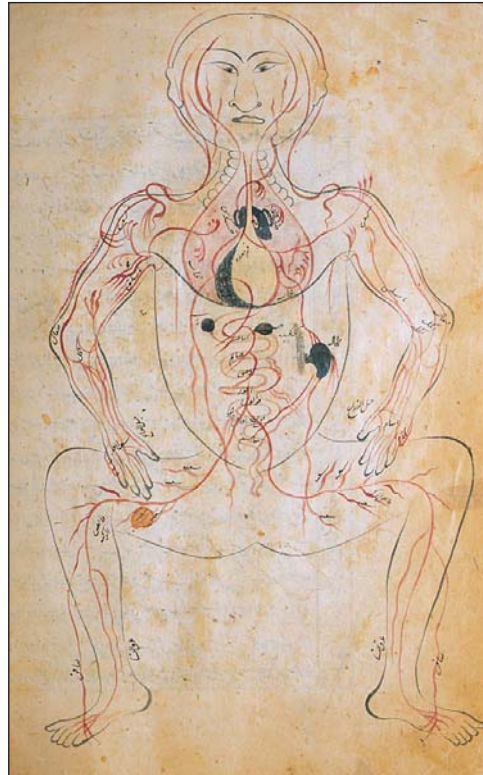


Good clinical diagnostic practice

A guide for clinicians in developing countries to
the clinical diagnosis of disease and to making
proper use of clinical diagnostic services



WHO Regional Publications, Eastern Mediterranean Series 27

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proper use of clinical diagnostic services

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Cairo 2005

WHO Library Cataloguing in Publication Data

Carter, Jane.

Good clinical diagnostic practice: a guide for clinicians in developing countries to the clinical diagnosis of disease and to making proper use of clinical diagnostic services / by Jane Carter..... [et al.] .

p. (WHO Regional Publications, Eastern Mediterranean Series; 27)

ISBN : 978-92-9021-393-2

1. Clinical Laboratory Techniques 2. Clinical laboratory procedures I. Müller-Stöver, Irmela. II. Östensen, Harald III. Heuck, Claus Chr. IV. Title V. WHO Regional Office for the Eastern Mediterranean VI. Series

(NLM Classification: QY 25)

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Cover design by John Shimwell
Printed in Cairo, Egypt, by Fikra Advertising Agency

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Foreword

The range of diseases that affect and afflict humans continues to hinder development in many parts of the world—from communicable diseases to noncommunicable diseases, genetic diseases to lifestyle-related and behavioural diseases, those induced by hardship and by poverty to those induced by affluence, and those that result from natural and man-made disasters. Clinical diagnostic services provide physicians with a wide range of tools to help in their decision-making regarding appropriate treatment of all types of disease for their patients. At the same time, health technology is becoming more and more sophisticated throughout the world, including many parts of the developing world. However, diagnostic investigation of disease, whether by laboratory services or imaging services, becomes more expensive every year.

Meanwhile, equipment companies often market their products in developing countries in a manner which encourages primary health care physicians to diagnose relatively simple ailments with unnecessarily sophisticated tests. The primary health care system is overburdened in many developing countries, and in the absence of a family doctor system, patients have to resort to specialized physicians. The expense is overwhelming, both to individuals and to Ministries of Health, and in many cases is completely unnecessary. The traditional model of diagnosis by a primary health care physician to a regional hospital or other medical centres, with a small number of references to specialized centres, has been reversed.

This publication addresses these problems. It provides guidelines on the most common and necessary diagnostic tools in clinical practice,

especially for countries with minimal resources, and guides physicians on how to select the most appropriate services and laboratory investigations, at least cost. Great emphasis has been placed on improving diagnostic performance, on restoring good referral systems, and above all on promoting communication between clinicians and technicians in order to achieve good clinical diagnostic practice. I have no doubt this will be an invaluable tool for physicians in developing countries.



Hussein A. Gezairy MD FRCS
Regional Director for the Eastern Mediterranean

Preface

In many countries, there is a lack of communication between the clinical services and the laboratory and diagnostic imaging services. As a result, clinicians do not take appropriate advantage of, and consequently the patients do not benefit from, the information that could be provided by the diagnostic services if they were properly used. The reasons may be various.

- Clinicians play a pivotal role in patient education and in cooperation with all diagnostic services. However, clinicians may regard quality management of diagnostic services as a matter that is separate from their own area of responsibility. Therefore they are not aware of the need for, and may fail to add, sufficient information on a patient, which makes it difficult for a diagnostic service to provide clinically relevant results. Clinicians may feel that they do not have the time for such activities, and they may not see that clinical outcomes are in fact tied to the diagnostic processes being followed.
- Clinicians are rarely used to team-work and may feel uncomfortable working as a member of a team of health workers with different professional training or fewer credentials.
- The diagnostic service may not recognize the clinical importance of its observations in the management of a patient; and vice versa, the clinician may not be sufficiently aware of the relevance of a diagnostic observation to the clinical situation of a patient.

Studies in developed countries have revealed between 20% and 60% of orders for laboratory investigations are clinically unjustified. For example, more than 95% of orders for serum sodium measurements ordered in one

hospital setting were not medically relevant. In another example, clinicians were unable to draw conclusions from the results of serum protein electrophoresis in more than 95% of reports provided by the laboratory [1]. Consequently, the service provided by the laboratory is wasted, placing an unacceptable burden on the laboratory that is of no benefit to the health service. This observation applies equally to the diagnostic imaging services that receive unnecessary orders for investigations on patients who are not well prepared by the clinician.

These observations underline the need for intensive communication between the diagnostic services and the clinical staff. The better the collaboration between the clinician and the diagnostic services, the more patient care will benefit from improved quality health services.

During the past few years, the WHO Regional Office for the Eastern Mediterranean Office has published a series of books on the technical aspects of the appropriate management of laboratory and blood transfusion services, including quality control and quality assurance, local reagent production, and specimen collection in microbiology. The present work discusses important areas that are not under the direct control of laboratory or imaging services that influence the outcome of a diagnostic examination. These are things that should be known to all users of diagnostic services. The manual has been written for medical officers working in outpatient curative clinics in health centres and primary level hospitals. The aim of the manual is to improve clinical and diagnostic skills. The manual assumes that physicians have been trained in history-taking, physical examination and use of laboratory investigations; that they are provided with essential items of clinical diagnostic equipment; and that they have access to essential laboratory tests. Clinicians working in hospitals may also have access to basic diagnostic imaging facilities.

The authors would like to thank J. Richter, University Hospital, Düsseldorf, Germany, D. Mathay, Christian Medical College, Vellore, Tamil Nadu, India, and Norman D. Olson, Stanford University School of Medicine, Stanford, California, for their valuable comments on the manuscript.

The authors are grateful for the valuable support received from Dr Hussein A. Gezairy, WHO Regional Director for the Eastern Mediterranean, and Dr M.H. Khayat for their continuous support and encouragement.

Abbreviations

| | |
|--------------|--|
| AFI | amniotic fluid index |
| AFP | alpha-fetoprotein |
| ALT | alanine–leucine transaminase |
| AP | anterior–posterior |
| AST | alanine–serine transaminase |
| CK | creatine kinase |
| CRP | C-reactive protein |
| CSF | cerebrospinal fluid |
| DD | differential diagnosis |
| EBV | Epstein–Barr virus |
| ECG | electrocardiogram |
| ECS | endocervical swab |
| EDTA | ethylenediaminetetraacetic acid |
| ESR | erythrocyte sedimentation rate |
| G6PD | glucose-6-phosphate dehydrogenase |
| γ -GT | gamma-glutamyl transferase |
| GNID | Gram-negative intracellular diplococci |
| HAV | hepatitis A virus |
| HBsAg | hepatitis B surface antigen |
| HBsAb | hepatitis B surface antigen antibody |
| HBV | hepatitis B virus |
| HCT | haematocrit |
| HCV | hepatitis C virus |
| HbE | haemoglobin E |
| HDL | high density lipoprotein |
| HIV | human immunodeficiency virus |
| HSV | herpes simplex virus |
| LDH | lactate dehydrogenase |
| MCH | mean corpuscular haemoglobin |
| MCHC | mean corpuscular haemoglobin concentration |
| MCV | mean corpuscular volume of red blood cells |
| MSU | midstream urine |
| PSA | prostate specific antigen |

| | |
|-----|--|
| RBC | red blood cell count |
| RDW | red blood cell distribution width |
| SLE | systemic lupus erythematosus |
| U/L | units per litre |
| WBC | white blood cell count (leukocyte count) |

Glossary

Anaemia

The condition of having less than the normal total volume of red blood cells. The oxygen-carrying capacity of the blood is therefore decreased.

Bias (of a measuring instrument)

Systematic error of the indication of a measuring instrument.

Note: the bias of an instrument is normally estimated by averaging the error of indication over an appropriate number of repeated measurements.

Body-mass index (BMI)

Index relating body weight to height. The BMI is a person's weight in kilograms (kg) divided by height in metres (m) squared.

Overweight is a BMI of 25 or more for women and 29.9 or more for men.

Obesity is a BMI of 30 and above.

Some very muscular people may have a high BMI without undue health risks.

Coefficient of analytical variation (CV)

Standard deviation divided by the average of a sample of values of a variable measurable quantity

Note 1: the coefficient of variation is independent of the unit of measurement used since the unit is the same for standard deviation and average.

Note 2: when using the abbreviated form *coefficient of variation* it should be made clear whether a sample of values or a population of random variable values is being referred to.

Coefficient of intra-individual variation (CV_i)

Standard deviation divided by the average of values of a variable measurable quantity measured in an individual over a given period of time.

Precision of measurement

The closeness of agreement between independent test results obtained under stipulated conditions.

Note 1: precision depends only on the distribution of random errors and does not relate to the true value or the specified value.

Note 2: the measure of precision is usually expressed in terms of imprecision and computed as a standard deviation of the test results. Less precision is reflected by a larger standard deviation.

Note 3: *independent test results* means results obtained in a manner not influenced by any previous result on the same or similar test object. Quantitative measures of precision depend critically on the stipulated conditions. Repeatability and reproducibility are specific sets of extreme stipulated conditions.

Probe

See *Transducer*.

Reference interval (reference range)

The range of test values expected for a designated population of individuals; for example, 95% of individuals that are presumed to be healthy (or normal).

Red blood cell distribution width (RDW)

A measurement of the variability of red blood cell size. Higher numbers indicate greater variation in size. The normal range for the red cell distribution width (RDW) is 11%–15%. The RDW is a standard part of the complete red blood cell count of automated cell counters that also includes the concentration of red blood cells (RBC), the mean corpuscular volume (MCV), the mean haemoglobin of a red blood cell (MCH), and mean haemoglobin concentration of a red blood cell (MCHC).

Sensitivity, analytical

The change in response of a measuring instrument divided by the corresponding change in the stimulus.

Note 1: the sensitivity may depend on the value of the stimulus.

Note 2: the term *analytical sensitivity* should not be used as a synonym for *limit of detection*.

Specificity, analytical

The ability of a measurement procedure to determine solely the measurable quantity of the analyte it purports to measure.

Note: the analytical specificity is usually expressed in terms of unspecificity—that is, the effect of any component of the sample other than the analyte causing an indication of the measuring instrument and thereby introducing a systematic error of measurement.

Transducer

A device that converts one form of energy into another. For example, in ultrasonography, the transducer is the device which an examiner positions on, for example, a patient's abdomen. The transducer has a dual function: to produce ultrasound and send it into the patient; and to detect echoes by the reverse process.

Chapter 1

Introduction

Patients seek medical help for determination and treatment of various health problems. Sometimes a combination of the patient's history and a clinical examination by a primary level physician are enough to decide whether medical treatment is needed, and what treatment should be given. However, often laboratory investigations or diagnostic imaging procedures are required to confirm a clinically suspected diagnosis or to obtain more accurate information. For example, malaria may be suspected by the presence of fever and by excluding other causes of fever on history and physical examination, but a firm diagnosis is made on microscopic examination of a blood slide. In a second example, in a patient with acute abdominal pain, various underlying causes may be clinically suspected, but in most cases no firm diagnosis can be made without either ultrasound or X-ray examination. Otherwise, a potentially dangerous (and unnecessary, given the availability of the alternatives) abdominal operation would be the only way to establish a diagnosis.

1.1 Clinical assessment

History and physical examination should be carried out by medically qualified personnel using appropriate diagnostic instruments such as stethoscope, otoscope and sphygmomanometer. A list of essential clinical diagnostic equipment is given in Annex 1.

The clinician should identify the patient, understand the major complaint and ask questions in order to explore the underlying cause of the complaint and make a clinical diagnosis. A major concern is to obtain the correct history of the patient and to clearly understand the complaints and their duration. Information about the duration of symptoms is often unreliable. If pain or other symptoms have persisted for days, months or years it may be difficult to obtain an accurate history.

The physical examination should include a general examination and examination of the affected body system. The physical examination should take the privacy of the patient into consideration.

In some cases, diagnosis of a disease is evident from the history and observations made during the physical examination, for example in patients with hypertension or certain skin diseases. In other cases, the clinician will make a tentative diagnosis or a selection of differential diagnoses for which more detailed investigations by laboratory and/or diagnostic imaging services are needed for clarification. The clinical symptoms together with the medical history and physical examination of the patient guide the clinician to request a diagnostic investigation for confirmation or exclusion of a disease.

1.2 Diagnostic investigation

There are three phases in the process of diagnostic investigation:

- the pre-analytical phase
- the analytical phase
- the post-analytical phase.

The pre-analytical phase comprises the time and all processes for the preparation of a patient for a diagnostic investigation to the moment when the investigation is made. The analytical phase comprises the time and all processes of a diagnostic investigation. The post-analytical phase comprises the time and all processes for reporting the results of the diagnostic investigation to the person who then undertakes the medical management of the patient.

Errors made during each phase influence the clinical relevance of a diagnostic report, and precautions must be taken to avoid results that are misleading or provide false information. The analytical phase is under the

control of the diagnostic service, which has the responsibility for accurately performing the investigations. In contrast, during the pre-analytical and post-analytical phases, other personnel, including the medical doctor and paramedical personnel who are not working with the diagnostic service, are involved in the process; and errors made in these two phases influence the results such that they may no longer be clinically relevant.

Surveys in the clinical health services of developed countries revealed that 93% of errors identified are made during the pre-analytical and post-analytical phases, whereas only 7% of errors originate during the analytical phase, provided the diagnostic service has established an effective system for internal quality control. It was also observed that in an ambulatory general medical examination less than 5% of the most common laboratory tests contributed to a new diagnosis and 0.7% to 16% to a new therapy [2].

The diagnostic service must familiarize the clinician with the value of the information obtained from an investigation, including its diagnostic specificity. This requires constant communication between clinical staff and the diagnostic service.

Diagnostic reports are valuable only when the information can be used for patient management. It is therefore an obligation for the diagnostic service to provide the results to the clinician in a timely manner so that the results can be interpreted together with the clinical findings for the patient. If the findings do not fit with the patient's clinical picture, the clinician should discuss the problem with the laboratory and/or diagnostic imaging staff to find a reasonable explanation. Sometimes it may be useful for an experienced clinician to visit the diagnostic service to confirm the diagnosis of the disease himself. It has been proven that the communication between clinicians and diagnostic services of a hospital is most effective if daily consultations are held to discuss patients' clinical problems and observations made.

Chapter 2

Diagnostic imaging

2.1 Ultrasound examinations (ultrasonography)

Ultrasonography has a significant impact on diagnostic work. Today, ultrasonography is the most frequently used imaging modality in certain medical disciplines (gastroenterology, urology, obstetrics), although the implementation of ultrasonography in district hospitals is not yet standard in developing countries for the following reasons.

- Equipment is still expensive. Rarely can a district hospital purchase an ultrasound machine from its own budget. Currently, ultrasound equipment used in district hospitals in developing countries is usually the result of donations.
- The operation of ultrasound machines requires a constant power supply. Battery-operated equipment is available but expensive.
- A local after-sales service is often not available for repair if breakdown occurs.
- The clinical application of ultrasound investigation requires extensive education and continuing training, which is generally not provided at local training institutions.

Only very few countries have implemented regulations for the use of ultrasound examination, and examinations are often performed by insufficiently trained personnel. This may be of more harm than benefit to the patient because of the potential incorrect diagnoses made. Ultrasound

investigation should be a systematic examination using standardized sections and detailed delineation of all organs and performed only by sufficiently trained staff. The probe should not only be moved across the area where a pathological feature is expected, but a systematic examination of all organs and structures is obligatory. The person doing the ultrasound examinations must have sound medical knowledge as well as sufficient training in sonography; these are essential for correct and safe examinations. The interpretation of certain findings may be difficult for various reasons, such as obesity, uncooperative patients, a high amount of gas in the intestine, an empty bladder (catheter), in an investigation of emergency cases, or due to an inappropriate probe being used for the requested examination (this frequently occurs in infants).

Ultrasonography is an excellent initial examination procedure for many abdominal, gynaecological and obstetric disorders. During sonographic examination, high frequency sound waves transmitted into the body are partly or totally reflected (following the physical laws of reflection) to the surface (i.e. the receiver) when passing from one type of tissue to another. The distance from the surface to an organ in the body correlates with the time interval between the emission of the sound wave and the reception of the reflected portion. This time interval and the intensity of the reflected wave are registered by the computer and is used for “constructing” an ultrasonographic image.

Ultrasonography distinguishes well between various types of soft tissue. It is therefore predominantly used for abdominal examinations, including obstetric examinations. As the sound waves used in clinical settings do not sufficiently penetrate bony structures or air/gas, ultrasonography is not suitable for pulmonary examinations or for examinations of the skeleton and the brain, which is surrounded by bones. For the brain, however, there is one exception in newborns and infants where the fontanelles are still open. These openings can be used for ultrasound examination of the brain.

Annex 3 comprises two recipes for making contact gel for use in ultrasonography.

2.2 Conventional X-ray examinations

The principles behind X-ray imaging techniques are the same as for those for ordinary photography. The light (*visible*, *low-energy* for photography; *invisible* and *high-energy* for X-ray examinations) induces changes on a photographic film or in an electric detector. X-rays have more energy than visible light and can penetrate material that is opaque to visible light. The amount of X-rays penetrating a given material—in our case the human body—depends upon the material's physicochemical properties. More specifically, it depends upon the size of atoms in the material. In general, light atoms—those with low atomic weights—allow more of the X-rays to pass through than heavier atoms, i.e. with higher atomic weights.

In a broad sense the human body consists of three types of material: *soft tissue*, containing mainly light atoms, *bone* containing heavy atoms (minerals), and *air* (or some sort of gas) built up of very light atoms. A film exposed to X-rays that have penetrated a human body will show white or very bright areas (little exposure to X-rays), grey areas (more exposure), or nearly black areas (heavy exposure) depending upon the amounts of X-rays that penetrate various parts of the body. For example, bones appear very bright or white on film, because they absorb a large amount of X-rays, whereas gas-filled areas appear nearly black, because they let a large amount of X-rays pass through.

As soft tissues, including muscles, blood vessels, liver and kidneys, have nearly the same chemical composition (mainly hydrogen, oxygen, nitrogen and carbon), it is rarely possible to distinguish between these tissues on an X-ray film without using more complicated procedures of investigation (contrast agent for conventional X-rays or computed tomography). In such cases the method of choice for diagnostic imaging will often be sonography, which distinguishes better between various types of soft tissue.

2.3 Computed tomography

Computed tomography images are generated using the same principles as conventional X-ray images. In computed tomography, X-rays are

generated and allowed to penetrate the body and are picked up by detectors as electrical signals instead of creating an image on a photographic film via a chemical process. The signals are analysed by computer, which generates a picture showing an anatomical cross-section of the part of the body under investigation. The sensitivity of computed tomography is much higher than that of conventional X-ray systems. Different types of soft tissue may be more easily distinguished. The computed tomography images are built up digitally; therefore it is possible to manipulate the images on display (contrast, brightness, etc.) or to transmit the pictures electronically to other monitors within a hospital or to remote destinations (teleradiology).

2.4 Magnetic resonance imaging

Magnetic resonance imaging, or MRI, represents a new technique for diagnostic imaging in which the physical principle differs from X-ray, computed tomography and sonography. MRI is regarded as safe for the patient and in certain cases gives more diagnostic information than other examinations. However, the high costs and special training that is required for MRI makes this technology inappropriate for most small and mid-size hospitals.

2.5 Radiation protection of patients

There is no scientific evidence that diagnostic procedures that are not based on ionizing radiation (sonography and magnetic resonance imaging) are harmful to pregnant women and fetuses. However, too much exposure to ionizing radiation can be harmful and so any use of ionizing radiation for diagnostic purposes must be medically justified; the radiation dose applied should be according to the ALARA principle—*as low as reasonably achievable*. When accepting these rules, radiological examinations may even be considered in pregnant women without fearing harm to the patient or fetus, provided that the absorbed radiation dose to the embryo/fetus is well below the internationally agreed limit of 100 mGy.

For the purpose of this document it is assumed that hospitals will have one or two basic stationary X-ray machines, perhaps a mobile X-ray unit,

and a general purpose ultrasound machine. It is also assumed that no radiologist is available—or at least not necessarily on a permanent basis.

It should be emphasized that any diagnostic efforts are only justified when appropriate therapeutic measures can be taken. Where means for treatment are limited, diagnostic efforts should be limited accordingly. In such a situation the patient should be transferred to another hospital where treatment can be provided. The general recommendations are valid only for the “average patient”. For the individual patient techniques and procedures need to be tailored according to specific clinical problems and findings.

Chapter 3

Laboratory services and laboratory investigations

A proper request for laboratory investigations necessitates a knowledge of the pathology of a disease as well as the technical aspects of laboratory analysis. Clinicians should know beforehand the value of the information that they can expect from a laboratory with respect to the clinical situation of the patient. Surprisingly, even in a large general hospital with an intensive care unit, it was found that 82% of all laboratory results were within normal range [1]. There is no doubt that the number of normal results could be considerably reduced if the indication for orders were identified by the physician with more appropriate care. Experience has shown that a laboratory must also be proactive in collaborating with clinical staff to solve these problems, for the following reasons.

- The laboratory communicates with all departments of the health services. Therefore it is in a better position to address and develop solutions that are of common concern.
- There is a difference in the way problems are solved from the clinical and laboratory perspectives. The laboratory examines and analyses specimens and provides information that makes reference to scientific concepts that have been developed on the basis of statistically verified data. In contrast, the physician is concerned with the health problems of an individual. Clinical diagnosis is based on experience with individuals rather than statistical analysis, and the doctor focuses on medical history as well as physical and psychological observations of the patient.

- Very often a laboratory is insufficiently informed about the clinical situation and previous treatment of a patient. The laboratory is frequently confined to producing laboratory results without knowing all the pre-analytical elements that may have influenced the outcome of a measurement. In contrast, a physician takes laboratory results for granted and does not realize that their correct interpretation requires the knowledge of a variety of technical and biological factors. This is also true for the established reference intervals for laboratory indicators. The physician must be familiar with the reference values and reference intervals that are used by a laboratory when reviewing laboratory reports.

This section briefly outlines aspects of the pre-analytical and post-analytical phases of laboratory investigations that should be known by the physician and paramedical personnel. The reader is referred to the WHO Regional Office for the Eastern Mediterranean publication *Basics of quality assurance in laboratories at peripheral and intermediate level* to learn about other aspects that are part of the analytical phase [3].

3.1 Biological aspects

The concentrations of biological indicators in healthy persons vary within a given time period to a smaller or greater extent. The inter-individual variation of the indicators is expressed by the inter-individual coefficient of variation (CV_g). A laboratory method for quantitative measurement must be able to take into account intra-individual fluctuations; therefore the precision of measurement using a given method should have a CV which is less than the CV_g . Otherwise the method will not allow a comparison of results with sufficient confidence. As a widely accepted recommendation, methods should be used that have a $CV < 0.25CV_g$ [4]. Only methods that fulfil these criteria should be used to establish normal reference intervals from healthy populations. Visual comparative techniques for haemoglobin measurement using a simple filter paper method (haemoglobin colour scales) should not be used by medical laboratories, because the precision of this method is low and does not meet the analytical requirements of a laboratory test [3]. The

results obtained from such a test are very often misleading the physician to make a false diagnosis.

Physiological and/or behavioural conditions of the patient may influence laboratory measurements. They include:

- genetic and ethnic disposition
- age
- nutrition
- geographical factors
- biorhythmic fluctuations
- sex
- pregnancy
- physical exercise
- use of drugs and traditional medicines.

3.1.1 Genetic and ethnic disposition

Many genetic factors contribute to the variety of human physiognomy. Certain genetic factors, such as the human ABO blood groups, do not cause disease, but are important in health care. Other genetic factors may cause a disease in childhood (for example, phenylketonuria, thalassaemia, sickle-cell disease, glucose-6-phosphate dehydrogenase deficiency) or adulthood (for example, certain forms of muscular dystrophy, rheumatic disease). Other genetic factors may predispose to the clinical manifestation of a disease after a change in lifestyle. Thus, in a number of developing countries today there are more cases of diabetes mellitus or hyperlipoproteinaemia; in the past these diseases were less apparent as the population had a different lifestyle.

The prevalence of genetic diseases may vary from one population to another. Thalassaemias are predominant in the populations of the Eastern Mediterranean and South-East Asian regions of WHO, whereas haemoglobin E (HbE) disease is more prevalent in the populations of the Western Pacific Region; the highest prevalence of sickle-cell disease is among the African population. Phenylketonuria is more prevalent in the Caucasian population.

Reference intervals for laboratory indicators are used to distinguish between a normal and a pathological state of health. Textbooks state reference intervals derived from one population, but these may not necessarily be transferable to other populations. It is only a preliminary

solution to use normal reference intervals that were not established from the local population; the laboratory in collaboration with the physician should try hard to establish reference intervals for healthy individuals taken from the indigenous population.

There is surprisingly little information about ethnic disposition and reference intervals. The reference intervals for a number of laboratory indicators, including serum electrolytes, are the same in different ethnic groups. Interestingly, this seems also to be true for blood haemoglobin concentration. In ethnic groups with a high prevalence of thalassaemia (such as the indigenous people of Oman), the reference intervals for blood haemoglobin are the same as in other populations, although the normal reference intervals of other haematological indicators, including the MCV and WBC, are lower in these populations than in Caucasian populations [Nam D. Sultan Qaboos University Hospital, Al Khod, Oman. Private communication, 1999]. It is important to identify the ethnic disposition when establishing reference intervals for a healthy indigenous population. This requires close collaboration between the physician and the laboratory. Table 3.1 lists the means or lower limits of reference intervals a few indicators for which ethnic differences have been observed [WHO unpublished observation, 2001].

Table 3.1 Means or lower limits of reference intervals of indicators in different ethnic groups

| Indicator | Caucasian | Arab | African | Asian |
|----------------------------------|------------------|-------------|----------------|--------------|
| Creatine kinase (U/L) | 100 | | 180 | 115 |
| Pancreas α -amylase (U/L) | 90 | | 150 | |
| WBC* ($\times 1000$)/ μ L | 4.4 | 2.2** | 3.4 | 3.0*** |
| MCV* (fL) | 80 | 60** | 77 | 69 |

*lower limit of reference interval.

**Omani population.

***Indonesian population.

3.1.2 Age

Often, older text books mention reference intervals that were established in adults. However, more extensive epidemiological studies have revealed that the reference intervals remain constant during the whole period of life in only a few laboratory indicators, including some but not all serum electrolytes. The largest changes of reference intervals occur between the newborn and adolescent periods. For example, serum alkaline phosphatase activity that may be abnormally high in an adult may still be considered normal in an adolescent. Table 3.2 gives examples of age-dependent changes in selected laboratory indicators.

Table 3.2 **Age-related changes of laboratory indicators**

| Indicator | Change |
|----------------------|---------------------------------|
| Alkaline phosphatase | increased during adolescence |
| Bilirubin | considerably increased at birth |
| Cholesterol | increases with age |
| WBC | considerably increased at birth |

3.1.3 Nutrition

Nutrition affects many laboratory indicators in blood, plasma and serum as well as urine. Typically, serum triglyceride and glucose concentrations increase after the ingestion of a fatty and/or carbohydrate-rich meal. Creatinine concentrations are elevated in subjects who eat a lot of meat. As a rule, laboratory measurements of metabolic indicators are made in blood specimens from subjects who are in a baseline metabolic state. The physician should take measures to ensure that the patient meets optimal conditions for taking blood, which is usually after 12 hours fasting. Table 3.3 lists the changes of common laboratory indicators following the ingestion of a meal.

Table 3.3 **Nutritional effects on laboratory indicators**

| Indicator | Change |
|-----------------------------------|---------------|
| Alanine aminotransferase (ALAT) | increase 20% |
| Aspartate aminotransferase (ASAT) | increase 10% |
| Serum bilirubin | increase 15% |
| Serum glucose | increase 15% |
| Serum potassium | increase 10% |
| Serum phosphate | increase 15% |
| Serum triglycerides | increase 50% |

For certain investigations it is necessary to take blood several times during a day, for example, to establish a glucose profile. The laboratory should advise the clinician on the exact timing for taking blood; otherwise the results of the measurements cannot be properly evaluated and are not comparable.

3.1.4 Geographical factors

Red blood cell counts, haematocrit and haemoglobin levels are elevated in residents who live at higher altitudes (at 1400 metres and above). The elevated laboratory indicators are not caused by ethnic disposition but result from the lower oxygen concentration in the air at high altitude. The laboratory should take this effect into consideration when establishing reference intervals for populations who live at higher altitudes. Table 3.4 lists changes in some indicators that are due to altitude.

Table 3.4 Effect of altitude on mean concentrations of laboratory indicators

| Indicator | Change |
|------------------|---------------------|
| CRP | up to 65% at 3600 m |
| Haemoglobin | up to 8% at 1400 m |
| Haematocrit | up to 8% at 1400 m |
| Serum uric acid | up to 8% at 1400 m |

3.1.5 Biorhythmic fluctuations

Biorhythmic fluctuations occur in many laboratory indicators. These fluctuations may be daily, monthly or annually. The WBC is about 15% higher in the evening than in the morning; in contrast, blood haemoglobin is about 10% lower at night than during the day. Corticosteroids and thyroid hormone concentrations also fluctuate in a daily rhythm. Serum phosphate and iron concentrations are about 30% and 60% higher during the day than during the night. Urine sodium is highest during the early morning hours, whereas urine phosphate is highest during the evening. These observations make it evident that the time for collection of the specimen for analysis should be indicated on the request form.

In women the concentrations of sex hormones fluctuate in a monthly rhythm and are related to the menstrual cycle. Monthly changes also occur in serum iron, serum phosphate and serum protein concentrations in females. It is more difficult to demonstrate long-term rhythms in the concentrations of laboratory indicators, because they may be hidden behind nutritional effects and/or the effects of ageing.

Biorhythmic changes must also be considered in the diagnosis of certain parasitic infections, including malaria and microfilaria, and bacterial infections. Depending on the biorhythm in the proliferation of the parasite, the clinician must decide on the optimal timing for taking blood to collect material that has the highest content of parasites.

3.1.6 Sex

The reference intervals of certain laboratory indicators are gender dependent, including blood cells, serum enzymes, serum electrolytes, serum metabolites and hormones. Table 3.5 lists selected laboratory indicators with sex-dependent reference intervals.

Table 3.5 **Sex-related changes in certain laboratory indicators**

| Indicator | Male/female ratio of concentration |
|--------------------------------|------------------------------------|
| Bilirubin | increased |
| Serum creatinine | increased |
| Creatine kinase | increased |
| γ -glutamyl transferase | increased |
| Erythrocyte count | increased |
| Haematocrit | increased |
| Blood haemoglobin | increased |
| Serum transaminases | increased |
| Serum triglycerides | increased |
| Serum urea | increased |
| Serum uric acid | increased |
| HDL-cholesterol | decreased |

3.1.7 Pregnancy

In pregnancy the reference intervals of laboratory indicators in blood or serum, including clotting factors, serum enzyme activity, hormone levels, serum metabolites, blood cell concentrations and serum proteins, do not apply. Table 3.6 indicates typical changes in laboratory indicators commonly observed during pregnancy.

Table 3.6 **Changes in mean concentrations of laboratory indicators during pregnancy**

| Indicator | Change |
|--------------------------------|-----------|
| Serum alkaline phosphatase | increased |
| Erythrocyte sedimentation rate | increased |
| CRP | increased |
| Serum albumin | decreased |
| Serum proteins | decreased |
| Serum iron | decreased |

Tests for urine human chorionadotropin (hCG) are used for the diagnosis of early pregnancy. Some test kits show a positive result after only two weeks of fertilization; other tests are positive after four weeks or later. The laboratory and the clinician must be aware of these differences when different tests kits are used.

3.1.8 Physical exercise

Heavy physical exercise decreases the blood volume. Consequently, laboratory indicators confined to the blood compartment, including blood cells, serum enzyme activities and clotting factors, are increased. Certain hormones may be considerably decreased after prolonged physical exercise. Table 3.7 lists laboratory indicators that change during prolonged physical exercise (for example, long distance running).

Increased red blood cell count and haemoglobinuria are often seen after prolonged physical exercise; these findings could give rise to a misleading diagnosis.

Table 3.7 Effect of physical exercise on laboratory indicators

| Indicator | Increase |
|----------------------------|-----------------|
| Creatine kinase | 400% |
| Pyruvate kinase | 250% |
| Aspartate aminotransferase | 50% |
| Serum bilirubin | 50% |
| Serum urea | 30% |
| Urine RBC | elevated |

3.1.9 Drugs

Certain drugs and medicinal plants alter the concentrations of laboratory indicators in a patient. Drug effects are observed in the clotting system, serum enzyme activities and serum metabolites. The effects indicate the expected outcome (for example, vitamin K antagonists prolong the clotting time) or may be regarded as side-effects of drug treatment (for example, prolonged clotting time during treatment with cephalosporines). Often, the accidental observation of an abnormal laboratory result can be attributed to a drug that has been used for treatment of a patient. Table 3.8 lists certain drugs that are commonly used and their side effects.

Table 3.8 Drug effects on concentrations of laboratory indicators

| Indicator | Change |
|----------------------|--|
| Acetylsalicylic acid | reduced platelet aggregation |
| Alcohol | increased AST, γ -glutamyl transferase (chronic effect) |
| Anti-vitamin K | prolonged clotting time |
| Barbiturates | aminotransferases increased |
| Cephalosporines | prothrombin time prolonged; platelet aggregation inhibited |
| Heroin | increased cholesterol, serum potassium |
| Morphine | increased amylase, lipase, ALT |

3.2 Choice of laboratory indicators and test systems

In the diseased state, a number of laboratory indicators may be altered. For example, for the diagnosis of anaemia, measurements of several laboratory indicators (haemoglobin, haematocrit or red blood cell count) can be made.

For each individual laboratory indicator a range of tests may be available. However, the analytical property (specificity, sensitivity, precision, bias) may differ from one test system to another. The different characteristics makes it necessary to define the acceptability of a test by taking into account the specific needs of the health service to which a laboratory result is being provided. For example, the copper sulfate method may be acceptable for the distinction of anaemic from non-anaemic subjects for blood donation. However, in a clinical setting, where haemoglobin must be quantitatively measured for accurate diagnosis and monitoring of treatment of patients, this method is inappropriate, and more accurate methods must be used by the laboratory.

The laboratory should discuss the suitability of a laboratory test given the needs of the medical staff ordering the test. In addition to the performance of the test, the clinician and the laboratory must consider the costs of performing the test.

Sometimes a laboratory indicator can indicate an abnormality, but is not specific to make a diagnosis of a disease. A typical example of an indicator with no diagnostic specificity is the erythrocyte sedimentation rate (ESR). In fact, the majority of quantitative tests in clinical chemistry provide non-specific information, such as serum transaminase activity, which is elevated in a number of diseases. Often, only the combined use and interpretation of a selection of laboratory test results will provide conclusive information. Therefore, in practice a clinician uses a cluster of tests to make a clinical diagnosis of a disease.

Some tests are used as surrogate tests for the exclusion of certain diseases. For example, ALT activity in serum is measured to exclude high risk donors for transmitting an infectious disease. ALT activity is not a specific indicator of infectious disease. However, subjects suffering from liver damage usually have an elevated plasma ALT. Very often the damage is

caused by microbial infection. Tests with a low specificity are widely used for monitoring the development of a disease, because they are more cost-effective. The coagulation tests, prothrombin time and activated partial thromboplastin time belong to that group. These tests indicate an alteration of the coagulation system, but do not provide information on the individual clotting factor that has caused the alteration.

Certain tests are used for screening. Screening tests usually have a low clinical diagnostic specificity, whereas their diagnostic sensitivity should be high. For example, the mean corpuscular volume (MCV) of red blood cells unspecifically indicates an abnormality in a patient. It is low in thalassaemia, but also in iron deficiency and other diseases. Further investigations are needed to specify the underlying cause of the disease. In thalassaemia the size distribution of red blood cells, which is commonly expressed in the red blood cell distribution width, RDW, is narrow. In contrast, in iron-deficiency anaemia the MCV is low whereas the RDW is increased. However, the clinician should be aware that a patient may suffer both from thalassaemia and iron deficiency. Consequently, the MCV will be low and the RDW will be high in blood of such a patient.

Results of tests with high specificity are useful for the laboratory diagnosis of a disease. Microscopic investigations, as used in the diagnosis of parasitic infections, have a low diagnostic sensitivity but a high specificity, and positive observation by microscopy usually allows for a clinical diagnosis. A few quantitative tests are specific enough to confirm the diagnosis of a disease. For example, low or absent concentrations of clotting factors VIII or IX in a patient who is not on drug treatment provide conclusive information for the diagnosis of haemophilia A and B, respectively.

Some tests are useful to assess the acute clinical state of a patient, whereas they do not provide information on the long-term state in chronic disease. Typically, serum glucose levels indicate the actual situation of glucose metabolism in a patient. However, the metabolism of glucose is rapid, and elevated glucose concentrations in a patient do not reflect the diabetic state of the patient over a long period. For this, glycated haemoglobin A1c (HbA1c) is a better monitoring indicator. Similarly, specific IgM concentrations in serum are elevated during the acute phase of

infection by a viral agent, whereas elevated IgG concentrations are elevated in the post-acute state and chronic state of an infection.

3.3 Technical pre-analytical and post-analytical aspects

There are several steps during the pre-analytical phase that are not under the control of the laboratory services. The clinician and paramedical staff should be aware of errors that can be made during the handling of patient material for investigation [3]. These steps include:

- the preparation of the patient for the collection of specimens
- the collection of specimens for laboratory analysis
- the transport and storage of specimens prior to analysis.

Medical and paramedical staff can avoid errors during specimen collection if they are familiar with the sampling procedures, including the preparation of the patient and the use of appropriate instruments and devices for sampling.

Certain techniques for collection of specimens should only be applied by the clinician, such as collection of cerebrospinal fluid, pleural fluid, peritoneal fluid and arterial blood. Other techniques, including sputum and throat swab collection, urine and stool sampling, and collection of specimens from skin and wounds, can be performed by paramedical staff.

3.3.1 Blood

In some countries only medical personnel are allowed to collect blood; in other countries paramedical personnel are allowed to collect venous and capillary blood. Special attention must be taken in order to avoid haemolysis during sampling of blood or cerebrospinal fluid, since haemolysis has pronounced effects on the measurement of a number of laboratory indicators. The laboratory should inform the medical staff that haemolysed specimens must be rejected for certain measurements, because the results will not allow a conclusion on the clinical situation of the patient. Similarly, hyperlipidaemia and turbidity interferes with a number of measurements. Table 3.9 lists indicators for which the measurements are affected by haemolysis and hyperlipidaemia.

Table 3.9 Effect of haemolysis and hyperlipidaemia on the measurement of laboratory indicators

| Indicator | Effect |
|--------------------------------|------------------------------|
| Lactate dehydrogenase (LDH) | increased by haemolysis |
| Aspartate aminotransferase | increased by haemolysis |
| Alanine aminotransferase | increased by haemolysis |
| Creatine kinase | increased by haemolysis |
| Serum potassium | increased by haemolysis |
| Alkaline phosphatase | decreased by haemolysis |
| γ -glutamyl transferase | decreased by haemolysis |
| Serum uric acid | increased by hyperlipidaemia |
| Serum glucose | increased by hyperlipidaemia |

3.3.2 Cerebrospinal fluid

Special precautions must be taken for the collection and transportation of cerebrospinal fluid for haematological, immunological, clinical–chemical and bacteriological investigations.

A diagnosis of acute intracerebral bleeding can be made only from the observation of sanguineous cerebrospinal fluid. Therefore care must be taken to avoid accidental puncture of a vein during cerebrospinal fluid collection.

The cerebrospinal fluid must be transported to the laboratory as quickly as possible for microscopic, bacteriological and biochemical analysis. The laboratory should be informed in advance that cerebrospinal fluid samples are to be collected. White blood cells disappear within a short time and cannot be properly investigated after delayed transfer of the material to the laboratory. Similarly, glucose in cerebrospinal fluid is rapidly metabolized by enzymes of destroyed cells. Therefore, a glycolysis inhibitor should be added. Whenever possible, the cerebrospinal fluid specimens should be transported in a tube placed in a beaker with lukewarm water (30–37 °C).

3.3.3 Stool

Stool samples must be rapidly transferred to the laboratory for the examination of red blood cells and white (pus) cells, bacteria of characteristic shape and motility, and motile trophozoites. Stool for cysts, ova or helminth larvae must be examined within 24 hours. Hookworm larvae may hatch in stool that has been standing for some hours; larvae of *Strongyloides stercoralis* are only seen in fresh stool. Specimens for ova of *Enterobius vermicularis* are taken from the anal skin using a moistened swab or sticky tape.

3.3.4 Collection, storage and transport of specimens

The timing of sampling is important for laboratory investigations of indicators of metabolism. Blood should be collected in the morning before breakfast. The patient should avoid a “heavy” meal the evening before and should have fasted overnight.

Although it is more difficult to consider the timing for blood sampling in outpatients, patients should at least be instructed on how to prepare themselves for blood sampling. Errors in the collection of specimens (venous blood, capillary blood, cerebrospinal fluid, urine, stool, discharge, etc.) from a patient and their transport to the laboratory are described in detail in *Basics of quality assurance for intermediate and peripheral laboratories* [3].

The measurement of certain laboratory indicators will give different results depending on the origin of the collected blood. Venous blood glucose concentrations are about 5% to 10% lower than plasma glucose concentrations. These differences should be considered, when different techniques for blood collection and measurement are used.

Blood concentrations of laboratory indicators may differ when blood is taken from a patient in the horizontal or vertical position. The difference in results may be up to 15% for certain indicators. Table 3.10 indicates the changes in selected indicators as a consequence of the positioning of healthy subjects from the horizontal to the upright position. The differences may be more pronounced in diseased individuals.

Table 3.10 Changes in selected laboratory indicators from upright patient compared to horizontal patient

| Indicator | Change |
|----------------------|---------------|
| Erythrocytes | 15% increase |
| Haemoglobin | 5% increase |
| Haematocrit | 12% increase |
| WBC | 7% increase |
| Serum albumin | 8% increase |
| Alkaline phosphatase | 6% increase |
| Serum cholesterol | 10% increase |

changes in selected indicators as a consequence of the positioning of healthy subjects from the horizontal to the upright position. The differences may be more pronounced in diseased individuals.

Special attention should be paid when collecting blood from patients who are receiving infusion therapy. Plasma expanders expand the volume of blood and reduce the concentration of blood components. In addition, some plasma expanders affect certain enzyme reactions. As a rule, blood samples should not be taken from the same side of the body as the site of an infusion of fluid or drugs; rather the contra-lateral side should be used. Table 3.11 lists infusions that affect the measurement of laboratory indicators:

Changes also occur after surgical intervention. For example, urea and C-reactive protein (CRP) levels increase after surgical treatment, whereas albumin level may decrease.

Biochemical processes continue to proceed after blood collection. Blood cells metabolize, and blood enzymes continue to react. Therefore reagents are added to blood or cerebrospinal fluid containers to inhibit ongoing biological processes. Today, the containers (usually test-tubes) are specifically prepared for the transportation of blood, plasma or serum. The

Table 3.11 **Effect of infusion solutions on the measurement of selected laboratory indicators**

| Infusion | Affected laboratory indicator | Effect |
|-----------------|--------------------------------------|---|
| Citrate | clotting tests | prolonged |
| | pH of blood | decreased |
| Electrolytes | plasma electrolytes | increased |
| Glucose | serum glucose | increased |
| | serum potassium | decreased |
| | serum phosphate | decreased |
| | serum amylase | decreased |
| Fructose | uric acid | increased |
| Dextran | thrombin time | prolonged |
| | serum protein | increased (method dependent, biuret method) |
| | serum urea | decreased |
| | blood group serology | pseudo-agglutination |
| Immunoglobulins | viral tests | false positive |

tubes are marked with colours that can be easily identified and selected by personnel for collecting specimens for specific laboratory analyses. Table 3.12 lists the recommended containers with specific inhibitors and their purposes for analysing blood, plasma, serum or cerebrospinal fluid.

Anticoagulants are additives that inhibit blood and/or plasma from clotting so that the indicator to be measured is changed as little as possible before the analytical process. Anticoagulation is achieved by either the binding of calcium ions (EDTA, citrate) or by the inhibition of thrombin

Table 3.12 Specified containers for blood collection

| Indicator | Effect |
|---|--|
| Heparin | inhibition of clotting |
| EDTA | inhibition of platelet aggregation and enzyme activation |
| Citrate | inhibition of clotting |
| Sodium oxalate | calcium binding, inhibition of clotting |
| Glycolysis inhibitors (iodine acetate sodium) (sodium fluoride) | inhibition of glycolytic enzymes |
| Inhibitors of proteinolysis (aprotinine) | inhibition of proteases |
| Antibiotics | inhibition of bacterial growth |
| Gel separators | separation of blood cells from plasma |

activity (heparinates, hirudin). For citrate it is important that the blood is mixed in the following concentrations immediately after sample collection:

- one part 0.109 mol (3.2%) citric acid (pH 5.5 to 5.6) is mixed with nine parts blood for coagulation tests.
- one part of 0.109 mol (3.2%) citric acid (pH 5.5 to 5.6) is mixed with four parts blood to determine the erythrocyte sedimentation rate.

The colour codes of tubes containing anticoagulants for blood collection according to the ISO 6710 standard are:

| | |
|--------------------------|------------|
| EDTA | lavender |
| citrate 9:1 | light blue |
| citrate 4:1 | black |
| heparinate | green |
| no additives (for serum) | red. |

Storage and transport can change the nature of the specimen. The results of specimens that have been inadequately stored and transported may be incorrect and therefore give rise to inappropriate medical action. Therefore the physician should be familiar with the specific conditions of

transport and storage of specimens for laboratory analysis. This applies equally to blood, plasma, serum, cerebrospinal fluid, urine and stool. The laboratory must provide full and specific information to the physicians and paramedical staff on the use of appropriate containers and the conditions of transport and storage of specimens. The containers are different for investigations in clinical chemistry, haematology and microbiology. For example, EDTA tubes for the transportation of blood for cell counting cannot be used for certain clinical chemical investigations, such as calcium and alkaline phosphatase measurements, since the EDTA interferes with the measurement procedure. The use of antimicrobials as preservatives for microbiological investigations in blood and urine is obsolete, because they inhibit the growth of microorganisms. On the contrary, optimal conditions must be chosen to sustain the viability of microorganisms prior to culture.

The phlebotomist should adopt a standard procedure when collecting blood in more than one tube. The following sequence for blood collection has proved to be useful:

- tube for blood culture
- tube for serum (no additive in the tube)
- tube citrate plasma
- tube heparin blood
- tube EDTA
- tube with glycolytic inhibitor.

The phlebotomist must fill each tube containing an additive with the recommended volume of blood. Otherwise, the concentration of the additive will be too high or low, which may lead to incorrect results. For example, it is important to exactly mix 9 parts of blood with 1 part of 3.2% citrate solution. If the volume of blood added to a citrate-containing tube is too small, the clotting time will be artificially prolonged, not only because of an incorrect dilution of the clotting factors in the sample, but also, because the activation process of the plasma coagulation is inhibited.

The physician and paramedical staff should also be familiar with the optimal conditions of storage of specimens. For example, the plasma potassium concentration will rise significantly when blood is stored at 4 °C as well as at 30 °C or 37 °C for several hours. Significant changes are also observed in plasma enzyme activities (alanine aminotransferase) when blood

specimens are stored at 4° or 37 °C. Conversely, glucose concentration in blood decreases when stored under these conditions. Certain indicators are destroyed by bright light, such as bilirubin. This is why specimens should never be exposed to sunlight during storage and transportation.

These changes are more pronounced when blood rather than plasma or serum is stored. As a rule, plasma should be separated from blood cells as soon as possible to minimize the effects of storage, due to leakage of components from blood cells.

Needles and syringes and other sharp objects must be disposed of in leak proof containers after they are used for specimen collection in order to reduce the risk of infection and injury. The containers should be labelled clearly and placed close to where the specimens are routinely taken. All plastic syringes and needles must be used only once and properly disposed by incineration and/or destruction. Small instruments are available which completely destroy needles. Urine, stool and other body fluids may be flushed down the laboratory sluice or the toilet.

3.3.5 Pre-analytical aspects of microbiology

The outcome of microbiological investigations is important for the monitoring and treatment of individual patients, and for the investigations of diseases causing outbreaks and their surveillance. Bacteria and parasites may develop resistance against drugs used for antimicrobial therapy. The re-emergence of infectious diseases as the result of the development of antimicrobial resistance in microorganisms has become a worldwide concern. It is caused by a lack of communication between the diagnostic and therapeutic sectors in health care and the uncontrolled use of antimicrobials.

Paramedical staff may collect urethral discharge using sterile swabs (urethral swab) or directly on to clean glass slides. High vaginal swabs (HVS), endocervical swabs (ECS), cerebrospinal fluid, joint fluid, pleural fluid and peritoneal fluid are collected by the physician and submitted immediately to the laboratory for examination. It is wise to inform the laboratory in advance that these samples are about to be collected so they can be processed immediately. Skin scrapings and specimens of hair and nails are submitted dry to the laboratory in a clean jar or wrapped in a piece

of clean paper. All wet preparations for bacteriological and parasitological examination must be examined as soon as possible in the laboratory.

The technical aspects for collection and transport of clinical specimens for microbiological examination are outlined in detail in *Specimen collection and transport for microbiological investigation* [5]. The following rules are particularly important for the physician to remember.

1. The physician must decide upon the usefulness of a microbiological investigation. Whenever possible, use antimicrobial sensitivity data collected at regional sentinel sites, if the laboratory cannot provide investigations of antimicrobial sensitivity. Some bacteria are always susceptible to certain antimicrobials. Treatment can be immediately initiated without an antibiogram after the identification of the bacteria.
2. The appropriate material that must be collected for the diagnosis of an infectious disease in a patient. For example, observations from saliva rather than from expectorate of the lower respiratory tract are not useful in identifying the microorganism causing pneumonia.
3. The physician must indicate to the laboratory the current medical treatment of the patient, and antimicrobial therapy in particular.
4. Specimen collection must be made before (and not after) the start of antimicrobial therapy. Microorganisms that have already been exposed to antimicrobials may not grow adequately in culture, and the recommendations for antimicrobial therapy made by the laboratory may therefore be misleading.
5. The clinician must consider the appropriate timing of specimen collection. In patients with fever, the specimen should be collected when the temperature is highest. Often this is during evening hours. For the diagnosis of certain parasitic infections (plasmodium, microfilaria) the biorhythm of the parasite must be considered.
6. The physician must collect an adequate volume of the specimen using sterile equipment, place it in a sterile container and deliver the sample under the appropriate conditions of temperature to the laboratory as soon as possible for investigation. Some microorganisms (*Meningococci*, *Chlamydia*, *Bordetella pertussis*) are fragile. Urine should be transported at 4 °C to limit the growth of bacteria in the urine. A pinch of boric acid can be added to limit growth of bacteria

during transport. Blood, cerebrospinal fluid and genital tract discharge material should be transported at body or room temperature. (see Section 3.3.2 on cerebrospinal fluid).

7. The physician must collect the specimen for microbial examination in the appropriate transport medium to ensure the viability of the organism. When blood is collected in culture bottles the minimal blood volume should be:
 - 1 mL from children below the age of 2;
 - 5 mL in persons who are 11 years and above.
 Blood for bacterial investigation should never be stored in the refrigerator.
8. Physicians must understand the meaning of the terms used to describe the properties of microorganisms as reported in antimicrobial susceptibility test¹ results. Otherwise they will not be able to make the right choice of antimicrobials for treatment.

¹ An antimicrobial susceptibility test is performed for two main purposes:

- to guide the clinician in selecting the best antimicrobial agent for treating an individual patient;
- to accumulate epidemiological information on the resistance of microorganisms of public health importance within the community.

The result of the antimicrobial susceptibility test, as reported to the clinician, follows the classification of the microorganism into different categories of susceptibility. The Kirby-Bauer method and its modifications recognize three categories:

- Susceptible. An organism is called “susceptible” to a drug when the infection caused by it is likely to respond to treatment with this drug, at the recommended dosage.
- Intermediate covers two situations.

It is applicable to strains that are “moderately susceptible” to an antibiotic that can therefore be used for treatment at a higher dosage (e.g. β -lactamase) because of its low toxicity, or because the antibiotic is concentrated in the focus of infection (e.g. in the urine).

It also applies to strains that show “intermediate susceptibility”. In this situation, the intermediate category serves as a buffer zone between susceptible and resistant to a more toxic antibiotic (e.g. aminoglycoside) that cannot be used at a higher dosage.

As most physicians are not familiar with the subtle, although clinically important, distinction between intermediate and moderate susceptibility, many laboratories use the designation “intermediate” for reporting purposes.

- *Resistant*. This term implies that the organism does not respond to a given drug, irrespective of the dosage and the location of the infection.

In certain situations, such as for testing the response of *Staphylococci* to benzyl penicillin, only the categories “susceptible” and “resistant” (corresponding to the production of β -lactamase) are used.

The ultimate decision to use a particular antimicrobial, and the dosage to be given will depend not only on the results of the susceptibility tests, but also on their interpretation by the physician. Other factors, such as the pathogenic significance of the microorganism, side-effects and pharmacokinetic properties of the drug, its diffusion into and concentration at different body

9. The physician and the laboratory should consult each other when deciding on the introduction of a new antimicrobial. For such a decision it may be pertinent to take the usage of antimicrobials in farming into account. Certain antimicrobials used as so-called “growth factors” in animal breeding may cause antimicrobial resistance in micro-organisms that may infect mankind but maintain their resistance to antimicrobials used for human therapy. The physician must be aware that the misuse and overuse of antimicrobials will promote antimicrobial resistance.
10. The laboratory should provide a report that indicates the pathogenic bacteria and their antimicrobial susceptibility. The report should not mention the normal flora that was identified by culture in order to avoid misinterpretation of results.

3.3.6 Pre- and post-analytical aspects of immunology

Immunological and serological tests are increasingly used for the diagnosis of diseases and for monitoring the treatment or progress of a disease. Immunological tests are more expensive, and unfortunately physicians may be only marginally aware of the clinical value of these tests. This may result in serious problems arising from the inappropriate use of tests, or interpretation of the test results without considering the performance of the tests. Various factors may contribute to the difficulties of using immunological tests.

- Certain immunological tests were previously designed to diagnose a disease, but today, the usefulness of these tests is no longer accepted. For example, the Widal test can be dangerously misleading and should no longer be used in clinical practice.
- A number of diagnostic immunological reagents are not standardized. Consequently, results obtained by different test systems cannot be compared. The physician is rarely aware of these differences and conclusions are made that may have serious consequences for the

sites, the immune status of the patient, and the state of liver and kidney function of the host, will also have to be considered.

patient (e.g. false diagnosis of a tumour or viral infection). This poses particular problems for laboratory services in developing countries.

- In developing countries, interruption of the supply of reagents forces laboratories to change from one test system to another. The information is not passed on to the physician, who may come to the wrong conclusion when comparing results that were established by different test systems.
- Certain immunological tests were developed for monitoring a disease. Some of these tests have a low diagnostic specificity; nevertheless they are mistakenly used for the diagnosis of a disease (e.g. certain tumour markers).
- Tests that are intended serve a specific purpose are used for other purposes, and the results obtained may lead to the wrong conclusion. For example, certain tests for the detection of HBV surface antigen are used in the control of donated blood although their low diagnostic sensitivity may insufficiently indicate that the donation is not infectious.
- Immunological reagents may be subject to cross-reactions under certain circumstances, and the results must be interpreted with caution.

3.3.7 Validation of laboratory results

All laboratory results must be validated by the laboratory from both a technical and a medical point of view before they are reported to the physician. The laboratory has an obligation to ensure that all results are correct within accepted limits of uncertainty.

The technical validation of laboratory results focuses on the exclusion of errors, such as:

- inappropriate material provided to the laboratory for analysis
- inappropriate handling of the material prior to and during analysis
- inappropriate execution of measurement (including wrong calibration, use of inappropriate reagents, inappropriate measurement conditions, incorrect reading and calculation)
- incorrect transcription of results.

The medical validation identifies errors that may have been made during the pre-analytical phase at the time of collection and transport of specimens (which may not be under the control of the laboratory). During the medical validation the results are compared with the clinical state of the patient. The medical validation includes a plausibility control of the value of the measurement with the suspected pathobiochemical status of a patient. For example, a measured serum potassium concentration of 12 mmol/L is not compatible with life. Consequently, such a result in a report is not plausible knowing that the patient is alive; obviously an error was made during sampling, transportation or storage of the specimen. The error could have been caused by prolonged storage of the specimen prior to the laboratory examination or by sampling from a site where the patient was receiving a potassium-containing salt infusion. There may also be other causes that explain the elevated serum potassium concentration, which was correctly measured from a technical point of view.

A comparison of results with previous results on the same patient often helps to identify inappropriate procedures (e.g. use of inappropriate tubes for blood collection), undetected accidents during laboratory measurement (e.g. fibrin clots in serum), and errors of transcription of results.

The importance of the information on the medical history of the patient for the interpretation of laboratory observations also applies to tests that provide a “yes” or “no” answer. For example, the following tests were found to be an occasionally falsely positive:

- tests for antibodies against HIV and other viruses (anti-HCV, anti-rubella, anti-HAV-IgM, anti-EBV, anti-HSV)
- tests for bacterial infections
- tests for autoimmune antibodies
- tests for rheumatic factors
- hypergammaglobulinaemia.

This is why it is sometimes necessary to make an additional laboratory investigation using a different test principle in order to confirm that the result is truly positive.

Chapter 4

Approaches to clinical problem-solving

Clinical problem-solving is a process of finding out what is wrong with a patient, starting with the patient's presenting complaint. The stages of clinical problem-solving should be followed step by step, in order to arrive at the best possible diagnosis and to plan appropriate management.

The sequence of events used in making a diagnosis is:

- history-taking
- physical examination
- selection of laboratory tests and interpretation of results
- use of diagnostic facilities, e.g. X-ray, ultrasound.

The first step to make a diagnosis of a disease is the exploration of the medical history, followed by the physical examination of the patient. The second step is the ordering of diagnostic investigations.

4.1 Medical history-taking

The medical history consists of:

- complaints or symptoms presented by the patient
- further information obtained from inquiry by the clinician.

The time needed to gather a medical history depends on the nature of the problem. The physician should aim to spend at least 10 minutes with every patient, but complicated problems may require longer. Physicians should familiarize themselves with local terminology used by the community to describe clinical conditions and diseases. Knowledge of the local dialect and

local beliefs assists in communicating with patients. An interpreter may be needed.

In hospitals the medical history of a patient together with the observations that were made during the physical examination are kept on record. The medical doctor examining the patient is requested to enter all important information into a pre-printed record form if available. Such a form is useful for examining the patient in a systematic way, to follow up a patient during subsequent visits, and for communication with other clinical experts who may have inspected the patient from a different medical point of view. An example of a record form is shown in Annex 2.

A medical history proceeds as follows:

- history of present illness
- systemic inquiry (review of systems)
- past history
- social history
- family history
- drug history.

Questions are asked in order to explain the chief complaint and clarify the likely differential diagnoses. Where there are several symptoms, it useful to ask the order in which they occurred. Questions should always be specific and useful. One of the most useful questions is “Have you ever had the same problem before?”.

When patients complain of pain, useful questions to delineate the problem are:

- the site (where is the pain?)
- radiation (does it spread elsewhere?)
- severity (how bad is it? Does it stop you carrying out normal activities?)
- character (what is the pain like? Stabbing, burning, dull, etc?)
- aggravating and relieving factors (what brings the pain on? What relieves the pain?)
- duration of the pain (how long have you had it?).

The most useful questions to ask relate to the “system” involved (see the sections devoted to systemic inquiry below).

With experience, two or three specific questions will lead the clinician to the most likely diagnosis. The clinician will also learn which questions related to the other “systems” could be relevant to the patient’s problem.

The following lists give most of the major questions that could be asked about a “system”. It is important that answers to all questions are entered into the pre-printed record form. Note that the questions remain *specific* and *useful* in leading to a possible diagnosis.

- *General*
weight loss
night sweats
fever
oedema
enlarged lymph nodes

- *Ear, nose and throat*
ear pain
deafness
discharge from the ears
tinnitus (ringing or buzzing in the ears)
sore throat
difficulty or pain in swallowing
hoarseness of the voice
pain in the face (over the sinuses)
nasal discharge (runny nose)
nose bleeding
painful teeth
soreness/ulcers of the mouth or tongue
bleeding of the gums

- *Eyes*
loss of vision
double vision
eye pain
itching of the eyes
discharge from the eyes

- *Cardiovascular system*
central chest pain
palpitations
shortness of breath (on exertion, at rest, at night, lying flat)
cough
sputum (colour, consistency, blood-stained)
swelling of the ankles (oedema)
tenderness of calf or veins

- *Respiratory system*
chest pain (site, with inspiration)
shortness of breath (at rest, exertion)
cough
sputum (colour, consistency, amount)
wheezing

- *Gastrointestinal system*
vomiting (with or without blood)
appetite, ability to take fluids
diarrhoea or constipation (frequency, amount, consistency, colour,
presence of blood or mucus)
flatus (excessive or absent)
abdominal pain (site, type, severity, aggravating/relieving factors)

- *Genitourinary system*
painful urination
colour of urine (blood, dark)
difficulty in passing urine
frequent passing of small volumes of urine
urinary incontinence
loin pain
passage of stones

- *Genitourinary system: males*
urethral discharge: colour
genital ulcers

testicular pain or swelling
enlarged inguinal lymph nodes

- *Genitourinary system: females*
pregnancies: number, complications
menstruation: regular, heavy, painful
vaginal discharge: colour, irritation, smell
genital ulcers
enlarged inguinal lymph nodes
pelvic pain

- *Endocrine system*
swelling of the neck
body growth
hair distribution
polyuria (passing excessive quantities of urine)
polydipsia (excessive thirst)

- *Skin, hair, nails*
itching, pain
rash: distribution, colour, type, sensation
ulcers
discharge
bruising, bleeding
baldness
hair/nail changes: shape, colour

- *Joints, muscles*
joints: pain, swelling, redness, heat
deformity
stiffness

- *Central nervous system*
headache
visual disturbance

photophobia
deafness, tinnitus
weakness of face, limbs (especially one-sided)
difficulty in swallowing
numbness, tingling (one side, “glove and stocking” distribution)
difficulty speaking
difficulty walking, abnormal gait
control of urination or defecation
convulsions
coma

- *Psychiatric status*
depression
anxiety
hallucinations
sleep disturbances

- *Past history*
previous surgical operations, and reasons
previous admissions to hospital, and reasons
previous accidents or injuries
previous severe illnesses

- *Social history*
marital status
religion
occupation
diet
hobbies, other activities
smoking
alcohol intake
recent travel

- *Family history*
hereditary diseases: history of illness in parents, siblings (sisters and brothers) and children
infectious diseases: history of illness in those living close to the patient, e.g. spouse, relations, friends
- *Drug history*
recent or previous use of medicines including herbal remedies.

4.2 General examination

Every patient must have a general examination performed including examination of the head, eyes (conjunctivae), mouth, neck, the skin and the extremities, all of which may provide clues to the cause of the patient's illness. The observations of the general examination should also be entered into the pre-printed record form. A complete general examination includes the following:

- general appearance (cleanliness, emaciation or obesity, marasmus, degree of illness)
- general mood, level of consciousness, ability to walk or sit (in a child), gait, posture
- obvious deformities

| | |
|--------------------|--|
| hair | hair colour and texture, fungal infection, loss of hair (alopecia) |
| pallor | conjunctivae, mouth and tongue, nailbeds, palms |
| jaundice | sclera, mouth and frenulum of the tongue |
| cyanosis | mouth, lips and tongue, nailbeds |
| mouth | poor teeth, oral thrush, oral ulcers, enlarged or inflamed tonsils, mouth opening, tongue protrusion |
| state of hydration | dry mucous membranes, lack of tears, loss of skin turgidity, sunken fontanelle |
| ears | discharge, external ears, ear drums |

| | |
|-------------------------|---|
| swellings of the neck | enlargement of the thyroid, lymph nodes |
| fingers and nails | clubbing, nail pitting |
| peripheral oedema | pitting of the skin |
| peripheral skin lesions | rashes, ulcers |

- vital signs: temperature, pulse rate, respiration rate, blood pressure
- body weight.

4.2.1 Respiratory system

The respiratory system is examined with the patient sitting up, or with a child sitting on its mother's lap. The patient should remove the shirt completely for the examination of the chest. Examine both the anterior and posterior parts of the chest; there is more posterior lung area available for examination than anterior.

- *Inspection*: shape and movement of the chest: symmetrical/asymmetrical, deformities. Respiratory rate.
- *Character of respirations*: wheezing (delayed expiration); respiratory distress: flaring of the alae nasae, use of accessory muscles, chest indrawing (suprasternal/clavicular, intercostal, subcostal); Kussmaul breathing (air hunger); Cheyne–Stokes breathing: periods of deep breathing alternating with apnoea; finger clubbing.
- *Palpation*: trachea central or deviated, chest expansion equal or asymmetrical on both sides, tenderness, vocal fremitus (feeling while the patient speaks).
- *Percussion*: resonant (normal); hyper-resonant, dull, stony dull.

- *Auscultation*: normal (vesicular) breath sounds, reduced or absent breath sounds, bronchial breathing, rhonchi, crackles, pleural rub, vocal resonance (auscultating while the patient speaks).

Note: always compare the two sides of the body in your examination.

4.2.2 Cardiovascular system

The cardiovascular system is examined with the patient lying on his/her back on a couch, propped up at a 45° angle. A child can be sitting on its mother's lap.

- *Inspection*: cyanosis, finger clubbing, position and character of apex beat, redness of veins in legs, jugular venous pulse rate.
- *Palpation*: rate and rhythm of pulse, position and character of apex beat, jugular venous pressure, thrills (palpable murmurs), peripheral (or sacral) oedema, tenderness of calf veins.
- *Percussion*: the heart borders can be percussed to determine the size of the heart.
- *Auscultation*: heart sounds I and II; murmurs (systolic or diastolic); extra sounds, pericardial rub, bruits over arteries (carotid, aortic). Listen over the four valves of the heart to see where murmurs are loudest:
 - mitral: left fifth intercostal space in the mid-clavicular line
 - aortic: right second intercostal space adjacent to the sternum
 - pulmonary: left second intercostal space adjacent to the sternum
 - tricuspid: right fourth intercostal space adjacent to the sternum.

4.2.3 Abdominal system

The abdomen is examined with the patient lying flat on his/her back on a couch, with arms at the sides and knees slightly flexed. Ask the patient to relax and breathe gently. Small children can be examined lying on the

mother's lap. Hernias are best examined with the patient standing up and asking the patient to cough or strain.

- *Inspection*: distension, movement with respiration, visible peristalsis, scars, striae, dilated veins, umbilical hernia, enlarged liver or spleen, masses.
- *Palpation*: tenderness, rigidity, organs (liver, spleen, kidneys), masses, hernias (umbilical, inguinal, femoral), direction of blood flow in dilated veins, thrills (arterio-venous fistulae).
- *Percussion*: extent of liver and spleen; differentiation of enlarged spleen from enlarged kidney; detection of peritoneal fluid (ascites), shifting dullness.
Always percuss from resonant to dull.

- *Auscultation*: bowel sounds (normal, increased, silent), arterial bruits (aorta, renal arteries), continuous murmurs (arterio-venous fistulae).

Always compare the two sides of the body in your examination.

- *Differentiation of spleen from kidney*
On inspiration, the spleen moves diagonally down, the kidney moves vertically down.
The spleen has a notch, the kidney does not have a notch.
The spleen is dull to percussion; the kidney is resonant to percussion.
The upper part of the spleen cannot be palpated; the upper part of the kidney can be palpated (in slim patients).

- *Rectal examination*
Rectal examination should be performed in cases of anal irritation or pain, where there is blood or mucus coating the stool, and in patients with prostatic symptoms. The examination is performed wearing examination gloves and with the patient lying curled up in the left lateral position.

Inspection: peri-anal skin, fissures, haemorrhoids, ulcers, polyps.

Inspection of finger after withdrawal: colour of faeces, blood, pus, mucus.

Palpation (with lubricated, gloved finger): tenderness, tone of anal sphincter, faecal masses, rectal masses, tenderness, prostate for hardness or irregularity.

4.2.4 Genitourinary system

Wear examination gloves and have all instruments, a light or torch, and sterile swabs ready to hand.

Male patients

- *Inspection:* distribution of pubic hair, appearance of penis, presence of prepuce, site of external urethral orifice, discharge (colour, consistency), ulcers, scrotum for redness or swelling, oedema of skin, ulceration, inguinal swellings.
- *Palpation:* withdraw prepuce to examine for ulcers, massage for discharge, presence of both testes in the scrotum, scrotal or testicular swellings, trans-illumination, inguinal swellings.

Female patients

The patient is best examined lying flat on her back with legs drawn up and knees apart. Cover the lower abdomen with a sheet. Vaginal examination requires the presence of a chaperone.

- *Inspection:* vulva for ulcers, swellings, vaginal discharge (colour, consistency), urethral discharge.

Inspection using a vaginal speculum

This procedure should be performed to examine the vagina and cervix. Use a sterile speculum lubricated with water only (antiseptics may destroy pathogenic organisms).

Insert the speculum sideways into the lower part of the vagina.

Rotate the blades through 90° so that they are lying flat anteriorly and posteriorly.

Gently open the blades and identify the cervix.
Tighten the screw to keep the speculum in place.
Note ulcers, irregularity, bleeding of the cervix.
Observe the source (cervical, vaginal) of the discharge.
Note colour, consistency of the discharge.
Collect an endocervical swab (ECS) from the cervical canal.
Collect a high vaginal swab (HVS) from the posterior fornix.
Gently withdraw the speculum. Observe discharge on the speculum.

- *Palpation (using index and middle fingers of right hand)*: direction of cervix, irregularity, tenderness on movement.
- *Palpation (bimanually)*: size, position of uterus, each lateral fornix for tenderness and swellings of fallopian tubes or ovaries, pouch of Douglas inferiorly.

4.2.5 Musculoskeletal system (muscles, joints and back)

- *Inspection*: swelling, redness, position of joints. Muscle wasting, fibrillation. Posture upright, anteriorly, posteriorly and laterally. Spinal movements during flexion, extension, lateral flexion and rotation. Gait during walking. Walking on tip-toes and heels.
- *Palpation*: tenderness, range of motion, crepitus, fluctuation. Straight leg raising and ankle dorsiflexion. Spine for local tenderness.

Note: always compare the two sides of the body in your examination.

4.2.6 Skin

Typical features on the skin very often provide the first information on a disease in a patient. The features may be caused by an infection (bacterial, viral, fungal, protozoan), metabolic disorder, malignant disease or exposure to harmful agents (allergens, toxins).

- *Inspection:* rashes/ulcers; type, site, distribution, arrangement, shape, colour, inflammation, swelling, discharge, oedema, excoriations, eczema (dry, seborrhoeic), exanthema, pustules, pyoderma, bullae, gangrene, creeping eruptions, abscesses, cyanosis, erysipelas, erythema, alopecia, herpes, plaques, vitiligo, hyperpigmentation, urticaria, burns, tumours, cysts, atheroma, fibroma, haemangioma, lipoma, keloids, warts, condyloma, naevi; insects and microorganisms: ticks, lice, mites, tinea (fungi), larvae.
- *Palpation:* rashes/ulcers; tenderness, anaesthesia, raised edges.

4.2.7 Endocrine system

- *Inspection:* obesity; acromegalic face, hands and feet; increased water intake; weight loss; weight distribution; exophthalmos; lid lag; thyroid swelling; resting tremor; distribution of body hair; breast mass, indrawn nipple.
- *Palpation:* texture of hair and skin; pulse rate; blood pressure; thyroid swelling; breast mass; abdominal mass.

4.2.8 Nervous system

- *Mental functions:* appearance, cooperation, orientation, memory, emotional state, intelligence, conversation, speech, level of consciousness.
- *Cranial nerves*

| | | |
|-----|-------------|---|
| I | Olfactory | sense of smell |
| II | Optic nerve | visual acuity, visual fields, optic fundus |
| III | Oculomotor | eye movements, nystagmus, squint, pupils (size, light, accommodation) |
| IV | Trochlea | control of superior oblique muscle that moves the eye |

| | | |
|------|------------------|--|
| V | Trigeminal | sensation of face, cornea, anterior $\frac{2}{3}$ of tongue; open mouth, clench jaw, jaw movements from side to side |
| VI | Abducens | motor nerve for the lateral rectus muscle that moves the eye outward |
| VII | Facial | taste (anterior $\frac{2}{3}$ of tongue), facial movements |
| VIII | Auditory | hearing, balance |
| IX | Glossopharyngeal | sensation, taste to posterior $\frac{2}{3}$ tongue, swallowing, |
| X | Vagus | movement of palate, uvula, pharyngeal reflex |
| XI | Accessory | sternomastoid, trapezius (turn head, shrug shoulders) |
| XII | Hypoglossal | tongue movements |

- *Motor functions:* muscle bulk, muscle tone (flaccid, spastic/clasp-knife, cog-wheel, lead-pipe), muscle power, tendon reflexes, abdominal reflexes, plantar reflex.
- *Sensation:* light touch, pain (pin prick), temperature, position sense, vibration, recognition of size, shape, weight.
- *Coordination:* finger to nose, heel to knee, standing with eyes closed (Romberg sign).
- *Gait:* spastic, stamping, reeling, high-stepping, scissors.
- *Involuntary movements:* epilepsy, tremor, choreiform, athetosis.
- *Meningeal irritation:* neck stiffness, Kernig sign (passively extending the knee with the hip fully flexed).
- *Raised intracranial pressure:* bulging fontanelle, papilloedema.

Note: always compare the two sides of the body in your examination.

Chapter 5

Examination of clinical symptoms and signs

Observations that commonly present in medical practice and ways of approaching the diagnosis in a systematic way are discussed in the following sections:

- fever
- anaemia (pallor)
- diarrhoea
- cough and shortness of breath
- skin diseases (rashes and ulcers)
- jaundice
- oedema
- sexually transmitted infections
- coma or altered consciousness
- acute and non-acute abdominal pain
- accidents and injuries
- complicated pregnancy
- malignancy.

Chapter 6 discusses the contribution of diagnostic services in the control of epidemics. Chapter 7 considers noncommunicable diseases. The signs and symptoms of common diseases and disorders and the laboratory test that should be considered, are summarized in Table 5.1

Table 5.1 Use of essential laboratory tests

| Clinical condition | Investigation required | Specimen | Technique |
|--|--|--|---|
| Anaemia | Haemoglobin estimation or haematocrit | Capillary or anticoagulated venous blood | Haemoglobin Reverse Field stain |
| | Peripheral blood film | | Differential blood film |
| | Sickle-cell screen | | Sodium metabisulfite slide test |
| Anaemia, weight loss | Stool for ova and larvae | Stool | Direct saline preparation |
| Abdominal pain | Blood in stool, blood haemoglobin | | Formol-ether concentration method and microscopy |
| | | | Hb, haemocult |
| Fever, mental confusion, severe headache, signs of meningitis, unconsciousness | Cerebrospinal fluid for bacteria, parasites, viruses | Cerebrospinal fluid | Microscopy and culture |
| | Blood for bacteria, parasites | Fresh blood | Differential blood cell count |
| | | | Cerebrospinal fluid blood cell count Special viral tests |
| Fever, arthritis/ arthralgia | Total and differential white blood cell count | Capillary or anticoagulated venous blood | Improved Neubauer chamber |
| | Blood film for malaria parasites | | Reverse Field stain |
| | Sickle-cell anaemia | | Blood microscopy, serological test, sickle cell test |
| | Bacterial and viral infections | | |
| Fever, lymphangitis, lymphadenitis | Blood film for microfilariae, white blood cell microscopy | Capillary or anticoagulated venous blood | Direct examination Knott concentration method |
| | | Lymph knot puncture | Field stain Serological tests for toxoplasmosis, etc. |
| | | | |
| Fever, lymphadenopathy, apathy, skin oedema, headache, coma | Blood film, lymph gland puncture, subcutaneous (chancre) fluid, for <i>Trypanosoma</i> | Capillary or anticoagulated venous blood | Direct microscopy Buffy coat microscopy |
| | | Lymph gland fluid | Field stain |
| | | Subcutaneous fluid | Reverse Field stain |
| | | | |
| Fever, weight loss, splenomegaly | Blood cell count; | Skin biopsy | Reverse Field stain |
| | WBC microscopy | | |
| | Leishmania | | |

Table 5.1 Use of essential laboratory tests (continued)

| Clinical condition | Investigation required | Specimen | Technique |
|-------------------------------|--|---|--|
| Relapsing fever | Blood film for <i>Borrelia</i> | Capillary or anticoagulated venous blood | Field stain |
| | <i>Plasmodium vivax</i> , <i>P. ovale</i> , <i>P. malaria</i> | | Reverse Field stain |
| | WBC count, WBC microscopy, | | |
| Urethral discharge/urethritis | Urethral discharge for <i>Neisseria gonorrhoeae</i> , pus cells | Urethral swab or urethral smear | Gram stain |
| | | First voided urine | Bacterial culture |
| | First voided urine for <i>Trichomonas vaginalis</i> (in males) | Fresh midstream urine | Direct microscopic examination of sediment |
| | | | Urine dipsticks |
| | Urine for glucose, bacteria, protein, haemoglobin | | Colorimetric or strips |
| | Midstream urine for microscopy | | Microalbuminuria |
| Haematuria | Urine for <i>Schistosoma</i> ova (in endemic areas) | Terminal urine | Microscopy of urine sediment |
| | Urine for bacteria | | |
| | | | |
| Genital ulcer | Exudate for <i>Treponema pallidum</i> | Exudate from genital ulcer | Dark-field examination |
| | Lymphogranuloma venereum | <i>Chlamydia trachomatis</i> | Bacterial culture |
| | <i>Haemophilus ducreyi</i> | | |
| Vaginal discharge | High vaginal swab for <i>Trichomonas vaginalis</i> , <i>Candida albicans</i> and bacterial vaginosis | High vaginal swab | Direct saline and 10% potassium hydroxide preparations |
| | | Endocervical swab | Gram stain |
| | Endocervical swab for <i>Neisseria gonorrhoeae</i> , pus cells | | |
| Diarrhoea/dysentery | Stool for vibrios | Fresh stool (within 1 hour of collection) | Direct examination |
| | Stool for blood cells and protozoa and bacteria | | Dark-field examination |
| | | | Direct saline, eosin preparations, |
| | | | Stool cultures |

Table 5.1 Use of essential laboratory tests (concluded)

| Clinical condition | Investigation required | Specimen | Technique |
|--|---|--|---|
| Fibrous skin nodules, blindness | Skin snip for onchocerca microfilariae | Skin snip | Direct examination |
| Skin ulcer | Skin smear for acid-fast bacilli | Skin slit smear | Modified Ziehl–Neelsen stain |
| | Skin exudate for <i>Treponema pallidum</i> | Exudate from skin lesion | Skin smear for bacteria (<i>Mycobacterium ulcerans</i>) |
| | Syphilis screening test | Serum | Dark field microscopy |
| | Syphilis confirmatory test | | VDRL screening test |
| | Tropical ulcer | | Confirmatory test |
| Fungal infection of skin, nails and hair | Skin, hair, nails for fungus | Skin scrapings, hair, nail clippings | 10% potassium hydroxide preparation |
| Pre-eclampsia | Urine for protein | Random urine | Urine dipsticks |
| Chronic cough with expectorate | Sputum, gastric washings for acid-fast bacilli, <i>Paragonimus westermani</i> | Sputum | Ziehl–Neelsen stain microscopy |
| | | Gastric washings | |
| Antenatal screening | Haemoglobin estimation | Capillary or anticoagulated venous blood | Haemoglobin |
| | Syphilis screening test | | VDRL screening test |
| | Urine for protein and glucose | Random urine | Urine dipsticks |
| Eye infection in the elderly | <i>Chlamydia trachomatis</i> | Conjunctival swab | Gram stain |
| Eye infection in the newborn | Conjunctival swab for <i>Neisseria gonorrhoeae</i> , chlamydia, pus cells | Conjunctival swab | Gram stain |

5.1 Fever

In someone with good health, the body temperature is maintained by the thermoregulatory centre in the brain within a narrow range, despite extremes of environmental conditions and physical activity: 36.5–37.5 °C (oral). Normal body temperature varies throughout the day (diurnal variation) and is higher in the evening. Fever is defined as body temperature above normal.

Substances called *pyrogens*, which are derived mainly from viruses and bacteria, reset the thermoregulatory centre’s “thermostat” at a higher level. During infection, heat is generated by shivering (chills, rigours) and

lost through sweating and dilation of peripheral blood vessels (warm extremities).

5.1.1 Types of fever

- *Acute*: for a short time.
- *Chronic*: more than two weeks duration.
- *Intermittent*: falls to normal in regular periodical intervals.
- *Persistent*: without significant diurnal variation.
- *Relapsing*: short febrile periods between one or several days of normal temperature.

5.1.2 Causes of fever

The most common cause of fever is infection. Infection may be due to organisms such as viruses, bacteria, fungi or parasites. Fever may also be due to inflammatory processes in the body. Common and important conditions that are associated with fever, and their causative agents, include the following.

Infectious fever

- *Viral infections*
 - *Main clinical manifestation*: tonsillitis, laryngitis, pharyngitis, tracheitis, laryngotracheobronchitis (LTB or croup), bronchitis, bronchiolitis, pneumonia.
 - *Main viral agents*: measles, mumps, chicken pox, haemorrhagic fevers, respiratory syncytial virus, rhinovirus, adenovirus, influenza virus, mumps virus, varicella-zoster virus, vaccinia, coxsackievirus, human immunodeficiency virus (HIV), hepatitis virus (HAV, HBV, HCV), flavivirus.
- *Bacterial infections*
 - *Main clinical manifestation*: tonsillitis, otitis media, sinusitis, dental abscess, bronchitis, bronchiectasis, pneumonia, lung abscess, urinary tract infection, pelvic inflammatory disease (PID), cellulitis/ulcers, septic arthritis, osteomyelitis, meningitis, secondary syphilis, typhoid (enteric fever), enterocolitis,, relapsing fever,

- *Main bacterial agents:* plague, group A β -haemolytic streptococci, *Streptococcus pneumoniae*, *Mycobacterium tuberculosis*, *Haemophilus influenzae*, *Staphylococcus aureus*, *Mycoplasma pneumoniae*, *Klebsiella pneumoniae*, *Yersinia pestis*, *Escherichia coli*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Neisseria meningitidis/gonorrhoeae*, *Treponema pallidum*, *Salmonella typhi*, *Salmonella paratyphi*, *Shigella* spp., *Campylobacter jejuni*, *Brucella abortus/suis/melitensis*, *Bacillus anthracis*, *Borrelia recurrentis/duttoni*.
- *Rickettsial infections:* typhus, fièvre boutonneuse.
- *Fungal infections:* meningitis (*Cryptococcus neoformans*, *Aspergillus*).
- *Protozoan infections:* malaria (*Plasmodium* spp.), trypanosomiasis (*Trypanosoma* spp.), visceral leishmaniasis (*Leishmania donovani*).
- *Helminthic infections:* schistosomiasis (*Schistosoma mansoni*, *S. haematobium*), filariasis.

Noninfectious fever

- *Inflammatory diseases:* rheumatoid arthritis, auto-immune diseases.
- *Malignancy:* lymphoma.
- *Injury:* crushing injury.
- *Acute haemolytic episodes:* sickle-cell crisis, thalassaemia.
- *Thrombosis:* pulmonary embolus, myocardial infarction (heart attack).
- *Drug reactions.*
- *Allergic reaction.*

Diagnosis

Often, the history and physical examination of the patient give a hint to the cause of the fever, although sometimes its origin cannot be identified (pyrexia of unknown origin; see below). Laboratory investigations depend on the presenting complaint of the patient and the severity of the illness. Questions should be asked in order to find any localized cause of the fever. The following information and investigations may be pertinent.

- *History*
 - duration
 - timing
 - night sweats
 - enlarged lymph glands
 - sore throat, runny nose
 - ear pain, sinus pain
 - painful teeth, facial oedema
 - headache, photophobia, vomiting
 - convulsions, altered consciousness
 - cough, sputum, chest pain, shortness of breath, wheezing
 - diarrhoea (blood, mucus), abdominal pain
 - painful urination, haematuria, loin pain
 - skin rash, ulcer
 - joint swelling, joint pain, bone pain
 - bleeding from mucous membranes into skin
 - drug ingestion.

- *Physical examination*
 - rapid pulse, rapid respiratory rate (exception: slow pulse in typhoid fever)
 - pallor, jaundice
 - stiff neck, bulging fontanelle, photophobia, Kernig sign
 - red throat, pus on tonsils, red bulging eardrums, sinus tenderness
 - decayed teeth
 - respiratory distress (use of accessory muscles, chest indrawing, grunting, nasal flaring), rhonchi, bronchial breathing, pleural rub
 - abdominal tenderness, liver or spleen enlargement, masses, ascites
 - loin/pelvic tenderness
 - skin rash, ulcer, lymphangitis
 - swollen tender joints
 - bone tenderness, swelling
 - bleeding, petechiae
 - lymphadenopathy.

- *Laboratory investigations*
 - haemoglobin
 - total and differential blood cell count
 - blood slide for parasites and *Borrelia*
 - sputum for acid-fast bacilli
 - fresh stool for pus cells, red cells, ova
 - midstream urine (MSU) for pus cells, bacteria
 - coagulation tests (in suspected bleeding disorder)
 - cerebrospinal fluid for white cells (total and differential), bacteria, fungi, protozoa
 - microscopic examination of body fluids for white cells (total and differential), bacteria, fungi
 - lymph gland puncture for trypanosomes, acid-fast bacilli
 - syphilis screening test.
- *Diagnostic imaging*
 - chest X-ray for pneumonia, pulmonary tuberculosis
 - facial X-ray for chronic sinusitis
 - bone/joint X-ray for osteomyelitis, septic arthritis
 - ultrasound for amoebic liver abscess, extrapulmonary tuberculosis, septic arthritis.

5.1.3 Acute fever

Acute fever has a duration of less than two weeks and is most often caused by bacterial, viral or protozoan infection. In tropical climates patients and small children may often suffer from fever due to dehydration. Rarely fever may be caused by an allergy. A meticulous interview should aim to identify a possible risk of infection of the patient (e.g. intake of infected milk, water or food; insect or animal bite). Acute fever may be diagnosed according to the flowchart in Figure 5.1.

Look for signs of localized infection:

- jaundice
- red throat/pus on tonsils
- bulging red ear drums

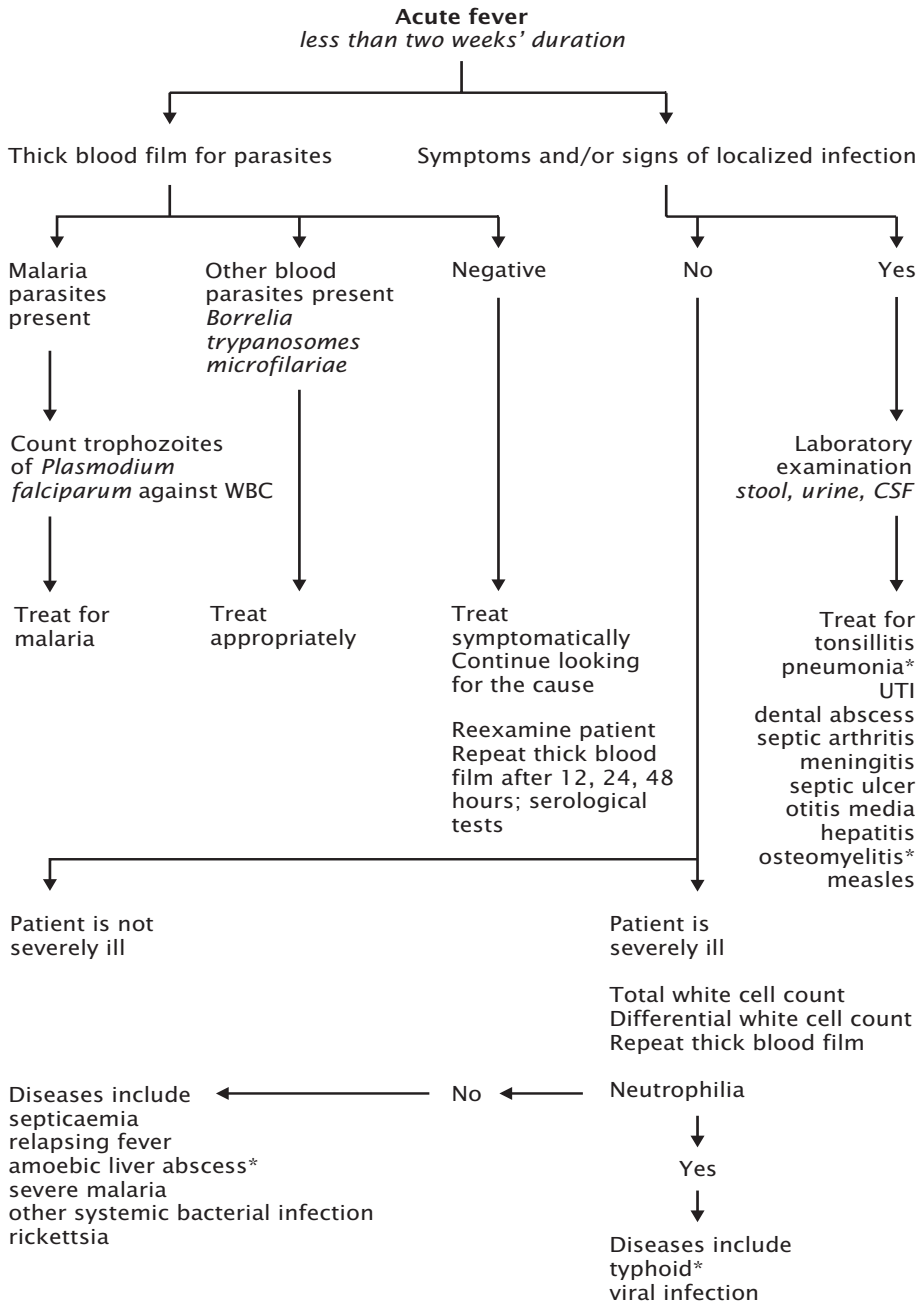


Figure 5.1 Flowchart for the diagnosis of chronic fever

- decayed teeth, facial swelling
- lung crepitations, bronchial breathing
- abdominal/loin tenderness, enlarged organs
- joint/bone swelling, heat, tenderness
- skin rash, ulcer, bleeding
- lymphadenopathy
- neck stiffness, bulging fontanelle.

5.1.4 Chronic fever

Chronic fever is fever of more than two weeks' duration. Although chronic fever may occasionally be observed after microbial infection, more often patients suffer from a chronic disease (such as rheumatic fever) or a malignant disease. Usually temperature elevation is not as high as in acute fever. By contrast with acute fever, it is less easy to directly identify the causative agent if the fever is of microbial origin. Therefore specific serological tests may help to establish a diagnosis. The flowchart in Figure 5.2 provides guidance in the diagnosis of chronic fever.

Pyrexia of unknown origin is fever of >38.3 °C on several occasions that lasts more than three weeks' duration and no diagnosis can be established.

5.1.5 Guidelines for laboratory investigations

Total and differential white blood cell count

The total white cell count (WBC) does not provide a diagnosis, but provides the physician with an indication of the type of infection in a patient. Causes of an increased white count include most bacterial infections (e.g. septic abortion, septicaemia, pneumonia, bacterial meningitis), parasitic infections and allergic reactions, inflammation and leukaemias. Certain bacterial infections, such as typhoid fever (*Salmonella typhi*) and brucellosis, cause a reduction in the white count. Certain drugs may also reduce the white blood cell count, e.g. chloramphenicol, anti-tuberculous drugs. It is important to remember that the normal reference interval of white blood cell concentrations varies with age of the patient. Newborns normally have white blood cell levels that are far above the normal WBC levels in adults.

The total white cell count must be made at the same time as the differential count so that the actual number of each type of cell can be calculated. This provides the clinician with very useful information. For example, an increase in lymphocytes suggests a viral infection and an increase in neutrophils suggests a bacterial infection. An increase in eosinophils suggests a parasitic infection or allergies. An increase in monocytes suggests tuberculosis, brucellosis, chronic inflammation, mononucleosis or tumours.

The flow chart on chronic fever (Figure 5.2) suggests differential diagnoses for different white cell count types.

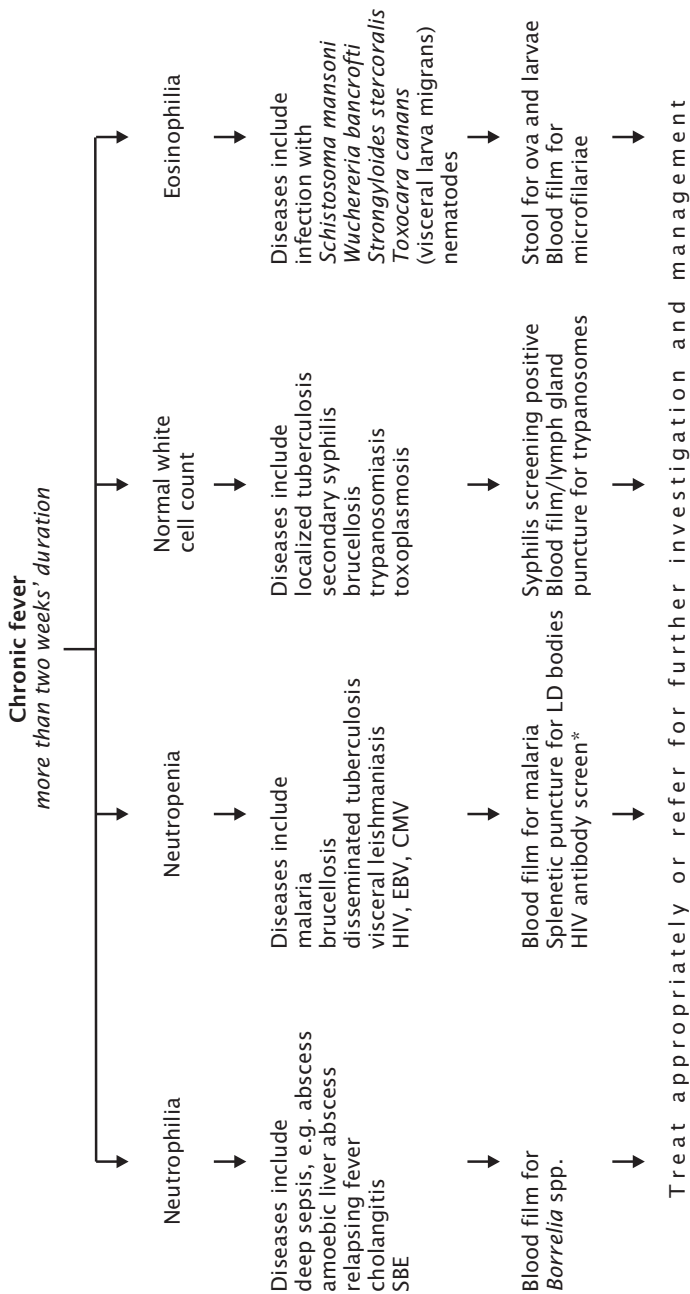
The diagnosis of typhoid fever is difficult to confirm in the peripheral clinic, where blood cultures (the only exact test for typhoid fever) are usually not available. The diagnosis is made using a combination of the clinical symptoms (fever, abdominal pain, headache), signs (slow pulse rate, splenomegaly) and the total white blood count (neutropenia and eosinopenia). The Widal test is misleading and should no longer be used. Patients without fever are not suffering from typhoid fever (although they may be carriers of *Salmonella typhi*), and the Widal test cannot be interpreted in these patients. Carriers can only be diagnosed by culture of the stool and urine.

Thick blood film (blood slide)

The thick blood film is examined by microscopy for the detection of blood parasites. A thick blood film should be ordered even if the patient has already taken antimalarial drugs. It may take two or three days after effective treatment for the blood film to become negative for malaria parasites. If treatment is ineffective, the blood film remains positive.

Plasmodium trophozoites are the active form of malaria infection in blood and are present when the patient has symptoms of malaria. If trophozoites of *P. falciparum* malaria are detected, the level of parasitaemia should be measured by counting the trophozoites against 200 white blood cells in a thick blood film. This is important in order to:

- measure the severity of the infection
- monitor the response to treatment
- recognize resistance to treatment as soon as possible.



*Test may not be available.

Figure 5.2 Flowchart for the diagnosis of chronic fever

Thin blood films are used to confirm malaria parasite species, as the appearance (morphology) of parasites is better preserved. Other blood parasites, such as trypanosomes, *Borrelia* and microfilariae, may also be seen on thin blood films.

It is possible that a blood film may be negative in a patient who has malaria. If the parasite count is very low, parasites may be missed on the blood film. In addition, patients with severe (cerebral) malaria may have negative blood films because the late forms of *P. falciparum* (schizonts) become fixed to the capillary walls of internal organs (such as the brain). Therefore, the treatment of severely ill patients for malaria may be justified even when the blood slide is negative. In patients who are not severely ill, the blood slide may be repeated two or three times, in order to confirm the diagnosis. If the blood slide still remains negative, it is unlikely the patient has malaria.

Gametocytes seen in the blood film are not a cause of fever. Gametocytes are the sexual form of the malaria parasite and are not active until they are taken up by a biting mosquito. Gametocytes appear after untreated or poorly treated malaria infections and may persist in the blood for up to five weeks. If the patient has fever and gametocytes are seen, look for another cause of fever, such as trophozoites in the blood, or another cause of fever altogether, e.g. otitis media.

Malaria has no specific symptoms and signs to distinguish it from other febrile illnesses. It is therefore not possible to make a diagnosis of malaria on clinical grounds alone. The diagnosis of malaria must be confirmed by demonstrating the presence of parasites in blood. "Clinical malaria" is not a recognized medical entity and has resulted in a great overdiagnosis of malaria infection. This problem has contributed to the increasing resistance of malaria parasites to treatment drugs.

Counting malaria parasites

Counting malaria parasites against 200 white blood cells is the recommended method for measuring parasite density in a thick blood film. Other methods, e.g. the plus (+) system, or using the terminologies "mild", "moderate" or "severe", are not recommended because these methods are based on the opinion of the observer and are affected by the thickness of the

blood film. For example, two thick films prepared from the same blood sample could be prepared differently so that one film is spread more thinly than the other. In the thinner blood film, there will “appear” to be fewer malaria parasites. This could mislead the clinician into believing that the parasite count is decreasing and the treatment is effective, which could lead to a dangerous management decision for the patient.

In malaria infection white cell count is used as a marker against which to measure the rise and fall in the parasite count by microscopy. A comparison with red blood cell count is obsolete, because red cell counting by microscopy is far too imprecise.

Table 5.2 illustrates how the parasite count can be used in clinical practice.

When blood cells are counted using an automated cell counter, the count of parasite infected red blood cells per 1000 red blood cells provides a more accurate estimate, since the assumption must not be made that the white blood cells remain constant in patients suffering from malaria.

Parasite counting is only used in *P falciparum* infections. In other malaria infections, parasite counts are too low for counting to be of any value. In addition, drug resistance is not such a major problem as in *P falciparum* infections. Other parasites, such as *Trypanosoma*, *Borrelia* and microfilariae, are never counted.

Table 5.2 **Parasite count during malaria infection**

| Day 0 | Day 3 | Day 7 | Day 14 | Assessment |
|-------|-------|-------|--------|---|
| 680. | 160 | 0 | 0 | Good response to therapy |
| 790 | 280 | 176 | 0 | Parasites not cleared by Day 7; change to second-line therapy |
| 520. | 60 | 490 | | Resistance to therapy; change drug |
| 2460 | 2536 | 2795 | | Resistance to therapy; change drug |

Lymph gland puncture

Lymph glands are enlarged in the chronic form of trypanosome infection and in tuberculosis infection and also some malignant diseases. In developing countries, lymph gland puncture is mainly performed to detect *Trypanosoma gambiense* if none are seen in a thick blood film and for tuberculosis. The fluid is examined using a wet preparation technique and staining as for a thin blood film for trypanosomes, and using the Ziehl–Neelsen staining technique for acid-fast bacilli.

Cerebrospinal fluid and other body fluids

Simple tests on cerebrospinal fluid and other body fluids, e.g. joint fluid, pleural fluid, peritoneal (ascitic) fluid, are extremely useful in the preliminary diagnosis of meningitis and other infections. Macroscopic appearance is vital: if the fluid is cloudy, there is likely to be infection present.

Cerebrospinal fluid is one of the most urgent samples to be examined in the laboratory. Before collection of cerebrospinal fluid and other body fluids the laboratory should be informed in advance.

The total white cell count in body fluids other than blood is normally fewer than 5 WBC/mm³ (fewer than 30 WBC/mm³ in neonates). An increased neutrophil count suggests bacterial infection, while an increased lymphocyte count suggests a viral infection or chronic infection, e.g. tuberculosis. In cerebrospinal fluid, the expected results in common forms of meningitis are listed in Table 5.3. Common and less common bacterial pathogens responsible for meningitis are listed in Table 5.4.

Table 5.3 WBC in cerebrospinal fluid of patients suffering from infection

| Cerebrospinal fluid- WBC count/mm³ | Predominant WBC type | Type of meningitis |
|--|-----------------------------|---------------------------|
| 500–2000 | Neutrophils | Bacterial |
| 50–500 | Lymphocytes | Tuberculous |
| 20–500 | Lymphocytes | Viral |

Table 5.4 Bacteria causing meningitis in adults and infants

| Patient group | Common pathogens | Gram stain reaction | Less common pathogens | Gram stain reaction |
|----------------------|------------------------|---|--|-----------------------------|
| Neonates | <i>E. coli</i> | Gram-negative bacillus | <i>L. monocytogenes</i> | Gram-positive coccobacillus |
| | Group B streptococcus | Gram-positive coccus | <i>S. pneumoniae</i> | Gram-positive coccus |
| | | | <i>Pseudomonas</i> spp. | Gram-negative bacillus |
| | | | <i>St. aureus</i> | Gram-positive coccus |
| Infants and children | <i>H. influenzae</i> | Gram-negative bacillus | <i>St. aureus</i> | Gram-positive coccus |
| | <i>N. meningitidis</i> | Gram-negative intracellular diplococcus | Gram-negative bacilli, e.g. <i>E. coli</i> | Gram-negative bacillus |
| | <i>S. pneumoniae</i> | Gram-positive coccus | | |
| Adults | <i>N. meningitidis</i> | Gram-negative intracellular diplococcus | <i>L. monocytogenes</i> | Gram-positive coccobacillus |
| | <i>S. pneumoniae</i> | Gram-positive coccus | <i>St. aureus</i> | Gram-positive coccus |
| | | | Gram-negative bacilli, e.g. <i>E. coli</i> | Gram-negative bacillus |

If antibiotic treatment has already been started, Gram stain may be negative. It may be possible to identify the causative agent using commercially prepared latex agglutination tests. However, these are very expensive.

In general, an increase in protein indicates an infection. Increased protein may also indicate blockage of the spinal canal or a tumour. The blood sugar must always be tested at the same time. Normal cerebrospinal fluid

glucose is approximately 70% of the blood glucose level. A reduced glucose level indicates bacterial infection.

In endemic areas cerebrospinal fluid must always be examined in trypanosome infection to differentiate early from late infection. This has important implications for drug choice and management. In these cases, an increase in leukocyte count and protein level may also be considered as an indication of cerebrospinal fluid involvement.

In patients with neurological complications in relapsing fever, *Borrelia* organisms may be seen in the cerebrospinal fluid deposit stained with a Romanowsky stain.

5.1.6 HIV infection

Infection with the human immunodeficiency virus (HIV) is a cause of persistent fever (> one month)—one of the features of acquired immune deficiency syndrome (AIDS). Other features of HIV infection include generalised lymphadenopathy, oral-pharyngeal candidiasis, recurrent bacterial infections (pneumonia, meningitis, septic arthritis, impetigo, osteomyelitis, etc), tuberculosis, chronic diarrhoea, central nervous system disease, skin rash (impetigo, eczema, generalized pruritic dermatitis), Kaposi sarcoma and failure to thrive (in children). The diagnosis of HIV infection is made using an HIV screening test to detect antibodies to HIV in serum. In an individual with no symptoms and signs of AIDS, two tests employing different principles are carried out to confirm the diagnosis. In patients with clinical criteria for AIDS, a single test is sufficient. The HIV test may be negative in the early stages of the disease, before antibodies have developed (window period). The test may also be negative in the very late stages of the disease, when the immune system is unable to produce antibodies.

Children born to HIV infected mothers may have a positive HIV test up to 18 months of age due to the presence of maternal antibodies, even if the child is not infected. Children with symptoms and signs of AIDS most likely have HIV infection. Children of more than 18 months of age with a positive HIV test have HIV infection.

The staging of HIV infection is made using a combination of clinical and laboratory criteria. The 1993 revised Centers for Disease Control and Prevention (CDC) classification is given below.

| <i>CD4 count categories</i> | | <i>Clinical category</i> | | |
|-----------------------------|------------------------------------|--|--|----------------------------------|
| | | A | B | C |
| | CD4 count/μL | Asymptomatic, acute primary infection, persistent generalized lymphadenopathy | Symptomatic, not A or C, indicative of defective cell-mediated immunity | AIDS indicator conditions |
| 1 | ≥ 500 | A1 | A2 | A3 |
| 2 | 200–499 | B1 | B2 | B3 |
| 3 | < 200 | C1 | C2 | C3 |

CD4 counts: should be based on the lowest recorded accurate CD4 count, not necessarily the most recent one.

Clinical categories: apply to adults (> 13 years) with documented HIV infection. Once a category C condition has occurred, the patient remains in category C.

Shaded areas: AIDS.

Clinical conditions

Category A

Acute HIV infection (fever, joint pains, generalised lymphadenopathy, maculopapular rash)

Persistent generalized lymphadenopathy

Category B

Oral candidiasis

Frequent vaginal/vulval candidiasis

Persistent fever

Persistent diarrhoea

Herpes zoster (more than 1 episode/more than one dermatome)

Cervical abnormalities/cervical cancer

Pelvic inflammatory disease/tubo-ovarian abscess

Peripheral neuropathy

Category C

Opportunistic infection

Malignancy

Candida infection of oesophagus, trachea, bronchi, lungs

Invasive cervical cancer

Persistent diarrhoea due to *Cryptosporidium*, *Isospora*

Kaposi sarcoma

Cytomegalovirus infection

Burkitt lymphoma

Pneumocystis carinii pneumonia

Non-Hodgkins lymphoma

Recurrent bacterial pneumonia

Recurrent *Salmonella* septicaemia

Toxoplasmosis brain abscess

Cryptococcus neoformans meningitis

Herpes simplex extensive skin infection or involving lungs/oesophagus

Mycobacterium avium complex infection

Others

HIV wasting syndrome (weight loss > 10% body weight)

HIV-related encephalopathy

The 1994 revised Centers for Disease Control and Prevention classification for children less than 13 years of age is given below. HIV infected children are classified according to their immunological status (based on CD4 counts) or their clinical status.

CD4 counts

| Immunological category | Age | | | | | |
|------------------------------|----------|-------|-----------|-------|------------|-------|
| | < 1 year | | 1–5 years | | 6–12 years | |
| | /μL | % | /μL | % | /μL | % |
| 1 no immunosuppression | 1500 | 25 | 1000 | 25 | 500 | 25 |
| 2 moderate immunosuppression | 750–1499 | 15–24 | 500–999 | 15–24 | 200–499 | 15–24 |
| 3 severe immunosuppression | <750 | <15 | <500 | <15 | <200 | <15 |

Clinical category

Category N: asymptomatic

No signs and symptoms considered to be the results of HIV infection

Only ONE of the conditions listed in Category A

Category A: Mildly symptomatic

Lymphadenopathy (> 0.5 cm at more than one site – bilateral = one site)

Hepatomegaly

Splenomegaly

Dermatitis

Parotitis

Recurrent upper respiratory tract infection, sinusitis, otitis media

Category B: moderately symptomatic

Anaemia (Hb < 80g/L); neutropenia (< 1000/ μ L); thrombocytopenia (<100 000/ μ L) for more than 30 days

Bacterial pneumonia, meningitis or sepsis

Oropharyngeal candidiasis for > 2 months (children > 6 months of age)

Cardiomyopathy

Cytomegalovirus infection (onset before 1 month of age)

Diarrhoea, recurrent or persistent

Hepatitis

Herpes simplex stomatitis, recurrent (> 2 episodes in 1 year)

Herpes simplex bronchitis, pneumonitis, oesophagitis (onset before 1 month of age)

Herpes zoster (at least 2 episodes; more than 1 dermatome)

Leiomyosarcoma

Lymphoid interstitial pneumonia

Nephropathy

Persistent fever (> 1 month)

Category C: severely symptomatic

Serious bacterial infections, multiple or recurrent (at least 2 culture confirmed) within a 2 year period (septicaemia; pneumonia; meningitis; bone/joint infection; abscess (excluding skin, otitis media))

Candida infection: oesophageal, pulmonary (bronchi, trachea, lungs)

Cryptococcus infection, extra-pulmonary

Persistent diarrhoea with *Cryptosporidium*, *Isospora*

Cytomegalovirus disease (onset after 1 month of age)

Herpes simplex mucocutaneous infection, bronchitis, pneumonitis for more than 1 month (onset after 1 month of age)

Mycobacterium infection, disseminated

Pneumocystis carinii pneumonia

Kaposi sarcoma

Lymphoma of brain

Burkitt lymphoma

Salmonella septicaemia (non-typhoid); recurrent

Toxoplasmosis brain abscess (onset after 1 month of age)

Encephalopathy (present for more than 2 months; no other concurrent illness): failure to attain developmental milestones; impaired brain growth; acquired symmetric motor deficit

Wasting syndrome: weight loss > 10%; <5th percentile on weight for height chart on 2 consecutive measurements

Persistent fever (> 30 days)

5.1.7 Guidelines for diagnostic imaging

X-ray

In patients where chronic sinusitis is not responding adequately to treatment, a standard series of radiographs of the sinuses: anteroposterior (AP), lateral and AP, Walters—or occipitomeatal—and lateral) might be justified. Frontal and maxillary sinuses are well demonstrated by a standard AP and a Walters projection, the latter specifically to expose the maxillary sinuses sufficiently well. When densities in one or both of the maxillary sinuses are observed, it is important to know whether fluid is present. An additional Walters projection with the patient's head tilted some 10–20 degrees to the right or left will normally solve that problem easily (water–air line stays horizontal!).

Inflammatory processes, and especially abscesses originating from the teeth, are mostly diagnosed clinically, and diagnostic imaging is normally not indicated. However, when a clinical diagnosis cannot be made, the presence of an abscess within the bony structures can be fairly well demonstrated with conventional radiography.

With persisting clinical problems, radiological examinations may be considered to exclude more serious diseases, such as malignant disease, or inflammatory processes. It is important to obtain images of good diagnostic quality including all necessary projections, and such examinations should not be carried out with mobile X-ray equipment: such equipment will normally produce images of inferior quality. This is especially true for lateral projections of the lumbar spine and the lumbosacral junction.

When ordering X-ray examinations of the spine, it is crucial to communicate the clinical findings to the radiologist or technician in charge of the examinations; the various parts of the spine must be targeted separately. A “whole column” or “thoracolumbar column” in one exposure in order to save film should not be carried out as even in children this will produce an inadequate film. A sufficiently good quality image needs to be achieved. Otherwise, the radiation exposure to the patient as well as the use of resources is questionable.

Clinical symptoms, mostly pain, in the extremities and joints should be referred for diagnostic imaging as soon as possible when malignancy or an inflammatory process is suspected. High-quality radiography will give

sufficient diagnostic information to decide on the treatment to be given. Inflammatory processes such as osteomyelitis are normally not seen until 10–14 days after onset. In such cases, a “negative” X-ray does not exclude the presence of bone infection, and the examination should be repeated after some days if the clinical symptoms persist or become worse.

The reasons for symptoms such as pain, swelling, or reduced motion of joints can often be diagnosed clinically. In the early stages, acute inflammatory processes can be diagnosed on X-ray by the presence of fluid in the joint. In the later stages, there will be damage to the bony structures. Inflammatory processes may be recognized when bony structures are already affected or eventually damaged.

Ultrasound

One of the most outstanding sonographic diagnoses in tropical diseases presenting with fever is amoebic liver abscess. The abscess appears as a hypoechoic round lesion, and is sometimes associated with pleural effusion and/or pericardial effusion. The wall of the abscess is usually thin, and the size can vary between small and filling almost the whole lobe of the liver. Multiple abscesses may also occur. Since the abscess contains necrotic material and not pus, gas-forming organisms are not present and hyperechoic areas are missing. The appearance of the lesion does not exclude other causes of disease affecting the liver. In 80%–90% of cases, the right lobe of the liver is affected. In about 70% of cases, the abscess is single.

During treatment sonographic control is compulsory. At the start of treatment, the abscess may increase in size; and the reduction in size of a large abscess may take several weeks. Sometimes calcification remains for months or years.

In developing countries, extrapulmonary tuberculosis is common. Abdominal tuberculosis with big para-aortic lymph nodes may be detected. The kidneys may be infected, and miliary tuberculosis of the liver and the spleen is sometimes visible (often related to HIV infection). These forms of tuberculosis can be combined with ascites.

The diagnosis of pleural effusion or empyema associated with pulmonary tuberculosis can also be made on ultrasound scanning (see sections on respective diseases).

5.2 Anaemia (pallor)

Anaemia is a symptomatic diagnosis in individuals who have a reduced red blood cell mass. The red cell mass is not routinely determined; instead surrogate measurements are made, such as the red blood cell concentration, haematocrit and/or blood haemoglobin concentration.

Haemoglobin is contained inside red blood cells. Red blood cells are produced in the bone marrow and circulate in the bloodstream. The function of haemoglobin is to carry oxygen from the lungs to the body tissues. In anaemia the amount of red pigment (haemoglobin) in the blood is below the normal level. Haemoglobin levels are the same in healthy persons of different ethnic groups, but vary with altitude, sex and age. The normal reference intervals for haemoglobin in blood in subjects living at altitudes below 1300 m are:

| | |
|-----------------------------------|-------------|
| neonates (<24 hrs) | 160–250 g/L |
| children aged 6 months to 6 years | 110–150 g/L |
| children aged 6–14 years | 120–160 g/L |
| adult males | 130–180 g/L |
| adult females, non-pregnant | 120–160 g/L |
| adult females, pregnant | 110–140 g/L |

It is very important to recognize anaemia early. Anaemia is an unhealthy condition: patients who are anaemic may not be able to carry out their normal daily activities. Children who are anaemic may function poorly at school and may not be able to play well in sports. Anaemia also affects the normal physical and mental development of infants. In pregnancy, anaemia may slow the growth of the baby in the uterus leading to a low-birth-weight infant and increased risk of death of the baby.

Many blood transfusions may be avoided if anaemia is detected and treated early. If patients with mild or moderate anaemia are treated until the haemoglobin reaches normal levels, then diseases that cause an acute fall in haemoglobin such as malaria will not lead to dangerously low levels that require transfusion. Unfortunately, the importance of mild anaemia is not recognized. Mild anaemia is frequently not detected and often it is ignored.

It should be remembered that although blood transfusions can be life saving, they can also be at risk for infection—particularly in countries with a high prevalence of bloodborne disease—or dangerous in case of immunoincompatibility. Subjects who have even mild signs of anaemia should be prevented from blood donation.

5.2.1 Causes of anaemia

Anaemia is not a disease itself, but is due to underlying disease or disorder in the patient. This is important to remember, as the correct management includes treating the cause as well as replacing essential substances. Some causes of anaemia are serious illnesses that may endanger the life of the patient. The various forms of anaemia can be systematically distinguished according to the underlying pathological causes and the microscopic features of red blood cells.

Etiological classification of anaemias

Primary(nonacquired) anaemias

Non-regenerative anaemias

Proliferation defects

Erythropoetic displacement

Stem cell proliferation defect

Acute leukaemias

Myeloproliferative syndromes

Lymphomas

Tumour metastases

Storage diseases

Regenerative anaemias

Increased haemolysis

RBC membrane defects (hereditary spherocytosis, elliptocytosis,

paroxysmal nocturnal

haemoglobinuria),

haemoglobinopathies (thalassaemias,

Hb-H disease, sickle-cell disease),

Enzyme defects (G6PD deficiency)

Secondary (acquired) anaemias

| | |
|--------------------------------|--|
| Malnutrition | Iron, vitamin B12, folate, iodine deficiency |
| Intoxication | Alcohol, drugs, poisons |
| Irradiation (aplastic anaemia) | |
| Chronic diseases | Chronic infection (e.g. hookworm, schistosomiasis, <i>Trichuris trichiura</i> , <i>Giardia lamblia</i> infection, tuberculosis, visceral leishmaniasis, trypanosomiasis, HIV), autoimmune disease, liver disease, inflammation, diabetes |
| Organ diseases | Liver, kidney, thyroid, small intestine, adrenal gland |
| Increased haemolysis | Immune haemolysis Toxins (e.g. malaria, Wilson disease) Mechanical destruction (e.g. heart valves) |
| Haemorrhage, acute or chronic | Injury post-partum haemorrhage; peptic ulcer, Malignancies |

In some countries secondary forms of anaemia (e.g. due to malaria) may dominate; in other countries they may be primary forms (e.g. in populations with a high prevalence of thalassaemias). Very often there may be combined factors causing anaemia (e.g. malnutrition and infections). The patients who are most susceptible to anaemia are pregnant and lactating women, premature infants and all children under 5 years of age.

There are four main causes of anaemia.

- *Deficiency anaemia*: insufficient dietary intake of essential nutrients (including iron, folic acid and vitamin B12) or increased demand (due to increased requirements in pregnancy and lactation, or to compensate for losses, such as iron loss in hookworm infection) to enable the bone marrow to produce enough haemoglobin and red cells.

- *Bone marrow suppression*: inability of the bone marrow to produce enough haemoglobin and red cells due to severe systemic infections (protozoan infection: leishmania), metabolic diseases, malignancy.
- *Haemolysis*: increased destruction of red cells, e.g. due to genetic conditions (e.g. sickle-cell anaemia) or acquired conditions, e.g. infection (e.g. malaria); drugs (e.g. methyl dopa), autoimmune disease, intoxication.
- *Bleeding*: a large loss of red cells, e.g. due to injury, peptic ulceration, bleeding from the uterus, or a slow chronic loss of red cells, e.g. due to hookworm, schistosomiasis, menorrhagia, intestinal tumour.

Note that a slow loss of red cells over a period of time leads to iron deficiency.

5.2.2 Investigation of anaemia

The clinical symptoms of anaemia vary considerably; they may be subtle or severe. The following symptoms can be seen in anaemic patients.

- *History*
 - headache
 - fatigue, weakness, dizziness
 - buzzing of the ear
 - irritability
 - sore tongue and mouth
 - dyspnoea, especially during exercise
 - tachycardia, especially during exercise
 - palpitations
 - oedema
 - fever
 - bloody diarrhoea, dark stool (melaena)
 - blood in urine
 - epigastric pain
 - heavy menstrual periods (menorrhagia)
 - amenorrhoea
 - loss of libido

acute joint pain, swelling
pregnancy status, multiple pregnancies, breast feeding
diet, able to feed/breastfeed.

- *Physical examination*

rapid pulse, rapid respiratory rate, raised temperature, low blood pressure

general appearance (wasting, marasmus)

low weight for age (children)

hair colour and texture (children)

oedema of both feet (children)

palpitations

pallor of conjunctivae, mucous membranes, nailbeds, palms and soles

smooth tongue

signs of cardiac insufficiency:

in adults: ankle oedema

crackles in lung bases (fluid)

enlarged liver

raised jugular venous pressure

in infants: grunting

intercostal or subcostal retractions

nasal flaring

enlarged liver

epigastric tenderness

pregnant uterus

red, hot joints (sickle-cell anaemia)

jaundice, enlarged liver, enlarged spleen

shock.

Note: clinical symptoms and signs of anaemia may not be clearly evident in mild anaemia.

- *Laboratory indicators*

The laboratory indicators commonly determined to establish the diagnosis of anaemia are:

- blood haemoglobin
- haematocrit
- red blood cell count.

These indicators measure concentrations rather than amounts; they are accepted as suitable with the assumption that the total blood volume in a patient remains unchanged. In patients suffering from chronic anaemia the blood volume is almost normal. However, in certain conditions the laboratory indicators may still be within the normal reference interval although the patient is anaemic (e.g. acute blood loss, where the erythrocyte concentration remains unchanged during the first hours). In pseudo-anaemia the indicators may be below the reference interval, although the individual may even have an elevated red cell mass: in pregnancy the red blood cell mass is increased; however the plasma volume is increased to a higher extent. Therefore a pregnant woman is pseudo-anaemic when the blood haemoglobin concentration is $120 \text{ g/L} > \text{Hb} > 110 \text{ g/L}$; true anaemia exists in pregnant women with less than 110 g Hb/L .

Although the above three laboratory indicators are measured in order to diagnose anaemia, additional laboratory indicators must be investigated to determine the exact cause of anaemia. They include the erythrocyte indices (RDW, MCV, MCH, MCHC), microscopic examination of the size and shape of red blood cells and additional blood constituents (e.g. reticulocyte count, serum iron, serum transferrin, ferritin) as well as specific investigations to exclude infectious microorganisms (e.g. parasites in blood, stool or urine, leishmania, *Mycobacterium tuberculosis*) or other disease causing anaemia (e.g. systemic lupus erythematosus, malignant diseases)

5.2.3 Microscopic features of anaemia

When a patient becomes anaemic, the red blood cells may change their size, shape and appearance, depending on the cause of the anaemia. Therefore, examination of the appearance of the red blood cells (red blood cell morphology) is a useful way of identifying the cause of anaemia. In an anaemic patient, the red blood cells may appear:

- *microcytic*: small, e.g. in iron deficiency, thalassaemia
- *macrocytic*: large, e.g. in folic acid deficiency, liver disease
- *normocytic*: normal, e.g. in malaria, or after haemorrhage.

These features are useful for the differential diagnosis of anaemia (Table 5.5)

There are features of red blood cells under the microscope that are specific for certain diseases, for example:

- spherocytes in hereditary spherocytosis
- sickle cells in sickle-cell anaemia
- basophilic stippling in heavy metal (lead) poisoning.

5.2.4 Guidelines for laboratory investigations

Haemoglobin estimation

Pallor is not a sensitive sign for the presence of anaemia. Patients with mild anaemia may not appear pale. When pallor is seen, the patient already has moderate or severe anaemia. Therefore the haemoglobin level must be checked in all patients who have a high risk of developing anaemia (children under 5, pregnant and lactating women).

The presence of symptoms and signs of anaemia may not correlate well with the haemoglobin level. Patients who develop anaemia rapidly, e.g. after haemorrhage, may have clinical symptoms and signs of anaemia when the haemoglobin level is just below normal. Patients who develop anaemia slowly, e.g. due to hookworm infestation, may not show clinical symptoms and signs of anaemia until the haemoglobin level is very low.

If the haemoglobin level does not match with the patient's clinical picture, consult the laboratory. Errors that can occur in the laboratory include poor mixing of blood, and excessive squeezing of the finger after a fingerprick. Therefore the result of haemoglobin measurement may be incorrect and may need to be repeated.

Physician should be familiar with the method of haemoglobin estimation used in the laboratory. Some methods are inaccurate because they use the principle of visual colour comparison (Tallqvist, Lovibond, Sahli). These methods cannot be used effectively to measure haemoglobin level or monitor a patient's response to treatment; therefore they should not be used in a hospital, even at bed side.

Table 5.5 Thin blood film microscopy

| Microcytic red cells | | | |
|--|------------------------------------|--|------------------------------|
| <i>Iron deficiency</i> | <i>Vitamin A deficiency</i> | <i>Chronic conditions (sometimes)</i> | <i>Lead poisoning</i> |
| <i>Main causes</i> | <i>Main cause</i> | | |
| Dietary deficiency | Dietary deficiency | Chronic infection | Basophilic stippling |
| Pregnancy | | Autoimmune disease | |
| Lactation | | Liver disease | |
| Bleeding | | Renal insufficiency | |
| conditions causing chronic blood loss, e.g. gastric ulcer, menorrhagia, malignancies | | Diabetes | |
| Infections causing chronic blood loss: hookworm, <i>Trichuris trichiura</i> , <i>Schistosoma mansoni</i> , <i>S. haematobium</i> , <i>Entamoeba histolytica/dispar</i> | | | |
| <i>Test</i> | | | |
| Stool for ova and larvae | | | |
| Stool for trophozoites and cysts | | | |
| Macrocytic red cells | | | |
| <i>Megaloblastic changes</i> | | <i>No megaloblastic changes</i> | |
| Oval macrocytes | | Large round red cells | |
| Hypersegmented polymorphs | | Megaloblasts | |
| Hypersegmented polymorph neutrophils | | | |
| Reduced platelet count | | | |

Table 5.5 Thin blood film microscopy (concluded)

| | |
|--|---|
| <p><i>Main causes</i></p> <p>Folic acid deficiency</p> <p>Dietary deficiency</p> <p>Pregnancy</p> <p>Lactation</p> <p>Chronic haemolysis, e.g. sickle-cell disease</p> <p>Vitamin B12 deficiency</p> <p><i>Diphyllobothrium latum</i> infection</p> <p>Haematinics</p> | <p><i>Main causes</i></p> <p>Liver disease</p> <p>Reticulocytosis due to: bleeding, haemolysis, response to haematinics, dietary deficiency</p> |
| <p><i>Test</i></p> <p>Stool for <i>D. latum</i> ova</p> | <p><i>Test</i></p> <p>Appropriate investigations</p> |
| <p><i>Findings</i></p> <p>Thin blood film may also show Howell–Jolly bodies</p> | <p><i>Findings</i></p> <p>Thin blood film may also show target cells, in liver disease</p> |

Note: reticulocytes are large, young red cells that stain slightly bluish.

Normocytic red cells

| Blood loss, acute (haemorrhage) | Blood destruction (haemolysis) | Bone marrow suppression |
|---|---|---|
| <p><i>Main causes</i></p> <p>Haemorrhage from gastrointestinal tract, uterus</p> <p>Trauma, including burns and surgery</p> | <p><i>Main causes</i></p> <p>Malaria</p> <p>Sickle-cell anaemia</p> <p>G6PD deficiency</p> <p>Autoimmune haemolytic anaemia</p> | <p><i>Main causes</i></p> <p>Malaria</p> <p>Cancer</p> <p>Chronic infections, e.g.: tuberculosis, amoebic abscess, trypanosomiasis, visceral leishmaniasis</p> <p>Chronic conditions, e.g.: malnutrition, renal disease, liver disease, aplastic anaemia, leukaemia</p> |
| <p><i>Test</i></p> <p>Appropriate investigations</p> | <p><i>Test</i></p> <p>Blood film for malaria</p> <p>Sickle-cell screen</p> | <p><i>Test</i></p> <p>Appropriate investigations</p> |
| <p><i>Findings</i></p> <p>Thin blood film may also show spherocytes, in burns</p> | <p><i>Findings</i></p> <p>Thin blood film may also show sickle cells, in sickle-cell disease</p> | |

The haematocrit is a screening test for haemoglobin that requires a supply of capillary tubes. Accurate methods for haemoglobin estimation and monitoring recovery after treatment are: haemoglobinometer, colorimeter, electronic blood cell counters.

Examination of the appearance of red cells is an excellent guide to the cause of anaemia. However, the correct recognition of red cell abnormalities requires considerable technical skill and experience, and this therefore may not be possible in every laboratory. In secondary anaemias, microcytic red blood cells are always a sign of a late stage of the existing anaemia.

Reticulocytes are young red cells that appear large and stain bluish on a peripheral blood film. They can be properly counted in a specially stained reticulocyte preparation. The presence of reticulocytes usually indicates normally functioning bone marrow. Reticulocytes are seen in three major instances: after bleeding, haemolysis, and during haematinic therapy for deficiency anaemia.

Sickle-cell screening

Haemoglobin S (HbS), an abnormal kind of haemoglobin, can be inherited from one (sickle-cell trait) or both (sickle-cell disease) parents. Patients with sickle-cell disease have the severe form of the disease, which is evident from childhood. Patients with sickle-cell trait have a normal blood picture, but may develop problems under certain conditions, e.g. anaesthesia. Patients from areas where sickle-cell disease is common should have a sickle-cell screen performed if they are planning to undergo general anaesthesia.

The sickle-cell screening test cannot distinguish patients with sickle-cell disease from those with sickle-cell trait. All patients who have a positive sickle-cell screening test should have a confirmatory test (haemoglobin electrophoresis) performed in a referral centre in order to fully characterize the type of haemoglobin abnormality. This assists in the management of the disease and also provides guidance if the patient is planning to have children.

Patients with sickle-cell disease are susceptible to infection with *Pneumococcus*, *Meningococcus*, *Haemophilus* and *Salmonella* species. Adult patients are also susceptible to severe *P. falciparum* malaria infections.

Thalassaemia screening

Thalassaemias are a group of haemolytic anaemias that are prevalent in Mediterranean and south-east Asian populations. Different forms of thalassaemia are distinguished by biochemical analysis (α -thalassaemia, δ - β -thalassaemia, β -thalassaemia). The inherited diseases are caused by an altered synthesis of haemoglobin, which results in insufficient formation of red blood cells. As in sickle-cell anaemia, the biochemical defect can be inherited from one parent (thalassaemia trait) or from both parents (thalassaemia disease). In populations with thalassaemia and sickle-cell disease, some patients may suffer from both disorders (HbS- β -thalassaemia disease).

Clinical signs

Subjects with thalassaemia trait (thalassaemia minor) usually do not show signs of anaemia. Thalassaemia patients with α -thalassaemia or δ - β -thalassaemia show signs of severe anaemia (thalassaemia major) accompanied by jaundice, gallstones, splenomegaly and ulcers on the lower legs. Often the faces of these patients have a mongoloid appearance which results from hyperactivity of the bone marrow, causing hyperplasia of the facial bones. Signs of anaemia are less pronounced in patients with β -thalassaemia.

Laboratory indicators

- RBC below normal
- erythrocytes with diffuse basophilic stippling
- poikilocytosis
- anisocytosis
- MCV reduced
- target cells
- reticulocyte number increased.

The differential diagnosis of thalassaemia is made by electrophoresis of the α -, β - and δ - chains of haemoglobin.

Glucose-6-phosphate dehydrogenase deficiency screening

Glucose-6-phosphate dehydrogenase deficiency (G6PD) is a group of X-chromosomal inherited diseases that is fully expressed only in males. The disease is transmitted only from the mother and never from father to son. Female carriers of the gene defect have two red cell populations, one of which behaves normal whereas the other population exhibits reduced G-6PD activity. Therefore some heterozygotic females appear to be normal, whereas other female carriers are fully affected. The disease is prevalent in Mediterranean and sub-Saharan populations, although the genetic patterns of G6PD deficiency in these groups are different.

In G6PD deficiency the lifespan of red blood cells is shortened, and the cells are haemolysed when exposed to certain drugs (e.g. primaquine during treatment of *P. vivax* malaria; phenylhydrazine-like drugs), vegetables (fava bean), diabetic acidosis, or during the neonatal period of life. Consequently patients with G6PD deficiency may develop anaemia that may occasionally be accompanied by hyperbilirubinaemia and the formation of methaemoglobin. In severe haemolytic episodes the patient may suffer from back pain and his urine may turn dark.

Laboratory indicators

- haemoglobin reduced
- elevated reticulocyte count
- Heinz bodies
- serum bilirubin elevated
- methaemoglobin
- haemoglobinuria.

Stool examination

Hookworm, *S. mansoni*, *E. histolytica* and *T. trichiura* infestation of bowel cause a slow loss of red blood cells leading to iron deficiency anaemia. Hookworm infestation also causes loss of proteins, and heavy infestation can lead to malnutrition. Heavy *G. lamblia* infestation may cause malabsorption and lack of essential nutrients. *D. latum* (the fish tapeworm) is an unusual helminth that consumes vitamin B12 in the bowel, leading to B12

deficiency and megaloblastic anaemia. It is found in persons who eat raw or undercooked fresh-water fish.

Guidelines for diagnostic imaging

X-ray

In thalassaemia, the skeleton shows signs of bone marrow hyperactivity (bone marrow hyperplasia).

Ultrasound

Sickle-cell disease involves various organs, and sonographic findings are important (ultrasound for hepatosplenomegaly, gallstones and renal inflammation/infection in sickle-cell disease). The kidneys and urinary system are often affected. Chronic inflammatory processes lead to parenchymal scarring, normally depicted as a focal indentation of the renal parenchyma associated with a dilated pelvicaliceal system. Septic kidneys can also occur, and pus may be visible within the collecting system as echogenic material that shifts with positional change. The liver is enlarged; the spleen is extremely enlarged and can even reach the pelvis.

5.3 Diarrhoea

Diarrhoea is a change in normal stool pattern characterized by passing three or more unformed stools in a 24 hour period, or a single stool with blood and/or mucous. Diarrhoea stool mixed with blood is called dysentery. Diarrhoea is due to a disease or infection in the bowel (jejunum and/or caecum) (enteral causes of diarrhoea) or secondary to a disease or infection elsewhere in the body (parenteral causes of diarrhoea).

Enteral causes of diarrhoea include:

- bacterial infections or toxins, e.g. infection with *Campylobacter jejuni*, *Vibrio cholerae*, *Escherichia coli*, *Staphylococcus aureus*, *Clostridium perfringens*, shigella (bacillary dysentery), salmonella
- viral infections, e.g. infection with rotavirus, Norwalk virus

- protozoan infections, e.g. infection with *Entamoeba histolytica/dispar*, *Balantidium coli*, *Giardia lamblia*, *Cryptosporidium parvum*, *Isospora belli*
- poisoning, e.g. kerosene, liquid paraffin
- malabsorption, probably due to repeated protozoan, bacterial and viral infections or allergic reactions (coeliac disease)
- lactase deficiency, often following bowel infections or kwashiorkor.
- malignancy of the bowel, e.g. carcinoma of the colon.
- helminthic infections (e.g. infection with *Trichuris trichiura*, *Strongyloides stercoralis*) and trematode infections (e.g. infection with *Schistosoma mansoni*) rarely cause diarrhoea in infants.

Some of the enteral causes of diarrhoea are associated with fever.

Bloody diarrhoea (dysentery) is always due to enteral causes.

Parenteral causes of diarrhoea include:

- malaria
- otitis media
- pneumonia
- measles
- urinary tract infection
- HIV infection
- disorders of the pancreas
- treatment with antibiotics.

Diarrhoea due to parenteral causes is more common in children and is usually associated with fever.

5.3.1 Types of diarrhoea

Diarrhoea can also be classified according to the presence or absence of blood in the stool (dysentery) and fever, respectively. These are the most important factors to note when making a diagnosis of the cause of diarrhoea. Diarrhoea can be classified as:

- *acute*: starts suddenly and lasts from a few hours up to one or two weeks. Bacterial infections usually cause diarrhoea within 24 hours, whereas viruses may cause diarrhoea more than two days after exposure, which may be combined with vomiting (see Tables 5.6a and 5.6b).

- *persistent* (relapsing or chronic): diarrhoea lasting two or more weeks. The causes may be bacterial or protozoan infection, allergic reactions (e.g. gluten) or enzyme defects (e.g. lactase deficiency).

5.3.2 Investigation of diarrhoea

When taking a history and examining a patient with diarrhoea, two factors should be kept in mind: the level of hydration and the cause of the diarrhoea.

The assessment of a patient with diarrhoea is summarized as follows (see Tables 5.6 and 5.7).

Table 5.6a **Acute diarrhoea with blood (less than two weeks' duration)**

| Fever | No fever |
|---------------------------------------|---|
| <i>Main causes</i> | <i>Main causes</i> |
| <i>Shigella</i> (bacillary) dysentery | <i>Entamoeba histolytica</i> * (amoebiasis) |
| <i>Schistosoma mansoni</i> | <i>Trichuris trichiura</i> |
| Rotavirus (in children) | <i>Giardia lamblia</i> |
| * <i>Salmonella enterocolitis</i> | <i>Balantidium coli</i> |
| <i>Campylobacter enterocolitis</i> | |
| <i>E. coli</i> (enteropathogenic) | |
| <i>Test</i> | <i>Test</i> |
| Fresh stool | Fresh stool |
| <i>Findings</i> | <i>Findings</i> |
| Pus cells, red blood cells | Red blood cells |
| | <i>E. histolytica/dispar</i> trophozoites |
| | <i>Giardia lamblia</i> |
| | <i>B. coli</i> trophozoites |
| | <i>S. mansoni</i> ova |
| | <i>T. trichiura</i> ova |

*occasionally with fever.

Table 5.6b Acute diarrhoea without blood (less than two weeks' duration)

| Fever | | Elevated temperature or no fever | |
|---|--|--|--|
| <i>Main causes</i> | <i>Main causes</i> | | |
| Salmonella enteritis | Viral gastroenteritis, e.g. rotavirus | Cholera (severe watery diarrhoea) | <i>Strongyloides stercoralis</i> (fatty diarrhoea) |
| Shigella (bacillary) enteritis | <i>C. perfringens</i> * | | |
| <i>Campylobacter</i> enteritis | <i>E. coli</i> (toxigenic)* | | |
| Malaria, especially <i>P falciparum</i> | <i>S. aureus</i> * | | |
| Almost any infection in a child: UTI, pneumonia, otitis media, tonsillitis, viral infection | <i>E. histolytica/dispar</i> | | |
| | <i>B. coli</i> | | |
| | Poisoning | | |
| <i>Test</i> | <i>Test</i> | <i>Test</i> | <i>Test</i> |
| Examine patient for local infection Blood film for malaria Fresh stool | Fresh stool | Fresh stool for dark field examination | Fresh stool |
| <i>Findings</i> | <i>Findings</i> | <i>Findings</i> | <i>Findings</i> |
| Pus cells | Negative in viral infections and food poisoning <i>E. histolytica /dispar</i> trophozoites <i>B. coli</i> trophozoites | Motile vibrios of <i>Vibrio cholerae</i> | <i>S. stercoralis</i> larvae** |

*food poisoning.

** Baermann test.

- *History*
duration of diarrhoea (how many days)
frequency of diarrhoea (how many times a day)
amount of diarrhoeal stool (quantity of stool)
consistency/colour of stool, e.g. watery, blood-stained, mucoid, fatty

Table 5.7 **Persistent (chronic) diarrhoea (more than two weeks' duration)**

| Fever and wasting | Blood, no fever | Fatty diarrhoea |
|---|--|---|
| <i>Causes include</i> | <i>Causes include</i> | <i>Causes include</i> |
| Tuberculous enteritis Visceral leishmaniasis <i>Cryptosporidium</i> , <i>Isospora</i> infection HIV infection | <i>Schistosoma mansoni</i> <i>Trichuris trichiuria</i> <i>E. histolytica/dispar</i> (amoebiasis) Colitis ulcerosa Crohn disease | <i>Giardia lamblia</i> (giardiasis) <i>Strongyloides stercoralis</i> Tropical sprue Chronic pancreatitis |
| <i>Test</i> | <i>Test</i> | <i>Test</i> |
| Modified stool Ziehl–Neelsen | Fresh stool | Stool concentration technique |
| <i>Findings</i> | <i>Findings</i> | <i>Findings</i> |
| <i>Cryptosporidium</i> oocysts | <i>E. histolytica/dispar</i> trophozoites <i>S. mansoni</i> ova <i>T. trichiura</i> ova | <i>G. lamblia</i> cysts |
| <i>Test</i> | | <i>Test</i> |
| Other specific concentration technique | | Other specific concentration technique |
| <i>Findings</i> | | <i>Other possibilities</i> |
| <i>Isospora belli</i> oocysts | | <i>Giardia lamblia</i> trophozoites <i>Strongyloides stercoralis</i> larvae |
| Treat appropriately | Treat appropriately | Treat appropriately |

vomiting
 excessive thirst
 ability to drink/breastfeed
 urine output
 lethargy, restlessness
 fever

abdominal pain
diet
other people affected, e.g. household
symptoms of other infections (see Section 5.1 on fever).

- *Physical examination*
general condition, e.g. lethargic, irritable, confused, unconscious
rapid pulse, rapid respiratory rate, raised temperature
sunken eyes
dry mucous membranes (mouth and tongue)
poor skin turgor
no tear production
sunken fontanelle
severe undernutrition
pallor
hair changes
hepatosplenomegaly
abdominal tenderness.
signs of other infections (see Section 5.1 on fever).

Guidelines for laboratory investigations

- Stool examination is not helpful in mild acute watery diarrhoea of up to two days' duration, except in severe diarrhoea in the case of suspected cholera. Stool examination is useful in acute dysentery and in persistent diarrhoea (more than two weeks' duration).
- Stool: macroscopic appearance, red cells, pus cells, bacteria of characteristic shape and motility, trophozoites, cysts, larvae, ova; concentration method.
- Blood slide for malaria.
- Haemoglobin.

Guidelines for diagnostic imaging investigations

- X-ray for bowel malignancy.

- Ultrasound for schistosomiasis, colitis ulcerosa, bacterial colitis, abdominal tuberculosis, diverticulitis and malignancies.
- Tests for other infections (see Section 5.1 on fever).
Other causes of fresh blood in stool which may occur without diarrhoea include:
 - carcinoma
 - *E. coli* infection
 - haemorrhoids
 - anal fissure
 - *S. mansoni* infection
 - causes of occult blood in stool include:
 - meat in the diet
 - drugs (aspirin)
 - parasite infections
 - malignancies.

Guidelines for laboratory investigations

Occult blood test (only applicable after food intake without meat)

Melaena is black stool smelling typically of blood. Melaena indicates significant bleeding from the stomach and/or upper intestinal tract. During the passage through the bowel the blood is altered, which explains the change in colour from red to black. After an intake of iron tablets, the stool also appears black which could be mistaken for melaena, except melaena stool is soft and tarry, and the stool in iron therapy is usually hard.

Direct stool examination

One of the most important examinations is the macroscopic appearance of stool. For example, a patient may report passing loose, bloody stools (dysentery), yet the stool appears normal. This is vital information for the clinician, who then needs to explore further the history given by the patient. The laboratory should always report on the macroscopic appearance of stool. Identification of enteric causes of acute mild to moderate watery diarrhoea is difficult and is not clinically important, as long as dehydration is

corrected. Causes include viral infections and mild bacterial infections, which do not require specific treatment. Acute watery diarrhoea may also be due to parenteral causes, such as malaria, which must be investigated. Stool examination is performed if the diarrhoea persists.

In severe watery diarrhoea, dark field microscopy examination of stool may give an immediate presumptive diagnosis of cholera, by recognizing the characteristic shape and motility of *Vibrio cholerae* organisms.

Immunocompromised patients, such as patients with AIDS, may develop severe and persistent diarrhoea due to the following intestinal organisms: *Entamoeba histolytica*, *Cryptosporidium parvum*, *Isospora belli*, *Cyclospora cayetanensis*, *Microsporidia*. *Cryptosporidium* is detected using modified Ziehl Neelsen stain of stool; *Isospora* is recognised by direct stool examination. *Cyclospora* and *Microsporidium* require specialized laboratory procedures for detection (fluorescent staining; special stains). Unfortunately treatment is rarely effective. In immunocompetent individuals, these infections cause self-limiting diarrhoea for which specific treatment is not required. Persistent diarrhoea in AIDS patients may also be due to the direct effect of HIV on the bowel wall cells.

In patients with bloody diarrhoea (dysentery), stool examination is helpful. Direct examination of stool in dysentery is a very rapid procedure, and a laboratory can be requested to perform this test as an emergency. Microscopic examination of stool distinguishes bacterial from parasitic causes of dysentery, which is vital for selecting appropriate management. In bacterial dysentery, stool contains red cells and pus cells, although the type of bacteria cannot be determined (this requires stool culture). Bacterial identification may be important for epidemiological purposes, e.g. during epidemics (see Chapter 6). In parasitic infection, trophozoites (*E histolytica/dispar*) and ova (*S mansoni*, *T trichiura*) are seen and require specific treatment.

Note: hookworm and malaria never cause bloody diarrhoea.

Enterobius vermicularis causes anal itching and is common in children. The correct specimen for investigation of *Enterobius vermicularis* infection is an anal swab, not stool examination.

If a patient reports seeing worms in the stool, a stool examination should be performed.

Larvae seen on examination of fresh stool are likely to be *Strongyloides stercoralis*. Active larvae seen in stale stool are likely to be hookworm, especially if hookworm ova are also seen. Other pathogens may also be present, e.g. *S. mansoni* ova.

In healthy individuals, *Cryptosporidium*, *Blastocystis hominis* and *Isospora belli* cause acute self-limiting watery diarrhoea (especially in children) for which specific treatment is usually not required. These protozoa may cause severe and persistent diarrhoea in patients with reduced immunity, e.g. HIV sufferers.

Trichomonas hominis infection is usually non-pathogenic. However, heavy infections may cause diarrhoea and require treatment.

Direct examination of stool for parasites is not a very sensitive test, as only a small part of the stool is examined. If in doubt, the stool examination may need to be examined by a concentration technique several times if necessary.

Guidelines for diagnostic imaging investigations

X-ray

In most cases, conventional, plain abdominal radiographs will add little information to what can be found clinically and from laboratory tests. Pathological calcifications indicating some sort of parasitic disease may be detected. Also, severe inflammatory bowel disease with dilatation of bowel loops can be observed. Furthermore, high-quality radiographs may reveal the presence of pathologic soft tissue masses (tumours) and displaced organs, but even in the hands of a well trained radiologist, the amount of information to be extracted from such images is limited.

Barium studies such as a small bowel “pass through”, or barium enema using either single or double contrast technique for the large bowel are good diagnostic tools when performed correctly. However, both

equipment (fluoroscopy with image intensifier) and well trained operators are required. Otherwise, such examinations are not recommended.

Ultrasound

Intestinal schistosomiasis (see Section 5.6 on jaundice).

5.4 Cough and shortness of breath

Cough is an explosive expiration to clear the airway of secretions and foreign bodies. Shortness of breath (dyspnoea) is an abnormally uncomfortable awareness of breathing. Coughing may be initiated voluntarily or as a reflex action. Coughing is an essential mechanism to keep the airway clear for the vital process of breathing. Shortness of breath is a change in the normal breathing pattern appropriate to the metabolic demands of the body.

Cough and shortness of breath share many of the same causes. Cough is due to irritation of the “cough receptors” in the respiratory mucous membranes, which can occur when there is infection or oedema (excess fluid) in the membranes. The major mechanism that induces shortness of breath is a reduction in the amount of oxygen carried in the bloodstream. The common causes of cough and shortness of breath are therefore due to:

- diseases of the respiratory system (airway or lungs)
- diseases of the heart.

Diseases of the respiratory system causing cough and/or shortness of breath are given below. The organisms listed are some of the common agents causing infections of the respiratory system.

- Viral infections: tonsillitis, laryngitis, pharyngitis, tracheitis, laryngo-tracheo-bronchitis (LTB or croup), bronchitis, bronchiolitis, pneumonia (respiratory syncytial virus, adenovirus, influenza virus, mumps virus, varicella-zoster virus, vaccinia, coxsackievirus).
- Bacterial infections: tonsillitis, bronchitis, emphysema, pneumonia, lung abscess, pneumonic plague (Group A β -haemolytic streptococci, *Streptococcus pneumoniae*, *Mycobacterium tuberculosis*, *Haemophilus influenzae*, *Staphylococcus aureus*, *Mycoplasma*

pneumoniae, *Klebsiella pneumoniae*, *Yersinia pestis*, *Bordetella pertussis*).

- Chlamydial infections: pneumonia (*Chlamydia pneumoniae*).
- Fungal infections: pharyngitis, pneumonia (*Candida* spp., *Aspergillus* spp.).
- Parasitic infections: pneumonia, pneumonitis (*Paragonimus westermani*, *Pneumocystis carinii*, larvae of *Ascaris lumbricoides*, *Strongyloides stercoralis*, hookworm).
- Asthma.
- Pneumothorax: spontaneous, emphysema bullae, lung abscess, malignancy, chest trauma.
- Pleural effusion: pneumonia, malignancy.
- Empyema: pneumonia, or spread from a nearby structure, e.g. subdiaphragmatic abscess.
- Pleural abscess: amoeba, tuberculosis.
- Pneumoconiosis: silicosis, coal dust, asbestosis.
- Malignancy: carcinoma of the bronchus.

Diseases of the heart or cardiovascular system causing cough and shortness of breath include the following.

- Heart failure due to rheumatic heart disease, ischaemic heart disease, left heart insufficiency, congenital abnormalities of the heart, hypertension, etc. Heart failure leads to accumulation of fluid in the lungs (pulmonary oedema).
- Myocarditis, e.g. caused by viral, bacterial or trypanosome infection
- Pericarditis, e.g. due to viral infection, bacterial infection (staphylococci, pneumococci, streptococci, meningococci, *Haemophilus influenzae*, *Mycobacterium tuberculosis*).
- *M. tuberculosis* is a cause of constrictive pericarditis.
- Pulmonary embolism.

Shortness of breath can occur in patients with:

- severe anaemia
- diabetic ketoacidosis and other severe metabolic disorders of the body
- septicaemia

- severe malaria
- severe kyphoscoliosis.

5.4.1 Types of cough and shortness of breath

Cough can be classified as:

- *Acute*: less than 3 weeks duration. Viral infections of the respiratory system are usually acute; also acute bacterial bronchitis or pneumonia, some forms of heart failure, and pulmonary embolus.
- *Chronic*: more than three weeks' duration. Causes of chronic cough include tuberculous pneumonia, passage of larvae of helminths through the lungs, trematodes, chronic bronchitis, bronchiectasis, malignancy, asthma.

Cough can also be classified as:

Productive: where there is production of sputum. The nature of the sputum can give important clues to the cause of the cough (see Table 5.8).

Non-productive: where there is no sputum. The cough is a dry cough.

Shortness of breath can be:

- *of sudden onset (acute)*: foreign body inhalation (in young children!), oedema of the glottis, pneumothorax
- *on exertion*: cardiac failure, anaemia, constrictive pericarditis
- *at rest*: pneumothorax, pulmonary embolus, heart failure, pleural effusion
- *on lying flat (orthopnoea)*: heart failure, chronic bronchitis
- *in acute episodes*: asthma, bronchiectasis
- *in acute episodes at night (paroxysmal nocturnal dyspnoea)*: heart failure
- *chronic*: severe chronic bronchitis or emphysema, asthma, pneumoconiosis, severe kyphoscoliosis.

Table 5.8 The nature of sputum

| White | Green | Grey-yellowish | Large amounts of pus |
|---|---------------------|--|--------------------------------|
| Allergic Viral infection | Bacterial infection | Tuberculosis | Lung abscess Bronchiectasis |
| Blood-tinged | Frothy/pink tinged | Frank blood | |
| Pneumonia Pneumonic plague <i>P. westermani</i> infection | Pulmonary oedema | Bronchitis Tuberculosis Malignancy Rheumatic heart disease <i>P. westermani</i> infection Pulmonary embolus | |

5.4.2 Investigation of cough and shortness of breath

- *History*
 - duration
 - aggravating, relieving factors
 - sore throat
 - sputum (colour consistency, amount)
 - wheezing
 - chest pain (localized)
 - ankle swelling
 - phlebitis of the legs
 - fever
 - weight loss
 - night sweats
 - occupation
 - contacts
 - smoking.

- *Physical examination*
rapid/irregular pulse, rapid respiratory rate, raised temperature,
 raised/lowered blood
 pressure
wheeze, stridor
pallor
cyanosis
inflammation/swelling of the pharynx
use of accessory muscles of respiration, chest indrawing
trachea deviated
asymmetric chest wall movement
displaced apex beat
heart murmurs (systolic, diastolic)
signs of cardiac failure.
bronchial breathing
rhonchi, crackles
pleural rub
phlebitis in the legs.

- *Physical examination, adults*
oedema
crackles in lung bases (fluid)
enlarged liver
raised jugular venous pressure.

- *Physical examination, infants*
grunting
intercostal and subcostal indrawing
nasal flaring
enlarged liver
hyperresonance/dullness to percussion.

- *Laboratory investigations*
sputum for acid-fast bacilli
sputum for larvae
sputum or stool for ova of *Paragonimus westermani*.

Guidelines for diagnostic imaging investigations

- Chest X-ray for pneumonia, pleural effusion, enlarged heart, pulmonary congestion, airway obstruction or pneumothorax.
- Ultrasound of the chest for pleural effusion, pleural lesions.

Children with pneumonia

For children at rest, danger levels for fast breathing are:

| | |
|-----------------------------|-------------------------------|
| Aged <2 months: | 60 or more breaths per minute |
| Aged 2 months to 12 months: | 50 or more breaths per minute |
| Aged 12 months to 5 years: | 40 or more breaths per minute |

In children with pneumonia, crepitations and bronchial breathing may be hard to hear. Therefore in children aged two months to five years, pneumonia is diagnosed as follows:

| | |
|---|-----------------------|
| Fast breathing only: | pneumonia |
| Fast breathing and chest indrawing: | severe pneumonia |
| Fast breathing, chest indrawing and cyanosis: | very severe pneumonia |

In children younger than two months of age, pneumonia must be considered if there is one or more of any of the following: fast breathing, severe chest in-drawing, convulsions, stopped feeding well, abnormally sleepy, stridor, wheezing, fever $>38^{\circ}\text{C}$, low temperature $< 35.5^{\circ}\text{C}$, central cyanosis, grunting.

Guidelines for laboratory investigations**Sputum for acid-fast bacilli**

The first sputum sample is collected when the patient is first seen at the health facility. The patient is then given a container to collect sputum early the next morning, before eating (early morning sputum sample), and the third sample is collected when the patient attends the health facility the next day. Three samples are therefore collected within two visits to the health facility.

Although three samples of sputum are usually examined for pulmonary tuberculosis, this is not a fixed requirement. If the first sputum sample is positive, a second sample is usually checked to ensure there are no clerical or administrative errors. A third sample is not required. If all three samples are negative (and the diagnosis is strongly suspected), several further samples may be requested, e.g. six or more.

Negative smears do not rule out pulmonary tuberculosis. Patients with pulmonary tuberculosis and immune deficiency, e.g. HIV infection, are more likely to produce negative smears.

P. westermani infection of the lungs may mimic pulmonary tuberculosis.

Guidelines for imaging investigations

X-ray

It is advisable to start with a simple posterior-anterior-radiograph with the patient in the upright position. If the patient is unable to stand, an anterior-posterior-radiograph of the chest with the patient on a stretcher or on the examination table will do. Major pathological processes such as pulmonary consolidation due to pneumonia (including tuberculosis), clinically significant atelectasis, tumours, heart failure with pulmonary congestion, lung abscesses, parasitic and fungal infections, and pleural fluid are demonstrated sufficiently well for initial diagnostic purposes. However, the image quality needs to be good. It is important that the examinations are performed in an X-ray department using stationary equipment and not with mobile equipment. Most patients can be transported (or can walk) to the X-ray department for examination. The use of mobile units should be restricted to those patients who cannot be moved.

Foreign bodies swallowed and stuck in the throat can usually be located by conventional radiography using one lateral projection of the region. However, a “normal” image does not exclude the presence of a foreign body since many such “articles”, including most fish bones, are not sufficiently radiopaque to be detected. When technically possible, additional lateral and AP projections taken during the swallowing of diluted contrast media (barium suspension or water-soluble contrast medium) may be of

help. However, such procedures normally require fluoroscopy and the presence of a radiologist.

Symptoms of upper airway obstruction and dysphagia may rarely indicate the presence of a retropharyngeal process, usually an abscess. Conventional X-ray examination such as a lateral radiograph of the neck structures may strengthen the suspicion or confirm the diagnosis; however more sophisticated and reliable diagnostic information cannot be obtained from conventional radiography alone. Computer tomography would be the method of choice if available. A very well trained ultrasound operator might be able to supply some diagnostic information, but that will highly depend on his or her skills.

Pain in the chest may have a multitude of causes. A proper clinical evaluation of the patient normally gives sufficient information to make a diagnosis and to decide on appropriate treatment. Diagnostic imaging should only be considered to confirm a clinical diagnosis. The diagnosis of *Echinococcus* infection of the lung is made by chest X-ray.

In the presence of symptoms indicating heart failure and pulmonary congestion, a proper clinical evaluation followed by appropriate treatment should be given the highest priority. A chest radiograph may be indicated when complications such as pneumonia are suspected, or when the patient's condition does not improve in spite of adequate treatment. It might be of some value to take a chest radiograph to evaluate the course of treatment, or before discharging the patient from hospital after treating the complications.

When diagnostic imaging for the diagnosis of pulmonary disease is needed, plain PA and lateral chest radiographs with the patient in the upright position will give sufficient diagnostic information to decide upon treatment. When the patient is unable to stand upright, a normal AP radiograph of the chest with the patient lying on her/his back on the examination table, will be enough (mobile X-ray equipment to be avoided whenever possible!). In such cases, additional valuable information on the presence and quantity of pleural fluid, can be obtained by placing the patient on her/his side, and making an examination with a horizontal X-ray beam (lateral decubitus position).

Ultrasound

Sonography may be of some value when evaluating pleural fluid and pathologic processes that are located close to, or affecting the, chest wall. Cardiac and pericardial disease may be visualized by ultrasonography (“echocardiography”). Such examinations require specially trained operators and often more sophisticated equipment than generally available in small hospitals and clinics. Congestion of the liver with or without ascites due to right heart insufficiency from congenital or acquired heart disease can be demonstrated.

5.5 Skin diseases

Diseases of the skin lead to changes in the appearance, feel and function of the skin. The hair and nails are part of the skin structure and may also be affected by the same diseases that affect the skin. Skin disease may be due to local or external factors or systemic diseases of the body. Alterations of the skin are among the best indicators of serious disease of the body. Clinicians must be able to distinguish skin diseases from those features on the skin that indicate an underlying disease, including malignant disease (e.g. breast cancer), infectious disease (viral [e.g. HIV, herpes], bacterial [e.g. leprosy] and parasitic [e.g. leishmania]), malnutrition, metabolic disease (e.g. Addison disease), systemic disease (e.g. lupus erythematosus). The most important diagnostic tool for identifying skin diseases is accurate observation.

Skin lesions may be caused by a range of agents.

- Viral infection: measles (rubeola), chickenpox (varicella), rubella, herpes (*Herpes simplex*, *Herpes zoster*), warts, molluscum contagiosum, dengue, etc.
- Rickettsial infection: typhus (*Rickettsia* spp.).
- Bacterial infection: impetigo (*Staphylococcus aureus*), erysipelas (Group A streptococci), cellulitis, folliculitis, furuncles (boils), abscesses (mainly from staphylococci), syphilis (*Treponema pallidum*), plague (*Yersinia pestis*), leprosy (*Mycobacterium leprae*), anthrax (*Bacillus anthracis*), tuberculosis (*Mycobacterium tuberculosis*), Buruli ulcer (*Mycobacterium ulcerans*), etc.

- Fungal infection: candidiasis, tinea, pityriasis versicolor (*Candida albicans*, *Trichophyton* spp., *Epidermophyton* spp., *Microsporum* spp.), Madura foot (*Actinomadura madurae*), etc.
- Protozoan infection: trypanosoma chancre (*Trypanosoma* spp.); cutaneous leishmaniasis (*Leishmania infantum*, *L. tropica*), Calabar swelling (microfilariae).
- Helminthic infection: onchocerciasis (*Onchocerca volvulus*), guinea worm (*Dracunculus medinensis*), cutaneous larva migrans (*Ancylostoma braziliense*), larva currens (*Strongyloides stercoralis*), etc.
- Ectoparasite infection: scabies (*Sarcoptes scabiei*), jiggers (*Tunga penetrans*), lice (*Pediculus* spp.), fleas, etc.
- Allergic conditions: urticaria, allergies to drugs (e.g. Stevens–Johnson syndrome, toxic epidermal necrolysis), food, chemicals, intestinal helminths, schistosomiasis (Katayama fever).
- Autoimmune disease: Werlhoff disease
- Inflammatory conditions: eczema, psoriasis, acne, pityriasis rosea, lichen planus.
- Blistering (bullous conditions): pemphigus, pemphigoid, erythema multiforme, dermatitis, herpetiformis.
- Connective tissue disorders: systemic lupus erythematosus, discoid lupus, scleroderma.
- Nutritional deficiencies: vitamin A deficiency, vitamin C deficiency (scurvy), niacin deficiency (pellagra), etc.
- Genetic conditions: albinism.
- Metabolic diseases: diabetes mellitus.
- Organ diseases: hepatic disease, adrenal disease.
- Blood disorders: sickle-cell disease, thalassaemias.
- Vascular disorders: varicose ulcers, atherosclerotic vessel disease.
- Injuries: cut wounds, ulcers, burns, calluses.
- Malignant disorders: squamous cell carcinoma, basal cell carcinoma, melanoma, Kaposi sarcoma.
- Others: vitiligo.
- Haemorrhagic fever: petechiae (dengue, Rift Valley, Congo–Crimean).

5.5.1 Types of skin lesion

Skin lesions are classified and described according to the following features:

- *flat lesions*: macules, petechiae (small spots of blood in the skin)
- *raised lesions*: papules, wheals, vesicles/bullae, pustules, nodules, cysts, abscesses, plaques, keloids
- *depressed lesions*: ulcers, scars, excoriation, sinuses, atrophy
- *shape*: linear, circular, serpiginous
- *arrangement*: single, grouped
- *distribution*: localized, regional, generalized, following a dermatome pattern, areas of pressure
- *exudate*: discharge, crusts, bleeding
- *colour*: red, pale, etc.
- *sensation*: itching, pain, anaesthesia.

Chronic ulcers on the skin are often due to irritation, as with bedsores, and they may become infected and inflamed as they grow. Very often the patient may have an underlying disease that reduces the resistance to external mechanic or invasive irritants. Patients may suffer from painful or painless chronic ulcers (see Table 5.9).

5.5.2 Investigation of skin disease

- *History*
 - fever
 - pain
 - itching
 - sensation (numbness, burning, altered sensation)
 - scaling
 - duration
 - site
 - drug history
 - occupation, exposure
 - diet
 - family members affected.

Table 5.9 Examination of chronic ulcers

| Painful | Painless |
|---------------------|---|
| Tropical ulcer | Leprosy |
| Guinea worm | Anthrax |
| Sickle-cell disease | Syphilis (gumma) |
| Varicose | Buruli ulcer |
| Atherosclerotic | Cutaneous leishmaniasis |
| | Tuberculosis |
| | Diabetes |
| | Malignancy |
| <i>Test</i> | <i>Test</i> |
| Sickle-cell screen | Skin smear or tissue fluid for acid-fast bacilli and other bacteria |
| | Skin biopsy or fluid for LD bodies |
| | VDRL |
| | Urine/blood for glucose |

- Physical examination**
 raised temperature, rapid pulse, rapid respiratory rate, high blood pressure
 general condition (emaciated, etc)
 pallor
 jaundice
 oedema
 hair and nail changes (hair loss, ridges, clubbing)
 mucous membranes (ulcers, lesions, bleeding)

lesion type: shape, arrangement, distribution, colour, edges (raised or not raised), surface features (smooth, rough, thickened), sensation.

lymphadenopathy (local, generalized)

lesion discharge, bleeding, scaling, scab.

- *Laboratory investigations*
 - skin scrapings for fungus
 - skin snip for microfilariae (onchocerciasis)
 - skin snip for Leishman–Donovan (LD) bodies
 - subcutaneous fluid for trypanosomes
 - skin slit smear for acid-fast bacilli
 - skin puncture for histological/microbial examination
 - blood slide for microfilaria (loa loa during the day, *Wuchereria bancrofti* at night)
 - skin smear or tissue fluid for bacteria/acid-fast bacilli
 - stool for ova and larvae
 - anal swab for *Enterobius vermicularis*
 - sickle-cell screen
 - serum for syphilis screening
 - urine and blood for glucose.
- *Diagnostic imaging investigations*
 - ultrasound for skin abscesses, Kaposi sarcoma and filariasis.

Guidelines for laboratory investigations

Many skin diseases are identified by inspection. Scabies is recognized by burrows (fine wavy dark lines a few millimetres long with a papule at one end); pediculosis (lice) by the presence of greyish-white nits (ova) on the hair shafts, which cannot be dislodged; active lice may also be seen. *Strongyloides stercoralis* (larva currens) causes an itchy wheal which comes and goes in a few hours; the dog hookworm (*Ancylostoma braziliense*) causes a slow moving wheal.

Many simple microscopic laboratory tests are available for the investigation of skin diseases. These should be used wherever possible to identify the cause.

In developing countries most causes of skin disease are infectious in origin. Some skin diseases are caused by sexually transmitted infections. These include venereal warts (condylomata lata caused by syphilis; condylomata acuminata caused by the human papilloma virus), the rash of secondary syphilis (non-itchy macular rash on the palms and soles), molluscum contagiosum (umbilicated papules caused by pox virus), pubic (crab) lice (caused by the louse *Phthirus pubis*) and scabies (caused by the mite *Sarcoptes scabiei*).

Differentiate chronic fungal infection from inflammatory or allergic conditions by examination of skin scrapings for fungal elements using the potassium hydroxide (KOH) technique. Do not treat fungal infection with steroid creams, which encourage the fungus to spread.

Many skin diseases (especially in children) are due to inadequate hygiene, and improve with daily washing of the body with soap and water, e.g. fungal skin infections, scabies.

Most skin conditions require several weeks of treatment to heal completely.

Skin diseases associated with acquired immune deficiency syndrome (AIDS) include generalised pruritic dermatitis, impetigo, eczema, scabies with secondary bacterial infection, recurrent *Herpes zoster* vesicular rash and Kaposi sarcoma of the skin and oral cavity. Recurrent severe “oral thrush” due to infection with *Candida* spp, and extensive mouth ulcers due to *H simplex* infection are significantly associated with AIDS. Kaposi sarcoma appears as red/purplish skin tumours that may also affect the gastrointestinal tract and lung.

Remember, secondary syphilis is a cause of skin disease, particularly a non-itchy macular rash on the palms and soles.

Guidelines for diagnostic imaging investigations

Ultrasound

Skin abscesses

Sonography can be useful if the appropriate probe is available (75 MHz). The size and position of the abscess, and its relationship to nearby organs can be demonstrated. This information may be important when deciding if surgical intervention requires general or only local anaesthesia.

Two special clinical features may occur.

- Pyomyositis, in which the abscesses affect the muscles. Pyomyositis is common between the ages of 5 and 25, and occurs in patients who live in poor conditions, or suffer from HIV and tuberculosis infection. In 90% of cases, the abscesses are caused by *Staphylococcus aureus*, but the reason for their occurrence is unknown. Single muscles or a group can be involved (mainly the quadriceps femoris and latissimus dorsi). Sonographically one can depict how many layers are affected and the size and depth of the infection can be described.
- Buruli ulcer is endemic in central Africa. It is caused by *Mycobacterium ulcerans* and affects only the upper layers of the skin.

Kaposi sarcoma

Kaposi sarcoma is particularly common in patients with AIDS. It can develop in all organs except the ovaries. In 90% of cases the sarcoma is found in males; however, the AIDS-related Kaposi sarcoma has no sexual preference. Tumour nodes in various forms can be depicted sonographically. The tumour nodes may be present on the skin as well as in internal organs.

Filariasis

Scanning can be helpful to see if the enlarged lymph nodes and redundant skin (hanging groins) of onchocerciasis are combined with hernias or hydroceles.

5.6 Jaundice

Jaundice is a yellow colouring of the skin, mucous membranes and sclera of the eyes due to an increase in bilirubin in the blood. Bilirubin is produced from the normal breakdown processes of haemoglobin. Bilirubin is normally present in small amounts in the blood, but this is clinically undetectable. When jaundice is clinically detectable, this indicates an underlying disorder.

5.6.1 Types of jaundice

There are three types of jaundice.

- *Pre-hepatic or haemolytic*: due to an increased amount of unconjugated bilirubin in the blood. This may be due to over-production of bilirubin (haemolysis) or defective conjugation of bilirubin in the liver. Haemolysis leads to increased urobilinogen in the urine, and the stools may appear slightly darker.
- *Hepatic*: due to liver disease. There is an increase of both conjugated and unconjugated bilirubin in the blood, and bilirubin appears in the urine. The stool appears normal.
- *Post-hepatic or obstructive*: due to obstructed excretion of bile. There is an increase of conjugated bilirubin in the blood, and bilirubin appears in the urine. In total obstruction, the stools appear pale and bulky, and there is an absence of urobilinogen in the urine.

5.6.2 Causes of jaundice

The causes of jaundice can be inborn errors of disease, incompatibility of blood groups, malnutrition, poisoning, side-effect of drugs, cancer or infections.

Pre-hepatic or haemolytic jaundice

- Increased destruction of red cells (haemolysis): malaria, G6PD deficiency, sickle-cell anaemia, Rhesus incompatibility in neonates, etc.
- Vitamin B12, folic acid deficiency (severe).
- Immaturity of the liver (neonates, prematurity).
- Congenital defects (rare).

Hepatic jaundice

- Viral infections of the liver: hepatitis A, B, C, E; yellow fever; Marburg/Ebola virus infection, Rift Valley fever, etc.
- Rickettsial infections of the liver: typhus.
- Bacterial infections of the liver: typhoid, syphilis, leptospirosis, *Borrelia* infection (relapsing fever), septicæmia, etc.
- Parasitic infections of the liver: malaria, toxoplasmosis, *Fasciola hepatica* infestation, *Echinococcus* cyst, *Entamoeba histolytica* liver abscess, etc.
- Drugs: isoniazid, phenytoin, methyldopa, halothane anaesthesia.
- Chemicals: aflatoxin, alcohol, insecticides, herbal remedies.
- Tumours of the liver: primary hepatoma, metastatic tumours from other sites.

Posthepatic or obstructive jaundice

- Gall stones.
- Biliary tract occlusion by *Ascaris lumbricoides* or *Fasciola hepatica*.
- Tumour of the head of the pancreas.
- Drugs: oral contraceptives, chlorpromazine, etc.
- Pregnancy (can cause cholestasis).
- Acute pancreatitis (due to oedema of the head of the pancreas), pancreas carcinoma.

5.6.3 Investigation of jaundice

- *History*
 - fever
 - hair changes
 - vomiting blood (haematemesis)
 - bruising, bleeding from the mucous membranes (mouth, nose, bowel)
 - abdominal pain: type, severity, duration
 - dark urine
 - dark or pale stools
 - skin rash, itching of the skin
 - drug ingestion, recent anaesthesia

alcohol ingestion
pregnancy status
family members.

- *Physical examination*
raised temperature, rapid pulse, rapid respiratory rate
emaciated condition
hair and nail changes
skin rash, bruising, striae, excoriations
lymphadenopathy
abdominal tenderness
enlarged liver or spleen
ascites
distended abdominal veins.
- *Laboratory investigations*
urine for bilirubin, urobilinogen
blood film for parasites, *Borrelia*
haemoglobin estimation
thin blood film for red cell morphology
total and unconjugated serum bilirubin
sickle-cell screen
stool for ova
syphilis screening
serum transaminases (ALT, AST)
alkaline phosphatase
serum amylase
hepatitis virus antibodies (HAV, HBV, HCV).
- *Diagnostic imaging*
X-ray for gallstones
ultrasound for liver cirrhosis, liver tumours, *Echinococcus* cysts,
gallstones and other gall bladder conditions, pancreatic tumour
or inflammation, enlarged biliary tract system.

Guidelines for laboratory investigations

A summary of the laboratory findings in the different types of jaundice are listed in Table 5.10.

Tests for viruses causing hepatitis (hepatitis B, C, etc) are serological tests carried out in laboratories with these facilities. A viral haemorrhagic fever screen is carried out by national or regional reference laboratories. Viral hepatitis due to hepatitis B and C viruses is a major complication of HIV/AIDS.

Table 5.10 Laboratory findings in jaundice

| | Pre-hepatic | Hepatic | Post-hepatic |
|--|---|--|--------------|
| <i>Urine</i> | | | |
| Bilirubin | 0 | + | ++ |
| Urobilinogen | ↑ | + | 0 |
| <i>Serum</i> | | | |
| Conjugated bilirubin | N | ↑↑ | ↑↑↑ |
| Unconjugated bilirubin | ↑↑ | ↑ | ↑ |
| <i>Indicative results of other tests</i> | Blood film for malaria Hb Sickle-cell screen Thin blood film for sickle cells, megaloblastic changes | Liver function tests: ALT, AST Alkaline phosphatase, amylase, γ -glutamyl transferase HAV, HBV, HCV antibodies Stool for <i>Ascaris lumbricoides</i> ova Blood film for parasites, <i>Borrelia</i> Syphilis screening test Blood cultures Serology for antibodies to <i>E. histolytica</i> | |

Key:

0: no bilirubin.

Test results of semiquantitative tests (urine dipstick): + slightly elevated, ++ elevated; +++ strongly elevated;

Quantitative measurements in serum: ↑ slightly above normal, ↑↑ elevated, ↑↑↑ strongly elevated.

Toxoplasmosis is usually an asymptomatic infection and reactivation of the disease is a feature of patients with acquired immune deficiency syndrome (AIDS). The diagnosis is made using a serological test; demonstration of the protozoan in tissues or body fluids is sometimes possible.

Guidelines for diagnostic imaging examinations

X-ray examination

Symptoms related to the biliary tract

Clinical examination of patients with acute abdominal pain originating from biliary tract disease may be difficult, especially in the absence of jaundice. However, the medical history combined with clinical and laboratory examinations may point towards the biliary tract, and diagnostic imaging may be required. The method of choice for evaluating biliary tract obstruction is ultrasonography. Where ultrasonography is not available, conventional abdominal radiographs including chest X-ray to exclude pulmonary causes of upper abdominal pain may be considered; however, diagnostic information is limited to the detection of radiopaque (calcified) structures indicating cholelithiasis. Only about 10% of gall stones are radiopaque. Cholecystography with contrast medium given orally could be considered by a well trained radiologist in clinically subacute or chronic stages of biliary tract disease, when clinical and laboratory findings do not give clear evidence for biliary tract obstruction. Cholangiography (intravenously injected contrast medium) is considered to be risky.

Ultrasound

Fatty liver

In normal patients the liver is only slightly more echogenic than the parenchyma of the kidney. Fatty metamorphosis of the liver shows an abnormally echogenic texture of the liver compared with that of the kidney. In fatty metamorphosis the vessels remain normal. This condition is reversible. A fatty liver never causes jaundice.

Liver cirrhosis

The end-stage of parenchymal liver disease is not reversible. In liver cirrhosis the intrahepatic vessels are not in an orderly and straight fashion and therefore they are difficult to trace. The parenchyma is extremely echogenic, sometimes also irregular. Portal hypertension associated with liver cirrhosis shows an enlarged main portal vein, splenic vein and superior mesenteric vein. Ascites may be observed. Jaundice may or may not occur in liver cirrhosis.

Intestinal schistosomiasis

Intestinal schistosomiasis caused by *Schistosoma mansoni* shows specific sonographic features. About 10% of patients develop hepatosplenomegaly with liver fibrosis, portal hypertension and ascites. In schistosomiasis only the periportal parenchyma is affected, depicting as hyperechogenic areas, whereas the rest of the parenchyma appears almost normal. About 30% of patients develop only hepatosplenomegaly. In these patients the differential diagnosis from other tropical diseases causing hepatosplenomegaly is only possible through laboratory examination.

Note: schistosomiasis never causes jaundice.

Amoebic liver abscess

See Section 5.1 on fever.

Echinococcus cysts

See Section 5.12.2 on non-acute abdominal pain.

In both conditions jaundice may develop when the biliary tract system is compressed.

Hepatoma

Liver tumours due to primary hepatocellular carcinoma are endemic in some areas. Sonographically they are often associated with invasion of the hepatic vein and the inferior vena cava, and these structures need to be examined closely (DD: *Echinococcus granulosus*, *E. multilocularis* in the

northern non-tropical hemisphere). The boundary between the malignant and normal tissue should be determined to define the degree of infiltration for staging purposes.

Liver metastasis

Liver metastases may be visible, mainly as round (bull's eyes) or irregular hypoechoic or hyperechoic lesions, or occasionally as diffuse infiltration. In the presence of carcinoma in other parts of the body, liver metastasis should be assessed in order to explore if radical or only palliative surgery shall be performed.

When the infiltrative growing of hepatomas and metastases are reaching the biliary tract system, jaundice usually develops.

Gallbladder disorders

The following disorders may be considered if the patient has fasted for about 6 hours prior to the examination:

Cholelithiasis: gallstones of about 2 mm to 3 mm in size can be detected, independent of their composition. The diagnosis is enhanced by acoustic shadowing distal to the gallstone.

All types of gallstones demonstrate shadowing distal to the gallbladder. To elicit a shadow distal to the gallstone, the gallstone must be imaged in near normal angulation (perpendicular to the skin) to the incident beam and within the optimal focal zone of the transducer.

It is helpful to examine the patient in several positions to mobilize the stones. Stones of different sizes can be measured; occasionally the gallbladder is packed with a number of stones and only shadowing can be observed. Jaundice may develop in case of obstruction of the biliary tract system by one or more stones.

Cholecystitis: in cholecystitis from bacterial infection or in a gall bladder containing gallstones the gall bladder wall is usually thickened; in addition there may be distension of the gallbladder.

Cholecystitis is normally not accompanied by jaundice.

Miscellaneous disorders: The most common disorder of the gallbladder is "sludge" that is diagnosed by the presence of echogenic

material in the gallbladder due to irregular emptying. The biliary tract system is not involved.

Gallbladder carcinoma: gallbladder carcinoma is often associated with gallstones and can be observed as a focal thickening of the wall. Periportal lymph nodes may be enlarged. Carcinoma of the gallbladder causes jaundice when invading the bile tract.

Polyps of the gallbladder: polyps appear as echogenic intraluminal stationary projections without shadowing. Gall bladder polyps do not normally cause jaundice.

Pancreas

Demonstration of the pancreas is often difficult and sometimes impossible. Perivisceral and mesenteric fat and gas within the bowel can interfere with the examination. In order to get a better picture of the pancreas the stomach can be distended with water (the patient should drink three or four 80 mL glasses of water).

Acute pancreatitis usually causes an enlarged pancreas with intraparenchymal oedema with or without haemorrhage. The texture of the pancreas is hypoechoic or of mixed echogenicity. Pancreatic cysts may appear after recovery. The biliary tract system is rarely involved.

Pancreatic carcinoma may depict as an area of decreased echogenicity (most often in the head of the pancreas) but it cannot be confidently distinguished sonographically from pancreatitis. If a tumour can be identified as such, it is normally at an advanced stage and has often reached the biliary tract system.

Distended bile ducts can be visualized in obstructive jaundice due to a pancreatic tumour, pancreatitis or liver flukes. Jaundice is always present.

5.7 Oedema

Oedema is an accumulation of tissue fluid in the extravascular space (outside the bloodstream). Oedema indicates a local obstructive or inflammatory process or a serious underlying systemic disease.

Oedema may be localized, affecting a limited area or part of the body, or generalized, affecting dependent parts of the body. Pleural effusion,

peritoneal effusion (ascites) and pericardial effusion are types of oedema where tissue fluid is accumulated in body spaces. Pitting oedema is the persistence of indentation of the skin following pressure.

About one-third of total body water is present in the body outside cells (extracellular space). Fluid in the extracellular space consists of plasma (in the bloodstream) and tissue fluid. Normally, plasma volume represents about 25% of the extracellular fluid, and the remainder is interstitial (tissue) fluid. Oedema occurs when fluid is forced from the bloodstream into the tissues, or when there is reduced removal of fluid from the tissues by the lymphatic system. This can be due to:

- reduced protein concentration in the blood resulting from e.g. malnutrition, liver disease
- increased pressure in the bloodstream caused by e.g. venous obstruction, cardiac failure
- reduced removal of fluid from the tissues caused by e.g. obstructed lymphatic vessels
- damage to capillary blood vessels resulting from e.g. inflammation.

5.7.1 Causes of oedema

Localized oedema (see Table 5.11)

- Obstruction/poor flow in venous or lymphatic vessels: varicose veins, venous thrombosis, lymphatic filariasis, tumours, cysts, etc.
- Inflammation of the skin due to: bacterial infection, ulcers, cutaneous anthrax, leprosy, trypanosomal chancre, onchocerciasis, Calabar swelling (*Loa loa*), allergies, etc.
- Puffiness of the face is seen in nephrotic syndrome (that may be caused by *Plasmodium malariae* or trypanosome infection).

Table 5.11 Causes of localized oedema

| | |
|---|--|
| <p><i>Obstruction/poor flow in venous or lymphatic vessels due to</i></p> <ul style="list-style-type: none"> varicose veins venous thrombosis filariasis tumours/cysts: | <p><i>Inflammation due to</i></p> <ul style="list-style-type: none"> cellulitis ulceration trypanosomiasis, <i>Loa loa</i>, onchocerciasis cutaneous anthrax leprosy hypersensitivity reaction (allergies) |
| <p><i>Tests</i></p> <ul style="list-style-type: none"> Blood film for microfilariae/trypanosomes Subcutaneous fluid for trypanosomes Skin slit smear for leprosy Skin snip for onchocerciasis | |

Generalized oedema (see Table 5.12)

- Insufficient dietary protein (malnutrition): famine, malnutrition, tropical sprue, *Giardia lamblia* infestation.
- Loss of protein from the gut: hookworm infestation, tuberculous enteritis.
- Loss of protein from the kidney: nephrotic syndrome (*P. malariae*), glomerulonephritis.
- Inability to excrete fluid: renal failure.
- Inability to produce/metabolize protein: hepatic failure.
- Inability of the heart to pump blood: heart failure due to rheumatic heart disease damaging the heart valves, myocardial infarction, congenital heart disease, disease of heart muscle (cardiomyopathy) due to alcohol, vitamin B1 deficiency, filariasis etc.
- Hypothyroidism: myxoedema.

5.7.2 Investigation of oedema

- *History*
 - fever
 - weight loss or gain
 - diet
 - night sweats

Table 5.12 Causes of generalized oedema

| Inadequate protein intake/absorption | Protein loss from the gut | Protein loss from the kidney | Hepatic failure |
|---|--|--|------------------------|
| Cardiac disease | Tuberculous enteritis | Inability to excrete fluid | |
| Famine | Hookworm infestation | Nephrotic syndrome | |
| Heart failure due to malnutrition, rheumatic heart disease, tropical sprue, myocardial infarction | | Glomerulonephritis | |
| Congenital heart disease | | Renal failure | |
| <i>Tests**</i> | <i>Tests</i> | <i>Tests</i> | <i>Tests</i> |
| Serum protein determination Protein electrophoresis ECG | Sputum for acid-fast bacilli Stool for hookworm ova | Urine protein determination White blood cells in urine Red blood cells in urine Casts | Liver function tests** |

*special investigations: Rf factors, small bowel biopsy.

**ALT, AST, HBsAg.

local pain
milky urine
dark urine
fatty, pale stool
cough and sputum
allergies
drug intake
alcohol intake.

- *Physical examination*
raised temperature, rapid or slow pulse, rapid respiratory rate, high blood pressure
wasting
weight gain
hair colour and texture
puffy face
skin ulcers, rashes
lymphadenopathy
tender, inflamed, thickened lymphatic vessels
tender/varicose veins
enlarged liver or spleen
abdominal masses
ascites
peripheral oedema
signs of cardiac failure.
- *Physical examination: adults*
ankle oedema (on both ankles)
crackles in lung bases (fluid)
enlarged liver
raised jugular venous pressure.
- *Physical examination: infants*
grunting
intercostal or subcostal retractions
nasal flaring
enlarged liver.
- *Laboratory investigations*
blood film for microfilariae, trypanosomes, *Plasmodium malariae*
subcutaneous fluid for trypanosomes
skin snip for onchocerciasis
skin slit smear for leprosy
stool for trophozoites, cysts, ova

microscopic examination of urine for protein, white cells, red cells, casts

sputum for acid-fast bacilli. Liver function tests (LFTs) include serum bilirubin, transaminases, alkaline phosphatase and gamma GT. Renal function tests include blood urea, serum creatinine and electrolytes. These are biochemical tests performed in laboratories with these facilities.

Thyroid function tests are performed on serum in national or regional reference laboratories.

A lymph gland or breast lump may be removed and submitted to a reference laboratory for histopathological examination to demonstrate conditions including inflammation, e.g. tuberculosis infection; malignancy, e.g. lymphoma, carcinoma of the breast.

- *Diagnostic imaging*
Ultrasound for liver cirrhosis, ascites, renal abnormalities.

Guidelines for diagnostic imaging investigations

X-ray

Chest X-ray

See Section 5.4 on cough/shortness of breath.

Ultrasound

Nephrotic syndrome

Nephrotic syndrome in children is demonstrated as enlargement and hyperechogenicity of the kidneys. Sonographic finding may also be seen in schistosomiasis, onchocerciasis, tuberculosis, liver cirrhosis and others.

5.8 Urinary tract infection (UTI)

The urinary tract consists of the urethra, bladder, ureters, pelvis of the kidneys and the collecting ducts within the kidney. Urinary tract infections

are common and occur more frequently in females than males, except in infancy. The organisms causing of urinary tract infection are mainly the following microorganisms:

- bacterial infections: *Escherichia coli*, *Klebsiella* spp., *Proteus* spp., *Enterococcus* spp., *Pseudomonas* spp., *Staphylococcus aureus*
- fungal infections: *Candida albicans*
- helminthic infections: *Schistosoma haematobium*.

Fungal infections occur mainly in immunosuppressed patients. *Staphylococcus aureus* causes abscesses of the kidney and is usually spread through the bloodstream.

Lower urinary tract infections are infections of the urethra and the bladder (cystitis). Symptoms include: dysuria (painful or burning micturition), increased frequency of micturition and suprapubic pain. Infection occurs by organisms ascending the urethra.

Upper urinary tract infections include infection of the kidney (pyelonephritis). Symptoms include fever and loin pain, as well as symptoms of lower urinary tract infection (dysuria). Infection occurs by organisms ascending the urethra or by spread from the bloodstream.

The symptoms of *lower urinary tract infection* are often confused with the symptoms of *urethritis* caused by sexually transmitted infections, because both cause symptoms of painful urination (dysuria). In many cases the symptoms are identical: however, urinary tract infection is never accompanied by discharge.

It is important to recognize these two separate entities because the diagnostic methods, treatment and management of patients are different.

Guidelines for laboratory investigations

Urine examination

Urine examination is the most poorly ordered of all laboratory investigations at primary health care level. Examination of the urine is performed for several purposes, and for each purpose a different sample of urine is collected. Tests include: chemical testing for glucose, protein or urobilinogen (spot urine), microscopic examination for urethritis (first part of the first morning urine), urinary tract infection (midstream urine),

tuberculosis (early morning urine), *Schistosoma haematobium* (terminal urine) and microbial culture for diagnosis of bacteria and assessment of antimicrobial drug resistance. Ordering urinalysis without indicating the clinical history or test required is not helpful as the laboratory is unable to advise the patient what specimen to collect and is unclear what test to perform. The laboratory should return such requests to the clinician for clarification.

In male patients, dysuria is almost always due to urethritis caused by sexually transmitted organisms. Discharge may be absent or reduced due to previous inadequate treatment. If there is no obvious discharge, collect a urethral swab for examination. If the swab is negative, request the patient to collect the first few drops of the first morning urine the next day and bring the sample to the laboratory. The laboratory will examine the urine deposit after centrifugation, and if pus cells are present, a Gram stain should be performed to detect Gram-negative intracellular diplococci (presumptive evidence of *Neisseria gonorrhoeae*). More than 10 pus cells/high power field in the absence of Gram-negative intracellular diplococci indicates non-gonococcal urethritis (mainly *Chlamydia*).

Ordering an examination of urine with discharge without providing information on the medical history of the patient indicates that the relevant examination has not been performed by the clinician, and wastes the time and resources of the laboratory and the patient.

The following factors predispose to urinary tract infections:

- urethral stricture
- renal/bladder stones
- prostatic hypertrophy
- tumours of the urinary tract
- bladder catheterization
- chronic anti-microbial therapy
- diabetes mellitus
- pregnancy
- immunosuppressed patients
- neurogenic bladder (paralysed patients).

5.8.1 Investigation of urinary tract infections

- *History*
 - fever
 - painful urination
 - blood in urine (haematuria)
 - difficulty in passing urine (frequency, dribbling, nocturia)
 - history of passing stones
 - previous urethritis due to sexually transmitted infection
 - pregnancy
 - previous drug treatment
 - other systemic disease, e.g. diabetes, immunosuppression.
- *Physical examination*
 - raised temperature
 - suprapubic, loin tenderness
 - indwelling catheter
 - pregnancy.
- *Laboratory investigations*
 - midstream urine (MSU) for cells, bacteria, casts, crystals
 - random urine for glucose, protein
 - terminal urine for *Schistosoma haematobium* ova
 - total and differential white blood cell count
 - blood glucose.

5.9 Sexually transmitted infections

Sexually transmitted infections are transmitted mainly (although not exclusively) through sexual contact. Sexually transmitted infections may be caused by viruses, bacteria, fungi and parasites.

The agents that cause sexually transmitted infections may also be transmitted through:

- direct contact
- blood transfusion

- use of non-sterile, infected needles and instruments
- from mother to child, either *in utero*, during delivery or through breastfeeding.

Sexually transmitted infections can result in severe pain and can lead to deformity of the genital area and infertility. The local infections may be transmitted by direct contact with the child at the time of delivery, e.g. neonatal conjunctivitis due to *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, and neonatal pneumonia due to *Chlamydia trachomatis*, which may lead to blindness and death.

Local infections of the genital tract, especially those that cause ulceration, enhance the transmission of the human immunodeficiency virus (HIV), the virus that causes AIDS.

Some sexually transmitted infections may lead to severe or fatal systemic disease, e.g. syphilis (*Treponema pallidum*), acute septic arthritis (*Neisseria gonorrhoeae*), HBV infection and HIV infection. Some infections may be transmitted to the child *in utero* (*Treponema pallidum*, HIV infection) leading to congenital abnormalities, abortion and death.

Some sexually transmitted infections may be alleviated by drug therapy but cannot be permanently cured, e.g. *Herpes simplex*, HIV infection.

5.9.1 Microorganisms causing sexually transmitted infections

- Viral infection: *Herpes simplex*, hepatitis B (HBV); human immunodeficiency virus (HIV), human papilloma virus (HPV).
- Chlamydial infection: *Chlamydia trachomatis* (lymphogranuloma venereum).
- Bacterial infection: *Neisseria gonorrhoeae* (gonorrhoea), *Gardnerella vaginalis* (bacterial vaginosis), *Haemophilus ducreyi* (chancroid), *Treponema pallidum* (syphilis), *Calymmatobacterium granulomatis* (lymphogranuloma inguinale).
- Fungal infection: *Candida albicans*.
- Protozoan infection: *Trichomonas vaginalis*.
- Ectoparasitic infection: *Phthirus pubis* (crab lice).

5.9.2 Types of sexually transmitted infection

Sexually transmitted infections cause the following major clinical syndromes.

- *Urethral discharge/urethritis*: painful urination, urethral discharge (common in male patients). Infection of the urethra may spread to involve the seminal vesicles, epididymis and testes in men; and the Bartholin glands in women. Causative agents are: *Chlamydia trachomatis* (watery discharge, painful urination), *Neisseria gonorrhoeae* (thick, pus discharge, painful urination), *Trichomonas vaginalis* (uncommon: watery discharge, often asymptomatic).
- *Vaginal discharge and/or vulval pruritus*: painful/burning urination, irritating/foul smelling vaginal discharge in women. Agents that cause infection of the vagina are: *Candida albicans* (white, curdsh irritating discharge); *Trichomonas vaginalis* (profuse greenish, frothy, irritating discharge); *Gardnerella vaginalis* (foul smelling, non-irritating discharge).
- *Lower abdominal pain in females*: pelvic pain with or without vaginal discharge. Infection of the cervix spreads to involve the uterus, fallopian tubes, ovaries and peritoneum. Main causative agents are: *Chlamydia trachomatis* (watery discharge), *Neisseria gonorrhoeae* (pus discharge).
- *Genital ulcers*: ulceration of the genital organs in men and women (including the cervix in women), associated with inguinal lymphadenopathy. Causative agents are: *Herpes simplex* (painful vesicles in crops, recurrent); *Haemophilus ducreyi* (multiple, painful, ragged ulcers), *Chlamydia trachomatis* (ulcer painless and heals quickly, prominent matted inguinal lymphadenopathy), *Treponema pallidum* (usually painless—unless secondarily infected—single ulcer), *Calymmatobacterium granulomatis* (single or multiple, raised, painless, beefy papule).
- *Neonatal conjunctivitis (ophthalmia neonatorum)*: conjunctivitis and discharge in babies within one month of birth. Causative agents are: *Chlamydia trachomatis* (watery discharge), *Neisseria gonorrhoeae* (pus discharge). Conjunctivitis in neonates may also be due to non-sexually transmitted infections, e.g. staphylococcus, streptococcus.

In addition to these syndromes, there are important systemic diseases that are sexually transmitted.

- *Syphilis*: a bacterial infection caused by *Treponema pallidum* which occurs in three major stages:
primary syphilis: genital ulcer disease
secondary syphilis: skin rash, mouth ulcers, fever, lymphadenopathy, genital warts
tertiary syphilis: cardiac and neurological disease.
Between each stage the patient may have long symptom-free periods. Syphilis is transmitted to the fetus *in utero* after the fourth month of pregnancy, resulting in congenital infection and deformity.
- *HIV infection*: human immunodeficiency virus is the virus that causes AIDS. HIV is transmitted mainly by sexual contact but also through blood transfusion, use of contaminated needles and instruments, and from mother to child, at the time of birth and from breast milk. Infection results in a slow destruction of the body's immune system resulting in severe infection (opportunistic infections) and malignancy. Infected individuals may remain well for many years before symptoms develop, but they are still infectious to others.
- *Human papilloma virus (HPV)*: this virus is associated with the development of carcinoma of the uterine cervix.

5.9.3 Investigation of sexually transmitted infections

- *History*
fever
painful urination
urethral or vaginal discharge
genital ulcer: pain
pelvic/vulval pain or swelling (in women)
swelling/pain in genital organs (in men)
enlarged inguinal lymph nodes
conjunctival discharge (in babies)
skin rash
mouth ulcers

joint pain and swelling
contacts, partners
previous drug treatment.

- *Physical examination*

raised temperature
generalized or inguinal lymphadenopathy
skin rash
tender, swollen, red joints
mouth ulcers
conjunctival inflammation and discharge (in babies)
pubic lice
genital ulcers, swelling
genital warts
urethral discharge
vaginal/cervical discharge (on speculum examination)
pelvic tenderness and swelling (on bimanual examination).

- *Laboratory investigations*

urethral discharge: wet preparation for *Trichomonas vaginalis*, pus cells; Gram stain for pus cells, Gram-negative intracellular diplococci (*Neisseria gonorrhoeae*)

first part of the first morning urine: deposit for *Trichomonas vaginalis*, pus cells; Gram stain for pus cells, Gram-negative intracellular diplococci (*Neisseria gonorrhoeae*)

high vaginal swab (HVS): wet preparation for *Candida albicans*, *Trichomonas vaginalis*, “clue cells” (*Gardnerella vaginalis*); potassium hydroxide preparation for *Candida albicans*; Gram stain for *Candida albicans*, “clue cells”

endocervical swab (ECS): Gram stain for pus cells, Gram-negative intracellular diplococci (*Neisseria gonorrhoeae*)

conjunctival swab: Gram stain for pus cells, Gram-negative intracellular diplococci (*Neisseria gonorrhoeae*)

dark field illumination of genital ulcer fluid for spirochaetes (*Treponema pallidum*)

serum for syphilis screening
hepatitis B screening and HIV-antibody testing.

Guidelines for diagnostic imaging

X-ray

hysterosalpingography (HSG) for tubal patency.

Ultrasound

bladder thickening/calcification
bladder stones
bladder tumours
renal cysts
hydronephrosis
testicular torsion
tubo-ovarian abscess
pelvic masses
advanced carcinoma of the cervix
scrotal abnormalities.

5.9.4 Urethral discharge/urethritis

There is a normal “physiological” discharge in all women which varies in amount according to the stage of the menstrual cycle. Some women are not aware of this, and therefore it is important for the clinician to examine the nature and amount of the discharge. In addition, infection is not the only cause of discharge. Discharge may be due to cervical erosions, malignancy or foreign bodies. Itchy or bloody discharge is always abnormal. Examination of the cervix and vagina in females complaining of discharge is an important part of the physical examination.

Patients of both sexes complaining of dysuria should be asked about the presence of discharge. If discharge is present, a full examination of the genital area must be performed by the clinician, wearing gloves. A sample of discharge should be submitted to the laboratory for examination. In male patients, urethral discharge is collected by the clinical or laboratory staff on to a slide or using a swab. In female patients, samples of discharge (HVS and ECS) are collected

using sterile swabs after direct speculum examination of the cervix and vagina. Speculum examination must be performed by the examining clinician and not by a nurse or the laboratory staff. The HVS and ECS samples should be clearly labelled so that the laboratory can distinguish them. Urethral swabs may also be collected in female patients. The specimens must be taken immediately to the laboratory for examination to detect motile organisms (*Trichomonas vaginalis*).

Male patients with dysuria (painful urination) are likely to have urethritis due to a sexually transmitted infection. Urinary tract infection is uncommon in males. Always question and examine male patients for urethral discharge and collect a urethral smear or urethral swab.

Female patients with dysuria may have a urinary tract infection or a sexually transmitted infection causing urethritis and/or vaginal discharge. Always question female patients about vaginal discharge, and if present, investigate accordingly (see Figure 5.3).

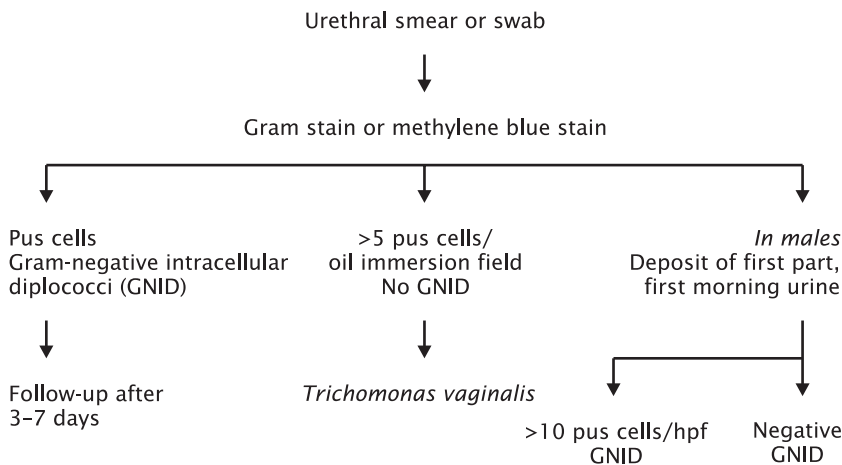


Figure 5.3 Flowchart for the differential diagnosis of urethral discharge/dysuria

Comparison of dysuria caused by UTI and STI

The diagnosis of UTI is made by considering the following:

- UTI occurs more commonly in adult female patients
- there is no history of sexual contact
- there is no discharge.

UTI is confirmed by finding >5 pus cells/hpf (high-powered field of microscope) in a correctly collected midstream urine (MSU) sample.

Table 5.13 compares the clinical findings caused by sexually transmitted infections (STI) and (UTI).

5.9.5 Vaginal discharge

The agents that cause vaginal discharge may also cause dysuria in female patients. Always question female patients with dysuria about vaginal discharge.

Perform speculum examination; examine the cervix; take both a high vaginal swab (HVS) and an endocervical swab (ECS) (see Table 5.14).

5.9.6 Neonatal conjunctivitis

Gonorrhoeal or chlamydia infection may cause serious disability of neonates. Therefore, all neonates with conjunctival discharge *must* be investigated and treated promptly, in order to avoid blindness. The differential diagnosis of *Neisseria gonorrhoeae* and *Chlamydia* infection is outlined in Table 5.15.

5.9.7 Lower abdominal pain in women

Figure 5.4 presents a flow diagram for the symptomatic diagnosis of lower abdominal pain in women.

5.9.8 Genital ulcers

Genital ulcers may cause dysuria in both male and female patients. Always examine the patient carefully. Genital ulcers in females may occur on the cervix or the walls of the vagina. Genital ulcers due to syphilis (*Treponema pallidum*) may be painful if they are secondarily infected with bacteria.

Table 5.13 Dysuria caused by sexually transmitted infections and urinary tract infections

| | STI | UTI |
|--|--|---|
| Symptom | Dysuria | Dysuria |
| Presence of urethral/vaginal discharge | Yes | No |
| Common causative organisms | <i>N. gonorrhoea</i> <i>C. trachomatis</i> <i>T. vaginalis</i> | <i>E. coli</i> <i>Proteus</i> spp. <i>Klebsiella</i> spp. <i>Enterococcus</i> spp. <i>Pseudomonas</i> spp., etc. |
| Source of organisms | Infected partner | Bowel flora |
| Mode of transmission | Sexual contact | Local spread/ contamination |
| Mode of spread of disease | Genital tract | Urinary tract |
| Sex ratio | M:F = 1:1 | F > M |
| Age group affected | Sexually active group | All ages, including babies, children and the elderly |
| Laboratory tests | Urethral smear, swab, HVS/ECS | Midstream urine (MSU) |
| Treatment | Penicillin Ampicillin Augmentin Septrin | Septrin Ampicillin |
| Dosage regimens | High single dose | 3–7 days |
| Treatment of contact | Yes | No |

Table 5.14 Differential diagnosis and treatment of vaginal discharge

| High vaginal swab | | Endocervical swab | |
|--|---|--|--|
| <i>Test</i> Wet preparation 10% KOH preparation Gram stain | | <i>Test</i> Gram stain | |
| <i>Findings</i> Yeast positive | <i>Findings</i> Clue cells +ve KOH test | <i>Findings</i> <i>Trichomonas vaginalis</i> | <i>Findings</i> Pus cells: Gram-negative intracellular diplococci |
| <i>Treatment</i> Candidiasis treatment | <i>Treatment</i> Bacterial vaginosis treatment | <i>Treatment</i> <i>Trichomonas</i> treatment | <i>Treatment</i> First line gonorrhoea and <i>Chlamydia</i> treatment |
| <i>Follow up after seven days</i> | | | |

Table 5.15 Diagnosis of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* infection

| | | |
|---|---|--|
| <i>Test</i> Gram stain of discharge | | |
| <i>Findings</i> Pus cells Gram-negative intracellular diplococci (GNID) | <i>Findings</i> Pus cells No Gram-negative intracellular diplococci | |
| <i>Treatment</i> Treat for gonorrhoea, neonatal conjunctivitis | <i>Treatment</i> Examine and treat mother and her contacts for gonorrhoea and <i>Chlamydia</i> | <i>Treatment</i> Treat for <i>Chlamydia</i> , neonatal conjunctivitis |

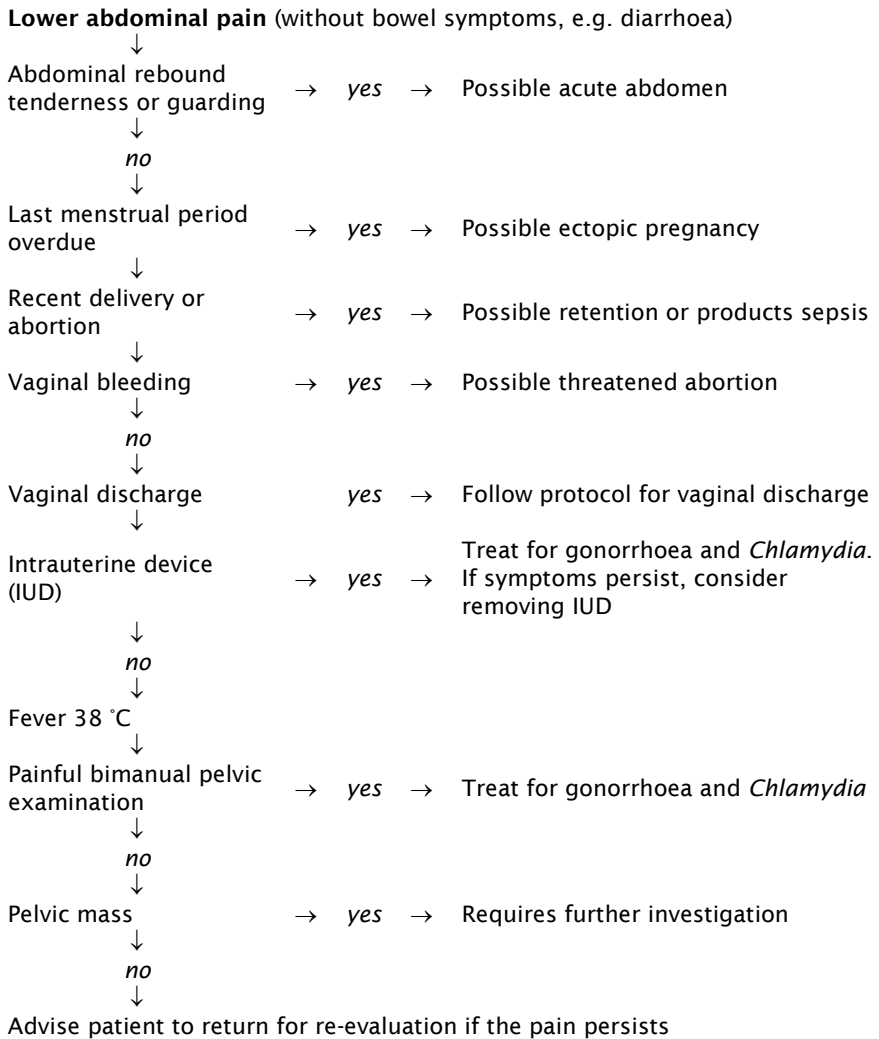


Figure 5.4 **A flow diagram for the symptomatic diagnosis of lower abdominal pain in women**

Examination of genital ulcers

Screening tests for syphilis (VDRL) may be negative in the early stages of the disease (primary chancre) as antibodies have not yet developed (see Figure 5.5). Early and effective treatment may prevent the development of antibodies. Screening tests are always positive in secondary syphilis.

Screening tests may become negative or weak during the late stages of the disease due to reduced activity of *Treponema pallidum*. In late stages of syphilis (and in patients with suspected central nervous system involvement) a specific test, e.g. TPHA (*Treponema pallidum* haemagglutination assay), must always be performed.

The VDRL (or RPR) test is a screening test for syphilis, and consists of non-specific antigen (cardiolipin) coated on to carbon antigen particles. Patients with syphilis develop antibodies that cause the particles to agglutinate. Since the antigen used is not derived from *T. pallidum*, non-specific (false positive) reactions may occur; however, this may be of little significance as the treatment of syphilis is simple and economical.

False positive screening tests for syphilis may occur in malaria, tuberculosis, leprosy, pregnancy, hepatitis, malignancy, lupus erythematosus, etc.

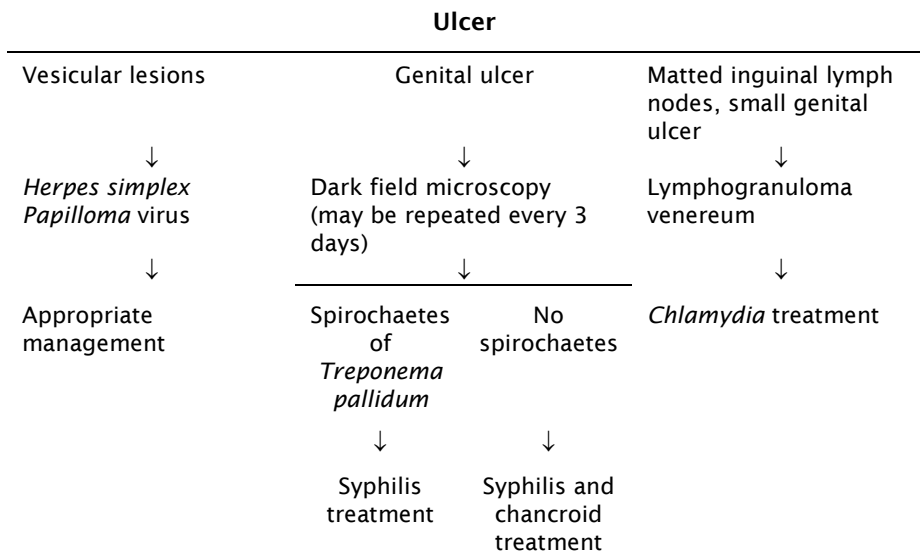


Figure 5.5 Diagnosis of genital ulcers

The VDRL test is also a very useful test because it provides a measure of the activity of the disease. In order to quantify antibodies, the patient's serum is diluted until the agglutination reaction disappears (titration).

Genital ulcers and all features of secondary syphilis heal spontaneously without treatment. A VDRL titre is carried out to determine the patient's response to treatment. Patients who are treated for syphilis should have the VDRL titre checked every three to six months until antibodies can no longer be detected. *T. pallidum* cannot be cultured on artificial media.

Congenital syphilis can be prevented by treating syphilis in pregnant women before the fourth month of pregnancy. After the fourth month, the *T. pallidum* organism crosses the placenta and can infect the fetus.

Guidelines for diagnostic imaging investigations of the female genital tract

X-ray

Conventional radiography is of very little value for evaluating gynaecological problems. In small hospitals and clinics the only imaging technique of value is ultrasonography. Special radiological examinations such as hysterosalpingography (HSG) should only be considered when a radiologist is available. Patients with complex clinical symptoms and malignant disease should be transferred to hospitals with facilities for computer tomography examinations before planning surgical intervention or radiotherapy.

Ultrasound

The chronic stage of urogenital schistosomiasis, caused by *Schistosoma haematobium*, shows typical sonographic features. The wall of the bladder is thickened and irregular with fibrotic bladder tissue. Calcification of the bladder wall may be visible. In more advanced stages, various findings are possible, such as contraction (shrinking) of the bladder, and dilation or deformity of the distal ureter, which may cause hydronephrosis. In addition, bladder stones may be present. There is a

proven link between schistosomiasis and bladder carcinoma in endemic areas.

In chronic sexually transmitted infection in males, there may be thickening of the bladder wall. Hydronephrosis may be a late manifestation of urethral stricture. Another cause of urinary obstruction is an enlarged prostate. The size of the prostate can be measured by ultrasonography. Prostate cancer is shown by tissue with different echoes and an irregular border, sometimes infiltrating the surrounding organs.

Although the most commonly used probe is not very specific for scrotal scanning, hydroceles can be differentiated from inflammatory processes and big tumours. Hydroceles appear as fluid around the testicle. Tumours show a disorganized texture; in an inflammatory process the testicles appear thickened.

Torsion of the testes exhibits an irregular texture with echogenic areas corresponding to haemorrhage, but it is difficult to make the diagnosis in the early stages with the normally used transducer.

Late stages of sexually transmitted infection in women with acute or chronic pelvic inflammation show various features that may be difficult to differentiate on transabdominal scanning. Transvaginal scanning is preferred to demonstrate pelvic organs but this type of probe is not usually available.

A tubo-ovarian abscess appears as a mass with low-level echoes arising from the inflammatory fluid. Fluid in the pouch of Douglas is common. In late stages of sexually transmitted infection, complex pelvic masses may occur which can fill the entire pelvis, and which contain fluid and/or solid masses, pus, clots or cellular debris. The differential diagnosis of extrauterine pregnancy can be extremely difficult (see Section 5.13.3 on complicated pregnancy).

Scanning is only helpful in advanced stages of cervical cancer. Typically enlargement and irregularity of the borders of the cervix and infiltration of the bladder are seen. Stenosis of the cervix due to carcinoma may give the appearance of a distended uterus with haematometra.

Congenital abnormalities of the kidney such as congenital polycystic kidney disease can also lead to urinary tract infection. Solitary cysts of the kidney are often noted with no other renal abnormality.

5.10 Altered consciousness, coma and shock

A patient with altered consciousness may present himself as aggressive, excited, in a state of delirium or unconsciousness. The altered consciousness of a patient should be considered as highly critical. An unconscious patient is in a state of shock or coma, that are life threatening. The causes of shock and coma are different as is their treatment. Both conditions require immediate intensive care that should be monitored using the appropriate clinical and laboratory indicators. Table 5.16 summarizes the causes of altered consciousness.

5.10.1 Investigation of altered consciousness

- *History*
 - headache
 - photophobia
 - vomiting
 - fever
 - head injury
 - history of diabetes
 - history of hypertension
 - history of renal disease
 - alcohol or other drug abuse
 - use of local herbal remedies
 - exposure to chemicals, carbon monoxide
 - pregnancy
 - history of epilepsy.

- *Physical examination*
 - level of consciousness and orientation
 - increased temperature, rapid or slow pulse, rapid/laboured breathing,
blood pressure (hypertension/hypotension)
 - head wound
 - bulging fontanelle
 - neck stiffness, Kernig sign, photophobia

Table 5.16 Causes of altered consciousness

| Infection | Metabolic | Poisoning | Head injury | Vascular | Neural |
|--|--------------------------------|-----------------|-----------------------------|--------------------------|----------------------|
| Meningitis | Hypoglycaemia | Carbon monoxide | Extradural haematoma | Stroke | Grand mal convulsion |
| Malaria | Hyperglycaemia | Alcohol | Hypertensive encephalopathy | Subdural haematoma | Brain tumour |
| Septicaemia | | Chemicals | | | Eclampsia |
| Brain abscess | | Opiates | | | |
| Trypanosomiasis | | Drug overdose | | | |
| | | Local herbs | | | |
| <i>Signs</i> | <i>Signs</i> | <i>Signs</i> | <i>Signs</i> | <i>Signs</i> | <i>Signs</i> |
| Fever | History of diabetes | Focal signs | Head wound | Raised blood pressure | History of epilepsy |
| Neck stiffness | Insulin use | | Focal signs | Unequal pupils | |
| Unequal pupils | Hypoglycaemic drugs | | Kernig sign | History of renal disease | |
| Bulging fontanelle | | | | | |
| Kernig sign | | | | | |
| <i>Tests</i> | <i>Tests</i> | | | | |
| Blood film for parasites | Blood glucose | | | | |
| Cerebrospinal fluid for total and differential | Urine chemistry and microscopy | | | | |
| WBC | Serum creatinine/blood urea | | | | |
| Gram stain | | | | | |
| Ziehl–Neelsen stain | | | | | |
| Negative stain | | | | | |
| Cerebrospinal fluid protein | | | | | |
| Cerebrospinal fluid culture | | | | | |

pupils: dilated, constricted, non-reactive, unequal
papilloedema, retinal exudates, retinal haemorrhages
focal weakness/paralysis
urine retention/incontinence.

- *Laboratory investigations*
blood haemoglobin, haematocrit
blood film for parasites
gram stain, Ziehl–Neelsen stain, negative staining
blood glucose
blood gases
serum urea,
serum potassium
serum creatinine
serum transaminases
plasma clotting factors
cerebrospinal fluid for protein, total white cell count, differential white
cell count, trypanosomes,
cerebrospinal fluid culture and antimicrobial sensitivity
urine ketone bodies
urine glucose
urine pH
urine osmolality
cross-match.

Guidelines for diagnostic imaging

X-ray

Skull X-ray for fractures (see Section 5.11 on accidents and injuries).

5.10.2 Shock

Shock is a critical condition in which the circulatory system fails to maintain adequate blood flow. This sharply curtails the delivery of oxygen and nutrients to vital organs. It also compromises the kidney and so curtails

the removal of wastes from the body. Shock is a major medical emergency. It is common after blood loss from serious injury.

Shock may result from:

- insufficient cardiac output of blood to maintain blood pressure
- disproportionate distribution of blood between organs of the body.

Table 5.17 summarizes the common causes and laboratory findings of various forms of shock.

Typical clinical signs of a shock are low blood pressure and tachycardia; rapid but weak pulse; low to absent urine production; tachypnoea; confusion; stupor. In the milder form of shock the patient may still be conscious, but confused and reacting slowly. Hands and feet may feel cold and moist and appear pale or cyanotic. In heavy shock the patient is unconscious.

The diagnostic indicators for monitoring shock treatment are ECG, blood pressure, Hb, RBC, blood glucose, blood gases and urine volume.

5.10.3 Coma

Coma is a state of unconsciousness from which the patient cannot be aroused, even by powerful stimuli. The coma may be accompanied by signs of delirium. In deep coma, even primitive body reflexes cannot be triggered. Relative degrees of coma include stupor and drowsiness, although there is no clear distinction between them. The level of coma can be defined using the Blantyre Coma Scale as follows.

Best motor response

| | |
|--|---|
| Localizes painful stimulus (pressure with blunt end of pencil on sternum or supra-orbital ridge) | 2 |
| Withdraws limb from painful stimulus (pressure with horizontal pencil on nailbed of finger or toe) | 1 |
| No response or inappropriate response | 0 |

Best verbal response

| | |
|---|---|
| Cries or speaks appropriately with painful stimulus | 2 |
| Moans or abnormal cry with painful stimulus | 1 |
| No vocal response to painful stimulus | 0 |

Eye movement

| | |
|---|---|
| Watches or follows (e.g. mother's face) | 1 |
| Fails to watch or follow | 0 |
| Maximum score | 5 |
| Minimum score | 0 |

Diabetic coma is caused by impaired glucose and fatty acid metabolism. The early signs include weight loss, nausea, confusion, gasping for breath and a characteristically sweet foetor similar to that of acetone ("acetone breath").

There are three forms of diabetic coma: hyperosmolar, ketoacidotic and hypoglycaemic coma. The clinical and laboratory indicators to distinguish between the different forms of diabetic coma are shown in Table 5.18.

A patient suffering from hyperosmolar coma may still react despite of the highly elevated blood glucose levels.

In severe cases of viral (e.g. HBV, yellow fever virus, haemorrhagic fever viruses) or protozoan (e.g. *Plasmodium falciparum*) infection patients may suffer from high fever and hepatic failure, accompanied by jaundice and coma. Complications of liver cirrhosis from chronic HBV infection include mental confusion, coma, fluid accumulation (ascites), internal bleeding and kidney failure.

Encephalitis in viral infection with high fever and convulsions may also result in a coma. Occasionally the encephalitis may eventuate in central nervous system impairment or death.

Table 5.17 Common causes of shock

| Type of shock | Common causes | Laboratory findings |
|---|--|---|
| Hypovolemic shock | Acute blood loss, e.g. from peptic ulcer, aortic aneurism, extra-uterine gravidity, septic abortion, trauma, surgery Loss of body fluid, e.g. in acute diarrhoea, kidney disease, diabetes mellitus, cholera Acute adrenal insufficiency Drug effect (e.g. diuretic drug treatment) | Hb normal to low HCT normal to low Serum electrolytes Creatinine high Blood glucose very low Urine ketone high |
| Cardiogenic shock | Cardiac arrhythmia Myocardial infarction Pulmonary embolism | Hb normal HCT normal Enzymes (CK, AST, ALT) elevated LDH very high |
| Vasodilatation (relative hypovolemic shock) | | |
| i. neurogenic shock | Cerebral trauma | |
| ii. septic shock | Bacterial infection with fever and shivering (in severe cases no fever and shivering) | WBC high to very low Respiratory alkalosis |
| iii. Dengue shock syndrome and haemorrhagic fever | Dengue virus Haemorrhagic fever viruses | Thrombopenia leukopenia |
| iv. anaphylactic shock | Allergic reaction | |
| v. acute adverse blood transfusion reaction | ABO incompatibility reactions | ABO blood groups and cross-match Urine haemoglobin |
| vi. toxic shock | <i>Staphylococcus aureus</i> toxin, poisons medicinal herbs | Serum transaminases Plasma clotting factors |

Table 5.18 Clinical and laboratory findings in diabetic coma

| | Hyperosmolar coma | Ketoacidotic coma | Hypoglycaemic coma |
|---------------------------|-------------------------|---------------------------|-----------------------|
| Development | hours | days | minutes |
| Preceding stress or fever | often | often | absent |
| Physical condition | very sick | extremely sick | very weak |
| Breathing | normal to tachypnoeic | very deep (Kussmaul type) | normal |
| Skin | very dry | dry and red | moist and pale |
| Infection | frequent | frequent | absent |
| Mouth | dry | dry | saliva increased |
| Thirst | pronounced | pronounced | absent |
| Vomitus | occasionally | frequent | rare |
| Abdominal pain | occasionally | frequent | absent |
| Breath | accelerated | accelerated | normal and flat |
| Foetor | no acetone | acetone | no acetone |
| Blood pressure | low | low | normal |
| Urine glucose | elevated | elevated | absent |
| Urine ketones | normal | elevated | absent |
| Urine osmolality | >360 mOsmol/L | <320 mOsmol/L | |
| Blood glucose | >500 mg/dL (>30 mmol/L) | >300 mg/dL (<18 mmol/L) | <50 mg/dL (<3 mmol/L) |
| Serum bicarbonate | elevated | < 10 meq/L | >22 meq/L |
| Serum potassium | elevated | elevated | low |

Poisoning may be more common than is currently recognized. Poisoning may be accidental or deliberate from ingestion of toxic foods or chemicals, overdoses of drugs or medicinal herbs or to exposure to toxic gases. A common cause of poisoning is carbon monoxide, a tasteless gas formed during combustion in the absence of sufficient oxygen. Carbon monoxide poisons by preferentially binding to haemoglobin. Carbon monoxide poisoning may be more common than is currently recognized. Patients may have symptoms of carbon monoxide poisoning but be unaware of the reasons for their symptoms. The early symptoms of carbon monoxide poisoning are nonspecific. They include prolonged headache and nausea. Advanced exposure to carbon monoxide results in cardiovascular collapse, coma and death.

A person with heat stroke has a body temperature above 41 °C. Other symptoms include confusion, combativeness, bizarre behaviour, faintness, staggering, strong rapid pulse, dry flushed skin, lack of sweating, delirium and coma.

Haemolytic–uraemic syndrome is a condition involving break-up of red blood cells and kidney failure. There is clumping of platelets within the kidneys' small blood vessels with resultant reduced blood flow. This leads to kidney failure. Haemolytic–uraemic syndrome is the most common cause of acute kidney failure in infants and young children.

There are many causes of haemolytic–uraemic syndrome including *Shigella*, drugs, tumours, pregnancy and systemic lupus erythematosus (SLE). One of the most prominent causes today of haemolytic–uraemic syndrome is *Escherichia coli* O157:H7.

Typically patients with haemolytic–uraemic syndrome suffer from anaemia and thrombocytopenia, which causes abnormal bleeding. Seizures and coma can also occur. Cases typically begin with severe abdominal cramps and diarrhoea, which may become bloody by the second or third day. Nausea and vomiting are present in approximately half of the patients. Most patients recover in seven to ten days, but some go on to develop the severe form of the disease.

Guidelines for laboratory investigations

A patient who presents in altered consciousness requires an immediate assessment and immediate therapy to prevent further nervous system damage. Treatment requires repeated clinical control (ECG, pulse rate, blood pressure) and laboratory measurements of metabolic indicators (e.g. haemoglobin, RBC, blood and urine glucose, urea, potassium and urine ketone bodies) and blood gases (if available) at frequent intervals to monitor the success of treatment of the patient.

Hypertension is only recognised clinically by blood pressure examination. The patient may not be aware of having underlying hypertension.

Ketones may be seen in urine in healthy fasting individuals, or in patients who are not eating because of nausea or vomiting, or other illness; ketones together with glucose in urine indicates diabetic ketoacidosis.

A blood glucose level less than 2.8 mmol/L (50 mg/dl) *during a symptomatic episode* indicates hypoglycaemia.

Repeated laboratory measurements of metabolic indicators are required at frequent intervals, e.g. glucose, urea, to monitor the success of treatment.

Central nervous system disease in patients with acquired immune deficiency syndrome (AIDS) may be due to the effects of the human immunodeficiency virus (HIV) itself, to infection or malignancy. HIV virus causes dementia. Opportunistic infections include encephalitis due to cytomegalovirus, Herpes simplex; meningitis due to *Cryptococcus neoformans*; brain abscess due to *Toxoplasma gondii*; and brain tumour, e.g. lymphoma.

Guidelines for diagnostic imaging investigations

Less than 0.5% of acute headaches are due to serious intracranial disease. Consequently, patients with headache but no additional neurological symptoms normally do not need diagnostic imaging of any kind.

Patients with suspected intracranial disease should be transferred to a hospital where CT, cerebral angiography and possibly MRI examinations can be performed, and where the necessary treatment can be given.

5.11 Accidents and injuries

An injury or accident is an event that occurs suddenly and requires immediate attention, to prevent worsening of the condition, to prevent complications, such as infection, and sometimes to save life.

5.11.1 Types of accident or injury

For practical purposes, accidents and injuries may be grouped as follows:

- trauma to the head
- trauma to the chest
- trauma to the abdomen
- trauma to the skeleton and soft tissues
- multiple trauma.

Other accidents that do not involve trauma include:

- poisoning
- burns and scalds
- emergencies occurring in childbirth (see section 5.12.2 on complicated pregnancy).

5.11.2 Investigation of accidents and injuries

- *History*
 - nature of accident, sequence of events
 - time of accident
 - headache
 - visual disturbance
 - difficulty in breathing
 - vomiting: colour, amount
 - pain: site
 - bleeding: site and intensity
 - limited movement of limbs, loss of sensation
 - confusion, loss of consciousness
 - seizures

pre-treatment

contact with poisons (swallowed, inhaled, absorbed through the skin, instilled into the eye, injected).

- *Physical examination*
vital signs: temperature, blood pressure, pulse, respirations
level of consciousness (see Section 5.10.3 on coma)
pupils: size, equal, reactive
eye: burns, lacerations
skin: burns, lacerations
bones: crepitation, swelling
foreign bodies
examination of relevant systems.
- *Laboratory investigations*
haemoglobin
urine for blood
blood grouping.

Guidelines for diagnostic imaging investigations

X-ray

Head

X-rays are often requested for investigation of head injuries. In general, however, conventional skull X-rays are of very limited value because dangerous and often life threatening intracranial injuries are normally not visible. The lack of skull fractures does not say anything about damage to the brain or other intracranial structures.

Suspected facial injuries do justify X-ray examination. In addition, unconscious patients should have an X-ray examination of the cervical spine. An absolute minimum would be a lateral view performed with a mobile X-ray unit.

Foreign bodies located in the eye can be demonstrated when they are metallic or otherwise radiopaque.

Chest

Patients with chest trauma should be examined radiologically to evaluate possible lesions of the lungs and mediastinal structures. A plain chest radiograph will exclude pneumothorax, atelectasis, pleural fluid collection and other serious damage. The diagnostic quality of images and radiation safety are more difficult to ensure using mobile X-ray units, and wherever possible the patient should be examined in an X-ray department using stationary equipment. Only very few patients are in a condition preventing them from transportation to the X-ray unit for imaging.

A chest X-ray to exclude a simple rib fracture is not indicated in most cases. In the absence of serious injuries or symptoms, a rib fracture can be easily diagnosed by clinical examination. High-quality radiographs are needed for the diagnosis of pneumothorax or other lesions.

Abdomen

Abdominal trauma requires extensive diagnostic examination, which may be difficult.

In the absence of external or penetrating injuries, it may be impossible to diagnose intra-abdominal injuries with certainty, although medical staff may be able to indicate the likelihood of such injuries. In these cases, additional diagnostic examinations are required to obtain more exact information.

Conventional abdominal X-ray examinations should be considered if ultrasound is not available, as they can offer valuable information on intra-abdominal lesions. These examinations may not be of sufficiently high quality when made under emergency conditions. If more sophisticated radiological examinations, including the use of contrast medium and abdominal computer tomography are not available, surgical intervention, such as exploratory laparotomy, may be required.

Skeleton

Although most injuries of the skeleton are diagnosed clinically, it may be difficult to give adequate treatment without information from diagnostic imaging. Mobile X-ray units are often not suitable for producing images of adequate diagnostic quality even when operated by skilled personnel. This is

true for injuries and fractures of the pelvis, the hips and lumbar spine, where lateral projections are of great importance.

At least two projections positioned at right angles to each other are required. Special views may be necessary according to the type and location of the injury/fracture. The X-ray operator should discuss the clinical situation of the patient with the clinician in order to tailor the examination properly.

Ultrasound

Patients with abdominal trauma who are suspected to be suffering internal lesions should have their abdomens examined as soon as possible. Sonography can be performed at the same time as life-saving treatment. The examination does not require any special preparation of the patient, although gas in the bowel often makes examinations difficult. Most intra-abdominal lesions such as intraperitoneal bleeding, severe injuries of the liver, spleen and kidneys can be identified within minutes by adequately trained personnel.

Splenic rupture and haematomas appear as echogenic and later, hypoechoic masses within or outside the spleen. Surrounding fluid represents partial rupture or laceration of the spleen.

Renal contusion and laceration have a variable appearance. Haematomas appear as hypoechoic masses within or surrounding the kidney. At a later stage they become echogenic.

Joints

Ultrasound cannot be used to evaluate injuries of the skeleton. However ultrasound can be used for examination of the joints. Intra-articular fluid, including accumulation of blood or pus in the joint, may be difficult to diagnose on physical examination, especially in the shoulder and hip joints. In such cases, a well trained ultrasonography operator will be able to make the diagnosis provided that the appropriate probe is available. It is, however, not possible to specify the type of fluid in a joint, and fluid aspiration is needed to obtain more information.

Chest

Sonographic examination of the chest is usually made with the patient sitting in a stationary chair leaning forward on a pillow. Pleural fluid should be collected on inspiration and expiration. Normally, the air-containing lung produces an echogenic interface at the thoracic wall. Effusions appear as hypoechoic accumulations between the thoracic wall and the lung. Simple effusions tend to change in configuration with respiration. Paradoxical motion of the diaphragm may also be documented.

Ultrasound can be used to delineate lesions of muscles, fascia and ligaments such as complete tears and haematomas (although this needs special training and a 75 MHz transducer).

5.12 Acute and non-acute abdomen

5.12.1 Acute abdominal pain

Acute abdomen is a serious abdominal crisis of acute onset characterized by pain and usually associated with vomiting, abdominal distension, fever and altered bowel function. Acute abdomen may be associated with shock, where there is acute circulatory failure marked by coldness of the skin, hypotension and tachycardia. A patient with acute abdomen may have a serious underlying disease which could lead to a fatal outcome. Early evaluation and appropriate therapy (including surgical intervention) must be carried out without delay. Acute abdomen may occur in pregnancy. In pregnancy, the position of the appendix may be altered due to the enlarged uterus.

Acute abdomen is not a diagnosis in itself, but is a term applied to an acute abdominal crisis which may be due to one of many causes. The causes of acute abdomen include:

- *Acute intestinal obstruction*: e.g. intussusception, strangulated/incarcerated hernia, mass of *Ascaris lumbricoides* (in children), bowel torsion, volvulus, adhesions.
- *Inflammation of abdominal organs*: e.g. gastroenteritis, acute appendicitis, acute cholecystitis, acute pancreatitis, pyelitis/pyelonephritis, acute mesenteric adenitis, acute salpingitis/

pyosalpinx, ruptured liver abscess, severe amoebic colitis, complication after laparotomy.

- *Perforation with spreading peritonitis*: e.g. perforated peptic ulcer, perforated gut (e.g. typhoid perforation), ruptured tubal (ectopic) pregnancy.
- *Vascular and tubular structures obstruction/leakage*: e.g. ureteric colic (stone in ureter), biliary colic, twisted ovarian cyst, acute mesenteric thrombosis, leaking abdominal aortic aneurysm.
- *Non-surgical abdominal crisis*: e.g. sickle-cell crisis, malaria, diabetic crisis, acute porphyria, lobar pneumonia, myocardial infarction, *Herpes zoster*, tertiary syphilis (*Treponema pallidum*), familial Mediterranean fever, periodic syndrome in children.

5.12.2 Non-acute abdominal pain

Non-acute abdominal pain lasts typically more than several days, and often several weeks duration. It is not excessively severe, and is usually not accompanied by high fever. Many causes of non-acute abdominal pain can be diagnosed by correct investigation, and treatment or cure is available. In some cases there may be progression to a severe abdominal disorder if the condition is not treated early.

Causes of non-acute abdominal pain or discomfort include:

- peptic ulcer disease, e.g. gastric, duodenal ulcer, hiatus hernia
- chronic pancreatitis, e.g. recurrent acute pancreatitis due to alcohol ingestion, gall stones, etc.
- small intestinal infections, e.g. *Ascaris lumbricoides*, hookworm, *Strongyloides stercoralis*, *Giardia lamblia*, tuberculous enteritis
- large intestinal (colorectal) infections, e.g. *Entamoeba histolytica/dispar*, *Schistosoma mansoni*, *Trichuris trichiura*
- hepatitis, e.g. viral, bacterial, parasitic causes (see Section 5.6 on jaundice)
- biliary disease, e.g. cholecystitis
- diseases with tender hepatosplenomegaly, e.g. malaria (tropical splenomegaly syndrome), visceral leishmaniasis (kala azar), *Schistosoma mansoni*, *Echinococcus* cysts, brucellosis, malignant lymphoma, chronic leukaemia

- pelvic masses, e.g. fibroids, ovarian cysts
- malignancy, e.g. gastric, hepatic, pancreatic, ovarian, renal tumours, teratoma, abdominal Burkitt lymphoma.

Tables 5.19 and 5.20 summarize the causes and clinical and diagnostic findings of acute and non-acute abdominal pain respectively.

5.12.3 Investigation of acute abdomen and non-acute abdominal pain

- *History*
 - fever
 - vomiting, haematemesis
 - localized/generalized abdominal pain
 - abdominal cramps, continuous or intermittent
 - loin pain
 - abdominal distension
 - constipation, no passage of wind
 - diarrhoea, blood in stool
 - dysuria, haematuria
 - vaginal discharge, vaginal bleeding
 - amenorrhoea
 - previous surgery
 - previous similar episodes.
- *Physical examination*
 - general condition (acutely ill; in pain; wasted)
 - posture (unable to stand; leaning forward)
 - raised temperature, low blood pressure
 - dehydration
 - pallor, jaundice
 - abdominal distension, localized/generalized tenderness, guarding, rebound tenderness
 - surgical scars
 - abdominal mass

Table 5.19 Causes and clinical and diagnostic findings in acute abdominal pain

| | <i>Main causes</i> | <i>Signs/symptoms</i> | <i>Tests</i> |
|---|-------------------------------------|---|---|
| Intestinal obstruction | Strangulated/incarcerated hernia | Intermittent colicky pain | X-ray: gas, fluid levels |
| | Intussusception | Continuous vomiting, stomach contents (bile, faecal matter) | Ultrasound |
| | Mass of <i>Ascaris lumbricoides</i> | Constipation (no wind) | |
| | Bowel torsion | Distended abdomen | |
| | | Visible peristalsis | |
| | Adhesions | Generalized/localized tenderness | |
| | | Cough tenderness: hernial rings, male genitalia | |
| | | High-pitched tinkling sounds | |
| | | Mass on rectal examination | |
| | | Stool mucoid/bloody | |
| | <i>A. lumbricoides</i> ova | | |
| Inflammation of abdominal organs | <i>Main causes</i> | <i>Signs/symptoms</i> | <i>Tests</i> |
| | Gastroenteritis | Localized pain (pointing test) | Urine: pus cells, red cells, casts, bacteria, parasites |
| | Acute appendicitis | Pain becomes worse | Stool for red cells, pus cells, characteristic bacteria |
| | Acute cholecystitis | Vomiting with pain | ECS: pus cells, GNID |
| | Acute pancreatitis | Diarrhoea (gastroenteritis) | Total and differential white blood cell count |
| | Pyelitis/pyelonephritis | Fever | Ultrasound |
| | Acute mesenteric adenitis | Tenderness on superficial/deep palpation | |
| | Acute salpingitis/pyosalpinx | Abdominal rigidity/guarding | |
| | | Rebound tenderness | |
| | | Abdominal mass | |
| | Vaginal discharge | | |
| | Cervical excitation | | |
| | Tender pelvic mass | | |
| | Rectal examination tenderness | | |
| | Raised temperature | | |
| Perforation | <i>Main causes</i> | <i>Signs/symptoms</i> | <i>Tests</i> |
| | Perforated peptic ulcer | Excruciating pain not relieved by analgesics | Pregnancy test positive |
| | Perforated bowel, e.g. typhoid | Shoulder tip pain | X-ray: free gas under diaphragm |
| | Ruptured tubal pregnancy | Amenorrhoea | Ultrasound |
| | | Board-like rigidity | |
| | Silent abdomen | | |

Table 5.19 **Causes and clinical and diagnostic findings in acute abdominal pain (concluded)**

| Vascular/tubular obstruction/ leakage | <i>Main causes</i> | <i>Signs/symptoms</i> | <i>Tests</i> |
|--|-----------------------------------|--|---|
| | Ureteric colic | Intermittent colicky pain | Urine: pus cells, red cells, crystals |
| | Biliary colic | Severe localized abdominal/loin pain | X-ray: gallstones/ureteric opacities (stones) |
| | Twisted ovarian cyst | Tenderness on superficial/deep palpation | Ultrasound |
| | Acute mesenteric thrombosis | Abdominal rigidity/guarding | |
| | Leaking abdominal aortic aneurysm | | |
| Non-surgical | <i>Main causes</i> | <i>Signs/symptoms</i> | <i>Tests</i> |
| | Sickle-cell crisis | Tenderness on superficial/deep palpation | Urine and blood sugar |
| | Malaria | Bronchial breathing | Sickle-cell screen |
| | Diabetic crisis | Skin vesicles | Blood for malaria |
| | Acute porphyria | | VDRL |
| | Lobar pneumonia | | Chest X-ray |
| | Myocardial infarction | | Ultrasound |
| | <i>Herpes zoster</i> | | |
| | Syphilis | | |
| | Familial Mediterranean fever | | |

enlarged liver, spleen

absent, tinkling or increased bowel sounds

rectal examination: mass, tenderness

vagina/cervix (on speculum examination): pus, blood

pelvis (on bimanual examination): tenderness, tender pelvic mass, cervical excitation.

A person with heat stroke has a body temperature above 41 °C. Other symptoms include confusion, combativeness, bizarre behaviour, faintness, staggering, strong rapid pulse, dry flushed skin, lack of sweating, delirium and coma.

Haemolytic–uraemic syndrome is a condition involving break-up of red blood cells and kidney failure. There is clumping of platelets within the kidneys' small blood vessels with reduced blood flow. This leads to kidney failure. Haemolytic–uraemic syndrome is the most common cause of acute kidney failure in infants and young children.

Table 5.20 Causes, clinical and diagnostic findings in non-acute abdominal pain

| Peptic ulcer disease | Pancreatic disease | Hepatic/biliary disease | Hepatospleno-megaly | Pelvic disease | Enteric infection | Miscellaneous |
|---|---|---|---|--|--|---|
| <p>Causes</p> <p>Gastric ulcer</p> <p>Duodenal ulcer</p> <p>Hiatus hernia</p> <p>Gastric carcinoma</p> | <p>Causes</p> <p>Chronic pancreatitis</p> <p>Carcinoma</p> | <p>Causes</p> <p>Hepatitis</p> <p>Cholecystitis</p> <p>Carcinoma</p> | <p>Causes</p> <p>Malaria</p> <p>Kala azar</p> <p><i>S. mansoni</i></p> <p><i>Echinococcus</i> cyst carcinoma</p> <p>Brucellosis</p> <p>Leukaemia/lymphoma</p> | <p>Causes</p> <p>Fibroids</p> <p>Ovarian cysts</p> <p>Ovarian</p> <p>Ovarian cyst carcinoma</p> | <p>Causes</p> <p><i>A lumbricoides</i></p> <p>Hookworm</p> <p><i>T. trichiura</i></p> <p><i>S. stercoralis</i></p> <p><i>G. lamblia</i></p> <p><i>E. histolytica/dispar</i></p> <p>Tuberculous enteritis</p> <p><i>S. mansoni</i></p> | <p>Causes</p> <p>Renal tumours</p> <p>Burkitt lymphoma</p> |
| <p>Tests</p> <p>Hb</p> <p>Barium swallow</p> | <p>Tests</p> <p>Hb</p> <p>Ultrasound</p> | <p>Tests</p> <p>Hb</p> <p>Liver function tests</p> <p>Cholecystogram</p> | <p>Tests</p> <p>Hb</p> <p>Blood film for parasites</p> <p>Total and differential WBC</p> <p>Peripheral blood film</p> <p>Splenic aspirate for LD bodies</p> <p>Stool for ova</p> <p>Ultrasound</p> | <p>Tests</p> <p>Hb</p> <p>Ultrasound</p> | <p>Tests</p> <p>Hb</p> <p>Stool for trophozoites, cysts, ova</p> <p>Ultrasound</p> | <p>Tests</p> <p>Hb</p> <p>Ultrasound</p> |

There are many causes of haemolytic–uraemic syndrome including *Shigella*, drugs, tumours, pregnancy and systemic lupus erythematosus (SLE). One of the most prominent causes today of haemolytic–uraemic syndrome is *Escherichia coli* O157:H7.

Typically patients with haemolytic–uraemic syndrome suffer from anaemia and thrombocytopenia, which causes abnormal bleeding. Seizures and coma also occur. Cases typically begin with severe abdominal cramps and diarrhoea, which may become bloody by the second or third day. Nausea and vomiting are present in about half of the patients. Most patients recover in seven to ten days, but some go on to develop the severe form of the disease.

- *Laboratory investigations*
 - haemoglobin
 - blood film for malaria parasites
 - total and differential white blood cell count
 - sickle-cell screen
 - urine for protein, glucose, blood
 - MSU for pus cells, red cells, casts, crystals
 - fresh stool: macroscopic appearance, red cells, pus cells, bacteria of characteristic shape and motility, cysts, trophozoites, larvae, ova
 - endocervical swab (ECS) for pus cells, Gram-negative intracellular diplococci (GNID)
 - blood for glucose
 - pregnancy test
 - VDRL.

- *Other investigations*
 - Aspiration of abdominal fluid, or fluid from the pouch of Douglas

- *Diagnostic imaging: acute abdominal pain*
 - X-ray of abdomen*
 - free air: erect and left lateral decubitus (perforation)
 - fluid levels: supine, erect, left and right lateral decubitus (obstruction)
 - renal stones: plain and intravenous pyelogram (IVP).

Chest X-ray

for free air: upright (perforation).

Ultrasound

fluid in bowel, peristalsis (obstruction)

enlarged sigmoid colon (sigmoid volvulus)

bowel invagination (intussusception)

intra-abdominal fluid (peritonitis)

ectopic pregnancy, intra-abdominal abscess, hydrosalpinx and tubo-ovarian abscess.

- *Diagnostic imaging: non-acute abdominal pain*

X-ray of abdomen

cholecystogram

barium swallow.

Ultrasound of abdomen

hepatosplenomegaly

Echinococcus cyst

pelvic masses, e.g. ovarian cyst, fibroid, ovarian carcinoma

abdominal tumours, e.g. Burkitt lymphoma, Wilms tumour, other lymphomas, teratomas, etc.

Guidelines for diagnostic imaging*X-ray: acute abdomen*

Diagnostic imaging is helpful to plan correct surgical intervention and to avoid unnecessary and potentially dangerous surgical intervention.

For suspected perforated gastric ulcer, an X-ray should be performed as soon as possible. The following views should be obtained: plain antero-posterior (AP) with the patient lying down; lateral decubitus with the patient lying on the left side; and chest X-ray with the patient in the upright position to look for free air in the peritoneal cavity. For the lateral decubitus view, the patient should be left in this position for a few minutes to allow the air to

rise. The chest X-ray may be the best view for visualizing free air under the diaphragm.

For suspected gastrointestinal obstruction, the following views should be obtained: plain AP with the patient supine and standing up; left and right decubitus; and a chest X-ray to look for fluid levels. It may be possible to determine the level of obstruction (jejunum, ileum, colon). Intestinal obstruction caused by a large bowel volvulus may be identified. Fluid levels at all levels of the bowel are seen in paralytic ileus.

In some patients with abdominal obstruction, the patient may be given diluted water-soluble contrast medium to drink, and the passage of the contrast followed through the bowel for a few hours in order to localize the site of obstruction. In some cases, this procedure will resolve the obstruction. The patient must *never* receive barium suspension for examination.

In a child with a suspected ileocolic intussusception, radiological reposition may be performed, but this must be carried out only by an experienced radiologist.

For suspected renal colic, a plain AP abdominal X-ray may show radiopaque stones. An intravenous pyelogram may also be made if well trained radiological staff are available and a physician is present during the injection of the contrast medium. The procedure can be limited to two to three images: one taken before the contrast medium is injected and one taken 15–20 minutes afterwards. Ultrasound is a preferable procedure for the demonstration of renal stones.

Ultrasound: acute abdomen

In case of gastrointestinal obstruction, distended, multiple fluid-filled loops of bowel are likely to be caused by either paralytic ileus or mechanical small bowel obstruction. Obstruction of the colon is likely to be due to sigmoid volvulus, which in some regions is endemic in adult males. Typically, abnormal thickening of the sigmoid wall and enlarged target configurations are seen. Increased or decreased peristalsis can also be noted.

The characteristic appearance of intussusception is of a “doughnut” or “target”, with the image of two hypoechoic rings.

Peritonitis appears as intra-abdominal fluid with different echoes, according to the consistency of the fluid (pus, blood, clots).

Perforation of peptic ulcers and typhoid bowel show air in the abdominal cavity.

Intra-abdominal abscesses (subphrenic abscess, abscesses between loops of bowel, pelvic abscess, perinephric abscess) can be demonstrated as masses with or without a wall and various echogenity within the respective area. The distinction between hydrosalpinx and tubo-ovarian abscess and ectopic pregnancy is difficult. A tubo-ovarian abscess usually has a complex internal appearance with low-level echoes arising from the inflammatory fluid but ectopic pregnancy may mimic this appearance.

Amoebic colitis, acute pancreatitis, appendicitis, acute pelvic inflammatory disease in women, ectopic pregnancy, liver abscess: see under the respective sections.

X-ray: non-acute abdominal pain

A cholecystogram using fat-soluble contrast medium, given orally, can be performed by an experienced radiologist. A negative examination (“normal gallbladder”) does not rule out the presence of gallbladder disease; however the presence of stones gives a clear diagnosis.

An intravenous cholangiogram examination should only be performed in hospitals with well trained radiological and anaesthetic staff, due to the danger of severe adverse reactions from the contrast medium.

Barium swallow using either a single contrast or double contrast technique for examining the stomach and the duodenum should be reserved for hospitals with qualified radiologists.

Ultrasound: non-acute abdominal pain

Echinococcus cysts of the liver show a typical appearance of multiple cysts with calcification, although this appearance does not exclude other cystic diseases such as liver abscess and amoebic abscesses.

Ovarian cysts range from small cysts, e.g. corpus luteum cysts, to huge ovarian masses filling the whole pelvis. The echoes seen in those cysts vary according to the internal fluid, e.g. blood, pus or clots. There may be involvement of other organs. Other pelvic masses may indicate ovarian carcinoma.

Most solid masses in the pelvis arise from the uterus. Fibroids are the most common. They appear as single or multiple masses within the uterus, which can be considerably enlarged. Larger fibroids can be pedunculated and appear as extra-uterine masses. Non-calcified fibroids are hypoechoic relative to the surrounding myometrium; high echogenic areas result from calcification. A low-lying caecum filled with faeces can mimic a pelvic mass.

Abdominal masses in children include Burkitt lymphoma, other lymphoma, Wilms tumour and teratoma. Many Burkitt lymphomas occur in the abdomen, located around the kidney, ovary, liver or retroperitoneum. They are large tumours which do not appear to arise from a specific organ. Other lymphomas are often associated with mesenteric lymphadenopathy and present as rounded hypoechoic masses usually located near the midline at the root of the mesentery. Occasionally they develop septation, the so-called “sandwich” sign. Wilms tumour develops in children between 2 and 4 years of age and grows as an intrarenal mass, poorly differentiated from the kidney. In 10% of cases, both kidneys are involved. Wilms tumours often grow into the inferior vena cava, whereas neuroblastomas displace the abdominal vessels. The appearance of teratomas is related to their composition, e.g. fat, hair, bone, teeth.

For the appearance of tuberculous enteritis, see Section 5.7 on oedema.

Children with “periodic syndrome” have pain for 1 day, are pale, vomit, have fever and normal stool examination. The major causes are non-specific colic or mesenteric adenitis usually associated with a viral infection. “Periodic syndrome” is a diagnosis of exclusion.

5.13 Pregnancy

The following information should be collected when examining a pregnant woman.

- *History*
 - age
 - date of last menstrual period
 - bleeding time of menstruation
 - pain (unilateral?)
 - fever
 - nausea and vomiting
 - cramping
 - previous abortions
 - previous illnesses (e.g. diabetes, sexually transmitted infection)
 - current illnesses
 - trauma
 - previous operations
 - drugs
 - attempt to induce abortion
 - mental retardation in the family
 - previous anomalous infant
 - dyspnoea
 - fetal movements
 - seizures
 - vaginal discharge
 - twins in the family.

- *Physical examination*
 - assessment of pregnancy
 - rapid pulse, raised temperature
 - general appearance (additional illness, acute and chronic, e.g. malaria, cardiac failure)
 - shock
 - abdominal tenderness
 - oedema
 - pallor of e.g. mucous membranes, nails
 - vaginal examination (assessment of bleeding, size of uterus, assessment of cervical os)
 - blood pressure.

- *Laboratory examinations*
 - haemoglobin
 - urine for protein
 - blood glucose
 - pregnancy test
 - cross-matching (if necessary).

A pregnancy test is carried out on a sample of urine. Although a random urine sample can be used, an early morning urine sample is more sensitive. The test can become positive as early as a few days after the first missed period, but a negative test does not rule out early pregnancy.

- *Ultrasound*

Ultrasound examination in pregnancy is indicated when the observations of the midwife are not consistent with the history of the patient. Common indications for scanning during normal pregnancy are:

 - estimation of gestational age (after first trimester)
 - confirmation of the presence of a pregnancy and fetal viability
 - multifetal pregnancy
 - date/size discrepancy
 - fetal position (see Section 5.13.5 on ultrasound in pregnancy).

5.13.1 Diseases of pregnancy

Pre-eclampsia/eclampsia

Pre-eclampsia is a disease occurring after 20 weeks of gestation. The symptoms of pre-eclampsia are hypertension and proteinuria. In mild pre-eclampsia elevated blood pressure is below 160/110 mmHg and proteinuria is 0.4 g to 5 g protein in urine per 24 hours. In severe pre-eclampsia blood pressure is above 160/110 mmHg on two occasions at least 6 hours apart, and urine protein is more than 5 g/24 hours.

In eclampsia the typical signs of pre-eclampsia are combined with tonic-clonic grand mal seizures during or after delivery. The disease results from generalized constriction of the arterioles. The cause of the arteriolar constriction is unknown.

Maternal complications are seizures, cerebral haemorrhage, renal failure, thrombocytopenia, hepatic failure, pulmonary oedema, HELLP syndrome (haemolytic anaemia, elevated liver enzymes, low platelet count). There is a risk of pre-term delivery and caesarean section.

Fetal complications are acute and chronic placental insufficiency, placental infarction and abruption, intrapartal fetal distress, stillbirth, oligohydramnios and growth retardation

Diseases of pregnancy include the following:

- hyperemesis gravidarum
- Rh incompatibility
- pregnancy-induced hypertension
- gestational diabetes.

5.13.2 Diseases occurring during pregnancy

The following diseases may cause complications to mother and child or both. Therefore, in pregnant women these diseases need special attention and treatment.

- chronic renal disease
- heart disease
- respiratory diseases
- endocrine diseases
- diabetes, hypertension, coagulation disorders
- drug misuse
- syphilis
- rubella
- cytomegaly virus
- toxoplasma
- HIV
- hepatitis B
- malaria
- listeria.

Urinary tract infection occurs more frequently in pregnant women, whose muscles lining the ureters are more relaxed and because of the pressure of the uterus. Urinary tract infection may be asymptomatic in

pregnant women. A midstream urine sample should be examined by microscopy to exclude an infection.

Anaemia due to iron and folic acid deficiency is more common in pregnant and lactating women, who have an increased demand for iron and folic acid for haemoglobin biosynthesis. Haemoglobin should be determined in all pregnant women as soon as possible and for some time after delivery. Women should receive iron and folic acid supplementation during pregnancy and lactation.

5.13.3 Complicated pregnancy

Complicated pregnancy is defined as any problem occurring during pregnancy. At the level of district hospitals in developing countries about 60% of pregnancies are complicated. Complications in pregnancy can be separated into those which are most likely to occur at any time in pregnancy, and those related to the different trimesters or delivery. The complications that may occur during pregnancy are listed in Table 5.21.

Investigation of complicated pregnancy

- *History*
 - duration of pregnancy (date of last menstrual period)
 - abdominal/pelvic pain: site, type
 - vaginal bleeding/discharge: type, amount, clots, products of conception
 - fetal movements
 - attempts to induce abortion
 - systemic illness: diabetes, renal disease, heart disease, hypertension.
 - past obstetrical history: pregnancy, abortion, complications, congenital abnormalities, multiple pregnancy, surgery
 - family history of twins
 - trauma
 - shortness of breath

Table 5.21 Complications in pregnancy

| First trimester | Second trimester | Third trimester | Delivery | General |
|--|--|--|--|--|
| Abortion Ectopic pregnancy Molar pregnancy Hyperemesis gravidarum Retention of urine <i>Infections</i> Rubella <i>Toxoplasma gondii</i> | Abortion Pre-eclampsia/eclampsia Small for date Large for date | Pre-eclampsia/eclampsia Ante-partum haemorrhage Hydramnios Oligohydramnios Cytomegalovirus Varicella zoster | Pre-term labour Uterine rupture Cord prolapse Fetal distress Multiple pregnancy Malpresentations Cephalo-pelvic disproportion Fetal death Rhesus incompatibility Postmaturity | Anaemia Urinary tract infection Maternal disease: diabetes, hypertension, cardiac disease <i>Infections</i> HIV Hepatitis B <i>Herpes simplex</i> <i>C. trachomatis</i> <i>N. gonorrhoeae</i> Malaria |
| Laboratory investigations Hb Blood for parasites Urine chemistry MSU microscopy Pregnancy test Blood glucose Toxoplasma test Ultrasound | Laboratory investigations Hb Blood for parasites Urine chemistry Blood glucose Blood typing Ultrasound | Laboratory investigations Hb Urine for protein Viral tests Ultrasound | Laboratory investigations Hb Blood for parasites Urine chemistry Blood glucose Blood typing Ultrasound | Laboratory investigations Hb Gram stain HIV test Blood for parasites |

seizures
fever
drug use
symptoms of systemic infection.

- *Physical examination:*

general condition (acutely ill, in pain, clinical shock)
increased temperature, rapid pulse, rapid respiratory rate, low blood pressure/high blood pressure
dehydration
pallor
oedema
abdominal/pelvic tenderness, localized/generalized, guarding rebound tenderness
palpable uterus, uterine size, uterine mass
dehydration
vagina/cervix on speculum examination¹: blood, products of conception
pelvis on bimanual examination¹: tenderness, tender pelvic mass, open cervical os
signs of systemic infection.

- *Laboratory investigations*

haemoglobin
blood film for malaria parasites
total and differential white blood cell count, platelet estimate
urine for glucose, protein
MSU for pus cells, red cells, casts
endocervical swab (ECS) for pus cells, Gram-negative intracellular diplococci (GNID)
blood for glucose, urea/creatinine
pregnancy test
VDRL
blood typing and cross-matching.

¹ This procedure should not be performed if there is suspected placental bleeding or threatened abortion.

- *Diagnostic imaging*
ultrasound for:
 - estimation of gestational age (date/size discrepancy)
 - confirmation of pregnancy and fetal viability
 - diagnosis of ectopic pregnancy
 - evaluation of uterine bleeding (assessment of abortion)
 - investigation of molar pregnancy
 - multiple pregnancy
 - placental disorders
 - amniotic fluid
 - fetal disorders
 - malformations/malpresentations.

Complications occurring at different stages of pregnancy are discussed in the following sections.

First trimester (1–3 months)

Abortion (85% of cases): mainly due to fetal causes, e.g. inappropriate development of the fetus due to chromosomal abnormalities, or maternal illness, e.g. malaria.

Types of abortion

- *Threatened abortion*: cervical os closed, uterus correct size for dates.
- *Inevitable abortion*: rhythmical pains, dilatation of the cervix.
- *Incomplete abortion*: partial expulsion of products of conception. Cervical os open, uterus small for dates.
- *Complete abortion*: complete expulsion of all products of conception. Cervical os closed, non-pregnant uterus.
- *Missed abortion*: death of fetus, complete retention of products of conception.
- *Recurrent abortion*: more than three consecutive abortions.
- *Septic abortion*: usually due to attempted criminal abortion. Patient is febrile and suffers from severe pelvic pain.
- *Ectopic pregnancy* (implantation of the ovum outside the uterine cavity): e.g. inside the fallopian tube (95%), cervix, ovary, abdominal

or pelvic cavity, due to tubal diseases such as sexually transmitted infections, use of intrauterine devices.

- *Molar pregnancy* (tumour of the products of conception: 80% are benign; 15% are locally invasive; 5% are malignant).
- *Uterus too large for date*.
- *Hyperemesis gravidarum*: vomiting in pregnancy severe enough to cause profound metabolic changes.
- *Retention of urine*: due to elongation of the urethra and compression by a retroverted uterus.
- *Infection*: e.g. rubella virus, *Toxoplasma gondii*.

Second trimester (4–6 months)

- *Abortion* (15% of cases): mainly due to maternal causes, e.g. cervical incompetence, abnormalities of the uterus (fibroids, septate/bicornuate uterus), diabetes mellitus, hypertension, chronic renal disease, infection (e.g. syphilis, malaria, *Herpes simplex*, *Listeria monocytogenes*).
- *Pre-eclampsia/eclampsia*: see Section 5.13.1 on diseases of pregnancy.

Disorders of fetal growth

Small for gestational age

Definition: fetuses less than the 10th percentile for growth are termed small for gestational age.

Causes:

- a. Decreased growth potential
- 10% to 15% due to congenital abnormalities (e.g. Down syndrome or any other trisomy, Turner syndrome, anencephaly, neural tube defects)
- intrauterine infections of various origins, e.g. cytomegaly, rubella)
- exposure to teratogens (e.g. alcohol, cigarettes)
- small maternal stature
- pregnancies at high altitudes
- female fetus.

- b. Intrauterine growth restriction
 - decreased nutrition and oxygen transmitted across the placenta
 - maternal causes: hypertension, renal failure, anaemia, malnutrition
 - placental causes: placenta praevia, placental infarction.
- c. Additional causes of small babies according to the gestational age
 - multiple gestations, oligohydramnios.

Large for gestational age

Definition: estimated fetal weight higher than the 90th percentile (birth weight more than 4500 g) is termed large for gestational age.

Causes include: diabetes mellitus, maternal obesity, multiparity, advanced maternal age, large maternal stature, male fetus.

Third trimester (7–9 months)

Pre-eclampsia/eclampsia

See section 5.13.1 on diseases of pregnancy.

Ante partum haemorrhage

- Definition: any vaginal bleeding in late pregnancy.
- Bleeding is the main complication of the third trimester; it often leads to pre-term labour and delivery.
- Clinical feature: vaginal bleeding, tenderness of the abdomen or back pain, abnormal contractions, fetal distress, shock, pre-term labour, pre-term rupture of the membranes, intrauterine growth restriction, malpresentation, congenital disorders.

Causes:

- a. Placental (50%)
 - *Placenta praevia* (low-lying placenta which covers the internal cervical os; complete means total covering, marginal means the edge of the placenta reaches the margin of the os).

Placenta praevia is occasionally combined with placenta accreta (abnormal adherence), placenta increta (invading the myometrium) and placenta percreta (invades the uterine membranes).

Mothers with a history of smoking, previous caesarean section, multiparty, multiple gestation, increased maternal age and erythroblastosis, are at high risk of developing placenta praevia. Bleeding results from small disruptions in the placental attachment during the normal development and thinning of the lower uterine segment during the third trimester. Placenta praevia should never be assessed by vaginal examination. This must be avoided.

- *Placental abruption* (separation of the placenta from the uterine wall). About 30% of haemorrhage in the third trimester is due to placental abruption. The main risk for placental abruption is hypertension, trauma, short umbilical cord, hydramnios, old maternal age, drug misuse, pre-term rupture of membranes. Haemorrhage appears revealed, concealed or external. The uterus is tender, painful contractions can be reported.

b. Maternal

- Uterine rupture due to uterine scars, abdominal trauma, abnormal placentation, overdistension, multiparty, large fetus, abnormal position of the fetus.
- Clinical features: sudden onset, shock, fetal distress or disappearance of fetal heart beat, pain, vaginal bleeding.

c. Fetal

- Fetal vessel rupture mainly due to velamentous cord insertion (cord between amnion and chorion, unprotected from the membranes).
- Causes: mainly multiple pregnancies.

d. Non-obstetric causes

- Cervicitis.
- Benign or malign neoplasm.
- Laceration of the vagina.
- Varices.

- Pelvic trauma.
- Clotting disorders.
- Polyhydramnios: due to maternal causes (diabetes mellitus, benign placental tumours) and fetal causes (multiple pregnancy, anencephaly, oesophageal/duodenal atresia, absence of kidneys, hydrops foetalis)
- Oligohydramnios: due to poor placental function, fetal growth retardation, renal agenesis.
- Malpresentation: breech, transverse position—may be due to fetal congenital abnormality.
- High head near term: poor position of the fetus, angle of the pelvic brim, pelvic tumours, pelvic disproportion, hydramnios, placenta praevia.
- Cephalopelvic disproportion: contracted pelvis, large fetal head, diabetes.
- Fetal death causes: diabetes, *Herpes simplex*, malaria, hypertension, chronic renal disease.
- Infection, e.g. cytomegalovirus, *Varicella zoster*.
- Rhesus incompatibility.
- Postmaturity.

Disorders of amniotic fluid

The normal amount of amniotic fluid is 800 mL at about 28 weeks and 500 mL at 40 weeks.

Oligohydramnios

- Definition: lack of amniotic fluid.
- Clinical feature: uterus small for date, uterus feels full of fetus, labour often preterm.
- Causes: decreased secretion by the fetal kidneys or increased resorption by the placenta, swallowed “by the fetus, or leaked out into the vagina, due to fetal congenital abnormalities, decreased placental perfusion or ruptured membranes.

Polyhydramnios

- Definition: excess of amniotic fluid.

- Clinical features: increased symphysiofundal height, tense uterus, bigger than date. Difficulty to feel any fetal parts.
- Causes: diabetes mellitus of the mother, multiple gestations, hydrops (Rh incompatibility, congenital abnormalities)

Multiple gestations

Definition of multiple gestations

- Monocygote: a fertilized ovum divides into two separate ova.
- Dicygote: an ovulation produced two ova and both are fertilized.
- Triplet pregnancy (rare).

Clinical features

In multiple pregnancies complications including pre-term labour, cord prolapse, pre-eclampsia, congenital abnormalities, malpresentation and twin–twin transfusion syndrome are more frequent. The patient should be referred to a hospital with an obstetric facility to avoid complications during delivery. Normally a multiple gestation is suspected when a date-size discrepancy of the uterus has been diagnosed. Very often the medical history of the pregnant woman reveals a history of twins in the family.

5.13.4 Complications during labour and delivery

Pre-term labour

Definition: labour before 37 weeks of gestation with change of the cervix. Reasons include:

- maternal infections (e.g. syphilis, malaria)
- uterine rupture
- fetal distress: due to placental insufficiency, abruptio placentae, cord prolapse, maternal cardiac disease, fetal abnormalities
- fetal infections: e.g. hepatitis B, malaria, *Herpes simplex*, HIV, neonatal conjunctivitis (*Neisseria gonorrhoeae*, *Chlamydia trachomatis*), neonatal pneumonia (*C. trachomatis*)
- premature spontaneous rupture of the membranes

Definition: rupture of the membranes before onset of labour

- Clinical feature: Leaking of vaginal fluid, pain
- Chorio-amnionitis
Definition: infection of the amniotic fluid.
Clinical feature: Maternal fever, fetal tachycardia, uterine tenderness, smelling vaginal discharge.
 - Fetal death
Definition: lack of fetal heart rate at or beyond 20 weeks of gestation
Causes: all complications mentioned above (in addition: cord compression, utero-placental insufficiency).
 - Other causes of pre-term labour:
multiple pregnancy
polyhydramnios
ante partum haemorrhage
uterine abnormalities.

Obstruction, malpositions and malpresentations

a. Cephalopelvic dysproportion

- Definition: absolute: no possibility for vaginal delivery
- Relative: large baby, able to pass in case of normal labour.
- Clinical feature: high head at term, obstruction of labour.
- Causes: pelvis of the mother too small, polyhydramnios, multiple pregnancy, fetal abnormalities (e.g. hydrocephalus).

b. Breech presentation

- Clinical feature: head can be felt in the fundus (Leopold manoeuvres).
Fetal heart near the fundus, breech can be palpated in the pelvis or by vaginal examination.

c. Cord prolapse

- Clinical feature: cord can be felt ahead of the presenting part. Often combined with malpresentations, pre-term delivery, multiparity, small baby.

d. Other malpresentations

- Shoulder-presentation, brow-presentation, face presentation and occipito-posterior presentation are rare.

5.13.5 Ultrasound investigations during pregnancy and delivery

Ultrasound examinations are made when pathological features are expected, or when the findings of the midwives are not consistent with the history of the patient. Often the suspected diagnosis is confirmed during scanning. The person making the examination should not tell the pregnant women the diagnosis during the investigation, not only in severe findings such as fetal death or ectopic pregnancy but also confirming a twin pregnancy or an intact pregnancy. The observations and their consequences should be rather discussed with the patient after the examination in appropriate surroundings. It may be even advisable to tell the findings to a nurse or midwife who comes from the same community as the patient and therefore may be more qualified to discuss the problems the patient may have to face.

Estimation of gestational age

Uncertainty about gestational age occurs when patients cannot accurately remember the date of the last menstrual period, or when menstruation had not resumed due to breast feeding. From 7 weeks on, fetal heart movements are visible in abdominal scanning. From 8–12 weeks, an estimation of fetal length can be made (crown–rump length). During the second and third trimesters, biparietal diameter and femur length are used to demonstrate fetal growth. Abdominal circumference can also be measured but is less accurate. Tables for fetal age assessment are usually provided within the operating manual of the scanner.

In case of decreased fetal growth, both parameters are less than the 10th percentile according to the tables. The abdominal circumference can be assessed as a third parameter, although it is less accurate.

When all parameters, such as biparietal diameter, femur length and abdominal circumference, are 10 to 15% higher than expected, they indicate that a fetus is too large for its gestational age.

Confirmation of pregnancy and fetal viability

Assessment of fetal viability includes presence of fetal heart movements (from 7 weeks on in abdominal scanning).

Signs of fetal death include lack of fetal heartbeat, oligohydramnios (scanty amniotic fluid), hydrops foetalis (generalized oedema of the fetus), overlapping of the cranial sutures.

Ectopic pregnancy

Any pelvic mass in a woman of childbearing age should be considered an ectopic pregnancy until proved otherwise. An unruptured ectopic pregnancy appears as a complex mass between 1.5–2.5 cm consisting of an echoic centre and an echogenic ring. With a ruptured ectopic pregnancy there is intraperitoneal fluid. The blood is anechoic when unclotted, but moderately echogenic when clotted. There is also blood in the pouch of Douglas. If the ultrasound investigation is difficult, it should be repeated several times and confirmed by a second investigator. Ectopic pregnancy can mimic a complex adnexal mass, especially the “chronic ectopic pregnancy” in combination with sexually transmitted infection where the typical signs of acute abdomen are missing. Severe anaemia is often present, and a pregnancy test can be helpful.

Assessment of abortion

Incomplete abortion shows lack of a definable embryo. Missed abortion shows retention of products of conception with a non-viable fetus.

Molar pregnancy

Molar pregnancy shows a typical pattern of multiple small anechogenic structures within the echogenic tissue.

Uterine disorders

Uterine fibroids appear as hypoechoic masses inside the uterus, or may be pedunculated, in addition to an existing pregnancy. Calcified fibroids are hyperechoic. A bicornuate uterus shows a normal pregnancy in one horn, with a thickened endometrium in the other horn.

Placental disorders

Placental abnormalities are well demonstrated by ultrasound. In suspected fetal growth retardation, the following may be demonstrated: abnormally small placenta, areas of thrombosis and placental infarction reflecting premature senescence.

Ultrasound can identify placenta praevia with 95% accuracy. Placing the patient in the Trendelenburg position may assist in obtaining a precise picture. Abruption of the placenta can only be demonstrated by the presence of a retroplacental clot, in rare cases.

Amniotic disorders

The amniotic fluid index (AFI) is calculated by dividing the maternal abdomen into quadrants, finding the largest vertical pocket in each quadrant, and adding the vertical measures of each pocket. An AFI of less than 5 is considered oligohydramnios. An AFI of greater than 20 indicates polyhydramnios.

Fetal disorders

Fetal abnormalities can be clinically suspected when there is evidence of oligohydramnios or hydramnios. However, not all anatomical abnormalities of the fetus can be detected by ultrasound.

Multifetal pregnancy

Sonographically it is important to be aware of two types of twin-pregnancy. The dizygotic type has two amniotic cavities and two placentas. In the monozygotic type the twins have only one amniotic sac. Complications are more frequent in the monozygotic type. Cord torsions are most frequently observed in this type.

Chorio-amnionitis

Elevated fetal heart rate. Organisms changing the amniotic fluid can be depicted as irregular echoes.

Chapter 6

Epidemics

An *endemic disease* is a disease which is usually present in a community at all times but with relatively low incidence. Something that is endemic is typically restricted or peculiar to a locality or region. An *epidemic disease* is a disease which occurs in more than usual numbers in a community. Therefore, an epidemic is usually recognized by an increase in the numbers of cases of a disease. Even a single case of a disease may constitute an epidemic if the disease is not normally present in the community, e.g. Ebola haemorrhagic fever, plague. Most diseases that cause epidemics are highly infectious. Most endemic diseases are only moderately or not very infectious. An increase in the number of cases of a disease may occur *without* an epidemic. A *pandemic* occurs when an epidemic becomes very widespread and affects a whole region, a continent, or the entire world.

Outpatient morbidity data most closely resemble diseases present in the community. Therefore figures for disease prevalence (the number of cases over a period of time, e.g. a month or a year, in a particular location) can be examined to know if there is an increase in numbers of cases of a disease. This is usually done by collecting numbers of cases (disease statistics) in routine health facility work. For example, patients attending an outpatient clinic are (or should be) recorded daily in a register.

An epidemic always starts with a disease in a few individuals. It is the responsibility of the clinician to take an epidemic into consideration when establishing the diagnosis of a disease in a patient. It is also his or her responsibility to alert the health services if a suspected risk for an epidemic

presents and take preventive measures as appropriate to avoid the risk of spreading the disease within the local population and extending the disease outside the local area.

The risk of an epidemic due to an infectious agent depends on:

- *the means of transmitting the agent.* Means of transmitting infectious diseases include: droplet infection, direct contact (including sexual transmission, animal bites, etc), ingestion of contaminated food and water, and through vectors, e.g. mosquito bites.
- *the immunization/immune status of the population.* Diseases in which there is a high degree of natural immunity in certain populations include hepatitis A and Epstein–Barr virus. Diseases for which effective immunization is available include: poliomyelitis, measles, diphtheria (*Corynebacterium diphtheriae*), tetanus, yellow fever, hepatitis B, rubella, meningococcal infection types A, C, Y and W 135 (*Neisseria meningitidis*), rabies, influenza.

A decision to act rapidly to manage an epidemic therefore depends on:

- the severity of the disease
- the risk of spread of the disease within the local population
- the number of cases expected to occur
- the risk of social and economic disruption
- the danger of regional, national and international transmission.

Confirming the nature of the disease is done through detailed examination of the affected individuals, following the standard procedures:

- history-taking (symptoms of disease)
- physical examination (signs of disease).

Laboratory examination consists of tests that can be done onsite, and tests that are referred to higher centres (for which specimens are taken onsite). Table 6.1 list major presenting features of epidemic conditions.

Table 6.1 Major clinical presenting features of epidemic conditions

| Major presenting feature | Major causes of epidemics |
|-------------------------------------|--|
| Fever | Typhoid (<i>Salmonella typhi</i> , <i>Salmonella paratyphi</i>) Brucellosis (<i>Brucella abortus</i> , <i>Brucella suis</i> , <i>Brucella melitensis</i>) Malaria (<i>Plasmodium</i> spp.) Dengue fever Yellow fever Relapsing fever (<i>Borrelia recurrentis</i>) Leptospirosis (<i>Leptospira</i> spp.) Rift Valley fever |
| Fever with rash | Measles Rubella Varicella Typhus (<i>Rickettsia</i> sp) |
| Localized skin rash | Anthrax (<i>Bacillus anthracis</i>) Guinea worm (<i>Dracunculus medinensis</i>) |
| Fever and haemorrhage | Dengue fever Yellow fever Ebola and Marburg virus diseases Endemic haemorrhagic fever viruses (e.g. Crimean–Congo, West Nile etc.) |
| Fever and lymphadenopathy | Filariasis (<i>Wuchereria bancrofti</i>) Visceral leishmaniasis (<i>Leishmania donovani</i>) Plague (<i>Yersinia pestis</i>) Trypanosomiasis (<i>Trypanosoma</i> spp.) |
| Fever and neurological disease | Meningitis (<i>Neisseria meningitidis</i> , <i>Haemophilus influenzae</i> , <i>Cryptococcus neoformans</i>) Viral encephalitis Rabies Poliomyelitis |
| Fever and respiratory tract disease | Diphtheria (<i>Corynebacterium diphtheriae</i>) Whooping cough (<i>Bordetella pertussis</i>) Anthrax (<i>Bacillus anthracis</i>) Pneumonic plague (<i>Yersinia pestis</i>) Legionellosis Pneumonia (<i>Streptococcus pneumoniae</i>) Tuberculosis (<i>M. tuberculosis</i>) Viral laryngo-tracheobronchitis Viral influenza |

Table 6.1 **Major clinical presenting features of epidemic conditions (concluded)**

| Major presenting feature | Major causes of epidemics |
|--|---|
| Gastrointestinal disease with or without fever (watery diarrhoea, dysentery) | <i>Vibrio cholera</i> <i>Shigella</i> spp.) <i>Salmonella</i> spp. <i>Campylobacter</i> enteritis <i>Escherichia coli</i> enteritis <i>Entamoeba histolytica</i> Viral enteritis due to rotavirus <i>Clostridium perfringens</i> |
| Fever and jaundice | Hepatitis A Hepatitis B Hepatitis E <i>Leptospira</i> spp. <i>Plasmodium</i> spp. Yellow fever <i>Borrelia recurrentis</i> |

6.1 The role of the laboratory in the investigation of epidemics

6.1.1 Tests to be done on-site

The testing that can be carried out on-site depends on the availability of equipment, reagents and qualified staff. Simple tests may provide definitive diagnosis of parasitic infections, but provide only presumptive diagnosis of viral and bacterial infections. Certain rapid tests can also verify the diagnosis of viral infections (e.g. HIV, HBV). The following tests may be performed:

- field stained thick and thin films of blood, chancre fluid, lymph gland fluid, splendid aspirate material for parasites: malaria, *Borrelia* spp., leishmania organisms, trypanosomes
- wet preparations of stool for: cholera (*Vibrio cholerae*), pus cells, red blood cells, *Campylobacter* spp., trophozoites of *Entamoeba histolytica/dispar*.

Other tests that may assist with the diagnosis are:

- haemoglobin estimation
- total and differential white blood cell count
- Ziehl–Neelsen stain
- blood glucose using reagent strips
- chemical testing of urine using reagent strips.

6.1.2 Initial tests to be done at the laboratory base

This requires either the transfer of the patient (in case of suspected meningitis) or transfer of specimens to the laboratory base. Cerebrospinal fluid must be collected using a strict aseptic technique.

The following preliminary tests are performed:

- total cell counts
- chemical analysis: glucose and protein
- microscopy of the spun deposit for:
 - Gram stain (GNID suggestive of *Neisseria meningitidis*, Gram-negative rods suggestive of *Haemophilus influenzae*, Gram-positive cocci suggestive of *Streptococcus pneumoniae*).
 - Field stain: differential white cell count, *Borrelia* spp.
 - Ziehl–Neelsen stain: for *Mycobacteria* spp.
 - India ink: for *Cryptococcus neoformans*.

Specimen transfer for the following tests:

- total and differential white blood cell count
- blood concentration technique for trypanosomes
- blood films for further examination.
- stool for further examination.

Specimens are transported to the laboratory base as follows:

- blood films: slides cleaned of oil, wrapped in tissue paper.
- whole blood: anticoagulated using EDTA, in leak-proof containers, in a coolbox.
- stool: clean, wide-mouthed, leak-proof containers.

6.1.3 Tests to be referred to the central laboratory

- Swabs for culture: in appropriate transport media, e.g. rectal swabs for *Vibrio cholerae* in alkaline peptone water; rectal swabs for other enteric pathogens in Cary–Blair transport medium.
- Stool for culture, e.g. for *Shigella*, *Salmonella*.
- Serum for serological tests, e.g. haemorrhagic fevers, yellow fever: 0.5–1 ml in a clean, dry leak-proof tube.
- Cerebrospinal fluid for *Neisseria meningitidis*: 2–5 mL (1–2 mL in children) in a sterile bottle.
- Blood for culture: blood collected aseptically and inoculated into blood culture media, e.g. for typhoid (*Salmonella typhi*).
- Water for bacteriological analysis for faecal coliforms, *Vibrio cholerae*, etc: 0.5–1 L water collected in a clean, leak-proof sterile container.
- Post mortem samples, e.g. rectal swabs, autopsy specimens.

Chapter 7

Noncommunicable diseases

The major noncommunicable disease complexes that are increasingly affecting populations of developing countries and that are important in public health care are:

- cardiovascular disease
- diabetes mellitus
- hypertension
- diseases of the thyroid
- malignancies.

Biochemical, genetic, nutritional and behavioural factors contribute to the development of these diseases. Whereas the majority of infectious diseases show clinical manifestation within hours, days, weeks or months, with some exceptions the clinical symptoms of noncommunicable diseases develop slowly over years or decades. Moreover, in the early stage of a noncommunicable disease the clinical symptoms may be subtle and are therefore often overlooked by the physician.

It is important to diagnose risk factors and advise individuals at risk on appropriate measures (e.g. changes in nutritional habits and behaviour) to prevent the clinical manifestation of noncommunicable disease.

7.1 Cardiovascular disease

The risk factors for cardiovascular disease are:

- smoking

- obesity (see *body-mass index* in the glossary)
- lack of physical exercise
- hypertension
- diabetes mellitus
- hyperlipoproteinaemia.

The risk factors are diagnosed by the medical history, physical examination, including the measurement of blood pressure, and laboratory investigations as appropriate. Laboratory indicators may be abnormal in a subject at risk although the disease may not yet be clinically apparent. In patients with manifest cardiovascular disease additionally ECG and X-ray examinations may show abnormalities. Cardiovascular disease may also develop as chronic disease after streptococcal, *Treponema pallidum* or trypanosomal infection.

Large and longitudinal epidemiological studies revealed a close relationship between hyperlipoproteinaemia, in particular hypercholesterolaemia, and cardiovascular disease. This is why today serum lipids and serum apolipoproteins are measured as part of the risk assessment for cardiovascular disease.

7.1.1 Laboratory indicators

- Total serum cholesterol.
- Serum triglycerides.
- LDL cholesterol.
- Apolipoprotein A1 and apolipoprotein B.

Apolipoproteins A1 and B correlate better with the degree of coronary heart disease than low density lipoprotein cholesterol. The concept of apolipoproteins is appreciated, but determination of these proteins is not frequently requested by physicians.

The main complications of cardiovascular disease are coronary heart disease, which may be complicated by myocardial infarction, stroke and also atheromatous peripheral vascular disease.

The most commonly available tests to assess cardiac injury include creatine kinase (CK), lactate dehydrogenase (LDH) and myoglobin.

Diagnostic imaging

Imaging procedures may be useful and medically indicated in order primarily to evaluate the extent of cardiovascular disease, to plan medical or surgical intervention and to follow up on treatment.

At peripheral level chest radiographs (PA and lateral) give extensive diagnostic information on size and shape of the heart and on vascularization of the lungs. Thus, early stages of pulmonary congestion may be diagnosed radiologically before clinical symptoms arise. More sophisticated imaging procedures such as angiography or ultrasound of the heart (echocardiography) are normally applied in large referral hospitals only.

7.2 Diabetes mellitus

Diabetes mellitus is a clinical syndrome that is typically characterized by impaired glucose metabolism. However, the protein, fat and purine metabolisms are also affected. The cause of the metabolic disorder is an imbalance between the action of insulin and insulin-counteracting hormones (steroids, glucagon, parathyroid hormone, thyroid hormone, etc.). Long standing metabolic imbalance leads to clinical complications of diabetes.

Two major clinical forms of diabetes mellitus are distinguished:

- juvenile diabetes (type 1), mainly caused by insulin insufficiency
- adult-onset diabetes (type 2), mainly caused by insufficient response of tissue to insulin stimulation of the cell metabolism.

Diabetic mothers have increased risk of birth defects (15%–20%) compared with the general population (3%–5%). Therefore mother and child health care programmes play a major role in detecting and following up diabetes mellitus during pregnancy. The typical features of juvenile and adult onset diabetes mellitus are listed in Table 7.1

Acute clinical symptoms of diabetes mellitus result from acute alterations of glucose and insulin metabolism. They may be life-threatening when the patient is in a diabetic hyperosmolar, ketoacidotic or hypoglycaemic coma (see Section 5.10.3 on coma).

Clinical symptoms from chronic disease result from altered organ and tissue functions that are caused by impaired glucose metabolism over long

periods. The symptoms and laboratory indicators of clinically manifest diabetes mellitus are listed in Table 7.2.

7.2.1 Laboratory indicators

Blood, plasma or serum glucose.

Glucose 24 hour-profile.

Glucose tolerance test.

Urine glucose.

Microalbumin in urine.

Glycated haemoglobin (HbA1c) or fructosamine.

Special laboratory indicators

insulin, pro-insulin, C-peptide

insulin antibodies.

The laboratory diagnosis of diabetes mellitus is conveniently made from fasting or postprandial hyperglycaemia in a patient. Elevated urinary glucose may be found in diabetic patients without renal insufficiency whose blood glucose levels are above 180 mg/dL (165 mmol/L). However, in patients with renal insufficiency, urinary glucose may be observed even at normal blood glucose levels.

Table 7.1 **Features of juvenile and adult-onset diabetes mellitus**

| | Juvenile | Adult-onset |
|--------------------|-----------------|--------------------------------|
| Age of onset | < 25 years | > 40 years |
| Body weight | slim | overweight |
| Vascular symptoms | microangiopathy | atherosclerosis |
| Genetic burden | low | high |
| Insulin metabolism | lack of insulin | inappropriate insulin response |

Table 7.2 **Clinical symptoms and laboratory indicators of diabetes mellitus**

| Clinical symptom | | Laboratory indicator |
|---------------------------------------|---|---|
| Thirst | | Glycosaemia |
| Hunger | | Glucosuria |
| Weight loss | | Glucose intolerance |
| Polyuria | | HbA1c, fructosamine Insulin |
| Ketoacidosis | Vomiting | Urine ketone bodies Nausea Ketone breathing |
| | Signs of acute abdomen Anorexia Coma | |
| Frequent infections and inflammations | Cystitis Pyelonephritis Gingivitis Abscesses | Bacteriuria |
| Microangiopathy | Retinopathy (loss of vision) Renal insufficiency | Microalbuminuria, proteinuria Haematuria |
| | Ulcers | Serum creatinine |
| Polyneuropathy (loss of sensibility) | | |
| Sexual impotence | | |
| Diarrhoea and constipation | | |
| Hypertension | | |
| Macroangiopathy | Cardiovascular disease | |

Urinary glucose determination is a simple, but not an optimal method to control therapy. Urine glucose determination should only be made if no other tests are available. More accurate tests for control and prognosis of diabetes mellitus include the following.

Glycated haemoglobin and fructosamine

Glycated haemoglobin (HbA1c) is a retrospective indicator for blood glucose levels over a longer period (8–10 weeks). HbA1c gives a better index than sporadic blood glucose estimations in the control of diabetes mellitus. Clinical laboratories measure glycated haemoglobin using different assays. Clinicians should be familiar with the assay used in their own laboratory, and laboratories should always use the same assay to ensure comparability of results in the control of individual diabetic patients.

The fructosamine assay measures glycated serum albumin. However, glycated albumin has a shorter biological life time (about 60 days) than HbA1c (about 120 days). From a clinical point of view both indicators seem to be equally valid.

Microalbuminuria

Microalbuminuria is a good index of urinary albumin excretion in minute amounts and is used to detect early diabetic nephropathy especially in type 1 diabetes. Simple test procedures for the detection of microalbuminuria are available.

The special tests used for the differential diagnosis of diabetes are normally reserved for central laboratories. The discussion of the use of these tests is beyond the scope of this document.

7.2.2 Diagnostic imaging

Imaging procedures may be indicated to further evaluate organ complications of diabetes mellitus, be it cardiac, vascular, renal, or other organ manifestations. For the heart, plain radiography (PA and lateral views) is normally sufficient. Kidneys are best examined by ultrasound, whereas vascular complications may need angiography eventually, in addition to Doppler examinations.

7.3 Hypertension

Individuals with elevated blood pressure suffer from hypertension. Patients with hypertension may suffer from retinopathy, kidney failure, early

development of congestive heart failure and/or cerebrovascular disease. Surveys have identified socioeconomic status, body weight, age, nutrition, organ damage (kidney), hormone and metabolic disorders as causal factors for the development of hypertension. Epidemiological studies showed that populations of African origin are more prone to develop hypertension than Caucasian populations who live in the same environment. Moreover a family history of elevated blood pressure is one of the strongest risk factors for future development of hypertension in individuals.).

No specific cause can be identified in more than 95% of patients with hypertension. These patients are diagnosed as suffering from primary hypertension. The small minority of patients in whom a specific cause has been identified are diagnosed as having secondary hypertension. Selected causes of secondary hypertension are listed in Table 7.4.

Table 7.4 Selected causes of secondary hypertension

| | |
|---------------------------------|--|
| Renal disorders | |
| Pregnancy induced | |
| Surgically induced | |
| Coarctation of aorta | |
| Exogenous substance or medicine | Hormonal contraceptives Corticosteroids Non-steroidal anti-inflammatory drugs Sympaticomimetics |
| Cocaine | |
| Lead | |
| Endocrine disorders | Hypothyroidism Hyperthyroidism Adrenal disease (phaeochromcytoma) Hypophysis tumour Carcinoid tumour |
| Neurological disorders | Brain tumour Encephalitis |

7.3.1 Clinical assessment of patients with hypertension

The diagnostic investigation of a subject with hypertension has several goals:

- confirm a chronic elevation of blood pressure
- assess the overall cardiovascular risk
- evaluate existing organ damage or concomitant disease
- search for possible causes.

A superficial investigation is unacceptable since hypertension is a life-long disease, and therapy may have serious implications on the patient. Medical history of the patient provides important information (lifestyle, hereditary risk, nutritional habits, etc). Accurate physical examination is not limited to measurement of blood pressure but should concentrate on finding possible signs suggesting secondary hypertension. A single measurement of blood pressure is often not sufficient. Measurement should be repeated over a period of several days and at different times during the day. Blood pressure can be optimally assessed by continuous measurement during a period of 24 hours.

7.3.2 Laboratory investigations

The minimum laboratory investigation needed is a matter of debate. However investigations should progress from the most simple to the more complicated tests. The tests listed in Table 7.5 may be considered.

Table 7.5 **Laboratory investigations for hypertensive patients**

| | |
|----------------------------|---|
| Strongly recommended tests | Urine analysis (dipstick) Serum creatinine Blood glucose Serum cholesterol Plasma potassium |
| Additional tests | Plasma uric acid Haemoglobin and haematocrit Urine culture |

7.3.3 Diagnostic imaging

As part of an initial evaluation of arterial hypertension, chest radiographs should be made under standard conditions (PA and lateral view, erect patient, minimum distance between X-ray tube and patient 140 cm). The main reason is to establish a baseline with regard to shape and size of the heart and the pulmonary vascularization. In the absence of organ complications already caused by hypertension, no further diagnostic imaging procedures are needed.

Further imaging examinations such as echocardiography, examination of the kidneys, and/or renal arteries (Doppler and/or angiography) would depend upon the clinical situation.

See also Section 7.1.1 on cardiovascular disease.

7.4 Diseases of the thyroid

Diseases of the thyroid gland are among the most abundant endocrine disorders worldwide, second to diabetes. Thyroid disease may result from excessive thyroid hormone activity (hyperthyroidism) or from insufficient hormone activity (hypothyroidism). Hyper- and hypothyroidism may be due to diseases of the thyroid gland, malfunction of the pituitary gland or malfunction in the hypothalamus. Goitre or active thyroid nodules may be endemic in some areas due to dietary deficiency of iodine, which must be available for the biosynthesis of thyroid hormone. Patients with goitre may not show clinical signs of hyper- or hypothyroidism. The thyroid gland may also be the site of inflammatory disease (thyroiditis) and of various types of tumours (adenoma).

Thyroid diseases can be serious and even life-threatening but are usually curable. The typical symptoms are the listed in Table y.6.

Common forms of hyperthyroidism are:

- immunogenic diffuse hyperthyroidism enlarged, soft thyroid (Basedow or Graves disease)
- thyroid storm thyroid nodules (not obligatory)
- multifocal goitre multifocal nodules
- thyroid carcinoma (papillary, folicular, solid) nodules

- subacute thyroiditis de Quervain asymmetrically enlarged, hard thyroid gland
 - iatrogenic hyperthyroidism normal thyroid gland.
- Rarely, other diseases may produce symptoms of hyperthyroidism due to thyroid-stimulating hormone (TSH production).

Common forms of hypothyroidism are:

- iodine deficiency (endemic cretinism) very enlarged thyroid gland
- primary hypothyroidism (myxoedema) no or dislocated thyroid gland
- autoimmune thyroiditis (Hashimoto thyroiditis) enlarged painless thyroid gland
- iatrogenic hypothyroidism normal thyroid gland.

7.4.1 Laboratory indicators

Unspecific laboratory indicators for thyroid disease are elevated white blood cell count and elevated blood sedimentation rate (BSR) indicating an inflammatory process (thyroiditis). Serum creatine kinase (CK) activity may be highly elevated in hyperthyroidism.

Thyroid-stimulating hormone (TSH) is the primary indicator for the laboratory diagnosis of hyper- and hypothyroidism. Low TSH levels the blood of a patient with clinical symptoms confirm the diagnosis of hyperthyroidism. Conversely, high levels of TSH are confirmatory for hypothyroidism in a patient with clinical symptoms of suppressed thyroid function. A differential diagnosis of different forms of hyper-or hypothyroidism requires the measurement of free T4 (FT4) and free T3 (FT3) [6]. In autoimmune thyroiditis (Hashimoto; de Quervain) thyroid auto-antibodies are elevated. Typically, in de Quervain thyroiditis giant cells are detected by histological examination in a thyroid gland aspiration, which are absent in Hashimoto thyroiditis.

Table 7.6 Clinical signs of hyperthyroidism and hypothyroidism

| Hyperthyroidism | Hypothyroidism |
|--|---|
| | Cretinism (neonatal) |
| | Growth retardation (during adolescence) |
| | Retarded tooth development |
| Tremor | Change in behaviour, loss of intelligence |
| Hyperreactivity | Hyporeactivity |
| Heat intolerance | |
| Fever | Hypothermia |
| Moist skin | Dry skin |
| Diarrhoea | Constipation |
| Hypocapnia | Hypercapnia |
| Fatigue and weakness | |
| Hypomenorrhoea | Menorrhagia |
| Increasing appetite | |
| Weight loss | |
| Tachycardia | Bradycardia |
| Ophthalmopathy: lacrimation, light sensitivity, orbital oedema | Reflexes: fast contraction, but slow relaxation |
| Pretibial myxoedema | |
| | Cramps |
| Goitre | Goitre |
| Fever | |
| Jaundice | |
| Psychosis | Psychosis |
| Coma | Coma |

Severe maternal hypothyroidism due to iodine deficiency or thyroid blocking agents may lead to cretinism in newborns if untreated. It is of vital importance that this condition is recognized. In many countries screening of newborns by measuring thyroid stimulating hormone (TSH) has therefore become mandatory. Sampling should be performed during the first–second or fifth–seventh day after birth.

7.4.2 Diagnostic imaging

Two complementary methods are recommended. Imaging of the thyroid is sufficiently done by ultrasonography. Where available, nuclear medicine examinations (scintigraphy) are applied to evaluate the *functional* status of the thyroid. Other imaging methods are of little value.

Subclinical thyroid diseases have subtle clinical manifestations and may mimic other diseases. Non-thyroidal conditions, e.g. renal failure, liver disease, fulminant infections and metabolic diseases may cause adaptive responses of the thyroid. Furthermore, thyroid diseases may be only partly responsible for a complex presentation of symptoms. It is therefore important to differentiate the various conditions to guide the physician in the correct diagnosis and treatment.

7.5 Malignancies (cancer)

Although malignant diseases are commonly considered as noncommunicable diseases, there is enough evidence demonstrating that certain types of cancer are caused by infective agents, whereas others are caused by environmental factors, lifestyle or genetic disposition. Combined factors increase the risk to a patient of developing cancer. With increasing life expectancy of populations in developing countries the diagnosis of malignant disease gains importance. In fact certain types of cancer occur almost exclusively in developing countries and are closely linked to the prevalence of certain communicable diseases (e.g. HBV infection and liver cancer). The causative agents of certain types of cancer are listed in Table 7.7.

The clinical symptoms of cancer are often unspecific (fever, fatigue, weakness, weight loss, etc.) or they may vary according to the function of

the organs that are affected. Sometimes the clinical symptoms observed in a patient are caused by cancer metastases in other parts of his/her body than by the genuine tumour, thus complicating the search for a diagnosis.

Table 7.7 Possible causes of cancer

| Infective agent | Cancer |
|---------------------------------------|--------------------------------------|
| HBV, HCV, flukes | Liver |
| Papilloma virus | Cervix |
| HIV | Kaposi sarcoma |
| <i>Helicobacter pylori</i> , EBV, HIV | Non-Hodgkin lymphoma |
| Epstein–Barr virus | Nasopharyngeal |
| Epstein–Barr virus, HIV | Hodgkin disease |
| Schistosoma | Bladder |
| HTLV-1 | Leukaemia |
| Other causes | |
| Tobacco | Lung, bladder |
| Asbestos | Lung |
| Contaminated food (aflatoxin B1) | Liver |
| Salt | Stomach |
| Meat | Colon, rectum |
| Ultraviolet radiation | Skin |
| Nuclear radiation | Blood, thyroid |
| Obesity* | Uterus, kidney, gall bladder, breast |

*see *body-mass index* in the glossary.

7.5.1 Laboratory indicators

A number of laboratory indicators in body fluids may be abnormal without being specific enough to make a diagnosis of cancer (e.g. haemoglobin, ESR, CRP, transaminases, phosphatases, etc.). Often the diagnosis of cancer requires histological and/or cytological examination of biopsy material. Only very few laboratory indicators (AFP, PSA) are specific for certain types of cancer, such as atypical blood cells for certain types of blood cancer. The so-called tumour markers are not useful make a diagnosis but are helpful to monitor the development of cancer during therapy.

7.5.2 Diagnostic imaging




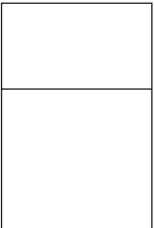
Apart from screening examination, which will not be further evaluated here, indications for diagnostic imaging of malignant disease should be dictated by the clinical situation. Two main areas can be distinguished: to diagnose and evaluate a primary malignant tumour; and to search for metastases, preferentially in the liver, bones, lung or brain.

Relevant clinical information is essential for the imaging department to make a correct diagnosis. The clinical problems should be discussed with staff of the radiologist and other relevant staff of the imaging department, to find the best possible approach to the problems. Open-ended requests such as “ultrasound of abdomen”, without specifying what to look for and what may be suspected clinically, are most inappropriate and of no value.

Annexes

1. Instruments for physical examination

Sphygmomanometer
Stethoscope
Ophthalmoscope
Hammer, brush and needle
Tongue depressor
Otoscope
Torch
Rule
Weighing scale
Speculum
Gloves

| | | |
|-----------------------------|-----------------------|---|
| Physical examination | Height | Weight |
| Integument | | Nutritional state |
| | | Strength |
| Head | | |
| Oral cavity | Teeth | |
| Neck | |  |
| Thyroid | | |
| Thorax | | |
| Breast | |  |
| Lung | Percussion | |
| | Auscultation | |
| Heart | Heartbeat |  |
| | Heart sounds | |
| | Heart murmurs | |
| | Horizontal | Right Left |
| | Upright | Right Left |
| Blood pressure | | |
| Blood pressure | | |
| Pulse | | |
| Blood vessels | | |
| Carotid artery | Dorsalis pedis artery | |
| Abdomen | | |
| Inguinal canal | |  |
| Liver | | |
| Spleen | | |
| Lymph nodes | | |
| Neck | Axilla | Groin |
| Kidneys | | |
| Spinal column | | |
| Extremities | | |
| Genitals | | |
| Rectal examination | | |
| Prostate | | |
| Nervous system | | |
| Reflexes | | |
| Mental state | | |

*Additional information***1. Problem**

Solution

Therapy

Disease Progress

2. Problem

Solution

Therapy

Disease Progress

3. Ultrasonography contact gel preparation

The following recipes describe the composition and preparation of two contact gels for ultrasound examinations. The first gel is less expensive. However occasionally allergic reactions have been reported in some individuals. The second gel is more expensive, but it seems to be less allergenic and is stable over a longer period when kept at normal temperatures.

Devices needed for preparation:

- scale
- 15 L flask
- stirrer
- waterbath or heater
- vacuum pump.

Gel 1

Composition

| | |
|--|----------|
| • polyacrylic acid (USP grade) mol. weight 4 million | 85 g |
| • sodium hydroxide (NaOH) 5% aqueous solution | 510 g |
| • parabene* | 10 g |
| • propylene glycol (USP grade) | 50 g |
| • glycerol (USP grade) | 1 553 g |
| • distilled water | 7 793 g |
| • total | 10 000 g |

**parabene:*

| | |
|---------------------------------|------|
| <i>methyl-4-hydroxybenzoate</i> | 70 g |
| <i>propyl-4-hydroxybenzoate</i> | 30 g |

Preparation

- Dissolve parabene (methylene-4-hydroxybenzoate and propyl-4-hydroxybenzoate) in propylene glycol under heating.
- Add glycerol and distilled water to the solution under strong stirring.
- Add the solid polyacrylic acid slowly to the solution while stirring.

- Stir under vacuum for 10 minutes to de-gas and homogenize the mixture.
- Neutralize the mixture while stirring while adding slowly sodium hydroxide solution (5%). Strong stirring is important to prevent a sudden increase of viscosity while adding the sodium hydroxide.
- Measure the pH of the mixture. The pH should be 6.7. Adjust the pH, if necessary.
- Pour the gel into plastic, elastic bottles for use.

Gel 2

Composition

| | |
|---|----------|
| • Polyacrylic acid (USP grade), mol. weight 4 million | 48 g |
| • Sodium hydroxide (NaOH), 15% aqueous solution | 108 g |
| • Glycerol 85% | 1 800 g |
| • Euxyl K 400* | 120 g |
| • Distilled water | 10 032 g |
| <hr/> | |
| • Total | 12 000 g |
| *Euxyl K 400: | |
| 12-dibrom-24-dicyanobutane | 20% |
| Phenoxyethanol | 80% |

Preparation

- Dissolve 12 g Euxyl K 400 in 1800 g of glycerol (85%) in a flask.
- Add 9532 g of distilled water and mix thoroughly.
- Add slowly 48 g solid polyacrylic acid.
- Leave the mixture over night.
- The next morning stir the mixture under vacuum to de-gas.
- Mix 15% of sodium solution with 500 g distilled water.
- Add the sodium hydroxide dilution to the mixture slowly while stirring to neutralize.
- Stir the final mixture under vacuum for 20 minutes.
- Control the pH. The pH should be 6.7. Adjust the pH, if necessary.
- Pour the gel into plastic, elastic bottles for use.

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The cover illustration is taken from *Tashrih-i badan-i insan* (The anatomy of the human body) by Mansur ibn Muhammad ibn Ahmad ibn Yusuf ibn Ilyas (fl. ca. 1390). The illustrations in this work are the earliest preserved anatomical illustrations of the entire human body from the Islamic world.

The figure shows the venous system, with the figure drawn frontally and the internal organs indicated in opaque watercolours. Copy completed by scribe Hasan ibn Ahmad, working in Isfahan, on 8 December 1488 (4 Muharram 894 H).

From the online exhibition Islamic medical manuscripts at the National Library of Medicine. <http://www.nlm.nih.gov/hmd/arabic/welcome.html> (February 2005).