Part 3

The reproductive years

Chapter 7

The mother and fetus in pregnancy

For most women, childbearing is a major event in their lives. The basic changes of pregnancy are covered in this chapter; the rest of pregnancy and childbirth are discussed in Chapters 8–14 and a short chapter, Chapter 15, covers those aspects the obstetrician should know about the newborn child.

Maternal changes in pregnancy

During pregnancy, oestrogen increases vascularity and progesterone permits muscular relaxation and softening of the connective tissue sheath of the vagina by an increase in fluid. Over 38 weeks the tube becomes much more stretchable so that, by full term, the vagina and vulva permit the passage of an infant with a head diameter of approximately 10 cm. The perineum with the squamous epithelium in the region of the fourchette does not always stretch so readily and so may tear on occasions.

Pregnancy causes alterations not just in the mother's pelvis and abdomen but the whole body. Adaptations in the function of various systems occur to minimize the stresses imposed and are interlinked smoothly so the function of the whole organism does not deteriorate.

Uterus

By term, a litre of blood can be in the uterine vasculature. Branches increase in size, number and diameter from each side of the uterus. The placental site gets preferential blood supply. Penetrating branches pass through the myometrium, under the surface of the decidua. They become spiral arteries and penetrate the decidua. In early pregnancy their exits into the placental bed pool are narrow, but trophoblast invasion by 16 weeks normally widens them into deltas so reducing resistance and improving flow. If invasion is incomplete, flow is restricted so that:

- in late pregnancy, the fetus gets fewer nutrients for growth;
- in labour, the fetus gets less O_2 and so fetal distress follows more readily.

The uterus grows through hypertrophy of the myometrial cells rather than by an increase in numbers of myometrial cells. From 28 weeks the lower third of the uterus thins and becomes less vascular forming the lower segment of the uterus (hence lower segment Caesarean section).

Metabolism

Increased to provide for:

- Growth of fetus and placenta.
- Increased growth of the uterus.
- Increased growth of support systems.
- Preparation for lactation.

Weight increase (Table 7.1)

Usually 10–14 kg (22–30 lb) in whole pregnancy. For example:

0–14 weeks: 2 kg (4.5 lb)—may be a loss because of vomiting;

13–28 weeks: 5 kg (11 lb);

28–40 weeks: 5 kg (11 lb)—may be a loss in last 2–3 weeks because of diminution of amniotic fluid.

The rest is extracellular fluid, fat and protein storage—6 kg.

A sharp increase in the mother's weight gain in late pregnancy may indicate increased water retention, a facet of pre-eclampsia. Weight loss, if persistent, may reflect poor fetal progress although there is little precision in this and many obstetricians do not use weight as a measure of well-being.

Protein

The fetus needs little protein in early pregnancy so the woman is in negative balance.

Two-thirds of the fetal protein is acquired in the last 12 weeks (a half in last 4 weeks). Also maternal uterus and breasts use much protein in growing tissues and storage occurs for lactation. Approximately 12 g of nitrogen a day are needed for the development of these and the fetus.

Carbohydrate

Pregnancy is diabetogenic and calorie need is slightly increased.

Fat

The fetus accumulates fat late, from 2% of the fetal body weight at 32 weeks to 12% at term. Fetal neolipogenesis accounts for most of the baby's fat with low transfer rate of precursors across the placenta. The mother has a higher circulating lipid and lipoprotein level.

Table 7.1 Breakdown of approximate weight increase during pregnancy.

Fetus	3.5 kg	7 lb
Placenta	0.5	1
Amniotic fluid	1.5	2
Uterus	1.0	2
Blood increase	1.5	3
Breasts	1.0	2
Total	9.0 kg	17 lb

Calcium

The fetus utilizes calcium late, taking from the long bones of the mother. If the stores are insufficient the fetus still utilizes calcium leading to maternal osteomalacia. Maternal serum calcium levels stay steady.

Iron

Iron is mostly passed to the fetus in the last weeks of pregnancy. It is stored in the liver. The mother may have poor iron stores because of:

- too little in diet, therefore give supplements;
- too poor absorption.

Cardiovascular system

Load

Pregnancy is an increased load so more work is required by the heart.

- Growing fetal tissues which have high O_2 consumption rates.
- Hypertrophied uterus and breasts require more O_2.
- Increased muscular effort by mother to cope with weight gain of 10–14 kg (22–30 lb).
- In last weeks of pregnancy, the placental bed may act like an arteriovenous fistula. More work is required to overcome this shunt.

Cardiac output

Increased needs are met by increasing cardiac output.

$$\text{Cardiac output} = \text{stroke volume} \times \text{pulse rate}.$$

In pregnancy, pulse rate is raised but most increase in output comes from larger stroke volume with enlarged heart chambers and muscle hypertrophy.

Output increases rapidly in the first trimester by up to 40% and steadies for the rest of pregnancy (Fig. 7.1).

During labour, cardiac output can increase by a further 2 l/min in association with uterine contractions.

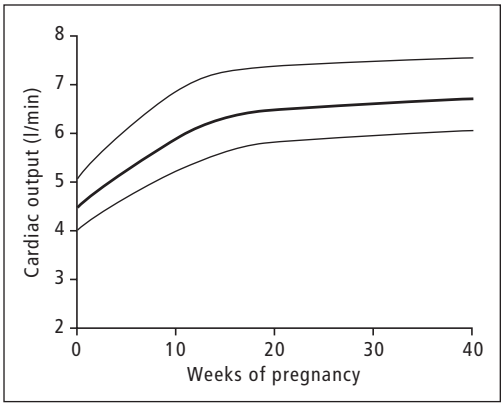


Figure 7.1 Cardiac output in pregnancy in normal women. The lines on the graph represent the mean ± 2 SD of the mean.

Systolic and diastolic pressure is much lower in early and mid-pregnancy, rising in the last trimester. Peripheral resistance is decreased and, since cardiac output is raised, pulse pressure is increased.

Blood volume

Return of blood to the heart is maintained by an increased blood volume. Plasma volume increases more than red cells so that relative haemodilution occurs. This used to be called physiological anaemia, but this is a bad term, for no pathological process can be physiological.

Heart changes

Pregnancy is a hyperkinetic state. The heart is:

- Enlarged.
- Pushed up.
- Unfolded upon aorta.

These changes produce electrocardiogram (ECG) and X-ray changes which are normal for pregnancy, but may appear pathological if interpreted without knowledge of pregnancy.

There are also sometimes extra murmurs, normal hypervolaemic sounds such as the systolic ejection murmur and that over the internal mammary arteries supplying the breasts.

Respiratory system

Pressure of the growing uterus forces the diaphragm up and lower ribs out but vital capacity is not reduced in late pregnancy.

Raised progesterone levels increase respiratory rate.

Urinary tract

Renal function

- Renal plasma flow increases by 30–50%.
- Glomerular filtration rate increases by 30–50%.
- Tubular re-absorption increases by 30–50%.
- Patchy glomerular leak happens occasionally (e.g. glucose).

Lower urinary tract

- Bladder more irritated as growing uterus pushes on it.
- Ureters:
  (a) Longer, wider, lower tone because of progesterone effects.
  (b) Stasis in ureter and pelvis of kidney may lead to infection.

Alimentary tract

- Teeth more susceptible to spreading caries and gingivitis because of increased cortisone levels.
- Nausea and vomiting.
- Hypomotility of gut may lead to constipation.
- Hypochlorhydria—regurgitation of alkaline chyle into stomach.
- Slow emptying of gall bladder.
- Increased gastro-oesophageal reflux.

Early fetal development

Fetal development is well documented in most mammalian species including the human.

Since many women cannot time the precise act of coitus at which fertilization occurred, it is conventional to date pregnancy in weeks from the 1st day of the last normal menstrual period (LNMP). The difference in the clinical timing of pregnancy and biological age (from conception) is readily

understood on realizing that no-one becomes pregnant in the first half of a menstrual cycle. The first 14 days of pregnancy do not exist using the 1st day of the LNMP as a method of timing (Fig. 7.2).

The following milestones are particularly important.

Four weeks (from LNMP) or 14 days biological life

- Sac 2–3 mm.
- Ectoderm, Mesoderm, Endoderm } formed.
- Yolk sac formed.

Six weeks (from LNMP)

- Sac 20–25 mm; embryo 10 mm—can be seen on ultrasound.
- A cylinder with head and tail end formed.
- Pulsation of heart tube.
- Body stalk (umbilical cord) formed.
- Villi appear in cytotrophoblast.

Eight weeks (from LNMP)

- Sac 30–50 mm; fetus 20 mm (Figs 7.3 and 7.4).
- Sex glands differentiated.
- Limbs well formed, toes and fingers present.
- Centres of ossification present.

Twelve weeks (from LNMP)

- Sac 100 mm; fetus 90 mm.
- Primary development of all organ systems.
- Nails on fingers and toes.

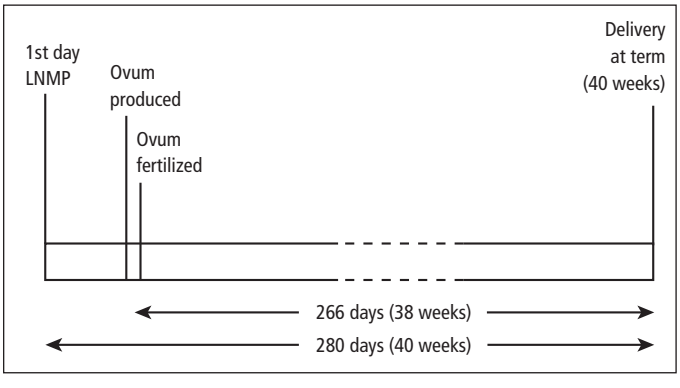


Figure 7.2 The differences between the actual length of gestation and the calculated length of pregnancy from the LNMP.

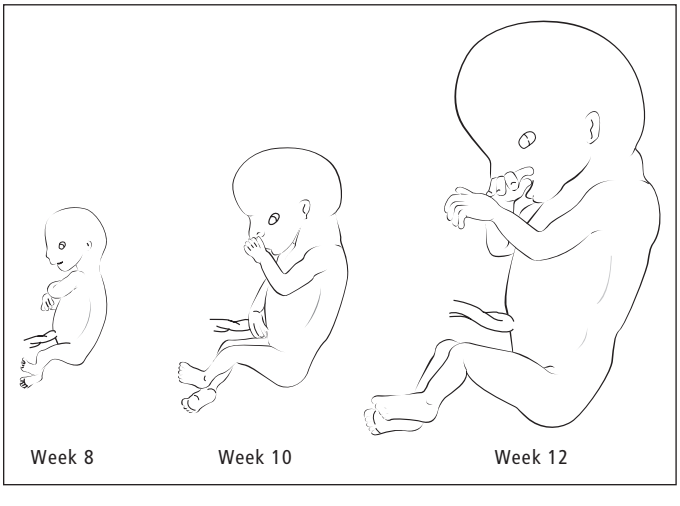


Figure 7.3 Different stages of fetal growth. The fetus at 8, 10 and 12 weeks are shown two-thirds of actual size.

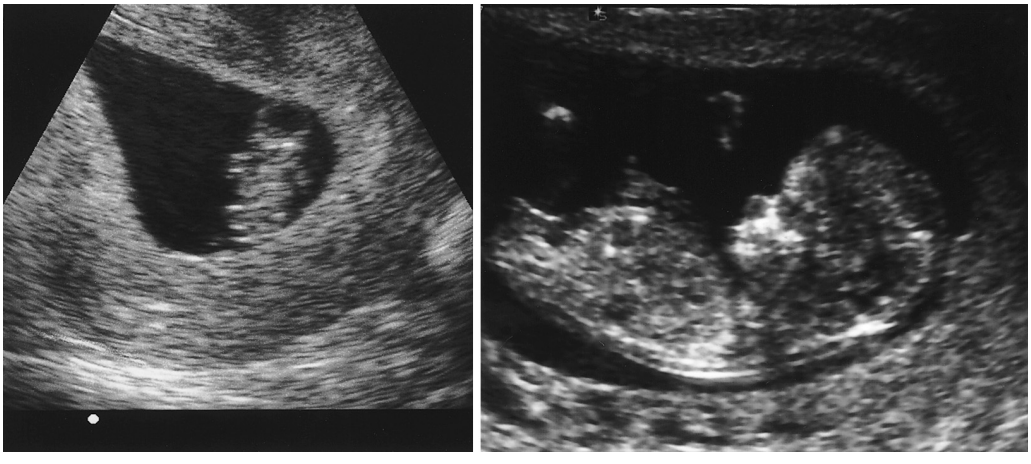
(a)  (b)

Figure 7.4 Different stages of fetal growth. (a) Ultrasound showing a sac at 7 weeks. (b) Ultrasound showing a sac and fetus at 12 weeks.

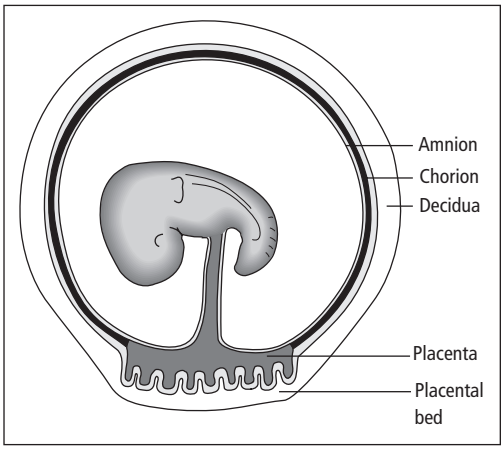


Figure 7.5 Formation of placenta in relation to fetus and fetal membranes.

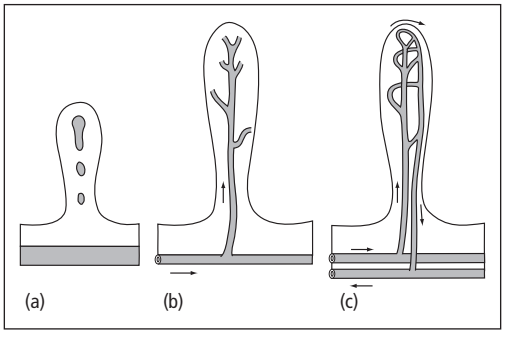


Figure 7.6 Development of blood vessels in the villi. (a) Mesoderm appears *in situ* in the core of a villus of proliferating trophoblast cells. (b) Blood vessels form and join up with those in the mesoderm layer. (c) Capillaries from arterial side circulate blood back to veins.

Early placental development

The placenta (Fig. 7.5) is formed from:

- chorion
- decidua basalis

} covered by amnion.

Villi are buds from chorionic plate. At first they are made of cytotrophoblast tissue only. Mesoderm appears *in situ* in the centre of the core of each villus (Fig. 7.6).

In this mesodermal core, angioblastic strands are formed. The cells on the edge of these become the endothelium of blood vessels and the central cells, the red blood cells. The vessels of the villus join the vessels formed in the mesoderm. By 22 days, the fetal heart pumps blood and a functioning circulation starts.

By eight weeks, the villi are 200 μm in diameter with a well-organized circulatory system and a

double layer of epithelium (cytotrophoblast covered by a cellular syncytiotrophoblast).

Further demands of fetal metabolism require swifter exchanges at the placenta. These come as a result of:

1 Greater surface area—longer and branching villi.
2 Thinning of epithelium so that syncytiotrophoblast is in direct contact with blood capillary.
3 Nuclei in syncytiotrophoblast migrate from areas over capillaries where exchange actually occurs.
4 Localized dome-like swellings occur on the villi protruding into the intervillous space. These areas are especially thin-walled and are probably the site of much of the gas exchange.

Villi are like fronds of seaweed under water as the maternal blood circulates around them (Fig. 7.7). As the placenta grows, fetal size is proportional to the surface area available for exchange at first. The number of stem villi does not increase after the 12th week. Hence the number of lobules is now fixed. The rest of growth is by proliferation and by growth of peripheral villi.

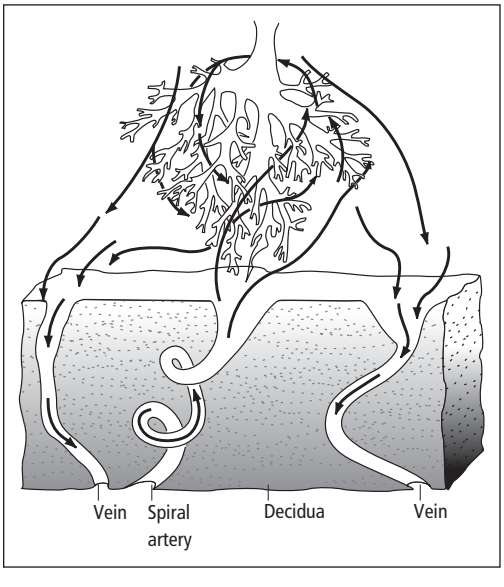


Figure 7.7 Circulation of maternal blood around fine exchange villi.

Fetal physiology

The major functions will be reviewed particularly where they differ from adult physiological patterns.

Cardiovascular system

The heart is beating by 22 days and can be detected with vaginal ultrasound at 5 weeks (from LNMP).

There are bypasses in the system since the lungs are not used; less than 10% of blood goes through them (Fig. 7.8). These bypasses include:

- foramen ovale between the right and left atria so that the majority of oxygenated blood passes straight to the left side of the heart.
- ductus arteriosus from the pulmonary artery to the aorta so that only a small amount of blood from the right side of the heart goes into the lungs and the rest can use the bypass into the aorta.

Umbilical blood flow increases with fetal weight. This increase is disproportionate, but with enhanced O_2 carrying capacity of the fetal blood, the total O_2 transport is increased. Flow is about 100 ml/kg/min, as measured experimentally, but may be greater *in vivo*.

Fetal haemoglobin

HbA (adult haemoglobin) differs from HbF (fetal haemoglobin) by a 25% alteration of amino acid radicals in chains. At any given Po_2, the O_2 dissociation curve of HbF is to the left of HbA so it has greater O_2 affinity (Fig. 7.9). The fetus has higher Hb concentration than the adult (18 g/dl in the blood compared with 13 g/dl) allowing further O_2 uptake at the placenta and greater release to tissues. Production of HbF diminishes before birth and has usually ceased by the age of one year (Fig. 7.10).

Respiratory system

Within 1–2 minutes this has to adjust from an intrauterine to an independent state. Vascular loops occur in the lungs by 18 weeks. Alveoli develop by 22 weeks.

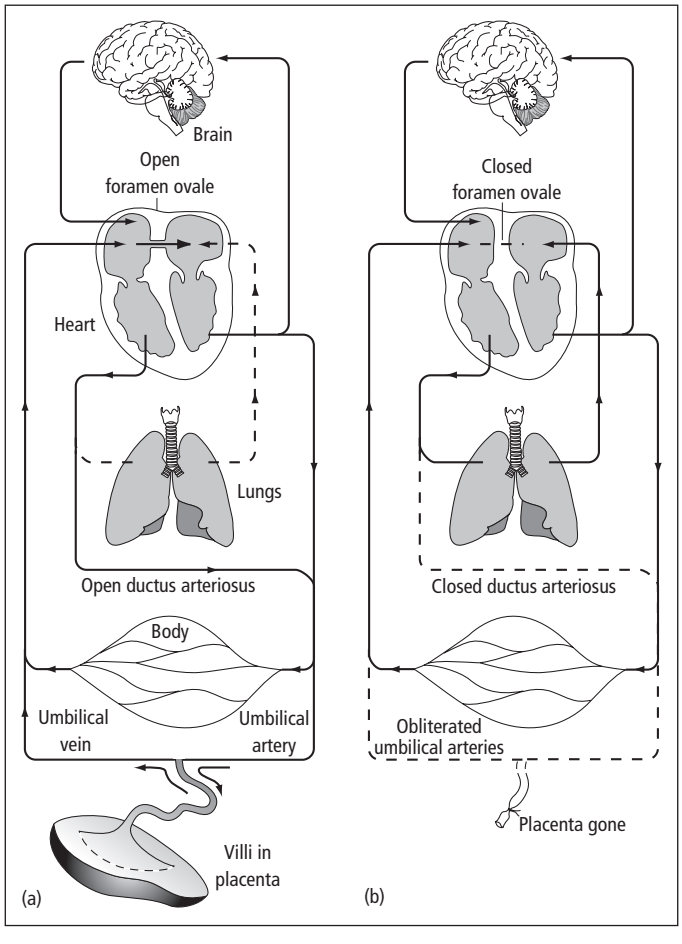


Figure 7.8 (a) The fetal circulation. (b) The neonatal circulation. Note closure of bypasses after birth.

Surface tension of alveolar epithelium is decreased by surfactant lipoproteins, which are not present in the immature fetus. Hence if they are born prematurely it is difficult to open up their lungs and respiratory distress syndrome occurs. Production of surfactant increases after 34 weeks.

Before birth, the alveoli are closed and the trachea is filled with lung fluid. This is different from amniotic fluid and is secreted from glandular cells in the periphery of the bronchiolar system. Small spontaneous chest movements occur, but if the fetus is made hypoxic, larger efforts are made; then (and only then) is amniotic fluid drawn into the trachea. Most non-stressed infants are born with a respiratory tract filled with lung fluid, not amniotic fluid.

Fetal development is mostly by growth (Fig. 7.11); most congenital defects that are going to occur will have been formed by 10 weeks. The critical periods in the development of the human embryo are shown in Fig. 7.12.

Growing from one cell to six billion demands organization of cells into functioning systems so that all can metabolize under optimal conditions. The rate of growth is greatest in the first weeks. Cellular increase is under the control of maternal and fetal hormones; at first, oestrogens are most influential, then later insulin-like growth factors. In very early pregnancy oestrogens regulate the supply of nutrients in uterine fluid. Later they regulate the course of the blood supply to the placental bed.

After mid-pregnancy, growth is also determined by placental transfer. This could be impaired by:

1 A low environment supply from the mother of:
- oxygen—only has effect in last weeks, e.g. living at high altitudes;
- nutrients—shows with extremes of specific deprivation or general starvation.

2 Reduced blood flow to the placental bed. This follows lack of normal invasion of the arcuate arteries by trophoblasts at 16–18 weeks. This can be estimated by Doppler ultrasound.

3 Poor exchange across the syncytiotrophoblast membrane; if this should be reduced a smaller baby results.

Overall growth is determined by:

1 Genetic factors inherited from both parents.

2 Placental transfer of nutrients dependent on:
- placental bed flow rates;
- placental membrane transfer.

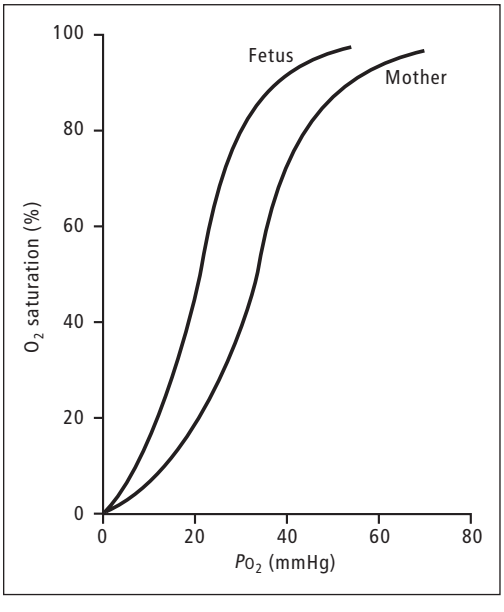


Figure 7.9 Oxyhaemoglobin dissociation curves for human maternal and fetal blood at pH 7.4 and 37°C.

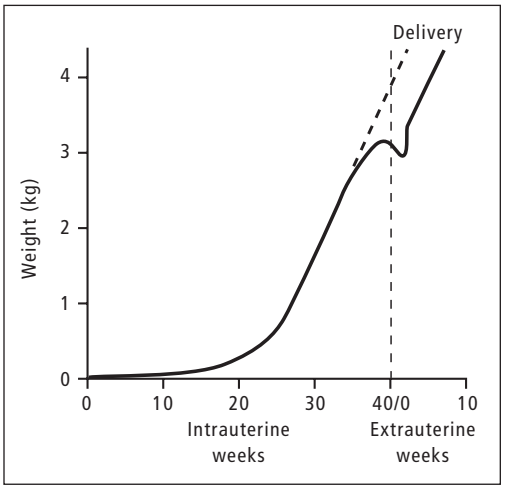


Figure 7.11 The weight gain of the fetus and newborn child. The growth potential falls off in the last few weeks of pregnancy. Note that, after the immediate weight drop, neonatal growth continues at the same incremental rate as it did in the uterus.

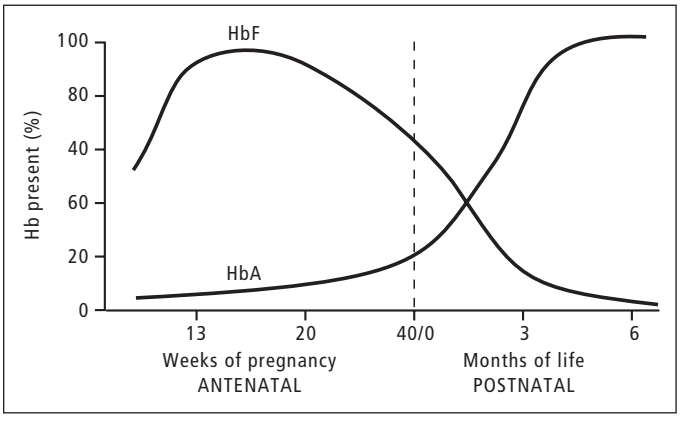


Figure 7.10 Proportion of HbF and HbA present at different stages of fetal and postnatal life.

Changes that occur in the fetus at birth

- Closure of the ductus arteriosus
- Closure of the foramen ovale

} Occurs with the first breath so that 100% of deoxygenated blood passes through the lungs.

- Obliteration of the umbilical arteries and veins (Fig. 7.8b).

Placental physiology

Exchange

The placenta is the fetal exchange station. Compare Fig. 7.13a and Fig. 7.13b. Figure 7.13a is an adult with organs of homeostasis (kidney, skin and lung) communicating with the outside environment—the air in the case of humans. Figure 7.13b shows the fetal situation where these same homeostatic organs only communicate with the amniotic sac—a closed cavity. All exchange must take place via the placenta to the mother and thence (using her kidneys, skin and lungs) to the outside. The placenta is called the lung of the fetus but is also its liver and kidneys. Transfer of nutrients, waste products, etc., occur predominantly by diffusion but active transport mechanisms exist for larger molecules.

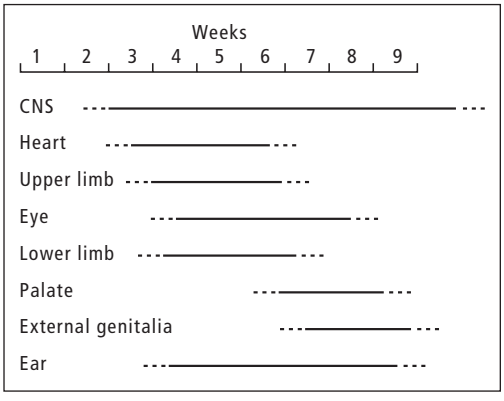


Figure 7.12 Critical periods of various areas of the human embryo. Abnormalities are likely to follow if appropriate teratogens act on tissues at these sensitive times.

Placental hormones

The placenta has a second set of functions, that of an endocrine organ making hormones that regulate the following:

1 Rate of growth of fetus.

2 Activity of uterus to:
- prevent premature expulsion of fetus;
- encourage labour contractions at correct time.

3 Activity of other organs:
- breasts;
- ligaments of pelvis in pregnancy.

The hormones made by the placenta are detailed below.

- *Chorionic gonadotrophin*
  - Made in: cytotrophoblast.
  - Function: prolongs corpus luteum (early); may control progesterone metabolism (late).

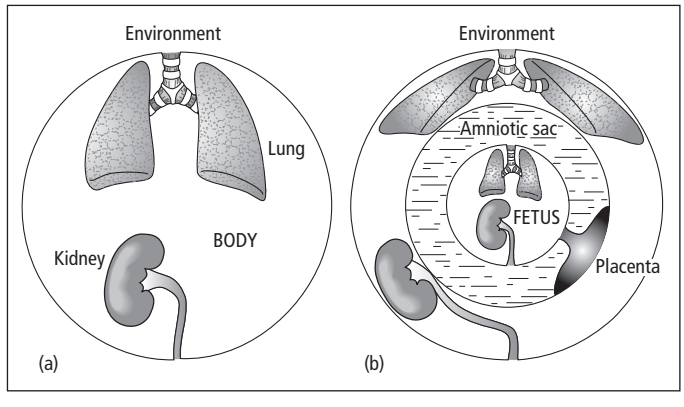


Figure 7.13 (a) Non-pregnant woman. (b) The fetal environment in the pregnant woman.

- *Oestrogens*
  - Made in: all tissues of placenta.
  - Function: stimulate uterine growth and development.
- *Progesterone*
  - Made in: cytotrophoblast.
  - Function: damps down intrinsic uterine action in pregnancy.
- *Human placental lactogen*
  - Made in: syncytiotrophoblast.
  - Function: alters glucose and insulin metabolism; may initiate lactation.

Placental tissues age. Maximum efficiency is at 37–38 weeks; many functions deteriorate after this.

Beware extrapolations between transfer and endocrine functions of the placenta. Correlations may not be valid.

The fetus and placenta at term

The fetus

The anatomical features of the fetus which most concern the obstetrician are those found in the mature fetus after 36 weeks' gestation. The most important area is that which is largest, hardest and most difficult to deliver—the head.

The head

Certain measurements should be remembered (Fig. 7.14). These diameters engage in the maternal pelvic brim at different degrees of flexion of the fetal head on the neck.

The intracranial arrangement of meninges is important (Fig. 7.15) because, under stress, it can be damaged to produce intracranial haemorrhage.

The body

The rest of the fetus will usually pass where the head leads. The bisacromial diameter of the shoulders is about 10 cm.

Placenta

A discoid with 15–20 lobules packed together.

- *Fetal surface*. Covered with amnion (not chorion which fuses with the placental edge). Fetal vessels

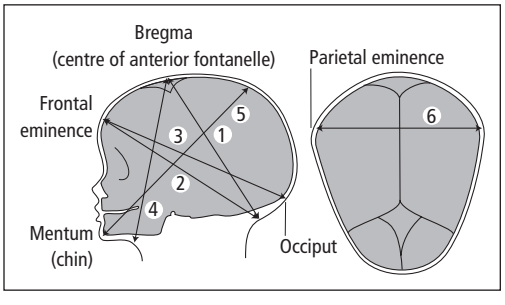


Figure 7.14 The important diameters of the fetal head of a 3-kg baby:
1 Suboccipitobregmatic, 10 cm: vertex presentation
2 Suboccipitofrontal, 11 cm: various flexions of cephalic presentations
3 Occipitofrontal, 12 cm
4 Submentobregmatic, 10 cm: face presentation
5 Mentovertical, 13 cm: brow presentation
6 Biparietal, 10 cm

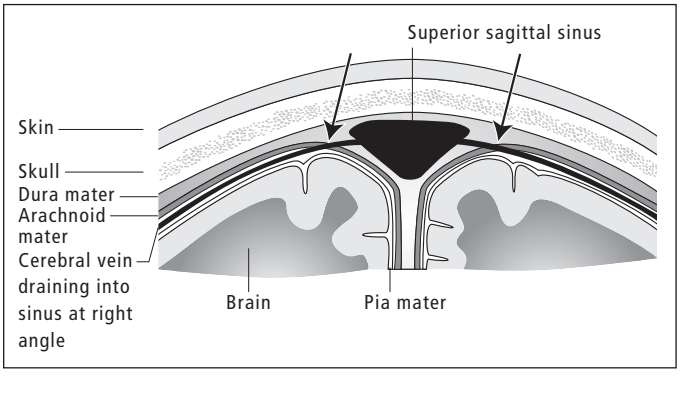


Figure 7.15 Arrangement of the meninges showing how cerebral veins traverse them. If much intracranial movement occurs, the arachnoid moves with the brain but the dura stays with the skull. Hence the vein can be torn at the arrowed sites.

(arteries paler than veins) course over it diving into each lobule as an end vessel.

• *Maternal surface*. Lobules of compressed villi (like seaweed out of water) separated from each other by sulci.

Maternal side of the placental circulation

Maternal blood is in vessels except in the placental bed where it is in contact with foreign tissues (syncytiotrophoblast of villi). Spiral arteries (about 200) lead blood from the uterine arteries to the placental bed pool. Maternal blood spurts under arterial blood pressure, loses way against a mass of villi and passes laterally, pushed by *vis a tergo* to the placental bed veins scattered over the floor of the placental bed.

Measurement of blood flow to the placental bed has been very difficult because it involved direct measurement in animals (unphysiological) or indirect methods with electromagnetic flow meters in humans (imprecise). Now indirect measurements with Doppler ultrasound allow more precise non-invasive flow studies in humans.

Maternal blood flow to the uterus is 100–150 ml/kg/min in late pregnancy, of which 80–85% goes to the placenta.

Abnormal implantation

• *Placenta accreta*. Villi penetrate decidua just into the myometrial layer; difficulty in separation.

• *Placenta increta*. Villi penetrate deeply into myometrium. Even more difficult to separate.

• *Placenta percreta*. Villi penetrate to subperitoneal myometrium. Impossible to separate.

The three diagnoses above cannot usually be differentiated clinically. They are pathological ones made at sectioning a uterus after removal.

• *Placenta praevia*. Implantation in the lower segment of the uterus.

Umbilical cord

At term the umbilical cord is about 50 cm long, 2 cm in diameter. It contains two arteries and a vein which is derived from the left umbilical vein of the embryo. (The right one usually disappears.) For types of cord insertion, see Fig. 7.16.

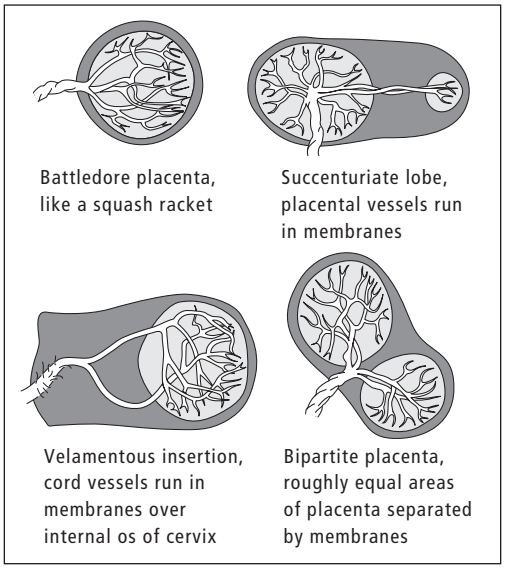


Figure 7.16 Types of umbilical cord insertion.

Box 7.1 Diagnostic uses of checking amniotic fluid

- Chromosome content of amniocytes and fetal skin cells in genetic diseases
- Rhesus effect measuring bilirubin breakdown products
- Metabolic upset of the fetus
- Infection of the amniotic cavity in premature rupture of membranes
- Respiratory maturity by measuring the lecithin–sphingomyelin ratio

Arteries spiral and give a cord-like appearance. Possibly their pattern wrapped around the vein allows their pulsations to help massage blood back along the umbilical vein. The vessels are packed and protected by a viscous fluid—Wharton's jelly.

There are no nerves in the cord or placenta. Hence ligation and cutting the umbilical cord does not hurt the fetus.

Amniotic fluid

This surrounds the fetus.

- Produced:
  - in early pregnancy: from amnion over placenta and sac;
  - in late pregnancy: from fetal urine as well.
- Volume:
  - increase to 38 weeks; 500–1500 ml.
- Osmolality:
  - decreases in late pregnancy.
- Creatinine:
  - increases in late pregnancy.
- Acid–base:
  - normally accumulation of CO_2 and fixed acid causes a slight reduction in pH (about 7.15–7.20).

Amniotic fluid can be removed at amniocentesis and used to diagnose a number of factors (Box 7.1).

Self-assessment

7.1 Fill in the blanks in the following sentences from the list below.
In pregnancy the maternal cardiac output increases principally because of a greater (1) _____. Haemoglobin concentrations decrease because of an increased (2) _____ despite an increased (3) _____. The uterus grows by (4) _____ with a blood flow at term of (5) _____ ml/kg/min.
(a) 100–150
(b) red cell volume
(c) stroke volume
(d) 200–250
(e) hypertrophy
(f) plasma volume
(g) pulse rate
(h) red cell mass
(i) mitosis
(j) mean haemoglobin concentration

7.2 Which of the following statements are true?
(a) Fetal haemoglobin shifts the oxygen dissociation curve to the right of that for haemoglobin A.
(b) At birth, changes in the neonatal circulation enable the entire circulating volume to enter the pulmonary tree.
(c) In fetal life oxygenated blood from the umbilical arteries flows directly to the left side of the heart.
(d) During fetal life the lungs are filled with amniotic fluid.
(e) Exposure to teratogens is more likely to cause congenital abnormalities in the first trimester of pregnancy.

7.3 The functions of the placenta include which of the following?
(a) Transfer of oxygen from the mother to the fetus.
(b) Transfer of urea from the mother to the fetus.
(c) Prevention of premature labour.
(d) Transfer of nutrients from the fetus to the mother.
(e) Regulation of fetal metabolism of insulin and glucose.

7.4 The smallest diameters of the fetal skull include which of the following?
(a) Mentovertical.
(b) Submentobregmatic.
(c) Suboccipitobregmatic.
(d) Biparietal.
(e) Occiptofrontal.