chorionic gonadotropin test results. ACOG Committee Opinion 278. *Obstet Gynecol*. 2002;100:1057.

American College of Obstetricians and Gynecologists. Ultrasonography in pregnancy. ACOG Practice Bulletin No. 101. *Obstet Gynecol*. 2009;113:451.

Doubilet PM, Benson CB, Bourne T, et al. Diagnostic criteria for nonviable pregnancy early in the first trimester. *N Engl J Med*. 2013;369:1443.

Farquhar CM. Ectopic pregnancy. *Lancet*. 2005;366:583.

Practice Committee of American Society for Reproductive Medicine. Medical treatment of ectopic pregnancy: a committee opinion. *Fertil Steril*. 2013;100:638.

Rausch ME, Barnhart KT. Serum biomarkers for detecting ectopic pregnancy. *Clin Obstet Gynecol*. 2012;55:418.

Seeber BE, Barnhart KT. Suspected ectopic pregnancy. *Obstet Gynecol*. 2006;107:399.

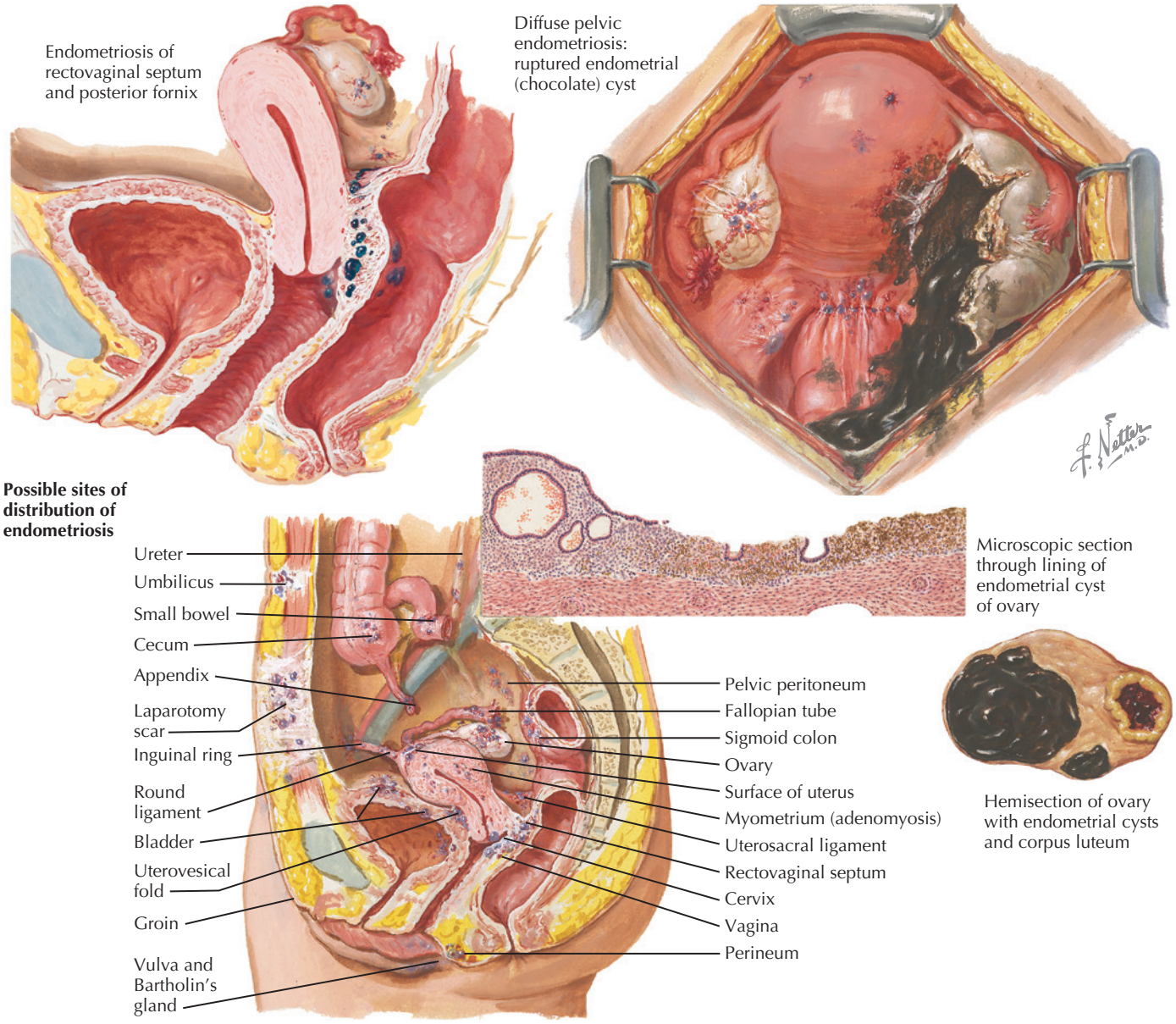


Figure 144.1 Appearance of and possible sites of distribution of endometriosis

- Corpus luteum cysts
- Ovarian neoplasia
- Adenocarcinoma of the large bowel (endometrial implants may be difficult to differentiate grossly from a primary neoplasm of the large bowel)

Associated Conditions: Infertility, nulliparity, pelvic pain, dyspareunia (deep thrust), uterine retroversion, premenstrual and menstrual pain, intermenstrual bleeding, and adenomyosis (20% of these patients).

WORKUP AND EVALUATION

Laboratory: No evaluation indicated. CA-125 is not useful for screening or follow-up.

Imaging: No imaging indicated; pelvic or transvaginal ultrasonography, or magnetic resonance imaging (MRI) may demonstrate endometriomas or signs of scarring (nonspecific, a detection ratio and specificity of approximately 78% for implants, sensitivity and specificity of 91%–95%).

Special Tests: None indicated.

Diagnostic Procedures: The ultimate diagnosis of endometriosis rests on direct inspection of the involved area (laparoscopy or laparotomy), supported by histologic confirmation.

Pathologic Findings

Endometriosis is characterized by endometrial glands and stroma found in locations other than the endometrium. Nests of endometrial glands and stroma may occur in many distant locations throughout the body, although they are most common in the pelvis (60% on the surfaces of the ovaries). Vulva implants occur in 1 in 500 patients with endometriosis, generally at the site of an episiotomy or obstetric laceration. Evidence of old hemorrhage (hemosiderin-laden macrophages) is often present.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Analgesics (nonsteroidal antiinflammatory drugs), modification of periods (oral contraceptives), suppression of periods (gonadotropin-releasing hormone [GnRH] agonists, danazol sodium, oral progestins, long-acting progestins, continuous oral contraceptives).

Specific Measures: The selection of therapy depends on many factors—reliability of diagnosis, the extent of disease and symptoms, the patient's desire for fertility, and degree of involvement with other organs. Endometriomata of greater than 5 cm generally require surgical therapy. Surgical therapy may be conservative (resection of lesions) or definitive (hysterectomy, oophorectomy).

Diet: No specific dietary changes indicated.

Activity: No restriction.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP013 (Endometriosis), AP136 (Evaluating Infertility), and AP137 (Treating Infertility).

Drug(s) of Choice

GnRH agonists for 6 months—leuprolide acetate (Lupron) 3.75 mg IM monthly; nafarelin acetate (Synarel) 200 mcg intranasal in morning and in opposite nostril at bedtime; goserelin acetate (Zoladex) 3.6 mg implant monthly.

Contraindications: Known or suspected pregnancy, breastfeeding, undiagnosed vaginal bleeding.

Precautions: A decrease in bone mass of 5%–7% during a 6-month course of therapy with GnRH agonists has been documented. This is believed to be reversible.

Add-Back Therapy: Progestins, low-dose estrogens, or both may be used to suppress bothersome side effects without reducing efficacy.

Alternative Drugs

- Danazol sodium 200 mg PO four times a day for 6–9 months (80% of patients experience side effects and 10%–20% discontinue therapy because of them)
- Continuous combination oral contraceptives (monophasic or long-cycle formulation) taken daily for 6–9 months (if breakthrough bleeding occurs, the dose is doubled for 5 days)
- Medroxyprogesterone acetate 30 mg PO daily or 150 mg IM every 3 months for 6–9 months.

FOLLOW-UP

Patient Monitoring: Any therapy must be reevaluated at no less than 6-month intervals. History and physical evaluations are usually sufficient.

Prevention/Avoidance: None.

Possible Complications: Pelvic scarring, chronic pelvic pain, erosion into bowel or urinary tract resulting in hematochezia or hematuria. Endometriosis has been associated with an increased risk of ovarian epithelial tumors.

Expected Outcome: Endometriosis is never considered to be "cured." Symptoms may be resolved and progression of the disease may be halted through medical or surgical therapy, but 5%–15% of patients have a recurrence after 1 year and 40%–50% have a recurrence by 5 years. The success of therapy and the risk of recurrence are proportional to the extent of the initial disease. Up to 40% of patients may eventually conceive with therapy. Endometriosis generally regresses after menopause (natural or surgically induced).

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy once pregnancy is achieved. Pregnancy may actually resolve symptoms of endometriosis and promote regression of implants in some patients.

ICD-10-CM Codes: N80.9 (Endometriosis, unspecified) (Codes N80.0-N80.8 used for specific sites).

REFERENCES

LEVEL II

Bazot M, Lafont C, Rouzier R, et al. Diagnostic accuracy of physical examination, transvaginal sonography, rectal endoscopic sonography, and magnetic resonance imaging to diagnose deep infiltrating endometriosis. *Fertil Steril*. 2009;92:1825.

Friedman AJ, Hornstein MD. Gonadotropin-releasing hormone agonist plus estrogen-progestin "add-back" therapy for endometriosis-related pelvic pain. *Fertil Steril*. 1993;60:236.

Legras A, Mansuet-Lupo A, Rousset-Jablonski C, et al. Pneumothorax in women of child-bearing age: an update classification based on clinical and pathologic findings. *Chest*. 2014;145:354.

Pearce CL, Templeman C, Rossing MA, et al. Association between endometriosis and risk of histological subtypes of ovarian cancer: a pooled analysis of case-control studies. *Lancet Oncol*. 2012;13:385.

Wright S, Valdes CT, Dunn RC, et al. Short-term Lupron or Danazol therapy for pelvic endometriosis. *Fertil Steril*. 1995;63:504.

LEVEL III

American College of Obstetricians and Gynecologists. Management of endometriosis. Practice Bulletin No. 113. *Obstet Gynecol*. 2010;116:223.

American College of Obstetricians and Gynecologists. Noncontraceptive uses of hormonal contraceptives. Practice Bulletin No. 110. *Obstet Gynecol*. 2010;115:206.

Appleyard TL, Mann CH, Khan KS. Guidelines for the management of pelvic pain associated with endometriosis: a systematic appraisal of their quality. *BJOG*. 2006;113:7497.

Engemise S, Gordon C, Konje JC. Endometriosis. *BMJ*. 2010;340:c2168.

Giudice LC, Kao LC. Endometriosis. *Lancet*. 2004;364:1789.

Winkel CA. Evaluation and management of women with endometriosis. *Obstet Gynecol*. 2003;102:397.

EPITHELIAL STROMAL OVARIAN TUMORS

145

INTRODUCTION

Description: The most common type of ovarian tumors (65% of ovarian tumors, 95% of ovarian malignancies). Endometrial stromal tumors are derived from the surface (celomic) epithelium and the ovarian stroma and include serous (20%–50%), mucinous (15%–25%), endometrioid (5%), clear cell (<5%), and Brenner (2%–3%) types. Epithelial tumors are categorized as benign (adenoma), malignant (adenocarcinoma), or of an intermediate form (borderline malignant adenocarcinoma or tumors of low malignant potential). Some have proposed that these tumors originate in the fallopian tubes (unproven).

Prevalence: Two of three ovarian tumors and 95% of ovarian malignancies; 12.7 of 100,000 women.

Predominant Age: Benign tumors—age 20–29 years; malignant tumors—half are in women older than 50 years (average age is 63 years).

Genetics: No genetic pattern, though mutations of the BRCA1 and BRCA2 genes impart a two- to three-fold increase in risk. Other genes have been implicated but represent a small number of cases.

ETIOLOGY AND PATHOGENESIS

Causes: Unknown.

Risk Factors: Family history, high-fat diet, advanced age, endometriosis, nulliparity, early menarche, late menopause, white race, higher economic status, cigarette smoking (mucinous type only). Oral contraception, high parity, and breastfeeding reduce risk.

SIGNS AND SYMPTOMS

- Asymptomatic
- Weight loss
- Increasing abdominal girth despite constant or reduced caloric intake
- Ascites
- Adnexal mass (multilocular or partly solid masses in patients older than 40 years are likely to be malignant; the risk of a mass being malignant is one in three for women older than 45 years versus <1% for women 20–45 years of age)
- Vague lower abdominal discomfort
- Pleural effusion and shortness of breath

DIAGNOSTIC APPROACH

Differential Diagnosis

- Functional cyst (corpus luteum, follicular)
- Endometriosis
- Hydrosalpinx
- Paratubal cyst
- Appendiceal abscess
- Ectopic pregnancy
- Pedunculated leiomyomata
- Pelvic or horseshoe kidney
- Gastrointestinal malignancy (colon, stomach)

Associated Conditions: None. In patients with advanced malignant disease, bowel obstruction, ascites, and inanition are common.

WORKUP AND EVALUATION

Laboratory: As indicated before surgery. β-Human chorionic gonadotropin or α-fetoprotein levels may be elevated in some tumors. The CA-125 level may be useful for monitoring disease response to treatment or progression, but it is not a good prognostic test. Only 80% of epithelial ovarian tumors express CA-125, and many benign and other malignant processes (lung, breast, and pancreas) may cause CA-125 to become higher than normal.

Imaging: Preoperative evaluation (computed tomography or ultrasonography) for possible lymph node enlargement or intra-abdominal spread is indicated for patients in whom malignancy is a significant possibility.

Special Tests: A frozen-section histologic evaluation (intraoperative consultation) should be considered for any ovarian mass that appears suspicious for malignancy.

Diagnostic Procedures: History, physical examination, and imaging. Final diagnosis is established by histologic evaluation.

Pathologic Findings

Varies with cell type. Malignant epithelial tumors are more likely to be bilateral than are benign epithelial neoplasms.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, supportive therapy based on symptoms.

Specific Measures: Generally, requires surgical exploration and extirpation. In benign disease or tumors of borderline malignant potential, the uterus and other ovary generally may be spared. Adjunctive chemotherapy (platinum-based and paclitaxel [Taxol]) or radiation therapy is often included, based on the location and stage of the disease. It currently is not recommended that a grossly normal opposite ovary be bisected to look for a contralateral mass.

Diet: No specific dietary changes indicated, except those imposed by advanced disease.

Activity: No restriction, except that imposed by advanced disease.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP096 (Cancer of the Ovary) and AP075 (Ovarian Cysts).

Drug(s) of Choice

None, except as adjunctive or symptomatic therapy.

Contraindications: See individual agents.

Precautions: Alkylating agents are associated with an increased risk of future leukemia (10% by 8 years after therapy).

Interactions: See individual agents.

FOLLOW-UP

Patient Monitoring: Careful follow-up for recurrent pelvic disease or enlargement of the remaining ovary (if any). This is generally performed by pelvic examination, augmented with ultrasonography in selected patients. In patients suspected of having recurrent disease and other selected patients, second-look surgery may be desirable to assess progress and discover occult disease. Estrogen therapy does not have a negative influence on the disease-free interval and overall survival in women who have had ovarian carcinoma.

Prevention/Avoidance: None. Prophylactic bilateral salpingo-oophorectomy for those with known BRCA mutations.

Possible Complications: Spread and advancement of malignant tumors.

Expected Outcome: Generally good.

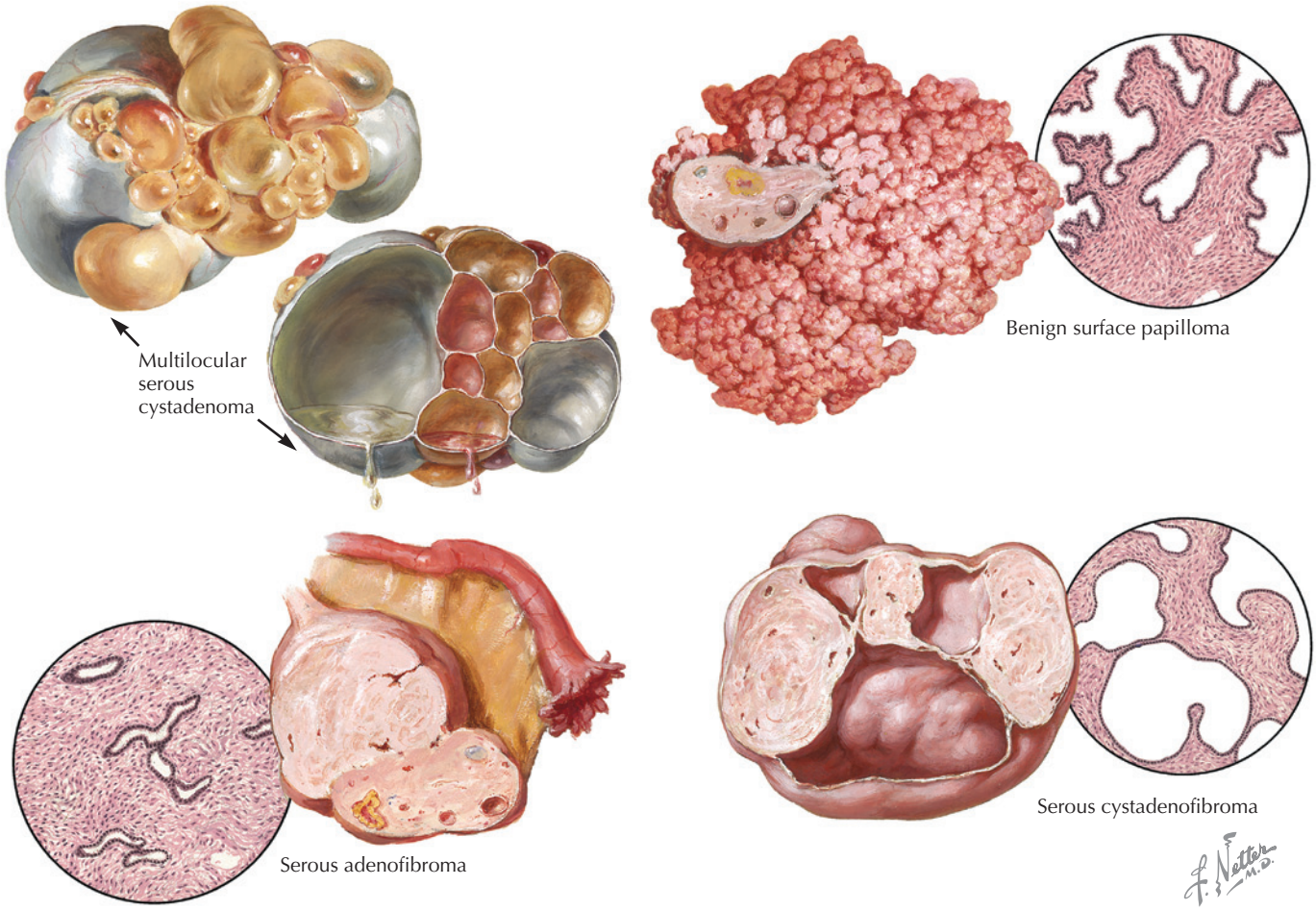


Figure 145.1 Cystadenoma, adenofibroma, papilloma, and cystadenofibroma

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: Based on the cause and type.

REFERENCES

LEVEL I

Guidozzi F, Daponte A. Estrogen replacement therapy for ovarian carcinoma survivors: a randomized controlled trial. *Cancer*. 1999;86:1013.

LEVEL II

Finch A, Beiner M, Lubinski J, et al. Salpingo-oophorectomy and the risk of ovarian, fallopian tube, and peritoneal cancers in women with a BRCA1 or BRCA2 mutation. *JAMA*. 2006;296:185.

Gates MA, Rosner BA, Hecht JL, et al. Risk factors for epithelial ovarian cancer by histologic subtype. *Am J Epidemiol*. 2010;171:45.

Marchbanks PA, Wilson H, Bastos E, et al. Cigarette smoking and epithelial ovarian cancer by histologic type. *Obstet Gynecol*. 2000;95:255.

LEVEL III

American College of Obstetricians and Gynecologists. Management of adnexal masses. ACOG Practice Bulletin No. 83. *Obstet Gynecol*. 2007; 110:201.

Berek JS, Crum C, Friedlander M. Cancer of the ovary, fallopian tube, and peritoneum. *Int J Gynaecol Obstet*. 2012;119(suppl 2):S118.

Bhoola S, Hoskins WJ. Diagnosis and management of epithelial ovarian cancer. *Obstet Gynecol*. 2006;107:1399.

Salvador S, Gilks B, Köbel M, et al. The fallopian tube: primary site of most pelvic high-grade serous carcinomas. *Int J Gynecol Cancer*. 2009;19:58.

GERM CELL TUMOR

146

INTRODUCTION

Description: Germ cell tumors contain cells that echo the three layers of embryonic tissue (ectoderm, mesoderm, and endoderm) or extraembryonic elements.
Prevalence: Second most frequent ovarian neoplasm (25% of tumors) and the most common ovarian tumor in women younger than 30 years (70%).
Predominant Age: Younger than 30 years; most common malignancy in women in their teens and 20s.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Unknown (may differentiate from primitive germ cells).
Risk Factors: None known.

SIGNS AND SYMPTOMS

- Asymptomatic
- Ovarian enlargement (ovarian masses in premenarchal girls are most often germ cell tumors)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Benign adnexal masses (corpus luteum, follicular cyst)
- Endometriosis
- Hydrosalpinx
- Paratubal cyst
- Appendiceal abscess
- Ectopic pregnancy
- Pedunculated leiomyomata
- Pelvic or horseshoe kidney
- Nongynecologic pelvic masses

Associated Conditions: Varies with the cell type.

WORKUP AND EVALUATION

Laboratory: As indicated before surgery. β-Human chorionic gonadotropin or α-fetoprotein may be elevated in some tumors (dysgerminoma, primary choriocarcinoma). The CA-125 level may be useful for monitoring disease response to treatment or progression, but it is not a good prognostic test. Only 80% of epithelial ovarian tumors express CA-125, and many benign and other malignant tumors (lung, breast, and pancreas) may also cause an increase in the CA-125 level that is higher than normal.
Imaging: Preoperative evaluation (computed tomography or ultrasonography) for possible lymph node enlargement or intra-abdominal spread is indicated for patients in whom malignancy is a significant possibility.
Special Tests: None indicated.
Diagnostic Procedures: History, physical examination, imaging. Final diagnosis is established by histologic evaluation.

Pathologic Findings

Germ cell tumors include dysgerminoma (45% of malignant germ cell tumors), endodermal sinus tumors (10%), embryonal carcinoma, choriocarcinoma, teratomas (immature, mature, solid and cystic, struma ovarii, carcinoid), and mixed forms. Approximately one-third of germ cell tumors in women younger than 21 years are malignant.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, supportive therapy based on symptoms.
Specific Measures: Surgical exploration and resection (often with salvage of the ovary in the case of teratomas). Immature (malignant) teratomas are often treated with an adjunctive chemotherapy (vincristine, actinomycin D, and cyclophosphamide); endodermal sinus tumors should all be treated with chemotherapy after surgical resection.
Diet: No specific dietary changes indicated, except those imposed by advanced disease.
Activity: No restriction, except that imposed by advanced disease.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP096 (Cancer of the Ovary) and AP075 (Ovarian Cysts).

Drug(s) of Choice

- Vincristine 1.5 mg/m^2 IV weekly for 12 weeks, actinomycin D, and cyclophosphamide (0.5 mg of actinomycin D with 5–7 mg/kg/day cyclophosphamide IV daily for 5 days every 4 weeks).
- Adjunctive or symptomatic therapy.

Contraindications: See individual agents.
Precautions: Alkylating agents are associated with an increased risk for future leukemia (10% by 8 years after therapy).
Interactions: See individual agents.

Alternative Drugs

Chemotherapy for endodermal sinus tumors may alternately include actinomycin D, 5-fluorouracil, and cyclophosphamide.

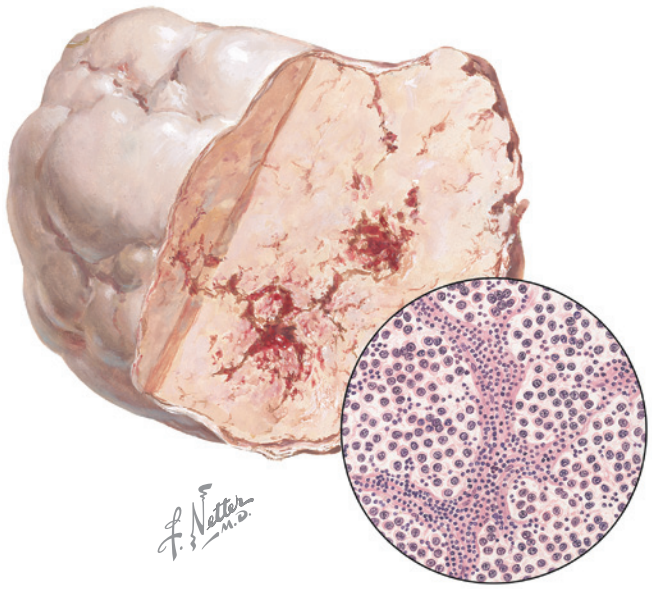


Figure 146.1 Dysgerminoma

FOLLOW-UP

Patient Monitoring: Careful follow-up for recurrent pelvic disease or enlargement of the remaining ovary (if any). This is generally performed by pelvic examination, augmented with ultrasonography in selected patients. In patients suspected with recurrent disease and other selected patients, second-look surgery may be desirable to assess progress and discover occult disease.
Prevention/Avoidance: None
Possible Complications: Spread and advancement in the case of malignant tumors.
Expected Outcome: Generally good.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: Based on the cause and type.

REFERENCES

LEVEL II

Koonings PP, Campbell K, Mishell DR Jr, et al. Relative frequency of primary ovarian neoplasms: a 10-year review. *Obstet Gynecol*. 1989;74:921.

Mais V, Ajossa S, Mallarini G, et al. No recurrence of mature ovarian teratomas after laparoscopic cystectomy. *BJOG*. 2003;110:624.

LEVEL III

American College of Obstetricians and Gynecologists. Management of adnexal masses. ACOG Practice Bulletin No. 83. *Obstet Gynecol*. 2007;110:201.

Berek JS, Crum C, Friedlander M. Cancer of the ovary, fallopian tube, and peritoneum. *Int J Gynaecol Obstet*. 2012;119(suppl 2):S118.

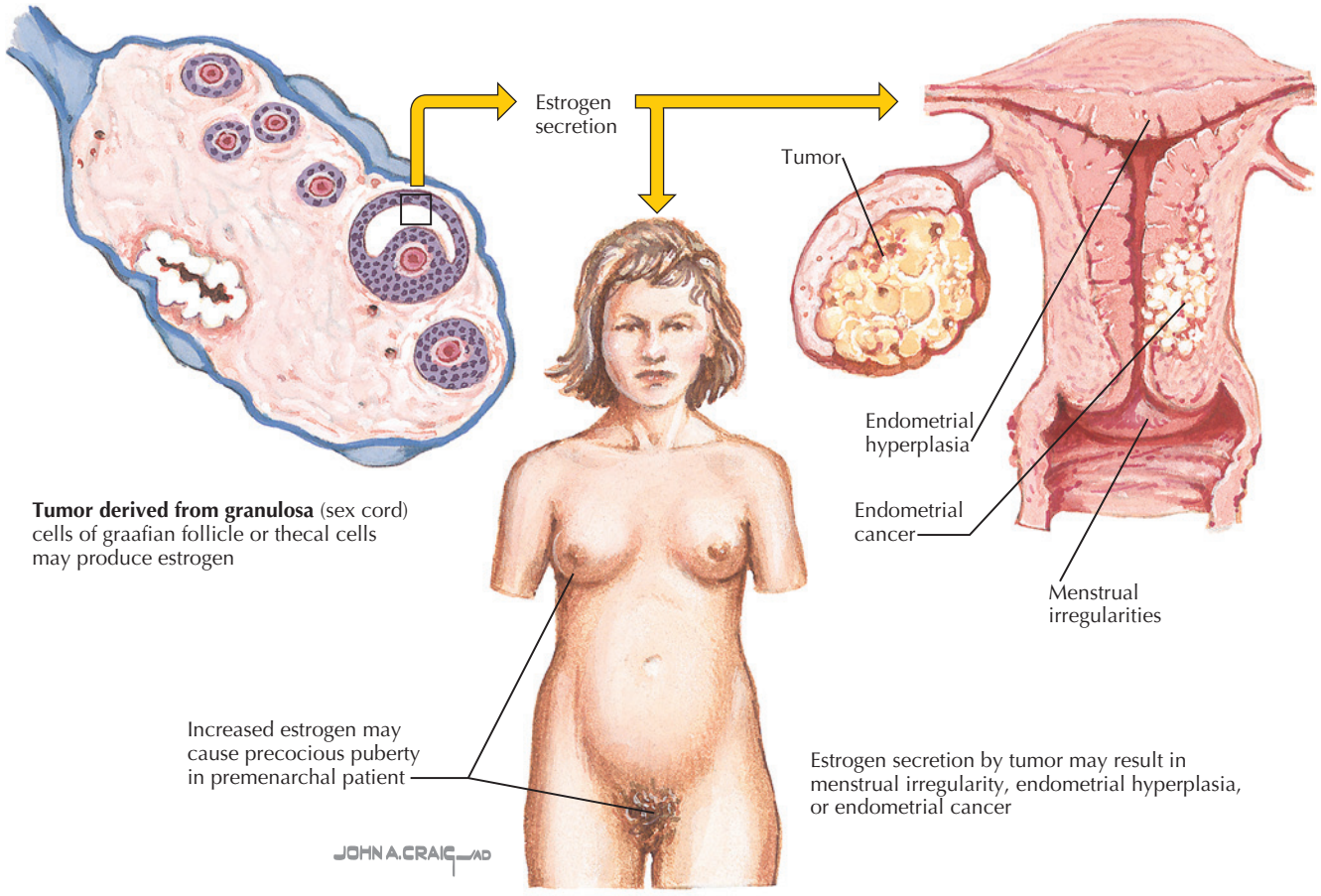


Figure 147.1 Stromal (sex cord) ovarian tumor

approximately 70% of cases. Poorly differentiated tumors may be confused with adenocarcinomas (especially small cell carcinoma).

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, supportive therapy based on symptoms.
Specific Measures: Surgical exploration and resection. Because fewer than 5% of these tumors are bilateral, conservative surgery is generally indicated for tumors at stage IA or lower. Chemotherapy (cisplatin, doxorubicin) and radiotherapy have been used for recurrent disease.
Diet: No specific dietary changes indicated, except those imposed by advanced disease.
Activity: No restriction, except that imposed by advanced disease.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP096 (Cancer of the Ovary) and AP075 (Ovarian Cysts).

Drug(s) of Choice

Adjunctive (unproved benefit) or symptomatic therapy.
Contraindications: See individual agents.
Precautions: Alkylating agents are associated with an increased risk of future leukemia (10% by 8 years after therapy).
Interactions: See individual agents.

Alternative Drugs

Chemotherapy with alternative use of actinomycin D, 5-fluorouracil, and cyclophosphamide.

FOLLOW-UP

Patient Monitoring: Careful follow-up for recurrent pelvic disease or enlargement of the remaining ovary (if any). This is generally performed by pelvic examination, augmented with ultrasonography in selected cases. In those suspected of having recurrent disease and other selected patients, second-look surgery may be desirable to assess progress and discover occult disease.
Prevention/Avoidance: None.
Possible Complications: Recurrences are frequent, even 5 years after initial therapy. In 10% of patients the tumor is diagnosed when it ruptures, causing pain or intraperitoneal bleeding.
Expected Outcome: Prognosis does not correlate with the histologic pattern of the tumor: 90% of tumors found are stage I and the prognosis is good (90% 10-year survival). A poorer prognosis is associated with tumors more than 15 cm in size that have ruptured or that have a high mitotic rate or aneuploidy.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: Specific to cell type and location.

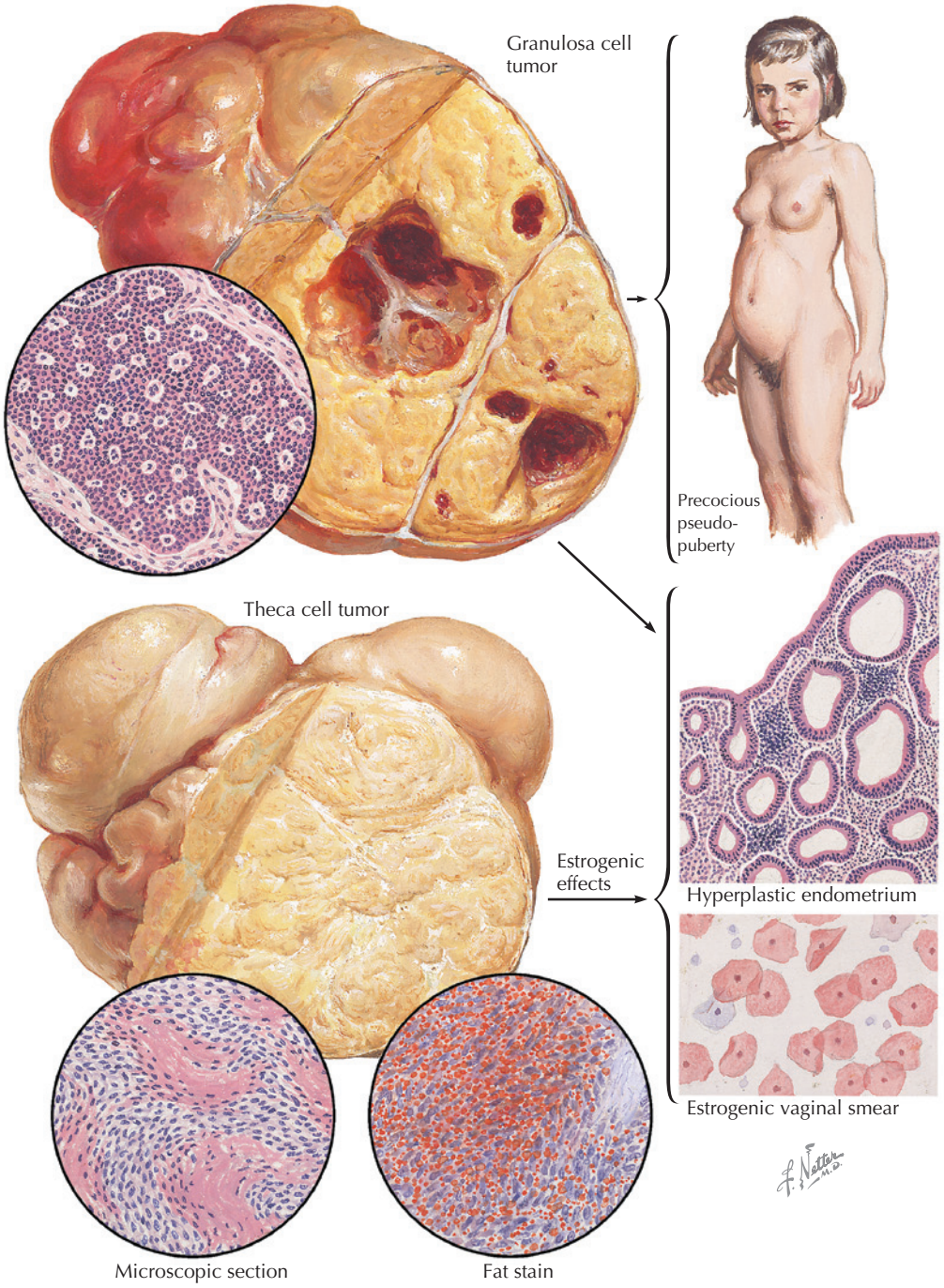


Figure 147.2 Granulosa and theca cell tumors

REFERENCES

LEVEL II

Auranen A, Sundström J, Ijäs J, et al. Prognostic factors of ovarian granulosa cell tumor: a study of 35 patients and review of the literature. *Int J Gynecol Cancer*. 2007;17:1011.

Chang HL, Pahlavan N, Halpern EF, et al. Serum Müllerian inhibiting substance/anti-Müllerian hormone levels in patients with adult granulosa cell tumors directly correlate with aggregate tumor mass as determined by pathology or radiology. *Gynecol Oncol*. 2009;114:57.

Homesley HD, Bundy BN, Hurteau JA, et al. Bleomycin, etoposide, and cisplatin combination therapy of ovarian granulosa cell tumors and other stromal malignancies: A Gynecologic Oncology Group study. *Gynecol Oncol*. 1999;72:131.

Mom CH, Engelen MJ, Willemse PH, et al. Granulosa cell tumors of the ovary: the clinical value of serum inhibin A and B levels in a large single center cohort. *Gynecol Oncol*. 2007;105:365.

LEVEL III

American College of Obstetricians and Gynecologists. Management of adnexal masses. ACOG Practice Bulletin No. 83. *Obstet Gynecol*. 2007;110:201.

Schumer ST, Cannistra SA. Granulosa cell tumor of the ovary. *J Clin Oncol*. 2003;21:1180.

HYDROSALPINX (CHRONIC PELVIC INFLAMMATORY DISEASE)

INTRODUCTION

Description: Recurrent or chronic adnexal infections may result in a cystic dilation of the fallopian tube (hydrosalpinx), which may present as an adnexal mass.
Prevalence: Forty percent of female infertility is a result of tubal damage, including the most severe form hydrosalpinx.
Predominant Age: 15–25 years.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Recurrent or chronic adnexal infection. This is the end-stage condition of pyosalpinx.

Risk Factors: Early (age) sexual activity, multiple sexual partners, pelvic inflammatory disease, sexually transmitted infections (STIs; *Chlamydia*, gonorrhea), uterine instrumentation (hysterosalpingography, intrauterine contraceptive device placement, endometrial biopsy, dilation and curettage), and douching. Damage from previous surgery or adhesions can also cause hydrosalpinx.

SIGNS AND SYMPTOMS

- Asymptomatic (most common)
- Vague lower abdominal pressure or chronic pelvic pain
- Infertility

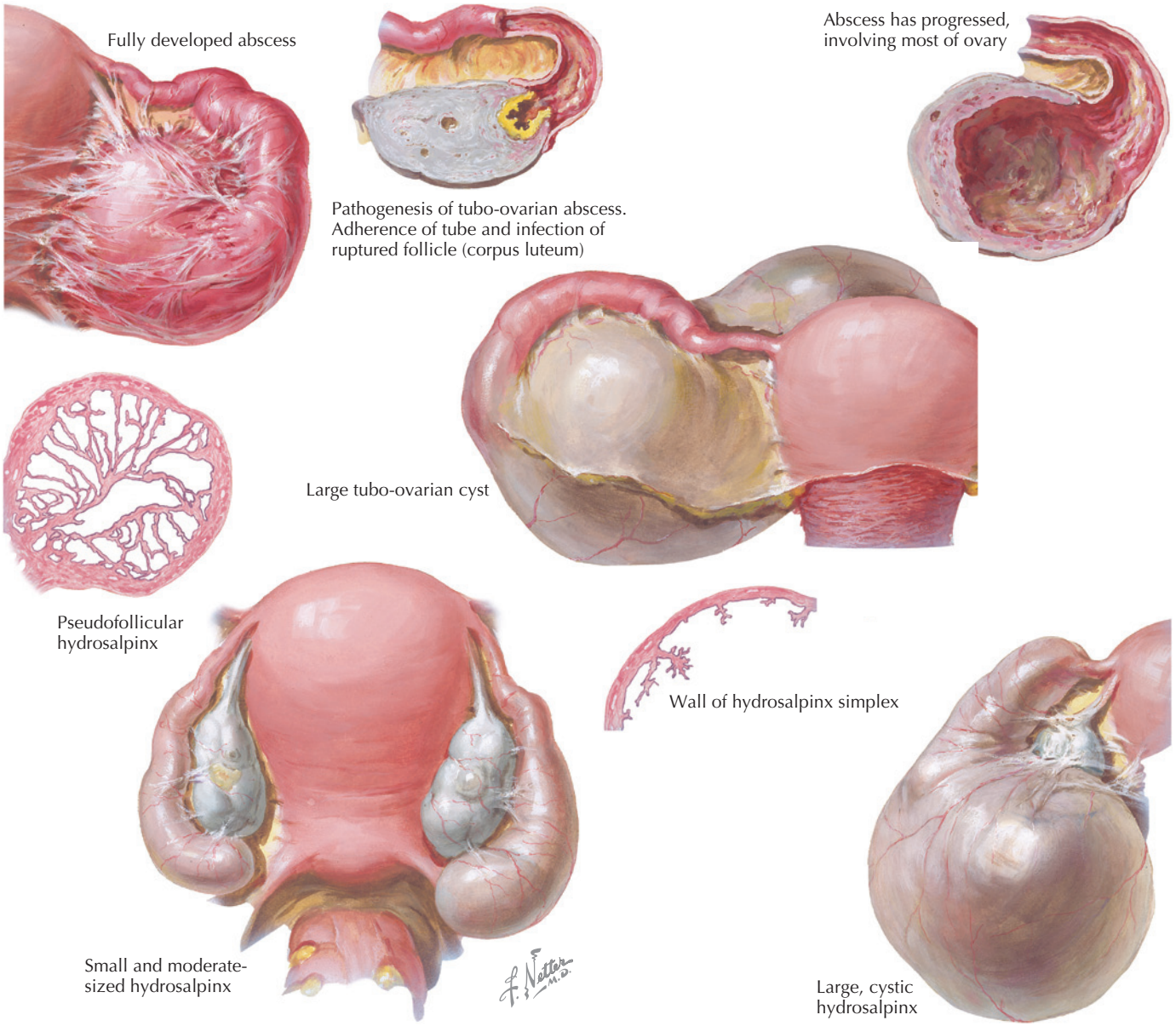


Figure 148.1 Types of abscesses and cysts

- Unilateral or bilateral cystic masses (often elongated or sausage-shaped). Data indicate that a clinical diagnosis of symptomatic pelvic inflammatory disease has a positive predictive value for salpingitis of only 65%.

DIAGNOSTIC APPROACH

Differential Diagnosis

- Functional cysts (follicle, corpus luteum)
- Epithelial tumors (cystic or solid)
- Ovarian cysts
- Paratubal or paraovarian cysts
- Uterine leiomyomata
- Ectopic pregnancy
- Tubo-ovarian abscess
- Endometrioma
- Appendiceal abscess

Associated Conditions: Pelvic pain, infertility, and STIs.

WORKUP AND EVALUATION

Laboratory: Complete blood count or erythrocyte sedimentation rate if active infection is suspected. Screening for coexistent STIs should be strongly considered.

Imaging: Ultrasonography (abdominal or transvaginal), computed tomography (CT), or magnetic resonance imaging (MRI) may be used but are more expensive without providing greater specificity.

Special Tests: None indicated.

Diagnostic Procedures: History, physical examination, and ultrasonography.

Pathologic Findings

Chronic induration and inflammation with cystic dilation of the fallopian tube and flattening and atrophy of the epithelial lining. The fluid found is generally sterile.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, including screening for other STIs.

Specific Measures: Generally requires surgical evaluation and therapy (laparoscopy or laparotomy).

Diet: No specific dietary changes indicated.

Activity: No restriction.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP077 (Pelvic Inflammatory Disease), AP009 (How to Prevent Sexually Transmitted Infections), AP099 (Chronic Pelvic Pain), AP071 (Gonorrhea, Chlamydia, and Syphilis), AP136 (Evaluating Infertility), AP137 (Treating Infertility), and AP020 (When Sex Is Painful).

Drug(s) of Choice

Broad-spectrum antibiotics if active infection is suspected. Most hydrosalpinges are sterile and are the inactive end-stage disease.

FOLLOW-UP

Patient Monitoring: Normal health maintenance, periodic surveillance for other STIs.

Prevention/Avoidance: Avoidance of STIs (barrier contraception, "safe sex"), screening for those at risk, and aggressive treatment.

Possible Complications: Chronic pelvic pain, infertility, increased risk of hysterectomy and oophorectomy, two-fold increase in ovarian cancer.

Expected Outcome: Surgical therapy (salpingectomy or salpingo-oophorectomy) is curative. Neosalpingostomy may be considered when fertility is to be maintained, but the success of this procedure is inversely proportional to the size of the hydrosalpinx and is generally less than 15%. More often, in vitro fertilization (IVF), bypassing the damaged tubes, is recommended, although the success rates are lower in these patients. For this reason, some advocate surgical excision of the damaged tubes prior to undertaking IVF.

MISCELLANEOUS

Pregnancy Considerations: Successful pregnancy is much less likely because of the increased risk of infertility and ectopic pregnancy.

ICD-10-CM Codes: N70.11 (Chronic salpingitis), N70.12 (Chronic oophoritis), and N70.13 (Chronic salpingitis and oophoritis).

REFERENCES

LEVEL I

Ness RB, Trautmann G, Richter HE, et al. Effectiveness of treatment strategies of some women with pelvic inflammatory disease: a randomized trial. *Obstet Gynecol*. 2005;106:573.

LEVEL II

Lin HW, Tu YY, Lin SY, et al. Risk of ovarian cancer in women with pelvic inflammatory disease: a population-based study. *Lancet Oncol*. 2011;12:900.

Trent M, Haggerty CL, Jennings JM, et al. Adverse adolescent reproductive health outcomes after pelvic inflammatory disease. *Arch Pediatr Adolesc Med*. 2011;165:49.

LEVEL III

American College of Obstetricians and Gynecologists. Dual therapy for gonococcal infections. Committee Opinion No. 645. *Obstet Gynecol*. 2015;126:e95.

American College of Obstetricians and Gynecologists. Expedited partner therapy in the management of gonorrhea and chlamydial infection. Committee Opinion No. 632. *Obstet Gynecol*. 2015;125:1526.

Centers for Disease Control and Prevention. Recommendations for the Laboratory-Based Detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae*—2014. *MMWR Recomm Rep*. 2014;63(RR-2).

LeFevre ML, U.S. Preventive Services Task Force. Screening for chlamydia and gonorrhea: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2014;161:902.

Soper DE. Pelvic inflammatory disease. *Obstet Gynecol*. 2010;116:419.

Workowski KA, Bolan GA, Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep*. 2015;64:1.

KRUKENBERG TUMOR

149

INTRODUCTION

Description: A Krukenberg tumor is a metastatic tumor (generally from the gastrointestinal tract) that is characterized by large signet-ring cells. The most common site or origin is the stomach or large intestine.
Predominant Age: Postmenopausal.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Metastatic spread of carcinoma from the gastrointestinal tract (most commonly the stomach or colon). Metastatic breast cancer may appear similar histologically.
Risk Factors: None known.

SIGNS AND SYMPTOMS

- Asymptomatic
- Adnexal enlargement (bilateral solid adnexal masses in an older patient should always suggest the possibility of a gastrointestinal tract source)
- Metastatic tumors from the gastrointestinal tract to the ovary can be associated with sex hormone production, usually estrogen.

DIAGNOSTIC APPROACH

Differential Diagnosis

- Benign adnexal masses (corpus luteum, follicular cyst)
- Endometriosis
- Hydrosalpinx

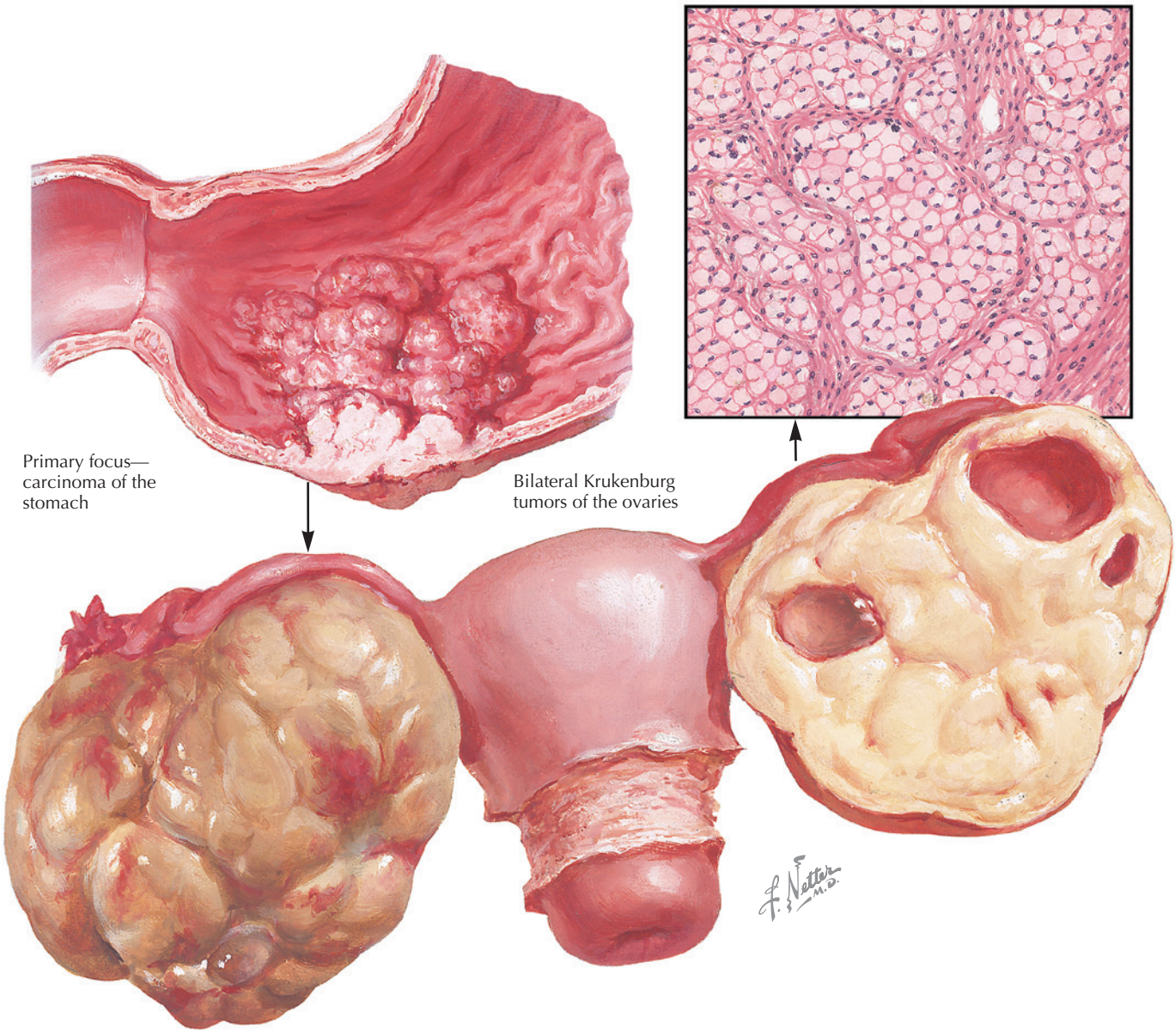


Figure 149.1 Krukenburg tumors of stomach and ovaries

- Paratubal cyst
- Appendiceal abscess
- Ectopic pregnancy
- Pedunculated leiomyomata
- Pelvic or horseshoe kidney
- Nongynecologic pelvic masses
- Breast cancer
- Lung cancer

Associated Conditions: Gastrointestinal or breast malignancy.

WORKUP AND EVALUATION

Laboratory: As indicated before surgery.

Imaging: Preoperative evaluation (computed tomography or ultrasonography) for possible lymph node enlargement or intra-abdominal spread is indicated for patients in whom malignancy is a significant possibility. Radiographic evaluation of the gastrointestinal tract. Mammography as indicated based on differential diagnosis and routine screening needs.

Special Tests: Esophagoscopy, gastroscopy, sigmoidoscopy, or colonoscopy should be considered as a part of the evaluation when a gastrointestinal source is being sought.

Diagnostic Procedures: History, physical examination, and imaging. Final diagnosis is established by histologic evaluation.

Pathologic Findings

Nests of mucin-filled signet-ring cells in a cellular stroma.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, establishment of location of primary tumor (most often stomach or large intestine).

Specific Measures: Therapy of the original tumor.

Diet: No specific dietary changes indicated except those dictated by the original tumor and its therapy.

Activity: No restrictions except those dictated by the original tumor and its therapy.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP096 (Cancer of the Ovary) and AP075 (Ovarian Cysts).

Drug(s) of Choice

None (based on primary tumor and its therapy).

FOLLOW-UP

Patient Monitoring: Based on primary tumor.

Prevention/Avoidance: None.

Possible Complications: Progression and spread of the primary tumor is generally well under way when the ovarian sites are discovered.

Expected Outcome: Generally poor, with an unlikely 5-year survival rate.

MISCELLANEOUS

Pregnancy Considerations: Does not directly threaten pregnancy except by the jeopardy caused to the mother.

ICD-10-CM Codes: C79.60 (Secondary malignant neoplasm of unspecified ovary).

REFERENCES

LEVEL II

de Palma P, Wronski M, Bifernino V, et al. Krukenberg tumor in pregnancy with virilization. A case report. *Eur J Gynaecol Oncol*. 1995;16:59.

Kakushima N, Kamoshida T, Hirai S, et al. Early gastric cancer with Krukenberg tumor and review of cases of intramucosal gastric cancers with Krukenberg tumor. *J Gastroenterol*. 2003;38:1176.

LEVEL III

Al-Agha OM, Nicastri AD. An in-depth look at Krukenberg tumor: an overview. *Arch Pathol Lab Med*. 2006;130:1725.

American College of Obstetricians and Gynecologists. Management of adnexal masses. ACOG Practice Bulletin No. 83. *Obstet Gynecol*. 2007;110:201.

Fuchs CS, Mayer RJ. Gastric carcinoma. *N Engl J Med*. 1995;333:32.

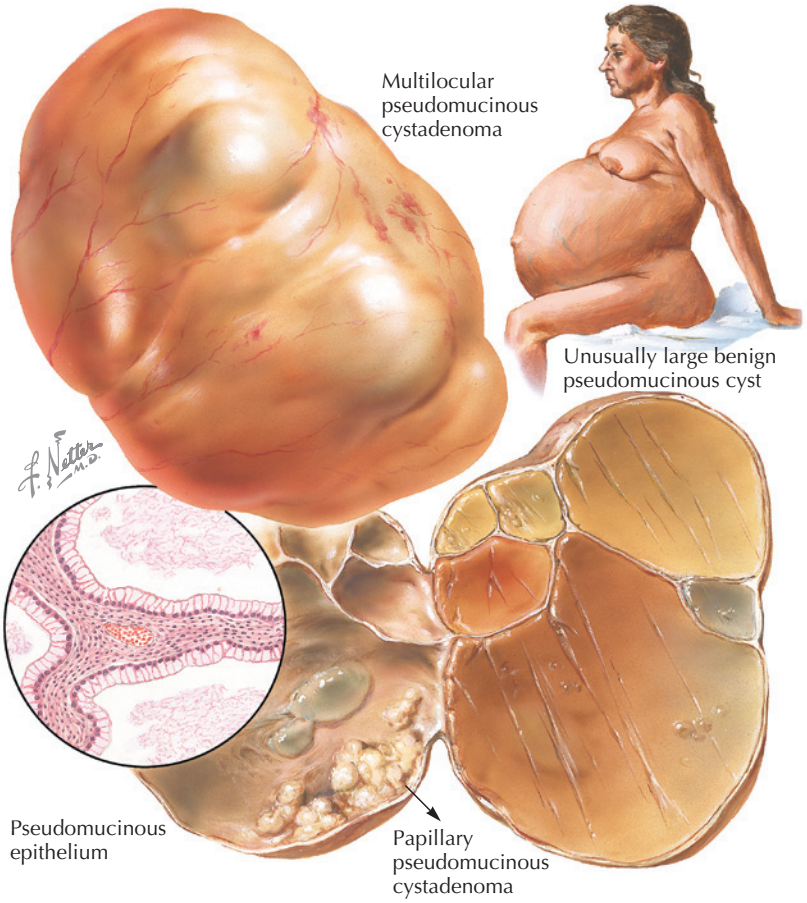


Figure 150.1 Pseudomucinous cystadenoma

race, higher economic status. Oral contraception, high parity, and breastfeeding reduce the risk.

SIGNS AND SYMPTOMS

- Asymptomatic
- Vague lower abdominal symptoms
- Adnexal mass (bilateral in 5% of benign and 10%–20% of malignant lesions) up to 50 cm in diameter (average, 15–30 cm)
- Pleural effusion and shortness of breath

DIAGNOSTIC APPROACH

Differential Diagnosis

- Benign adnexal masses (corpus luteum, follicular cyst)
- Endometriosis
- Hydrosalpinx
- Paratubal cyst
- Appendiceal abscess
- Ectopic pregnancy
- Pedunculated leiomyomata
- Pelvic or horseshoe kidney
- Nongynecologic pelvic masses

Associated Conditions: Pseudomyxoma peritonei.

WORKUP AND EVALUATION

- **Laboratory:** As indicated before surgery. CA-125 levels may be useful for monitoring disease response to treatment or progression, but this is not a good prognostic test. Only 80% of epithelial ovarian tumors express CA-125, and many benign and other malignant processes (lung, breast, and pancreas) may also cause an increase in CA-125 levels that are higher than normal.
- **Imaging:** No imaging indicated.
- **Special Tests:** A frozen-section histologic evaluation should be considered for any ovarian mass that appears suspicious for malignancy.
- **Diagnostic Procedures:** History, physical examination, and imaging. Final diagnosis is established by histologic evaluation.

Pathologic Findings

Gross—smooth translucent cyst wall with infrequent papillary areas. Microscopic—epithelial cells filled with mucin that resemble cells of the endocervix or intestinal epithelium. Mucinous tumors have a higher chance of being of borderline malignant potential (grade 0) than do other epithelial tumors.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, supportive therapy based on symptoms.

Specific Measures: Generally require surgical exploration and extirpation. In benign disease or tumors of borderline malignant potential, the uterus and other ovary generally may be spared. Adjunctive chemotherapy (platinum-based and paclitaxel [Taxol]) or radiotherapy is often included, based on the location and stage of malignant disease.

Diet: No specific dietary changes indicated, except those imposed by advanced disease.
Activity: No restriction, except that imposed by advanced disease.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP096 (Cancer of the Ovary) and AP075 (Ovarian Cysts).

Drug(s) of Choice

None, except as adjunctive or symptomatic therapy.
Contraindications: See individual agents.
Precautions: Alkylating agents are associated with an increased risk of future leukemia (10% by 8 years after therapy).
Interactions: See individual agents.

FOLLOW-UP

Patient Monitoring: Careful follow-up for recurrent pelvic disease or enlargement of the remaining ovary (if any). This is generally performed by pelvic examination, augmented with ultrasonography in selected patients. In those suspected of having recurrent disease and other selected patients, second-look surgery may be desirable to assess progress and discover occult disease.
Prevention/Avoidance: None. Prophylactic bilateral salpingo-oopherectomy for those with known BRCA mutations.
Possible Complications: Perforation of the tumor capsule with rupture, which may lead to the seeding of the peritoneal cavity (pseudomyxoma peritonei, 2%–5% of patients).
Expected Outcome: Tumors with borderline malignant potential tend to grow slowly, and patients have prolonged survival with these tumors (the 20-year survival rate of patients with stage III disease is 40%). Of ovarian malignancies, mucinous cystadenocarcinoma has one of the best 5-year survival rates (40%).

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. More than 10% of tumors with borderline malignant potential are discovered during pregnancy.
ICD-10-CM Codes: Specific to the cell type and location.

REFERENCES

LEVEL II

Chao A, Chao A, Yen YS, et al. Abdominal compartment syndrome secondary to ovarian mucinous cystadenoma. *Obstet Gynecol*. 2004; 104:1180.

Gates MA, Rosner BA, Hecht JL, et al. Risk factors for epithelial ovarian cancer by histologic subtype. *Am J Epidemiol*. 2010;171:45.

Kalapotharakos G, Högberg T, Bergfeldt K, et al. Long term survival in women with borderline ovarian tumors: a population-based survey of borderline ovarian tumors in Sweden 1960-2007. *Acta Obstet Gynecol Scand*. 2015.

Koonings PP, Campbell K, Mishell DR Jr, et al. Relative frequency of primary ovarian neoplasms: a 10-year review. *Obstet Gynecol*. 1989; 74:921.

Stewart Massad L, Gao F, Hagemann I, et al. Clinical Outcomes among Women with Mucinous Adenocarcinoma of the Ovary. *Gynecol Obstet Invest*. 2015.

van Dessel T, Hameeteman TM, Wagenaar SS. Mucinous cystadenocarcinoma in pregnancy. Case report. *Br J Obstet Gynaecol*. 1988;95:527.

LEVEL III

Acs G. Serous and mucinous borderline (low malignant potential) tumors of the ovary. *Am J Clin Pathol*. 2005;123:S13.

American College of Obstetricians and Gynecologists. Management of adnexal masses. ACOG Practice Bulletin No. 83. *Obstet Gynecol*. 2007; 110:201.

Berek JS, Crum C, Friedlander M. Cancer of the ovary, fallopian tube, and peritoneum. *Int J Gynaecol Obstet*. 2012;119(suppl 2):S118.

Bhoola S, Hoskins WJ. Diagnosis and management of epithelial ovarian cancer. *Obstet Gynecol*. 2006;107:1399.

Carter J, Carson LF, Moradi MM, et al. Pseudomyxoma peritonei: a review. *Int J Gynecol Cancer*. 1991;1:243.

Link CJ Jr, Reed E, Sarosy G, et al. Borderline ovarian tumors. *Am J Med*. 1996;101:217.

Massad LS Jr, Hunter VJ, Szpak CA, et al. Epithelial ovarian tumors of low malignant potential. *Obstet Gynecol*. 1991;78:1027.

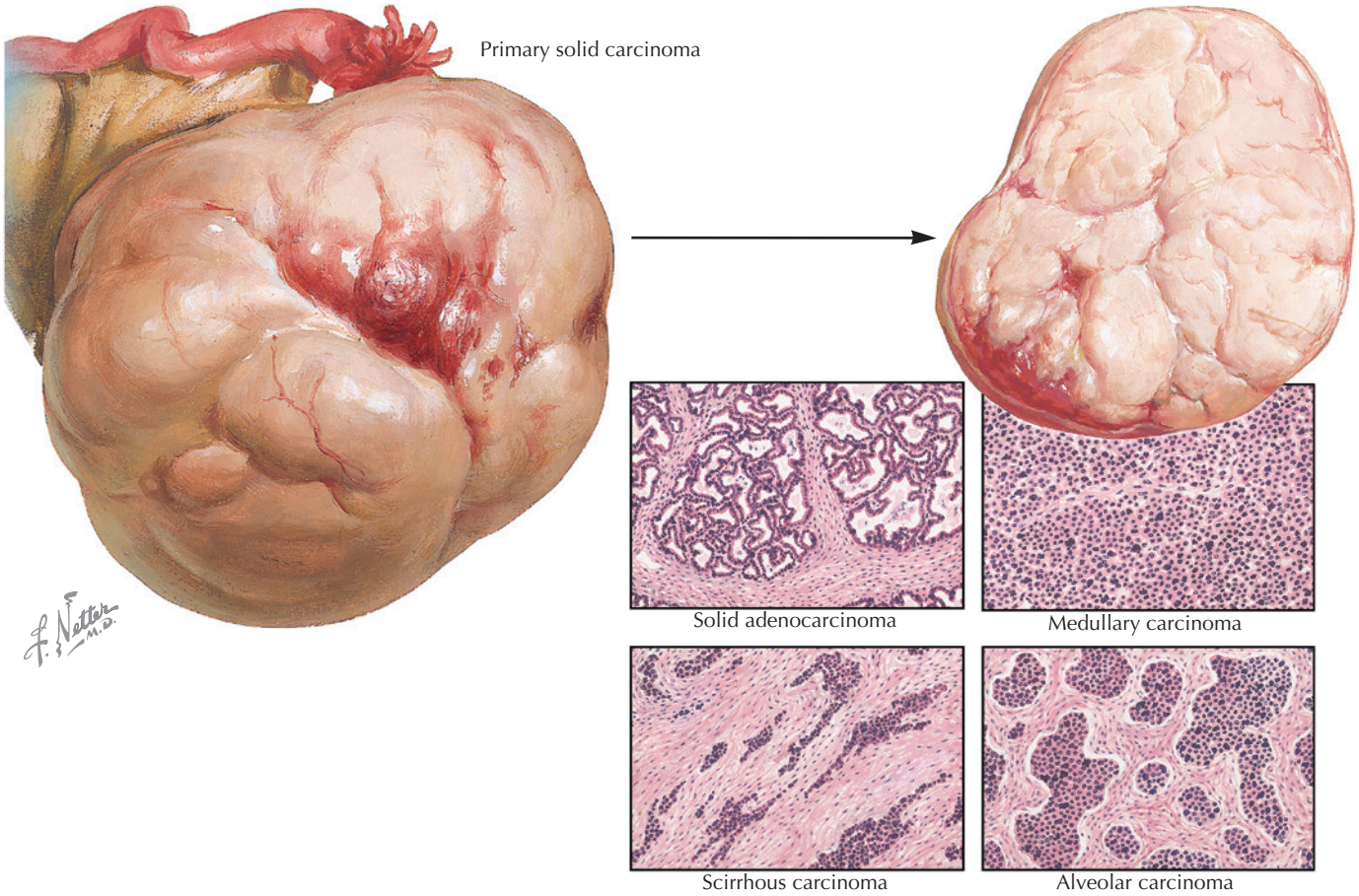


Figure 151.1 Primary solid, medullary, scirrhous, and alveolar ovarian carcinomas

SIGNS AND SYMPTOMS

- Asymptomatic until late in the disease (most diagnosed at stage III or IV)
- Weight loss
- Increasing abdominal girth despite constant or reduced caloric intake
- Ascites
- Adnexal mass (multilocular or partly solid masses in patients older than age 40 years likely to be malignant; ovarian masses in premenarchal girls are most often germ cell tumors)
- Vague lower abdominal discomfort (severe pain uncommon)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Benign adnexal masses (corpus luteum, follicular cyst)
- Nongynecologic pelvic masses
- Hepatic, renal, or cardiac disease, resulting in weight loss and ascites
- Endometriosis
- Hydrosalpinx
- Ectopic pregnancy (reproductive-aged women)
- Pedunculated leiomyomata
- Pelvic or horseshoe kidney
- Gastrointestinal malignancy

Associated Conditions: Breast cancer, endometrial cancer.

WORKUP AND EVALUATION

Laboratory: Serum testing for tumor markers, such as CA-125, lipid-associated sialic acid, carcinoembryonic antigen, α-fetoprotein, and lactate dehydrogenase (LDH), should be reserved for following the progress of patients with known malignancies and not for prognostic evaluation.

Imaging: Ultrasonography, magnetic resonance imaging (MRI), and computed tomography (CT) are helpful in evaluating patients suspected of having ovarian cancer. The normal postmenopausal ovary is typically 1.5–2 cm in size. Asymptomatic simple cysts of less than 5 cm diameter can be generally conservatively followed. Routing screening using transvaginal ultrasonography has not been shown to be cost effective without the presence of significant risk factors or symptoms.

Special Tests: A frozen-section histologic evaluation (intraoperative consultation) should be considered for any ovarian mass that appears suspicious for malignancy. Flow cytometry may be of prognostic value.

Diagnostic Tests: History, physical examination, and imaging. Final diagnosis is established by histologic evaluation.

Pathologic Findings

More than 90% of ovarian cancer is of the epithelial cell type, thought to arise from pluripotential mesothelial cells of the visceral peritoneum of the ovarian capsule. Lymphatic spread occurs in

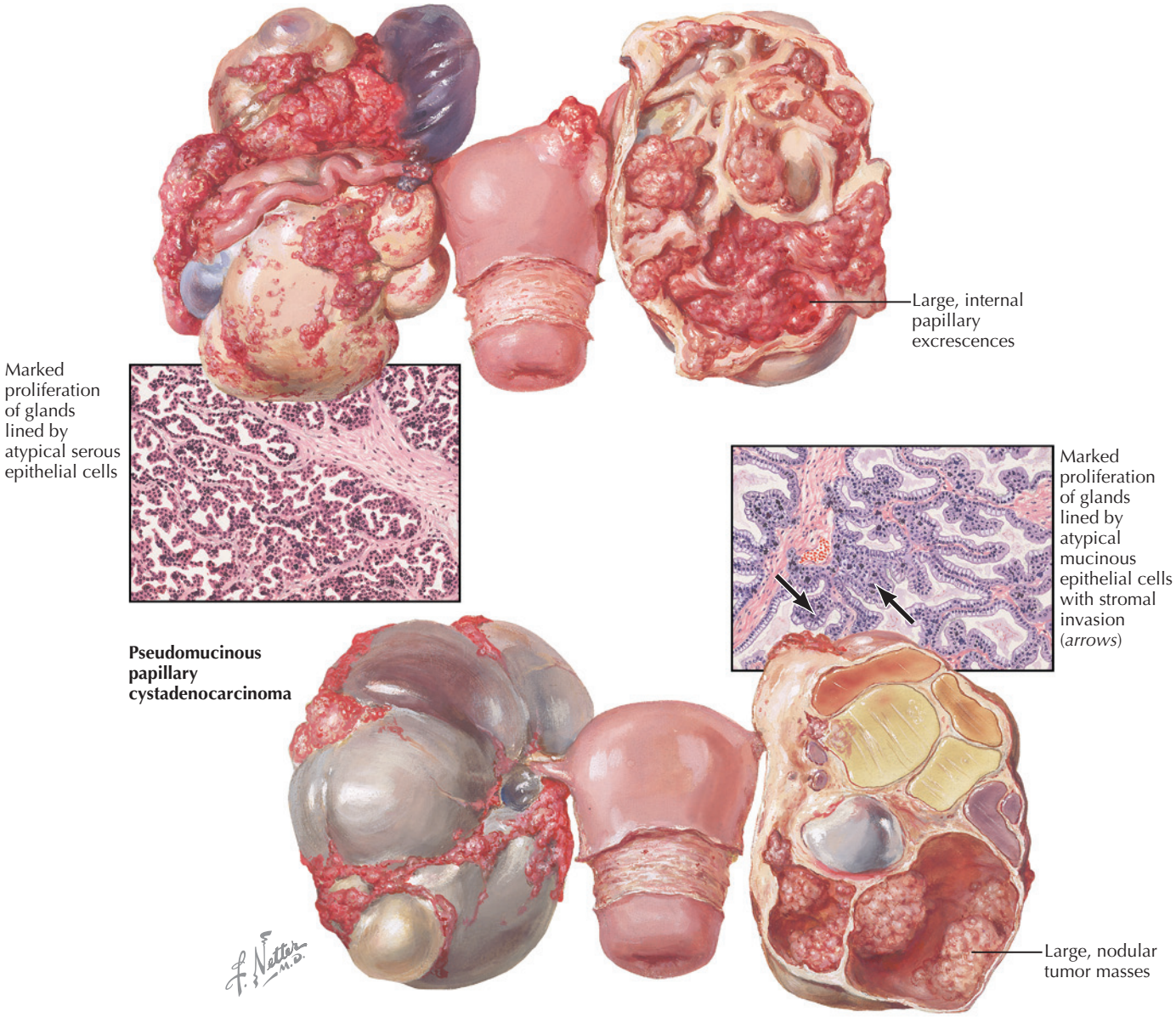


Figure 151.2 Papillary serous cystadenocarcinoma

approximately 20% of tumors that appear grossly confined to the ovary.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, supportive therapy based on symptoms.

Specific Measures: Ovarian cancer is a disease that requires surgical exploration and extirpation (generally including the uterus and contralateral ovary). Adjunctive chemotherapy (platinum-based and paclitaxel [Taxol]) or radiotherapy is often included based on the location and stage of the disease. Immune modulator therapy is being evaluated but remains unproven.

Diet: No changes except those imposed by advanced disease. Parenteral nutrition may be required before or after surgery in advanced disease.

Activity: No restriction, except that imposed by advanced disease.

Patient Education: Reassurance; American College of Obstetricians and Gynecologists Patient Education Pamphlet AP096 (Cancer of the Ovary) and AP075 (Ovarian Cysts).

Drug(s) of Choice

None, except as an adjunctive therapy.

Precautions: Alkylating agents are associated with an increased risk for future leukemia (10% by 8 years after therapy).

FOLLOW-UP

Patient Monitoring: As yet, there are no effective screening tools for the early detection of primary ovarian cancer. Ultrasonography, MRI, CT, and biochemical markers such as CA 125, which are useful for evaluating a suspicious mass or following the progress of treatment, are not of value for mass screening. In those suspected of having recurrent disease and other selected patients,

second-look surgery may be desirable to assess progress and discover occult disease. When second look surgery is negative, the associated 5-year survival is approximately 50%.

Prevention/Avoidance: For those few patients at a truly high risk (familial cancer syndromes), prophylactic salpingo-oophorectomy, performed after childbearing is completed, is preferable to any attempt at prolonged surveillance with current technology. Even this aggressive step does not preclude the development of ovarian cancer; up to 10% of ovarian cancers are found in women who have had bilateral oophorectomies.

Possible Complications: Ascites, pulmonary effusion, small bowel obstruction, disease progression, and death.

Expected Outcome: Ovarian cancer has the highest mortality of any gynecologic cancer, resulting in more deaths annually than cervical and endometrial cancer combined. If discovered early in the process and treated with aggressive surgical resection and adjunctive therapy, disease-free survival is possible. Survival is affected by stage, grade, cell type, and residual tumor after surgical resection. Survival (5-year) by stage: stage I, 80%; stage II, 60%; stage III, 25%; stage, IV 15%. Serous adenocarcinoma has the poorest prognosis of the epithelial types.

MISCELLANEOUS

Pregnancy Considerations: Does not threaten pregnancy except by the jeopardy caused to the mother.

ICD-10-CM Codes: Based on the type and stage.

REFERENCES

LEVEL II

Gates MA, Rosner BA, Hecht JL, et al. Risk factors for epithelial ovarian cancer by histologic subtype. *Am J Epidemiol*. 2010;171:45.

Helder-Woolderink JM, Blok EA, Vasen HF, et al. Ovarian cancer in Lynch syndrome; a systematic review. *Eur J Cancer*. 2016;55:65.

Jaaback K, Johnson N, Lawrie TA. Intraperitoneal chemotherapy for the initial management of primary epithelial ovarian cancer. *Cochrane Database Syst Rev*. 2016;(1):CD005340.

Lacey JV Jr, Greene MH, Buys SS, et al. Ovarian cancer screening in women with a family history of breast or ovarian cancer. *Obstet Gynecol*. 2006;108:1176.

Tangjitgamol S, Manusirivithaya S, Laopaiboon M, et al. Interval debulking surgery for advanced epithelial ovarian cancer. *Cochrane Database Syst Rev*. 2016;(1):CD006014.

van Nagell JR Jr, DePriest PD, Ueland FR, et al. Ovarian cancer screening with annual transvaginal sonography: findings of 25,000 women screened. *Cancer*. 2007;109:1887.

LEVEL III

American College of Obstetricians and Gynecologists. Hereditary breast and ovarian cancer syndrome. ACOG Practice Bulletin No. 103. *Obstet Gynecol*. 2009;113:957.

American College of Obstetricians and Gynecologists. Hereditary cancer syndromes and risk assessment. Committee Opinion No. 634. *Obstet Gynecol*. 2015;125:1538.

American College of Obstetricians and Gynecologists. Management of adnexal masses. ACOG Practice Bulletin No. 83. *Obstet Gynecol*. 2007;110:201.

American College of Obstetricians and Gynecologists. Salpingectomy for ovarian cancer prevention. Committee Opinion No. 620. *Obstet Gynecol*. 2015;125:279.

American College of Obstetricians and Gynecologists. The role of the obstetrician–gynecologist in the early detection of epithelial ovarian cancer. Committee Opinion No. 477. *Obstet Gynecol*. 2011;117:742.

Berek JS, Crum C, Friedlander M. Cancer of the ovary, fallopian tube, and peritoneum. *Int J Gynaecol Obstet*. 2012;119(suppl 2):S118.

Bhoola S, Hoskins WJ. Diagnosis and management of epithelial ovarian cancer. *Obstet Gynecol*. 2006;107:1399.

Cannistra SA. Cancer of the ovary. *N Engl J Med*. 2004;351:2519.

Farthing A. Conserving fertility in the management of gynaecological cancers. *BJOG*. 2006;113:129.

Hartmann LC, Lindor NM. The role of risk-reducing surgery in hereditary breast and ovarian cancer. *N Engl J Med*. 2016;374:454.

Marth C, Walker JL, Barakat RR, et al. Results of the 2006 Innsbruck International Consensus Conference on intraperitoneal chemotherapy in patients with ovarian cancer. *Cancer*. 2007;109:645.

Troso-Sandoval TA, Lichtman SM. Chemotherapy of ovarian cancer in elderly patients. *Cancer Biol Med*. 2015;12:292.

U.S. Preventive Services Task Force. Screening for ovarian cancer: recommendation statement. U.S. Preventive Services Task Force. *Am Fam Physician*. 2005;71:759.

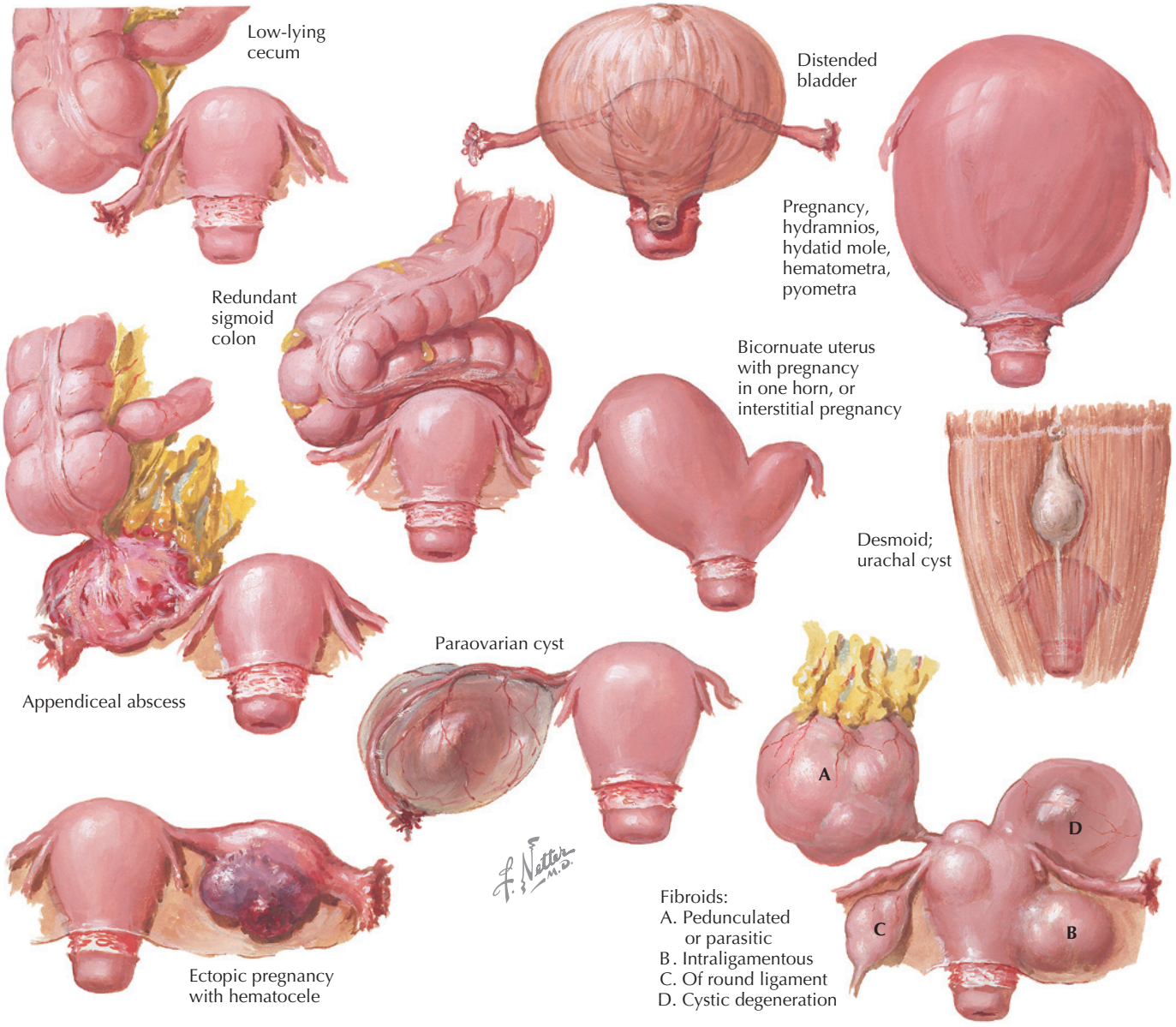


Figure 152.1 Differential diagnosis of ovarian cysts

bleeding, enlarge and become symptomatic. Approximately 25% of ovarian enlargements in reproductive-aged women represent true neoplasia, with only approximately 10% being malignant. The largest group of benign ovarian tumors are those that arise from the epithelium of the ovary and its capsule. Despite the diversity of tumors with epithelial beginnings, the most common ovarian tumor in young reproductive-aged women is the cystic teratoma or dermoid, which originates from a germ cell. These tumors are derived from primary germ cells and include tissues from all three embryonic germ layers (ectoderm, mesoderm, and endoderm).

Strategies: History and physical examinations are generally sufficient to establish the presence of the mass. No laboratory tests are of specific help in the global diagnosis of ovarian cysts. Laboratory investigations may support specific diagnoses. Ultrasonography, computed tomography, and magnetic resonance imaging are of limited value in evaluating asymptomatic masses in young patients. Exceptions to this are patients in whom clinical assessment is impractical or inadequate (eg, massive obesity) or those in whom malignancy is suspected. Serum testing for tumor markers, such as CA-125, lipid-associated sialic acid, carcinoembryonic antigen, α-fetoprotein, and lactate dehydrogenase (LDH), should be reserved for following the progress of patients with known malignancies and not for prognostic evaluation.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP075 (Ovarian Cysts).

IMPLEMENTATION

Special Considerations: Some authors favor giving young patients with small, presumably benign, cystic masses ovulation suppression therapy, such as oral contraceptives, to hasten the process of regression. Regression rates of 65%–75% are often cited for this approach, but this strategy is largely a matter of personal choice because definitive studies are lacking. Physiologic ovarian enlargements, including follicular or corpus luteum cysts, should

not be present if a patient is using oral contraceptives (ovulation may not be fully suppressed in women using some progestin-only contraceptives). For this reason, patients who are already using oral contraceptives and develop adnexal masses are more likely to have pathologic conditions that will not regress, increasing the possibility that eventual surgical exploration is required. Peri- and postmenopausal patients may still have benign processes as a cause of an adnexal mass, but the likelihood of a malignant process is increased (up to one-third of cases), altering management. In these patients, masses larger than 6 cm generally prompt surgical exploration and excision, although some authors suggest this threshold should be increased to 10 cm. Transvaginal ultrasonography to measure and track masses has allowed masses that once would have required exploration to be conservatively followed up. As in younger patients, the size, shape, mobility, and consistency of the mass should be estimated. Irregular, immobile, or mixed-character masses (solid and cystic) are more likely to be malignant and deserve immediate consultation with a surgeon for exploration. The final diagnosis of ovarian cancer must be surgically made.

REFERENCES

LEVEL II

Geomini PM, Kluivers KB, Moret E, et al. Evaluation of adnexal masses with three-dimensional ultrasonography. *Obstet Gynecol*. 2006;108:1167.

Rufford BD, Jacobs IJ, Menon U. Feasibility of screening for ovarian cancer using symptoms as selection criteria. *BJOG*. 2007;114:59.

Whitecar MP, Turner S, Higby MK. Adnexal masses in pregnancy: a review of 130 cases undergoing surgical management. *Am J Obstet Gynecol*. 1999;181:19.

LEVEL III

American College of Obstetricians and Gynecologists. Management of adnexal masses. ACOG Practice Bulletin No. 83. *Obstet Gynecol*. 2007;110:201.

American College of Obstetricians and Gynecologists. The role of the obstetrician–gynecologist in the early detection of epithelial ovarian cancer. Committee Opinion No. 477. *Obstet Gynecol*. 2011;117:742.

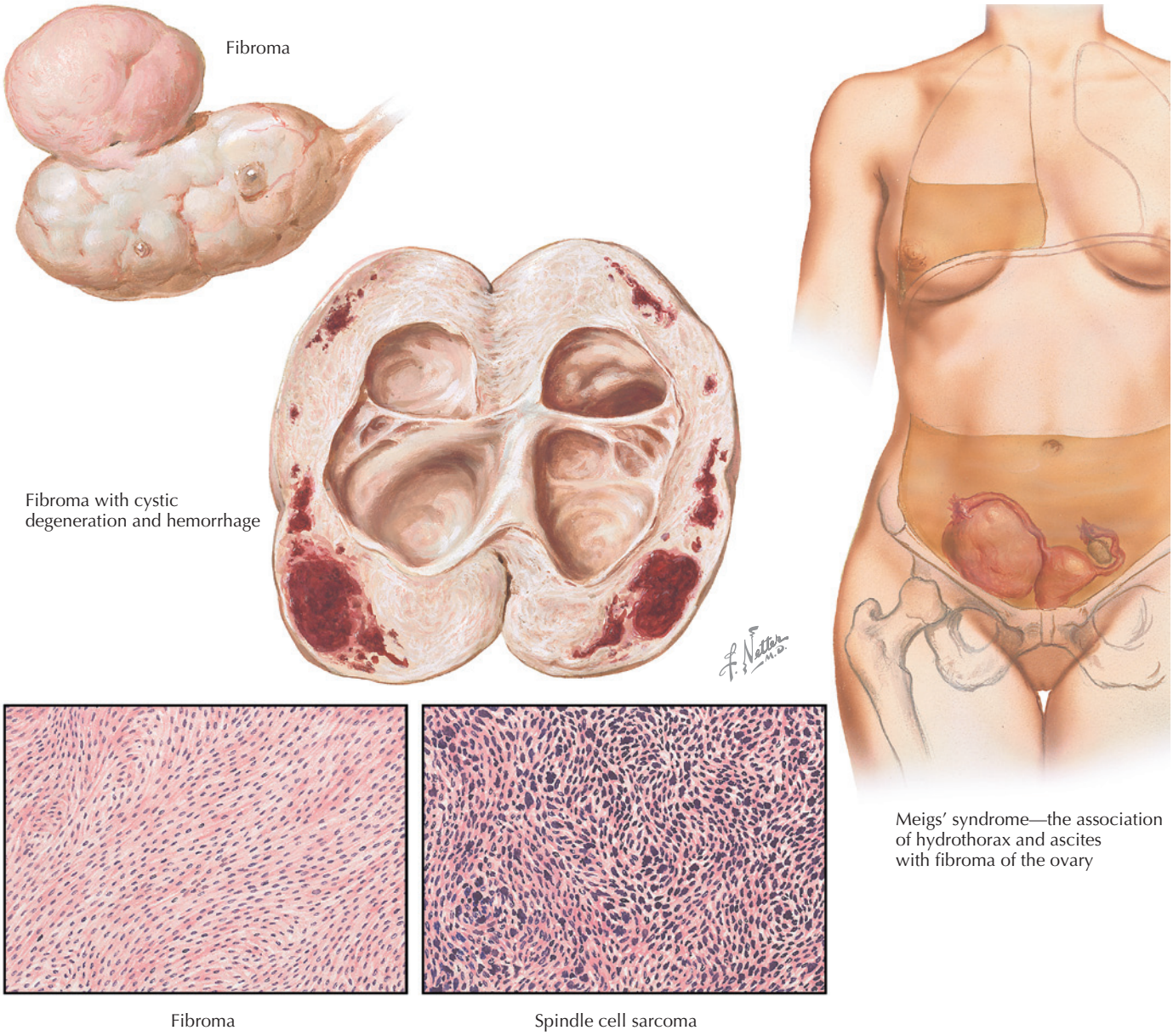


Figure 153.1 Ovarian fibroma

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, supportive therapy based on symptoms.
Specific Measures: Surgical exploration and resection are adequate. In older women, hysterectomy and removal of the contralateral ovary are generally performed. Fibromas of low malignant potential are rare.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP096 (Cancer of the Ovary) and AP075 (Ovarian Cysts).

Drug(s) of Choice

Adjunctive or symptomatic therapy.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: Uncommon. Torsion or bleeding may occur. Fibromas of low malignant potential that are adherent or that are ruptured may recur.
Expected Outcome: Simple surgical excision is generally curative.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. Hormonally active tumors (thecoma) may disrupt menstrual patterns and ovulation, leading to reduced fertility.
ICD-10-CM Codes: D27.9 (Benign neoplasm of unspecified ovary).

REFERENCES

LEVEL II

Brun JL. Demons syndrome revisited: a review of the literature. *Gynecol Oncol*. 2007;105:796.

Geomini PM, Kluivers KB, Moret E, et al. Evaluation of adnexal masses with three-dimensional ultrasonography. *Obstet Gynecol*. 2006;108:1167.

Leung SW, Yuen PM. Ovarian fibroma: a review on the clinical characteristics, diagnostic difficulties, and management options of 23 cases. *Gynecol Obstet Invest*. 2006;62:1.

Onderoglu LS, Gultekin M, Dursun P, et al. Bilateral ovarian fibromatosis presenting with ascites and hirsutism. *Gynecol Oncol*. 2004;94:223.

LEVEL III

American College of Obstetricians and Gynecologists. Management of adnexal masses. ACOG Practice Bulletin No. 83. *Obstet Gynecol*. 2007; 110:201.

Burket RL, Rauh JL. Gorlin's syndrome. Ovarian fibromas at adolescence. *Obstet Gynecol*. 1976;47:43s.

Meigs JV. Fibroma of the ovary with ascites and hydrothorax. Meigs' syndrome. *Am J Obstet Gynecol*. 1954;67:962.

Meigs JV, Armstrong SH, Hamilton HH. A further contribution to the syndrome of fibroma of the ovary with fluid in the abdomen and chest, Meigs' syndrome. *Am J Obstet Gynecol*. 1943;46:19.

Roth LM. Recent advances in the pathology and classification of ovarian sex cord-stromal tumors. *Int J Gynecol Pathol*. 2006;25:199.

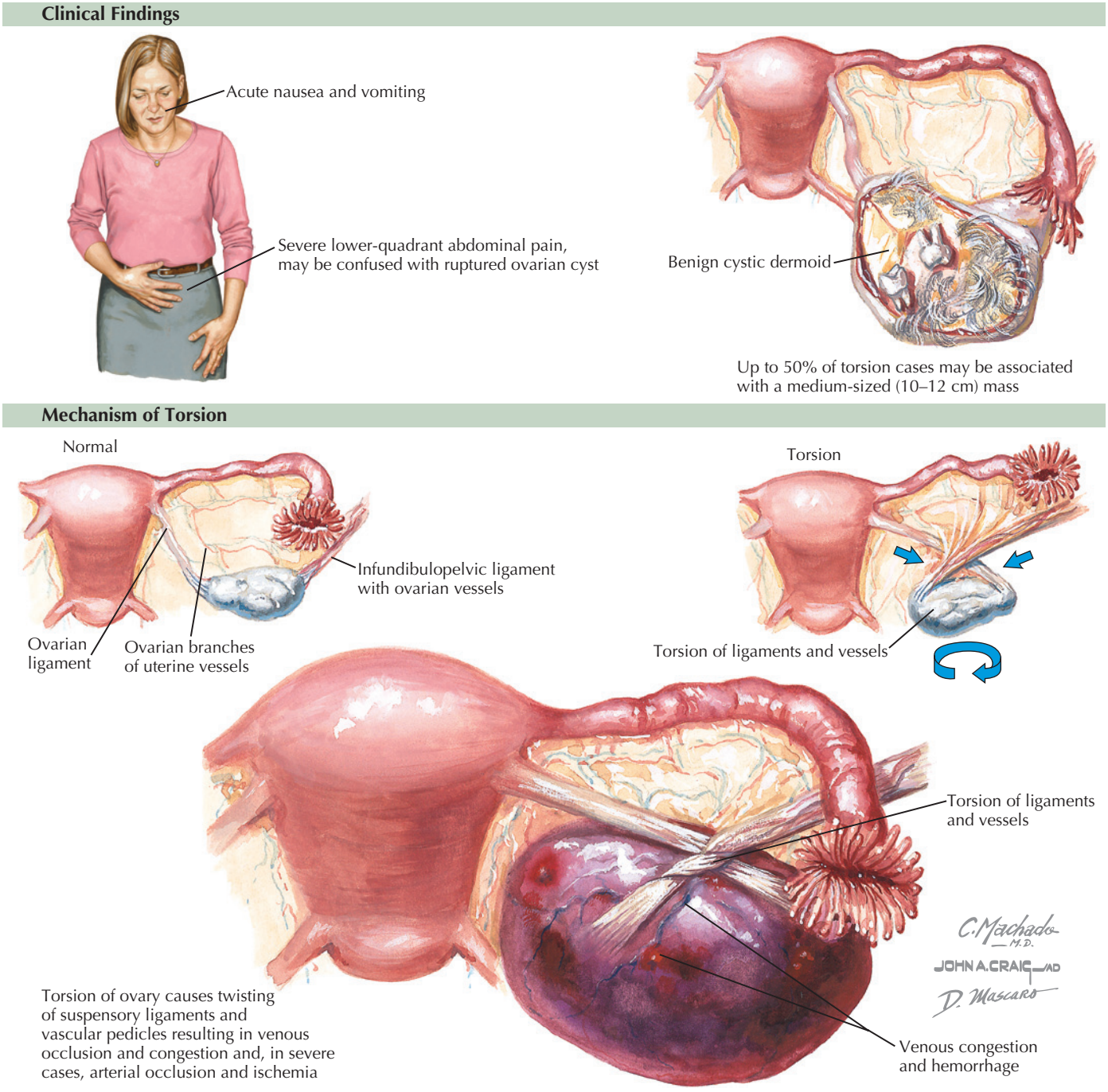


Figure 154.1 Clinical findings and mechanism of ovarian torsion

FOLLOW-UP

Patient Monitoring: Normal health maintenance as follow-up.
Prevention/Avoidance: None.
Possible Complications: Complete loss of the involved ovary.
Expected Outcome: A part or all of the ovary may be salvaged in some patients if intervention occurs early enough in the process.

MISCELLANEOUS

Pregnancy Considerations: Twenty percent of cases occur during pregnancy; peak risk is between 10 and 17 weeks gestation.
ICD-10-CM Codes: N83.53 (Torsion of ovary, ovarian pedicle, and fallopian tube).

REFERENCES

LEVEL II

Ashwal E, Hiersch L, Krissi H, et al. Characteristics and management of ovarian torsion in premenarchal compared with postmenarchal patients. *Obstet Gynecol*. 2015;126:514.

Huchon C, Fauconnier A. Adnexal torsion: a literature review. *Eur J Obstet Gynecol Reprod Biol*. 2010;150:8.

Rody A, Jackisch C, Klockenbusch W, et al. The conservative management of adnexal torsion—A case-report and review of the literature. *Eur J Obstet Gynecol Reprod Biol*. 2002;101:83.

LEVEL III

American College of Obstetricians and Gynecologists. Management of adnexal masses ACOG Practice Bulletin 83. *Obstet Gynecol*. 2007;110:201.

Breech LL, Hillard PJ. Adnexal torsion in pediatric and adolescent girls. *Curr Opin Obstet Gynecol*. 2005;17:483.

Cass DL. Ovarian torsion. *Semin Pediatr Surg*. 2005;14:1486.

Giuntoli RL 2nd, Vang RS, Bristow RE. Evaluation and management of adnexal masses during pregnancy. *Clin Obstet Gynecol*. 2006;49:492.

Oelsner G, Shashar D. Adnexal torsion. *Clin Obstet Gynecol*. 2006;49:459.

Strickland JL. Ovarian cysts in neonates, children and adolescents. *Curr Opin Obstet Gynecol*. 2002;14:459.

PID has a positive predictive value (PPV) for salpingitis of 65%–90% compared with laparoscopy.

Diagnostic Tests: History, physical examination, and ultrasonography. Diagnostic criteria are shown in the following table. Empiric treatment of PID should be started in sexually active women at risk for sexually transmitted infections (STIs) if they are experiencing pelvic or lower abdominal pain, if no cause for the illness other than PID can be identified, and if they have cervical motion or cervical or uterine tenderness. The "gold standard" for establishing the diagnosis is endometrial biopsy, transvaginal sonography, or magnetic resonance imaging techniques showing thickened, fluid-filled tubes with or without free pelvic fluid or tubo-ovarian complex, but these are used almost exclusively in the research setting.

Pathologic Findings

Inflammation of the fallopian tubes, ovaries, and surrounding peritoneal surfaces.

Table 155.1 Diagnostic Criteria for Pelvic Inflammatory Disease

Must Have All Three*:	• Abdominal tenderness • Adnexal tenderness • Cervical tenderness
Must Have at Least One:	• Positive Gram stain or laboratory documentation of cervical infection with *N. gonorrhoeae* or *C. trachomatis* • Temperature > 38°C • White blood cell count > 10,000 • Elevated erythrocyte sedimentation rate • Elevated C-reactive protein • Cervical friability • Increased white blood cells in vaginal fluid • Pus on culdocentesis or laparoscopy • Tubo-ovarian abscess

*Some advocate treating solely based on the presence of any one of these to reduce the risk of undertreatment.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Rapid evaluation, cervical cultures, supportive therapy (fluids, analgesics, and antipyretics).

Specific Measures: Aggressive antibiotic therapy. For a rare few, hysterectomy may be required. Rupture of a tubo-ovarian abscess, with subsequent septic shock, may be life threatening.

Diet: No specific dietary changes indicated.

Activity: Pelvic rest. Ambulatory care is possible with early mild infections; hospitalization may be required.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP077 (Pelvic Inflammatory Disease), AP009 (How to Prevent Sexually Transmitted Infections), AP099 (Pelvic Pain), AP071 (Gonorrhea, Chlamydia, and Syphilis), and AP020 (When Sex Is Painful).

Drug(s) of Choice

- Ambulatory care—ceftriaxone 250 mg IM in a single dose plus doxycycline 100 mg PO twice a day for 14 days, with or without metronidazole 500 mg twice a day for 14 days; cefoxitin 2 g IM plus probenecid 1 g PO combined with a 14-day course of doxycycline 100 mg twice daily; or a combination of ceftriaxone 250 mg IM plus a 14-day course of doxycycline both with or without metronidazole 500 mg twice a day for 14 days. Fluoroquinolone-resistant gonorrhea is now widespread in the United States, making this class of antibiotics no longer appropriate for the treatment of gonorrhea, and hence, PID.
- Hospitalized patients—cefotetan 2 g IV every 12 hours or cefoxitin 2 g IV every 6 hours with doxycycline 100 mg every 12 hours PO or IV is recommended. For mixed infections, clindamycin 900 mg IV every 8 hours plus an aminoglycoside such as gentamicin 2 mg/kg loading doses then 1.5 mg/kg every 8 hours will give better protection.
- After discharge—doxycycline 100 mg PO twice a day or clindamycin 450 mg four times a day for 14 days.

Contraindications: See individual agents.

Precautions: See individual agents.

Interactions: See individual agents.

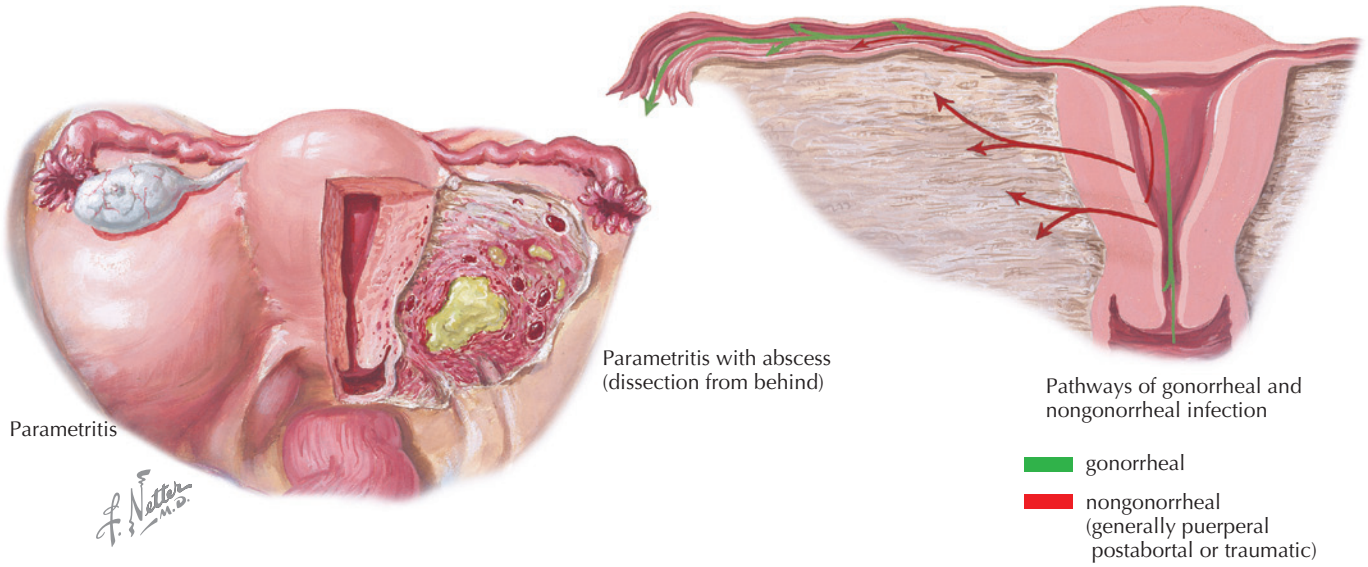


Figure 155.1 Parametritis and gonorrheal/nongonorrheal infection

Alternative Drugs

- Spectinomycin 2 g in a single intramuscular dose.
- Augmentin 500 mg three times a day for 10 days may also be used with similar results.
- Excellent results have been reported with the combination of clindamycin and aztreonam 2 g IM every 8 hours.
- Piperacillin 4 g combined with tazobactam 500 mg given IV every 8 hours may also be used but has given cure rates of only 90% (5% improved).
- Amoxicillin/clavulanic acid and doxycycline were effective in obtaining short-term clinical response in a single clinical trial; however, gastrointestinal symptoms limit compliance.

FOLLOW-UP

Patient Monitoring: Hospitalized care is indicated when differential diagnosis includes ectopic pregnancy or appendicitis, HIV, immunosuppression, IUCD use, nulliparity, paralytic ileus, peritonitis or toxicity, pregnancy, previous treatment failure, significant gastrointestinal symptoms, significant morbidity, temperature >39°C, tubo-ovarian abscess, uncertain or complicated differential diagnosis, unreliable patient, or white blood cell count >20,000 or <4000.

Prevention/Avoidance: Prevention of these sequelae is based on prevention of infection (barrier contraception, safe sex practices), screening for those at risk, and aggressive treatment. As with most STIs, the partners of patients with PID should be screened for gonococcal, chlamydial, or HIV infections and treated accordingly.

Possible Complications: Approximately one in four women with acute PID experiences medical sequelae. PID often leads to tubal factor infertility (8%), ectopic pregnancy (9%), and chronic abdominal pain (18%). The risk of infertility approximately doubles with each subsequent episode, resulting in a 40% rate of infertility after only three episodes. Women with documented salpingitis have a four-fold increase in their rate of ectopic pregnancy, and 5%–15% of women require surgery because of damage caused by PID. Peritoneal involvement may spread to include perihepatitis (Fitz-Hugh-Curtis syndrome). Rupture of a tubo-ovarian abscess, with subsequent septic shock, may be life threatening. Death from pelvic infections or their complications (for women aged 15–45 years) is reported to be 0.29 of 100,000.

Expected Outcome: Early, aggressive therapy is generally associated with resolution, but the possibility of recurrence or sequelae is significant.

MISCELLANEOUS

Pregnancy Considerations: Often associated with reduced fertility and an increased risk of ectopic pregnancy. Once pregnancy is established, the risk of new infection is reduced because of obstruction of the upper genital tract by the gestation. Scarring from previous infections may cause pain when stretched by the enlarging uterus.

ICD-10-CM Codes: N73.0 (Acute parametritis and pelvic cellulitis), others based on chronicity, structures involved, and relation to pregnancy.

REFERENCES

LEVEL I

Ness RB, Trautmann G, Richter HE, et al. Effectiveness of treatment strategies of some women with pelvic inflammatory disease: a randomized trial. *Obstet Gynecol*. 2005;106:573.

LEVEL II

Gaitán H, Angel E, Diaz R, et al. Accuracy of five different diagnostic techniques in mild-to-moderate pelvic inflammatory disease. *Infect Dis Obstet Gynecol*. 2002;10:171.

Latthe P, Mignini L, Gray R, et al. Factors predisposing women to chronic pelvic pain: systematic review. *BMJ*. 2006;332:749.

Ness RB, Hillier SL, Kip KE, et al. Bacterial vaginosis and risk of pelvic inflammatory disease. *Obstet Gynecol*. 2004;104:761.

Satterwhite CL, et al. Sexually transmitted infections among U.S. women and men: Prevalence and incidence estimates, 2008. *Sex Transm Dis*. 2013;40:187.

Tepper NK, Steenland MW, Gaffield ME, et al. Retention of intrauterine devices in women who acquire pelvic inflammatory disease: a systematic review. *Contraception*. 2013;87:655.

Trent M, Haggerty CL, Jennings JM, et al. Adverse adolescent reproductive health outcomes after pelvic inflammatory disease. *Arch Pediatr Adolesc Med*. 2011;165:49.

Whiteman MK, Kuklina E, Jamieson DJ, et al. Inpatient hospitalization for gynecologic disorders in the United States. *Am J Obstet Gynecol*. 2010;202:541e1.

LEVEL III

American College of Obstetricians and Gynecologists. Dual therapy for gonococcal infections. Committee Opinion No. 645. *Obstet Gynecol*. 2015;126:e95.

American College of Obstetricians and Gynecologists. Expedited partner therapy in the management of gonorrhea and chlamydial infection. Committee Opinion No. 632. *Obstet Gynecol*. 2015;125:1526.

Centers for Disease Control and Prevention. Recommendations for the Laboratory-Based Detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae*—2014. *MMWR Recomm Rep*. 2014;63(RR–2).

LeFevre ML, U.S. Preventive Services Task Force. Screening for chlamydia and gonorrhea: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2014;161:902.

Soper DE. Pelvic inflammatory disease. *Obstet Gynecol*. 2010;116:419.

156 PSEUDOMYXOMA PERITONEI

INTRODUCTION

Description: Pseudomyxoma peritonei is the intraperitoneal spread of a mucin-secreting tumor (either a mucinous cystadenoma or carcinoma), which results in recurrent abdominal masses, often-massive ascites, and multiple bowel obstructions. This tumor may frequently begin in the appendix.
Prevalence: Two of 10,000 laparotomies and 2%–5% of ovarian mucinous tumors (16% in mucinous cystadenocarcinomas).
Predominant Age: Middle to late reproductive age.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Spread, rupture, spill, or leakage of a primary appendiceal tumor or other gastrointestinal or ovarian tumor. Recent histologic studies suggest that in the majority of patients the appendix is the primary tumor source. In rare cases, metaplasia by the cells of the peritoneal surface may account for this tumor.
Risk Factors: Rupture or leakage of an ovarian mucinous tumor at the time of surgical resection. This role has been debated in recent literature.

SIGNS AND SYMPTOMS

- Accumulation of large amounts of mucinous material in the peritoneal cavity
- Recurrent bowel obstruction
- Implants of tumor on the omentum, undersurface of the diaphragm, pelvis, right retrohepatic space, left abdominal gutter, and ligament of Treitz. (In contrast to carcinoma the peritoneal surface of the bowel is generally spared; metastasis outside the peritoneal cavity does not occur.)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Disseminated ovarian cancer
- Metastatic colon cancer
- Disseminated leiomyomata
- Ascites

Associated Conditions: Gastrointestinal tumors, bowel obstruction.

WORKUP AND EVALUATION

Laboratory: As indicated before surgery. Serum testing for tumor markers, such as CA-125, lipid-associated sialic acid, carcinoembryonic antigen, and α-fetoprotein, should be reserved for following the progress of patients with known malignancies and not for prognostic evaluation.
Imaging: Ultrasonography or computed tomography may be helpful in determining the extent of disease.
Special Tests: None indicated.
Diagnostic Tests: History, physical examination, and imaging. Final diagnosis is established by histologic evaluation.

Pathologic Findings

Perforation of the capsule of a mucinous tumor with rupturing and seeding of the peritoneal cavity. Most often associated with malignant tumors, although benign mucinous neoplasms may perforate and result in pseudomyxoma peritonei as well. Tumors of the ovary and appendix may be synchronous, making the determination of origin difficult or impossible.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, supportive therapy based on symptoms.
Specific Measures: Surgical exploration and extirpation. Extensive bowel resection is often required because of diffuse peritoneal implants of tumor. Reoperation is common.
Diet: No specific dietary changes indicated, except those imposed by advanced disease.
Activity: No restriction, except that imposed by advanced disease.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP075 (Ovarian Cysts), AP096 (Cancer of the Ovary), and AP080 (Preparing for Surgery).

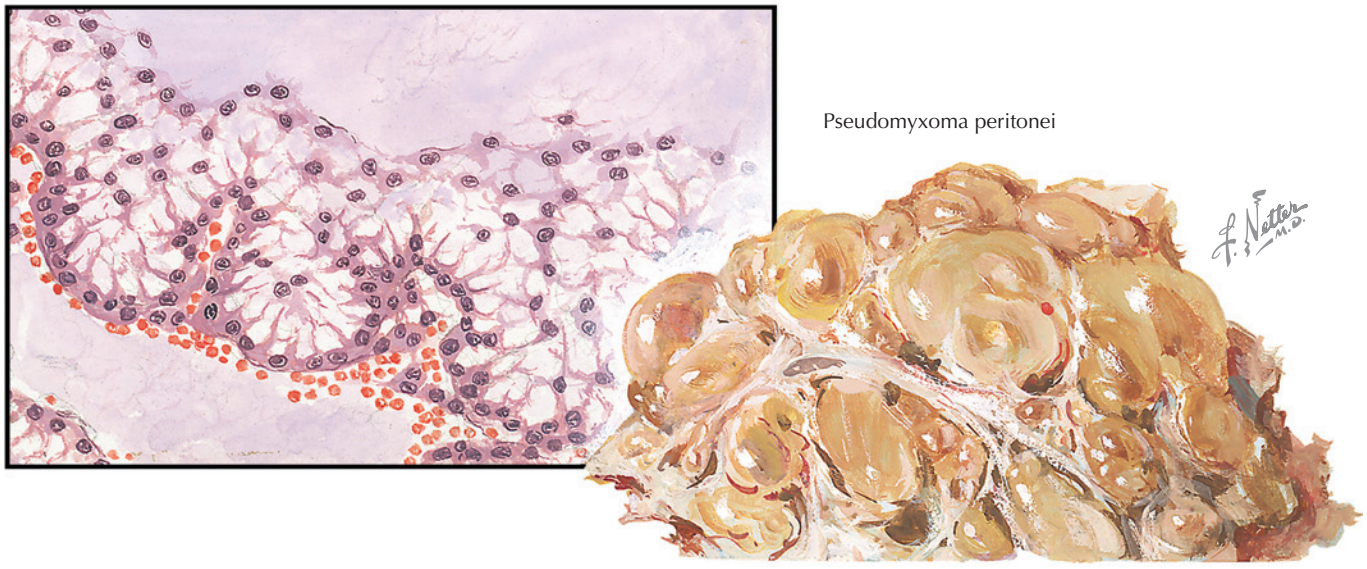


Figure 156.1 Pseudomyxoma peritonei

Drug(s) of Choice

None, except as an adjunctive or symptomatic therapy. Chemotherapy (systemic or intraperitoneal alkylating agents) and mucolytic agents have not been shown to be effective. One publication has advocated intraperitoneal hyperthermic perfusion, but efficacy has not been established.

Precautions: Alkylating agents are associated with an increased risk of future leukemia (10% by 8 years after therapy).

FOLLOW-UP

Patient Monitoring: Careful follow-up for recurrent pelvic disease or enlargement of the remaining ovary (if any). This is generally performed by pelvic examination, augmented with ultrasonography in selected patients.

Prevention/Avoidance: Care in the handling and surgical removal of ovarian masses.

Possible Complications: Generally follows an indolent course with progressive bowel dysfunction, intercurrent infection, inanition, and death.

Expected Outcome: The prognosis is better for the patient when the tumor arises from adenomas (appendiceal or ovarian; 5-year survival rate is 85%) than if it comes from a carcinoma (5-year survival is <60%) or peritoneal carcinomatosis (<10%).

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.

ICD-10-CM Codes: C78.6 (Secondary malignant neoplasm of retroperitoneum and peritoneum).

REFERENCES

LEVEL II

Bryant J, Clegg AJ, Sidhu MK, et al. Systematic review of the Sugarbaker procedure for pseudomyxoma peritonei. *Br J Surg*. 2005;92:153.

Geisinger KR, Levine EA, Shen P, et al. Pleuropulmonary involvement in pseudomyxoma peritonei: morphologic assessment and literature review. *Am J Clin Pathol*. 2007;127:135.

Kusamura S, Younan R, Baratti D, et al. Cytoreductive surgery followed by intraperitoneal hyperthermic perfusion: analysis of morbidity and mortality in 209 peritoneal surface malignancies treated with closed abdomen technique. *Cancer*. 2006;106:1144.

Ronnett BM, Kurman RJ, Zahn CM, et al. Pseudomyxoma peritonei in women: a clinicopathologic analysis of 30 cases with emphasis on site of origin, prognosis, and relationship to ovarian mucinous tumors of low malignant potential. *Hum Pathol*. 1995;26:509.

Yan TD, Links M, Xu ZY, et al. Cytoreductive surgery and perioperative intraperitoneal chemotherapy for pseudomyxoma peritonei from appendiceal mucinous neoplasms. *Br J Surg*. 2006;93:1270.

LEVEL III

Acs G. Serous and mucinous borderline (low malignant potential) tumors of the ovary. *Am J Clin Pathol*. 2005;123:S13.

Jones DH. Pseudomyxoma peritonei. *Br J Clin Pract*. 1965;19:675.

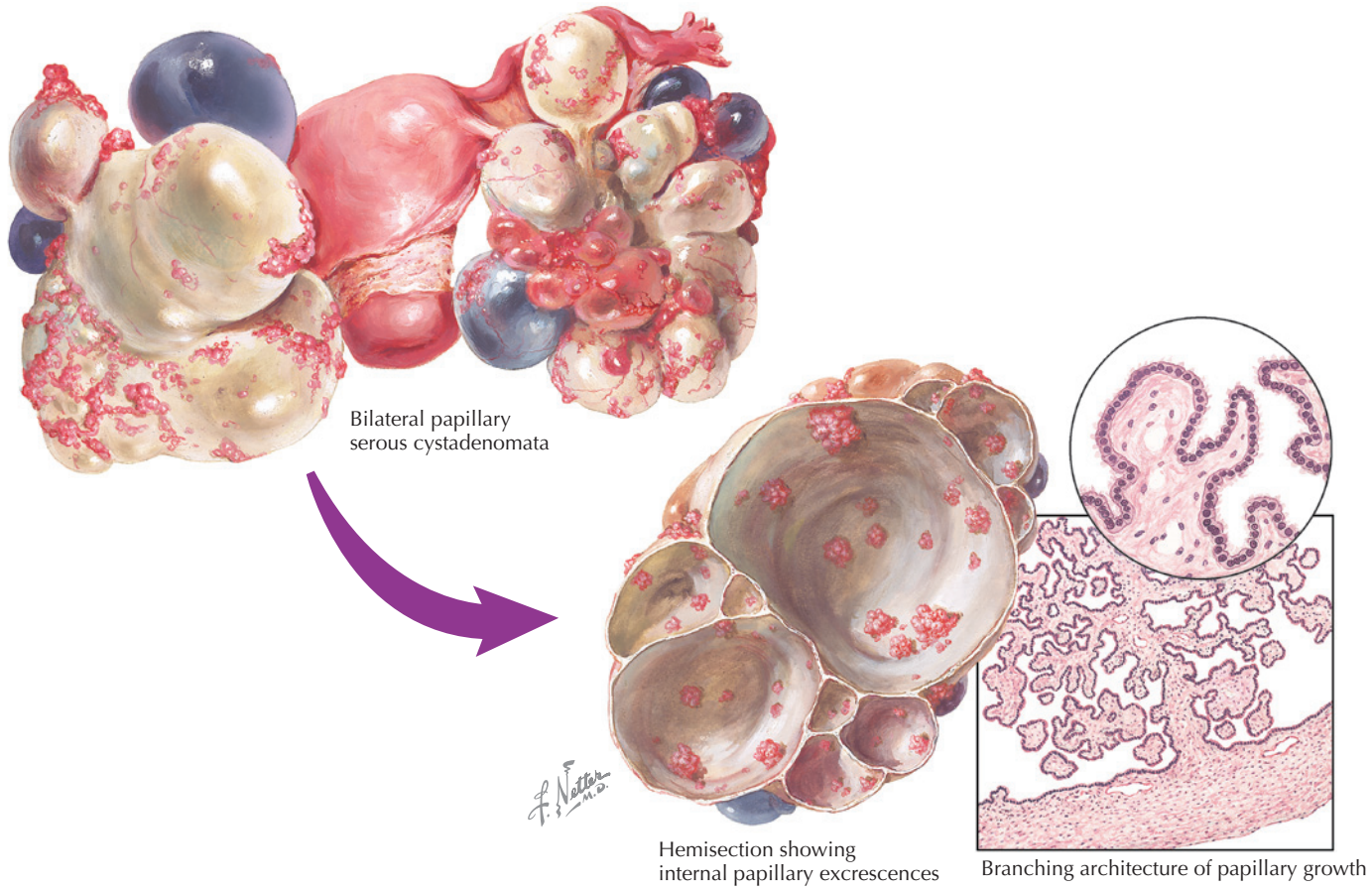


Figure 157.1 Serous cystadenomata

malignant processes (lung, breast, and pancreas) may also cause an increase in CA-125 levels that are higher than normal.

Imaging: No imaging indicated.

Special Tests: A frozen-section histologic evaluation should be considered for any ovarian mass that appears suspicious for malignancy.

Diagnostic Tests: History, physical examination, and imaging. Final diagnosis is established by histologic evaluation.

Pathologic Findings

Serous tumors are more likely to be found with poorer differentiation and discovered late in the disease process. Papillary surface carcinomas of the ovary are most likely to be serous in type. The diagnosis is made on the basis of the histologic analysis of the cyst wall and not on the characteristics of the cyst fluid.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, supportive therapy based on symptoms.

Specific Measures: Generally require surgical exploration and extirpation. In benign disease or tumors of borderline malignant potential the uterus and other ovary may be generally spared. Adjunctive chemotherapy (platinum-based and paclitaxel [Taxol]) or radiotherapy is often included based on the location and stage of the disease.

Diet: No specific dietary changes indicated, except those imposed by an advanced disease.

Activity: No restriction, except that imposed by advanced disease.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP096 (Cancer of the Ovary) and AP075 (Ovarian Cysts).

Drug(s) of Choice

None, except as adjunctive or symptomatic therapy.

Precautions: Alkylating agents are associated with an increased risk of future leukemia (10% by 8 years after therapy).

FOLLOW-UP

Patient Monitoring: Careful follow-up for recurrent pelvic disease or enlargement of the remaining ovary (if any). This is generally performed by pelvic examination, augmented with ultrasonography in selected patients. In patients suspected of having a recurrent disease and other selected patients, second-look surgery may be desirable to assess progress and discover occult disease.

Prevention/Avoidance: None.

Possible Complications: Torsion, hemorrhage, progression, and spread of malignant disease.

Expected Outcome: Generally good for benign tumors; the prognosis for malignant tumors is based on stage. Overall, the 5-year survival rate for malignant serous carcinomas is approximately 20%. Of malignant serous carcinomas, 75% are at an advanced stage at the time of diagnosis.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.

ICD-10-CM Codes: Specific to cell type and location.

REFERENCES

LEVEL II

Flynn MK, Niloff JM. Outpatient minilaparotomy for ovarian cysts. *J Reprod Med*. 1999;44:399.

Gates MA, Rosner BA, Hecht JL, et al. Risk factors for epithelial ovarian cancer by histologic subtype. *Am J Epidemiol*. 2010;171:45.

Rufford BD, Jacobs IJ, Menon U. Feasibility of screening for ovarian cancer using symptoms as selection criteria. *BJOG*. 2007;114:59.

Timmerman D, Testa AC, Bourne T, et al., International Ovarian Tumor Analysis Group. Logistic regression model to distinguish between the benign and malignant adnexal mass before surgery: a multicenter study by the International Ovarian Tumor Analysis Group. *J Clin Oncol*. 2005;23:8794.

Vuento MH, Pirhonen JP, Makinen JI, et al. Evaluation of ovarian findings in asymptomatic postmenopausal women with color Doppler ultrasound. *Cancer*. 1995;76:1214.

LEVEL III

Acs G. Serous and mucinous borderline (low malignant potential) tumors of the ovary. *Am J Clin Pathol*. 2005;123:S13.

American College of Obstetricians and Gynecologists. Management of adnexal masses. ACOG Practice Bulletin 83. *Obstet Gynecol*. 2007;110: 201.

Fromm GL, Gershenson DM, Silva EG. Papillary serous carcinoma of the peritoneum. *Obstet Gynecol*. 1990;75:89.

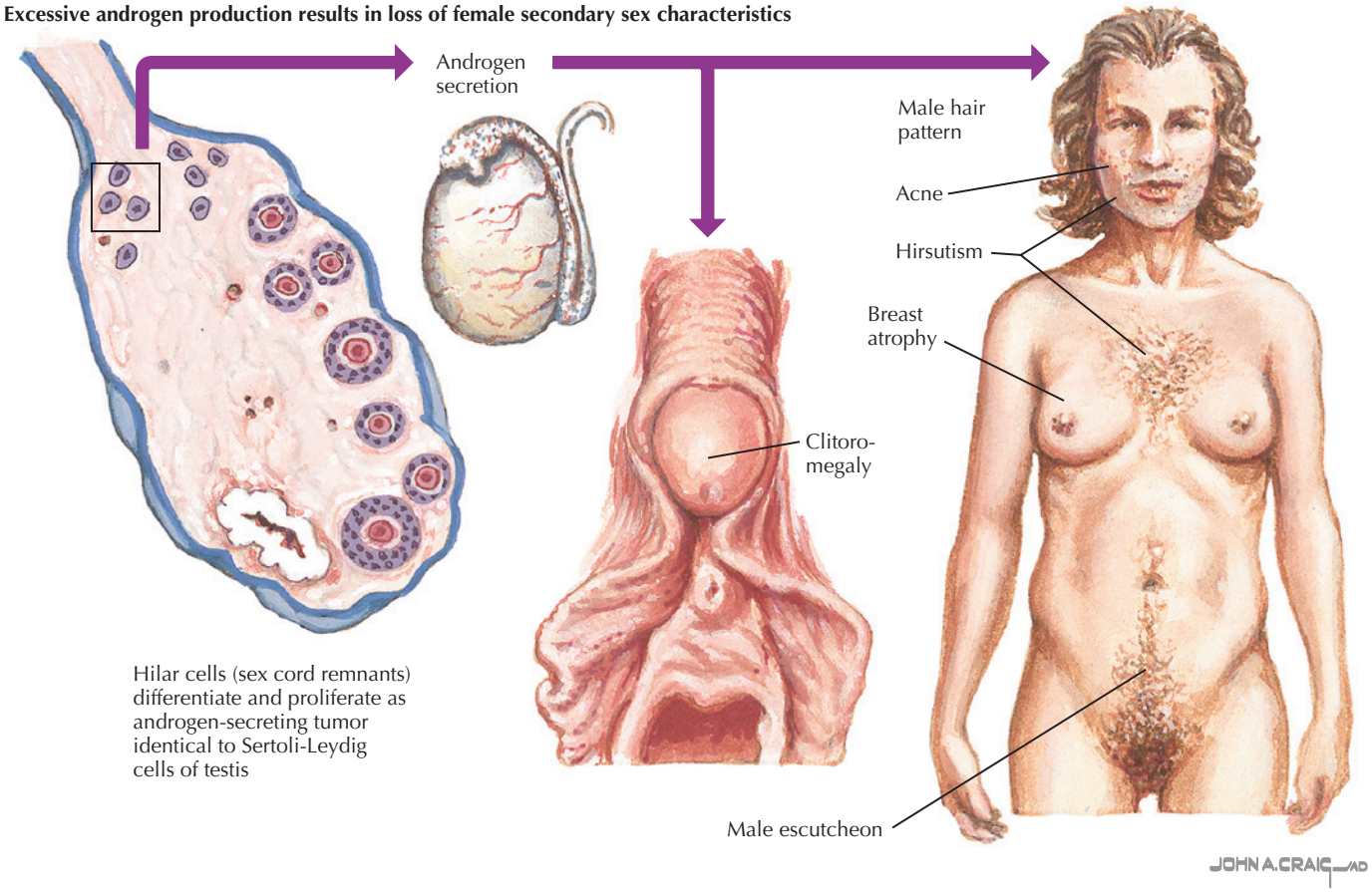


Figure 158.1 Excessive androgen production

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, supportive therapy based on symptoms.

Specific Measures: Surgical exploration and resection. Young patients with stage IA disease may be treated with unilateral salpingo-oophorectomy. Undifferentiated tumors or advanced-stage disease require a more aggressive surgical resection and may be treated with adjunctive chemotherapy (vincristine, actinomycin D, and cyclophosphamide) or radiotherapy.

Diet: No specific dietary changes indicated.

Activity: No restriction.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP096 (Cancer of the Ovary) and AP075 (Ovarian Cysts).

Drug(s) of Choice

- Vincristine 1.5 mg/m^2 IV weekly for 12 weeks; actinomycin D and cyclophosphamide (0.5 mg of actinomycin D + 5–7 mg/kg/day of cyclophosphamide) IV daily for 5 days every 4 weeks. Adjunctive or symptomatic therapy as required.
- Precautions—alkylating agents are associated with an increased risk for future leukemia (10% by 8 years after therapy).

FOLLOW-UP

Patient Monitoring: Careful follow-up and normal health maintenance.

Prevention/Avoidance: None.

Possible Complications: Disease progression or spread (<20%). Recurrence occurs within 1 year in two-thirds of patients with advanced-stage disease.

Expected Outcome: These tumors behave as low-grade malignancies and have 5-year survival rates of 70%–90%. Survival is poor for higher stage and poorly differentiated tumors. Menses may be anticipated to return approximately 4 weeks after tumor removal. Excessive hair often regresses but does not disappear; clitoral enlargement and voice changes (if present) are unlikely to reverse.

MISCELLANEOUS

Pregnancy Considerations: Pregnancy unlikely in the presence of these tumors. No direct effect on the pregnancy, if they coexist. Hormonal effects on the fetus could be postulated, but tumors with significant hormonal function generally preclude pregnancy.

ICD-10-CM Codes: Based on the location and tumor character.

REFERENCES

LEVEL II

Al-Agha OM, Huwait HF, Chow C, et al. FOXL2 is a sensitive and specific marker for sex cord-stromal tumors of the ovary. *Am J Surg Pathol*. 2011;35:484.

Gheorghisan-Galateanu A, Fica S, Terzea DC, et al. Sertoli-Leydig cell tumor—A rare androgen secreting ovarian tumor in postmenopausal women. Case report and review of literature. *J Cell Mol Med*. 2003;7:461.

Gui T, Cao D, Shen K, et al. A clinicopathological analysis of 40 cases of ovarian Sertoli-Leydig cell tumors. *Gynecol Oncol*. 2012;127:384.

Heravi-Moussavi A, Anglesio MS, Cheng SW, et al. Recurrent somatic DICER1 mutations in nonepithelial ovarian cancers. *N Engl J Med*. 2012;366:234.

Tomlinson MW, Treadwell MC, Deppe G. Platinum based chemotherapy to treat recurrent Sertoli-Leydig cell ovarian carcinoma during pregnancy. *Eur J Gynaecol Oncol*. 1997;18:44.

LEVEL III

American College of Obstetricians and Gynecologists. Management of adnexal masses. ACOG Practice Bulletin 83. *Obstet Gynecol*. 2007;110:201.

Borer JG, Tan PE, Diamond DA. The spectrum of Sertoli cell tumors in children. *Urol Clin North Am*. 2000;27:529.

Roth LM. Recent advances in the pathology and classification of ovarian sex cord-stromal tumors. *Int J Gynecol Pathol*. 2006;25:199.

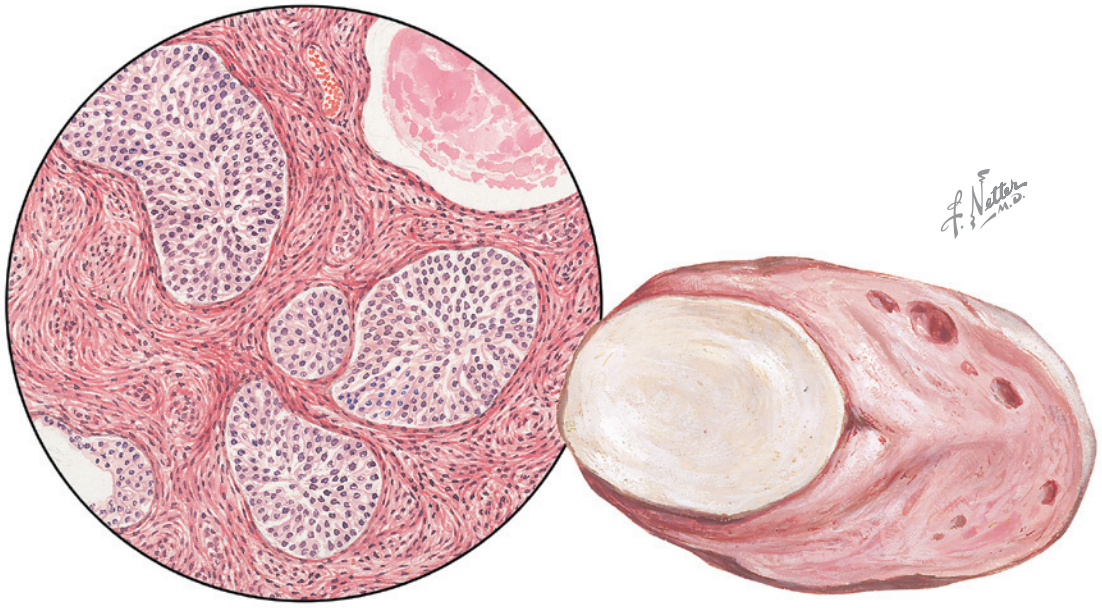


Figure 159.1 Brenner tumor

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: The rare malignant form has a poor prognosis despite surgical therapy. Chemotherapy has not been proved to be effective.
Expected Outcome: Most Brenner tumors are benign and are cured by simple oophorectomy.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: D27.9 (Benign neoplasm of unspecified ovary), D39.10 (Neoplasm of uncertain behavior of unspecified ovary), C56.9 (Malignant neoplasm of unspecified ovary).

REFERENCES

LEVEL II

Arnogiannaki N, Grigoriadis C, Zygouris D, et al. Proliferative Brenner tumor of the ovary. Clinicopathological study of two cases and review of the literature. *Eur J Gynaecol Oncol*. 2011;32:576.

Rufford BD, Jacobs IJ, Menon U. Feasibility of screening for ovarian cancer using symptoms as selection criteria. *BJOG*. 2007;114:59.

Silverberg SG. Brenner tumor of the ovary. A clinicopathologic study of 60 tumors in 54 women. *Cancer*. 1971;28:588.

Yang DM, Heller DS, Ganesh V, et al. Brenner tumor of the ovary with extensive stromal luteinization presenting in pregnancy: report of a case and review of the literature. *J Matern Fetal Neonatal Med*. 2002;12:281.

Yoshida M, Obayashi C, Tachibana M, et al. Coexisting Brenner tumor and struma ovarii in the right ovary: case report and review of the literature. *Pathol Int*. 2004;54:793.

LEVEL III

American College of Obstetricians and Gynecologists. Management of adnexal masses. ACOG Practice Bulletin No. 83. *Obstet Gynecol*. 2007; 110:201.

Austin RM, Norris HJ. Malignant Brenner tumors and transitional cell carcinoma of the ovary. *Int J Gynecol Pathol*. 1987;6:29.

Chen KT, Hoffmann KD. Malignant Brenner tumor of the ovary. *J Surg Oncol*. 1988;39:260.

Hampton HL, Huffman HT, Meeks GR. Extraovarian Brenner tumor. *Obstet Gynecol*. 1992;79:844.

Miles PA, Norris HJ. Proliferative and malignant Brenner tumors of the ovary. *Cancer*. 1972;30:174.

Roth LM, Dallenbach-Hellweg G, Czernobilsky B. Ovarian Brenner tumors. I: Metaplastic, proliferating and of low malignant potential. *Cancer*. 1985;56:582.

SECTION X

Breast Diseases and Conditions

This page intentionally left blank

ACCESSORY NIPPLES (POLYTHELIA)

160

INTRODUCTION

Description: Accessory nipples are supernumerary nipples found along defined developmental lines known as the "milk lines."
Prevalence: Observed in 0.22%–2.5% of women and in up to 5%–6% of Asian women.
Predominant Age: Congenital in origin.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Developmental abnormality.
Risk Factors: More common in males and in African Americans.

SIGNS AND SYMPTOMS

- Asymptomatic
- Most commonly found below a normal left breast. It is more common to have one or more extra nipples (polythelia) than to have true accessory breasts (polymastia).

DIAGNOSTIC APPROACH

Differential Diagnosis

- Skin papilloma
- Nevis

Associated Conditions: Polymastia, duplicate renal arteries.

WORKUP AND EVALUATION

Laboratory: No evaluation indicated.
Imaging: No imaging indicated. Some advocate ultrasonographic evaluation of the renal system for possible associated anomalies.
Special Tests: None indicated.
Diagnostic Procedures: History, physical examination.

Pathologic Findings

None.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and reassurance.
Specific Measures: None.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance, instruction on monthly breast self-examination. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP026 (Benign Breast Problems and Conditions).

Drug(s) of Choice

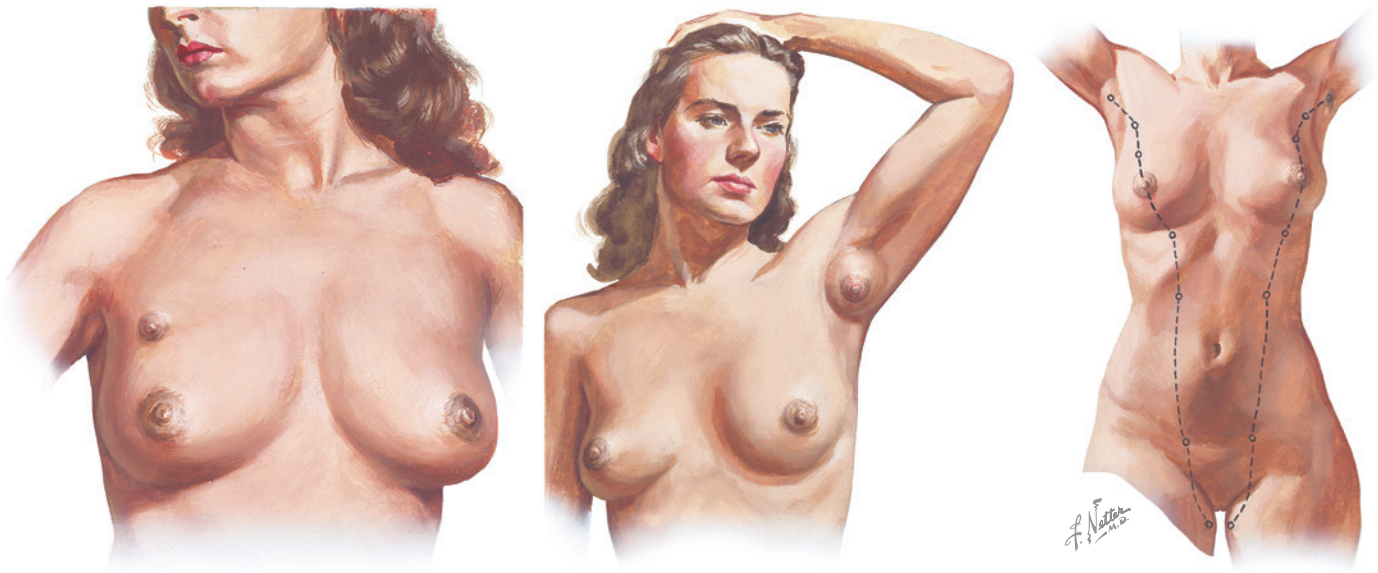
None

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, although occasionally accessory nipples undergo hypertrophy during pregnancy.
ICD-10-CM Codes: Q83.3 (Accessory nipple) and Q83.1 (Accessory breast).



Polythelia | Polymastia | The milk lines

Figure 160.1 Accessory nipples (polythelia and polymastia)

REFERENCES

LEVEL II

Brown J, Schwartz RA. Supernumerary nipples and renal malformations: a family study. *J Cutan Med Surg*. 2004;8:170.

Casey HD, Chasan PE, Chick LR. Familial polythelia without associated anomalies. *Ann Plast Surg*. 1996;36:101.

Ferrara P, Giorgio V, Vitelli O, et al. Polythelia: still a marker of urinary tract anomalies in children? *Scand J Urol Nephrol*. 2009;43:47.

LEVEL III

Greydanus DE, Matytsina L, Gains M. Breast disorders in children and adolescents. *Prim Care*. 2006;33:455.

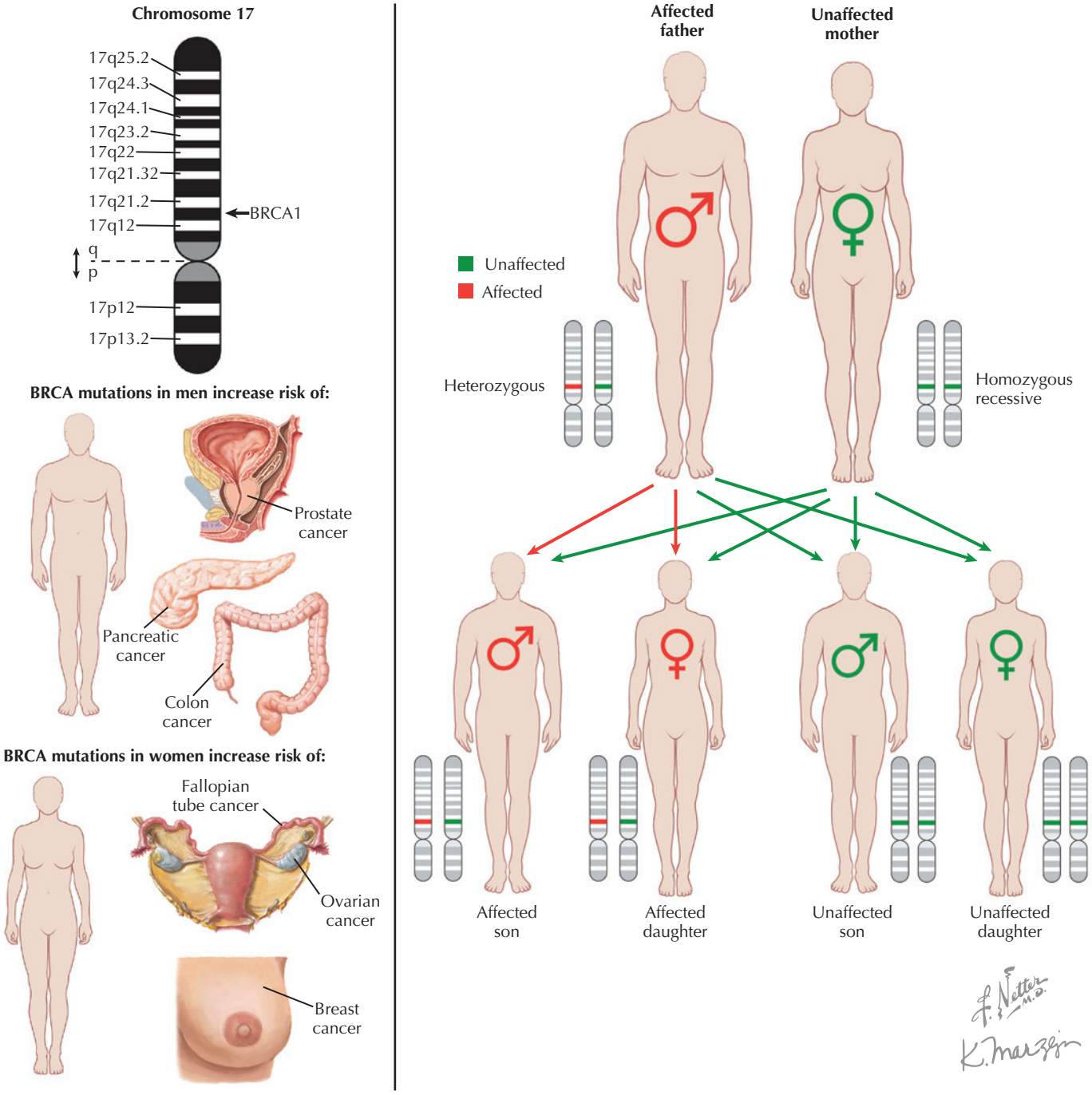


Figure 161.1 *BRCA1* and *BRCA2* mutations

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP026 (Benign Breast Problems and Conditions) and AP178 (Mammography and Other Screening Tests for Breast Problems).

IMPLEMENTATION

Special Considerations: While *BRCA* testing is covered by many health insurance policies, the long-term impact on insurance coverage in the face of a positive test is unclear.

REFERENCES

LEVEL II

Couch FJ, Hart SN, Sharma P, et al. Inherited mutations in 17 breast cancer susceptibility genes among a large triple-negative breast cancer cohort unselected for family history of breast cancer. *J Clin Oncol*. 2015;33:304.

Gabai-Kapara E, Lahad A, Kaufman B, et al. Population-based screening for breast and ovarian cancer risk due to BRCA1 and BRCA2. *Proc Natl Acad Sci USA*. 2014;111:14205.

King MC, Marks JH, Mandell JB, et al. Breast and ovarian cancer risks due to inherited mutations in BRCA1 and BRCA2. *Science*. 2003;302:643.

Molina-Montes E, Pérez-Nevot B, Pollán M, et al. Cumulative risk of second primary contralateral breast cancer in BRCA1/BRCA2 mutation carriers with a first breast cancer: a systematic review and meta-analysis. *Breast*. 2014;23:721.

Malone KE, Daling JR, Doody DR, et al. Prevalence and predictors of BRCA1 and BRCA2 mutations in a population-based study of breast cancer in white and black American women ages 35 to 64 years. *Cancer Res*. 2006;66:8297.

Manchanda R, Legood R, Burnell M, et al. Cost-effectiveness of population screening for BRCA mutations in Ashkenazi Jewish women compared with family history-based testing. *J Natl Cancer Inst*. 2015;107:380.

Mersch J, Jackson MA, Park M, et al. Cancers associated with BRCA1 and BRCA2 mutations other than breast and ovarian. *Cancer*. 2015;121:269.

Phillips KA, Milne RL, Rookus MA, et al. Tamoxifen and risk of contralateral breast cancer for BRCA1 and BRCA2 mutation carriers. *J Clin Oncol*. 2013;31:3091.

Rebbeck TR, Mitra N, Wan F, et al. Association of type and location of BRCA1 and BRCA2 mutations with risk of breast and ovarian cancer. *JAMA*. 2015;313:1347.

LEVEL III

American College of Obstetricians and Gynecologists. Breast cancer screening. Practice Bulletin No. 122. *Obstet Gynecol*. 2011;118:372.

American College of Obstetricians and Gynecologists. Hereditary breast and ovarian cancer syndrome. ACOG Practice Bulletin No. 103. *Obstet Gynecol*. 2009;113:957.

Couch FJ, Nathanson KL, Offit K. Two decades after BRCA: setting paradigms in personalized cancer care and prevention. *Science*. 2014;343:1466.

Hampel H, Bennett RL, Buchanan A, et al. A practice guideline from the American College of Medical Genetics and Genomics and the National Society of Genetic Counselors: referral indications for cancer predisposition assessment. *Genet Med*. 2015;17:70.

Yoshida K, Miki Y. Role of BRCA1 and BRCA2 as regulators of DNA repair, transcription, and cell cycle in response to DNA damage. *Cancer Sci*. 2004;95:866.

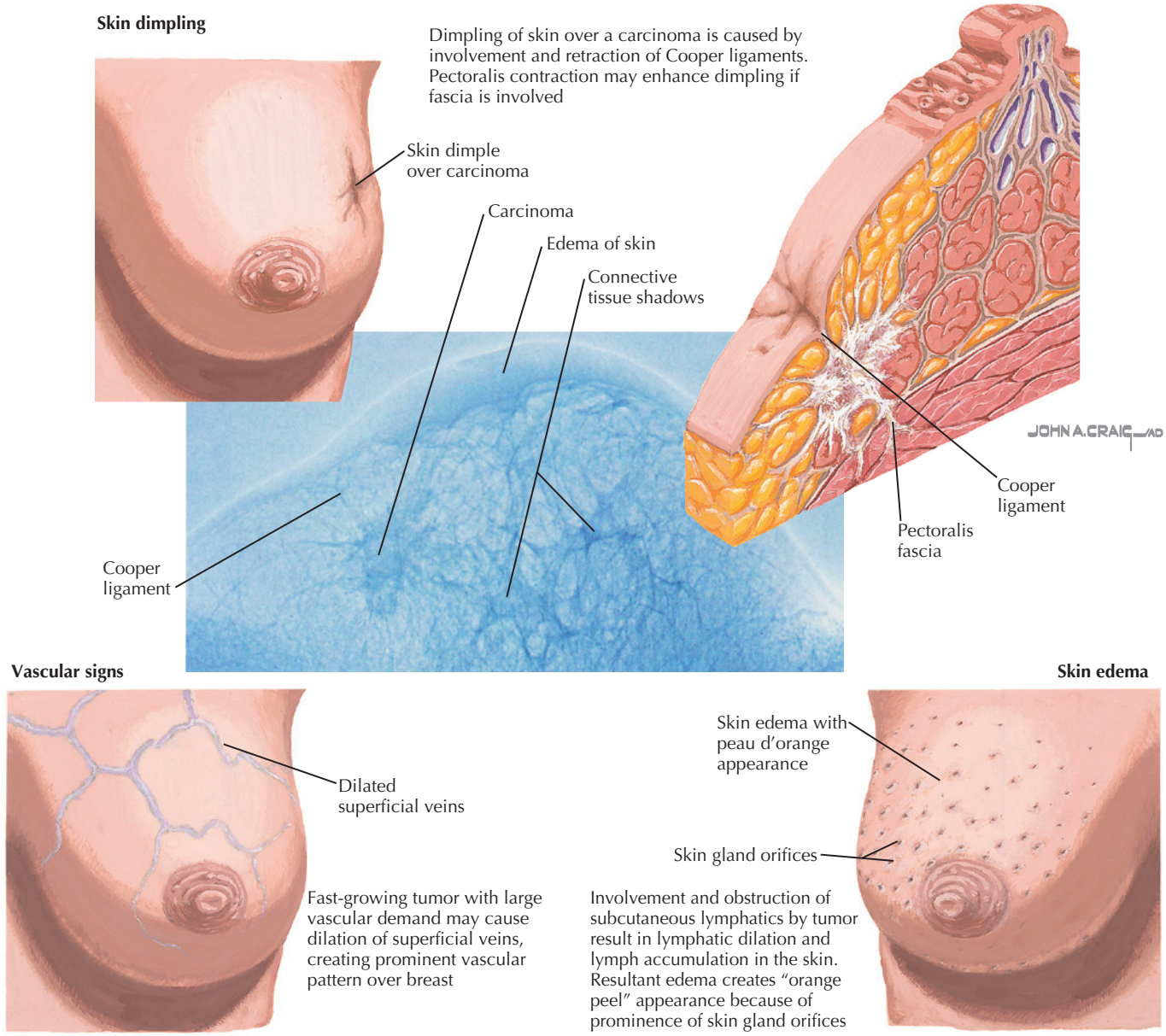


Figure 162.1 Clinical signs of breast cancer

Digital radiography, thermal imaging (thermography), transillumination, mammoscintigraphy, ductography, and other techniques have not been shown to be comparable or superior to mammography.

Special Tests: Fine needle aspiration (FNA) of cells from a breast mass can provide histologic confirmation of malignancy and help direct definitive therapy.

Diagnostic Procedures: Up to one-fourth of all breast cancers are detected during routine examination. Excisional biopsy with or without radiographic control provides the only definitive diagnosis.

Pathologic Findings

Based on the cell type. At the time of diagnosis, 70% of breast cancers show signs of invasion. Ductal carcinoma is the most common type, accounting for 65%–85% of cases.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and staging. If surgical treatment affects pectoralis muscles, physical or occupational therapy may speed return to function.

Specific Measures: Surgical resection with or without adjunctive chemotherapy.

Diet: Moderation in alcohol use recommended to reduce risk.

Activity: No restriction.

Patient Education: Instruction on breast self-awareness. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP026 (Benign Breast Problems and Conditions) and AP178 (Mammography and Other Screening Tests for Breast Problems).

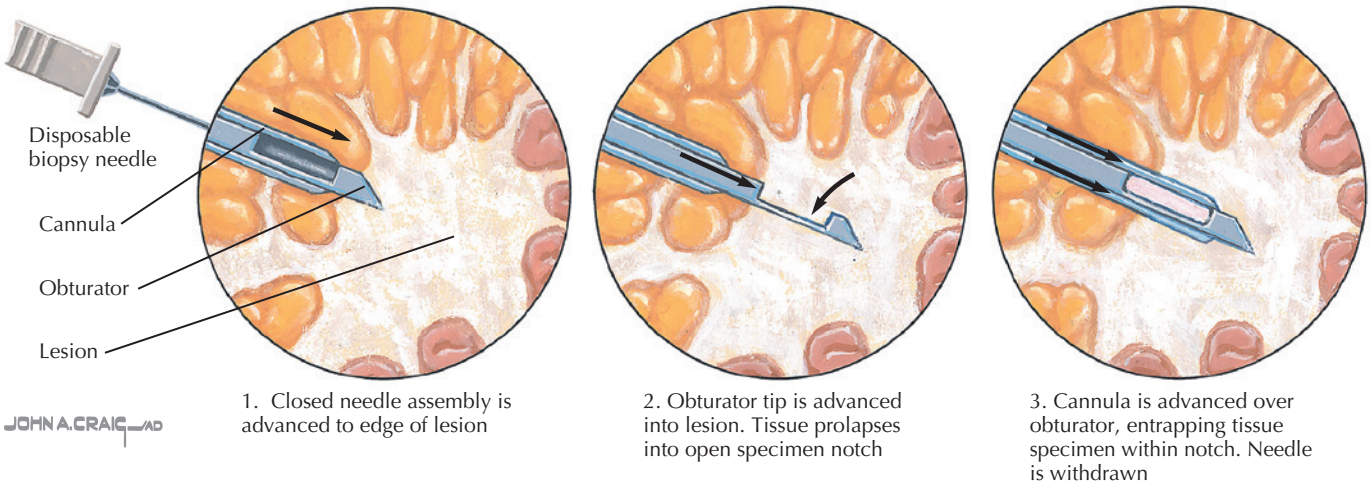


Figure 162.2 Needle breast biopsy

Drug(s) of Choice

Adjuvant chemotherapy considered for stages I and II disease (cyclophosphamide, methotrexate, fluorouracil, anthracyclines, or taxanes, single agent or in combination).

Contraindications: Strict guidelines for hepatic and renal function before chemotherapy.

Precautions: Increased risk of infection during chemotherapy.

ALTERNATIVE THERAPY

- Adjunctive or palliative radiotherapy is often recommended.
- Agents that suppress cancer growth by interfering with surface proteins that are involved with cell division are under evaluation. An example of this approach is trastuzumab (Herceptin), approved by the U.S. Food and Drug Administration (FDA) in 1998.
- A number of studies suggest that estrogen therapy (for other indications) can actually reduce the mortality of patients who are being treated for breast cancer.

FOLLOW-UP

Patient Monitoring: Watch for recurrence (60% risk in first 5 years).

Prevention/Avoidance: Reduced dietary fat and alcohol have been suggested, but effects are unproven. Routine mammography. Prophylactic use of tamoxifen was approved by the FDA late in 1998 for use in women at a high risk. Selective estrogen receptor modulators (SERMs) have been effective in reducing the incidence of recurrence or the development of primary lesions for those at increased risk. Prophylactic mastectomy for those at highest risk should be considered.

Possible Complications: Postoperative lymphedema, seroma, wound infections, or breakdown. Chemotherapy is associated with nausea, vomiting, alopecia, leukopenia, stomatitis, fatigue, and infections. Tamoxifen therapy is associated with hot flashes, menstrual irregularity, endometrial hyperplasia, or carcinoma. Radiotherapy associated with fibrosis and scarring, brachial neuropathy, and pulmonary fibrosis.

Expected Outcome: Breast cancer disseminates through vascular and lymphatic routes, in addition to direct infiltration. There is also a growing trend to view breast cancer as a multifocal disease. Breast cancer survival depends less on a cell type than it does on the size of the tumor and stage of disease. The 10-year survival rate is based on the stage: stage I, 95%; stage II, 40%; stage III, 15%; and stage IV (metastatic), 0%. More than 60% of cases are stage I at diagnosis.

MISCELLANEOUS

Pregnancy Considerations: Breast cancer occurs infrequently during pregnancy, accounting for only 2%–3% of all cancers: no effect on pregnancy. Pregnancy often results in a delay in diagnosis but does not appreciably affect clinical course.

ICD-10-CM Codes: C50.XXX (subcodes based upon gender and location), Z17.0 [Estrogen receptor positive status (ER+)], and Z17.1 [Estrogen receptor negative status (ER–)].

REFERENCES

LEVEL I

Pritchard KI, Shepherd LE, O'Malley FP, et al., National Cancer Institute of Canada Clinical Trials Group. HER2 and responsiveness of breast cancer to adjuvant chemotherapy. *N Engl J Med*. 2006;354:2103.

Turnbull L, Brown S, Harvey I, et al. Comparative effectiveness of MRI in breast cancer (COMICE) trial: a randomised controlled trial. *Lancet*. 2010;375:563.

Vogel VG, Costantino JP, Wickerham DL, et al., National Surgical Adjuvant Breast and Bowel Project (NSABP). Effects of tamoxifen vs raloxifene on the risk of developing invasive breast cancer and other disease outcomes: the NSABP Study of Tamoxifen and Raloxifene (STAR) P-2 trial. *JAMA*. 2006;295:2727.

LEVEL II

Collaborative Group on Hormonal Factors in Breast Cancer. Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58,209 women with breast cancer and 101,986 women without the disease. *Lancet*. 2001;358:1389.

Coombs NJ, Taylor R, Wilcken N, et al. Hormone replacement therapy and breast cancer: estimate of risk. *BMJ*. 2005;331:347.

Lacey JV Jr, Greene MH, Buys SS, et al. Ovarian cancer screening in women with a family history of breast or ovarian cancer. *Obstet Gynecol*. 2006;108:1176.

Punglia RS, Morrow M, Winer EP, et al. Local therapy and survival in breast cancer. *N Engl J Med*. 2007;356:2399.

LEVEL III

American College of Obstetricians and Gynecologists. Hereditary breast and ovarian cancer syndrome. ACOG Practice Bulletin No. 103. *Obstet Gynecol*. 2009;113:957.

American College of Obstetricians and Gynecologists. Breast cancer screening. Practice Bulletin No. 122. *Obstet Gynecol*. 2011;118:372.

American College of Obstetricians and Gynecologists. Management of gynecologic issues in women with breast cancer. Practice Bulletin No. 126. *Obstet Gyencol*. 2012;119:666.

American College of Obstetricians and Gynecologists. Management of women with dense breasts diagnosed by mammography. Committee Opinion No. 625. *Obstet Gynecol*. 2015;125:750.

Barthelmes L, Davidson LA, Gaffney C, et al. Pregnancy and breast cancer. *BMJ*. 2005;330:1375.

Loibl S, von Minckwitz G, Gwyn K, et al. Breast carcinoma during pregnancy. International recommendations from an expert meeting. *Cancer*. 2006;106:237.

Saslow D, Boetes C, Burke W, et al., American Cancer Society Breast Cancer Advisory Group. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA Cancer J Clin*. 2007;57:75.

Smith I, Chua S. Medical treatment of early breast cancer. III: Chemotherapy. *BMJ*. 2006;332:161.

Smith I, Chua S. Medical treatment of early breast cancer. IV: Neoadjuvant treatment. *BMJ*. 2006;332:223.

in diameter. Small cysts have a firm character and are filled with clear fluid, giving the cyst a bluish cast. Larger cysts may have a brown color resulting from hemorrhage into the cyst. Inspissated secretions or milk may form a cystic dilation of ducts (galactocele, ductal ectasia) that may be palpable as a cystic mass. Variable degrees of fibrosis and inflammation may be seen in the surrounding stroma. Leakage of cyst fluid into the surrounding tissue induces an inflammatory response that may alter physical findings and imitate cancer. The microscopic findings associated with breast cysts depend on the pathophysiologic changes involved.

Strategies: The diagnosis and management of cystic masses in the breast are based on history, physical examination, and aspiration, with the occasional adjunctive use of mammography and ultrasonography (ultrasonography is useful in differentiating solid and cystic breast masses but it has limited spatial resolution and cannot be used to differentiate benign and malignant tissues). Needle aspiration with a 22- to 25-gauge needle may be both diagnostic and therapeutic. If the cyst disappears completely and does not re-form by 1-month follow-up examination, no further therapy is required. Fluid aspirated from patients with fibrocystic changes is customarily straw colored. Fluid that is dark brown or green occurs in cysts that have been present for a long time, but it is innocuous. Bloody fluid requires further evaluation. Cytologic evaluation of the fluid obtained is of little value. After aspiration of a cyst, the patient should be rechecked in 2–4 weeks. Recurrence of the cyst or the presence of a palpable mass should prompt additional evaluation, such as fine needle aspiration (FNA) or open biopsy.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP026 (Benign Breast Problems and Conditions) and AP076 (Mammography and Other Screening Tests for Breast Problems).

IMPLEMENTATION

Special Considerations: Whereas most cystic changes in the breast are not associated with malignancy and are not premalignant, the presence of atypia in any of the cellular components requires special attention because this is associated with an approximately five-fold increased risk for malignancy. In women older than 35 years, mammography before aspiration should be considered because of the increased incidence of malignancy. Once aspiration has been attempted, mammography should be delayed by several weeks because of artifactual changes induced by the manipulation, making mammograms difficult to interpret. Patients with a history of multiple cysts or diffuse fibrocystic change or a strong family history of breast disease should have close follow-up, including mammography, to delve for other occult lesions.

REFERENCES

LEVEL II

Dixon JM, McDonald C, Elton RA, et al. Risk of breast cancer in women with palpable breast cysts: a prospective study. Edinburgh Breast Group. *Lancet*. 1999;353:1742.

Tea MK, Grimm C, Heinz-Peer G, et al. The predictive value of suspicious sonographic characteristics in atypical cyst-like breast lesions. *Breast*. 2011;20:165.

LEVEL III

American College of Obstetricians and Gynecologists. Breast cancer screening. Practice Bulletin No. 122. *Obstet Gynecol*. 2011;118:372.

American College of Obstetricians and Gynecologists. Diagnosis and management of benign breast disorders. Practice Bulletin No. 164. *Obstet Gynecol*. 2016;127:e141.

Lucas JH, Cone DL. Breast cyst aspiration. *Am Fam Physician*. 2003;68:1983.

Santen RJ, Mansel R. Benign breast disorders. *N Engl J Med*. 2005;353:275.

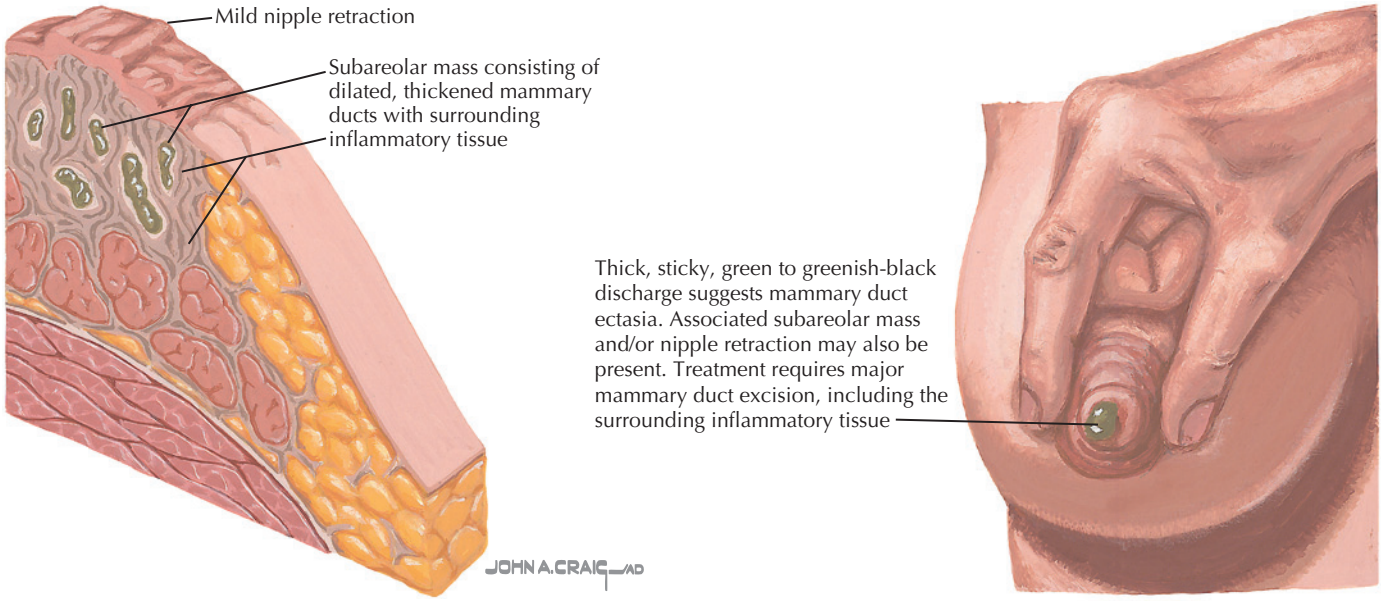


Figure 164.1 Breast (mammary) duct ectasia

Imaging: No imaging indicated.
Special Tests: None indicated.
Diagnostic Procedures: History and physical examination. Biopsy confirms the diagnosis. The characteristic discharge may be easily demonstrated during clinical examination.

Pathologic Findings

Dilation of the ducts with the atrophy of the epithelium, thickening of the underlying wall, and inflammatory reaction in the duct wall and surrounding tissue.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and reassurance.
Specific Measures: No further therapy is needed unless warranted by the patient's symptoms. When therapy is required, surgical excision with a cone of tissue surrounding the duct is curative.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Instruction on monthly breast self-examination. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP026 (Benign Breast Problems and Conditions) and AP076 (Mammography and Other Screening Tests for Breast Problems).

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: Secondary infection and abscess formation.
Expected Outcome: Gradual resolution of symptoms, complete resolution with surgical excision.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: N60.49 (Mammary duct ectasia of unspecified breast).

REFERENCES

LEVEL II

Duchesne N, Skolnik S, Bilmer S. Ultrasound appearance of chronic mammary duct ectasia. *Can Assoc Radiol J*. 2005;56:297.
Dixon JM, McDonald C, Elton RA, et al. Risk of breast cancer in women with palpable breast cysts: a prospective study. Edinburgh breast group. *Lancet*. 1999;353:1742.
Rahal RM, de Freitas-Junior R, Paulinelli RR. Risk factors for duct ectasia. *Breast J*. 2005;11:262.
Richards T, Hunt A, Courtney S, et al. Nipple discharge: a sign of breast cancer? *Ann R Coll Surg Engl*. 2007;89:124.

LEVEL III

American College of Obstetricians and Gynecologists. Diagnosis and management of benign breast disorders. Practice Bulletin No. 164. *Obstet Gynecol*. 2016;127:e141.
Dixon JM. Periductal mastitis/duct ectasia. *World J Surg*. 1989;13:715.
Greydanus DE, Matytsina L, Gains M. Breast disorders in children and adolescents. *Prim Care*. 2006;33:455.
Hamed H, Fentiman IS. Benign breast disease. *Int J Clin Pract*. 2001;55:461.
Hughes LE. Non-lactational inflammation and duct ectasia. *Br Med Bull*. 1991;47:272.
Santen RJ, Mansel R. Benign breast disorders. *N Engl J Med*. 2005;353:275.

165 BREAST FAT NECROSIS

INTRODUCTION

Description: Trauma to the breast may result in necrosis of fatty tissues, leading to an ill-defined mass that can mimic cancer.
Prevalence: Uncommon.
Predominant Age: Reproductive age.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Fat necrosis is most often the result of trauma, although the causative event cannot be identified (or recalled) in approximately one-half of patients. May also follow surgical intervention in the breast such as biopsy or augmentation.
Risk Factors: Trauma to the breast.

SIGNS AND SYMPTOMS

- Solitary, irregular, ill-defined, tender mass that is easily confused with cancer
- Skin retraction sometimes present
- Fine, stippled calcification and stellate or infiltrative fibrosis often seen on mammograms

DIAGNOSTIC APPROACH

Differential Diagnosis

- Cancer
- Lipoma

Associated Conditions: Mastalgia.

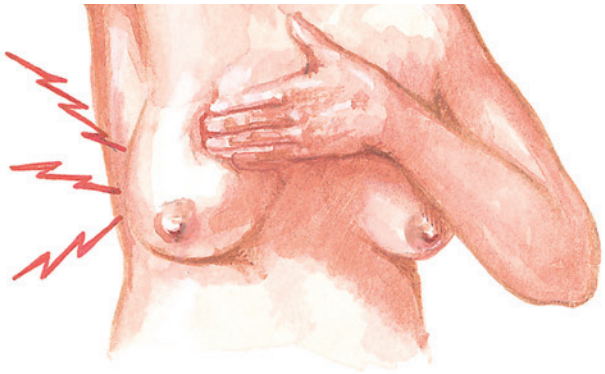
Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: Mammography findings mimic cancer.
Special Tests: Open biopsy often required to establish the diagnosis.
Diagnostic Procedures: Even with a history of trauma, the commonality of findings between fat necrosis and cancer with physical examination, mammography, and ultrasonography generally mandates further evaluation and biopsy.

Pathologic Findings

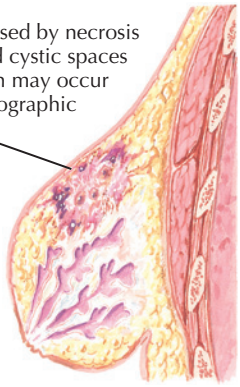
Diffuse changes consistent with necrosis and fibrosis of tissue. Hemorrhage and cystic spaces ("oil cysts") are common. Calcification of older lesions may occur. Histiocytic foam cells with mitotic figures and pleomorphism are common.

Fat Necrosis of Breast

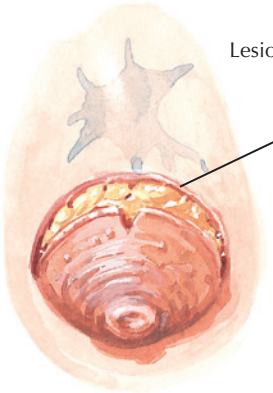


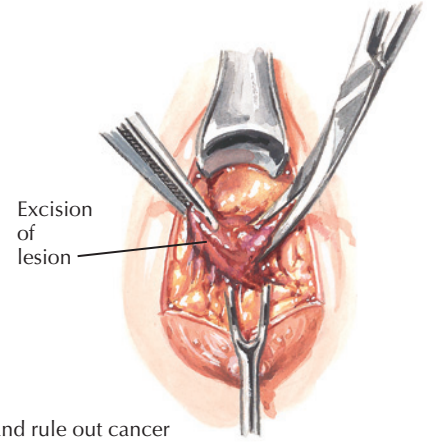
Trauma to breast may result in fat necrosis, an ill-defined, irregular, tender mass that may be confused with cancer both clinically and radiographically

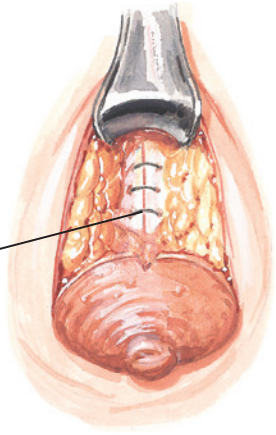
Diffuse changes in breast caused by necrosis and fibrosis. Hemorrhage and cystic spaces are common and calcification may occur in older lesions, giving a radiographic picture similar to cancer



Excision Biopsy for Fat Necrosis







Excisional biopsy indicated to confirm diagnosis and rule out cancer

Figure 165.1 Appearance and excision biopsy for fat necrosis

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation.
Specific Measures: Excisional biopsy.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Instruction on monthly breast self-examination. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP026 (Benign Breast Problems and Conditions) and AP076 (Mammography and Other Screening Tests for Breast Problems).

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Normal health maintenance, periodic mammography screening.
Prevention/Avoidance: Minimize the risk of trauma.
Possible Complications: An occult malignancy may be missed if a mass is presumed to be fat necrosis without tissue evaluation for confirmation.
Expected Outcome: With excision, complete resolution.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: N64.1 (Fat necrosis of breast).

REFERENCES

LEVEL II

Chala LF, de Barros N, de Camargo Moraes P, et al. Fat necrosis of the breast: mammographic, sonographic, computed tomography, and magnetic resonance imaging findings. *Curr Probl Diagn Radiol*. 2004; 33:106.

Gatta G, Pinto A, Romano S, et al. Clinical, mammographic and ultrasonographic features of blunt breast trauma. *Eur J Radiol*. 2006;59:327.

LEVEL III

American College of Obstetricians and Gynecologists. Diagnosis and management of benign breast disorders. Practice Bulletin No. 164. *Obstet Gynecol*. 2016;127:e141.

Amin AL, Purdy AC, Mattingly JD, et al. Benign breast disease. *Surg Clin North Am*. 2013;93:299.

Atasoy MM, Oren NC, Ilica AT, et al. Sonography of fat necrosis of the breast: correlation with mammography and MR imaging. *J Clin Ultrasound*. 2013;41:415.

Guray M, Sahin AA. Benign breast diseases: classification, diagnosis, and management. *Oncologist*. 2006;11:435.

Santen RJ, Mansel R. Benign breast disorders. *N Engl J Med*. 2005;353:275.

Soo MS, Kornguth PJ, Hertzberg BS. Fat necrosis in the breast: sonographic features. *Radiology*. 1998;206:261.

Tan PH, Lai LM, Carrington EV, et al. Fat necrosis of the breast—A review. *Breast*. 2006;15:313.

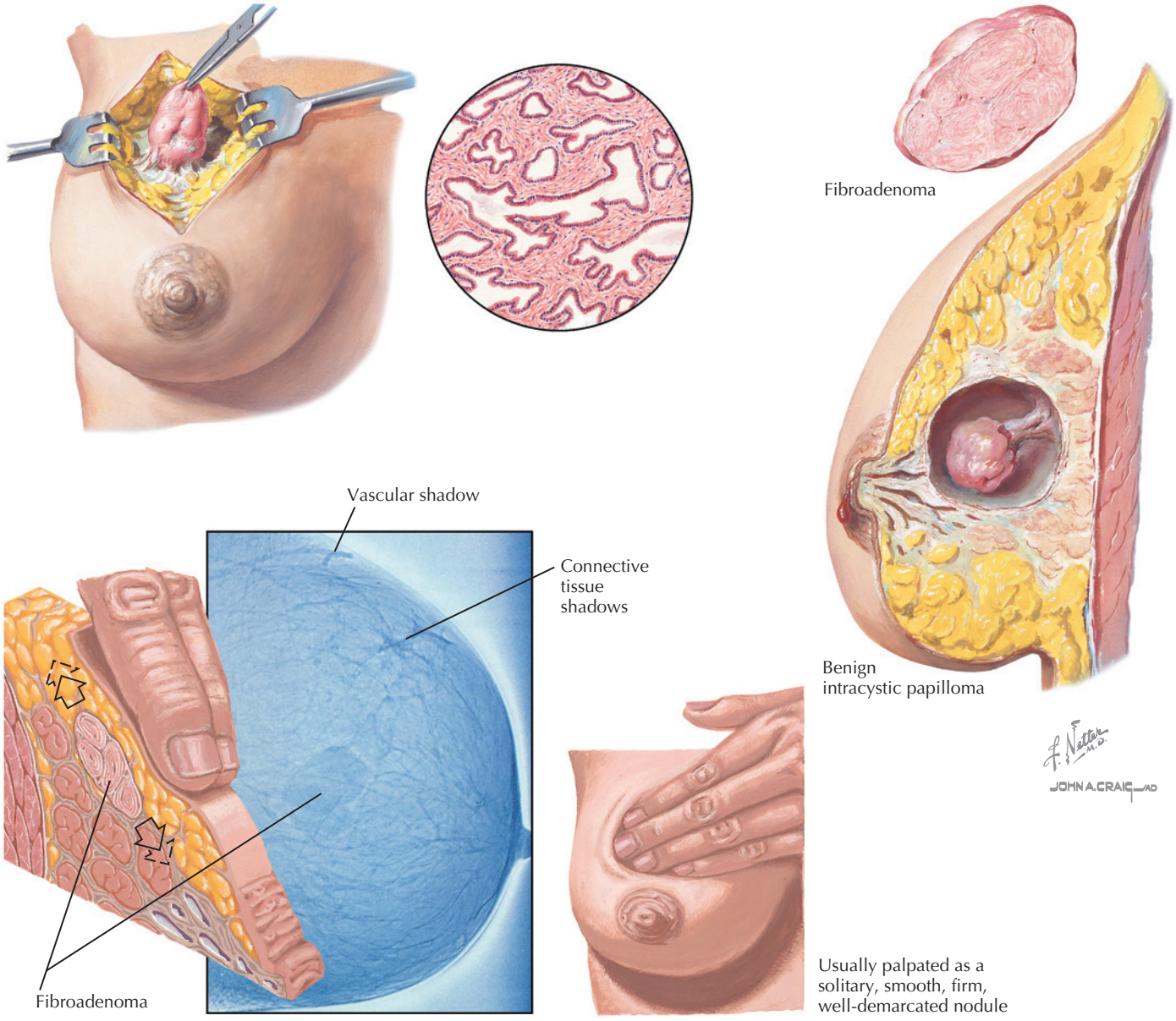


Figure 166.1 Fibroadenoma

tan–white fibrous whorls bulge from the surface when cut. Hemorrhagic infarcts are common.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Reassurance and observation may be sufficient for small, asymptomatic tumors.
Specific Measures: Primary therapy is surgical excision, although tamoxifen and danazol have been used. Cyroablation therapy has been evaluated but has not displaced surgery as the primary management.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Instruction on monthly breast self-examination. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP026 (Benign Breast Problems and Conditions) and AP076 (Mammography and Other Screening Tests for Breast Problems).

Drug(s) of Choice

Danazol sodium 50–200 mg PO twice a day (therapy should start during menstruation or pregnancy must be ruled out). Side effects may be significant and recurrence is likely after therapy is discontinued.
Contraindications: Danazol sodium is contraindicated in pregnancy (category X drug). It may also worsen epilepsy, migraine headaches, and cardiac or renal function.
Interactions: Danazol sodium may prolong prothrombin time in patients receiving warfarin.

Alternative Drugs

Tamoxifen has been advocated in some studies.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.

Prevention/Avoidance: Combination oral contraceptives provide some protection when taken for more than 1 year.

Possible Complications: Hemorrhage into the fibroadenoma may result in pain or rapid growth of the tumor. Malignant change is extremely rare.

Expected Outcome: Lesions tend to grow over time without treatment. Prognosis with surgical excision is excellent and fair with medical therapy. After menopause, fibroadenomas tend to regress and become hyalinized, but they may remain unchanged or grow with estrogen replacement therapy.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy; fibroadenomas may grow rapidly during pregnancy.

ICD-10-CM Codes: D24.1 (Benign neoplasm of right breast).

REFERENCES

LEVEL II

El-Wakeel H, Umpleby HC. Systematic review of fibroadenoma as a risk factor for breast cancer. *Breast*. 2003;12:302.

Harvey JA, Nicholson BT, Lorusso AP, et al. Short-term follow-up of palpable breast lesions with benign imaging features: evaluation of 375 lesions in 320 women. *AJR Am J Roentgenol*. 2009;193:1723.

Littrup PJ, Freeman-Gibb L, Andea A, et al. Cryotherapy for breast fibroadenomas. *Radiology*. 2005;234:63.

Nurko J, Mabry CD, Whitworth P, et al. Interim results from the FibroAdenoma Cryoablation Treatment Registry. *Am J Surg*. 2005;190:647.

LEVEL III

American College of Obstetricians and Gynecologists. Diagnosis and management of benign breast disorders. Practice Bulletin No. 164. *Obstet Gynecol*. 2016;127:e141.

Greydanus DE, Matytsina L, Gains M. Breast disorders in children and adolescents. *Prim Care*. 2006;33:455.

Hamed H, Fentiman IS. Benign breast disease. *Int J Clin Pract*. 2001;55:461.

Houssami N, Cheung MN, Dixon JM. Fibroadenoma of the breast. *Med J Aust*. 2001;174:185.

Hung WK, Ying M, Chan CM, et al. Minimally invasive technology in the management of breast disease. *Breast Cancer*. 2009;16:23.

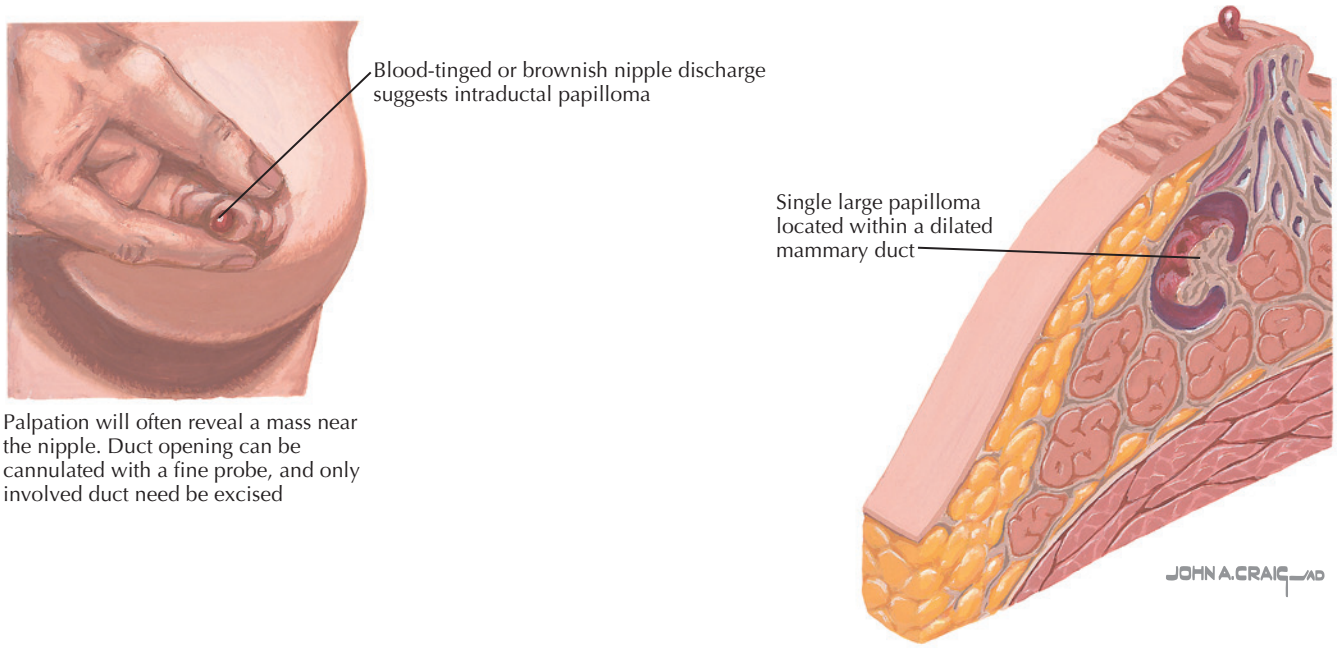


Figure 167.1 Solitary intraductal papilloma

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP026 (Benign Breast Problems and Conditions) and AP076 (Mammography and Other Screening Tests for Breast Problems).

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: Atypia of the epithelial cells may occur and increases the possibility of malignancy.
Expected Outcome: Surgical excision is both diagnostic and therapeutic.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: N64.9 (Disorder of breast, unspecified).

REFERENCES

LEVEL II

Lewis JT, Hartmann LC, Vierkant RA, et al. An analysis of breast cancer risk in women with single, multiple, and atypical papilloma. *Am J Surg Pathol*. 2006;30:665.

Nakhlis F, Ahmadiyeh N, Lester S, et al. Papilloma on core biopsy: excision vs. observation. *Ann Surg Oncol*. 2015;22:1479.

Wen X, Cheng W. Nonmalignant breast papillary lesions at core-needle biopsy: a meta-analysis of underestimation and influencing factors. *Ann Surg Oncol*. 2013;20:94.

LEVEL III

American College of Obstetricians and Gynecologists. Diagnosis and management of benign breast disorders. Practice Bulletin No. 164. *Obstet Gynecol*. 2016;127:e141.

Ganesan S, Karthik G, Joshi M, et al. Ultrasound spectrum in intraductal papillary neoplasms of breast. *Br J Radiol*. 2006;79:843.

Santen RJ, Mansel R. Benign breast disorders. *N Engl J Med*. 2005;353:275.

Valdes EK, Feldman SM, Boolbol SK. Papillary lesions: a review of the literature. *Ann Surg Oncol*. 2007;14:1009.

Vargas HI, Romero L, Chlebowski RT. Management of bloody nipple discharge. *Curr Treat Options Oncol*. 2002;3:157.

FIBROCYSTIC BREAST CHANGE

168

INTRODUCTION

Description: Fibrocystic breast changes are characterized by stromal and ductal proliferation that results in cyst formation, diffuse thickening, cyclic pain, and tenderness. The term fibrocystic change encompasses a multitude of different processes and older terms, including fibrocystic disease. It is the most common of all benign breast conditions, accounting for its linguistic demotion to "change" from the designation "disease."

Prevalence: 60%–75% of all women.

Predominant Age: Most common between the age of 30–50 years; 10% of women younger than 21 years.

Genetics: A family history of fibrocystic change is often present, but causality is difficult to establish.

ETIOLOGY AND PATHOGENESIS

Causes: The cause or causes of fibrocystic change are unknown, but it is postulated to arise from an exaggerated response to hormones. A role for progesterone has been suggested based on the common occurrence of premenstrual breast swelling and tenderness. Other proposed sources for fibrocystic changes are altered ratios of estrogen and progesterone or an increased rate of prolactin secretion, but none of these has been conclusively established.

Risk Factors: Methylxanthine intake has been proposed, but hard data are lacking. There is no evidence that oral contraceptive use increases the risk of these changes.

SIGNS AND SYMPTOMS

- Asymptomatic (50%)
- Cyclic, diffuse, bilateral pain and engorgement, with worst symptoms that occur just before menses (the pain associated with fibrocystic change often radiates to the shoulders or upper arms)
- Multiple cysts and nodules intermixed with scattered bilateral nodularity typical, ropy thickening, especially in the upper outer quadrants of the breast

DIAGNOSTIC APPROACH

Differential Diagnosis

- Fibroadenoma
- Carcinoma
- Fat necrosis
- Lipoma
- Radiculitis (Tietze syndrome)

Associated Conditions: Mastalgia, fibroadenoma.

Workup and Evaluation

Laboratory: No evaluation indicated.

Imaging: Mammography may be used to assist with the diagnosis or to provide a baseline, but it is not necessary for diagnosis. Mammography is more difficult in the younger women who predominantly have these complaints. Ultrasonography may be of more help when imaging is deemed necessary.

Special Tests: If the patient has a cystic breast mass, needle aspiration with a 22- to 25-gauge needle may be both diagnostic and therapeutic. Fine needle aspiration (FNA) or core biopsy may be required if malignancy is suspected.

Diagnostic Procedures: Diagnosis is based on symptoms and physical findings rather than histologic evaluation.

Pathologic Findings

Fibrocystic changes appear in three steps: (1) proliferation of stroma, especially in the upper outer quadrants of the breast, is observed; (2) proliferation of the ducts and alveolar cells occurs, adenosis ensues, and cysts are formed; and (3) larger cysts are found and pain generally decreases. Proliferative changes may be extensive (although usually benign) in any of the involved tissues.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Mechanical support (a well-fitting brassiere worn day and night), analgesics, and reassurance. Cold compresses or ice may be helpful for acute exacerbations.

Specific Measures: Diuretics (such as spironolactone or hydrochlorothiazide administered before menstrual periods) and nonsteroidal antiinflammatory agents (NSAIDs) for analgesia may be necessary. For severe symptoms, danazol, bromocriptine, tamoxifen, or gonadotropin-releasing hormone (GnRH) agonists may be required. Patients with intractable pain refractory to medical management may rarely require subcutaneous mastectomy.

Diet: Reduction in methylxanthine intake is often beneficial. Premenstrual restriction of salt or fluids is useful for selected patients. The roles of vitamins A and E are unknown.

Activity: No restriction. To reduce discomfort, good breast support is recommended during vigorous activity.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AAP026 (Benign Breast Problems and Conditions) and AP076 (Mammography and Other Screening Tests for Breast Problems).

Drug(s) of Choice

- Combination oral contraceptives (70%–90% chance of success).
- Spironolactone 50 mg PO twice a day given 7–10 days before periods.
- Danazol sodium 200 mg PO twice a day (therapy should start during menstruation or pregnancy must be ruled out). Side effects may be significant, and recurrence is likely to occur after therapy is discontinued.
- Bromocriptine 2.5 mg PO daily (with food) may be increased after 3–7 days if required.

Contraindications: Spironolactone is contraindicated in the presence of anuria, renal insufficiency, or hyperkalemia. Danazol sodium is contraindicated in pregnancy (category X). It may also worsen epilepsy, migraine headaches, and cardiac or renal function. Bromocriptine is contraindicated in patients with uncontrolled hypertension or in those known to be sensitive to ergot alkaloids.

Precautions: Diuretics must be used with care to avoid fluid and electrolyte disturbances. Bromocriptine may cause hypotension during the first several days of therapy. Care should also be used with patients who have compromised hepatic or renal function.

Interactions: Spironolactone enhances the action of other diuretics and increases digoxin levels. Danazol sodium may prolong prothrombin time in patients being administered warfarin.

Alternative Drugs

- Hydrochlorothiazide 25 mg PO at bedtime for 7–10 days before menses. Gonadotropin-releasing hormone agonists (Lupron) 3.75 mg IM monthly for no more than 6 months.
- Tamoxifen has had a response rate of up to 70% in some trials.

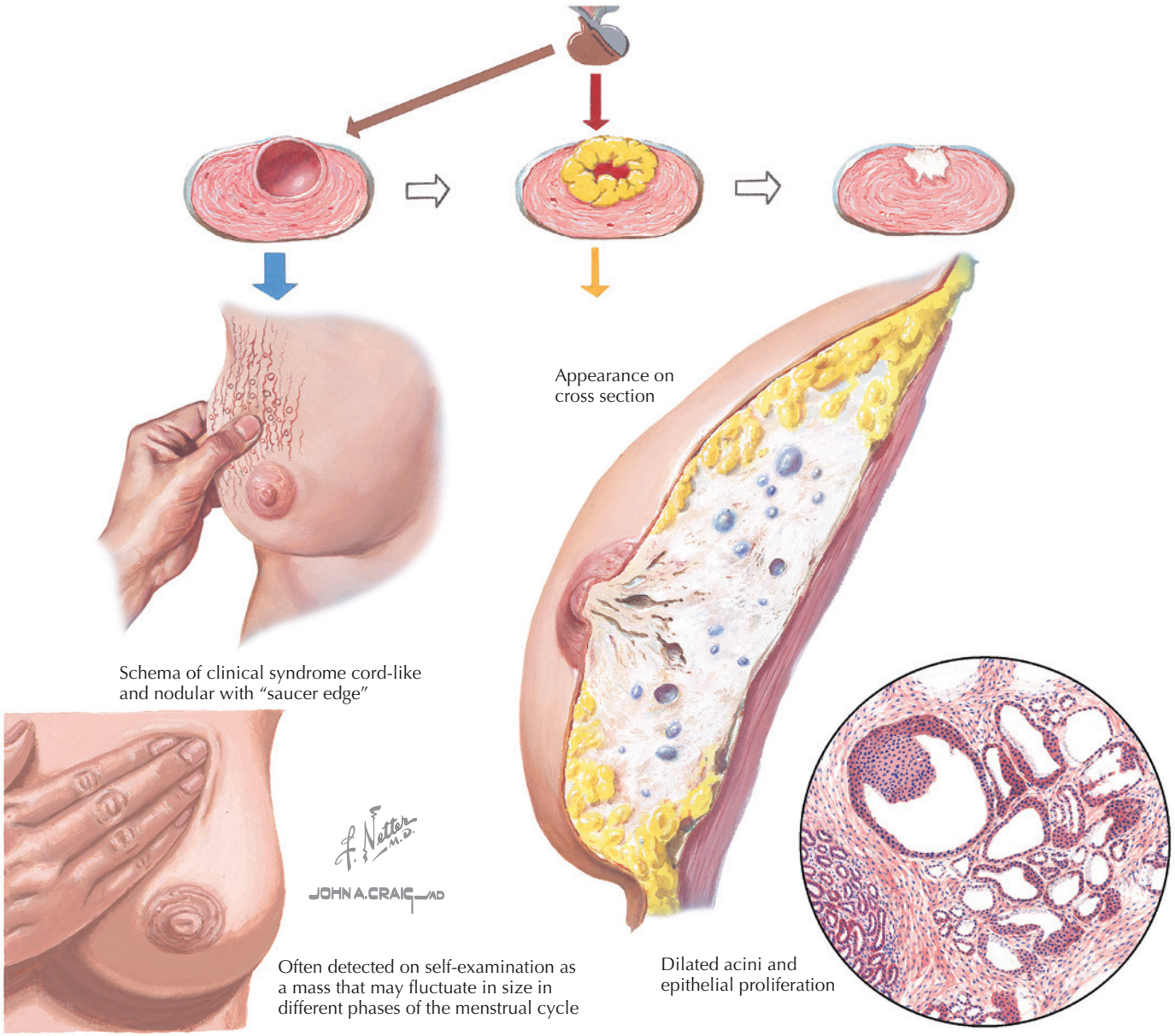


Figure 168.1 Fibrocystic breast change

FOLLOW-UP

Patient Monitoring: Patients with mastalgia but no dominant mass may be safely rechecked at a different portion of the next menstrual cycle. After aspiration of a cyst (yielding clear fluid and complete loss of the mass), the patient should be rechecked in 2–4 weeks. Recurrence of the cyst or the presence of a palpable mass should prompt additional evaluations, such as FNA or open biopsy.

Prevention/Avoidance: None.

Possible Complications: When atypia is found in hyperplastic ducts or apocrine cells, there is a five-fold increase in the risk of developing carcinoma in the future.

Expected Outcome: Symptomatic relief can be generally achieved with a combination of diet changes, analgesics, and specific medications. The underlying pathologic features remain unchanged or progress.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy. The hormonal changes of pregnancy may worsen symptoms.

ICD-10-CM Codes: N60.19 (Diffuse cystic mastopathy of unspecified breast).

REFERENCES

LEVEL I

Ernster VL, Mason L, Goodson WH 3rd, et al. Effects of caffeine-free diet on benign breast disease: a randomized trial. *Surgery*. 1982;91:263.

Oksa S, Luukkaala T, Mäenpää J. Toremifene for premenstrual mastalgia: a randomised, placebo-controlled crossover study. *BJOG*. 2006;113:713.

LEVEL II

Boyle CA, Berkowitz GS, LiVolsi VA, et al. Caffeine consumption and fibrocystic breast disease: a case control epidemiologic study. *J Natl Cancer Inst*. 1984;72:1015.

LEVEL III

American College of Obstetricians and Gynecologists. Diagnosis and management of benign breast disorders. Practice Bulletin No. 164. *Obstet Gynecol*. 2016;127:e141.

Drukker BH. Fibrocystic change of the breast. *Clin Obstet Gynecol*. 1994; 37:903.

Drukker BH, deMendonca WC: Fibrocystic change and fibrocystic disease of the breast. *Obstet Gynecol Clin North Am*. 1987;14:685.

Ferguson CM, Powel RW. Breast masses in young women. *Arch Surg*. 1989;124:1338.

Maddox PR, Mansel RE. Management of breast pain and nodularity. *World J Surg*. 1989;13:699.

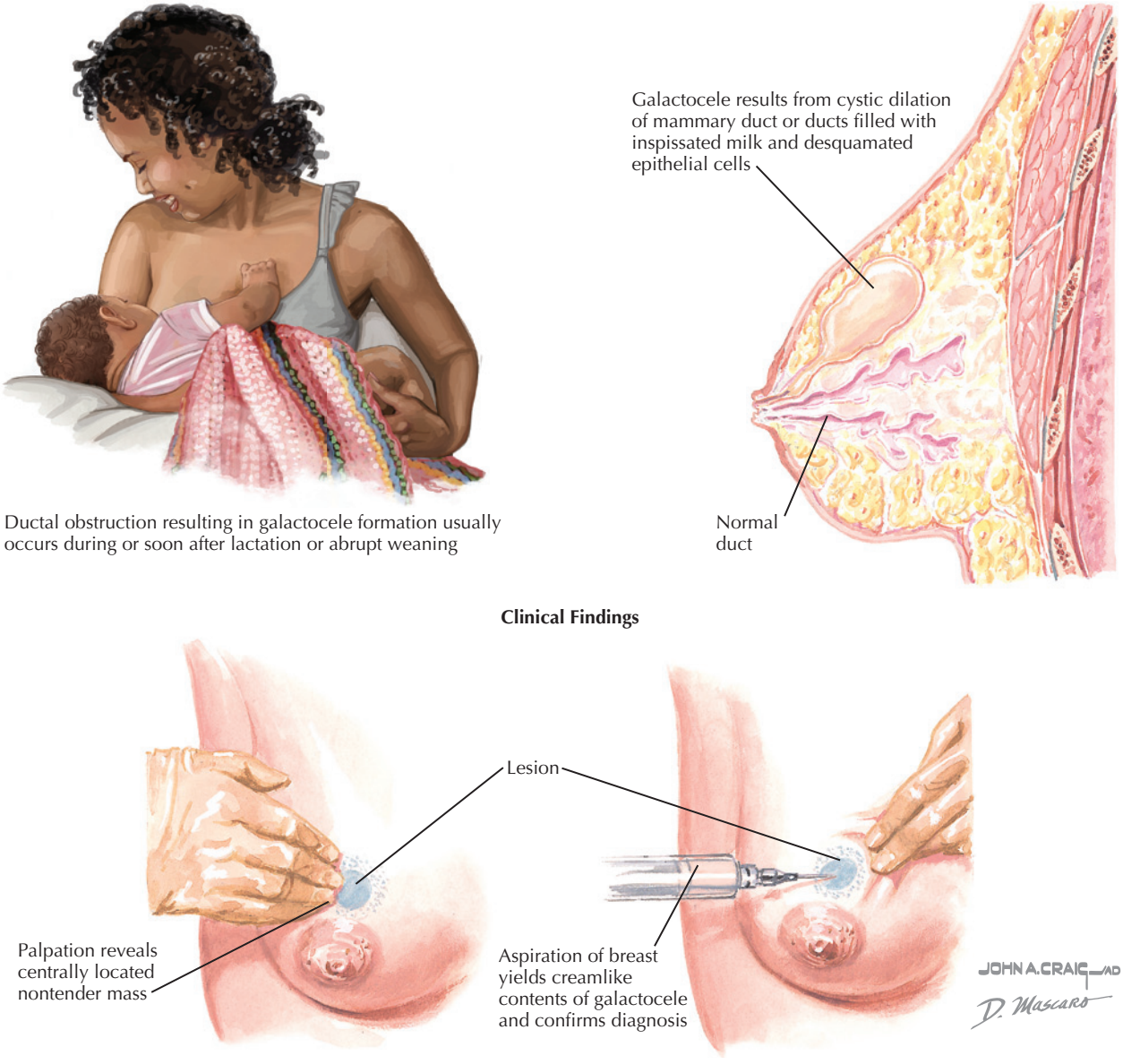


Figure 169.1 Clinical findings in galactocele

REFERENCES

LEVEL III

Santen RJ, Mansel R. Benign breast disorders. *N Engl J Med*. 2005;353:275.
Winker JM. Galactocele of the breast. *Am J Surg*. 1964;108:357.

GALACTORRHEA

170

INTRODUCTION

Description: Spontaneous, bilateral nipple discharge (milky fluid only).
Prevalence: Uncommon, but reports vary from 1% to 30%, depending on the population studied.
Predominant Age: Reproductive age.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Pituitary adenoma (generally <10 mm), disruptions in thyroid or prolactin hormone levels, pharmacologic (most often those drugs that affect dopamine or serotonin), second-generation H_2 receptor antagonists (cimetidine), autoimmune disease (sarcoid, lupus), Cushing's disease, herpes zoster, chest wall/breast stimulation or irritation, physiologic changes during pregnancy or after childbirth and/or breastfeeding, specific foods (licorice). No cause may be found in up to 50% of cases.
Risk Factors: None known.

SIGNS AND SYMPTOMS

- Bilateral, spontaneous, milky discharge from both breasts
- Often symptoms of underlying pathologic condition (eg, hypothyroidism, Cushing disease, or pituitary enlargement)
- Amenorrhea common

DIAGNOSTIC APPROACH

Differential Diagnosis

- Pregnancy
- Breast cancer
- Chronic nipple stimulation
- Hypothyroidism
- Sarcoidosis
- Lupus
- Cirrhosis or hepatic disease

Associated Conditions: One-third of patients with an elevated prolactin level experience amenorrhea or infertility. Prolonged amenorrhea is associated with an increased risk for osteoporosis, vaginal and genital atrophic changes, dyspareunia, and libidinal dysfunction.

Workup and Evaluation

Laboratory: Pregnancy should always be considered if menses are absent. There is a poor correlation between serum prolactin levels and the size or detectability of a pituitary lesion. Thyroxine (T_4) and thyroid-stimulating hormone (TSH) levels based on the differential diagnosis being considered.
Imaging: Computed tomography or magnetic resonance imaging (preferred) are frequently indicated.
Special Tests: Testing of visual fields may be indicated.

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: When prolactin levels are low and a coned-down view of the sella turcica is normal, observation alone may be sufficient. If observation is chosen, periodic re-evaluation is required to check for the emergence of slow-growing tumors.
Specific Measures: Treatment with bromocriptine is recommended for patients who desire pregnancy or for those with distressing degrees of galactorrhea or to suppress intermediate-sized pituitary tumors. Rapidly growing tumors, tumors that are large at the time of discovery, or those that do not respond to bromocriptine therapy may require surgical therapy.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance, discuss treatment options. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP136 (Evaluating Infertility) and AP029 (Breastfeeding Your Baby).

Drug(s) of Choice

If the prolactin level is elevated—dopamine agonists (cabergoline 0.25–1.0 mg orally once or twice per week).
Contraindications: Uncontrolled hypertension, pregnancy.
Precautions: With medical therapy—nausea, orthostatic hypotension, drowsiness, syncope, hypertension, or seizures.
Interactions: Medical therapy may interact with phenothiazines or butyrophenones.

Alternative Drugs

- Bromocriptine (Parlodel) 2.5 mg daily, gradually increased to three times a day.
- Estrogen supplementation may be indicated in selected patients.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. If a pituitary adenoma is present, periodic assessment of visual fields should be considered.
Prevention/Avoidance: None.
Possible Complications: Visual field loss; symptoms may return after medication is discontinued.
Expected Outcome: Generally good depending on cause. Prolactin levels should be measured every 6–12 months, and visual fields should be reassessed yearly. The pituitary should be re-evaluated every 2–5 years, based on initial diagnosis.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, although pregnancy may cause pituitary adenomas to grow rapidly.
ICD-10-CM Codes: N64.3 (Galactorrhea not associated with childbirth), N91.2 (Amenorrhea, unspecified), and O92.6 (Galactorrhea) should only be used in conjunction with pregnancy and breastfeeding.

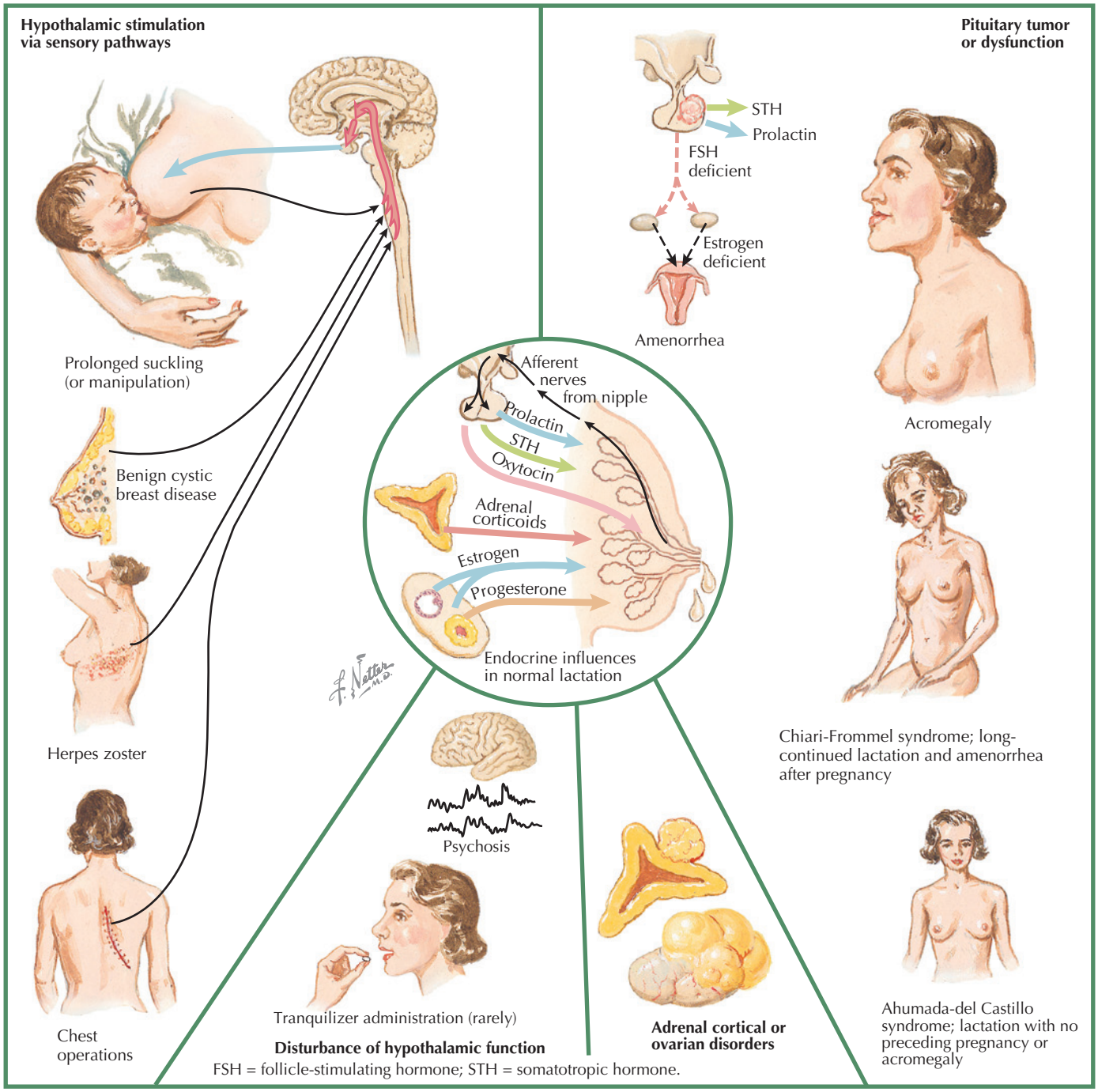


Figure 170.1 Pathogenesis of galactorrhea

REFERENCES

LEVEL II

Basile FV, Basile AR. Diagnosis and management of galactorrhea after breast augmentation. *Plast Reconstr Surg*. 2015;135:1349.

Schlechte J, Dolan K, Sherman B, et al. The natural history of untreated hyperprolactinemia: a prospective analysis. *J Clin Endocrinol Metab*. 1989;68:412.

LEVEL III

Molitch ME. Medication-induced hyperprolactinemia. *Mayo Clin Proc*. 2005;80:1050.

Sakiyama R, Quan M. Galactorrhea and hyperprolactinemia. *Obstet Gynecol Surv*. 1983;38:689.

Santen RJ, Mansel R. Benign breast disorders. *N Engl J Med*. 2005;353:275.

Schlechte JA. Clinical practice. Prolactinoma. *N Engl J Med*. 2003;349:2035.

MAMMOGRAPHY

171

THE CHALLENGE

To improve the use of breast imaging to detect occult disease.

Scope of the Problem: First developed in 1965 the widespread use of mammography has been credited with reducing the mortality rate of breast cancer by up to 30%. Unfortunately, not all women undergo appropriate screening on a regular basis. One study indicated that only 39% of women aged 50–59 years and 36% of women aged 60–69 years had undergone a mammogram in the preceding year. In another study, only 24% of women older than 65 years followed the current recommendations for annual examinations. It has been estimated that breast cancer mortality could be reduced by as much as 50% if all women older than 40 years underwent annual screening. In one study, 6 cancers per 1000 screening mammograms were found, and 3 additional cancers per 1000 annual repeat studies were detected.

Objectives: To appropriately use mammography for evaluating breast complaints and to improve compliance with screening guidelines.

TACTICS

Relevant Pathophysiology: Mammography is the best currently available mode of screening for early lesions. Mammography localizes, documents, objectifies, and identifies other occult pathologic changes. Approximately 85% of breast cancers found by mammography are early stage lesions versus 54%–70% found by physicians and 38%–64% of tumors found by the patient herself during breast self-examination. Approximately 35% of breast cancers are found with an abnormal mammogram, without a palpable mass present. Mammography can identify small lesions (1–2 mm), calcifications, or other changes suspicious for malignancy approximately 2 years before a lesion is clinically palpable. The 10-year disease-free survival rate for patients with these lesions is 90%–95%. The average lesion found on breast self-examination is 2.5 cm, and half of these patients have nodal involvement. For these patients, 10-year survival falls to between 50% and 70%. More than one-third of occult breast cancers have calcifications, making the otherwise-undetected tumors visible through mammography.

Strategies: The American Cancer Society guidelines for mammographic screening for low-risk women are as follows.

- Mammography should be performed every year from the age of 45 to 54 years, but women should have the opportunity to begin annual screening between the ages of 40 and 44 years.
- Annual or bi-annual mammogram from the age of 55 years and onward. If the patient has a first-degree relative with premenopausal breast cancer, screening should begin approximately 5 years before the age at which the relative's cancer was diagnosed.

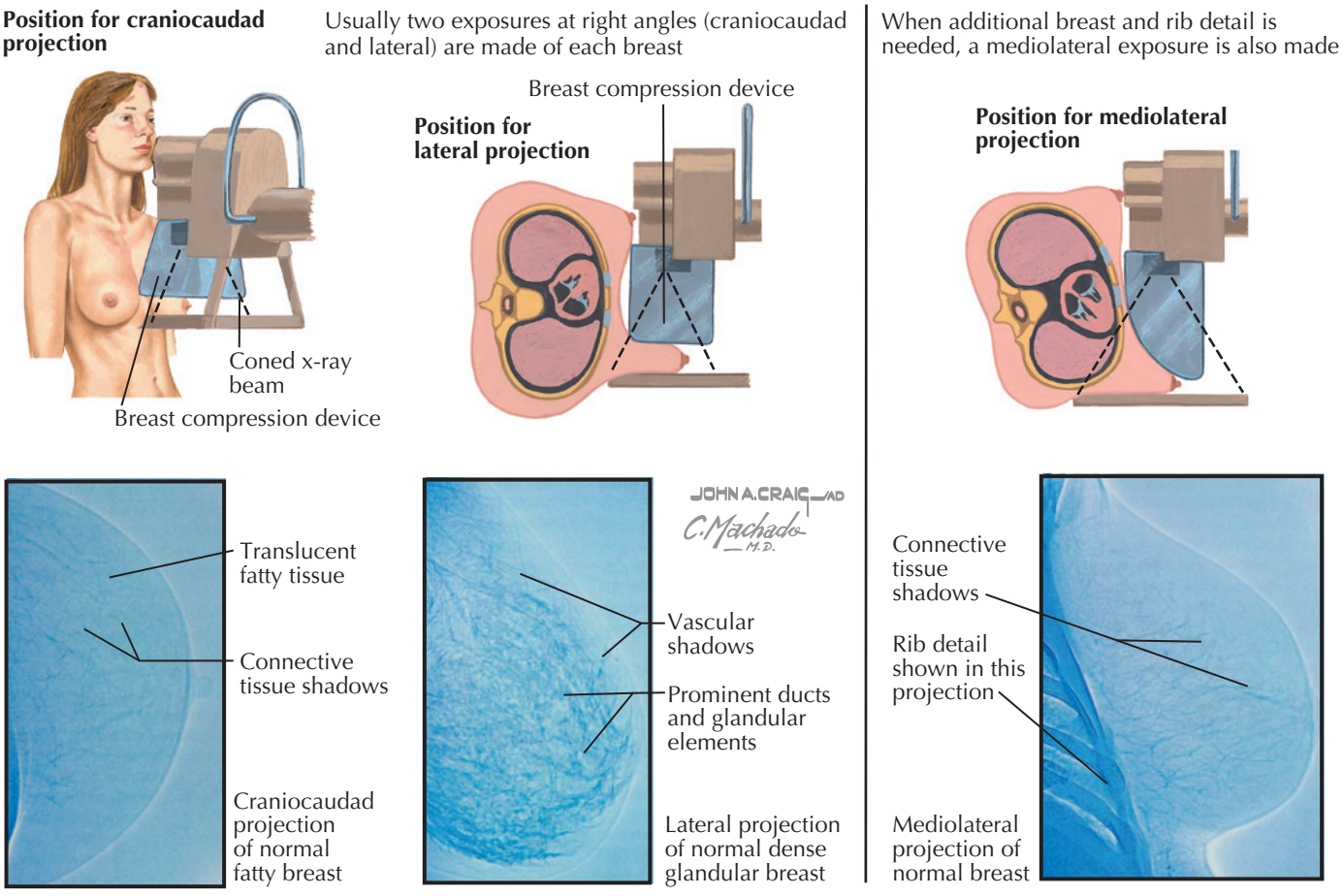


Figure 171.1 Mammography

- Women should continue screening mammography as long as their overall health is good and they have a life expectancy of 10 years or longer.
- For patients at an increased risk for breast cancer (strong family history or genetic abnormality, such as mutations of *BRCA1* or *BRCA2*) mammography should be augmented by magnetic resonance imaging (MRI) studies.

Patient Education: Instruction on the need for and timing of mammography. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP026 (Benign Breast Problems and Conditions) and AP076 (Mammography and Other Screening Tests for Breast Problems).

IMPLEMENTATION

Special Considerations: Mammography in younger women is more difficult to interpret than that in older women because of the greater tissue density present during the reproductive years. While the increasing ability to diagnose cancer in older women parallels their increasing risk, breast cancers in younger women are more easily missed. This diagnostic difficulty and the relatively higher rate of false-positive study results that necessitate further evaluation have raised questions about routine screening of women younger than 50 years. The finding of clusters of calcification that often are associated with cancer is nonspecific. Of calcification clusters found on mammography, 75% result from benign disease. Overall, mammography is approximately 85% accurate in diagnosing malignancy, with a 10%–15% false-negative rate. For this reason, mammography provides an adjunct to clinical impressions and the definitive procedure of biopsy, but it does not replace them. Approximately 10% of mammographic studies require additional views. Between 1% and 2% of screening studies necessitate histologic evaluation to establish a diagnosis. Mammographic radiation exposure is minimal (less than 1 rad). Based on this level of exposure, mammography might induce up to five new lifetime cancers for every 1 million women ages 40–44 years screened and less than 1 per 1 million for women aged 60–64 years (background risk is 115 and 292 for these age groups, respectively). Therefore, the risk for death caused by radiation exposure is approximately equivalent to that encountered by driving a car 220 miles, riding a bicycle for 10 miles, or smoking 1.5 cigarettes.

REFERENCES

LEVEL I

Turnbull L, Brown S, Harvey I, et al. Comparative effectiveness of MRI in breast cancer (COMICE) trial: a randomised controlled trial. *Lancet*. 2010;375:563.

LEVEL II

Armstrong K, Moye E, Williams S, et al. Screening mammography in women 40 to 49 years of age: a systematic review for the American College of Physicians. *Ann Intern Med*. 2007;146:516.

Bleyer A, Welch HG. Effect of three decades of screening mammography on breast-cancer incidence. *N Engl J Med*. 2012;367:1998.

Friedewald SM, Rafferty EA, Rose SL, et al. Breast cancer screening using tomosynthesis in combination with digital mammography. *JAMA*. 2014; 311:2499.

Gartlehner G, Thaler K, Chapman A, et al. Mammography in combination with breast ultrasonography versus mammography for breast cancer screening in women at average risk. *Cochrane Database Syst Rev*. 2013;(4):CD009632.

Lazarus E, Mainiero MB, Schepps B, et al. BI-RADS lexicon for US and mammography: interobserver variability and positive predictive value. *Radiology*. 2006;239:385.

Mandelblatt J, Saha S, Teutsch S, et al., Cost Work Group of the U.S. Preventive Services Task Force. The cost-effectiveness of screening mammography beyond age 65 years: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med*. 2003;139:835.

Moss SM, Cuckle H, Evans A, et al., Trial Management Group. Effect of mammographic screening from age 40 years on breast cancer mortality at 10 years' follow-up: a randomised controlled trial. *Lancet*. 2006;368: 2053.

Myers ER, Moorman P, Gierisch JM, et al. Benefits and harms of breast cancer screening: a systematic review. *JAMA*. 2015;314:1615.

LEVEL III

American College of Obstetricians and Gynecologists. Breast cancer screening. Practice Bulletin No. 122. *Obstet Gynecol*. 2011;118:372.

American College of Obstetricians and Gynecologists. Management of women with dense breasts diagnosed by mammography. Committee Opinion No. 625. *Obstet Gynecol*. 2015;125:750.

American College of Radiology. *Breast Imaging Reporting and Data System (BI-RADS)*. 4th ed. Reston, VA: American College of Radiology; 2003.

Euhus D, Di Carlo PA, Khouri NF. Breast cancer screening. *Surg Clin North Am*. 2015;95:991.

Gilbert FJ, Tucker L, Young KC. Digital breast tomosynthesis (DBT): a review of the evidence for use as a screening tool. *Clin Radiol*. 2016;71:141.

Independent UK Panel on Breast Cancer Screening. The benefits and harms of breast cancer screening: an independent review. *Lancet*. 2012;380(9855):1778.

Lewin JM, D'Orsi CJ, Hendrick RE. Digital mammography. *Radiol Clin North Am*. 2004;42(871):vi.

Løberg M, Lousdal ML, Bretthauer M, et al. Benefits and harms of mammography screening. *Breast Cancer Res*. 2015;17:63.

Nelson HD, Tyne K, Naik A, et al., US Preventive Services Task Force. Screening for breast cancer: an update for the US Preventive Services Task Force. *Ann Intern Med*. 2009;151:727.

Oeffinger KC, Fontham ETH, Etzioni R, et al. Breast Cancer Screening for Women at Average Risk: 2015 Guideline Update From the American Cancer Society. *JAMA*. 2015;314:1599.

Qaseem A, Snow V, Sherif K, et al., Clinical Efficacy Assessment Subcommittee of the American College of Physicians. Screening mammography for women 40 to 49 years of age: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2007;146:511.

Saslow D, Boetes C, Burke W, et al., American Cancer Society Breast Cancer Advisory Group. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA Cancer J Clin*. 2007;57:75.

MASTITIS (LACTATIONAL)

172

INTRODUCTION

Description: Mastitis is an infection of one or more ductal complexes of the breast, generally associated with breastfeeding and potentially causing significant morbidity if not recognized and aggressively treated.
Prevalence: 2%–10% of women who are breastfeeding after delivery.
Predominant Age: Reproductive age; 2–6 weeks after delivery.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Infection comes from organisms carried in the nose and mouth of a nursing infant, most commonly *Staphylococcus aureus* and *Streptococcus* species. Common agents include β-hemolytic streptococci, *Haemophilus influenzae, H. parainfluenzae, Escherichia coli*, and *Klebsiella pneumoniae*.
Risk Factors: Diabetes, steroid use, heavy cigarette smoking, nipple excoriation or cracking, and retracted (inverted) nipples.

SIGNS AND SYMPTOMS

- Firm, sore, red, and tender portion of the breast, most commonly in the upper outer quadrant
- High fever, tachycardia, headaches, anorexia, and malaise
- Axillary nodes tender or enlarged
- In patients who are not breastfeeding a palpable, recurrent mass, accompanied by a multicolored discharge from the nipple or adjacent to a Montgomery follicle

DIAGNOSTIC APPROACH

Differential Diagnosis

- Breast abscess
- Blocked (plugged) duct
- Breast engorgement
- Galactocele

Associated Conditions: Breast engorgement.

Workup and Evaluation

Laboratory: A complete blood count documents an elevated white blood cell count but is not required for diagnosis. Cultures of the mother's milk and the infant's nose and mouth may be helpful but are not required.
Imaging: No imaging indicated.
Special Tests: None indicated.
Diagnostic Procedures: History and physical examinations combined with the knowledge of the condition of the breast at or before delivery.

Pathologic Findings

Swelling and obstruction of the involved ducts with inflammation. When present in nonpregnant and postmenopausal women, it may be accompanied by squamous metaplasia. When well established, ductal thickening may lead to nipple retraction.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Mild fluid restriction, analgesics, ice packs, and support (well-fitting brassiere). In mild cases, it is not necessary to cease breastfeeding.
Specific Measures: Prompt and aggressive antibiotic therapy is indicated. Breastfeeding from the opposite side or pumping or expression of the involved breast may be helpful. If tenderness or fever do not promptly decrease, abscess must be suspected and prompt surgical drainage, usually under general anesthesia, is required.
Diet: No specific dietary changes indicated.
Activity: No restriction.

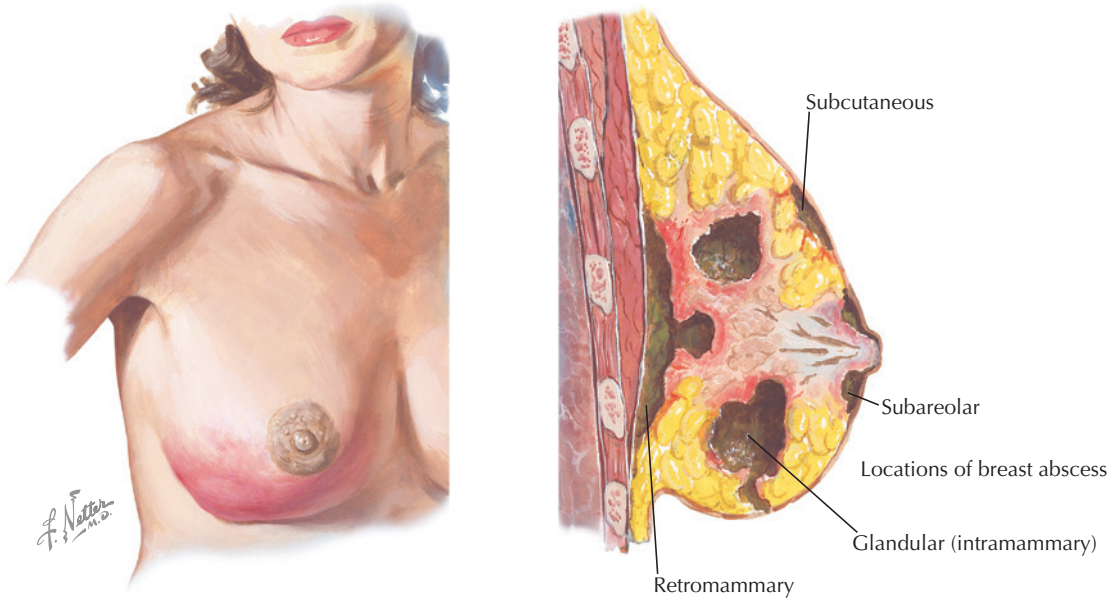


Figure 172.1 Acute mastitis

Patient Education: Reassurance, support, specific suggestions. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP029 (Breastfeeding Your Baby).

Drug(s) of Choice

Dicloxacillin 500 mg PO four times daily or cephalexin 500 mg PO four times daily. Cefaclor 250 mg PO three times a day or amoxicillin/clavulanate (Augmentin) 250 mg PO three times a day may also be used.

Contraindications: Known or suspected allergy.

Precautions: If response to therapy is not prompt, surgical drainage is required.

Alternative Drugs

- Penicillin G or erythromycin 250–500 mg PO four times a day
- Erythromycin ethylsuccinate (EES) 400 mg PO four times a day for 10 days.
- The level of erythromycin achieved in milk is very high.
- In severe infections, empiric inpatient therapy with vancomycin 15–20 mg/kg/dose every 8–12 hours (not to exceed 2 g per dose) may be indicated.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. Watch for the development of an abscess.

Prevention/Avoidance: Attention to normal hygiene practices during breastfeeding (hand washing, avoid drying agents). Avoid cracking or fissuring of nipples. Use breast or nipple shields when cracked nipples are present.

Possible Complications: Progression of infection, abscess formation, scarring, squamous metaplasia, ductal ectasia. Abscesses may form even while a patient is receiving antibiotic therapy.

Expected Outcome: Generally good with aggressive therapy.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.

ICD-10-CM Codes: O91.219 (Nonpurulent mastitis associated with pregnancy, unspecified trimester).

REFERENCES

LEVEL II

Amir LH, Forster D, McLachlan H, et al. Incidence of breast abscess in lactating women: report from an Australian cohort. *BJOG*. 2004;111:1378.

Jahanfar S, Ng CJ, Teng CL. Antibiotics for mastitis in breastfeeding women. *Cochrane Database Syst Rev*. 2013;(2):CD005458.

Peters F, Flick-Fillies D. Hand disinfection to prevent puerperal mastitis. *Lancet*. 1991;338:831.

LEVEL III

Dixon JM, Khan LR. Treatment of breast infection. *BMJ*. 2011;342:d396.

Michie C, Lockie F, Lynn W. The challenge of mastitis. *Arch Dis Child*. 2003;88:818.

Scott-Conner CE, Schorr SJ. The diagnosis and management of breast problems during pregnancy and lactation. *Am J Surg*. 1995;170:401.

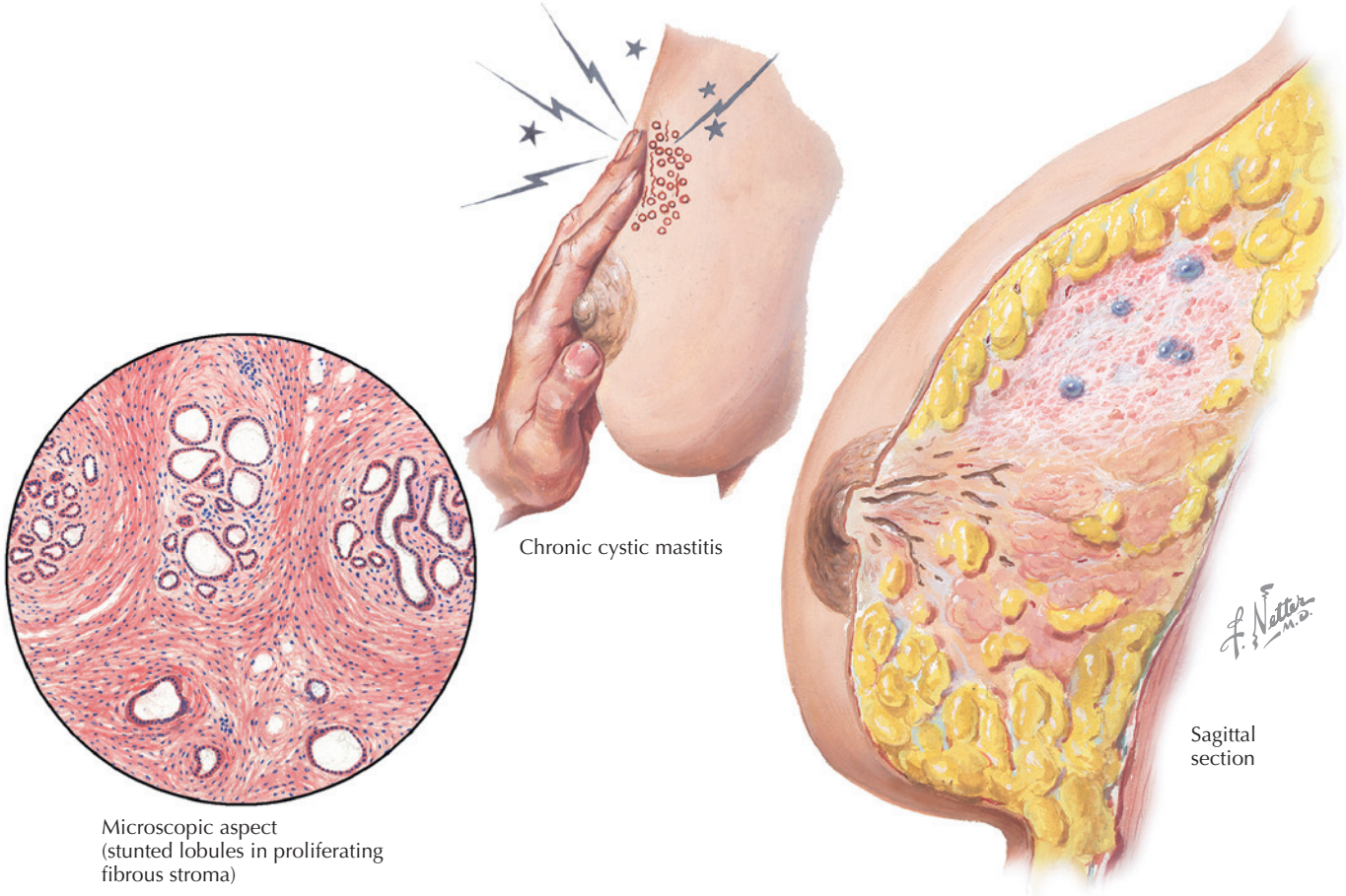


Figure 173.1 Chronic cystic mastitis

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: Mammography may be indicated for other reasons but seldom directly assists in the evaluation of mastalgia.
Special Tests: None indicated.
Diagnostic Procedures: History and physical examinations. The presence of scattered bilateral nodularity suggests fibrocystic change.

Pathologic Findings

Based on pathophysiologic changes present.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Analgesics, mechanical support (a well-fitting brassiere worn day and night), local heat, smoking cessation, reassurance.
Specific Measures: Caffeine restriction, medical treatment of underlying pathophysiologic changes (eg, fibrocystic change).
Diet: A reduction in methylxanthine intake may be beneficial. Premenstrual restriction of salt or fluids is recommended for selected patients. The role of vitamins A and E is unknown.
Activity: No restriction. To reduce discomfort, good mechanical breast support is recommended during vigorous activity.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP026 (Benign Breast Problems and Conditions) and AP076 (Mammography and Other Screening Tests for Breast Problems).

Drug(s) of Choice

- Combination oral contraceptives (70%–90% chance of success).
- Spironolactone 50 mg PO twice a day administered 7–10 days before periods.
- Danazol sodium 200 mg PO twice a day (therapy should start during menstruation or pregnancy must be ruled out). Side effects may be significant, and recurrence is likely after therapy is discontinued.
- Bromocriptine 2.5 mg PO daily (with food) may be increased after 3–7 days if needed.

Contraindications: Spironolactone is contraindicated in the presence of anuria, renal insufficiency, or hyperkalemia. Danazol sodium is contraindicated in pregnancy (category X). It may also worsen epilepsy, migraine headaches, and cardiac or renal function. Bromocriptine is contraindicated in patients with uncontrolled hypertension or in patients known to be sensitive to ergot alkaloids.
Precautions: Diuretics must be used with care to avoid fluid and electrolyte disturbances. Bromocriptine may cause hypotension during the first several days of therapy. Care should also be exercised with patients who have compromised hepatic or renal function.
Interactions: Spironolactone enhances the action of other diuretics and increases digoxin levels. Danazol sodium may prolong prothrombin time in patients receiving warfarin.

Alternative Drugs

- Hydrochlorothiazide 25 mg PO at bedtime for 7–10 days before menses.
- Gonadotropin-releasing hormone agonists—leuprolide acetate (Lupron) 3.75 mg IM monthly for no more than 6 months.
- Evening primrose oil and chasteberry have shown efficacy in limited trials, but standardization of both therapy and active ingredients in varying preparations limits the ability to completely evaluate these as therapeutic options.

FOLLOW-UP

Patient Monitoring: Patients with mastalgia but no dominant mass may be safely rechecked at a different portion of the next menstrual cycle.

Prevention/Avoidance: None.

Expected Outcome: Symptomatic relief can generally be achieved with a combination of diet changes, analgesics, and specific medications.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, although pregnancy may induce mastalgia.

ICD-10-CM Codes: N64.4 (Mastodynia).

REFERENCES

LEVEL I

Gorins A, Perret F, Tournant B, et al. A French double-blind crossover study (danazol versus placebo) in the treatment of severe fibrocystic breast disease. *Eur J Gynaecol Oncol*. 1984;5:85.

Ioannidou-Mouzaka L, Niagassas M, Galanos A, et al. Pilot study on the treatment of cyclical mastodynia with Quinagolide. *Eur J Gynaecol Oncol*. 1999;20:117.

Oksa S, Luukkaala T, Mäenpää J. Toremifene for premenstrual mastalgia: a randomised, placebo-controlled crossover study. *BJOG*. 2006;113:713.

LEVEL II

Boyle CA, Berkowitz GS, LiVolsi VA, et al. Caffeine consumption and fibrocystic breast disease: a case control epidemiologic study. *J Natl Cancer Inst*. 1984;72:1015.

Scurr J, Hedger W, Morris P, et al. The prevalence, severity, and impact of breast pain in the general population. *Breast J*. 2014;20:508.

Srivastava A, Mansel RE, Arvind N, et al. Evidence-based management of Mastalgia: a meta-analysis of randomised trials. *Breast*. 2007;16:503.

Winkler UH, Schindler AE, Brinkmann US, et al. Cyclic progestin therapy for the management of mastopathy and mastodynia. *Gynecol Endocrinol*. 2001;15:37.

LEVEL II

American College of Obstetricians and Gynecologists. Breast cancer screening. Practice Bulletin No. 122. *Obstet Gynecol*. 2011;118:372.

American College of Obstetricians and Gynecologists. Diagnosis and management of benign breast disorders. Practice Bulletin No. 164. *Obstet Gynecol*. 2016;127:e141.

BeLieu RM. Mastodynia. *Obstet Gynecol Clin North Am*. 1994;21:461.

Carranza-Lira S, Garduno-Hernandez MP, Caisapanta DA, et al. Evaluation of mastodynia in postmenopausal women taking hormone therapy. *Int J Gynaecol Obstet*. 2005;89:158.

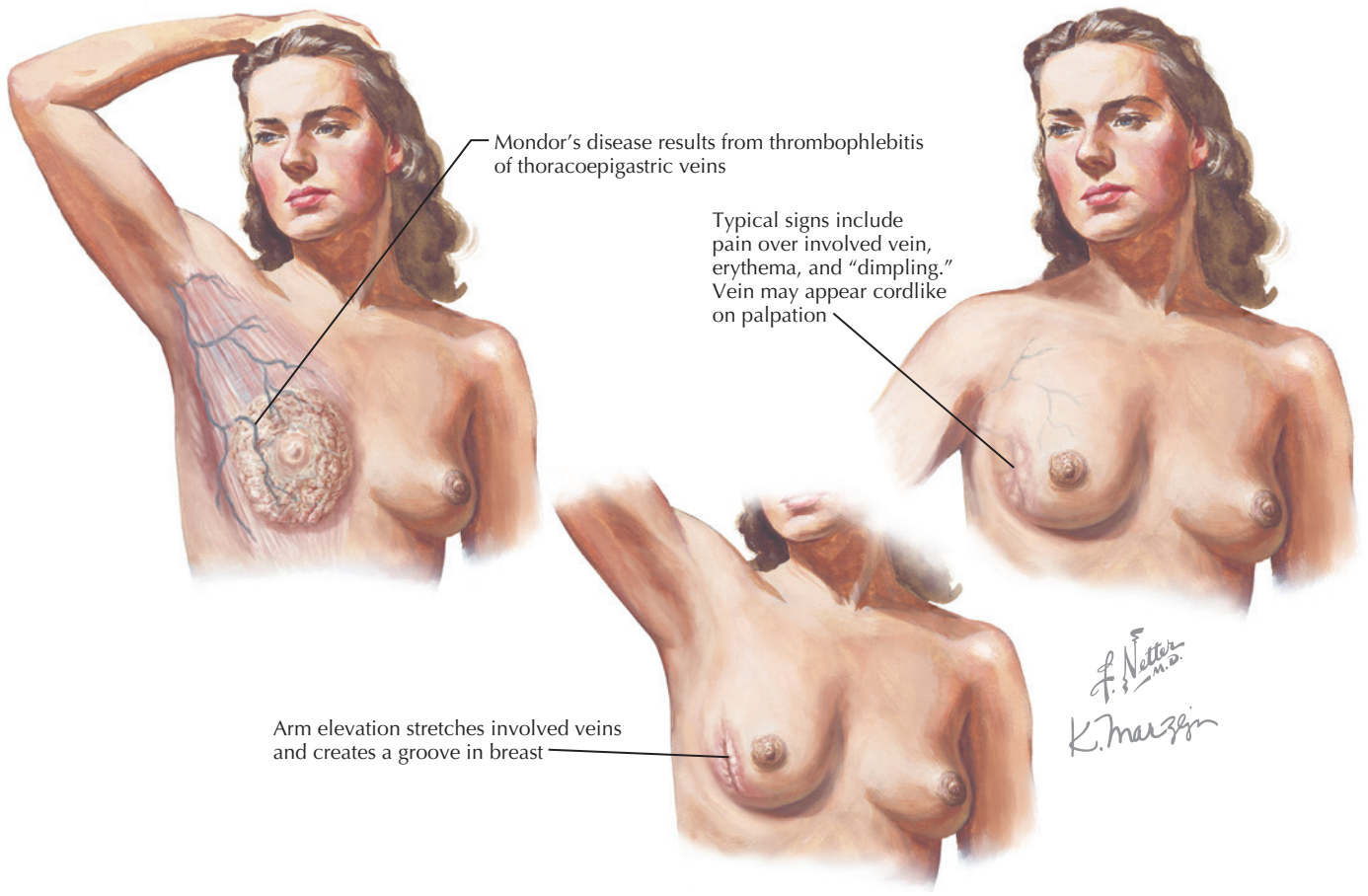


Figure 174.1 Mondor disease

Imaging: Mammography may be required to rule out other processes, but the diagnosis is generally established by examination and history.
Special Tests: On rare occasions, biopsy may be required to establish the diagnosis.
Diagnostic Procedures: History and physical examinations. Accentuation of dimpling or the formation of a groove over the affected vein often occurs when the ipsilateral arm is raised during physical examination.

Pathologic Findings

Thrombophlebitis of the superficial veins.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and reassurance, symptomatic therapy.
Specific Measures: Analgesics and heat reduce symptoms. The condition generally resolves in 2–3 weeks, but it may take 6 weeks or longer.
Diet: No specific dietary changes indicated.
Activity: No restriction. Good mechanical support improves comfort during vigorous activity.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP026 (Benign Breast Problems and Conditions), AP029 (Breastfeeding Your Baby), and AP076 (Mammography and Other Screening Tests for Breast Problems).

Drug(s) of Choice

Nonsteroidal antiinflammatory agents (NSAIDs). Antibiotics and anticoagulants have little effect on the course of the disease and are not indicated.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: Avoidance of breast trauma.
Possible Complications: Unlikely.
Expected Outcome: Mondor disease is self-limiting, although full resolution may take 8–10 weeks.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: I80.8 (Phlebitis and thrombophlebitis of other sites).

REFERENCES

LEVEL II

Pasta V, D'Orazi V, Sottile D, et al. Breast Mondor's disease: diagnosis and management of six new cases of this underestimated pathology. *Phlebology*. 2015;30:564.

Salemis NS, Vasilara G, Lagoudianakis E. Mondor's disease of the breast as a complication of ultrasound-guided core needle biopsy: management and review of the literature. *Breast Dis*. 2015;35:73.

LEVEL III

Camiel MR. Mondor's disease in the breast. *Am J Obstet Gynecol*. 1985; 152:879.

Duff P. Mondor's disease in pregnancy. *Obstet Gynecol*. 1981;58:117.

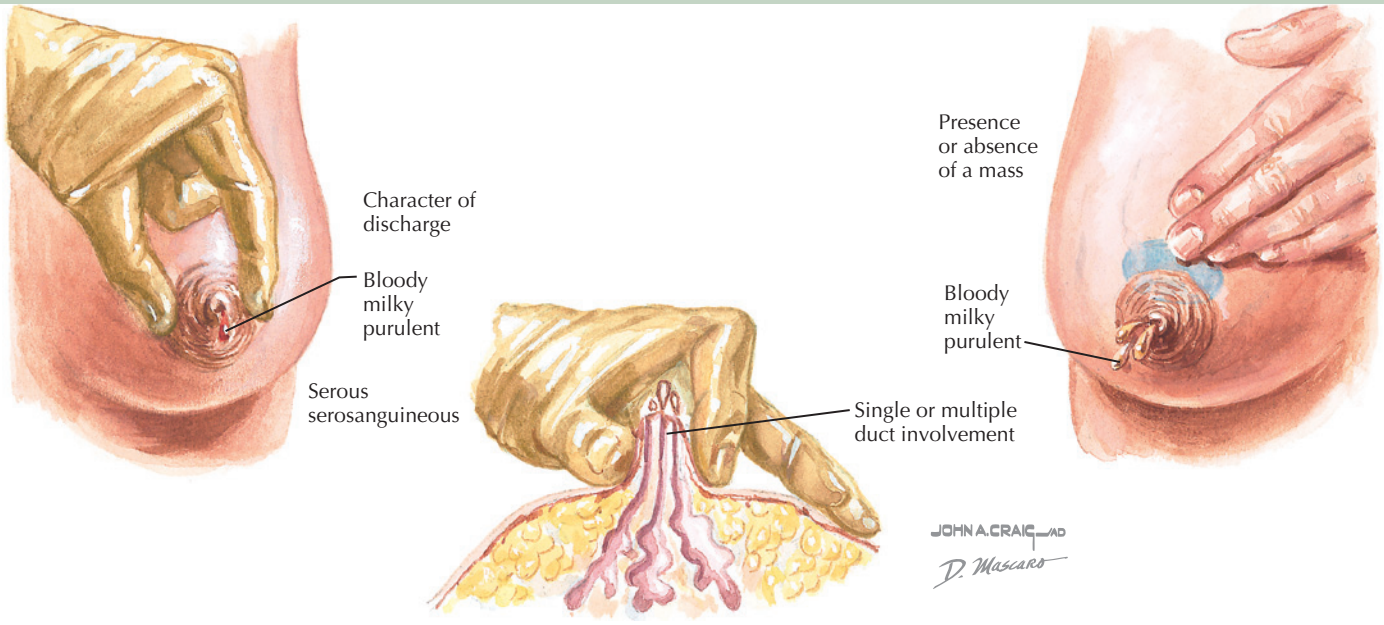
Laroche JP, Galanaud J, Labau D, et al. Mondor's disease: what's new since 1939? *Thromb Res*. 2012;130(suppl 1):S56.

Oldfield MC. Mondor's disease. A superficial phlebitis of the breast. *Lancet*. 1962;1:994.

Pugh CM, DeWitty RL. Mondor's disease. *J Natl Med Assoc*. 1996;88:359.

Samlaska CP, James WD. Superficial thrombophlebitis. II. Secondary hypercoagulable states. *J Am Acad Dermatol*. 1990;23:1.

Clinical Considerations



Management Algorithm For Nipple Discharge

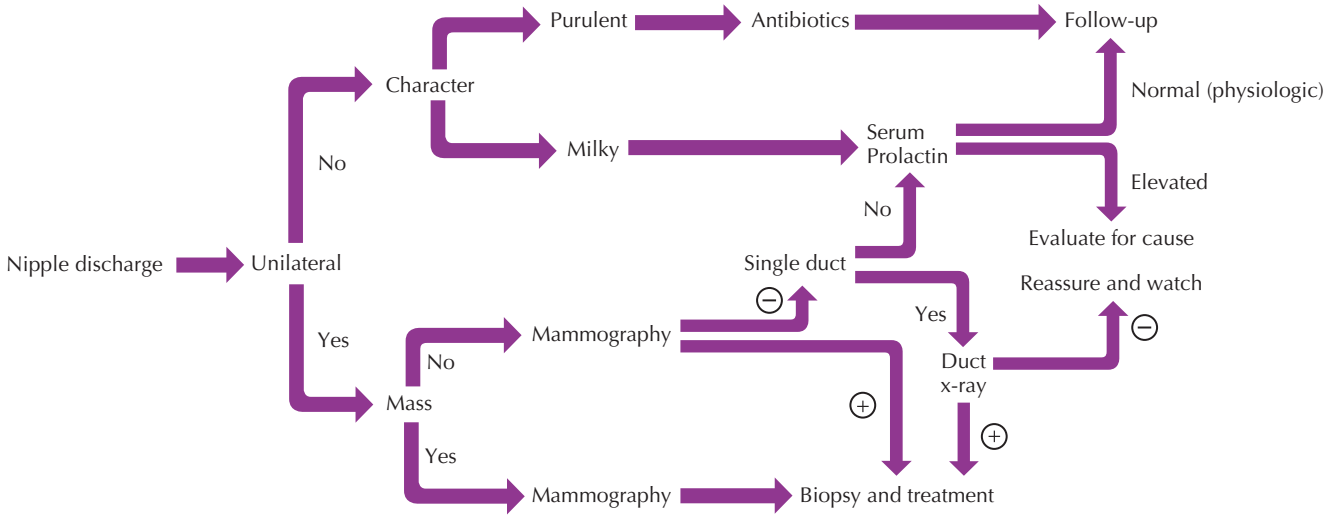


Figure 175.1 Clinical consideration and management of nipple discharge

Expected Outcome: Surgical excision of the involved duct may be required for diagnosis and treatment.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy.
ICD-10-CM Codes: N64.52 (Nipple discharge).

REFERENCES

LEVEL II

Alcock C, Layer GT. Predicting occult malignancy in nipple discharge. *ANZ J Surg.* 2010;80:646.

Chen L, Zhou WB, Zhao Y, et al. Bloody nipple discharge is a predictor of breast cancer risk: a meta-analysis. *Breast Cancer Res Treat.* 2012;32:9.

Kooistra BW, Wauters C, van de Ven S, et al. The diagnostic value of nipple discharge cytology in 618 consecutive patients. *Eur J Surg Oncol.* 2009; 35:573.

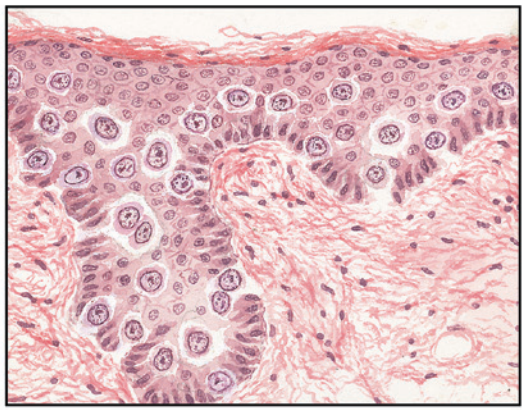
Morrogh M, Morris EA, Liberman L, et al. The predictive value of ductography and magnetic resonance imaging in the management of nipple discharge. *Ann Surg Oncol.* 2007;14:3369.

LEVEL III

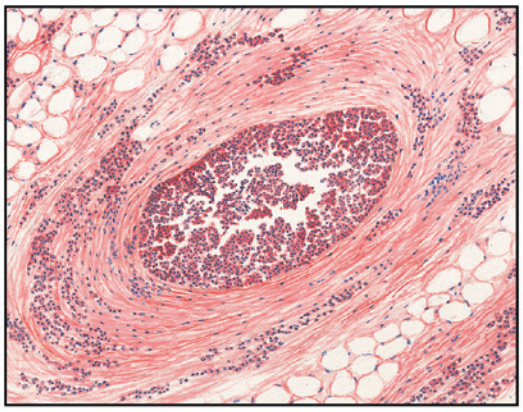
American College of Obstetricians and Gynecologists. Diagnosis and management of benign breast disorders. Practice Bulletin No. 164. *Obstet Gynecol.* 2016;127:e141.

Escobar PF, Crowe JP, Matsunaga T, et al. The clinical applications of mammary ductoscopy. *Am J Surg.* 2006;191:211.

Falkenberry SS. Nipple discharge. *Obstet Gynecol Clin North Am*. 2002;29: 21.
Fentiman IS, Hamed H. Assessment of breast problems. *Int J Clin Pract*. 2001;55:458.
Hamed H, Fentiman IS. Benign breast disease. *Int J Clin Pract*. 2001;55:461.
Hussain AN, Policarpio C, Vincent MT. Evaluating nipple discharge. *Obstet Gynecol Surv*. 2006;61:278.
Masood S, Khalbuss WE. Nipple fluid cytology. *Clin Lab Med*. 2005; 25(787):vii.
Sakorafas GH. Nipple discharge: current diagnostic and therapeutic approaches. *Cancer Treat Rev*. 2001;27:275.
Santen RJ, Mansel R. Benign breast disorders. *N Engl J Med*. 2005;353:275.
Vargas HI, Romero L, Chlebowski RT. Management of bloody nipple discharge. *Curr Treat Options Oncol*. 2002;3:157.



Paget cells in epidermis



Duct invasion

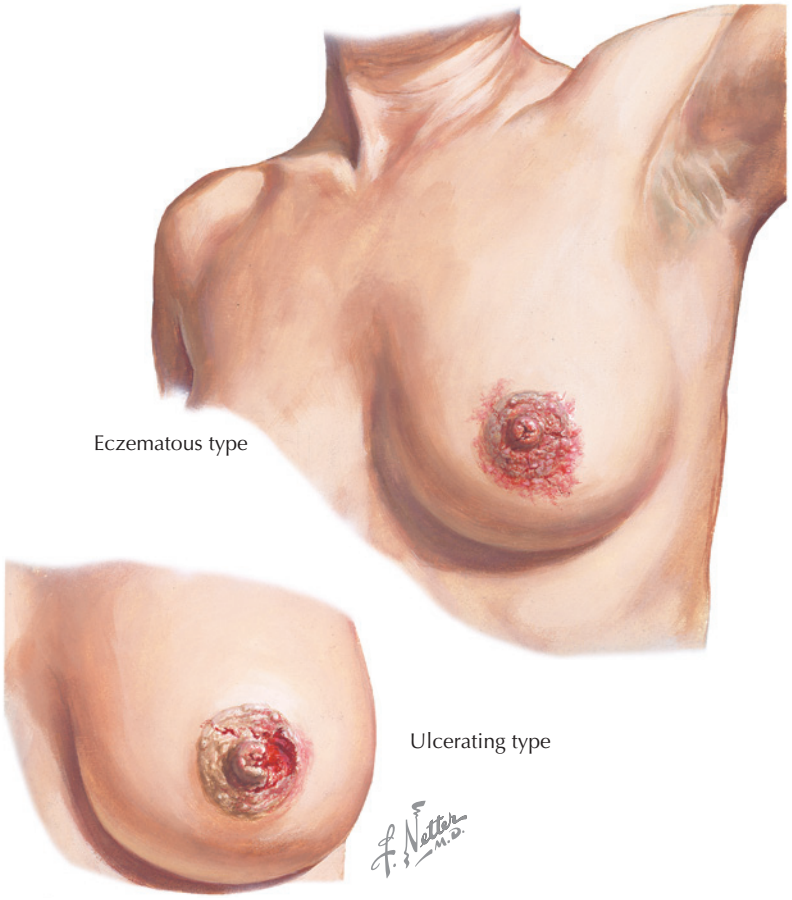


Figure 176.1 Types of Paget disease of the breast

REFERENCES

LEVEL I

Bijker N, Rutgers EJ, Duchateau L, EORTC Breast Cancer Cooperative Group, et al. Breast-conserving therapy for Paget disease of the nipple: a prospective European Organization for Research and Treatment of Cancer study of 61 patients. *Cancer*. 2001;91:472.

LEVEL II

Caliskan M, Gatti G, Sosnovskikh I, et al. Paget's disease of the breast: the experience of the European Institute of Oncology and review of the literature. *Breast Cancer Res Treat*. 2008;112:513.

Chen CY, Sun LM, Anderson BO. Paget disease of the breast: changing patterns of incidence, clinical presentation, and treatment in the U.S. *Cancer*. 2006;107:1448.

Marshall JK, Griffith KA, Haffty BG, et al. Conservative management of Paget disease of the breast with radiotherapy: 10- and 15-year results. *Cancer*. 2003;97:2142.

Morrogh M, Morris EA, Liberman L, et al. MRI identifies otherwise occult disease in select patients with Paget disease of the nipple. *J Am Coll Surg*. 2008;206:316.

LEVEL III

Jamali FR, Ricci A Jr, Deckers PJ. Paget's disease of the nipple-areola complex. *Surg Clin North Am*. 1996;76:365.

Lloyd J, Flanagan AM. Mammary and extramammary Paget's disease. *J Clin Pathol*. 2000;53:742.

This page intentionally left blank

SECTION XI

Reproductive, Genetic, and Endocrine Conditions

This page intentionally left blank

ABNORMAL PUBERTY

177

THE CHALLENGE

To evaluate patients who do not experience the normal events of puberty when expected and to provide reassurance with appropriate or timely diagnosis and intervention when more sinister processes are at work. Abnormal (precocious) puberty is estimated to affect approximately 1 in 10,000 girls.

Scope of the Problem: For all patients with precocious puberty (pubertal changes before the age of 7 years or cyclic menstruation before the age of 10 years) the possibility of a serious process, either central or peripheral, must be evaluated. (Because of evolving changes in maturation rates, these traditional ages should be adjusted downward by 1 year for African American girls). Precocious puberty is customarily divided into two classifications: true or gonadotropin-releasing hormone (GnRH) dependent (70%) and precocious pseudopuberty that is independent of GnRH control. For most girls older than 4 years, no specific cause is discovered for early development. In contrast, the most common cause of precocious change in girls younger than 4 years is a central nervous system lesion, most often hamartomas of the hypothalamus. Even when the sequence of events appears normal, a serious process (such as a slowly progressing brain tumor) must be aggressively sought initially and watched for with long-term continuing follow-up. Delayed puberty is a relatively uncommon problem in girls. When it occurs, the possibility of a genetic or hypothalamic–pituitary abnormality must be considered, along with a moderately large number of other possibilities. Based on the average age and normal variation of puberty, any girl who has not exhibited breast budding by the age of 13 years requires preliminary investigation. Similarly, girls who do not menstruate by the age of 15 or 16 years, regardless of other sexual development, should be evaluated. Patients should also be evaluated any time there is a disruption in the normal sequence of puberty or when there is patient or parental concern. Patients with significant abnormalities of either height or weight should be evaluated for chromosomal abnormalities or endocrinopathies.

Objectives of Management: To establish the cause of advanced or delayed events of puberty with appropriate speed and care, without adding to the trauma of adolescence.

TACTICS

Relevant Pathophysiology: True precocious puberty, also known as complete, isosexual, or central precocity, is related to the early activation of the hypothalamic–pituitary–gonadal axis. In 75% of patients, there is no indication of how or why the normal processes of puberty are accelerated. In the remaining one-fourth a central nervous system abnormality is the cause. A number of central nervous system pathologic conditions may result in the activation of GnRH secretion and the early onset of pubertal changes. Precocious pseudopuberty is also referred to as incomplete or peripheral and may be iso- or heterosexual. In these patients, there may be secretion of sex steroids or human chorionic gonadotropin from sources other than the pituitary. More than 10% of girls with precocious puberty have an ovarian tumor. These tumors are palpable in 80% of patients or may be readily detected by ultrasonography or tomographic studies. Bleeding is heavy and irregular in character, befitting escape from the normal control mechanisms. One of the most common chromosomal causes of absent (delayed) menstruation is the premature ovarian failure found in patients with Turner syndrome (45,X). The absence of one X chromosome results in accelerated ovarian follicular atresia to such an extent that by the age of puberty, no functionally competent follicles remain. The appearance of these patients is noteworthy for short stature, webbed neck (pterygium colli), a shield-like chest with widely spaced nipples, and an increased carrying angle of the arms (cubitus valgus). Buccal smears do not demonstrate Barr bodies, and chromosomal analysis confirms the diagnosis. Because these women will not undergo any secondary sexual maturation, referral to a specialist for counseling and management of replacement hormonal manipulations is advisable. Deletions of only a part of the long arm of the X chromosome have been shown to be associated with premature ovarian failure, with the earliest failures associated with the greatest deletions.

Strategies: The evaluation of patients with precocious puberty is focused on detecting possible life-threatening disease and defining the velocity of the process. When the diagnosis of true precocious puberty is established, generally by exclusion, treatment with GnRH agonists usually halts the progression of change. This therapy is expensive and effective only if the observed changes are under central control. GnRH may also be suppressed using medroxyprogesterone acetate (Depo-Provera) with doses of 100–200 mg intramuscularly administered every 2–4 weeks. This therapy is less likely to control bone growth abnormalities than the GnRH agonist treatment. Without any therapy, approximately 50% of girls will not reach 5 feet in height. The evaluation of patients with delayed pubertal development must begin with a general history, including general health, weight and height records, and family history, including the pubertal experience of others in the family. Physical examination should identify the type and degree of sexual development present. The presence of breast changes generally indicates the production of estrogen, and the development of pubic or axillary hair indicates the production of androgens. Laboratory evaluation should include serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin measurements; skull radiographs; and thyroid function studies. Bone age, chromosomal or cytologic studies, and pelvic ultrasonography or other imaging studies may also be indicated. Because of the significance of the potential causes of disordered puberty, most of these patients should be evaluated by or in consultation with a specialist.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlets AP041 (Your Changing Body-Especially for Teens) and AP049 (Your First Period-Especially for Teens).

IMPLEMENTATION

Special Considerations: Although precocious puberty is most often heralded by the sequence of increased growth, thelarche, and adrenarche, these events may simultaneously occur, or menarche itself may be the first indication. Idiopathic or constitutional precocious puberty is associated with a normal reproductive life and normal age of menopause. The greatest risk for abnormality comes from the early closure of the bony growth plates that often leaves these patients with short stature. Therapy is worth considering for young children to achieve adult height and to avoid the social and emotional stresses that early maturation can entail. If the cause of delayed puberty is found to be hypogonadism, hormonal therapy initiates and sustains the development of normal secondary sex characteristics. Hormonal therapy also allows for normal height and bone mass deposition to be achieved. Adolescents require much less hormone therapy than do adults or postmenopausal women. Therapy usually begins with unopposed estrogen at a dose of 0.3 mg of conjugated estrogen, 0.5 mg of estradiol, or their equivalent daily. In 6–12 months, this dose is approximately doubled and medroxyprogesterone acetate is added (10 mg for the first 12 days of the month). This combination results in regular menstruation but is insufficient for contraception. Normal pubertal development generally proceeds when the patient reaches a bone age of 13 years.

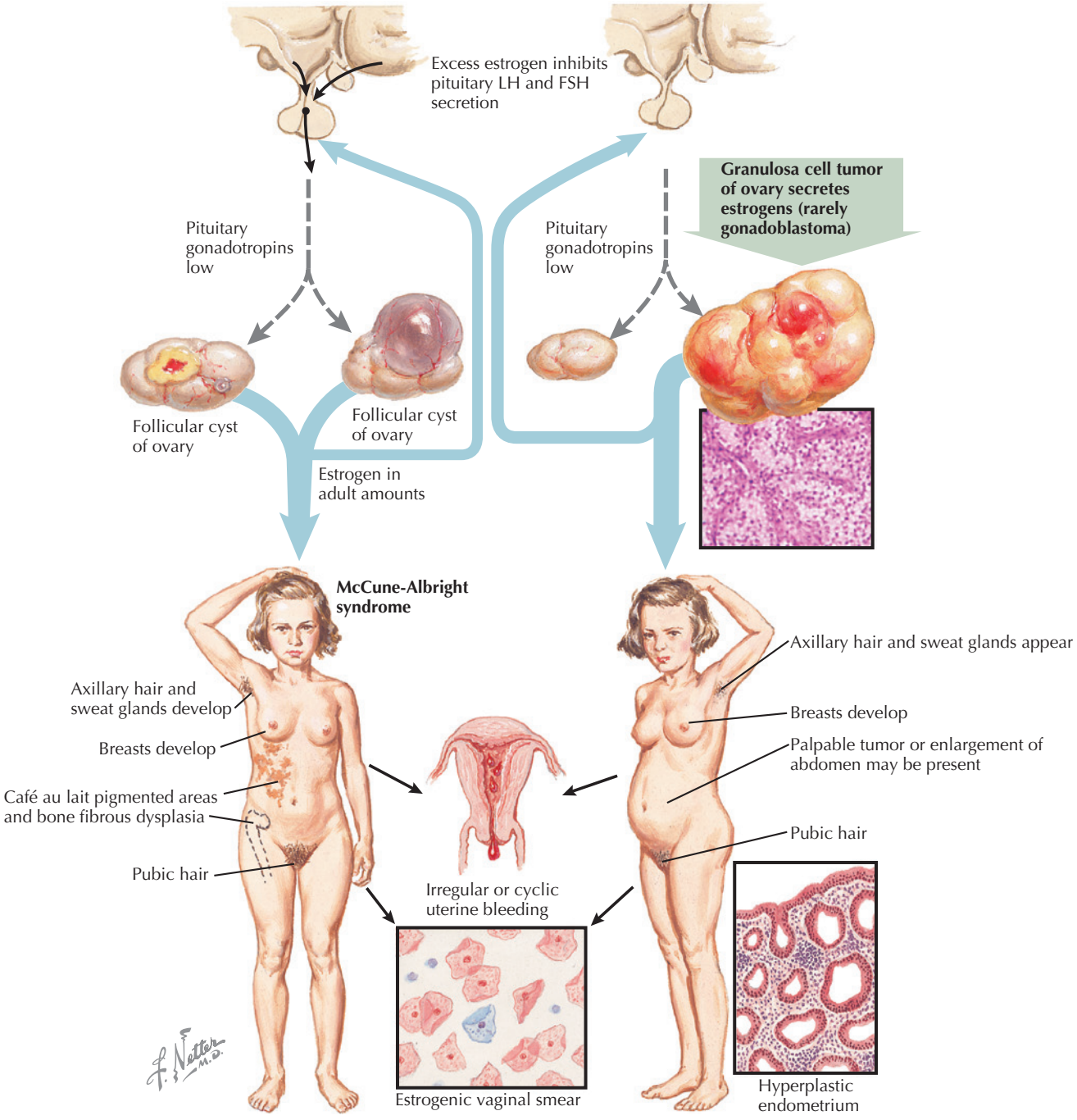


Figure 177.1 Causes of female sexual precocity

REFERENCES

LEVEL II

Armengaud JB, Charkaluk ML, Trivin C, et al. Precocious pubarche: distinguishing late-onset congenital adrenal hyperplasia from premature adrenarche. *J Clin Endocrinol Metab*. 2009;94:2835.

Houk CP, Kunselman AR, Lee PA. Adequacy of a single unstimulated luteinizing hormone level to diagnose central precocious puberty in girls. *Pediatrics*. 2009;123:e1059.

Lee PA, Klein K, Mauras N, et al. Efficacy and safety of leuprolide acetate 3-month depot 11.25 milligrams or 30 milligrams for the treatment of central precocious puberty. *J Clin Endocrinol Metab*. 2012;97:1572.

LEVEL III

American College of Obstetricians and Gynecologists. Menstruation in girls and adolescents: using the menstrual cycle as a vital sign. Committee Opinion No. 651. *Obstet Gynecol*. 2015;126:e143.

American College of Obstetricians and Gynecologists. Primary ovarian insufficiency in adolescents and young women. Committee Opinion No. 605. *Obstet Gynecol*. 2014;123:193.

AMENORRHEA: PRIMARY

178

INTRODUCTION

Description: Primary amenorrhea is the absence of normal menstruation in a patient without previously established cycles.
Prevalence: Uncommon.
Predominant Age: Mid to late teens.
Genetics: One-third caused by chromosomal abnormalities such as 45,XO, 46,XY gonadal dysgenesis, or 46,XX q5 X long-arm deletion.

ETIOLOGY AND PATHOGENESIS

Causes: Gonadal abnormalities (failure, 60% of patients)—autoimmune ovarian failure (Blizzard syndrome), gonadal dysgenesis, pure gonadal dysgenesis, 45,XO (Turner syndrome), 46,XY gonadal dysgenesis (Swyer syndrome), 46,XX q5 X chromosome long-arm deletion, mixed or mosaic, follicular depletion, autoimmune disease, infection (eg, mumps), infiltrative disease processes (eg, tuberculosis, galactosemia), iatrogenic ovarian failure (eg, alkylating chemotherapy, irradiation), ovarian insensitivity syndrome (resistant ovary [Savage] syndrome), 17α-hydroxylase deficiency, polycystic ovary syndrome (PCOS, 7%), chronic anovulation of pubertal onset. Extragonadal anomalies (40%)—congenital absence of uterus and vagina (15%; Müllerian agenesis), constitutional delay, imperforate hymen, male pseudohermaphroditism (testicular feminization/androgen insensitivity syndrome), pituitary–hypothalamic dysfunction, transverse vaginal septum.
Risk Factors: None known.

SIGNS AND SYMPTOMS

- No period by the age of 13 years with no secondary sex changes
- No period by the age of 15 years regardless of secondary sex changes
- No period by 2 years after the start of secondary sex changes

Evaluation should not be delayed any time there is the suggestion of a chromosomal abnormality or an obstructed genital tract.

DIAGNOSTIC APPROACH

Differential Diagnosis

- Pregnancy before first cycle
- Obstructed outflow tract (making menstruation cryptic)
- Gonadal dysgenesis
- Uterine agenesis
- Androgen insensitivity syndrome
- Mayer–Rokitansky–Küster–Hauser syndrome

Associated Conditions: Infertility, abnormal stature (short or tall), and cardiac changes in some congenital syndromes; hypertension and hypokalemic alkalosis in 17α-hydroxylase deficiency, virilization, or hirsutism; and cyclic pelvic pain with outflow obstruction. Renal and skeletal abnormalities may also occur. Prolonged amenorrhea is associated with an increased risk for osteoporosis.

Workup and Evaluation

Laboratory: The development of sexual hair or breasts provides an outward sign of androgen and estrogen production, respectively.
Imaging: Based on conditions being considered. If a normal vagina or uterus is not apparent, pelvic ultrasonography should be performed to evaluate the upper genital tract.
Special Tests: Based on conditions being considered.
Diagnostic Procedures: Laparoscopy to evaluate internal organs and gonads may be required.

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Determination of underlying cause(s).
Specific Measures: Based on the diagnosis and specific needs of the patient.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP049 (Your First Period-Especially for Teens) or AP041 (Your Changing Body-Especially for Teens).

Drug(s) of Choice

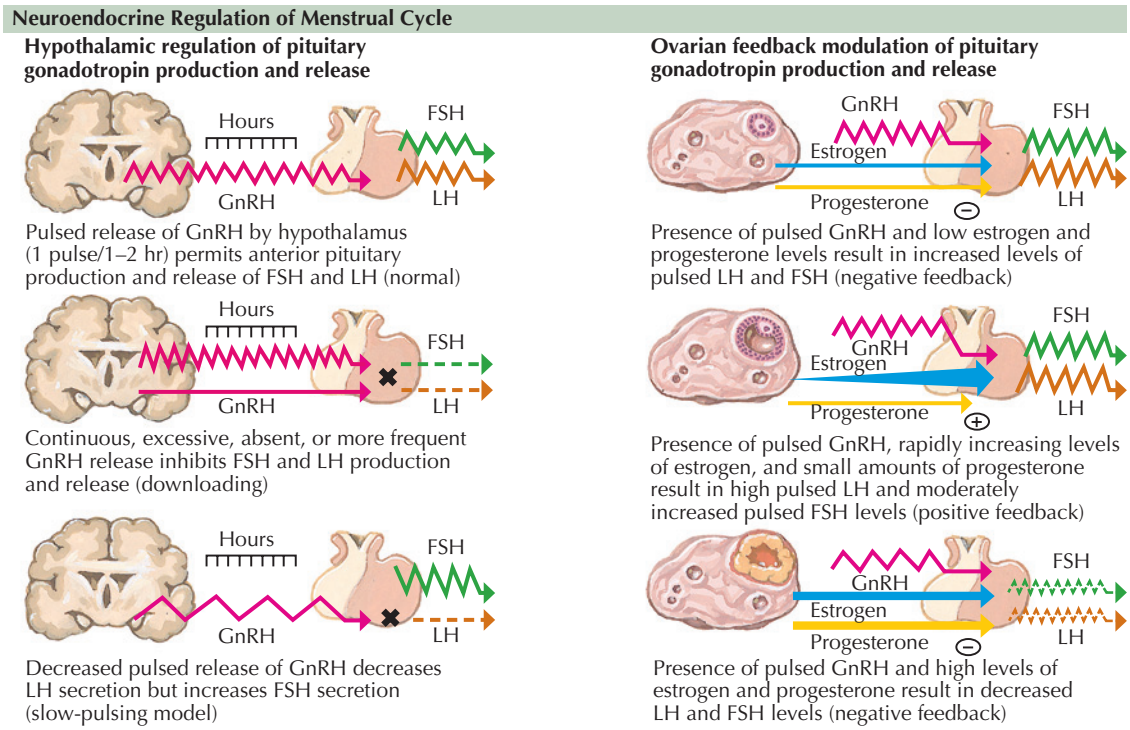
Based on the underlying cause. Hormone replacement may be required or desirable for many patients.

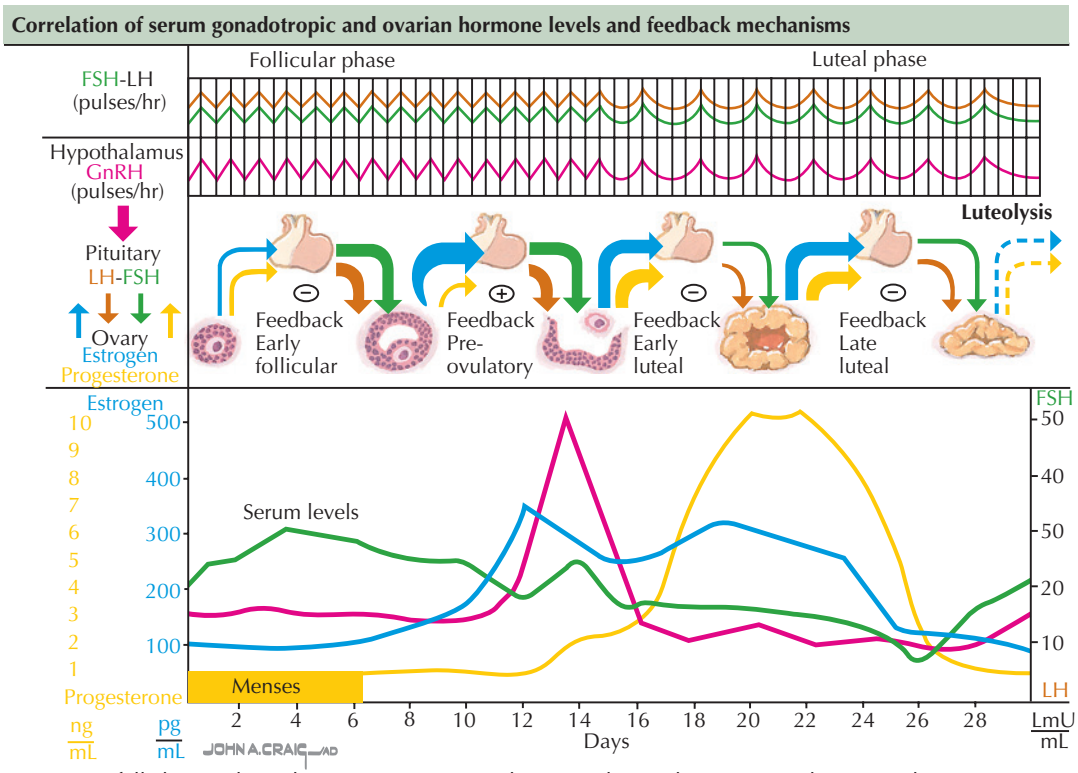
FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: Risk for gonadal malignancy is increased if a Y chromosome is present. Risk for osteoporosis is present if the patient is hypoestrogenic and does not undergo replacement therapy. Extensive damage to the upper tract may occur if obstruction is not corrected.
Expected Outcome: Menstruation and fertility may be restored for many of these patients if there are no structural or chromosomal conditions that preclude the possibility (uterine agenesis, androgen insensitivity syndrome, gonadal dysgenesis).

MISCELLANEOUS

Pregnancy Considerations: Infertility common. If pregnancy is achieved, there are no effects except those imposed by underlying cause.
ICD-10-CM Codes: N91.2 (Amenorrhea, unspecified).





FSH, follicle-stimulating hormone; GnRH, gonadotropin-releasing hormone; LH, luteinizing hormone.

Figure 178.1 Amenorrhea: primary

REFERENCES

LEVEL III

American College of Obstetricians and Gynecologists. Menstruation in girls and adolescents: using the menstrual cycle as a vital sign. Committee Opinion No. 651. *Obstet Gynecol*. 2015;126:e143.

American College of Obstetricians and Gynecologists. Müllerian agenesis: diagnosis, management, and treatment. Committee Opinion No. 562. *Obstet Gynecol*. 2013;121:1134.

American College of Obstetricians and Gynecologists. Primary ovarian insufficiency in adolescents and young women. Committee Opinion No. 605. *Obstet Gynecol*. 2014;123:193.

Practice Committee of the American Society for Reproductive Medicine. Current evaluation of amenorrhea. *Fertil Steril*. 2006;86:S148.

AMENORRHEA: SECONDARY

INTRODUCTION

Description: Secondary amenorrhea is the absence of normal menstruation in a patient with previously established cycles.
Prevalence: Common.
Predominant Age: Reproductive age (menarche to menopause).
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Most common—pregnancy. Other causes—end organ: Asherman syndrome, outflow obstruction; ovarian (40%): polycystic ovary syndrome (PCOS, 30%), menopause, resistant ovary (Savage) syndrome, toxin exposure, surgery, autoimmune disease; central (hypothalamic, 35%), behavioral, and others: anorexia, obesity, athletics (overtraining), drugs/medications, nutritional deprivation, psychogenic (stress); medical: adenoma, craniopharyngioma, Sheehan syndrome, tuberculosis, sarcoid, empty sella syndrome; virilizing syndromes: PCOS, adrenal hyperplasia, virilizing tumors.
Risk Factors: Unprotected intercourse, exposure to toxins or radiation, surgery, overtraining, eating disorders, psychosocial stress.

SIGNS AND SYMPTOMS

- Absent menstruation—may be associated with symptoms that suggest the cause.

DIAGNOSTIC APPROACH

Differential Diagnosis

- Pregnancy
- Menopause (natural or premature)
- Exogenous hormone use
- Virilization
- Metabolically active ovarian tumor
- Lactational amenorrhea

Associated Conditions: Endometrial hyperplasia, osteoporosis in hypoestrogenic states.

Workup and Evaluation

Laboratory: A pregnancy test is always indicated and is the first step in evaluation.
Imaging: Based on conditions being considered.
Special Tests: Women who are younger than 30 years who have ovarian failure should have a karyotype performed.
Diagnostic Procedures: Based on conditions being considered.

Pathologic Findings

None

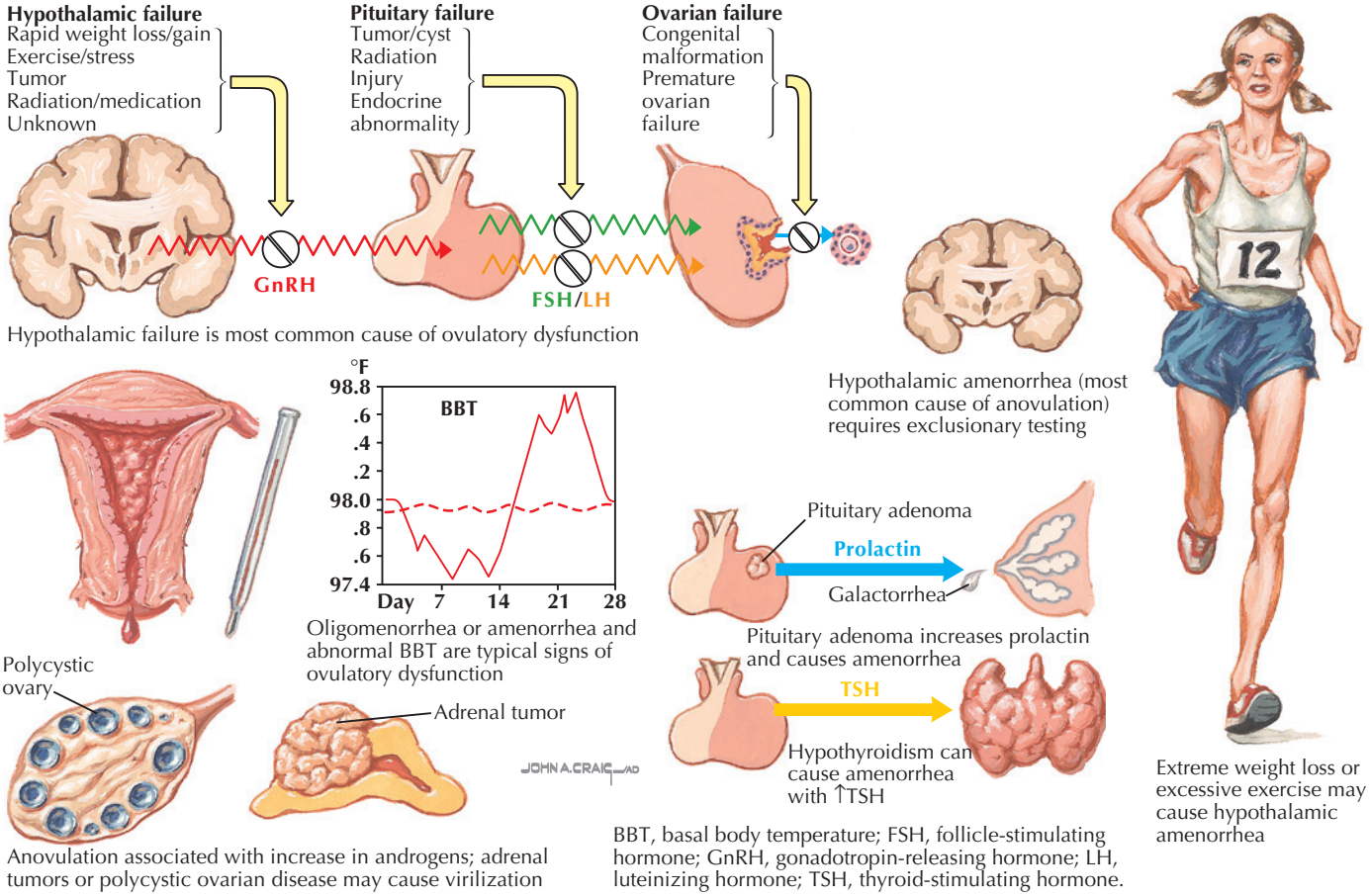


Figure 179.1 Causes of ovulatory dysfunction in amenorrhea (secondary)

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Determination of underlying cause(s). If a pathologic condition has been ruled out and pregnancy is not desired, reassurance only. Evaluation should not be delayed any time there is the suggestion of an abnormality or pregnancy.

Specific Measures: Periodic (every 3–6 months) progestin withdrawal to prevent endometrial hyperplasia and to re-evaluate status. Specific therapy is based on the underlying cause (such as estrogen/progestin therapy for menopause). Treatment is focused on restoring or inducing ovulation if pregnancy is desired.

Diet: No specific dietary changes indicated.

Activity: No restriction.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlets AP049 (Your First Period-Especially for Teens) or AP041 (Your Changing Body-Especially for Teens), AP121 (Polycystic Ovary Syndrome), and AP047 (The Menopause Years).

Drug(s) of Choice

Based on the diagnosis (eg, thyroid replacement for hypothyroidism, estrogen and progestin therapy for ovarian failure, periodic oral or transvaginal progestin therapy, or ovulation induction for anovulation).

Contraindications: All medical interventions are contraindicated until pregnancy has been ruled out.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. Watch for changing status or intercurrent pregnancy.

Prevention/Avoidance: None (contraception).

Possible Complications: Endometrial hyperplasia with continued estrogen (unopposed) exposure.

Expected Outcome: Most causes of secondary amenorrhea may be successfully treated with the return of menstruation.

MISCELLANEOUS

Pregnancy Considerations: Pregnancy must be ruled out.

ICD-10-CM Codes: N91.2 (Amenorrhea, unspecified).

REFERENCES

LEVEL III

American College of Obstetricians and Gynecologists. Menstruation in girls and adolescents: using the menstrual cycle as a vital sign. Committee Opinion No. 651. *Obstet Gynecol*. 2015;126:e143.

American College of Obstetricians and Gynecologists. Müllerian agenesis: diagnosis, management, and treatment. Committee Opinion No. 562. *Obstet Gynecol*. 2013;121:1134.

American College of Obstetricians and Gynecologists. Polycystic ovary syndrome. ACOG Practice Bulletin No. 108. *Obstet Gynecol*. 2009;114:936.

American College of Obstetricians and Gynecologists. Primary ovarian insufficiency in adolescents and young women. Committee Opinion No. 605. *Obstet Gynecol*. 2014;123:193.

Bloomfield D. Secondary amenorrhea. *Pediatr Rev*. 2006;27:113.

Gordon CM. Clinical practice. Functional hypothalamic amenorrhea. *N Engl J Med*. 2010;363:365.

Haller E. Eating disorders. A review and update. *West J Med*. 1992;157:658.

Kakuno Y, Amino N, Kanoh M, et al. Menstrual disturbances in various thyroid diseases. *Endocr J*. 2010;57:1017.

Perkins RB, Hall JE, Martin KA. Neuroendocrine abnormalities in hypothalamic amenorrhea: spectrum, stability, and response to neurotransmitter modulation. *J Clin Endocrinol Metab*. 1999;84:1905.

Practice Committee of the American Society for Reproductive Medicine. Current evaluation of amenorrhea. *Fertil Steril*. 2006;86:S148.

Rosenfield RL. Clinical review: adolescent anovulation: maturational mechanisms and implications. *J Clin Endocrinol Metab*. 2013;98:3572.

Sabatini S. The female athlete triad. *Am J Med Sci*. 2001;322:193.

Walshe JM, Denduluri N, Swain SM. Amenorrhea in premenopausal women after adjuvant chemotherapy for breast cancer. *J Clin Oncol*. 2006;24:5769.

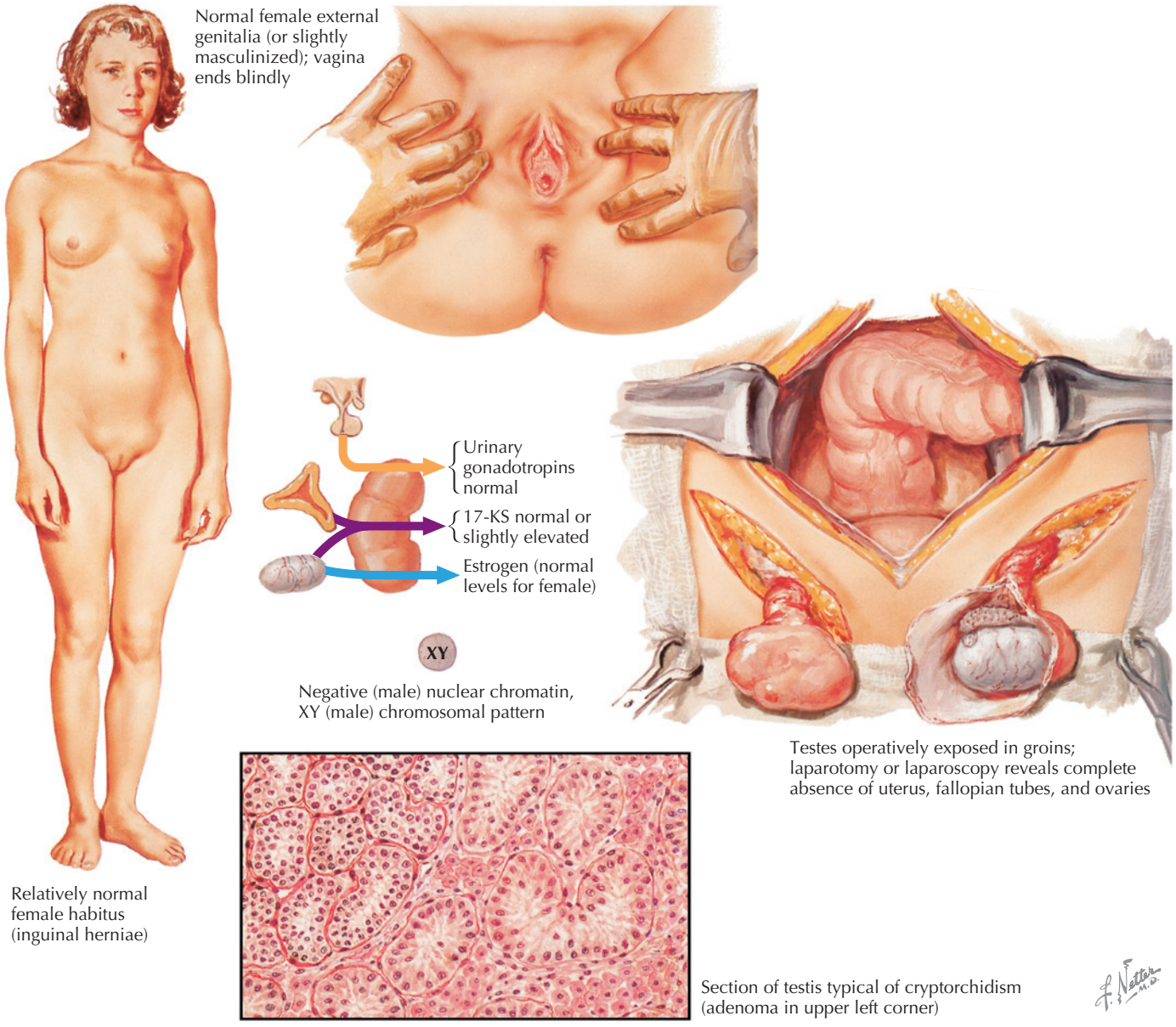


Figure 180.1 Androgen insensitivity syndrome

- Short or absent blind vaginal pouch
- Scant or no pubic or axillary hair
- Gonads (testes) may be palpable in the inguinal canal or labioscrotal folds
- Inguinal hernia (50%)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Pregnancy before first cycle
- Obstructed outflow tract (making menstruation cryptic)
- Gonadal dysgenesis
- Uterine agenesis
- Complete lack of Müllerian development (Mayer–Rokitansky–Küster–Hauser syndrome)

Associated Conditions: Infertility, amenorrhea, mildly impaired visual-spatial ability, horseshoe kidney.

Workup and Evaluation

Laboratory: Measurement of gonadotropins, estrogen, and testosterone (not required for diagnosis).
Imaging: Ultrasonography may be used to confirm the absence of the uterus, although it is not required for diagnosis.
Special Tests: Chromosomal analysis confirms the diagnosis.
Diagnostic Procedures: History and physical examination should provide the suggestion, confirmed by chromosomal analysis.

Pathologic Findings

The presence of testicular tissue in the labioscrotal folds.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and reassurance.

Specific Measures: Surgical extirpation of the gonads must be performed because of a 25%–30% risk of malignant gonadal tumor formation. This should not be performed until complete breast development has occurred and there has been epiphyseal closure (age, 18 years). Genetic counseling should be offered to siblings.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Frank discussion about the syndrome and its effects (infertility and amenorrhea). Patients should be informed that they carry an abnormal sex chromosome without mentioning the Y chromosome specifically because of the "male" connotations this carries. In addition, the term gonads should be used rather than testes when discussing the need for removal.

Drug(s) of Choice

None. Estrogen replacement therapy is generally not necessary after the removal of the gonads; the insensitivity of the peripheral tissues to the effects of circulating androgens results in unopposed estrogen effects from the low levels of estrogen that come from adrenal and peripheral conversion sources.

FOLLOW-UP

Patient Monitoring: Normal health maintenance once the diagnosis is established and the gonads are removed (at the appropriate time).
Prevention/Avoidance: None.
Possible Complications: There is a 25%–30% risk for malignant gonadal tumor formation if the testes are not removed (rare before the age of 25 years).
Expected Outcome: These patients are phenotypically, behaviorally, and psychologically female and continue to lead normal lives with the exception of infertility and amenorrhea.

MISCELLANEOUS

Pregnancy Considerations: These patients are infertile.
ICD-10-CM Codes: E29.8 (Other testicular dysfunction).

REFERENCES

LEVEL III

American College of Obstetricians and Gynecologists. Müllerian agenesis: diagnosis, management, and treatment. Committee Opinion No. 562. *Obstet Gynecol*. 2013;121:1134.

Baxter RM, Arboleda VA, Lee H, et al. Exome sequencing for the diagnosis of 46,XY disorders of sex development. *J Clin Endocrinol Metab*. 2015;100:E333.

Deans R, Creighton SM, Liao LM, et al. Timing of gonadectomy in adult women with complete androgen insensitivity syndrome (CAIS): patient preferences and clinical evidence. *Clin Endocrinol (Oxf)*. 2012;76:894.

Griffin JE, Wilson JD. The syndromes of androgen resistance. *N Engl J Med*. 1980;302:198.

Hiort O. The differential role of androgens in early human sex development. *BMC Med*. 2013;11:152.

Hyun G, Kolon TF. A practical approach to intersex in the newborn period. *Urol Clin North Am*. 2004;31:435, viii.

Kaprova-Pleskacova J, Stoop H, Brüggenwirth H, et al. Complete androgen insensitivity syndrome: factors influencing gonadal histology including germ cell pathology. *Mod Pathol*. 2014;27:721.

Quigley CA, De Bellis A, Marschke KB, et al. Androgen receptor defects: historical, clinical, and molecular perspectives. *Endocr Rev*. 1995;16:271.

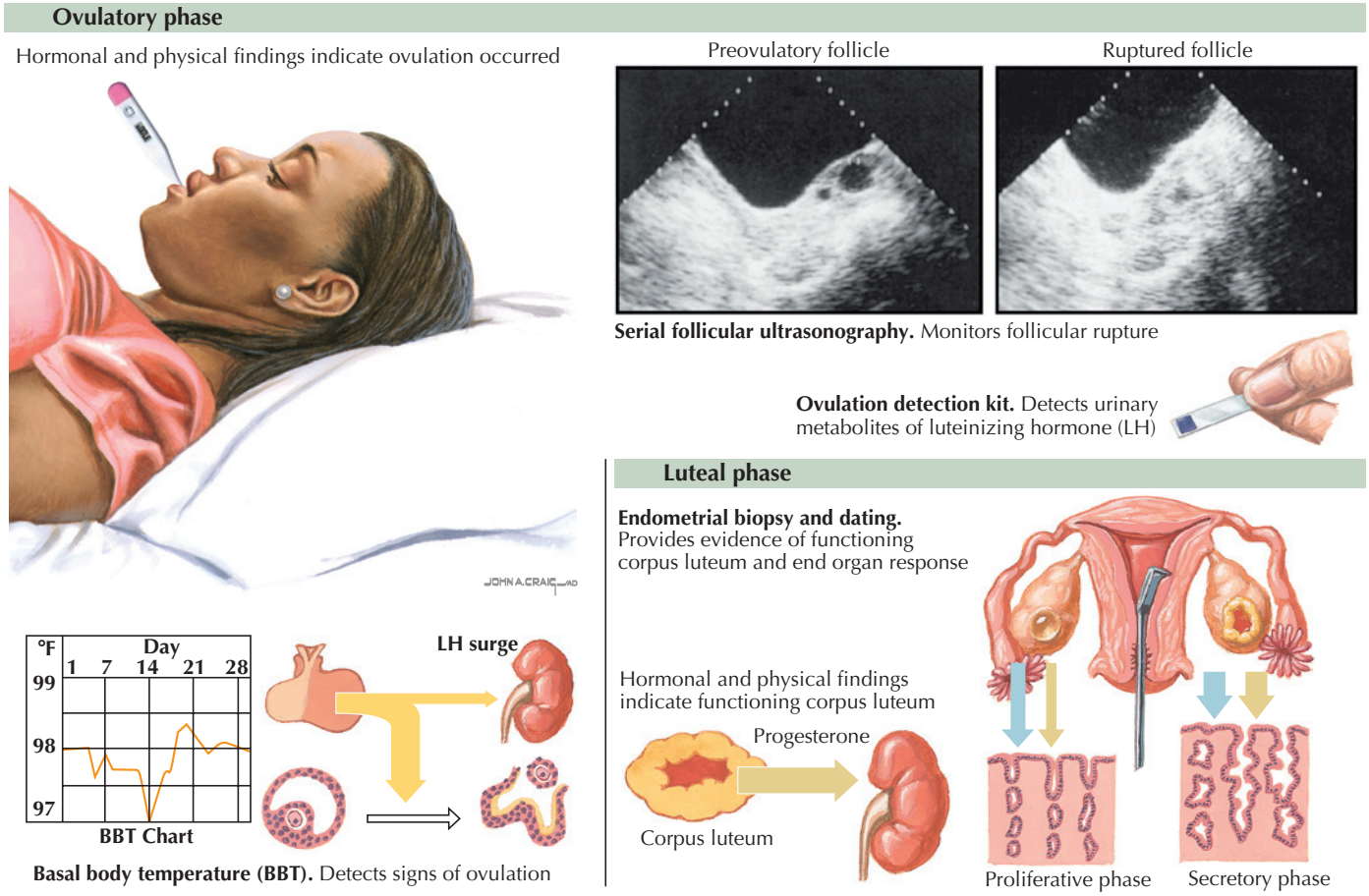


Figure 181.1 Assessment of ovulation

- Congenital abnormality of the outflow tract causing amenorrhea
- Cervical stenosis resulting in amenorrhea

Associated Conditions: Infertility, dysfunctional uterine bleeding, endometrial hyperplasia, and endometrial cancer.

Workup and Evaluation

Laboratory: Follicle-stimulating hormone (FSH), prolactin, thyroid function studies (eg, sensitive thyroid-stimulating hormone [TSH]), others as clinically indicated.
Imaging: No imaging indicated.
Special Tests: Basal body temperature charting may be used to detect ovulation, but other laboratory tests are more specific for establishing the cause.
Diagnostic Procedures: Endometrial biopsy performed during the presumed luteal phase. May also be helpful when endometrial hyperplasia, resulting from chronic estrogen exposure, is being considered.

Pathologic Findings

Endometrial—proliferative changes only, hyperplasia possible with prolonged anovulation.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation
Specific Measures: If pregnancy is desired, induction of ovulation. If pregnancy is not desired, periodic progestin therapy.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlets AP136 (Evaluating Infertility), AP137 (Treating Infertility), AP095 (Abnormal Uterine Bleeding), AP121 (Polycystic Ovary Syndrome), and AP047 (The Menopause Years).

Drug(s) of Choice

Ovulation Induction: clomiphene citrate 50 mg PO daily on days 5–10 of the menstrual cycle, may be increased to 100 mg PO daily on days 5–10 of the menstrual cycle if ovulation does not occur. Metformin (1500 mg/day) as an adjunctive treatment for ovulation induction (considered now as first-line therapy for polycystic ovary syndrome).
Progestin Withdrawal: medroxyprogesterone acetate 5–10 mg for 1–14 days each month.
Contraindications: Undiagnosed amenorrhea or bleeding.
Precautions: Progestins should not be used until pregnancy has been ruled out.

Alternative Drugs

- Aromatase inhibitors are efficacious as primary agents for ovulation induction (eg, letrozole; 2.5 mg or 5 mg administered for 5 days, beginning on cycle days 3–5).
- Norethindrone acetate 5–10 mg for 10–14 days each month for progestin withdrawal.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: Infertility, dysfunctional uterine bleeding, endometrial hyperplasia.
Expected Outcome: For many patients, normal ovulation and fertility may be restored.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy once pregnancy is achieved. The risk for multiple gestations is increased with clomiphene citrate therapy.
ICD-10-CM Codes: N97.0 (Anovulation).

REFERENCES

LEVEL I

Eisenhardt S, Schwarzmann N, Henschel V, et al. Early effects of metformin in women with polycystic ovary syndrome: a prospective randomized, double-blind, placebo-controlled trial. *J Clin Endocrinol Metab*. 2006;91:946.

Legro RS, Brzyski RG, Diamond MP, et al. Letrozole versus clomiphene for infertility in the polycystic ovary syndrome. *N Engl J Med*. 2014;371:119.

LEVEL II

Franik S, Kremer JA, Nelen WL, et al. Aromatase inhibitors for subfertile women with polycystic ovary syndrome. *Cochrane Database Syst Rev*. 2014;(2):CD010287.

Lord JM, Flight IH, Norman RJ. Metformin in polycystic ovary syndrome: systematic review and meta-analysis. *BMJ*. 2003;327:951.

LEVEL III

American College of Obstetricians and Gynecologists. Diagnosis of abnormal uterine bleeding in reproductive-aged women. Practice Bulletin No. 128. *Obstet Gynecol*. 2012;120:197.

American College of Obstetricians and Gynecologists. Endometrial cancer. Practice Bulletin No. 149. *Obstet Gynecol*. 2015;125:1006.

American College of Obstetricians and Gynecologists. Noncontraceptive uses of hormonal contraceptives. Practice Bulletin No. 110. *Obstet Gynecol*. 2010;115:206.

American College of Obstetricians and Gynecologists. Management of abnormal uterine bleeding associated with ovulatory dysfunction. Practice Bulletin No. 136. *Obstet Gynecol*. 2013;122:176.

American College of Obstetricians and Gynecologists. Menstruation in girls and adolescents: using the menstrual cycle as a vital sign. Committee Opinion No. 651. *Obstet Gynecol*. 2015;126:e143.

American College of Obstetricians and Gynecologists. Müllerian agenesis: diagnosis, management, and treatment. Committee Opinion No. 562. *Obstet Gynecol*. 2013;121:1134.

American College of Obstetricians and Gynecologists. Polycystic ovary syndrome. ACOG Practice Bulletin No. 108. *Obstet Gynecol*. 2009;114:936.

American College of Obstetricians and Gynecologists. Primary ovarian insufficiency in adolescents and young women. Committee Opinion No. 605. *Obstet Gynecol*. 2014;123:193.

Casper RF, Mitwally MF. Review: aromatase inhibitors for ovulation induction. *J Clin Endocrinol Metab*. 2006;91:760. Epub 2005 Dec 29.

De Vos M, Devroey P, Fauser BC. Primary ovarian insufficiency. *Lancet*. 2010;376:911.

Guzick DS. Polycystic ovary syndrome. *Obstet Gynecol*. 2004;103:181.

Hamilton-Fairley D, Taylor A. Anovulation. *BMJ*. 2003;327:546.

182 ASSISTED REPRODUCTION

THE CHALLENGE

To use advanced reproductive technology to assist couples who experience difficulty in conceiving through normal means.
Scope of the Problem: 10%–15% of couples who are infertile require or benefit from assisted reproductive technologies.
Objectives of Management: To achieve a successful pregnancy (carried to term) with minimal intervention. The treatment of an infertile couple is based on identifying the impediment to fertility and overcoming or bypassing it to achieve pregnancy. A number of techniques are available to accomplish this end. Most are less exotic than their acronyms suggest (Table 182.1). Among infertile couples seeking treatment, 85%–90% can be treated with conventional medical and surgical procedures and do not require assisted reproductive technologies such as in vitro fertilization (IVF).

TACTICS

Relevant Pathophysiology: The success of the treatment depends to a great extent on the identified cause of infertility because some problems are more easily overcome than others. It must be recognized that success is also a function of the age of the woman. It is also true that the rate of spontaneous pregnancy loss rapidly increases after the age of 35 years, adversely affecting success.
Strategies: Often a good starting point in the treatment of infertility is a frank and open discussion about sexuality and the physiology of conception. When couples have intercourse four or more times per week, more than 80% achieve pregnancy in the first 6 months of trying. In contrast, only approximately 15% of couples conceive when intercourse happens less than once a week. Intercourse should be maintained on an every-other-day cycle for the period from 3–4 days before the presumed ovulation until 2–3 days after that time. When ovulation disorders are encountered, ovulation induction or control may be used to enhance the likelihood of pregnancy. Tubal factor infertility may be addressed by either surgical repair of the damage or by bypassing the tubes completely through IVF and embryo transfer (IVF/ET). Success rates for surgical repair, including the reversal of previous sterilization procedure, are highly variable. Technologies, such as intracellular sperm injection, may allow fertility with as few as one sperm per oocyte.

Table 182.1 Abbreviations for Techniques

Abbreviation	Technique
AID	Artificial insemination, donor (using donor sperm, occasionally referred to as TDI or therapeutic donor insemination)
AIH	Artificial insemination, homologous (using the partner's sperm)
BT	Basal body temperature
GIFT	Gamete intrafallopian transfer (gametes placed in the fallopian tube for fertilization)
HSG	Hysterosalpingogram or uterine cavity radiograph
ICSI	Intracytoplasmic sperm injection
IUI	Intrauterine insemination (placement of either donor or husband sperm directly into the uterine cavity)
IVF/ET	In vitro fertilization with embryo transfer
PCT	Postcoital test or Huhner–Sims test
SPA	Sperm penetration assay (also known as a hamster egg test or zona-free egg penetration test)
ZIFT	Zygote intrafallopian transfer (fertilization takes place in vitro and the zygote is transferred to the fallopian tube to be transported into the uterine cavity)

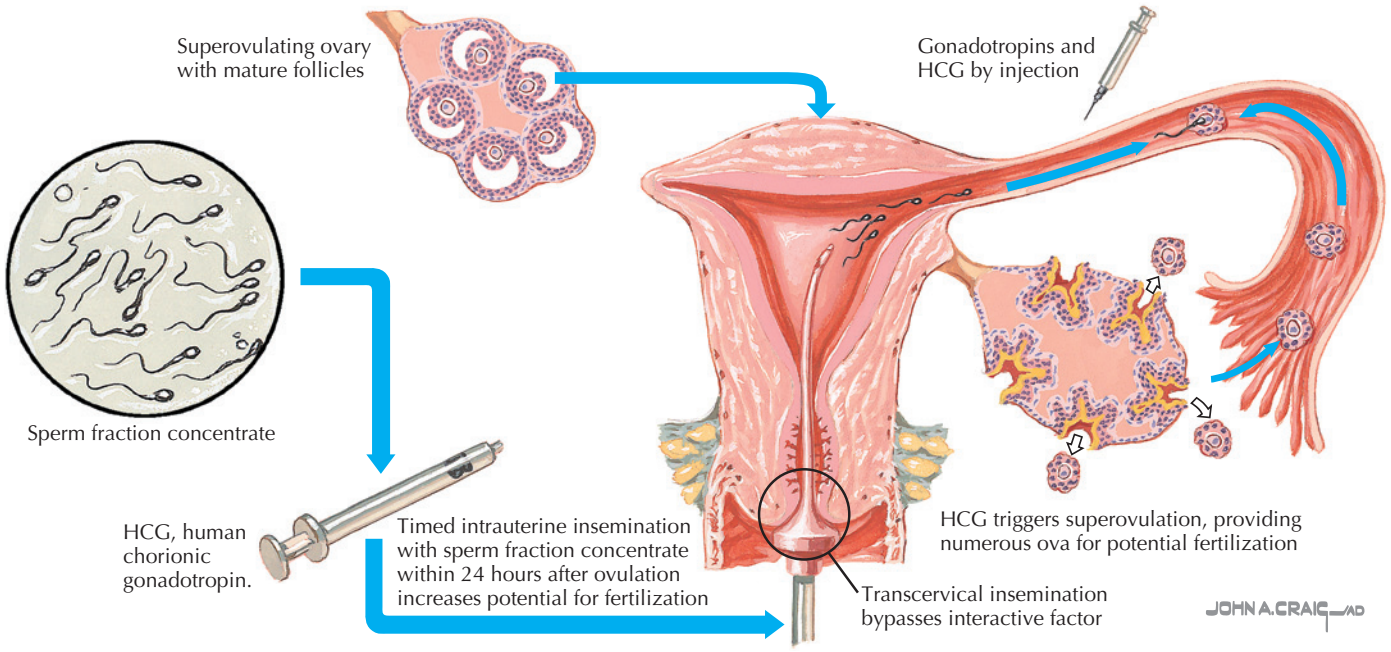


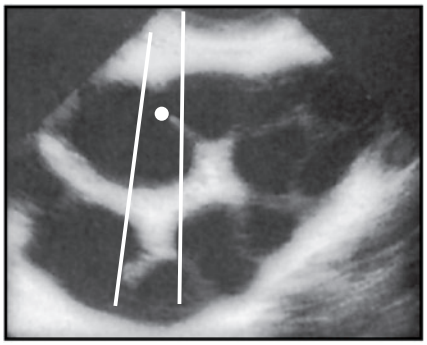
Figure 182.1 Basic options in assisted reproduction

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlets AP136 (Evaluating Infertility) and AP137 (Treating Infertility).

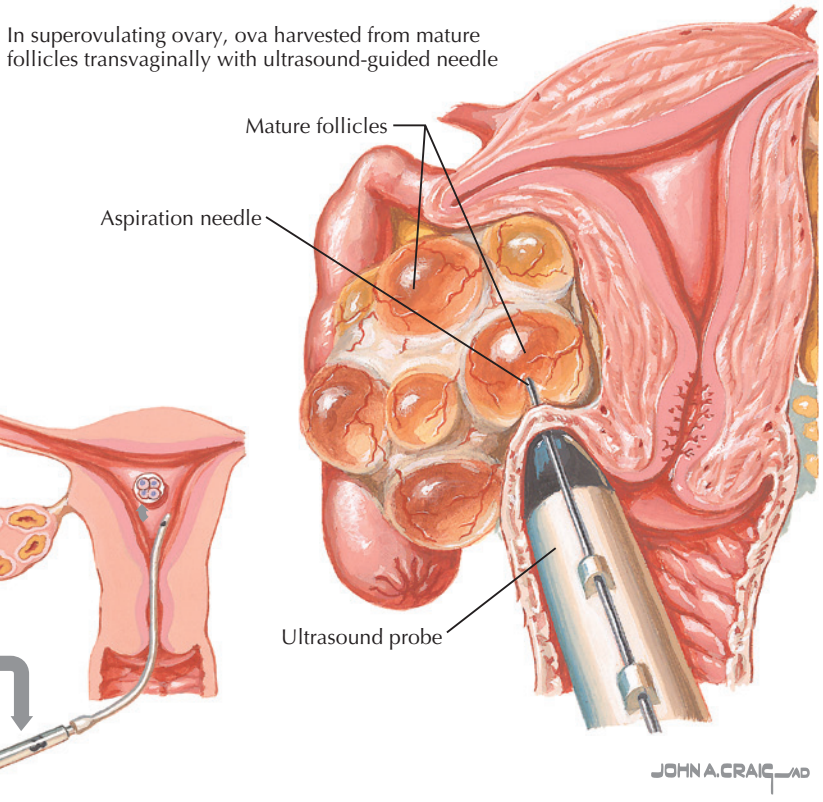
IMPLEMENTATION

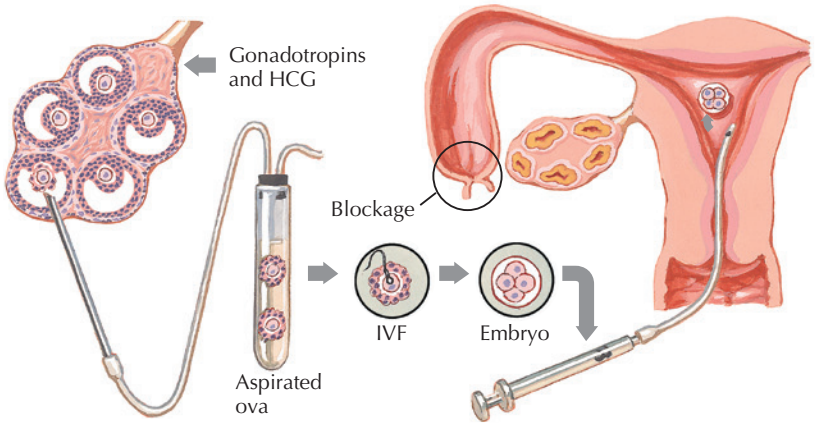
Special Considerations: Patients experiencing infertility are usually extremely motivated, following to the letter any suggestion made by the healthcare team. Hence, care must be taken that during the evaluation and treatment of infertility the couple's relationship is not destroyed in the process. In the end, there is no guarantee that efforts will result in a conception, so the healthcare team must not damage what is present in the quest of something that may not be. Couples should be reminded that if they miss having intercourse at the "right time" in a given month, remember that ovulations are like commuter trains—there is probably another one on its way. If the couple is in the mood for "making love," in any of its myriad forms, they should not worry about what the temperature chart is doing. To do otherwise is the fodder of cinematic comedy and divorce lawyers. Because infertility does not threaten life or health, many insurance providers do not cover the cost of its evaluation or treatment. A frank and open discussion about the time and expense involved in infertility evaluation allows the couple to make informed choices and avoids unnecessary financial or emotional hardship in the future.

All types of assisted reproductive technologies involving ovarian stimulation are associated with an increased incidence of multiple gestations (40%). The majority of these pregnancies are twins (25%), and 5% are higher-order gestations.



Ultrasonogram of follicular aspiration



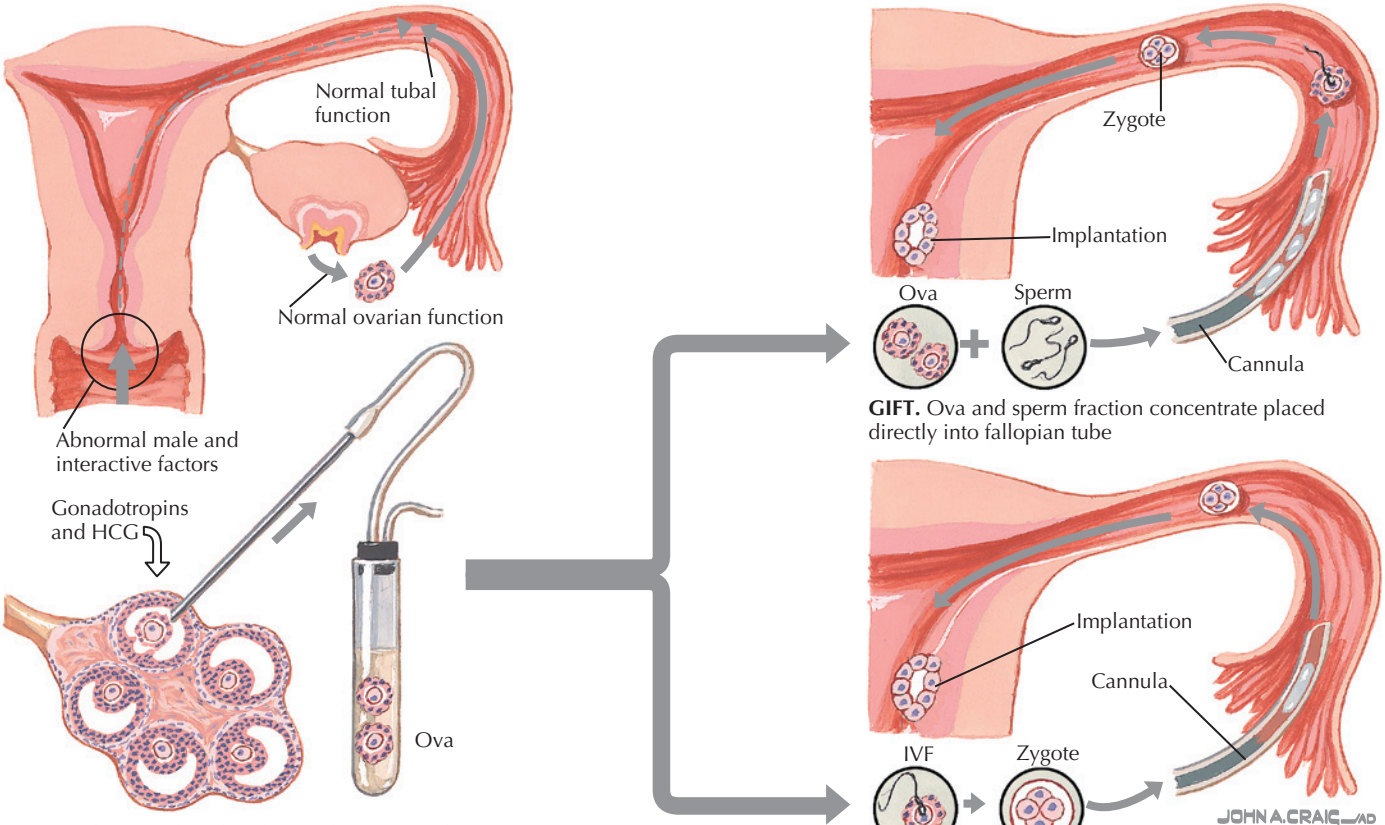


Hormonal stimulation induces superovulation; ova aspirated from mature follicles

HCG, human chorionic gonadotropin.

Ova fertilized in vitro (IVF) with sperm fraction concentrate. Embryo transferred directly into uterus, bypassing tubal occlusion

Figure 182.2 Advanced option: in vitro fertilization



Superovulation induced with gonadotropins and HCG. Ova aspirated from mature follicles for intrafallopian transfer techniques

HCG, human chorionic gonadotropin.

GIFT. Ova and sperm fraction concentrate placed directly into fallopian tube

ZIFT. Ova fertilized in vitro (IVF); resulting zygotes placed directly into fallopian tube

Figure 182.3 Advanced options: Gamete intrafallopian transfer (GIFT) and zygote intrafallopian transfer (ZIFT)

REFERENCES

LEVEL III

American College of Obstetricians and Gynecologists. Management of abnormal uterine bleeding associated with ovulatory dysfunction. Practice Bulletin No. 136. *Obstet Gynecol*. 2013;122:176.

American College of Obstetricians and Gynecologists. Multifetal gestations: twin, triplet, and higher-order multifetal pregnancies. Practice Bulletin No. 144. *Obstet Gynecol*. 2014;123:1118.

American College of Obstetricians and Gynecologists. Polycystic ovary syndrome. ACOG Practice Bulletin No. 108. *Obstet Gynecol*. 2009;114:936.

American College of Obstetricians and Gynecologists. Perinatal risks associated with assisted reproductive technology. ACOG Committee Opinion 324. *Obstet Gynecol*. 2005;106:1143.

American College of Obstetricians and Gynecologists. Preimplantation Genetic Screening for Aneuploidy. ACOG Committee Opinion No. 430. *Obstet Gynecol*. 2009;113:766.

American College of Obstetricians and Gynecologists. Surrogate motherhood. ACOG Committee Opinion No. 397. *Obstet Gynecol*. 2008;111:465.

American College of Obstetricians and Gynecologists. Using preimplantation embryos for research. ACOG Committee Opinion 347. *Obstet Gynecol*. 2006;108:1305.

Braude P, Rowell P. Assisted conception. II—In vitro fertilisation and intracytoplasmic sperm injection. *BMJ*. 2003;327:852.

Braude P, Rowell P. Assisted conception. III—Problems with assisted conception. *BMJ*. 2003;327:920.

Ory SJ. The national epidemic of multiple pregnancy and the contribution of assisted reproductive technology. *Fertil Steril*. 2013;100:929.

Rowell P, Braude P. Assisted conception. I—General principles. *BMJ*. 2003;327:799.

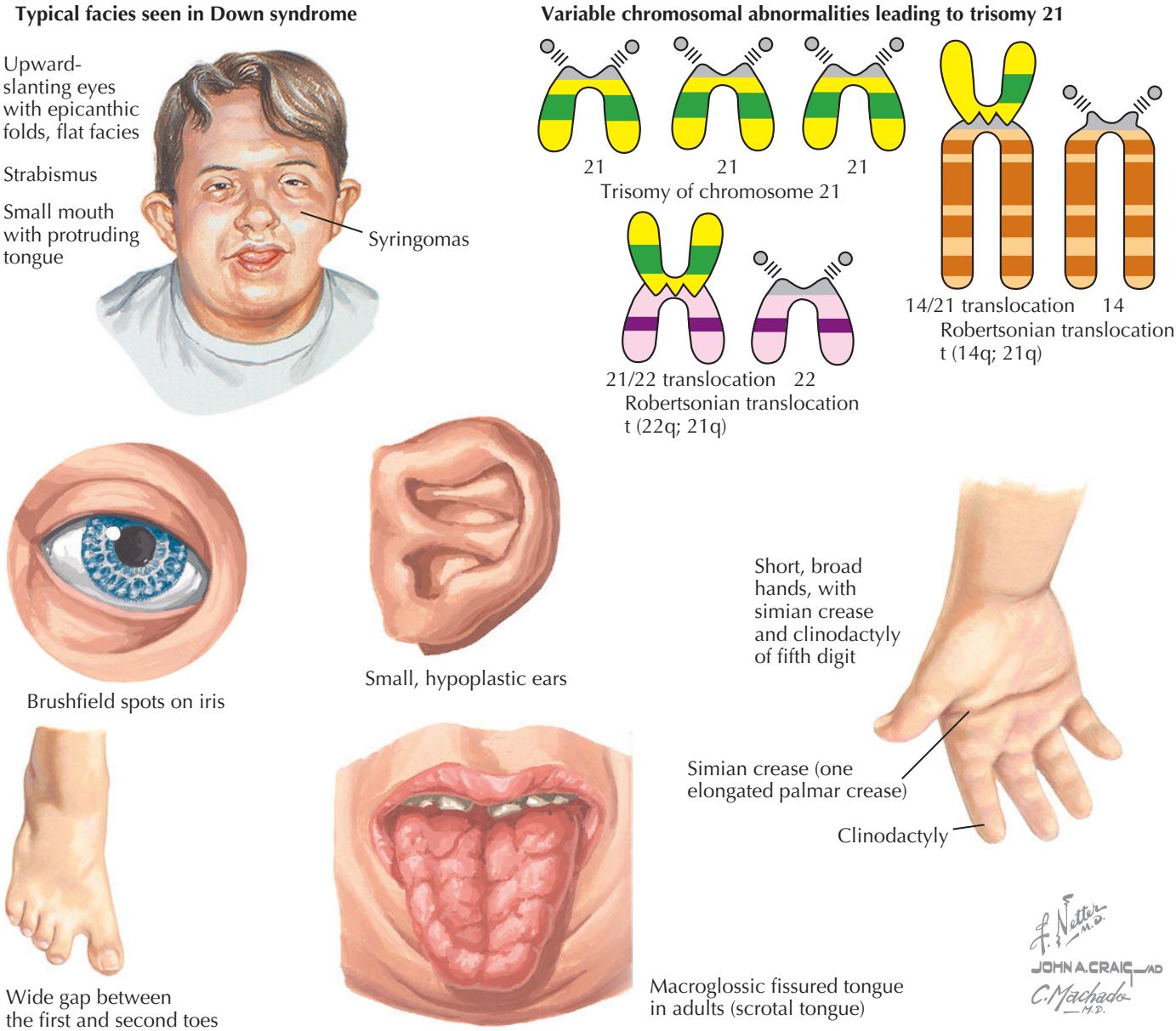


Figure 183.1 Characteristics and variable chromosomal abnormalities in trisomy 21 Down syndrome

villus sampling or amniocentesis may be performed for antenatal diagnosis. Testing for cell-free DNA in maternal blood can detect more than 99% of affected pregnancies.

Diagnostic Procedures: History, physical examination, chromosomal analysis (antenatal or after birth). The presence of a whorl on the ball of the foot generally indicates a normal child, not a trisomy.

Pathologic Findings

Physical changes as noted. Alzheimer plaques common after the age of 20 years.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Genetic and cardiac evaluation and counseling. Assessment of abilities and assistance with activities of daily living as appropriate.

Specific Measures: Based on the needs of the individual. Parental support and counseling are vital.

Diet: No specific dietary changes indicated.

Activity: No restriction, except if cardiac abnormalities are present.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlets AP094 (Genetic Disorders) and AP060 (Having a Baby After Age 35).

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Normal health maintenance, monitor for renal or cardiac complications.

Prevention/Avoidance: Recurrence rate is 1% for true trisomy, 16%–20% for translocation, and 100% for trisomy involving chromosome 12.

Possible Complications: Congenital heart disease (50%), bowel obstruction (10%), Hirschsprung disease (3%), thyroid disease (5%–8%), and Alzheimer disease.

Expected Outcome: One-third of patients have normal development during the first year of life; growth, language, and mental development slow thereafter. Life expectancy is reduced by cardiac and other associated anomalies. Life potential varies from ability to live and work within sheltered environment to profound restriction. Premature aging is common, with life expectancy of 50–60 years.

MISCELLANEOUS

Pregnancy Considerations: Chorionic villus sampling (9–10 weeks) or amniocentesis (13–15 weeks) should be offered for patients at risk by age or other factors. Maternal serum α-fetoprotein (low) or triple or quadruple screening (combinations of maternal serum α-fetoprotein, β-human chorionic gonadotropin, estriol, PAPP-A, placental growth factor, and inhibin A in maternal serum) should be performed at 14–16 weeks. Pregnancy is possible for patients with Down syndrome; recurrence rate is 50%.

ICD-10-CM Codes: Q90.9 (Down syndrome, unspecified).

REFERENCES

LEVEL I

Bahado-Singh RO, Wapner R, Thom E, First Trimester Maternal Serum Biochemistry and Fetal Nuchal Translucency Screening Study Group, et al. Elevated first-trimester nuchal translucency increases the risk of congenital heart defects. *Am J Obstet Gynecol*. 2005;192:1357.

Canick JA, Lambert-Messerlian GM, Palomaki GE, First and Second Trimester Evaluation of Risk (FASTER) Trial Research Consortium, et al. Comparison of serum markers in first-trimester Down syndrome screening. *Obstet Gynecol*. 2006;108:1192.

Malone FD, Canick JA, Ball RH, First- and Second-Trimester Evaluation of Risk (FASTER) Research Consortium, et al. First-trimester or second-trimester screening, or both, for Down's syndrome. *N Engl J Med*. 2005; 353:2001.

Malone FD, D'Alton ME, Society for Maternal-Fetal Medicine. First-trimester sonographic screening for Down syndrome. *Obstet Gynecol*. 2003;102:1066.

LEVEL II

Freeman SB, Allen EG, Oxford-Wright CL, et al. The National Down Syndrome Project: Design and implementation. *Public Health Rep*. 2007;122:62.

Lou S, Mikkelsen L, Hvidman L, et al. Does screening for Down's syndrome cause anxiety in pregnant women? A systematic review. *Acta Obstet Gynecol Scand*. 2015;94:15.

Norton ME, Jacobsson B, Swamy GK, et al. Cell-free DNA analysis for noninvasive examination of trisomy. *N Engl J Med*. 2015;372:1589.

Sonek JD, Cicero S, Neiger R, et al. Nasal bone assessment in prenatal screening for trisomy 21. *Am J Obstet Gynecol*. 2006;195:1219.

LEVEL III

American College of Obstetricians and Gynecologists. Cell-free DNA screening for fetal aneuploidy. Committee Opinion No. 640. *Obstet Gynecol*. 2015;126:e31.

American College of Obstetricians and Gynecologists. Ethical issues in genetic testing. ACOG Committee Opinion No. 410. *Obstet Gynecol*. 2008;111:1495.

American College of Obstetricians and Gynecologists. Invasive prenatal testing for aneuploidy. ACOG Practice Bulletin No. 88. *Obstet Gynecol*. 2007;110:1459.

American College of Obstetricians and Gynecologists. Screening for fetal chromosomal abnormalities. ACOG Practice Bulletin 77. *Obstet Gynecol*. 2007;109:217.

American College of Obstetricians and Gynecologists. The use of chromosomal microarray analysis in prenatal diagnosis. Committee Opinion No. 581. *Obstet Gynecol*. 2013;122:1374.

American College of Obstetricians and Gynecologists. Ultrasonography in pregnancy. ACOG Practice Bulletin No. 101. *Obstet Gynecol*. 2009;113: 451.

Lott IT, Dierssen M. Cognitive deficits and associated neurological complications in individuals with Down's syndrome. *Lancet Neurol*. 2010; 9:623.

Nicolaides KH. Nuchal translucency and other first-trimester sonographic markers of chromosomal abnormalities. *Am J Obstet Gynecol*. 2004;191: 45.

Reddy UM, Mennuti MT. Incorporating first-trimester Down syndrome studies into prenatal screening: executive summary of the National Institute of Child Health and Human Development workshop. *Obstet Gynecol*. 2006;107:167.

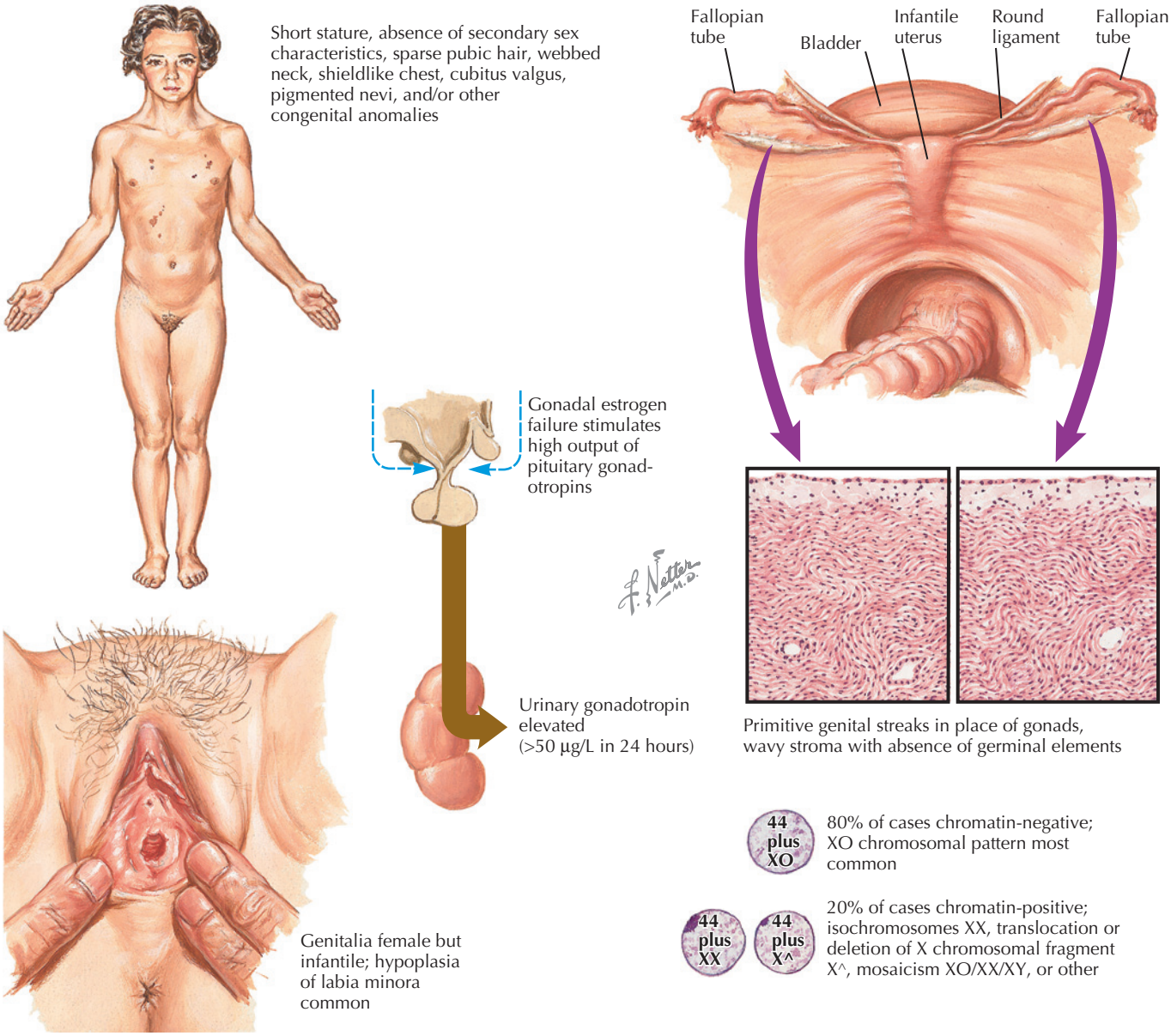


Figure 184.1 Gonadal dysgenesis

ETIOLOGY AND PATHOGENESIS

Causes: Pure gonadal dysgenesis—45,XO (Turner syndrome); 46,XY gonadal dysgenesis (Swyer syndrome); 46,XX q5 X chromosome long-arm deletion, mixed or mosaic (50%).
Risk Factors: Translocations involving the X chromosome (rare).

SIGNS AND SYMPTOMS

Based on the amount of chromatin lost

- Primary amenorrhea and infertility (the most common cause of failure to begin menstruation is gonadal dysgenesis; in approximately 60% of women with primary amenorrhea, an abnormality of gonadal differentiation or function has occurred during the fetal or neonatal period)
- Absent or grossly abnormal gonad development

DIAGNOSTIC APPROACH

Differential Diagnosis

- Polycystic ovary syndrome
- Hypothyroidism
- Growth hormone deficiency or glucocorticoid excess
- Androgen insensitivity syndrome (male pseudohermaphroditism, testicular feminization)
- Intersex abnormality
- Enzymatic defects (such as 17α-hydroxylase deficiency)
- Structural genital tract abnormalities (uterine and/or vaginal agenesis or an imperforate hymen)
- Ovarian insensitivity syndrome (resistant ovary [Savage] syndrome)
- Follicular depletion (autoimmune disease, infection [mumps], infiltrative disease processes [tuberculosis, galactosemia])

Associated Conditions: Amenorrhea, infertility, incomplete or abnormal external genitalia, and premature menopause.

Workup and Evaluation

Laboratory: Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels are high (nonspecific). FSH is usually elevated in gonadal dysgenesis. Assessment of thyroid function, prolactin, or growth hormone if indicated by the differential diagnosis being considered.
Imaging: Pelvic ultrasonography to evaluate the presence and condition of upper genital tract organs.
Special Tests: Karyotype.
Diagnostic Procedures: History, physical examination, karyotyping.

Pathologic Findings

Abnormal karyotype. Germ cell involution occurs soon after they migrate into the undifferentiated gonad. This results in fibrous streak gonads that are hormonally inactive.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, screening for associated defects, counseling about menstrual and fertility issues.
Specific Measures: Hormone replacement therapy. When there is a mosaicism involving a Y chromosome, surgical extirpation of the gonads must be performed because of a 25%–30% risk of malignant gonadal tumors. Timing of gonadal removal in patients with a Y chromosome is generally delayed until pubertal changes are complete.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Extensive counseling about sexual maturation and fertility.

Drug(s) of Choice

Adolescents are much more sensitive to the effects of estrogen than are postmenopausal women, allowing doses in the range of 0.3 mg of conjugated estrogen, 0.5 mg of estradiol, or their equivalent, daily. After 6–12 months of therapy at this level, the dose should be doubled and a progestin (eg, medroxyprogesterone acetate 10 mg for the first 12 days of the month) should be added, or the patient's treatment should be switched to combination oral contraceptives. This generally results in regular menstruation, and normal pubertal development proceeds on its own when the patient reaches a bone age of 13 years.
Contraindications: Undiagnosed amenorrhea.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: Prenatal chromosomal analysis for those known to carry translocations (detection only, not prevention, although the couple may choose not to continue the pregnancy based on the findings).
Possible Complications: Gonadal malignancy or virilization in those with Y chromatin present. Others based on cause.
Expected Outcome: Reasonably normal lives with the exception of fertility.

MISCELLANEOUS

Pregnancy Considerations: These patients may be infertile. In pure gonadal dysgenesis and XX/XY mosaicism, a uterus is present. Consequently, some patients may achieve pregnancy. Pregnancy is associated with a 50% chance of aneuploidy.
ICD-10-CM Codes: Q50.01 (Congenital absence of ovary, unilateral), Q50.02 (Congenital absence of ovary, bilateral), and Q50.32 (Ovarian streak).

REFERENCES

LEVEL II

Gravholt CH, Fedder J, Naeraa RW, et al. Occurrence of gonadoblastoma in females with Turner syndrome and Y chromosome material: a population study. *J Clin Endocrinol Metab*. 2000;85:3199.

Ogata T, Muroya K, Matsuo N, et al. Turner syndrome and Xp deletions: clinical and molecular studies in 47 patients. *J Clin Endocrinol Metab*. 2001;86:5498.

LEVEL III

American College of Obstetricians and Gynecologists. Menstruation in girls and adolescents: using the menstrual cycle as a vital sign. Committee Opinion No. 651. *Obstet Gynecol*. 2015;126:e143.

American College of Obstetricians and Gynecologists. Müllerian agenesis: diagnosis, management, and treatment. Committee Opinion No. 562. *Obstet Gynecol*. 2013;121:1134.

American College of Obstetricians and Gynecologists. Primary ovarian insufficiency in adolescents and young women. Committee Opinion No. 605. *Obstet Gynecol*. 2014;123:193.

Bondy CA, Turner Syndrome Study Group. Care of girls and women with Turner syndrome: a guideline of the Turner Syndrome Study Group. *J Clin Endocrinol Metab*. 2007;92:10.

Master-Hunter T, Heiman DL. Amenorrhea: evaluation and treatment. *Am Fam Physician*. 2006;73:1374.

Park SY, Jameson JL. Minireview: transcriptional regulation of gonadal development and differentiation. *Endocrinology*. 2005;146:1035.

Ranke MB, Saenger P. Turner's syndrome. *Lancet*. 2001;358:309.

Sybert VP, McCauley E. Turner's syndrome. *N Engl J Med*. 2004;351:1227.

185 HIRSUTISM

INTRODUCTION

Description: Hirsutism refers to increased or excessive hair growth only. It may be idiopathic (hypertrichosis) or caused by androgen-stimulated excessive growth. Hypertrichosis involves increased hair on the extremities and tends to be ethnic, racial, or familial in origin. This is not considered hirsutism.
Prevalence: 5%–10% of women; variable within ethnic groups; 60% of women with Cushing disease.
Predominant Age: After puberty.
Genetics: Influenced by the number of hair follicles present, a function of race and ethnicity.

ETIOLOGY AND PATHOGENESIS

Causes: Familial, idiopathic, increased hair follicle androgens (5α-reductase). Increased androgen production—ovarian (polycystic ovary syndrome, hilus cell hyperplasia/tumor, arrhenoblastoma, adrenal rest), adrenal (congenital adrenal hyperplasia [10%–15% of women with hirsutism], Cushing disease, virilizing carcinoma or adenoma). Drugs—minoxidil, androgens (including Danocrine), phenytoin, diazoxide. Other (hypothyroidism, hyperprolactinemia). Follicle size and type (vellus or terminal) of hair can change in response to numerous factors, particularly androgens.
Risk Factors: Androgen use, danazol sodium, minoxidil, phenytoin, and diazoxide.

SIGNS AND SYMPTOMS

- Increased or excessive hair growth, primarily along the angle of the jaw, upper lip, and chin.
- For most patients, hirsutism dates from puberty
- Menstrual irregularity or amenorrhea (60%)
- Acne (40%)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Virilization (especially when hirsutism is in a male pattern)
- Familial hypertrichosis
- Cushing disease (truncal obesity, facial rounding, cervicodorsal fat deposition [buffalo hump], and red or purple striae are often not fully developed)
- Polycystic ovary syndrome
- Iatrogenic hirsutism (patients may use steroids for a number of reasons, legal and otherwise, and may not recognize the possibility of virilizing side effects; the use of danazol sodium [eg, for endometriosis therapy] also may be associated with increased hair growth)
- Acromegaly
- Hypothyroidism
- Hyperprolactinemia
- Anorexia nervosa

Associated Conditions: Obesity, menstrual irregularity, amenorrhea, infertility, acne, oily skin, increased libido, alopecia, acanthosis nigricans.

Workup and Evaluation

Laboratory: Evaluation for possible virilizing process (prolactin, dehydroepiandrosterone sulfate [DHEA-s], follicle-stimulating hormone [FSH], thyroid screening). Patients suspected of having adrenal sources of hyperandrogenicity may be screened by measuring 24-hour urinary-free cortisol, by performing adrenocorticotropic hormone (ACTH) stimulation tests, or by performing an overnight dexamethasone suppression test. Circulating testosterone is generally normal or only mildly elevated (>1.5 ng/mL). Of patients with idiopathic hirsutism, 80% have elevated levels of 3α-diol-G (metabolite of 5α-reductase).
Imaging: No imaging indicated, except as indicated by physical or laboratory findings.
Special Tests: Clitoral index may be useful if virilization is suspected. The clitoral index is defined as the vertical dimension times the horizontal dimension, in millimeters. The normal range is from 9 to 35 mm, with borderline values in the range of 36–99 mm. Values of more than 100 mm indicate severe hyperandrogenicity and should prompt aggressive evaluation and referral. Hirsutism may be quantified using the Ferriman-Gallwey scoring system, though cutoff scores should be adjusted based upon ethnicity (>8 for Whites and Blacks, >9–10 for Mediterranean, Hispanic, and Middle Eastern women).
Diagnostic Procedures: History and physical examination, Ferriman–Gallwey score greater than 8.

Pathologic Findings

Based on underlying pathophysiologic conditions.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, shaving, depilatories, or electrolysis. Topical treatment of acne (if present). Weight reduction if obesity is present.
Specific Measures: Suppressive therapies reduce the growth of new hair, but once a hair follicle is induced, or turned on, it continues to grow. For this reason, shaving, depilatories, or electrolysis may be required. These are satisfactory only if combined with other therapies to reduce new growth.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Instruction on management of unwanted hair. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP121 (Polycystic Ovary Syndrome).

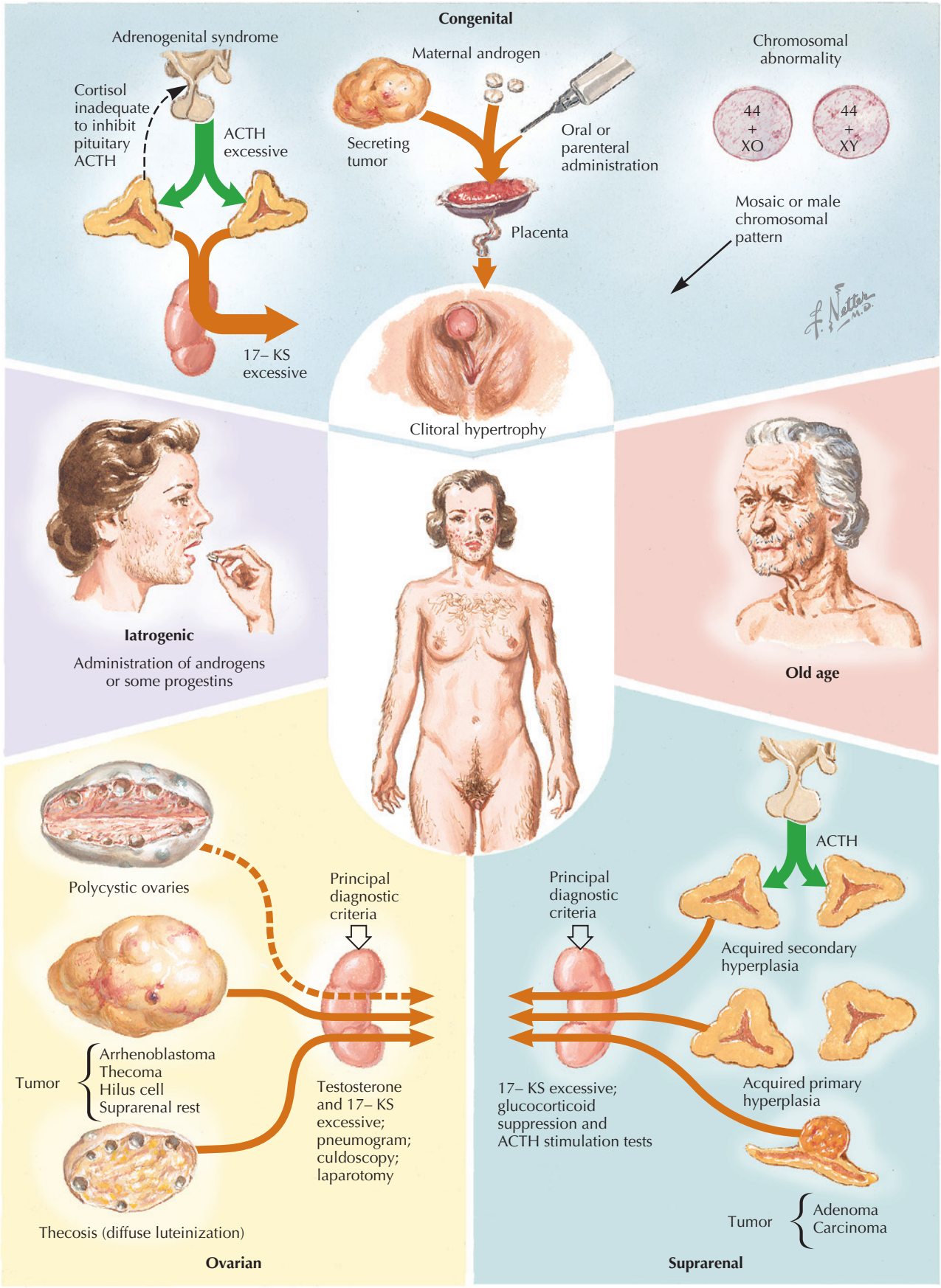
Drug(s) of Choice

- 5α-reductase inhibitors (finasteride 5 mg PO daily).
- Polycystic ovary syndrome—combination oral contraceptives: spironolactone 100–200 mg PO daily, medroxyprogesterone acetate (Depo-Provera 150–300 mg IM every 3 months, metformin 1500 mg/day, or other insulin sensitizers). Aromatase inhibitors may be used if ovulation induction is desired (eg, letrozole 2.5 mg or 5 mg administered for 5 days, beginning on cycle days 3–5).
- Hyperandrogenicity of adrenal origin—cortisol administration. If DHEA-s is elevated, dexamethasone 0.25–0.5 mg PO every bedtime may be added.

Contraindications: Pregnancy (spironolactone and finasteride are category X drugs and patients of child-bearing potential must use reliable contraception).

FOLLOW-UP

Patient Monitoring: Normal health maintenance once a diagnosis is established. Contraception and weight maintenance should also



ACTH, adrenocorticotropic hormone.

Figure 185.1 Causes of hirsutism

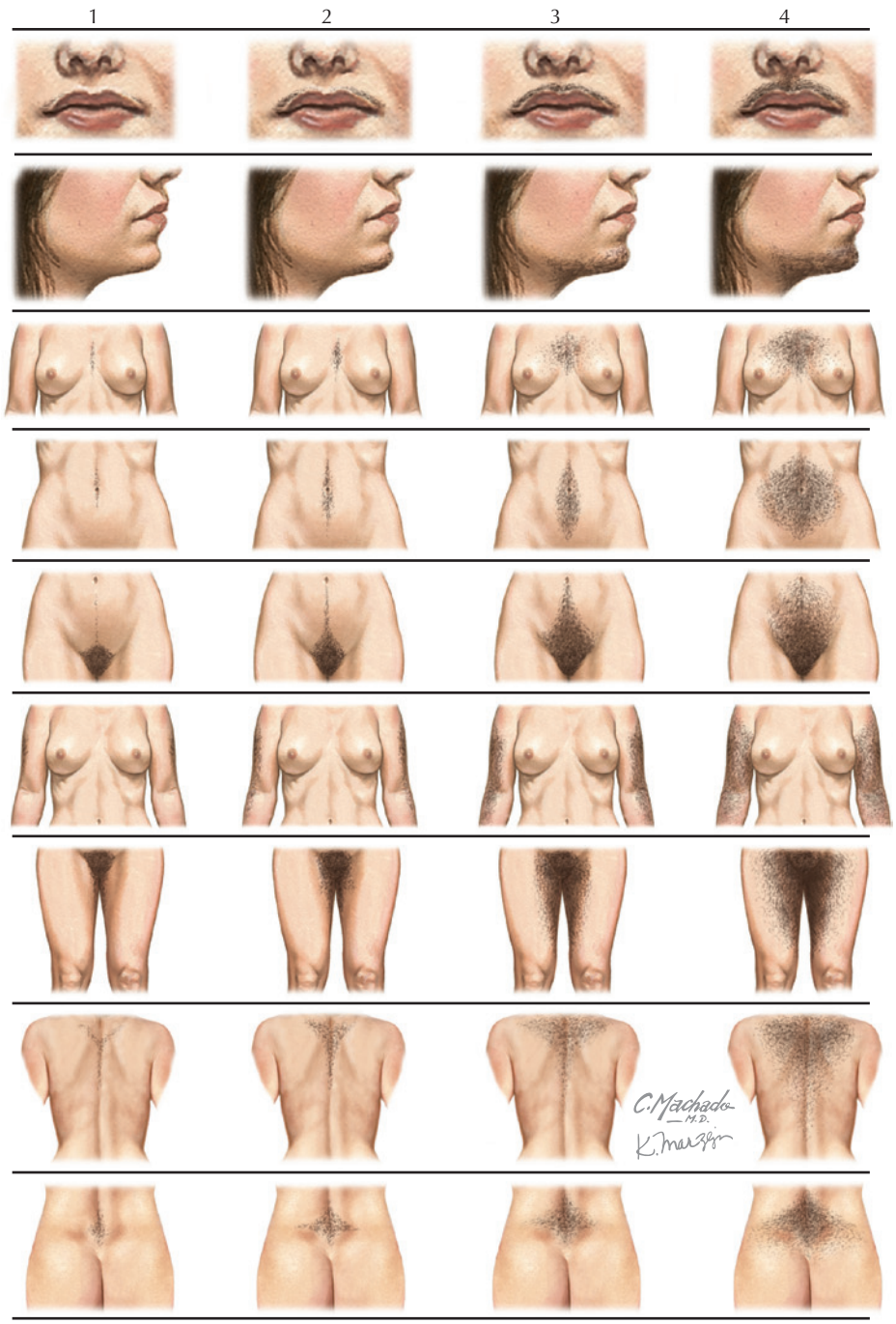


Figure 185.2 Hirsutism and virilization

be addressed. There is an increased risk of diabetes for patients with polycystic ovaries.

Prevention/Avoidance: None.

Possible Complications: Permanent induction of hair changes. Chronic anovulation is associated with increased risk of endometrial hyperplasia and cancer.

Expected Outcome: Approximately 70% response after 1 year of therapy may be expected.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, although some metabolic causes of hirsutism may result in reduced fertility or virilization of a fetus.

ICD-10-CM Codes: L68.0 (Hirsutism) and L68.9 (Hypertrichosis, unspecified).

REFERENCES

LEVEL I

Azziz R, Ehrmann D, Legro RS, et al., PCOS/Troglitazone Study Group. Troglitazone improves ovulation and hirsutism in the polycystic ovary syndrome: a multicenter, double blind, placebo-controlled trial. *J Clin Endocrinol Metab*. 2001;86:1626.

Moghetti P, Tosi F, Tosti A, et al. Comparison of spironolactone, flutamide, and finasteride efficacy in the treatment of hirsutism: a randomized, double blind, placebo-controlled trial. *J Clin Endocrinol Metab*. 2000;85:89.

LEVEL II

Guido M, Romualdi D, Giuliani M, et al. Drospirenone for the treatment of hirsute women with polycystic ovary syndrome: a clinical, endocrinological, metabolic pilot study. *J Clin Endocrinol Metab*. 2004;89:2817.

Harborne L, Fleming R, Lyall H, et al. Metformin or antiandrogen in the treatment of hirsutism in polycystic ovary syndrome. *J Clin Endocrinol Metab*. 2003;88:4116.

Ibanez L, Lopez-Bermejo A, del Rio L, et al. Combined low-dose pioglitazone, flutamide, and metformin for women with androgen excess. *J Clin Endocrinol Metab*. 2007;92:1710.

Ibanez L, Valls C, Potau N, et al. Sensitization to insulin in adolescent girls to normalize hirsutism, hyperandrogenism, oligomenorrhea, dyslipidemia, and hyperinsulinism after precocious pubarche. *J Clin Endocrinol Metab*. 2000;85:3526.

LEVEL III

American College of Obstetricians and Gynecologists. Noncontraceptive uses of hormonal contraceptives. Practice Bulletin No. 110. *Obstet Gynecol*. 2010;115:206.

American College of Obstetricians and Gynecologists. Polycystic ovary syndrome. ACOG Practice Bulletin No. 108. *Obstet Gynecol*. 2009;114:936.

Azziz R. The evaluation and management of hirsutism. *Obstet Gynecol*. 2003;101:995.

Bergfeld WF. Hirsutism in women. Effective therapy that is safe for long-term use. *Postgrad Med*. 2000;107:93, 99.

Curran DR, Moore C, Huber T. Clinical inquiries. What is the best approach to the evaluation of hirsutism? *J Fam Pract*. 2005;54:465.

Escobar-Morreale HF, Carmina E, Dewailly D, et al. Epidemiology, diagnosis and management of hirsutism: a consensus statement by the Androgen Excess and Polycystic Ovary Syndrome Society. *Hum Reprod Update*. 2012;18:146.

Ferriman D, Gallwey JD. Clinical assessment of body hair growth in women. *J Clin Endocrin*. 1961;21:1440.

Rosenfield RL. Clinical practice. Hirsutism. *N Engl J Med*. 2005;353:2578.

Setji TL, Brown AJ. Polycystic ovary syndrome: diagnosis and treatment. *Am J Med*. 2007;120:128.

HYPERPROLACTINEMIA

186

INTRODUCTION

Description: Hyperprolactinemia is the pathologic elevation of serum prolactin levels. The finding of elevated levels of prolactin is nonspecific with respect to the cause, thereby requiring careful clinical evaluation.

Prevalence: Uncommon; reports vary from 1% to 30%, depending on the population studied.

Predominant Age: Reproductive age.

Genetics: No genetic pattern. A germline loss-of-function mutation in the prolactin receptor gene (*PRLR*) has been reported.

ETIOLOGY AND PATHOGENESIS

Causes: Pituitary adenoma (most common). Pharmacologic—most often those that affect dopamine or serotonin: major tranquilizers (phenothiazines), trifluoperazine (Stelazine), and haloperidol (Haldol); some antipsychotic medications; metoclopramide (Reglan); less often, α-methyldopa and reserpine. Other—herpes zoster, chest wall/breast stimulation or irritation, physiologic during pregnancy, or after childbirth and/or breastfeeding. Most act by blocking gonadotropin-releasing hormone (GnRH) release, thus lowering luteinizing hormone (LH).

Risk Factors: Exposure to known pharmacologic agents, specific disease processes (Table 186.1).

SIGNS AND SYMPTOMS

- Asymptomatic
- Bilateral, spontaneous milky discharge from both breasts (75%)
- Amenorrhea (30%)
- Large adenoma, clinical appearance of impingement on the optic nerve or adjacent structures
- Fertility may be impaired even without menstrual cycle disruption

DIAGNOSTIC APPROACH

Differential Diagnosis

- Pregnancy
- Breast cancer
- Chronic nipple stimulation
- Hypothyroidism
- Sarcoidosis
- Lupus
- Cirrhosis or hepatic disease
- Radiculopathy (herpetic)

Associated Conditions: One-third of patients with elevated prolactin levels experience amenorrhea or infertility. Prolonged amenorrhea is associated with an increased risk of osteoporosis.

Workup and Evaluation

Laboratory: Serum prolactin level. Pregnancy should always be considered if menses are absent.

Imaging: Computed tomography (CT) or magnetic resonance imaging (MRI) to evaluate the pituitary and surrounding bony structures; MRI is now preferred.

Table 186.1 Sources of Elevated Prolactin Levels

Pharmacologic (Examples)	Pathophysiologic Causes
Anesthetics	Central nervous system
Central nervous system: dopamine-depleting agents	Cavernous sinus thrombosis
α-Methyldopa	Infection
Monoamine oxidase inhibitors	Neurofibromas
Reserpine	Temporal arteritis
Dopamine receptor blocking agents	Tumors and cysts (all types)
Domperidone	Hypothalamic
Haloperidol	Craniopharyngioma
Metoclopramide	Glioma
Phenothiazines	Granulomas
Pimozide	Histiocytosis disease
Sulpiride	Sarcoid
Dopamine reuptake blockers	Tuberculosis
Nomifensine	Irradiation damage
Histamine H2-receptor antagonists	Pituitary stalk transaction
Cimetidine	Surgical
Hormones	Traumatic
Estrogens	Pseudocyesis (functional)
Oral contraceptives	Pituitary lesions
Thyrotropin-releasing hormone	Acromegaly
Opiates	Mixed growth hormone or adrenocorticotropic hormone–prolactin-secreting adenoma
Stimulators of serotoninergic inhibitors	Prolactinoma
Amphetamines	Somatic sources
Hallucinogens	Breast augmentation or reduction
	Bronchogenic carcinoma
	Chest wall trauma
	Chronic nipple stimulation
	Cushing syndrome
	Herpes zoster
	Hypernephroma
	Hypothyroidism
	Pregnancy
	Renal failure
	Upper abdominal surgery

Special Tests: Assessment of visual fields may be indicated.
Diagnostic Procedures: History, physical examination, and laboratory determination of prolactin levels.

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: When prolactin levels are low and a coned-down view of the sella turcica is normal, observation alone may be sufficient. If observation is chosen, periodic re-evaluation is required to check for the emergence of slow-growing tumors.
Specific Measures: Treatment with a dopamine receptor agonist (bromocriptine, pergolide, or cabergoline) is recommended for patients who desire pregnancy or for those with distressing degrees of galactorrhea or to suppress intermediate-sized pituitary tumors. Rapidly growing tumors, tumors that are large at the time of discovery, or those that do not respond to bromocriptine therapy may have to be treated surgically.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlets AP136 (Evaluating Infertility) and AP137 (Treating Infertility).

Drug(s) of Choice

Bromocriptine (Parlodel) 2.5 mg daily increased gradually to three times a day.
Contraindications: Uncontrolled hypertension, pregnancy.
Precautions: With medical therapy—may experience nausea, orthostasis, drowsiness, or syncope; rarely may produce hypertension or seizures.
Interactions: Medical therapy may interact with phenothiazines or butyrophenones.

Alternative Drugs

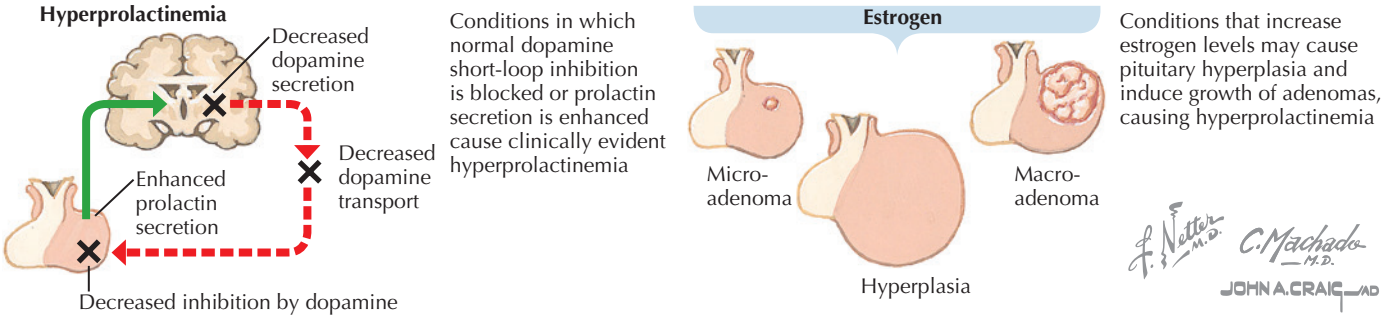
- Intravaginal bromocriptine (associated with lower rates of side effects).
- Cabergoline (0.25–1.0 mg orally once or twice per week) may also be used.

FOLLOW-UP

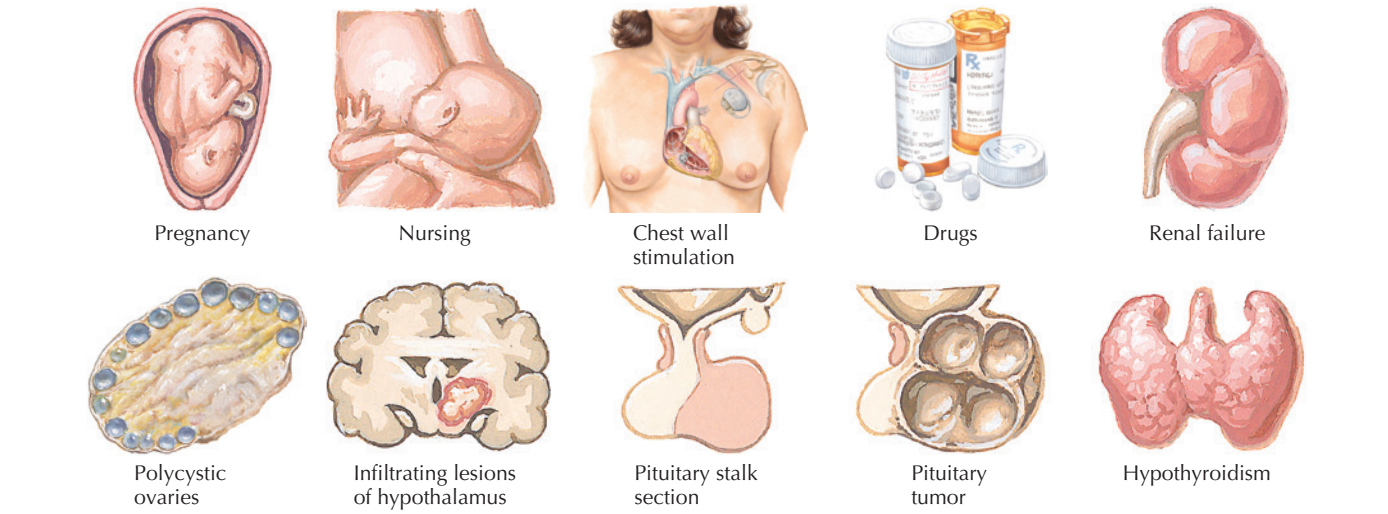
Patient Monitoring: Normal health maintenance. If a pituitary adenoma is present, periodic assessment of visual fields should be considered.
Prevention/Avoidance: None.
Possible Complications: Visual field loss, symptoms may return after medication is discontinued. Chronic anovulation is associated with an increased risk of endometrial hyperplasia and cancer. Cabergoline and pergolide have been associated with valvular heart disease in patients with Parkinson disease.
Expected Outcome: Generally good depending on cause. Prolactin levels should be measured every 6–12 months, and visual fields should be reassessed yearly. The pituitary should be re-evaluated every 2–5 years, based on the initial diagnosis. Approximately 10% of patients undergoing oral therapy will not experience return of prolactin to normal level.

MISCELLANEOUS

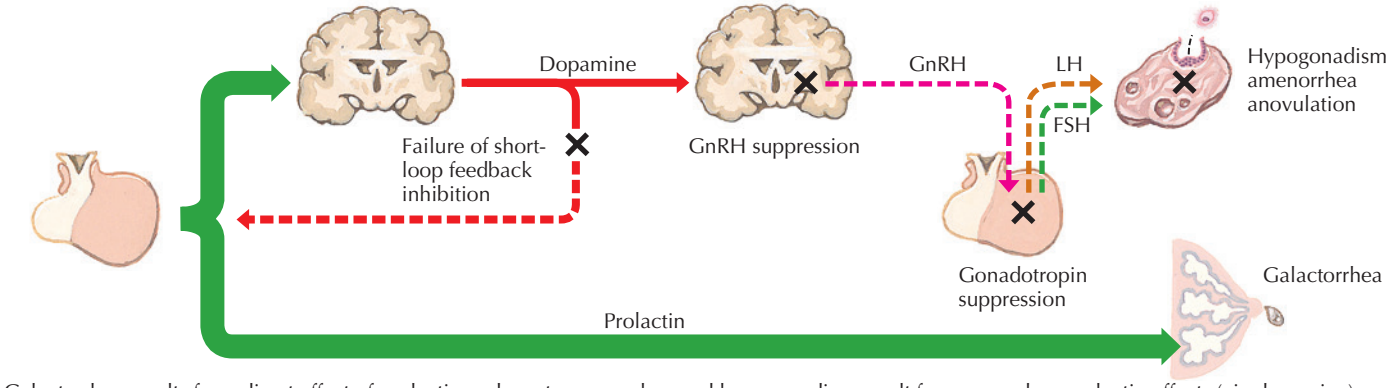
Pregnancy Considerations: No effect on pregnancy. Pregnancy may cause adenomas to grow rapidly.
ICD-10-cm Codes: E22.1 (Hyperprolactinemia).



Conditions associated with hyperprolactinemia



Mechanisms in galactorrhea-amenorrhea syndromes



Galactorrhea results from direct effect of prolactin on breast; amenorrhea and hypogonadism result from secondary prolactin effects (via dopamine) on GnRH and gonadotropin production and release
FSH, follicle-stimulating hormone; GnRH, gonadotropin-releasing hormone; LH, luteinizing hormone.

Figure 186.1 Hyperprolactinemia

REFERENCES

LEVEL I

Webster J, Piscitelli G, Polli A, et al. A comparison of cabergoline and bromocriptine in the treatment of hyperprolactinemic amenorrhea. Cabergoline Comparative Study Group. *N Engl J Med*. 1994;331:904.

LEVEL II

Auriemma RS, Pivonello R, Perone Y, et al. Safety of long-term treatment with cabergoline on cardiac valve disease in patients with prolactinomas. *Eur J Endocrinol*. 2013;169:359.

Schlechte J, Dolan K, Sherman B, et al. The natural history of untreated hyperprolactinemia: a prospective analysis. *J Clin Endocrinol Metab*. 1989;68:412.

Wang AT, Mullan RJ, Lane MA, et al. Treatment of hyperprolactinemia: a systematic review and meta-analysis. *Syst Rev*. 2012;1:33.

LEVEL III

American College of Obstetricians and Gynecologists. Management of abnormal uterine bleeding associated with ovulatory dysfunction. Practice Bulletin No. 136. *Obstet Gynecol*. 2013;122:176.

American College of Obstetricians and Gynecologists. Polycystic ovary syndrome. ACOG Practice Bulletin No. 108. *Obstet Gynecol*. 2009;114:936.

American College of Obstetricians and Gynecologists. Primary ovarian insufficiency in adolescents and young women. Committee Opinion No. 605. *Obstet Gynecol*. 2014;123:193.

Casanueva FF, Molitch ME, Schlechte JA, et al. Guidelines of the Pituitary Society for the diagnosis and management of prolactinomas. *Clin Endocrinol (Oxf)*. 2006;65:265.

Melmed S, Casanueva FF, Hoffman AR, et al. Diagnosis and treatment of hyperprolactinemia: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2011;96:273.

Molitch ME. Medication-induced hyperprolactinemia. *Mayo Clin Proc*. 2005;80:1050.

Schlechte JA. Clinical practice. Prolactinoma. *N Engl J Med*. 2003;349:2035.

Serri O, Chik CL, Ur E, et al. Diagnosis and management of hyperprolactinemia. *CMAJ*. 2003;169:575.

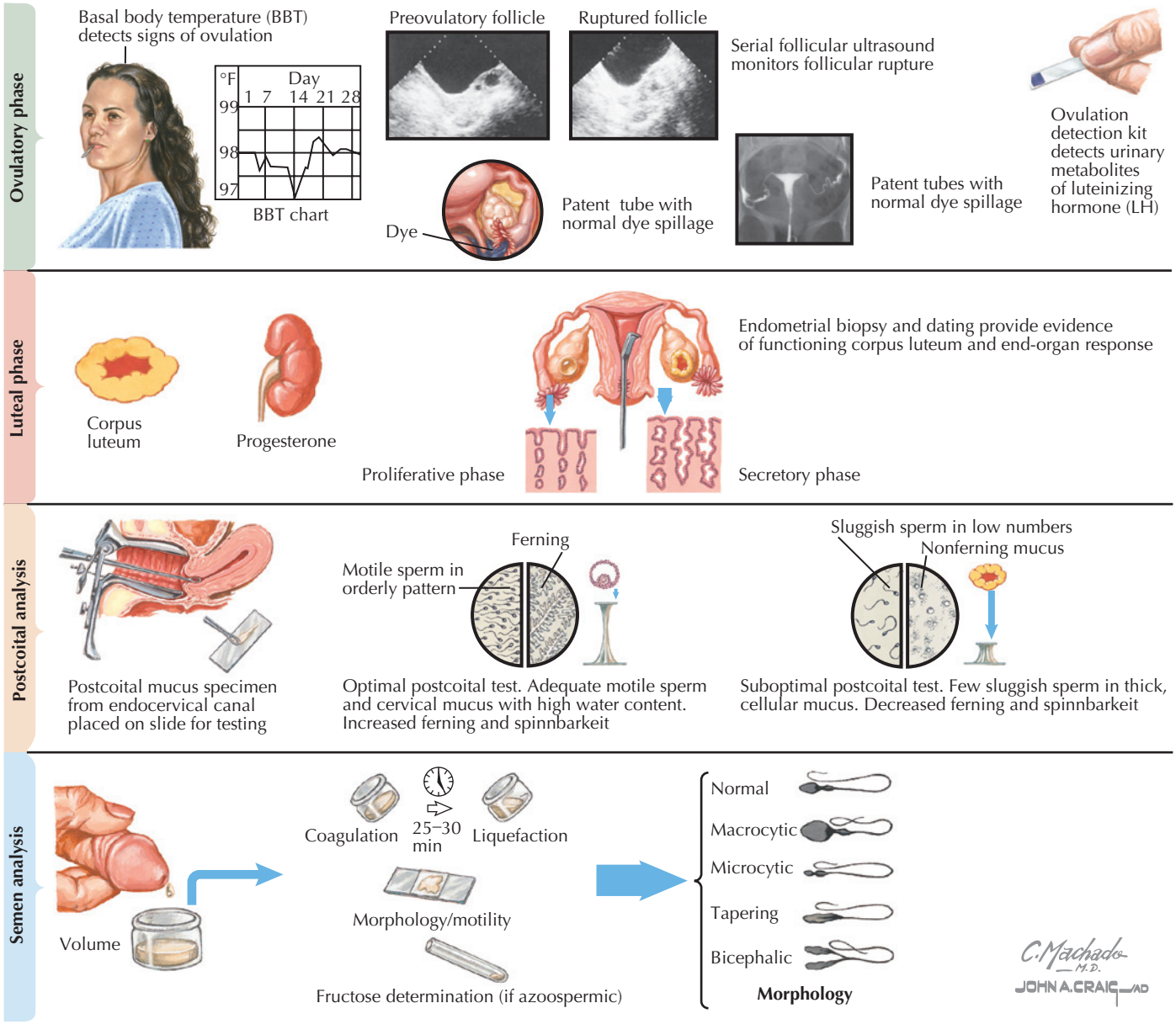


Figure 187.1 Infertility evaluation

the evaluation of infertility proceeds, couples should be instructed to continue attempting pregnancy through intercourse timed to the most fertile days of the cycle.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlets AP136 (Evaluating Infertility) and AP137 (Treating Infertility).

Drug(s) of Choice

- Based on diagnosis of cause.
- Secondary infertility (ovulation induction)—clomiphene citrate 50 mg PO daily on days 5–10 of the menstrual cycle; may be increased to 100 mg PO daily on days 5–10 of the menstrual cycle if ovulation does not occur. Metformin 1500 mg/day as an adjunctive treatment for ovulation induction (considered now as first-line therapy for polycystic ovary syndrome).

Contraindications: Undiagnosed infertility.

Precautions: The possibility of ovarian hyperstimulation must be considered and close follow-up should be maintained if ovulation induction is attempted.

Alternative Drugs

Gonadotropin-releasing hormone (GnRH) agonists may be used to control the hormonal environment during ovulation induction. Human gonadotropins may be used to induce ovulation but are associated with an increased risk of multiple ovulations and multiple gestations if pregnancy ensues.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Expected Outcome: Less than 40% of couples with primary infertility conceive after 6 years of therapy compared with more than 50% of secondary infertility couples who conceive within 3 years.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy once pregnancy is achieved. Some causes of impaired fertility are associated with a greater risk of early pregnancy loss.
ICD-10-CM Codes: N97.9 (Female infertility, unspecified) (other more specific classifications based on the cause).

REFERENCES

LEVEL II

Legro RS, Barnhart HX, Schlaff WD, et al. Cooperative Multicenter Reproductive Medicine Network. Clomiphene, metformin, or both for infertility in the polycystic ovary syndrome. *N Engl J Med*. 2007;356:551.

Reddy UM, Wapner RJ, Rebar RW, et al. Infertility, assisted reproductive technology, and adverse pregnancy outcomes: executive summary of a National Institute of Child Health and Human Development workshop. *Obstet Gynecol*. 2007;109:967.

LEVEL III

American College of Obstetricians and Gynecologists. Adoption. Committee Opinion No. 528. *Obstet Gynecol*. 2012;119:1320.

American College of Obstetricians and Gynecologists. Aromatase inhibitors in gynecologic practice. ACOG Committee Opinion No. 412. *Obstet Gynecol*. 2008;112:405.

American College of Obstetricians and Gynecologists. Female age-related fertility decline. Committee Opinion No. 589. *Obstet Gynecol*. 2014;123:719.

American College of Obstetricians and Gynecologists. Oocyte cryopreservation. Committee Opinion No. 584. *Obstet Gynecol*. 2014;123:221.

American College of Obstetricians and Gynecologists. Ovarian reserve testing. Committee Opinion No. 618. *Obstet Gynecol*. 2015;125:268.

American College of Obstetricians and Gynecologists. Polycystic ovary syndrome. ACOG Practice Bulletin No. 108. *Obstet Gynecol*. 2009;114:936.

American College of Obstetricians and Gynecologists. Surrogate motherhood. ACOG Committee Opinion No. 397. *Obstet Gynecol*. 2008;111:465.

Braude P, Rowell P. Assisted conception. II—In vitro fertilisation and intracytoplasmic sperm injection. *BMJ*. 2003;327:852.

Braude P, Rowell P. Assisted conception. III—Problems with assisted conception. *BMJ*. 2003;327:920.

Hamilton-Fairley D, Taylor A. Anovulation. *BMJ*. 2003;327:546.

Practice Committee of the American Society for Reproductive Medicine. Definitions of infertility and recurrent pregnancy loss. *Fertil Steril*. 2008;90:S60.

Practice Committee of American Society for Reproductive Medicine. Diagnostic evaluation of the infertile female: a committee opinion. *Fertil Steril*. 2012;98:302.

Rowell P, Braude P. Assisted conception. I—General principles. *BMJ*. 2003;327:799.

Smith S, Pfeifer SM, Collins JA. Diagnosis and management of female infertility. *JAMA*. 2003;290:1767.

Van Voorhis BJ. Outcomes from assisted reproductive technology. *Obstet Gynecol*. 2006;107:183.

Van Voorhis BJ. Clinical practice. In vitro fertilization. *N Engl J Med*. 2007;356:379.

- Polycystic ovary syndrome
- Prolactin-secreting tumor
- Hypothalamic dysfunction

Associated Conditions: Dyspareunia, vulvodynia, atrophic vulvitis, osteoporosis, increased risk of cardiovascular disease (most apparent with premature menopause), hot flashes and flushes, sleep disturbances, stress urinary incontinence, and others.

WORKUP AND EVALUATION

Laboratory: Usually not necessary. When the diagnosis of ovarian failure must be confirmed, measurement of serum follicle-stimulating hormone (FSH) is sufficient. Levels of greater than 100 mIU/mL are diagnostic, although lower levels (40–50 mIU/mL) may be sufficient to establish a diagnosis when symptoms are also present. Serum estradiol levels may be determined (generally less than 15 pg/mL) but are less reliable as a marker of ovarian failure. A pregnancy test is always indicated in women who are perimenopausal and sexually active and not using contraception.

Imaging: No imaging indicated. Standard imaging does not document bone loss of less than 30%.

Special Tests: A vaginal maturation index may be obtained but is generally not required for diagnosis. Bone densitometry may be indicated for those at special risk. When noncyclic bleeding occurs in these patients, endometrial biopsy should be strongly considered. Women younger than the age of 30 years who have ovarian failure should have a karyotype performed.

Pathologic Findings

Vaginal, vulvar, and endometrial atrophy. Thinned ovarian stroma with few, inactive oocytes. Accelerated calcium loss from bone for approximately 7–10 years following menopause.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Health maintenance, annual mammogram, annual pelvic and rectal examinations, thyroid and cholesterol screening every 5 years or as indicated, tetanus booster shot every 10 years, pneumococcus vaccine as indicated. The value of the routine pelvic examinations for women of advanced age has been questioned, but has yet to achieve consensus.

Specific Measures: For symptom relief—systemic estrogen (estrogen/progestin) therapy (less than 1% of women do not benefit from therapy). Topical estrogen supplements.

Diet: Adequate dietary calcium (1000–1500 mg/day).

Activity: No restriction. Weightbearing activity to promote bone health and cardiovascular fitness training/maintenance.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlets AP047 (The Menopause Years), AP048 (Preventing Osteoporosis), and AP028 (Vaginitis).

Drug(s) of Choice

- Most common drug doses shown.
- Oral estrogens—conjugated equine estrogens 0.625–1.25 mg/day, diethylstilbestrol, esterified estrogens 0.625–1.25 mg/day, ethinyl estradiol 0.05 mg/day, micronized estradiol 0.5–1 mg/day, piperazine estrone sulfate, estropipate, quinestrol.
- Injectable estrogens—conjugated equine estrogens, estradiol benzoate, estradiol cypionate, estradiol valerate (oil), estrone (aqueous), ethinyl estradiol, polyestradiol phosphate.
- Topical estrogens—17β-estradiol (transdermal) 0.05–0.10 mg/day, conjugated equine estrogens 0.625 mg/g, estradiol 0.1 mg/g, estropipate 1.5 mg/g.

Contraindications: Systemic therapy—active liver disease, carcinoma of the breast (current), chronic liver damage (impaired function), endometrial carcinoma (current), recent thrombosis (with or without emboli), unexplained vaginal bleeding. Relative contraindications/special considerations—endometriosis, familial hyperlipidemia, gallbladder disease, hypertension (uncontrolled), migraine headaches, seizure disorders, thrombophlebitis (unknown risk), uterine leiomyomas. Topical use—known sensitivity to vehicle.

Precautions: Continuous estrogen exposure without periodic or concomitant progestins increases the risk for endometrial carcinoma by six- to eightfold. Continuous estrogen/progestin therapy frequently results in random vaginal bleeding, but biopsy or other investigation is still warranted. Patients undergoing cyclic estrogen/progestin therapy should experience vaginal bleeding only after the withdrawal of progestin; biopsy or other investigation is warranted for other bleeding or heavy menses.

Interactions: Raloxifene should not be used with cholestyramine. Most therapies alter the effects of warfarin therapy.

Alternative Drugs

- Raloxifene (Evista) 60 mg PO daily—reduces breast cancer risk but does not provide relief for hot flashes or vaginal dryness
- Progestin therapy (oral, vaginal, or injectable; effective for hot flashes, may reduce bone loss, but has no effect on coronary artery disease or urogenital atrophy)
- Clonidine (oral or transdermal)
- Bellergal-S (phenobarbital, ergotamine tartrate, belladonna)
- Bisphosphonates (alendronate [Fosamax] and others; for osteoporosis)
- Topical moisturizers for atrophic vaginitis
- Botanical agents have not been shown to be efficacious for most menopausal symptoms or for osteoporosis prevention.

FOLLOW-UP

Patient Monitoring: Normal health maintenance. Serious consideration should be given to a trial of therapy discontinuation after 2 or more years.

Prevention/Avoidance: Estrogen replacement therapy at menopause. The use of progestins is required if the patient retains her uterus to reduce the risk of iatrogenic endometrial hyperplasia or cancer. Therapy may be oral (such as medroxyprogesterone acetate [Provera] 5–10 mg PO daily for 12–14 days per month or 2.5 mg PO daily) or vaginal (progesterone bioadhesive gel [Crinone] 4%–8%, 45 mg [1.125 g] intravaginally every other day for six doses per month).

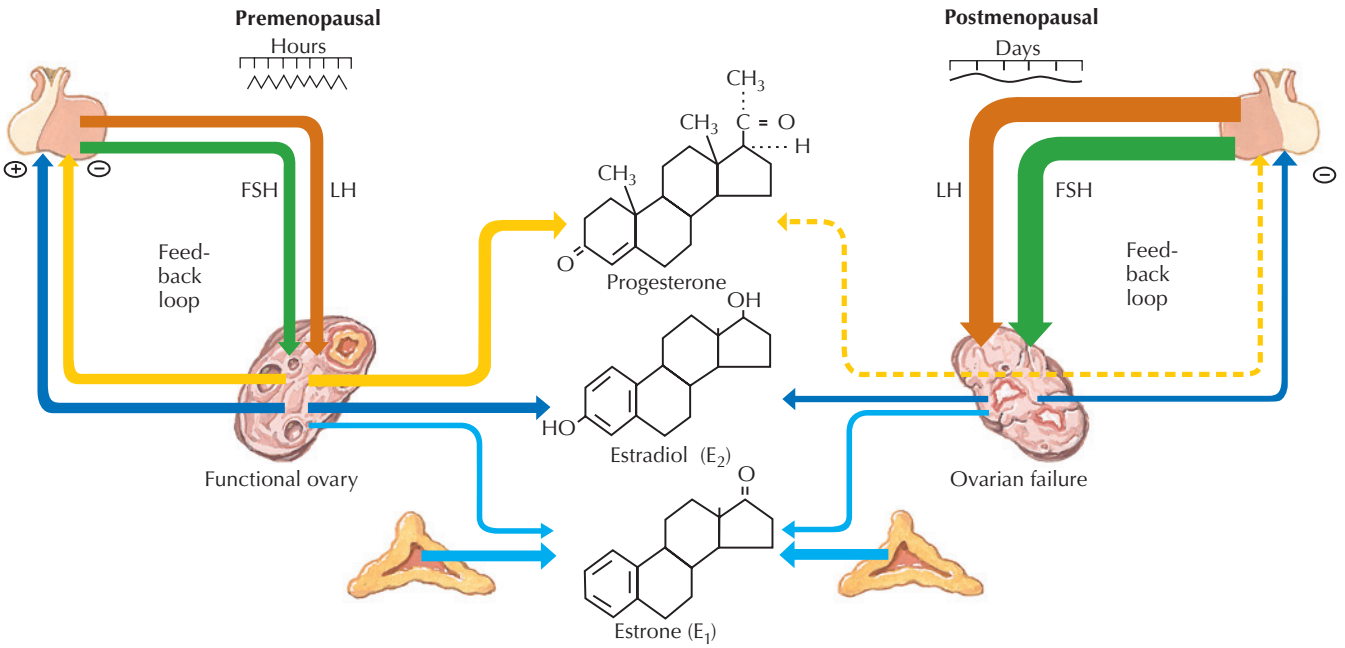
Possible Complications: Endometrial hyperplasia if the uterus is present and progestins are not used; vaginal bleeding (predictable or otherwise).

Expected Outcome: Reversal of symptoms, reestablishment of normal physiology with treatment. Selective estrogen receptor modulators (also called SERMS or tissue-specific estrogens) may provide protection against cardiac, bone, and colon cancer and Alzheimer disease with reduced rates of risk for both breast and endometrial cancer.

MISCELLANEOUS

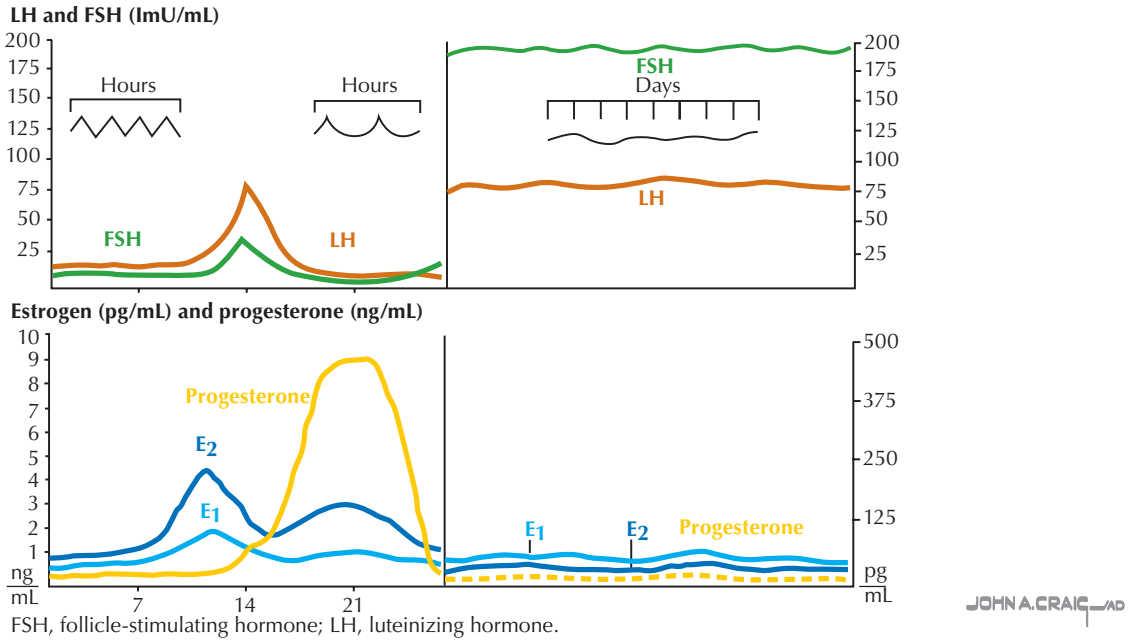
Pregnancy Considerations: Menopause is associated with the loss of fertility.

ICD-10-CM Codes: N95.1 (Menopause or female climacteric states), E28.310 (Symptomatic premature menopause), and E89.40/E89.41 (Asymptomatic/Symptomatic postprocedural ovarian failure).



Hormone levels increase and decrease cyclically during menstrual cycle. Modulation occurs by pulsatile releases of gonadotropins and positive and negative feedback loops

In postmenopausal period, gonadotropin levels increase and ovarian hormone levels decrease secondary to ovarian failure. Endogenous estrogen is primarily of adrenal origin, and E_1 to E_2 ratio is reversed



FSH, follicle-stimulating hormone; LH, luteinizing hormone.

Figure 188.1 Pituitary and ovarian hormone changes in menopause

REFERENCES

LEVEL III

American College of Obstetricians and Gynecologists. Compounded bioidentical menopausal hormone therapy. Committee Opinion No. 532. *Obstet Gynecol*. 2012;120:411.

American College of Obstetricians and Gynecologists. Hormone therapy and heart disease. Committee Opinion No. 565. *Obstet Gynecol*. 2013; 121:1407.

American College of Obstetricians and Gynecologists. Management of menopausal symptoms. Practice Bulletin No. 141. *Obstet Gynecol*. 2014; 123:202.

American College of Obstetricians and Gynecologists. Osteoporosis. Practice Bulletin No. 129. *Obstet Gynecol*. 2012;120:718.

American College of Obstetricians and Gynecologists. Postmenopausal estrogen therapy: route of administration and risk of venous thromboembolism. Committee Opinion No. 556. *Obstet Gynecol*. 2013;121:887.

POLYCYSTIC OVARY SYNDROME

189

INTRODUCTION

Description: Polycystic ovary syndrome (PCOS) consists of amenorrhea, hirsutism, insulin resistance, and obesity in association with enlarged, multicystic ovaries.
Prevalence: Up to 5% of women; 30% of secondary amenorrhea. The most common hormonal disorder among women of reproductive age.
Predominant Age: Begins at menarche.
Genetics: No genetic pattern established; suggestion of increased family tendency.

ETIOLOGY AND PATHOGENESIS

Causes: The exact pathophysiology of PCOS is not well established, but increased amplitude of gonadotropin-releasing hormone (GnRH) pulsation and abnormal secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) during puberty are considered to result in excess androgen. Elevated levels of LH persist and may be used to help establish the diagnosis. Insulin resistance is a prominent aspect of this syndrome.
Risk Factors: Borderline adrenal hyperplasia, occult hypothyroidism, and childhood obesity.

SIGNS AND SYMPTOMS

- Anovulation and amenorrhea (75%–80%)
- Infertility (75%)
- Excessive hair growth, primarily along the angle of the jaw, upper lip, and chin (70%)
- Obesity (50%; "apple-shaped" obesity centered around the lower half of the torso)
- Acanthosis nigricans
- Acne

DIAGNOSTIC APPROACH

Differential Diagnosis

- Virilization (especially when hirsutism is in a male pattern)
- Familial hypertrichosis
- Cushing disease (truncal obesity, facial rounding, cervicodorsal fat deposition [buffalo hump], and red or purple striae are often not fully developed)

Associated Conditions: Increased risk for cardiovascular disease (adverse lipid profiles), diabetes (insulin resistance in 50% of patients), hypertension, and infertility.

Workup and Evaluation

Laboratory: Elevated levels of LH may be used to help establish the diagnosis (a two-to-one ratio of LH to FSH is considered diagnostic). Evaluation for possible virilizing process (prolactin, FSH, thyroid screening). Patients suspected of having adrenal sources of hyperandrogenicity may be screened by measuring 24-hour urinary-free cortisol, by performing adrenocorticotropin hormone (ACTH) stimulation tests, or an overnight dexamethasone suppression test. Serum testosterone (total) is generally 70–120 ng/mL and androstenedione is 3–5 ng/mL. Dehydroepiandrosterone sulfate (DHEA-s) is elevated in approximately 50% of patients.
Imaging: Ultrasonography (abdominal or transvaginal) may identify ovarian enlargement or the presence of multiple small follicles (12 or more follicles per ovary). Magnetic resonance imaging (MRI) or computed tomography (CT) may be used to evaluate the adrenal glands.
Special Tests: None indicated.
Diagnostic Procedures: History, physical examination, imaging and laboratory evaluations. May be confirmed at laparoscopy, but seldom required for diagnosis (Box 189.1). Hyperandrogenism is based on clinical signs and does not require laboratory confirmation.

Pathologic Findings

The ovaries are enlarged with a thickened white capsule. They contain multiple follicles in varying stages of development. Luteinization of theca cells may be present.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation. Weight loss is often associated with resolution of symptoms and a return of menstrual function in patients with mild or early PCOS.
Specific Measures: Medical therapy has replaced surgical treatment. Treatment depends on desire for pregnancy; if pregnancy is desired, then ovulation induction may be required.
Diet: No specific dietary changes indicated; weight loss or control desirable.
Activity: No restriction.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP121 (Polycystic Ovary Syndrome).

Drug(s) of Choice

- Combination oral contraceptives (less than 50-mg formulation and a progestin other than norgestrel).
- If DHEA-s is elevated, dexamethasone 0.25 to 0.5 mg PO every bedtime may be added to oral contraceptives.
- Spironolactone 100–200 mg PO daily.
- Metformin 1500 mg/day as an adjunctive treatment for ovulation induction (considered now as first-line therapy for PCOS).

Contraindications: Pregnancy (spironolactone is a category X drug and patients of child-bearing potential must use reliable contraception).

Alternative Drugs

GnRH analogs and clomiphene citrate may be used.

FOLLOW-UP

Patient Monitoring: Normal health maintenance once diagnosis and management have been implemented. There is an increased risk for diabetes in patients with polycystic ovaries. Weight control and contraception should also be addressed.

Box 189.1 2003 ROTTERDAM CRITERIA

Patient must have two or more of the following:
1. Oligo-ovulation and/or anovulation
2. Excess androgen activity
3. Polycystic ovaries (by gynecologic ultrasonography)

Data based on Welt CK, Gudmundsson JA, Arason G, et al. Characterizing discrete subsets of polycystic ovary syndrome as defined by the Rotterdam Criteria: the impact of weight on phenotype and metabolic features. *J Clin Endocrinol Metab*. 2006;91:4842

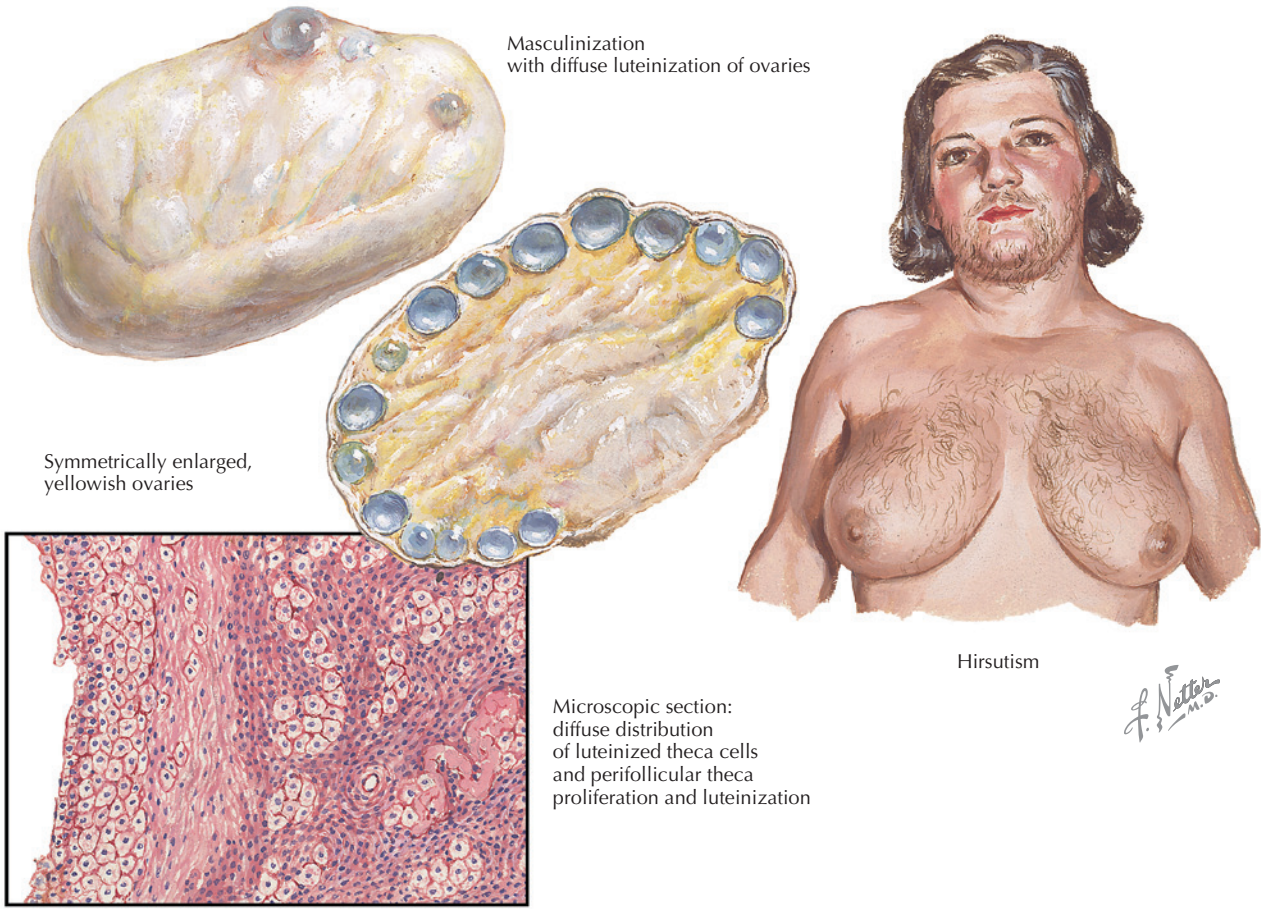


Figure 189.1 Polycystic ovarian disease

Prevention/Avoidance: Role of normalized weight debated.
Possible Complications: Chronic anovulation is associated with osteoporosis and endometrial hyperplasia or carcinoma.
Expected Outcome: Generally good response to medical therapy.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, although fertility is often reduced.
ICD-10-CM Codes: E28.2 (Polycystic ovarian syndrome).

REFERENCES

LEVEL I

Bridger T, MacDonald S, Baltzer F, et al. Randomized placebo-controlled trial of metformin for adolescents with polycystic ovary syndrome. *Arch Pediatr Adolesc Med*. 2006;160:241.

Eisenhardt S, Schwarzmann N, Henschel V, et al. Early effects of metformin in women with polycystic ovary syndrome: a prospective randomized, double-blind, placebo-controlled trial. *J Clin Endocrinol Metab*. 2006;91:946.

Legro RS, Brzyski RG, Diamond MP, et al. Letrozole versus clomiphene for infertility in the polycystic ovary syndrome. *N Engl J Med*. 2014;371:119.

Legro RS, Zaino RJ, Demers LM, et al. The effects of metformin and rosiglitazone, alone and in combination, on the ovary and endometrium in polycystic ovary syndrome. *Am J Obstet Gynecol*. 2007;196:402.e1.

Moll E, Bossuyt PM, Korevaar JC, et al. Effect of clomifene citrate plus metformin and clomifene citrate plus placebo on induction of ovulation in women with newly diagnosed polycystic ovary syndrome: randomised double blind clinical trial. *BMJ*. 2006;332:1485.

LEVEL II

Costello MF, Shrestha B, Eden J, et al. Metformin versus oral contraceptive pill in polycystic ovary syndrome: a Cochrane review. *Hum Reprod*. 2007;22:1200.

Franik S, Kremer JA, Nelen WL, et al. Aromatase inhibitors for subfertile women with polycystic ovary syndrome. *Cochrane Database Syst Rev*. 2014;(2):CD010287.

Legro RS, Barnhart HX, Schlaff WD, et al. Cooperative Multicenter Reproductive Medicine Network. Clomiphene, metformin, or both for infertility in the polycystic ovary syndrome. *N Engl J Med*. 2007;356:551.

Lord JM, Flight IH, Norman RJ. Metformin in polycystic ovary syndrome: systematic review and meta-analysis. *BMJ*. 2003;327:951.

Moran LJ, Hutchison SK, Norman RJ, et al. Lifestyle changes in women with polycystic ovary syndrome. *Cochrane Database Syst Rev*. 2011;CD007506.

Pasquali R, Gambineri A, Pagotto U. The impact of obesity on reproduction in women with polycystic ovary syndrome. *BJOG*. 2006;113:1148.

Tang T, Lord JM, Norman RJ, et al. Insulin-sensitising drugs (metformin, rosiglitazone, pioglitazone, D-chiro-inositol) for women with polycystic ovary syndrome, oligo amenorrhoea and subfertility. *Cochrane Database Syst Rev*. 2012;(5):CD003053.

LEVEL III

American College of Obstetricians and Gynecologists. Diagnosis of abnormal uterine bleeding in reproductive-aged women. Practice Bulletin No. 128. *Obstet Gynecol*. 2012;120:197.

American College of Obstetricians and Gynecologists. Noncontraceptive uses of hormonal contraceptives. Practice Bulletin No. 110. *Obstet Gynecol*. 2010;115:206.

American College of Obstetricians and Gynecologists. Management of abnormal uterine bleeding associated with ovulatory dysfunction. Practice Bulletin No. 136. *Obstet Gynecol*. 2013;122:176.

American College of Obstetricians and Gynecologists. Menstruation in girls and adolescents: using the menstrual cycle as a vital sign. Committee Opinion No. 651. *Obstet Gynecol*. 2015;126:e143.

American College of Obstetricians and Gynecologists. Polycystic ovary syndrome. ACOG Practice Bulletin No. 108. *Obstet Gynecol*. 2009;114:936.

Carmina E, Lobo RA. Polycystic ovary syndrome (PCOS): arguably the most common endocrinopathy is associated with significant morbidity in women. *J Clin Endocrinol Metab*. 1999;84:1897.

Dewailly D, Lujan ME, Carmina E, et al. Definition and significance of polycystic ovarian morphology: a task force report from the Androgen Excess and Polycystic Ovary Syndrome Society. *Hum Reprod Update*. 2014;20:334.

Ehrmann DA. Polycystic ovary syndrome. *N Engl J Med*. 2005;352:1223.

Guzick DS. Polycystic ovary syndrome. *Obstet Gynecol*. 2004;103:181.

Hopkinson ZE, Sattar N, Fleming R, et al. Polycystic ovarian syndrome: the metabolic syndrome comes to gynaecology. *BMJ*. 1998;317:329.

Legro RS, Arslanian SA, Ehrmann DA, et al. Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2013;98:4565.

Martin KA, Chang RJ, Ehrmann DA, et al. Evaluation and treatment of hirsutism in premenopausal women: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2008;93:1105.

Setji TL, Brown AJ. Polycystic ovary syndrome: diagnosis and treatment. *Am J Med*. 2007;120:128.

Siassakos D, Wardle P. Polycystic ovary syndrome and pregnancy outcome: red herring or red flag? *BJOG*. 2007;114:922.

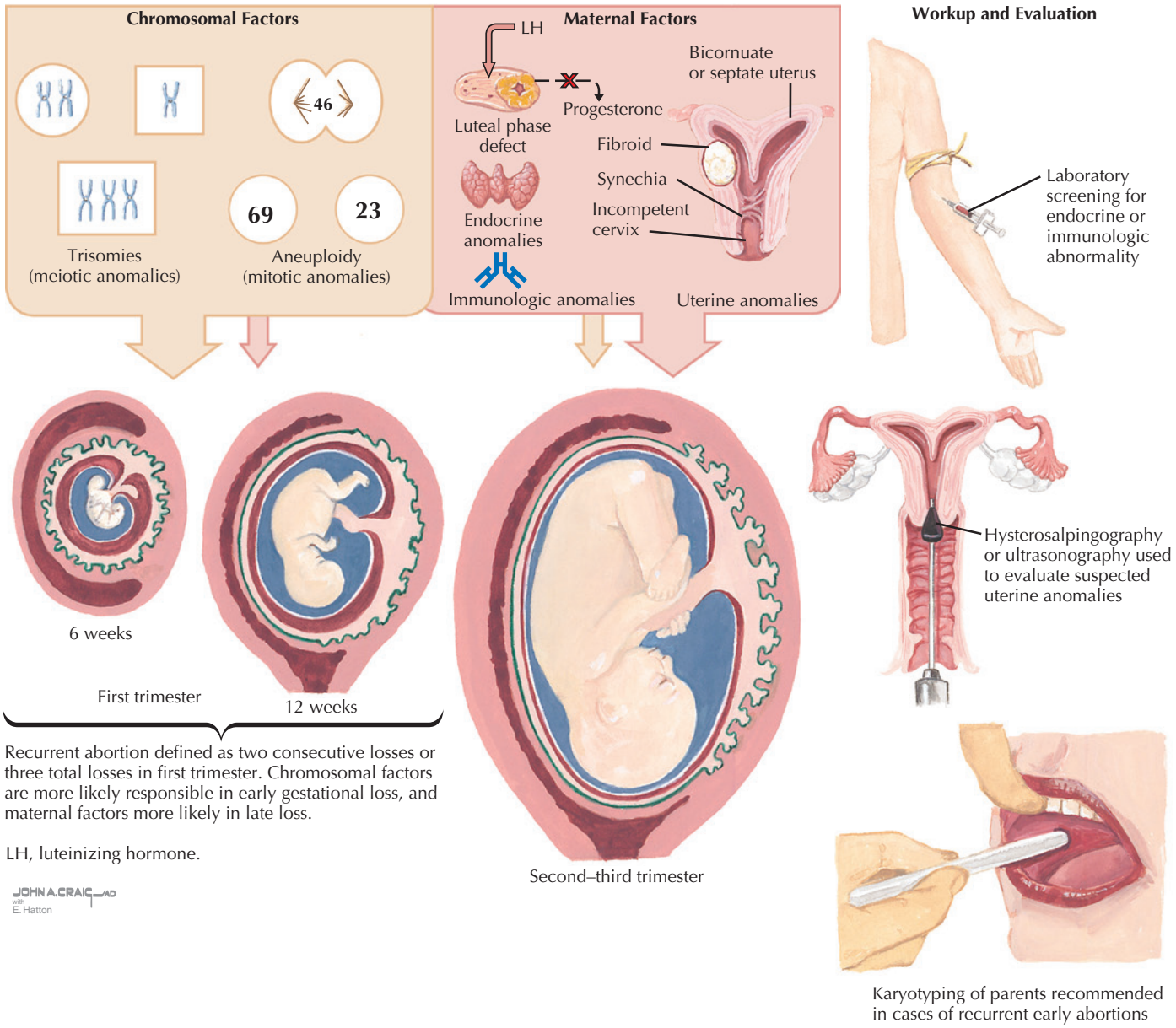


Figure 190.1 Chromosomal factors, workup, and evaluation

Diagnostic Procedures: Hysteroscopy may be of limited value (indicated only when a uterine factor is strongly considered).

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Support and evaluation.
Specific Measures: Those with parental chromosomal anomalies may be offered donor oocytes or artificial insemination with donor sperm. Uterine anomalies or submucous fibroids may be treated, although care must be taken to recognize the possibility of continued failure for other reasons and the possible impact of future delivery options.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlets AP100 (Repeated Miscarriage) and AP090 (Early Pregnancy Loss).

Drug(s) of Choice

None. Progesterone and thyroid supplements have not been shown to reduce the risk for pregnancy loss. When immunologic factors are present (antiphospholipid syndrome), the use of low-dose aspirin and subcutaneous heparin (5000 units twice daily) has reduced the rate of subsequent loss but has no effect in the absence of documented immunologic factors.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: Based on the underlying pathologic condition.
Expected Outcome: Based on the underlying pathologic condition.

MISCELLANEOUS

Pregnancy Considerations: When because of correctable factors, future pregnancies will not be affected.
ICD-10-CM Codes: O26.20 (Pregnancy care for patient with recurrent pregnancy loss, unspecified trimester).

REFERENCES

LEVEL I

Coomarasamy A, Williams H, Truchanowicz E, et al. A Randomized Trial of Progesterone in Women with Recurrent Miscarriages. *N Engl J Med*. 2015;373:2141.

Dolitzky M, Inbal A, Segal Y, et al. A randomized study of thromboprophylaxis in women with unexplained consecutive recurrent miscarriages. *Fertil Steril*. 2006;86:362.

LEVEL II

Franssen MT, Korevaar JC, van der Veen F, et al. Reproductive outcome after chromosome analysis in couples with two or more miscarriages: index [corrected]-control study. *BMJ*. 2006;332:759.

Haas DM, Ramsey PS. Progestogen for preventing miscarriage. *Cochrane Database Syst Rev*. 2013;(10):CD003511.

Jaslow CR, Carney JL, Kutteh WH. Diagnostic factors identified in 1020 women with two versus three or more recurrent pregnancy losses. *Fertil Steril*. 2010;93:1234.

Sotiriadis A, Makrigiannakis A, Stefos T, et al. Fibrinolytic defects and recurrent miscarriage: a systematic review and meta-analysis. *Obstet Gynecol*. 2007;109:1146.

Thangaratinam S, Tan A, Knox E, et al. Association between thyroid autoantibodies and miscarriage and preterm birth: meta-analysis of evidence. *BMJ*. 2011;342:d2616.

Wong LF, Porter TF, Scott JR. Immunotherapy for recurrent miscarriage. *Cochrane Database Syst Rev*. 2014;(10):CD000112.

LEVEL III

American College of Obstetricians and Gynecologists. Antiphospholipid syndrome. Practice Bulletin No. 132. *Obstet Gynecol*. 2012;120:1514.

American College of Obstetricians and Gynecologists. Cerclage for the management of cervical insufficiency. Practice Bulletin No. 142. *Obstet Gynecol*. 2014;123:372.

American College of Obstetricians and Gynecologists. Early pregnancy loss. Practice Bulletin No. 150. *Obstet Gynecol*. 2015;125:1258.

Kolte AM, Bernardi LA, Christiansen OB, et al. Terminology for pregnancy loss prior to viability: a consensus statement from the ESHRE early pregnancy special interest group. *Hum Reprod*. 2015;30:495.

Practice Committee of the American Society for Reproductive Medicine. Current clinical irrelevance of luteal phase deficiency: a committee opinion. *Fertil Steril*. 2015;103:e27.

Practice Committee of American Society for Reproductive Medicine. Definitions of infertility and recurrent pregnancy loss: a committee opinion. *Fertil Steril*. 2013;99:63.

Rai R, Regan L. Recurrent miscarriage. *Lancet*. 2006;368:601.

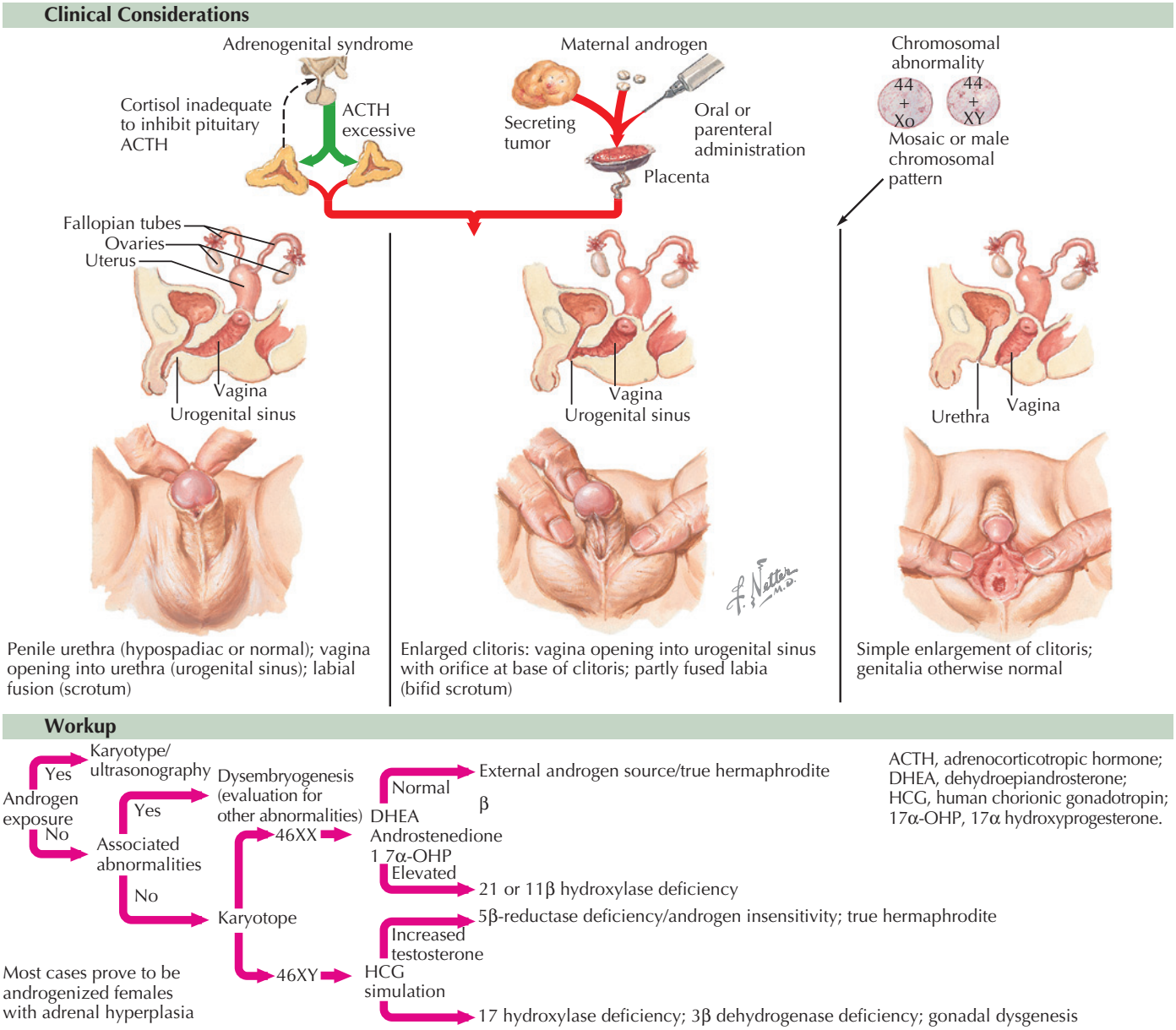


Figure 191.1 Clinical considerations and workup of ambiguous genitalia

- Vaginal agenesis
- Imperforate hymen
- Other enzymatic defects

Associated Conditions: Premature puberty, infertility, sexual dysfunction, and gender dysphoria.

Workup and Evaluation

Laboratory: Electrolytes, hormonal and enzymatic function.
Imaging: Ultrasonography may be used to assess the internal genitalia, but it is seldom necessary for an initial diagnosis.
Special Tests: Karyotyping may be desirable, but a buccal smear to detect Barr bodies is often sufficient.
Diagnostic Procedures: Systematic examination of the genitalia (mons and groin, clitoris/phallus, urethral opening, labioscrotal folds, vaginal opening, posterior fourchette and perineum, anus and anal patency—the penis has a midline frenulum; the clitoris has two lateral folds that extend to the labia minora), karyotype, laboratory testing. A multidisciplinary team may be required to complete the evaluation.

Pathologic Findings

Based on the cause.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Rapid assessment and treatment as if congenital adrenal hyperplasia is present should be instituted until the possibility has been ruled out. The assigning of gender must be made as soon as possible after delivery but should be delayed until a gender can be established considering all available evidence. Many experts argue against the use of names that are gender ambiguous such as Leslie, Terry, or Jamie.

Specific Measures: Therapy is medical and surgical—medical therapy to reverse the effects of enzyme defects and surgical therapy for cosmetics and sexual function. Surgery is often delayed until late infancy or adolescence (based on the type of reconstruction planned). If a Y-chromosome cell line is present, removal of the gonads is indicated. For many, this may be delayed until puberty is complete.
Diet: No specific dietary changes indicated.
Activity: No restriction.

Drug(s) of Choice

For congenital adrenal hyperplasia—cortisol 12–18 mg/m^2 or prednisone 3.5–5 mg/m^2 or higher to maintain adrenal suppression.

FOLLOW-UP

Patient Monitoring: Normal health maintenance, continuing support for enzymatic defects.
Prevention/Avoidance: Avoidance of agents with androgenic activity during pregnancy (drugs and food supplements).
Possible Complications: Failure to establish a clear, unambiguous gender (sex of rearing) can result in lifelong social and psychologic problems and may limit future surgical reconstruction and sexual options.
Expected Outcome: With early detection, successful growth and development appropriate to gender may be anticipated. With reconstruction, even severe anatomic deformities can be corrected to provide cosmetic and sexually acceptable results.

MISCELLANEOUS

Pregnancy Considerations: Based on cause—androgenized females are fully fertile and have normal pregnancies; males with isolated hypospadias or cryptorchidism may be fertile; all others are sterile.
ICD-10-CM Codes: Q56.4 (Indeterminate sex, unspecified) and Q56.3 (Pseudohermaphroditism, unspecified).

REFERENCES

LEVEL III

Bidarkar SS, Hutson JM. Evaluation and management of the abnormal gonad. *Semin Pediatr Surg.* 2005;14:118.

Brown J, Warne G. Practical management of the intersex infant. *J Pediatr Endocrinol Metab.* 2005;18:3.

Jaaskelainen J, Tiitinen A, Voutilainen R. Sexual function and fertility in adult females and males with congenital adrenal hyperplasia. *Horm Res.* 2001;56:73.

Lee PA, Houk CP, Ahmed SF, et al. Consensus statement on management of intersex disorders. International Consensus Conference on Intersex. *Pediatrics.* 2006;118:e488.

Low Y, Hutson JM, Murdoch Children's Research Institute Sex Study Group. Rules for clinical diagnosis in babies with ambiguous genitalia. *J Paediatr Child Health.* 2003;39:406.

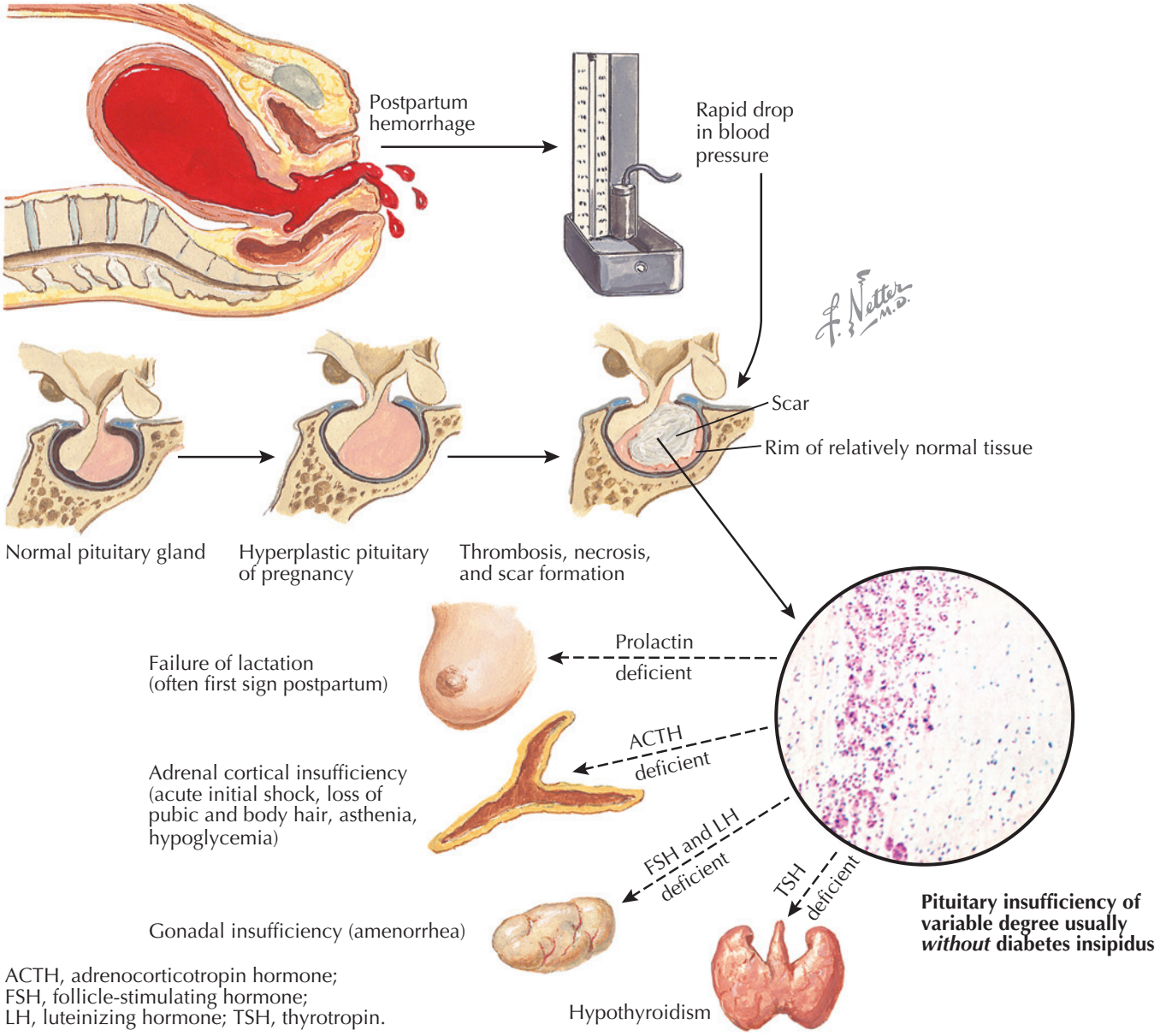


Figure 192.1 Sheehan syndrome

Special Tests: None indicated.
Diagnostic Procedures: History and laboratory evaluations.

Pathologic Findings

Necrosis of the pituitary gland.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation (rapid; potentially life-threatening through loss of adrenal and thyroid hormones).
Specific Measures: Hormone replacement (thyroid, adrenal, and ovarian steroids).
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Patients must be carefully instructed when continuation of adrenal and thyroid hormone replacement therapy is required.

Drug(s) of Choice

Hormone replacement (thyroid, adrenal, and ovarian steroids).

FOLLOW-UP

Patient Monitoring: Careful follow-up of thyroid and adrenal functions is required.
Prevention/Avoidance: Maintenance of adequate perfusion and oxygenation when postpartum hemorrhage occurs.
Possible Complications: Failure to diagnose the loss of pituitary function can result in life-threatening adrenal insufficiency and hypothyroidism.
Expected Outcome: With timely diagnosis and hormone replacement, normal life and function may be expected.

MISCELLANEOUS

Pregnancy Considerations: Without ovulation induction and assisted reproduction, pregnancy is unlikely.
ICD-10-CM Codes: E23.0 (Hypopituitarism).

REFERENCES

LEVEL II

Antonypillai CN, Wass JA, Warrell DA, et al. Hypopituitarism following envenoming by Russell's vipers (*Daboia siamensis* and *D. russelii*) resembling Sheehan's syndrome: first case report from Sri Lanka, a review of the literature and recommendations for endocrine management. *QJM*. 2011;104:97.

Atmaca H, Tanriverdi F, Gokce C, et al. Posterior pituitary function in Sheehan's syndrome. *Eur J Endocrinol*. 2007;156:563.

Feinberg EC, Molitch ME, Endres LK, et al. The incidence of Sheehan's syndrome after obstetric hemorrhage. *Fertil Steril*. 2005;84:975.

LEVEL III

Benvenga S, Campenni A, Ruggeri RM, et al. Clinical review 113: hypopituitarism secondary to head trauma. *J Clin Endocrinol Metab*. 2000;85:1353.

Keleştimur F. Sheehan's syndrome. *Pituitary*. 2003;6:181.

Lamberts SW, de Herder WW, van der Lely AJ. Pituitary insufficiency. *Lancet*. 1998;352:127.

Miller KK, Biller BM, Hier J, et al. Androgens and bone density in women with hypopituitarism. *J Clin Endocrinol Metab*. 2002;87:2770.

Schneider HJ, Aimaretti G, Kreitschmann-Andermahr I, et al. Hypopituitarism. *Lancet*. 2007;369:1461.

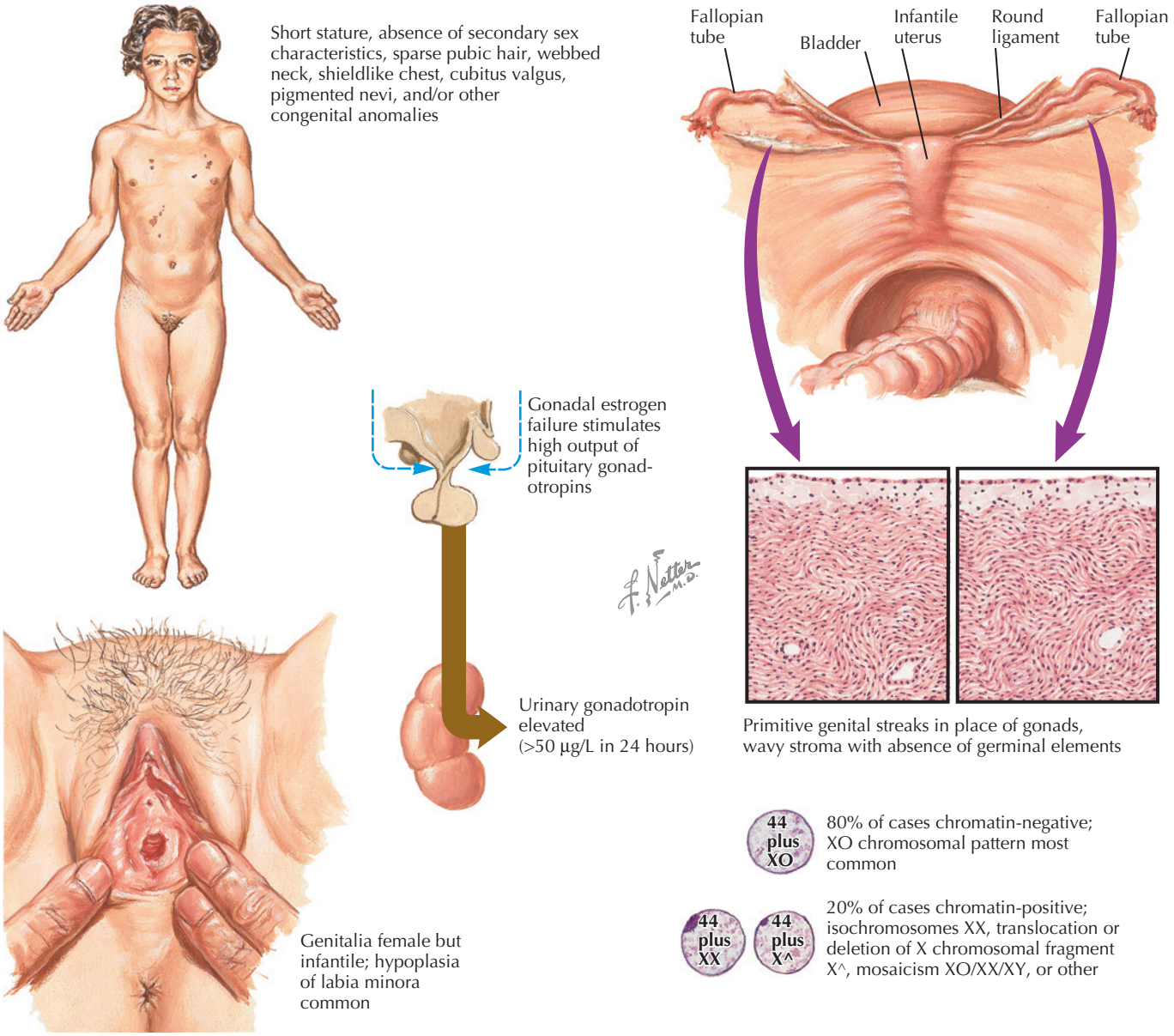


Figure 193.1 Turner syndrome

Patient Education: Extensive counseling about stature, sexual maturation, and fertility.

Drug(s) of Choice

Adolescents are much more sensitive to the effects of estrogen than are postmenopausal women, allowing doses in the range of 0.3 mg of conjugated estrogen, 0.5 mg of estradiol, or their equivalent daily. After 6–12 months of therapy at this level, the dose should be doubled and a progestin (eg, medroxyprogesterone acetate 10 mg for the first 12 days of the month) should be added, or the patient's therapy should be switched to combination oral contraceptives. This generally results in regular menstruation, and normal pubertal development proceeds on its own when the patient reaches a bone age of 13 years. Growth hormone (0.05 mg/kg SC daily) may be effective if given before the age of 10 years.

Contraindications: Undiagnosed amenorrhea.

FOLLOW-UP

Patient Monitoring: Screening for cardiac and renal anomalies, periodic hearing and thyroid testing (annual), monitoring of growth. Screening of serum lipids and glucose and pelvic examinations to detect gonadal neoplasia should be annually performed.

Prevention/Avoidance: Prenatal chromosomal analysis for those known to carry translocations (detection only, not prevention, although the couple may choose not to continue the pregnancy based on the findings).

Possible Complications: Renal or cardiac complications. New-onset breast growth or sexual hair growth should suggest the development of a gonadal tumor.

Expected Outcome: Reasonably normal life with the exception of infertility.

MISCELLANEOUS

Pregnancy Considerations: These patients are infertile. Individuals with a mosaic karyotype may be fertile but pregnancy is associated with a 50% chance of aneuploidy. Aortic dissection or rupture that has been reported in women with Turner syndrome becoming pregnant through in vitro fertilization (IVF) with donor oocytes.

ICD-10-CM Codes: Q96.9 (Turner's syndrome, unspecified).

REFERENCES

LEVEL I

Blum WF, Crowe BJ, Quigley CA, et al. SHOX Study Group. Growth hormone is effective in treatment of short stature associated with short stature homeobox-containing gene deficiency: two-year results of a randomized, controlled, multicenter trial. *J Clin Endocrinol Metab*. 2007;92:219.

Sas TC, de Muinck Keizer-Schrama SM, Stijnen T, et al. Normalization of height in girls with Turner syndrome after long-term growth hormone treatment: results of a randomized dose-response trial. *J Clin Endocrinol Metab*. 1999;84:4607.

LEVEL II

Gravholt CH, Fedder J, Naeraa RW, et al. Occurrence of gonadoblastoma in females with Turner syndrome and Y chromosome material: a population study. *J Clin Endocrinol Metab*. 2000;85:3199.

Hadnott TN, Gould HN, Gharib AM, et al. Outcomes of spontaneous and assisted pregnancies in Turner syndrome: the U.S. National Institutes of Health experience. *Fertil Steril*. 2011;95:2251.

Ogata T, Muroya K, Matsuo N, et al. Turner syndrome and Xp deletions: clinical and molecular studies in 47 patients. *J Clin Endocrinol Metab*. 2001;86:5498.

Piippo S, Lenko H, Kainulainen P, et al. Use of percutaneous estrogen gel for induction of puberty in girls with Turner syndrome. *J Clin Endocrinol Metab*. 2004;89:3241.

Sagi L, Zuckerman-Levin N, Gawlik A, et al. Clinical significance of the parental origin of the X chromosome in Turner syndrome. *J Clin Endocrinol Metab*. 2007;92:846.

LEVEL III

American College of Obstetricians and Gynecologists. Screening for fetal chromosomal abnormalities. ACOG Practice Bulletin 77. *Obstet Gynecol*. 2007;109:217.

American College of Obstetricians and Gynecologists. Primary ovarian insufficiency in adolescents and young women. Committee Opinion No. 605. *Obstet Gynecol*. 2014;123:193.

American College of Obstetricians and Gynecologists. Menstruation in girls and adolescents: using the menstrual cycle as a vital sign. Committee Opinion No. 651. *Obstet Gynecol*. 2015;126:e143.

Bondy CA, Turner Syndrome Study Group. Care of girls and women with Turner syndrome: a guideline of the Turner Syndrome Study Group. *J Clin Endocrinol Metab*. 2007;92:10.

Chu CE, Connor JM. Molecular biology of Turner's syndrome. *Arch Dis Child*. 1995;72:285.

Doswell BH, Visootsak J, Brady AN, et al. Turner syndrome: an update and review for the primary pediatrician. *Clin Pediatr (Phila)*. 2006;45:301.

Practice Committee of the American Society for Reproductive Medicine. Increased maternal cardiovascular mortality associated with pregnancy in women with Turner syndrome. *Fertil Steril*. 2006;86:S127.

Sybert VP, McCauley E. Turner's syndrome. *N Engl J Med*. 2004;351:1227.

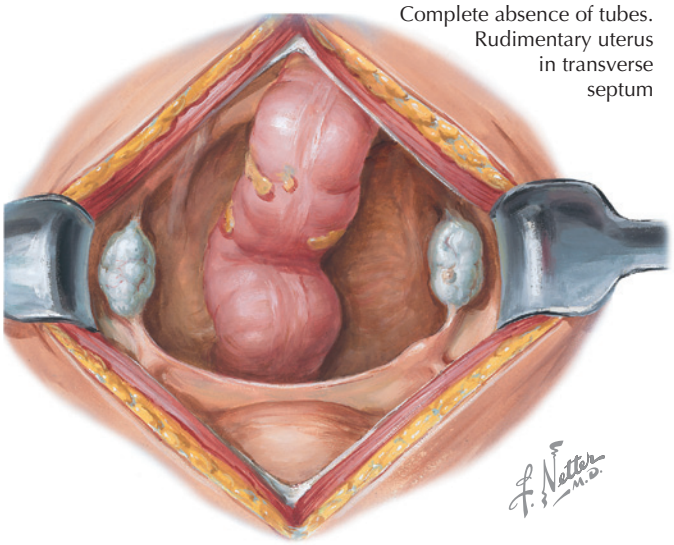


Figure 194.1 Uterine agenesis

Associated Conditions: Primary amenorrhea, infertility, urinary tract abnormalities (25%–40%), skeletal abnormalities (12%), congenital rectovaginal fistula, imperforate anus, and hypospadias.

Workup and Evaluation

Laboratory: Serum follicle-stimulating hormone (FSH; to differentiate hypogonadal hypogonadism and gonadal dysgenesis).
Imaging: No imaging indicated. Ultrasonography may be used to assist the diagnosis but is generally not indicated. Intravenous pyelography should be considered.
Special Tests: Measurement of height, weight, and arm span. A karyotype or buccal smear may be performed but is generally not necessary.
Diagnostic Procedures: History, physical examination, imaging procedures.

Pathologic Findings

One or both fallopian tubes and some fibrous tissue may be present in the normal location of the uterus. Normal ovaries, with normal cyclic ovarian function, are usually present.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and education.
Specific Measures: Patients may require surgical removal of abnormal gonads (after puberty: age 18 years) because of an increased risk for malignancy if Y-chromatin material is present. Fertility may be achieved through in vitro fertilization with implantation into a host uterus.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Frank discussion about the syndrome and its effects (infertility and amenorrhea).

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: Renal, skeletal, and cardiac abnormalities are more common in these patients.
Expected Outcome: Normal life expectancy without reproductive capability. Fertility may be achieved through in vitro fertilization with implantation into a host uterus.

MISCELLANEOUS

Pregnancy Considerations: Normal pregnancy is not possible.
ICD-10-CM Codes: Q51.0 (Agenesis and aplasia of uterus).

REFERENCES

LEVEL III

American College of Obstetricians and Gynecologists. Müllerian agenesis: diagnosis, management, and treatment. Committee Opinion No. 562. *Obstet Gynecol*. 2013;121:1134.

Dwyer PL, Rosamilia A. Congenital urogenital anomalies that are associated with the persistence of Gartner's duct: a review. *Am J Obstet Gynecol*. 2006;195:354.

Fisher K, Esham RH, Thorneycroft I. Scoliosis associated with typical Mayer-Rokitansky-Küster-Hauser syndrome. *South Med J*. 2000;93:243.

Grimbizis GF, Gordts S, Di Spiezio Sardo A, et al. The ESHRE/ESGE consensus on the classification of female genital tract congenital anomalies. *Hum Reprod*. 2013;28:2032.

Griffin JE, Edwards C, Madden JD, et al. Congenital absence of the vagina. The Mayer-Rokitansky-Kuster-Hauser syndrome. *Ann Intern Med*. 1976;85:224.

Jayasinghe Y, Rane A, Stalewski H, et al. The presentation and early diagnosis of the rudimentary uterine horn. *Obstet Gynecol*. 2005;105:1456.

Troiano RN, McCarthy SM. Mullerian duct anomalies: imaging and clinical issues. *Radiology*. 2004;233:19.

VAGINAL AGENESIS

195

INTRODUCTION

Description: Vaginal agenesis is the congenital absence of the vagina, most often associated with an absence of the uterus (Mayer–Rokitansky–Küster–Hauser syndrome). Seven to ten percent of these women have functional endometrium within either a uterus that is obstructed, a rudimentary uterine horn, or cavitated Müllerian remnants.
Prevalence: Reported to vary from 1 of 4000 to 1 of 10,500 female births.
Predominant Age: Generally not diagnosed until puberty, often following a delay of 2–3 years or more.
Genetics: No genetic pattern (accident of development), although in some inbred communities there is a suggestion that an autosomal recessive gene is present.

ETIOLOGY AND PATHOGENESIS

Causes: Failure of the endoderm of the urogenital sinus and the epithelium of the vaginal vestibule to fuse and perforate during embryonic development. This process is normally completed by the 21st week of gestation. Patients with a congenital absence of the vagina but with a uterus present represent an extreme form of transverse vaginal septum.
Risk Factors: None known.

SIGNS AND SYMPTOMS

- Vaginal obstruction (absence)
- Primary amenorrhea
- Cyclic abdominal pain
- Hematometra (if a uterus or uterine remnant is present)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Imperforate hymen
- Hermaphroditism
- Androgen insensitivity syndrome (testicular feminization)
- Mayer–Rokitansky–Küster–Hauser syndrome (75% have vaginal agenesis and 25% have shortened vaginal pouch)
- Transverse vaginal septum

Associated Conditions: Endometriosis, infertility, chronic pelvic pain, sexual dysfunction, hematometra (when uterus is present), urologic abnormalities (25%–40%), and skeletal abnormalities (10%–15%).

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: Ultrasonography, magnetic resonance imaging (MRI), or computed tomography (CT) to determine the presence and status of the upper genital tract structures. Intravenous pyelography should be considered.
Special Tests: Karyotyping or buccal smear should be considered. Laparoscopy may be desirable in some patients to confirm the diagnosis, although this is generally not necessary.
Diagnostic Procedures: History and physical examination (including rectal examination).

Pathologic Findings

The ovaries are usually normal and the fallopian tubes are present.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and reassurance.
Specific Measures: Surgical creation of a vagina if intercourse is desired. May be created by a flap procedure (McIndoe procedure) or progressive perineal pressure techniques (Ingram dilators or bicycle seat). Patients with androgen insensitivity should have their gonads (testes) removed to prevent seminoma (generally after puberty is complete); patients with Mayer–Rokitansky–Küster–Hauser syndrome have normal ovaries and should not have them removed.
Diet: No specific dietary changes indicated.
Activity: No restriction.

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Normal health maintenance. Patients in whom a neovagina is created must be monitored for narrowing.
Prevention/Avoidance: None.
Possible Complications: Hematocolpos, endometriosis, sexual dysfunction. If a neovagina is created, it will scar and stenose if it is not used frequently or maintained with the use of a dilator.
Expected Outcome: Sexual function can generally be restored through the creation of a neovagina. The presence of a uterus is associated with cyclic pain and often must be removed. Except as an egg donor, fertility is unlikely to be restored.

MISCELLANEOUS

Pregnancy Considerations: Generally not a consideration. Patients may be able to achieve reproduction as egg donors.
ICD-10-CM Codes: Q52.4 (Other congenital malformations of vagina).

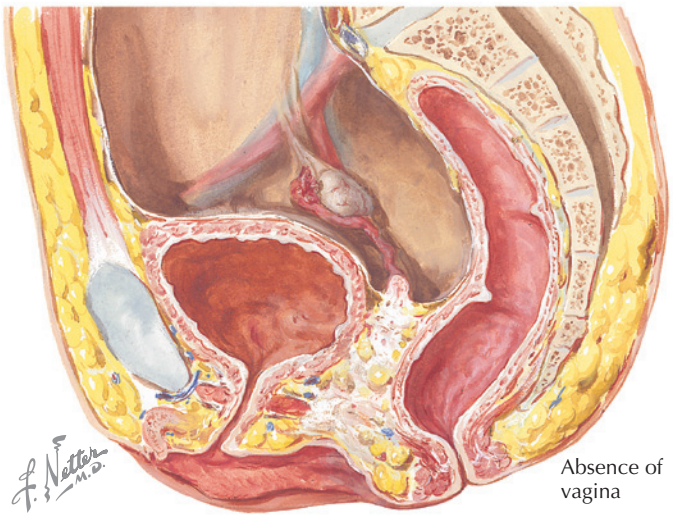


Figure 195.1 Vaginal agenesis

REFERENCES

LEVEL II

Bianchi S, Frontino G, Ciappina N, et al. Creation of a neovagina in Rokitansky syndrome: comparison between two laparoscopic techniques. *Fertil Steril*. 2011;95:1098.

Fedele L, Bianchi S, Frontino G, et al. Laparoscopic findings and pelvic anatomy in Mayer-Rokitansky-Küster-Hauser syndrome. *Obstet Gynecol*. 2007;109:1111.

Gargollo PC, Cannon GM Jr, Diamond DA, et al. Should progressive perineal dilation be considered first line therapy for vaginal agenesis? *J Urol*. 2009;182:1882.

Ingram JM. The bicycle seat stool in the treatment of vaginal agenesis and stenosis: a preliminary report. *Am J Obstet Gynecol*. 1981;140:867.

Woodhouse CR. The sexual and reproductive consequences of congenital genitourinary anomalies. *J Urol*. 1994;152:645.

LEVEL III

American College of Obstetricians and Gynecologists. Müllerian agenesis: diagnosis, management, and treatment. Committee Opinion No. 562. *Obstet Gynecol*. 2013;121:1134.

Giacalone PL, Laffargue F, Faure JM, et al. Ultrasound-assisted laparoscopic creation of a neovagina by modification of Vecchietti's operation. *Obstet Gynecol*. 1999;93:446.

Griffin JE, Edwards C, Madden JD, et al. Congenital absence of the vagina. The Mayer-Rokitansky-Küster-Hauser syndrome. *Ann Intern Med*. 1976; 85:224.

Hensle TW, Chang DT. Vaginal reconstruction. *Urol Clin North Am*. 1999; 26:39, vii.

Lindenman E, Shepard MK, Pescovitz OH. Müllerian agenesis: an update. *Obstet Gynecol*. 1997;90:307.

Tolhurst DE, van der Helm TW. The treatment of vaginal atresia. *Surg Gynecol Obstet*. 1991;172:407.

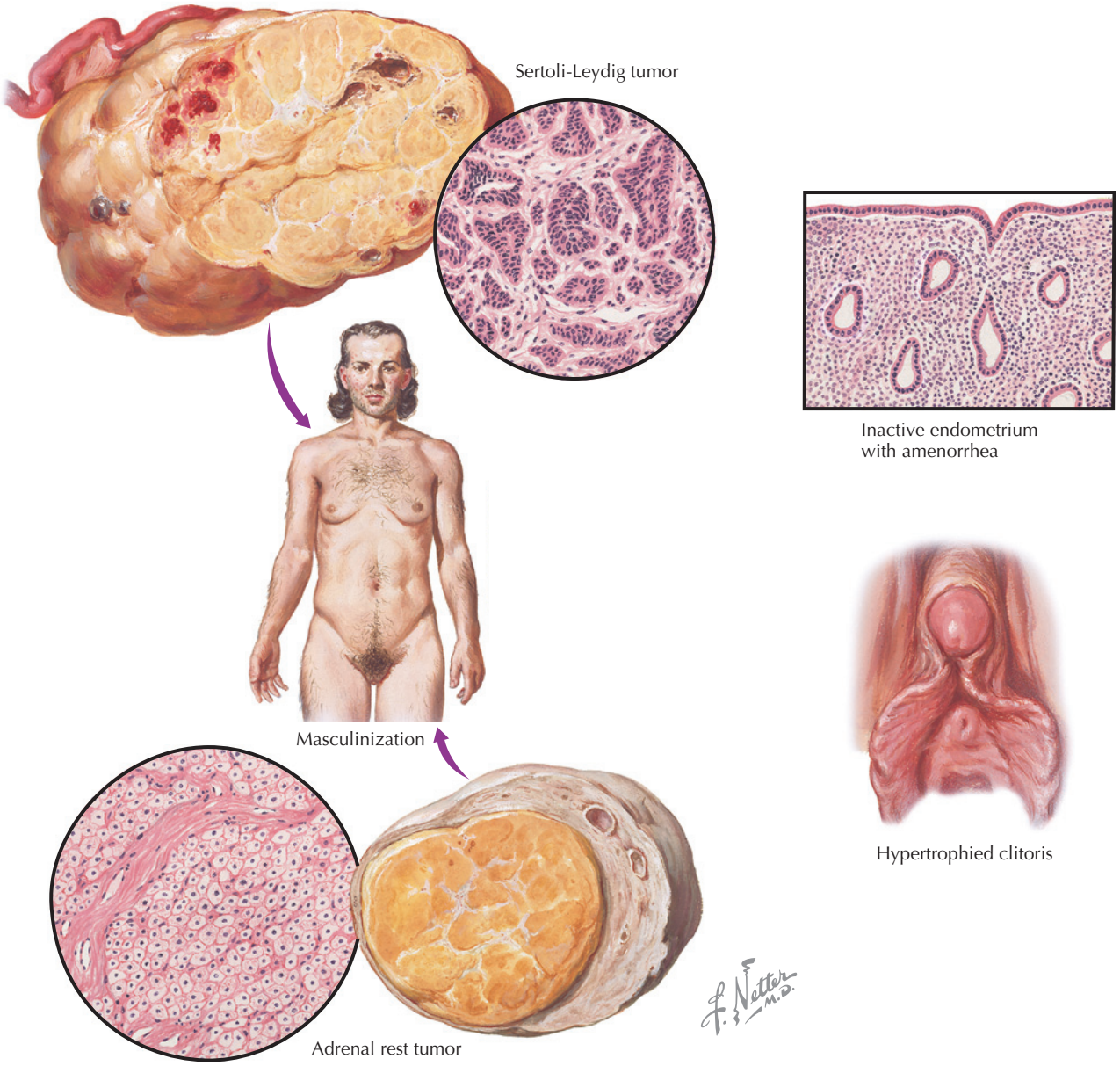


Figure 196.1 Masculinizing neoplasms

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and support, shaving, depilatories, or electrolysis. Topical treatment of acne (if present).
Specific Measures: Patients with polycystic ovary syndrome often do well with oral contraceptive suppression of ovarian function or with the use of spironolactone. Patients with hyperandrogenicity of adrenal origin respond well to cortisol administration, which results in a reduction of the production of androgenic precursors. Tumors require surgical removal.
Diet: No specific dietary changes indicated.
Activity: No restriction.

Drug(s) of Choice

- Polycystic ovary syndrome—combination oral contraceptives, spironolactone 100–200 mg PO daily, medroxyprogesterone acetate (Depo-Provera 150–300 mg IM every 3 months).
- Hyperandrogenicity of adrenal origin—cortisol administration.

Contraindications: Pregnancy (spironolactone is teratogenic; patients of child-bearing potential must use reliable contraception.)

FOLLOW-UP

Patient Monitoring: Normal health maintenance once diagnosis and management have been implemented. There is an increased risk for diabetes in patients with polycystic ovaries.
Prevention/Avoidance: None.
Possible Complications: Permanent loss of feminine attributes and induction of hirsutism, lowering of voice, and others. Chronic anovulation is associated with an increased risk for endometrial hyperplasia and cancer.
Expected Outcome: Good, with appropriate diagnosis and treatment.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy, although some metabolic causes of virilization of the mother may result in reduced fertility or virilization of a fetus.

ICD-10-CM Codes: E25.9 (Adrenogenital disorder, unspecified) (others based on the diagnosis).

REFERENCES

LEVEL I

Azziz R, Ochoa TM, Bradley EL Jr, et al. Leuprolide and estrogen versus oral contraceptive pills for the treatment of hirsutism: a prospective randomized study. *J Clin Endocrinol Metab*. 1995;80:3406.

Moghetti P, Tosi F, Tosti A, et al. Comparison of spironolactone, flutamide, and finasteride efficacy in the treatment of hirsutism: a randomized, double blind, placebo-controlled trial. *J Clin Endocrinol Metab*. 2000;85:89.

LEVEL II

Alpañés M, González-Casbas JM, Sánchez J, et al. Management of postmenopausal virilization. *J Clin Endocrinol Metab*. 2012;97:2584.

Guido M, Romualdi D, Giuliani M, et al. Drospirenone for the treatment of hirsute women with polycystic ovary syndrome: a clinical, endocrinological, metabolic pilot study. *J Clin Endocrinol Metab*. 2004;89:2817.

LEVEL III

American College of Obstetricians and Gynecologists. Polycystic ovary syndrome. ACOG Practice Bulletin No. 108. *Obstet Gynecol*. 2009;114:936.

American College of Obstetricians and Gynecologists. Noncontraceptive uses of hormonal contraceptives. Practice Bulletin No. 110. *Obstet Gynecol*. 2010;115:206.

Azziz R. The evaluation and management of hirsutism. *Obstet Gynecol*. 2003;101:995.

Conn JJ, Jacobs HS. Managing hirsutism in gynaecological practice. *Br J Obstet Gynaecol*. 1998;105:687.

Ehrmann DA. Polycystic ovary syndrome. *N Engl J Med*. 2005;352:1223.

Ehrmann DA, Rosenfield RL. Clinical review 10: an endocrinologic approach to the patient with hirsutism. *J Clin Endocrinol Metab*. 1990;71:1.

Gordon CM. Menstrual disorders in adolescents. Excess androgens and the polycystic ovary syndrome. *Pediatr Clin North Am*. 1999;46:519.

Harborne L, Fleming R, Lyall H, et al. Metformin or antiandrogen in the treatment of hirsutism in polycystic ovary syndrome. *J Clin Endocrinol Metab*. 2003;88:4116.

Rosenfield RL. Clinical practice. Hirsutism. *N Engl J Med*. 2005;353:2578.

Tagatz GE, Kopher RA, Nagel TC, et al. The clitoral index: a bioassay of androgenic stimulation. *Obstet Gynecol*. 1979;54:562.

SECTION XII

Obstetrics: General Considerations

This page intentionally left blank

PRECONCEPTIONAL CARE AND COUNSELING

197

THE CHALLENGE

In many ways, prenatal care is the prototypical example of preventive medicine. Preconceptional care is directed toward ensuring the optimal health of the prospective mother and doing those things that will remove preventable impediments to a healthy outcome for the pregnancy. The care these women receive during this and the prenatal phase of their lives is critical to both their health and the success of the pregnancy.

Scope of the Problem: In the United States, approximately 4 million women give birth each year, and more than 90% of American women will bear children during their lifetime. Twenty percent or more of women have one or more risk factors that could adversely affect a pregnancy if not addressed. Therefore, women who receive delayed (after 12 weeks of pregnancy) or no prenatal care are at a risk for having undetected or preventable complications of pregnancy that can result in significant maternal or fetal morbidity or mortality.

Objectives of Management: To protect the health and well-being of mother, fetus, and neonate through screening and optimizing a woman's health and knowledge before conceiving a pregnancy.

TACTICS

Relevant Pathophysiology: The initiation of folic acid supplementation at least 1 month before pregnancy has been shown to reduce the incidence of neural tube defects such as spina bifida and anencephaly. Because organogenesis begins early in pregnancy, starting folic acid supplementation after neural tube closure (28 days after conception) has no demonstrated benefit in reducing neural tube defects. Similarly, adequate glucose control

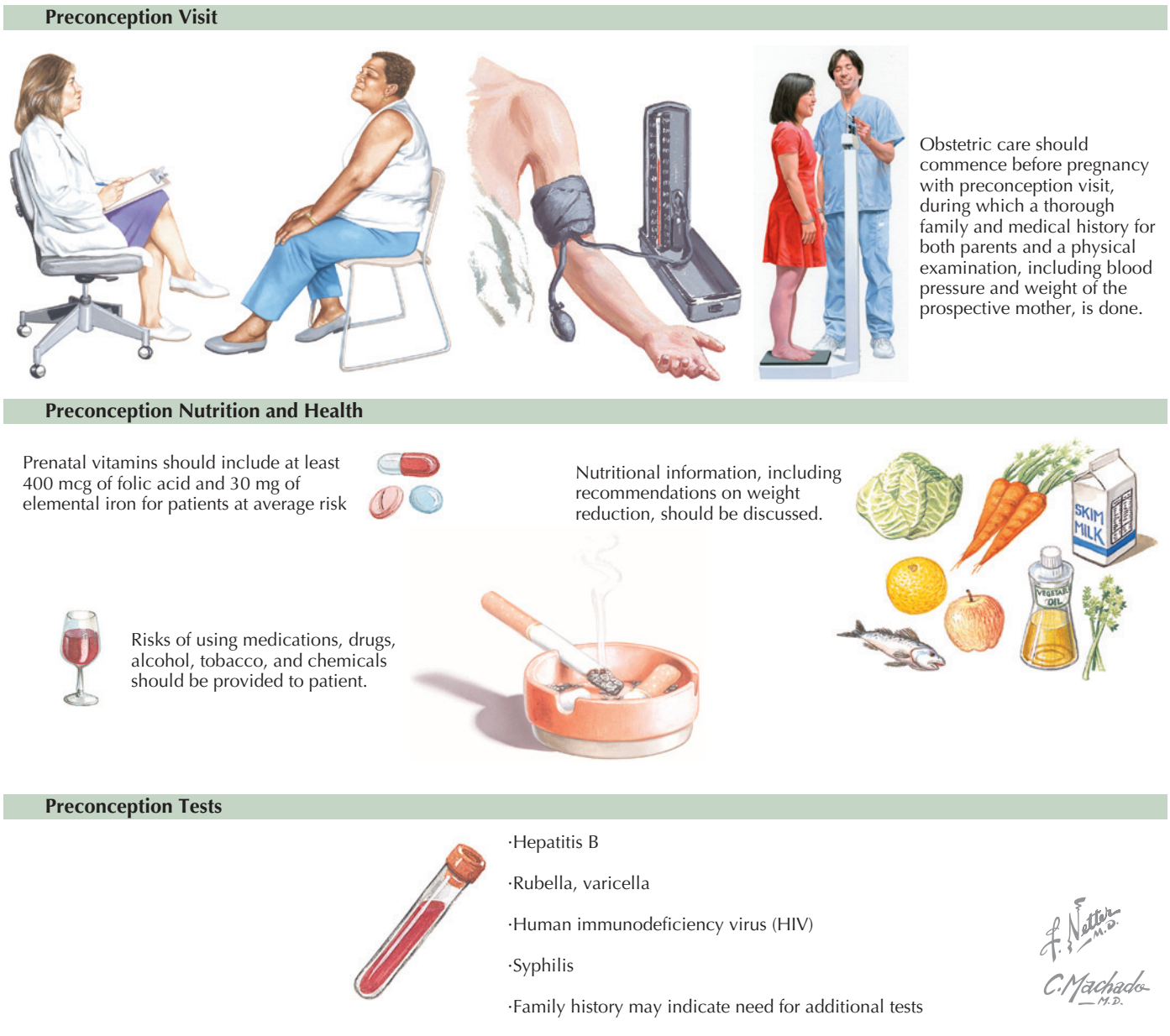


Figure 197.1 Preconception visit, nutrition and health, and tests

in a woman with diabetes before conception and throughout pregnancy decreases maternal morbidity, spontaneous abortion, fetal malformation, fetal macrosomia, intrauterine fetal death, and neonatal morbidity. Reducing the risk of infectious diseases that can have adverse effects on the mother or fetus if contracted during pregnancy, through vaccination (eg, rubella) or avoidance (eg, toxoplasmosis), is a proven preventive strategy.

Strategies: Ideally, obstetric care should commence before pregnancy with a preconception visit, during which a thorough family and medical history for both parents is taken and a physical examination of the prospective mother is performed. Both before and between pregnancies, pre-existing conditions that may affect conception, pregnancy, or both should be identified, and appropriate management plans should be formulated with the goal of a "healthy" subsequent pregnancy. Nearly half of all pregnancies in the United States are unintended, making the challenge of preconception care more difficult. As a result, effective preconceptional care must address pregnancy planning for women who seek care in anticipation of a planned pregnancy and, just as importantly, for all women with childbearing potential.

- General evaluations are directed toward establishing optimal maternal health, providing nutritional counseling, and instituting appropriate prophylaxis. This generally takes the form of genetic screening or the detection of maternal diseases that will alter or be altered by the future pregnancy. Based on the age, ethnic origin, race, or family history, couples may be identified who are at increased risk for chromosomal or enzymatic abnormalities, such as sickle cell trait, thalassemia, or Tay-Sachs disease carrier state. A family history that is positive for certain diseases, such as cystic fibrosis and congenital hearing loss, indicates the need for additional screening.
- The evaluation should focus on many aspects of the woman's life that can adversely influence the outcome of the pregnancy: undiagnosed, untreated, or poorly controlled medical conditions; immunization history; medication use; occupational and environmental exposures; nutritional issues; tobacco and substance use; and any other high-risk behaviors. Social and mental health issues that may affect the woman's ability to access and participate in prenatal care should also be addressed.
- Before pregnancy is the optimal time for immunizing against hepatitis B, rubella, and varicella, as well as screening for human immunodeficiency virus and syphilis infections; if found, treatment should be initiated to prevent the transmission of the disease to the fetus. The patient should be counseled on ways to prevent infection with toxoplasmosis, cytomegalovirus, and parvovirus. Anemia, hypothyroidism, urinary tract infections, and other conditions may be identified and nutritional counseling and weight reduction may be affected before pregnancy. Admonitions about the risks of using medications, drugs, alcohol, and tobacco and avoidance of chemicals such as solvents and pesticides during early pregnancy may be given.
- Patients considering pregnancy in the immediate future should be prescribed prenatal vitamins, folic acid supplements, or both. Prenatal vitamins should include at least 400 mcg of folic acid and 30 mg of elemental iron for patients at an average risk. The dosage of folic acid should be increased to 1 mg/day for women with diabetes mellitus, epilepsy, or hemoglobinopathies. Patients who have given birth to a child with neural tube defects should take 4 mg of folic acid per day for subsequent pregnancies. Higher levels of supplementation should not be achieved by taking excess multivitamins because of the risk of vitamin A toxicity.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Booklets AP056 (Good Health Before Pregnancy: Preconceptional Care), AB012 (Planning Your Pregnancy), AP001 (Nutrition During Pregnancy), AP103 (Having a Baby-Especially for Teens), AB005 (You and Your Baby: Prenatal Care, Labor and Delivery, and Postpartum Care), AP060 (Having a Baby After Age 35), and AP032 (A Father's Guide to Pregnancy).

IMPLEMENTATION

Special Considerations: If the patient has significant medical problems, the impact of pregnancy on these problems and the implications for the pregnancy may be determined, and where possible, the risks may be reduced before conception. Medications for hypertension, epilepsy, thromboembolism, depression, and anxiety should be reviewed and changed, if necessary, before the patient becomes pregnant.

REFERENCES

LEVEL II

Milunsky A, Jick H, Jick SS, et al. Multivitamin/folic acid supplementation in early pregnancy reduces the prevalence of neural tube defects. *JAMA*. 1989;262:2847.

LEVEL III

American Academy of Pediatrics, American College of Obstetricians and Gynecologists. *Guidelines for perinatal care*. 7th ed. Elk Grove Village, IL: AAP; Washington, DC: ACOG; 2012.

American College of Obstetricians and Gynecologists. *Access to women's health care. ACOG Statement of Policy*. Washington, DC: ACOG; 2003.

American College of Obstetricians and Gynecologists. Neural tube defects. ACOG Practice Bulletin 44. *Obstet Gynecol*. 2003;102:203.

American College of Obstetricians and Gynecologists. Pregestational diabetes mellitus. ACOG Practice Bulletin 60. *Obstet Gynecol*. 2005; 105:675.

American College of Obstetricians and Gynecologists. Screening for Tay–Sachs disease. ACOG Committee Opinion No. 318. *Obstet Gynecol*. 2005;106:893.

American College of Obstetricians and Gynecologists. The importance of preconception care in the continuum of women's health care. ACOG Committee Opinion 313. *Obstet Gynecol*. 2005;106:665.

American Diabetes Association. Preconception care of women with diabetes. *Clinical Diabetes*. 2000;18:124.

Botto LD, Moore CA, Khoury MJ, et al. Neural-tube defects. *N Engl J Med*. 1999;341:1509.

Iqbal MM. Prevention of neural tube defects by periconceptional use of folic acid. *Pediatr Rev*. 2000;21:58.

Johnson K, Posner SF, Biermann J, et al. Recommendations to improve preconception health and health care—United States. *MMWR Recomm Rep*. 2006;55:1.

Lu MC, Kotelchuck M, Culhane JF, et al. Preconception care between pregnancies: the content of internatal care. *Matern Child Health J*. 2006;10:107.

ROUTINE PRENATAL CARE: FIRST TRIMESTER

198

THE CHALLENGE

Despite the dramatic and vulnerable changes that the conceptus undergoes in the first 14 weeks of gestation, many patients are unaware of their pregnancy or delay seeking prenatal care. Evidence suggests that it is during this period the foundations of a successful pregnancy and even the future health of the adult individual are set. Although most pregnant women would deliver healthy infants without any prenatal care, obstetric care is designed to promote optimal health throughout the course of normal pregnancy while screening for and managing any complications that may develop.

Scope of the Problem: Approximately one-fourth of pregnant women do not receive care during the first trimester.

Objectives of Management: To protect the health and well-being of mother and fetus.

TACTICS

Relevant Pathophysiology: During the first trimester of gestation, the developing embryo implants in the endometrium (except in the case of ectopic pregnancies), the placental attachment to the mother is created, and the major structures and organs of the body are formed. The developing embryo is sensitive to exposures to toxins, medications, radiation, and the effects of maternal conditions that can disrupt this process. Errors in this process may result in major disruptions in structure or function of the fetus or even the complete loss of the pregnancy. At approximately the 12th week of gestation, the placenta takes over hormonal support for the pregnancy from the corpus luteum. If this transition does not smoothly occur, the pregnancy can be lost.

Strategies: At the first prenatal visit, a comprehensive history should be taken, including previous pregnancy outcome(s), if any, and any medical or surgical conditions that may affect pregnancy. This should include past medical history, information pertinent to genetic screening, and any events in the course of the current pregnancy. Special attention should also be given to diet, tobacco or alcohol use, and any medications or substances used. Routine laboratory studies should be conducted, and the patient should be given instructions concerning routine prenatal care, warning signs of complications, and who to contact with questions or problems (Box 198.1). A complete physical examination should be performed, including a Pap test (based upon screening guidelines) and tests for sexually transmitted infections.

- It is important early in the course of pregnancy to establish an accurate gestational age and estimated date of confinement (EDC, or due date). This information is needed to manage later complications of pregnancy and to determine the timing of evaluations (eg, neural tube screening, 1-hour glucose challenge testing, Rh prophylaxis). If needed, transvaginal and transabdominal ultrasonographic techniques allow gestational age determination with an approximate 7- to 10-day accuracy when performed during the first trimester.
- At each visit, the patient should be asked about any problems such as vaginal bleeding, nausea/vomiting, dysuria, or vaginal

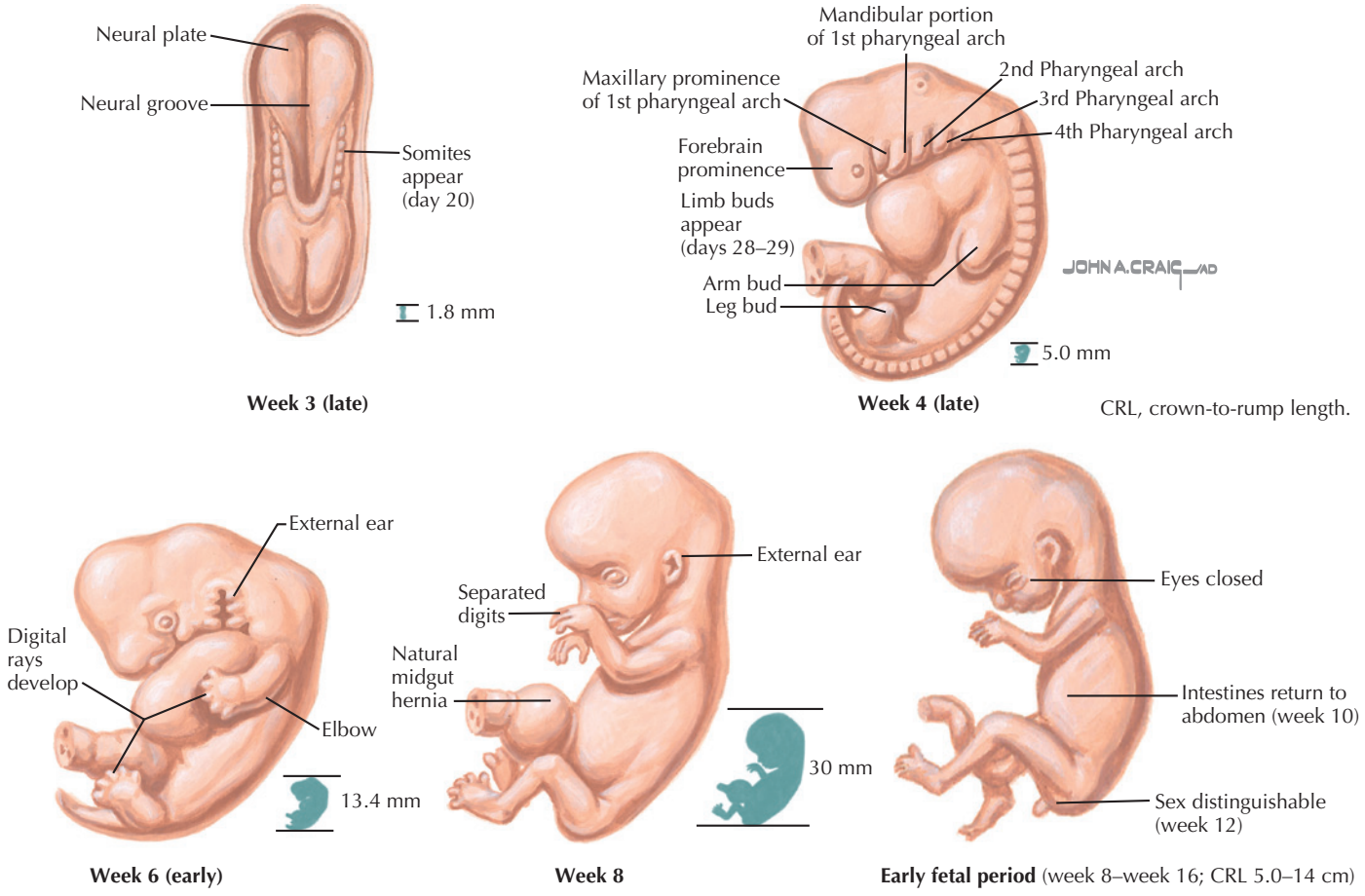


Figure 198.1 Developmental events of the first trimester

Box 198.1 COMMONLY ORDERED INITIAL LABORATORY AND OTHER TESTS

- Complete blood count
- Urinalysis and urine culture and sensitivity
- Blood group, Rh, antibody screen
- Serologic test for syphilis (rapid plasma reagin [RPR], Venereal Disease Research Laboratory [VDRL])
- Human immunodeficiency virus (HIV) titer by enzyme-linked immunosorbent assay (ELISA); Western blot if HIV+ by ELISA
- Hepatitis B surface antigen
- Rubella titer
- Cervical cytology (Pap test) based upon screening guidelines
- Testing for *Neisseria gonorrhoeae*
- Hemoglobin electrophoresis (selected patients)
- Maternal serum screening for open neural tube defects (triple or quad screen) at 15–20 weeks (maternal serum α-fetoprotein plus other markers)

discharge. Each prenatal visit should include measurements of blood pressure and weight and an assessment for edema. (Blood pressure generally declines at the end of the first trimester, increasing again in the third trimester.) A clean-catch urine sample should be tested (most often by dipstick) for protein and signs of infection. Obstetric assessments should include uterine size by pelvic examination or fundal height measurement and documentation of the presence and rate of fetal heart tones by the use of a fetal Doppler ultrasound device. (The fetal heart may not be routinely detected by a Doppler device until 12 weeks or later.)

- Patients at a low risk may be followed at 4-week intervals until 28 weeks of gestation.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Booklets AP001 (Nutrition During Pregnancy), AB005 (You and Your Baby: Prenatal Care, Labor and Delivery, and Postpartum Care), AP032 (A Father's Guide to Pregnancy), AP060 (Having a Baby After Age 35), AP090 (Early Pregnancy Loss), AP0103 (Having a Baby-Especially for Teens), AP119 (Exercise During Pregnancy), AP126 (Morning Sickness: Nausea and Vomiting of Pregnancy), AP133 (Routine Tests in Pregnancy), AP156 (How Your Baby Grows During Pregnancy), and AP165 (Screening Tests for Birth Defects).

IMPLEMENTATION

Special Considerations: Between 4% and 8% of pregnant women are victims of "battering" and will benefit from counseling or help finding shelters and other social supports. In the United States, suicide, homicide, and trauma associated with auto accidents where seat belts were not used account for three-fourths of maternal mortality. These are all areas in which proactive counseling and assistance can have a positive impact on reducing morbidity or mortality.

If a genetic evaluation of the fetus is indicated, chorionic villus sampling may be performed between the 10th and 12th week of gestation. Screening for cystic fibrosis should be offered to all patients during either the first or second trimester.

REFERENCES

LEVEL III

American Academy of Pediatrics, American College of Obstetricians and Gynecologists. *Guidelines for perinatal care*. 7th ed. Elk Grove Village, IL: AAP; Washington, DC: ACOG; 2012.

American College of Obstetricians and Gynecologists. *Prevention of Rh D alloimmunization. ACOG Practice Bulletin 4*. Washington, DC: ACOG; 1999.

American College of Obstetricians and Gynecologists. Air travel during pregnancy. ACOG Committee Opinion 264. *Obstet Gynecol*. 2001;98:1187.

American College of Obstetricians and Gynecologists. Exercise during pregnancy and the postpartum period. ACOG Committee Opinion 267. *Obstet Gynecol*. 2002;99:171.

American College of Obstetricians and Gynecologists. Neural tube defects. ACOG Practice Bulletin 44. *Obstet Gynecol*. 2003;102:203.

American College of Obstetricians and Gynecologists. Guidelines for diagnostic imaging during pregnancy. ACOG Committee Opinion 299. *Obstet Gynecol*. 2004;104:647.

American College of Obstetricians and Gynecologists. Management of alloimmunization during pregnancy. ACOG Practice Bulletin No. 75. *Obstet Gynecol*. 2006;108:457.

American College of Obstetricians and Gynecologists. Screening for fetal chromosomal abnormalities. ACOG Practice Bulletin 77. *Obstet Gynecol*. 2007;109:217.

American College of Obstetricians and Gynecologists. Invasive prenatal testing for aneuploidy. ACOG Practice Bulletin No. 88. *Obstet Gynecol*. 2007;110:1459.

American College of Obstetricians and Gynecologists. Anemia in pregnancy. ACOG Practice Bulletin No. 95. *Obstet Gynecol*. 2008;112:201.

American College of Obstetricians and Gynecologists. Ultrasonography in pregnancy. ACOG Practice Bulletin No. 101. *Obstet Gynecol*. 2009;113:451.

American College of Obstetricians and Gynecologists. Cytomegalovirus, parvovirus B19, varicella zoster, and toxoplasmosis in pregnancy. Practice Bulletin No. 151. *Obstet Gynecol*. 2015;125:1510.

American College of Obstetricians and Gynecologists. Thyroid disease in pregnancy. Practice Bulletin No. 148. *Obstet Gynecol*. 2015;125:996.

Prevention of neural tube defects: Results of the Medical Research Council Vitamin Study. MRC Vitamin Study Research Group. *Lancet*. 1991;338:131.

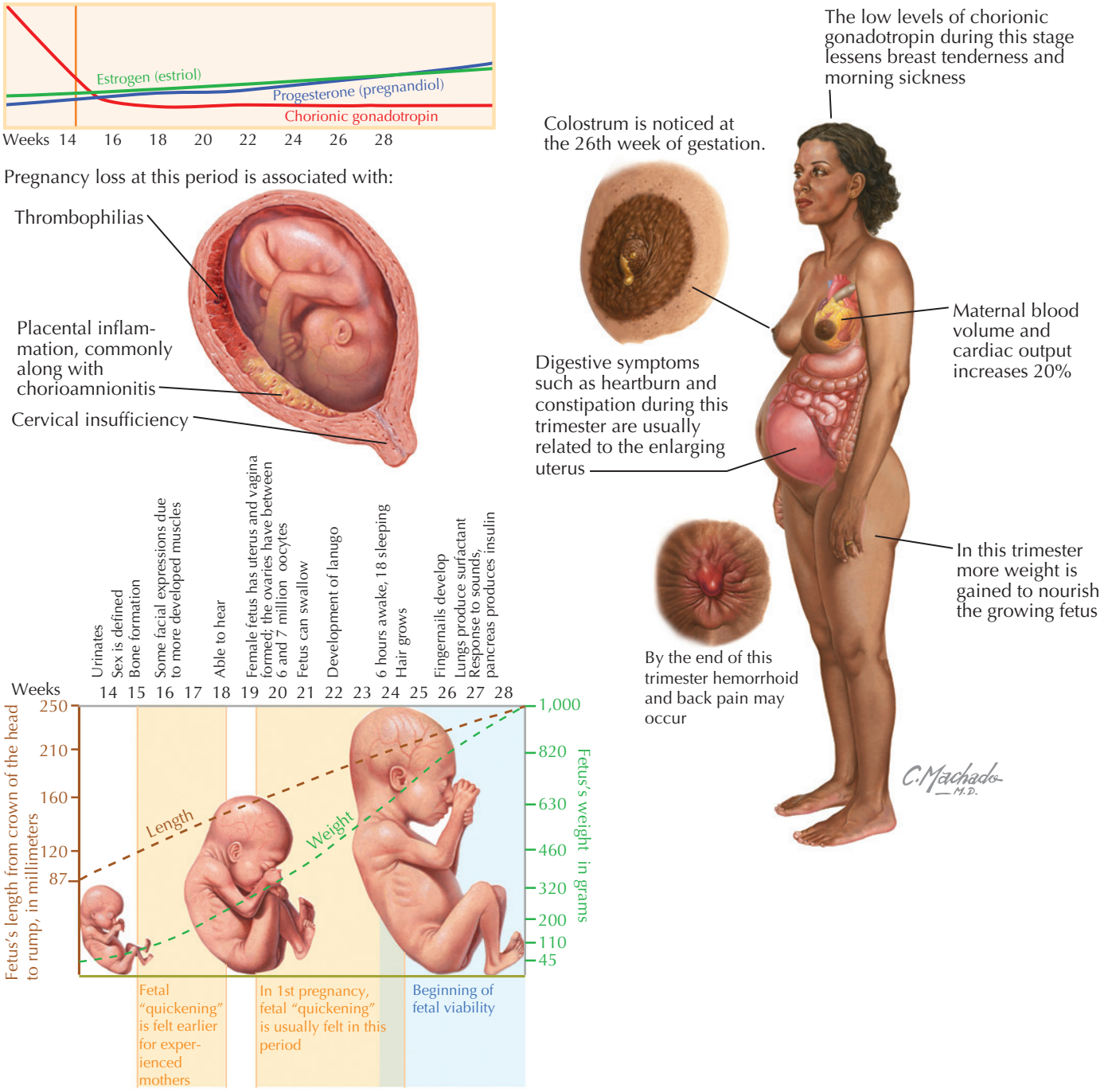


Figure 199.1 Developmental events of the second trimester

Objectives of Management: To protect the health and well-being of the mother and fetus.

TACTICS

Relevant Pathophysiology: During the second trimester of gestation, levels of human chorionic gonadotropin plateau and often decline, easing many of the early maladies of pregnancy such as breast tenderness and morning sickness, although the growing uterus may now bring on heartburn and constipation. The risk for early pregnancy loss has passed (except for infrequent cases of cervical incompetence and preterm labor) and the fetus grows from being just 3 inches in length at 14 weeks to weighing approximately 2 pounds by the end of the second trimester. There is an increase in maternal blood volume and cardiac output (20% greater) to feed the needs of the growing pregnancy. The first detectable movements of the baby (quickening) occur during this trimester (generally at approximately 16–20 weeks of gestation) and the female fetus has the most egg cells of any point in her life (oocytes peak at 6–7 million at approximately 16–20 weeks of gestation, declining to approximately 1 million at birth). Fetal viability (ability to survive apart from the mother) begins at

approximately 24 weeks, although intact survival at this stage is unlikely. Toward the end of this trimester maternal hemorrhoids and low back pain may occur. Colostrum (the first form of breast milk) is present by 26 weeks of gestation.

Strategies: At each visit, patients should be asked about any problems such as vaginal bleeding, nausea/vomiting, dysuria, or vaginal discharge. Each prenatal visit should include measurements of blood pressure and weight and an assessment for edmea. (Blood pressure generally declines at the end of the first trimester, increasing again in the third trimester.) A clean-catch urine sample should be tested (most often by dipstick) for protein and signs of infection. Obstetric assessments should include uterine size by fundal height measurement and documentation of the presence and rate of fetal heart tones by the use of a fetal Doppler ultrasound device.

- Screening for open neural tube and other defects (via measurement of maternal serum alpha-fetoprotein and other markers) is generally performed between 15 and 20 weeks.
- Toward the end of this trimester, a repeat measurement of hemoglobin is taken, glucose screening (usually 1-hour glucose challenge at 28 weeks for patients at a low risk) is performed, and prophylactic treatment with Rh D immune globulin is given for patients who are Rh negative.
- Patients at low risk may be followed at 4-week intervals until the end of this trimester. Routine use of ultrasonography to screen low-risk pregnancies in not currently recommended.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Booklets AP001 (Nutrition During Pregnancy), AB005 (You and Your Baby: Prenatal Care, Labor and Delivery, and Postpartum Care), AP060 (Having a Baby After Age 35), AP0103 (Having a Baby-Especially for Teens), AP119 (Exercise During Pregnancy), AP133 (Routine Tests in Pregnancy), and AP156 (How Your Baby Grows During Pregnancy).

IMPLEMENTATION

Special Considerations: If a genetic evaluation of the fetus is indicated, an amniocentesis may be performed between the 12th and 21st weeks of gestation. Screening for cystic fibrosis should be offered to all patients during either the first or second trimester.

REFERENCES

LEVEL III

American Academy of Pediatrics, American College of Obstetricians and Gynecologists. *Guidelines for perinatal care*. 7th ed. Elk Grove Village, IL: AAP; Washington, DC: ACOG; 2012.

American College of Obstetricians and Gynecologists. *Prevention of Rh D alloimmunization. ACOG Practice Bulletin 4*. Washington, DC: ACOG; 1999.

American College of Obstetricians and Gynecologists. Air travel during pregnancy. ACOG Committee Opinion 264. *Obstet Gynecol*. 2001;98:1187.

American College of Obstetricians and Gynecologists. Exercise during pregnancy and the postpartum period. ACOG Committee Opinion 267. *Obstet Gynecol*. 2002;99:171.

American College of Obstetricians and Gynecologists. Neural tube defects. ACOG Practice Bulletin 44. *Obstet Gynecol*. 2003;102:203.

American College of Obstetricians and Gynecologists. Guidelines for diagnostic imaging during pregnancy. ACOG Committee Opinion 299. *Obstet Gynecol*. 2004;104:647.

American College of Obstetricians and Gynecologists. Management of alloimmunization during pregnancy. ACOG Practice Bulletin No. 75. *Obstet Gynecol*. 2006;108:457.

American College of Obstetricians and Gynecologists. Screening for fetal chromosomal abnormalities. ACOG Practice Bulletin 77. *Obstet Gynecol*. 2007;109:217.

American College of Obstetricians and Gynecologists. Invasive prenatal testing for aneuploidy. ACOG Practice Bulletin No. 88. *Obstet Gynecol*. 2007;110:1459.

American College of Obstetricians and Gynecologists. Anemia in pregnancy. ACOG Practice Bulletin No. 95. *Obstet Gynecol*. 2008;112:201.

American College of Obstetricians and Gynecologists. Ultrasonography in pregnancy. ACOG Practice Bulletin No. 101. *Obstet Gynecol*. 2009;113:451.

American College of Obstetricians and Gynecologists. Cerclage for the management of cervical insufficiency. Practice Bulletin No. 142. *Obstet Gynecol*. 2014;123:372.

American College of Obstetricians and Gynecologists. Thyroid disease in pregnancy. Practice Bulletin No. 148. *Obstet Gynecol*. 2015;125:996.

American College of Obstetricians and Gynecologists. Cytomegalovirus, parvovirus B19, varicella zoster, and toxoplasmosis in pregnancy. Practice Bulletin No. 151. *Obstet Gynecol*. 2015;125:1510.

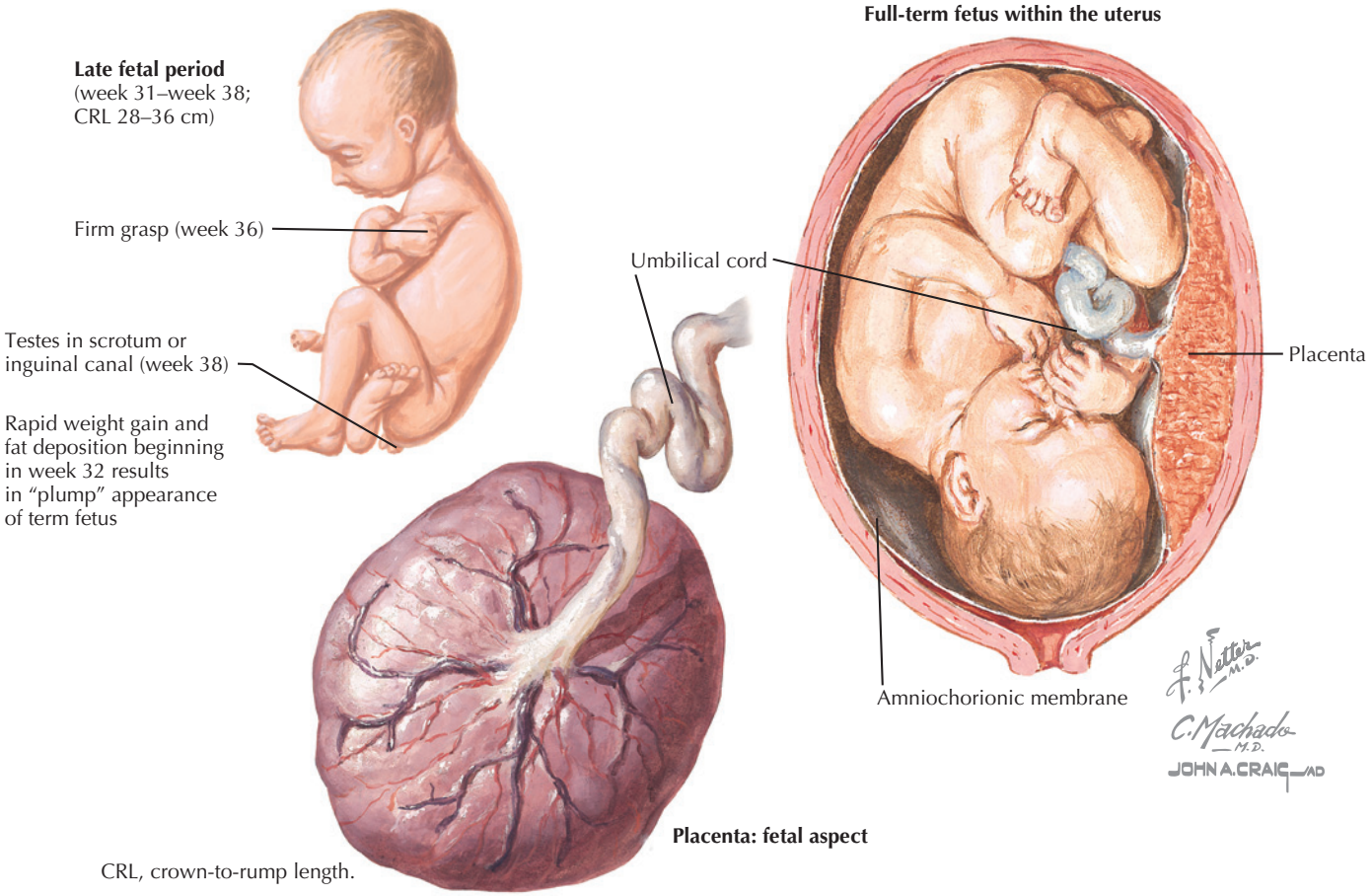


Figure 200.1 Developmental events of the third trimester

cardiac output reaches its maximum. By the 29th week, the fetus has 300 bones, although many of them will fuse after birth, leaving the adult with a total of 206. The fetal presenting part begins to descend into the maternal pelvis in the last month of pregnancy, resulting in a decline in fundal height, improved respiratory and gastric function, and greater pelvic pressure and discomfort. Late in this trimester, changes in the cervix begin the preparations for dilation and effacement during labor and delivery.

Strategies: At each visit, patients continue to be asked about any problems such as vaginal bleeding, nausea/vomiting, dysuria, or vaginal discharge. Each prenatal visit should include measurements of blood pressure and weight and an assessment for edema. A clean-catch urine sample should be tested (most often by dipstick) for protein and signs of infection. Obstetric assessments should include uterine size by fundal height measurement and documentation of the presence and rate of fetal heart tones using a fetal Doppler ultrasound device. Fundal height in centimeters will generally match the gestational age of the pregnancy up to between 31 and 34 weeks. All measurements should be made with the patient's bladder empty; a full bladder can add up to 3 cm to the measurement. Vaginal examinations to assess the dilation and effacement of cervix may be indicated for those with a history of premature labor or those experiencing symptoms of labor. (Routine cervical checks near term are not normally necessary or useful.)

- For selected patients, "kick counts" may be used to assess the overall health of the fetus. In general, the detection of more than four fetal movements over the course of an hour indicates a healthy fetus. All patients should be encouraged to monitor their baby's activity levels and be evaluated for any prolonged reduction or absence in activity.
- At approximately 35–37 weeks of gestation a culture for group B streptococcus should be obtained to identify patients who are carriers and will require antibiotic treatment during labor. Some practitioners choose to just treat all patients during labor based on a review of risk factors. Both strategies are equally acceptable.
- Planning and preparation for breastfeeding should be undertaken during this trimester. No special physical preparation is needed for successful breastfeeding, but discussion, questions, and the acquisition of needed supplies (eg, nursing bra) are best taken care of before delivery.
- For high-risk pregnancies, antenatal testing (nonstress test, contraction stress test, biophysical profile) should be considered and implemented as indicated.
- Patients at low risk may be followed at 2-week intervals until approximately the 36th week, when visits occur at weekly intervals (or more often as dictated by the course of the pregnancy).

Patient Education: American College of Obstetricians and Gynecologists Patient Education Booklets AP001 (Nutrition During Pregnancy), AB005 (You and Your Baby: Prenatal Care, Labor and Delivery, and Postpartum Care), AP060 (Having a Baby After Age 35), AP069 (What to Expect After Your Due Date), AP079 (If Your Baby is Breech), AP098 (Special Test for Monitoring Fetal Health), AP0103 (Having a Baby-Especially for Teens), AP119 (Exercise During Pregnancy), AP133 (Routine Tests in Pregnancy), and AP156 (How Your Baby Grows During Pregnancy).

IMPLEMENTATION

Special Considerations: Patients at high risk should be rechecked for sexually transmitted infections (HIV, syphilis, gonorrhea, and chlamydia) toward the end of pregnancy.

REFERENCES

LEVEL III

American Academy of Pediatrics, American College of Obstetricians and Gynecologists. *Guidelines for perinatal care*. 7th ed. Elk Grove Village, IL: AAP; Washington, DC: ACOG; 2012.

American College of Obstetricians and Gynecologists. *Prevention of Rh D alloimmunization. ACOG Practice Bulletin 4*. Washington, DC: ACOG; 1999.

American College of Obstetricians and Gynecologists. Air travel during pregnancy. ACOG Committee Opinion 264. *Obstet Gynecol*. 2001;98: 1187.

American College of Obstetricians and Gynecologists. Exercise during pregnancy and the postpartum period. ACOG Committee Opinion 267. *Obstet Gynecol*. 2002;99:171.

American College of Obstetricians and Gynecologists. Guidelines for diagnostic imaging during pregnancy. ACOG Committee Opinion 299. *Obstet Gynecol*. 2004;104:647.

American College of Obstetricians and Gynecologists. Management of alloimmunization during pregnancy. ACOG Practice Bulletin No. 75. *Obstet Gynecol*. 2006;108:457.

American College of Obstetricians and Gynecologists. Anemia in pregnancy. ACOG Practice Bulletin No. 95. *Obstet Gynecol*. 2008;112:201.

American College of Obstetricians and Gynecologists. Ultrasonography in pregnancy. ACOG Practice Bulletin No. 101. *Obstet Gynecol*. 2009;113: 451.

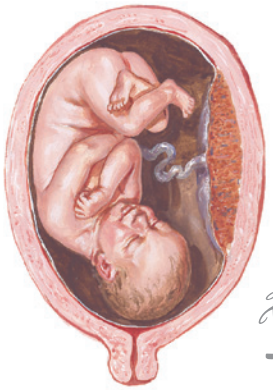
American College of Obstetricians and Gynecologists. Prediction and prevention of preterm birth. Practice Bulletin No. 130. *Obstet Gynecol*. 2012;120:964.

American College of Obstetricians and Gynecologists. Cerclage for the management of cervical insufficiency. Practice Bulletin No. 142. *Obstet Gynecol*. 2014;123:372.

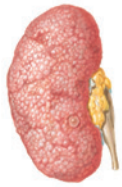
Noninvasive testing used to identify ''high-risk'' fetus and to elicit signs of deteriorating status to allow intervention and prevent mortality

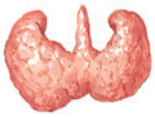
Testing based on premise that marginal fetal oxygenation limits fetal ability to modulate fetal heart rate in response to fetal movement or to placental ischemia as a result of uterine contraction. Fetal heart rate should show acceleration to movement or contraction

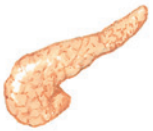
Nonstress Test (NST)
Contraction Stress Test (CST)
Biophysical Profile (BPP)



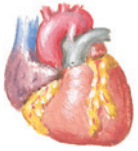
Some Conditions That Suggest Need for Antepartum Testing


Chronic renal disease

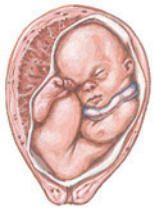

Hyperthyroidism


Diabetes mellitus

Maternal hypertension


Maternal cyanotic heart disease

Intrauterine growth restriction


Reduced fetal movement

Management Flowchart for Antepartum Fetal Testing

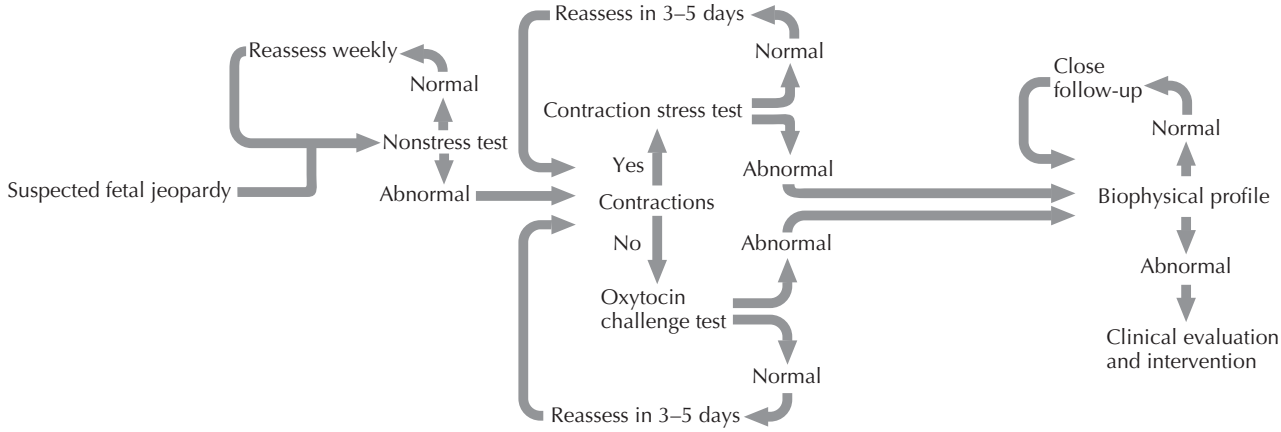


Figure 201.1 Antepartum fetal testing

testing must be viewed in the context of the clinical picture. The choice of timing and test must be made on clinical grounds, degree of risk, and the availability and expertise of those who will perform and interpret the test. Normal test results generally warrant further testing in a few days to a week. Positive or nonreassuring test results suggest the need for a more invasive test (eg, NST to CST, CST to BPP) or more direct intervention in the course of the pregnancy (delivery). Despite the extent of the study that has accompanied these technologies, all studies must always be interpreted in light of all available clinical factors.

REFERENCES

LEVEL I

Brown VA, Sawers RS, Parsons RJ, et al. The value of antenatal cardiotocography in the management of high-risk pregnancy: a randomized controlled trial. *Br J Obstet Gynaecol*. 1982;89:716.

Chauhan SP, Doherty DD, Magann EF, et al. Amniotic fluid index vs single deepest pocket technique during modified biophysical profile: a randomized clinical trial. *Am J Obstet Gynecol*. 2004;191:661.

Kidd LC, Patel NB, Smith R. Non-stress antenatal cardiotocography—A prospective randomized clinical trial. *Br J Obstet Gynaecol*. 1985;92:1156.

Lumley J, Lester A, Anderson I, et al. A randomized trial of weekly cardiotocography in high-risk obstetric patients. *Br J Obstet Gynaecol*. 1983;90:1018.

Vintzileos AM, Antsaklis A, Varvarigos I, et al. A randomized trial of intrapartum electronic fetal heart rate monitoring versus intermittent auscultation. *Obstet Gynecol*. 1993;81:899.

LEVEL II

Grivell RM, Alfirevic Z, Gyte GM, et al. Antenatal cardiotocography for fetal assessment. *Cochrane Database Syst Rev*. 2015;(9):CD007863.

Nageotte MP, Towers CV, Asrat T, et al. The value of a negative antepartum test: contraction stress test and modified biophysical profile. *Obstet Gynecol*. 1994;84:231.
Nageotte MP, Towers CV, Asrat T, et al. Perinatal outcome with the modified biophysical profile. *Am J Obstet Gynecol*. 1994;170:1672.
Tan KH, Sabapathy A, Wei X. Fetal manipulation for facilitating tests of fetal wellbeing. *Cochrane Database Syst Rev*. 2013;(12):CD003396.

LEVEL III

American College of Obstetricians and Gynecologists. Antepartum fetal surveillance. Practice Bulletin No. 145. *Obstet Gynecol*. 2014;124:182.
American College of Obstetricians and Gynecologists. Fetal growth restriction. Practice Bulletin No. 134. *Obstet Gynecol*. 2013;121:1122.
American College of Obstetricians and Gynecologists. Management of late-term and postterm pregnancies. Practice Bulletin No. 146. *Obstet Gynecol*. 2014;124:390.
Signore C, Freeman RK, Spong CY. Antenatal testing—a reevaluation: executive summary of a Eunice Kennedy Shriver National Institute of Child Health and Human Development workshop. *Obstet Gynecol*. 2009;113:687.
Zimmer EZ, Divon MY. Fetal vibroacoustic stimulation. *Obstet Gynecol*. 1993;81:451.

202 BIOPHYSICAL PROFILE

THE CHALLENGE

The biophysical profile is one of the several tests used to evaluate fetal health and reserve. Of the tests used for fetal assessment, the biophysical profile is the most technologically intensive and most expensive, but it carries the lowest false-positive and false-negative rates (0.6–1/1000).

Scope of the Problem: Of pregnancies, 3%–12% are at risk because of gestations that extend beyond term and more may be compromised by maternal disease states that affect fetal health or placental function (eg, hypertension, diabetes), resulting in abnormalities of fetal growth and amniotic fluid volume and other problems.

Objectives of Test: To assess fetal health and reserve.

TACTICS

Relevant Pathophysiology: The biophysical profile is based on the fetal heart rate response to activity (as in the nonstress test) but also adds the assessment of fetal tone, activity, and breathing as evaluated by ultrasonography. These parameters of activity often reflect the impact of acute and subacute stress. The volume of amniotic fluid (also measured by ultrasonography) can be indicative of fetal risk as reductions are often associated with either maternal or fetal compromise (most often reduced fetal urine output in the face of chronic stress).

Strategies: The biophysical profile is made up of five assessments of fetal well-being: the volume of amniotic fluid present, the frequency of fetal breathing movements, fetal tone, gross body movements, and the results of a nonstress test. Each parameter is scored as present or absent (0 or 2 scale), and then scores are totaled (Table 202.1). A score of 8 or 10 is considered normal, and the risk for fetal death within 1 week is low (0.4–0.6/1000 births); 6 is equivocal and suggests further evaluation; and a score of 4 or less is abnormal and augurs for immediate intervention. A score of 0 is invariably associated with significant fetal acidemia.

Patient Education: Reassurance; American College of Obstetricians and Gynecologists Patient Education Booklet AP098 (Special Tests for Monitoring Fetal Health).

IMPLEMENTATION

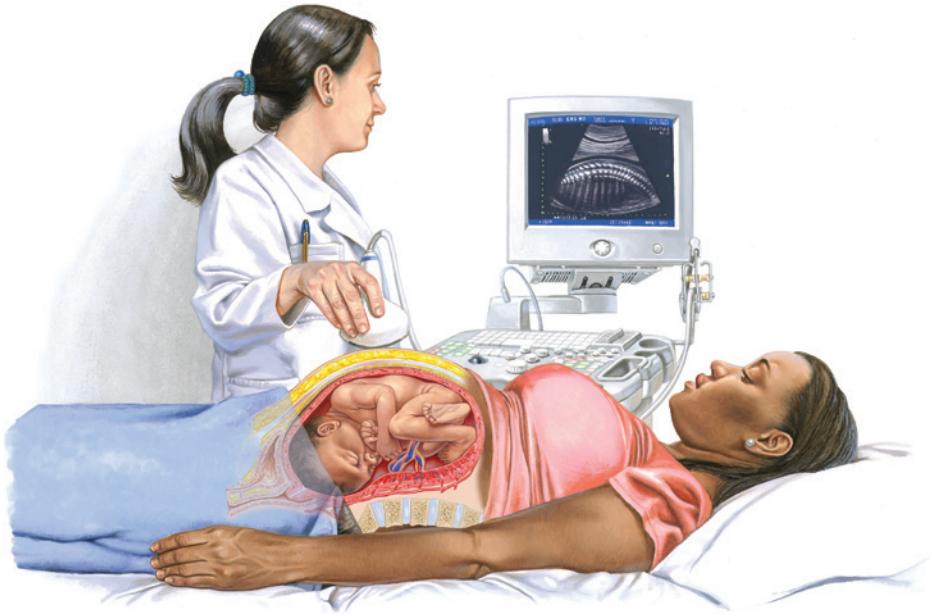
Special Considerations: Approximately 97% of biophysical profiles will be normal. The false-normal rate of biophysical profiles is approximately 1/1000 tests. False-positive test results occur in 1.5% of patients. The use of antenatal steroids can alter fetal heart and physical activity for up to 4 days following administration, resulting in lower scores.

Despite the extent of study that has accompanied the biophysical profile, these studies must always be interpreted in light of all available clinical factors.

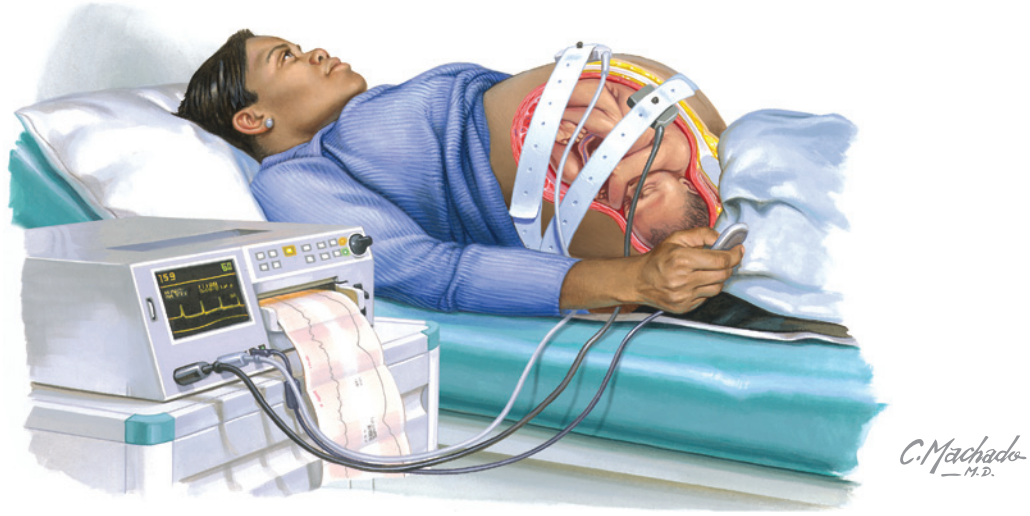
Table 202.1 Biophysical Profile Score

Profile Parameter	Normal (=2 points)	Abnormal (=0 points)
Amniotic fluid volume	At least 1 pocket of 1 cm in 2 perpendicular planes	No fluid or no pockets >1 cm
Fetal breathing movements (FBM)	≥1 FBM of 30-s duration in 30 min	No FBM of 30-s duration in 30 min
Fetal tone	≥1 episode of active extension and return or hand opening and closing	No or slow extension, poor return or no activity
Gross body movements	≥3 body or limb movements in 30 min	≤2 body or limb movements in 30 min
Reactive fetal heart rate	Reactive nonstress test	Nonreactive nonstress test

The biophysical profile score is established by summing the values obtained on each of the five-component tests.



An ultrasound is used for four of the five factors in the biophysical profile (fetal breathing, movement, tone, and fluid volume).



The fifth factor in a biophysical profile is the heart rate response to activity, which is measured by a nonstress test.

Figure 202.1 Biophysical profile

REFERENCES

LEVEL I

Chauhan SP, Doherty DD, Magann EF, et al. Amniotic fluid index vs single deepest pocket technique during modified biophysical profile: a randomized clinical trial. *Am J Obstet Gynecol.* 2004;191:661.

LEVEL II

Dayal AK, Manning FA, Berck DJ, et al. Fetal death after normal biophysical profile score: an eighteen-year experience. *Am J Obstet Gynecol.* 1999; 181:1231.

Lalor JG, Fawole B, Alfirevic Z, et al. Biophysical profile for fetal assessment in high risk pregnancies. *Cochrane Database Syst Rev.* 2008; CD000038.

Manning FA, Harman CR, Morrison I, et al. Fetal assessment based on fetal biophysical profile scoring. IV. An analysis of perinatal morbidity and mortality. *Am J Obstet Gynecol.* 1990;138:575.

Moore TR, Piacquadio K. A prospective evaluation of fetal movement screening to reduce the incidence of antepartum fetal death. *Am J Obstet Gynecol.* 1989;160:1075.

Nageotte MP, Towers CV, Asrat T, et al. The value of a negative antepartum test: contraction stress test and modified biophysical profile. *Obstet Gynecol.* 1994;84:231.

Ott WJ, Mora G, Arias F, et al. Comparison of the modified biophysical profile to a "new" biophysical profile incorporating the middle cerebral artery to umbilical artery velocity flow systolic/diastolic ratio. *Am J Obstet Gynecol.* 1998;178:1346.

Yoon BH, Romero R, Roh CR, et al. Relationship between the fetal biophysical profile score, umbilical artery Doppler velocimetry, and fetal blood acid-base status determined by cordocentesis. *Am J Obstet Gynecol.* 1993;169:1586.

LEVEL III

American College of Obstetricians and Gynecologists. Antepartum fetal surveillance. Practice Bulletin No. 145. *Obstet Gynecol*. 2014;124:182.

American College of Obstetricians and Gynecologists. Management of late-term and postterm pregnancies. Practice Bulletin No. 146. *Obstet Gynecol*. 2014;124:390.

Magann EF, Doherty DA, Field K, et al. Biophysical profile with amniotic fluid volume assessments. *Obstet Gynecol*. 2004;104:5.

Signore C, Freeman RK, Spong CY. Antenatal testing—a reevaluation: executive summary of a Eunice Kennedy Shriver National Institute of Child Health and Human Development workshop. *Obstet Gynecol*. 2009;113:687.

THE CHALLENGE

Fetal health may be assessed using the contraction stress test (also called "oxytocin challenge test"). This test is somewhat analogous to an exercise stress test for the evaluation of adult cardiac function as problems or weaknesses that are normally compensated for at rest may become apparent with stress. In the contraction stress test the fetal–placental–maternal unit is stressed through uterine contractions. The resulting periodic deprivation of uterine blood flow can be used to evaluate the robustness of the fetal–placental condition.

Scope of the Problem: Of pregnancies, 3%–12% are at risk because of gestations that extend beyond term. More pregnancies may be compromised by maternal disease states that affect fetal health or placental function (eg, hypertension, diabetes), resulting in abnormalities of fetal growth and amniotic fluid volume and other problems.

Objectives of the Test: To assess fetal health and reserve.

TACTICS

Relevant Pathophysiology: During uterine contractions, uterine intramural pressure exceeds perfusion pressure, resulting in transient ischemia and loss of blood delivery to the intervillous spaces. When the fetus and placenta are healthy, this loss of blood flow causes no change in fetal tissue oxygenation, and there is no compensatory or reactive change in fetal heart rate. When the fetal–placental or placental–maternal relationships have been degraded, this brief loss of perfusion may be sufficient to cause a reduction in heart rate in the same way as that seen in labor when late decelerations are found.

Strategies: If uterine contractions spontaneously occur, the contraction stress test may directly proceed. To perform the oxytocin challenge test, there must be no contraindications to the use of oxytocin. Fetal heart rate and uterine activity monitoring are established, and contractions are induced using oxytocin or through intermittent nipple stimulation. Contractions must occur at a rate of three per 10 minutes for at least three 10-minute periods. A normal stress test should show normal fetal heart rate variability and the absence of periodic decelerations. Accelerations with fetal activity are reassuring.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlets AP098 (Special Tests for Monitoring Fetal Health) and AP015 (Fetal Heart Rate Monitoring During Labor).

IMPLEMENTATION

Special Considerations: If contractions spontaneously occur at a rate of at least three every 10 minutes, the term "contraction stress test" is generally used, whereas the term "oxytocin challenge test" is used when contractions must be induced through oxytocin administration. Like most tests of fetal status, the contraction stress test has a moderate false-positive rate. Consequently, the interpretation of a positive test result must be made in the perspective of other information about the mother and fetus, including the results of other tests such as the nonstress test or biophysical profile.

REFERENCES

LEVEL I

Freeman RK, Anderson G, Dorchester W. A prospective multi-institutional study of antepartum fetal heart rate monitoring. II. Contraction stress test versus nonstress test for primary surveillance. *Am J Obstet Gynecol*. 1982;143:778-781.

Lipitz S, Barkai G, Rabinovici J, et al. Breast stimulation test and oxytocin challenge test in fetal surveillance: a prospective randomized study. *Am J Obstet Gynecol*. 1987;157:1178.

LEVEL II

Nageotte MP, Towers CV, Asrat T, et al. Perinatal outcome with the modified biophysical profile. *Am J Obstet Gynecol*. 1994;170:1672.

Nageotte MP, Towers CV, Asrat T, et al. The value of a negative antepartum test: contraction stress test and modified biophysical profile. *Obstet Gynecol*. 1994;84:231.

LEVEL III

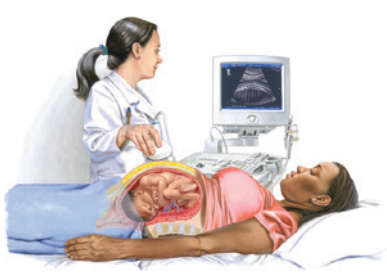
American College of Obstetricians and Gynecologists. Antepartum fetal surveillance. Practice Bulletin No. 145. *Obstet Gynecol*. 2014;124:182.

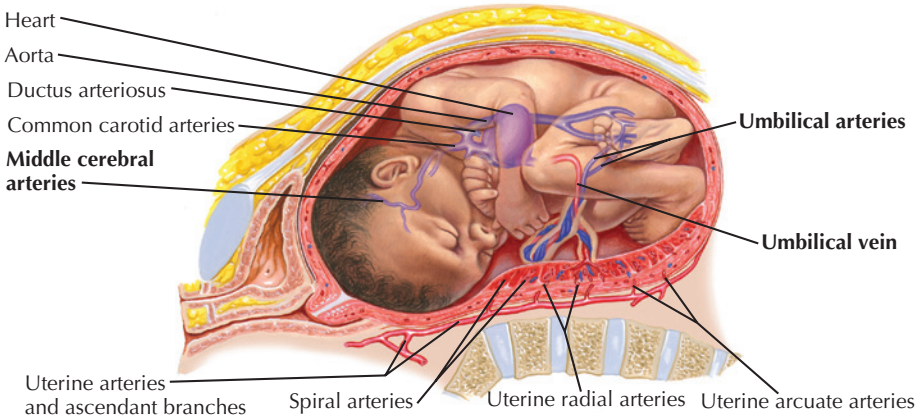
American College of Obstetricians and Gynecologists. Management of late-term and postterm pregnancies. Practice Bulletin No. 146. *Obstet Gynecol*. 2014;124:390.

Freeman RK. Contraction stress testing for primary fetal surveillance in patients at high risk for uteroplacental insufficiency. *Clin Perinatol*. 1982;9:265.

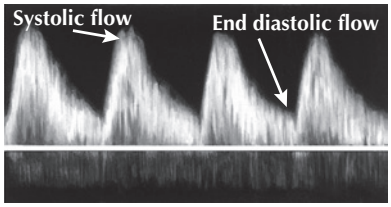
Signore C, Freeman RK, Spong CY. Antenatal testing—a reevaluation: executive summary of a Eunice Kennedy Shriver National Institute of Child Health and Human Development workshop. *Obstet Gynecol*. 2009;113:687.

Doppler flow studies constitute a group of tests used to evaluate fetal health and reserve through the assessment of blood flow characteristics in fetal and uterine vessels and fetal heart. Routinely, though, only the study of umbilical and cerebral blood vessels is of major relevance.



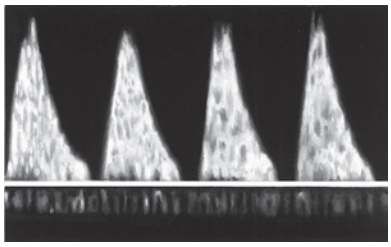


Current applications of Doppler flow studies are generally limited to cases of fetal intrauterine growth restriction (IUGR). Babies with abnormal umbilical artery Doppler blood flow results have a significantly higher rate of cesarean section delivery for fetal distress, longer stays in the neonatal intensive care unit, and increased neonatal morbidity regardless of whether they were of normal size or growth restricted.

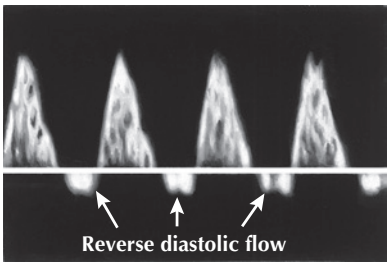


Normal blood flow in umbilical arteries.

C. Machado M.D.



Absent end diastolic flow in umbilical arteries is associated with significant fetal compromise.



Presence of reverse diastolic flow in umbilical arteries indicates extreme case of fetal-placental compromise.

Figure 204.1 Doppler flow studies (Doppler velocimetry)

the velocity of blood flow in vessels because the frequency of sound reflected from moving blood cells is slightly altered in proportion to the velocity of the blood flow (and the cosine of the angle of incidence).

- During the cardiac cycle, blood flow within the fetal circulation is pulsatile, with the difference in flow during systole and diastole gradually declining with gestational age and other factors. In the umbilical artery, this systolic to diastolic (S/D) ratio decreases from approximately four at 20 weeks to less than three at 30 weeks, and finally to around two near term. Much of this change is mediated by the health and function of the placenta, and when this is compromised, diastolic flow diminishes. In extreme cases of fetal–placental compromise, diastolic flow may be absent or even show reversal of flow direction. Absent end-diastolic flow is associated with significant fetal compromise. Babies with abnormal umbilical artery Doppler blood flow results have a significantly higher rate of cesarean delivery for fetal distress, longer stays in the neonatal intensive care unit, and increased neonatal morbidity regardless of whether they were of normal size or growth restricted.
- When there is fetal anemia, the associated increased cardiac output and relatively lower blood viscosity result in increased blood flow in the middle cerebral artery. This flow can be measured and used to evaluate fetuses with alloimmunization. Fetuses with blood flow greater than 1.5 times the median (multiples of median or MoM) are correctly identified with anemia with only a 12% false-positive rate. Increased middle cerebral artery blood flow has also been proposed as a marker for altered blood flow before other indicators of hypoxemia may be present.
- Uterine artery blood flow increases from approximately 50 mL/min in early gestation to 500–750 mL/min by term. Doppler flow studies of the uterine artery have been used in an effort to predict the development of preeclampsia and other complications. Unfortunately, uterine artery Doppler flow velocity appears to have limited diagnostic accuracy in predicting preeclampsia, intrauterine growth restriction (IUGR), and perinatal death.

Strategies: Doppler flow studies may be used to assess blood flow in the umbilical blood vein and arteries, fetal brain, and fetal heart. A Doppler flow study is often used when a fetus has intrauterine growth restriction or abnormalities of amniotic fluid volume.

- Blood flow in the fetal ductus arteriosus can be assessed when the fetus has been exposed to nonsteroidal antiinflammatory drugs.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Booklet AP098 (Special Tests for Monitoring Fetal Health).

IMPLEMENTATION

Special Considerations: Despite its usefulness in evaluating the fetus at risk, intrapartum umbilical artery Doppler velocimetry is a poor predictor of adverse perinatal outcomes.

Studies suggest that even such factors as a cholesterol-lowering diet can influence umbilical artery blood-flow patterns.

Notwithstanding the extent of study that has accompanied these technologies, Doppler flow studies must always be interpreted in light of all available clinical factors.

REFERENCES

LEVEL I

Omtzigt AM, Reuwer PJ, Bruinse HW. A randomized controlled trial on the clinical value of umbilical Doppler velocimetry in antenatal care. *Am J Obstet Gynecol*. 1994;170:625.

Whittle MJ, Hanretty KP, Primrose MH, et al. Screening for the compromised fetus: a randomized trial of umbilical artery velocimetry in unselected pregnancies. *Am J Obstet Gynecol*. 1994;170:555.

Williams KP, Farquharson DF, Bebbington M, et al. Screening for fetal well-being in a high-risk pregnant population comparing the nonstress test with umbilical artery Doppler velocimetry: a randomized controlled clinical trial. *Am J Obstet Gynecol*. 2003;188:1366-1371.

Zimmerman R, Carpenter RJ Jr, Durig P, et al. Longitudinal measurement of peak systolic velocity in the fetal middle cerebral artery for monitoring pregnancies complicated by red cell alloimmunisation: a prospective multicentre trial with intention-to-treat. *BJOG*. 2002;109:746.

LEVEL II

Alfirevic Z, Stampalija T, Medley N. Fetal and umbilical Doppler ultrasound in normal pregnancy. *Cochrane Database Syst Rev*. 2015;(4): CD001450.

Farrell T, Chien PF, Gordon A. Intrapartum umbilical artery Doppler velocimetry as a predictor of adverse perinatal outcome: a systematic review. *Br J Obstet Gynaecol*. 1999;106:783.

Konje JC, Howarth ES, Kaufmann P, et al. Longitudinal quantification of uterine artery blood volume flow changes during gestation in pregnancies complicated by intrauterine growth restriction. *BJOG*. 2003;110:301.

Morris RK, Malin G, Robson SC, et al. Fetal umbilical artery Doppler to predict compromise of fetal/neonatal wellbeing in a high-risk population: systematic review and bivariate meta-analysis. *Ultrasound Obstet Gynecol*. 2011;37:135.

Ott WJ, Mora G, Arias F, et al. Comparison of the modified biophysical profile to a "new" biophysical profile incorporating the middle cerebral artery to umbilical artery velocity flow systolic/diastolic ratio. *Am J Obstet Gynecol*. 1998;178:1346.

Papageorghiou AT, Yu CK, Erasmus IE, et al. Assessment of risk for the development of pre-eclampsia by maternal characteristics and uterine artery Doppler. *BJOG*. 2005;112:703.

Picklesimer AH, Oepkes D, Moise KJ Jr, et al. Determinants of the middle cerebral artery peak systolic velocity in the human fetus. *Am J Obstet Gynecol*. 2007;197:526.e1.

LEVEL III

American College of Obstetricians and Gynecologists. Antepartum fetal surveillance. Practice Bulletin No. 145. *Obstet Gynecol*. 2014;124:182.

American College of Obstetricians and Gynecologists. Fetal growth restriction. Practice Bulletin No. 134. *Obstet Gynecol*. 2013;121:1122.

American College of Obstetricians and Gynecologists. Management of late-term and postterm pregnancies. Practice Bulletin No. 146. *Obstet Gynecol*. 2014;124:390.

American College of Obstetricians and Gynecologists. Ultrasonography in pregnancy. ACOG Practice Bulletin No. 101. *Obstet Gynecol*. 2009;113: 451.

Chien PF, Arnott N, Gordon A, et al. How useful is uterine artery Doppler flow velocimetry in the prediction of pre-eclampsia, intrauterine growth retardation and perinatal death? An overview. *BJOG*. 2000;107:196.

Detti L, Johnson SC, Diamond MP, et al. First-trimester Doppler investigation of the uterine circulation. *Am J Obstet Gynecol*. 2006;195:1210.

Divon MY. Umbilical artery Doppler velocimetry: clinical utility in high-risk pregnancies. *Am J Obstet Gynecol*. 1996;174:10.

Karsdorp VH, van Vugt JM, van Geijn HP, et al. Clinical significance of absent or reversed end diastolic velocity waveforms in umbilical artery. *Lancet*. 1994;344:1664.

Pattinson RC, Norman K, Odendaal HJ. The role of Doppler velocimetry in the management of high risk pregnancies. *Br J Obstet Gynaecol*. 1994; 101:114.

Signore C, Freeman RK, Spong CY. Antenatal testing—a reevaluation: executive summary of a Eunice Kennedy Shriver National Institute of Child Health and Human Development workshop. *Obstet Gynecol*. 2009; 113:687.

Society for Maternal-Fetal Medicine Publications Committee, Berkley E, Chauhan SP, et al. Doppler assessment of the fetus with intrauterine growth restriction. *Am J Obstet Gynecol*. 2012;206:300.

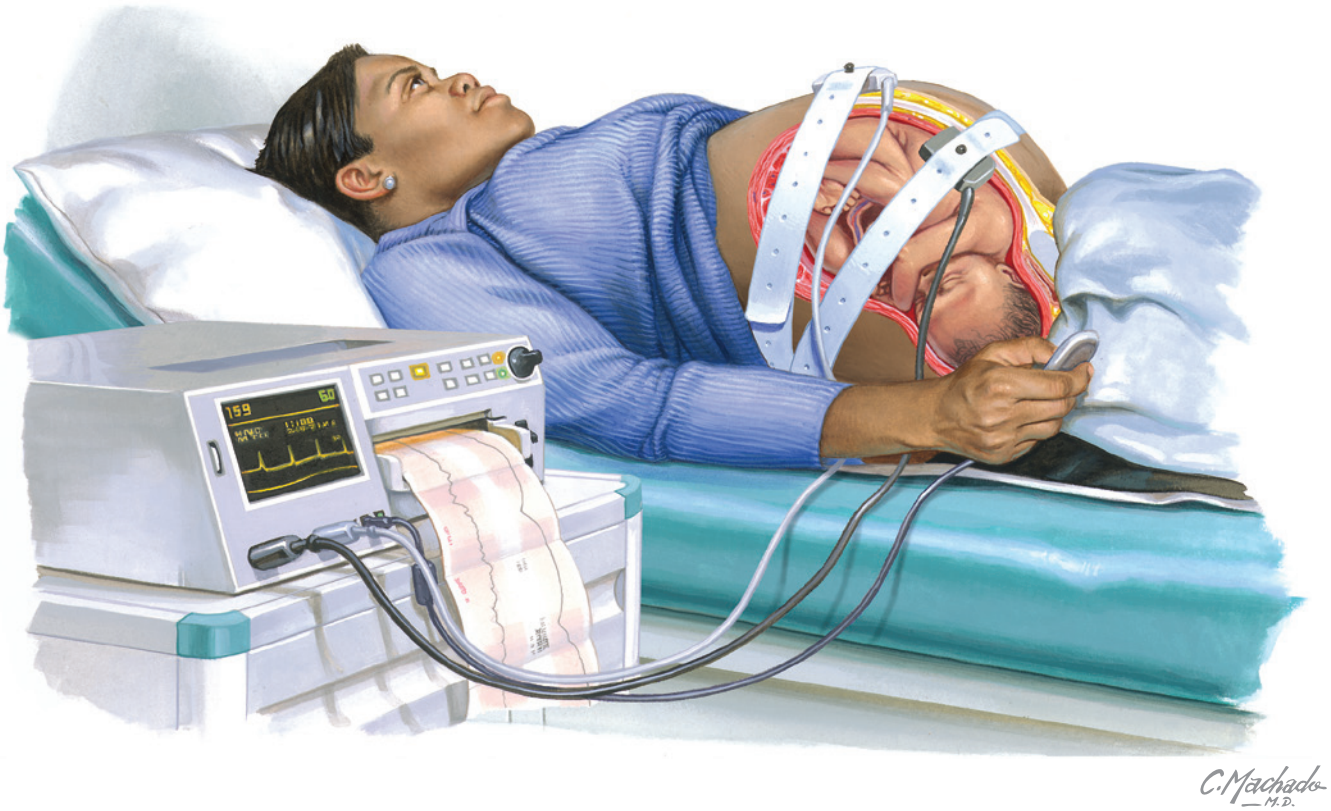


Figure 205.1 Nonstress testing

A reactive NST is a good predictor of adequate fetal oxygenation, and most reactive fetuses do well for at least another week.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlets AP098 (Special Tests for Monitoring Fetal Health) and AP015 (Fetal Heart Rate Monitoring During Labor).

IMPLEMENTATION

Special Considerations: To increase the reliability of the NST, the patient should not have recently smoked. The NST is more easily performed than the contraction stress test, but it has the highest false-positive rate (up to 90% of positive tests) and the highest risk for a false-negative test result (1.4 of 1000). The NST of the healthy preterm fetus is frequently nonreactive: from 24 to 28 weeks of gestation, up to 50% of NSTs may not be reactive, and from 28 to 32 weeks of gestation, 15% of NSTs are not reactive. Variable decelerations may be observed in up to 50% of NSTs. If sporadic and brief (<30 seconds), they are inconsequential and do not indicate fetal compromise or the need for intervention. Repetitive variable decelerations (at least three in 20 minutes), even if mild, have been associated with an increased risk of cesarean delivery for fetal indications. Because of these factors, the interpretation of a nonreactive test must be made in the perspective of other information about the mother and fetus, including the results of other tests such as the contraction stress test or biophysical profile (see also "Antepartum Testing").

REFERENCES

LEVEL II

Anyaegbunam A, Brustman L, Divon M, et al. The significance of antepartum variable decelerations. *Am J Obstet Gynecol*. 1986;155:707.

Bishop EH. Fetal acceleration test. *Am J Obstet Gynecol*. 1981;141:905.

Lavin JP Jr, Miodovnik M, Barden TP. Relationship of nonstress test reactivity and gestational age. *Obstet Gynecol*. 1984;63:338.

Meis PJ, Ureda JR, Swain M, et al. Variable decelerations during nonstress tests are not a sign of fetal compromise. *Am J Obstet Gynecol*. 1986;154:586.

Nageotte MP, Towers CV, Asrat T, et al. Perinatal outcome with the modified biophysical profile. *Am J Obstet Gynecol*. 1994;170:1672.

Pazos R, Vuolo K, Aladjem S, et al. Association of spontaneous fetal heart rate decelerations during antepartum nonstress testing and intrauterine growth retardation. *Am J Obstet Gynecol*. 1982;144:574.

Tan KH, Sabapathy A, Wei X. Fetal manipulation for facilitating tests of fetal wellbeing. *Cochrane Database Syst Rev*. 2013;(12):CD003396.

Tan KH, Smyth RM, Wei X. Fetal vibroacoustic stimulation for facilitation of tests of fetal wellbeing. *Cochrane Database Syst Rev*. 2013;(12):CD002963.

LEVEL III

American College of Obstetricians and Gynecologists. Antepartum fetal surveillance. Practice Bulletin No. 145. *Obstet Gynecol*. 2014;124:182.

American College of Obstetricians and Gynecologists. Fetal growth restriction. Practice Bulletin No. 134. *Obstet Gynecol*. 2013;121:1122.

American College of Obstetricians and Gynecologists. Management of late-term and postterm pregnancies. Practice Bulletin No. 146. *Obstet Gynecol*. 2014;124:390.

Druzin ML, Fox A, Kogut E, et al. The relationship of the nonstress test to gestational age. *Am J Obstet Gynecol*. 1985;153:386.

Graca LM, Cardoso CG, Clode N, et al. Acute effects of maternal cigarette smoking on fetal heart rate and fetal body movements felt by the mother. *J Perinat Med*. 1991;19:385.

Signore C, Freeman RK, Spong CY. Antenatal testing—a reevaluation: executive summary of a Eunice Kennedy Shriver National Institute of Child Health and Human Development workshop. *Obstet Gynecol*. 2009;113:687.

NORMAL LABOR

206

THE CHALLENGE

Description: Labor is the rhythmic contraction of the uterus that leads to progressive cervical effacement and dilatation. When effective, this leads to descent and eventual expulsion of the fetus. Labor may or may not culminate in the delivery of the fetus. It is generally divided into three stages: first stage—from the onset of labor to complete cervical dilation, although the exact time of onset is almost impossible to establish; second stage—from complete cervical dilation to the delivery of the fetus; and third stage—from fetal delivery to expulsion of the placenta. Some add a fourth stage, recovery, which spans the time from delivery to 1 hour after. The first stage of labor is often subdivided into a latent phase (to cervical dilation of 3–4 cm) and an active phase (from 4 cm to complete), although these remain inconsistently defined and difficult to pinpoint. Labor is anticipated to follow a predictable sequence and time course. However, factors, such as active labor management and pain control, have raised concern about using traditional standards.

Scope of the Problem: Unless cesarean delivery is performed in advance, all pregnant women eventually go into labor.

Objectives of Management: To safely monitor and manage the processes of labor to ensure the health and safety of the mother and baby.

TACTICS

Relevant Pathophysiology: The physiologic changes that lead to the initiation of labor are many, complex, deeply interconnected, and incompletely delineated. The mean duration of human singleton pregnancy is 280 days (40 weeks) from the first day of the last menstrual period, although "term" is defined as between 259 and 293 days. It is clear that the complex interaction of maternal signaling molecules (progestins and estrogens, prostaglandins, oxytocin, relaxin, nitrous oxide and others), fetal molecules (cortisol, estrogen and others), and uterine distention reduce contractile inhibition and induce an increase in uterine oxytocin and prostaglandin receptors, ion channels, and cellular gap junctions. The latter appear necessary to effect coordinated contractions that create a pressure gradient from the top of the uterus toward the cervix. Intrinsic slow and fast waves of myometrial cell depolarization become more and more effective in producing local, and then regional, muscle depolarization and contraction (mediated through ATP-dependent binding of myosin to actin). Increasing pressure on the cervix causes stretch, neural signaling, and the local release of prostaglandins (predominantly PGF_{2a}), reinforcing uterine contraction and oxytocin sensitivity in an ever-increasing positive feedback loop, eventually leading to the rhythmic contractions of labor. Despite the importance of this positive feedback loop, most researchers view the onset of labor as the loss of inhibition rather than an active process.

For most viviparous animals, the fetus and placenta appear to control the timing of labor onset. In humans, this is considered to occur because of the changes in the hypothalamic–pituitary–adrenal axis, increasing fetal cortisol, inducing placental enzymatic functions that downregulate inhibitory factors, such as progesterone. (Progesterone inhibits uterine contractions early in pregnancy, but progesterone withdrawal is not a prerequisite for labor in humans and progesterone levels are not markedly different before or during labor.) Placental estrogens upregulate myometrial gap junctions and uterotonic receptors (L-type calcium channels and oxytocin receptors), while the placental and cervical production of prostaglandins increase, furthering inducing their receptors and facilitating cervical ripening (PGE_2) and contractions (PGF_{2a}). The pivotal role these molecules play can be seen by the delay caused by the use of prostaglandin synthesis inhibitors such as nonsteroidal antiinflammatory agents (NSAIDs).

Oxytocin is the most potent endogenous uterotonic peptide and is clinically important in the management of labor. However, oxytocin levels do not significantly differ in labor from those found in the weeks before labor begins (although fetal production does seem to increase). This reinforces the importance of the increase in number of oxytocin receptors in the myometrium (up to 200-fold) at term. In addition to oxytocin's myometrial effects, it also indirectly acts by enhancing amniotic and decidual prostaglandin synthesis.

Successful delivery of the infant depends upon the interaction of three variables: power (uterine contractions), passenger (fetus), and passage (both bony pelvis and pelvic soft tissues). The fetus typically undergoes a series of movements (the cardinal movements of labor), which allow it to traverse the convoluted birth passage. Abnormalities in any of the three variables may result in a failure of the fetus to progress, necessitating either operative vaginal delivery (forceps or vacuum assist) or cesarean delivery.

The strength or power of labor may be quantified through the calculation of "Montevideo units" (MVUs), which are a surrogate for uterine work (area under the pressure curve minus the baseline or resting pressure). Montevideo units are calculated by summing the peak pressure achieved above (minus) the baseline for all contractions in a 10-minute period. This requires that the rupture of the fetal membranes and placement of a pressure measurement catheter has occurred to obtain the pressure data. Labors with sustained MVUs of 200–250 are considered "adequate," and are generally associated with successful delivery. Uterine activity does vary based on the labor stage; approximately 100 MVUs in latent labor, 175 MVUs in active labor, and 250 MVUs during the second stage.

Strategies: For most women the onset and progress of labor are natural, automatic, and productive. Generally, the process of labor will result in a change of cervical dilation of about 1 cm/h from 5 to 9 cm of dilation. This rate of change can be affected by parity, the use of analgesics, active management of contractions, fetal size, maternal height or weight, and other factors. The median time to dilate from 4 to 10 cm in nulliparas and multiparas is 5.3 hours and 3.8 hours, respectively. Traditionally, the rupture of the fetal membranes was considered to hasten the progress of labor, but studies have failed to support this. The median duration of the second stage of labor is 1.1 hours for nulliparas and 0.4 hours for multiparas, with 95% of women delivering by 3.5 and 2 hours, respectively. Meta-analysis suggests that strict dependence on these times is not supported and that clinical decisions must be made using all available information not simply progress over time.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlets AP004 (How to Tell When Labor Begins), AP006 (Cesarean Birth), AP015 (Fetal Heart Rate Monitoring During Labor), AP069 (What to Expect After Your Due Date), AP070 (Vaginal Birth After Cesarean Delivery: Deciding on a Trial of Labor After Cesarean Delivery), AP079 (If Your Baby Is Breech), AP086 (Medications for Pain Relief During Labor and Delivery), AP087 (Preterm Labor and Birth), AP103 (Having a Baby-Especially for Teens), AP154 (Labor Induction), AP181 (Elective Delivery Before 39 Weeks), and AP192 (Assisted Vaginal Delivery).

IMPLEMENTATION

Special Considerations: Protraction of labor and arrest of progress disorders are common. Depending on the population studied and the definitions used, these may occur in as many as 20% of

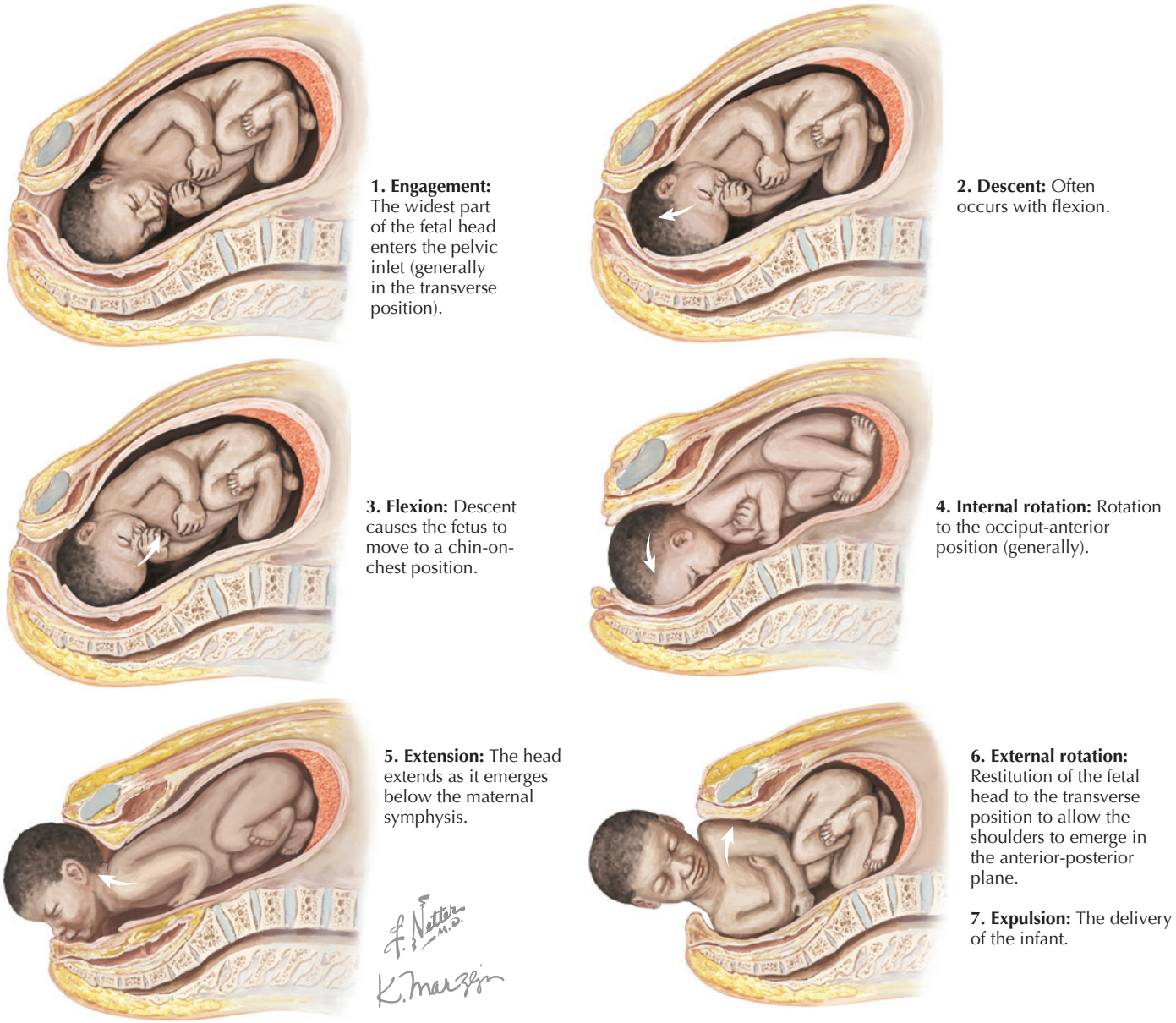


Figure 206.1 Seven* cardinal fetal movements of delivery. *Some authors combine descent and flexion into a single step, yielding six cardinal movements.

successful labors (up to 35% in some samples). Active use of oxytocin is associated with shortening the time to delivery but is not associated with a meaningful change in the cesarean delivery rate.

The use of epidural anesthesia is associated with a slight increase in labor duration and the likelihood of operative delivery but not an increased rate of cesarean delivery.

REFERENCES

LEVEL I

Sadler LC, Davison T, McCowan LM. A randomized controlled trial and meta-analysis of active management of labour. *BJOG*. 2000;107:909.

LEVEL II

Alexander JM, Lucas MJ, Ramin SM, et al. The course of labor with and without epidural analgesia. *Am J Obstet Gynecol*. 1998;178:516.

Anim-Somuah M, Smyth RM, Jones L. Epidural versus non-epidural or no analgesia in labour. *Cochrane Database Syst Rev*. 2011;(12):CD000331.

Bugg GJ, Siddiqui F, Thornton JG. Oxytocin versus no treatment or delayed treatment for slow progress in the first stage of spontaneous labour. *Cochrane Database Syst Rev*. 2013;(6):CD007123.

Cheng YW, Shaffer BL, Nicholson JM, et al. Second stage of labor and epidural use: a larger effect than previously suggested. *Obstet Gynecol*. 2014;123:527.

Laughon SK, Berghella V, Reddy UM, et al. Neonatal and maternal outcomes with prolonged second stage of labor. *Obstet Gynecol*. 2014;124:57.

Lavender T, Hart A, Smyth RM. Effect of partogram use on outcomes for women in spontaneous labour at term. *Cochrane Database Syst Rev*. 2013;(7):CD005461.

Le Ray C, Fraser W, Rozenberg P, et al. Duration of passive and active phases of the second stage of labour and risk of severe postpartum haemorrhage in low-risk nulliparous women. *Eur J Obstet Gynecol Reprod Biol*. 2011;158:167.

Nelson DB, McIntire DD, Leveno KJ. Relationship of the length of the first stage of labor to the length of the second stage. *Obstet Gynecol*. 2013; 122:27.

Smyth RM, Markham C, Dowswell T. Amniotomy for shortening spontaneous labour. *Cochrane Database Syst Rev*. 2013;(6):CD006167.

Wei SQ, Luo ZC, Xu H, et al. The effect of early oxytocin augmentation in labor: a meta-analysis. *Obstet Gynecol*. 2009;114:641.

Wei S, Wo BL, Qi HP, et al. Early amniotomy and early oxytocin for prevention of, or therapy for, delay in first stage spontaneous labour compared with routine care. *Cochrane Database Syst Rev*. 2013;(8):CD006794.

Zhang J, Landy HJ, Branch DW, et al. Contemporary patterns of spontaneous labor with normal neonatal outcomes. *Obstet Gynecol*. 2010;116:1281.

Zhang J, Troendle J, Mikolajczyk R, et al. The natural history of the normal first stage of labor. *Obstet Gynecol*. 2010;115:705.

LEVEL III

American College of Obstetricians and Gynecologists. Intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. ACOG Practice Bulletin No. 106. *Obstet Gynecol*. 2009;114:192.

American College of Obstetricians and Gynecologists. Induction of labor. ACOG Practice Bulletin No. 107. *Obstet Gynecol*. 2009;114:386.

American College of Obstetricians and Gynecologists. Vaginal birth after previous cesarean delivery. Practice Bulletin No. 115. *Obstet Gynecol*. 2010;116:450.

American College of Obstetricians and Gynecologists. Management of intrapartum fetal heart rate tracings. Practice Bulletin No. 116. *Obstet Gynecol*. 2010;116:1232.

American College of Obstetricians and Gynecologists. Use of prophylactic antibiotics in labor and delivery. Practice Bulletin No. 120. *Obstet Gynecol*. 2011;117:1472.

American College of Obstetricians and Gynecologists. Antepartum fetal surveillance. Practice Bulletin No. 145. *Obstet Gynecol*. 2014;124:182.

American College of Obstetricians and Gynecologists. Management of late-term and postterm pregnancies. Practice Bulletin No. 146. *Obstet Gynecol*. 2014;124:390.

American College of Obstetricians and Gynecologists. Management of preterm labor. Practice Bulletin No. 159. *Obstet Gynecol*. 2016;127:e29.

American College of Obstetricians and Gynecologists. Premature rupture of membranes. Practice Bulletin No. 160. *Obstet Gynecol*. 2016;127:e39.

American College of Obstetricians and Gynecologists, Society for Maternal-Fetal Medicine. Obstetric care consensus no. 1: safe prevention of the primary cesarean delivery. *Obstet Gynecol*. 2014;123:693.

Bugg GJ, Siddiqui F, Thornton JG. Oxytocin versus no treatment or delayed treatment for slow progress in the first stage of spontaneous labour. *Cochrane Database Syst Rev*. 2013;(6):CD007123.

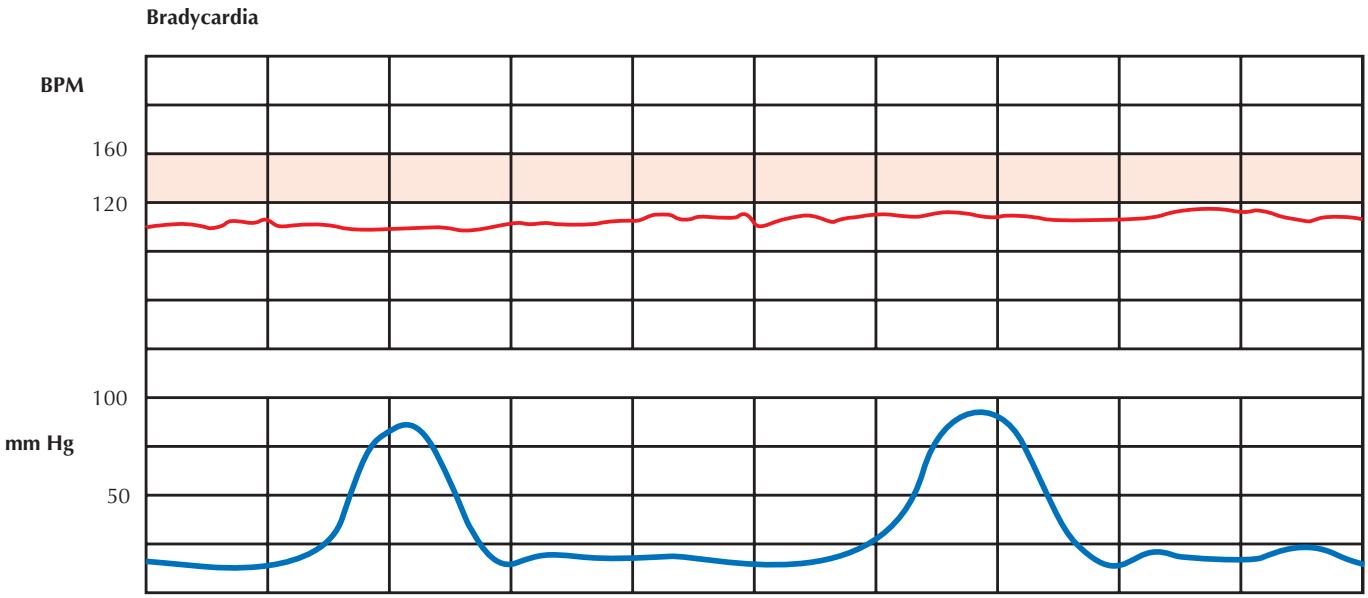
Fuchs AR, Fuchs F, Husslein P, et al. Oxytocin receptors and human parturition: a dual role for oxytocin in the initiation of labor. *Science*. 1982; 215:1396.

Kenyon S, Ullman R, Mori R, et al. Care of healthy women and their babies during childbirth: summary of NICE guidance. *BMJ*. 2007;335:667.

Millen KR, Kuo K, Zhao L, et al. Evidence-based guidelines in labor management. *Obstet Gynecol Surv*. 2014;69:209.

Zakar T, Hertelendy F. Progesterone withdrawal: key to parturition. *Am J Obstet Gynecol*. 2007;196:289.

Zakar T, Mesiano S. How does progesterone relax the uterus in pregnancy? *N Engl J Med*. 2011;364:972.



BPM, beats per minute.

Figure 207.1 Bradycardia

Imaging: Ultrasonography may identify abnormalities of the placenta (abruption) but plays a minor role in the evaluation of the fetus with bradycardia.
Special Tests: Fetal scalp pH or pulse oximetry (when available) may be of assistance in determining the fetal status.
Diagnostic Procedures: Clinical evaluation of mother and fetus.

Pathologic Findings

Based on underlying pathophysiologic conditions.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Maternal hydration, change in maternal position (lateral recumbent), maternal oxygen therapy.
Specific Measures: Aggressive fetal and maternal evaluation, amnioinfusion, tocolytics (when hypertonus is involved), expedited delivery in the face of nonreassuring changes.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Booklets AP015 (Fetal Heart Rate Monitoring During Labor) and AP098 (Special Tests for Monitoring Fetal Health).

Drug(s) of Choice

Tocolytics may be used if uterine tetany is thought to play a causative role in fetal stress.
Contraindications: Tocolytics are relatively contraindicated in the absence of a diagnosis.

FOLLOW-UP

Patient Monitoring: Continued maternal and fetal assessment.
Prevention/Avoidance: Adequate maternal hydration, left lateral recumbent position for labor.
Possible Complications: Progressive deterioration of fetal status unless underlying processes are identified and corrected.
Expected Outcome: With aggressive diagnosis and management, outcome will generally be good.

MISCELLANEOUS

Other Notes: Intrapartum fetal heart rate monitoring is only one part of the overall evaluation of mother and fetus. This modality must be used to augment clinical judgment and not replace it.

REFERENCES

LEVEL I

Rees SG, Thurlow JA, Gardner IC, et al. Maternal cardiovascular consequences of positioning after spinal anaesthesia for Caesarean section: left 15 degree table tilt vs. left lateral. *Anaesthesia*. 2002;57:15.

LEVEL II

Alfirevic Z, Devane D, Gyte GM. Continuous cardiotocography (CTG) as a form of electronic fetal monitoring (EFM) for fetal assessment during labour. *Cochrane Database Syst Rev*. 2013;(5):CD006066.

Graham EM, Petersen SM, Christo DK, et al. Intrapartum electronic fetal heart rate monitoring and the prevention of perinatal brain injury. *Obstet Gynecol*. 2006;108:656.

Mardirosoff C, Dumont L, Boulvain M, et al. Fetal bradycardia due to intrathecal opioids for labour analgesia: a systematic review. *BJOG*. 2002;109:274.

LEVEL III

American College of Obstetricians and Gynecologists. Intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. ACOG Practice Bulletin No. 106. *Obstet Gynecol*. 2009;114:192.

American College of Obstetricians and Gynecologists. Management of intrapartum fetal heart rate tracings. Practice Bulletin No. 116. *Obstet Gynecol*. 2010;116:1232.

American College of Obstetricians and Gynecologists. Antepartum fetal surveillance. Practice Bulletin No. 145. *Obstet Gynecol*. 2014;124:182.

Hon EH. Additional observations on "pathologic" bradycardia. *Am J Obstet Gynecol*. 1974;118:428.

Parer JT, King T. Fetal heart rate monitoring: is it salvageable? *Am J Obstet Gynecol*. 2000;182:982.

Rosen MA. Paracervical block for labor analgesia: a brief historic review. *Am J Obstet Gynecol*. 2002;186:S127.

Schifrin BS. Fetal heart rate monitoring during labor. *JAMA*. 1972;222:196.

FETAL HEART RATE TESTING: PERIODIC CHANGES

208

INTRODUCTION

Description: Periodic changes in the fetal heart rate in conjunction with uterine contractions may occur. These may indicate fetal stress when they are persistent or become progressively deeper or longer lasting. Recurrent decelerations are defined as occurring with ≥50% of contractions during a 20-minute period. In the United States, decelerations in the fetal heart rate are classified by their relationship to uterine activity: early, late, and variable (Box 208.1). The shape of the deceleration is also significant in the classification. Accelerations higher than the baseline often accompany fetal movement and are reassuring.

Prevalence: Mild and transient periodic decelerations are not uncommon during the course of normal labor. Accelerations are documented in virtually all normal labors.

Predominant Age: Reproductive age.

Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes

- Accelerations
  - Physiologic response to fetal activity or external stimuli (acoustic stimulation, scalp stimulation, fetal scalp blood sampling). Compensatory accelerations also occur following variable decelerations. These changes reflect an intact neurohormonal cardiovascular control system
- Early decelerations
  - Physiologic response to head compression; dural stimulation mediated via the vagus nerve ("diving reflex"). These changes are not associated with hypoxia, acidemia, or low Apgar scores
- Variable decelerations
  - Compensatory response to intermittent obstruction of umbilical blood flow
- Late decelerations
  - Decreased fetal oxygenation with reflex bradycardia or myocardial depression. This type of deceleration suggests the greatest fetal stress despite the relatively modest change in heart rate

Risk Factors: Early—occiput posterior position, cephalopelvic disproportion. Variable—low amniotic fluid volume, cord prolapse, abnormal lie. Late—placental aging, reduced placental perfusion (maternal disease, vascular spasm, medications).

Box 208.1 CLASSIFICATION OF FETAL HEART RATE PATTERNS

Category I: predictive of normal fetal acid-base balance. Seen in 15% of tracings.
- Baseline rate: 110–160 bpm
- Moderate baseline FHR variability
- No late or variable decelerations
- Early decelerations may be present or absent
- Accelerations may be present or absent

Category II: intermediate risk. Continued close observation warranted. Seen in 85% of tracings.
- Dose not meet the criteria for either category I or III

Category III: predictive of abnormal fetal acid-base status. Intervention may be required. Seen in <1% of tracings.
- Either
  - Absent baseline FHR variability and any of the following:
    - Recurrent late decelerations
    - Recurrent variable decelerations
    - Bradycardia
- Or
  - Sinusoidal pattern

SIGNS AND SYMPTOMS

- Accelerations
  - Abrupt increase in fetal heart rate that reaches a maximum within 30 seconds
- Early decelerations
  - Shallow U-shaped, with gradual onset and resolution, generally (10–30 beats/min [bpm]), that reaches a nadir at the peak of uterine activity; rarely associated with heart rates below 100–110 bpm
- Variable decelerations
  - Slowing with abrupt onset and return, frequently associated with accelerations before, after, or both; variable in depth and duration but coincide with the compression of the umbilical cord during contraction
- Late decelerations
  - U-shaped, with gradual onset and resolution, generally shallow (10–30 bpm), and reaches a nadir after the peak of uterine activity; often associated with decreased variability. Generally, not diagnosed unless present with more than 50% of contractions.

DIAGNOSTIC APPROACH

Differential Diagnosis

Early Decelerations

- Head compression (less common; generally results in a more gradual deceleration that is proportional to the strength and duration of the contraction but may reflect maternal expulsive efforts)

Variable Decelerations

- Cord compression
- Cord prolapse

Late Decelerations

- Uterine hypertonus or tachysystole
- Conduction anesthesia
- Maternal hypotension
- Placental abruption
- Medication effects

Associated Conditions: Oligohydramnios, preeclampsia, eclampsia, maternal hypertension, transient maternal hypotension, intrauterine growth restriction, placental abruption.

Workup and Evaluation

Laboratory: No evaluation indicated.

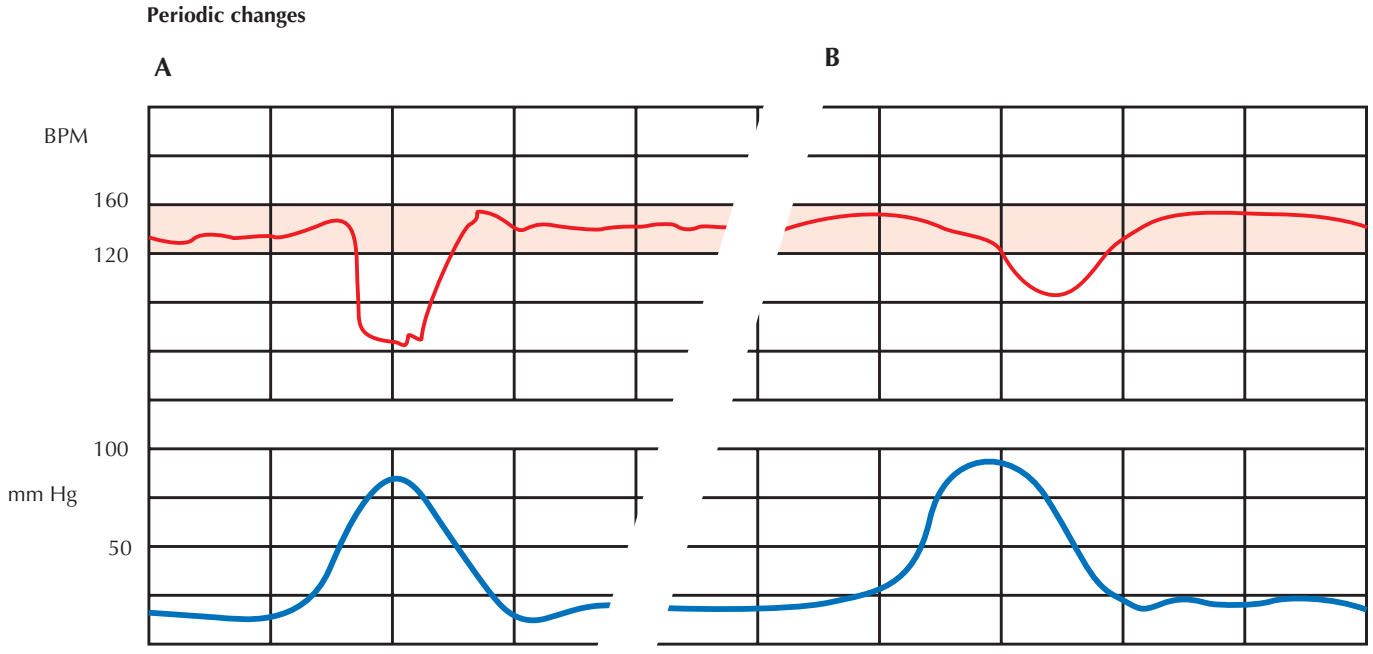
Imaging: Ultrasonography may be used to assess possible causes.

Special Tests: Fetal scalp pH or pulse oximetry (when available) may be of assistance in determining the fetal status.

Diagnostic Procedures: Clinical evaluation of mother and fetus. Fetal monitoring patterns are often classified into three categories (see Box 208.1), which suggest the level of clinical concern.

Pathologic Findings

An elongated umbilical cord or an umbilical cord wrapped around the neck is frequently observed in the presence of variable decelerations. Placental findings often reflect underlying maternal or fetal disease associated with late decelerations.



Variable decelerations (A) are generally sharp in contour, coincide with the contraction in a variable manner, and may have associated accelerations before or after. Late decelerations (B) are subtle with their nadir occurring after the peak of the contraction.

BPM, beats per minute.

Figure 208.1 Periodic changes

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Maternal hydration, change in maternal position (lateral recumbent), maternal oxygen therapy.
Specific Measures: Aggressive fetal and maternal evaluation, amnioinfusion, tocolytics (when hypertonus is involved), expedited delivery in the face of nonreassuring changes.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Booklets AP015 (Fetal Heart Rate Monitoring During Labor) and AP098 (Special Tests for Monitoring Fetal Health).

Drug(s) of Choice

Tocolytics may be used if uterine tetany or tachysystole are considered to play a role in fetal stress.
Contraindications: Tocolytics are relatively contraindicated in the absence of a diagnosis.

FOLLOW-UP

Patient Monitoring: Continued maternal and fetal assessment.
Prevention/Avoidance: Adequate maternal hydration, left lateral recumbent position for labor. Continued assessment of fetal status in postdate pregnancies.
Possible Complications: Progressive deterioration of fetal status unless underlying processes are identified and corrected.
Expected Outcome: With aggressive diagnosis and management, outcome will generally be good.

MISCELLANEOUS

Other Notes: Intrapartum fetal heart rate monitoring is only one part of the overall evaluation of mother and fetus. This modality must be used to augment clinical judgment and not replace it.

REFERENCES

LEVEL I

Ellison PH, Foster M, Sheridan-Pereira M, et al. Electronic fetal heart monitoring, auscultation, and neonatal outcome. *Am J Obstet Gynecol*. 1991;164:1281.

Rinehart BK, Terrone DA, Barrow JH, et al. Randomized trial of intermittent or continuous amnioinfusion for variable decelerations. *Obstet Gynecol*. 2000;96:571.

LEVEL II

Alfirevic Z, Devane D, Gyte GM. Continuous cardiotocography (CTG) as a form of electronic fetal monitoring (EFM) for fetal assessment during labour. *Cochrane Database Syst Rev*. 2013;(5):CD006066.

Bhide A, Chandraharan E, Acharya G. Fetal monitoring in labor: implications of evidence generated by new systematic review. *Acta Obstet Gynecol Scand*. 2016;95:5.

Devane D, Lalor JG, Daly S, et al. Cardiotocography versus intermittent auscultation of fetal heart on admission to labour ward for assessment of fetal wellbeing. *Cochrane Database Syst Rev*. 2012;(2):CD005122.

Graham EM, Petersen SM, Christo DK, et al. Intrapartum electronic fetal heart rate monitoring and the prevention of perinatal brain injury. *Obstet Gynecol*. 2006;108:656.

Grimes DA, Peipert JF. Electronic fetal monitoring as a public health screening program: the arithmetic of failure. *Obstet Gynecol*. 2010;116:1397.

LEVEL III

American College of Obstetricians and Gynecologists. Intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. ACOG Practice Bulletin No. 106. *Obstet Gynecol*. 2009;114:192.

American College of Obstetricians and Gynecologists. Management of intrapartum fetal heart rate tracings. Practice Bulletin No. 116. *Obstet Gynecol*. 2010;116:1232.

American College of Obstetricians and Gynecologists. Antepartum fetal surveillance. Practice Bulletin No. 145. *Obstet Gynecol*. 2014;124:182.

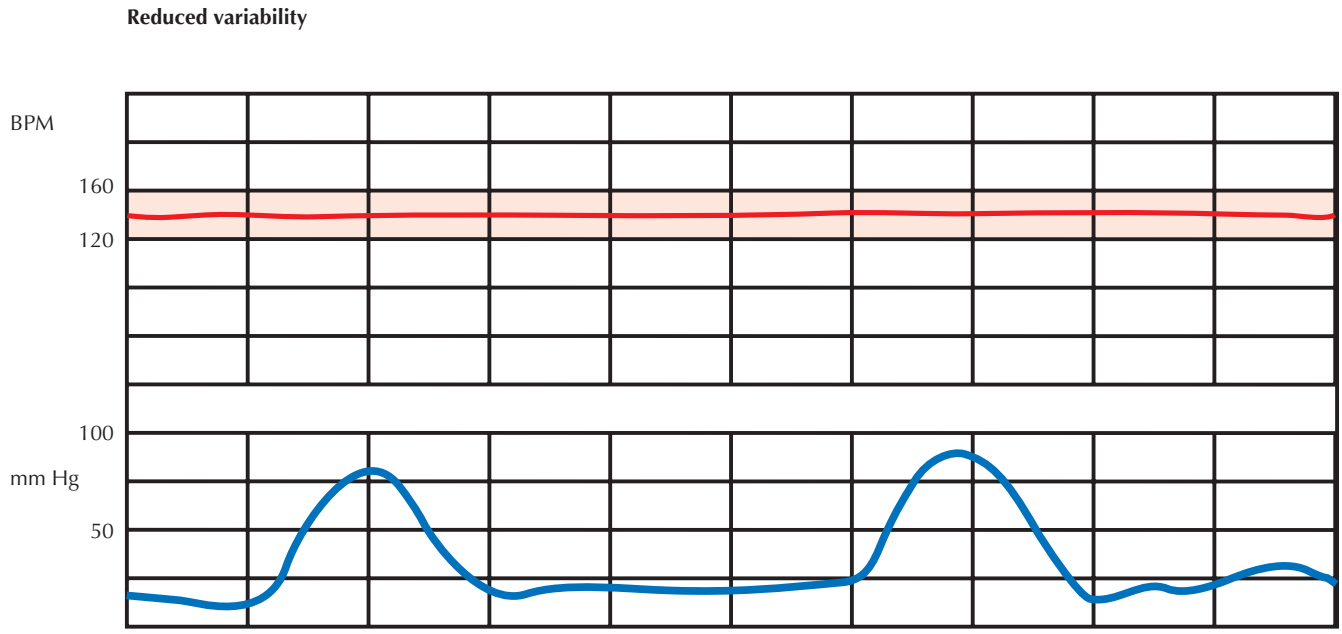
Burrus DR, O'Shea TM Jr, Veille JC, et al. The predictive value of intrapartum fetal heart rate abnormalities in the extremely premature infant. *Am J Obstet Gynecol*. 1994;171:1128.

Grimes DA, Peipert JF. Electronic fetal monitoring as a public health screening program: the arithmetic of failure. *Obstet Gynecol*. 2010;116:1397.

Larmay HJ, Strasburger JF. Differential diagnosis and management of the fetus and newborn with an irregular or abnormal heart rate. *Pediatr Clin North Am*. 2004;51:1033.

Parer JT, King T. Fetal heart rate monitoring: is it salvageable? *Am J Obstet Gynecol*. 2000;182:982.

Schifrin BS. Fetal heart rate monitoring during labor. *JAMA*. 1972;222:196.



BPM, beats per minute.

Figure 209.1 Reduced variability

MISCELLANEOUS

Other Notes: When the fetal heart rate is increased, there is an apparent reduction in beat-to-beat variability based solely on physiologic constraints and does not reflect fetal stress.

Intrapartum fetal heart rate monitoring is only one part of the overall evaluation of mother and fetus. This modality must be used to augment clinical judgment and not replace it.

REFERENCES

LEVEL I

Hallak M, Martinez-Poyer J, Kruger ML, et al. The effect of magnesium sulfate on fetal heart rate parameters: a randomized, placebo-controlled trial. *Am J Obstet Gynecol*. 1999;181:1122.

LEVEL II

Alfirevic Z, Devane D, Gyte GM. Continuous cardiotocography (CTG) as a form of electronic fetal monitoring (EFM) for fetal assessment during labour. *Cochrane Database Syst Rev*. 2013;(5):CD006066.

Davidson SR, Rankin JHG, Martin CB Jr, et al. Fetal heart rate variability and behavioral state: analysis by poser spectrum. *Am J Obstet Gynecol*. 1992;167:717.

Graham EM, Petersen SM, Christo DK, et al. Intrapartum electronic fetal heart rate monitoring and the prevention of perinatal brain injury. *Obstet Gynecol*. 2006;108:656.

Grimes DA, Peipert JF. Electronic fetal monitoring as a public health screening program: the arithmetic of failure. *Obstet Gynecol*. 2010;116:1397.

Siira SM, Ojala TH, Vahlberg TJ, et al. Marked fetal acidosis and specific changes in power spectrum analysis of fetal heart rate variability recorded during the last hour of labour. *BJOG*. 2005;112:418.

LEVEL III

American College of Obstetricians and Gynecologists. Intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. ACOG Practice Bulletin No. 106. *Obstet Gynecol*. 2009;114:192.

American College of Obstetricians and Gynecologists. Management of intrapartum fetal heart rate tracings. Practice Bulletin No. 116. *Obstet Gynecol*. 2010;116:1232.

American College of Obstetricians and Gynecologists. Antepartum fetal surveillance. Practice Bulletin No. 145. *Obstet Gynecol*. 2014;124:182.

Burrus DR, O'Shea TM Jr, Veille JC, et al. The predictive value of intrapartum fetal heart rate abnormalities in the extremely premature infant. *Am J Obstet Gynecol*. 1994;171:1128.

Parer JT, King T. Fetal heart rate monitoring: is it salvageable? *Am J Obstet Gynecol*. 2000;182:982.

Samueloff A, Langer O, Berkus M, et al. Is fetal heart rate variability a good predictor of fetal outcome? *Acta Obstet Gynecol Scand*. 1994;73:39.

Schifrin BS. Fetal heart rate monitoring during labor. *JAMA*. 1972;222:196.

FETAL HEART RATE TESTING: TACHYCARDIA

210

INTRODUCTION

Description: Tachycardia is an increase in the baseline heart rate, generally above 160 beats/min (bpm). Mild tachycardia is generally defined as 161–180 bpm, and severe tachycardia as greater than 180 bpm for more than 3 minutes.
Prevalence: Mild fetal tachycardia is observed during approximately 2% of labors.
Predominant Age: Reproductive age.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Maternal fever (most common), intra-amniotic infection (fetal tachycardia may occur even before maternal fever is present), fetal congenital heart disease, depressed fetal oxygenation, fetal acidosis, fetal anemia or blood loss, medication effects (atropine, terbutaline), maternal hypotension.
Risk Factors: Maternal, fetal, or uterine infection.

SIGNS AND SYMPTOMS

- Increased fetal heart rate (baseline) above 160 bpm (frequently associated with an apparent loss of beat-to-beat variability)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Maternal fever (chorioamnionitis)
- Intra-amniotic infection
- Congenital heart disease
- Fetal anemia or blood loss
- Medication effects
- Uterine rupture

Associated Conditions: Chorioamnionitis, maternal fever, maternal dehydration.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated.
Special Tests: Fetal scalp pH or pulse oximetry (when available) may be of assistance in determining the fetal status.
Diagnostic Procedures: Clinical evaluation of mother and fetus.

Pathologic Findings

Based on underlying pathophysiologic conditions.

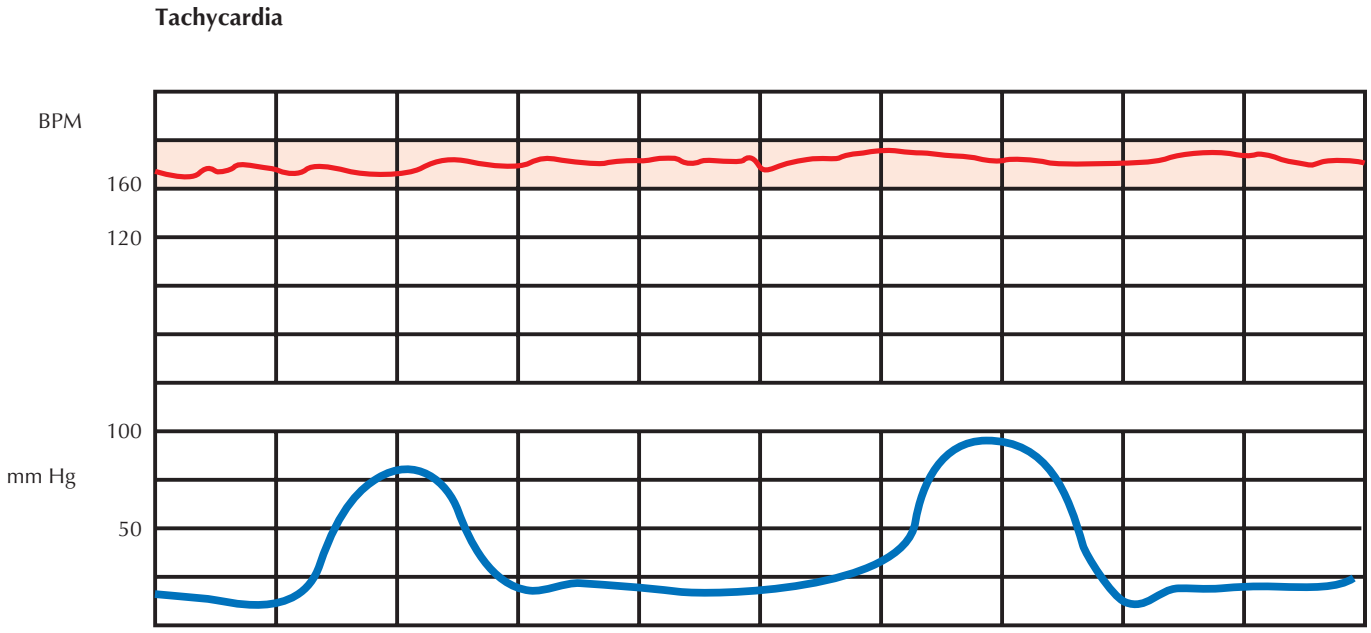
MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Maternal hydration, change in maternal position (lateral recumbent), maternal oxygen therapy.
Specific Measures: Aggressive fetal and maternal evaluation, amnioinfusion, tocolytics (when hypertonus is involved), expedited delivery in the face of nonreassuring changes.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Booklets AP015 (Fetal Heart Rate Monitoring During Labor) and AP098 (Special Tests for Monitoring Fetal Health).

Drug(s) of Choice

None. Digoxin therapy for selected persistent fetal tachyarrhythmias, such as fetal supraventricular tachycardia, may be indicated.



BPM, beats per minute.

Figure 210.1 Tachycardia

FOLLOW-UP

Patient Monitoring: Continued maternal and fetal assessment.
Prevention/Avoidance: Adequate maternal hydration, reduced number of cervical examinations in patients at risk for infection (premature rupture of the membranes).
Possible Complications: Progressive deterioration of fetal status unless underlying processes are identified and corrected.
Expected Outcome: With aggressive diagnosis and management, outcome will generally be good.

MISCELLANEOUS

Other Notes: When the fetal heart rate is increased, there is an apparent reduction in beat-to-beat variability based solely on physiologic constraints and does not reflect fetal stress.
Intrapartum fetal heart rate monitoring is only one part of the overall evaluation of mother and fetus. This modality must be used to augment clinical judgment and not replace it.

REFERENCES

LEVEL II

Alfirevic Z, Devane D, Gyte GM. Continuous cardiotocography (CTG) as a form of electronic fetal monitoring (EFM) for fetal assessment during labour. *Cochrane Database Syst Rev*. 2013;(5):CD006066.

Graham EM, Petersen SM, Christo DK, et al. Intrapartum electronic fetal heart rate monitoring and the prevention of perinatal brain injury. *Obstet Gynecol*. 2006;108:656.

LEVEL III

American College of Obstetricians and Gynecologists. Intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. ACOG Practice Bulletin No. 106. *Obstet Gynecol*. 2009;114:192.

American College of Obstetricians and Gynecologists. Management of intrapartum fetal heart rate tracings. Practice Bulletin No. 116. *Obstet Gynecol*. 2010;116:1232.

American College of Obstetricians and Gynecologists. Antepartum fetal surveillance. Practice Bulletin No. 145. *Obstet Gynecol*. 2014;124:182.

Burrus DR, O'Shea TM Jr, Veille JC, et al. The predictive value of intrapartum fetal heart rate abnormalities in the extremely premature infant. *Am J Obstet Gynecol*. 1994;171:1128.

Gardiner HM. Fetal echocardiography: 20 years of progress. *Heart*. 2001; 86:II12.

Jones LM, Garmel SH. Successful digoxin therapy of fetal supraventricular tachycardia in a triplet pregnancy. *Obstet Gynecol*. 2001;98:921.

Larmay HJ, Strasburger JF. Differential diagnosis and management of the fetus and newborn with an irregular or abnormal heart rate. *Pediatr Clin North Am*. 2004;51:1033.

Parer JT, King T. Fetal heart rate monitoring: is it salvageable? *Am J Obstet Gynecol*. 2000;182:982.

Parer JT, Livingston EG. What is fetal distress? *Am J Obstet Gynecol*. 1990; 162:1421.

Schifrin BS. Fetal heart rate monitoring during labor. *JAMA*. 1972;222:196.

van Engelen AD, Weijtens O, Brenner JI, et al. Management outcome and follow-up of fetal tachycardia. *J Am Coll Cardiol*. 1994;24:1371.

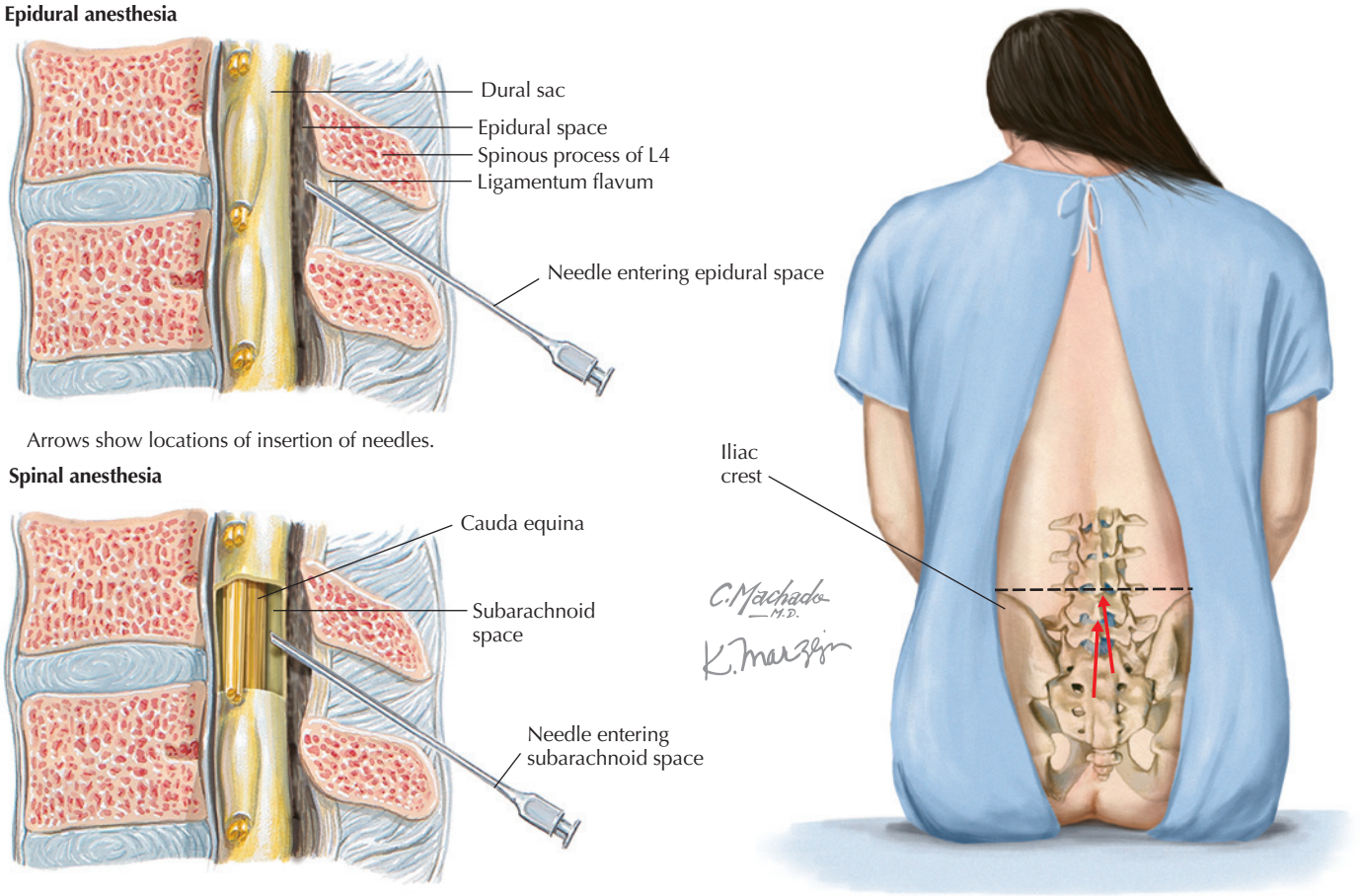


Figure 211.1 Lumbar puncture and epidural anesthesia

or local infiltration, are good options for the perineal discomfort of the final processes of delivery (and repair if necessary), but provide little or no relief for the other aspects of labor and delivery pain. More versatile, effective, and longer lasting are the neuraxial techniques such as epidural, spinal, or combined epidural-spinal techniques. These are particularly well suited to the needs of cesarean or operative deliveries. Caudal anesthesia is effective for the discomfort of the late stages of labor but has fallen out of use in favor of the more versatile epidural options.

Patient Education: Reassurance; American College of Obstetricians and Gynecologists Patient Education Pamphlet AP086 (Medications for Pain Relief During Labor and Delivery).

IMPLEMENTATION

Special Considerations: Epidural and spinal techniques may not be used in the face of uncorrected coagulopathy, infection near the site of administration, uncorrected hypovolemia, or increased intracranial pressure. The use of epidural anesthesia is associated with a slight increase in labor duration and the likelihood of operative delivery but not an increased rate of cesarean delivery. Under emergent conditions, rapid sequence intubation and induction of general anesthesia may be required, but risks anesthetizing the fetus as well.

REFERENCES

LEVEL II

Anim-Somuah M, Smyth RM, Jones L. Epidural versus non-epidural or no analgesia in labour. *Cochrane Database Syst Rev*. 2011;CD000331.

Freeman LM, Bloemenkamp KW, Franssen MT, et al. Patient controlled analgesia with remifentanil versus epidural analgesia in labour: randomised multicentre equivalence trial. *BMJ*. 2015;350:h846.

Gupta JK, Hofmeyr GJ, Shehmar M. Position in the second stage of labour for women without epidural anaesthesia. *Cochrane Database Syst Rev*. 2012;(5):CD002006.

Jones L, Othman M, Dowswell T, et al. Pain management for women in labour: an overview of systematic reviews. *Cochrane Database Syst Rev*. 2012;(3):CD009234.

Klomp T, van Poppel M, Jones L, et al. Inhaled analgesia for pain management in labour. *Cochrane Database Syst Rev*. 2012;(9):CD009351.

Osterman MJK, Martin JA. *Epidural and spinal anesthesia use during labor: 27-state reporting area, 2008*. National vital statistics reports; Vol 59 no 5. Hyattsville, MD: National Center for Health Statistics; 2011.

Othman M, Jones L, Neilson JP. Non-opioid drugs for pain management in labour. *Cochrane Database Syst Rev*. 2012;(7):CD009223.

Torvaldsen S, Roberts CL, Bell JC, et al. Discontinuation of epidural analgesia late in labour for reducing the adverse delivery outcomes associated with epidural analgesia. *Cochrane Database Syst Rev*. 2004; CD004457.

Ullman R, Smith LA, Burns E, et al. Parenteral opioids for maternal pain relief in labour. *Cochrane Database Syst Rev*. 2010;CD007396.

LEVEL III

American College of Obstetricians and Gynecologists. Obstetric analgesia and anesthesia. ACOG Practice Bulletin No. 36. *Obstet Gynecol*. 2002; 100:177.

American College of Obstetricians and Gynecologists. Pain relief during labor. ACOG Committee Opinion No. 295. *Obstet Gynecol*. 2004;104:213.

American College of Obstetricians and Gynecologists. Analgesia and cesarean delivery rates. ACOG Committee Opinion No. 339. *Obstet Gynecol*. 2006;107:1487.

Leighton BL, Halpern SH, Wilson DB. Lumbar sympathetic blocks speed early and second stage induced labor in nulliparous women. *Anesthesiology*. 1999;90:1039.

Rogers R, Gilson G, Kammerer-Doak D. Epidural analgesia and active management of labor: effects on length of labor and mode of delivery. *Obstet Gynecol*. 1999;93:995.

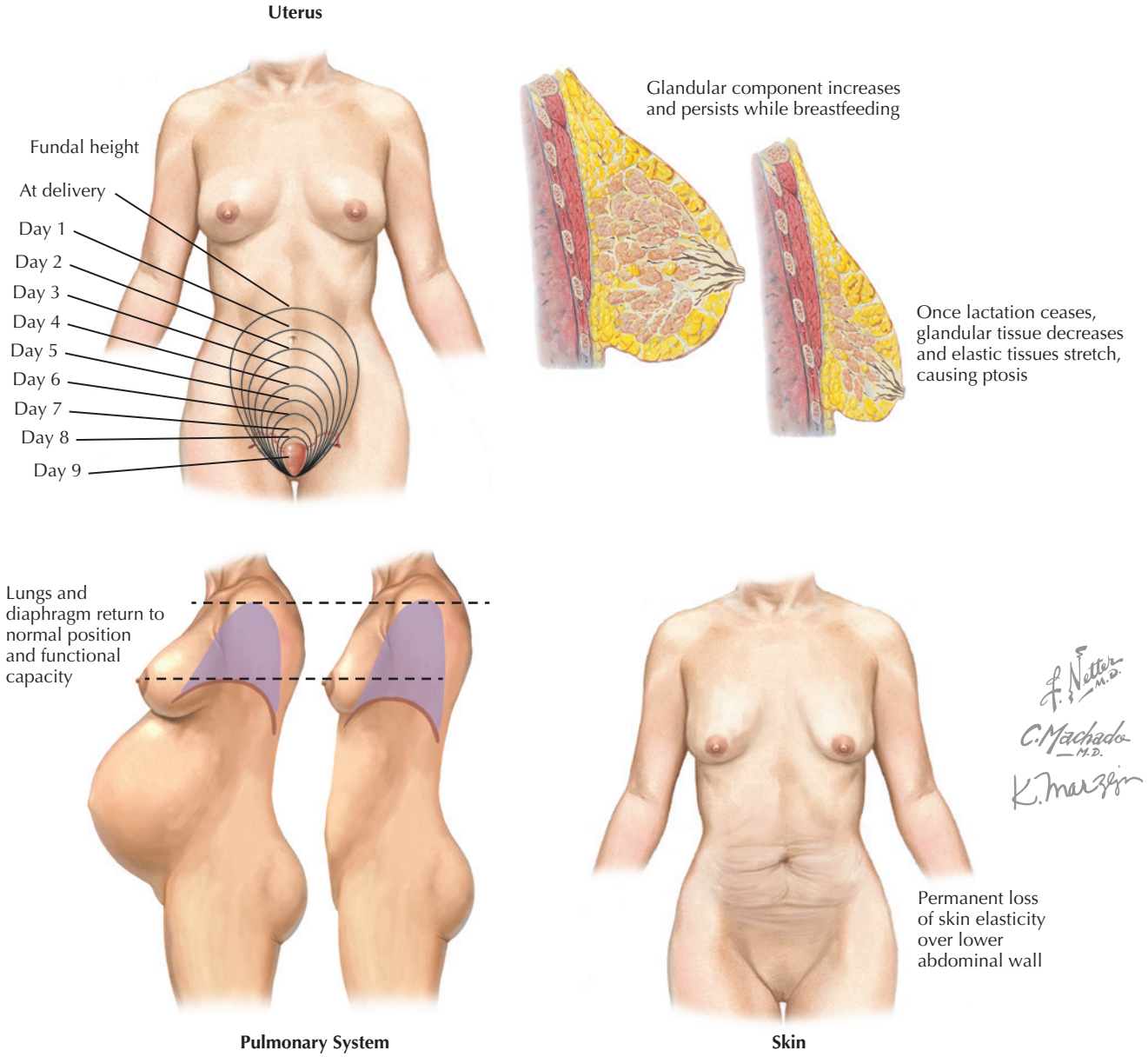


Figure 212.1 Normal postpartum changes

glomerular filtration rate and other functional changes in the kidney that are induced by pregnancy resolve over a similar time course.

Musculoskeletal system: With the loss of the forward displaced mass of the fetus, uterus, and amniotic fluid, the patient's center of gravity abruptly moves backward to its normal location. This forces a rapid return to the normal upright stance of pre-pregnancy. When this is combined with the bending and lifting associated with newborn care, low back discomfort is common. The abdominal wall musculature regains most, if not all, of its normal tone and strength, but the diastasis of the rectus muscles may persist.

Skin and hair: Striae, when present, fade from red to silvery but are permanent as is some loss of skin elasticity over the lower abdominal wall. Following delivery, there is a reversal in the ratio of growing (anagen) and resting (telogen) hair follicles. This causes the appearance of accelerated hair loss (telogen effluvium), which is self-limited and lasts between 6 and 12 months.

Strategies: Awareness of the changes that are induced by pregnancy and the associated reversals required to regain the pre-pregnant state are important to understand so that they may be monitored for normality or intervention instituted when the sequence is incomplete.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlets AP029 (Breastfeeding Your Baby), AP091 (Postpartum Depression), AP131 (Exercise After Pregnancy), AB005 (You and Your Baby: Prenatal Care, Labor and Delivery, and Postpartum Care), AB020 (Birth Control), and AP052 (Postpartum Sterilization).

IMPLEMENTATION

Special Considerations: It is common (25%–50%) for women to experience shivering during the first 30 minutes after delivery. The exact etiology of this phenomenon is not known, but it is normal and self-limited.

REFERENCES

LEVEL II

Amorim Adegboye AR, Linne YM. Diet or exercise, or both, for weight reduction in women after childbirth. *Cochrane Database Syst Rev*. 2013;(7):CD005627.

Benson MD, Haney E, Dinsmoor M, et al. Shaking rigors in parturients. *J Reprod Med*. 2008;53:685.

Deussen AR, Ashwood P, Martis R. Analgesia for relief of pain due to uterine cramping/involution after birth. *Cochrane Database Syst Rev*. 2011;(5):CD004908.

East CE, Begg L, Henshall NE, et al. Local cooling for relieving pain from perineal trauma sustained during childbirth. *Cochrane Database Syst Rev*. 2012;(5):CD006304.

Jackson E, Glasier A. Return of ovulation and menses in postpartum nonlactating women: a systematic review. *Obstet Gynecol*. 2011;117:657.

Lim JL. Post-partum voiding dysfunction and urinary retention. *Aust N Z J Obstet Gynaecol*. 2010;50:502.

Mulder FE, Hakvoort RA, Schoffelmeer MA, et al. Postpartum urinary retention: a systematic review of adverse effects and management. *Int Urogynecol J*. 2014;25:1605.

Oladapo OT, Fawole B. Treatments for suppression of lactation. *Cochrane Database Syst Rev*. 2012;(9):CD005937.

Sherman D, Lurie S, Frenkel E, et al. Characteristics of normal lochia. *Am J Perinatol*. 1999;16:399.

LEVEL III

American College of Obstetricians and Gynecologists. *Prevention of Rh D isoimmunization*. ACOG Practice Bulletin 4. Washington, DC: ACOG; 1999.

American College of Obstetricians and Gynecologists. Postpartum hemorrhage. ACOG Practice Bulletin No. 76. *Obstet Gynecol*. 2006;108:1039.

American College of Obstetricians and Gynecologists. Use of psychiatric medications during pregnancy and lactation. ACOG Practice Bulletin No. 92. *Obstet Gynecol*. 2008;111:1001.

American College of Obstetricians and Gynecologists. Health care for pregnant and postpartum incarcerated women and adolescent females. Committee Opinion No. 511. *Obstet Gynecol*. 2011;118:1198.

American College of Obstetricians and Gynecologists. Access to postpartum sterilization. Committee Opinion No. 530. *Obstet Gynecol*. 2012;120:212.

American College of Obstetricians and Gynecologists. Emergent therapy for acute-onset, severe hypertension during pregnancy and the postpartum period. Committee Opinion No. 623. *Obstet Gynecol*. 2015;125:521.

American College of Obstetricians and Gynecologists. Physical activity and exercise during pregnancy and the postpartum period. Committee Opinion No. 650. *Obstet Gynecol*. 2015;126:e135.

American College of Obstetricians and Gynecologists. Screening for perinatal depression. Committee Opinion No. 630. *Obstet Gynecol*. 2015;125:1268.

American College of Obstetricians and Gynecologists. Optimizing support for breastfeeding as part of obstetric practice. Committee Opinion No. 658. *Obstet Gynecol*. 2016;127:e86.

Leeman LM, Rogers RG. Sex after childbirth: postpartum sexual function. *Obstet Gynecol*. 2012;119:647.

Shin GH, Toto EL, Schey R. Pregnancy and postpartum bowel changes: constipation and fecal incontinence. *Am J Gastroenterol*. 2015;110:521.

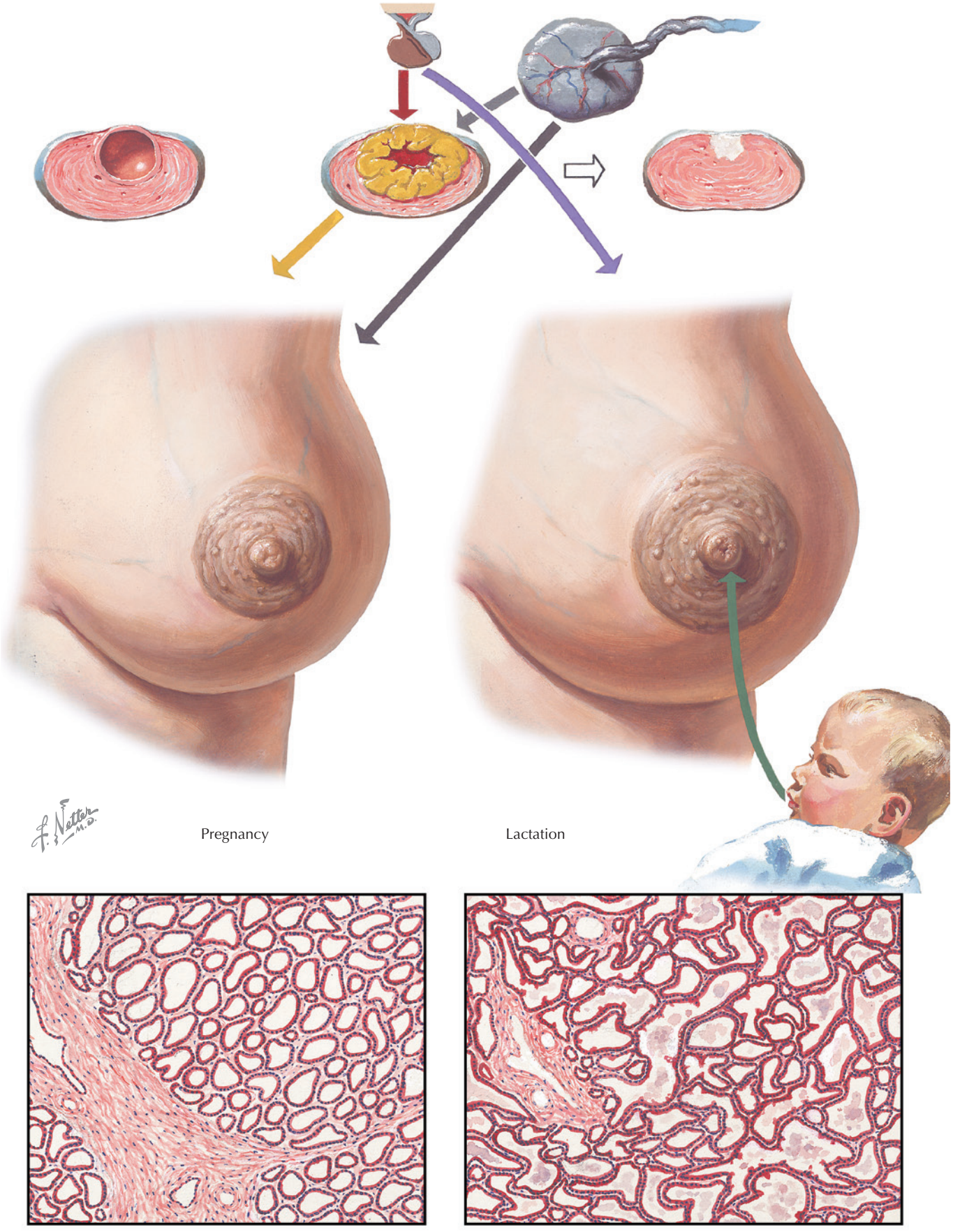


Figure 213.1 Lactation

compressive binding provide the greatest relief. Medication to suppress lactation is generally not effective.

Patient Education: Reassurance, support, specific suggestions. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP029 (Breastfeeding Your Baby).

IMPLEMENTATION

Special Considerations: Breastfeeding is contraindicated in patients with human immunodeficiency virus (HIV), cytomegalovirus, hepatitis B virus infections, and human T-cell lymphotropic virus type I or type II and in those who have active untreated tuberculosis or varicella or active herpes simplex virus with breast lesions. Substances of abuse (including alcohol) pass to breast milk, as do some medications. Breastfed infants often lose weight in the first few days and do not regain birth weight until as late as day 10. Growth spurts often occur at approximately 10 days, 6 weeks, 3 months, and 4–6 months. If the infant fails to thrive, support and evaluation are in order. Care must be taken to wash the hands (and any equipment used) well before breastfeeding or breast manipulation. The nipples and the infant's face should also be clean before each feeding. Fresh breast milk may be safely kept for 6–10 hours at room temperature or 72 hours under refrigeration. Breast milk may also be frozen and kept for 6 months in a home freezer or 12 months at –20°C. Thawed breast milk should be used within 24 hours and may not be refrozen. Breast milk should never be warmed in a microwave oven. The volume of milk required for each feeding varies widely but is normally between 2 and 5 oz for newborns, 4–6 oz for infants 2–4 months of age, and 5–7 oz for babies 4–6 months old. One study found that 65% of women with augmentation mammoplasty have lactation insufficiency.

REFERENCES

LEVEL I

Lavender T, Baker L, Smyth R, et al. Breastfeeding expectations versus reality: a cluster randomised controlled trial. *BJOG*. 2005;112:1047.

Mattar CN, Chong YS, Chan YS, et al. Simple antenatal preparation to improve breastfeeding practice: a randomized controlled trial. *Obstet Gynecol*. 2007;109:73.

Wolfberg AJ, Michels KB, Shields W, et al. Dads as breastfeeding advocates: results from a randomized controlled trial of an educational intervention. *Am J Obstet Gynecol*. 2004;191:708.

LEVEL II

Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease. *Lancet*. 2002;360:187.

Coutinho SB, de Lira PI, de Carvalho Lima M, et al. Comparison of the effect of two systems for the promotion of exclusive breastfeeding. *Lancet*. 2005;366:1094.

Dennis CL, Jackson K, Watson J. Interventions for treating painful nipples among breastfeeding women. *Cochrane Database Syst Rev*. 2014;(12):CD007366.

Jahanfar S, Ng CJ, Teng CL. Antibiotics for mastitis in breastfeeding women. *Cochrane Database Syst Rev*. 2013;(2):CD005458.

Mangesi L, Dowswell T. Treatments for breast engorgement during lactation. *Cochrane Database Syst Rev*. 2010;(9):CD006946.

Østbye T, Krause KM, Swamy GK, et al. Effect of breastfeeding on weight retention from one pregnancy to the next: results from the North Carolina WIC program. *Prev Med*. 2010;51:368.

Pisacane A, Continisio GI, Aldinucci M, et al. A controlled trial of the father's role in breastfeeding promotion. *Pediatrics*. 2005;116:e494.

Sadeharju K, Knip M, Virtanen SM, et al. Finnish TRIGR Study Group. Maternal antibodies in breast milk protect the child from enterovirus infections. *Pediatrics*. 2007;119:941.

LEVEL III

American Academy of Pediatrics, American College of Obstetricians and Gynecologists. *Breastfeeding handbook for physicians*. Elk Grove Village, IL: AAP; Washington, DC: ACOG; 2006.

American College of Obstetricians and Gynecologists. Breastfeeding: Maternal and infant aspects. Special report from ACOG. *ACOG Clin Rev*. 2007;12:1S.

American College of Obstetricians and Gynecologists. Use of psychiatric medications during pregnancy and lactation. ACOG Practice Bulletin No. 92. *Obstet Gynecol*. 2008;111:1001.

American College of Obstetricians and Gynecologists. Breastfeeding in underserved women: increasing initiation and continuation of breastfeeding. Committee Opinion No. 570. *Obstet Gynecol*. 2013;122:423.

American College of Obstetricians and Gynecologists. Marijuana use during pregnancy and lactation. Committee Opinion No. 637. *Obstet Gynecol*. 2015;126:234.

American College of Obstetricians and Gynecologists. Guidelines for diagnostic imaging during pregnancy and lactation. Committee Opinion No. 656. *Obstet Gynecol*. 2016;127:e75.

American College of Obstetricians and Gynecologists. Optimizing support for breastfeeding as part of obstetric practice. Committee Opinion No. 658. *Obstet Gynecol*. 2016;127:e86.

Friedman NJ, Zeiger RS. The role of breast-feeding in the development of allergies and asthma. *J Allergy Clin Immunol*. 2005;115:1238.

Gray GE, McIntyre JA. HIV and pregnancy. *BMJ*. 2007;334:950.

Michalopoulos K. The effects of breast augmentation surgery on future ability to lactate. *Breast J*. 2007;13:62.

Sachs HC, Committee On Drugs. The transfer of drugs and therapeutics into human breast milk: an update on selected topics. *Pediatrics*. 2013;132:e796.

SECTION XIII

Obstetric Conditions and Concerns

This page intentionally left blank

ABNORMALITIES OF PLACENTAL IMPLANTATION 214

INTRODUCTION

Description: Failure of the normal process of decidua formation results in a placental implantation in which the villi directly adhere to (accreta; 79%), invade into (increta; 14%), or go through (percreta; 7%) the myometrium. One portion (partial) or all (total) of the placenta may be involved.
Prevalence: Difficult to assess; estimates vary from 1 in 1667 to 1 in 70,000 pregnancies (average 1 in 7000). The incidence has been increasing in parallel with the rate of cesarean delivery.
Predominant Age: Reproductive age; average age is 29 years.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Abnormal decidua formation at the time of placental implantation. Imperfect development of the fibrinoid (Nitabuch) layer. Abnormal site of placental implantation (previa, 64% of placenta accreta, cornual or lower uterine segment, or uterine scars such as site of previous cesarean delivery).
Risk Factors: Placenta previa (5% without previous uterine surgery; 15%–70% with previous surgery), previous cesarean delivery (risk increases with number; 2.4% of those with three or more procedures), multigravidity (1 of 500,000 for parity <3; 1 of 2500 for parity >6), older maternal age (>35 years), previous uterine curettage, previous uterine sepsis, previous manual removal of the placenta, leiomyomata, uterine malformation, prior abortion, endometrial ablation. Eighty percent of patients have a history of a uterine surgical procedure.

SIGNS AND SYMPTOMS

- Failure of normal placental separation
- Abnormally heavy bleeding after delivery of the placenta (may be life threatening)
- History of antepartum hemorrhage

DIAGNOSTIC APPROACH

Differential Diagnosis

- Placenta previa
- Uterine rupture with expulsion of the placenta
- Uterine rupture at the time of manual removal of the placenta

Associated Conditions: Placenta previa (15%), postpartum hemorrhage.

Workup and Evaluation

Laboratory: Complete blood count after delivery to assess blood loss (which may be excessive).
Imaging: Ultrasonography, Doppler ultrasonography, or magnetic resonance imaging (MRI) have been used to make the diagnosis before labor in many cases. Low-lying placentas noted in studies performed at less than 30 weeks may "migrate," leaving the cervix free at term (up to 90% of cases).
Special Tests: None indicated.
Diagnostic Procedures: Generally diagnosed only at delivery by failure of the normal separation mechanism. Final diagnosis is established histologically.

Pathologic Findings

Absence of the decidua basalis (replaced by loose connective tissue). The decidua parietalis may be normal or absent. The villi may be separated from the myometrial cells by a layer of fibrin.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Aggressive fluid and blood support as necessary. Oxytocin or other uterotonic agents to promote uterine contractions after placental delivery (if accomplished).
Specific Measures: Most patients require hysterectomy. If the invasion of the myometrium is incomplete and the bladder is spared, conservative management by uterine packing may be possible. Any time the diagnosis is considered, preparations for hysterectomy, including anesthesia, instruments, and adequate blood, should be ready before any attempt is made to free the placenta.
Diet: Nothing by mouth until the patient's condition has been stabilized.
Activity: Bed rest until the patient's condition has been stabilized.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlets AP038 (Bleeding During Pregnancy), AP006 (Cesarean Birth), and AP025 (Ultrasound Exams).

Drug(s) of Choice

Uterotonics should be available, and broad-spectrum antibiotics should be prophylactically administered.

FOLLOW-UP

Patient Monitoring: Hemodynamic monitoring during the acute diagnosis and treatment.
Prevention/Avoidance: Patients at a high risk may be examined by ultrasonography or MRI in an attempt to identify the absence of the subplacental hypoechoic zone or the presence of lacunar blood-flow patterns. If present, plans for autologous blood donation and elective cesarean hysterectomy may be made. The absence of these findings does not rule out this possibility.
Possible Complications: Life-threatening hemorrhage may occur; maternal mortality of 2%–6% has been reported for treatment by hysterectomy and up to 30% for conservative management. Coagulopathy secondary to blood loss and replacement is common. Adult respiratory distress syndrome and renal failure when significant hemorrhage occurs. Spontaneous rupture of the uterus may occur before labor. Rupture of the uterus or inversion may occur during attempts to remove the placenta.
Expected Outcome: Most patients go to term with normal fetal development. If the possibility is recognized and appropriate treatment is rendered, maternal survival is probable, although loss of the uterus is common. It is hypothesized that small areas of accreta may result in placental cotyledon(s) being torn from the placenta and that these cotyledons may become placental polyps.

MISCELLANEOUS

ICD-10-CM Codes: O43.21 (All types, without hemorrhage), O43.239 (Placenta percreta, unspecified trimester), related; O73.0 (Retained placenta without hemorrhage).

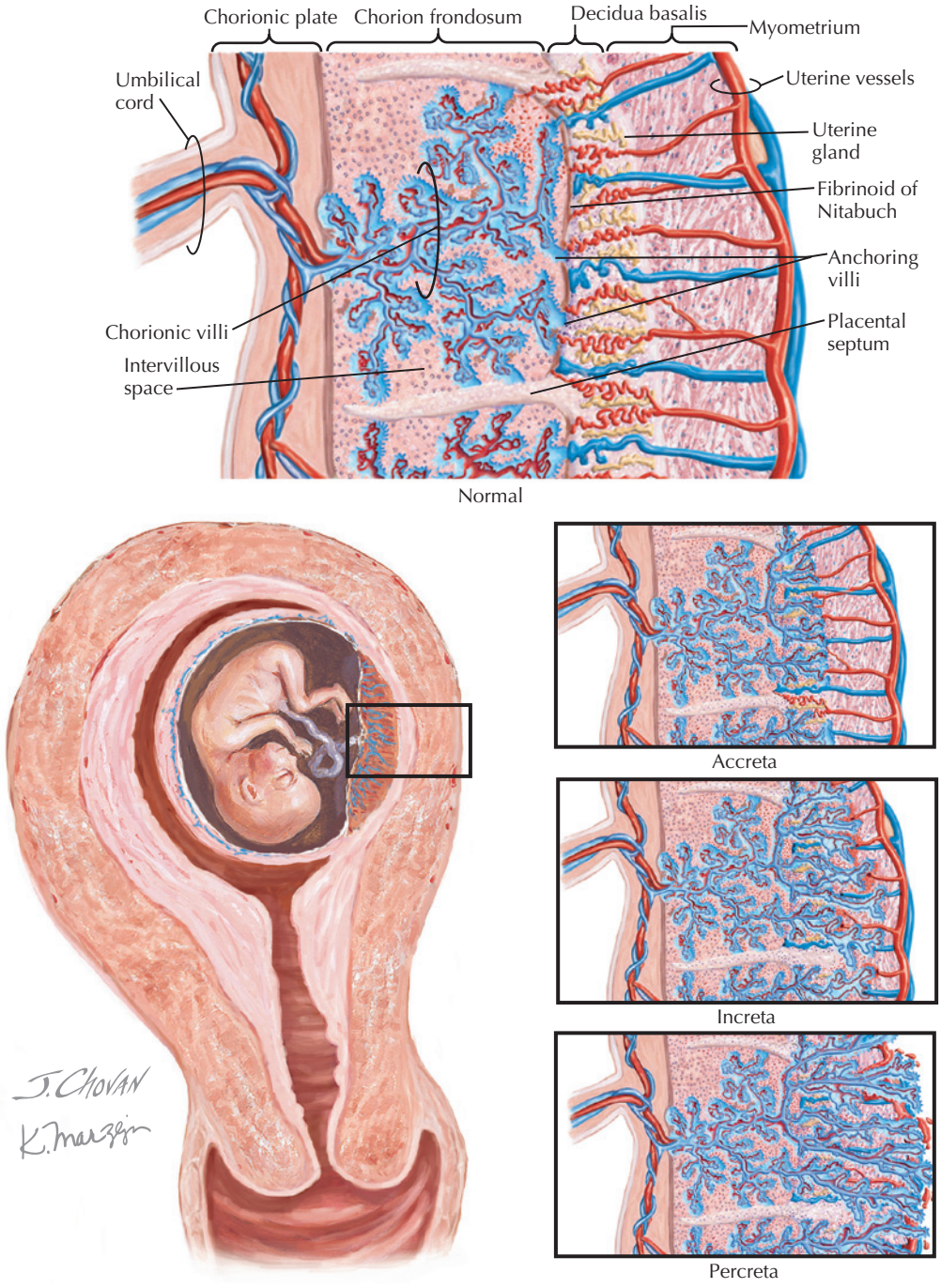


Figure 214.1 Abnormalities of placental implantation

REFERENCES

LEVEL II

Bowman ZS, Eller AG, Kennedy AM, et al. Accuracy of ultrasound for the prediction of placenta accreta. *Am J Obstet Gynecol*. 2014;211:177.e1.

Clausen C, Lönn L, Langhoff-Roos J. Management of placenta percreta: a review of published cases. *Acta Obstet Gynecol Scand*. 2014;93:138.

Eller AG, Bennett MA, Sharshiner M, et al. Maternal morbidity in cases of placenta accreta managed by a multidisciplinary care team compared with standard obstetric care. *Obstet Gynecol*. 2011;117:331.

Salim R, Chulski A, Romano S, et al. Precesarean Prophylactic balloon catheters for suspected placenta accreta: A randomized controlled trial. *Obstet Gynecol*. 2015;126:1022.

Tantbirojn P, Crum CP, Parast MM. Pathophysiology of placenta creta: the role of decidua and extravillous trophoblast. *Placenta*. 2008;29:639.

Warshak CR, Ramos GA, Eskander R, et al. Effect of predelivery diagnosis in 99 consecutive cases of placenta accreta. *Obstet Gynecol*. 2010;115:65.

LEVEL III

American College of Obstetricians and Gynecologists. Postpartum hemorrhage. ACOG Practice Bulletin 76. *Obstet Gynecol*. 2006;108:1039.

American College of Obstetricians and Gynecologists. Endometrial ablation: ACOG Practice Bulletin 81. *Obstet Gynecol*. 2007;109:1233.

American College of Obstetricians and Gynecologists. Placenta accreta. Committee Opinion No. 529. *Obstet Gynecol*. 2012;120:207.

Oyelese Y, Smulian JC. Placenta previa, placenta accreta, and vasa previa. *Obstet Gynecol*. 2006;107:927.

ACTIVE MANAGEMENT OF LABOR

THE CHALLENGE

Active management of labor is a system of labor management that is designed to promote effective labor and reduce the need for cesarean delivery.

Scope of the Problem: Cesarean birth rate for nulliparous patients approximates or exceeds 30% in most areas. Active management has been associated with cesarean delivery rates of less than 5% for its developers (Ireland).

Objectives of Management: To reduce cesarean delivery rates through a system of management that includes education, strict criteria for labor and abnormal progress, one-on-one care, and the use of high-dose oxytocin (when needed).

TACTICS

Relevant Pathophysiology: As developed in Ireland, the active management of labor is based on the following:

- Patient education
- Strict criteria for the diagnosis of labor, the determination of abnormal progress, and the diagnosis of fetal compromise
- One-on-one nursing care during labor
- Use of high-dose oxytocin infusion (when needed)
- Peer review of all operative deliveries

Strategies: In Ireland, where this technique was developed, the active management of labor is restricted to nulliparous patients with singleton pregnancies in vertex presentation with no evidence of fetal compromise. Women are carefully instructed to come to the hospital early in labor. Labor is confirmed by the presence of complete effacement, passage of the mucous plug, or rupture of the membranes. If these criteria are met, the patient is admitted to the hospital, and the membranes are ruptured within 1 hour (if not already ruptured). Vaginal examination is performed hourly, and the administration of high-dose oxytocin is initiated if dilation falls below 1 cm/h. Oxytocin is initiated at 6 mU/min, and the dose is increased every 15 minutes until a maximum of 40 mU/min is reached, active labor is established, or hyperstimulation occurs. As a part of this process, one-on-one nursing care is provided, and the fetal status is assessed by auscultation every 5 minutes. Fetal compromise is diagnosed by fetal scalp pH. Cesarean delivery is performed if delivery is not imminent 12 hours after admission or if fetal compromise is diagnosed.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP004 (How to Tell When Labor Begins).

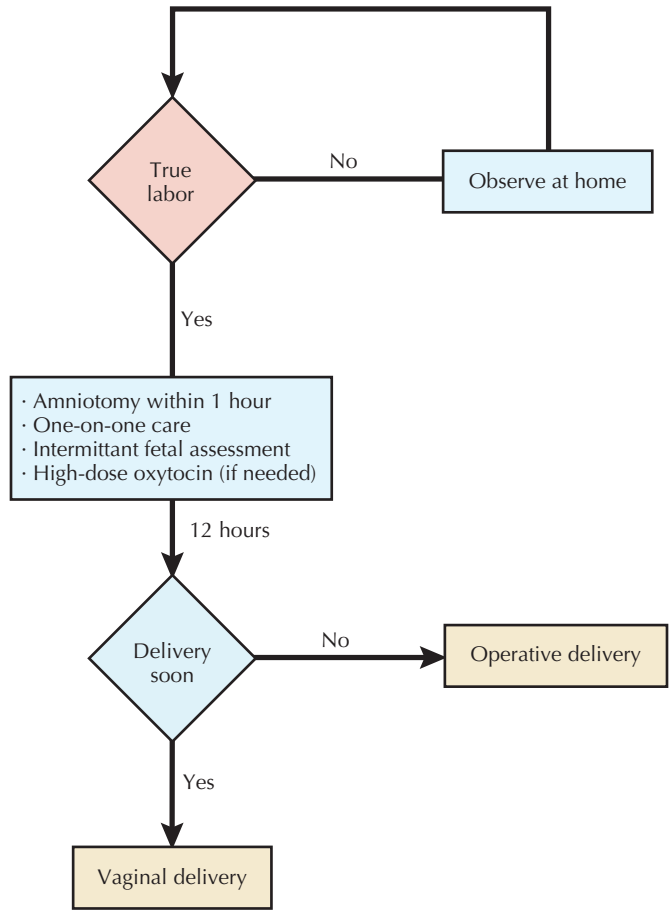


Figure 215.1 Active management of labor

IMPLEMENTATION

Special Considerations: The Irish experience with the active management of labor has resulted in a reduced rate of births by cesarean delivery without untoward events. Which elements of the management (education, early amniotomy, intensive nursing, aggressive use of oxytocin, or methods of establishing distress) are directly responsible for this success is unknown. Attempts to apply only some elements of the program have generally not yielded the same reductions in cesarean section rates. It should be noted that conduction (epidural) anesthesia is also less common in Ireland.

REFERENCES

LEVEL I

Bolnick JM, Velazquez MD, Gonzalez JL, et al. Randomized trial between two active labor management protocols in the presence of an unfavorable cervix. *Am J Obstet Gynecol*. 2004;190:124.

Cohen GR, O'Brien WF, Lewis L, et al. A prospective randomized study of the aggressive management of early labor. *Am J Obstet Gynecol*. 1987;157:1174.

Frigoletto FD Jr, Lieberman E, Lang JM, et al. A clinical trial of active management of labor. *N Engl J Med*. 1995;333:745.

Lavender T, Alfirevic Z, Walkinshaw S. Partogram action line study: a randomised trial. *Br J Obstet Gynaecol*. 1998;105:976.

Pattinson RC, Howarth GR, Mdluli W, et al. Aggressive or expectant management of labour: a randomised clinical trial. *BJOG*. 2003;110:457.

Sadler LC, Davison T, McCowan LM. A randomised controlled trial and meta-analysis of active management of labour. *BJOG*. 2000;107:909.

Shetty A, Stewart K, Stewart G, et al. Active management of term prelabour rupture of membranes with oral misoprostol. *BJOG*. 2002;109:1354.

LEVEL II

Brown HC, Paranjothy S, Dowswell T, et al. Package of care for active management in labour for reducing caesarean section rates in low-risk women. *Cochrane Database Syst Rev*. 2013;(9):CD004907.

Bakker JJ, Janssen PF, van Halem K, et al. Internal versus external tocodynamometry during induced or augmented labour. *Cochrane Database Syst Rev*. 2013;(8):CD006947.

Bugg GJ, Siddiqui F, Thornton JG. Oxytocin versus no treatment or delayed treatment for slow progress in the first stage of spontaneous labour. *Cochrane Database Syst Rev*. 2013;(6):CD007123.

Fraser W, Vendittelli F, Krauss I, et al. Effects of early augmentation of labour with amniotomy and oxytocin in nulliparous women: a meta-analysis. *Br J Obstet Gynaecol*. 1998;105:189.

Frigoletto FD Jr, Lieberman E, Lang JM, et al. A clinical trial of active management of labor. *N Engl J Med*. 1995;333:745.

Kenyon S, Tokumasu H, Dowswell T, et al. High-dose versus low-dose oxytocin for augmentation of delayed labour. *Cochrane Database Syst Rev*. 2013;(7):CD007201.

Laughon SK, Berghella V, Reddy UM, et al. Neonatal and maternal outcomes with prolonged second stage of labor. *Obstet Gynecol*. 2014;124:57.

Rouse DJ, Owen J, Hauth JC. Active-phase labor arrest: oxytocin augmentation for at least 4 hours. *Obstet Gynecol*. 1999;93:323.

Satin AJ, Leveno KJ, Sherman ML, et al. High-dose oxytocin: 20- versus 40-minute dosage interval. *Obstet Gynecol*. 1994;83:234.

Smyth RM, Markham C, Dowswell T. Amniotomy for shortening spontaneous labour. *Cochrane Database Syst Rev*. 2013;(6):CD006167.

Vogel JP, West HM, Dowswell T. Titrated oral misoprostol for augmenting labour to improve maternal and neonatal outcomes. *Cochrane Database Syst Rev*. 2013;(9):CD010648.

Wei SQ, Luo ZC, Xu H, et al. The effect of early oxytocin augmentation in labor: a meta-analysis. *Obstet Gynecol*. 2009;114:641.

Wei S, Wo BL, Qi HP, et al. Early amniotomy and early oxytocin for prevention of, or therapy for, delay in first stage spontaneous labour compared with routine care. *Cochrane Database Syst Rev*. 2013;(8):CD006794.

LEVEL III

American College of Obstetricians and Gynecologists. Induction of labor. ACOG Practice Bulletin No. 107. *Obstet Gynecol*. 2009;114:386.

American College of Obstetricians and Gynecologists, Society for Maternal-Fetal Medicine. Obstetric care consensus no. 1: safe prevention of the primary cesarean delivery. *Obstet Gynecol*. 2014;123:693.

Leighton BL, Halpern SH, Wilson DB. Lumbar sympathetic blocks speed early and second stage induced labor in nulliparous women. *Anesthesiology*. 1999;90:1039.

Millen KR, Kuo K, Zhao L, et al. Evidence-based guidelines in labor management. *Obstet Gynecol Surv*. 2014;69:209.

Peaceman AM, Socol ML. Active management of labor. *Am J Obstet Gynecol*. 1996;175:363.

Rogers R, Gilson G, Kammerer-Doak D. Epidural analgesia and active management of labor: effects on length of labor and mode of delivery. *Obstet Gynecol*. 1999;93:995.

Spong CY, Berghella V, Wenstrom KD, et al. Preventing the first cesarean delivery: summary of a joint Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, and American College of Obstetricians and Gynecologists Workshop. *Obstet Gynecol*. 2012;120:1181.

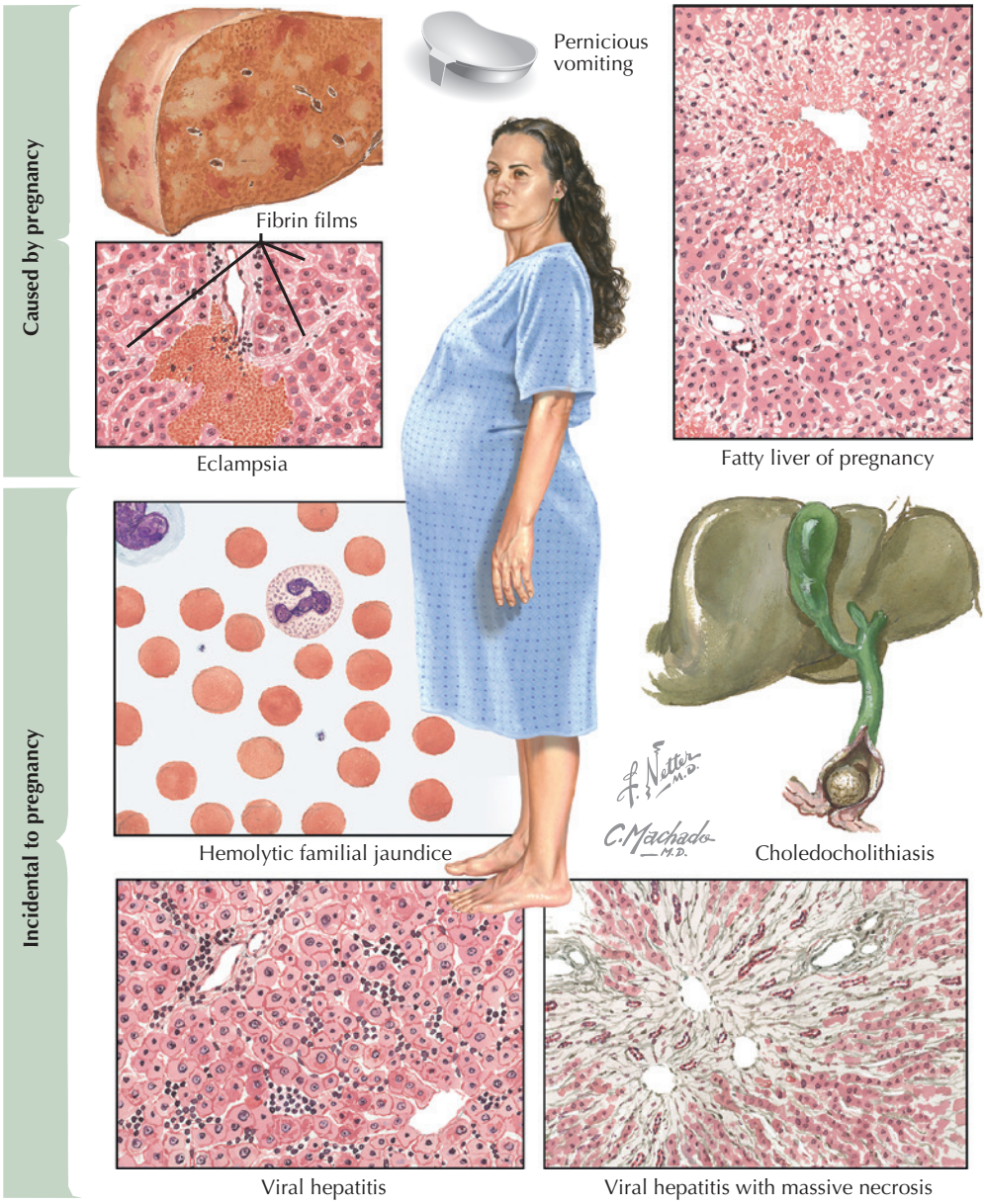


Figure 216.1 Liver diseases caused by pregnancy and incidental to pregnancy

Associated Conditions: Hypoglycemia and hepatic coma, coagulopathy, renal failure, sepsis, aspiration, circulatory collapse, pancreatitis, and gastrointestinal bleeding are all common.

Workup and Evaluation

Laboratory: Complete blood count, evaluation of liver function, serum bilirubin, clotting studies, serum ammonia.
Imaging: Ultrasonography, computed tomography, or magnetic resonance imaging may demonstrate the fatty metamorphosis, but false-negative results may be as high as 80%.
Special Tests: None indicated.
Diagnostic Procedures: History, physical, and laboratory examinations.

Pathologic Findings

Grossly the liver is small, soft, yellow, and greasy. Histologically, there are swollen hepatocytes with microvesicular fat and central nuclei and periportal sparing. There may also be lipid accumulation within renal tubular cells.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Rapid evaluation, supportive measures (fluids, glucose, and clotting factors), and prompt delivery of the fetus, regardless of gestational age.
Specific Measures: The only specific measure is delivery, which generally arrests the process. The decision between cesarean or vaginal birth remains uncertain and controversial. Transfusion with fresh-frozen plasma, cryoprecipitate, whole blood, packed red blood cells, and platelets may be necessary if surgery is planned or bleeding ensues. Liver transplantation may have to be considered in selected patients.
Diet: Nothing by mouth.
Activity: Strict bed rest. Often requires admission to intensive care facilities.

Drug(s) of Choice

No specific medications. Other medications based on the symptoms and condition.

FOLLOW-UP

Patient Monitoring: Intensive monitoring for circulatory, renal, and hepatic collapse. Often the fetus is severely compromised (often dead at the time of diagnosis) and also requires intensive monitoring.

Prevention/Avoidance: None.

Possible Complications: At one time, this was frequently fatal for both the mother (75%) and fetus (90%). Lower mortality rates have been reported in recent studies (as low as 10% maternal and 20% fetal mortality). Hypoglycemia and hepatic coma (60% of patients), coagulopathy (55%), and renal failure (50%) may occur. Sepsis, aspiration, circulatory collapse, pancreatitis, and gastrointestinal bleeding are all common.

Expected Outcome: May be fatal for both the mother and fetus. If the diagnosis is established and delivery is accomplished in time, recovery is marked by acute pancreatitis and ascites (almost universal). Transient diabetes insipidus is common during recovery, occurring approximately 7–10 days after delivery. For patients who receive rapid and supportive care, eventual recovery is complete and recurrence is rare. Most laboratory values normalize within 7–10 days after delivery.

MISCELLANEOUS

ICD-10-CM Codes: O26.611 (Liver and biliary tract disorders in pregnancy, first trimester), O26.612 (Liver and biliary tract disorders in pregnancy, second trimester), and O26.613 (Liver and biliary tract disorders in pregnancy, third trimester).

REFERENCES

LEVEL II

Fesenmeier MF, Coppage KH, Lambers DS, et al. Acute fatty liver of pregnancy in 3 tertiary care centers. *Am J Obstet Gynecol*. 2005;192:1416.

Ibdah JA, Okajima Y, Kang XS, et al. A fetal fatty-acid oxidation disorder as a cause of liver disease in pregnant women. *N Engl J Med*. 1999;340:1723.

Knight M, Nelson-Piercy C, Kurinczuk JJ, et al. A prospective national study of acute fatty liver of pregnancy in the UK. *Gut*. 2008;57:951.

Nelson DB, Yost NP, Cunningham FG. Hemostatic dysfunction with acute fatty liver of pregnancy. *Obstet Gynecol*. 2014;124:40.

Yang Z, Yamada J, Zhao Y, et al. Prospective screening for pediatric mitochondrial trifunctional protein defects in pregnancies complicated by liver disease. *JAMA*. 2002;288:2163-2166.

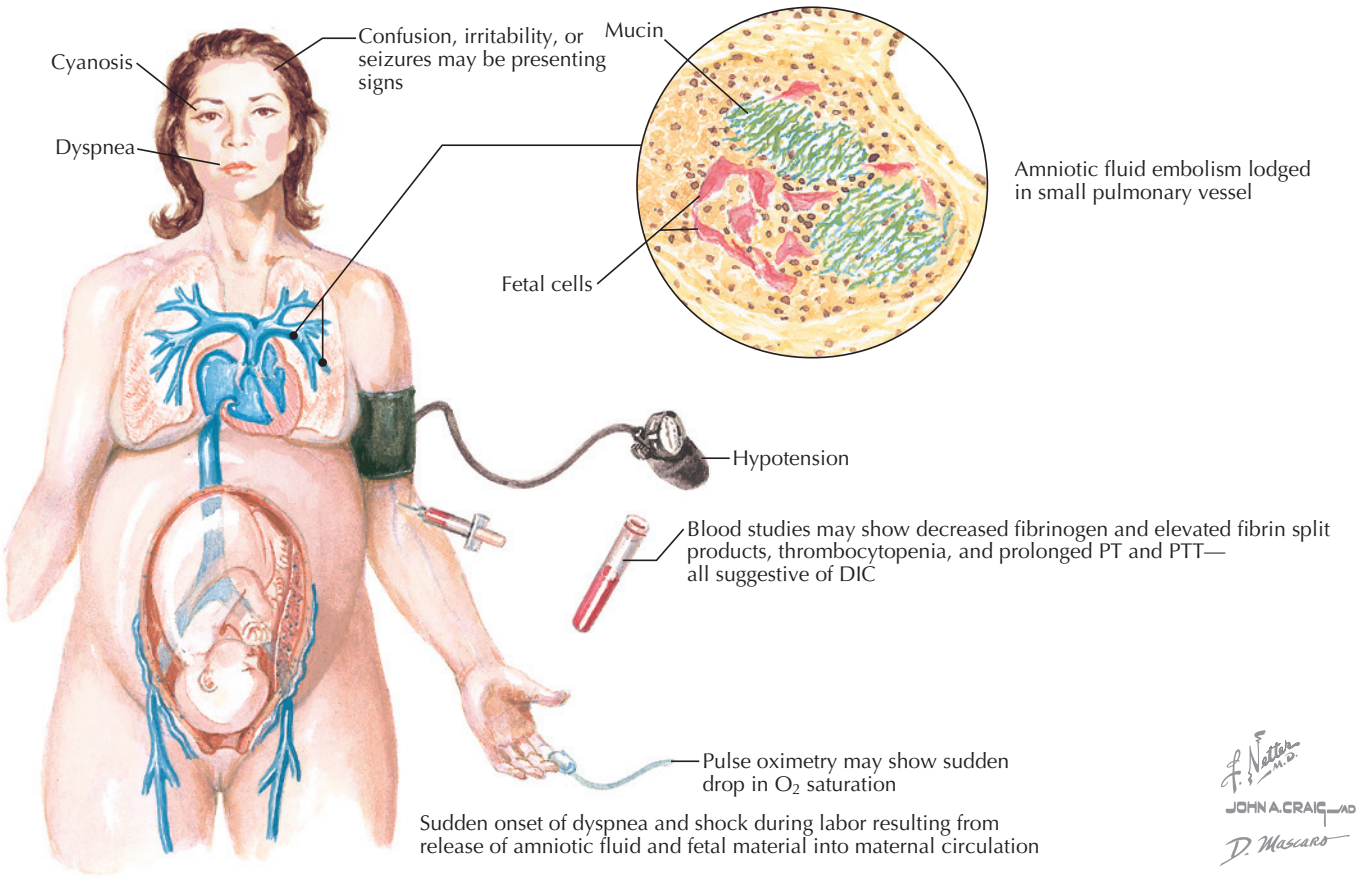
LEVEL III

Ibdah JA. Acute fatty liver of pregnancy: an update on pathogenesis and clinical implications. *World J Gastroenterol*. 2006;12:7397.

Ko H, Yoshida EM. Acute fatty liver of pregnancy. *Can J Gastroenterol*. 2006;20:25.

Rajasri AG, Srestha R, Mitchell J. Acute fatty liver of pregnancy (AFLP)—An overview. *J Obstet Gynaecol*. 2007;27:237.

Steingrub JS. Pregnancy-associated severe liver dysfunction. *Crit Care Clin*. 2004;20:763, xi.



Clinical Features of Amniotic Fluid Embolism

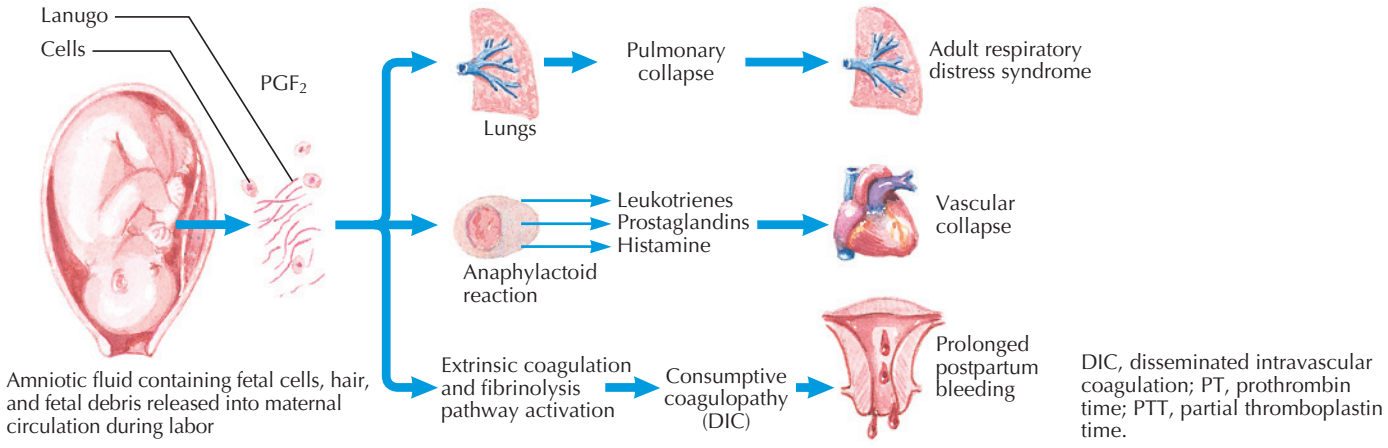


Figure 217.1 Amniotic fluid embolism

Workup and Evaluation

Laboratory: Coagulation studies, blood gas measurements, renal function studies, all on an ongoing basis.
Imaging: May help in managing pulmonary complications but generally not helpful in establishing the diagnosis.
Special Tests: Continuous monitoring of oxygen saturation and invasive hemodynamic monitoring (pulmonary artery catheter) essential.
Diagnostic Procedures: History and physical examination. Exclusion of other causes.

Pathologic Findings

Fetal squamous cells and lanugo present in the pulmonary vascular space (typical but not sensitive or specific). Initial acute pulmonary hypertension and right ventricular failure (lasting 15–30 minutes), followed by left ventricular dysfunction.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Aggressive airway control and cardiovascular resuscitation (including myocardial support, inotropic agents and

fluids, high-concentration oxygen therapy). The use of vasopressors has been reported to be successful. Correction and support for clotting defects (blood and platelets, fresh-frozen plasma, and cryoprecipitate as indicated).

Specific Measures: None. In women who suffer cardiac arrest before delivery, perimortem cesarean delivery should be considered to improve newborn outcome. In those who have not suffered arrest, maternal considerations generally take precedence.

Diet: Nothing by mouth until condition resolved.

Activity: Bed rest until condition resolved.

Drug(s) of Choice

No specific medications. Other medications as needed for cardiovascular, pulmonary, renal, and coagulation support.

FOLLOW-UP

Patient Monitoring: Intensive hemodynamic monitoring (arterial and central venous) required. Laboratory testing in anticipation of coagulopathy.

Prevention/Avoidance: None.

Possible Complications: Acute mortality rates with amniotic fluid embolism approximate 50%. Of women who survive, 50% have a life-threatening bleeding diathesis. Renal failure is common, as are pulmonary edema and adult respiratory distress syndrome. Of women who suffer cardiac arrest during the initial phase, only 8% survive neurologically intact. Overall maternal mortality approaches 80%. More than half of the neonates that survive have neurologic impairment.

Expected Outcome: Prolonged and complicated course for those who survive.

MISCELLANEOUS

Other Notes: The most devastating effects of amniotic fluid embolism appear to be mediated through the anaphylactic reaction induced. Experimental studies indicate that pretreatment with inhibitors of leukotriene synthesis can prevent the development of symptoms in experimental settings.

ICD-10-CM Codes: O88.113 (Amniotic fluid embolism in pregnancy, third trimester) and O88.12 (Amniotic fluid embolism in childbirth).

REFERENCES

LEVEL II

Aguilera LG, Fernandez C, Plaza A, et al. Fatal amniotic fluid embolism diagnosed histologically. *Acta Anaesthesiol Scand*. 2002;46:334.

Benson MD, Kobayashi H, Silver RK, et al. Immunologic studies in presumed amniotic fluid embolism. *Obstet Gynecol*. 2001;97:510.

Knight M, Tuffnell D, Brocklehurst P, et al. Incidence and risk factors for amniotic-fluid embolism. *Obstet Gynecol*. 2010;115:910.

Martin SR, Foley MR. Intensive care in obstetrics: an evidence-based review. *Am J Obstet Gynecol*. 2006;195:673.

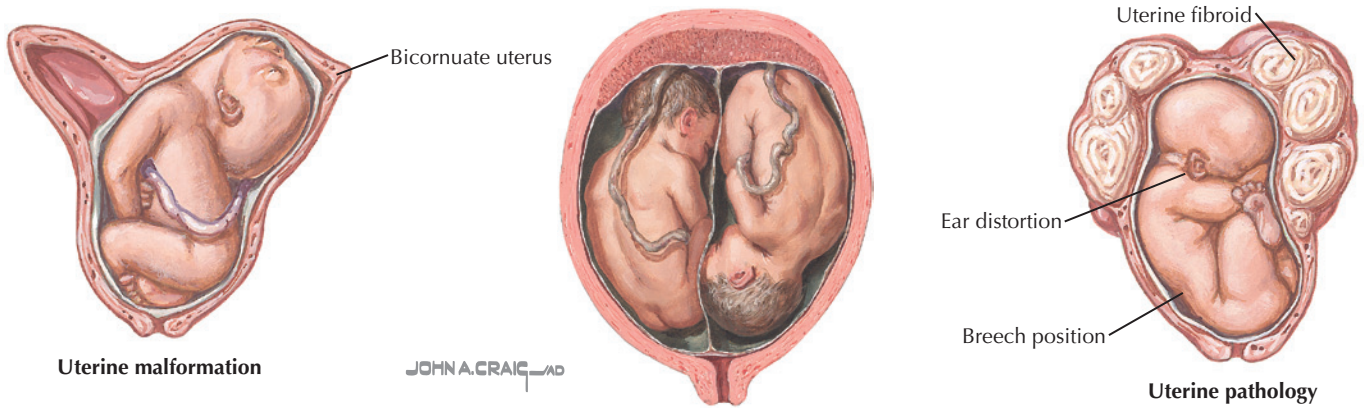
LEVEL III

Clark SL. Amniotic fluid embolism. *Obstet Gynecol*. 2014;123:337.

Gist RS, Stafford IP, Leibowitz AB, et al. Amniotic fluid embolism. *Anesth Analg*. 2009;108:1599.

Green BT, Umana E. Amniotic fluid embolism. *South Med J*. 2000;93:721.

Moore J, Baldisseri MR. Amniotic fluid embolism. *Crit Care Med*. 2005; 33:S279.



Conditions that cause intrauterine crowding can lead to abnormal fetal positions

Figure 218.1 Breech birth

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Fetal and maternal monitoring and support.
Specific Measures: External version, evaluation for route of delivery. External version is successful in >50% of patients. It is estimated that 338 cesarean deliveries would need to be performed to prevent one perinatal death.
Diet: No specific dietary changes indicated; nothing by mouth if the patient is in labor because of the increased risk for operative delivery.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP079 (If Your Baby Is Breech).

Drug(s) of Choice

None (tocolytics may be used to assist with external version procedures).

FOLLOW-UP

Patient Monitoring: Fetal and maternal monitoring as with normal labor.

Prevention/Avoidance: None.
Possible Complications: Prolapse of umbilical cord, entrapment of the fetal head, birth trauma.
Expected Outcome: Breech deliveries are associated with an increased risk for congenital anomalies, intracranial hemorrhage, growth restriction, neurologic disorders, and mortality, but the role of breech presentation and the delivery route are unclear. Much of the morbidity traditionally associated with breech presentation and delivery is because of factors that predispose to breech (congenital anomalies, prematurity).

MISCELLANEOUS

Pregnancy Considerations: The route of delivery must be determined on an individual basis based on fetal and maternal factors, the availability of needed resources, and the skill of the obstetrician. Vaginal delivery may be considered if labor is normal, fetal weight is 2000–3800 g, fetal status is normal, the pelvis is adequate, fetal head position is normal, and normal progression of cervical dilation and fetal descent are maintained. Cesarean delivery does not eliminate the possibility of head entrapment during extraction of the fetus (approximately 1% of cases).
ICD-10-CM Codes: O32.1XX0 (Maternal care for breech presentation, not applicable or unspecified).

REFERENCES

LEVEL I

Hannah ME, Whyte H, Hannah WJ, et al.; Term Breech Trial Collaborative Group. Maternal outcomes at 2 years after planned cesarean section versus planned vaginal birth for breech presentation at term: the international randomized Term Breech Trial. *Am J Obstet Gynecol*. 2004; 191:917.

Whyte H, Hannah ME, Saigal S, et al.; Term Breech Trial Collaborative Group. Outcomes of children at 2 years after planned cesarean birth versus planned vaginal birth for breech presentation at term: the International Randomized Term Breech Trial. *Am J Obstet Gynecol*. 2004; 191:864.

LEVEL II

Alfirevic Z, Milan SJ, Livio S. Caesarean section versus vaginal delivery for preterm birth in singletons. *Cochrane Database Syst Rev*. 2013;(9): CD000078.

Ford JB, Roberts CL, Nassar N, et al. Recurrence of breech presentation in consecutive pregnancies. *BJOG*. 2010;117:830.

Hofmeyr GJ, Hannah M, Lawrie TA. Planned caesarean section for term breech delivery. *Cochrane Database Syst Rev*. 2015;(7):CD000166.

Hofmeyr GJ, Kulier R, West HM. External cephalic version for breech presentation at term. *Cochrane Database Syst Rev*. 2015;(4):CD000083.

Lyons J, Pressey T, Bartholomew S, et al. Delivery of breech presentation at term gestation in Canada, 2003-2011. *Obstet Gynecol*. 2015;125:1153.

Palencia R, Gafni A, Hannah ME, et al.; Term Breech Trial Collaborative Group. The costs of planned cesarean versus planned vaginal birth in the Term Breech Trial. *CMAJ*. 2006;174:1109.

Rietberg CC, Elferink-Stinkens PM, Visser GH. The effect of the Term Breech Trial on medical intervention behaviour and neonatal outcome in The Netherlands: an analysis of 35,453 term breech infants. *BJOG*. 2005;112:205.

Vistad I, Klungsøyr K, Albrechtsen S, et al. Neonatal outcome of singleton term breech deliveries in Norway from 1991 to 2011. *Acta Obstet Gynecol Scand*. 2015;94:997.

Vlemmix F, Bergenhenegouwen L, Schaaf JM, et al. Term breech deliveries in the Netherlands: did the increased cesarean rate affect neonatal outcome? A population-based cohort study. *Acta Obstet Gynecol Scand*. 2014;93:888.

LEVEL III

Alarab M, Regan C, O'Connell MP, et al. Singleton vaginal breech delivery at term: still a safe option. *Obstet Gynecol*. 2004;103:407.

American College of Obstetricians and Gynecologists. Mode of term singleton breech delivery. ACOG Committee Opinion 340. *Obstet Gynecol*. 2006;108:235.

American College of Obstetricians and Gynecologists. External cephalic version. Practice Bulletin No. 161. *Obstet Gynecol*. 2016;127:e54.

Burke G. The end of vaginal breech delivery. *BJOG*. 2006;113:969.

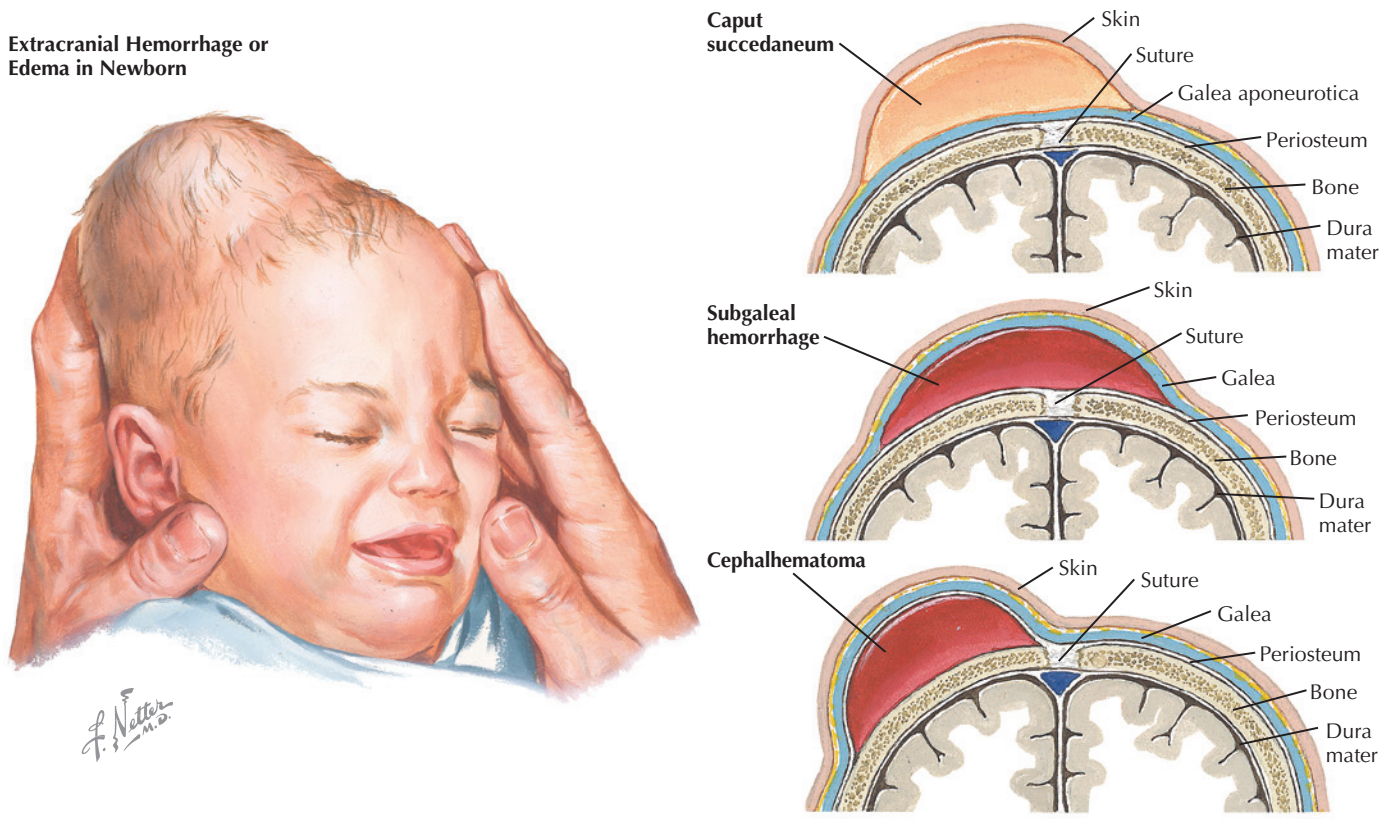


Figure 219.1 Caput succedaneum

REFERENCES

LEVEL III

Anshelevich A, Osterhoudt KC, Introcaso CE, et al. Picture of the month–quiz case. Halo scalp ring. *Arch Pediatr Adolesc Med*. 2010;164:673.

Choi JW, Lee CH, Suh SI. Scalp swelling crossing the suture line on skull radiograph: is it always a sign of caput succedaneum? *Pediatr Radiol*. 2006;36:364.

Gerscovich EO, McGahan JP, Jain KA, et al. Caput succedaneum mimicking a cephalocele. *J Clin Ultrasound*. 2003;31:98.

Gilboa Y, Kivilevitch Z, Kedem A, et al. Caput succedaneum thickness in prolonged second stage of labour: a clinical evaluation. *Aust N Z J Obstet Gynaecol*. 2013;53:459.

Parker LA. Part 1: Early recognition and treatment of birth trauma: injuries to the head and face. *Adv Neonatal Care*. 2005;5:288.

Petrikovsky BM, Schneider E, Smith-Levitin M, et al. Cephalhematoma and caput succedaneum: do they always occur in labor? *Am J Obstet Gynecol*. 1998;179:906.

Rawal S, Modi N, Lacey S, et al. *Escherichia coli* septicaemia arising as a result of an infected caput succedaneum. *Eur J Pediatr*. 2006;165:66.

Sauvageau A, Belley-Cote EP, Racette S. Utility of the caput succedaneum in the forensic investigation of neonaticide: a case report. *Med Sci Law*. 2007;47:262.

CARDIOVASCULAR DISEASE IN PREGNANCY 220

THE CHALLENGE

Cardiac disease is one of the major causes of nonobstetric maternal mortality. While in the past patients with congenital or significant heart disease did not survive to the reproductive age, it is now common for these patients to become pregnant, be it planned or unplanned.

Scope of the Problem: Cardiac disease complicates approximately 1% of all pregnancies. Mitral valve prolapse may be observed in 5%–7% of pregnant women. The type and severity of risk vary with the type of lesion and the functional abilities of the patient (Table 220.1). Patients with valvular disease have an increased risk for thromboembolic disease, subacute bacterial endocarditis, cardiac failure, and pulmonary edema during and after pregnancy.

Table 220.1 Cardiac (Maternal) Mortality Associated With Pregnancy

Group I (Mortality <1%)	• Atrial septal defect • Bioprosthetic valve • Mitral stenosis (functional class I and II) • Patent ductus arteriosus • Pulmonic/tricuspid disease • Tetralogy of Fallot, corrected • Ventricular septal defect
Group II (Mortality 5%–15%)	• Aortic stenosis • Coarctation of aorta, without valvular involvement
	IIA • Marfan Syndrome with Normal Aorta • Mitral stenosis (functional class III and IV) • Previous myocardial infarction • Uncorrected tetralogy of Fallot
	IIB • Artificial Valve • Mitral stenosis with atrial fibrillation
Group III (Mortality 25%–50%)	• Coarctation of aorta, with valvular involvement • Marfan syndrome with aortic involvement • Pulmonary hypertension

Congenital heart disease accounts for 20% of maternal cardiac deaths.

Objectives of Management: Identify patients at risk because of cardiovascular conditions, provide realistic counseling regarding the risk to mother and fetus, and work to reduce this risk. The basis of antepartum management consists of frequent evaluations of maternal cardiac status and fetal well-being, combined with the avoidance of conditions or actions that increase cardiac workload. The latter includes the treatment or avoidance of anemia, prompt treatment of any infection or fever, limitation of strenuous activity, and adherence to appropriate weight gain.

TACTICS

Relevant Pathophysiology: By midpregnancy, there is a 40% increase in cardiac output, a 30%–50% increase in intravascular volume, and an average 10 mm Hg drop in blood pressure because of reduced peripheral resistance; this results in an increase in demand that may be fatal. Cardiac output shows an additional increase in the immediate postpartum period, as up to 500 mL of additional blood enters the maternal circulation because of uterine contractions and rapid loss of uterine volume. Cardiac complications, such as peripartum cardiomyopathy, may occur up to 6 months after delivery. Valvular heart disease is the most commonly encountered cardiac complication of pregnancy, with rheumatic valvular disease being the most frequent type. The severity of the associated valvular lesion determines the degree of risk associated with pregnancy. Approximately 90% of these patients have mitral stenosis, which may result in worsening obstruction as cardiac output increases during the pregnancy. When severe or associated with atrial fibrillation, the risk for cardiac failure during pregnancy is increased.

Table 220.2 New York Heart Association Classification of Heart Disease

Classification	Symptoms
Class I	No cardiac decompensation
Class II	No symptoms of decompensation at rest Minor limitations of physical activity
Class III	No symptoms of decompensation at rest Marked limitations of physical activity
Class IV	Symptoms of decompensation at rest Discomfort with any physical activity

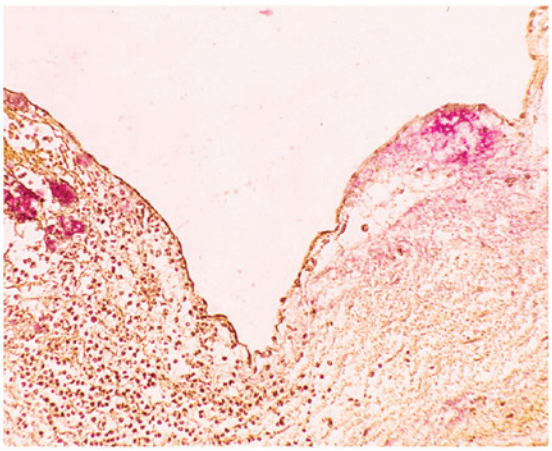
Strategies: The New York Heart Association classification of heart disease is a useful guide to the risk for pregnancy (Table 220.2). Patients with class I or II disease, such as those with septal defects, patent ductus arteriosus, or mild mitral or aortic valvular disease, generally do well during pregnancy, although their fetuses are at greater risk for prematurity and low birth weight. Patients with class III or IV disease caused by primary pulmonary hypertension, uncorrected tetralogy of Fallot, Eisenmenger syndrome, or other conditions rarely do well, with pregnancy inducing a significant risk for death, often in excess of 50%. Patients with this degree of cardiac decompensation should be advised to avoid pregnancy or consider termination based on careful consultation with specialists in both cardiology and high-risk obstetrics. The ZAHARA score, validated in a single retrospective observational cohort study, allows one to predict adverse maternal cardiac events. Other scoring systems (eg, CARPREG risk score) exist but have not been universally adopted.

IMPLEMENTATION

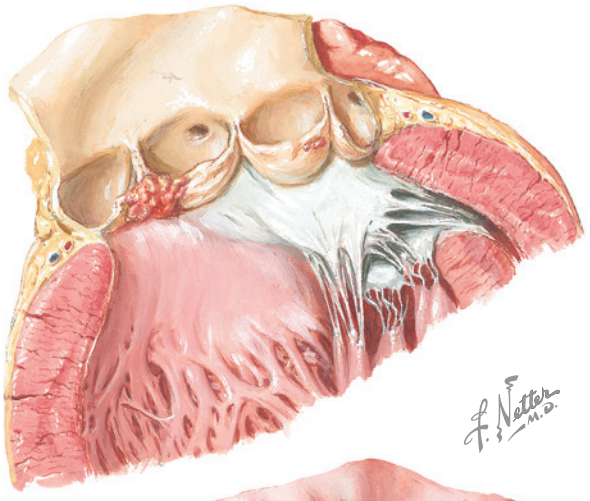
Special Considerations: Most patients with mitral valve prolapse do well. The rare patient with left atrial and ventricular enlargement may develop dysfunction during the course of pregnancy. The severity of the disease and impact on the atrium and ventricle may be assessed by echocardiography.

Peripartum cardiomyopathy is rare but uniformly severe. Occurring in the last month of pregnancy or during the first 6 months after delivery, it is similar to other cardiomyopathies in symptoms and findings. Most often a specific cause is not identified, and the cause remains unknown. This process presents a particularly grave risk, necessitating early suspicion and aggressive consultative management. Patients at highest risk are those in their 30s, who are multiparous, African-American, have delivered twins, or have had preeclampsia.

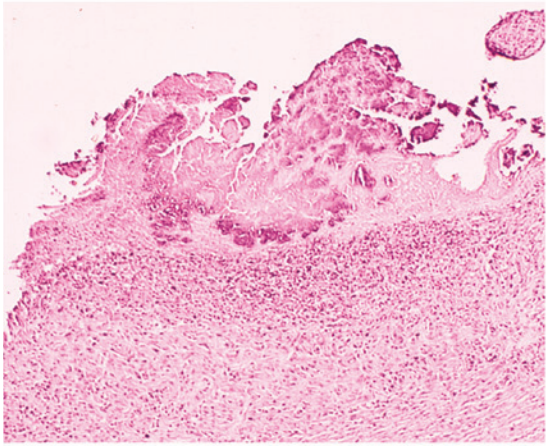
Unusual cardiac conditions, such as idiopathic hypertrophic subaortic stenosis and the structural anomalies associated with Marfan syndrome, are associated with maternal moralities of 25%–50% or higher. The presence of such conditions demands realistic preconception counseling, and early transfer for specialized care, should a pregnancy occur.



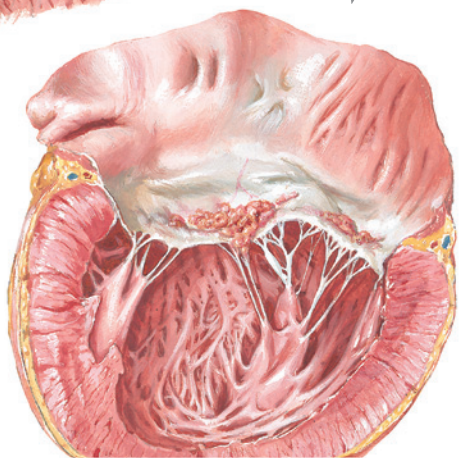
Deposit of platelets and organisms (stained dark), edema, and leukocytic infiltration in very early bacterial endocarditis of aortic valve



Early vegetations of bacterial endocarditis on bicuspid aortic valve



Development of vegetations containing clumps of bacteria on tricuspid valve



Early vegetations of bacterial endocarditis at contact line of mitral valve

Figure 220.1 Cardiovascular disease in pregnancy

REFERENCES

LEVEL II

Canobbio MM, Morris CD, Graham TP, et al. Pregnancy outcomes after atrial repair for transposition of the great arteries. *Am J Cardiol*. 2006;98:668.

Drenthen W, Boersma E, Balci A, et al. Predictors of pregnancy complications in women with congenital heart disease. *Eur Heart J*. 2010;31:2124.

Roos-Hesselink JW, Ruys TP, Stein JI, et al. Outcome of pregnancy in patients with structural or ischaemic heart disease: results of a registry of the European Society of Cardiology. *Eur Heart J*. 2013;34:657.

Siu SC, Sermer M, Colman JM, et al. Cardiac Disease in Pregnancy (CARPREG) Investigators. Prospective multicenter study of pregnancy outcomes in women with heart disease. *Circulation*. 2001;104:515.

LEVEL III

Elkayam U, Bitar F. Valvular heart disease and pregnancy: Part I: Native valves. *J Am Coll Cardiol*. 2005;46:223.

Elkayam U, Bitar F. Valvular heart disease and pregnancy: Part II: Prosthetic valves. *J Am Coll Cardiol*. 2005;46:403.

Milewicz DM, Dietz HC, Miller DC. Treatment of aortic disease in patients with Marfan syndrome. *Circulation*. 2005;111:e150.

Murali S, Baldisseri MR. Peripartum cardiomyopathy. *Crit Care Med*. 2005;33:S340.

Reimold SC, Rutherford JD. Clinical practice. Valvular heart disease in pregnancy. *N Engl J Med*. 2003;349:52.

Sliwa K, Fett J, Elkayam U. Peripartum cardiomyopathy. *Lancet*. 2006;368:687.

Stout KK, Otto CM. Pregnancy in women with valvular heart disease. *Heart*. 2007;93:552.

Thorne SA. Pregnancy in heart disease. *Heart*. 2004;90:450.

Thorne S, MacGregor A, Nelson-Piercy C. Risks of contraception and pregnancy in heart disease. *Heart*. 2006;92:1520.

Uebing A, Steer PJ, Yentis SM, et al. Pregnancy and congenital heart disease. *BMJ*. 2006;332:401.

221 CERVICAL INSUFFICIENCY

INTRODUCTION

Description: Cervical insufficiency is characterized by the asymptomatic dilation of the internal os during pregnancy. This generally leads to the dilation of the entire cervical canal during the second trimester with the subsequent risk for rupture of the membranes, expulsion of the fetus, or both.
Prevalence: 1 of 54 to 1 of 1842 pregnancies (as a result of uncertain diagnostic criteria); appears to be declining.
Predominant Age: Reproductive age.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Iatrogenic (most common); damage from cervical dilation at the time of dilation and curettage (D&C) or other manipulation, damage caused by surgery (conization). Congenital tissue defect, uterine anomalies (uterus didelphys), obstetric lacerations, in utero exposure to diethylstilbestrol (DES).
Risk Factors: In utero exposure to diethylstilbestrol (rare now), uterine anomalies, connective tissue disorders (eg, Ehlers–Danlos syndrome).

SIGNS AND SYMPTOMS

- History of second-trimester pregnancy loss (generally three or more) accompanied by the spontaneous rupture of the membranes without labor or rapid, painless, preterm labor.
- Prolapse and ballooning of the fetal membranes into the vagina without labor.

DIAGNOSTIC APPROACH

Differential Diagnosis

- Uterine anomalies
- Chorioamnionitis, cervicitis
- Chromosomal anomaly (balanced translocation)

Associated Conditions: Premature rupture of the membranes, premature (preterm) delivery, and recurrent second trimester pregnancy loss.

Workup and Evaluation

Laboratory: No evaluation indicated beyond that for routine prenatal care.
Imaging: Ultrasonography before cervical cerclage to ensure normal fetal development. Although cervical length can be measured by ultrasonography, routine use of this has not proved to be an effective screening tool except in the face of a high-risk history (then beginning approximately at 14 weeks of gestation). Normal cervical length is approximately 4.1 cm (±1.02 cm) between 14 and 28 weeks and gradually decreases in length to 40 weeks, when it averages between 2.5 and 3.2 cm. Signs of cervical funneling and cervical shortening are associated with an increased risk for preterm delivery, but management in the absence of other risk factors is unclear.

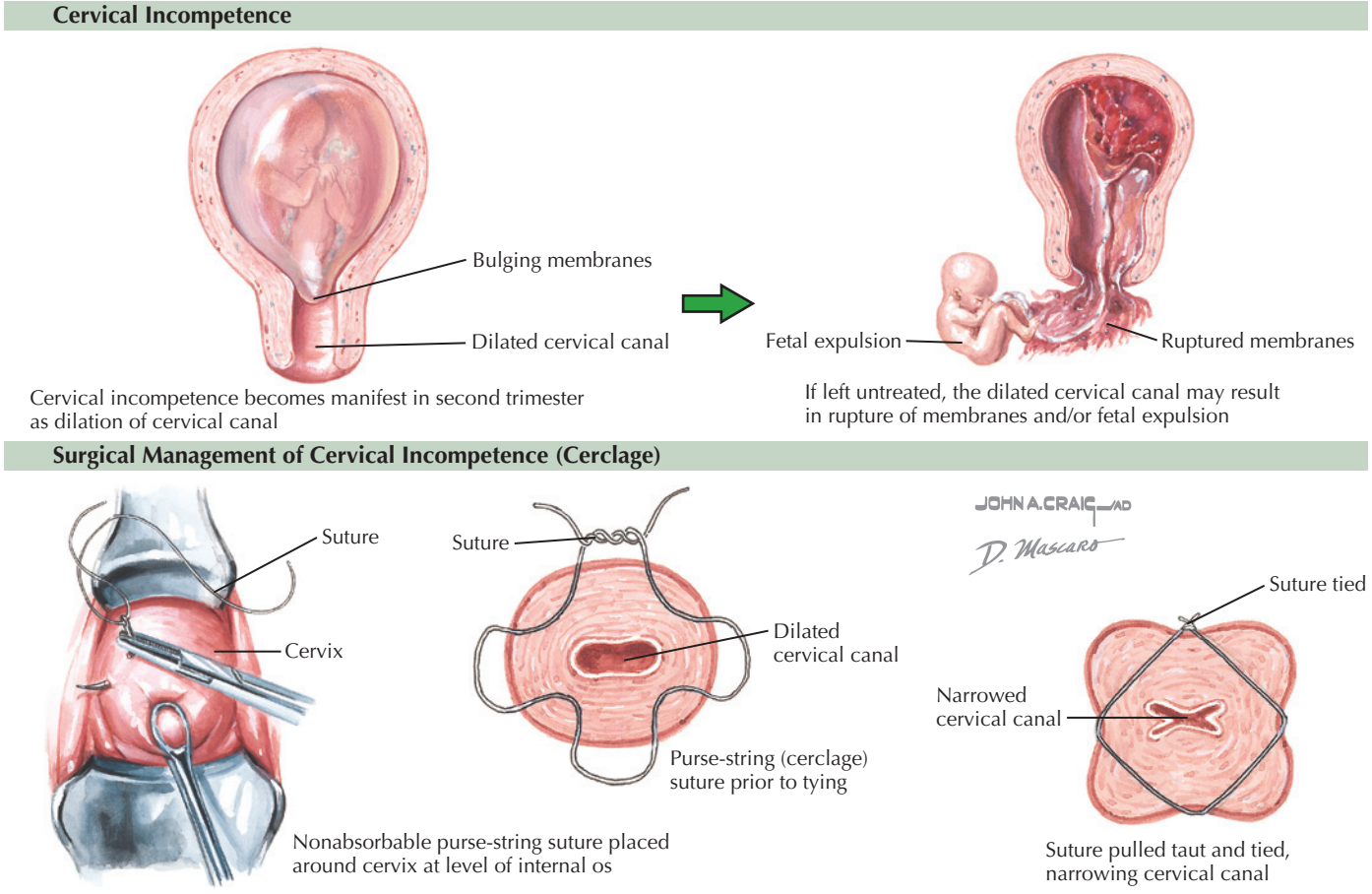


Figure 221.1 Cervical insufficiency and surgical management

Special Tests: None indicated. Frequent vaginal or ultrasonographic examinations beginning around the time of previous cervical change or the second trimester, whichever is earlier. Attempts to define or identify cervical incompetence by hysterosonography, pull-through techniques with inflated catheter balloons, measurement of cervical resistance to cervical dilators, magnetic resonance imaging, and others have not gained clinical acceptance.

Diagnostic Procedures: History.

Pathologic Findings

Painless dilation of the cervix.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, frequent prenatal visits with monitoring for cervical change.

Specific Measures: Cervical cerclage (placement of a concentric nonabsorbable suture at the level of the inner cervical os) is generally performed between 10 and 14 weeks of gestation. When the suture is vaginally placed, it is generally removed at 38 weeks of gestation. If labor occurs before this point, the suture must be immediately removed. Cervical cerclage is occasionally transabdominally performed. These sutures are intended to remain permanently and preclude vaginal delivery. The use of lever pessaries (such as the Smith–Hodge) has been reported to give outcomes similar to that obtained by cerclage, but this modality is infrequently used. Bleeding, uterine contractions, obvious infection, or rupture of the membranes is a contraindication to cerclage. Because of scarring after cerclage, approximately 15% of patients require cesarean delivery.

Diet: No specific dietary changes indicated.

Activity: Restriction of activity is often suggested, but evidence that this alters the outcome of pregnancy is lacking. After 24 weeks of pregnancy, bed rest may be the only therapy available because cerclage may bring on labor.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlets AP100 (Repeated Miscarriage) and AP110 (Loop Electrosurgical Excision Procedure).

Drug(s) of Choice

In women with prior second trimester pregnancy loss suggestive of cervical insufficiency, randomized trials of hydroxyprogesterone caproate prophylaxis (from 16 to 20 weeks to 36 weeks) have reduced the risk for recurrent preterm birth. Prophylactic antibiotics and beta mimetics have not been shown to be effective.

FOLLOW-UP

Patient Monitoring: Frequent prenatal visits with monitoring for cervical change in patients thought to be at high risk. If a cerclage is placed, planned removal of cerclage at 38 weeks of gestation is advisable.

Prevention/Avoidance: Care to avoid overdilation of the cervix when surgical manipulation is required.

Possible Complications: Continued fetal loss, chorioamnionitis, cervical avulsion, or uterine rupture if labor occurs and the cerclage is not removed.

Expected Outcome: With correct diagnosis and cervical cerclage, fetal survival increases from 20% to more than 80%.

MISCELLANEOUS

ICD-10-CM Code: N88.3 (Incompetence of cervix uteri).

REFERENCES

LEVEL I

Goya M, Pratcorona L, Merced C, et al. Cervical pessary in pregnant women with a short cervix (PECEP): an open-label randomised controlled trial. *Lancet*. 2012;379:1800.

LEVEL II

Abdel-Aleem H, Shaaban OM, Abdel-Aleem MA. Cervical pessary for preventing preterm birth. *Cochrane Database Syst Rev*. 2013;(5): CD007873.

Berghella V, Rafael TJ, Szychowski JM, et al. Cerclage for short cervix on ultrasonography in women with singleton gestations and previous preterm birth: a meta-analysis. *Obstet Gynecol*. 2011;117:663.

Chan YY, Jayaprakasan K, Tan A, et al. Reproductive outcomes in women with congenital uterine anomalies: a systematic review. *Ultrasound Obstet Gynecol*. 2011;38:371.

Drakeley AJ, Roberts D, Alfirevic Z. Cervical cerclage for prevention of preterm delivery: meta-analysis of randomized trials. *Obstet Gynecol*. 2003;102:621.

Ehsanipoor RM, Seligman NS, Saccone G, et al. Physical examination-indicated cerclage: a systematic review and meta-analysis. *Obstet Gynecol*. 2015;126:125.

LEVEL III

American College of Obstetricians and Gynecologists. Cerclage for the management of cervical insufficiency. Practice Bulletin No. 142. *Obstet Gynecol*. 2014;123:372.

Romero R, Espinoza J, Erez O, et al. The role of cervical cerclage in obstetric practice: can the patient who could benefit from this procedure be identified? *Am J Obstet Gynecol*. 2006;194:1.

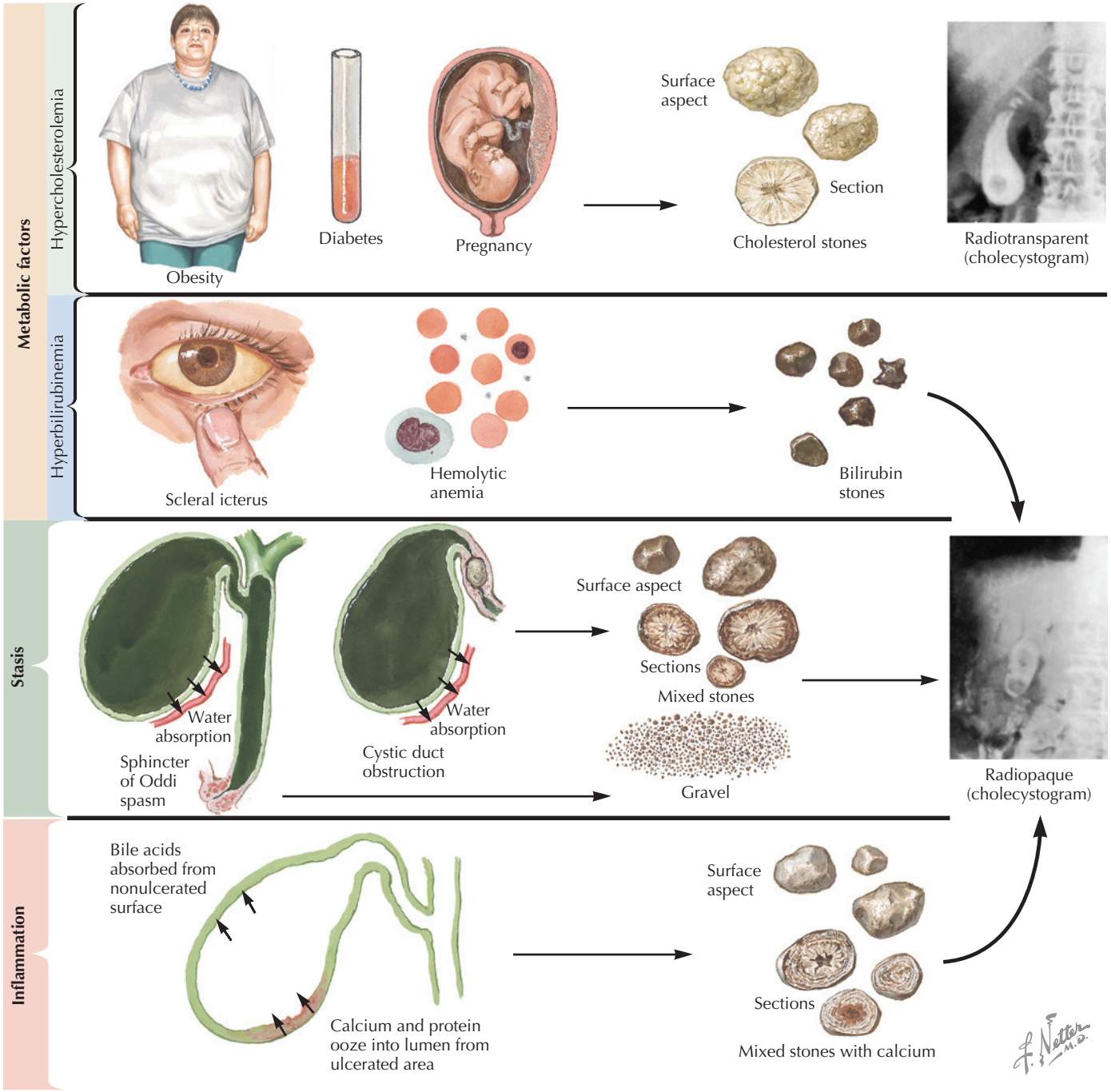


Figure 222.1 Cholecystitis

ETIOLOGY AND PATHOGENESIS

Causes: The metabolic alteration leading to cholesterol stones (gallstones) is considered to be a disruption in the balance between hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase and cholesterol 7α-hydroxylase. HMG-CoA controls cholesterol synthesis, whereas cholesterol 7α-hydroxylase controls the rate of bile acid formation. Patients who form cholesterol stones have elevated HMG-CoA levels and depressed cholesterol 7α-hydroxylase levels. This change in ratio increases the risk for cholesterol precipitation. During pregnancy, there is an increased rate of bile synthesis, increased cholesterol saturation of bile, and a reduced rate of gallbladder emptying, increasing the risk for stone formation and obstruction. These physiologic changes reverse by approximately 2 months after delivery.

Risk Factors: Cholecystitis is associated with an increased maternal age, multiparity, multiple gestation, and a history of previous attacks.

SIGNS AND SYMPTOMS

Unchanged by pregnancy

- May be confused with symptoms of pregnancy
- Fatty food intolerance
- Variable right upper quadrant pain with radiation to the back or scapula

- Nausea or vomiting (often mistaken for "indigestion" or "morning sickness")
- Fever is usually associated with cholangitis

DIAGNOSTIC APPROACH

Differential Diagnosis

- Labor
- Preeclampsia
- Placental accident (abruption)
- Cholestasis of pregnancy
- Gastroenteritis
- Esophageal reflux
- Malabsorption
- Irritable bowel syndrome
- Peptic ulcer disease
- Coronary artery disease
- Pneumonia
- Appendicitis

Associated Conditions: Jaundice, cirrhosis, pancreatitis, ileus, and premature labor.

Workup and Evaluation

Laboratory: Supportive, but often not diagnostic—complete blood count, serum bilirubin, amylase, alkaline phosphatase, and aminotransferase concentrations.

Imaging: Ultrasonography of the gallbladder (96% accurate in making the diagnosis of sludge or stone in the gallbladder); can visualize stones as small as 2 mm.

Special Tests: None indicated.

Diagnostic Procedures: History, physical examination, ultrasonography, and laboratory investigation.

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Watchful waiting, dietary modifications aimed at reducing cholesterol and fatty food exposure.

Specific Measures: Cholelithiasis may be treated with supportive and oral therapy; surgical extirpation may be required. Cholecystectomy during pregnancy is associated with a 5% fetal loss rate, which increases to approximately 60% if pancreatitis is present at the time of surgery.

Diet: Nothing by mouth during acute attacks or until the diagnosis is established (some patients require nasogastric suction during acute attacks). Reduced fatty food and cholesterol at other times.

Activity: No restriction.

Drug(s) of Choice

Ursodeoxycholic acid (Actigall) 8–10 mg/day divided in two to three doses. When cholecystitis is present, intravenous fluids, nasogastric suction, analgesics, and antibiotics (cephalosporin) are appropriate.

Contraindications: Known allergy, acute cholecystitis, abnormal liver function, calcified stones (not cholesterol based).

Interactions: See warning for individual agents.

FOLLOW-UP

Patient Monitoring: Normal prenatal care once acute episode is resolved.

Prevention/Avoidance: None.

Possible Complications: Acute cholecystitis, pancreatitis, ascending cholangitis, peritonitis, internal fistulization (to the gastrointestinal tract), premature labor or delivery.

Expected Outcome: Cholecystitis—generally good with either oral or surgical therapy.

MISCELLANEOUS

ICD-10-CM Code: K80.20 (Calculus of gallbladder without cholecystitis without obstruction, others based on obstruction or inflammation).

REFERENCES

LEVEL II

Graham G, Baxi L, Tharakan T. Laparoscopic cholecystectomy during pregnancy: a case series and review of the literature. *Obstet Gynecol Surv*. 1998;53:566.

Igbinosa O, Poddar S, Pitchumoni C. Pregnancy associated pancreatitis revisited. *Clin Res Hepatol Gastroenterol*. 2013;37:177.

Silvestri MT, Pettker CM, Brousseau EC, et al. Morbidity of appendectomy and cholecystectomy in pregnant and nonpregnant women. *Obstet Gynecol*. 2011;118:1261.

LEVEL III

Barone JE, Bears S, Chen S, et al. Outcome study of cholecystectomy during pregnancy. *Am J Surg*. 1999;177:232.

Ducarme G, Maire F, Chatel P, et al. Acute pancreatitis during pregnancy: a review. *J Perinatol*. 2014;34:87.

Indar AA, Beckingham IJ. Acute cholecystitis. *BMJ*. 2002;325:639.

Nesbitt TH, Kay HH, McCoy MC, et al. Endoscopic management of biliary disease during pregnancy. *Obstet Gynecol*. 1996;87:806.

Smith RP, Nolan TE. Gallbladder disease and women: etiology, diagnosis and therapy. *Female Patient*. 1992;17:99.

223 CHORIOAMNIONITIS

INTRODUCTION

Description: Chorioamnionitis is the inflammation of the fetal membranes. This may be associated with prolonged or premature rupture of the membranes or a primary cause of premature labor.
Prevalence: 40% of premature deliveries.
Predominant age: Reproductive age.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Infection by organisms that ascend from the vaginal canal, most often when the membranes have been ruptured. Studies indicate that bacteria (specifically *Escherichia coli*) can permeate intact chorioamnionic membranes. Infection may also occur by hematogenous, transabdominal, or transfallopian routes.
Risk factors: Prolonged rupture of the membranes, frequent pelvic examinations, bacterial or trichomonas vaginitis, vaginal or cervical infection with *Chlamydia trachomatis*, smoking, anemia, vaginal bleeding.

SIGNS AND SYMPTOMS

- May be asymptomatic
- Fever (>100.5°F, 38°C)
- Tachycardia (maternal and fetal)
- Uterine irritability and tenderness
- May result in premature rupture of the membranes or preterm labor
- Maternal signs of infection (elevated white blood count and sedimentation rate)
- Purulent cervical discharge (late)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Placental abruption
- Intraabdominal infection (eg, appendicitis)
- Pyelonephritis
- Pneumonia
- Pulmonary embolism
- Wound infection (episiotomy, abdominal incision following cesarean delivery or tubal ligation)
- Breast engorgement
- Drug fever

Associated Conditions: Endometritis, fetal infections (pneumonia, skin infections, septicemia), and oligohydramnios have been linked to clinical chorioamnionitis. Dysfunctional labor and postpartum hemorrhage are more common. Cerebral palsy has been linked to intrauterine infection and the associated inflammatory processes.

Workup and Evaluation

Laboratory: White blood count and red cell sedimentation rate. Gram stain of amniotic fluid (a negative test carries a 99% specificity). Cultures may be obtained and may be of assistance in management, but the diagnosis is made on clinical grounds. Amniocentesis for culture has not been shown to improve pregnancy outcome. There is no clear evidence to support the use of C-reactive protein for the early diagnosis of chorioamnionitis.
Imaging: No imaging indicated.
Special Tests: A biophysical profile of the fetus may be of assistance in planning management (if time and maternal condition permit).
Diagnostic Procedures: Physical examination, cultures.

Pathologic Findings

Invasion of the chorion by mononuclear and polymorphonuclear leukocytes (nonspecific).

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation and antibiosis.
Specific Measures: Expedited delivery (induction of labor, augmentation of labor).
Diet: No specific dietary changes indicated except as dictated by obstetric management.
Activity: No restriction except as dictated by obstetric management.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Booklet AP087 (Preterm Labor and Birth).

Drug(s) of Choice

Broad-spectrum antibiotic coverage based on organism suspected or detected by culture.

- Ampicillin 2 g IV every 6 hours plus gentamicin 1.5 mg/kg every 8 hours
- Cefoxitin (2 g IV every 6 to 8 hours)
- Ticarcillin/clavulanate (Timentin) 3.1 g IV every 6 hours
- Imipenem cilastatin (Primaxin) 0.5 g IV every 6 hours
- Ampicillin/sulbactam (Unasyn) 3.0 g IV every 6 hours

Contraindications: Known or suspected allergy. See individual agents for additional considerations.
Precautions: See individual agents.
Interactions: See individual agents.

Alternative Drugs

- Mezlocillin 4 g IV every 4 to 6 hours; piperacillin 3–4 g IV every 4 hours.
- Antipyretics have been advocated to reduce the risk of fetal morbidity.

FOLLOW-UP

Patient Monitoring: Increased need for fetal and maternal monitoring for the effects of infection and for the associated labor.
Prevention/Avoidance: Restricted vaginal examinations in labor after rupture of the membranes.
Possible Complications: Significant sepsis may occur, in rare cases to the extent that hysterectomy may be required. There is an increased risk for dysfunctional labor and postpartum hemorrhage. If antibiotic therapy does not provide improvement in 24–48 hours, consider the possibility of abscess or septic pelvic thrombophlebitis.
Expected Outcome: With early recognition, aggressive antibiosis, and expedited delivery, maternal response should be expected to be good. Fetal outcome is based on the gestational age at delivery.

MISCELLANEOUS

Pregnancy Considerations: When chorioamnionitis is present, delivery generally must be expedited.
Other Notes: Up to 20% of women with preterm labor can have bacteria recovered by amniocentesis without evidence of overt

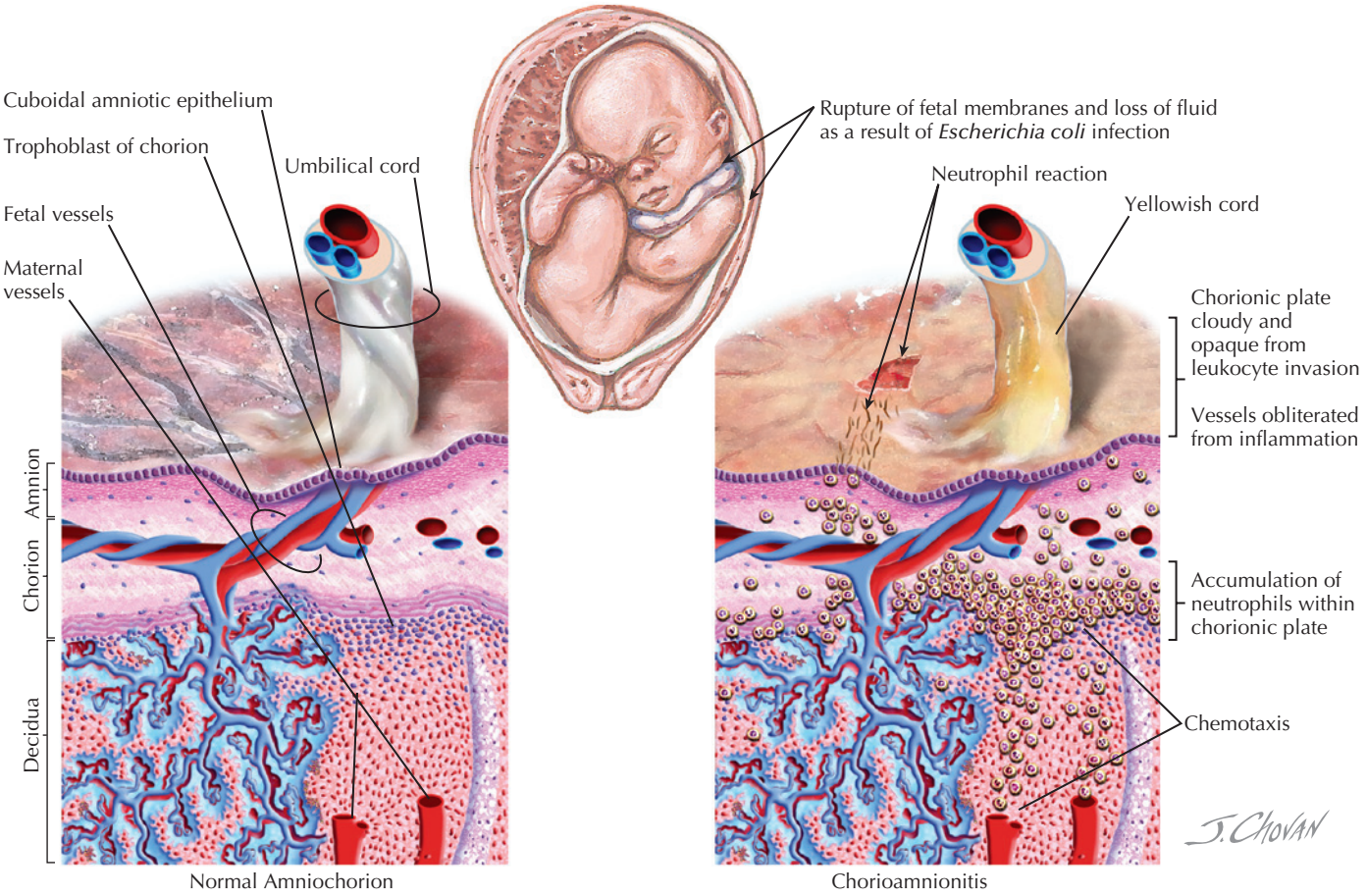


Figure 223.1 Chorioamnionitis

clinical infection. Chorioamnionitis is not an indication for cesarean delivery.

ICD-10-CM Code: O41.1230 (Chorioamnionitis, third trimester, not applicable or unspecified).

REFERENCES

LEVEL I

Locksmith GJ, Chin A, Vu T, et al. High compared with standard gentamicin dosing for chorioamnionitis: a comparison of maternal and fetal serum drug levels. *Obstet Gynecol*. 2005;105:473.

LEVEL II

Cahill AG, Duffy CR, Odibo AO, et al. Number of cervical examinations and risk of intrapartum maternal fever. *Obstet Gynecol*. 2012;119:1096.

Chapman E, Reveiz L, Illanes E, et al. Antibiotic regimens for management of intra-amniotic infection. *Cochrane Database Syst Rev*. 2014;(12):CD010976.

Chi BH, Mudenda V, Levy J, et al. Acute and chronic chorioamnionitis and the risk of perinatal human immunodeficiency virus-1 transmission. *Am J Obstet Gynecol*. 2006;194:174.

Kenyon S, Boulvain M, Neilson J. Antibiotics for preterm rupture of the membranes: a systematic review. *Obstet Gynecol*. 2004;104:1051.

Livingston JC, Llata E, Rinehart E, et al. Gentamicin and clindamycin therapy in postpartum endometritis: the efficacy of daily dosing versus dosing every 8 hours. *Am J Obstet Gynecol*. 2003;188:149.

Mackeen AD, Packard RE, Ota E, et al. Antibiotic regimens for postpartum endometritis. *Cochrane Database Syst Rev*. 2015;(2):CD001067.

Rouse DJ, Landon M, Leveno KJ, et al. National Institute of Child Health and Human Development, Maternal-Fetal Medicine Units Network. The Maternal-Fetal Medicine Units cesarean registry: Chorioamnionitis at term and its duration-relationship to outcomes. *Am J Obstet Gynecol*. 2004;191:211.

Shatrov JG, Birch SC, Lam LT, et al. Chorioamnionitis and cerebral palsy: a meta-analysis. *Obstet Gynecol*. 2010;116:387.

Trochez-Martinez RD, Smith P, Lamont RF. Use of C-reactive protein as a predictor of chorioamnionitis in preterm prelabour rupture of membranes: a systematic review. *BJOG*. 2007;114:796.

Ugwumadu A, Reid F, Hay P, et al. Oral clindamycin and histologic chorioamnionitis in women with abnormal vaginal flora. *Obstet Gynecol*. 2006;107:863.

Wu YW, Colford JM Jr. Chorioamnionitis as a risk factor for cerebral palsy: a meta-analysis. *JAMA*. 2000;284:1417.

LEVEL III

American College of Obstetricians and Gynecologists. Premature rupture of membranes. Practice Bulletin No. 160. *Obstet Gynecol*. 2016;127:e39.

Gibbs RS, Schrag S, Schuchat A. Perinatal infections due to group B streptococci. *Obstet Gynecol*. 2004;104:1062.

Simhan HN, Canavan TP. Preterm premature rupture of membranes: diagnosis, evaluation and management strategies. *BJOG*. 2005;112:32.

224 DIABETES MELLITUS IN PREGNANCY

THE CHALLENGE

To diagnose and manage disturbances of glucose metabolism to minimize the risk associated with diabetes in mothers and fetuses. Diabetes and pregnancy have profound effects on each other, making a familiarity with the interactions between mother, fetus, and the diabetic process a requirement to provide optimal care.

Scope of the Problem: Diabetes mellitus is the most common medical complication of pregnancy, affecting 2%–7% of patients (varying in direct proportion to the prevalence of type 2 diabetes in a given population or ethnic group). Patients who had gestational diabetes in a previous pregnancy have a 33%–50% likelihood of recurrence in a subsequent pregnancy. Patients with type 1 diabetes are at greater risk for maternal complications (diabetic ketoacidosis, glucosuria, hyperglycemia, polyhydramnios, preeclampsia, pregnancy-induced hypertension, preterm labor, retinopathy, urinary tract infections, postpartum uterine atony). The offspring of women with diabetes have a three-fold greater risk for congenital anomalies (3%–6%) than children of mothers without diabetes (1%–2%). Most common among these anomalies are cardiac and limb deformities. Other fetal complications include fetal demise, polyhydramnios, hyperbilirubinemia, hypocalcemia, hypoglycemia, macrosomia, polycythemia, prematurity, respiratory distress syndrome, and spontaneous abortion.

Objectives of Management: To return serum glucose levels to as close to normal as possible through a combination of diet, exercise, oral hypoglycemic agents, and insulin (for selected patients). Optimal management of diabetes begins before pregnancy. Optimal management also requires patient and family education and involvement. For the established patient with diabetes, this teaching is directed to the need for tighter control and more frequent monitoring. The woman with newly diagnosed diabetes requires general instruction about her disease and the unique aspects of diabetes during pregnancy. With respect to the fetus, the goal of treatment is to reduce the likelihood of macrosomia and its consequences. Neonatal hypoglycemia may also be reduced.

TACTICS

Relevant Pathophysiology: Human placental lactogen, made in abundance by the growing placenta, promotes lipolysis and decreases glucose uptake and gluconeogenesis. This anti-insulin effect is sufficient to tip borderline patients into a diabetic state or prompt readjustments in the insulin dosage used by patients with insulin-dependent diabetes. Estrogen, progesterone, and placental insulinase further complicate the management of diabetes, making diabetic ketoacidosis more common. High renal plasma flow and diffusion rates that exceed tubular reabsorption result in a physiologic glucosuria of approximately 300 mg/day. This physiologic glucosuria, combined with the poor correlation between urinary glucose and blood glucose levels, makes the urinary glucose screening useless to detect or monitor diabetes during pregnancy (once the standard).

Box 224.1 INDIVIDUALS AT LOW RISK FOR GESTATIONAL DIABETES (MUST MEET ALL CRITERIA)

- Age younger than 25 years
- No known diabetes in first-degree relative
- Not a member of an ethnic group with an increased risk for the development of type 2 diabetes (examples of high-risk ethnic groups include women of Hispanic, African, Native American, South or East Asian, or Pacific Islands ancestry)
- Body mass index of 25 or less
- No previous history of abnormal glucose tolerance
- No previous history of adverse obstetric outcomes usually associated with gestational diabetes mellitus

Strategies: The severity of diabetes may be classified by either the American Diabetes Association (ADA) classification or by the White classification schemes, although the latter has been rendered less useful by improvements in fetal assessment, neonatal care, and the metabolic management of the pregnant patient. The use of these classifications makes comparisons of published data meaningful and may help to predict the relative risk to the pregnant mother and fetus. Patients with American Diabetes Association–defined type 2 disease are often overweight and their diabetes may be controlled with strict diet or with minimal oral hypoglycemic agent or insulin therapy. Gestational diabetes is reversible, although these patients have a greater incidence of glucose intolerance in subsequent pregnancies or with aging. Because of the increased risk for fetal anomalies, a determination of maternal serum α-fetoprotein and early ultrasonographic studies are of great importance for these patients. Antenatal testing and active management of late pregnancy and labor induction are all indicated for selected patients with diabetes. When there is an estimated fetal weight of 4500 g or more, cesarean delivery may be considered because it may reduce the likelihood of permanent brachial plexus injury in the infant.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlets AP176 (A Healthy Pregnancy for Women With Diabetes), AP177 (Gestational Diabetes), and AP142 (Diabetes and Women).

IMPLEMENTATION

Special Considerations: Screening for gestational diabetes is conducted by measuring the plasma glucose level at 1 hour after ingestion of a 50-g glucose load and is performed between 24–28 weeks of gestation. Jelly beans can be substituted for the usual glucose beverage (28 standard-sized jelly beans = 50 g simple carbohydrate) but this method has poor sensitivity (40%) when compared with glucose polymer solutions (80%–90%). The upper limit of normal for such a test is 130 mg/dL (A screening test threshold of 140 mg/dL has 10% less sensitivity than a threshold of 130 mg/dL but fewer false-positive results; either threshold is acceptable). If a patient's value exceeds this threshold, a formal 3-hour glucose tolerance test is performed. Approximately15% of patients have an abnormal screening test, and approximately the same proportion have an abnormal 3-hour test. For a 3-hour glucose tolerance test, the patient must ingest a minimum of 150 g/day of glucose for the 3 days preceding the test. A fasting glucose level is determined, and a 100-g glucose load is consumed. Plasma glucose levels are then measured at 1, 2, and 3 hours. If two or more values are abnormal, the diagnosis of gestational diabetes may be made. If only one value is abnormal, the test is considered equivocal and should be repeated in 4–6 weeks. Studies indicate that screening may be omitted for selected individuals who are very low risk by selection criteria (see Box 224.1).

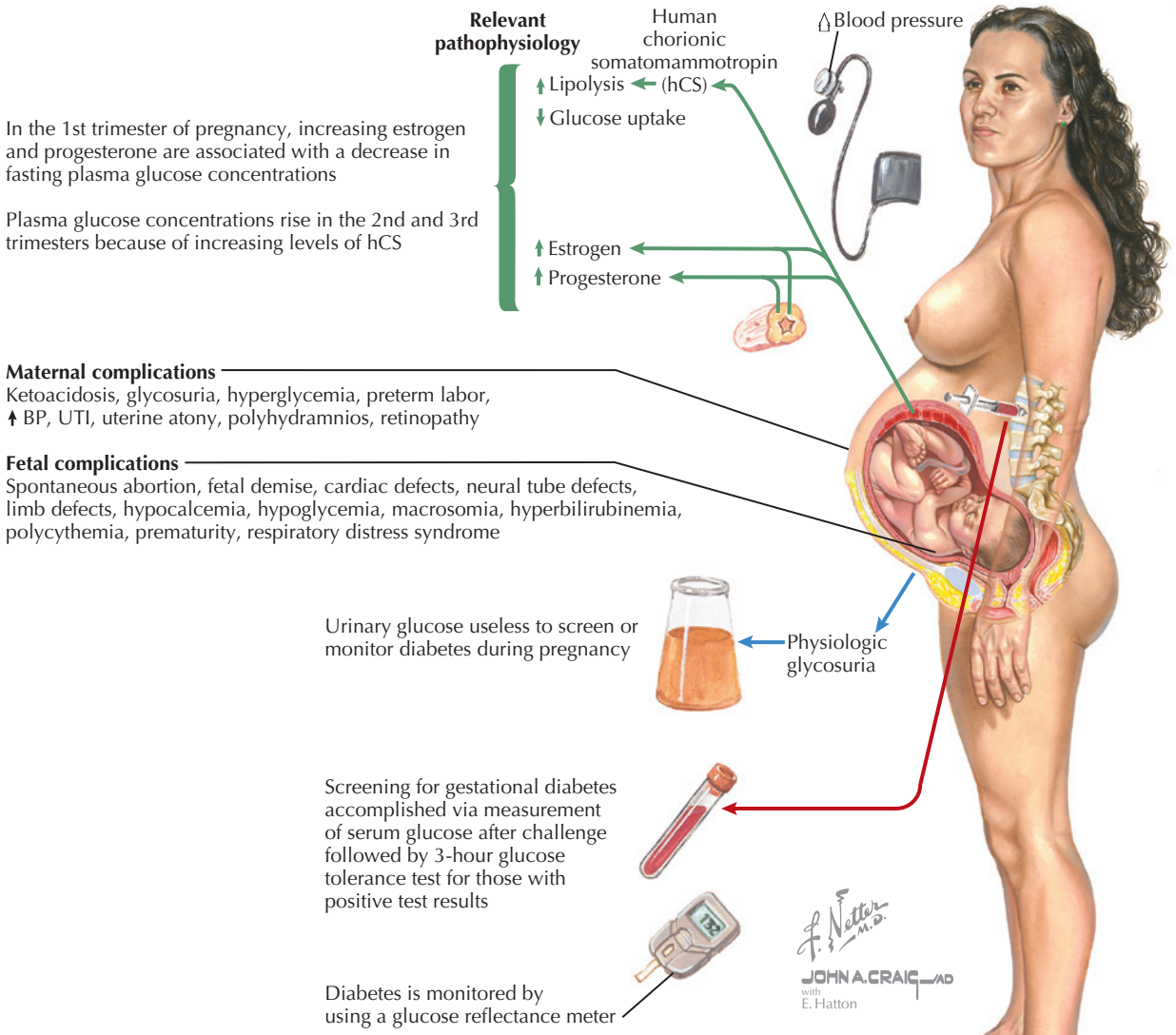


Figure 224.1 Relevant pathophysiology in gestational diabetes

REFERENCES

LEVEL I

Jensen DM, Molsted-Pedersen L, Beck-Nielsen H, et al. Screening for gestational diabetes mellitus by a model based on risk indicators: a prospective study. *Am J Obstet Gynecol*. 2003;189:1383.

Langer O, Conway DL, Berkus MD, et al. A comparison of glyburide and insulin in women with gestational diabetes mellitus. *N Engl J Med*. 2000;343:1134.

LEVEL II

Bain E, Crane M, Tieu J, et al. Diet and exercise interventions for preventing gestational diabetes mellitus. *Cochrane Database Syst Rev*. 2015;(4):CD010443.

Crowther CA, Hiller JE, Moss JR, et al. Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) Trial Group. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. *N Engl J Med*. 2005;352:2477.

Farrar D, Duley L, Medley N, et al. Different strategies for diagnosing gestational diabetes to improve maternal and infant health. *Cochrane Database Syst Rev*. 2015;(1):CD007122.

Feldman RK, Tieu RS, Yasumura L. Gestational Diabetes Screening: The International Association of the Diabetes and Pregnancy Study Groups Compared With Carpenter-Coustan Screening. *Obstet Gynecol*. 2016;127:10.

Han S, Middleton P, Crowther CA. Exercise for pregnant women for preventing gestational diabetes mellitus. *Cochrane Database Syst Rev*. 2012;(7):CD009021.

Lamar ME, Kuehl TJ, Cooney AT, et al. Jelly beans as an alternative to a fifty-gram glucose beverage for gestational diabetes screening. *Am J Obstet Gynecol*. 1999;181:1154.

Russo LM, Nobles C, Ertel KA, et al. Physical activity interventions in pregnancy and risk of gestational diabetes mellitus: a systematic review and meta-analysis. *Obstet Gynecol*. 2015;125:576.

LEVEL III

American College of Obstetricians and Gynecologists. Pregestational diabetes mellitus. ACOG Practice Bulletin 60. *Obstet Gynecol*. 2005;105:675.

American College of Obstetricians and Gynecologists. Gestational diabetes mellitus. Practice Bulletin No. 137. *Obstet Gynecol*. 2013;122:406.

American College of Obstetricians and Gynecologists. Medically indicated late-preterm and early-term deliveries. Committee Opinion No. 560. *Obstet Gynecol*. 2013;121:908.

American College of Obstetricians and Gynecologists. Antepartum fetal surveillance. Practice Bulletin No. 145. *Obstet Gynecol*. 2014;124:182.

American Diabetes Association. 2. Classification and Diagnosis of Diabetes. *Diabetes Care*. 2016;39(suppl 1):S13.

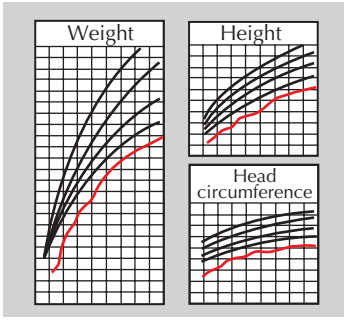
Buchanan TA, Xiang AH. Gestational diabetes mellitus. *J Clin Invest*. 2005;115:485.

Hod M, Kapur A, Sacks DA, et al. The International Federation of Gynecology and Obstetrics (FIGO) Initiative on gestational diabetes mellitus: a pragmatic guide for diagnosis, management, and care. *Int J Gynaecol Obstet*. 2015;131(suppl 3):S173.

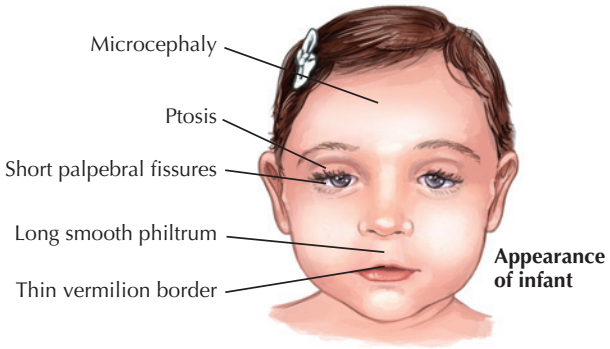
Moyer VA, U.S. Preventive Services Task Force. Screening for gestational diabetes mellitus: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2014;160:414.

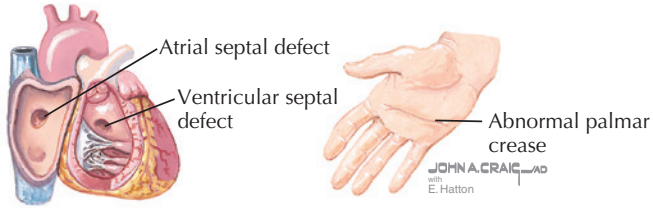
Taylor R, Davison JM. Type 1 diabetes and pregnancy. *BMJ*. 2007;334:742.

Alcohol consumption in excess of 3 oz/day during pregnancy is considered ''high risk.'' Although identifiable effects are seldom seen with consumption less than 1 oz/day, there is no assurance of safety at that level



Developmental deficiency is common. Prognosis is most influenced by degree of maternal alcohol consumption, extent and severity of malformation pattern, including growth retardation





Cardiac and skeletal anomalies are common

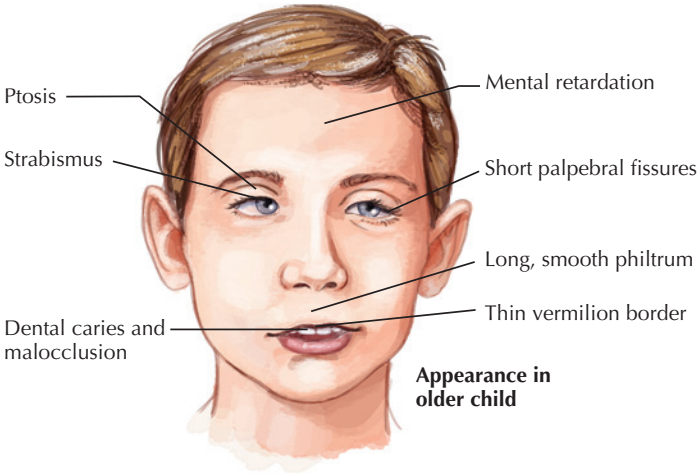


Figure 225.1 Clinical features in fetal alcohol syndrome

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Normal health maintenance, surveillance for dental caries (more common in these children) and cardiac and ophthalmic problems.

Prevention/Avoidance: Reduction or elimination of alcohol use during pregnancy. No safe level of exposure has been demonstrated, although sporadic use of less than 1 oz of alcohol per day has not been associated with the syndrome.

Possible Complications: Higher rate of spontaneous miscarriage in heavy users of alcohol.

Expected Outcome: Infants affected by fetal alcohol syndrome vary from mildly to profoundly mentally retarded. Similarly, structural anomalies are variable but lifelong.

MISCELLANEOUS

ICD-10-CM Code: P04.3 (Newborn [suspected to be] affected by maternal use of alcohol) and Q86.0 (Fetal alcohol syndrome [dysmorphic]).

REFERENCES

LEVEL II

Centers for Disease Control and Prevention (CDC). Alcohol use among pregnant and nonpregnant women of childbearing age - United States, 1991-2005. *MMWR Morb Mortal Wkly Rep*. 2009;58:529.

Floyd RL, Sobell M, Velasquez MM, et al. The Project CHOICES Efficacy Study Group. Preventing alcohol-exposed pregnancies: a randomized controlled trial. *Am J Prev Med*. 2007;32:1.

Henderson J, Gray R, Brocklehurst P. Systematic review of effects of low-moderate prenatal alcohol exposure on pregnancy outcome. *BJOG*. 2007; 114:243.

American College of Obstetricians and Gynecologists. At-risk drinking and alcohol dependence: obstetric and gynecologic implications. Committee Opinion No. 496. *Obstet Gynecol*. 2011;118:383.

LEVEL III

American College of Obstetricians and Gynecologists. Alcohol abuse and other substance use disorders: ethical issues in obstetric and gynecologic practice. Committee Opinion No. 633. *Obstet Gynecol*. 2015;125:1529.

Chudley AE, Conry J, Cook JL, et al. Public Health Agency of Canada's National Advisory Committee on Fetal Alcohol Spectrum Disorder. Fetal alcohol spectrum disorder: Canadian guidelines for diagnosis. *CMAJ*. 2005;172:S1.

Cook JL, Green CR, Lilley CM, et al. Fetal alcohol spectrum disorder: a guideline for diagnosis across the lifespan. *CMAJ*. 2016;188:191.

Floyd RL, O'Connor MJ, Sokol RJ, et al. Recognition and prevention of fetal alcohol syndrome. *Obstet Gynecol*. 2005;106:1059.

Sokol RJ, Delaney-Black V, Nordstrom B. Fetal alcohol spectrum disorder. *JAMA*. 2003;290:2996.

Williams JF, Smith VC. Committee On Substance Abuse. Fetal Alcohol Spectrum Disorders. *Pediatrics*. 2015;136:e1395.

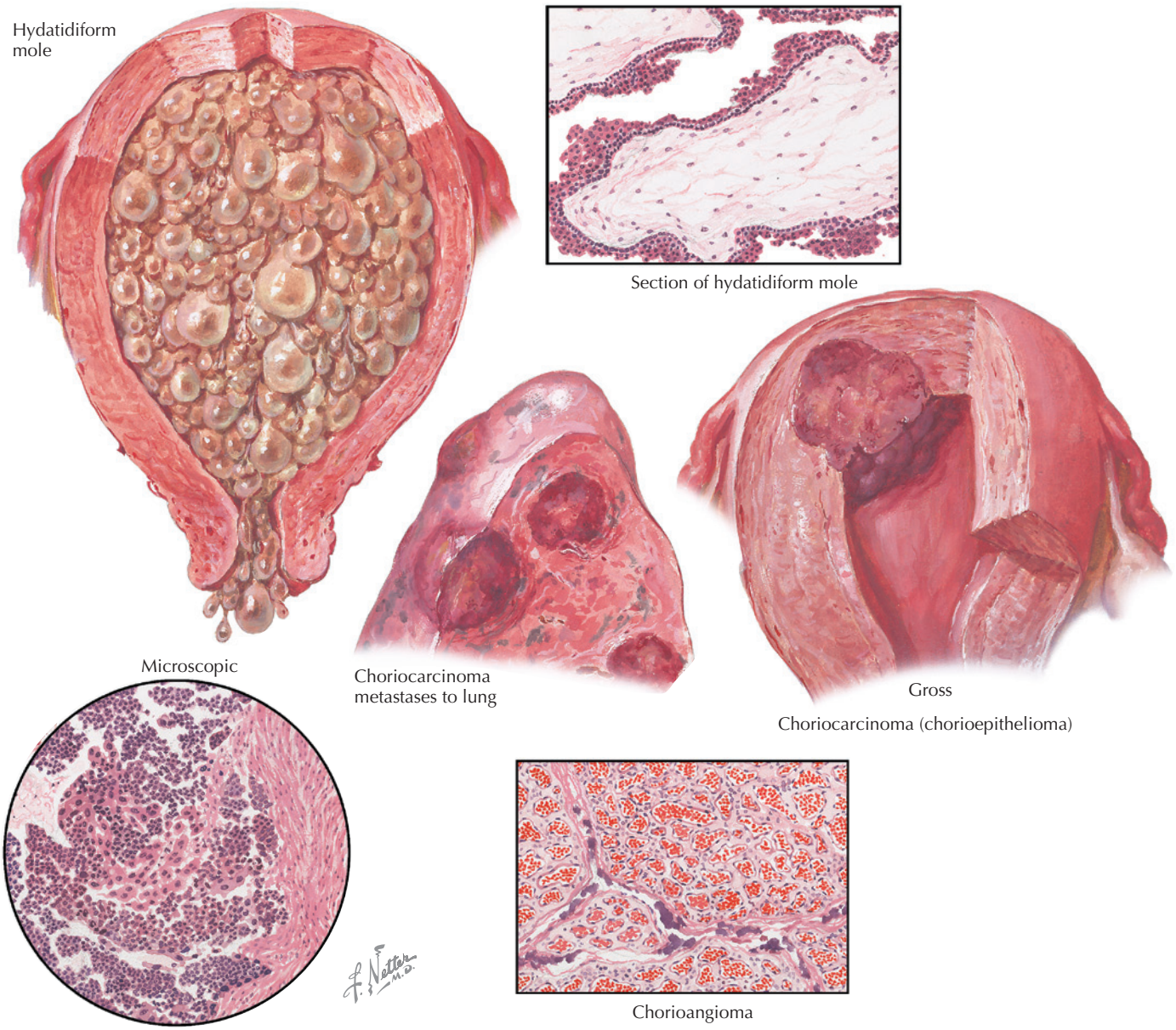


Figure 226.1 Gestational trophoblastic disease

accomplished via suction curettage. Because of the large size of some molar pregnancies and a tendency toward uterine atony, concomitant oxytocin administration is advisable and blood for transfusion must be immediately available, should it be needed.

Diet: No specific dietary changes indicated.

Activity: No restriction.

Drug(s) of Choice

None. Oxytocin or methylergonovine maleate (Methergine) is used to help contract the uterus during surgical evacuation. Primary or recurrent malignant trophoblastic disease is generally treated with chemotherapy (methotrexate, actinomycin D, chlorambucil, or cyclophosphamide [Cytoxan], singly or in combination).

FOLLOW-UP

Patient Monitoring: After the uterus has been emptied, the patient must be closely followed for at least 1 year for the possibility of recurrent benign or malignant disease. Any change in the patient's examination, an increase in β-hCG titers, or a failure of the β-hCG level to fall below 10 mIU/mL by 12 weeks after evacuation must be evaluated for the possibility of a recurrent benign or malignant disease. Serum hCG levels are generally monitored every 2 weeks until three consecutive tests are negative, then monthly for 6–12 months. (Proteolytic enzymes and heterophilic antibodies found in 3%–4% of individuals can cause a falsely positive hCG test [up to 800 ImU/mL has been reported] and can lead to inappropriate therapy).

Prevention/Avoidance: None.

Possible Complications: Gestational trophoblastic neoplasia is notable for the possibility of malignant transformation, although fewer than 10% of patients develop malignant changes. In general, the larger or more advanced the molar pregnancy, the greater the risk of pulmonary complications, bleeding, trophoblastic emboli, or fluid overload during evacuation.

Expected Outcome: Approximately 80% of molar pregnancies follow a benign course after an initial therapy. Between 15% and 25% of patients develop invasive disease, and 3%–5% eventually have metastatic lesions. The prognosis for patients with primary

or recurrent malignant trophoblastic disease is generally good (>90% cure rate). The theca lutein cysts often found in molar pregnancies may take several months to regress after evacuation of the uterine contents. Fewer than 5% of patients will require hysterectomy to achieve a cure for choriocarcinoma.

MISCELLANEOUS

Pregnancy Considerations: Pregnancy should be delayed for at least 1 year after a molar pregnancy to avoid confusion between normal pregnancy and recurrent disease. These patients have no higher rate of abortions, stillbirths, congenital anomalies, prematurity, or other complications of pregnancy with future gestations. The placenta from any subsequent pregnancies should be sent for histologic evaluation.

ICD-10-CM Codes: O01.9 (Hydatidiform mole, unspecified) and D39.2 (Neoplasm of uncertain behavior of placenta).

REFERENCES

LEVEL I

Covens A, Filiaci VL, Burger RA, et al.; Gynecologic Oncology Group. Phase II trial of pulse dactinomycin as salvage therapy for failed low-risk gestational trophoblastic neoplasia: a Gynecologic Oncology Group study. *Cancer*. 2006;107:1280.

Goldstein DP, Goldstein PR, Bottomley P, et al. Methotrexate with citrovorum factor rescue for nonmetastatic gestational trophoblastic neoplasms. *Obstet Gynecol*. 1976;48:321.

LEVEL II

Matsui H, Iitsuka Y, Suzuka K, et al. Early pregnancy outcomes after chemotherapy for gestational trophoblastic tumor. *J Reprod Med*. 2004;49:531.

LEVEL III

American College of Obstetricians and Gynecologists. Diagnosis and treatment of gestational trophoblastic disease. ACOG Practice Bulletin 53. *Obstet Gynecol*. 2004;103:1365.

Berkowitz RS, Goldstein DP. Clinical practice. Molar pregnancy. *N Engl J Med*. 2009;360:1639.

Goldstein DP, Berkowitz RS. Current management of gestational trophoblastic neoplasia. *Hematol Oncol Clin North Am*. 2012;26:111.

Lurain JR. Gestational trophoblastic disease I: epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. *Am J Obstet Gynecol*. 2010;203:531.

Seckl MJ, Sebire NJ, Berkowitz RS. Gestational trophoblastic disease. *Lancet*. 2010;376:717.

Smith HO. Gestational trophoblastic disease epidemiology and trends. *Clin Obstet Gynecol*. 2003;46:541.

Soper JT. Gestational trophoblastic disease. *Obstet Gynecol*. 2006;108:176.

Figure 227.1 Gingivitis

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, encourage good oral hygiene, smoking cessation, warm saline rinses (twice a day), periodic dental care. Infection, abscess, or sources of sepsis require prompt treatment, regardless of the stage of pregnancy.
Specific Measures: Removal of irritating factors (plaque).
Diet: Ensure adequate nutrition.
Activity: No restriction.
Patient Education: Reinforce the need for periodic dental care.

Drug(s) of Choice

Penicillin V 250–500 mg PO every 6 hours, topical corticosteroids (triamcinolone in Orabase).
Contraindications: Known or suspected allergy.
Precautions: Watch for possible overgrowth of vaginal fungal flora if penicillin is used.
Interactions: See individual agents.

Alternative Drugs

Other antibiotics based on smear or culture results.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: Good dental hygiene (daily brushing and flossing), periodic evaluation and cleaning.
Possible Complications: Severe periodontal disease, tooth loss.
Expected Outcome: Generally improves after delivery if hormonal change is the cause; can recur if dental hygiene is not maintained.

MISCELLANEOUS

ICD-10-CM Code: K05.10 Chronic gingivitis, plaque induced.

REFERENCES

LEVEL II

Boggess KA, Edelstein BL. Oral health in women during preconception and pregnancy: implications for birth outcomes and infant oral health. *Matern Child Health J*. 2006;10:S169.
Gazolla CM, Ribeiro A, Moyses MR, et al. Evaluation of the incidence of preterm low birth weight in patients undergoing periodontal therapy. *J Periodontol*. 2007;78:842.
Lopez NJ, Da Silva I, Ipinza J, et al. Periodontal therapy reduces the rate of preterm low birth weight in women with pregnancy-associated gingivitis. *J Periodontol*. 2005;76:2144.
Pretorius C, Jagatt A, Lamont RF. The relationship between periodontal disease, bacterial vaginosis, and preterm birth. *J Perinat Med*. 2007;35:93.
Vergnes JN, Sixou M. Preterm low birth weight and maternal periodontal status: a meta-analysis. *Am J Obstet Gynecol*. 2007;196:135. e1.
Xiong X, Buekens P, Fraser WD, et al. Periodontal disease and adverse pregnancy outcomes: a systematic review. *BJOG*. 2006;113:135.

LEVEL III

American College of Obstetricians and Gynecologists. Oral health care during pregnancy and through the lifespan. Committee Opinion No. 569. *Obstet Gynecol*. 2013;122:417.
Barak S, Oettinger-Barak O, Oettinger M, et al. Common oral manifestations during pregnancy: a review. *Obstet Gynecol Surv*. 2003;58:624.
Ferguson JE 2nd, Hansen WF, Novak KF, et al. Should we treat periodontal disease during gestation to improve pregnancy outcomes? *Clin Obstet Gynecol*. 2007;50:454.
Klebanoff M, Searle K. The role of inflammation in preterm birth—Focus on periodontitis. *BJOG*. 2006;113:43.
Michalowicz BS, Hodges JS, DiAngelis AJ, et al.; OPT Study. Treatment of periodontal disease and the risk of preterm birth. *N Engl J Med*. 2006; 355:1885.
Offenbacher S. Maternal periodontal infections, prematurity, and growth restriction. *Clin Obstet Gynecol*. 2004;47:808.
Scannapieco FA, Bush RB, Paju S. Periodontal disease as a risk factor for adverse pregnancy outcomes. A systematic review. *Ann Periodontol*. 2003;8:70.
Shub A, Swain JR, Newnham JP. Periodontal disease and adverse pregnancy outcomes. *J Matern Fetal Neonatal Med*. 2006;19:521.
Stoopler ET, Kuperstein AS. Pregnancy gingivitis and pregnancy tumour. *J Obstet Gynaecol Can*. 2012;34:509.

228 HELLP SYNDROME

INTRODUCTION

Description: Hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome is considered to be a variant of pregnancy-induced hypertension (PIH) and preeclampsia, which are dominated by hepatic and hematologic changes.
Prevalence: 0.1%–0.8% of pregnancies; up to 20% of patients with severe preeclampsia.
Predominant Age: Reproductive age. Eighty percent of cases are diagnosed prior to 37 weeks of gestation.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Unknown. Genetic, endocrine/metabolic (including altered prostaglandin production), uteroplacental ischemia, immunologic. A connection to fetal long-chain 3-hydroxyacyl CoA dehydrogenase (LCHAD) deficiency has been proposed.

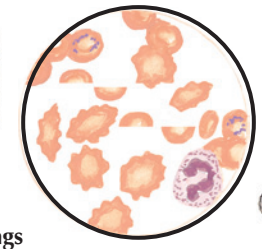
Risk Factors: Older than 40 years, African-American race, family history of pregnancy-induced hypertension, renal disease, antiphospholipid syndrome, diabetes mellitus, multiple gestation, past history of preeclampsia or HELLP syndrome. Chronic hypertension increases the risk for pregnancy-induced hypertension.

SIGNS AND SYMPTOMS

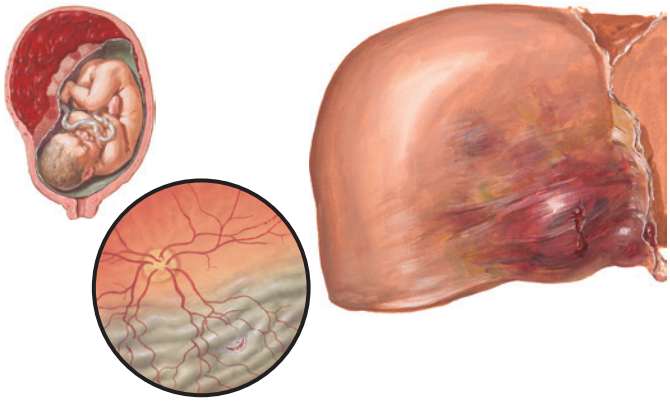
- Preeclampsia or eclampsia with hemolysis, thrombocytopenia (the degree of thrombocytopenia is predictive of the severity of the disease and the likelihood of poor outcome), elevated hepatic transaminase levels (any or all; blood pressure may be normal in up to 20% of patients)
- Right upper quadrant or epigastric pain
- Nausea, vomiting, and malaise

HELLP Syndrome (Hemolysis, Abnormal Liver Function Tests, Low Platelets)

Clinical symptoms
Nausea, vomiting
Right upper quadrant pain
Jaundice



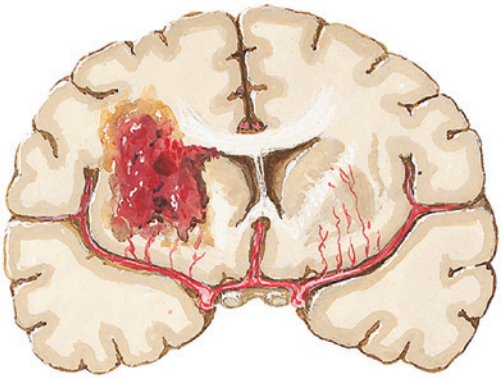
Laboratory findings
- Hemolysis (with schistocytes seen on peripheral smear)
- Elevated liver function tests
- Low platelet count



Complications
- Placental abruption
- Hepatic subcapsular hematoma
- Retinal detachment
- Acute kidney injury
- Pulmonary edema
- Disseminated intravascular coagulation (DIC)

Eclampsia

Clinical symptoms
- Generalized, tonic-clonic seizure
- Early symptoms may include:
  Blurred vision
  Severe frontal or occipital headache
  Altered mental status



Complications
- Cerebral hemorrhage

Figure 228.1 HELLP syndrome

DIAGNOSTIC APPROACH

Differential Diagnosis

- Preeclampsia or eclampsia
- Secondary hypertension
- Improper blood pressure measurement (wrong cuff size, position, technique), resulting in false elevation of readings
- Multiple pregnancy
- Molar pregnancy
- Primary hepatic disease and acute fatty liver of pregnancy

Associated Conditions: Intrauterine growth restriction, prematurity.

Workup and Evaluation

Laboratory: Liver and renal function studies (eg, enzymes, renal clearance, 24-hour urinary protein), platelet counts, clotting studies (platelet counts of >50,000/mm^3 are generally not associated with spontaneous bleeding).

Imaging: Ultrasonography to monitor fetal growth (frequently restricted).

Special Tests: Assessment of fetal lung maturation may be performed, but if maternal disease is severe, management is based on maternal factors and not fetal maturation.

Diagnostic Procedures: Measurement of blood pressure, laboratory confirmation.

Pathologic Findings

HELLP syndrome is a multiorgan process, including the renal, hepatic, hematologic, and nervous systems.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, support, and preparation for delivery.

Specific Measures: Patients with HELLP syndrome often represent the sickest patients with preeclampsia or eclampsia. The only true treatment is delivery. The presence of HELLP syndrome generally militates against conservative treatment for any but the briefest stabilization period.

Diet: No specific dietary changes indicated.

Activity: No restriction.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP034 (Preeclampsia and High Blood Pressure During Pregnancy).

Drug(s) of Choice

For mild to moderate chronic hypertension, α-methyldopa is considered to be the first-line therapy.

During labor or labor induction, magnesium sulfate is often used to reduce the chance of seizures or to provide fetal neuroprotection for fetuses below 32 weeks (4 g IV for 20 minutes, then 2–3 g/h IV continuous infusion; therapeutic range 4–8 mg/dL).

If blood pressure is >180 torr systolic or 110 torr diastolic—hydralazine HCl 5–10 mg IV bolus every 20 minutes as needed or labetalol 20 mg IV bolus every 10 minutes as needed to a maximum of 300 mg in 24 hours. Sodium nitroprusside may be used for extreme disease.

Steroids have been advocated, but their use has not been supported by large, well-designed randomized, double-blind, placebo-controlled trials.

Contraindications: Angiotensin-converting enzyme (ACE) inhibitors are teratogenic and are contraindicated in pregnancy. Diuretics should be avoided in pregnancy because of the possibility of adverse fetal effects caused by reduced plasma volume. Despite the common occurrence of edema, these patients have constricted circulatory volume.

Precautions: Central hemodynamic monitoring should be considered if blood pressure is high or potent agents are used.

Alternative Drugs

Verapamil or nifedipine may also be used to acutely reduce blood pressure.

FOLLOW-UP

Patient Monitoring: Increased maternal and fetal surveillance, antenatal testing.

Prevention/Avoidance: The value of low-dose aspirin therapy or calcium supplementation remains unproved.

Possible Complications: Maternal—cardiac decompensation, stroke, pulmonary edema (10%) and respiratory failure, renal failure (5%), disseminated intravascular coagulation (DIC), subcapsular or intraparenchymal liver hematoma, seizures and seizure-related injuries (6%), retinal detachment, intracranial hemorrhage, coma, and death (0.5%–5% mortality). Fetal risk (growth restriction and death) is directly proportional to both the degree of proteinuria and the level of maternal diastolic blood pressure. Placental abruption may occur in up to 10% of cases.

Expected Outcome: HELLP syndrome generally resolves after delivery, but the risk for recurrence with future pregnancies or elevated blood pressure in later life is increased.

MISCELLANEOUS

ICD-10-CM Codes: O14.20 (HELLP syndrome, unspecified trimester) and O14.10 (Severe preeclampsia, unspecified trimester).

REFERENCES

LEVEL II

Fitzpatrick KE, Hinshaw K, Kurinczuk JJ, et al. Risk factors, management, and outcomes of hemolysis, elevated liver enzymes, and low platelets syndrome and elevated liver enzymes, low platelets syndrome. *Obstet Gynecol*. 2014;123:618.

Thangaratinam S, Ismail KM, Sharp S, et al. Tests in Prediction of Pre-eclampsia Severity Review Group. Accuracy of serum uric acid in predicting complications of pre-eclampsia: a systematic review. *BJOG*. 2006;113:369.

Woudstra DM, Chandra S, Hofmeyr GJ, et al. Corticosteroids for HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome in pregnancy. *Cochrane Database Syst Rev*. 2010;(9):CD008148.

LEVEL III

American College of Obstetricians and Gynecologists. Emergent therapy for acute-onset, severe hypertension during pregnancy and the postpartum period. Committee Opinion No. 623. *Obstet Gynecol*. 2015;125:521.

American College of Obstetricians and Gynecologists. First-trimester risk assessment for early-onset preeclampsia. Committee Opinion No. 638. *Obstet Gynecol*. 2015;126:e25.

American College of Obstetricians and Gynecologists. Hypertension in pregnancy: executive summary. *Obstet Gynecol*. 2013;122:1122.

American College of Obstetricians and Gynecologists. Magnesium sulfate use in obstetrics. Committee Opinion No. 652. *Obstet Gynecol*. 2016;127:e52.

American College of Obstetricians and Gynecologists. Thrombocytopenia in pregnancy. In: *ACOG Practice Bulletin 6*. Washington, DC: ACOG; 1999.

American College of Obstetricians and Gynecologists, Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. *Obstet Gynecol*. 2013;122:1122.

229 HEPATITIS IN PREGNANCY

INTRODUCTION

Description: Hepatitis is one of the most serious infections that occur during pregnancy.
Prevalence: Hepatitis—0.1%–1.5% of pregnancies (one-third of Americans have antibodies to hepatitis A). The prevalence of hepatitis in pregnancy has declined in the past 15 years.
Predominant Age: Reproductive age.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Five different forms of hepatitis may be involved. Hepatitis A is caused by a ribonucleic acid (RNA) virus that is transmitted by fecal–oral contamination and accounts for 30%–50% of acute disease. Hepatitis B is caused by a small DNA virus that accounts for 40%–45% of occurrences. It is estimated that acute hepatitis B occurs in 1–2 of 1000 pregnancies and that chronic infections are present in 5–15 of 1000 pregnancies. Hepatitis B is transmitted by parenteral and sexual contact. Hepatitis B is easily sexually transmitted: 25% of people who have sexual contact with an infected person become infected. Hepatitis C (non-A, non-B) accounts for 10%–20% of cases and is caused by a single-stranded RNA virus spread by parenteral exposure. Hepatitis D is caused by an RNA virus that requires coinfection with the hepatitis B virus. Significant mortality and long-term consequences may occur from this less common infection. Hepatitis E, G, and other forms of non-A, non-B hepatitis are uncommon but may occur during pregnancy as well.
Risk Factors: Groups at greatest risk for hepatitis B are intravenous drug users, hemophiliacs, homosexuals, and healthcare workers. Poor hand washing habits, multiple sexual partners, a history of sexually transmitted infection, tattoos, and multiple blood transfusions (hepatitis C) increase the risk for an infection as well.

SIGNS AND SYMPTOMS

Unchanged by pregnancy
- Fever (60%), malaise (70%), fatigue, anorexia (50%), nausea (80%)
- Variable right upper quadrant pain (50%)
- Upper abdominal tenderness with hepatomegaly
- Dark urine (85%) and acholic stools
- Jaundice a possibility in up to 60%
- Coagulopathy or encephalopathy (fulminant infections only)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Acute fatty liver of pregnancy
- Toxic hepatic injury
- Cholestasis of pregnancy
- Severe preeclampsia
- Mononucleosis
- Cytomegalovirus hepatitis
- Lupoid hepatitis
- Viral enteritis

Associated Conditions: Jaundice, cirrhosis, pancreatitis, nephritis, and ileus. If cirrhosis is present; premature delivery, intrauterine growth restriction, intrauterine infection, and intrauterine fetal demise.

Workup and Evaluation

Laboratory: Hepatitis during pregnancy is diagnosed in the manner similar for nonpregnant patients; serum chemistry abnormalities indicate active hepatic disease (marked elevation of alanine aminotransferase, aspartate aminotransferase, and bilirubin), and immunochemical analysis indicates the presence of infection and the phase of the clinical course. In severe cases, coagulation studies should be performed. Routine screening of all pregnant patients is recommended.
Imaging: None indicated.
Special Tests: Percutaneous liver biopsy may be helpful but is generally not required.
Diagnostic Procedures: History, physical examination, ultrasonography (limited value), and laboratory investigation.

Pathologic Findings

Viral hepatitis is distinguished from other hepatic injuries by the characteristic pattern of injury and infiltrate.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Patients with encephalopathy or coagulopathy or who are severely debilitated should be hospitalized. Nutritional support is generally required. Fluid intake and electrolyte levels must be maintained. The upper abdomen should be protected from trauma. Sexual contact should be avoided until the partner(s) receive prophylaxis.
Specific Measures: Prophylaxis should be considered for anyone at risk (eg, travel to endemic area, sexual partners). Acute exposure should be treated with immune globulin (see Follow-up). Tenofovir disoproxil fumarate 300 mg daily or lamivudine 100 mg daily are both suitable options during pregnancy because both have been safely used, and the risk for developing resistance is low. Antiviral therapy is usually unnecessary, except in cases of acute liver failure or protracted severe hepatitis.
Diet: Maintain good nutrition.
Activity: The upper abdomen should be protected from trauma.
Patient Education: Patients should be instructed regarding risk factors and modes of spread to limit risk for family contacts and future recurrences. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP125 (Protecting Yourself Against Hepatitis B and Hepatitis C).

Drug(s) of Choice

Those necessary for support only; others of limited or unproved value.

FOLLOW-UP

Patient Monitoring: Normal prenatal care once the acute episode is resolved. Continued monitoring for chronic liver dysfunction or carrier state (where applicable).
Prevention/Avoidance: Active immunization of those at risk before a pregnancy is planned. Patients exposed to hepatitis A may be administered γ-globulin in the manner similar for nonpregnant patients. Patients exposed to hepatitis B or those found to be carriers may receive either active immunization with hepatitis vaccine or passive immunization with hepatitis B immunoglobulin (HBIG). To be effective, HBIG should be administered within 48 hours of exposure. The infants of these mothers should receive both forms of immunization. Infants born to mothers with hepatitis B infection should be given HBIG 0.5 mL and hepatitis B vaccine (separate site) within 12 hours of birth, with follow-up vaccinations at 1–6 months of age.

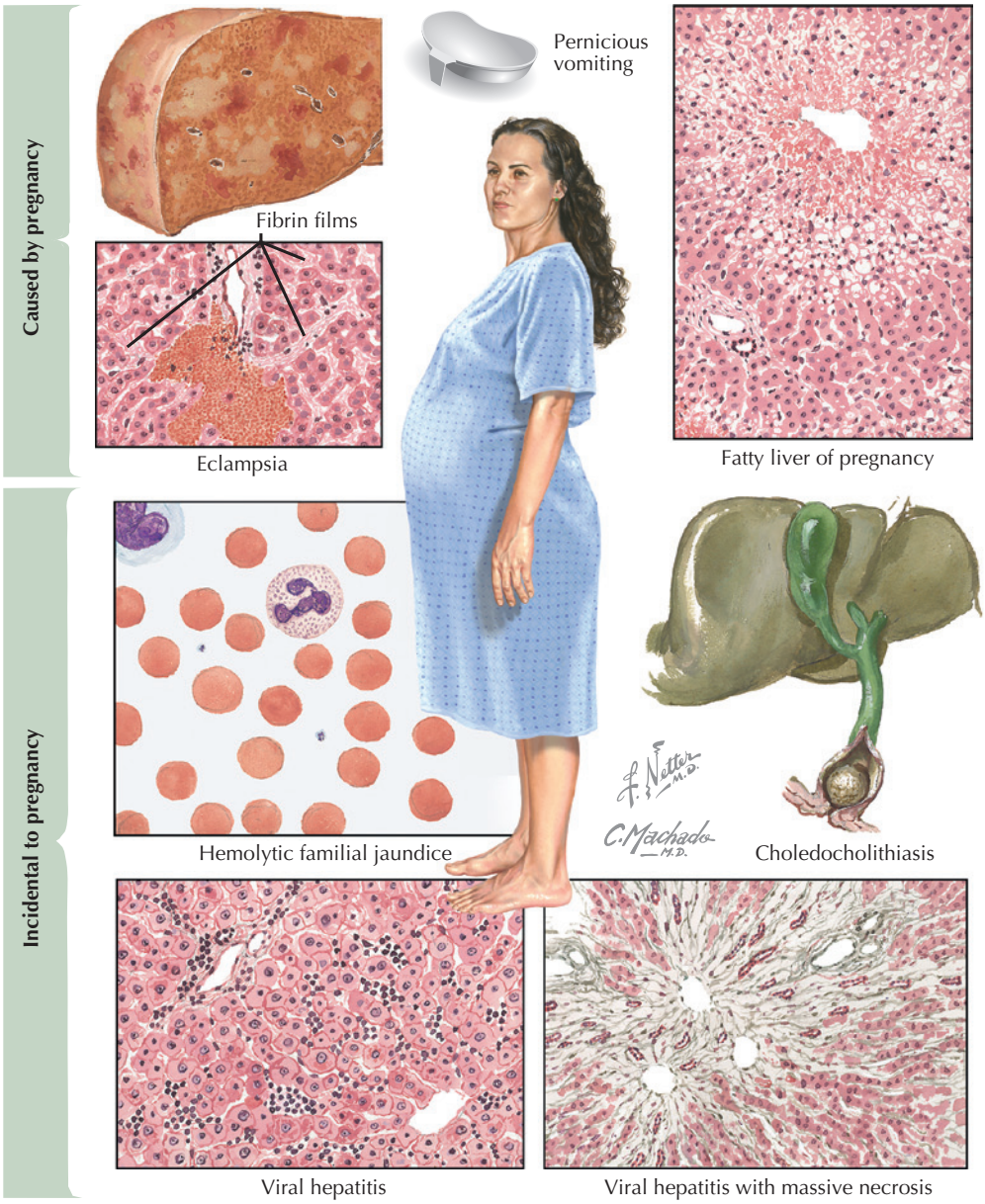


Figure 229.1 Liver diseases caused by pregnancy and incidental to pregnancy

Possible Complications: Mortality from acute hepatitis varies with the type of hepatitis and severity of infection but is generally in the range of 2–10 of 1000 cases. Serious complications of hepatitis A are uncommon. Vertical transmission of hepatitis B to the developing fetus can pose a significant risk. Of women seropositive for hepatitis B surface antigen (HbsAg), 10%–20% transmit the virus to their neonates in the absence of immunoprophylaxis. In women who are seropositive for both HBsAg and hepatitis B envelope antigen (HbeAg), vertical transmission is approximately 90%. In patients with acute hepatitis B, vertical transmission occurs in up to 10% of neonates when infection occurs in the first trimester and in 80%–90% of neonates when acute infection occurs in the third trimester. The majority (90%) of untreated infants become chronic carriers, capable of infecting others. These infants are also at increased risk for cirrhosis and hepatic cancer. Neonatal infection rates vary with gestation and are highest in the third trimester (exposure to blood and fluids at delivery). Patients with the envelope antigen have an 80% chance of vertical transmission of the infection. Hepatitis D leads to chronic hepatitis in 80% of patients with rapid appearance of cirrhosis in 15%; mortality approaches 25%. Chronic liver disease and liver failure may follow infection with hepatitis B, C, or D.

Expected Outcome: Of patients, 85%–90% experience complete resolution of symptoms; 10%–15% of patients with hepatitis B become chronic carriers (10%–15% of these develop serious long-term liver problems including cirrhosis and hepatocellular carcinoma). Patients with hepatitis C or D have a more than 80% risk of chronic hepatitis with cirrhosis and liver failure in 20%–25%.

MISCELLANEOUS

ICD-10-CM Code: O98.519 (Other viral diseases complicating pregnancy, unspecified trimester).

REFERENCES

LEVEL II

European Paediatric Hepatitis C Virus Network. Effects of mode of delivery and infant feeding on the risk of mother-to-child transmission of hepatitis C virus. European Paediatric Hepatitis C Virus Network. *BJOG*. 2001;108:371.

Schillie S, Walker T, Veselsky S, et al. Outcomes of infants born to women infected with hepatitis B. *Pediatrics*. 2015;135:e1141.

Shi Z, Yang Y, Ma L, et al. Lamivudine in late pregnancy to interrupt in utero transmission of hepatitis B virus: a systematic review and meta-analysis. *Obstet Gynecol*. 2010;116:147.

LEVEL III

American College of Obstetricians and Gynecologists. Hepatitis B, hepatitis C, and human immunodeficiency virus infections in obstetrician–gynecologists. Committee Opinion 655. *Obstet Gynecol*. 2016;127:e70.

American College of Obstetricians and Gynecologists. Viral Hepatitis in Pregnancy. ACOG Practice Bulletin No. 86. *Obstet Gynecol*. 2007;110:941.

Guntupalli SR, Steingrub J. Hepatic disease and pregnancy: an overview of diagnosis and management. *Crit Care Med*. 2005;33:S332.

Poland GA, Jacobson RM. Clinical practice: prevention of hepatitis B with the hepatitis B vaccine. *N Engl J Med*. 2004;351:2832.

- Promethazine (Phenergan) 25 mg PO or rectally every 4–6 hours
- Metoclopramide (Reglan) 10 mg PO four times a day
- Meclizine (Antivert) 12.5–25 mg PO four times a day

Contraindications: See individual agents.

Precautions: Promethazine (Phenergan) is a class C agent (risk for teratogenesis in animals but unknown risk in humans). Metoclopramide (Reglan) and meclizine (Antivert) are class B agents (no known human risk).

FOLLOW-UP

Patient Monitoring: Normal health maintenance, monitoring of fetal growth.

Prevention/Avoidance: None.

Possible Complications: Maternal dehydration and metabolic compromise. Rupture or tears of the esophagus and pneumothorax have been reported as a result of vomiting.

Expected Outcome: Generally good, although relapses in severe cases are common (25%–30%).

MISCELLANEOUS

Pregnancy Considerations: If nutrition is maintained, no effect on pregnancy. May recur with subsequent pregnancies.

ICD-10-CM Codes: O21.0 (hyperemesis gravidarum [mild]) and O21.1 (with metabolic disturbance).

REFERENCES

LEVEL I

Heazell A, Thorneycroft J, Walton V, et al. Acupressure for the in-patient treatment of nausea and vomiting in early pregnancy: a randomized control trial. *Am J Obstet Gynecol*. 2006;194:815.

Knight B, Mudge C, Openshaw S, et al. Effect of acupuncture on nausea of pregnancy: a randomized, controlled trial. *Obstet Gynecol*. 2001;97:184.

Rosen T, de Veciana M, Miller HS, et al. A randomized controlled trial of nerve stimulation for relief of nausea and vomiting in pregnancy. *Obstet Gynecol*. 2003;102:129.

Tan PC, Khine PP, Vallikkannu N, et al. Promethazine compared with metoclopramide for hyperemesis gravidarum: a randomized controlled trial. *Obstet Gynecol*. 2010;115:975.

Yost NP, McIntire DD, Wians FH Jr, et al. A randomized, placebo-controlled trial of corticosteroids for hyperemesis due to pregnancy. *Obstet Gynecol*. 2003;102:1250.

LEVEL II

Borrelli F, Capasso R, Aviello G, et al. Effectiveness and safety of ginger in the treatment of pregnancy-induced nausea and vomiting. *Obstet Gynecol*. 2005;105:849.

Lacasse A, Rey E, Ferreira E, et al. Nausea and vomiting of pregnancy: what about quality of life? *BJOG*. 2008;115:1484.

Matthews A, Haas DM, O'Mathúna DP, et al. Interventions for nausea and vomiting in early pregnancy. *Cochrane Database Syst Rev*. 2015;(9):CD007575.

Veenendaal MV, van Abeelen AF, Painter RC, et al. Consequences of hyperemesis gravidarum for offspring: a systematic review and meta-analysis. *BJOG*. 2011;118:1302.

LEVEL III

American College of Obstetricians and Gynecologists. Nausea and vomiting of pregnancy. Practice Bulletin No. 153. *Obstet Gynecol*. 2015;126:e12.

Lee NM, Saha S. Nausea and vomiting of pregnancy. *Gastroenterol Clin North Am*. 2011;40:309.

McParlin C, O'Donnell A, Robson SC, et al. Treatment for hyperemesis gravidarum and nausea and vomiting in pregnancy. A systematic review. *JAMA*. 2016;316(13):1392-1401.

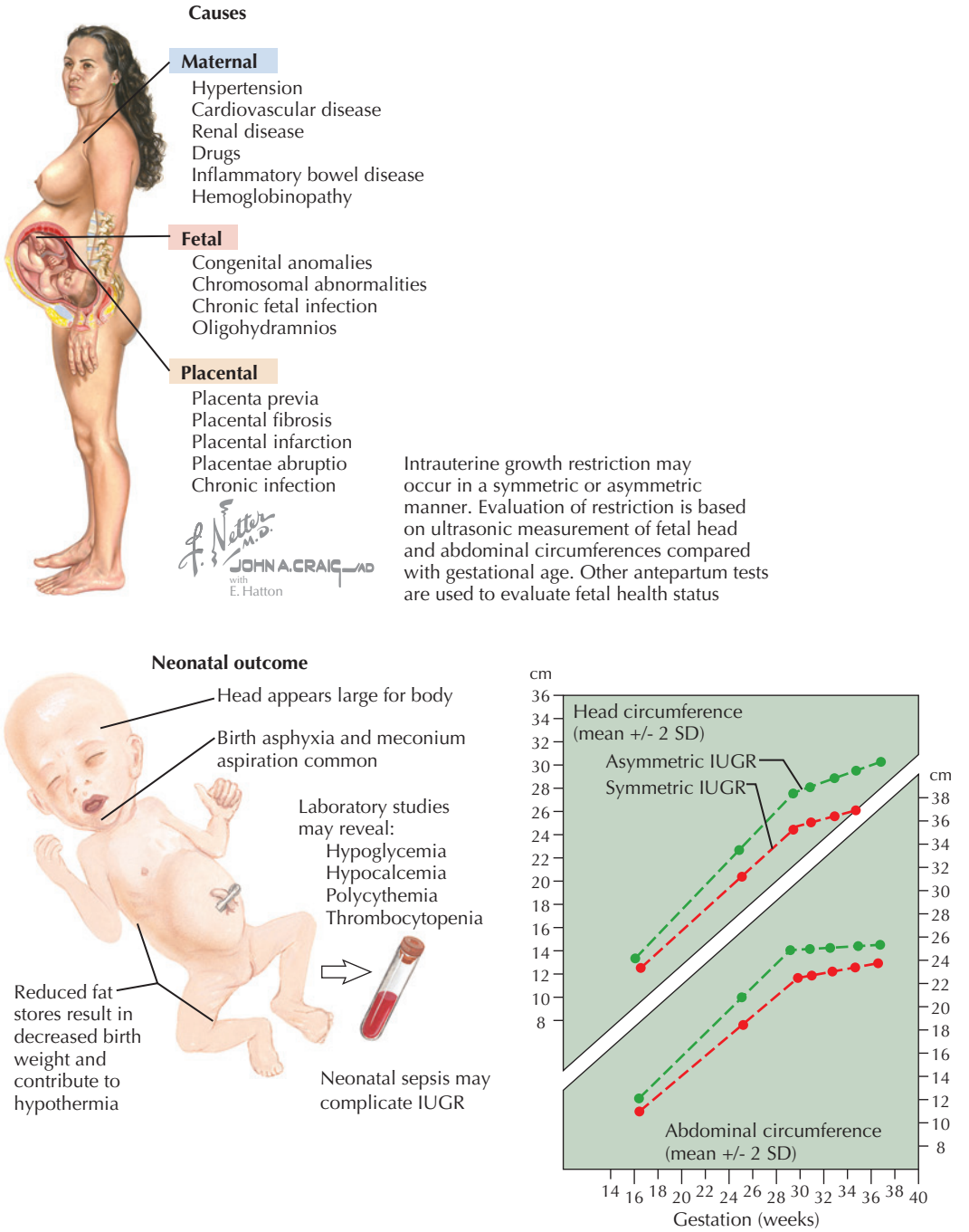


Figure 231.1 Intrauterine growth restriction

- Fetal growth that falls below the 5th–10th percentile for gestational age or demonstrates reduced growth velocity on serial examinations

DIAGNOSTIC APPROACH

Differential Diagnosis

- Inaccurate gestational age
- Congenital anomalies
- Multiple gestation
- Constitutionally small infants
- Extrauterine gestation

Associated Conditions: Prematurity, intrauterine fetal death, congenital anomalies, and oligohydramnios.

Workup and Evaluation

Laboratory: No evaluation indicated unless suggested by maternal disease.

Imaging: Ultrasonography with fetal biometry compared with curves specific to the location and population served. The diagnosis must also be based on serial examinations that provide information about the growth of the individual fetus.

Special Tests: When found in advanced gestations: fetal nonstress and contraction stress testing or biophysical profiling. The role of Doppler flow studies continues to be evaluated and is reliable only when placental dysfunction is the cause of the growth restriction.

Diagnostic Procedures: Physical examination, ultrasonography. (Physical examination may miss up to two-thirds of cases; ultrasonography can exclude or verify growth restriction in 90% and 80% of cases, respectively.) Intrauterine growth restriction must be distinguished from infants who are constitutionally small for gestational age who are not at increased risk. Asymmetric restrictions in growth argue against a constitutional cause. Early intrauterine insults are more likely to result in symmetric growth restriction; later insults result in asymmetry. Similarly, intrinsic factors generally cause symmetric restriction; extrinsic factors generally cause asymmetric restriction.

Pathologic Findings

Reduced fetal fat stores and reduced overall size compared with that expected for gestational age.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, ultrasonography with biometry. Cessation of tobacco and alcohol use (if present).

Specific Measures: Based on cause and stage of gestation. Early delivery is often necessary (the majority of fetal deaths occur after 36 weeks of gestation). Constitutionally small infants require no intervention.

Diet: No specific dietary changes indicated unless deficiencies identified.

Activity: No restriction except as dictated by maternal disease or fetal condition.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlets AP098 (Special Tests for Monitoring Fetal Health), AP025 (Ultrasound Exams), and AP156 (How Your Baby Grows During Pregnancy).

Drug(s) of Choice

None. Low-dose aspirin therapy has been advocated but has been abandoned.

FOLLOW-UP

Patient Monitoring: Enhanced fetal assessment, antenatal fetal testing (including nonstress testing, biophysical profiles, and contraction stress tests). Patients at risk because of maternal disease should have early assessment of fetal growth (biparietal diameter, head circumference, abdominal circumference, and femur length) with frequent reassessment as the pregnancy progresses. This may need to be done as often as every 2–3 weeks in severe cases. Careful fetal monitoring during labor.

Prevention/Avoidance: Management of maternal disease.

Possible Complications: Progressive deterioration of fetal status and intrauterine fetal demise. (There is an 8- to 10-fold increase in the risk for perinatal mortality; growth restriction is the second most important cause of perinatal morbidity after preterm delivery.) Long-term physical and neurologic sequelae are common. The risk for adverse outcome is proportional to the severity of growth restriction present. The presence of risk factors for intrauterine growth restriction increases the risk for fetal death by 2-fold in growth-restricted fetuses. The most immediate fetal morbidities are birth asphyxia, meconium aspiration, sepsis, hypoglycemia, hypocalcemia, hypothermia, polycythemia, thrombocytopenia, and pulmonary hemorrhage.

Expected Outcome: With early detection, progressive fetal growth can often be achieved, although many pregnancies may require early delivery or other interventions to ensure fetal well-being.

MISCELLANEOUS

ICD-10-CM Code: O36.5990 (Maternal care for other known or suspected poor fetal growth, unspecified trimester, not applicable or unspecified).

REFERENCES

LEVEL I

McKenna D, Tharmaratnam S, Mahsud S, et al. A randomized trial using ultrasound to identify the high-risk fetus in a low-risk population. *Obstet Gynecol*. 2003;101:626.

LEVEL II

Alfirevic Z, Stampalija T, Gyte GM. Fetal and umbilical Doppler ultrasound in high-risk pregnancies. *Cochrane Database Syst Rev*. 2013;(11):CD007529.

Barker ED, McAuliffe FM, Alderdice F, et al. The role of growth trajectories in classifying fetal growth restriction. *Obstet Gynecol*. 2013;122:248.

Grivell RM, Wong L, Bhatia V. Regimens of fetal surveillance for impaired fetal growth. *Cochrane Database Syst Rev*. 2012;(6):CD007113.

Gülmezoglu AM, Hofmeyr GJ. Betamimetics for suspected impaired fetal growth. *Cochrane Database Syst Rev*. 2001;(4):CD000036.

Lees CC, Marlow N, van Wassenaer-Leemhuis A, et al. 2 year neurodevelopmental and intermediate perinatal outcomes in infants with very preterm fetal growth restriction (TRUFFLE): a randomised trial. *Lancet*. 2015;385:2162.

LEVEL III

Alberry M, Soothill P. Management of fetal growth restriction. *Arch Dis Child Fetal Neonatal Ed*. 2007;92:F62.

American College of Obstetricians and Gynecologists. Ultrasonography in pregnancy. ACOG Practice Bulletin No. 101. *Obstet Gynecol*. 2009;113:451.

American College of Obstetricians and Gynecologists. Moderate caffeine consumption during pregnancy. Committee Opinion No. 462. *Obstet Gynecol*. 2010;116:467.

American College of Obstetricians and Gynecologists. Fetal growth restriction. Practice Bulletin No. 134. *Obstet Gynecol*. 2013;121:1122.

Baschat AA. Fetal responses to placental insufficiency: an update. *BJOG*. 2004;111:1031.

Chien PF, Arnott N, Gordon A, et al. How useful is uterine artery Doppler flow velocimetry in the prediction of pre-eclampsia, intrauterine growth retardation and perinatal death? An overview. *BJOG*. 2000;107:196.

Figueras F, Gardosi J. Intrauterine growth restriction: new concepts in antenatal surveillance, diagnosis, and management. *Am J Obstet Gynecol*. 2011;204:288.

Resnik R. Intrauterine growth restriction. *Obstet Gynecol*. 2002;99:490.

232 MULTIPLE GESTATION

INTRODUCTION

Description: Multiple gestation is two or more fetuses that coexist during the same gestation.

Prevalence: Occurs in 3.4% of births in the United States (but prevalence is increasing: 70% since 1980 when the rate was 1 in 53 births); 1/10,000 births for spontaneously occurring triplets. The increase in multiple births is considered to be because of the use of fertility drugs and an increased rate of childbearing in women older than 30 years, who are more likely to conceive multiples. Multiple gestations are responsible for a disproportionate share of perinatal morbidity and mortality. They account for 17% of all preterm births (before 37 weeks of gestation), 23% of early preterm births (before 32 weeks of gestation), 24% of low-birth weight infants (<2500 g), and 26% of very-low-birth weight infants (<1500 g). Hospital costs for women with multiple gestations are on an average 40% higher than those for women with gestational-age-matched singleton pregnancies because of their longer length of stay and increased rate of obstetric complications. Twin pregnancies account for approximately 96% of multiple gestations.

Predominant age: Reproductive age (becomes more common with increasing maternal age; four-fold increase from the age of 15 to 35 years).

Genetics: Dizygotic twins are more common in mothers who are themselves a dizygotic twin.

ETIOLOGY AND PATHOGENESIS

Causes: Monozygotic twins result from the cleavage of a single fertilized ova (4/1000 births). Dizygotic multiple gestations occur when there are multiple ova released and fertilized (naturally or through assisted ovulation. Table 232.1.).

Risk Factors: Ovulation induction (clomiphene therapy: 5%–10% multiple gestation rate), increased maternal age, parity, weight and height, African-American race.

SIGNS AND SYMPTOMS

- Uterus larger than dates
- Multiple fetal heart tones by auscultation or Doppler study

DIAGNOSTIC APPROACH

Differential Diagnosis

- Polyhydramnios
- Molar pregnancy

Table 232.1 Mechanisms of Twin Gestation Formation

Mechanism	Resulting Twin Pregnancy
Two ova, two sperm	Dizygotic (fraternal; 70% of cases)
Single ova, single sperm	Monozygotic ("identical")
• Division within 72 h	• Diamniotic, dichorionic
• Division between 4 and 8 days*	• Diamniotic, monochorionic
• Division between 8 and 13 days	• Monoamniotic, monochorionic
• Division after 10–13 days	• Conjoined twins

*Days after fertilization

Associated Conditions: Prematurity, cord accidents, intrauterine growth restriction (50%–60% of triplet or greater pregnancies), polyhydramnios, increased fetal morbidity and mortality, increased risk of congenital anomalies, abruptio placentae, placenta previa, hypertension, preeclampsia, anemia, acute fatty liver, gestational diabetes, hyperemesis gravidarum, pyelonephritis, cholestasis, thrombosis and embolism, postpartum hemorrhage, increased operative delivery rate. Twin-twin transfusion and cord entanglement for monochorionic twins.

Workup and Evaluation

Laboratory: No special evaluation indicated, although because of the higher incidence of gestational diabetes, screening is of greater importance. Abnormality of gestation-sensitive laboratory tests, such as maternal serum alpha-fetoprotein (MSAFP), is to be expected.

Imaging: Ultrasonography (considered definitive; reduces the rate of undiagnosed multiple gestation from 40% to <5%). Radiographic studies are generally inadequate to establish the presence or health of a multiple pregnancy, making routine use of X-rays undesirable.

Special Tests: Genetic amniocentesis may be considered (twin pregnancies have twice the rate of abnormalities: monozygotic = 2%–10% rate).

Diagnostic Procedures: History, physical examination, ultrasonography.

Pathologic Findings

Examination of the placenta can identify the type of pregnancy.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Adequate nutrition, diminished activity, frequent perinatal visits, monitoring of fetal growth (serial ultrasonography).

Specific Measures: Antenatal testing, prompt intervention for threatened preterm labor. Routine preterm hospitalization is not recommended.

Diet: Increase maternal intake by 300 kcal more than normal for pregnancy. Iron and folic acid supplementation.

Activity: Reduced activity as pregnancy progresses. Bed rest is unproven and carries an increased risk of vascular thromboembolic events.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Booklet AP188 (Multiple Pregnancy); Counseling regarding signs of pre-term labor AP087 (Preterm Labor and Birth), AP004 (How to Tell When Labor Begins).

Drug(s) of Choice

None. Tocolytic agents are often used when premature labor is threatened but are not useful as prophylaxis and are associated with an increased risk for side effects when used in these patients. The use of progestational agents to reduce the risk for preterm birth has been tested only in singleton pregnancies.

FOLLOW-UP

Patient Monitoring: Increased frequency of prenatal evaluations, antenatal fetal testing in late pregnancy. Counseling regarding signs of preterm labor.

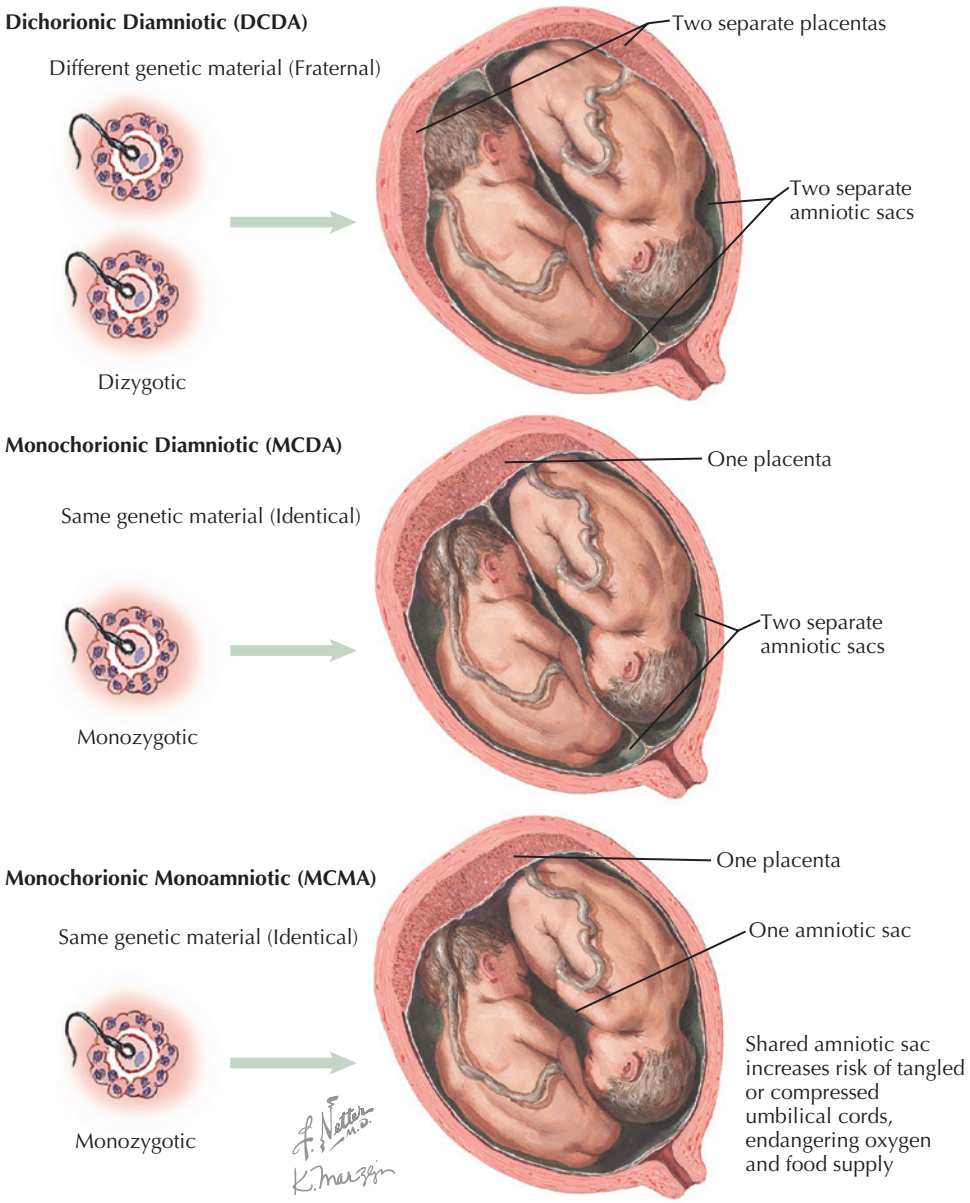


Figure 232.1 Multiple gestation: types of wins

Prevention/Avoidance: None. Some complications of multiple gestation may be reduced by increased surveillance and monitoring.

Possible Complications: Perinatal morbidity and mortality is two to five times higher than for singleton gestations. Preterm delivery (50%) is the most common cause of morbidity or mortality. Other complications: intrauterine growth restriction (12%–47% versus 5%–7% in singletons) or discordant growth, cord accidents, polyhydramnios, congenital anomalies (two times increase), malpresentation. Monozygotic twins have a 1% incidence of monoamniotic sacs that carries a 50% fetal mortality because of cord entanglement or conjoined twins. One-fifth of triplet pregnancies and one-half of quadruplet pregnancies result in at least one child with a major long-term handicap, such as cerebral palsy. Cerebral palsy occurs 17 times more often in triplet pregnancies and more than four times more often in twin pregnancies than in singleton pregnancies. When matched for gestational age at delivery, infants from multifetal pregnancies have a nearly three-fold greater risk of cerebral palsy.

Maternal Complications: Abruptio placenta, placentae previa, preeclampsia, anemia, hyperemesis gravidarum, pyelonephritis, cholestasis, postpartum hemorrhage, increased operative delivery rate.

Expected Outcome: Generally good, although delivery before term is common and there is an increased risk of operative delivery.

MISCELLANEOUS

Other Notes: Up to 50% of twin pregnancies identified in the early weeks will silently abort one fetus (with or without bleeding).

Most Common Presentation: Vertex/vertex (43%), vertex/other (38%), twin A other (19%).

ICD-10-CM Codes: O30.009 (Twin pregnancy, unspecified number of placentas and unspecified number of amniotic sacs, unspecified trimester), O30.109 (Triplet pregnancy, unspecified number of placentas and unspecified number of amniotic sacs, unspecified trimester), and O30.309 (Quadruplet pregnancy, unspecified number of placentas and unspecified number of amniotic sacs, unspecified trimester).

REFERENCES

LEVEL II

Blumenfeld YJ, Momirova V, Rouse DJ, et al. Accuracy of sonographic chorionicity classification in twin gestations. *J Ultrasound Med*. 2014;33:2187.

Crowther CA, Han S. Hospitalisation and bed rest for multiple pregnancy. *Cochrane Database Syst Rev*. 2010;(7):CD000110.

Rafael TJ, Berghella V, Alfirevic Z. Cervical stitch (cerclage) for preventing preterm birth in multiple pregnancy. *Cochrane Database Syst Rev*. 2014;(9):CD009166.

LEVEL III

American College of Obstetricians and Gynecologists. Perinatal risks associated with assisted reproductive technology. ACOG Committee Opinion 324. *Obstet Gynecol*. 2005;106:1143.

American College of Obstetricians and Gynecologists. Prediction and prevention of preterm birth. Practice Bulletin No. 130. *Obstet Gynecol*. 2012;120:964.

American College of Obstetricians and Gynecologists. Multifetal pregnancy reduction. Committee Opinion No. 553. *Obstet Gynecol*. 2013;121:405.

American College of Obstetricians and Gynecologists. Multifetal gestations: twin, triplet, and higher-order multifetal pregnancies. Practice Bulletin No. 144. *Obstet Gynecol*. 2014;123:1118.

Bahtiyar MO, Emery SP, Dashe JS, et al. The North American Fetal Therapy Network consensus statement: prenatal surveillance of uncomplicated monochorionic gestations. *Obstet Gynecol*. 2015;125:118.

Brown JE, Carlson M. Nutrition and multifetal pregnancy. *J Am Diet Assoc*. 2000;100:343.

233 OLIGOHYDRAMNIOS

INTRODUCTION

Description: Oligohydramnios is an abnormal reduction in the amount of amniotic fluid surrounding the fetus. At term, there should be approximately 800 mL of amniotic fluid present. Often defined as a single deepest pocket of amniotic fluid of 2 cm or less or an amniotic fluid index (sum of maximum vertical fluid pocket in each quadrant not containing umbilical cord or fetal extremities) of 5 cm or less on ultrasonography.

Prevalence: Rare in early pregnancy, common in postterm pregnancies (12%–25% at 41 weeks) and during labor following rupture of the fetal membranes.

Predominant Age: Reproductive age.

Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Unknown. Generally associated with a reduction in fetal urine production (renal agenesis, urinary tract obstruction, and fetal death), chronic amniotic leak or preterm rupture of the membranes (35%), maternal disease (hypertension, diabetes, uteroplacental insufficiency, preeclampsia).

Risk Factors: Fetal chromosomal or congenital abnormalities (approximately 50%; see Box 233.1), fetal growth restriction or demise, postterm pregnancy, multiple gestation (twin–twin transfusion), maternal hypertension, diabetes, preeclampsia, and prostaglandin synthetase inhibitors.

SIGNS AND SYMPTOMS

- Uterine size smaller than normal for stage of pregnancy
- Reduced amniotic fluid measured by ultrasonography

DIAGNOSTIC APPROACH

Differential Diagnosis

- Inaccurate gestational age

Box 233.1 ANOMALIES ASSOCIATED WITH OLIGOHYDRAMNIOS

- Amniotic band syndrome
- Cardiac anomalies: tetralogy of Fallot, septal defects
- Central nervous system: holoprosencephaly, meningocele, encephalocele, microcephaly
- Chromosomal: triploidy, trisomy 18, Turner syndrome
- Cloacal dysgenesis
- Cystic hygroma
- Diaphragmatic hernia
- Genitourinary tract: renal agenesis, renal dysplasia, urethral obstruction (posterior urethral valve), bladder exstrophy, Meckel-Gruber syndrome, ureteropelvic junction obstruction, prune-belly syndrome
- Hypothyroidism
- Multiple gestation: twin–twin transfusion syndrome, twin reverse arterial perfusion sequence (TRAP)
- Musculoskeletal: sirenomelia, sacral agenesis, absent radius, facial clefting
- VACTERL (vertebral, anal, cardiac, tracheoesophageal, renal, limb) association

- Intrauterine growth restriction
- Fetal anomalies
- Premature rupture of the membranes

Associated Conditions: Fetal—renal and urinary tract anomalies, intrauterine fetal growth restriction, pulmonary hypoplasia, musculoskeletal defects (clubfoot, amniotic bands, amputations), meconium-stained amniotic fluid. Fetal anomalies are present in 15%–25% of cases. Maternal—chronic disease (diabetes, hypertension).

Workup and Evaluation

Laboratory: No evaluation indicated.

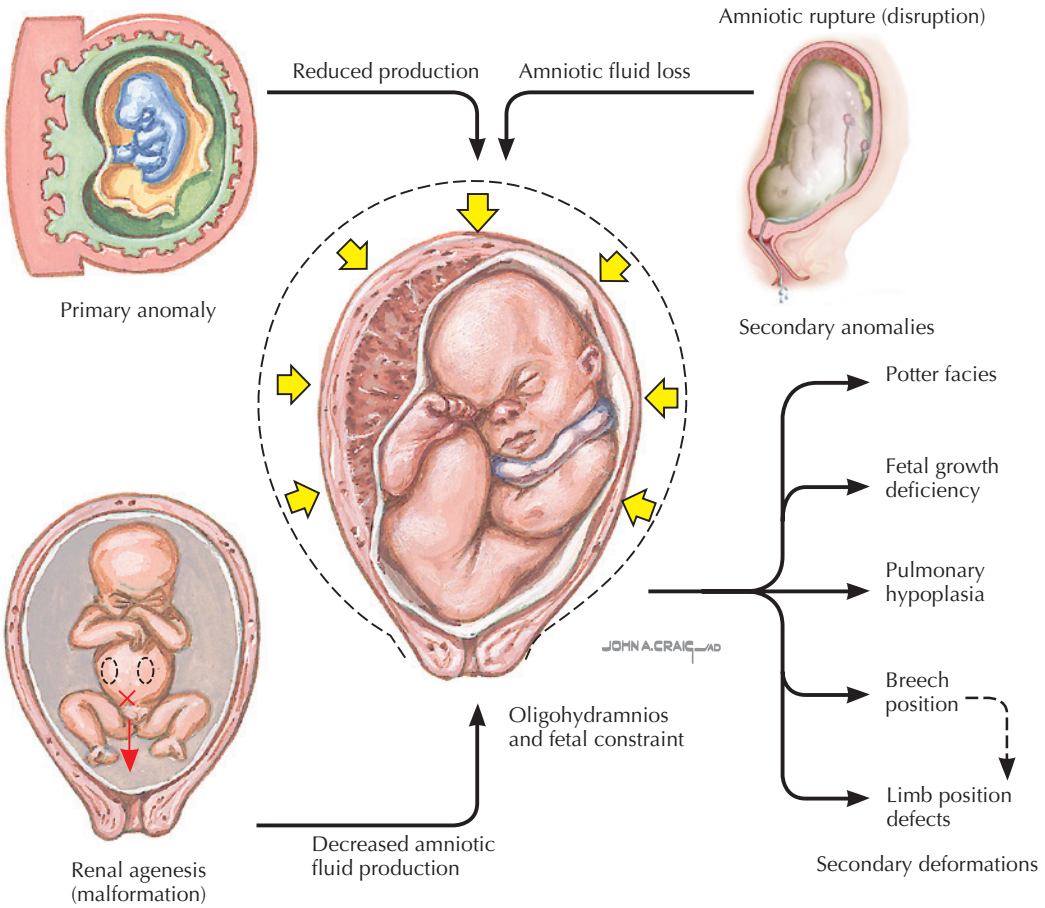


Figure 233.1 Events in oligohydramnios

Imaging: Amniotic fluid index calculated by adding the vertical depths of the largest pockets of amniotic fluid in each quadrant of the uterus (average at term = 12.5 cm, 95th percentile = 21.4). Borderline values should always be rechecked before any intervention is undertaken. Fetal anomalies may also be documented.
Special Tests: Nonstress or contraction stress testing to evaluate fetal health.
Diagnostic Procedures: Physical examination, ultrasonography.

Pathologic Findings

Reduced amniotic fluid (other findings based on the cause).

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation. Mild degrees may be managed expectantly. Maternal oral hydration may improve amniotic fluid volume.
Specific Measures: Amnioinfusion (the introduction of normal saline via an intrauterine catheter placed through the partially dilated cervix during labor) has been used to reduce the incidence of umbilical cord compression during labor. This does not reduce the risk for meconium aspiration.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlets AP069 (What to Expect After Your Due Date), AP025 (Ultrasound Exams), and AP098 (Special Tests for Monitoring Fetal Health).

Drug(s) of Choice

None

FOLLOW-UP

Patient Monitoring: Intensive fetal surveillance is required.
Prevention/Avoidance: None.
Possible Complications: Amniotic band syndrome (including partial limb amputation), pulmonary hypoplasia, premature labor, clubfoot, meconium-stained amniotic fluid, umbilical cord compression, and fetal death. The prognosis is inversely related to gestational age: the earlier the oligohydramnios occurs, the worse the outcome.
Expected Outcome: When oligohydramnios occurs in term or postterm pregnancies, it is associated with fetuses that do not tolerate labor well (five-fold to seven-fold increase in rate of cesarean delivery).

MISCELLANEOUS

ICD-10-CM Codes: 41.00X0 (Oligohydramnios, unspecified trimester, not applicable or unspecified), P01.2 (Newborn [suspected to be] affected by oligohydramnios), and O42.00 (Premature rupture of membranes, onset of labor within 24 hours of rupture, unspecified weeks of gestation).

REFERENCES

LEVEL I

Moses J, Doherty DA, Magann EF, et al. A randomized clinical trial of the intrapartum assessment of amniotic fluid volume: amniotic fluid index versus the single deepest pocket technique. *Am J Obstet Gynecol*. 2004;190:1564.

LEVEL II

Chauhan SP, Sanderson M, Hendrix NW, et al. Perinatal outcome and amniotic fluid index in the antepartum and intrapartum periods: a meta-analysis. *Am J Obstet Gynecol*. 1999;181:1473.

Nabhan AF, Abdelmoula YA. Amniotic fluid index versus single deepest vertical pocket as a screening test for preventing adverse pregnancy outcome. *Cochrane Database Syst Rev*. 2008;(3):CD006593.

Pitt C, Sanchez-Ramos L, Kaunitz AM, et al. Prophylactic amnioinfusion for intrapartum oligohydramnios: a meta-analysis of randomized controlled trials. *Obstet Gynecol*. 2000;96:861.

Sandruck JC, Grobman WA, Gerber SE. The effect of short-term indomethacin therapy on amniotic fluid volume. *Am J Obstet Gynecol*. 2005; 192:1443.

LEVEL III

American College of Obstetricians and Gynecologists. Ultrasonography in pregnancy. ACOG Practice Bulletin No. 101. *Obstet Gynecol*. 2009;113: 451.

American College of Obstetricians and Gynecologists. Antepartum fetal surveillance. Practice Bulletin No. 145. *Obstet Gynecol*. 2014;124: 182.

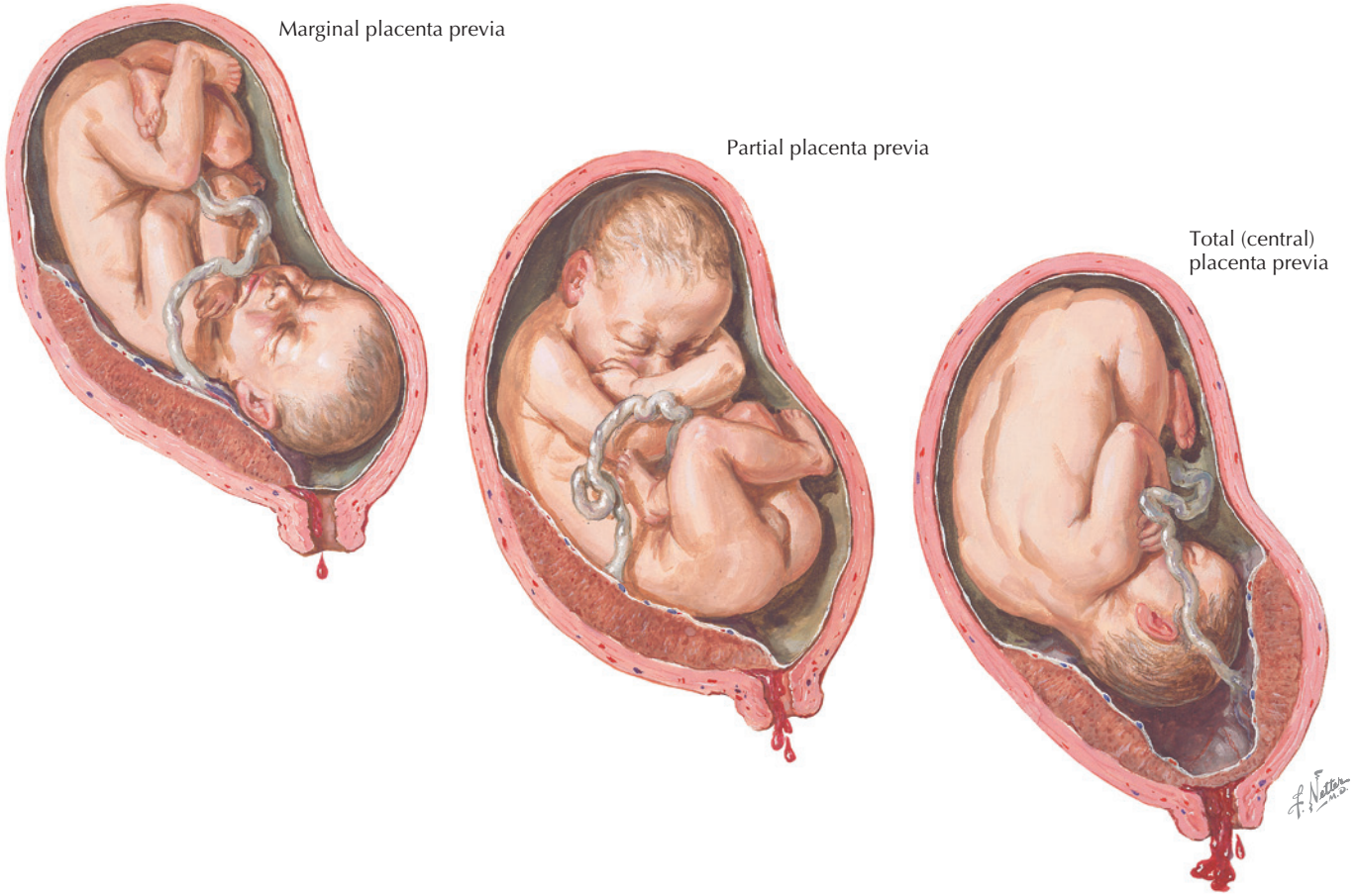


Figure 234.1 Placenta previa

Activity: Bed rest is generally indicated.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlets AP038 (Bleeding During Pregnancy), AP006 (Cesarean Birth), and AP025 (Ultrasound Exams).

Drug(s) of Choice

Fluid and blood product replacement as needed. Steroid therapy to accelerate fetal lung maturation has been advocated for patients remote from term. Oxytocin, methylergonovine maleate (Methergine), and prostaglandin (E_2) therapy to assist with uterine contraction after delivery. Rh (D) immunoglobulin should be administered as indicated in mothers who are Rh negative. If tocolysis is required, $MgSO_4$ is preferred.
Contraindications: β-Mimetic agents should not be used if there is significant maternal blood loss or hypotension.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: Catastrophic maternal hemorrhage, fetal anoxia. Coagulation defects may occur as a result of heavy or prolonged blood loss. Significant bleeding from the placental site may result in maternal compromise, and extensive measures (including hysterectomy) to achieve control must be taken. Preterm delivery represents the greatest source of morbidity for the fetus. Approximately 35% of infants whose mothers require transfusion require transfusion themselves.
Expected Outcome: Generally good—25%–30% of patients complete 36 weeks of gestation despite labor or repetitive bleeding.

MISCELLANEOUS

ICD-10-CM Code: O44.00 (Placenta previa specified as without hemorrhage, unspecified trimester) and O44.10 (Placenta previa with hemorrhage, unspecified trimester).

REFERENCES

LEVEL II

Rosenberg T, Pariente G, Sergienko R, et al. Critical analysis of risk factors and outcome of placenta previa. *Arch Gynecol Obstet*. 2011;284:47.
Rouse DJ, MacPherson C, Landon M, et al. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Blood transfusion and cesarean delivery. *Obstet Gynecol*. 2006;108:891.

LEVEL III

American College of Obstetricians and Gynecologists. Postpartum hemorrhage. ACOG Practice Bulletin No. 76. *Obstet Gynecol*. 2006; 108:1039.
American College of Obstetricians and Gynecologists. Ultrasonography in pregnancy. ACOG Practice Bulletin No. 101. *Obstet Gynecol*. 2009; 113:451.
American College of Obstetricians and Gynecologists. Medically indicated late-preterm and early-term deliveries. Committee Opinion No. 560. American College of Obstetricians and Gynecologists. *Obstet Gynecol*. 2013;121:908.

235 PLACENTAL ABRUPTION

INTRODUCTION

Description: Placental abruption is the premature separation of an otherwise normally implanted placenta before the delivery of the fetus. The term is generally applied only to above 20-week gestations.

Prevalence: 1 in 185–290 deliveries; sufficient to result in fetal death, 1 in 1600 deliveries (approximately 10% of third-trimester fetal demise).

Predominant Age: Reproductive age.

Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Pregnancy-induced hypertension (most common), trauma to the abdomen, decompression of an overdistended uterus (loss of amniotic fluid, delivery of a twin), cocaine use.

Risk Factors: Pregnancy-induced hypertension (most common). Prior abruption: 15% chance if one prior episode, 20%–25% for two or more prior events. Others: smoking more than 1 pack/day (2.5-fold increased risk; risk increases by 40% for each pack/day smoked), multiparity, alcohol abuse, cocaine use, polyhydramnios, maternal hypertension (five-fold increased risk), premature rupture of the membranes, external trauma, uterine leiomyomata or anomalies, increased age or parity, and multiple gestation.

SIGNS AND SYMPTOMS

(Highly variable)

- Vaginal bleeding (not universal; approximately 80%)
- Abdominal, back, or uterine pain (65%)
- Fetal bradycardia or late decelerations (60%)
- Uterine irritability, tachysystole, tetany, elevated baseline intrauterine pressure (20%–40%)
- Maternal hypotension or signs of volume loss (postural hypotension, shock)
- Fetal demise

DIAGNOSTIC APPROACH

Differential Diagnosis

- Uterine rupture
- Placenta or vasa previa
- Bloody show
- Chorioamnionitis
- Other sources of abdominal pain
- Preterm labor

Associated Conditions: Hypertension, preeclampsia, eclampsia, intrauterine fetal demise, postpartum hemorrhage, consumptive coagulopathy, tumultuous labor, premature delivery, and fetal bradycardia. There is a slight increase in the rate of congenital anomalies in these infants.

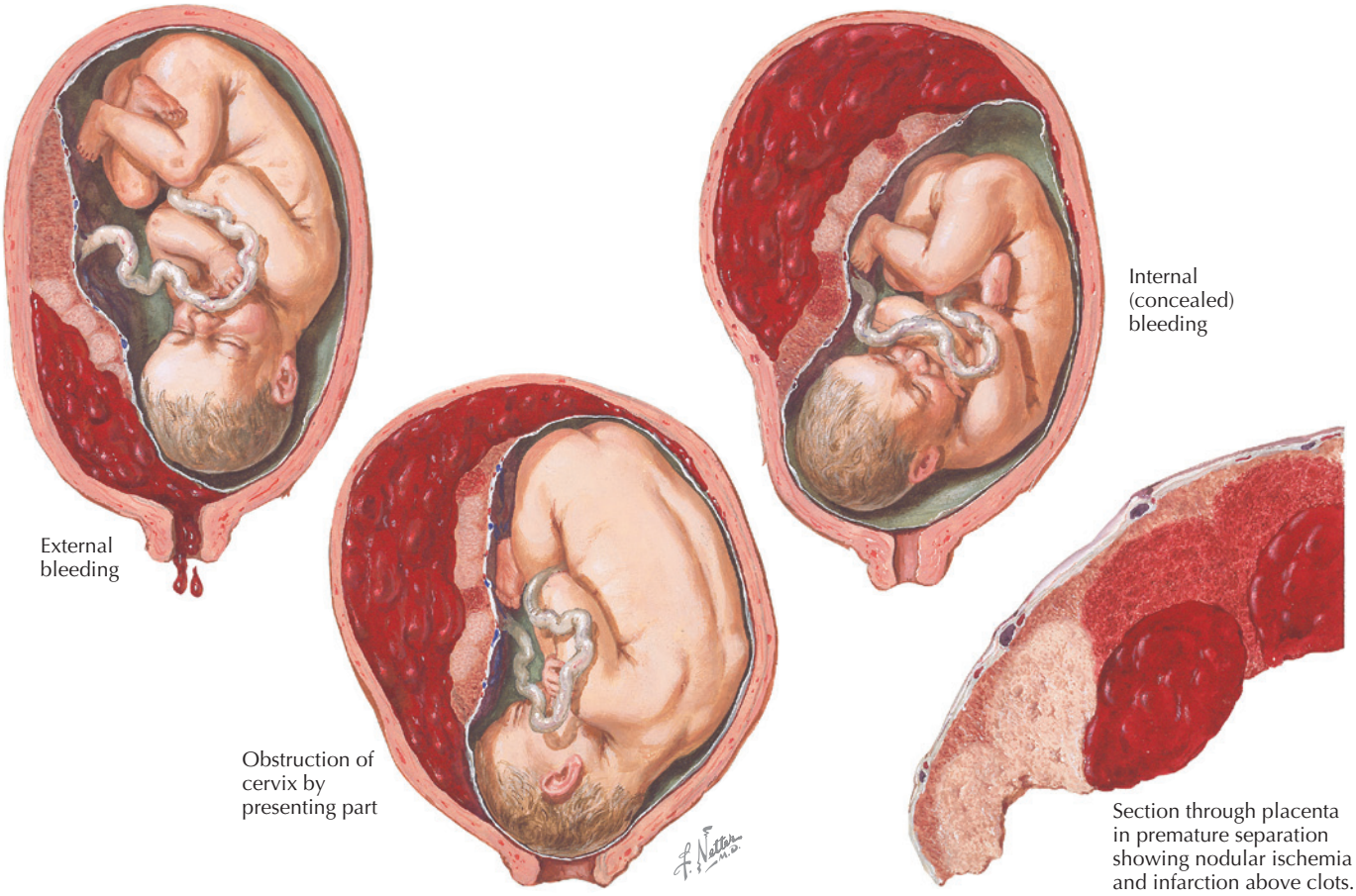


Figure 235.1 Placental abruption

Workup and Evaluation

Laboratory: Complete blood count, assessment of clotting function (bleeding time, prothrombin time, partial thromboplastin time, fibrinogen, D-dimer assay).

Imaging: Ultrasound may show signs of a retroplacental clot or collection of blood, but absence does not rule out abruption.

Special Tests: Kleihauer–Betke test for fetal–maternal transfusion, clot tube to assess possibility of coagulopathy, Apt test to identify fetal blood loss (vasa previa).

Diagnostic Procedures: History, physical examination, and laboratory evaluation. Fetal heart rate and uterine activity monitoring.

Pathologic Findings

Bleeding into the decidua basalia with hematoma formation, leading to progressive separation of the placenta and pressure necrosis. Acute anemia, evidence of clotting activation and consumption, histologically normal placenta.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Prompt evaluation, fluid support, cross-match blood or blood products, Rh typing (if not known).

Specific Measures: Fetal and uterine activity monitoring, monitoring of maternal condition (pulse, blood pressure, pulse oxygenation), expedited delivery when significant separation has occurred.

Diet: Nothing by mouth until the diagnosis is established and the patient's condition is stabilized.

Activity: Bed rest until the diagnosis is established and the patient's condition is stabilized.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP038 (Bleeding During Pregnancy). Often there is insufficient time for any more than the most basic information and counseling.

Drug(s) of Choice

None. Oxygen and intravenous fluid, Rh immune globulin if indicated.

Contraindications: Tocolytics should not be used until a diagnosis is established.

FOLLOW-UP

Patient Monitoring: Close attention to vaginal bleeding, fetal well-being, and maternal circulatory status.

Prevention/Avoidance: Eliminate modifiable risk factors. The risk of recurrence is estimated to be 9%–15%.

Possible Complications: Consumptive coagulopathy, maternal mortality 0.5%–1% and fetal mortality 20%–70% based on the size of the separation, the cause, and gestational age; 10%–15% neurologic sequelae in fetal survivors. Acute renal failure can occur with severe forms of abruption and hypovolemia.

Expected Outcome: Small abruption may be managed conservatively; larger separations may jeopardize mother and fetus and frequently require immediate delivery.

MISCELLANEOUS

ICD-10-CM Code: O45.8X9 (Other premature separation of placenta, unspecified trimester).

REFERENCES

LEVEL II

Ananth CV, Getahun D, Peltier MR, et al. Placental abruption in term and preterm gestations: evidence for heterogeneity in clinical pathways. *Obstet Gynecol*. 2006;107:785.

Ananth CV, Keyes KM, Hamilton A, et al. An international contrast of rates of placental abruption: an age-period-cohort analysis. *PLoS ONE*. 2015;10:e0125246.

Ananth CV, Smulian JC, Vintzileos AM. Incidence of placental abruption in relation to cigarette smoking and hypertensive disorders during pregnancy: a meta-analysis of observational studies. *Obstet Gynecol*. 1999;93:622.

Sibai BM, Lindheimer M, Hauth J, et al. Risk factors for preeclampsia, abruptio placentae, and adverse neonatal outcomes among women with chronic hypertension. National Institute of Child Health and Human Development Network of Maternal-Fetal Medicine Units. *N Engl J Med*. 1998;339:667.

Tikkanen M, Luukkaala T, Gissler M, et al. Decreasing perinatal mortality in placental abruption. *Acta Obstet Gynecol Scand*. 2013;92:298.

LEVEL III

Fretts RC. Etiology and prevention of stillbirth. *Am J Obstet Gynecol*. 2005;193:1923.

Oyelese Y, Ananth CV. Placental abruption. *Obstet Gynecol*. 2006;108:1005.

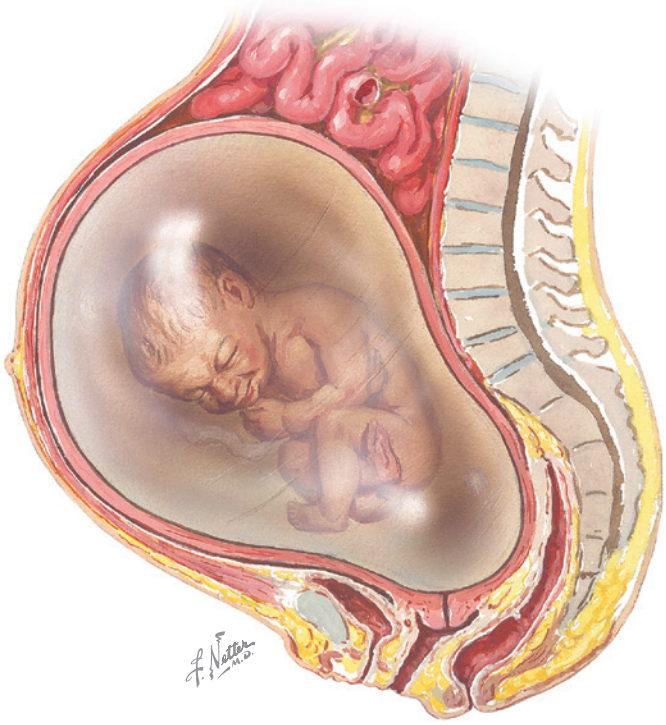


Figure 236.1 Polyhydramnios

Predominant Age: Reproductive age.
Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Idiopathic (40%), maternal diabetes (25%), multiple gestation, fetal anemia, fetal anomalies (50% of patients with severe hydramnios: central nervous system, gastrointestinal tract, chromosomal [trisomy 18 and 21]).
Risk Factors: Fetal anomalies that impair swallowing or alter urine production, multiple gestation (twin–twin transfusion), maternal diabetes, erythroblastosis.

SIGNS AND SYMPTOMS

- Uterine size larger than normal for stage of pregnancy
- Increased amniotic fluid measured by ultrasonography (amniotic fluid index [AFI] >24–25 cm)
- Dyspnea (especially when supine)
- Lower-extremity and vulvar edema
- Premature labor
- Difficulty palpating fetal parts or hearing fetal heart tones

DIAGNOSTIC APPROACH

Differential Diagnosis

- Inaccurate gestational age
- Normal multiple gestation
- Fetal anomalies
- Ascites
- Ovarian cyst

Associated Conditions: Anencephaly, esophageal atresia, prematurity, trisomy 21, fetal anemia, umbilical cord prolapse, fetal malposition, postpartum uterine atony, and placental abruption. When associated with fetal growth restriction, trisomy 18 should be considered. Perinatal mortality is increased by 2- to 5-fold.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: Amniotic fluid index calculated by adding the vertical depths of the largest pockets of amniotic fluid in each quadrant of the uterus (average at term = 12.5 cm, 95th percentile = 21.4). Fetal anomalies may also be documented.
Special Tests: None indicated.
Diagnostic Procedures: Physical examination, ultrasonography.

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation. Mild conditions may be expectantly managed. If dyspnea or abdominal pain is present, hospitalization may be required.
Specific Measures: Indomethacin therapy has been shown to be of help in some patients. Therapeutic amniocentesis may be used to transiently relieve maternal symptoms and in some cases allow prolongation of the gestation. If performed, the rate of withdrawal should be approximately 500 mL/h and limited to 1500–2000 mL total volume. Bed rest, diuretics, and salt and water restrictions are ineffective. Administration of steroids to accelerate fetal lung maturation as indicated by gestational age and risk for preterm delivery.
Diet: No specific dietary changes indicated.
Activity: No restriction except for those imposed by the enlarged uterus.
Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlets AP025 (Ultrasound Exams) and AP098 (Special Tests for Monitoring Fetal Health).

Drug(s) of Choice

Indomethacin 1.5–3.0 mg/kg/day.
Contraindications: Aspirin-sensitive asthma, inflammatory bowel disease, or ulcers.
Precautions: Use of nonsteroidal antiinflammatory agents has been associated with premature closure of the ductus arteriosus. This is generally transient and may be monitored by ultrasonography.

Alternative Drugs

None

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None.
Possible Complications: Premature labor and delivery (40%), abruptio placentae, maternal pulmonary compromise, umbilical cord prolapse, uterine atony.
Expected Outcome: Mild to moderate increases in fluid are not associated with significant risk. Severe polyhydramnios is often associated with significant fetal anomalies. Perinatal mortality is as high as 25%–30% in some studies. In general, the more severe the hydramnios, the greater the fetal risk.

MISCELLANEOUS

ICD-10-CM Codes: P01.3 (Newborn [suspected to be] affected by polyhydramnios).

REFERENCES

LEVEL II

Aviram A, Salzer L, Hiersch L, et al. Association of isolated polyhydramnios at or beyond 34 weeks of gestation and pregnancy outcome. *Obstet Gynecol*. 2015;125:825.

Dashe JS, McIntire DD, Ramus RM, et al. Hydramnios: anomaly prevalence and sonographic detection. *Obstet Gynecol*. 2002;100:134.

Many A, Hill LM, Lazebnik N, et al. The association between polyhydramnios and preterm delivery. *Obstet Gynecol*. 1995;86:389.

Pilliod RA, Page JM, Burwick RM, et al. The risk of fetal death in nonanomalous pregnancies affected by polyhydramnios. *Am J Obstet Gynecol*. 2015;213:410.e1.

Touboul C, Boileau P, Picone O, et al. Outcome of children born out of pregnancies complicated by unexplained polyhydramnios. *BJOG*. 2007; 114:489.

LEVEL III

Abhyankar S, Salvi VS. Indomethacin therapy in hydramnios. *J Postgrad Med*. 2000;46:176.

American College of Obstetricians and Gynecologists. Ultrasonography in pregnancy. ACOG Practice Bulletin No. 101. *Obstet Gynecol*. 2009;113: 451.

American College of Obstetricians and Gynecologists. Antepartum fetal surveillance. Practice Bulletin No. 145. *Obstet Gynecol*. 2014;124:182.

Kramer WB, Van den Veyver IB, Kirshon B. Treatment of polyhydramnios with indomethacin. *Clin Perinatol*. 1994;21:615.

Magann EF, Chauhan SP, Doherty DA, et al. A review of idiopathic hydramnios and pregnancy outcomes. *Obstet Gynecol Surv*. 2007;62:795.

Marino T. Ultrasound abnormalities of the amniotic fluid, membranes, umbilical cord, and placenta. *Obstet Gynecol Clin North Am*. 2004;31:177.

Underwood MA, Gilbert WM, Sherman MP. Amniotic fluid: not just fetal urine anymore. *J Perinatol*. 2005;25:341.

Education Pamphlets AP029 (Breastfeeding Your Baby) and AB005 (You and Your Baby: Prenatal Care, Labor and Delivery, and Postpartum Care).

Drug(s) of Choice

Analgesics. Medication to suppress lactation has little value, and recommendations for its use have been withdrawn.

FOLLOW-UP

Patient Monitoring: Normal health maintenance; watch for possible infection.

Prevention/Avoidance: Gradual weaning reduces engorgement.
Possible Complications: Ductal obstruction and ectasia (uncommon).
Expected Outcome: Generally resolves in 24–48 hours.

MISCELLANEOUS

ICD-10-CM Code: O92.29 (Other disorders of breast associated with pregnancy and the puerperium).

REFERENCES

LEVEL I

Anonymous. Single dose cabergoline versus bromocriptine in inhibition of puerperal lactation: randomised, double blind, multicentre study. European multicentre study group for cabergoline in lactation inhibition. *BMJ*. 1991;302:1367.

Dewhurst CJ, Harrison RF, Biswas S. Inhibition of puerperal lactation. A double blind study of bromocriptine and placebo. *Acta Obstet Gynecol Scand*. 1977;56:327.

Khosravan S, Mohammadzadeh-Moghadam H, Mohammadzadeh F, et al. The effect of hollyhock (Althaea officinalis L) leaf compresses combined with warm and cold compress on breast engorgement in lactating women: a randomized clinical trial. *J Evid Based Complementary Altern Med* 2015;pii:2156587215617106.

LEVEL II

Caballero-Gordo A, Lopez-Nazareno N, Calderay M, et al. Oral cabergoline. Single-dose inhibition of puerperal lactation. *J Reprod Med*. 1991;36:717.

Mangesi L, Dowswell T. Treatments for breast engorgement during lactation. *Cochrane Database Syst Rev*. 2010;(9):CD006946.

Renfrew MJ, Lang S, Martin L, et al. Feeding schedules in hospitals for newborn infants. *Cochrane Database Syst Rev*. 2000;(2):CD000090.

LEVEL III

American College of Obstetricians and Gynecologists. Breastfeeding in underserved women: increasing initiation and continuation of breastfeeding. Committee Opinion No. 570. *Obstet Gynecol*. 2013;122:423.

American College of Obstetricians and Gynecologists. Optimizing support for breastfeeding as part of obstetric practice. Committee Opinion No. 658. *Obstet Gynecol*. 2016;127:e86.

Berens PD. Breast pain: engorgement, nipple pain, and mastitis. *Clin Obstet Gynecol*. 2015;58:902.

Spitz AM, Lee NC, Peterson HB. Treatment for lactation suppression: little progress in one hundred years. *Am J Obstet Gynecol*. 1998;179:1485.

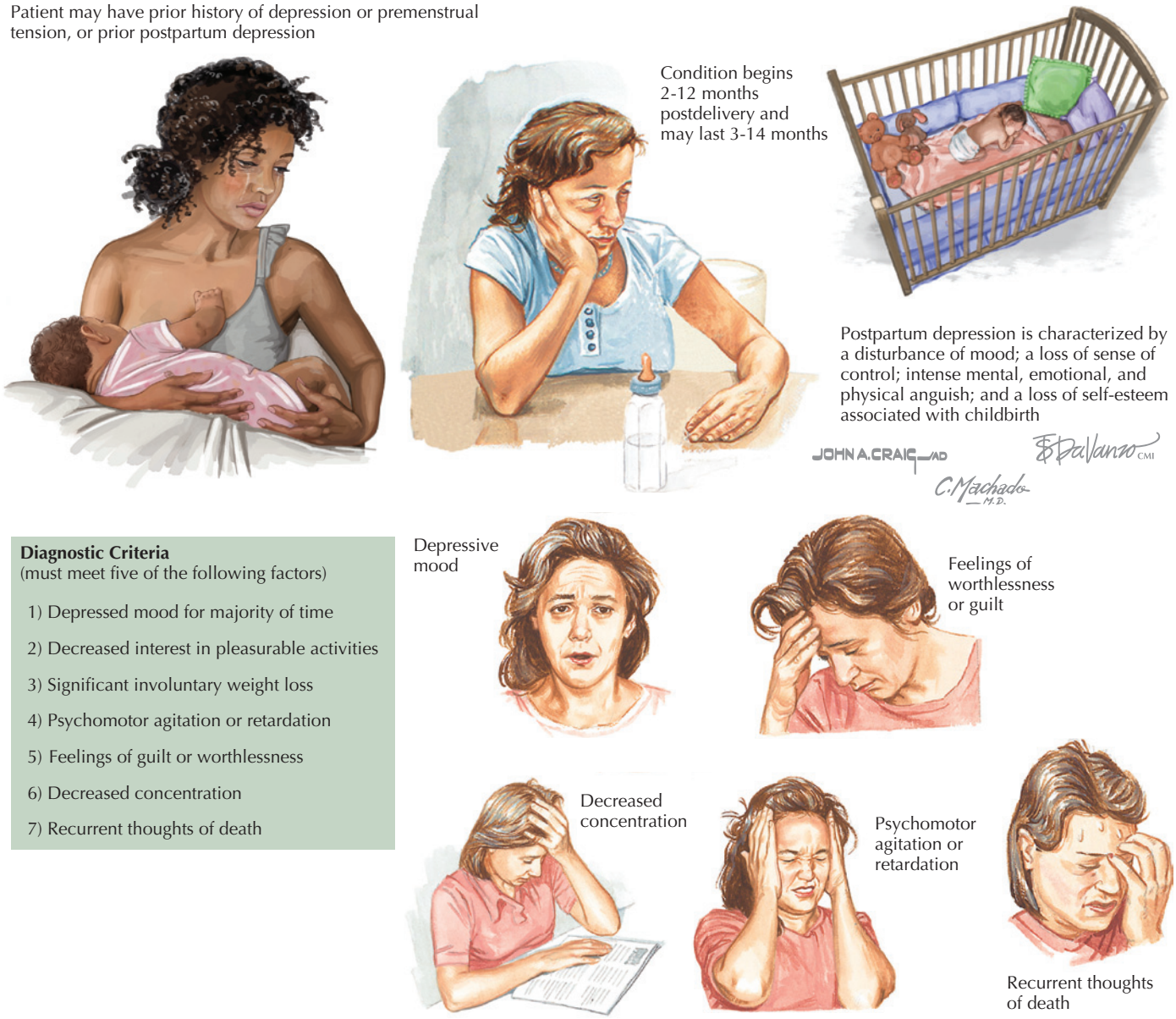


Figure 238.1 Postpartum depression

- Transient mood change ("postpartum blues;" 40%–80% of patients, onset within 2–3 days of delivery with resolution within 2 weeks)
- Substance abuse
- Eating disorders or other nonmood psychiatric disorders

Associated Conditions: None.

Workup and Evaluation

Laboratory: No evaluation indicated.
Imaging: No imaging indicated.
Special Tests: Beck Depression Inventory or the 10-item Edinburgh Postnatal Depression Scale may be used to screen for depression.
Diagnostic Procedures: History, suspicion.

Pathologic Findings

None

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Support, reassurance, and assistance with transition to motherhood. Postpartum exercise has been associated with a lower rate of depression.
Specific Measures: Psychotherapy, antidepressants, electroshock therapy.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: Reassurance, family support. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP091 (Postpartum Depression).

Drug(s) of Choice

- Selective serotonin reuptake inhibitors—fluoxetine (Prozac) 10–40 mg daily, paroxetine (Paxil) 20–50 mg daily, sertraline (Zoloft) 50–150 mg daily.

- For symptoms of appetite loss; loss of energy or interest in pleasure; psychomotor retardation; thoughts of hopelessness, guilt, or suicide—cyclic antidepressants (eg, amitriptyline, clomipramine, doxepin, imipramine, nortriptyline, bupropion, and others).
- For symptoms of increased appetite, sleepiness, high levels of anxiety, phobias, obsessive-compulsive disorders—monoamine oxidase (MAO) inhibitors (eg, isocarboxazid, phenelzine, tranylcypromine).

Contraindications: See individual agents.

Precautions: Use in pregnancy must be carefully weighed versus the potential effects (teratogenic) on the fetus. Some agents are associated with delayed cardiac conduction and disturbances in rhythm. Tricyclic agents, paroxetine, sertraline, and venlafaxine must be tapered over 2–4 weeks to discontinue.

Interactions: Virtually all agents may produce fatal interactions with monoamine oxidase inhibitors or antiarrhythmic medications. Monoamine oxidase inhibitors can also adversely interact with vasoconstrictors, decongestants, meperidine, and other narcotics.

Alternative Therapy

Electroshock therapy may still play a role in the treatment of major depression and mania in those who do not respond to other therapies or are at high risk for suicide.

FOLLOW-UP

Patient Monitoring: Follow up at 6 weeks, 3 and 6 months, and as needed.

Prevention/Avoidance: None for primary occurrence. For those with a history of prior postpartum depression, prophylactic treatment with antidepressants is associated with a reduced rate of recurrence. Postpartum exercise has been associated with a lower rate of depression.

Possible Complications: Progressive loss of function, impaired bonding, marital discord, infanticide or suicide.

Expected Outcome: Generally good response for mild to moderate depression with psychotherapy and medication; severe depression in 45%–65% of patients responds to medication. Recurrence rates are approximately 50% after a single episode, 70% after two episodes, and 90% with three or more episodes.

MISCELLANEOUS

Pregnancy Considerations: Tends to recur with subsequent pregnancies. Prophylactic treatment after delivery should be considered for these patients.

ICD-10-CM Codes: O99.340 (Other mental disorders complicating pregnancy, unspecified trimester), O90.6 (Postpartum mood disturbance), and O90.345 (Other mental disorders complicating the puerperium).

REFERENCES

LEVEL II

Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. *Br J Psychiatry*. 1987;150:782.

Dennis CL, Dowswell T. Psychosocial and psychological interventions for preventing postpartum depression. *Cochrane Database Syst Rev*. 2013;(2):CD001134.

Gavin NI, Gaynes BN, Lohr KN, et al. Perinatal depression: a systematic review of prevalence and incidence. *Obstet Gynecol*. 2005;106:1071.

Gold KJ, Johnson TR. Mothers at risk: maternal mental health outcomes after perinatal death. *Obstet Gynecol*. 2014;123(suppl 1):6S.

O'Connor E, Rossom RC, Henninger M, et al. Primary care screening for and treatment of depression in pregnant and postpartum women: Evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. 2016;315:388.

Pearson RM, Evans J, Kounali D, et al. Maternal depression during pregnancy and the postnatal period: risks and possible mechanisms for offspring depression at age 18 years. *JAMA Psychiatry*. 2013;70:1312.

Viguera AC, Tondo L, Koukopoulos AE, et al. Episodes of mood disorders in 2,252 pregnancies and postpartum periods. *Am J Psychiatry*. 2011;168:1179.

LEVEL III

American College of Obstetricians and Gynecologists. Use of psychiatric medications during pregnancy and lactation. ACOG Practice Bulletin No. 92. *Obstet Gynecol*. 2008;111:1001.

American College of Obstetricians and Gynecologists. Screening for perinatal depression. Committee Opinion No. 630. *Obstet Gynecol*. 2015;125:1268.

Beck A. *Depression Inventory*. Philadelphia: Center for Cognitive Therapy; 1991.

Brockington I. Postpartum psychiatric disorders. *Lancet*. 2004;363:303.

Cohen LS, Wang B, Nonacs R, et al. Treatment of mood disorders during pregnancy and postpartum. *Psychiatr Clin North Am*. 2010;33:273.

Halbreich U. The association between pregnancy processes, preterm delivery, low birth weight, and postpartum depressions—The need for interdisciplinary integration. *Am J Obstet Gynecol*. 2005;193:1312.

Miller LJ. Postpartum depression. *JAMA*. 2002;287:762.

Wisner KL, Chambers C, Sit DK. Postpartum depression: a major public health problem. *JAMA*. 2006;296:2616.

Prevalence: 3%–5% of all births; 250,000 cases per year; results in 150 maternal deaths (10%–15% of all maternal deaths; case-fatality rate of 6.4 deaths per 10,000 cases) and 3000 fetal deaths per year. Overall, hypertensive disease of some type occurs in approximately 12%–22% of pregnancies, and it is directly responsible for 17.6% of maternal deaths in the United States.
Predominant Age: Rare before 20 weeks of gestation. May uncommonly occur between 2 days and 6 weeks after delivery.
Genetics: Multifactorial, runs in families.

ETIOLOGY AND PATHOGENESIS

Causes: Unknown, genetic, endocrine/metabolic (including altered prostaglandin production), uteroplacental ischemia, immunologic all proposed.
Risk Factors: Prior history, body mass index > 26.1, African-American race, nulliparity (1.5-fold to 2-fold increase), older than 35 years (2-fold to 3-fold increase) or younger than 18 years, multifetal pregnancy, fetal hydrops, hydatidiform mole, thrombophilia.

SIGNS AND SYMPTOMS

- Hypertension without proteinuria or edema (gestational hypertension)
- Hypertension with proteinuria or edema (preeclampsia; severe preeclampsia: headache, abdominal pain, visual disturbances, thrombocytopenia, hemoconcentration, pulmonary edema)
- Hypertension and seizures (grand mal type; eclampsia)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Chronic (essential) hypertension
- Transient hypertension
- Chronic renal disease
- Acute or chronic glomerulonephritis
- Coarctation of the aorta
- Cushing's disease
- Systemic lupus erythematosus
- Periarteritis nodosa
- Obesity
- Epilepsy or other neurologic condition associated with seizure
- Encephalitis
- Cerebral aneurysm or tumor
- Lupus cerebritis
- Hysteria

Associated Conditions: Hypertension, heart disease, stroke, placental infarcts, and placental abruption.

Workup and Evaluation

Laboratory: Liver and renal function studies (enzymes, renal clearance, 24-hour urinary protein measurement).
Imaging: Ultrasonography to monitor fetal growth (frequently restricted).
Special Tests: Assessment of fetal lung maturation may be performed, but if maternal disease is severe, management is based on maternal factors and not fetal maturation. Invasive hemodynamic monitoring may be required for patients with the most severe cases.
Diagnostic Procedures: History, physical examination (with blood pressure), urinalysis (or "dipstick"), laboratory assessment. (For diagnostic criteris Table 239.1).

Pathologic Findings

Results of 24-hour urinary protein measurement is >300 mg/24 h, blood pressure >140/90 mm Hg, characteristic renal glomerular lesions (capillary endotheliosis), premature aging of the placenta, increased vascular reactivity, elevated liver enzymes, thrombocytopenia.

Table 239.1 Criteria for Preeclampsia

Preeclampsia (mild)	• Blood pressure ≥ 140 mm Hg systolic or ≥ 90 mm Hg diastolic after 20 weeks of gestation with previously normal blood pressure • Proteinuria (≥0.3 g/24 h) or 1+ dipstick protein
Severe preeclampsia (one or more)	• Blood pressure ≥ 160 mm Hg systolic or ≥ 110 mm Hg diastolic on two occasions at least 6 hours apart, while the patient is on bed rest. • Renal insufficiency (serum creatinine > 1.1 mg/dL or doubling of concentration in the absence of other causes) • Cerebral or visual disturbances • Pulmonary edema or cyanosis • Epigastric or right upper quadrant pain unresponsive to analgesia • Impaired hepatic function (transaminases >2-fold above normal) • Thrombocytopenia (<100,000/μL)

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Aggressive evaluation, frequent prenatal visits, increased fetal surveillance (fetal growth). Hospitalization is required for all but the most benign conditions (mild gestational hypertension, stable chronic hypertension with normal fetal growth). Weekly antenatal testing should be strongly considered.
Specific Measures: The only true treatment for preeclampsia or eclampsia is delivery. Management of symptoms may be used to get both mother and baby into optimal condition for delivery.
Diet: No specific dietary changes indicated except as dictated by labor or other management.
Activity: Bed rest with severe conditions or for women in the process of delivery.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP034 (High Blood Pressure During Pregnancy).

Drug(s) of Choice

Drug treatment of mild preeclampsia has generally been disappointing. Glucocorticoids are often administered to encourage fetal lung maturation. Drugs, such as labetalol or nifedipine, have been administered as part of conservative management protocols. These have generally resulted in prolongation of the gestation and improved fetal outcome but no reduction in catastrophic events such as placental abruption. Magnesium sulfate is often intravenously administered during labor to stabilize blood pressure and reduce the risk of seizures but is not associated with a reduction in fetal morbidity or mortality except below 32 weeks. Intravenous hydralazine may be used to acutely lower blood pressure during labor. Recent data suggest that antiplatelet/nonsteroidal antiinflammatory agents may reduce the risk for recurrence or complications, but definitive data are lacking.
Contraindications: Angiotensin-converting enzyme (ACE) inhibitors are contraindicated in pregnancy.

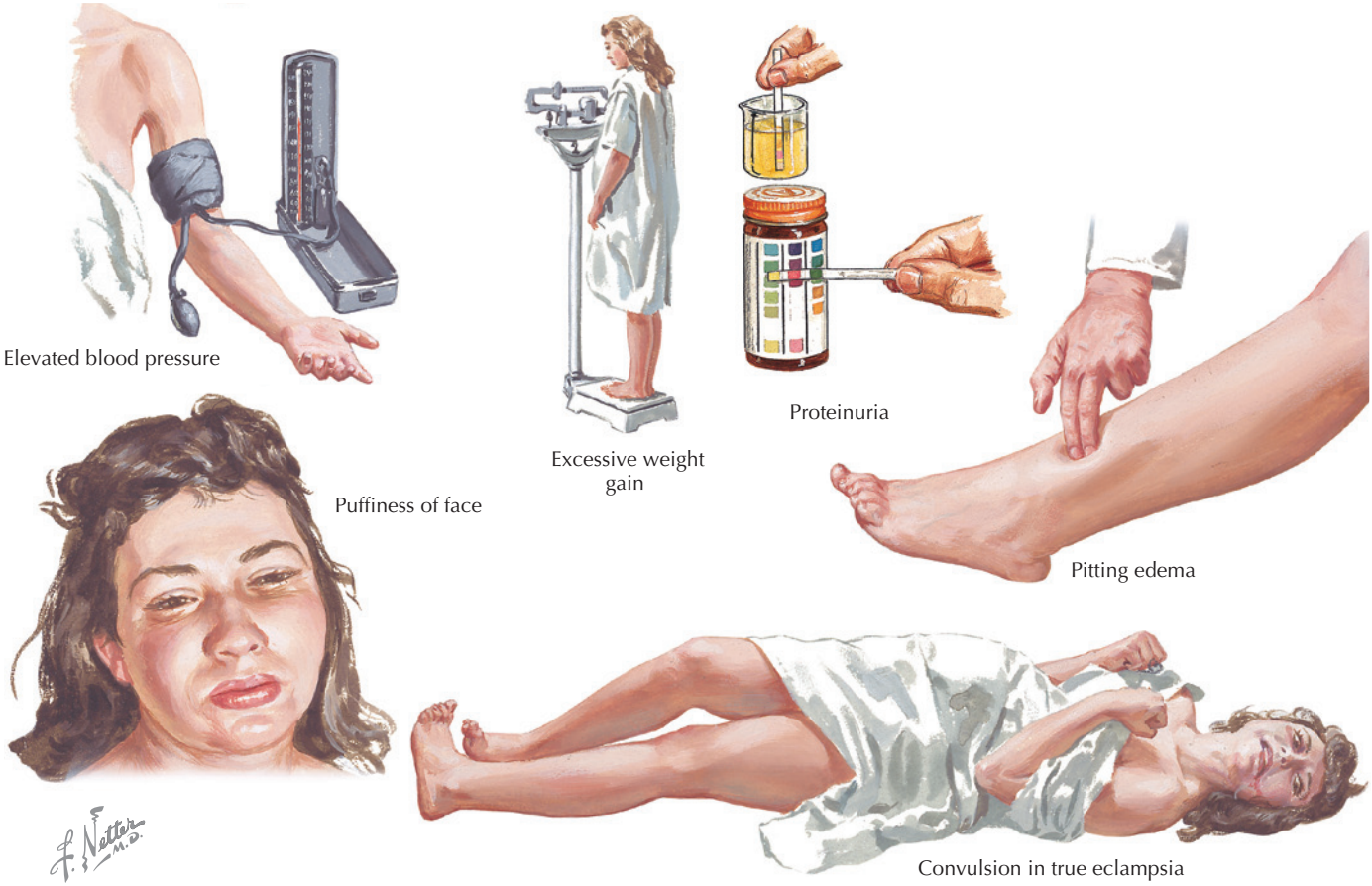


Figure 239.1 Clinical triad of preeclampsia and eclampsia

Precautions: Excessive levels (>10 mEg/L) of magnesium sulfate may result in respiratory paralysis and cardiac arrest.
Interactions: See individual agents.

Alternative Drugs

Verapamil, nimodipine, diazoxide, and nitroglycerin have all been studied or advocated at some time. Prophylactic treatment with aspirin has not been proved to be effective in preventing preeclampsia except in selected patients.

FOLLOW-UP

Patient Monitoring: Increased maternal and fetal surveillance (more frequent prenatal visits, laboratory tests, and ultrasonography evaluations).
Prevention/Avoidance: Early detection and treatment. Aggressive management of preeclampsia may reduce the risk for eclampsia. The use of prophylactic aspirin remains controversial and unproven. The risk for recurrence of preeclampsia in subsequent pregnancies is inversely proportional to the gestational age at which it occurred in the index pregnancy.
Possible Complications: Maternal—cardiac decompensation, stroke, pulmonary edema and respiratory failure, renal failure, seizures and seizure-related injuries, intracranial hemorrhage, coma, death (0.5%–5% mortality). Fetal risk (growth restriction and death) is directly proportional to the level of diastolic blood pressure. The risk to both mother and fetus dramatically increases in eclampsia.
Expected Outcome: Generally, gestational hypertension, preeclampsia, and eclampsia improve after delivery. Eclamptic seizures may occur up to 10 days after delivery but are uncommon beyond 48 hours.

MISCELLANEOUS

ICD-10-CM Codes: O14.00 (Mild to moderate preeclampsia, unspecified trimester), O14.10 (Severe preeclampsia, unspecified trimester), O15.9 (Eclampsia, unspecified as to time period), and O11.9 (Pre-existing hypertension with preeclampsia, unspecified trimester).

REFERENCES

LEVEL I

Broekhuijsen K, van Baaren GJ, van Pampus MG, et al. Immediate delivery versus expectant monitoring for hypertensive disorders of pregnancy between 34 and 37 weeks of gestation (HYPITAT-II): an open-label, randomised controlled trial. *Lancet*. 2015;385:2492.
Magpie Trial Follow-Up Study Collaborative Group. The Magpie Trial: A randomised trial comparing magnesium sulphate with placebo for pre-eclampsia. Outcome for children at 18 months. *BJOG*. 2007;114:289.

Magpie Trial Follow-Up Study Collaborative Group. The Magpie Trial: A randomised trial comparing magnesium sulphate with placebo for pre-eclampsia. Outcome for women at 2 years. *BJOG*. 2007;114:300.

LEVEL II

Al-Safi Z, Imudia AN, Filetti LC, et al. Delayed postpartum preeclampsia and eclampsia: demographics, clinical course, and complications. *Obstet Gynecol*. 2011;118:1102.

Ananth CV, Keyes KM, Wapner RJ. Pre-eclampsia rates in the United States, 1980-2010: age-period-cohort analysis. *BMJ*. 2013;347:f6564.

Askie LM, Duley L, Henderson-Smart DJ, et al.; PARIS Collaborative Group. Antiplatelet agents for prevention of preeclampsia: a meta-analysis of individual patient data. *Lancet*. 2007;369:1791.

Conde-Agudelo A, Villar J, Lindheimer M. World Health Organization systematic review of screening tests for preeclampsia. *Obstet Gynecol*. 2004;104:1367.

Duley L, Matar HE, Almerie MQ, et al. Alternative magnesium sulphate regimens for women with pre-eclampsia and eclampsia. *Cochrane Database Syst Rev*. 2010;CD007388.

Harmon QE, Huang L, Umbach DM, et al. Risk of fetal death with pre-eclampsia. *Obstet Gynecol*. 2015;125:628.

Li YH, Novikova N. Pulmonary artery flow catheters for directing management in pre-eclampsia. *Cochrane Database Syst Rev*. 2012;CD008882.

Lisonkova S, Sabr Y, Mayer C, et al. Maternal morbidity associated with early-onset and late-onset preeclampsia. *Obstet Gynecol*. 2014;124:771.

LEVEL III

American College of Obstetricians and Gynecologists. Hypertension in pregnancy: executive summary. *Obstet Gynecol*. 2013;122:1122.

American College of Obstetricians and Gynecologists. Emergent therapy for acute-onset, severe hypertension during pregnancy and the postpartum period. Committee Opinion No. 623. *Obstet Gynecol*. 2015;125:521.

American College of Obstetricians and Gynecologists. First-trimester risk assessment for early-onset preeclampsia. Committee Opinion No. 638. *Obstet Gynecol*. 2015;126:e25.

American College of Obstetricians and Gynecologists. Magnesium sulfate use in obstetrics. Committee Opinion No. 652. *Obstet Gynecol*. 2016;127:e52.

American College of Obstetricians and Gynecologists, Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. *Obstet Gynecol*. 2013;122:1122.

Brown MA, Mackenzie C, Dunsmuir W, et al. Can we predict recurrence of pre-eclampsia or gestational hypertension? *BJOG*. 2007;114:984.

Redman C. Hypertension in pregnancy: the NICE guidelines. *Heart*. 2011;97:1967.

Sibai BM. Diagnosis, prevention, and management of eclampsia. *Obstet Gynecol*. 2005;105:402.

Sibai BM. Imitators of severe preeclampsia. *Obstet Gynecol*. 2007;109:956.

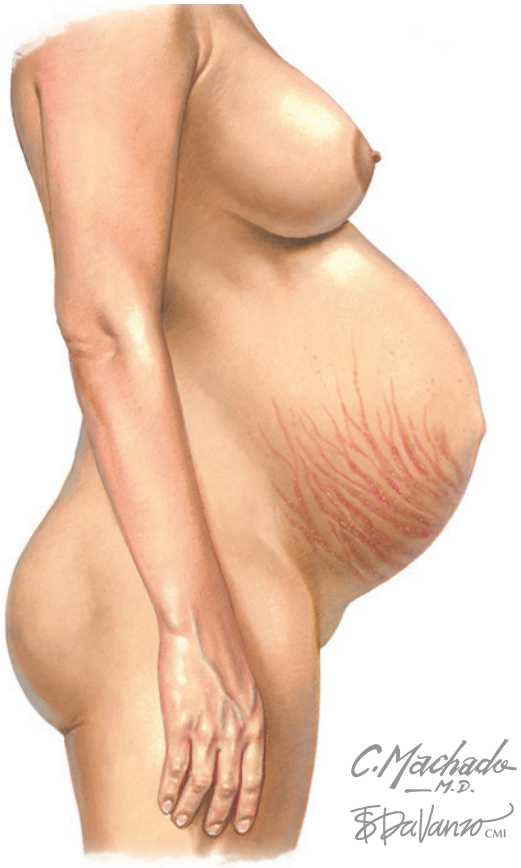


Figure 240.1 PUPPP on abdomen within striae

may be present. C3 and IgM or IgA deposits at the dermoepidermal junction or around blood vessels are found in approximately one-third of cases.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Skin hygiene, topical moisturizing creams or aqueous or emollient ointments, cold shower or iced cloths, mild sedation at night and the wearing of cotton gloves may reduce itching and skin damage.
Specific Measures: Topical corticosteroids to control itching.
Diet: No restriction.
Activity: No restriction, activity encouraged.
Patient Education: Reassurance.

Drug(s) of Choice

- Betamethasone dipropionate 0.05% spray or lotion, triamcinolone acetonide 0.025%–0.1% spray, cream, or ointment.
- Nonsedating oral antihistamines may also be used.
- Systemic corticosteroids (prednisone 0.5 mg/kg/day) may occasionally be needed.

Contraindications: See individual agents.
Precautions: Total dosage should be limited—see individual agents for maximum recommended dosage.

FOLLOW-UP

Patient Monitoring: Normal health maintenance.
Prevention/Avoidance: None known. Does not tend to recur in subsequent pregnancies.
Possible Complications: Skin breakdown or secondary infections from scratching.
Expected Outcome: Itching may worsen immediately following delivery, but most often resolves within 15 days. No long-term risk for either the mother or child.

MISCELLANEOUS

Pregnancy Considerations: No direct effect on pregnancy.
ICD-10-CM Codes: O26.86 (Pruritic urticarial papules and plaques of pregnancy [PUPPP])

REFERENCES

LEVEL II

Aronson IK, Bond S, Fiedler VC, et al. Pruritic urticarial papules and plaques of pregnancy: clinical and immunopathologic observations in 57 patients. *J Am Acad Dermatol*. 1998;39:933.

Ohel I, Levy A, Silberstein T, et al. Pregnancy outcome of patients with pruritic urticarial papules and plaques of pregnancy. *J Matern Fetal Neonatal Med*. 2006;19:305.

LEVEL III

Bechtel MA, Plotner A. Dermatoses of pregnancy. *Clin Obstet Gynecol*. 2015;58:104.

Giugliano E, Cagnazzo E, Servello T, et al. Pruritic urticarial papules and plaques of pregnancy. *J Obstet Gynaecol*. 2012;32:301.

Lawley TJ, Hertz KC, Wade TR, et al. Pruritic urticarial papules and plaques of pregnancy. *JAMA*. 1979;241:1696.

Shornick JK. Dermatoses of pregnancy. *Semin Cutan Med Surg*. 1998;17:172.

Vaughan Jones SA, Black MM. Pregnancy dermatoses. *J Am Acad Dermatol*. 1999;40:233.

Woolf RT, Abdul-Wahab A. A pruritic rash in pregnancy. *BMJ*. 2011;343:d5325.

PUERPERAL INFECTION

241

INTRODUCTION

Description: Although the term *puerperal infection* can be used to describe any infection during or after labor, it generally applies to the infection of the uterus and surrounding tissues after delivery. This can vary from mild to life-threatening severities. Some of the most severe infections may appear within hours of delivery and are often opportunistic and not associated with reliable risk factors. Vigilance and aggressive diagnosis and treatment are required.

Prevalence: Estimated to occur in 1%–3% of vaginal deliveries; approximately 15% if chorioamnionitis is present during labor. Following cesarean delivery: 2%–10% if antibiotic prophylaxis is administered during delivery and 50%–90% without antibiotic prophylaxis in some series.

Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Colonization and infection of the tissues of the uterus, peritoneum, or surrounding organs; typically, a polymicrobial infection (70%) that involves a mixture of two to three aerobes and anaerobes. The most common organisms are group B streptococci; other facultative streptococci; *Gardnerella vaginalis*; and *Escherichia coli*, *Bacteroides*, and *Peptostreptococcus* species. Infection by clostridia or group A streptococci may result in rapidly progressive soft-tissue (subcutaneous tissue, muscle, or myometrial) infection. Abscesses usually contain both aerobic and anaerobic bacteria such as *Bacteroides* species (*Bacteroides bivius, B. disiens*, or *B. fragilis*). Approximately 50% of ascending uterine infections involve *Chlamydia trachomatis*.

Risk Factors: Cesarean delivery (10- to 20-fold increase), invasive procedures during labor, prolonged rupture of the membranes, prolonged labor, multiple vaginal examinations, retained placental fragments, manual removal of the placenta, urinary catheter, bacterial vaginosis, intravenous line(s), low socioeconomic or nutritional status, maternal age, anemia, and chronic disease (diabetes).

SIGNS AND SYMPTOMS

- Fever (90%; >38.5°C by 24 hours) and tachycardia (often developing rapidly after delivery)
- Uterine tenderness (may be absent)
- Signs of septic or cardiovascular shock (hypotension, anxiety, disorientation, prostration)
- Impaired renal function (<20 mL/h urine production)
- Altered white blood count (<1000 or ≥25,000)
- Hemolysis or hemoconcentration
- Uterine subinvolution and excessive bleeding
- The United States Joint Commission on Maternal Welfare defines postpartum febrile morbidity as an oral temperature of ≥38.0°C (≥100.4°F) on any 2 of the first 10 days postpartum, exclusive of the first 24 hours.

DIAGNOSTIC APPROACH

Differential Diagnosis

- Urinary tract infections, including pyelonephritis (5% of patients; classical signs are routinely absent, urinalysis shows large numbers of white blood cells, and cultures are positive)
- Wound infection
- Atelectasis or pneumonitis
- Infection in intravenous line or site, contaminated fluids
- Disturbed abscess (old tubo-ovarian or appendiceal abscess)
- Septic thrombophlebitis
- Necrotizing fasciitis
- Transfusion reaction (when applicable)
- Amniotic fluid or pulmonary embolism
- Cardiogenic shock (drugs, cardiac disease, aortic dissection)
- Toxic shock syndrome
- Mastitis (2% of patients)

Associated Conditions: Septic shock, adult respiratory distress syndrome, acute renal failure, and disseminated intravascular coagulation.

Workup and Evaluation

Laboratory: Complete blood count, endometrial culture obtained by protected swab (if amniotic fluid or endometrial culture obtained within 24 hours of delivery is not available). Blood cultures are positive in 15%–25% of patients who are febrile but do not reflect the severity of the infection. Tissue culture (direct or by needle aspiration, when wound infections is suspected) and Gram stain.

Imaging: Ultrasonography may be useful in evaluating the possibility of pelvic abscess or gas formation. Computed tomography (CT) and magnetic resonance imaging (MRI) are useful for a more wide-ranging assessment.

Special Tests: Frozen-section histopathologic evaluation may be useful if necrotizing fasciitis is suspected.

Diagnostic Procedures: History, physical examination, cultures. The diagnosis is generally clinical.

Pathologic Findings

Evidence of inflammation and/or necrosis (based on tissue involved and severity of infections); edema and hyperemia with marked inflammatory infiltrates of the endometrial glands, primarily by neutrophils. This may invade the myometrium and parametrium with areas of necrosis and thrombosis. Endometritis is defined as five or more neutrophils per 400 high-power fields in the superficial endometrium and one or more plasma cells per 120 high-power fields in the endometrial stroma.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Evaluation, fluid replacement or resuscitation, antipyretics and analgesics (after a diagnosis has been established). Close monitoring, including intensive care, may be required when infection is severe. Consultation with an infectious-disease specialist may be desirable. Low-grade (<38°C) or intermittent fevers may not require treatment when present in the first 24 hours.

Specific Measures: Aggressive antibiotic therapy. Based on response, removal of infected products (if present), surgical exploration, abscess drainage (percutaneous or open), debridement, or hysterectomy may be required. Virtually all postpartum septic shock is caused by surgically treatable processes. Because of the expanded blood and tissue volume at and after delivery, antibiotic dosages must be increased by 40% over those used outside of pregnancy.

Diet: For patients who are acutely ill, nothing by mouth until condition is stabilized. For other patients, no specific dietary changes indicated.

Activity: Bed rest until patient's condition is stable, then a progressive return to normal activity.

Patient Education: Reassurance. American College of Obstetricians and Gynecologists Patient Education Pamphlet AP006 (Cesarean Birth).

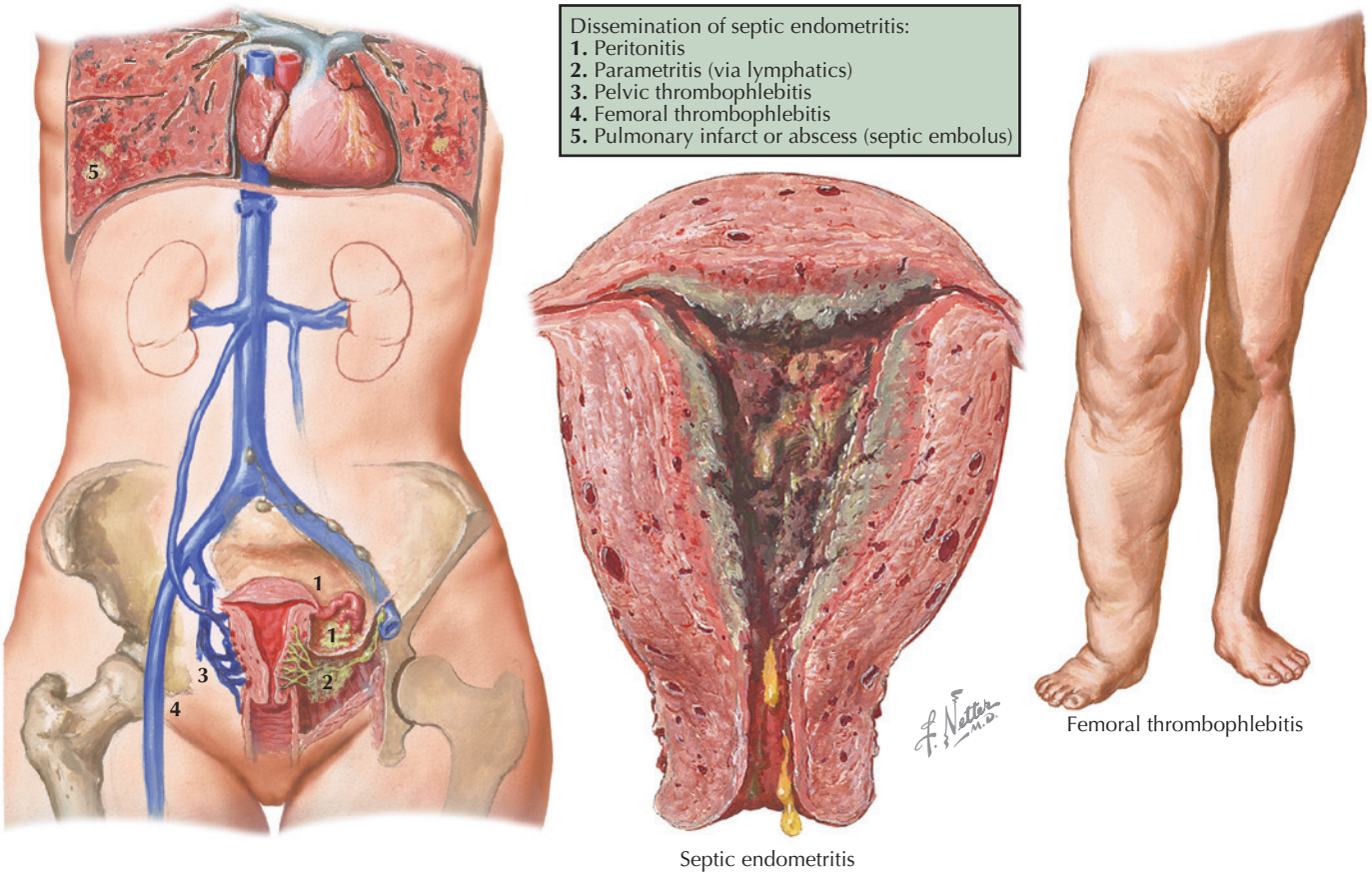


Figure 241.1 Puerperal infection

Drug(s) of Choice

Antibiotics should be administered to provide protection against gram-negative facultative and anaerobic bacteria. Moderate infections require double antibiotic treatment (clindamycin/gentamicin, 90%–97% effective); severe infections should be treated with triple therapy: an aminoglycoside or first-generation cephalosporin (for facultative bacteria); clindamycin, imipenem-cilastatin, or metronidazole (anaerobic bacteria); and penicillin or ampicillin (clostridia and synergistic action with aminoglycosides on enterococci). β-Lactam antibiotics (penicillin or cephalosporin) should be administered in dosages of 8–12 g/day.

Contraindications: See individual agents.

Precautions: Antibiotic dosages must be increased by up to 40% because of the altered physiologic state of pregnancy.

Interactions: See individual agents.

FOLLOW-UP

Patient Monitoring: When severe infections are present, intensive monitoring (including placement in an intensive care unit) may be required. This may include central venous access and monitoring, pulse oximetry, and careful (frequent if not continuous) blood pressure monitoring.

Prevention/Avoidance: Careful attention should be given to antisepsis, reduced numbers of vaginal examinations when the amniotic membranes have been ruptured, careful tissue handling during operative procedures, use of prophylactic antibiotics when risk factors are identified. Changing intravenous sites every 48 hours reduces the risk of infection. There is no evidence to support a role for vaginal antisepsis (chlorhexidine or similar) during labor, though benefit has been shown for its use prior to cesarean delivery. Parenteral prophylaxis at the time of cesarean delivery is appropriate. There are insufficient data to evaluate the role of prophylactic antibiotics after manual removal of the placenta or operative delivery.

Possible Complications: Progression of infection, abscess formation, septic thrombophlebitis, septic shock, adult respiratory distress syndrome, renal failure, cardiovascular collapse, death. If septic shock occurs, mortality rates of 20%–30% are common. Coagulopathy may develop. Necrotizing fasciitis is possible.

Expected Outcome: With timely diagnosis and appropriate therapy a complete recovery with no long-term sequelae should be expected. Approximately 90% of patients rapidly respond to antibiotic therapy (and/or percutaneous drainage of abscesses).

MISCELLANEOUS

ICD-10-CM Code: O86.89 (Other specified puerperal infections).

REFERENCES

LEVEL II

Cahill AG, Duffy CR, Odibo AO, et al. Number of cervical examinations and risk of intrapartum maternal fever. *Obstet Gynecol*. 2012;119:1096.

Chongsomchai C, Lumbiganon P, Laopaiboon M. Prophylactic antibiotics for manual removal of retained placenta in vaginal birth. *Cochrane Database Syst Rev*. 2006;CD004904.

Hopkins L, Smaill F. Antibiotic regimens for management of intra-amniotic infection. *Cochrane Database Syst Rev*. 2002;CD003254.

Liabsuetrakul T, Choobun T, Peeyananjarassri K, et al. Antibiotic prophylaxis for operative vaginal delivery. *Cochrane Database Syst Rev*. 2004; CD004455.

Lumbiganon P, Thinkhamrop J, Thinkhamrop B, et al. Vaginal chlorhexidine during labour for preventing maternal and neonatal infections (excluding Group B Streptococcal and HIV). *Cochrane Database Syst Rev*. 2004;CD004070.

Mackeen AD, Packard RE, Ota E, et al. Antibiotic regimens for postpartum endometritis. *Cochrane Database Syst Rev*. 2015;(2):CD001067.

Meaney-Delman D, Bartlett LA, Gravett MG, et al. Oral and intramuscular treatment options for early postpartum endometritis in low-resource settings: a systematic review. *Obstet Gynecol*. 2015;125:789.

Smaill FM, Gyte GM. Antibiotic prophylaxis versus no prophylaxis for preventing infection after cesarean section. *Cochrane Database Syst Rev*. 2010;CD007482

LEVEL III

American College of Obstetricians and Gynecologists. Prevention of early-onset group B streptococcal disease in newborns. Committee Opinion No. 485. *Obstet Gynecol*. 2011;117:1019.

American College of Obstetricians and Gynecologists. Use of prophylactic antibiotics in labor and delivery. Practice Bulletin No. 120. *Obstet Gynecol*. 2011;117:1472.

American College of Obstetricians and Gynecologists. Solutions for surgical preparation of the vagina. Committee Opinion No. 571. *Obstet Gynecol*. 2013;122:718.

American College of Obstetricians and Gynecologists. Management of preterm labor. Practice Bulletin No. 159. *Obstet Gynecol*. 2016;127:e29.

American College of Obstetricians and Gynecologists. Premature rupture of membranes. Practice Bulletin No. 160. *Obstet Gynecol*. 2016;127:e39.

Faro S. Postpartum endometritis. *Clin Perinatol*. 2005;32:803.

Maharaj D. Puerperal pyrexia: a review. Part I. *Obstet Gynecol Surv*. 2007; 62:393.

Maharaj D. Puerperal pyrexia: a review. Part II. *Obstet Gynecol Surv*. 2007; 62:400.

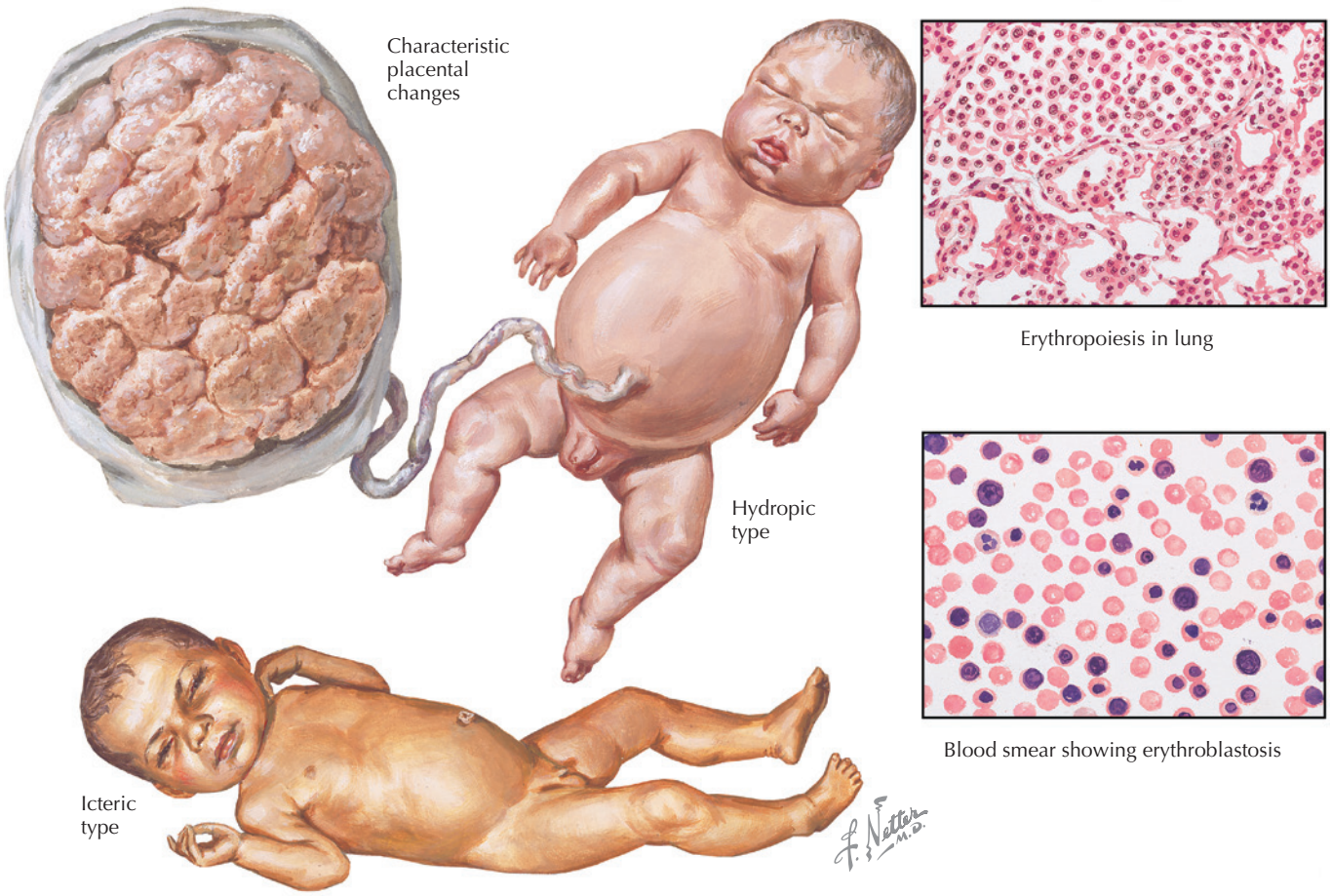


Figure 242.1 Rh incompatibility

Specific Measures: When antibody titers are ≤1:8, no intervention is required. When titers are ≥1:16 in albumin or 1:32 by an indirect Coombs test, amniocentesis or umbilical cord blood sampling should be considered. In severely affected fetuses, intrauterine transfusion may be required.
Diet: No specific dietary changes indicated.
Activity: No restriction.
Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP027 (The Rh Factor: How It Can Affect Your Pregnancy)

Drug(s) of Choice

None, if isoimmunization has occurred. Prophylaxis (with Rh-positive father): D immunoglobulin—50 mcg for miscarriage before 13 weeks of gestation or after chorionic villus sampling; 300 mcg after amniocentesis or ectopic pregnancy; at 28–30 weeks of gestation in unsensitized patients or after normal delivery (20 mcg/1 mL of D-positive cells [2 mL of whole blood] infused or lost into the patient's circulation).
Contraindications: Patients who are already sensitized to the D antigen should not receive D immunoglobulin.

FOLLOW-UP

Patient Monitoring: Normal prenatal care with increased surveillance of fetal growth and health.
Prevention/Avoidance: All patients should have their Rh type established and be tested for isoimmunization (indirect Coombs test) at the first prenatal visit. Those who are Rh negative should receive D immunoglobulin after delivery, amniocentesis, fetal demise, miscarriage, ectopic pregnancy, or any other time exposure to Rh-positive cells may have occurred. Prophylactic administration between 28 and 30 weeks of gestation is also standard.
Possible Complications: Isoimmunization with subsequent immune damage to fetal red cells leading to lysis, anemia, hydrops, and fetal death.
Expected Outcome: With prophylaxis, the risk for isoimmunization is estimated to be 0.3%.

MISCELLANEOUS

ICD-10-CM Code: O36.0190 (Maternal care for anti-D [Rh] antibodies, unspecified trimester, not applicable or unspecified).

REFERENCES

LEVEL II

Geifman-Holtzman O, Grotegut CA, Gaughan JP. Diagnostic accuracy of noninvasive fetal Rh genotyping from maternal blood—A meta-analysis. *Am J Obstet Gynecol*. 2006;195:1163.

Moise KJ Jr, Argoti PS. Management and prevention of red cell alloimmunization in pregnancy: a systematic review. *Obstet Gynecol*. 2012;120: 1132.

LEVEL III

American College of Obstetricians and Gynecologists. Prevention of Rh D isoimmunization. ACOG Practice Bulletin 4. Washington, DC, ACOG, 1999.

American College of Obstetricians and Gynecologists. Management of alloimmunization during pregnancy. ACOG Practice Bulletin 75. *Obstet Gynecol*. 2006;108:457.

Bianchi DW, Avent ND, Costa JM, et al. Noninvasive prenatal diagnosis of fetal Rhesus D: ready for Prime(r) Time. *Obstet Gynecol*. 2005;106:841.

Jabara S, Barnhart KT. Is Rh immune globulin needed in early first-trimester abortion? A review. *Am J Obstet Gynecol*. 2003;188:623.

Jones ML, Wray J, Wight J, et al. A review of the clinical effectiveness of routine antenatal anti-D prophylaxis for rhesus-negative women who are pregnant. *BJOG*. 2004;111:892.

Moise KJ Jr. Management of rhesus alloimmunization in pregnancy. *Obstet Gynecol*. 2002;100:600.

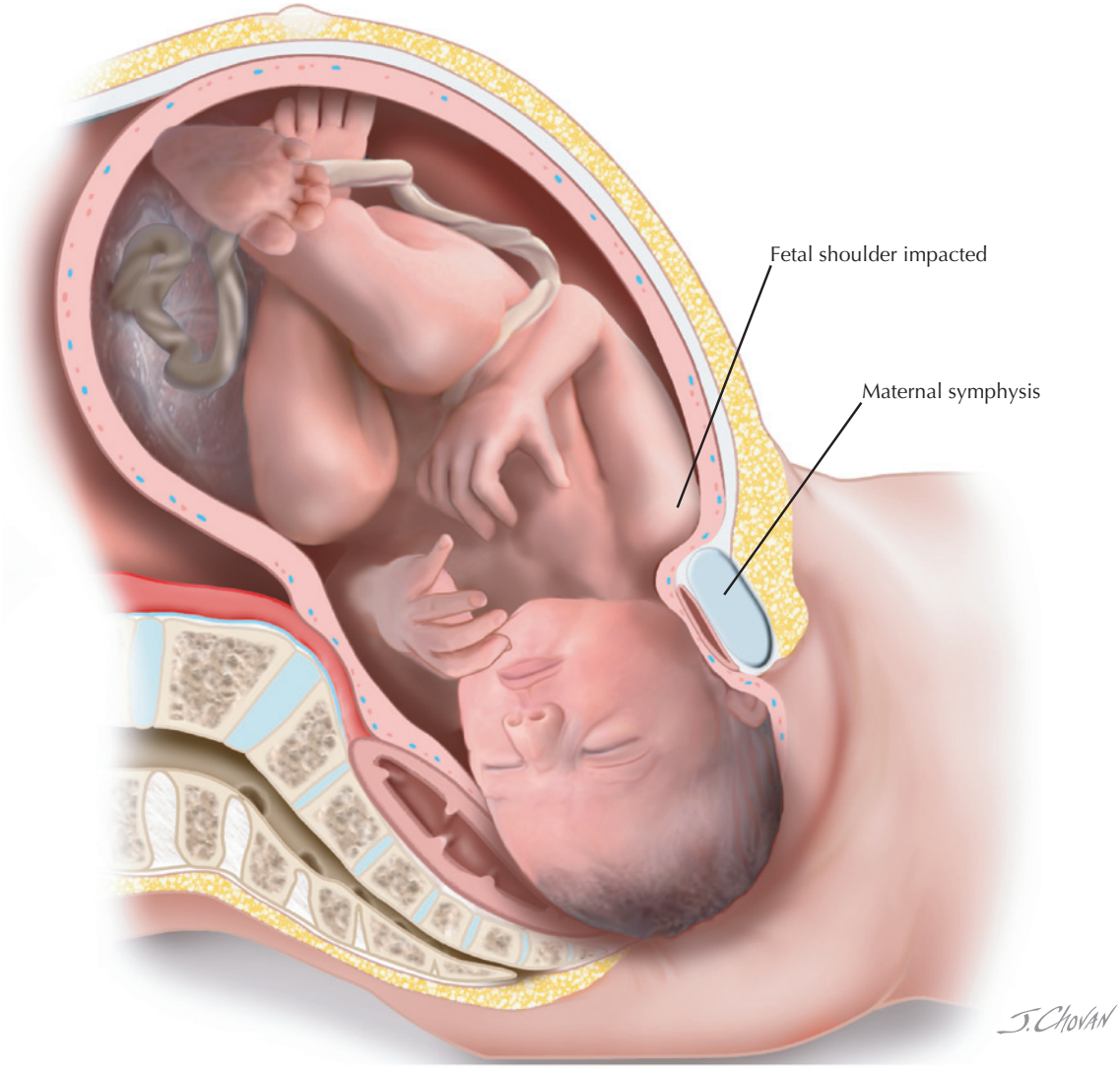


Figure 243.1 Shoulder dystocia

Cesarean delivery for fetuses ≥4500 g in diabetic pregnancies or ≥5000 g in other women (cesarean delivery for all suspected fetuses is not appropriate; operative delivery for ≥4000 g would result in 2345 procedures to prevent 1 permanent injury at a cost of $4.9 million annually). The risk of recurrence is estimated to be between 1% and 17%, although good data are lacking.

Possible Complications: Maternal—uterine atony, hemorrhage (11%), uterine rupture, urinary tract or rectal trauma (fourth degree laceration, 4%). Fetal/neonatal—asphyxia, death (up to 0.35%), brachial plexus injury (up to 40%, 10% persist), fractures (clavicular fracture [1.7%–9.5%], humerus fracture [0.1%–4.2%]). Data suggest that a significant proportion (34%–47%) of brachial plexus injuries are not associated with shoulder dystocia (in fact, 4% occur after cesarean delivery); clavicle or humerus fracture, neurologic damage.

Expected Outcome: Delivery can generally be accomplished, but 10%–30% of fetuses will experience long-term sequelae.

MISCELLANEOUS

ICD-10-CM Code: O66.0 (Obstructed labor due to shoulder dystocia).

REFERENCES

LEVEL II

Gherman RB, Chauhan S, Ouzounian JG, et al. Shoulder dystocia: the unpreventable obstetric emergency with empiric management guidelines. *Am J Obstet Gynecol*. 2006;195:657.

Gurewitsch ED, Johnson E, Hamzehzadeh S, et al. Risk factors for brachial plexus injury with and without shoulder dystocia. *Am J Obstet Gynecol*. 2006;194:486.

Hoffman MK, Bailit JL, Branch DW, et al. A comparison of obstetric maneuvers for the acute management of shoulder dystocia. *Obstet Gynecol*. 2011;117:1272.

Hofmeyr GJ, Shweni PM. Symphysiotomy for feto-pelvic disproportion. *Cochrane Database Syst Rev*. 2012;(10):CD005299.

Lerner H, Durlacher K, Smith S, et al. Relationship between head-to-body delivery interval in shoulder dystocia and neonatal depression. *Obstet Gynecol*. 2011;118:318.

McFarland MB, Langer O, Piper JM, et al. Perinatal outcome and the type and number of maneuvers in shoulder dystocia. *Int J Gynaecol Obstet*. 1996;55:219.

O'Leary JA. Cephalic replacement for shoulder dystocia: present status and future role of the Zavanelli maneuver. *Obstet Gynecol*. 1993;82:847.

Sagi-Dain L, Sagi S. The role of episiotomy in prevention and management of shoulder dystocia: a systematic review. *Obstet Gynecol Surv*. 2015;70:354.

Spain JE, Frey HA, Tuuli MG, et al. Neonatal morbidity associated with shoulder dystocia maneuvers. *Am J Obstet Gynecol*. 2015;212:353.e1.

Torki M, Barton L, Miller DA, et al. Severe brachial plexus palsy in women without shoulder dystocia. *Obstet Gynecol*. 2012;120:539.

LEVEL III

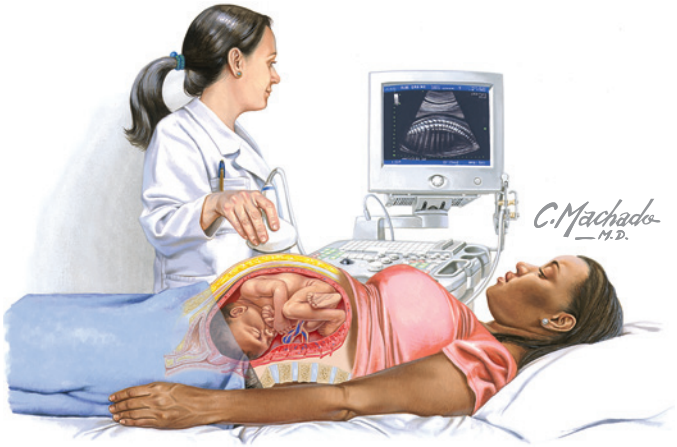
American College of Obstetricians and Gynecologists. Shoulder dystocia. ACOG Practice Bulletin 40. *Obstet Gynecol*. 2002;100:1045.

American College of Obstetricians and Gynecologists. Preparing for clinical emergencies in obstetrics and gynecology. Committee Opinion No. 590. *Obstet Gynecol*. 2014;123:722.

Gherman RB, Ouzounian JG, Goodwin TM. Brachial plexus palsy: an in utero injury? *Am J Obstet Gynecol*. 1999;180:1303.

Sandberg EC. The Zavanelli maneuver: a potentially revolutionary method for the resolution of shoulder dystocia. *Am J Obstet Gynecol*. 1985;152:479.

Sandberg EC. The Zavanelli maneuver: 12 years of recorded experience. *Obstet Gynecol*. 1999;93:312.



Whenever there is any significant bleeding during the third trimester of pregnancy it is vital to establish the location and condition of the placenta and fetus prior to any pelvic examination.

Figure 244.1 Ultrasound in third trimester bleeding

FOLLOW-UP

Patient Monitoring: Maternal—hemodynamic monitoring, direct inspection of bleeding. Fetal—fetal heart rate and biometry as indicated by obstetric considerations.

Prevention/Avoidance: None.

Possible Complications: Catastrophic maternal hemorrhage, fetal anoxia. Coagulation defects may occur as a result of heavy or prolonged blood loss. Preterm delivery represents the greatest source of morbidity for the fetus.

Expected Outcome: Good with most causes of bleeding, presuming early recognition and prompt management of the underlying cause.

MISCELLANEOUS

Pregnancy Considerations: No effect on pregnancy aside from those imposed by the underlying cause of the symptom of bleeding.

ICD-10-CM Codes: Based on the cause.

REFERENCES

LEVEL II

Bhandari S, Raja EA, Shetty A, et al. Maternal and perinatal consequences of antepartum haemorrhage of unknown origin. *BJOG*. 2014; 121:44.

Magann EF, Cummings JE, Niederhauser A, et al. Antepartum bleeding of unknown origin in the second half of pregnancy: a review. *Obstet Gynecol Surv*. 2005;60:741.

Towers CV, Pircon RA, Heppard M. Is tocolysis safe in the management of third-trimester bleeding? *Am J Obstet Gynecol*. 1999;180:1572.

LEVEL III

American College of Obstetricians and Gynecologists. Ultrasonography in pregnancy. ACOG Practice Bulletin No. 101. *Obstet Gynecol*. 2009; 113:451.

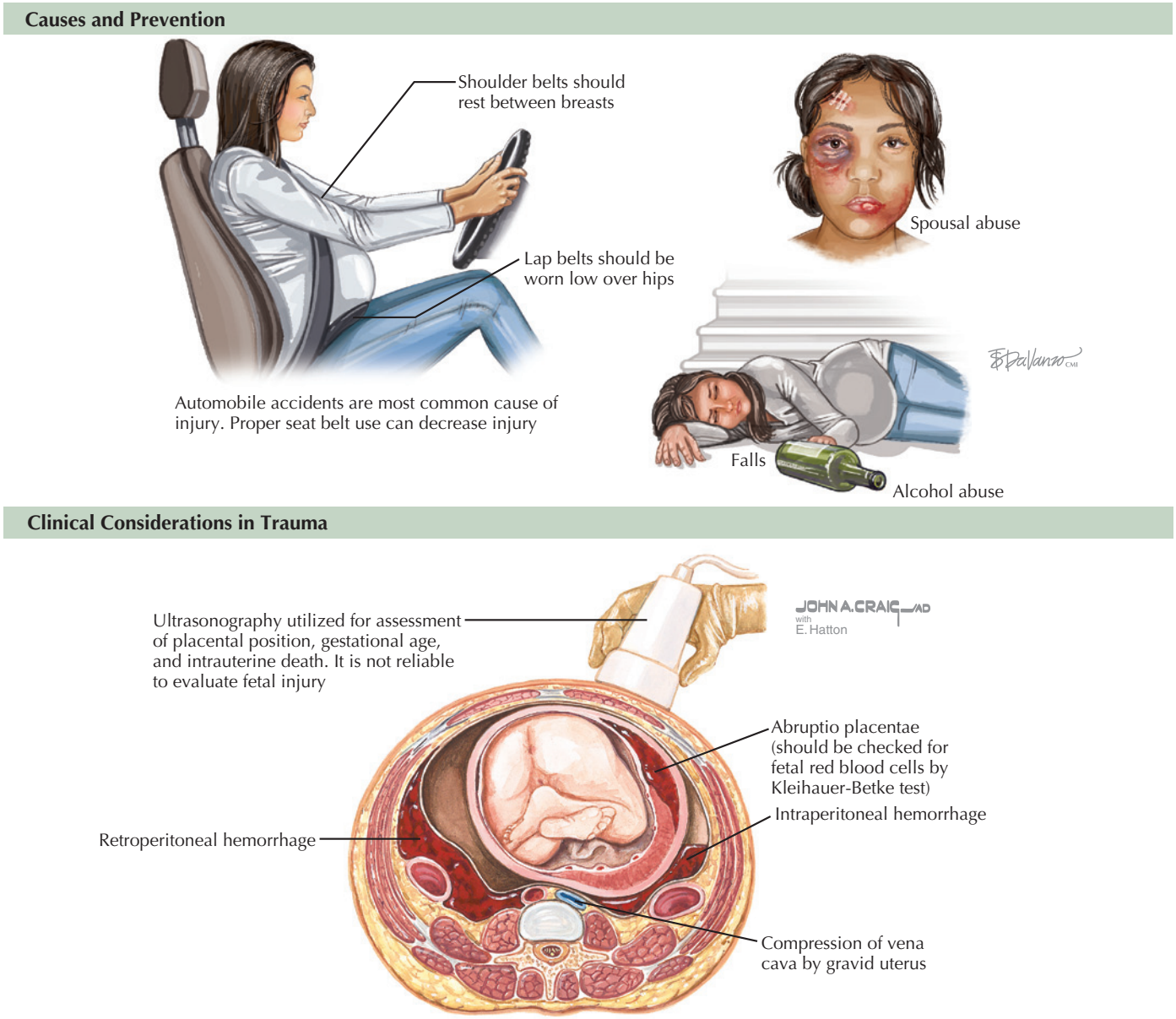


Figure 245.1 Blunt trauma in pregnancy

Workup and Evaluation

Laboratory: Based on the normal management of trauma.
Imaging: As needed for the management of trauma (unchanged by the pregnancy, trauma takes precedence). Ultrasonography for gestational age assessment, placental location, intrauterine death, and others (not reliable for assessment of fetal injury).
Special Tests: Peritoneal lavage under direct vision may be used to evaluate intraperitoneal hemorrhage. Kleihauer–Betke test for fetal–maternal hemorrhage.
Diagnostic Procedures: History, physical examination, imaging studies, and exploratory surgery when indicated.

Pathologic Findings

Based on the nature of the trauma.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Rapid assessment and stabilization (eg, administration of fluids and oxygen, cardiac and fetal heart rate monitoring based on gestational age), assessment of status (blood pressure, oxygen saturation, urinary output). Gestational age and fetal status must be established to inform other decisions. Tetanus prophylaxis should be provided as needed.
Specific Measures: The uterus should be displaced leftward, off the vena cava. All penetrating abdominal injuries must be surgically explored. The decision to surgically deliver the fetus must be based on the gestational age, fetal and maternal injuries, and the risk of death of the fetus if left in utero. Agonal cesarean delivery is only appropriate when there is imminent maternal death or cardiopulmonary resuscitation has been ineffective and delivery can be accomplished within four minutes. Prophylaxis for Rh isoimmunization should be given if fetal–maternal hemorrhage is

likely (up to 30% of cases). Antenatal glucocorticoids should be considered for women who are at a risk for preterm birth.

Diet: Nothing by mouth until the patient has been fully evaluated.

Activity: Bed rest until the patient has been fully evaluated.

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlets AP018 (Car Safety for You and Your Baby), AP055 (Travel During Pregnancy), and AP083 (Domestic Violence).

Drug(s) of Choice

Based on the injuries sustained. D immunoglobulin 300 mcg IM for each 30 mL of fetal blood thought to have been transfused to the mother (for Rh-incompatibility prophylaxis).

Precautions: Tocolytics should only be administered after abruption has been ruled out because medication side effects, such as tachycardia, may confuse the clinical picture. Vasopressors should be withheld until appropriate fluid resuscitation has been administered.

FOLLOW-UP

Patient Monitoring: Aggressive monitoring as appropriate for the trauma sustained, fetal heart rate monitoring.

Prevention/Avoidance: The incidence and severity of injuries can be reduced by the appropriate use of automobile safety restraints. The greatest injuries are observed when a pregnant woman is not using safety restraints during an automobile accident; injury is not usually caused by the restraints; air bags pose no increase in risk. Approximately 45% of pregnant women use safety restraints while driving. Lap belts should be worn low over the hips, and shoulder restraints should rest comfortably between the breasts. The use of approved infant seats to transport the newborn home and for all subsequent travel must also be encouraged in the strongest terms.

Possible Complications: Based on the injuries sustained.

Expected Outcome: Based on the trauma sustained; maternal generally good, fetal mortality 50%–75% for penetrating injuries involving the uterus.

MISCELLANEOUS

ICD-10-CM Code: O71.9 (Obstetrics trauma, unspecified) and P00.5 (Newborn [suspected to be] affected by maternal injury).

REFERENCES

LEVEL II

Fildes J, Reed L, Jones N, et al. Trauma: the leading cause of maternal death. *J Trauma*. 1992;32:643.

Mendez-Figueroa H, Dahlke JD, Vrees RA, et al. Trauma in pregnancy: an updated systematic review. *Am J Obstet Gynecol*. 2013;209:1.

Morris JA Jr, Rosenbower TJ, Jurkovich GJ, et al. Infant survival after cesarean section for trauma. *Ann Surg*. 1996;223:481.

Pearlman MD, Tintinalli JE, Lorenz RP. A prospective controlled study of outcome after trauma during pregnancy. *Am J Obstet Gynecol*. 1990;162:1502.

Schiff MA, Mack CD, Kaufman RP, et al. The effect of air bags on pregnancy outcomes in Washington State: 2002-2005. *Obstet Gynecol*. 2010;115:85.

Stewart DE, Cecutti A. Physical abuse in pregnancy. *Can Med Assoc J*. 1993;149:1257.

LEVEL III

American College of Obstetricians and Gynecologists. Intimate partner violence. Committee Opinion No. 518. *Obstet Gynecol*. 2012;119:412.

American College of Obstetricians and Gynecologists. Antepartum fetal surveillance. Practice Bulletin No. 145. *Obstet Gynecol*. 2014;124:182.

American College of Obstetricians and Gynecologists. Sexual assault. Committee Opinion No. 592. *Obstet Gynecol*. 2014;123:905.

Archer T. The pregnant trauma patient. *J Trauma*. 2007;62:S110.

Brown HL. Trauma in pregnancy. *Obstet Gynecol*. 2009;114:147.

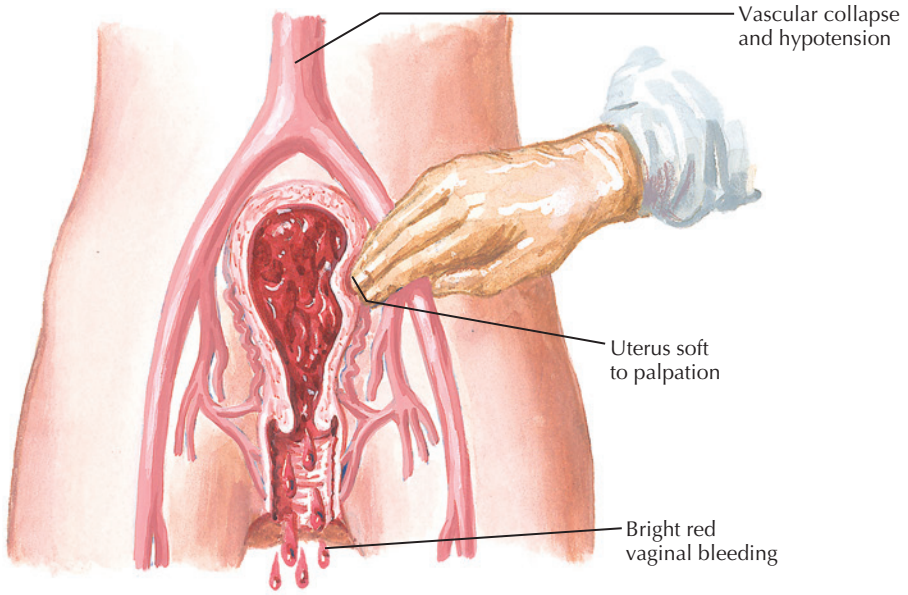
Edwards RK, Ripley DL, Davis JD, et al. Surgery in the pregnant patient. *Curr Probl Surg*. 2001;38:213.

Hendey GW, Votey SR. Injuries in restrained motor vehicle accident victims. *Ann Emerg Med*. 1994;24:77.

Mattox KL, Goetzl L. Trauma in pregnancy. *Crit Care Med*. 2005;33:S385.

Nash P, Driscoll P. ABC of major trauma. Trauma in pregnancy. *BMJ*. 1990;301:974.

Pearlman MD, Tintinalli JE, Lorenz RP. Blunt trauma during pregnancy. *N Engl J Med*. 1990;323:1609.



Uterine atony often presents as postpartum hemorrhage

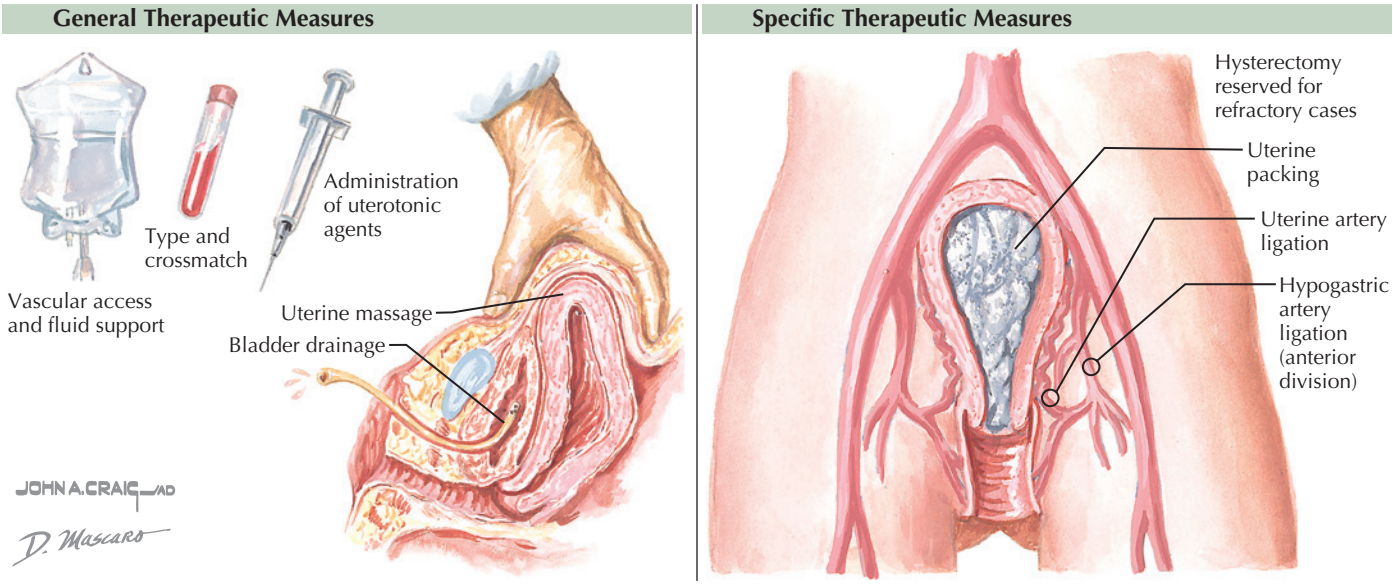


Figure 246.1 Uterine atony and postpartum hemorrhage

SIGNS AND SYMPTOMS

- Bright-red vaginal bleeding
- Loss of uterine tone palpable on abdominal examination
- Tachycardia, hypotension, and vascular collapse possible

DIAGNOSTIC APPROACH

Differential Diagnosis

- Retained placental fragments
- Genital tract lacerations (cervical, vaginal)
- Uterine rupture
- Uterine inversion
- Coagulopathy

Associated Conditions: Atony—uterine inversion and postpartum hemorrhage; hemorrhage—anemia, cardiovascular collapse, shock, death.

Workup and Evaluation

Laboratory: Hemoglobin or hematocrit to monitor status and volume of blood loss.
Imaging: Ultrasonography may be used to identify retained placental products but is generally not necessary.
Special Tests: None indicated.
Diagnostic Procedures: Physical examination (abdomen and vagina).

Pathologic Findings

Hemoglobin and hematocrit concentrations will not reflect the volume of blood lost until after equilibration has taken place at 6–24 hours.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Uterine atony should be suspected in any patient with excessive bleeding after delivery of placenta. If initial treatments do not appear to alter patient's bleeding (uterine massage, uterotonic agents such as oxytocin), other diagnoses should be considered while measures to treat atony continue. Rapid evaluation, fluid support or resuscitation (through large-bore access), massage of the uterine fundus. Type and crossmatch blood for possible transfusion. The bladder should be drained to allow the uterus to contract and to assess urinary output.

Specific Measures: Uterotonic agents (see later), uterine exploration (manual), uterine artery ligation (O'Leary stitch), hypogastric artery ligation, uterine packing, hysterectomy.

Diet: Nothing by mouth until a diagnosis is established and effective treatment is rendered.

Activity: Bed rest until a diagnosis is established and effective treatment is rendered.

Drug(s) of Choice

- Oxytocin 10–20 U/L of intravenous fluids, 100–300 mL administered as rapid infusion until uterine tone is reestablished, then 100–150 mL/h for the next several hours. Concentrations as high as 20–40 U/L may be used.
- Methylergonovine maleate (Methergine) 0.2 mg IM, may repeat in 5 minutes (produces tetanic contractions).
- 15-Methylprostaglandin F2α (carboprost tromethamine, Hemabate) 0.25 mg IM or 0.25–1 mg in 10 mL of normal saline injected into the myometrium (may repeat once).
- Misoprostol (synthetic prostaglandin E_1 analog Cytotec) 100–800 mg rectally or intravaginally administered.
- Iron replacement therapy.
- Broad-spectrum antibiotic treatment should be considered, especially if uterine packing is used.

Contraindications: Prostaglandin therapy is contraindicated in patients with asthma. Methergine should not be used in the presence of hypertension and may not be intravenously administered.

Precautions: The volume of fluids administered should be closely monitored to avoid inadvertent fluid overload. The placement of a bladder catheter to assess urinary output and to keep the bladder decompressed is desirable. When prostaglandins are used, side effects, such as diarrhea, hypertension, vomiting, fever, flushing, and tachycardia, are common.

Interactions: Magnesium sulfate and some halogenated anesthetic agents promote atony and work against uterotonic agents.

Alternative Drugs

Prostaglandin E_2 vaginal suppositories have been used, but newer agents and the techniques shown here are more effective and are more readily available.

FOLLOW-UP

Patient Monitoring: Normal postpartum care, follow-up complete blood count as needed.

Uterine atony (postpartum); anticipation of possible uterine atony, fundal massage, and oxytocin stimulation after delivery of the placenta.

Possible Complications: Hysterectomy, hemorrhagic shock, and cardiovascular collapse, Sheehan syndrome.

Expected Outcome: Most conditions respond to simple measures (uterine massage, oxytocin, methylergonovine maleate [Methergine]) if administered for the appropriate problem and in a timely way.

MISCELLANEOUS

ICD-10-CM Code: O72.1 (Other immediate postpartum hemorrhage).

REFERENCES

LEVEL I

Derman RJ, Kodkany BS, Goudar SS, et al. Oral misoprostol in preventing postpartum haemorrhage in resource-poor communities: a randomised controlled trial. *Lancet*. 2006;368:1248.

Hofmeyr GJ, Walraven G, Gulmezoglu AM, et al. Misoprostol to treat postpartum haemorrhage: a systematic review. *BJOG*. 2005;112:547.

Joshi VM, Otiv SR, Majumder R, et al. Internal iliac artery ligation for arresting postpartum haemorrhage. *BJOG*. 2007;114:356.

Khan RU, El-Refaey H. Pharmacokinetics and adverse-effect profile of rectally administered misoprostol in the third stage of labor. *Obstet Gynecol*. 2003;101:968.

Oleen MA, Mariano JP. Controlling refractory atonic postpartum hemorrhage with Hemabate sterile solution. *Am J Obstet Gynecol*. 1990;162:205.

LEVEL II

Alexander J, Thomas P, Sanghera J. Treatments for secondary postpartum haemorrhage. *Cochrane Database Syst Rev*. 2002;CD002867.

Begley CM, Gyte GM, Devane D, et al. Active versus expectant management for women in the third stage of labour. *Cochrane Database Syst Rev*. 2015;(3):CD007412.

Blomberg M. Maternal obesity and risk of postpartum hemorrhage. *Obstet Gynecol*. 2011;118:561.

Dionne MD, Deneux-Tharaux C, Dupont C, et al. Duration of expulsive efforts and risk of postpartum hemorrhage in nulliparous women: a population-based study. *PLoS ONE*. 2015;10:e0142171.

Duffy JM, Mylan S, Showell M, et al. Pharmacologic intervention for retained placenta: a systematic review and meta-analysis. *Obstet Gynecol*. 2015;125:711.

Hofmeyr GJ, Mshweshwe NT, Gülmezoglu AM. Controlled cord traction for the third stage of labour. *Cochrane Database Syst Rev*. 2015;(1):CD008020.

Le Ray C, Fraser W, Rozenberg P, et al. Duration of passive and active phases of the second stage of labour and risk of severe postpartum haemorrhage in low-risk nulliparous women. *Eur J Obstet Gynecol Reprod Biol*. 2011;158:167.

Rouse DJ, Leindecker S, Landon M, et al.; National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. The MFMU Cesarean Registry: uterine atony after primary cesarean delivery. *Am J Obstet Gynecol*. 2005;193:1056.

Westhoff G, Cotter AM, Tolosa JE. Prophylactic oxytocin for the third stage of labour to prevent postpartum haemorrhage. *Cochrane Database Syst Rev*. 2013;(10):CD001808.

LEVEL III

Abdul-Kadir R, McLintock C, Ducloy AS, et al. Evaluation and management of postpartum hemorrhage: consensus from an international expert panel. *Transfusion*. 2014;54:1756.

Albright CM, Rouse DJ, Werner EF. Cost savings of red cell salvage during cesarean delivery. *Obstet Gynecol*. 2014;124:690.

American College of Obstetricians and Gynecologists. Postpartum hemorrhage. ACOG Practice Bulletin 76. *Obstet Gynecol*. 2006;108:1039.

American College of Obstetricians and Gynecologists. Preparing for clinical emergencies in obstetrics and gynecology. Committee Opinion No. 590. *Obstet Gynecol*. 2014;123:722.

Conrad LB, Groome LJ, Black DR. Management of persistent postpartum hemorrhage caused by inner myometrial lacerations. *Obstet Gynecol*. 2015;126:266.

Ghezzi F, Cromi A, Uccella S, et al. The Hayman technique: a simple method to treat postpartum haemorrhage. *BJOG*. 2007;114:362.

Hensleigh PA. Anti-shock garment provides resuscitation and haemostasis for obstetric haemorrhage. *BJOG*. 2002;109:1377.

UTERINE INVERSION

INTRODUCTION

Description: Uterine inversion is the turning inside-out of the uterus immediately after delivery. Uncommon and often iatrogenic, this may be associated with catastrophic bleeding and cardiovascular collapse. The condition has also been reported in nonpregnant patients with intrauterine pathology, accounting for 5% of inversions.

Prevalence: 1 of 25,000 deliveries (estimates range from 1 in 1200–57,000 deliveries based on definitions and selection criteria).

Predominant Age: Reproductive age.

Genetics: No genetic pattern.

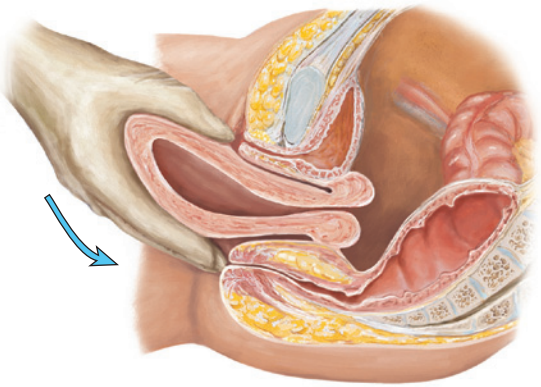
ETIOLOGY AND PATHOGENESIS

Causes: Iatrogenic (traction on the umbilical cord or downward pressure on the uterine fundus to facilitate delivery of the placenta; exact role remains controversial); abnormalities of placentation (accreta, increta, percreta).

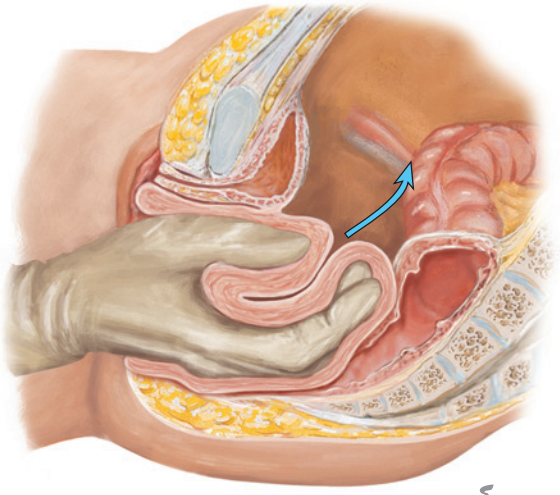
Risk factors: Uterine atony—multiparity (grand), uterine overdistention (multiple birth, polyhydramnios), prolonged labor, prolonged oxytocin stimulation, muscle-relaxant agents ($MgSO_4$), rapid labor. Less than 50% of cases have risk factors.

SIGNS AND SYMPTOMS

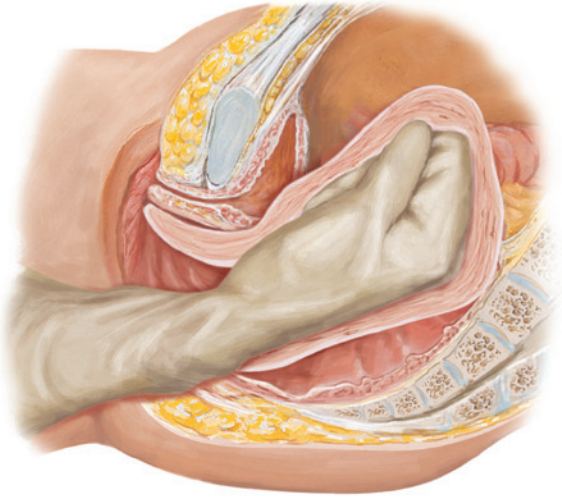
- A mass may be seen attached to or directly following the placenta as it delivers
- Bright-red vaginal bleeding



A. The fundus of the uterus is grasped by the operator's hand and gently pushed cephalward.



B. As the uterus is returned to the abdominal cavity, the body of the uterus must be allowed to revert to its normal configuration.



C. The examining hand is used to ensure that the fundus of the uterus is fully expanded into its normal position prior to the hand's being removed.

Figure 247.1 Uterine inversion

- Bradycardia from vagal stimulation
- Tachycardia, hypotension, and vascular collapse possible as a result of blood loss

DIAGNOSTIC APPROACH

Differential Diagnosis

- Uterine atony
- Retained placental fragments
- Genital tract lacerations
- Coagulopathy
- Prolapsed leiomyoma

Associated Conditions: Uterine atony, postpartum hemorrhage.

Workup and Evaluation

Laboratory: Hemoglobin or hematocrit to monitor status and volume of blood loss. Acute loss may not be reflected by these measures until equilibration has occurred in 6–24 hours.
Imaging: Ultrasonography may be used to verify the diagnosis, but this is unnecessary and delays the implementation of therapy.
Special Tests: None indicated.
Diagnostic Procedures: Pelvic examination.

Pathologic Findings

Inversion of the uterus.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Rapid evaluation, fluid support or resuscitation, call for anesthesia assistance.
Specific Measures: Discontinue uterotonic agents until replacement is accomplished. Uterine-relaxant agents (see later), manual replacement of uterine fundus (may require general anesthesia with a relaxant agent [halothane]), may require operative intervention (replacement or hysterectomy). Once the uterine wall has relaxed, gentle manual pressure should be placed on the fundus to displace it inward and upward until its normal position can be restored and the uterus returned to its normal configuration. Uterotonic agents are then used to obtain uterine contraction and hemostasis.
Diet: Nothing by mouth until a diagnosis is established and effective treatment is rendered.
Activity: Bed rest until a diagnosis is established and effective treatment is rendered.

Drug(s) of Choice

- Tocolytics—terbutaline 0.25 mg IV (may repeat once) or nitroglycerin 100–250 mcg IV (may repeat to a total of 1000 mcg).
- Broad-spectrum antibiotic prophylaxis (first-generation cephalosporin or clindamycin/gentamycin) should be instituted.

Contraindications: See individual agents.
Precautions: If nitroglycerine is used, blood pressure must be closely monitored (hypotension).

Alternative Drugs

Halothane general anesthesia may be required.

FOLLOW-UP

Patient Monitoring: Normal postpartum care, follow-up complete blood count as needed.
Prevention/Avoidance: Little or no traction on the umbilical cord or fundal pressure during the delivery of the placenta.
Possible Complications: Hysterectomy, hemorrhagic shock, and cardiovascular collapse.
Expected Outcome: Generally good if recognized and acted on promptly.

MISCELLANEOUS

Other Notes: Following replacement of the fundus, the possibility of uterine atony must be anticipated. If the placenta is still attached to the uterine wall, it should be left in place until after the uterine fundus has been reduced and returned to its normal location.
ICD-10-CM Code: O71.2 (Postpartum inversion of uterus).

REFERENCES

LEVEL II

Baskett TF. Acute uterine inversion: a review of 40 cases. *J Obstet Gynaecol Can*. 2002;24:953.

Hu CF, Lin H. Ultrasound diagnosis of complete uterine inversion in a nulliparous woman. *Acta Obstet Gynecol Scand*. 2012;91:379.

Lupovitch A, England ER, Chen R. Non-puerperal uterine inversion in association with uterine sarcoma: case report in a 26-year-old and review of the literature. *Gynecol Oncol*. 2005;97:938.

LEVEL III

American College of Obstetricians and Gynecologists. Postpartum hemorrhage. ACOG Practice Bulletin 76. *Obstet Gynecol*. 2006;108:1039.

Brar HS, Greenspoon JS, Platt LD, et al. Acute puerperal uterine inversion. New approaches to management. *J Reprod Med*. 1989;34:173.

Dufour P, Vinatier D, Puech F. The use of intravenous nitroglycerin for cervico-uterine relaxation: a review of the literature. *Arch Gynecol Obstet*. 1997;261:1.

Shah-Hosseini R, Evrard JR. Puerperal uterine inversion. *Obstet Gynecol*. 1989;73:567.

Tank Parikshit D, Mayadeo Niranjan M, Nandanwar YS. Pregnancy outcome after operative correction of puerperal uterine inversion. *Arch Gynecol Obstet*. 2004;269:214.

UTERINE RUPTURE

INTRODUCTION

Description: Uterine rupture is characterized by the breach of the uterine wall (new or after previous uterine surgery such as cesarean delivery) that may result in significant maternal or fetal morbidity or mortality. This should be distinguished from uterine scar dehiscence, in which there is a separation of an old scar that does not penetrate the uterine serosa or result in complications. Rupture of an intact uterus (without scars) does occur on rare occasions (1/5700–1/20,000 deliveries, approximately 10% of ruptures) and is generally associated with significant uterine distention (polyhydramnios, multiple gestation).

Prevalence: Found in 0.3%–3.7% of patients with a previous cesarean delivery and 5% of patients for whom vaginal birth after cesarean delivery (VBAC) fails. Uterine rupture rates in women with previous classical incisions and T-shaped incisions range between 4% and 12%. Approximately 7% of emergency cesarean hysterectomies are for rupture.

Predominant Age: Reproductive age.

Genetics: No genetic pattern.

ETIOLOGY AND PATHOGENESIS

Causes: Abnormal healing of a previous uterine scar, mechanical disruption of the uterine wall weakened by previous surgery, congenital anomalies (structural malformations, Ehlers–Danlos type IV), or abnormalities of placentation. The uterine wall may also be breached by injudicious manual removal of the placenta or manual exploration of the uterus after delivery of the placenta. Traumatic rupture of the uterus may occur with blunt trauma to the abdomen such as occurs to an unrestrained passenger during an automobile accident. The proper use of automobile lap and shoulder belts significantly reduces the risk for an injury to both mother and fetus. Air bags do not increase the risk for an injury.

Risk Factors: Previous uterine surgery (cesarean delivery; greatest for vertical incisions, myomectomy, septoplasty), multiple gestation, internal or external version, grand multiparity (20-fold increase), short interval between pregnancies, fetal malpresentation, polyhydramnios, oxytocin stimulation (unproved), low Bishop score, congenital anomalies, and disuse or misuse of vehicle passenger restraints. There is considerable evidence that cervical ripening with prostaglandin preparations increases the likelihood of uterine rupture (15-fold increase). Induction or augmentation of labor using mechanical means does not seem to increase the risk for rupture.

SIGNS AND SYMPTOMS

- Abrupt fetal distress (80% of cases)
- Abrupt loss of station (presenting part may cease to be present in the vagina)
- Vaginal bleeding (may not be present)
- Abdominal pain (may not be present; pain may be referred to the chest or diaphragm)
- Maternal circulatory collapse
- Uterine activity may persist despite expulsion of the fetus
- Hematuria (if rupture extends into the bladder)

DIAGNOSTIC APPROACH

Differential Diagnosis

- Uterine dehiscence
- Placental abruption
- Umbilical cord prolapse (causing abrupt fetal distress)
- Adnexal torsion
- Pulmonary or amniotic fluid embolism
- Abdominal pregnancy

Associated Conditions: Fetal demise, maternal blood loss.

Workup and Evaluation

Laboratory: Inter- and postoperative blood counts. Evaluation of clotting when significant bleeding has occurred.

Imaging: Ultrasonography may demonstrate uterine dehiscence, but the need for clinical intervention often precludes the examination.

Special Tests: Intensive fetal and maternal monitoring may be indicated.

Diagnostic Procedures: History and physical examinations (vaginal and abdominal).

Pathologic Findings

Separation of previous uterine scar or a new failure of the uterine wall muscle.

MANAGEMENT AND THERAPY

Nonpharmacologic

General Measures: Rapid evaluation, supportive measures as needed (fluids, blood products).

Specific Measures: Immediate operative delivery (most often by laparotomy), surgical exploration with the possibility of repair or hysterectomy. Ligation of one or both hypogastric arteries may be necessary.

Diet: Nothing by mouth once the diagnosis is made (pending surgical intervention).

Activity: Strict bed rest (pending surgical intervention).

Patient Education: American College of Obstetricians and Gynecologists Patient Education Pamphlet AP070 (Vaginal Birth After Cesarean Delivery: Deciding on a Trial of Labor After Cesarean Delivery).

Drug(s) of Choice

None. Supportive measures including fluids, blood products, and anesthetics (for immediate delivery) as needed. Prophylactic antibiotics are often recommended.

FOLLOW-UP

Patient Monitoring: Fetal and maternal monitoring must be maintained for those at a risk and intensified when the diagnosis is considered.

Prevention/Avoidance: Care in all uterine manipulations (eg, manual removal of the placenta, version, external pressure during delivery). Patients with a prior successful vaginal delivery have a greater likelihood of successful vaginal birth after cesarean delivery and a lower risk for uterine rupture than those without a successful vaginal delivery. One study has suggested that there is a lower rate of uterine rupture when a double-layer closure of the uterus is used at the time of cesarean delivery.

Possible Complications: Maternal morbidity or mortality possible (significantly reduced by fetal and maternal monitoring). Damage to the cervix, vagina, or bladder may occur as a part of the rupture. Fetal demise may occur in up to 50%–75% of fundal incision ruptures and 10%–15% of lower uterine segment ruptures. Long-term neurologic sequelae are common in infants who survive. Vertical uterine scars are associated with the greatest morbidity and mortality when a rupture occurs.

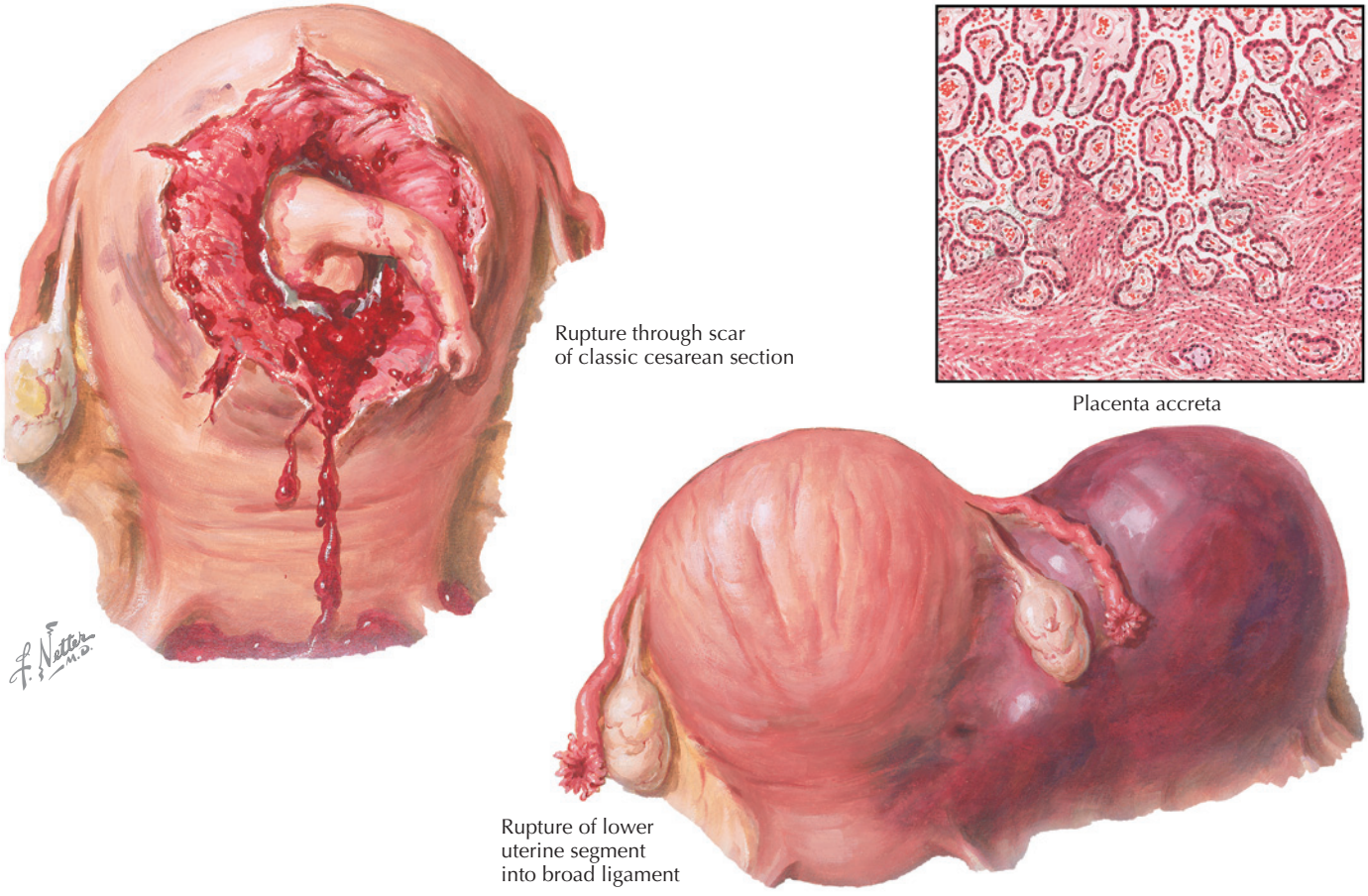


Figure 248.1 Uterine rupture

Expected Outcome: When diagnosed early and acted on promptly, a good outcome can be expected. If the uterus is repaired and preserved, the risk of recurrence in a subsequent pregnancy is approximately 20%.

MISCELLANEOUS

ICD-10-CM Codes: O71.1 (Rupture of uterus during labor), O71.00 (Rupture of uterus before onset of labor, unspecified trimester), and S37.60XA (Unspecified injury of uterus, initial encounter).

REFERENCES

LEVEL II

Budden A, Chen LJ, Henry A. High-dose versus low-dose oxytocin infusion regimens for induction of labour at term. *Cochrane Database Syst Rev*. 2014;(10):CD009701.

Bujold E, Bujold C, Hamilton EF, et al. The impact of a single-layer or double-layer closure on uterine rupture. *Am J Obstet Gynecol*. 2002;186:1326.

Bujold E, Mehta SH, Bujold C, et al. Interdelivery interval and uterine rupture. *Am J Obstet Gynecol*. 2002;187:1199.

Choy-Hee L, Raynor BD. Misoprostol induction of labor among women with a history of cesarean delivery. *Am J Obstet Gynecol*. 2001;184:1115.

Conde-Agudelo A, Rosas-Bermudez A, Kafury-Goeta AC. Effects of birth spacing on maternal health: a systematic review. *Am J Obstet Gynecol*. 2007;196:297.

Fox NS, Gerber RS, Mourad M, et al. Pregnancy outcomes in patients with prior uterine rupture or dehiscence. *Obstet Gynecol*. 2014;123:785.

Gibbins KJ, Weber T, Holmgren CM, et al. Maternal and fetal morbidity associated with uterine rupture of the unscarred uterus. *Am J Obstet Gynecol*. 2015;213:382.e1.

Guise JM, McDonagh MS, Osterweil P, et al. Systematic review of the incidence and consequences of uterine rupture in women with previous caesarean section. *BMJ*. 2004;329:19.

Kieser KE, Baskett TF. A 10-year population-based study of uterine rupture. *Obstet Gynecol*. 2002;100:749.

Landon MB, Spong CY, Thom E, et al.; National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Risk of uterine rupture with a trial of labor in women with multiple and single prior cesarean delivery. *Obstet Gynecol*. 2006;108:12.

Zelop CM, Shipp TD, Repke JT, et al. Effect of previous vaginal delivery on the risk of uterine rupture during a subsequent trial of labor. *Am J Obstet Gynecol*. 2000;183:1184.

LEVEL III

American College of Obstetricians and Gynecologists. Postpartum hemorrhage. ACOG Practice Bulletin 76. *Obstet Gynecol*. 2006;108:1039.

American College of Obstetricians and Gynecologists. Vaginal birth after previous cesarean delivery. Practice Bulletin No. 115. *Obstet Gynecol*. 2010;116:450.

Guise JM, Denman MA, Emeis C, et al. Vaginal birth after cesarean: new insights on maternal and neonatal outcomes. *Obstet Gynecol*. 2010;115:1267.

Macones GA, Cahill AG, Stamilio DM, et al. Can uterine rupture in patients attempting vaginal birth after cesarean delivery be predicted? *Am J Obstet Gynecol*. 2006;195:1148.

Miller DA, Goodwin TM, Gherman RB, et al. Intrapartum rupture of the unscarred uterus. *Obstet Gynecol*. 1997;89:671.

National Institutes of Health Consensus Development Conference Panel. National Institutes of Health Consensus Development conference statement: vaginal birth after cesarean: new insights March 8-10, 2010. *Obstet Gynecol*. 2010;115:1279.

SECTION XIV

Procedures

This page intentionally left blank

AMNIOCENTESIS

DESCRIPTION

Amniocentesis is the sampling of fluid from around the growing fetus for prenatal biochemical or genetic diagnosis. Amniocentesis may rarely be used to reduce the amount of amniotic fluid present in cases of polyhydramnios.

INDICATIONS

This procedure is used for assessing fetal genetics or metabolic disorders, lung maturity, fetal infection, or isoimmunization status. Therapeutic amniocentesis may be performed for reducing the fluid volume or instilling agents for fetal therapy or other purposes such as fetal imaging or diagnosing the rupture of fetal membranes. Amniocentesis is also a necessary step in other diagnostic and therapeutic procedures such as cordocentesis or fetal transfusion.

CONTRAINDICATIONS

Active skin infections near the site of needle placement. Relative; maternal fever of unknown origin, known or suspected allergies to materials used (eg, latex, skin preparation materials, local anesthetics), and uncorrected coagulopathy. While technically possible as early as 11 weeks of gestation, higher rates of fetal loss suggest that early amniocentesis should be delayed until or after 15–17 weeks. Amniocentesis may be technically difficult to accomplish in patients with multiple gestations.

REQUIRED EQUIPMENT

- Sterile gloves
- Skin preparation materials (eg, povidone–iodine and 70% isopropyl alcohol)
- Sterile gauze pads (2″ × 2″ or 4″ × 4″)
- Self-adhesive bandage
- Ultrasonography unit
- Fetal monitor or Doppler fetoscope
- Commercial amniocentesis tray

or

- 20- and 22-gauge spinal needles (or smaller), 20-cc syringe, three sterile 10-cc specimen tubes with caps (plain, without additive), sterile drape (one with a small fenestration, or multiple drapes)
- If desired: 1% lidocaine without epinephrine, 5-cc syringe, 22-gauge needle (if not included in amniocentesis kit)

TECHNIQUE

The indications, contraindications, risks, benefits, and complications should be reviewed and discussed with the patient, and informed consent should be obtained. The patient should be placed in the supine position with the head elevated at 20–30 degrees. If the pregnancy is advanced, the patient may empty her bladder and be placed in a slightly left decubitus position. Ultrasonography is used to assess fetal well-being, fetal lie, and placental position.

A suitable pocket of amniotic fluid should be identified using ultrasonography. Ideally, this pocket should be located away from the fetal face and placenta, but it should be accessible with a standard spinal needle. Areas around the fetal extremities are often best. The location of this pocket relative to the skin surface should be noted as a guide to needle insertion.

The skin of the abdominal wall over the selected pocket of amniotic fluid should be disinfected with a suitable skin preparation solution and technique of the examiner's choice. If a local anesthetic is to be used, it is established at this juncture using a sterile technique: a small skin wheal of local anesthetic is placed, and the proposed needle track is infiltrated with a total of less than 4–5 mL of anesthetic agent.

With the stylet in place, a 20- or 22-gauge spinal needle is perpendicularly passed through the skin, abdominal, and uterine walls into the amniotic sac. A slight pop or loss of resistance may be felt as the needle traverses the fascia. After entering the pocket of fluid, the stylet is removed from the needle. Free flow of fluid should be demonstrated. If free flow is not found, the needle should be rotated or tipped and rechecked prior to being advanced farther (with the stylet in place). Using ultrasonography to guide the needle's advancement may facilitate the placement of the needle into the pocket of the amniotic fluid. This can be particularly helpful when amniocentesis is performed early in pregnancy.

Once free flow of fluid has been demonstrated, a small syringe should be attached to the needle and 2–3 mL of fluid should be withdrawn. This fluid is discarded. Appropriate samples are now taken and placed in sterile specimen tubes. Determination of the amount of material needed and any special handling required for these specimens is dictated by the studies to be performed. If there is any doubt, consultation with the laboratory before initiating the procedure may help in identifying any special handling that must be used.

After the samples have been obtained, the needle is withdrawn and a self-adhesive bandage is applied to the site of needle puncture. The fetus should be monitored for a short period after the procedure. If bloody fluid was obtained, this monitoring period should be extended by 1–2 additional hours or longer, depending on other considerations. An appropriate procedure note should be entered into the patient's record.

COMPLICATIONS

Early amniocentesis is associated with a fetal loss rate of approximately 2.5% (vs. 0.7% for later procedures). Amniotic fluid leakage, frank rupture of fetal membranes, amnionitis (infection), bleeding, and possible isoimmunization of mothers who are Rh negative are all possible. The risk for direct fetal injury is small when the procedure is carefully performed. When amniocentesis is conducted in the presence of preterm premature rupture of membranes, failure

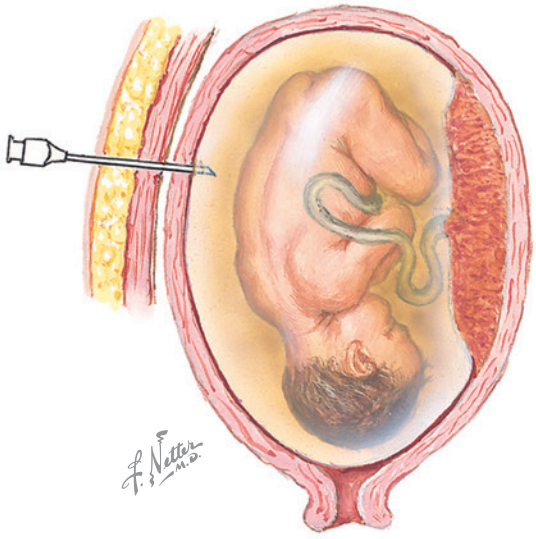


Figure 249.1 Amniocentesis

rates are higher. Bleeding and infection are always possible with any invasive procedure. Data suggest that prophylactic antibiotics reduce the risk for infection, but the impact is small.

FOLLOW-UP

When amniocentesis is performed after fetal viability (24 weeks), a period of electronic fetal heart rate monitoring (30 minutes) is recommended. If bloody fluid is obtained or the fetus or umbilical cord is perforated, this monitoring is generally increased (1–2 hours or longer, as clinically indicated). Patients should report persistent uterine cramping, vaginal bleeding or leakage of fluid, or fever. Rh (D) immunoglobulin should be administered as indicated in mothers who are Rh negative.

CPT CODE(S)

59000 Amniocentesis, any method
76946 Ultrasonic guidance for amniocentesis, physician supervision and interpretation

REFERENCES

LEVEL I

Giorlandino C, Cignini P, Cini M, et al. Antibiotic prophylaxis before second-trimester genetic amniocentesis (APGA): a single-centre open randomised controlled trial. *Prenat Diagn*. 2009;29:606.

Gordon MC, Ventura-Braswell A, Higby K, et al. Does local anesthesia decrease pain perception in women undergoing amniocentesis? *Am J Obstet Gynecol*. 2007;196:55.e1.

LEVEL II

Alfirevic Z, Sundberg K, Brigham S. Amniocentesis and chorionic villus sampling for prenatal diagnosis. *Cochrane Database Syst Rev*. 2004; CD003252.

Eddleman KA, Malone FD, Sullivan L, et al. Pregnancy loss rates after midtrimester amniocentesis. *Obstet Gynecol*. 2006;108:1067.

Mujezinovic F, Alfirevic Z. Analgesia for amniocentesis or chorionic villus sampling. *Cochrane Database Syst Rev*. 2011;CD008580.

Mujezinovic F, Alfirevic Z. Technique modifications for reducing the risks from amniocentesis or chorionic villus sampling. *Cochrane Database Syst Rev*. 2012;(8):CD008678.

Petrikovsky BM, Kaplan GP. Fetal responses to inadvertent contact with the needle during amniocentesis. *Fetal Diagn Ther*. 1995;10:83.

LEVEL III

American College of Obstetricians and Gynecologists. Screening for Tay–Sachs disease. ACOG Committee Opinion No. 318. *Obstet Gynecol*. 2005;106:893.

American College of Obstetricians and Gynecologists. Management of alloimmunization during pregnancy. ACOG Practice Bulletin 75. *Obstet Gynecol*. 2006;108:457.

American College of Obstetricians and Gynecologists. Preconception and prenatal carrier screening for genetic diseases in individuals of Eastern European Jewish descent. ACOG Committee Opinion No. 442. *Obstet Gynecol*. 2009;114:950.

American College of Obstetricians and Gynecologists. Cell-free DNA screening for fetal aneuploidy. Committee Opinion No. 640. *Obstet Gynecol*. 2015;126:e31.

Moise KJ Jr. Management of rhesus alloimmunization in pregnancy. *Obstet Gynecol*. 2002;100:600.

Mujezinovic F, Alfirevic Z. Procedure-related complications of amniocentesis and chorionic villous sampling: a systematic review. *Obstet Gynecol*. 2007;110:687.

Seeds JW. Diagnostic mid trimester amniocentesis: how safe? *Am J Obstet Gynecol*. 2004;191:607.

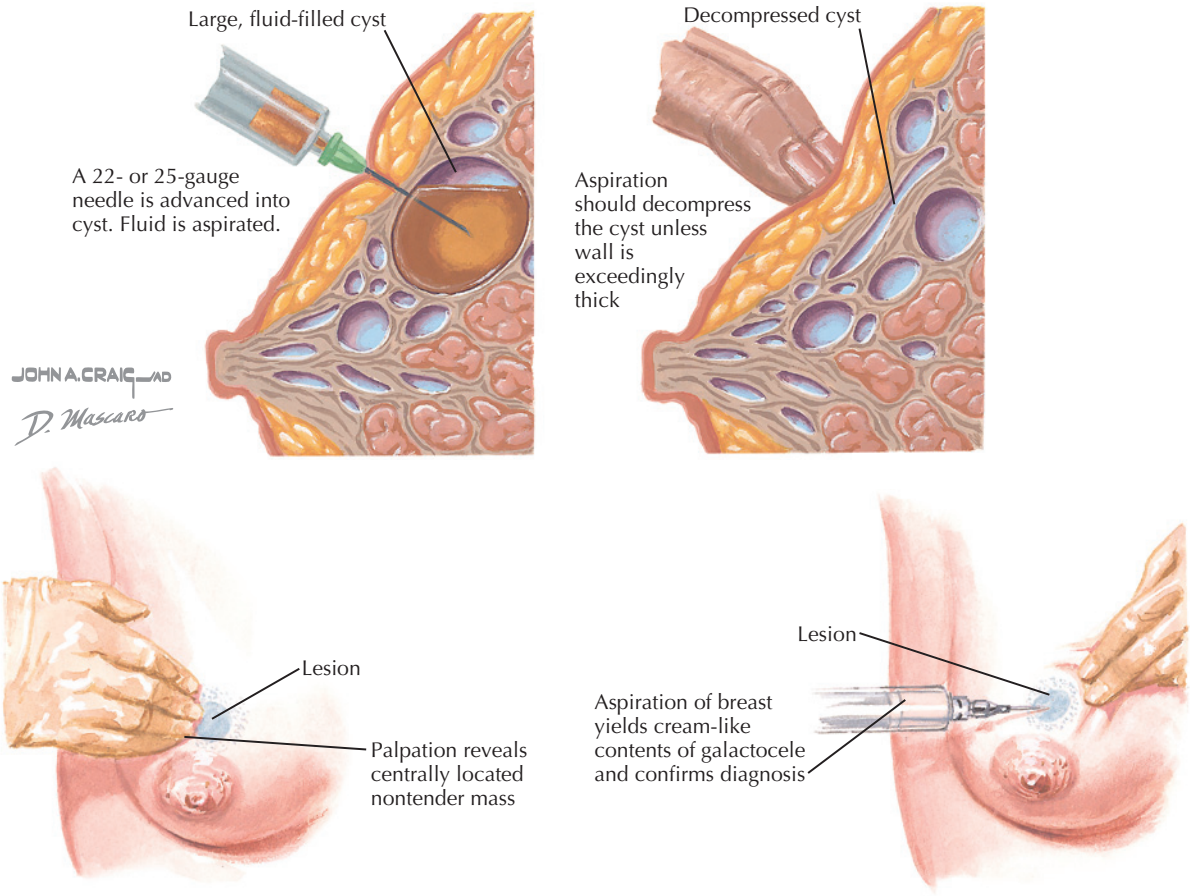


Figure 250.1 Aspiration of breast cyst

Fluid aspirated from patients with fibrocystic changes will customarily be straw colored. Fluid that is dark brown or green occurs in cysts that have been present for a long time but is equally innocuous. Because of high false-positive rates (up to 6%) and even higher false-negative rates (2%–22%), cytologic evaluation of the fluid obtained is of little value.

COMPLICATIONS

Hematoma, infection (rare).

FOLLOW-UP

If the cyst completely disappears and does not re-form at a 1-month follow-up examination, no further therapy is required. If no fluid is obtained, if the cyst re-forms within 2 weeks or must be repeatedly aspirated, or if a mass persists after the aspiration, biopsy should be performed.

CPT CODE(S)

19000 Puncture aspiration of cyst of breast
19001 Each additional cyst

REFERENCES

LEVEL II

Sanders LM, Lacz NL, Lara J. 16-year experience with aspiration of noncomplex breast cysts: cytology results with focus on positive cases. *Breast J*. 2012;18:443.

LEVEL III

Lucas JH, Cone DL. Breast cyst aspiration. *Am Fam Physician*. 2003;68:1983.

Morrow M. The evaluation of common breast problems. *Am Fam Physician*. 2000;61(2371):2385.

Parker SH, Stavros AT, Dennis MA. Needle biopsy techniques. *Radiol Clin North Am*. 1995;33:1171.

251 BARTHOLIN GLAND CYST/ABSCESS DRAINAGE

DESCRIPTION

Bartholin gland cyst/abscess drainage is an acute drainage of a symptomatic cystic dilation of the Bartholin gland.

INDICATIONS

Symptomatic cystic dilation or abscess of the Bartholin gland. Asymptomatic cysts in women younger than 40 years do not require treatment; in patients older than 40 years, biopsy is indicated. Mild Bartholin gland infections may also be treated with broad-spectrum antibiotics and frequent warm sitz baths.

CONTRAINDICATIONS

Incomplete evaluation of the vulvar lesion, bleeding diathesis, known or suspected allergy to agents used (eg, latex, iodine), uncorrected coagulopathy.

REQUIRED EQUIPMENT

- Skin preparation materials (alcohol, iodine- or hexachlorophene-based antibacterial solution [eg, Betadine, Hibiclens])
- Sterile gloves
- 1% lidocaine without epinephrine, 5-cc syringe, 22-gauge needle, analgesic skin-cooling spray or other topical analgesic
- 10-mL syringe
- Normal saline (for irrigation)
- Scalpel (#11 or #15 blade)
- Sterile gauze pads (2″ × 2″ or 4″ × 4″)
- Word catheter or iodoform gauze packing (1/4″ or 1/2″)

TECHNIQUE

After appropriate informed consent has been obtained from the patient, the skin of the vulva is disinfected. When an acute abscess is to be drained, the exquisite tenderness that is usually present dictates that this is gently performed; pain relief is best obtained by using an analgesic or skin-freezing spray. This technique may also be used for nonacute Bartholin cysts; local anesthesia using local or field infiltration is also appropriate. Abscesses should be incised at the point of least thickness overlying the mass (where the abscess is "pointing"). A vertical or "stab" incision is made, generally resulting in the abrupt release of purulent material. (Despite the apparent purulent character of the drained material, culture is generally of little use in the management of these cases). The size of this incision need only be of the order of 1 or 2 cm; sutures are generally not required. The abscess cavity may be gently irrigated with normal saline using a 10-mL syringe. A Word catheter should then be placed through the incision and inflated with a few milliliters of saline. As an alternative, iodoform gauze packing may be placed

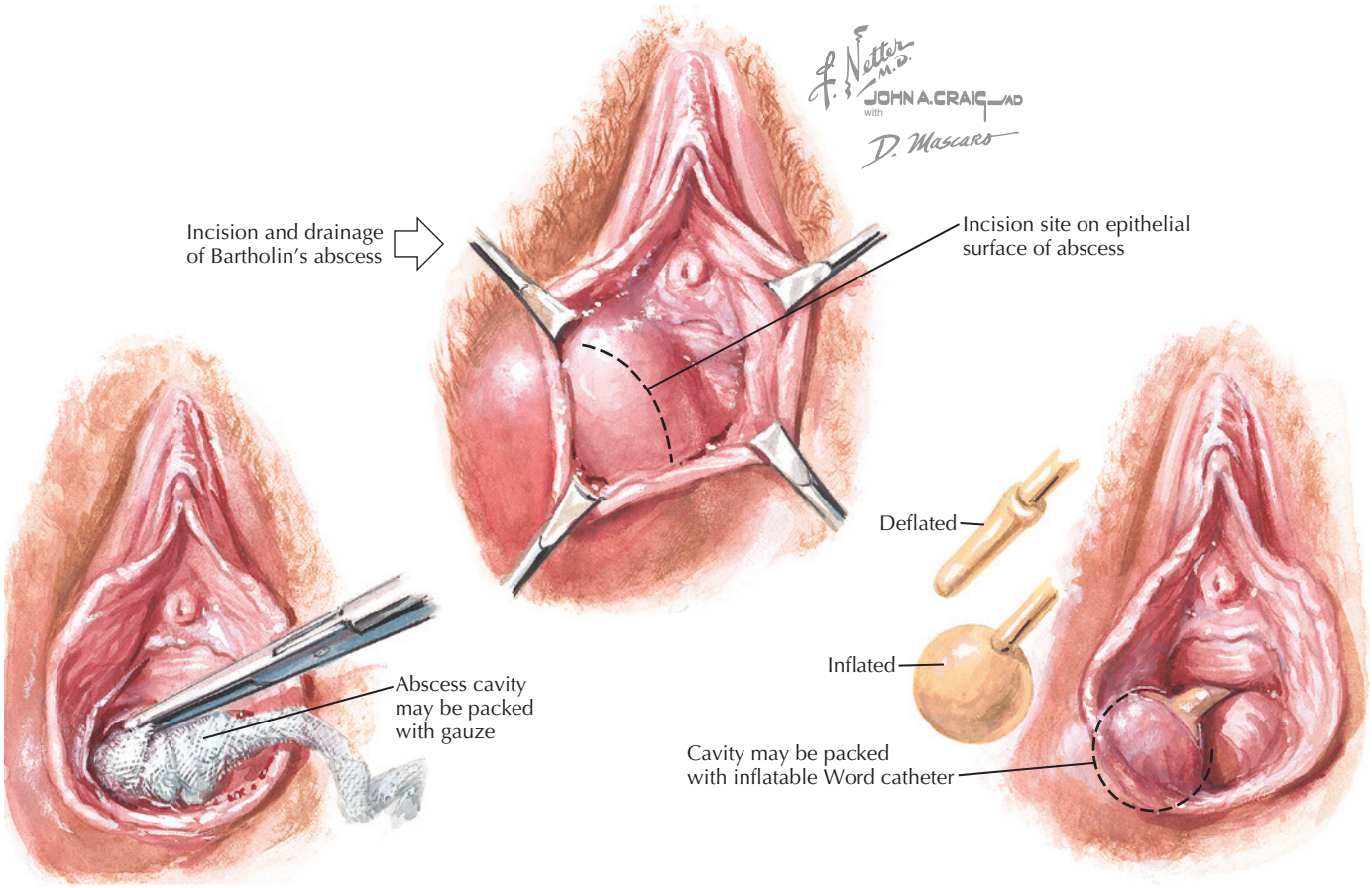


Figure 251.1 Bartholin gland cyst drainage

within the cavity with a 2- to 3-cm "tail" left outside the incision to facilitate eventual removal. Unless cellulitis is present, antibiotic therapy is not required.

When the cyst is not acutely inflamed, it should be stabilized and tensed by gentle finger pressure applied on either side of the affected labium, below the cyst. Incision in this case should be made within the hymeneal ring whenever possible. Incision length should be similar to that used for acute cases, and a Word catheter or iodoform gauze packing should be inserted in a similar manner.

COMPLICATIONS

Bleeding, hematoma, recurrence.

FOLLOW-UP

Word catheters should be left in place for 4–6 weeks. Iodoform gauze packing should be gradually removed over the course of several days. Recurrence is frequent, and many prefer marsupialization to simple drainage in all but the most acute cases.

CPT CODE(S)

56420 Incision and drainage of Bartholin gland abscess

REFERENCES

LEVEL II

Eilber KS, Raz S. Benign cystic lesions of the vagina: a literature review. *J Urol*. 2003;170:717.

Haider Z, Condous G, Kirk E, et al. The simple outpatient management of Bartholin's abscess using the Word catheter: a preliminary study. *Aust N Z J Obstet Gynaecol*. 2007;47:137.

Reif P, Ulrich D, Bjelic-Radisic V, et al. Management of Bartholin's cyst and abscess using the Word catheter: implementation, recurrence rates and costs. *Eur J Obstet Gynecol Reprod Biol*. 2015;190:81.

LEVEL III

Omole F, Simmons BJ, Hacker Y. Management of Bartholin's duct cyst and gland abscess. *Am Fam Physician*. 2003;68:135.

Wechter ME, Wu JM, Marzano D, et al. Management of Bartholin duct cysts and abscesses: a systematic review. *Obstet Gynecol Surv*. 2009;64:395.

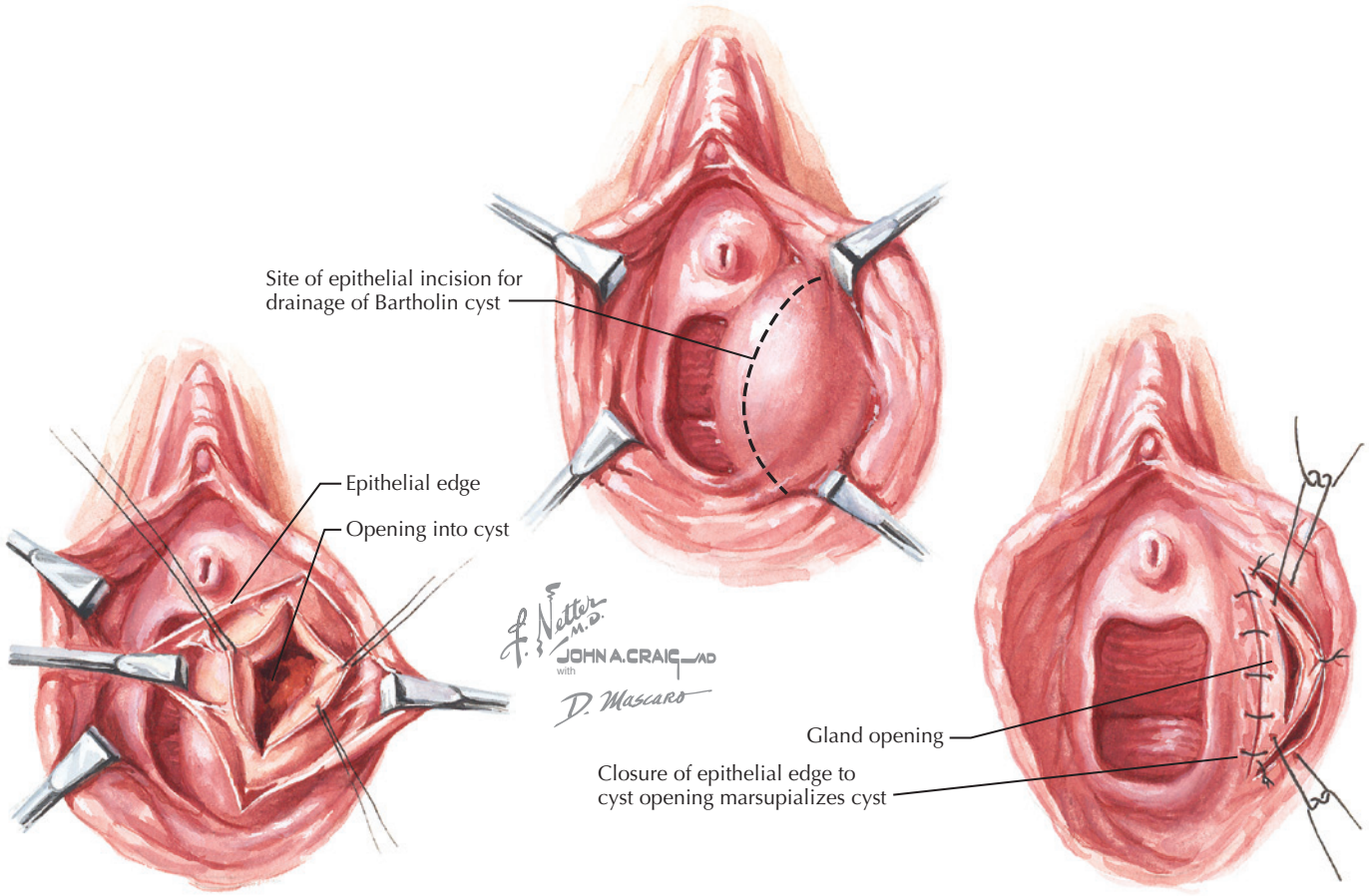


Figure 252.1 Bartholin gland marsupialization

FOLLOW-UP

Word catheters should be left in place for 4–6 weeks. Iodoform gauze packing should be gradually removed over the course of several days. Recurrence is frequent (5%–10% of cases).

CPT CODE(S)

56440 Marsupialization of Bartholin gland

REFERENCES

LEVEL II

Eilber KS, Raz S. Benign cystic lesions of the vagina: a literature review. *J Urol*. 2003;170:717.

Ozdegirmenci O, Kayikcioglu F, Haberal A. Prospective randomized study of marsupialization versus silver nitrate application in the management of bartholin gland cysts and abscesses. *J Minim Invasive Gynecol*. 2009; 16:149.

LEVEL III

Omole F, Simmons BJ, Hacker Y. Management of Bartholin's duct cyst and gland abscess. *Am Fam Physician*. 2003;68:135.

Wechter ME, Wu JM, Marzano D, et al. Management of Bartholin duct cysts and abscesses: a systematic review. *Obstet Gynecol Surv*. 2009;64: 395.

BREAST BIOPSY: CORE

DESCRIPTION

Core breast biopsy is a technique used to obtain small tissue samples for the histologic diagnosis of breast masses. It has become the preferred method of histologic diagnosis for breast masses.

INDICATIONS

Breast mass or suspicious lesion (palpable; nonpalpable masses may be sampled if image guidance is available).

CONTRAINDICATIONS

Local skin infection, known or suspected allergy to agents used (eg, latex, iodine). Core needle biopsy may not be suitable for patients who have very small or very hard breast lumps; masses close to the chest wall, nipple, or surface of the breast; calcifications that require magnification; or very small breasts. Patients who take blood thinners or aspirin should discontinue them before the procedure. Women who cannot remain still or in the supine position for 20–40 minutes because of physical illness or other problems are not good candidates for stereotactic core needle biopsy.

REQUIRED EQUIPMENT

- Skin preparation materials (alcohol, iodine- or hexachlorophene-based antibacterial solution [eg, Betadine, Hibiclens])
- Sterile gloves (if desired)
- 1% lidocaine without epinephrine, 5-cc syringe, 25-gauge needle
- Disposable core biopsy needle
- Scalpel (#11 blade), if desired
- Sterile gauze pads (2″ × 2″)
- Suitable tissue preservation/transportation medium (10% formalin solution or similar)
- Self-adhesive bandage
- Anxiolytics may be administered as needed

TECHNIQUE

After appropriate informed consent has been obtained from the patient, the skin is disinfected and a skin wheal of local anesthetic is injected at the site chosen for needle penetration. The patient may be either in the supine or prone position based on the location of the lesion to be biopsied, optimal access, and availability or need for image guidance. Using the fingers of the opposite hand to stabilize the area in question, the physician advances the needle into the area of concern by palpation or under image guidance using either stereotactic mammography or ultrasonography. Passage of the needle through the skin may be facilitated by a small incision if desired. A change in tissue resistance or a "gritty" sensation may be noticed as the needle enters some mass lesions.

Core biopsy needles generally have a specialized tip with a covering sheath and cutting edge. The needles are of large caliber (14 g) and are mounted onto a spring-loaded device that allows small

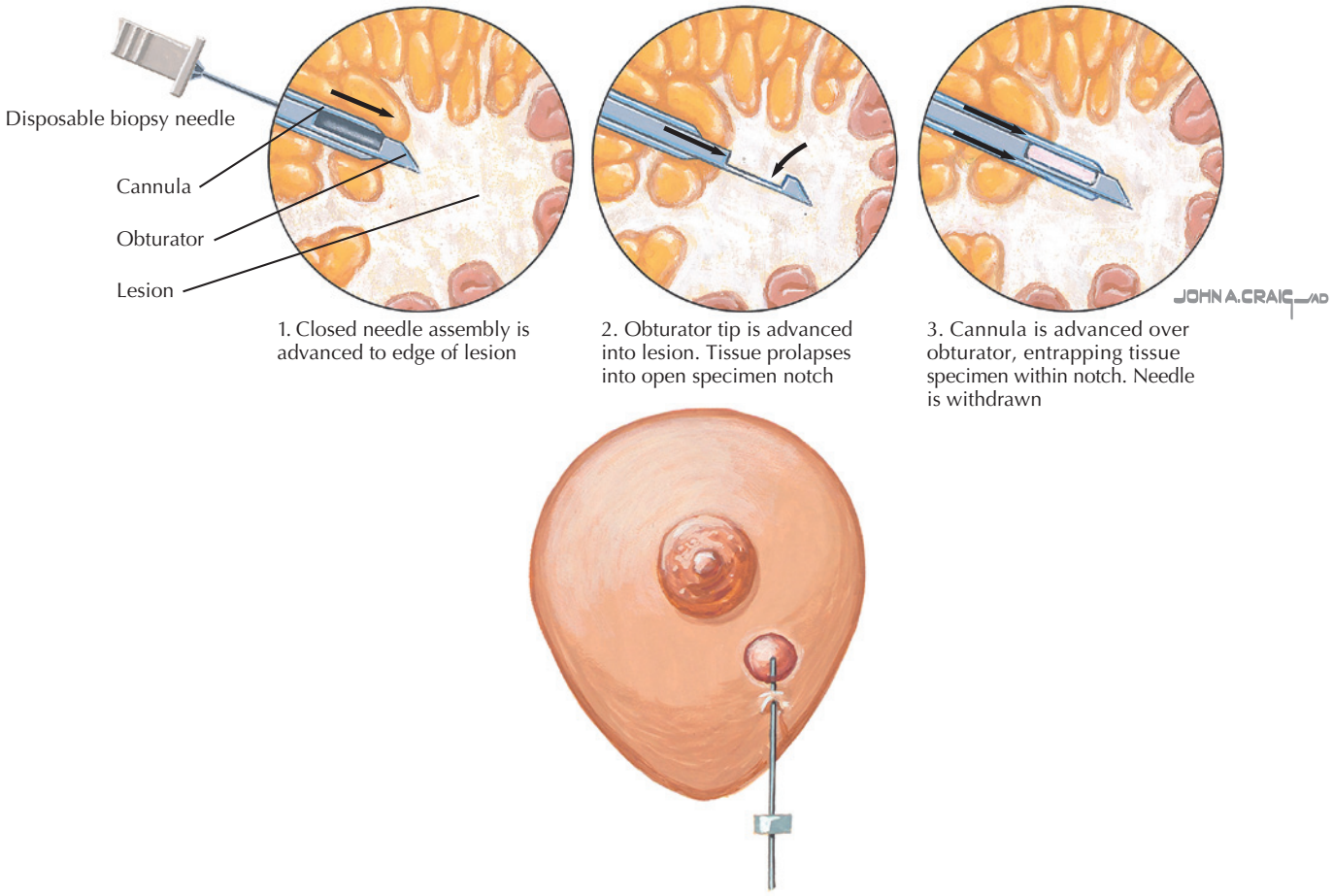


Figure 253.1 Needle biopsy

cylinders of tissue to be cut and collected within the notch of the needle. Techniques vary slightly based on the specific needle but commonly involve placing the tip just short of the tissue to be biopsied; then, the inner core is advanced into the tissue and the outer (cutting) sheath is advanced to free the tissue sample trapped in the inner portion of the needle. The needle is removed, tissue sample is extracted, and additional samples (as needed) are obtained in the same manner. Typically, samples are approximately 2-cm long and 0.16 cm in diameter.

Three to six separate core needle insertions are typically needed to obtain a sufficient sample of breast tissue. Patients may experience a slight pressure during core needle biopsy but should not experience any significant pain. At the close of the procedure, samples are sent to the pathology laboratory for diagnosis, and a light dressing is applied (a self-adhesive bandage suffices). Ice and gentle pressure may be applied for 15–30 minutes to minimize bruising.

Vacuum-assisted breast biopsy is able to remove approximately twice the amount of tissue compared with core needle biopsy while still offering the advantages of a minimally invasive procedure. The technique is the same as with core biopsy, differing only in the nature of the sampling device.

COMPLICATIONS

Bleeding, hematoma, infection.

FOLLOW-UP

The reported false-negative rate for malignancy with core biopsy is in the range of 2%–6.7%, with a mean rate of 4.4%. Approximately 10% of biopsy attempts will be inconclusive. Certain histologic results should be interpreted with caution: more than one half of all cases of atypical ductal hyperplasia (ADH) diagnosed with core biopsy prove malignant at surgery, and invasive carcinoma is found in up to one-third of core biopsy–confirmed ductal carcinoma in situ (DCIS).

CPT CODE(S)

19100 Biopsy of breast; percutaneous, needle core, not using imaging guidance (separate procedure)

19102 Biopsy of breast; percutaneous, needle core, using imaging guidance

19103 Biopsy of breast; percutaneous, automated vacuum assisted or rotating biopsy device, using imaging guidance

REFERENCES

LEVEL II

Brenner RJ, Fajardo L, Fisher PR, et al. Percutaneous core biopsy of the breast: effect of operator experience and number of samples on diagnostic accuracy. *AJR Am J Roentgenol*. 1996;166:341.

Bruening W, Fontanarosa J, Tipton K, et al. Systematic review: comparative effectiveness of core-needle and open surgical biopsy to diagnose breast lesions. *Ann Intern Med*. 2010;152:238.

Gutwein LG, Ang DN, Liu H, et al. Utilization of minimally invasive breast biopsy for the evaluation of suspicious breast lesions. *Am J Surg*. 2011;202:127.

Jackman RJ, Nowels KW, Rodriguez-Soto J, et al. Stereotactic, automated, large-core needle biopsy of nonpalpable breast lesions: false-negative and histologic underestimation rates after long-term follow-up. *Radiology*. 1999;210:799.

Lee CH, Philpotts LE, Horvath LJ, et al. Follow-up of breast lesions diagnosed as benign with stereotactic core-needle biopsy: frequency of mammographic change and false-negative rate. *Radiology*. 1999; 212:189.

Rich PM, Michell MJ, Humphreys S, et al. Stereotactic 14G core biopsy of non-palpable breast cancer: what is the relationship between the number of core samples taken and the sensitivity for detection of malignancy? *Clin Radiol*. 1999;54:384.

LEVEL III

American College of Obstetricians and Gynecologists. Breast cancer screening. Practice Bulletin No. 122. *Obstet Gynecol*. 2011;118:372.

Britton PD. Fine needle aspiration or core biopsy. *Breast*. 1999;8:1.

Staren ED, O'Neill TP. Ultrasound-guided needle biopsy of the breast. *Surgery*. 1999;126:629.

Strong JW, Worsham GF, Austin RM, et al. Stereotactic core biopsy of nonpalpable breast lesions. *J S C Med Assoc*. 1995;91:489.

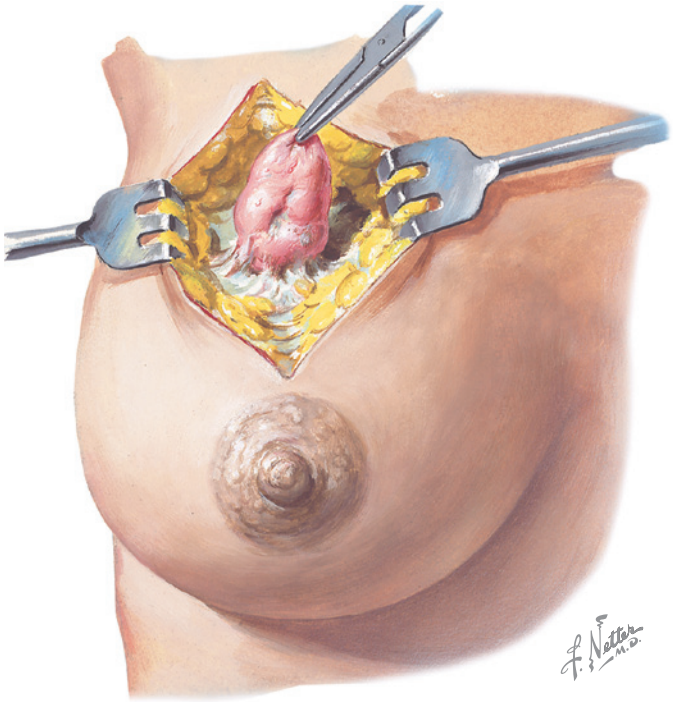


Figure 254.1 Open breast biopsy: masses are often not easily identified, requiring larger incision or needle localization using radiographic assistance.

- Self-adhesive skin tapes (if desired)
- Self-adhesive bandage
- Suitable tissue preservation/transportation medium (10% formalin solution or similar) (If estrogen and progesterone receptors are to be assessed, a sample of unpreserved tissue must be frozen within 30 minutes.)
- Anxiolytics may be administered as needed

TECHNIQUE

After appropriate informed consent has been obtained, the skin is disinfected, and the local anesthetic is injected at the selected site. The majority of biopsies can be performed with curvilinear incisions following the contours of the breast, often in the circumareolar area. An open biopsy should be performed using a scalpel rather than electrosurgical energy because thermal effects on the biopsy material may blur the margin of normal tissue around the tumor and cause abnormally low receptor levels. Thermal damage may also delay skin healing.

The dissection is carried to the area of concern through a combination of sharp and blunt techniques. A change in tissue character or a "gritty" sensation may be noticed as the tissue is dissected near some mass lesions. The mass or area of interest is excised, and hemostasis is obtained through electrosurgical energy or the placement of hemostatic sutures to close dead space. The skin may be closed using a running subcuticular suture or self-adhesive skin tapes.

At the close of the procedure, samples are sent to the pathology laboratory for diagnosis and light dressing is applied; a self-adhesive bandage often suffices. Ice and gentle pressure may be applied for 15–30 minutes to minimize bruising.

It is important to send the pathology laboratory a small sample (1 g of suspect tissue) to determine the presence or absence of estrogen and progesterone receptors. These receptors are heat labile; therefore, the tissue must be frozen within 30 minutes.

Nonpalpable masses may be localized through the placement of a small needle or sterile J-wire under fluoroscopic or ultrasonographic guidance. These are then used as guides for the open dissection. The specimen is removed with the wire or needle in place, and it is radiographed to confirm the removal of the suspect area. These techniques have been largely supplanted by computer-guided core biopsy techniques.

COMPLICATIONS

Bleeding, hematoma, infection.

FOLLOW-UP

If nonabsorbable suture material is used to close the skin, the stitches will need to be removed during a follow-up visit. The incidence of carcinoma in biopsies corresponds directly with the patient's age. Approximately 20% of breast biopsies in women age 50 are positive, and this figure increases to 33% in women aged 70 years or older.

CPT CODE(S)

19101 Biopsy of breast; open, incisional

REFERENCES

LEVEL II

Bluemke DA, Gatsonis CA, Chen MH, et al. Magnetic resonance imaging of the breast prior to biopsy. *JAMA*. 2004;292:2735.

Bruening W, Fontanarosa J, Tipton K, et al. Systematic review: comparative effectiveness of core-needle and open surgical biopsy to diagnose breast lesions. *Ann Intern Med*. 2010;152:238.

Chagpar AB, Scoggins CR, Sahoo S, et al. Biopsy type does not influence sentinel lymph node status. *Am J Surg*. 2005;190:551.

LEVEL III

American College of Obstetricians and Gynecologists. Breast cancer screening. Practice Bulletin No. 122. *Obstet Gynecol*. 2011;118:372.

Chang DS, McGrath MH. Management of benign tumors of the adolescent breast. *Plast Reconstr Surg*. 2007;120:13e.

255 CERVICAL CERCLAGE

DESCRIPTION

Cervical cerclage is the placement of a suture or tape to support and partially occlude the uterine cervix to reduce the risk for preterm delivery in the face of cervical insufficiency. A number of procedures have been described, but the most common and simplest is the McDonald cerclage, which is described here. Cervical cerclage may also be accomplished by placing the suture via an abdominal route, although this is a much more invasive procedure and the suture is generally left in place permanently, precluding vaginal delivery.

INDICATIONS

Cervical incompetence as documented by a history of preterm pregnancy loss associated with painless cervical dilation or prolapse and ballooning of the fetal membranes into the vagina without labor. Cerclage may be placed based on history or cervical shortening documented through ultrasonography. Prophylactic cervical cerclage is generally delayed until after 14 weeks so that early pregnancy losses from other factors may be resolved.

CONTRAINDICATIONS

Bleeding, uterine contractions, obvious infection, multiple gestation, or rupture of the membranes. Beyond 24–26 weeks, bed rest, pessary therapy or other treatments are often preferred because of the increased risk for surgically related labor.

REQUIRED EQUIPMENT

- Skin (vaginal) preparation materials (iodine-based antibacterial solution [eg, Betadine] or other suitable cleansing agents)
- Sterile gloves
- Number 1 or 2 permanent synthetic suture (Prolene or similar) or 5-mm woven tape (Mersilene or similar) on a medium blunt needle. (Monofilament sutures are easier to pass through the tissues, but a broader tape provides more support and less chance of suture erosion into or through the cervix.)
- Needle holder, long thumb forceps, suture scissors
- Retractors (two Deaver or right-angle retractors and/or weighted speculum)
- Sponge stick (may be useful to atraumatically grasp and manipulate the cervix)
- Foley or straight catheter (optional)
- External fetal heart rate monitor or Doppler fetal heart detector

TECHNIQUE

After appropriate informed consent has been obtained, ultrasonography should be performed to confirm a living fetus, exclude major fetal anomalies, and assess cervical length. Any obvious vaginal or cervical infections should be treated, and cultures for gonorrhea, chlamydia, and group B streptococci should be obtained prior to proceeding. Sexual intercourse is generally proscribed for 1 week before and after the procedure.

The anesthetized patient is placed in the dorsal lithotomy position, the vagina and cervix are disinfected, and the cervix is visualized using retractors. Some authors advise distending the maternal bladder to elevate the fetal presenting part, relieve pressure on the fetal membranes, and define the cervicovesical reflection. For right-handed surgeons, the needle is first placed entering the cervix at the 11–12-o'clock position near the inner cervical os, taking care to avoid injuring the bladder. The suture is passed below the surface of the cervix, incorporating some of the parenchyma, and exits at approximately the 10-o'clock position. The suture is then passed once again into the cervical tissue, entering at approximately the 8-o'clock position and exiting posteriorly near the 6- to 7-o'clock position. The circumferential suture is carried up the opposite side in a similar manner, terminating at approximately the 1-o'clock position, where it is firmly tied to the first portion of the suture. The suture should not cause blanching of the tissue but should narrow the cervix so that it will not admit a single gloved finger. The tied suture should be both tied and cut in such a manner as to facilitate eventual location and removal.

Based on the size of the cervix and needle chosen, it may be necessary to take additional suture passes to accomplish adequate circumferential support. Care should be taken such that the portions of the suture at the 3- and 9-o'clock positions are shallow or outside the cervical epithelium to minimize the risk to the descending cervical branches of the uterine vessels.

Following conclusion of the procedure, the fetal heart rate is monitored to assure normal fetal status. Prophylactic antibiotics or β-mimetic drugs have not been shown to be of any benefit in reducing the rate of complications or preterm labor. Some authors advocate prescribing a non-steroidal anti-inflammatory drug, such as indomethacin, for the first 12–24 hours after cerclage placement, but data are conflicting and the effects small.

When the suture is to be removed (generally at 38 weeks and always if labor ensues before that time), it may be carried out in the office or labor and delivery area by firmly grasping the knot or visible suture ends and applying traction to identify one side of the suture below the knot. Snipping this portion of the suture allows traction on the knot to pull the suture through the tissues for removal. An anesthetic may be required based on exposure, patient comfort, and provider or patient preference.

COMPLICATIONS

Preterm rupture of the membranes (1%–18%, up to 65% of emergent cases), chorioamnionitis (1%–7%, up to 35% of emergent cases), bleeding, and damage to adjacent structures (bladder or rectum). Scarring from the procedure may lead to cervical lacerations during labor (1%–13%) or failure of the cervix to dilate (2%–5%).

FOLLOW-UP

Fetal and maternal monitoring is generally performed for 12–24 hours or longer depending on clinical factors.

When the suture is placed vaginally, it is generally removed at 38 weeks of gestation. If labor occurs before this point, the suture must be removed immediately. Because of scarring after cerclage, approximately 15% of patients require cesarean delivery.

CPT CODE(S)

59320 Cerclage of cervix, during pregnancy; vaginal
59325 Cerclage of cervix, during pregnancy; abdominal

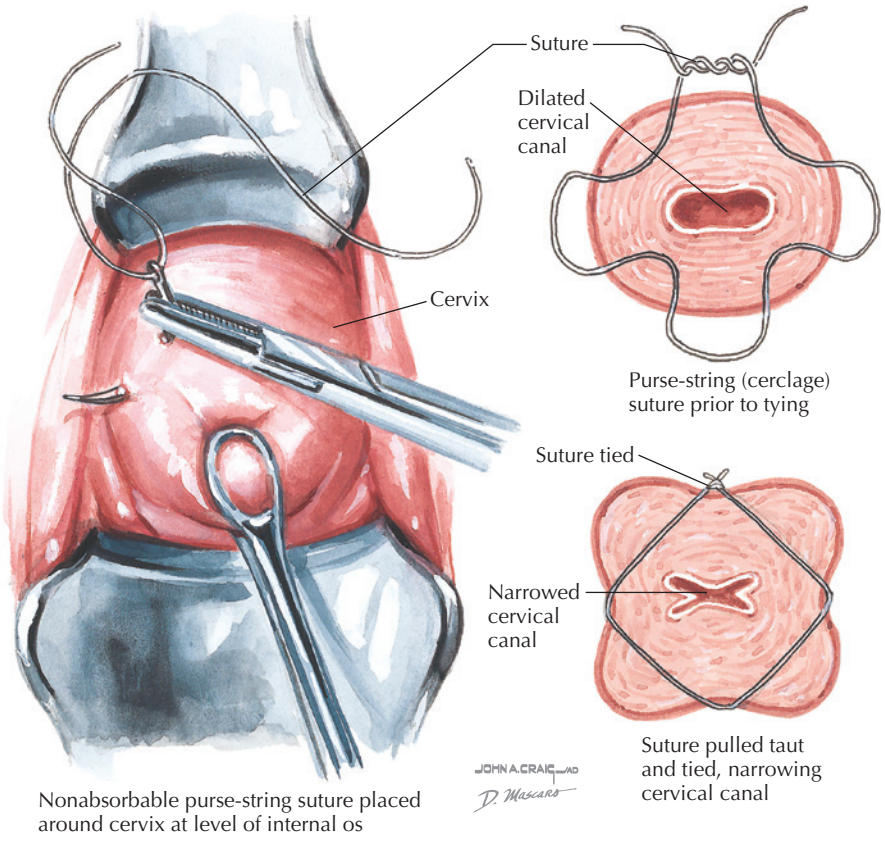


Figure 255.1 Surgical management of cervical incompetence (cerclage)

REFERENCES

LEVEL I

Althuisius SM, Dekker GA, Hummel P, et al. Cervical Incompetence Prevention Randomized Cerclage Trial: Emergency cerclage with bed rest versus bed rest alone. *Am J Obstet Gynecol*. 2003;189:907.

Berghella V, Odibo AO, Tolosa JE. Cerclage for prevention of preterm birth in women with a short cervix found on transvaginal ultrasound examination: a randomized trial. *Am J Obstet Gynecol*. 2004;191:1311.

Brix N, Secher NJ, McCormack CD, et al. Randomised trial of cervical cerclage, with and without occlusion, for the prevention of preterm birth in women suspected for cervical insufficiency. *BJOG*. 2013;120:613.

Owen J, Hankins G, Iams JD, et al. Multicenter randomized trial of cerclage for preterm birth prevention in high-risk women with shortened midtrimester cervical length. *Am J Obstet Gynecol*. 2009;201:375.e1.

Secher NJ, McCormack CD, Weber T, et al. Cervical occlusion in women with cervical insufficiency: protocol for a randomised, controlled trial with cerclage, with and without cervical occlusion. *BJOG*. 2007;114(649):e1.

To MS, Alfirevic Z, Heath VC, et al. Fetal Medicine Foundation Second Trimester Screening Group: Cervical cerclage for prevention of preterm delivery in women with short cervix: randomized controlled trial. *Lancet*. 2004;363:1849.

LEVEL II

Alfirevic Z, Stampalija T, Roberts D, et al. Cervical stitch (cerclage) for preventing preterm birth in singleton pregnancy. *Cochrane Database Syst Rev*. 2012;(4):CD008991.

Berghella V, Keeler SM, To MS, et al. Effectiveness of cerclage according to severity of cervical length shortening: a meta-analysis. *Ultrasound Obstet Gynecol*. 2010;35:468.

Berghella V, Rafael TJ, Szychowski JM, et al. Cerclage for short cervix on ultrasonography in women with singleton gestations and previous preterm birth: a meta-analysis. *Obstet Gynecol*. 2011;117:663.

Drakeley AJ, Roberts D, Alfirevic Z. Cervical cerclage for prevention of preterm delivery: meta-analysis of randomized trials. *Obstet Gynecol*. 2003;102:621.

Ehsanipoor RM, Seligman NS, Saccone G, et al. Physical examination-indicated cerclage: a systematic review and meta-analysis. *Obstet Gynecol*. 2015;126:125.

Harger JH. Cerclage and cervical insufficiency: an evidence-based analysis. *Obstet Gynecol*. 2002;100:1313.

Zaveri V, Aghajafari F, Amankwah K, et al. Abdominal versus vaginal cerclage after a failed transvaginal cerclage: a systematic review. *Am J Obstet Gynecol*. 2002;187:868.

LEVEL III

Althuisius SM, van Geijn HP. Strategies for prevention—Cervical cerclage. *BJOG*. 2005;112:51.

American College of Obstetricians and Gynecologists. Cerclage for the management of cervical insufficiency. Practice Bulletin No. 142. *Obstet Gynecol*. 2014;123:372.

McNamara HM. Problems and challenges in the management of preterm labour. *BJOG*. 2003;110:79.

Noori M, Helmig RB, Hein M, et al. Could a cervical occlusion suture be effective at improving perinatal outcome? *BJOG*. 2007;114:532.

256 CERVICAL CONIZATION (COLD KNIFE)

DESCRIPTION

Cervical conization is a diagnostic or therapeutic procedure that removes a cone-shaped specimen from the uterine cervix. Cold knife cone biopsy used to be the preferred treatment for removing abnormal cells, but now most cone biopsies are performed using the wire loop and electrosurgical energy (loop electrosurgical excision procedure [LEEP]/large loop excision of the transformation zone [LLETZ] cone). Cold knife cone biopsy is generally used for special situations such as when the size or shape of the specimen must be customized to a greater degree than allowed by loop procedures.

INDICATIONS

Histologically verified advanced epithelial atypia (for diagnosis or therapy) or inability to adequately evaluate the cervix through colposcopy.

CONTRAINDICATIONS

Coagulopathy, advanced pregnancy, known or suspected allergy to the agents used.

REQUIRED EQUIPMENT

- Skin (vaginal) preparation materials (iodine-based antibacterial solution [eg, Betadine] or other suitable cleansing agents)
- Sterile gloves
- 0 or 2-0 synthetic absorbable suture on a medium needle
- Needle holder, long thumb forceps, suture scissors
- Retractors (two Deaver or right-angle retractors and/or weighted speculum)
- Scalpel (#11 blade)
- Uterine sound (blunt probe) or small cervical dilator
- Sponge stick (may be useful to atraumatically grasp and manipulate the cervix)
- Electrosurgical generator, hand piece, and return electrode ("ground pad")
- Monsel solution or paste (ferric subsulfate)
- Histology fixative (10% formalin) in containers
- 5% acetic acid or Lugol solution (super-saturated potassium iodide) if colposcopy is to be performed
- Vaginal pack (optional)

TECHNIQUE

Cold knife conizations are generally performed under regional or general anesthesia. After providing appropriate informed consent, the anesthetized patient is placed in the dorsal lithotomy position, the vagina and cervix are disinfected, and the cervix is visualized using retractors. If necessary, a colposcopic examination, facilitated by acetic acid or Lugol solution, may be performed to further characterize any abnormalities present.

The procedure begins with the placement of hemostatic sutures (simple loop or figure-of-eight) at the 3- and 9-o'clock positions on

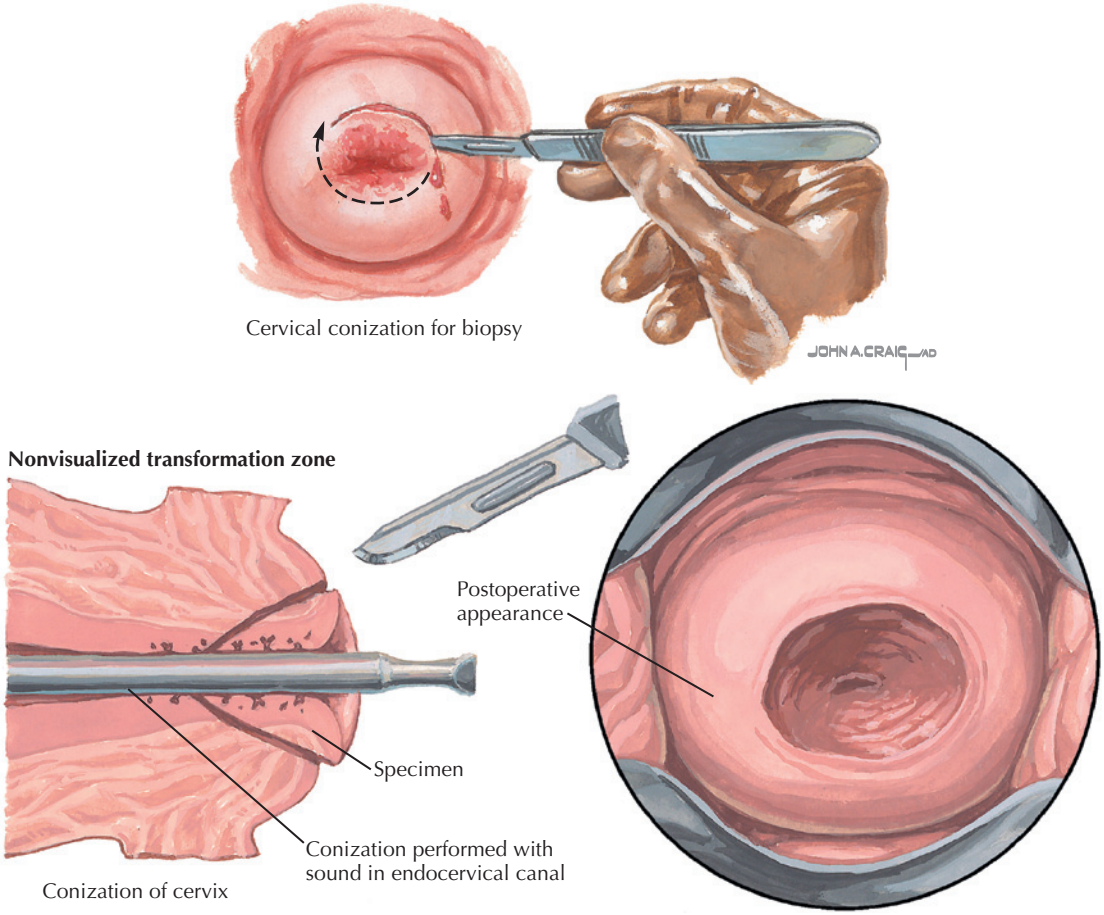


Figure 256.1 Cervical conization

the cervix near the cervicovaginal reflections bilaterally. These are generally tied and held to stabilize the cervix until the end of the procedure, although the role of these sutures in reducing blood loss has been debated and they may be omitted in certain cases. Dilute vasopressin (1 pressor unit/20 mL saline) or 1:200,000 epinephrine solution may be injected into the cervical parenchyma to further reduce blood loss. If desired, a blunt uterine probe or small cervical dilator is placed into the endocervical canal to guide the dissection.

A cone-shaped plug of cervical tissue is excised by sweeping the scalpel blade around the ectocervix with the blade angled inward to intersect the endocervical canal. The width and depth of the conization are determined by the anatomy of the cervix, the location of the transformation zone, and the lesion being treated; it must include the transformation zone and any specific lesion.

Hemostasis may be obtained through electrosurgical energy or the application of styptics such as Monsel solution. Some advocate general cautery of the cut surface of the cervix, although the resultant slough of damaged tissue may delay final healing. If desired, the ectocervical edges may be sewn with a running suture to provide hemostasis at the edge and to roll the edges inward. As an alternative, Sturmdorf stitches may be placed to partially reconstruct the external cervical os, although some argue that this may increase the risk of cervical stenosis. At the close of the procedure, the held tails of the hemostatic sutures may be either clipped (leaving the suture in place) or tied across the cervix to apply pressure or to hold a hemostatic pledget (oxidized regenerated cellulose [Surgicel or similar]) in place. Pelvic rest (no tampons, douching, or sexual intercourse) is generally advised for 2–3 weeks following the procedure, and the patient is instructed to return for heavy bleeding or bleeding that lasts more than 2 weeks.

COMPLICATIONS

Bleeding (acute and delayed, 5% to 10%, <1% transfusion rate), infection, uterine perforation, injury to the bladder or bowel, cervical stenosis, and cervical incompetence. Conization appears to approximately double the risk that a woman will subsequently have a preterm delivery, a low-birthweight infant, or premature rupture of the membranes.

FOLLOW-UP

The cervix is generally inspected at about 6 weeks after the procedure. Treatment success for cervical intraepithelial neoplasia is generally 95%.

CPT CODE(S)

57520 Conization of cervix, with or without fulguration, with or without dilation and curettage, with or without repair; cold knife or laser

REFERENCES

LEVEL I

Duggan BD, Felix JC, Muderspach LI, et al. Cold-knife conization versus conization by the loop electrosurgical excision procedure: a randomized, prospective study. *Am J Obstet Gynecol*. 1999;180:276.

Mathevet P, Dargent D, Roy M, et al. A randomized prospective study comparing three techniques of conization: cold knife, laser, and LEEP. *Gynecol Oncol*. 1994;54:175.

LEVEL II

El-Bastawissi AY, Becker TM, Daling JR. Effect of cervical carcinoma in situ and its management on pregnancy outcome. *Obstet Gynecol*. 1999;93:207.

Jackobsson M, Gissler M, Sainio S, et al. Preterm delivery after surgical treatment for cervical intraepithelial neoplasia. *Obstet Gynecol*. 2007; 109:309.

Kyrgiou M, Koliopoulos G, Martin-Hirsch P, et al. Obstetric outcomes after conservative treatment for intraepithelial or early invasive cervical lesions: systematic review and meta-analysis. *Lancet*. 2006;367:489.

Kyrgiou M, Tsoumpou I, Vrekoussis T, et al. The up-to-date evidence on colposcopy practice and treatment of cervical intraepithelial neoplasia: the Cochrane colposcopy and cervical cytopathology collaborative group (C5 group) approach. *Cancer Treat Rev*. 2006;32:516.

Martin-Hirsch PL, Kitchener H. Interventions for preventing blood loss during the treatment of cervical intraepithelial neoplasia. *Cochrane Database Syst Rev*. 2000;(2):CD001421.

Martin-Hirsch PL, Paraskevaidis E, Kitchener H. Surgery for cervical intraepithelial neoplasia. *Cochrane Database Syst Rev*. 2000;(2): CD001318.

Sadler L, Saftlas A, Wang W, et al. Treatment for cervical intraepithelial neoplasia and risk of preterm delivery. *JAMA*. 2004;291:2100.

LEVEL III

American College of Obstetricians and Gynecologists. Management of abnormal cervical cancer screening test results and cervical cancer precursors. Practice Bulletin No. 140. *Obstet Gynecol*. 2013;122:1338.

Morris M, Mitchell MF, Silva EG, et al. Cervical conization as definitive therapy for early invasive squamous carcinoma of the cervix. *Gynecol Oncol*. 1993;51:193.

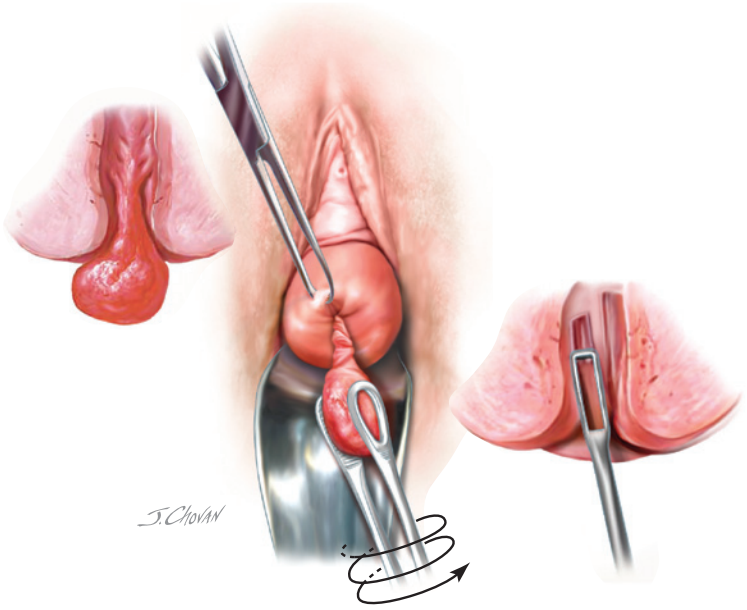


Figure 257.1 Cervical polypectomy

- Sterile or examination gloves
- Vaginal speculum
- Sponge stick or uterine packing forceps (fine scissors may be used but are seldom required)
- Kevorkian or similar endocervical curette
- Monsel solution or paste (ferric subsulfate) or silver nitrate–tipped sticks
- Histology fixative (10% formalin) in container

TECHNIQUE

The polyp is first visualized through the use of a standard vaginal speculum. Disinfection with a suitable solution may be performed, although most believe it is not required. The visible portion of the polyp is then grasped, and gentle traction, twisting through several revolutions, or excision accomplishes the removal of polyp. If the polyp is considered to arise from high in the endocervical canal, the base may be gently curetted with an endocervical curette. Curettage of the endocervical canal should also be considered to rule out a coexisting hyperplasia or cancer. Although malignancy is rare, all polyps should be submitted for histologic examination. The base of the polyp may be treated with chemical cautery (Monsel solution or silver nitrate), electrocautery, or cryocautery.

COMPLICATIONS

Bleeding

FOLLOW-UP

Although the histology of the polyp should be confirmed as benign, malignant degeneration of an endocervical polyp is extremely rare. The reported incidence is less than 1 in 200.

CPT CODE(S)

58999 Unlisted procedure, female genital system (nonobstetric)

REFERENCES

LEVEL II

Amesse LS, Taneja A, Broxson E, et al. Protruding giant cervical polyp in a young adolescent with a previous rhabdomyosarcoma. *J Pediatr Adolesc Gynecol*. 2002;15:271.

Esim Buyukbayrak E, Karageyim Karsidag AY, Kars B, et al. Cervical polyps: evaluation of routine removal and need for accompanying D&C. *Arch Gynecol Obstet*. 2011;283:581.

Pradhan S, Chenoy R. Dilatation and curettage in patients with cervical polyps: a retrospective analysis. *BJOG*. 1995;102:415.

CESAREAN DELIVERY

258

DESCRIPTION

Cesarean delivery (or cesarean section) is the delivery of the fetus through surgical incisions in the mother's abdomen and uterus. The rate of cesarean birth varies from 10% to 35% around the world, influenced by cultural factors and the availability of surgical care. In the United States, the rate of cesarean births increased by 5-fold for a 20-year period that ended in the early 1990s. The exact reasons for this are open to conjecture, but concerns about liability, almost universal use of electronic fetal monitoring, increasing birth weight, and an increased number of repeat cesarean deliveries have all been postulated. Despite this increase, only minor improvements in newborn outcomes have occurred as a result.

INDICATIONS

Cesarean delivery may be selected to accomplish fetal delivery when it is impossible, impractical, or unsafe for the baby to be vaginally delivered. Acute indications for cesarean delivery include fetal distress, hemorrhage from placenta previa, abruptio placentae, prolapse of the umbilical cord, and uterine rupture because these conditions require prompt delivery. Fetal intolerance to labor or failure of the labor to progress may also necessitate cesarean delivery. Less common are the anatomic or congenital conditions of mother or fetus that make vaginal delivery undesirable. An estimated 2.5% of all births in the United States are cesarean delivery on maternal request.

CONTRAINDICATIONS

Like most surgical procedures, the gross instability of the mother (eg, hypovolemia, hypotension, sepsis) and uncertainty about fetal status are relative contraindications. That said, there are rare instances where cesarean delivery must be performed to save a fetus when the mother is dying.

REQUIRED EQUIPMENT

Minimum requirements (for emergency procedures outside of the operating room):

- Sterile gloves, antiseptic solution or skin preparation swabs
- #10 scalpel
- Emergency delivery pack (bulb syringe, umbilical cord clamps, scissors, towels, and basin)
- Emergency cesarean pack (typically: 2 Kocher clamps, 4 Kelly clamps, 1-2 Allis clamps, 1 mayo scissors, 1 bandage scissors, 2 tissue forceps, 1 or 2 retractors [Richardson])
- An assistant is advantageous

Preferred requirements (operating room setting):

- Sterile gloves, antiseptic solution or skin preparation swabs
- Surgical gowns and gloves for the surgical team
- Sterile drape pack for abdominal surgery
- "Major abdominal surgery" instrument tray
- Sutures for uterine and fascial closure (eg, 0 or 00 delayed absorbable), and skin (eg, undyed 3-0 or 4-0 delayed absorbable, or 4-0 permanent to be removed a few days after the procedure)
- Umbilical cord clamps (2)
- Bulb suction (to clear the newborn's airway)
- Electrosurgical energy source and hand piece (optional)
- Surgical suction
- Sterile wound dressing materials and adhesive tape

TECHNIQUE

Following the establishment of appropriate anesthesia (generally a regional technique) and skin and vaginal preparation, the patient is draped in the usual fashion for lower abdominal surgery. Cesarean delivery may be accomplished through either a lower abdominal vertical midline or transverse (Pfannenstiel) incision. (Cesarean sections are not classified by the kind of abdominal incision made but rather as lower uterine segment (transverse or vertical) when the uterine incision is in the lower uterine segment or classical when the incision is in the upper, contractile portion of the uterus—the low-transverse form is described here.) Once the abdominal cavity has been entered and adequate exposure of the lower uterus has been secured, the bladder reflection is identified. If a "bladder flap" of visceral peritoneum is to be raised, an incision in the peritoneum overlying the lower segment is made and the peritoneum reflected inferiorly and superiorly to a distance of 1–2 cm. A transverse incision in the lower uterine segment is made (within the peritoneal flap, if one has been made), and this is carried down to the amniotic sac. The incision is then laterally widened and cephalad through a combination of blunt and sharp dissection at the surgeon's discretion. This incision must be able to accommodate the delivery of the fetus. The amniotic sac is entered, and the exact lie and position of the fetus are determined. Where possible, the fetal head is delivered through the uterine incision in the occiput-anterior position and extended to allow passage outside the abdomen by gentle upward traction. The delivery is completed, and the newborn is briefly dried, suctioned, and stimulated as needed. The umbilical cord is doubly clamped and cut, and the newborn is transferred from the sterile field to the pediatrician or other provider who will conduct the initial assessment and stabilization. If significant bleeding from the edge of the uterus is encountered, it is temporarily controlled using non-crushing clamps. The placenta may be spontaneously delivered by expulsion, by anterior–posterior pressure or by manual extraction. The uterine incision is closed in either 1 or 2 layers using delayed absorbable suture. Hemostasis must be established and verified before the abdominal wall closure is begun. The fascia is generally approximated using a delayed absorbable suture in a running fashion. The skin may be closed with skin staples or subcuticular sutures of either (undyed) delayed absorbable or permanent suture material—suture closure is associated with fewer wound complications and better cosmetic results. Following final sponge and needle counts a sterile dressing is applied.

COMPLICATIONS

Immediate complications of cesarean delivery include bleeding, infection, injury to adjacent organs or the fetus itself, and the possibility of additional surgery (including hysterectomy) based on the conditions at hand. Complications of surgical anesthesia, such as hypoxia, ischemic events (eg, stroke, myocardial infarction), aspiration, and embolism may also occur.

Because cesarean delivery is a major surgical procedure, the rate of maternal mortality is approximately 3- to 4-fold higher than that for vaginal delivery. Potential risks of cesarean delivery include a longer maternal hospital stay, an increased risk for respiratory problems for the baby, and greater complications in subsequent pregnancies, including increased risks for uterine rupture and placental implantation abnormalities. The risks for placenta previa, placenta accreta, and the need for cesarean hysterectomy all increase with each successive cesarean delivery.

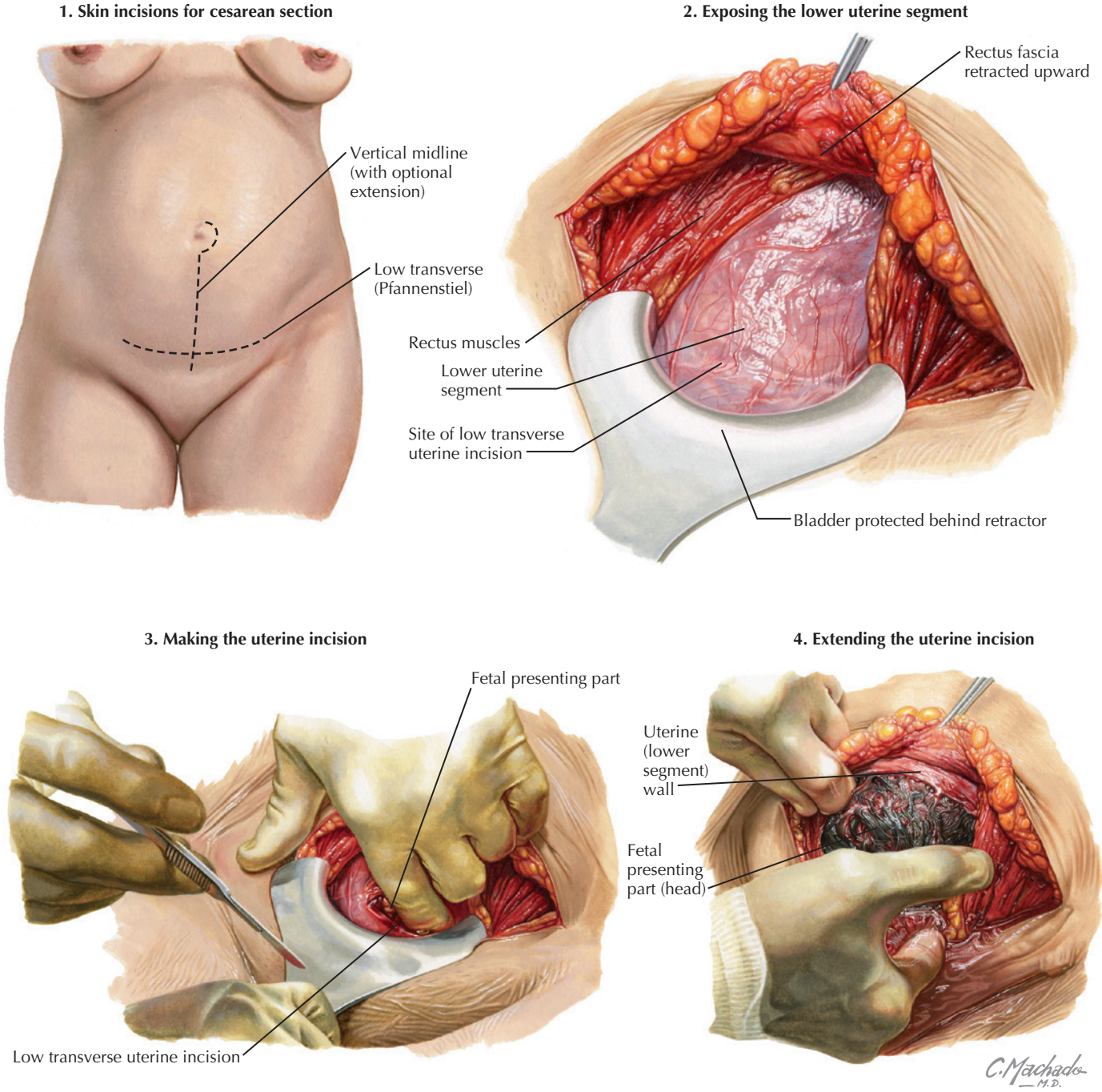


Figure 258.1 Cesarean delivery

FOLLOW-UP

Patients are generally seen within a week of hospital discharge to inspect the abdominal incision. If permanent sutures were used for skin closure, they are generally removed at or before this visit. Additional follow-up appointments are based on the healing of the wound or the presence of any complicating factors. A routine 6-week postpartum visit is also scheduled regardless of the route of delivery.

CPT CODE(S)

59510 Routine obstetric care including antepartum care, cesarean delivery, and postpartum care
59514 Cesarean delivery only
59515 Cesarean delivery only; including postpartum care

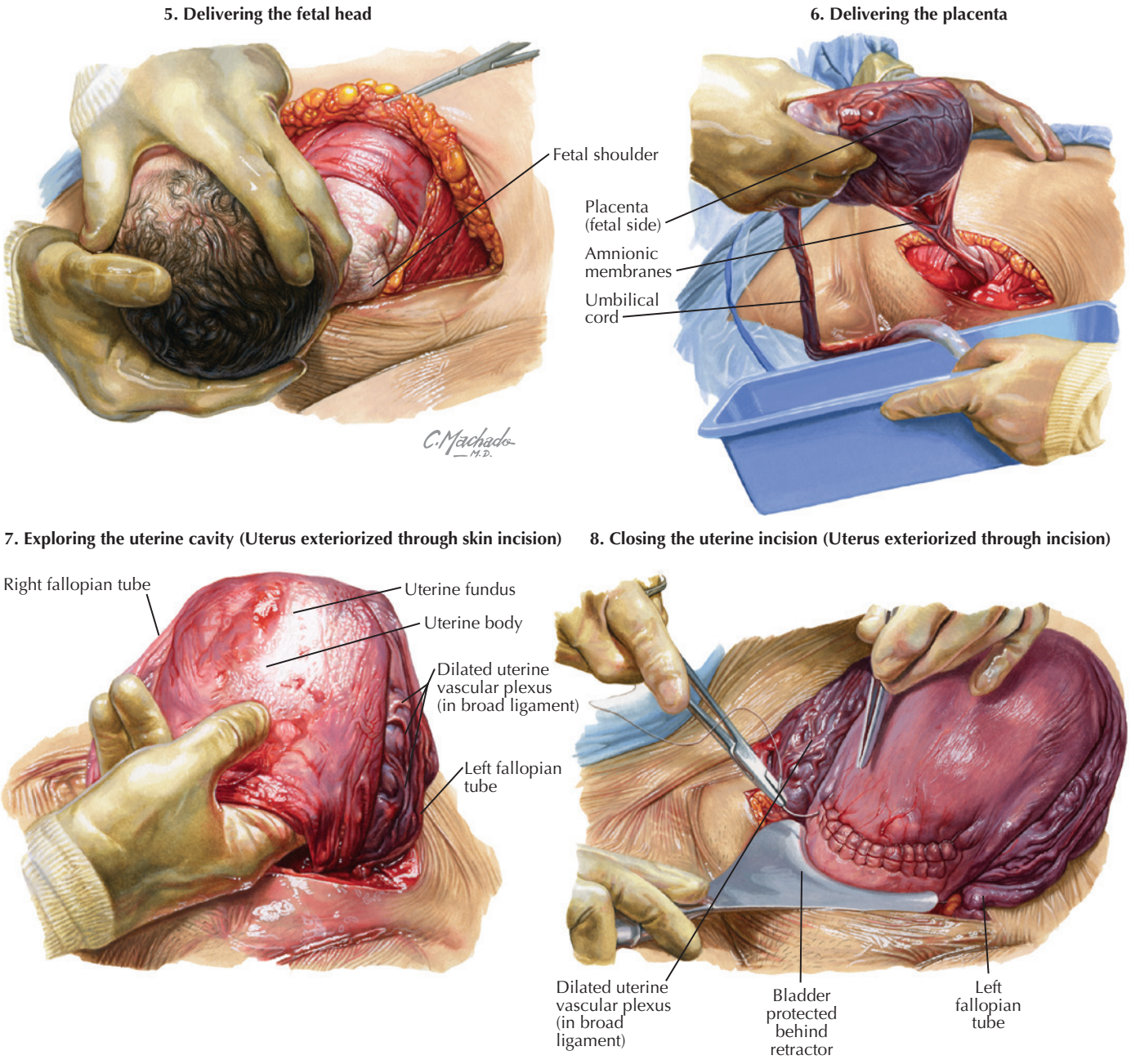


Figure 258.1, cont'd

REFERENCES

LEVEL II

Black M, Bhattacharya S, Philip S, et al. Planned cesarean delivery at term and adverse outcomes in childhood health. *JAMA*. 2015;314:2271.

Creanga AA, Bateman BT, Butwick AJ, et al. Morbidity associated with cesarean delivery in the United States: is placenta accreta an increasingly important contributor? *Am J Obstet Gynecol*. 2015;213:384.

Haas DM, Morgan S, Contreras K. Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections. *Cochrane Database Syst Rev*. 2014;(12):CD007892.

Molina G, Weiser TG, Lipsitz SR, et al. Relationship between cesarean delivery rate and maternal and neonatal mortality. *JAMA*. 2015;314:2263.

O'Callaghan M, MacLennan A. Cesarean delivery and cerebral palsy: a systematic review and meta-analysis. *Obstet Gynecol*. 2013;122:1169.

LEVEL III

American College of Obstetricians and Gynecologists. Obstetric analgesia and anesthesia. ACOG Practice Bulletin No. 36. *Obstet Gynecol*. 2002; 100:177.

American College of Obstetricians and Gynecologists. Vaginal birth after previous cesarean delivery. Practice Bulletin No. 115. *Obstet Gynecol*. 2010;116:450.

American College of Obstetricians and Gynecologists. Use of prophylactic antibiotics in labor and delivery. Practice Bulletin No. 120. *Obstet Gynecol*. 2011;117:1472.

American College of Obstetricians and Gynecologists. Cesarean delivery on maternal request. Committee Opinion No. 559. *Obstet Gynecol*. 2013;121:904.

259 CHORIONIC VILLUS SAMPLING

DESCRIPTION

A technique for obtaining fetal chorionic villus cells for cytogenetic or other testing, chorionic villus sampling (CVS) is usually performed between 10 and 13 weeks of gestation and involves the aspiration of the placental tissue using either percutaneous transabdominal or transcervical approaches. Transabdominal CVS can be performed at more than 13 weeks of gestation. A transvaginal approach similar to the transabdominal method has also been used for retroverted uteruses. Results from CVS have a higher diagnostic uncertainty (confined placental mosaicism) than those from amniocentesis, and the procedure is associated with slightly more complications than second trimester amniocentesis.

INDICATIONS

Genetic testing for fetal chromosome anomalies prompted by risk factors or an abnormal screening test result during the first trimester. Neural tube defects in the fetus cannot be detected by CVS.

CONTRAINDICATIONS

Thrombocytopenia or antiplatelet antibodies, active vaginal bleeding, or infection are relative contraindications. For transcervical CVS: cervical stenosis, cervical or lower uterine myomas. For transabdominal CVS: fetal position that blocks access to the placenta, known or suspected intraabdominal adhesions that could block access to the uterus. CVS may be technically difficult to accomplish in patients with multiple gestations. The risk for human immunodeficiency virus (HIV) vertical transmission associated with early invasive diagnostic techniques is lower than previously expected (3%) and similar to women who do not undergo the procedure.

REQUIRED EQUIPMENT

- Skin (or vaginal) preparation materials (iodine-based antibacterial solution [eg, Betadine] or other suitable cleansing agents)
- Sterile gloves
- Tissue transport medium (to be specified by the laboratory used and the test to be performed)
- Ultrasonography unit

For Transvaginal Approach

- Vaginal speculum
- Sponge stick (may be useful to atraumatically grasp and manipulate the cervix)
- Small (1.5 mm) aspiration cannula (with obturator) and 20- to 30-mL syringe; small biopsy forceps may be used as an alternative

For Transabdominal Approach

- 20- and 22-gauge spinal needles (or smaller), 20-cc syringe, three sterile 10-cc specimen tubes with caps (plain, without additive), sterile drape (one with a small fenestration or multiple drapes)
- If desired: 1% lidocaine without epinephrine, 5-cc syringe, 22-gauge needle (if not included in amniocentesis kit)

TECHNIQUE

The consensus is that CVS, both transabdominal and transcervical approaches, must be performed under ultrasonographic guidance. Ultrasonography is performed before CVS to confirm the gestational age of the fetus. Ultrasonography can also document multiple gestations and whether the multiples share a single placenta or each has its own. It is important to determine the number of placentas because each must be separately sampled to obtain an accurate genetic picture of each fetus.

In the transcervical technique, a speculum is used to visualize the cervix and it is cleansed with an antiseptic solution. The cervix may be stabilized with a sponge stick if needed. The cannula or biopsy tube is gently advanced through the cervix under ultrasonographic guidance until the tip is at the base of the placenta. The obturator is removed from the cannula, and the vacuum is applied to pull a sample of cells into the lumen of the cannula. The cannula is then withdrawn. The amount of tissue needed for the analysis is extremely small (10–25 mg) and represents only approximately 0.1% of the total amount of the placental tissue. The tissue sample obtained should be inspected for perceived adequacy, placed in the appropriate transport medium, labeled, and sent to the laboratory for analysis. Some clinicians prefer to place 10 mL of transport medium directly into the syringe used for suction to allow the aspirated material to enter the medium directly.

Small biopsy forceps may be substituted for the cannula and used in the same manner as with the cannula technique. Although there is some evidence to support the use of forceps as opposed to an aspiration cannula, the evidence is not strong enough to cause a change in practice, and the choice should be driven by operator experience and equipment availability.

When a transabdominal approach is selected, it is accomplished in a manner very similar to amniocentesis: the chorionic villus sample is obtained by passing a fine needle through the abdominal wall and into the placenta using ultrasonographic guidance. Published techniques for transabdominal CVS significantly vary both in the size of the needle used (18-gauge, 20-gauge, and others) and method of aspiration (negative pressure by syringe, negative pressure by vacuum aspirator). No published studies comparing clinical outcomes using different techniques exist.

For patients who are Rh-negative, prophylaxis with Rho(D) Rh-immunoglobulin should be administered.

COMPLICATIONS

Fetal loss rates following CVS are reported to be as high as 6%. Several randomized trials show almost identical miscarriage rates after transcervical CVS compared with the transabdominal approach. CVS is associated with a 14% risk for fetomaternal hemorrhage of more than 0.6 mL. Limb reductions have been associated with early (<9 weeks) CVS. There is some evidence that the focal disruption of the placenta at 13–14 weeks may increase the risk for hypertension/preeclampsia. The chance of getting a placental "mosaic" artifact is higher than with an amniocentesis. Vaginal spotting after CVS is reported in up to one-third of women; slightly heavier bleeding occurs in fewer than 6% of women. Bleeding is more common after transcervical compared with transabdominal CVS. Infection following CVS is very rare, although it is higher for the transcervical approach. Occult or gross rupture of the fetal membranes may occur.

FOLLOW-UP

Results are usually available in 2–3 weeks.

CPT CODE(S)

59015 Chorionic villus sampling, any method

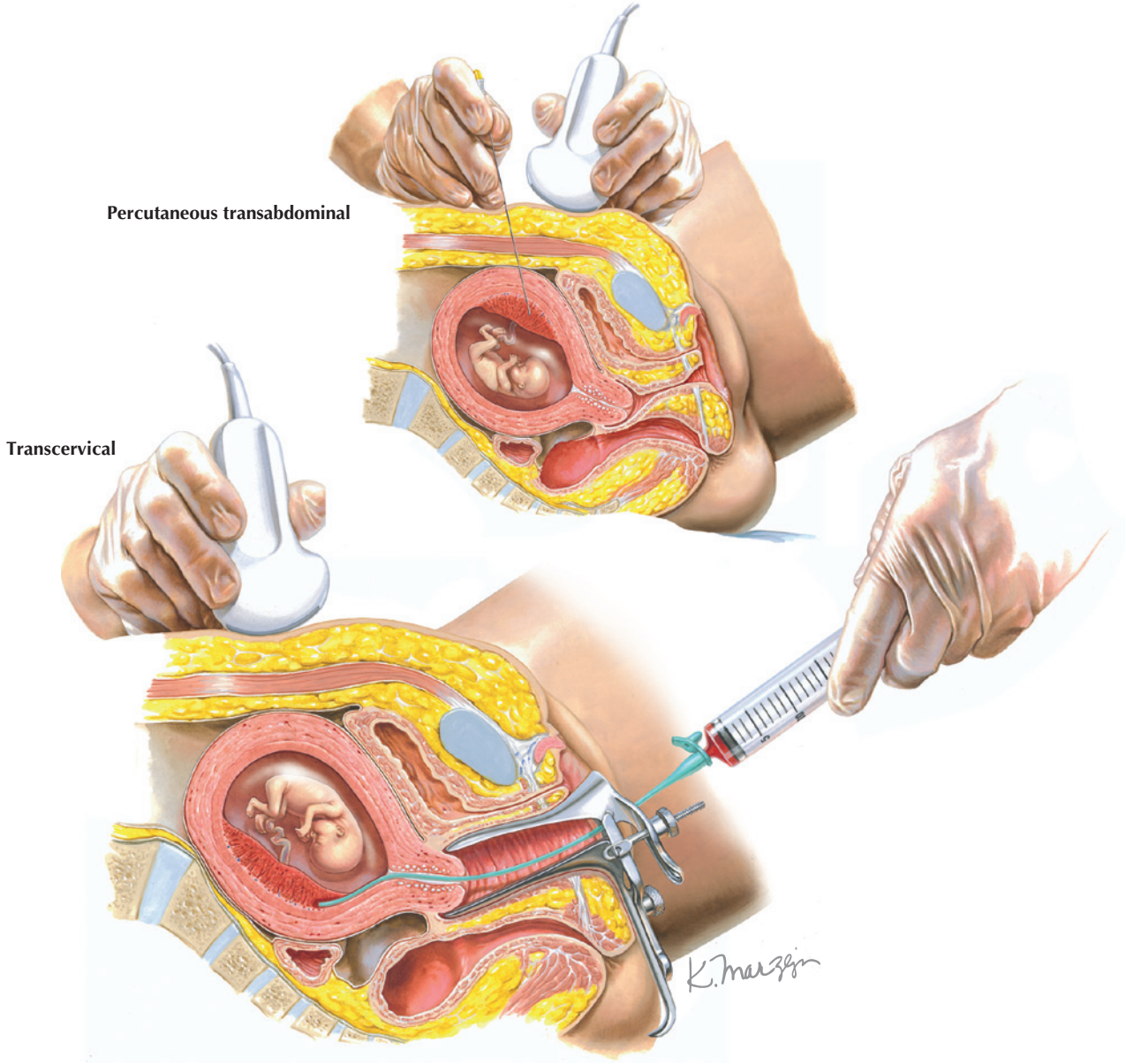


Figure 259.1 Chorionic villus sampling

REFERENCES

LEVEL I

Philip J, Silver RK, Wilson RD, et al.; NICHD EATA Trial Group. Late first-trimester invasive prenatal diagnosis: results of an international randomized trial. *Obstet Gynecol*. 2004;103:1164.

Sundberg K, Bang J, Smidt-Jensen S, et al. Randomised study of risk of fetal loss related to early amniocentesis versus chorionic villus sampling. *Lancet*. 1997;350:697.

LEVEL II

Akolekar R, Beta J, Picciarelli G, et al. Procedure-related risk of miscarriage following amniocentesis and chorionic villus sampling: a systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2015;45:16.

Alfirevic Z, Sundberg K, Brigham S. Amniocentesis and chorionic villus sampling for prenatal diagnosis. *Cochrane Database Syst Rev*. 2004;(3):CD003252.

Brambati B, Tului L, Guercilena S, et al. Outcome of first-trimester chorionic villus sampling for genetic investigation in multiple pregnancy. *Ultrasound Obstet Gynecol*. 2001;17:209.

Louis-Jacques A, Burans C, Robinson S, et al. Effect of commercial cell-free fetal DNA tests for aneuploidy screening on rates of invasive testing. *Obstet Gynecol*. 2014;123(suppl 1):67S.

Mujezinovic F, Alfirevic Z. Analgesia for amniocentesis or chorionic villus sampling. *Cochrane Database Syst Rev*. 2011;(11):CD008580.

Silver RK, Wilson RD, Philip J, et al.; NICHD EATA Trial Group. Late first-trimester placental disruption and subsequent gestational hypertension/preeclampsia. *Obstet Gynecol*. 2005;105:587.

Turner AL, Rad S, Afshar Y, et al. Declining rate of invasive procedures for prenatal diagnosis in the era of noninvasive prenatal testing. *Obstet Gynecol*. 2014;123(suppl 1):196S.

Young C, von Dadelszen P, Alfirevic Z. Instruments for chorionic villus sampling for prenatal diagnosis. *Cochrane Database Syst Rev*. 2013;(1):CD000114.

LEVEL III

American College of Obstetricians and Gynecologists. Screening for Tay–Sachs disease. ACOG Committee Opinion No. 318. *Obstet Gynecol*. 2005;106:893.

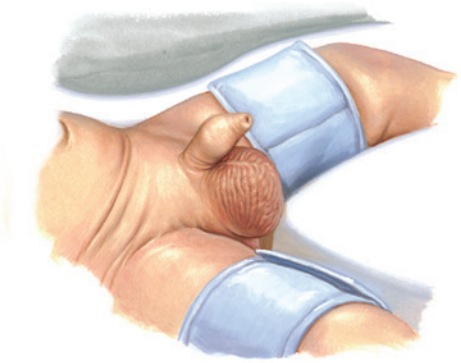
American College of Obstetricians and Gynecologists. Management of alloimmunization during pregnancy. ACOG Practice Bulletin No. 75. *Obstet Gynecol*. 2006;108:457.

American College of Obstetricians and Gynecologists. Preconception and prenatal carrier screening for genetic diseases in individuals of Eastern European Jewish descent. ACOG Committee Opinion No. 442. *Obstet Gynecol*. 2009;114:950.

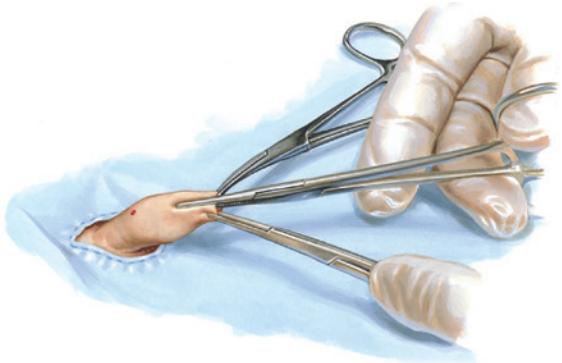
American College of Obstetricians and Gynecologists. Carrier screening for fragile X syndrome. Committee Opinion No. 469. *Obstet Gynecol*. 2010;116:1008.

American College of Obstetricians and Gynecologists. The use of chromosomal microarray analysis in prenatal diagnosis. Committee Opinion No. 581. *Obstet Gynecol*. 2013;122:1374.

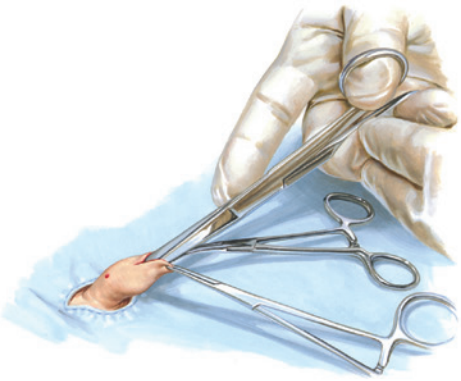
Mujezinovic F, Alfirevic Z. Procedure-related complications of amniocentesis and chorionic villous sampling: a systematic review. *Obstet Gynecol*. 2007;110:687.



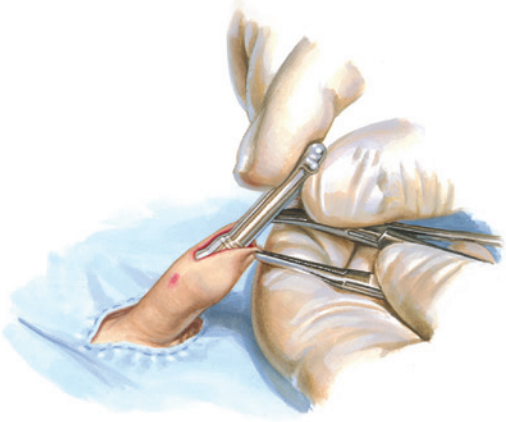
1. All circumcision techniques begin with the undiapered newborn restrained on an infant (papoose) board.



2. A hemostat is used to grasp the edge of the foreskin dorsal to the 3 and 9 o'clock positions (dorsal as 12 o'clock).

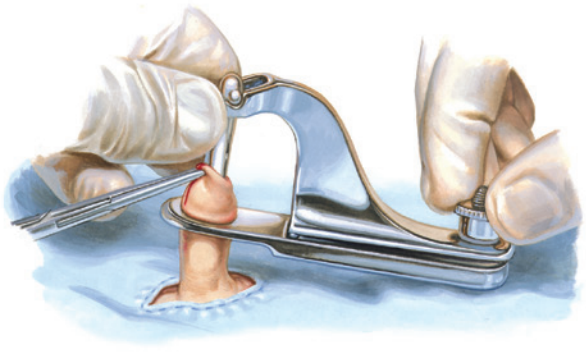


3. The crushed tissue is incised using scissors.

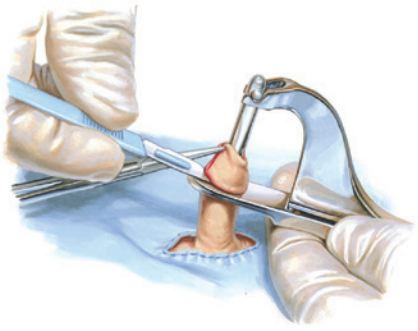


4. The bell of the Gomco clamp is placed under the foreskin, over the glans.

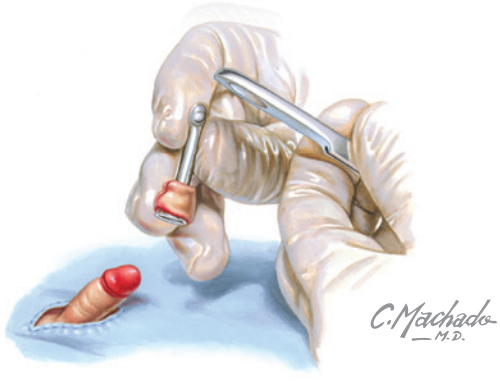
5. Placement of the bell through the baseplate may be facilitated by reaching through the opening with a hemostat.



6. The stem of the bell is placed into the top of the clamp and the thumb screw gently tightened.



7. A scalpel is used to excise all of the tissue above the baseplate of the clamp.



8. The Gomco clamp is loosened and the bell freed to conclude the procedure.

Figure 260.1

laterally to bluntly lyse any adhesions. Care must be taken to avoid disrupting either the ventral attachment or coronal reflection or to inadvertently canalize the urethra. The foreskin is tented away from the glans, and a straight hemostat is inserted along the dorsal line and clamped to a depth of one-third to one-half of the way to the coronal reflection. This is left in place for approximately 1 minute before it is removed, and the crushed tissue is incised using scissors. The glans must be avoided during both the clamping and incision process. The foreskin is next retracted, and any further adhesions are removed; if needed, the dorsal incision is extended by repeating the crush and cut process. The procedure is then completed based on the instrument preferred.

Plastibell

With the dissection of the foreskin free of the glans completed, the Plastibell string is placed as a loop near the base of the penis. The bell is placed under the foreskin and over the glans. This may be facilitated by upward traction on the edges of the foreskin grasped by hemostats and by downward pressure on the stem of the bell. When in a correct position, the bell should rest against the corona. The foreskin is pulled upward, ensuring even placement and positioning that leaves the groove in the bell well below the apex of the dorsal slit. The bell should freely move over the glans. While maintaining these relationships, the string is brought into position, resting in the groove of the bell. The string should be firmly pulled, and all aspects should be rechecked before the string is maximally tightened. Tension on the string is maintained for at least 30 seconds and then a square knot is placed.

The foreskin is cut just above the level of the string, with care taken not to cut too close to the string or to damage the string itself. The string is trimmed, and the stem of the Plastibell is broken off at its junction with the bell. Hemostasis should be confirmed, and a dressing may be applied if desired. The bell may be expected to slough off in 5–8 days, or it may be removed by cutting the ligature after a minimum of 36 hours.

Gomco Clamp

The Gomco clamp consists of a base plate, arm, bell, and thumbscrew. The bell of the Gomco clamp is placed under the foreskin and over the glans in the same manner as with the Plastibell. The bell and foreskin are then inserted through the opening in the baseplate of the clamp. This may be facilitated by reaching through the opening with a hemostat to help guide the foreskin. When the bell is passed through the baseplate, the foreskin must be brought completely through the opening and evenly drawn up on all sides. The entire length of the dorsal incision must be above the baseplate opening. The stem of the bell is placed into the top of the clamp, and the thumbscrew is gently tightened. The foreskin, bell, and shaft of the penis are again inspected before the final tightening is performed.

A scalpel is used to excise all of the tissue above the baseplate of the clamp. Care must be used to completely remove any tissue devitalized by the clamp. The Gomco clamp is loosened, and the bell is freed. The foreskin is freed from the bell by gentle traction using a gauze sponge. Hemostasis must be assured and may be assisted by pressure, the application of Monsel solution, or a fine suture. A petrolatum gauze dressing should be placed, and the newborn should be diapered.

Mogen Clamp

When the Mogen clamp is used, the infant is restrained and inspected, and the skin is prepared as for the other two methods. Hemostats are used to pull the foreskin upward, and the tip of the penis is transilluminated to identify the glans. The Mogen clamp is applied with its curved side toward the glans. It is slid into place over the foreskin from dorsal to ventral in a horizontal plane, and the provider adjusts it so that the desired amount of skin is distal to the clamp. The clamp is angled so that more skin is removed from the dorsal side of the penis. The glans is again inspected and palpated to ensure it is clear of the clamp, and the clamp is then tightened. A scalpel is used to cut the foreskin flush with the surface of the clamp. The clamp is left in place for approximately 1 minute before it is removed. If the Mogen clamp is left in place for more than 1 minute, the sides of the foreskin may become fused and difficult to separate. The sides of the foreskin are separated by downward traction, inspected, and dressed. A gauze pad may be used to help separate the sides of the foreskin if necessary, although excess bleeding may be encountered if too much force is used. (A small ventral "dog ear" will often be present when the clamp is removed. This will partially necrose and heal without cosmetic defect.)

Silver nitrate should not be used for hemostasis because of the risk of permanent staining of the tissues.

COMPLICATIONS

The exact incidence of complications after circumcision is not known, but data indicate that the rate is low (0.2%–0.6%), and the most common complications are local infection and bleeding. Rare complications include urinary fistulae, chordee, cysts, lymphedema, ulceration of the glans, necrosis of all or part of the penis, hypospadias, epispadias, impotence, and removal of too much tissue (sometimes causing secondary phimosis).

FOLLOW-UP

Following circumcision, the infant should be observed for at least 4 hours and should void before being released. The petrolatum gauze should be removed after 24 hours or if it becomes soiled. Petrolatum jelly should be applied at each diaper change until healing has occurred (approximately 7–10 days). At each diaper change the penile skin should be retracted to prevent adhesion formation.

CPT CODE(S)

54150 Circumcision, using clamp or other device with regional dorsal penile or ring block

54160 Circumcision, surgical excision other than clamp, device, or dorsal slit; neonate (28 days of age or less)

00920 Anesthesia for procedure on male external genitalia; not otherwise specified

REFERENCES

LEVEL I

Sinkey RG, Eschenbacher MA, Walsh PM, et al. The GoMo study: a randomized clinical trial assessing neonatal pain with Gomco vs Mogen clamp circumcision. *Am J Obstet Gynecol*. 2015;212:664.e1.

LEVEL II

Brady-Fryer B, Wiebe N, Lander JA. Pain relief for neonatal circumcision. *Cochrane Database Syst Rev*. 2004;(4):CD004217.

Jagannath VA, Fedorowicz Z, Sud V, et al. Routine neonatal circumcision for the prevention of urinary tract infections in infancy. *Cochrane Database Syst Rev*. 2012;(11):CD009129.

Stevens B, Yamada J, Ohlsson A. Sucrose for analgesia in newborn infants undergoing painful procedures. *Cochrane Database Syst Rev*. 2004;(3):CD001069.

Strimling BS. Partial amputation of glans penis during Mogen clamp circumcision. *Pediatrics*. 1996;97:906.

Weiss HA, Larke N, Halperin D, et al. Complications of circumcision in male neonates, infants and children: a systematic review. *BMC Urol*. 2010;10:2.

LEVEL III

American Academy of Pediatrics, Committee on Fetus and Newborn, Committee on Drugs, Section on Anesthesiology, Section on Surgery, Canadian Paediatric Society. Prevention and management of pain and stress in the neonate. Fetus and Newborn Committee. *Pediatrics*. 2000; 105:454-461.

Baskin LS, Canning DA, Snyder HM, et al. Treating complications of circumcision. *Pediat Emerg Care*. 1996;12:62.

Blank S, Brady M, Buerk E, et al. Male circumcision. *Pediatrics*. 2012;130: e756.

Niku SD, Stock JA, Kaplan GW. Neonatal circumcision. *Urol Clin North Am*. 1995;22:57.

Reynolds RD. Use of the Mogen clamp for neonatal circumcision. *Am Fam Physician*. 1996;54:177.

American Academy of Pediatrics Task Force on Circumcision. Circumcision policy statement. *Pediatrics*. 2012;130:585.

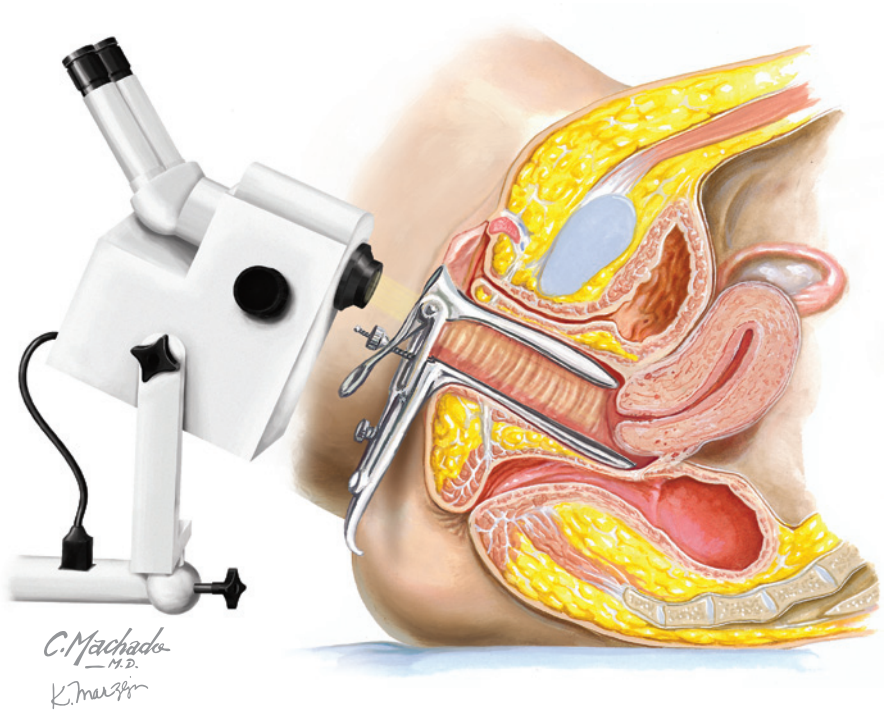


Figure 261.1 Colposcopy

Whenever possible, the biopsy should include the edge or border of the lesion. Biopsies should be placed in a buffered formalin solution for transport to the pathology laboratory.

Curettage of the endocervical canal (ECC) should be generally included to exclude the possibility of endocervical lesions above the limits of visibility. The ECC is especially helpful as a first stage in the evaluation of atypical glandular cells.

If bleeding from a biopsy site persists or is heavy, Monsel solution may be applied. Monsel solution should be applied only after all specimens have been obtained.

For colposcopy of the vulva, a weaker concentration of acetic acid will result in less burning and discomfort. Because of the relatively thicker epithelium of the vulva, the acetic acid must be left in contact with the tissues for a longer period (even if the stronger solution is chosen). Soaking a gauze sponge and allowing it to remain in contact with the skin for several minutes most easily accomplishes this.

COMPLICATIONS

Transient bleeding from biopsy sites. Infection at the biopsy site or endometrium is rare. Colposcopic examinations fail to visualize the squamocolumnar junction or the limits of any lesions present (inadequate studies) in approximately 15%–20% of premenopausal women.

FOLLOW-UP

Follow-up is dictated by the indication for the procedure and any lesions found. A review of the histology reports on any material removed may also alter the follow-up indicated. No specific procedure-related follow-up is needed, although if extensive biopsies are taken, pelvic rest (no tampons, douches, or sexual intercourse) for a period of time may be prudent. The patient should be advised to expect an increased vaginal discharge if biopsies were taken and Monsel solution was used. An abnormal discharge or vaginal bleeding should prompt a re-evaluation.

CPT CODE(S)

57452 Colposcopy (Vaginoscopy); (separate procedure)
57454 Colposcopy with biopsy(s) of the cervix and/or endocervical curettage
57460 Colposcopy with loop electrode excision procedure of the cervix
57500 Biopsy of cervix only, single or multiple
57505 Endocervical curettage (not done as part of a dilatation and curettage)

REFERENCES

LEVEL II

Gage JC, Hanson VW, Abbey K, et al. ASCUS LSIL Triage Study (ALTS) Group: Number of cervical biopsies and sensitivity of colposcopy. *Obstet Gynecol.* 2006;108:264.

Galaal K, Bryant A, Deane KH, et al. Interventions for reducing anxiety in women undergoing colposcopy. *Cochrane Database Syst Rev.* 2011;(12):CD006013.

Underwood M, Arbyn M, Parry-Smith W, et al. Accuracy of colposcopy-directed punch biopsies: a systematic review and meta-analysis. *BJOG.* 2012;119:1293.

LEVEL III

American College of Obstetricians and Gynecologists. Cervical cancer screening and prevention. Practice Bulletin No. 157. *Obstet Gynecol.* 2016;127:e1.

American College of Obstetricians and Gynecologists. Cervical cancer screening in low-resource settings. Committee Opinion No. 624. *Obstet Gynecol.* 2015;125:526.

American College of Obstetricians and Gynecologists. Gynecologic care for women with human immunodeficiency virus. Practice Bulletin No. 117. *Obstet Gynecol.* 2010;117:1492.

American College of Obstetricians and Gynecologists. Management of abnormal cervical cancer screening test results and cervical cancer precursors. Practice Bulletin No. 140. *Obstet Gynecol*. 2013;122: 1338.

American College of Obstetricians and Gynecologists. Management of vulvar intraepithelial neoplasia. Committee Opinion No. 509. *Obstet Gynecol*. 2011;118:1192.

Davis GD. Colposcopic examination of the vagina. *Obstet Gynecol Clin North Am*. 1993;20:217.

Massad LS, Einstein MH, Huh WK, et al. 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. *Obstet Gynecol*. 2013;121:829.

Safaeian M, Solomon D, Wacholder S, et al. Risk of precancer and follow-up management strategies for women with human papillomavirus-negative atypical squamous cells of undetermined significance. *Obstet Gynecol*. 2007;109:1325.

Wright VC. Understanding the colposcope. Optics, light path, magnification, and field of view. *Obstet Gynecol Clin North Am*. 1993;20:31.

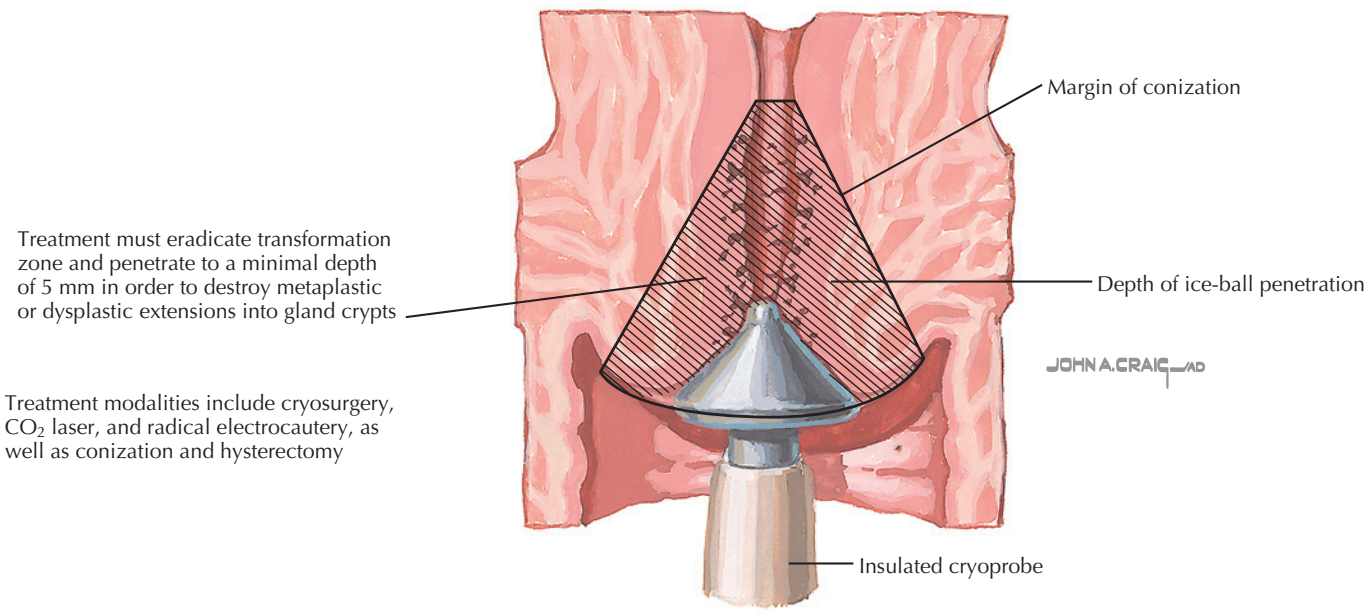


Figure 262.1 Cervical cryocautery

REFERENCES

LEVEL I

Mitchell MF, Tortolero-Luna G, Cook E, et al. A randomized clinical trial of cryotherapy, laser vaporization, and loop electrosurgical excision for treatment of squamous intraepithelial lesions of the cervix. *Obstet Gynecol*. 1998;92:737.

LEVEL II

Dolman L, Sauvaget C, Muwonge R, et al. Meta-analysis of the efficacy of cold coagulation as a treatment method for cervical intraepithelial neoplasia: a systematic review. *BJOG*. 2014;121:929.

Garrido JL. 30 years of colposcopic studies: validity of local destructives treatments. *Eur J Gynaecol Oncol*. 2015;36:323.

Loobuyck HA, Duncan ID. Destruction of CIN 1 and 2 with the Semm cold coagulator: 13 years' experience with a see-and-treat policy. *Br J Obstet Gynaecol*. 1993;100:465.

Martin-Hirsch PP, Paraskevaidis E, Bryant A, et al. Surgery for cervical intraepithelial neoplasia. *Cochrane Database Syst Rev*. 2013;(12): CD001318.

Ostergard DR. Cryosurgical treatment of cervical intraepithelial neoplasia. *Obstet Gynecol*. 1980;56:231.

Sauvaget C, Muwonge R, Sankaranarayanan R. Meta-analysis of the effectiveness of cryotherapy in the treatment of cervical intraepithelial neoplasia. *Int J Gynaecol Obstet*. 2013;120:218.

LEVEL III

American College of Obstetricians and Gynecologists. Management of abnormal cervical cancer screening test results and cervical cancer precursors. Practice Bulletin No. 140. *Obstet Gynecol*. 2013;122:1338.

Duncan I. Cold coagulation in the treatment of cervical intraepithelial neoplasia. *BJOG*. 2014;121:942.

Gage AA. Cryosurgery in the treatment of cancer. *Surg Gynecol Obstet*. 1992;174:73.

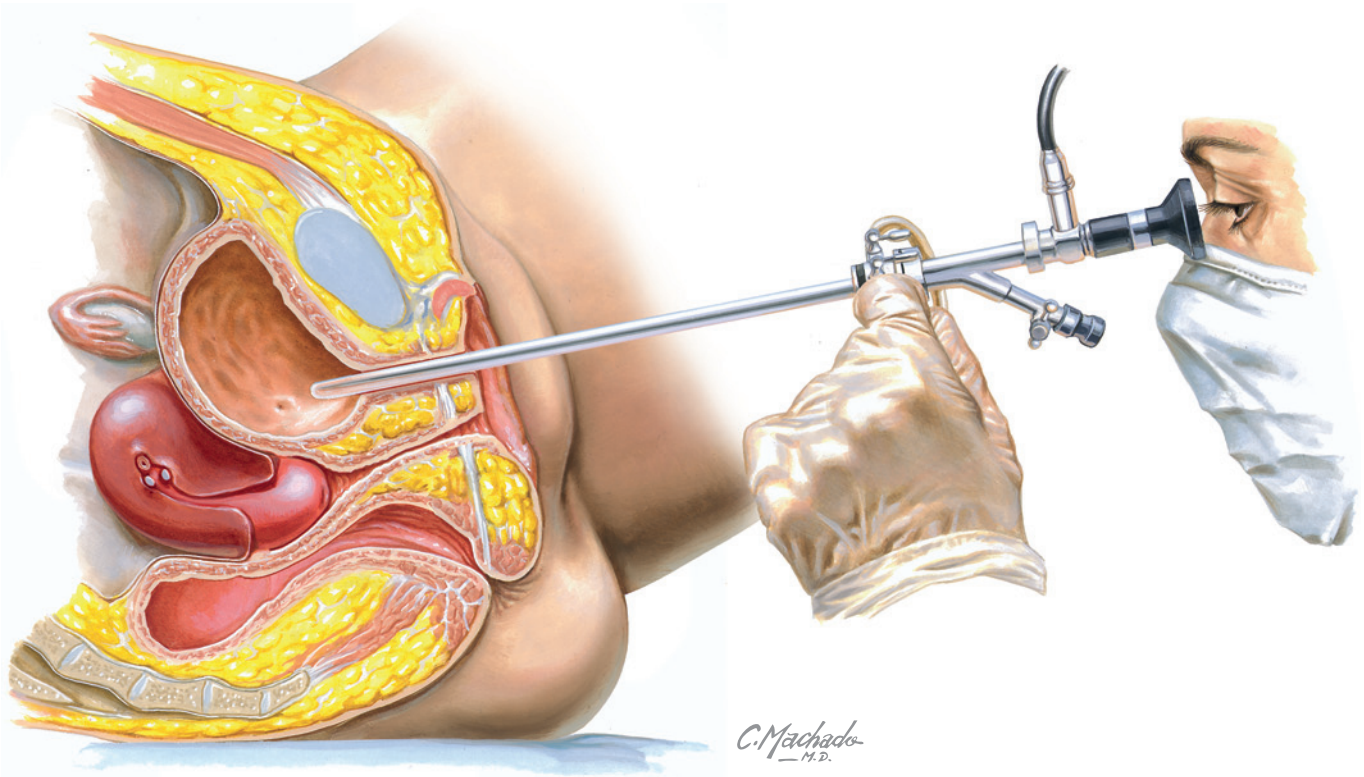


Figure 263.1 Cystourethroscopy

REQUIRED EQUIPMENT

- Skin (or vaginal) preparation materials (iodine-based antibacterial solution [eg, Betadine] or other suitable cleansing agents)
- Sterile gloves, antiseptic solution and sterile cotton balls, or skin preparation swabs
- Sterile urine specimen cup (with gradations)
- One liter of sterile saline (intravenous fluid without glucose is generally used) at room temperature (low-pressure carbon dioxide may also be used with suitable equipment). If electrocautery is to be performed, a nonconducting solution, such as glycine, should be used.
- Absorbent underpads
- 2% Xylocaine jelly in a mushroom-tipped syringe (optional) or tube with conical delivery cap
- Cystoscope (rigid or flexible, direct viewing or with a 30-degree or greater down-angle view; the latter is better for visualizing the bladder trigone and ureteral openings)
- Fiber-optic light source (compatible with type of cystoscope used)
- Fiber-optic light cord
- An assistant is advantageous

TECHNIQUE

Shortly before the procedure a single dose of prophylactic antibiotics is recommended to prevent urinary tract infection or septicemia for patients at a high risk for endocarditis, those who are neutropenic, and those with preoperative bacteriuria or an indwelling catheter.

Immediately prior to starting the procedure, the patient is asked to empty her bladder (in private and in her usual manner). The patient is placed in the dorsal lithotomy position, and the external urinary meatus and surrounding vulvar vestibule are cleansed with antiseptic solution. One to three milliliters of topical anesthetic, such as 2% Xylocaine, are introduced into the urethra. The procedure should be delayed for 5–15 minutes to enable full anesthesia.

With sterile technique, the patient is catheterized using a straight catheter, and any residual urine is caught, measured for volume, and sent for culture (if appropriate). With the catheter left in place, the bladder is slowly (to avoid inducing bladder spasm) filled with 100–200 mL of sterile saline, and the catheter is then removed. This step may be omitted if the cystoscope used is capable of retrograde filling of the bladder.

After the light guide is attached to both the cystoscope and light source, the tip of the cystoscope is placed at the external meatus and gently inserted under direct (or video) guidance. The cystoscope should be initially inserted with a slight downward angle and then gently rotated under the symphysis. A direct (forward looking) cystoscope may be used to facilitate the inspection of the internal sphincter (urethral–vesical junction) and the urethra itself. The entire lumen of the urethra, bladder wall, the trigone, and ureteral openings should be systematically examined. If problems are encountered viewing the trigone, using a cystoscope with a downward-viewing angle facilitates the process.

If the goal is to examine for ureteral patency, 5 mL of indigo carmine can be intravenously administered 10–15 minutes before the cystoscopy, followed by the observation of blue-stained urine from the ureteral orifices.

At the completion of the procedure, the patient may empty her bladder, or the bladder may be drained by catheter, as desired.

COMPLICATIONS

Infection, bleeding, dysuria, and urinary retention are possible, although unlikely. Perforation or bladder rupture is possible (more likely with biopsy).

FOLLOW-UP

Based on the indications.

CPT CODE(S)

52000 Cystoscopy

REFERENCES

LEVEL I

Choe JH, Kwak KW, Hong JH, et al. Efficacy of lidocaine spray as topical anesthesia for outpatient rigid cystoscopy in women: a prospective, randomized, double-blind trial. *Urology*. 2008;71:561.

LEVEL II

Bootsma AM, Laguna Pes MP, Geerlings SE, et al. Antibiotic prophylaxis in urologic procedures: a systematic review. *Eur Urol*. 2008;54:1270.

Gilmour DT, Das S, Flowerdew G. Rates of urinary tract injury from gynecologic surgery and the role of intraoperative cystoscopy. *Obstet Gynecol*. 2006;107:1366.

LEVEL III

American College of Obstetricians and Gynecologists. The role of cystourethroscopy in the generalist obstetrician–gynecologist practice. ACOG Committee Opinion 372. *Obstet Gynecol*. 2007;110:221.

American College of Obstetricians and Gynecologists. Urinary incontinence in women. Practice Bulletin No. 155. *Obstet Gynecol*. 2015;126:e66.

Olson ES, Cookson BD. Do antimicrobials have a role in preventing septicemia following instrumentation of the urinary tract? *J Hosp Infect*. 2000;45:85.

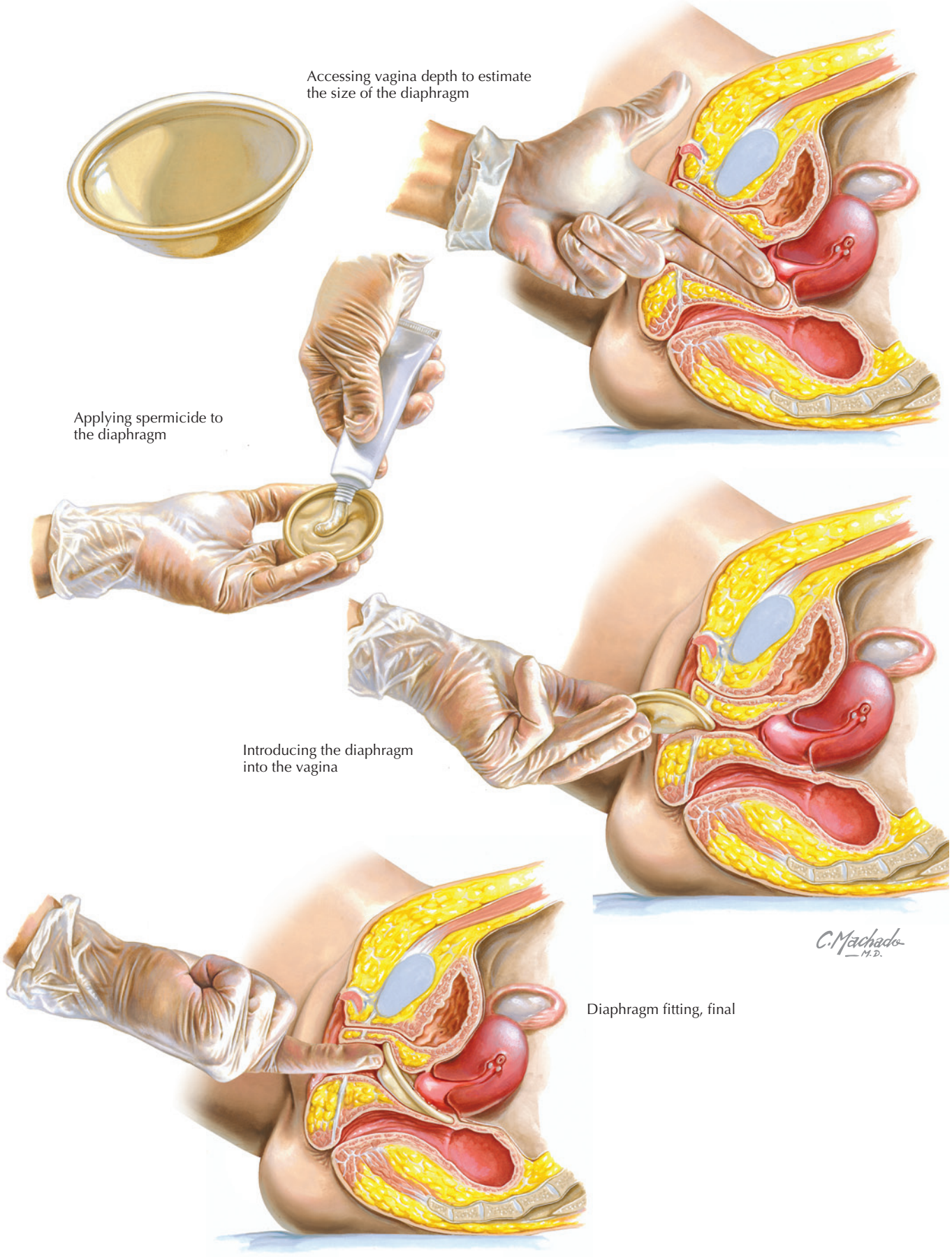


Fig. 264.1 Diaphragm fitting

FOLLOW-UP

As needed. If the patient has not had an opportunity to practice insertion, positioning, and removal in the office, this should be offered before the diaphragm is relied on for contraception.

CPT CODE(S)

57170 Diaphragm or cervical cap fitting with instructions

REFERENCES

LEVEL I

Ramjee G, van der Straten A, Chipato T, et al. The diaphragm and lubricant gel for prevention of cervical sexually transmitted infections: results of a randomized controlled trial. *PLoS ONE*. 2008;3:e3488.

LEVEL II

Cook L, Nanda K, Grimes D. Diaphragm versus diaphragm with spermicides for contraception. *Cochrane Database Syst Rev*. 2003;(1): CD002031.

de Bruyn G, Shiboski S, van der Straten A, et al. The effect of the vaginal diaphragm and lubricant gel on acquisition of HSV-2. *Sex Transm Infect*. 2011;87:301.

Ferreira A, Araújo M, Regina C, et al. Effectiveness of the diaphragm, used continuously, without spermicide. *Contraception*. 1993;48:29.

Mauck C, Lai J, Schwartz J, et al. Diaphragms in clinical trials: is clinician fitting necessary? *Contraception*. 2004;69:263.

LEVEL III

Allen RE. Diaphragm fitting. *Am Fam Physician*. 2004;69:97.

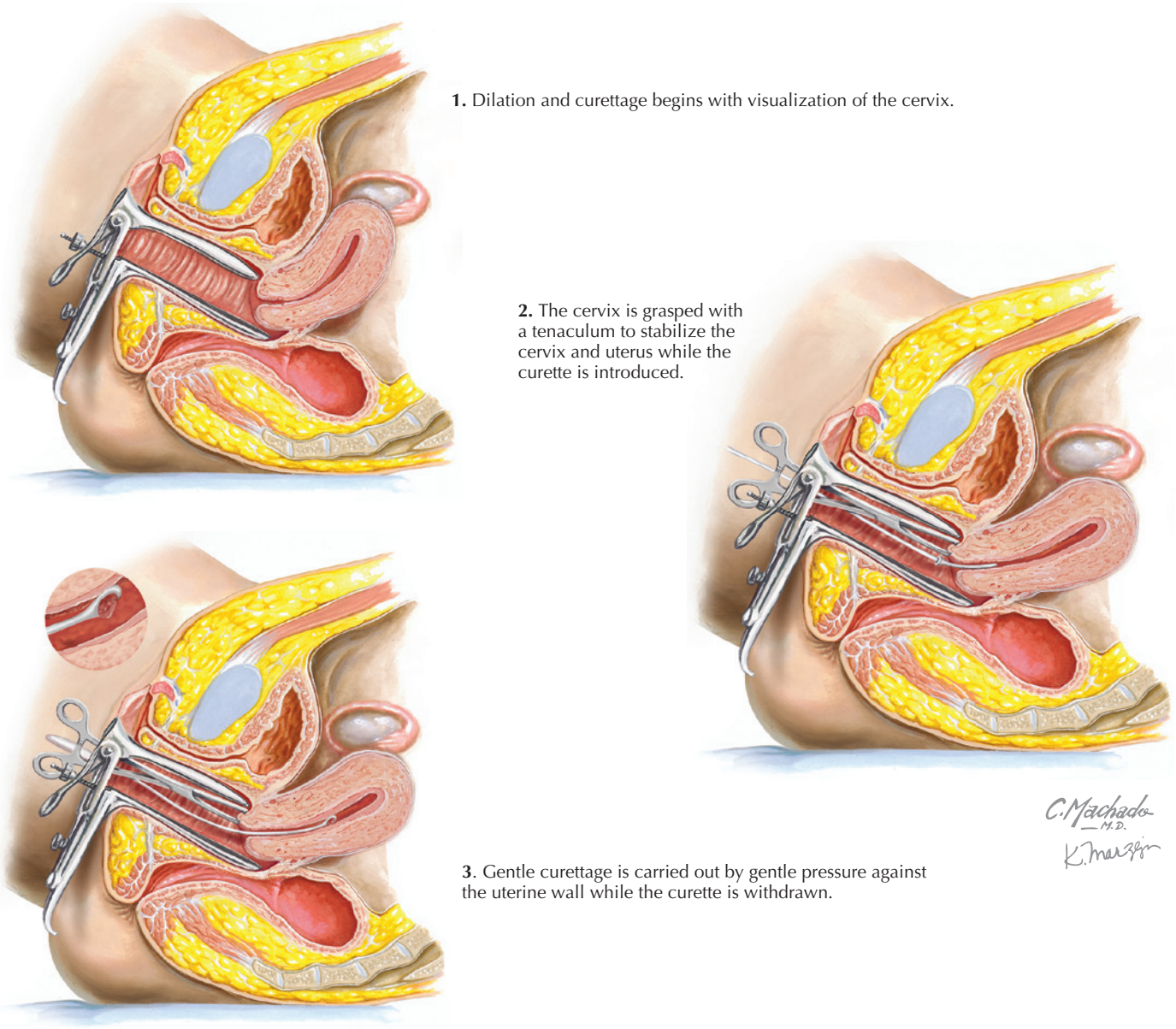


Figure 265.1 Dilation and curettage

be collected; placing a small polyethylene-covered surgical dressing below the cervix, on top of the posterior retractor, in the posterior vaginal fornix may facilitate this.

If a suction curette is used, it should be inserted to the level of the fundus with the suction off, then the suction applied and the curette withdrawn, curetting the uterine wall in the process. This withdrawal is often performed in a spiral manner to increase efficiency.

To ensure that all tissue is loosened by the curettage process (and for the possibility of intracavitary polyps), a small stone forceps is passed into the uterine cavity, opened, rotated 90 degrees, closed, and removed. This may be repeated as needed.

The procedure ends with the removal of the tenaculum or sponge stick used to grasp the cervix and the extraction of the speculum or retractors. The specimens obtained should be placed in a suitable fixative or transport media. Prophylactic antibiotic coverage is generally not indicated.

COMPLICATIONS

Uterine perforation, cervical laceration, infection (endometrial, myometrial, pelvic), hemorrhage (intraoperative or postoperative), uterine synechia (Asherman's syndrome)

FOLLOW-UP

Based on indications. Patients are generally advised to refrain from sexual intercourse, douching, or tampon use for 10–14 days.

CPT CODE(S)

58120 Dilation and curettage, diagnostic and/or therapeutic (nonobstetric)
59160 Curettage, postpartum
57558 Dilation and curettage of cervical stump

REFERENCES

LEVEL I

Trinder J, Brocklehurst P, Porter R, et al. Management of miscarriage: expectant, medical, or surgical? Results of randomised controlled trial (miscarriage treatment (MIST) trial). *BMJ*. 2006;332:1235.

LEVEL II

Hefler L, Lemach A, Seebacher V, et al. The intraoperative complication rate of nonobstetric dilation and curettage. *Obstet Gynecol*. 2009;113:1268.

Sotiriadis A, Makrydimas G, Papatheodorou S, et al. Expectant, medical, or surgical management of first-trimester miscarriage: a meta-analysis. *Obstet Gynecol*. 2005;105:1104.

LEVEL III

American College of Obstetricians and Gynecologists. Antibiotic prophylaxis for gynecologic procedures. ACOG Practice Bulletin No. 104. *Obstet Gynecol*. 2009;113:1180.

American College of Obstetricians and Gynecologists. Management of acute abnormal uterine bleeding in nonpregnant reproductive-aged women. Committee Opinion No. 557. *Obstet Gynecol*. 2013;121:891.

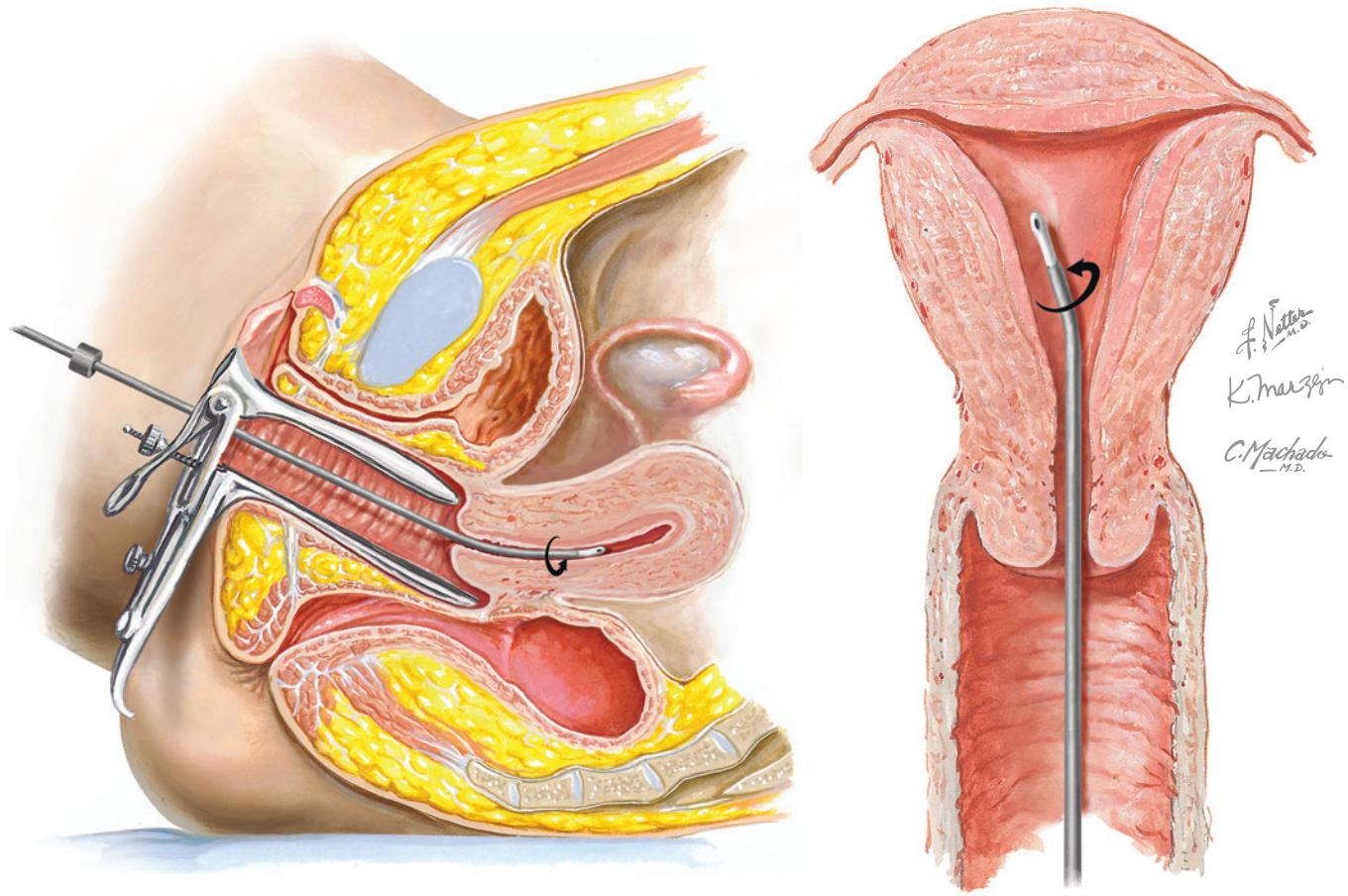


Figure 266.1 Endometrial biopsy

COMPLICATIONS

Uterine perforation (1– 2/1000), infection (endometrial, myometrial, pelvic). Vasovagal syncope during the procedure may occur but is generally transient.

FOLLOW-UP

Based on indications. Patients are generally advised to refrain from sexual intercourse, douching, or tampon use for 10–14 days.

CPT CODE(S)

58100 Endometrial sampling (biopsy) with or without endocervical sampling (biopsy) without cervical dilation, any method (separate procedure)

REFERENCES

LEVEL I

Nolan TE, Smith RP, Smith MT, et al. A prospective evaluation of an endometrial suction curette. *J Gynecol Surg*. 1992;8:231.

LEVEL II

Dijkhuizen FP, Mol BW, Brolmann HA, et al. The accuracy of endometrial sampling in the diagnosis of patients with endometrial carcinoma and hyperplasia—A meta-analysis. *Cancer*. 2000;89:1765.

Güney M, Oral B, Mungan T. Intrauterine lidocaine plus buccal misoprostol in the endometrial biopsy. *Int J Gynaecol Obstet*. 2007;97:125.

Law J. Histological sampling of the endometrium—A comparison between formal curettage and the Pipelle sampler. *Br J Obstet Gynaecol*. 1993;100:503.

Sierecki AR, Gudipudi DK, Montemarano N, et al. Comparison of endometrial aspiration biopsy techniques: specimen adequacy. *J Reprod Med*. 2008;53:760.

Williams AR, Brechin S, Porter AJ, et al. Factors affecting adequacy of Pipelle and Tao Brush endometrial sampling. *BJOG*. 2008;115:1028.

LEVEL III

American College of Obstetricians and Gynecologists. Diagnosis of abnormal uterine bleeding in reproductive-aged women. Practice Bulletin No. 128. *Obstet Gynecol*. 2012;120:197.

American College of Obstetricians and Gynecologists. Management of abnormal uterine bleeding associated with ovulatory dysfunction. Practice Bulletin No. 136. *Obstet Gynecol*. 2013;122:176.

American College of Obstetricians and Gynecologists. Tamoxifen and uterine cancer. Committee Opinion No. 601. *Obstet Gynecol*. 2014;123:1394.

American College of Obstetricians and Gynecologists. Endometrial cancer. Practice Bulletin No. 149. *Obstet Gynecol*. 2015;125:1006.

American College of Obstetricians and Gynecologists. Endometrial intraepithelial neoplasia. Committee Opinion No. 631. *Obstet Gynecol*. 2015;125:1272.

267 FORCEPS-AIDED DELIVERY

DESCRIPTION

Forceps-aided delivery is a method of assisting or expediting vaginal vertex delivery through the application of obstetric forceps. Discussion here is limited to low or outlet forceps with the fetus presenting within 45 degrees of directly occiput anterior.

INDICATIONS

Fetal: nonreassuring fetal status, acute fetal distress.
Maternal: fatigue, prolonged second stage of labor (nulliparous women: lack of continuing progress for 3 hours with regional anesthesia or 2 hours without regional anesthesia; multiparous women: lack of continuing progress for 2 hours with regional anesthesia or 1 hour without regional anesthesia), certain types of pulmonary, cardiac, or neurologic diseases.

CONTRAINDICATIONS

Incompletely dilated cervix, significant fetal malpresentation, unengaged fetal head, intact fetal membranes, inability to assess fetal position or obtain maternal cooperation, distorted or contracted maternal pelvic anatomy, gestational age less than 34 weeks, fetal demineralization or clotting disorder.

REQUIRED EQUIPMENT

- Standard equipment for spontaneous vaginal delivery, including sterile gowns and gloves
- Fetal heart rate monitor
- Traction forceps (Simpson, Tucker-McLane or similar)

TECHNIQUE

Adequate maternal anesthesia or analgesia should be ensured in all but the most extreme circumstances. Whenever possible, the maternal bladder should be emptied (by catheter). The exact position of the fetal head must be ascertained by the palpation of the sagittal suture and fontanels. All other preparations for vaginal delivery should be in place before forceps are applied.

Correct placement of forceps occurs only when the long axis of the blades corresponds to the occipitomental diameter, with the major portion of the blade lying over the face, the concave margins of the blades directed toward the sagittal suture (with the fetus in the occiput anterior position). To accomplish this, the left blade (both operator's and patient's left) is introduced into the vagina next to the fetal head using the operator's right hand or fingers within the vaginal canal. The vaginal hand is used as a guide to accomplish the placement, while the external hand provides only minimal

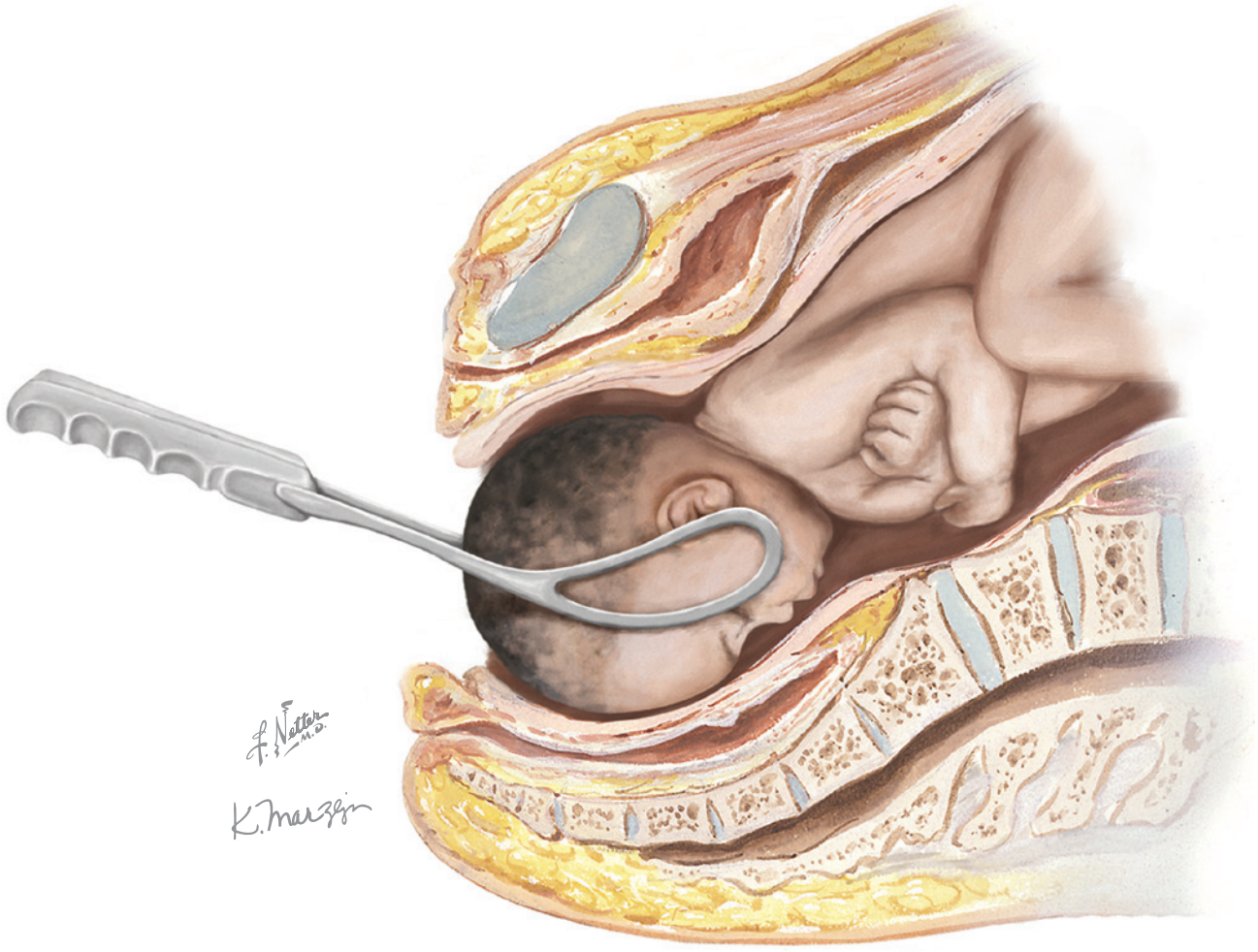


Figure 267.1 Forceps-aided delivery

support. The introduction is accomplished by starting with the handle perpendicular to the floor and the cephalic curve of the blade resting against the fetal head. The internal hand guides the blade inward, upward, and with a rotation that brings the forceps handle through a wide outward arc ending parallel to the floor. This arc is necessary to accommodate both the cephalic and pelvic curves of the device. A preliminary assessment of placement adequacy should be made before the right blade is placed. The right blade is placed in a similar arcing manner using the operator's left hand as the internal hand, with the right providing simple support.

Before the two forceps blades are articulated, the position on the fetal head should be verified. A correct position will be evident by the symmetry of the blades compared with the sagittal sutures and posterior fontanel. If necessary, one or both blades may be gently maneuvered (using fingers within the vagina) to accomplish optimal positioning. Removal and re-placement is sometimes necessary.

Traction is generally applied by the placement of the fingers on the upper surface of the handles or shanks and the thumbs below. Traction on the articulated forceps begins in a horizontal or slightly downward (axis of the maternal pelvic canal) manner. Traction should be intermittent and, when possible, coordinated with maternal expulsive efforts. To mimic the normal birth process, traction in the horizontal plane continues until the descending fetal head distends the vulva; an episiotomy, if required, may be performed at this point.

As the fetal head further distends the vulva, the axis of traction is gradually rotated upward, mimicking the normal extension process of the head as it rotates under the symphysis. Once the brow is palpable through the perineum the blades may be removed and the fetal head delivered by pressure on the perineum (modified Ritgen maneuver). More often the blades may be left in place until the fetal chin has cleared the perineum. The remainder of the delivery proceeds as with a spontaneous delivery.

COMPLICATIONS

It is difficult (if not impossible) to separate the effects of forceps-aided vaginal delivery from those of spontaneous vaginal delivery. Both randomized trials and meta-analysis studies have failed to demonstrate conclusive differences. Both forceps delivery and vacuum extraction have been associated with the development of maternal hematomas and possibly linked to pelvic floor injury. However, other factors associated with pelvic floor injury include normal spontaneous vaginal delivery, episiotomy, prolonged second stage of labor, and increased fetal size. Similarly, studies have failed to identify neonatal or fetal injuries or developmental abnormalities that can be directly linked to forceps delivery. The morbidity that previously had been considered to be because of operative vaginal delivery actually may have resulted from the process of abnormal labor that led to the need for an intervention.

CPT CODE(S)

59400 Routine obstetric care including antepartum care, vaginal delivery (with or without episiotomy, and/or forceps) and postpartum care

59610 Routine obstetric care including antepartum care, vaginal delivery (with or without episiotomy, and/or forceps) and postpartum care, after previous cesarean delivery

59409 Vaginal delivery only (with or without episiotomy and/or forceps)

59410 Vaginal delivery only (with or without episiotomy and/or forceps); including postpartum care

59612 Vaginal delivery only, after previous cesarean delivery (with or without episiotomy and/or forceps)

59614 Vaginal delivery only, after previous cesarean delivery (with or without episiotomy and/or forceps); including postpartum care

REFERENCES

LEVEL I

Carmona F, Martinez-Roman S, Manau D, et al. Immediate maternal and neonatal effects of low-forceps delivery according to the new criteria of The American College of Obstetricians and Gynecologists compared with spontaneous vaginal delivery in term pregnancies. *Am J Obstet Gynecol*. 1995;173:55.

LEVEL II

Aiken CE, Aiken AR, Brockelsby JC, et al. Factors influencing the likelihood of instrumental delivery success. *Obstet Gynecol*. 2014;123:796.

Burke N, Field K, Mujahid F, et al. Use and safety of Kielland's forceps in current obstetric practice. *Obstet Gynecol*. 2012;120:766.

de Vogel J, van der Leeuw-van Beek A, Gietelink D, et al. The effect of a mediolateral episiotomy during operative vaginal delivery on the risk of developing obstetrical anal sphincter injuries. *Am J Obstet Gynecol*. 2012;206:404.e1.

Ducarme G, Hamel JF, Bouet PE, et al. Maternal and neonatal morbidity after attempted operative vaginal delivery according to fetal head station. *Obstet Gynecol*. 2015;126:521.

Liabsuetrakul T, Choobun T, Peeyananjarassri K, et al. Antibiotic prophylaxis for operative vaginal delivery. *Cochrane Database Syst Rev*. 2014;(10):CD004455.

Nikpoor P, Bain E. Analgesia for forceps delivery. *Cochrane Database Syst Rev*. 2013;(9):CD008878.

O'Mahony F, Hofmeyr GJ, Menon V. Choice of instruments for assisted vaginal delivery. *Cochrane Database Syst Rev*. 2010;(11):CD005455.

Palatnik A, Grobman WA, Hellendag MG, et al. Predictors of failed operative vaginal delivery in a contemporary obstetric cohort. *Obstet Gynecol*. 2016;127:501.

Stock SJ, Josephs K, Farquharson S, et al. Maternal and neonatal outcomes of successful Kielland's rotational forceps delivery. *Obstet Gynecol*. 2013;121:1032.

Towner D, Castro MA, Eby-Wilkens E, et al. Effect of mode of delivery in nulliparous women on neonatal intracranial injury. *N Engl J Med*. 1999;341:1709.

Walsh CA, Robson M, McAuliffe FM. Mode of delivery at term and adverse neonatal outcomes. *Obstet Gynecol*. 2013;121:122.

LEVEL III

American College of Obstetricians and Gynecologists. Limitations of perineal lacerations as an obstetric quality measure. Committee Opinion No. 647. *Obstet Gynecol*. 2015;126:e108.

American College of Obstetricians and Gynecologists. Operative vaginal delivery. Practice Bulletin No. 154. *Obstet Gynecol*. 2015;126:e56.

268 HYSTEROSCOPY: DIAGNOSTIC

DESCRIPTION

Diagnostic hysteroscopy describes a number of techniques that allow the direct inspection of the endometrial cavity, endocervix, and fallopian tube ostia.

INDICATIONS

Dysfunctional uterine bleeding, postmenopausal bleeding, menorrhagia, abnormal endometrial thickening documented by ultrasonography, retained intrauterine contraceptives or other foreign bodies, infertility (eg, suspected müllerian anomalies), endometrial or pelvic infections (eg, tuberculosis), surveillance of (treated) endometrial cancer or other situations in which a visual or tissue diagnosis is indicated. Because of its more invasive nature, cost, and small, but not insignificant, risk for perforation or infection, this procedure is best suited for diagnosis and not screening.

CONTRAINDICATIONS

Patients who are medically unstable, viable (desired) pregnancy, known cervical or uterine cancer, active pelvic inflammatory disease, blood dyscrasia, active herpetic infection. Office hysteroscopy is a poor choice for patients who have cervical stenosis, high levels of anxiety, comorbidities, limited mobility, in whom there is difficulty visualizing the cervix, or the presence of uterine pathology that may require operative procedures.

REQUIRED EQUIPMENT

- Sterile gloves and operative drapes
- Skin preparation materials (generally an iodine-based antibacterial solution such as Betadine)
- Vaginal speculum or weighted vaginal speculum with Deaver or similar retractors
- Single tooth tenaculum or sponge stick
- Blunt uterine sound (optional)
- Hysteroscope (rigid or flexible) with light source. Rigid hysteroscopes generally include an outer sheath that surrounds the channels for the telescope, distending media inflow and outflow, and operative instruments. Rigid hysteroscopes offer better optical quality and are less expensive. Contact hysteroscopes that do not require an external light source (using ambient light instead) are available, but their limited field of view and the inability to convert to an operative procedure have resulted in their infrequent use. They are not discussed further here.
- Normal saline (intravenous fluid without glucose) at room temperature. Carbon dioxide may also be used as a distending medium.
- Equipment for infusing and monitoring the uterine distending media
- Hysteroscopes with more than 5-mm outside diameter require mechanical cervical dilation: Graduated cervical dilators (Hegar, Pratt, Rocket, Heaney, Hank, or similar; Goodell dilators are generally not preferred because of an increased risk of cervical laceration). Preoperative dilation is generally preferred and may

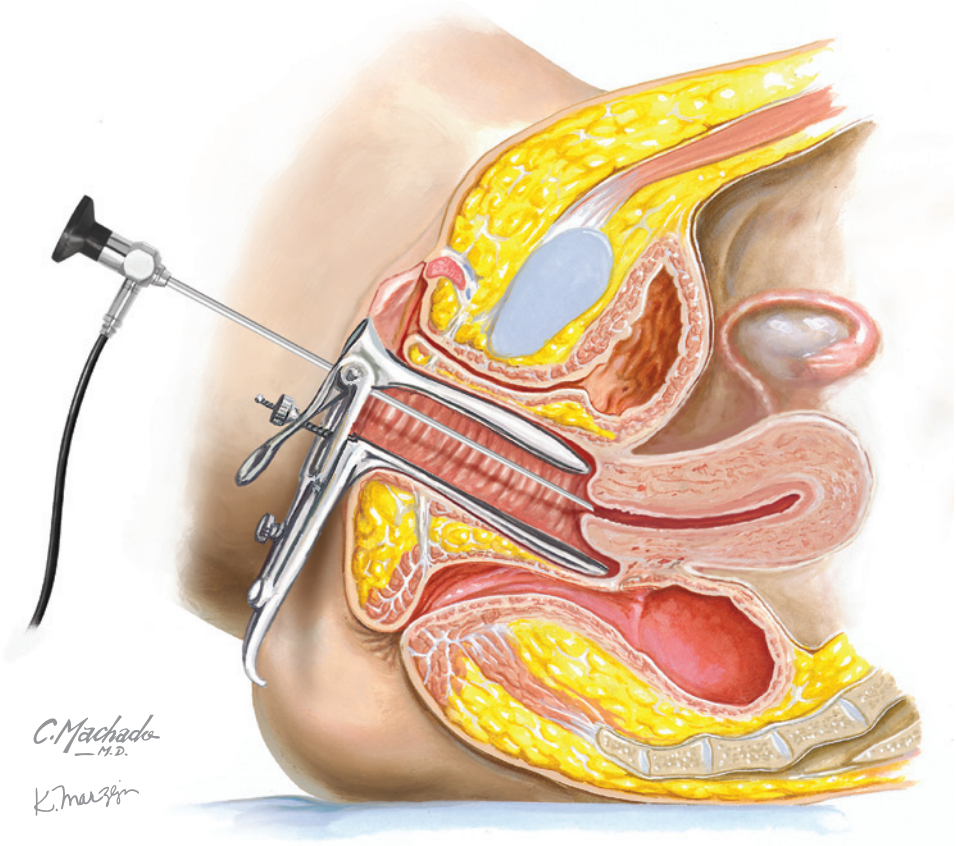


Figure 268.1 Diagnostic hysteroscopy

be accomplished with the aid of cervical ripening agents (eg, misoprostol, 200–400 mcg orally or intravaginally) or osmotic dilators (eg, laminaria).
- Video, photographic, or digital capture equipment may be attached to the hysteroscope as desired (optional).
- An assistant is advantageous.
- If local anesthesia is to be used, a syringe with 25- or 27-gauge 1.5-inch needle (or longer) for anesthetic injection, 1% or 2% lidocaine with or without 1:100,000 epinephrine
- Premedication with a nonsteroidal antiinflammatory agent can reduce intraoperative and postoperative pain.

TECHNIQUE

When possible, the proliferative phase of the menstrual cycle is best for the visualization of the uterine cavity. Bleeding can easily obscure inspection, and the procedure may have to be rescheduled. Most diagnostic hysteroscopy can be accomplished in the office or ambulatory setting with local anesthesia. Mild sedation may be appropriate for selected patients.

Before the procedure begins, the fit and completeness of the hysteroscope and its associated sheath, obturator, light cord, and fluid management tubing should be verified. Hysteroscopes are available with viewing angles that vary from 0 to 70 degree, with the optimal angle chosen based on the needs of the planned procedure and anticipated pathology; 0-degree scopes provide panoramic views and good delineation of the endocervix, angled scopes are helpful when the cavity is misshapen or pathology near the inner cervical os is anticipated.

Following informed consent, the patient is placed in the dorsal lithotomy position and sterile drapes placed as for colposcopy or cystoscopy. The cervix should be visualized, cleansed, and grasped by the anterior lip using a tenaculum or sponge stick. If desired, a paracervical block using lidocaine should be placed at this point and the anesthetic allowed a few minutes to take full effect. Some practitioners choose to sound the uterus with a blunt probe, but doing so may disrupt pathology and incite bleeding, which may lead to a suboptimal examination. For these reasons, it is generally not recommended.

The degree of dilation of the cervix is determined and dilated as needed to insure a snug fit over the hysteroscope's outer sheath. Distending media, most commonly normal saline, is used to distend the uterine cavity either just prior to or during the insertion of the viewing scope. The hysteroscope may be inserted into the uterine cavity under direct visualization (0-degree scope) or with the obturator in place until the tip of the sheath is within the uterine cavity. A careful and systematic inspection of the uterine cavity and tubal ostia is then carried out. Prior to the completion of the procedure, the pressure of the distending media should be gradually reduced under direct visualization to ensure that small lesions or excrescences have not been compressed and missed. The procedure concludes with the withdrawal of all instruments and verification of hemostasis.

COMPLICATIONS

Vasovagal syncope, uterine perforation, cervical laceration, infection (endometrial, myometrial, pelvic), hemorrhage (intraoperative or postoperative), fluid overload or gas embolus (based upon the distending media used), hyponatremia (with electrolyte-poor fluids).

FOLLOW-UP

Based on indications and findings.

CPT CODE(S)

58555 Hysteroscopy, diagnostic (separate procedure)

REFERENCES

LEVEL I

Batukan C, Ozgun MT, Ozcelik B, et al. Cervical ripening before operative hysteroscopy in premenopausal women: a randomized, double-blind, placebo-controlled comparison of vaginal and oral misoprostol. *Fertil Steril*. 2008;89:966.

Hassan A, Haggag H. Role of oral tramadol 50 mg in reducing pain associated with outpatient hysteroscopy: a randomised double-blind placebo-controlled trial. *Aust N Z J Obstet Gynaecol*. 2016;56:102.

Karakus S, Akkar OB, Yildiz C, et al. Comparison of Effectiveness of Laminaria versus Vaginal Misoprostol for Cervical Preparation Before Operative Hysteroscopy in Women of Reproductive Age: A Prospective Randomized Trial. *J Minim Invasive Gynecol*. 2016;23:46.

LEVEL II

Ahmad G, O'Flynn H, Attarbashi S, et al. Pain relief for outpatient hysteroscopy. *Cochrane Database Syst Rev*. 2010;CD007710.

Al-Fozan H, Firwana B, Al Kadri H, et al. Preoperative ripening of the cervix before operative hysteroscopy. *Cochrane Database Syst Rev*. 2015;(4):CD005998.

Cooper NA, Smith P, Khan KS, et al. A systematic review of the effect of the distension medium on pain during outpatient hysteroscopy. *Fertil Steril*. 2011;95:264.

Raimondo G, Raimondo D, D'Aniello G, et al. A randomized controlled study comparing carbon dioxide versus normal saline as distension media in diagnostic office hysteroscopy: is the distension with carbon dioxide a problem? *Fertil Steril*. 2010;94:2319.

Unfried G, Wieser F, Albrecht A, et al. Flexible versus rigid endoscopes for outpatient hysteroscopy: a prospective randomized clinical trial. *Hum Reprod*. 2001;16:168.

LEVEL III

American College of Obstetricians and Gynecologists. Antibiotic prophylaxis for gynecologic procedures. ACOG Practice Bulletin No. 104. *Obstet Gynecol*. 2009;113:1180.

American College of Obstetricians and Gynecologists. Diagnosis of abnormal uterine bleeding in reproductive-aged women. Practice Bulletin No. 128. *Obstet Gynecol*. 2012;120:197.

American College of Obstetricians and Gynecologists. Endometrial intraepithelial neoplasia. Committee Opinion No. 631. *Obstet Gynecol*. 2015;125:1272.

American College of Obstetricians and Gynecologists. Hysteroscopy. Technology Assessment in Obstetrics and Gynecology No. 7. *Obstet Gynecol*. 2011;117:1486.

Barbot J, Parent B, Dubuisson JB. Contact hysteroscopy: another method of endoscopic examination of the uterine cavity. *Am J Obstet Gynecol*. 1980;136:721.

269 HYSTEROSCOPY: POLYP AND LEIOMYOMA RESECTION

DESCRIPTION

Operative hysteroscopy enables the visual inspection and treatment of intracavitary and submucosal myometrial leiomyomata, which incorporates the use of mechanical or electrosurgical instruments.

INDICATIONS

Known or suspected endometrial polyp(s) or symptomatic intracavitary, submucosal, or intramural leiomyomata where there is a significant proportion of the lesion that protrudes into the uterine cavity.

CONTRAINDICATIONS

Patients who are medically unstable, viable (desired) pregnancy, known cervical or uterine cancer, active pelvic inflammatory disease, blood dyscrasia, active herpetic infection.

REQUIRED EQUIPMENT

- Sterile gloves and operative drapes
- Skin preparation materials (generally an iodine-based antibacterial solution such as Betadine)
- Vaginal speculum or weighted vaginal speculum with Deaver or similar retractors
- Single tooth tenaculum or sponge stick
- Blunt uterine sound (optional)
- Hysteroscope (rigid) with light source. Operating hysteroscopes include an outer sheath which surrounds channels for the telescope, distending media inflow and outflow, and operative instruments.
- Distending media. For operative procedures using monopolar electrosurgical instruments, a nonconductive fluid (eg, glycine) is required; bipolar electrosurgical procedures may use an isotonic fluid (eg, normal saline); mechanical procedures (eg, biopsy or morcellation) are generally done using saline.
- Equipment for infusing and monitoring the uterine distending media
- Hysteroscopes with >5-mm outside diameter (most operating sets) require mechanical cervical dilation via graduated cervical dilators (Hegar, Pratt, Rocket, Heaney, Hank, or similar; Goodell dilators are generally not preferred because of an increased risk of cervical laceration). Preoperative dilation is generally preferred and may be accomplished with the aid of cervical ripening agents (eg, misoprostol, 200–400 mcg orally or intravaginally) or osmotic dilators (eg, laminaria).
- Video, photographic, or digital capture equipment may be attached to the hysteroscope as desired (optional).
- If an electrosurgical technique is chosen, appropriate operative electrodes, electrosurgical generator, patient grounding pad with monitor, and isolated circuitry should be available.
- Histology fixative (10% formalin) in containers
- An assistant is advantageous.
- Premedication with a nonsteroidal antiinflammatory drug can reduce postoperative pain.

TECHNIQUE

There are three broad types of operative hysteroscopes: the traditional model with a retractable hand piece that can perform bipolar or monopolar electrosurgery; a second type using a morcellator that resects tissue and suctions it to a catchment device; and a third type that integrates a bipolar electrosurgical hand piece that resects and removes tissue through the operative sheath. The choice among these options will be driven by the procedure to be performed and the experience and preference of the operator.

Before the procedure begins, the fit and completeness of the hysteroscope and its associated sheath, obturator, light cord, and fluid management tubing should be verified. Hysteroscopes are available with viewing angles that vary from 0 to 70 degrees, with the optimal angle chosen based upon the needs of the planned procedure and anticipated pathology; 0-degree scopes provide panoramic views and good delineation of the endocervix, angled scopes are helpful when the cavity is misshapen or pathology near the inner cervical os is anticipated.

Following informed consent and the establishment of satisfactory anesthesia, the patient is placed in the dorsal lithotomy position, and sterile drapes are placed as for colposcopy or cystoscopy. The cervix should be visualized, cleansed, and grasped by the anterior lip using a tenaculum or sponge stick. The degree of dilation of the cervix is determined and dilated as needed to insure a snug fit over the hysteroscope's outer sheath.

Distending media is used to distend the uterine cavity either just prior to or during the insertion of the operating instruments. The hysteroscope may be inserted into the uterine cavity under direct vision (0-degree scope) or with the obturator in place until the tip of the sheath is within the uterine cavity. A careful and systematic inspection of the uterine cavity and tubal ostia is then conducted.

Electrosurgical Resection

Monopolar electrosurgical resection is generally conducted using a resectoscope that includes a U-shaped electrode, which carries the electrosurgical energy; bipolar resection tips are available in several shapes. The path to be resected, including the polyp or portion of leiomyoma to be removed, is inspected and a practice pass made. The electrosurgical generator is activated and the loop drawn toward the observing lens, removing a shallow strip of tissue. This is repeated as needed until the full resection has been accomplished. With larger lesions, it may be necessary to periodically irrigate the uterine cavity to improve visualization and to remove pathology specimens.

Morcellation

The morcellation device should be assembled following the manufacturer's directions. Once correct assembly has been verified, the morcellating device is inserted into the hysteroscope's operating channel. The correct alignment of the cutting head and fluid/tissue removal port must be verified. To resect tissue, the cutting port is placed against the side and base of the lesion and the device's cutting function is activated, moving the device laterally into and across the polyp or myoma. The device simultaneously resects and aspirates tissue to a collection point. The size of the bites taken by the device may provide a practical limit to the dimensions of lesions that can be addressed using this technology. At the conclusion of the resection, the device should either be retracted so that the cutting window is within the sheath of the hysteroscope or completely removed before withdrawing the scope from the uterus.

Fluid Management

Fluid overload is one of most common and potentially serious complications of operative hysteroscopy. Strict attention to the

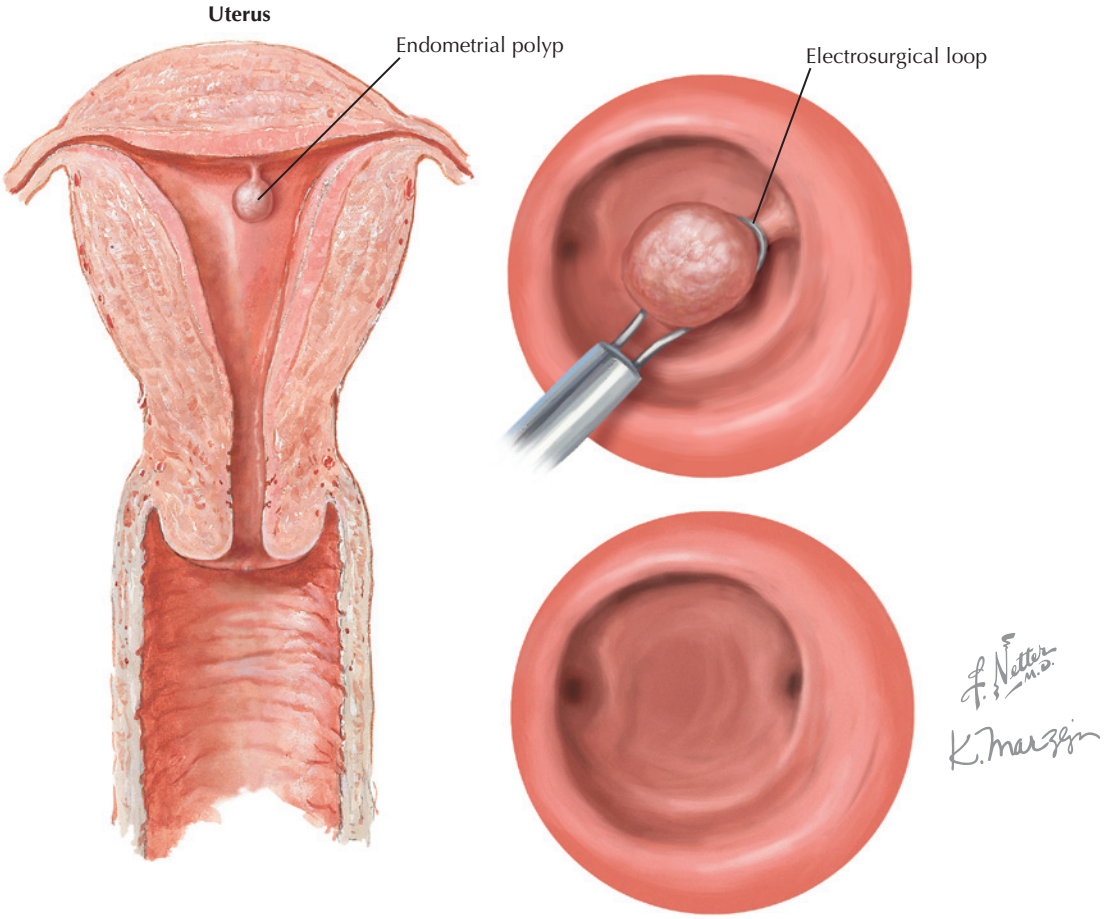


Figure 269.1 Polyp and leiomyoma resection (hysteroscopy)

balance of fluid infused and lost to the outside, minimizing the distending pressure and amount of raw surface created by the procedure, will all diminish the risk for this complication. Selecting a distending medium that minimizes risk and being prepared to promptly recognize and treat fluid overload are all required to ensure the safety of the procedure. If at any point in the procedure there is evidence of systemic absorption, such as a deficit of 750-mL electrolyte-poor fluids, 1000–1500 mL of a nonelectrolyte solution, or 2500 mL of an electrolyte solution, further infusion should be discontinued and the procedure terminated. In an outpatient setting or those with limited acute care and laboratory capabilities, discontinuing the procedure at a lower threshold should be considered.

Prior to the completion of the procedure, the pressure of the distending media should be gradually reduced under direct visualization to ensure that small lesions or excrescences have not been compressed and missed and that hemostasis of the surgical site(s) has been achieved. The procedure concludes with the withdrawal of all instruments and verification of cervical hemostasis. Any specimens removed should be placed in suitable transport media and sent for histopathologic examination.

COMPLICATIONS

Fluid overload, hyponatremia (with electrolyte-poor fluids), uterine perforation, cervical laceration, infection (endometrial, myometrial, pelvic), hemorrhage (intraoperative or postoperative).

FOLLOW-UP

Based on the indications and findings.

CPT CODE(S)

58558 Hysteroscopy, surgical; with sampling (biopsy) of endometrium and/or polypectomy, with or without D&C

58561 Hysteroscopy, surgical; with removal of leiomyomata

REFERENCES

LEVEL I

Karakus S, Akkar OB, Yildiz C, et al. Comparison of effectiveness of laminaria versus vaginal misoprostol for cervical preparation before operative hysteroscopy in women of reproductive age: a prospective randomized trial. *J Minim Invasive Gynecol*. 2016;23:46.

Muzii L, Bellati F, Pernice M, et al. Resectoscopic versus bipolar electrode excision of endometrial polyps: a randomized study. *Fertil Steril*. 2007;87:909.

LEVEL II

Emanuel MH, Wamsteker K. The Intra Uterine Morcellator: a new hysteroscopic operating technique to remove intrauterine polyps and myomas. *J Minim Invasive Gynecol*. 2005;12:62.

Nathani F, Clark TJ. Uterine polypectomy in the management of abnormal uterine bleeding: a systematic review. *J Minim Invasive Gynecol*. 2006; 13:260.

Preutthipan S, Herabutya Y. Hysteroscopic polypectomy in 240 premenopausal and postmenopausal women. *Fertil Steril*. 2005;83:705.

Smith PP, Middleton LJ, Connor M, et al. Hysteroscopic morcellation compared with electrical resection of endometrial polyps: a randomized controlled trial. *Obstet Gynecol*. 2014;123:745.

LEVEL III

American College of Obstetricians and Gynecologists. Alternatives to hysterectomy in the management of leiomyomas. ACOG Practice Bulletin No. 96. *Obstet Gynecol*. 2008;112:201.

American College of Obstetricians and Gynecologists. Antibiotic prophylaxis for gynecologic procedures. ACOG Practice Bulletin No. 104. *Obstet Gynecol*. 2009;113:1180.

American College of Obstetricians and Gynecologists. Diagnosis of abnormal uterine bleeding in reproductive-aged women. Practice Bulletin No. 128. *Obstet Gynecol*. 2012;120:197.

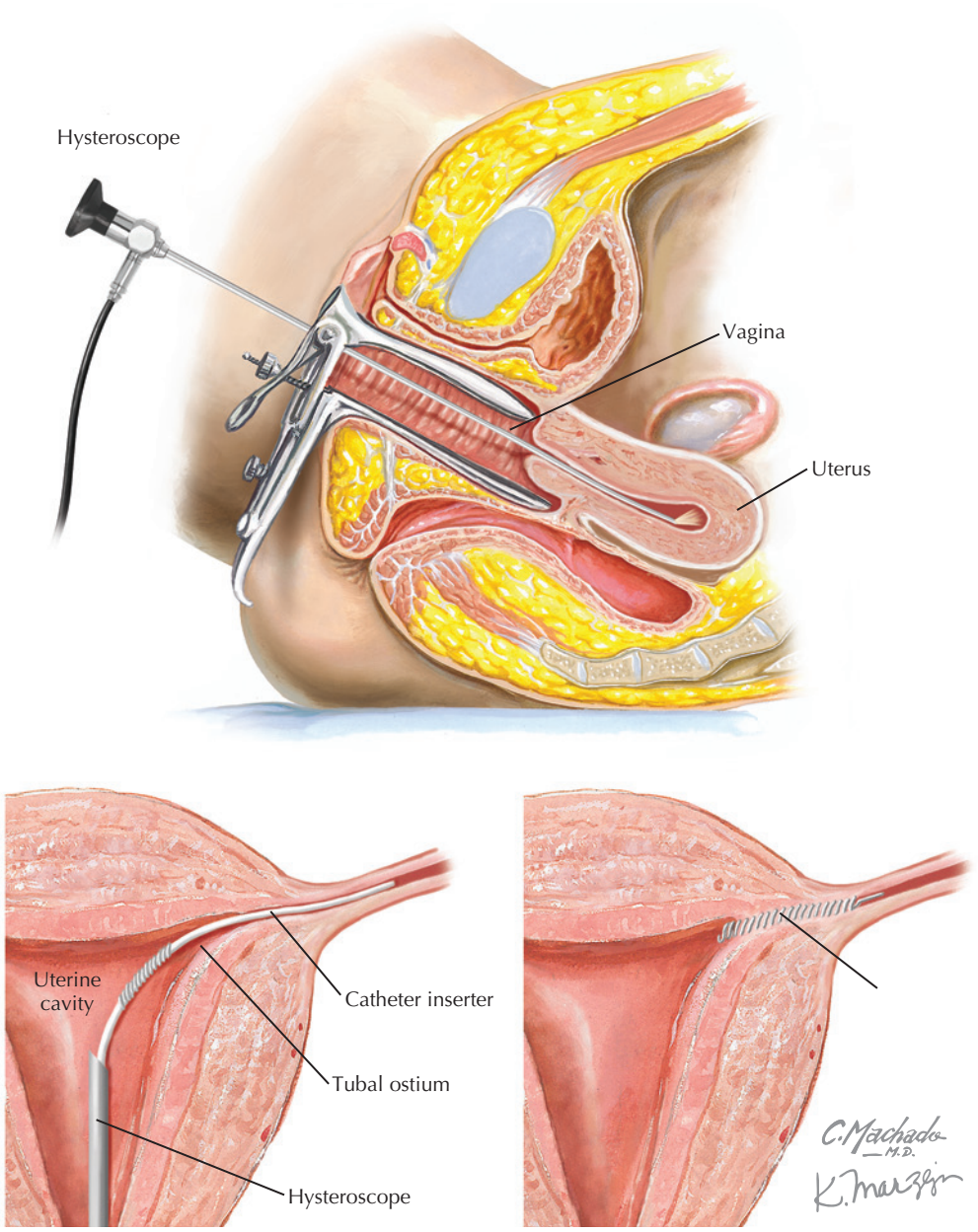


Figure 270.1 Hysteroscopic sterilization

the uterine cavity under direct visualization (0-degree scope) or with the obturator in place until the tip of the sheath is within the uterine cavity. A careful and systematic inspection of the uterine cavity and tubal ostia is then conducted.

Once both tubal ostia have been visualized, the insert deployment device may be opened onto the sterile field. The delivery system has an introducer sheath that must be inserted into the working channel of the hysteroscope. Through this sheath, the insertion system is passed though the hysteroscope and into the surgeon's view. The surgeon then advances the device until the black positioning marker is at the tubal ostium. A thumbwheel on the inserter is rotated backward until it can no longer rotate, retracting the delivery catheter and exposing the wound coil. A gold marker band should lie just outside the tubal ostium. The deployment button is depressed, and the thumbwheel is rotated again until it locks, unwinding and detaching the coil. The device delivery system is then removed, and the coil is inspected. The number of expanded coils that extend from the tubal ostium should be counted and recorded. There should be 3–8 expanded coils visible above the ostium, although 0–17 coils are considered acceptable by the manufacturer. If there are 18 or more expanded coils, the device must be removed and a new device used to reattempt placement. The second coil is placed in the same manner with a new introducer sheath. The procedure concludes with the withdrawal of all instruments and verification of hemostasis.

Three months after the procedure, a hysterosalpingogram should be performed to confirm tubal occlusion. Alternate contraception must be used until satisfactory device location and tubal occlusion is confirmed. If complete occlusion is not documented, follow up in an additional 3 months will often find sufficient scarring. A transvaginal ultrasonography alternative to hysterosalpingography has been approved but requires certification by the manufacturer.

COMPLICATIONS

Fluid overload, hyponatremia (with electrolyte-poor fluids), uterine perforation, cervical laceration, infection (endometrial, myometrial, pelvic), hemorrhage (intraoperative or postoperative).

FOLLOW-UP

Based on the indications and findings.

CPT CODE(S)

58565 Hysteroscopy, surgical; with bilateral fallopian tube cannulation to induce occlusion by placement of permanent implants

REFERENCES

LEVEL II

Hurskainen R, Hovi SL, Gissler M, et al. Hysteroscopic tubal sterilization: a systematic review of the Essure system. *Fertil Steril*. 2010;94:16.

Mao J, Pfeifer S, Schlegel P, et al. Safety and efficacy of hysteroscopic sterilization compared with laparoscopic sterilization: an observational cohort study. *BMJ*. 2015;351:h5162.

Miño M, Arjona JE, Cordón J, et al. Success rate and patient satisfaction with the Essure sterilisation in an outpatient setting: a prospective study of 857 women. *BJOG*. 2007;114:763.

Savage UK, Masters SJ, Smid MC, et al. Hysteroscopic sterilization in a large group practice: experience and effectiveness. *Obstet Gynecol*. 2009;114:1227.

Yunker AC, Ritch JM, Robinson EF, et al. Incidence and risk factors for chronic pelvic pain after hysteroscopic sterilization. *J Minim Invasive Gynecol*. 2015;22:390.

LEVEL III

American College of Obstetricians and Gynecologists. Antibiotic prophylaxis for gynecologic procedures. ACOG Practice Bulletin No. 104. *Obstet Gynecol*. 2009;113:1180.

Benefits and risks of sterilization. Practice Bulletin No. 133. American College of Obstetricians and Gynecologists. *Obstet Gynecol*. 2013;121:392.

Dhruva SS, Ross JS, Gariepy AM. Revisiting Essure–Toward safe and effective sterilization. *N Engl J Med*. 2015;373:e17.

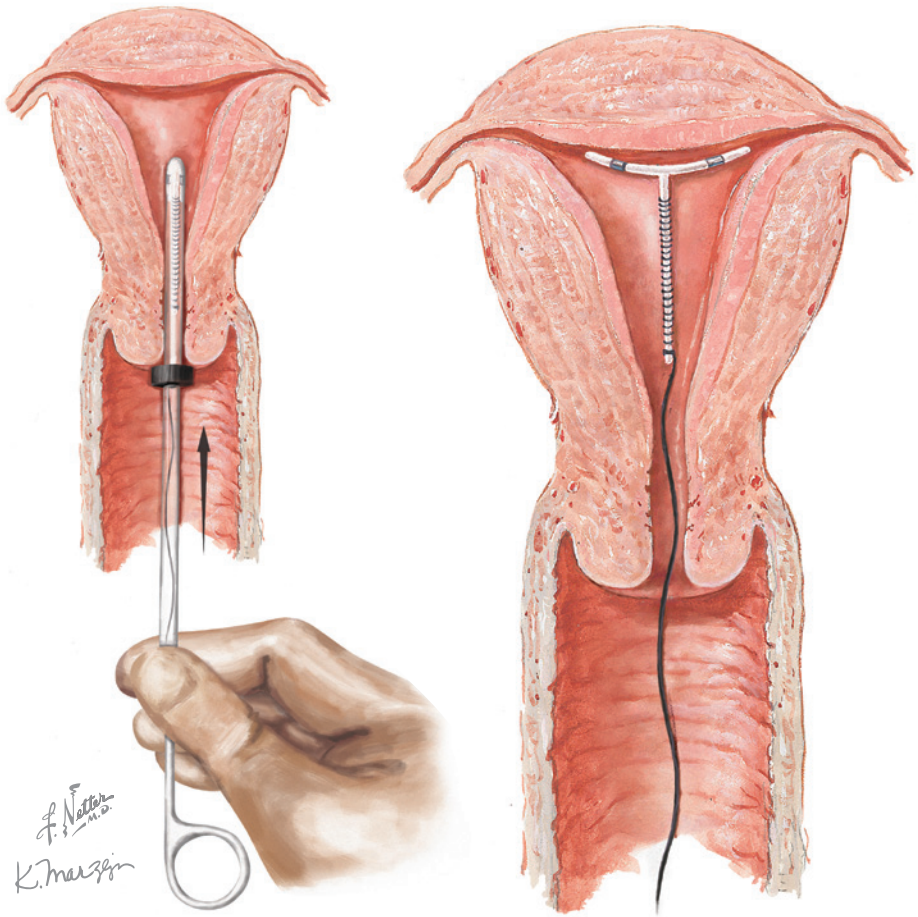


Figure 271.1 Intrauterine contraceptive device (IUCD) insertion

in position in the uterine cavity, withdrawing the placement instrument leaving the IUCD behind, verifying correct placement, and trimming the marker string(s).

ParaGuard T380A and Liletta

The IUCD must be loaded into its insertion device, which may be accomplished using either sterile gloves or a "no touch" technique. With sterile gloves the device is grasped, folded, and inserted into the distal end of the insertion tool. In the "no touch" method the same ends must be accomplished, but the IUCD in this case is manipulated through the outer package wrapper.

Once the IUCD is in the insertion device, the flexible flange is moved backward on the insertion tube until it corresponds to the expected or measured depth of the uterus. The IUCD and inserter are placed at the disinfected external cervical os and gently advanced until resistance indicates that the fundus has been reached. With the obturator held in place, the insertion tube is withdrawn, leaving the device in the correct position. The obturator should not be advanced as the insertion tube is withdrawn; the insertion tube may be slightly readvanced to ensure that the IUCD lies against the fundus and then is completely withdrawn. The string of the device should be trimmed at a point approximately 1–2 cm from the external os.

Mirena and Skyla

The levonorgestrel-containing IUCDs are supplied with a self-loading inserter. To insert this device, the package is opened, taking care to maintain the sterility of the contents. The threads of the IUCD must be freed from the base of the inserter, and the slider (located in the handle of the inserter) is advanced to the position closest to the IUCD itself. This will result in the arms of the IUCD folding inward and their distal knobs occluding the inserter tube. Once the IUCD is withdrawn into the insertion device, the flexible flange is moved backward on the insertion tube until it corresponds to the expected or measured depth of the uterus.

To place the IUCD in the uterine cavity, the tip of the IUCD and insertion tool are placed against the disinfected cervical os, and traction on the os is applied if needed. Gentle pressure is exerted, advancing until the flange is approximately 1.5–2 cm from the cervix. This will allow sufficient room for the arms of the IUCD to expand on deployment. While this position is maintained, the slider is pulled back. This will release the arms from the inserter tube. After 30 seconds are allowed for the arms to regain their full extension, at which point the inserter should be gently advanced until the flange meets the cervix, ensuring proper fundal placement of the device. Being careful not to entangle the threads, the device is now removed, and the threads are trimmed approximately 2–3 cm from the cervix.

Although an IUCD may be placed at any point in a menstrual cycle (after pregnancy has been ruled out), it is preferable to insert it 7–10 days after the onset of menstruation. Insertion at this point of the cycle is associated with a lower expulsion rate. The patient must be counseled to use a backup method of contraception during this cycle. If the IUCD is to be placed in the immediate postpartum period, the procedure is altered only by the lack of tenaculum use and the practice of leaving the string untrimmed until the 6-week

follow up visit. The IUCD may also be introduced on the end of a spongstick, if desired, omitting the inserter.

When gentle pressure does not result in the IUCD insertion tool's advancement through the cervix, a tenaculum may be used to stabilize the cervix. Traction on the tenaculum may result in some straightening of the canal, further aiding insertion. In some cases, it may be necessary to use a sterile uterine sound to identify the axis of the canal, provide modest cervical dilation, or confirm the depth of the uterine cavity.

IUCDs should not be left in the folded position inside the inserter for more than 1–2 minutes. Prolonged folding will result in a device that will not unfold properly in the uterine cavity, increasing the risk for expulsion or contraceptive failure.

COMPLICATIONS

Vasovagal reaction, pain, uterine perforation (approximately 1 in 1000 insertions), infection (uterine or pelvic, most common in the first 20 days after insertion), bleeding, expulsion of the device.

FOLLOW-UP

Generally, women should be re-evaluated 1–4 weeks after the IUCD placement. The patient should be advised to periodically verify the presence and length of the IUCD strings. Expulsion is most common during menstruation and during the first 6 months of use. Amenorrhea in a woman using the copper IUCD should prompt a pregnancy test. Any woman who misses a period and experiences pain should have ectopic pregnancy ruled out. Women should be instructed about warning signs of pelvic infection, particularly in the first month after the insertion of the device when the risk for pelvic infection is greater.

CPT CODE(S)

58300 Insertion of intrauterine device (IUD), not including the device
X4633 Charge for cost of copper IUD
X4634 Charge for cost of progesterone IUD

REFERENCES

LEVEL II

Cheng L, Che Y, Gülmezoglu AM. Interventions for emergency contraception. *Cochrane Database Syst Rev*. 2012;(8):CD001324.

Grimes DA, Schulz KF. Prophylactic antibiotics for intrauterine device insertion: a metaanalysis of the randomized controlled trials. *Contraception*. 1999;60:57.

Kavanaugh ML, Jerman J, Finer LB. Changes in use of long-acting reversible contraceptive methods among U.S. women, 2009-2012. *Obstet Gynecol*. 2015;126:917.

Lethaby AE, Cooke I, Rees M. Progesterone or progestogen releasing intrauterine systems for heavy menstrual bleeding. *Cochrane Database Syst Rev*. 2005;(4):CD002126.

Polis CB, Schaffer K, Blanchard K, et al. Advance provision of emergency contraception for pregnancy prevention. *Cochrane Database Syst Rev*. 2007;(2):CD005497.

Whiteman MK, Tyler CP, Folger SG, et al. When can a woman have an intrauterine device inserted? A systematic review. *Contraception*. 2013; 87:666.

Zhou L, Xiao B. Emergency contraception with Multiload Cu-375 SL IUD: a multicenter clinical trial. *Contraception*. 2001;64:107.

LEVEL III

American College of Obstetricians and Gynecologists. Access to emergency contraception. Committee Opinion No. 542. *Obstet Gynecol*. 2012; 120:1250.

American College of Obstetricians and Gynecologists. Adolescents and long-acting reversible contraception: implants and intrauterine devices. Committee Opinion No. 539. *Obstet Gynecol*. 2012;120:983.

American College of Obstetricians and Gynecologists. Emergency contraception. Practice Bulletin No. 152. *Obstet Gynecol*. 2015;126:e1.

American College of Obstetricians and Gynecologists. Increasing access to contraceptive implants and intrauterine devices to reduce unintended pregnancy. Committee Opinion No. 642. *Obstet Gynecol*. 2015;126:e44.

American College of Obstetricians and Gynecologists. Long-acting reversible contraception: implants and intrauterine devices. Practice Bulletin No. 121. *Obstet Gynecol*. 2011;118:184.

American College of Obstetricians and Gynecologists. Noncontraceptive uses of hormonal contraceptives. Practice Bulletin No. 110. *Obstet Gynecol*. 2010;115:206.

American College of Obstetricians and Gynecologists. Options for prevention and management of heavy menstrual bleeding in adolescent patients undergoing cancer treatment. Committee Opinion No. 606. *Obstet Gynecol*. 2014;124:397.

Buhling KJ, Zite NB, Lotke P, et al. Worldwide use of intrauterine contraception: a review. *Contraception*. 2014;89:162.

Stanford JB, Mikolajczyk RT. Mechanisms of action of intrauterine devices: update and estimation of postfertilization effects. *Am J Obstet Gynecol*. 2002;187:1699.

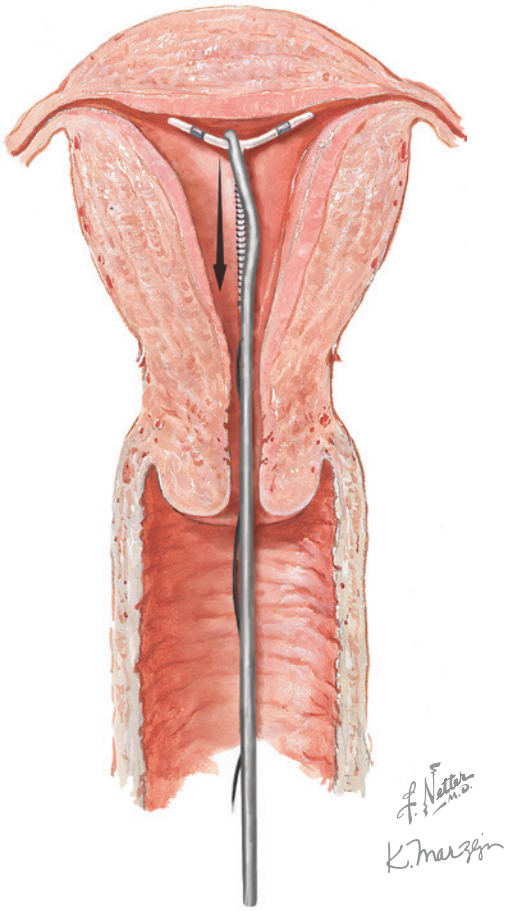


Figure 272.1 Intrauterine contraceptive device (IUCD) removal

REQUIRED EQUIPMENT

- Skin (vaginal) preparation materials (iodine-based antibacterial solution [eg, Betadine] or other suitable cleansing agents)
- Vaginal speculum
- Tenaculum
- Nonsterile examination gloves
- Uterine packing forceps or other long forceps
- IUD or "crochet" hook (optional)
- Cervical cytology brush (Cytobrush or similar; optional)

TECHNIQUE

The discomfort of an IUCD removal may be decreased by premedicating with a single oral dose of a nonsteroidal antiinflammatory drug administered in doses usually used to treat dysmenorrhea, through the use of 2% intracervical lidocaine gel, or both. Before beginning the procedure, the size, shape, and location of the uterus should be determined. The cervix should be visualized with the aid of a speculum. The cervix should be disinfected if reinsertion of a new device is planned.

When the IUCD string(s) are visible at the cervical os, gentle traction with uterine packing forceps or other suitable grasping device will result in the delivery of the IUCD. When the string is not apparent, gentle probing of the outer portion of the cervical canal with the forceps or a sterile crochet hook may locate the strings. A Cytobrush may also be placed in the endocervix and gently swept downward to locate the strings. These maneuvers will often yield the string that may then be grasped as previously described. If these maneuvers are unsuccessful in retrieving the IUCD, the cervix should be disinfected prior to any further attempts. Ultrasonography should be considered to ensure an intrauterine location of the IUCD. The possibility of an ongoing pregnancy must also be considered (if not already assessed).

An IUCD ("crochet") hook may be used under sterile conditions in the outpatient setting, or the IUCD may be removed in the operating room or ambulatory surgery setting where hysteroscopic guidance is available. In most cases, if a hook is to be used, a tenaculum to stabilize the cervix will be needed, and the hook is passed through the cervix to the level of the uterine fundus. As the hook is advanced, the device should be carefully monitored for vibrations, sounds, or a sensation that the tip has encountered the IUCD. Once the hook has reached the fundus (or the IUCD, if felt), the hook is slowly rotated 180–360 degrees and withdrawn. Moderate resistance to withdrawal is associated with capture of the IUCD, and persistent traction will often deliver the device. Even when no resistance is felt, removal of the hook will often deliver the string(s), allowing removal of the IUCD by conventional traction. If neither the IUCD nor its string has been retrieved after several attempts, the effort should be abandoned until the presence of the IUCD in the body has been confirmed and removal via hysteroscopy or laparoscopy is considered.

COMPLICATIONS

Vasovagal reaction, pain, uterine perforation (when a hook is used), infection (uterine or pelvic), bleeding.

FOLLOW-UP

Based on the contraceptive plans and the indications for removal.

CPT CODE(S)

58301 Removal of intrauterine device (IUD)

REFERENCES

LEVEL I

Bounds W, Hutt S, Kubba A, et al. Randomised comparative study in 217 women of three disposable plastic IUCD thread retrievers. *Br J Obstet Gynaecol*. 1992;99:915.

LEVEL II

Hov GG, Skjeldestad FE, Hilstad T. Use of IUD and subsequent fertility—Follow-up after participation in a randomized clinical trial. *Contraception*. 2007;75:88. [Epub 2006 Nov 14].

Hubacher D, Lara-Ricalde R, Taylor DJ, et al. Use of copper intrauterine devices and the risk of tubal infertility among nulligravid women. *N Engl J Med*. 2001;345:561.

Stanback J, Grimes D. Can intrauterine device removals for bleeding or pain be predicted at a one-month follow-up visit? A multivariate analysis. *Contraception*. 1998;58:357.

LEVEL III

Assaf A, Gohar M, Saad S, et al. Removal of intrauterine devices with missing tails during early pregnancy. *Contraception*. 1992;45:541.

Ben-Rafael Z, Bider D. A new procedure for removal of a "lost" intrauterine device. *Obstet Gynecol*. 1996;87:785.

Grimes DA. Intrauterine device and upper-genital-tract infection. *Lancet*. 2000;356:1013.

Johnson BA. Insertion and removal of intrauterine devices. *Am Fam Physician*. 2005;71:95.

Sachs BP, Gregory K, McArdle C, et al. Removal of retained intrauterine contraceptive devices in pregnancy. *Am J Perinatol*. 1992;9:139.

273 LEEP (LOOP ELECTROSURGICAL EXCISION PROCEDURE) AND LLETZ (LARGE LOOP EXCISION OF THE TRANSFORMATION ZONE) CONIZATIONS

DESCRIPTION

Cervical conization is a diagnostic or therapeutic procedure that removes a cone-shaped specimen from the uterine cervix. Loop electrocautery excisional procedure (LEEP, also known as large loop excision of the transformation zone [LLETZ]) uses electric current instead of a knife to remove the diseased cervical tissue.

INDICATIONS

Histologically verified advanced epithelial atypia (for diagnosis or therapy) or inability to adequately evaluate the cervix through colposcopy.

CONTRAINDICATIONS

Coagulopathy, advanced pregnancy, known or suspected allergy to the agents used.

REQUIRED EQUIPMENT

- Skin (vaginal) preparation materials (iodine-based antibacterial solution [eg, Betadine] or other suitable cervical cleansing agents)
- Sterile gloves
- Nonconductive vaginal speculum
- Electrosurgical generator with an output capability of at least 50 W in both coagulation and cutting modes, a variety of waveform outputs (pure cut, blended current, and coagulation current), patient grounding pad with monitor, and isolated circuitry
- A variety of loop electrodes (size and shape to be determined at the time of the procedure based on the size and shape of the cervix and lesion to be removed)
- A smoke evacuator with odor and viral filter
- Monsel paste (ferric subsulfate solution allowed to evaporate to the consistency of paste)
- 5% acetic acid or Lugol solution (super-saturated potassium iodide)
- Kevorkian or similar endocervical curette
- Histology fixative (10% formalin) in containers
- Syringe with 25- or 27-gauge 1.5 inch needle for anesthetic injection, 1% or 2% lidocaine with or without 1:100,000 epinephrine
- 12-inch needle holder, 2-0 absorbable suture material (or similar)

TECHNIQUE

After informed consent has been obtained, the patient is placed in the dorsal lithotomy position and a return electrode ("grounding

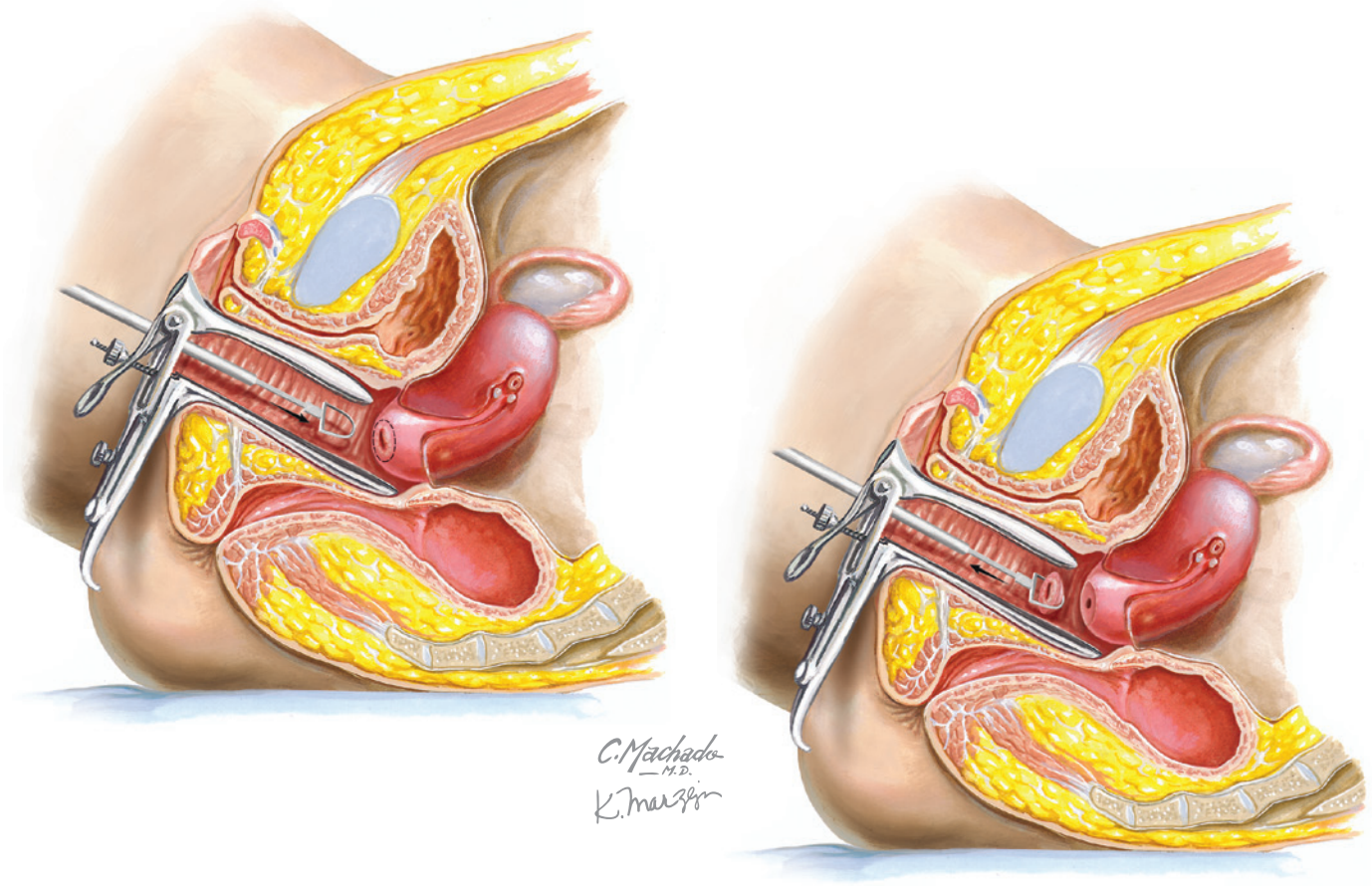


Figure 273.1 LEEP and LLETZ conizations

pad") is placed on the patient's thigh with the long edge directed toward the hip.

The cervix should be visualized using a nonconductive speculum with a smoke evacuator attachment. Acetic acid or Lugol solution may be applied to the cervix to delineate the area of abnormality.

The local anesthetic should be injected below the epithelium into the cervix at the 3-, 6-, 9-, and 12-o'clock positions. These injections should be approximately 3–5 mm deep. Vasopressin (1 pressor unit/20 mL saline) or 1:200,000 epinephrine solution may be added to this solution or separately injected. The appropriate loop electrode should be selected based on the size of the lesion to be treated: lesions confined to the external cervix are most often treated with a round loop, 2-cm wide and 0.8-cm deep; for a nulliparous, small cervix, a loop 1.5-cm wide and 0.7-cm deep is used; and for lesions extending into the endocervix, a square loop electrode, measuring1 × 1 cm, can be used.

The power setting for the electrosurgical generator depends on the manufacturer of the generator and the diameter of the loop: a 2-cm loop requires 35–45 W of power and a 1- × 1-cm loop requires 20–30 W of power. A blended current should be used.

The loop should be placed several millimeters lateral to the edge of the lesion, and a simulated pass of the loop over the lesion is made to ensure that there are no obstacles. The electrosurgical generator is then activated in the "cut" mode. The loop is pressed perpendicular into the tissue to a depth of 5–8 mm and then is dragged laterally across and through the endocervix, exiting at a point several millimeters past the lesions or beyond the transformation zone, whichever is farther. The resultant specimen should be dome shaped with the endocervical canal visible in the middle. Care should be taken to not press the loop greater than 4–5-mm deep at the lateral borders of the cervix due to the arterial blood supply located at the 3- and 9-o'clock positions of the cervix.

If the lesion is too large to be removed in a single pass, the central portion of the lesion is removed first using a 2-cm wide loop as described earlier. Additional passes are then made using the same loop to remove remaining lesions and the transformation zone, or a smaller loop may be used to extend the excision farther up the endocervical canal.

If a blended current is used, bleeding from the base of the excision site is generally minimal. If needed, hemostasis may be obtained by fulguration using the ball electrode or the application of Monsel solution.

Pelvic rest (no tampons, douching, or sexual intercourse) is generally advised for 2–3 weeks following the procedure, and the patient is instructed to return for heavy bleeding or bleeding that lasts more than 2 weeks.

COMPLICATIONS

Bleeding (acute and delayed), infection. Conization appears to approximately double the risk that a woman will subsequently have a preterm delivery, a low-birthweight infant, or premature rupture of the membranes.

FOLLOW-UP

The cervix is generally inspected at approximately 6 weeks after the procedure. Treatment success for cervical intraepithelial neoplasia is generally 95%.

CPT CODE(S)

57522 Conization of cervix, with or without fulguration, with or without dilation and curettage, with or without repair; loop electrode excision

REFERENCES

LEVEL I

Boardman LA, Steinhoff MM, Shackelton R, et al. A randomized trial of the Fischer cone biopsy excisor and loop electrosurgical excision procedure. *Obstet Gynecol*. 2004;104:745.

Mathevet P, Dargent D, Roy M, et al. A randomized prospective study comparing three techniques of conization: cold knife, laser, and LEEP. *Gynecol Oncol*. 1994;54:175.

LEVEL II

Jackobsson M, Gissler M, Sainio S, et al. Preterm delivery after surgical treatment for cervical intraepithelial neoplasia. *Obstet Gynecol*. 2007;109:309.

Kyrgiou M, Tsoumpou I, Vrekoussis T, et al. The up-to-date evidence on colposcopy practice and treatment of cervical intraepithelial neoplasia: The Cochrane Colposcopy & Cervical Cytopathology Collaborative Group (C5 group) approach. *Cancer Treat Rev*. 2006;32:516.

Martin-Hirsch PL, Paraskevaidis E, Kitchener H. Surgery for cervical intraepithelial neoplasia. *Cochrane Database Syst Rev*. 2000;(2): CD001318.

Phadnis SV, Atilade A, Young MP, et al. The volume perspective: a comparison of two excisional treatments for cervical intraepithelial neoplasia (laser versus LLETZ). *BJOG*. 2010;117:615.

Sadler L, Saftlas A, Wang W, et al. Treatment for cervical intraepithelial neoplasia and risk of preterm delivery. *JAMA*. 2004;291:2100.

Sjøborg KD, Vistad I, Myhr SS, et al. Pregnancy outcome after cervical cone excision: a case-control study. *Acta Obstet Gynecol Scand*. 2007; 86:423.

Vanichtantikul A, Charoenkwan K. Lidocaine spray compared with submucosal injection for reducing pain during loop electrosurgical excision procedure: a randomized controlled trial. *Obstet Gynecol*. 2013;122:553.

LEVEL III

American College of Obstetricians and Gynecologists. Management of abnormal cervical cancer screening test results and cervical cancer precursors. Practice Bulletin No. 140. *Obstet Gynecol*. 2013;122:1338.

274 PESSARY FITTING

DESCRIPTION

Pessaries are devices fitted and worn in the vagina to provide support to the pelvic organs. Pessaries are available in various sizes and shapes and are categorized as supportive (eg, ring, lever, Gellhorn, Gehrung, Shaatz) or space occupying (eg, doughnut, cube, inflatable).

INDICATIONS

Pelvic organ prolapse, urinary incontinence, cervical incompetence (lever or ring type), drug delivery. Pessaries are often used as either an alternative to surgery or as a presurgical trial (Box 274.1).

CONTRAINDICATIONS

Undiagnosed vaginal bleeding, significant vaginal atrophy, latex sensitivity. Patients who are unable or unwilling to manage the periodic insertion and removal of the device are poor candidates.

REQUIRED EQUIPMENT

- Vaginal speculum
- Water-soluble lubricant
- Nonsterile examination gloves
- Examples of appropriate pessaries in a variety of sizes (generally the "average size" and at least one size larger and smaller)

TECHNIQUE

Pessaries will not be well tolerated or provide optimal support in a patient who is poorly estrogenized. Therefore, a minimum of 30 days of topical estrogen therapy should be instituted prior to a trial of pessary therapy in these patients.

The type of pessary chosen for a given patient is determined by the anatomic defect and the symptoms the patient is experiencing. The most commonly used forms of pessary for pelvic relaxation are the ring (or doughnut), the ball, and the cube. The indications for various types of commonly used pessaries are shown in Box 274.1. The type of pessary that can be fitted is related to the severity of prolapse. Ring pessaries are frequently the first choice, followed by Gellhorn or other pessaries if the rings do not stay in place.

Pessaries are fitted and placed in the vagina in much the same way as a contraceptive diaphragm: the depth of the vagina and the integrity of the supporting structures of the vagina are gauged as a part of the pelvic examination. The size of pessary to be fitted is based on the findings of the pelvic examination. The pessary is lubricated with a water-soluble lubricant, folded or compressed, and inserted into the vagina. Some pessaries require specific maneuvers for their insertion; always consult the manufacturer's instructions.

The pessary is next adjusted so that it is in the proper position based on the type: ring and lever pessaries should sit behind the cervix (when present) and rest in the retropubic notch, the Gellhorn pessary should be entirely contained in the vagina with the plate resting above the levator plane, the Gehrung pessary must bridge the cervix with the limbs resting on the levator muscles on each side, and the ball or cube pessaries should occupy and occlude the upper vagina. All pessaries must allow the easy passage of an examining finger between the pessary and vaginal wall in all areas. The only situation wherein a pessary is allowed to exert any significant pressure beneath the urethra is in the case of those devices designed for the control of urinary incontinence.

After the pessary has been placed and the fit checked, the patient should be asked to strain. The pessary may slightly descend, but its integrity should be maintained and it should return to its normal position when the patient relaxes. The patient should be allowed to stand and walk a bit with the pessary in place to ensure comfort and retention. The pessary may then be removed (if a "fitting" pessary has been used) or may be left in place (if this is to be the patient's final device). If necessary, the process should be repeated until an appropriate, comfortable fit is obtained. The fit should also be confirmed at a follow-up visit in 5–7 days. In most patients (50%–73%) an appropriately sized pessary can be successfully fitted in one or two office visits.

The patient should be instructed on both the proper insertion and removal techniques. Ring pessaries should be removed by hooking a finger into the pessary's opening, gently compressing the device, and then withdrawing the pessary with gentle traction. Cube pessaries must also be compressed, but the suction created between the faces of the cube and vaginal wall must be broken by gently separating the device from the vaginal sidewall; the locator string often attached to these pessaries should not be used for traction. Inflatable pessaries should be deflated prior to removal. Gellhorn and Gehrung pessaries are removed by a reversal of their insertion procedures.

Box 274.1 INDICATIONS FOR COMMON PESSARIES

Malposition: Lever type (Hodge)
Prolapse
Uterine: Gellhorn, ring, doughnut, cube
Vaginal: Doughnut, cube, ball (Gehrung)
Cystocele/Rectocele: Gehrung, Shaatz
Incompetent cervix: Lever, ring
Incontinence: Doughnut, lever, ring
Preoperative: Based on the defect
Drug delivery: Specialized ring (17β-estradiol, medroxyprogesterone, prostaglandin E_2)

COMPLICATIONS

Vaginal erosion, bleeding, infection, vaginal discharge, pain, expulsion, urinary retention, fistula formation (rare with proper fit, care, and estrogen therapy).

FOLLOW-UP

An examination at 5–7 days after initial fitting is required to confirm proper placement, hygiene, and the absence of pressure-related problems (vaginal trauma or necrosis). Earlier evaluation (in 24–48 hours) may be advisable for patients who are debilitated or who require additional assistance. Follow-up should then occur in approximately 1 month and then quarterly for the duration of use. Some authors recommend maintaining a monthly schedule indefinitely, especially in those with limited abilities to maintain the device themselves.

CPT CODE(S)

57160 Fitting and insertion of pessary or other intravaginal support device (procedure only)

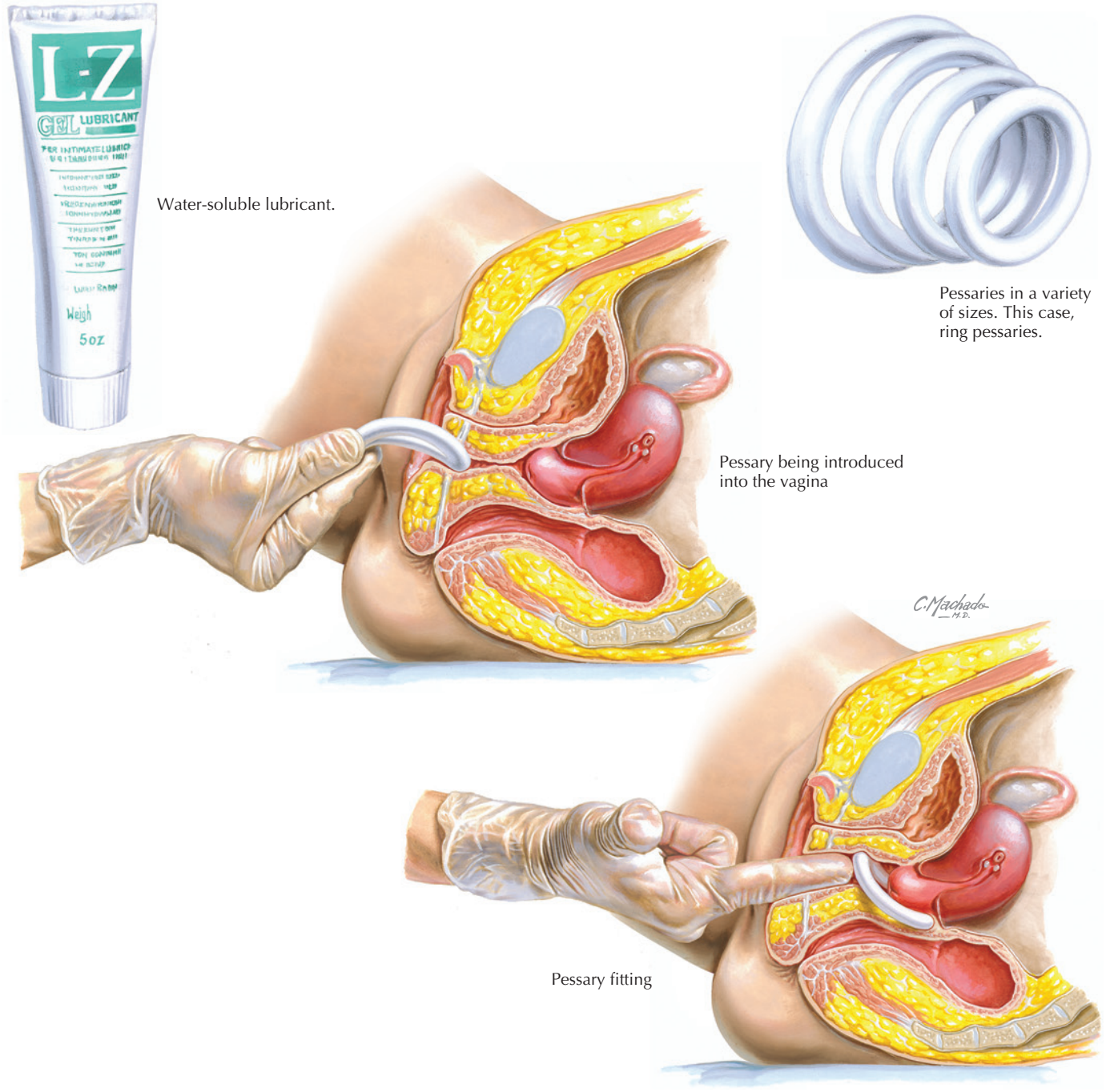


Figure 274.1 Pessary fitting

REFERENCES

LEVEL I

Cundiff GW, Amundsen CL, Bent AE, et al. The PESSRI study: symptom relief outcomes of a randomized crossover trial of the ring and Gellhorn pessaries. *Am J Obstet Gynecol*. 2007;196:405.e1.

LEVEL II

Adams E, Thomson A, Maher C, et al. Mechanical devices for pelvic organ prolapse in women. *Cochrane Database Syst Rev*. 2004;(2):CD004010.

Clemons JL, Aguilar VC, Tillinghast TA, et al. Risk factors associated with an unsuccessful pessary fitting trial in women with pelvic organ prolapse. *Am J Obstet Gynecol*. 2004;190:345.

Hagen S, Stark D, Maher C, et al. Conservative management of pelvic organ prolapse in women. *Cochrane Database Syst Rev*. 2004;(2): CD003882.

Mutone MF, Terry C, Hale D, et al. Factors which influence the short-term success of pessary management of pelvic organ prolapse. *Am J Obstet Gynecol*. 2005;193:89.

Patel M, Mellen C, O'Sullivan DM, et al. Impact of pessary use on prolapse symptoms, quality of life, and body image. *Am J Obstet Gynecol*. 2010; 202:499.e1.

Richter HE, Burgio KL, Brubaker L, et al. Continence pessary compared with behavioral therapy or combined therapy for stress incontinence: a randomized controlled trial. *Obstet Gynecol*. 2010;115:609.

Schaffer J, Nager CW, Xiang F, et al. Predictors of success and satisfaction of nonsurgical therapy for stress urinary incontinence. *Obstet Gynecol*. 2012;120:91.

Wu V, Farrell SA, Baskett TF, et al. A simplified protocol for pessary management. *Obstet Gynecol*. 1997;90:990.

LEVEL III

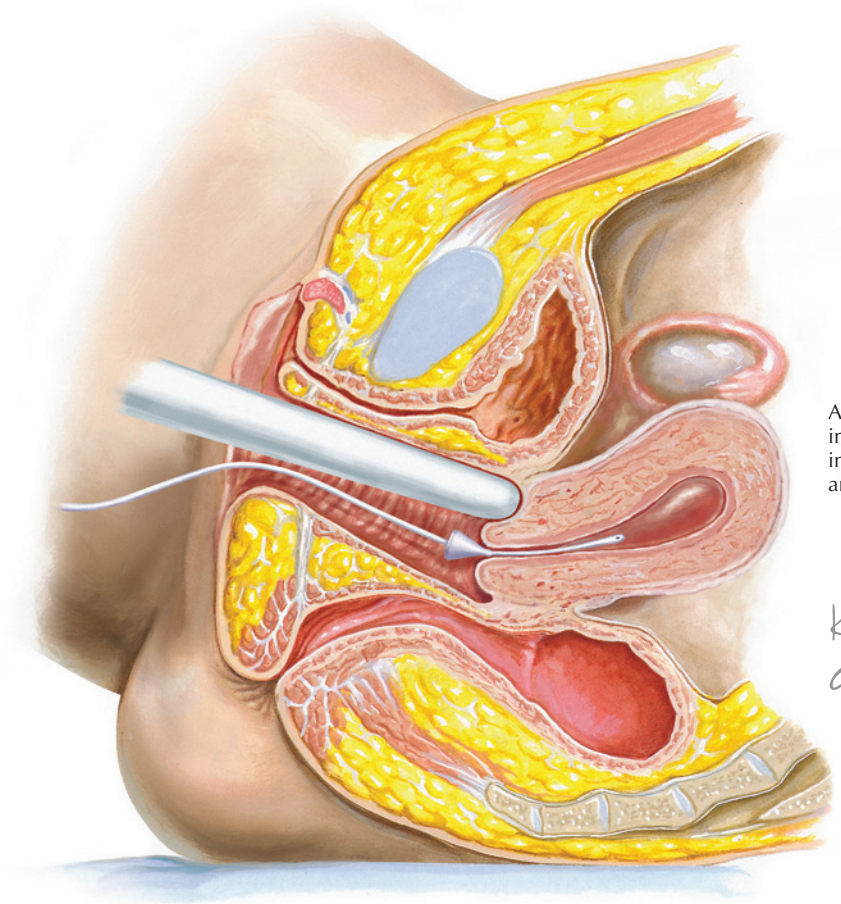
American College of Obstetricians and Gynecologists. Cerclage for the management of cervical insufficiency. Practice Bulletin No. 142. *Obstet Gynecol*. 2014;123:372.

American College of Obstetricians and Gynecologists. Evaluation of uncomplicated stress urinary incontinence in women before surgical treatment. Committee Opinion No. 603. *Obstet Gynecol*. 2014;123:1403.

Anders K. Devices for continence and prolapse. *BJOG*. 2004;111:61.

Jelovsek JE, Maher C, Barber MD. Pelvic organ prolapse. *Lancet*. 2007;369:1027.

Thakar R, Stanton S. Management of genital prolapse. *BMJ*. 2002;324:1258.



A small catheter or infant feeding tube is inserted into the uterine cavity so that sterile saline can be introduced to help visualize the uterine cavity and lining.

K. Marzga
C. Machado M.D.

Figure 275.1 Sonohysterography

COMPLICATIONS

Bleeding, infection (endometrial, myometrial, pelvic). Infection following sonohysterography is rare, and prophylactic antibiotics are not recommended unless indicated by factors such as valvular heart disease. Vasovagal syncope during the procedure may occur but is generally transient.

CPT CODE(S)

58340 Catheterization and introduction of saline or contrast material for saline infusion sonohysterography (SIS) or hysterosalpingography

76831 Saline infusion sonohysterography (SIS), with or without color flow Doppler hysterosonography

FOLLOW-UP

Based on the indications.

REFERENCES

LEVEL I

Guney M, Oral B, Bayhan G, et al. Intrauterine lidocaine infusion for pain relief during saline solution infusion sonohysterography: a randomized, controlled trial. *J Minim Invasive Gynecol.* 2007;14:304.

Spieldoch RL, Winter TC, Schouweiler C, et al. Optimal catheter placement during sonohysterography: a randomized controlled trial comparing cervical to uterine placement. *Obstet Gynecol.* 2008;111:15.

Tur-Kaspa I, Gal M, Hartman M, et al. A prospective evaluation of uterine abnormalities by saline infusion sonohysterography in 1,009 women with infertility or abnormal uterine bleeding. *Fertil Steril.* 2006;86:1731.

LEVEL II

Alborzi S, Parsanezhad ME, Mahmoodian N, et al. Sonohysterography versus transvaginal sonography for screening of patients with abnormal uterine bleeding. *Int J Gynaecol Obstet.* 2007;96:20.

Becker E Jr, Lev-Toaff AS, Kaufman EP, et al. The added value of transvaginal sonohysterography over transvaginal sonography alone in women with known or suspected leiomyoma. *J Ultrasound Med.* 2002;21:237.

La Sala GB, Blasi I, Gallinelli A, et al. Diagnostic accuracy of sonohysterography and transvaginal sonography as compared with hysteroscopy and endometrial biopsy: a prospective study. *Minerva Ginecol.* 2011;63:421.

LEVEL III

American College of Obstetricians and Gynecologists. The role of transvaginal ultrasonography in the evaluation of postmenopausal bleeding. ACOG Committee Opinion No. 440. *Obstet Gynecol.* 2009;114:409.

American College of Obstetricians and Gynecologists. Diagnosis of abnormal uterine bleeding in reproductive-aged women. Practice Bulletin No. 128. *Obstet Gynecol.* 2012;120:197.

American College of Obstetricians and Gynecologists. Sonohysterography. Technology Assessment in Obstetrics and Gynecology No. 8. *Obstet Gynecol*. 2012;119:1325.

American College of Obstetricians and Gynecologists. Endometrial intraepithelial neoplasia. Committee Opinion No. 631. *Obstet Gynecol*. 2015;125:1272.

American Institute of Ultrasound in Medicine, American College of Radiology, American College of Obstetricians and Gynecologists, Society of Radiologists in Ultrasound. AIUM practice guideline for the performance of sonohysterography. *J Ultrasound Med*. 2012;31:165.

Berridge DL, Winter TC. Saline infusion sonohysterography: technique, indications, and imaging findings. *J Ultrasound Med*. 2004;23:97.

Davis PC, O'Neill MJ, Yoder IC, et al. Sonohysterographic findings of endometrial and subendometrial conditions. *Radiographics*. 2002;22:803.

O'Neill MJ. Sonohysterography. *Radiol Clin North Am*. 2003;41:781.

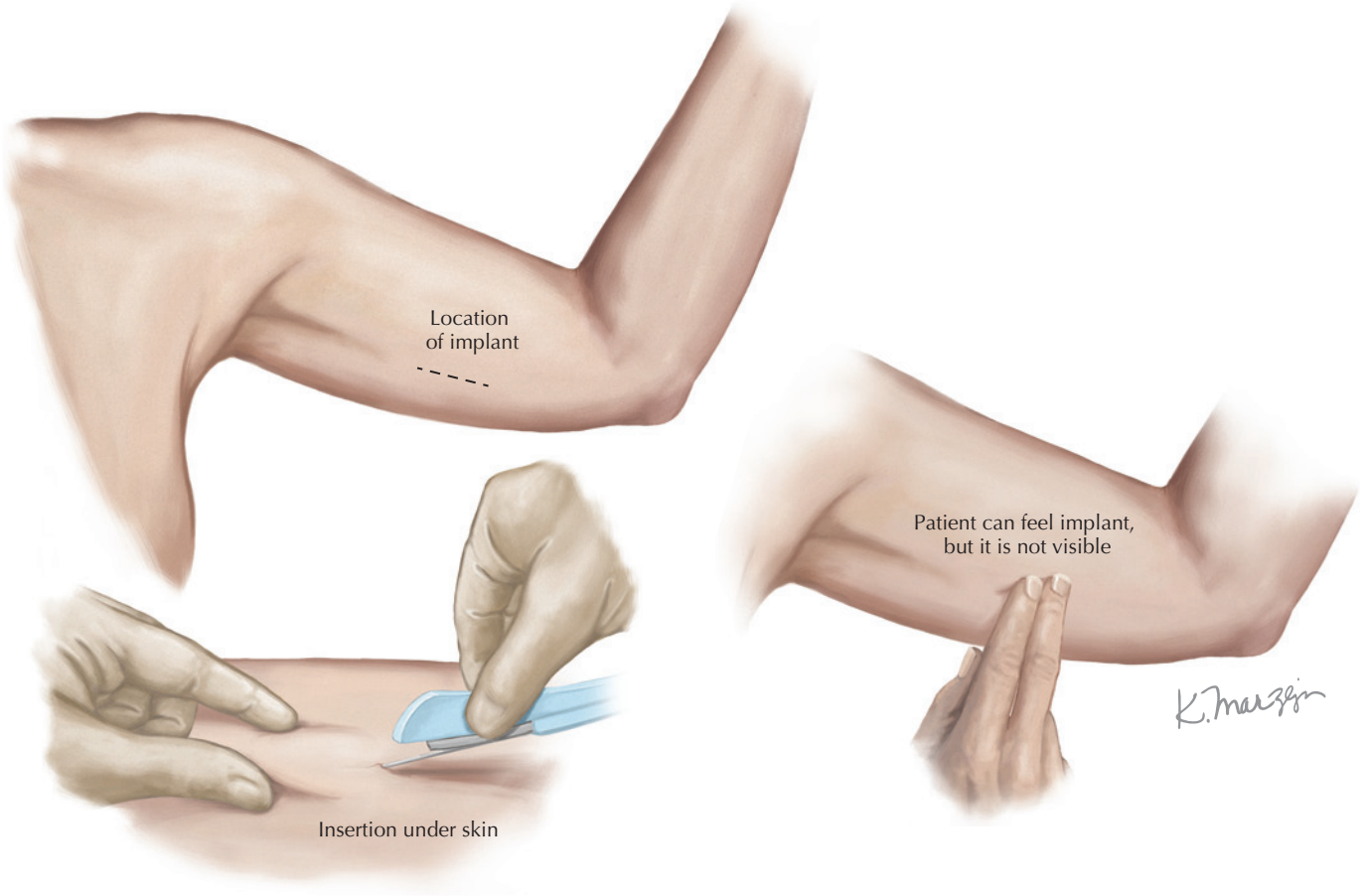


Figure 276.1 Subdermal contraceptive capsule insertion

pressure bandage may be placed for the first 24 hours, if desired. If the implant cannot be felt, check the applicator to make sure the implant is no longer in the insertion device (the applicator obturator is purple, while the implant is white). If there is uncertainty about the location of the implant, ultrasonography or X-ray may be used to determine its presence. The procedure should be documented in the chart to help guide the eventual removal process. Though post-placement discomfort is relatively minor, mild analgesics may be offered.

COMPLICATIONS

Local bruising, hematoma, infection, local irritation or rash, expulsion, neural or vascular injury (deep insertion), and allergic reaction.

FOLLOW-UP

Abstinence or back-up contraception is recommended for 7 days after insertion if the implant is placed more than 5 days after the start of the last menstrual period. No additional follow up is required until fertility is desired or 3 years have elapsed.

CPT CODE(S)

11981 Insertion, non-biodegradable drug delivery implant

REFERENCES

LEVEL II

Darney P, Patel A, Rosen K, et al. Safety and efficacy of a single-rod etonogestrel implant (Implanon): results from 11 international clinical trials. *Fertil Steril*. 2009;91:1646.

Levine JP, Sinofsky FE, Christ MF, et al. Assessment of Implanon insertion and removal. *Contraception*. 2008;78:409.

Wenzl R, van Beek A, Schnabel P, et al. Pharmacokinetics of etonogestrel released from the contraceptive implant Implanon. *Contraception*. 1998;58:283.

Winner B, Peipert JF, Zhao Q, et al. Effectiveness of long-acting reversible contraception. *N Engl J Med*. 2012;366:1998.

LEVEL III

Shulman LP, Gabriel H. Management and localization strategies for the nonpalpable Implanon rod. *Contraception*. 2006;73:325.

277 SUBDERMAL CONTRACEPTIVE CAPSULE REMOVAL

DESCRIPTION

Etonogestrel subdermal contraceptive implants provide reliable reversible contraception, but they must be removed after 3 years of use or if a return to fertility is desired.

INDICATIONS

Desired return of fertility or the completion of the useful life of the contraceptive implant.

CONTRAINDICATIONS

Local skin infection, known or suspected allergy to the agents used for the removal process.

REQUIRED EQUIPMENT

- Antiseptic solution and sterile cotton balls, or skin preparation swabs
- Sterile gloves
- Local anesthetic (eg, lidocaine, 1% without epinephrine, 2–5 mL), 3–5 mL syringe, 25-gauge needle
- Sterile 2″ × 2″ gauze
- Sterile drapes (helpful, but not required)
- Scalpel (#11 blade preferred)
- Sterile forceps (straight and curved mosquito)
- Sterile skin closure strips (1/4″)
- Adhesive bandage, pressure bandage (optional)
- Mild analgesics (nonsteroidal antiinflammatory drug or similar, if desired)

TECHNIQUE

Note that the following technique does not exactly match that recommended by the manufacturer (eg, making use of pressure bandage optional). Should a question arise, the manufacturer's procedure should be consulted.

Following informed consent, the patient should lie in the supine position with the implant-bearing arm elevated, flexed at the elbow, externally rotated and extended to approximately 90-degree angle from the body. The hand should rest comfortably at the level of the head. Some authors advocate having the arm extended, but mechanical support for the arm during the procedure may be difficult. The contraceptive implant should be palpated to identify any potential problems. If the rod is not palpable, the procedure must be postponed until the location can be determined by imaging studies.

The skin over the implant and surrounding area should be disinfected. The proximal (axillary) end of the contraceptive rod should be depressed or pushed distally to make the distal end apparent.

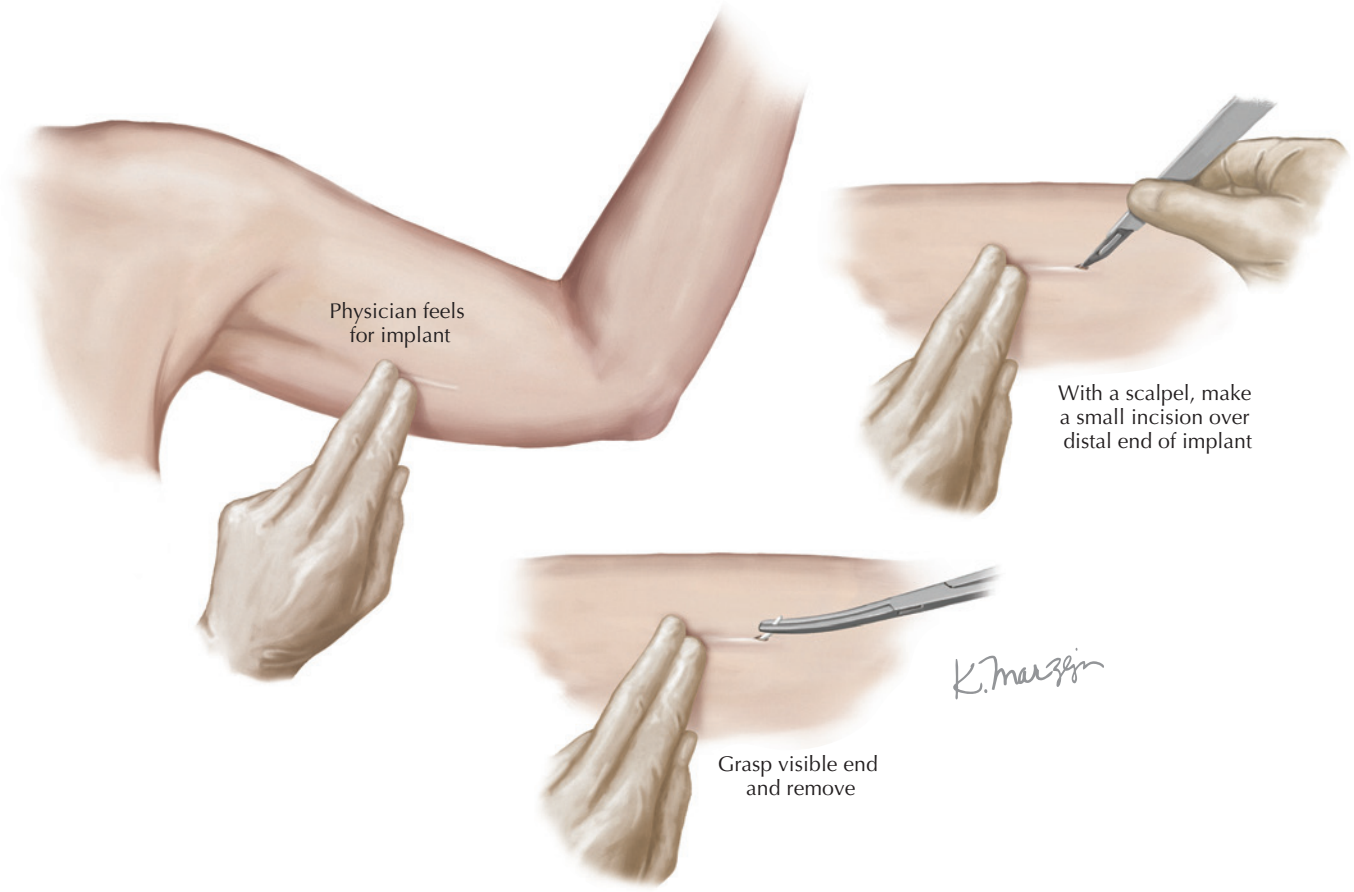


Figure 277.1 Subdermal contraceptive capsule removal

Local anesthesia should be established by injecting 0.5–1 mL of local anesthetic just below the distal end, elevating it slightly. Too much volume or injection above the rod will make removal difficult.

With the distal end of the implant again placed under outward and upward pressure, a 2–3-mm longitudinal skin incision is made over the end of the rod. The incision is deepened until a rubbery sensation against the point of the scalpel blade is felt (the rod encased in a fibrous sheath). While taking care not to cut the rod itself, this sheath should be scraped or incised, exposing the rod itself. The rod may then be expelled by further pressure on the proximal end, or it may be grasped at its end using a hemostat. If a hemostat is used, the rod should not be grasped significantly back from the tip because this can result in fracture of the rod, spill of contents, creation of fragments or incomplete removal. If the distal end is not readily delivered through the incision, the curved hemostat may be burrowed below the rod tip to facilitate delivery and scar tissue removal. Additional local anesthesia or extension of the incision is occasionally required. Complete removal of the 40-mm rod should be confirmed. If the patient wants to continue to use contraceptive implants, the new rod may be inserted through the same incision that was used for removal (with the addition of appropriate anesthesia) or the new implant can be placed in the other arm.

A sterile adhesive closure of the incision should be placed, and a sterile dressing or adhesive bandage should be applied. A pressure bandage may be placed for the first 24 hours, if desired. The procedure should be documented in the chart. Although postremoval discomfort is relatively minor, mild analgesics may be offered.

COMPLICATIONS

Local bruising, hematoma, infection, local irritation or rash, neural or vascular injury (removal of deep insertion), and allergic reaction.

FOLLOW-UP

Based on the alternate contraception plans, if any.

CPT CODE(S)

11976 Removal, implantable contraceptive capsules
11983 Removal with reinsertion, non-biodegradable drug delivery implant

REFERENCES

LEVEL II

Levine JP, Sinofsky FE, Christ MF. Implanon US Study Group. Assessment of Implanon insertion and removal. *Contraception*. 2008;78:409.

Wenzl R, van Beek A, Schnabel P, et al. Pharmacokinetics of etonogestrel released from the contraceptive implant Implanon. *Contraception*. 1998;58:283.

LEVEL III

Shulman LP, Gabriel H. Management and localization strategies for the nonpalpable Implanon rod. *Contraception*. 2006;73:325.

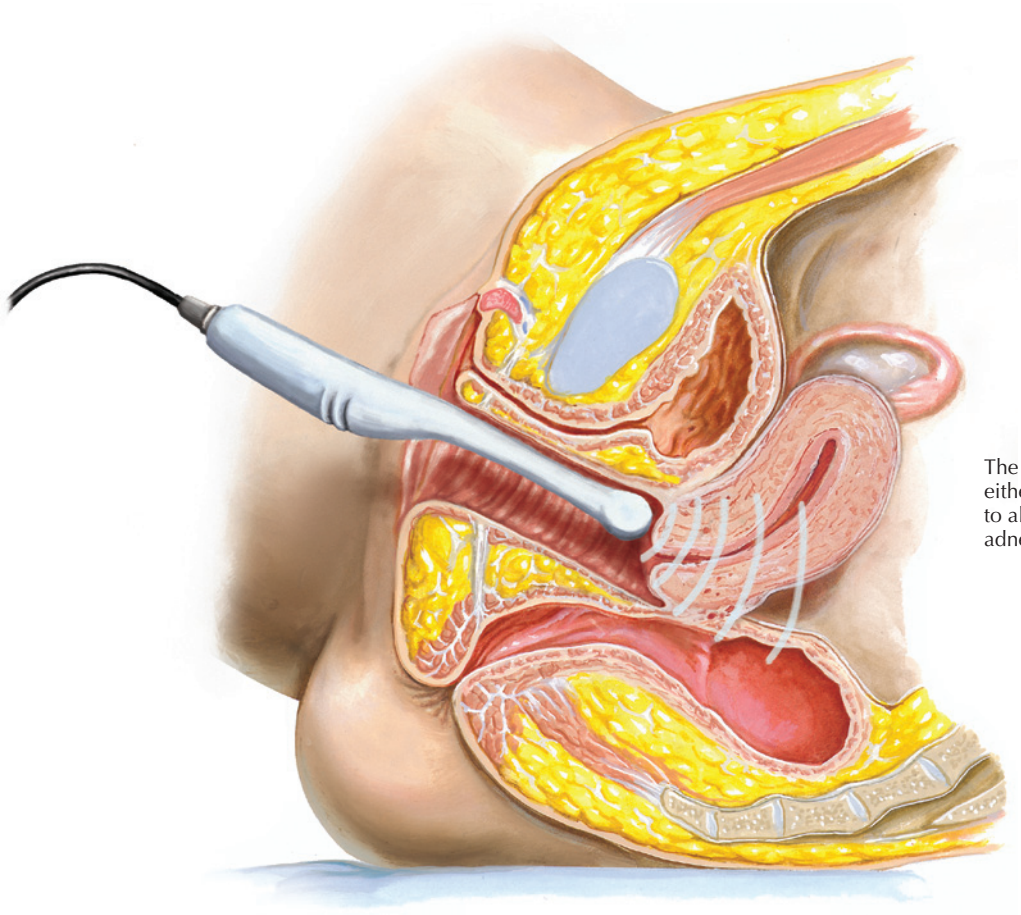


Figure 278.1 Transvaginal ultrasonography

The pelvic structures should be surveyed in a systematic manner by rocking the probe up and down, left and right so that all structures are fully seen. Rotating the probe 90 degrees to the right or left will change the plane of observation, further facilitating a full evaluation. Some ultrasonographic equipment is capable of forming three-dimensional renderings of the anatomy seen, but its superiority over other modalities remains to be demonstrated.

COMPLICATIONS

A small amount of discomfort (pelvic or vaginal fullness) may be experienced during the procedure, but this is considered normal.

FOLLOW-UP

Based on the indications.

CPT CODE(S)

76830 Ultrasound, transvaginal
76817 Ultrasound, pregnant uterus, real time with image documentation, transvaginal

REFERENCES

LEVEL III

American College of Obstetricians and Gynecologists. The role of transvaginal ultrasonography in the evaluation of postmenopausal bleeding. ACOG Committee Opinion No. 440. *Obstet Gynecol.* 2009; 114:409.

American College of Obstetricians and Gynecologists. Ultrasonography in pregnancy. ACOG Practice Bulletin No. 101. *Obstet Gynecol.* 2009; 113:451.

American College of Obstetricians and Gynecologists. The role of the obstetrician–gynecologist in the early detection of epithelial ovarian cancer. Committee Opinion No. 477. *Obstet Gynecol.* 2011;117:742.

American College of Obstetricians and Gynecologists. Diagnosis of abnormal uterine bleeding in reproductive-aged women. Practice Bulletin No. 128. *Obstet Gynecol.* 2012;120:197.

American College of Obstetricians and Gynecologists. Management of abnormal uterine bleeding associated with ovulatory dysfunction. Practice Bulletin No. 136. *Obstet Gynecol.* 2013;122:176.

American College of Obstetricians and Gynecologists. Endometrial intraepithelial neoplasia. Committee Opinion No. 631. *Obstet Gynecol.* 2015;125:1272.

TRIGGER POINT INJECTION

DESCRIPTION

Injection of steroids or local anesthetics into selected fascial and subcutaneous locations thought to give rise to pain and other symptoms. Response to trigger point injection routinely persists longer than the duration of action of the agent used. This frequently extends to permanent relief after only one or two anesthetic injections. Because of the rapid response to trigger point injections, they can be useful as a diagnostic tool.

INDICATIONS

A "trigger point" that induces or reproduces the patient's pain complaints. Musculoskeletal pain frequently radiates or is referred to areas distant from the source of the nociceptive signal. Trigger points are hypersensitive areas overlying muscles that induce muscular spasms and pain. They may be found throughout the body but are most common in the abdominal wall, back, and pelvic floor when pelvic pain is the complaint. Myofascial pain syndromes and fibromyalgia frequently demonstrate trigger point involvement.

CONTRAINDICATIONS

Known or suspected allergies to any of the agents used (latex, skin preparation materials, etc.), active skin infection, uncorrected blood dyscrasias.

REQUIRED EQUIPMENT

- Antiseptic solution and sterile cotton balls, or skin preparation swabs
- Local anesthetic (eg, lidocaine, 1% without epinephrine, 2–5 mL, 0.25% bupivacaine may also be used), 3–5 mL syringe, 25-gauge needle
- 22-gauge needle (1″–1.5″), an 18-gauge needle if a multi-dose vial is used
- 2.5–10 mL syringe for anesthetic infiltration
- Skin cleansing solution
- Alcohol wipes
- Sterile gloves (optional)
- Ice or ethyl chloride spray
- Skin marking pencil (optional)

Pelvic floor trigger points can be injected using a pudendal anesthesia kit

TECHNIQUE

The presence of a trigger point and the point of maximal tenderness must be established before any consideration of injection therapy. Most trigger points are located at or near areas of moving or sliding muscle surfaces, though they are not limited to these locations. Gentle palpation over the various muscle groups of the body is carried out using the flat of the hand or the fingertips. Trigger points

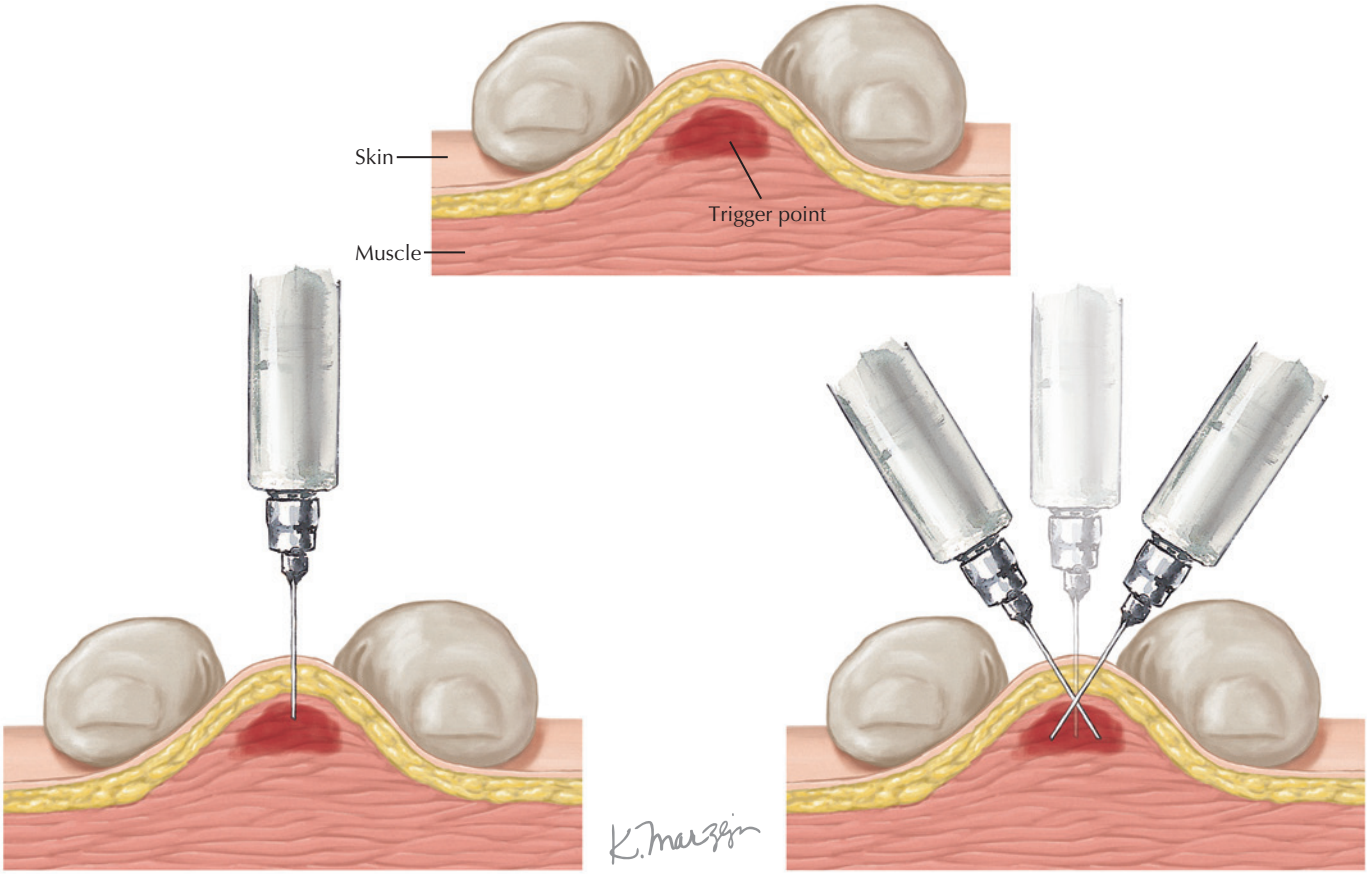


Figure 279.1 Trigger point injections

may occur in skin, ligaments, or periosteum in addition to muscles themselves; an area that is a trigger point will often be felt as an overly taut band of muscle. Compression of this site will elicit local tenderness and often reproduce the referred pain. Normal muscle should not be tender to firm compression and does not contain taut bands. The site of maximal tenderness should be noted, and this site may be marked with a skin marking pencil if desired. When evaluating possible trigger points in the lower abdominal wall, care must be taken to specify the origin of the tenderness elicited. This is especially true during bimanual pelvic examination. It should be apparent that tenderness is arising from the abdominal wall and not the uterus, adnexa, bladder, or bowel. To aid in this differentiation, ask the patient to lift her head and shoulders off the table or raise her heals with her legs straight. Pain arising from the abdominal wall will worsen with this maneuver whereas visceral pain may improve. The diagnosis of a trigger point is established solely on clinical grounds. There are no laboratory or imaging studies that will assist in the diagnosis.

A 22-gauge needle is selected for trigger point injection because of the amount of movement within tissue often required to probe for and block a taut muscle bundle. Thinner needles may bend or break under these circumstances. The length of the needle should be sufficient to allow the entire trigger point to be reached without indenting the skin or having the hub at the skin surface. The former will unduly distort landmarks and findings, and the latter avoids the possibility of a lost needle should the needle break or become separated from the hub during the injection maneuvers.

The patient should be made comfortable and warned that the process of injection may cause a very brief worsening of the referred pain. The skin over the point of maximal tenderness should be disinfected using a skin disinfecting agent or an alcohol wipe. Ice or a spray type topical anesthetic (eg, ethyl chloride) may be used to numb the skin prior to needle insertion, if desired. The skin should be held taut, and the needle inserted quickly at an acute angle to minimize discomfort. Skin tension should be maintained to minimize bleeding.

Once the needle has been inserted beneath the skin, the tip should be used as a probe to identify the taut band of muscle responsible for the patient's symptoms. Injection will be less successful if this band is not identified and specifically injected. With the needle at or in the taut muscle band, gentle aspiration should be performed to ensure against intravascular injection, and a small amount (1–3 mL) of anesthetic agent is then injected. The needle should then be moved from side to side of this original location, repeating the injection sequence. No more than 10 mL of any anesthetic agent should be used in one spot and no more than 30–40 mL used during any one session. Trigger points will often respond promptly to therapy, providing immediate feedback to confirm the diagnosis.

COMPLICATIONS

The most common complications of trigger point injection are local ecchymoses and anesthetic agent toxicity. The latter is best avoided by strictly limiting the total dose administered. Infection is rare if the skin is first disinfected and areas of frank infection avoided.

FOLLOW-UP

Based on the indications and findings.

CPT CODE(S)

11900 Injection, intralesional; up to and including seven lesions
11901 Injection, intralesional; more than seven lesions
20550 Injection(s); single tendon sheath, or ligament, aponeurosis (eg, plantar "fascia")

REFERENCES

LEVEL I

Boelens OB, Scheltinga MR, Houterman S, et al. Randomized clinical trial of trigger point infiltration with lidocaine to diagnose anterior cutaneous nerve entrapment syndrome. *Br J Surg*. 2013;100:217.

Gazi MC, Issy AM, Avila IP, et al. Comparison of acupuncture to injection for myofascial trigger point pain. *Pain Pract*. 2011;11:132.

LEVEL II

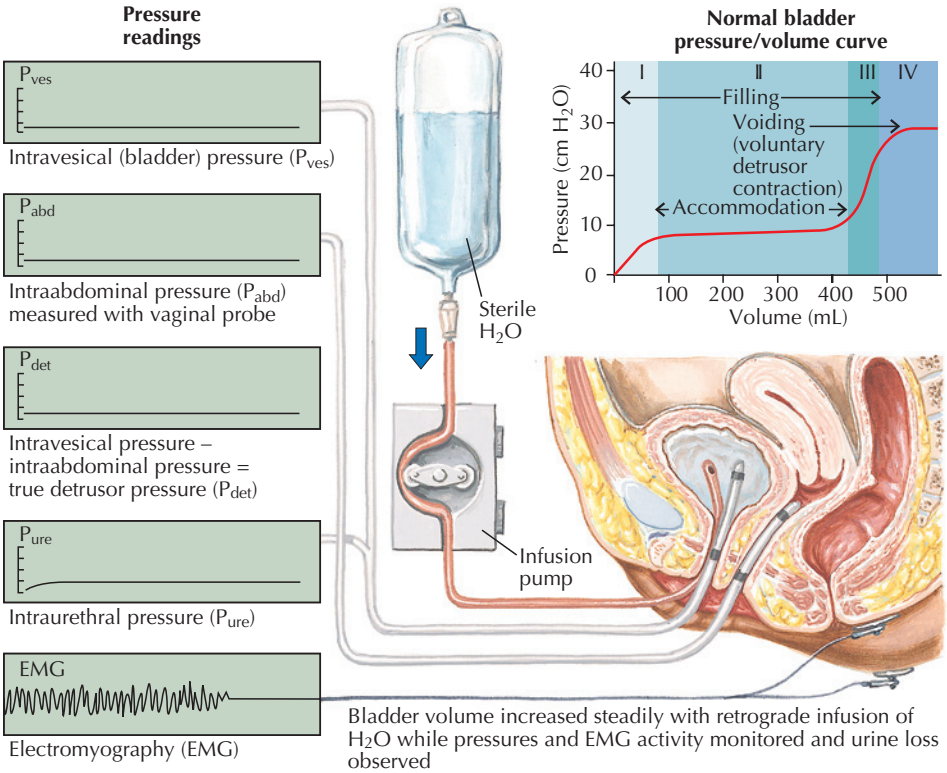
Langford CF, Udvari Nagy S, Ghoniem GM. Levator ani trigger point injections: An underutilized treatment for chronic pelvic pain. *Neurourol Urodyn*. 2007;26:59.

Montenegro ML, Braz CA, Rosa-e-Silva JC, et al. Anaesthetic injection versus ischemic compression for the pain relief of abdominal wall trigger points in women with chronic pelvic pain. *BMC Anesthesiol*. 2015;15:175.

LEVEL III

Borg-Stein J, Iaccarino MA. Myofascial pain syndrome treatments. *Phys Med Rehabil Clin N Am*. 2014;25:357.

White D, Staff T. HelpDesk Answers: Do trigger point injections effectively treat fibromyalgia? *J Fam Pract*. 2015;64:427.



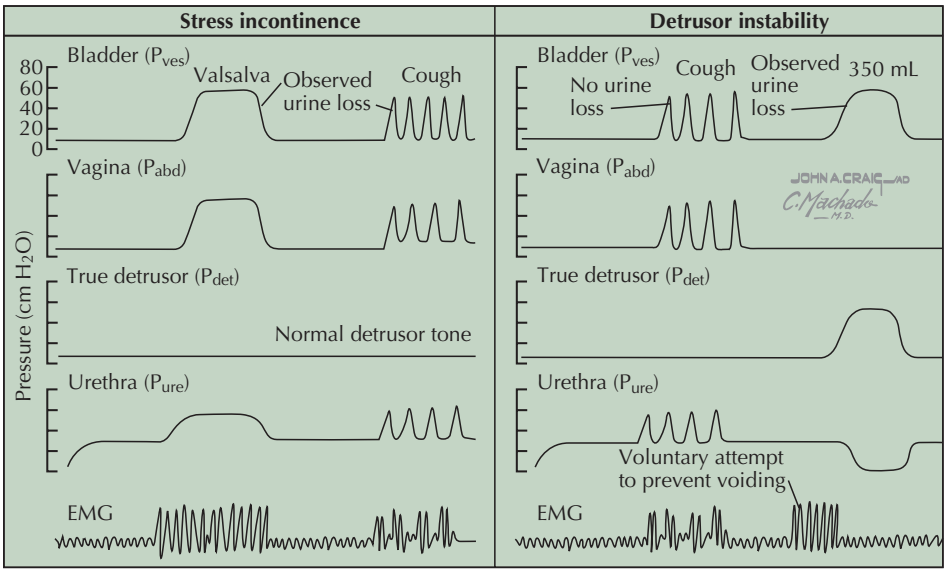


Figure 280.1 Urodynamics: complex

- One liter of sterile saline (intravenous fluid without glucose is generally used) at room temperature
- 2% lidocaine jelly in a mushroom-tipped syringe (optional)
- Intravenous or pump tubing (based on the specifics of the equipment used)
- Absorbent underpads
- Urodynamics testing unit (includes recording device, fluid pump, catheter puller, uroflowmetry commode)
- Printer for urodynamics reports
- An assistant is advantageous.

If Cystoscopy Is to Be a Part of the Procedure

- Cystoscope (rigid or flexible, direct viewing or with a 30-degree or greater down-angle view; the latter is better for visualizing the bladder trigone and ureteral openings)
- Fiberoptic light source (compatible with type of cystoscope used)
- Fiberoptic light cord

TECHNIQUE

Immediately before the procedure is initiated, the patient is asked to empty her bladder (in private and in her usual manner). The

patient is placed in the dorsal lithotomy position, and the external urinary meatus and surrounding vulvar vestibule are cleansed with an antiseptic solution. Then, 1–3 mL of topical anesthetic, such as 2% lidocaine, are introduced into the urethra.

With sterile technique, the patient is catheterized using a straight catheter, and any residual urine is collected, measured for volume, and sent for culture (if appropriate). The catheter is then removed.

A catheter-tip microtransducer or other pressure-recording catheter (specific to the equipment being used) is introduced into the bladder to record bladder and urethral pressure. A reference catheter is placed either in the vaginal or rectal canal to infer intraabdominal pressure. These catheters are secured by tape to the patient's thigh and attached to the urodynamic unit. The bladder is filled in a controlled manner (approximately 50 mL/min) using the pumping system supplied with the urodynamic equipment. The patient's first sensation of bladder fullness, the occurrence of a sense of urgency, and maximal bladder capacity are noted, and the patient is asked to cough several times. The resulting spikes in bladder and urethral pressures that occur are recorded, along with any urinary leakage. Leakage that occurs immediately after the cough, is prolonged, is associated with an increase in true bladder pressure, or is of large volume suggests detrusor instability.

If leak point pressures are to be measured, the volume of the bladder must be adjusted to 200 mL, and the pressure catheter must be no greater than 10 French in size. The true detrusor pressure is calculated by the subtraction of the reference pressure (from the vagina or rectum) from the pressures recorded from the urethra and bladder. The urodynamics equipment itself generally automatically performs this subtraction. The patient is asked to strain, and the pressure at which leakage occurs (if any) is noted.

Pressure measurements conclude with the reference pressure catheter being removed and urethral profilometry being performed. This is accomplished using the machine's catheter puller to remove the bladder catheter at a known rate while continuous pressures are recorded. Thus, pressure profiles are compiled by the urodynamic equipment; this may be repeated while the patient coughs to obtain a dynamic profile.

Cystoscopy is commonly performed as a part of complex urodynamic testing and is conducted at this point in the testing process.

Uroflowmetry is performed using the urodynamic equipment's commode, which is equipped to measure flow rate, volume, and time. These are automatically recorded and displayed in formats that are determined by the specific equipment.

Cystometrics are associated with a false-negative rate of approximately 50% and a false-positive rate of 15% in cases of urge incontinence.

COMPLICATIONS

Urinary tract infection, hematuria, dysuria, urinary retention.

FOLLOW-UP

Based on the indications and findings.

CPT CODE(S)

51726 Complex urodynamics
51772 Urethral profilometry
51741 Complex uroflowmetry

REFERENCES

LEVEL II

Glazener CM, Lapitan MC. Urodynamic investigations for management of urinary incontinence in adults. *Cochrane Database Syst Rev*. 2002;(3):CD003195.

Ward RM, Hampton BS, Blume JD, et al. The impact of multichannel urodynamics upon treatment recommendations for female urinary incontinence. *Int Urogynecol J Pelvic Floor Dysfunct*. 2008;19:1235.

LEVEL III

Abrams P, Blaivas JG, Stanton SL, et al. The standardization of terminology of lower urinary tract function produced by the International Continence Society Committee on Standardization of Terminology. *Scand J Urol Nephrol*. 1988;114:5.

American College of Obstetricians and Gynecologists. Evaluation of uncomplicated stress urinary incontinence in women before surgical treatment. Committee Opinion No. 603. *Obstet Gynecol*. 2014;123:1403.

American College of Obstetricians and Gynecologists. The role of cystourethroscopy in the generalist obstetrician–gynecologist practice. ACOG Committee Opinion 372. *Obstet Gynecol*. 2007;110:221.

American College of Obstetricians and Gynecologists. Urinary incontinence in women. Practice Bulletin No. 155. *Obstet Gynecol*. 2015;126:e66.

Decter RM, Harpster L. Pitfalls in determination of leak point pressure. *J Urol*. 1992;148:588.

Gilmour RF, Churchill BM, Steckler RE, et al. A new technique for dynamic analysis of bladder compliance. *J Urol*. 1993;150:1200.

Song JT, Rozanski TA, Belville WD. Stress leak point pressure: a simple and reproducible method utilizing a fiberoptic microtransducer. *Urology*. 1995;46:81.

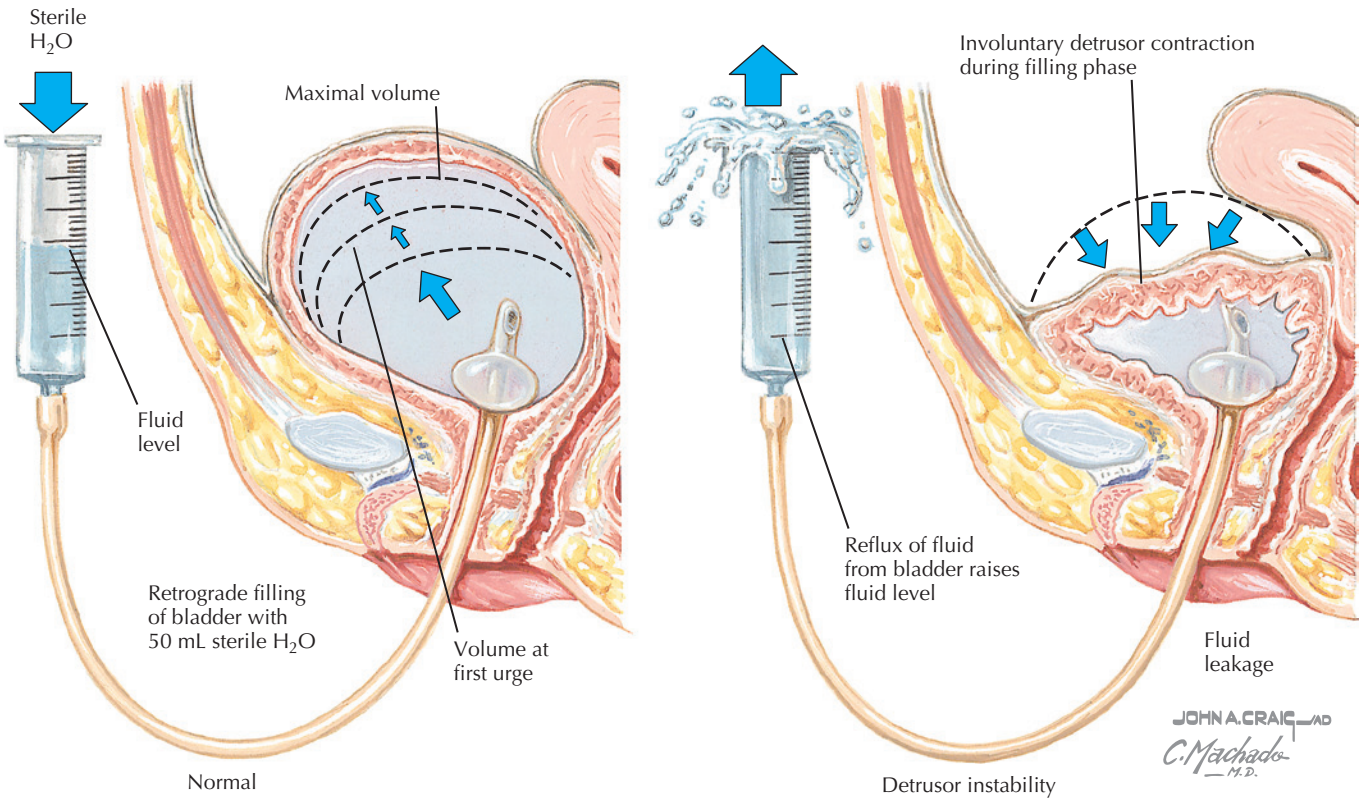


Figure 281.1 Urodynamics: simple

- Large catheter-tip syringe (without piston) or "Asepto" surgical irrigation syringe (without bulb)
- One liter of sterile water or saline (intravenous fluid without glucose is sufficient) at room temperature
- Intravenous tubing and measuring tape or ruler, or spinal manometer
- Commode or toilet
- Stopwatch or watch that allows counting of seconds
- Absorbent underpads
- 2% lidocaine jelly in a mushroom-tipped syringe (optional)
- An assistant is advantageous.

TECHNIQUE

Immediately before the procedure is started, the patient is asked to empty her bladder (in private and in her usual manner). The patient is placed in the dorsal lithotomy position, and the external urinary meatus and surrounding vulvar vestibule are cleansed with an antiseptic solution. Then, 1–3 mL of topical anesthetic, such as 2% lidocaine, are introduced into the urethra.

With a sterile technique, the patient is catheterized using a straight catheter, and any residual urine is collected, measured for volume, and sent for culture (if appropriate). The catheter tip or irrigation syringe is attached to the catheter to act as a funnel to fill the bladder with sterile water or saline. With the syringe held no more than 15 cm above the level of the symphysis and the catheter pinched off, fluid is poured into the syringe. The fluid is allowed to flow by gravity into the bladder at a rate that does not exceed 1–3 mL/s. This is often best accomplished in aliquots of 50 mL. The patient is asked to report her first sensation of bladder fullness, and the volume infused at that point is noted. Filling continues in 25-mL aliquots until the patient is unable to tolerate more, and this volume is recorded as the maximal bladder capacity. Any upward movement of the fluid column, intense sensation of urgency, or leakage around the catheter is abnormal, suggests detrusor instability, and should be noted.

For more exact measurements of bladder function, intravenous tubing, a spinal manometer (or limb of extra tubing), and a three-way connector may be connected to form a water-column manometer. In this configuration, filling proceeds as described with the exception that the pressure inside the fluid column may be directly monitored, and the presence of bladder contractions may be more easily detected. When this greater degree of accuracy is required, many prefer to proceed to formal urodynamic testing rather than commit to the additional preparation and time necessary to assemble this configuration.

Once the bladder has been filled and bladder compliance has been noted, the catheter is next removed and the patient is asked to cough several times. Urinary leakage at the time of cough should be noted. Leakage that occurs immediately after, is prolonged, or is of large volume suggests detrusor instability.

Filling the bladder with 200 mL of fluid and listening to the patient's voiding from outside a bathroom door or while the patient voids behind a screen can provide a simple assessment of voiding. The duration of flow may be timed with a stopwatch.

COMPLICATIONS

Urinary tract infection, dysuria, urinary retention.

FOLLOW-UP

Based on the indications and findings.

CPT CODE(S)

51725 Simple cystometrogram
51736 Simple uroflowmetry

REFERENCES

LEVEL II

Glazener CM, Lapitan MC. Urodynamic investigations for management of urinary incontinence in adults. *Cochrane Database Syst Rev*. 2002;(3): CD003195.

Sutherst JR, Brown MC. Comparison of single and multichannel cystometry in diagnosing bladder instability. *Br Med J (Clin Res Ed)*. 1984; 288:1720.

Thorp JM, Jones LH, Wells E, et al. Assessment of pelvic floor function: a series of simple tests in nulliparous women. *Int Urogynecol J Pelvic Floor Dysfunct*. 1996;7:94.

LEVEL III

Abrams P, Blaivas JG, Stanton SL, et al. The standardization of terminology of lower urinary tract function produced by the International Continence Society Committee on Standardization of Terminology. *Scand J Urol Nephrol*. 1988;114:5.

American College of Obstetricians and Gynecologists. Evaluation of uncomplicated stress urinary incontinence in women before surgical treatment. Committee Opinion No. 603. *Obstet Gynecol*. 2014;123:1403.

American College of Obstetricians and Gynecologists. Urinary incontinence in women. Practice Bulletin No. 155. *Obstet Gynecol*. 2015;126:e66.

Ouslander JG, Leach GE, Staskin DR. Simplified tests of lower urinary tract function in the evaluation of geriatric urinary incontinence. *J Am Geriatr Soc*. 1989;37:706.

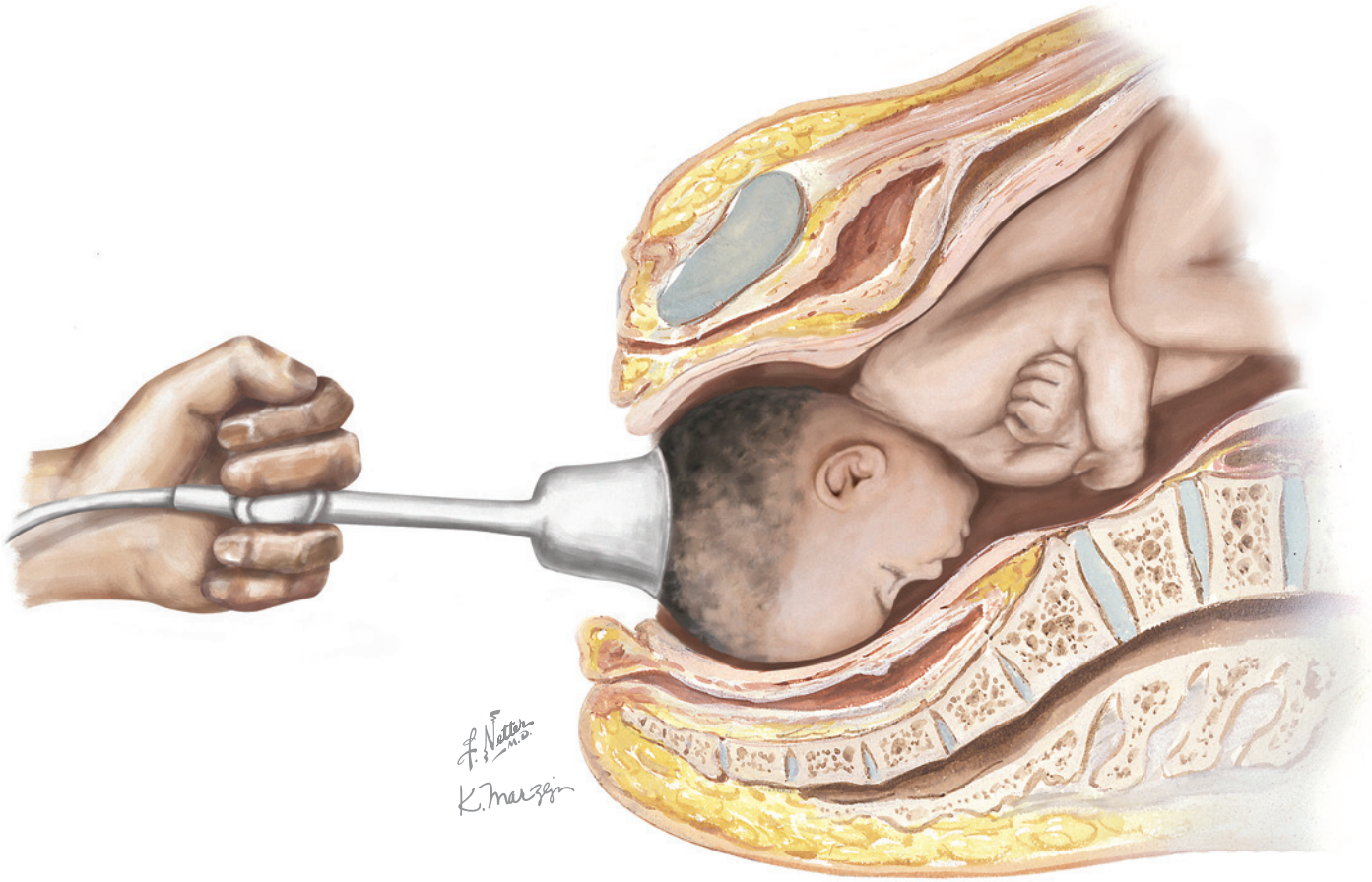


Figure 282.1 Vacuum-assisted delivery

traction in the horizontal plane continues until the descending fetal head distends the vulva. An episiotomy, if required, may be performed at this point.

As the fetal head further distends the vulva, the axis of traction is gradually rotated upward, following the normal extension process of the head as it rotates under the symphysis. Once the brow is palpable through the perineum, the suction may be released and the vacuum cup removed, allowing the fetal head to be delivered by pressure on the perineum (modified Ritgen maneuver). More often the cup may be left in place until the fetal chin has cleared the perineum. The remainder of the delivery proceeds as with a spontaneous delivery.

COMPLICATIONS

It is difficult (if not impossible) to separate the effects of vacuum-aided vaginal delivery from those of spontaneous vaginal delivery. Randomized trials and meta-analysis studies have failed to show conclusive differences. Both forceps delivery and vacuum extraction have been associated with the development of maternal hematomas and possibly linked to pelvic floor injury. However, other factors associated with pelvic floor injury include normal spontaneous vaginal delivery, episiotomy, prolonged second stage of labor, and increased fetal size. Similarly, studies have failed to identify neonatal or fetal injuries or developmental abnormalities that can be directly linked to vacuum-assisted delivery. Fetal scalp lacerations, cephalohematoma (14%–16%), subgaleal (subaponeurotic) hematoma (26–45/1000), intracranial hemorrhage, hyperbilirubinemia, and retinal hemorrhage are all possible. The higher rates of neonatal jaundice associated with vacuum delivery may be related to the higher rate of cephalohematoma. Overall, the incidence of serious complications with vacuum extraction is approximately 5%.

CPT CODE(S)

59400 Routine obstetric care including antepartum care, vaginal delivery (with or without episiotomy, and/or forceps), and postpartum care

59610 Routine obstetric care including antepartum care, vaginal delivery (with or without episiotomy, and/or forceps), and postpartum care, after previous cesarean delivery

59409 Vaginal delivery only (with or without episiotomy and/or forceps)

59410 Vaginal delivery only (with or without episiotomy and/or forceps), including postpartum care

59612 Vaginal delivery only, after previous cesarean delivery (with or without episiotomy and/or forceps)

59614 Vaginal delivery only, after previous cesarean delivery (with or without episiotomy and/or forceps), including postpartum care

REFERENCES

LEVEL II

Aiken CE, Aiken AR, Brockelsby JC, et al. Factors influencing the likelihood of instrumental delivery success. *Obstet Gynecol*. 2014;123:796.

de Vogel J, van der Leeuw-van Beek A, Gietelink D, et al. The effect of a mediolateral episiotomy during operative vaginal delivery on the risk of developing obstetrical anal sphincter injuries. *Am J Obstet Gynecol*. 2012;206:404.e1.

Ducarme G, Hamel JF, Bouet PE, et al. Maternal and neonatal morbidity after attempted operative vaginal delivery according to fetal head station. *Obstet Gynecol*. 2015;126:521.

Johanson R, Menon V. Soft versus rigid vacuum extractor cups for assisted vaginal delivery. *Cochrane Database Syst Rev*. 2000;CD000446.

Liabsuetrakul T, Choobun T, Peeyananjarassri K, et al. Antibiotic prophylaxis for operative vaginal delivery. *Cochrane Database Syst Rev*. 2014;(10):CD004455.

Lim FT, Holm JP, Schuitemaker NW, et al. Stepwise compared with rapid application of vacuum in ventouse extraction procedures. *Br J Obstet Gynaecol*. 1997;104:33.

O'Mahony F, Hofmeyr GJ, Menon V. Choice of instruments for assisted vaginal delivery. *Cochrane Database Syst Rev*. 2010;(11):CD005455.

Palatnik A, Grobman WA, Hellendag MG, et al. Predictors of failed operative vaginal delivery in a contemporary obstetric cohort. *Obstet Gynecol*. 2016;127:501.

Towner D, Castro MA, Eby-Wilkens E, et al. Effect of mode of delivery in nulliparous women on neonatal intracranial injury. *N Engl J Med*. 1999;341:1709.

Walsh CA, Robson M, McAuliffe FM. Mode of delivery at term and adverse neonatal outcomes. *Obstet Gynecol*. 2013;121:122.

LEVEL III

American College of Obstetricians and Gynecologists. Limitations of perineal lacerations as an obstetric quality measure. Committee Opinion No. 647. *Obstet Gynecol*. 2015;126:e108.

American College of Obstetricians and Gynecologists. Operative vaginal delivery. Practice Bulletin No. 154. *Obstet Gynecol*. 2015;126:e56.

INDEX

Note: Pages followed by *b*, *t*, or *f* refer to boxes, tables, or figures, respectively.

B

C

D

H

I

J

K

L

M

N

Q

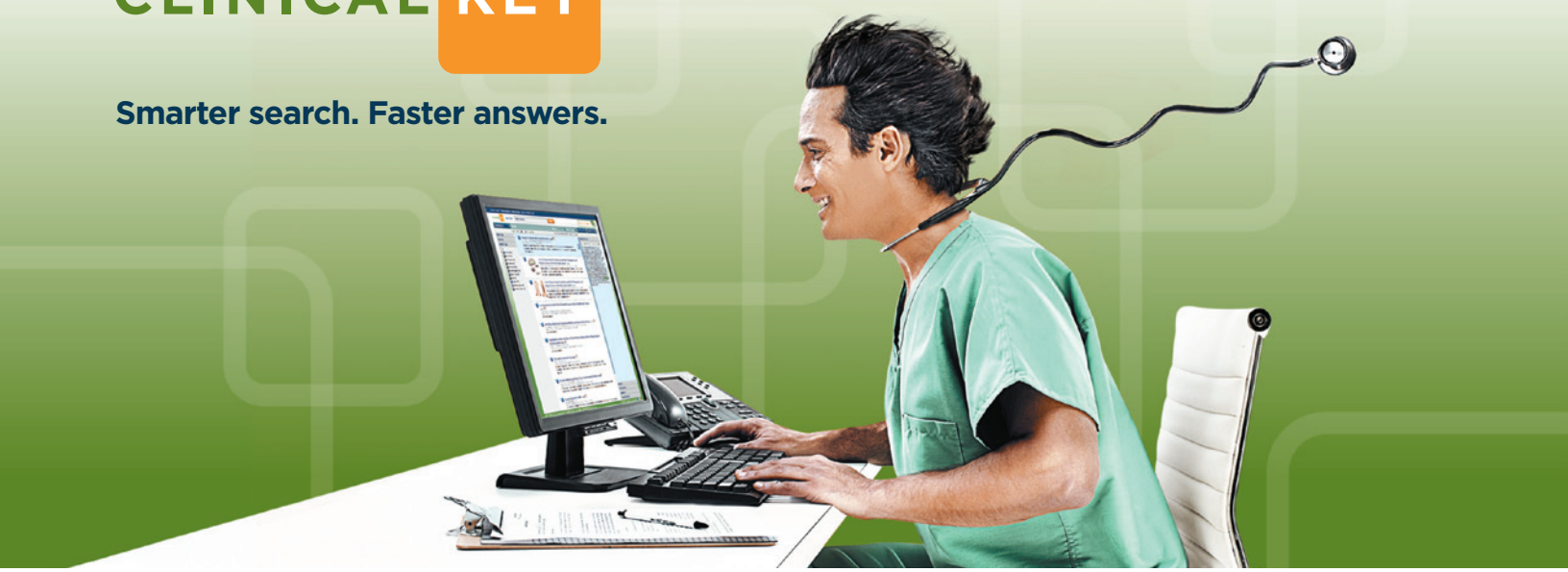
R

T

This page intentionally left blank

CLINICAL KEY™

Smarter search. Faster answers.



Smarter, Faster Search for Better Patient Care

Unlike a conventional search engine, ClinicalKey is specifically designed to serve doctors by providing three core components:

1 Comprehensive Content

The most current, evidence-based answers available for every medical and surgical specialty.

2 Trusted Answers

Content supplied by Elsevier, the world's leading provider of health and science information.

3 Unrivaled Speed to Answer

Faster, more relevant clinical answers, so you can spend less time searching and more time caring for patients.

Start searching with ClinicalKey today!

Visit ***ClinicalKey.com*** for more information and subscription options.

ELSEVIER