Human Embryology

Weeks 1-4

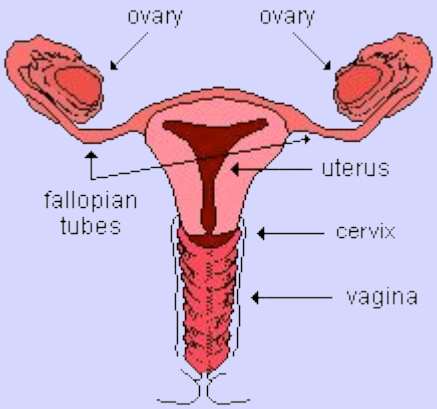
Week 1

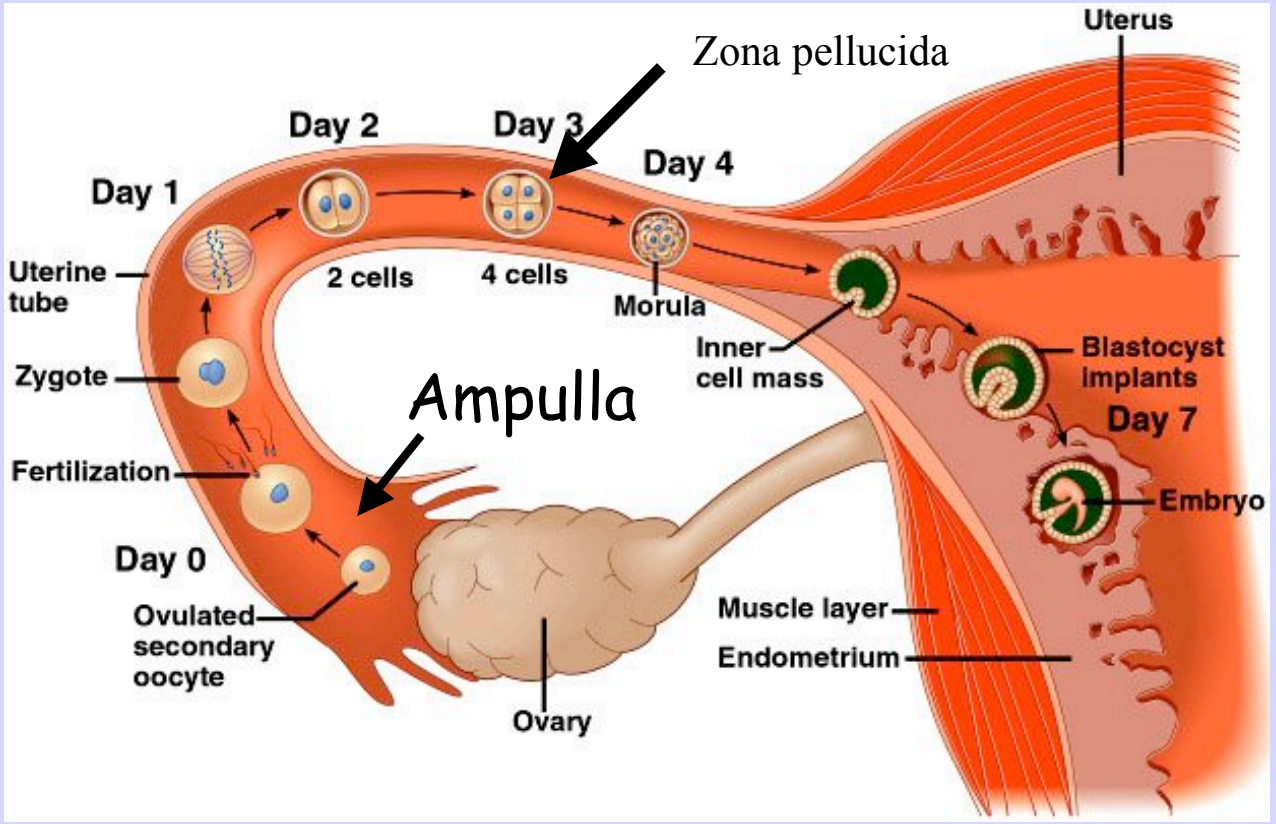
Fertilisation to Implantation

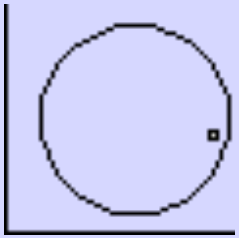
For this presentation embryonic age will be expressed as days or weeks from fertilisation. On this basis human pregnancy lasts about 266±3 days or 38 weeks.

Obstetricians time pregnancy from the last day of the menstrual period on the assumption that fertilisation takes place 2 weeks later. For obstetricians pregnancy lasts 280 days or 40 weeks.

The first week of human embryonic development



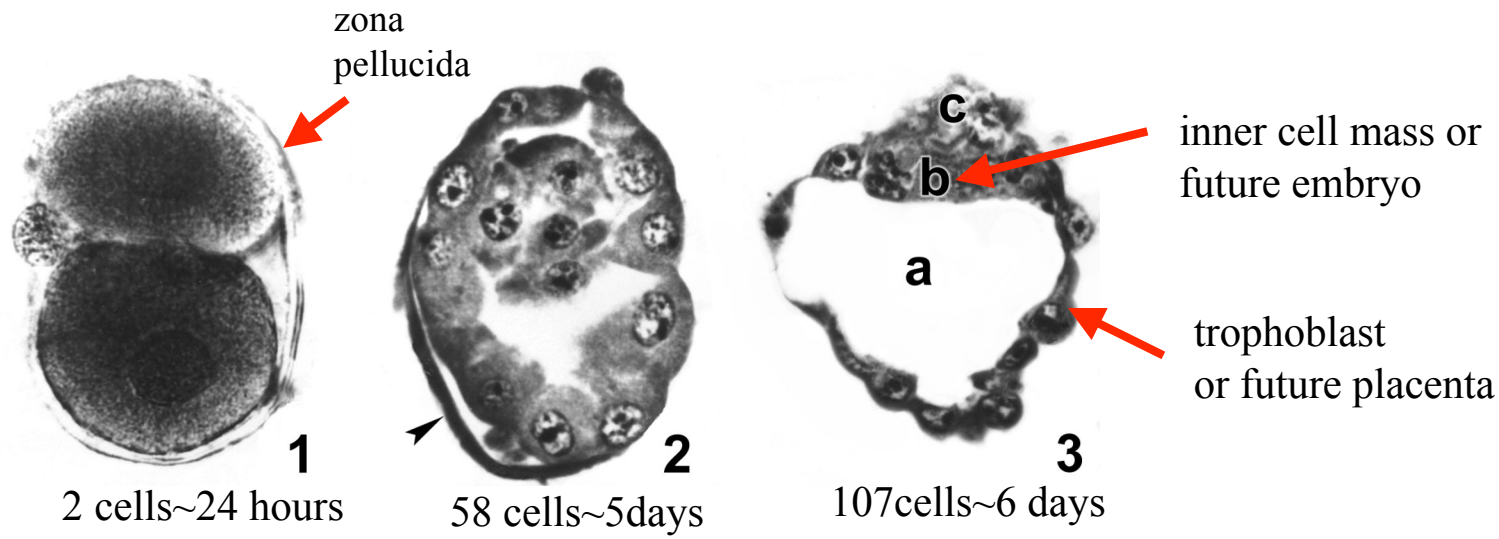


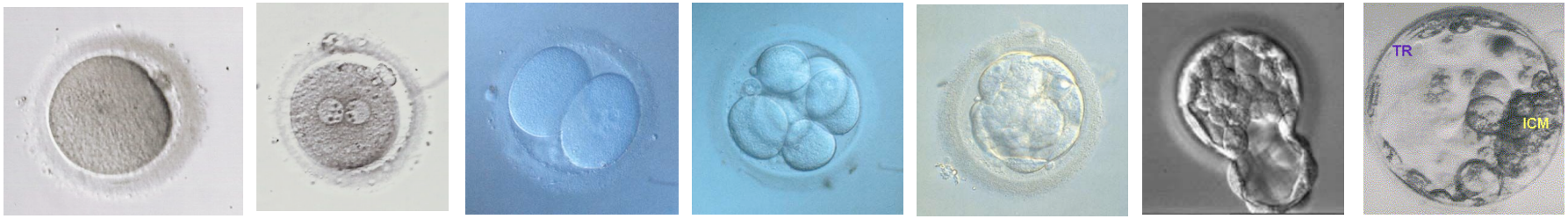


diameter of the uterine tube 1-2 cm

diameter of the zygote 0.12 mm

Human embryos in the first week of development





oocyte

fertilised egg or zygote – 2 nuclei egg and sperm

2-cell stage

8-cell stage (3 days)

morula

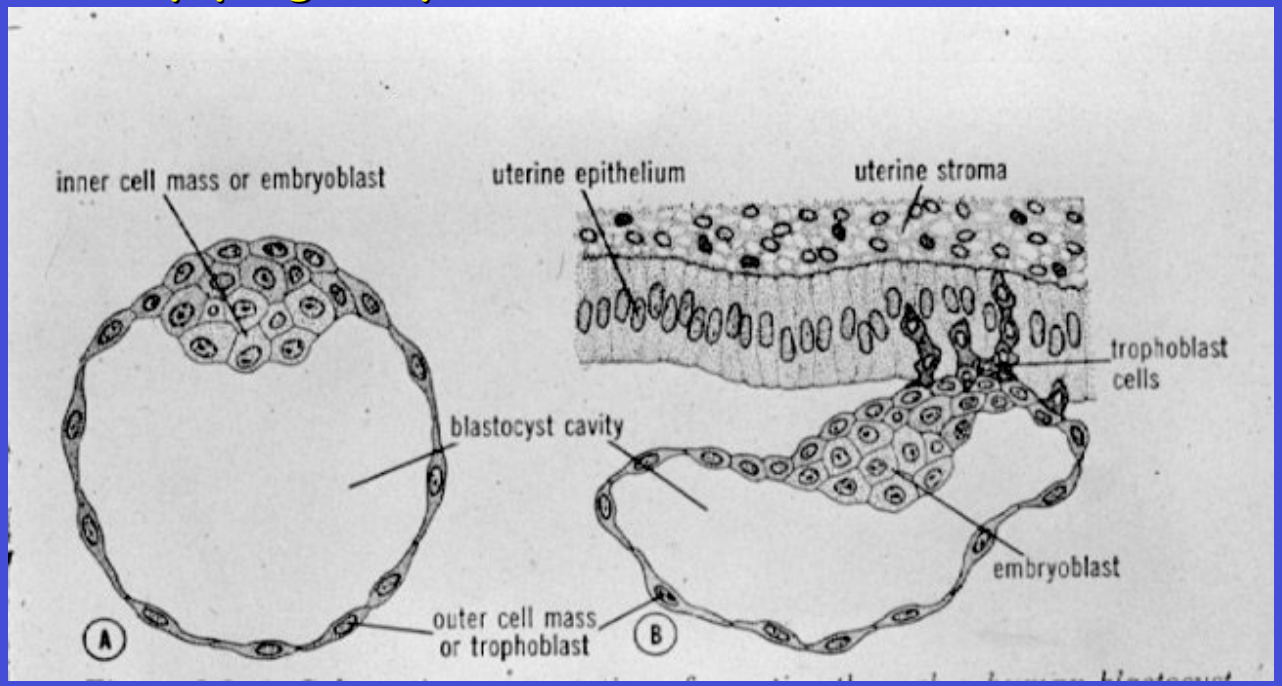
Embryo “hatching” From the zona pellucida

blastocyst


Three day old embryos

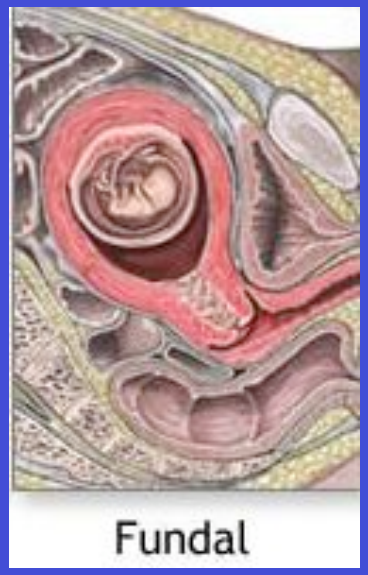
Implantation

To implant the developing embryo must pass through the uterine epithelium. This occurs about 7 days after fertilisation. The trophoblast produces
human chorionic gonadotropin (hCG) which maintains the corpus luteum of the ovary which in turn produces progestesterone which maintains early pregnancy. hCG can be detected in the maternal blood and forms the basis of the early pregnancy test. Detection in urine is less sensitive.



Ectopic Pregnancies

- Implantation in a non-uterine site occurs at a rate of about 0.25 – 1%.
- The ampulla of the uterine tube is the most common ectopic implantation site.



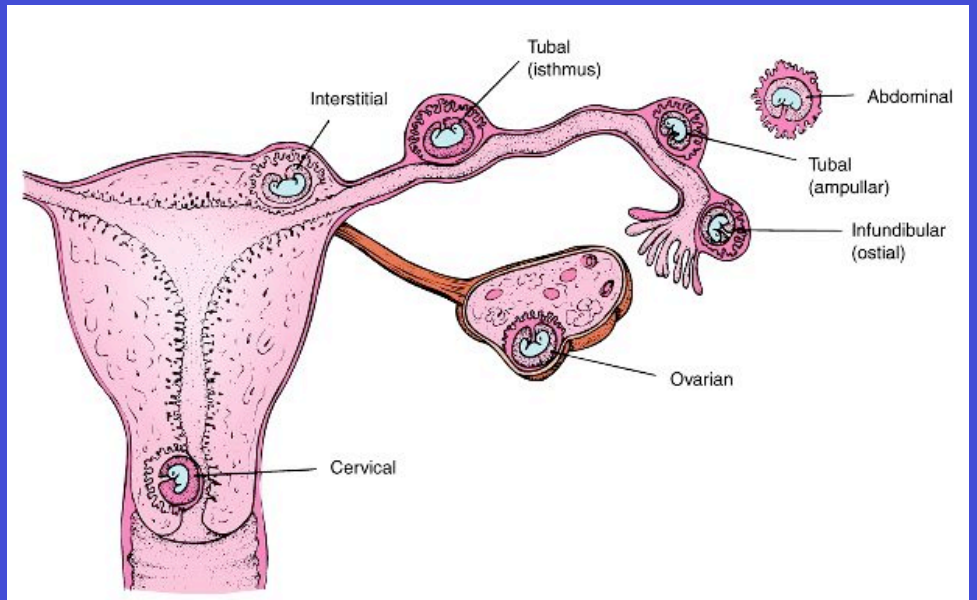
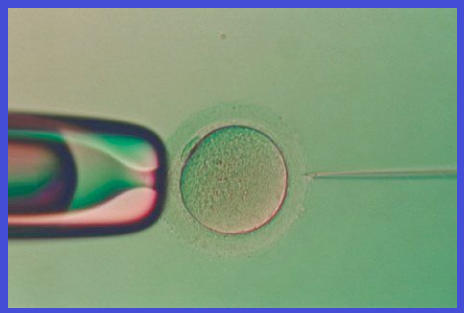


Figure 46-9 Sites of ectopic pregnancy.

In vitro fertilisation

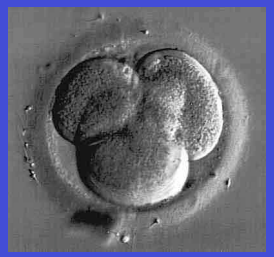
- The process by which one or more eggs (oocytes) are fertilised outside the body. Fertilisation is either achieved by placing a droplet of washed sperm (~50,000) onto each egg or if the sperm count is low a single sperm can be injected into each egg (Intra-Cytoplasmic Sperm Injection – ICSI).



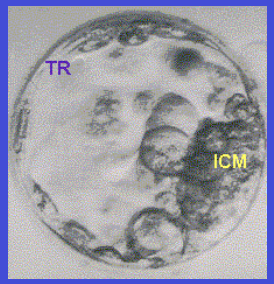
- Embryos can be placed into the uterus at the 6-8 cell stage (3-days culture) but some clinics culture the embryos for 5 or 6 days to ensure healthy blastocyst stage embryos are placed into the uterus.

oocyte

fertilised egg (zygote)



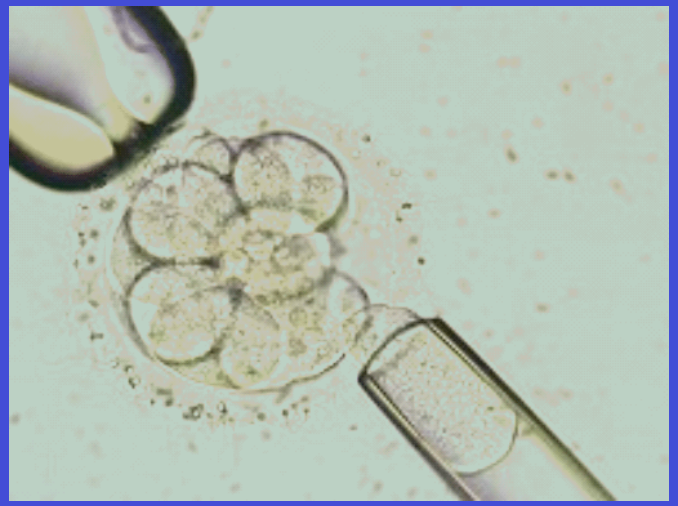
4-cell embryo

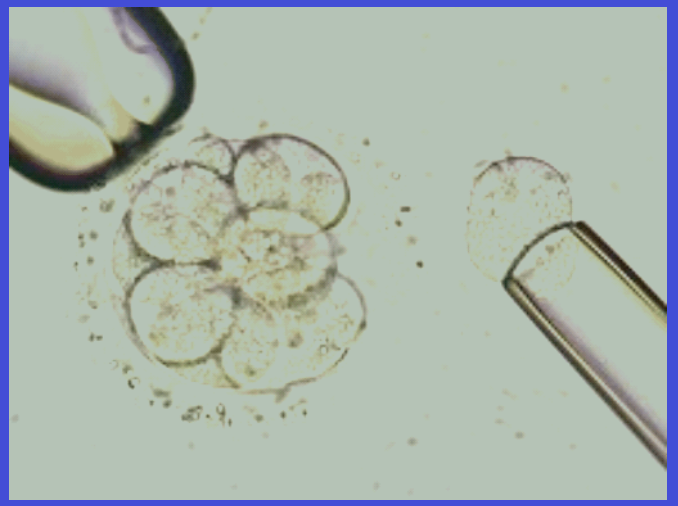


blastocyst

IVF and Preimplantation Genetic Diagnosis

- All cells in the early embryo (until about the 8-cell stage) are said to be totipotent. That means that each cell is capable of forming a complete human.
- So couples using IVF can use genetic screening of their embryos by having a cell removed from their embryo(s) and tested for its genotype. The embryo will still develop normally.
- More than 100 diseases can be detected including hemophilia A, muscular dystrophy, Tay-Sachs disease, cystic fibrosis and Down syndrome.



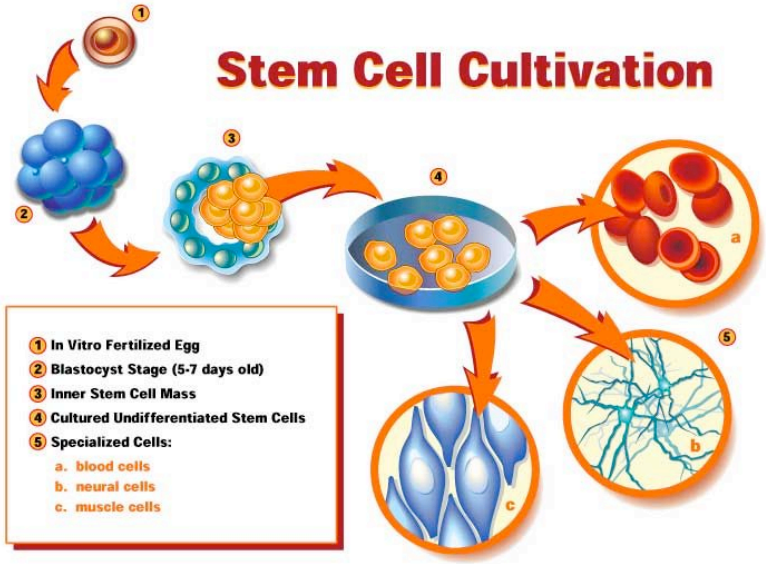


Stem Cell Research

- Stem cells are unspecialized cells that can renew themselves for long periods through cell division. Under certain experimental conditions, they can be induced to become cells with special functions such as the beating cells of the heart muscle or the insulin-producing cells of the pancreas.

- Human embryonic stem cells are obtained from the inner cell mass – the early embryo.

- In the USA it is forbidden to destroy a human embryo to obtain stem cells. So they are not allowed to remove the inner cell mass or totipotent cells. There is interest in the possibility that at the 8-cell stage the cells are no longer totipotent but are still pluripotent (ie can form the 240+ human cell types).



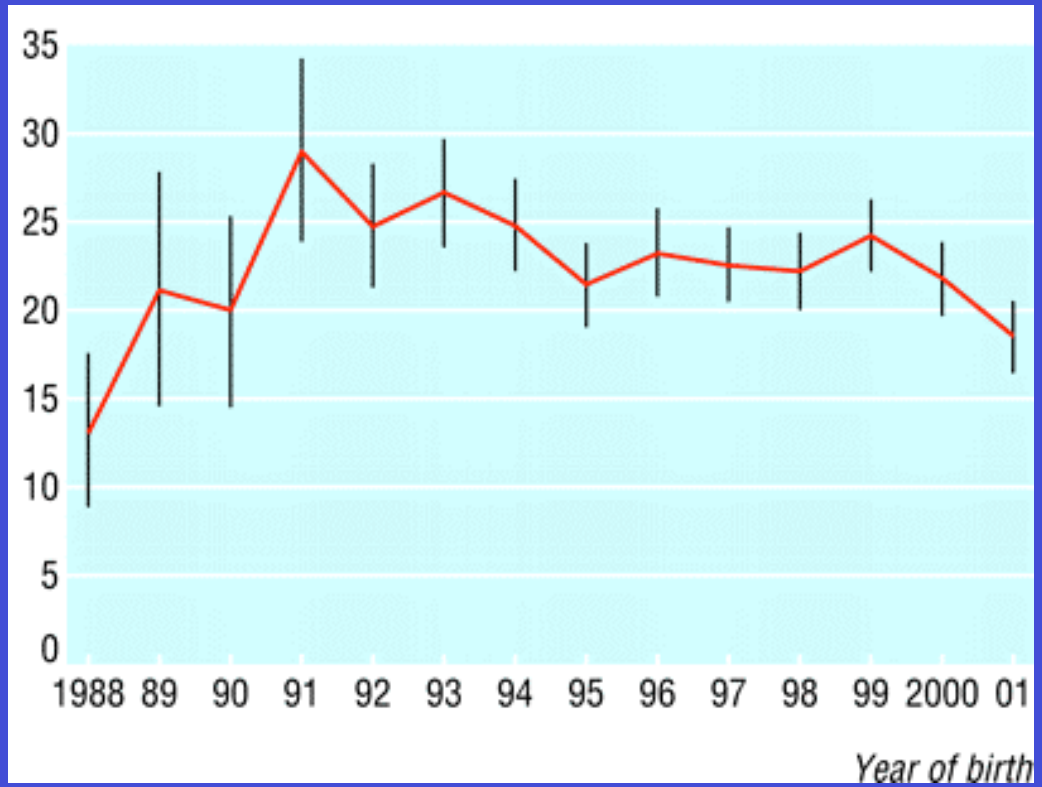
Multiple Gestations- TWINS

- About 1:80 human births (0.8%) is a twin pregnancy.
- About 2/3 of twins are fraternal (dizygotic) – derived from 2 eggs.
- One third (1:250) are identical twins (monozygotic)
- 35% of MZ twins divide between **2-8 cell stage**, get two babies with two amnions, two chorions, and either one fused or two separate placentas- cannot tell difference between these twins and fraternal until genetic testing is done.

  65% of MZ twins occur by **division of the inner cell mass after first week**. At this point two embryos will develop with two amniotic sacs, one chorionic sac and a common placenta.

- IVF has greatly increased the number of fraternal (dizygotic) twins and in 2001 the rate of twins in the USA was 3%.

Rate of twins in Sweden



In 1982 the twin rate was about 0.9%. Multiple births associated with IVF increased that rate to 1.7%.

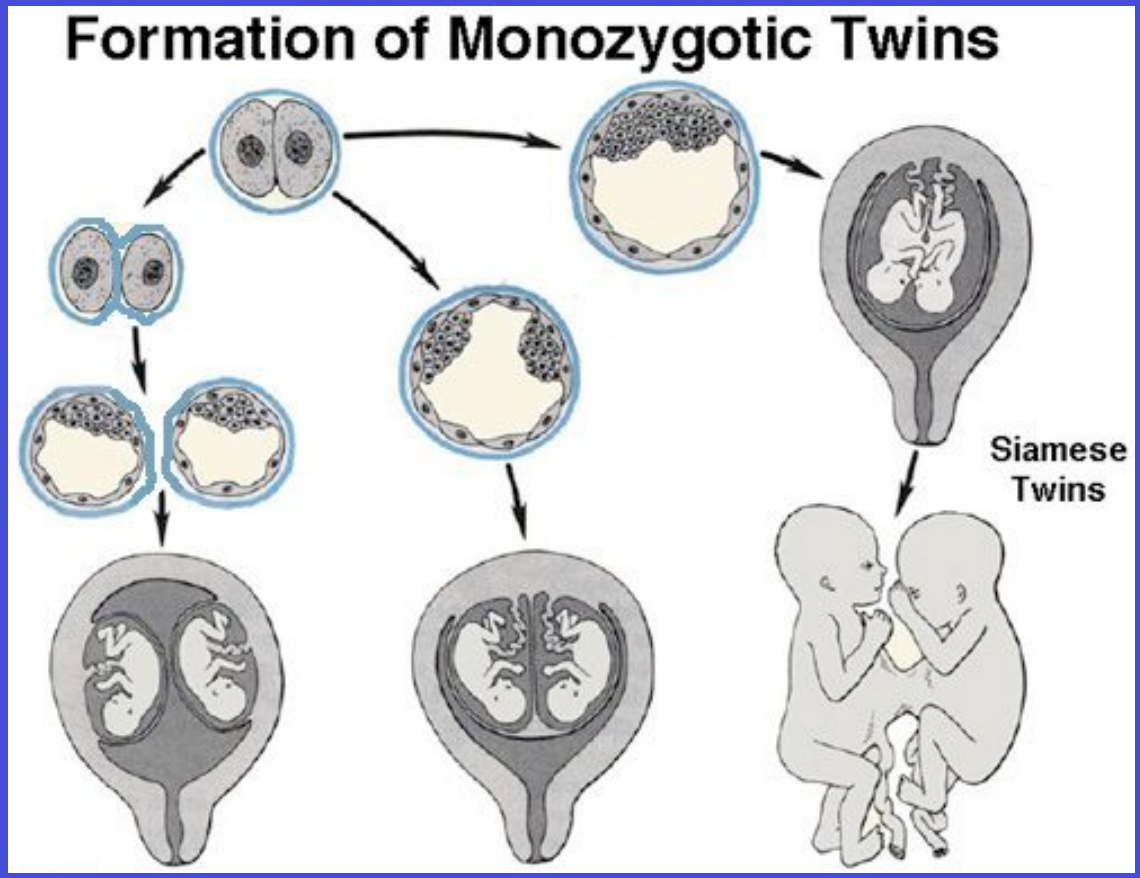
The first IVF child was born in Sweden in 1982. In early 1990s the number of embryos transferred to the uterus during IVF was reduced from 3 to 2. At present, the number of embryos transferred is being reduced further, from 2 to 1. Källén et al BMJ 2005;331:382-383

MONOZYGOTIC TWINS

(a) Separation at the two blastomere stage can lead to twinning.

(b) Splitting of the inner cell mass is the most common cause of identical twins.

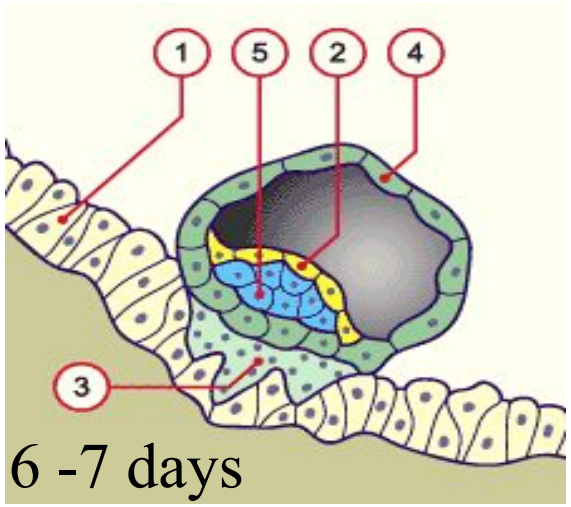
(c) Incomplete separation of the inner cell mass can lead to conjoined twins.

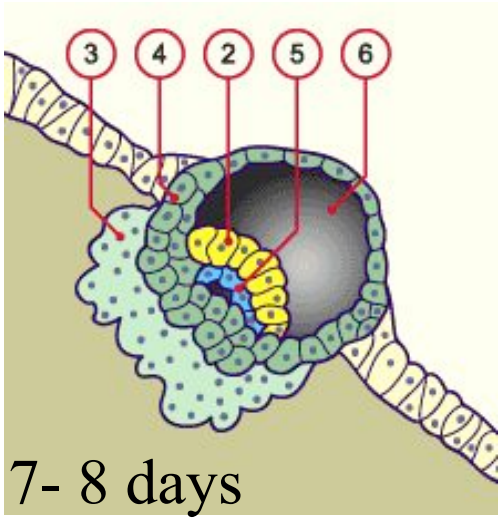


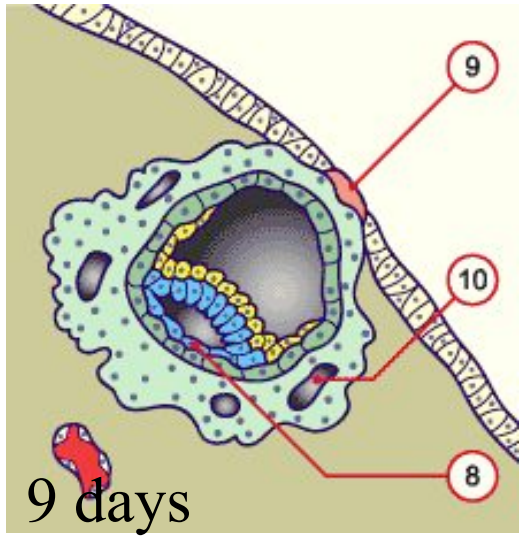
Week 2

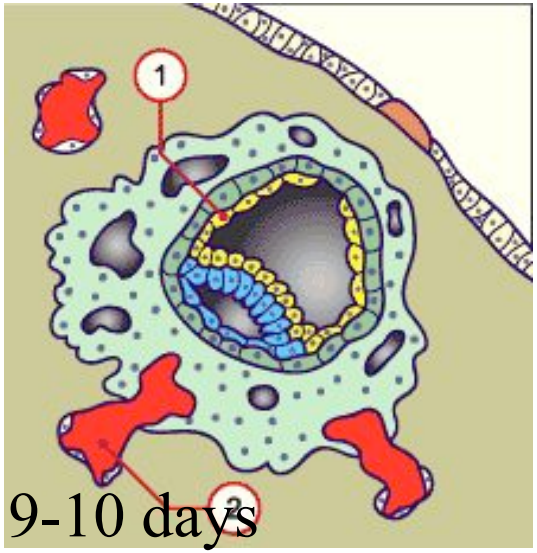
Implantation

Human implantation









1 = uterine epithelium

2 and 5 = inner cell mass or future embryo

3 and 4 = trophoblast or future placenta

3 = syncytiotrophoblast
4 = cytotrophoblast

6 = yolk sac cavity

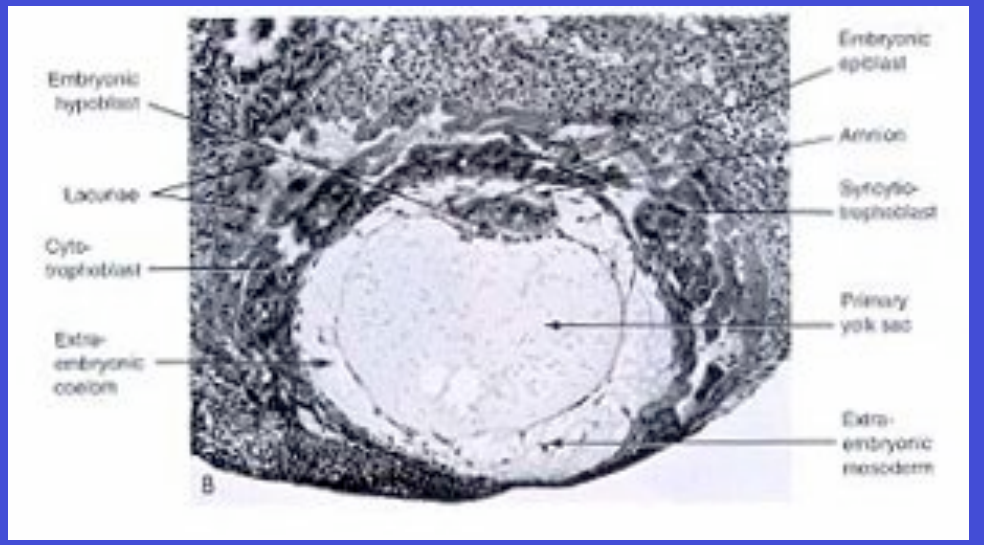
8 = amnion

9 = fibrin plug

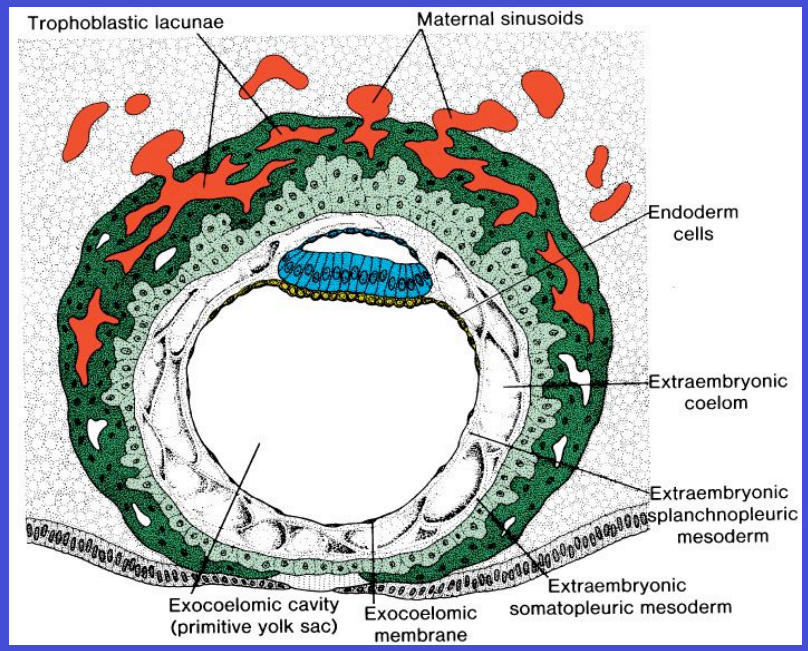
10 = intervillous spaces

http://www.embryology.ch/francais/gnidation/etape03.html

Implanted Human Blastocyst

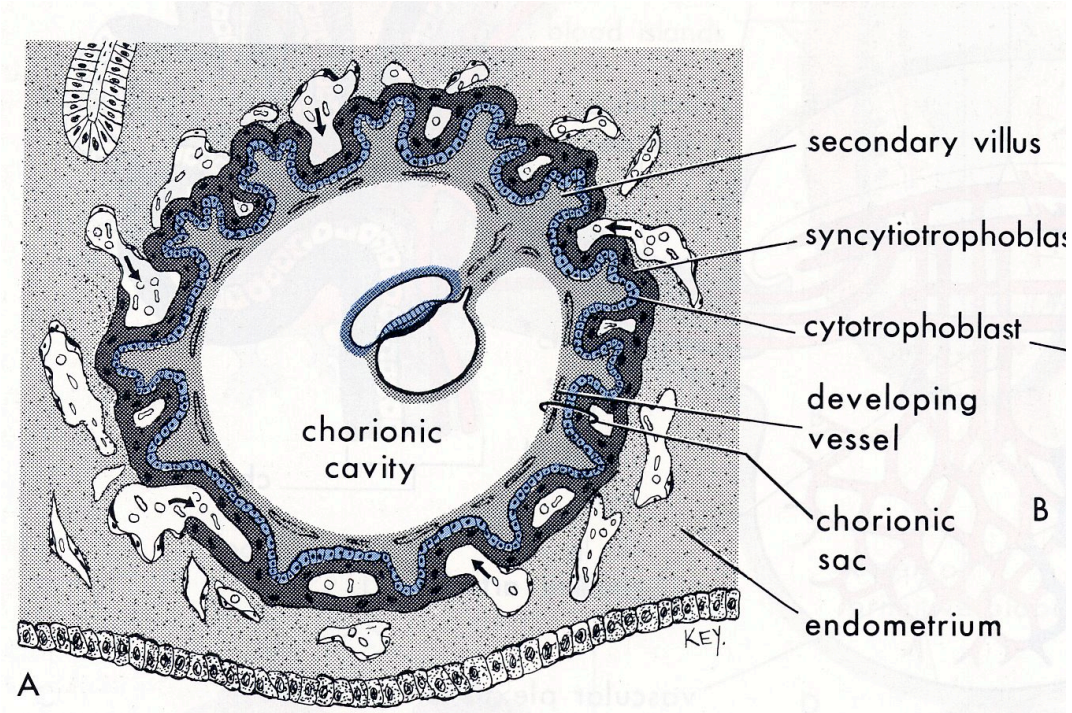


From The Developing Human
Moore and Persaud 6th Edition

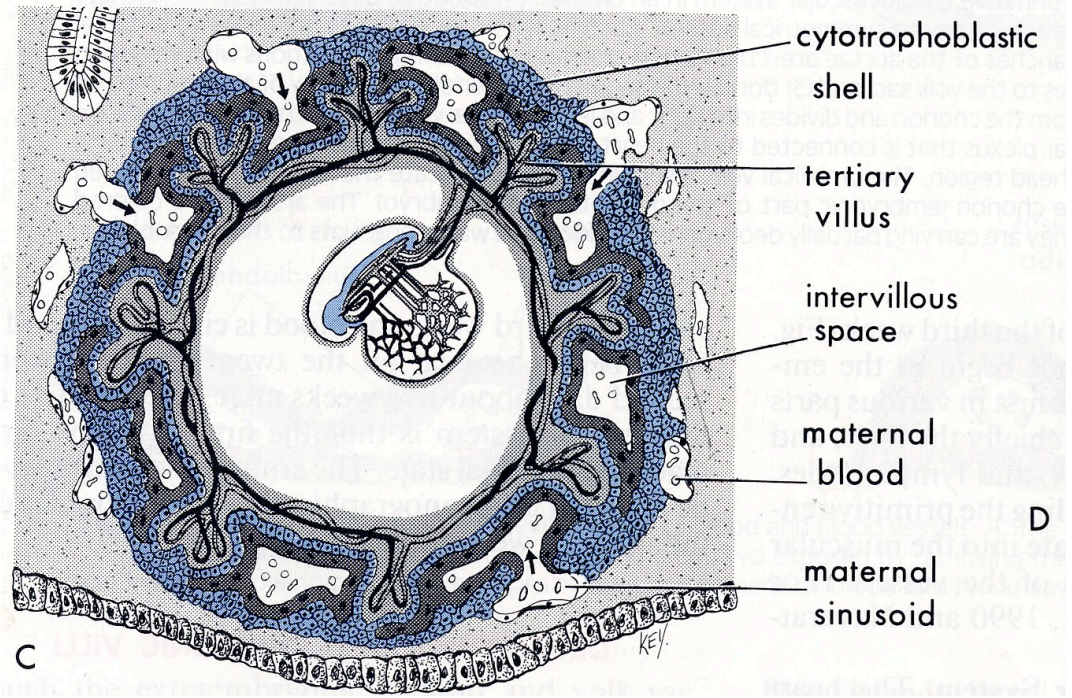


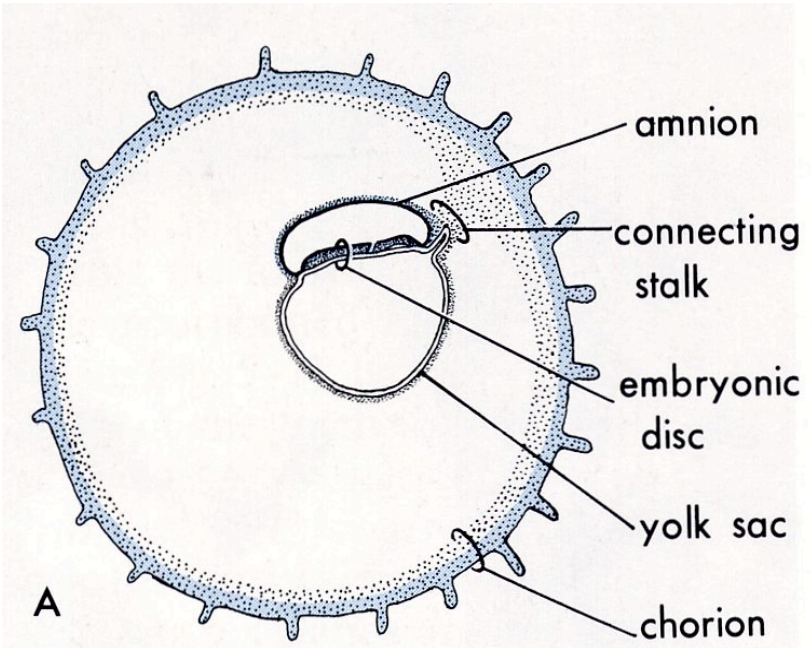
From Langman's Medical Embryology 9th Edition
Lippincott Williams & Wilkins

16 days gestation

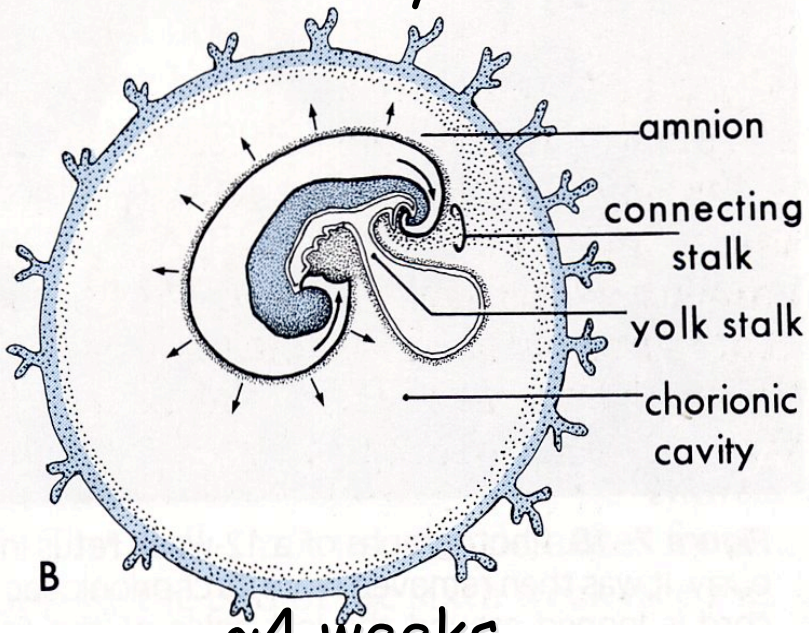


21 days circulation established

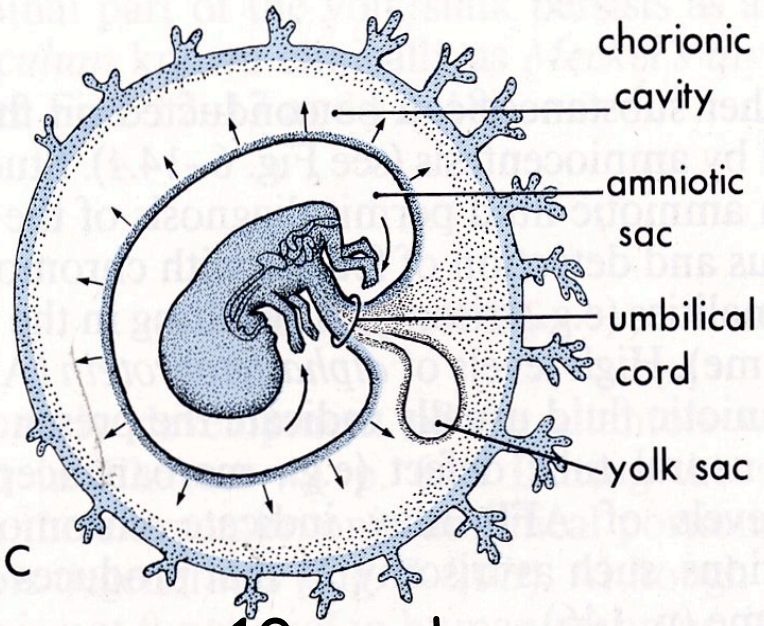




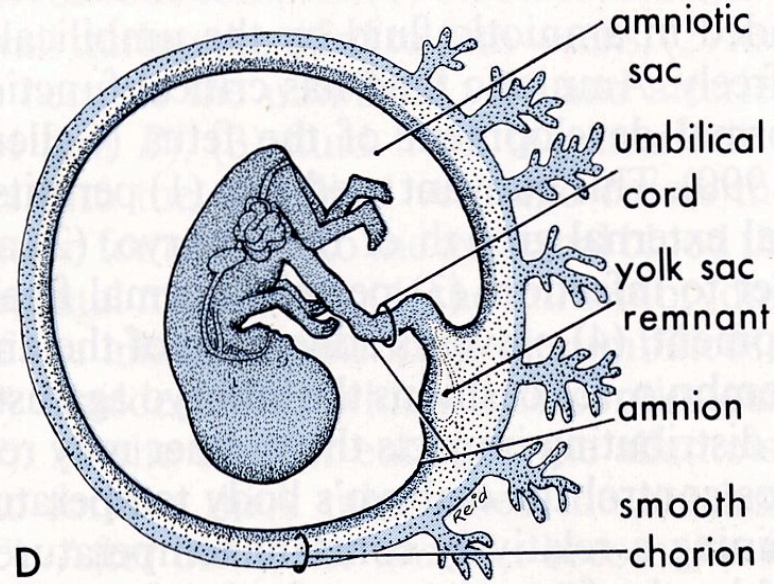
~16 days



~4 weeks



~10 weeks



~20 weeks

Week 3

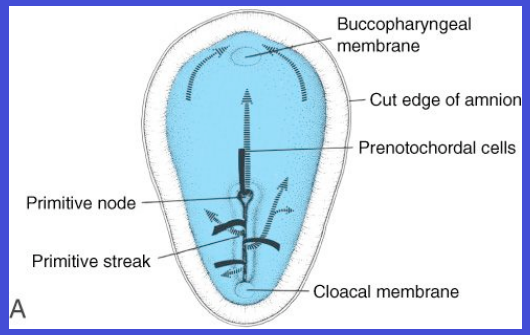
Gastrulation

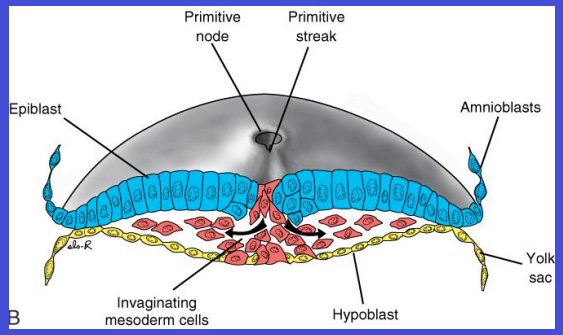
"The most important event in your life is not birth, marriage, or death, but gastrulation."- L. Wolpert.

Gastrulation

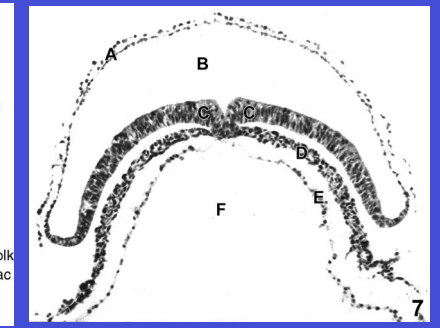
The inner cell mass in the 15-16 day human embryo consists of two layers – an upper epiblast and a lower hypoblast. Gastrulation converts this bilaminar disc into three layers. An upper **ectoderm**, a middle **mesoderm** and a lower **endoderm**.

14-day embryo





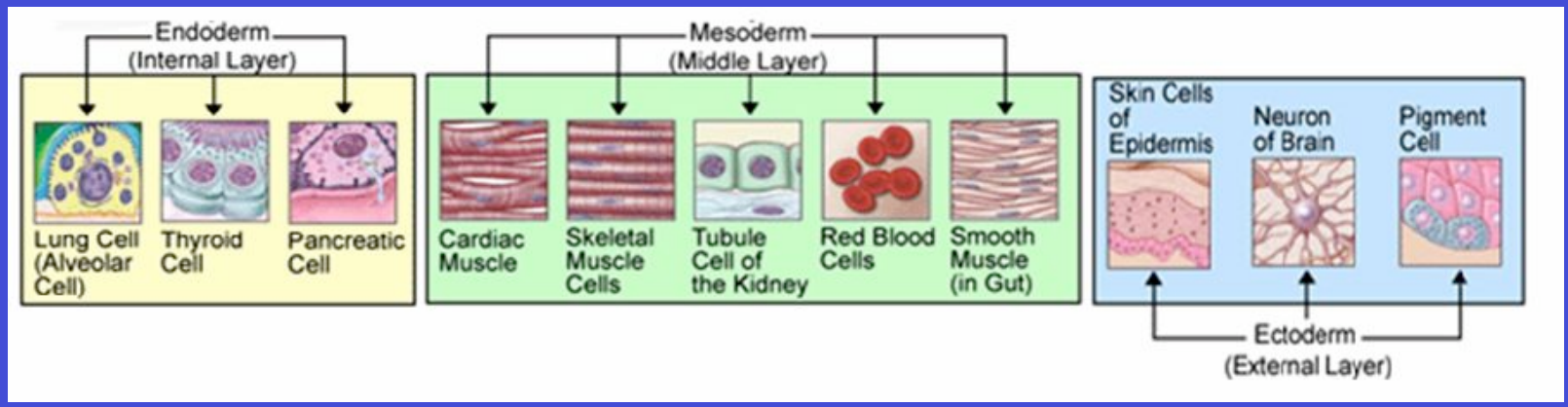
Gastrulation in a 16-day human embryo



18-day embryo

Germ layer cell fates

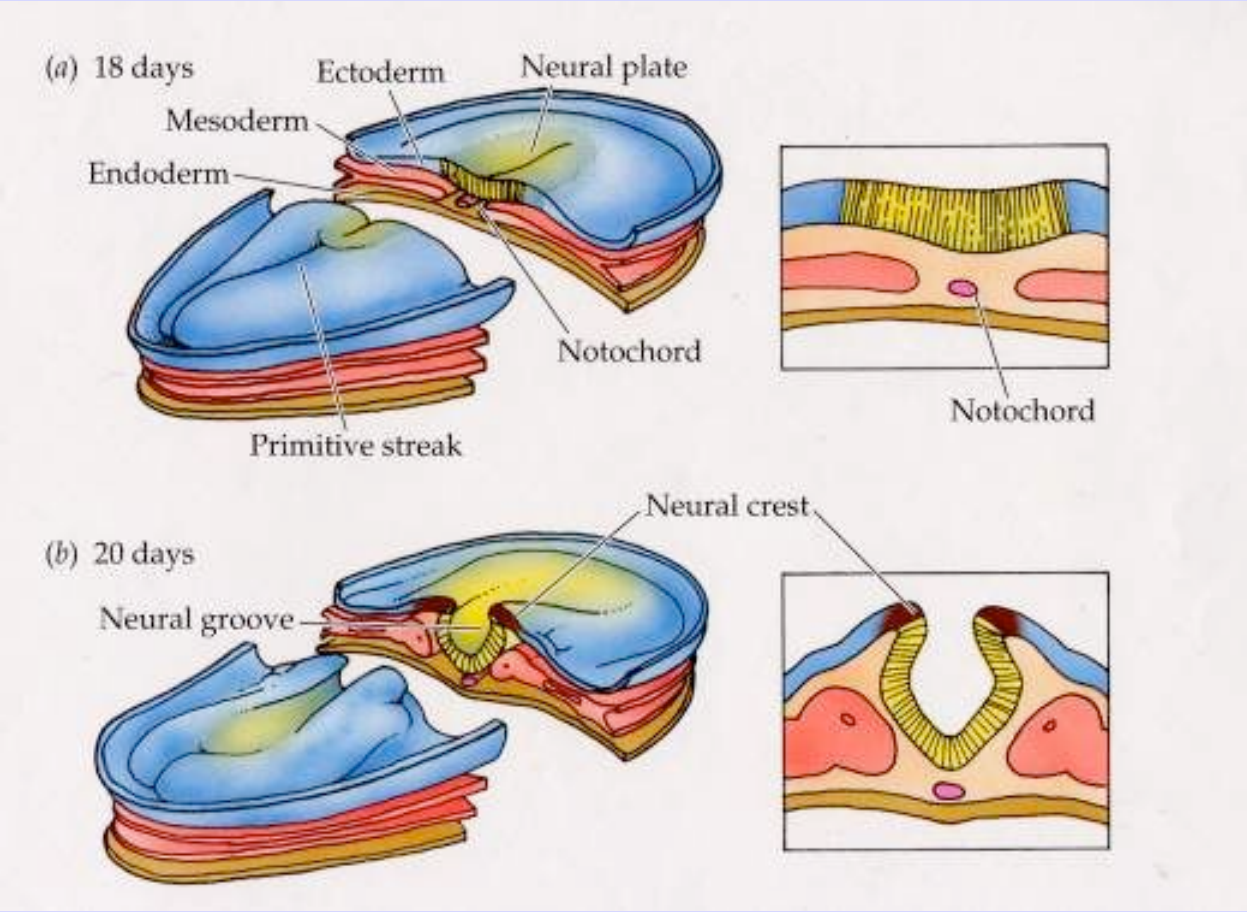
- Cells from each germ layer have specific fates
- Ectoderm:
  - Epidermis, hair, nails, etc.
  - Brain and nervous system
- Mesoderm:
  - Muscle, cardiovascular system, bones, blood, dermis, gonads, excretory systems, etc.
- Endoderm:
  - Inner lining of digestive tract
  - Lining of lungs
  - glands



Week 4

Neurulation

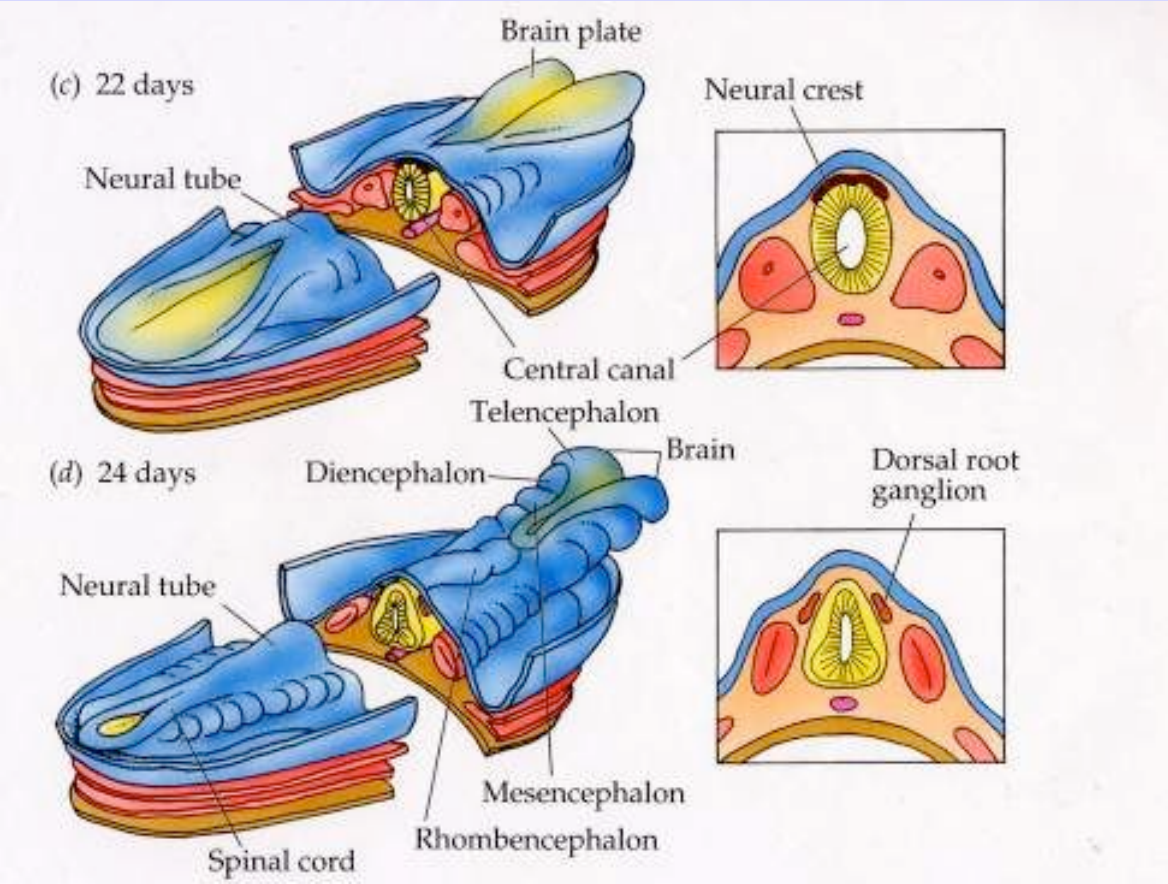
Nervous System Development in the Human Embryo



(a) At 18 days after conception the embryo consists of 3 layers of cells: endoderm, mesoderm, and ectoderm. Thickening of the ectoderm leads to the development of the neural plate.

(b) The neural groove begins to develop at 20 days.

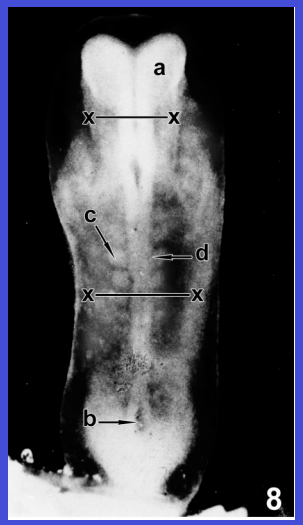
Nervous System Development in the Human Embryo



(c) At 22 days the neural groove has closed in the middle to form the neural tube. It remains open at either end.

(d) The anterior opening or neuropore closes day 25-26 and the posterior neuropore day 27-28.

Neural tube closure



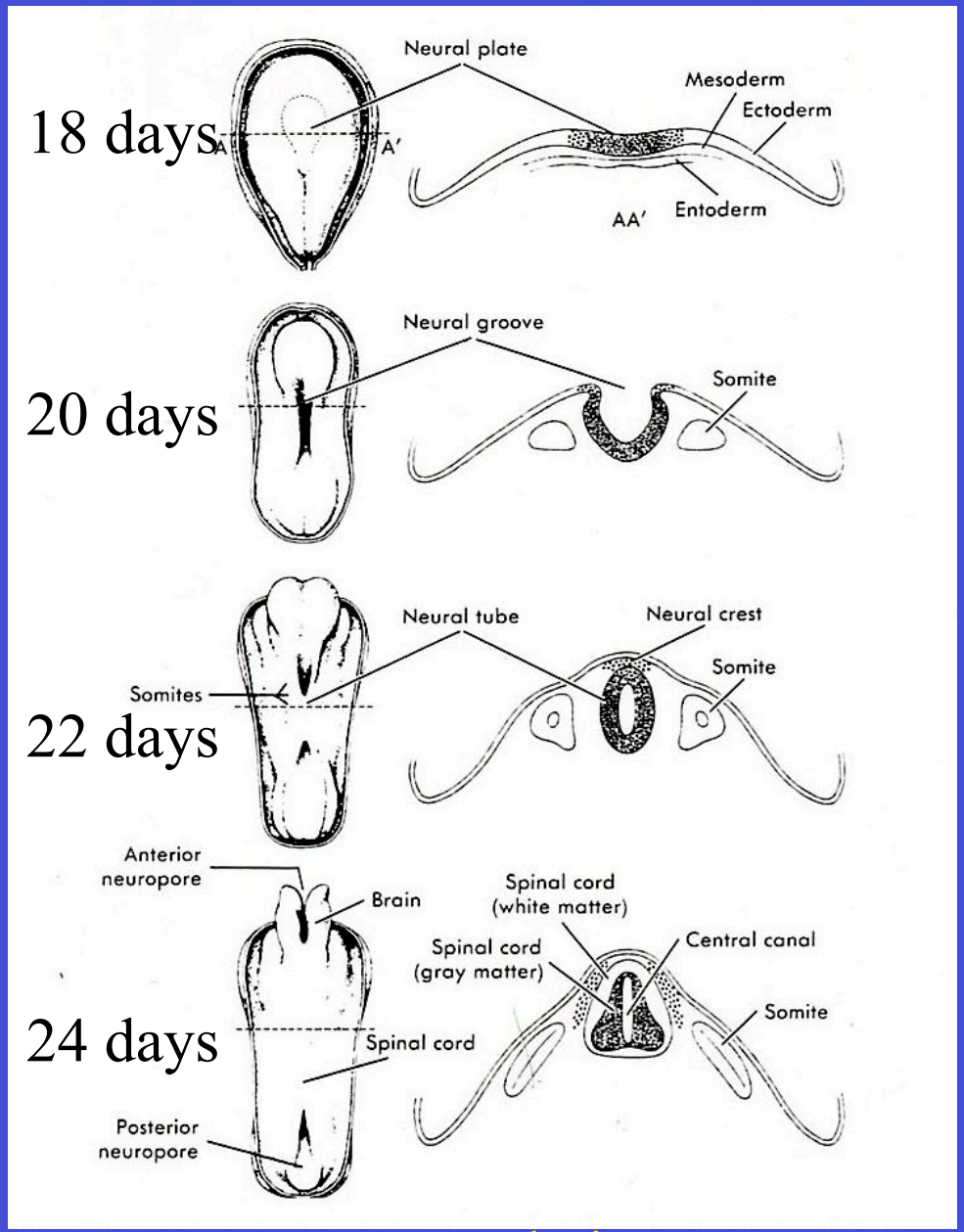
22-days

24-days

27-days~ 4mm

A 27-day embryo should have a completely closed neural tube. The heart is visible and has already started to beat.

Colour photo by Lennart Nilsson



Neurulation

Cowan WM The Development of the Brain Sci Am 1979; 241:112

Anencephaly

www.vh.org/.../FetalYoungCNS/Images/fig03.gif

Spina Bifida

Picture from Illustrated guide to malformations of the CNS at birth by N. C. Nevin and J. A. C. Weatherall 1983, Churchill Livingstone

Neural tube defects

The two neural tube defects spina bifida and anencephaly both have a prevalence of about 1:1000 live births.

The chances of having a child with either of these conditions can be greatly reduced by adequate folate intake. The U.S. Public Health Service in September 1992 recommended that all women of childbearing age capable of becoming pregnant consume 0.4 mg of folate daily to reduce their risk of having a pregnancy affected with spina bifida or other neural tube defects.

Use of the antiepileptic medications carbamazepine or valproic acid during early pregnancy is associated with an increased risk of spina bifida (perhaps 10-fold increase in risk). Folate does not appear to protect against this drug-induced birth defect.

Model of 4 week embryo ~ 4 mm length

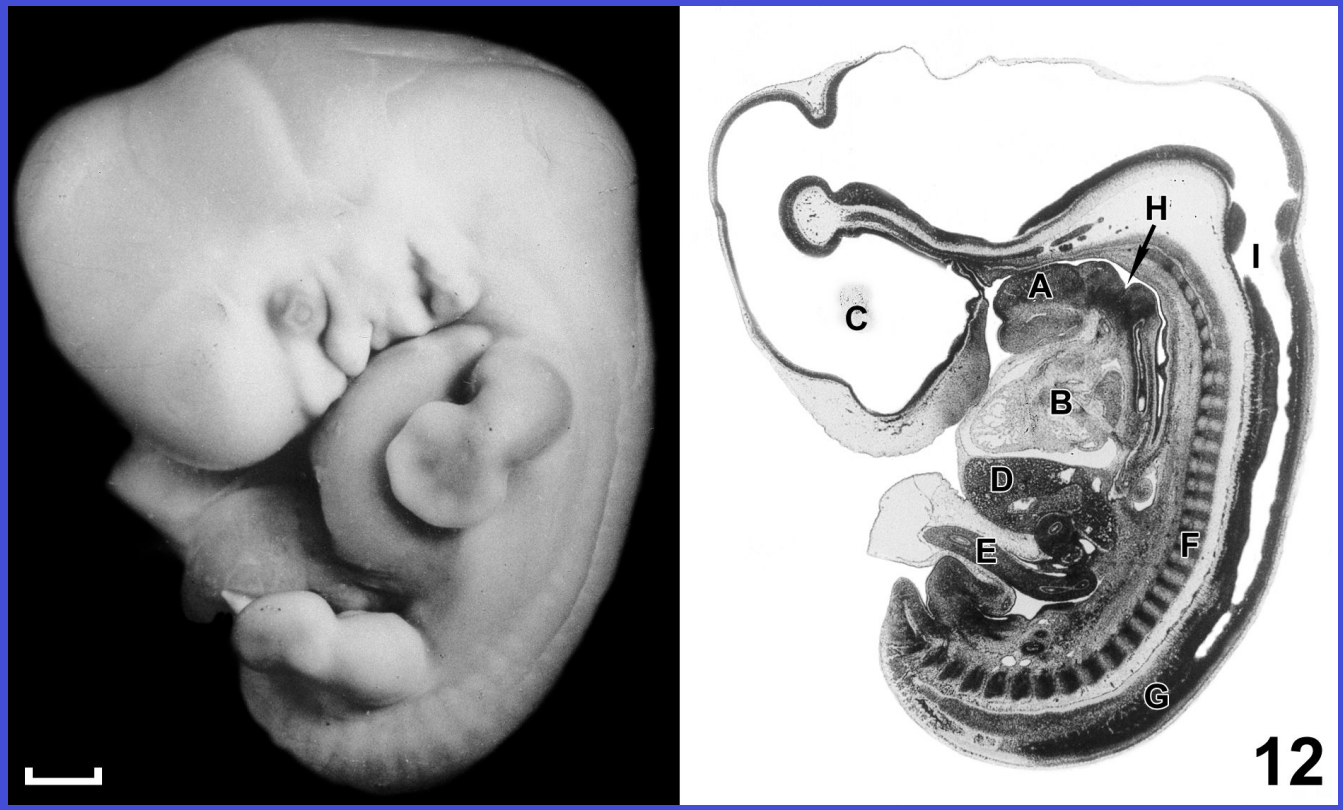
Weeks 5-8

Organogenic Period

32- day human embryo ~ 8 mm CR length

Organ system development is well underway. This is a critical time for development of the heart, limbs, eyes, upper lip, intestines.

44-day embryo ~ 13 mm length



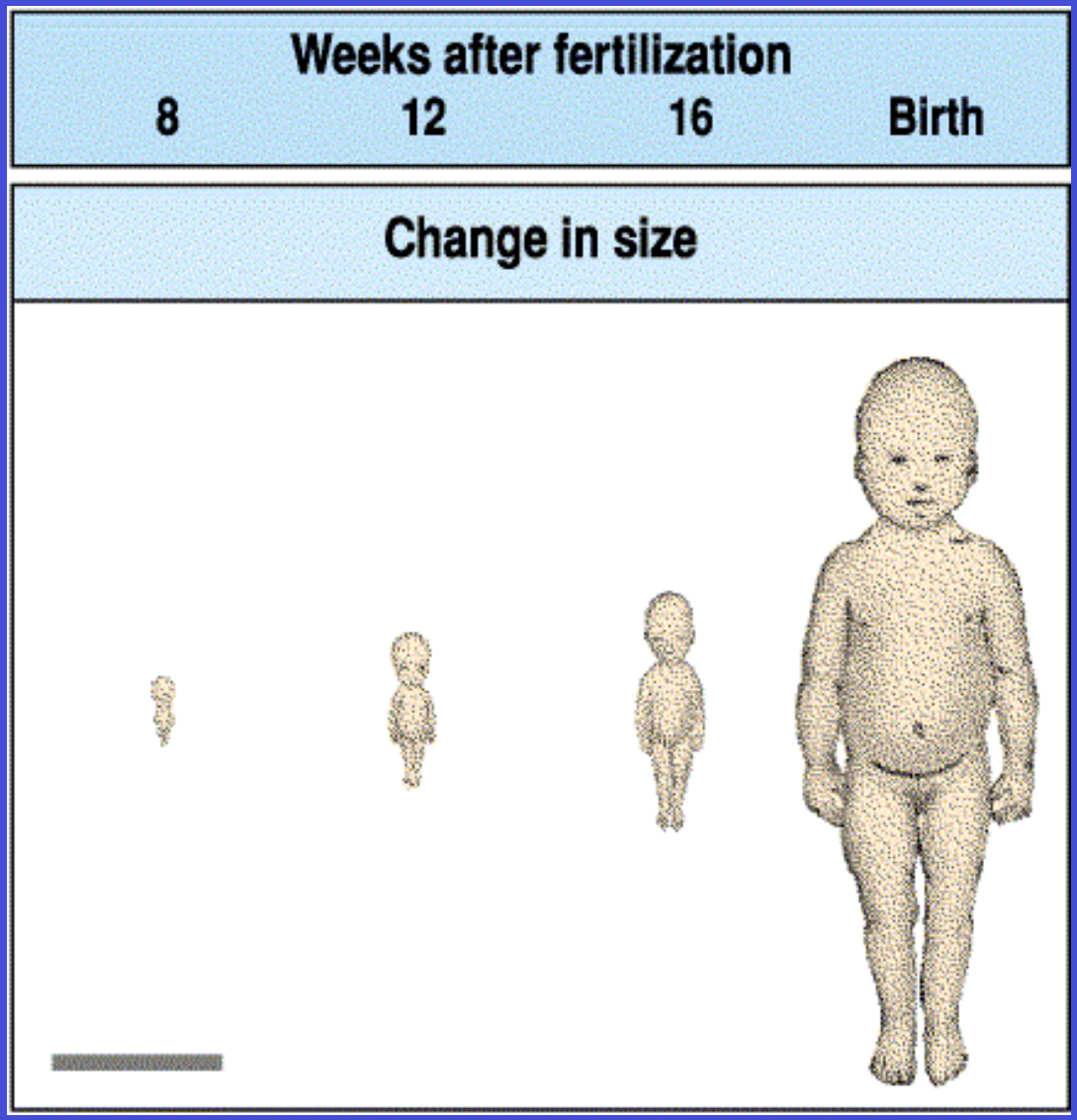
At this stage the embryo has completed much of its organogenesis. Still to be completed is the palate and external genitalia and brain development is ongoing.

8-week human fetus ~ 3cm in length

Organogenesis is largely complete – development of the external genitalia is still incomplete. The brain is about to start an 8-week period of massive neuronal cell formation for the cerebral cortex.

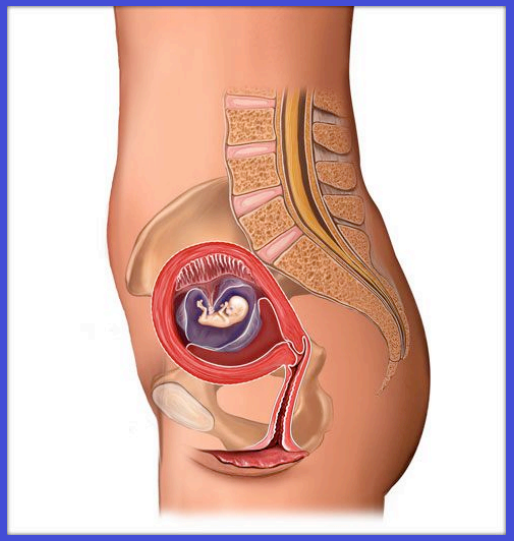
Weeks 9-38

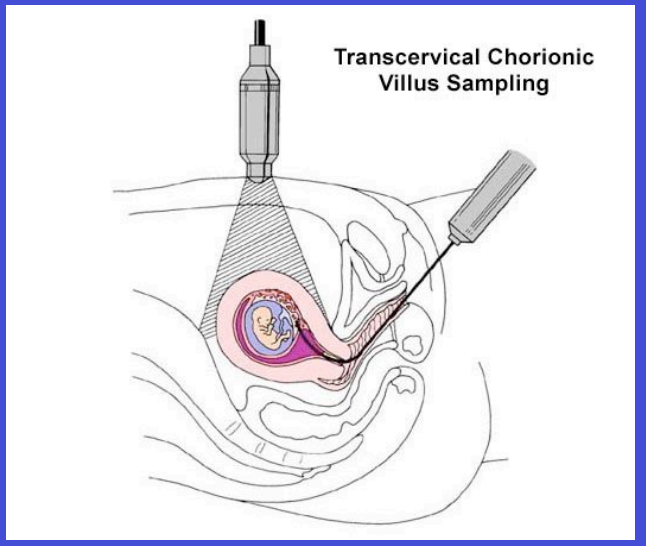
Fetal Period



An 8-week fetus is about 4 cm in length (crown-heel),
The newborn is about 50 cm (crown-heel)

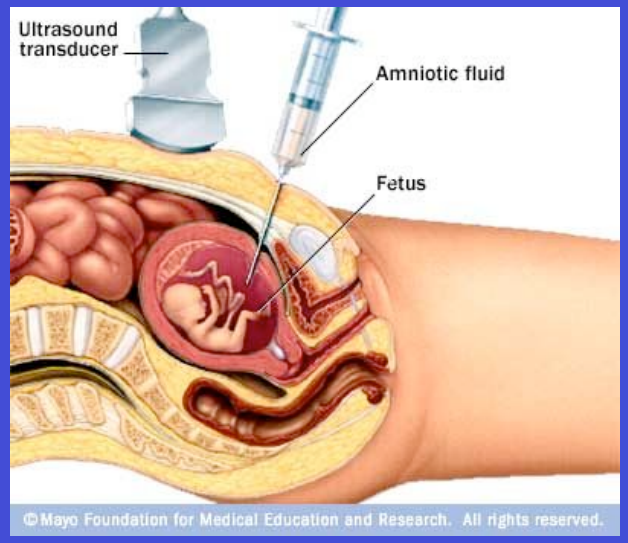
10-week human fetus ~ 6 cm in length.





Fetal heart beat can be monitored at this stage. Chorionic villous sampling is usually performed between 8 and 10 weeks. A small piece (villous) of the placenta is removed and cultured in the laboratory. Genetic results are usually available in ~2 weeks.

13-week human fetus ~ 10cm in length.



The fetus is surrounded by about 100 ml of amniotic fluid. Amniocentesis can be performed from about 13 to 18 weeks gestation. About 10-20 ml of fluid is removed, the fetal cells are separated and grown in culture and genetic results available in about 2 weeks. An α-fetoprotein test can be performed on the maternal blood. This protein is made by the fetus and is in higher concentrations in fetuses with neural tube defects.

16-week human fetus ~ 14cm in length, weight about 190 g.

An ultrasound dating scan can be given at 5-11 weeks to confirm pregnancy, exclude ectopic or molar pregnancies, confirm cardiac pulsation and measure the crown-rump length for dating. An anomaly scan is usually performed at 16-18 weeks to look for congenital malformations. Sex of the fetus can usually be determined at this stage.

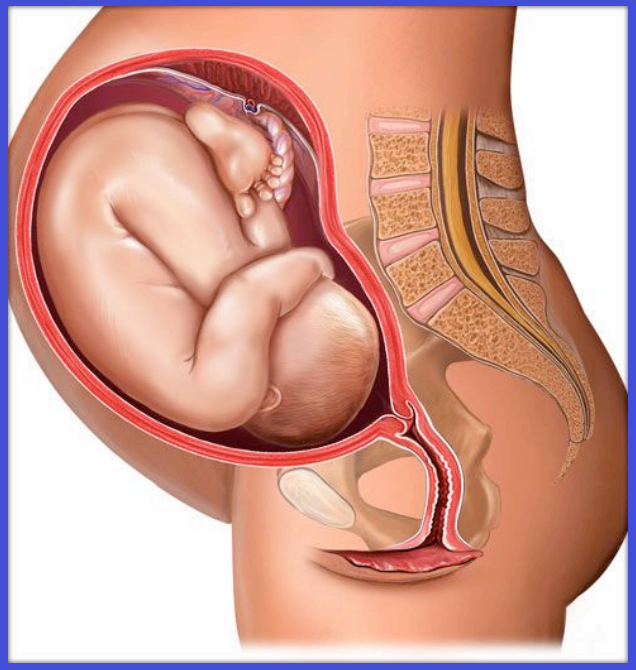
24-week human fetus ~ 23cm in length – weight about 760g.

Head hair appears, the fetus already has a downy hair (lanugo), skin is coated with vernix – a waxy secretion of sebaceous glands. 90% of premature babies born who weigh 800 g or more will survive. For those who weigh 500 g or more there is 40-50% survival.

Problems include (a) lack of body fat – difficulty keeping warm; (b) difficulty feeding; (c) hyperbilirubinemia; (d) apnea; (e) anemia; (f) respiratory distress syndrome due to lack of lung surfactant; (g) patent ductus arteriosus; (h) retinopathy

http://www.kidshealth.org/parent/growth/growing/preemies.html

38 weeks – term - crown-rump length about 36cm, crown heel 50 cm – weight about 3500g.



Eyes reopened at about 26 weeks, at about 30 weeks skin becomes thicker and subcutaneous fat appears.

FINISH!