3. **Tertiary villi** are like secondary villi except that there are blood capillaries in the mesoderm.

Details of the process of villus formation are as follows:

- The syncytiotrophoblast grows rapidly and becomes thick. Small cavities (called *lacunae*) appear in this layer (Fig. 6.7C). Gradually, the lacunae increase in size. At first they are irregularly arranged (Fig. 6.7D), but gradually, they come to lie radially (Figs 6.8A, 6.9) around the blastocyst. The lacunae are separated from one another by partitions of syncytium, which are called *trabeculae*. The lacunae gradually communicate with each other, so that eventually one large space is formed. Each trabeculus is now surrounded all around by this lacunar space (Fig. 6.8B).
Fig. 6.10: Uterine blood vessels in the decidua open into the lacunar space and fill it with maternal blood. (B) is a transverse section through trabeculae.

Fig. 6.11: Cells of cytotrophoblast grow into the syncytiotrophoblast of each trabeculus. The trabeculae are now called primary villi.
The syncytiotrophoblast (in which these changes are occurring) grows into the endometrium. As the endometrium is eroded, some of its blood vessels are opened up, and blood from them fills the lacunar space (Fig. 6.10).

Each trabeculus is, initially, made up entirely of syncytiotrophoblast (Fig. 6.10). Now the cells of the cytotrophoblast begin to multiply and grow into each trabeculus (Fig. 6.11A). The trabeculus thus comes to have a central core of cytotrophoblast covered by an outer layer of syncytiotrophoblast. It is surrounded by maternal blood, filling the lacunar space. The trabeculus is now called a primary villus (Fig. 6.11) and the lacunar space is now called the inter villous space.

Extra-embryonic mesoderm invades the centre of each primary villus (Fig. 6.12A). The villus now has a core of mesoderm (Fig. 6.12B) covered by cytotrophoblast and by syncytiotrophoblast. This structure is called a secondary villus.

Soon thereafter, blood vessels can be seen in the mesoderm forming the core of each villus. With their appearance, the villus is fully formed and is called a tertiary villus (Fig. 6.13). The blood vessels of the villus establish connections with the circulatory system of the embryo. Fetal blood now circulates through the villi, while maternal blood circulates through the inter villous space.

From Figs 6.11A, 6.12A and 6.13A, it will be seen that the cytotrophoblast, that grows into the trabeculus (or villus) does not penetrate the entire thickness of syncytiotrophoblast and, therefore, does not come in contact with the decidua.
**Fig. 6.13:** Blood capillaries invade the extra-embryonic mesoderm of each secondary villus thus converting it into a tertiary villus.

**Fig. 6.14:** Formation of cytотrophoblastic shell. Note that after formation of this shell the syncytiotrophoblast is no longer in contact with maternal tissues.
At a later stage, however, the cytotrophoblast emerges through the syncytium of each villus. The cells of the cytotrophoblast now spread out to form a layer that completely cuts off the syncytium from the decidua. This layer of cells is called the **cytotrophoblastic shell** (Fig. 6.14). The cells of this shell multiply rapidly and the placenta increases in size.

The villi that are first formed (as described above) are attached on the fetal side (Fig. 6.15) to the embryonic mesoderm and on the maternal side to the cytotrophoblastic shell. They are, therefore, called **anchoring villi**. Each anchoring villus consists of a stem (**truncus chori**); this divides into a number of branches (**rami chori**) which in turn divide into finer branches (**ramuli chori**). The ramuli are attached to the cytotrophoblastic shell. The anchoring villi give off numerous branches that grow into the inter villous space as free villi (Fig. 6.16). New villi also sprout from the chorionic side of the inter villous space. Ultimately, almost the whole inter villous space becomes filled with villi. As a result, the surface area available for exchanges between maternal and fetal circulations becomes enormous.

These, newly formed, villi at first consist only of syncytiotrophoblast. They are subsequently invaded by cytotrophoblast, mesoderm, and blood vessels, and pass through the stages of primary, secondary and tertiary villi, as described above.
FURTHER DEVELOPMENT OF THE PLACENTA

The placenta now becomes subdivided into a number of lobes, by septa that grow into the intervillous space from the maternal side (Fig. 6.17). Each such lobe of the placenta is often called a **maternal cotyledon**. If the placenta is viewed from the maternal side, the bases of the septa are seen as grooves (Fig. 6.18) while the cotyledons appear as convex areas bounded by the grooves. The number of lobes generally varies between 15 and 20. Each lobe contains a number of anchoring villi and their branches. One such villus and its branches constitute a **fetal cotyledon**. The fully formed placenta has 60-100 such fetal cotyledons. The placenta now forms a compact mass and is disc-shaped (Figs 6.17, 6.18).

At full term (9 months after onset of pregnancy), the placenta has a diameter of 6 to 8 inches and weighs about 500 g. After the birth of the child, the placenta is shed off along with the decidua. The maternal surface (formed by the decidual plate) is rough and is subdivided into cotyledons. The fetal surface (chorionic plate) is lined by amnion. It is smooth and is not divided into cotyledons. The umbilical cord is attached to this surface.
PLACENTAL MEMBRANE

In the placenta, maternal blood circulates through the intervillous space and fetal blood circulates through blood vessels in the villi. The maternal and fetal blood do not mix with each other. They are separated by a membrane, made up of the layers of the wall of the villus (Fig. 6.19A). These (from the fetal side) are as follows:

1. the endothelium of fetal blood vessels, and its basement membrane.
2. surrounding mesoderm (connective tissue).
3. cytotrophoblast, and its basement membrane.
4. syncytiotrophoblast.

These structures constitute the placental membrane or barrier. All interchanges of oxygen, nutrition and waste products take place through this membrane.

The total area of this membrane varies from 4 to 14 square metres. It is interesting to note that this is equal to the total absorptive area of the adult intestinal tract. As in the gut, the effective absorptive area is greatly increased by the presence of numerous microvilli on the surface of the syncytiotrophoblast.

In the later part of pregnancy, the efficiency of the membrane is increased, by disappearance of the cytotrophoblastic layer from most villi, and by considerable thinning of the connective tissue (Fig 6.19B). This membrane, which is at first 0.025 mm thick, is reduced to 0.002 mm. However, towards the end of pregnancy, a fibrinoid deposit appears on the membrane, and this reduces its efficiency.

Functions of Placenta

- The placenta enables the transport of oxygen, water, electrolytes and nutrition (in the form of carbohydrates, lipids, polypeptides, amino acids and vitamins) from maternal to fetal blood. A full term fetus takes up about 25 ml of oxygen per minute from maternal blood. Even a short interruption of oxygen supply is fatal for the fetus.
- It also provides for excretion of carbon dioxide, urea and other waste products produced by the fetus into the maternal blood.
Maternal antibodies (IgG, gammaglobulins or Immunoglobulins) reaching the fetus through the placenta give the fetus immunity against some infections (e.g. diphtheria and measles).

The placenta acts as a barrier and prevents many bacteria and other harmful substances from reaching the fetus. However, most viruses (including polio, measles and rubella) and some bacteria can pass across it. Drugs taken by the mother may also enter the fetal circulation and can produce congenital malformations.

As a rule, maternal hormones do not reach the fetus. However, synthetic progestins and synthetic oestrogens (e.g. diethylstilbestrol) easily cross the placenta and can have adverse effects on the fetus (including carcinoma in later life).

While permitting the exchange of several substances between the maternal and fetal blood, it keeps these blood streams separate, thereby preventing antigenic reactions between them.

The placenta synthesizes several hormones. These are probably produced in the syncytiotrophoblast.

- **Progesterone** secreted by the placenta is essential for maintenance of pregnancy after the fourth month (when the corpus luteum degenerates).
- **Oestrogens** (mainly estriol) produced by the placenta reach maternal blood and promote uterine growth and development of the mammary gland.

**Clinical Correlation**

**Human chorionic gonadotropin (hCG)** produced by the placenta is similar in its actions to the luteinizing hormone of the hypophysis cerebri. Gonadotropins are excreted through maternal urine where their presence is used as a test to detect a pregnancy in its early stages.

**Somatomammotropin (hCS)** has an anti-insulin effect on the mother. This leads to increased plasma levels of glucose and amino acids in the maternal circulation. In this way it increases availability of these materials for the fetus. It also enhances glucose utilization by the fetus.

**Circulation of Blood through the Placenta**

Blood flow through lacunar spaces in the syncytiotrophoblast begins as early as the 9th day of pregnancy. Thereafter, the maternal blood in the intervillous spaces is constantly in circulation.
Clinical Correlation contd...

Blood enters the intervillous space through maternal arteries that open into the space. The pressure of blood drives it right up to the chorionic plate. Blood from the intervillous spaces is drained by veins that also open into the same spaces.

In the fully formed placenta, the intervillous spaces contain about 150 ml of blood that is replaced in 15 to 20 seconds (i.e. three to four times per minute).

NORMAL SITE OF IMPLANTATION OF THE OVUM

The uterus can be divided into an upper part, consisting of the fundus and the greater part of the body, and a lower part, consisting of the lower part of the body and the cervix. These are called the upper uterine segment, and the lower uterine segment, respectively. It is the upper uterine segment that enlarges during pregnancy.

The placenta is normally attached only to the upper uterine segment (Fig. 6.21).

Abnormal Site of Implantation of the Ovum

Abnormal Implantation within the Uterus

The attachment of the placenta may extend partially, or completely, into the lower uterine segment. This condition is called placenta praevia. It causes difficulty during childbirth and may cause severe bleeding. Various degrees of placenta praevia may be recognized, as given below:

- **First degree:** The attachment of the placenta extends into the lower uterine segment, but does not reach the internal os (Fig. 6.22A).
- **Second degree:** The margin of the placenta reaches the internal os, but does not cover it (Fig. 6.22B).
- **Third degree:** The edge of the placenta covers the internal os, but when the os dilates during childbirth, the placenta no longer occludes it (Fig. 6.22C).
- **Fourth degree:** The placenta completely covers the internal os, and occludes the os even after it has dilated (Fig. 6.22D).

Implantation Outside the Uterus

When the ovum gets implanted at any site outside the uterus, this is called an *ectopic pregnancy*. This may be as follows:

- **Tubal pregnancy:** The blastocyst gets implanted in the uterine tube. Such a pregnancy cannot go on to full term, and may result in rupture of the tube. After rupture, the blastocyst may acquire a secondary implantation in the abdominal cavity (Fig. 6.23), giving rise to an abdominal pregnancy.
- **Interstitial tubal implantation:** The blastocyst may get implanted in the part of the uterine tube passing through the uterine wall.
- **Implantation in the ovary:** Fertilization and implantation may occur while the ovum is still in the ovary.
**Other Anomalies of Placenta**

Instead of being shaped like a disc, the placenta may be:
- **bifid**, when it consists of two discs (Fig. 6.24A);
- **lobed**, when it is divided into lobes (Fig. 6.24B);
- **diffuse**, when chorionic villi persist all round the blastocyst: the placenta is thin and does not assume the shape of a disc (Fig. 6.24C);
- **placenta succenturiata**, when a small part of the placenta is separated from the rest of it (Fig. 6.24D);

**Fig. 6.22**: Types of placenta praevia.

**Fig. 6.23**: Abnormal sites of implantation: (1) Normal site, (2) Placenta praevia, (3) Interstitial tubal implantation, (4) Tubal implantation, (5) Abdominal implantation, (6) Ovarian implantation.
fenestrated, when there is a hole in the disc (Fig. 6.24E); and

circumvallate, when the peripheral edge of the placenta is covered by a circular fold of
decidua (Fig. 6.24F).

The umbilical cord is normally attached to the placenta near the centre (Fig. 6.25A). However, this attachment may be:

- marginal, when the cord is attached at the margin of the placenta (Fig. 6.25B) (this type of placenta is called Battledore placenta); or
- furcate, when blood vessels divide before reaching the placenta (Fig. 6.25C).

When blood vessels are attached to amnion, where they ramify before reaching the placenta (Fig. 6.25D), the condition is referred to as velamentous insertion.

Fig. 6.25: Variations in attachment of umbilical cord to placenta: (A) Normal, (B) Marginal, (C) Furcate, (D) Velamentous insertion.
Chapter 6 – The Placenta, Fetal Membranes, Twinning

Fig. 6.26: Relationship of amniotic cavity, extra-embryonic coelom and uterine cavity. For description see text.

FETAL MEMBRANES

MUTUAL RELATIONSHIP OF AMNIOTIC CAVITY, EXTRA-EMBRYONIC COELOM AND UTERINE CAVITY

We have so far considered the fetal membranes (amnion and chorion), and the placenta, mainly in relation to the fetus. Let us now see their relationships to the uterine cavity. These are important, as they help us to understand some aspects of the process of childbirth. The changing relationships will be best understood by first reviewing Figs 4.6, 4.7 and 4.13 and then by studying Figs 6.26 to 6.28.

In Fig. 6.26 we see three cavities, namely, the uterine cavity, the extra-embryonic coelom, and the amniotic cavity. The outer wall of the extra-embryonic coelom is formed by chorion and the inner wall by amnion.
As the amniotic cavity enlarges, the extra-embryonic coelom becomes smaller and smaller. It is eventually obliterated, by fusion of amnion and chorion. The fused chorion and amnion form the amniochorionic membrane. From Fig. 6.27 it will be seen that the wall of the amniotic cavity is now formed by (i) amnion, (ii) chorion, and (iii) decidua capsularis, all three being fused to one another.

Further expansion of the amniotic cavity occurs at the expense of the uterine cavity. Gradually, the decidua capsularis fuses with the decidua parietalis, and the uterine cavity is also obliterated (Fig. 6.28). Still, further expansion of the amniotic cavity is achieved by enlargement of the uterus. Enlargement of the amniotic cavity is accompanied by an increase in the amount of amniotic fluid.

At the time of parturition (childbirth), the fused amnion and chorion (amniochorionic membrane) (along with the greatly thinned out decidua capsularis), constitute what are called the membranes. As the uterine muscle contracts, increased pressure in the amniotic fluid
INTRODUCTION

The epithelial lining of the various parts of the gastrointestinal tract is of endodermal origin. In the region of the mouth and the anal canal, however, some of the epithelium is derived from the ectoderm of the stomatodaeum and of the proctodaeum respectively.

We have seen that as a result of the establishment of the head and tail folds, part of the cavity of the yolk sac is enclosed within the embryo to form the primitive gut (Fig. 5.15). The primitive gut is in free communication with the rest of the yolk sac. The part of the gut cranial to this communication is the foregut, the part caudal to the communication is the hindgut, while the intervening part is the midgut (Fig. 13.1). Cranially, the foregut is separated from the stomatodaeum by the buccopharyngeal membrane. Caudally, the hindgut is separated from the proctodaeum by the cloacal membrane. At a later stage of development, these membranes disappear, and the gut opens to the exterior at its two ends.

While the gut is being formed, the circulatory system of the embryo undergoes considerable development. A midline artery, the dorsal aorta, is established and comes to lie just dorsal to the gut (Fig. 13.2). It gives off a series of branches to the gut. Those in the region of the midgut, initially, run right up to the yolk sac and are, therefore, called vitelline arteries. Subsequently, most of these ventral branches of the dorsal aorta disappear and only three of them remain; one for the foregut, one for the midgut and one for the hindgut. The artery of the abdominal part of the foregut is the coeliac, that of the midgut is the superior mesenteric and that of the hindgut is the inferior mesenteric.

The wide communication between the yolk sac and the midgut is gradually narrowed down (Fig. 13.2B) with the result that the midgut becomes tubular. Thereafter, the midgut assumes the form of a loop (Fig. 13.2C). The superior mesenteric artery now runs in the mesentery of this loop to its apex. The loop can, therefore, be said to have a proximal, or pre-arterial, segment and a distal, or postarterial, segment. A bud (called caecal bud) soon arises from the post-arterial segment very near the apex of the loop (Fig. 13.2D).

For a number of weeks, the midgut loop comes to lie outside the abdominal cavity of the embryo. It passes through the umbilical opening into a part of the extra-embryonic coelom that persists in relation to the most proximal part of the umbilical cord. The loop is subsequently withdrawn into the abdominal cavity.
Fig. 13.2: Establishment of the midgut loop. (A) Midgut in wide communication with the yolk sac. Note the vitelline artery passing from dorsal aorta to the yolk sac. (B) Yolk sac much smaller, and attached to midgut through a narrow vitello-intestinal duct. The original vitelline artery gives branches to the midgut. (C) The midgut increases in length and forms a loop. The loop has a prearterial segment and a postarterial segment. (D) Midgut loop passes out of abdominal cavity. The caecal bud arises from the postarterial segment.

While considering the formation of the allantoic diverticulum, it was seen that the diverticulum opens into the ventral aspect of the hindgut (Figs. 5.14, 13.1). The part of the hindgut caudal to the attachment of the allantoic diverticulum is called the cloaca. The cloaca soon shows a subdivision into a broad ventral part and a narrow dorsal part (Fig. 13.3). These two parts are separated from each other by the formation of the urorectal septum, which

Fig. 13.3: Formation of urorectal septum as seen in transverse sections. This septum divides the cloaca into the primitive urogenital sinus and the primitive rectum.
is first formed in the angle between the allantois and the cloaca (Figs. 13.4A, B). The ventral subdivision of the cloaca is now called the **primitive urogenital sinus**, and gives origin to some parts of the urogenital system. The dorsal part is called the **primitive rectum**. It forms the rectum, and part of the anal canal. The urorectal septum grows towards the cloacal membrane and eventually fuses with it (Fig. 13.4C). The cloacal membrane is now divided into a ventral **urogenital membrane**, related to the urogenital sinus, and a dorsal **anal membrane** related to the rectum. Mesoderm around the anal membrane becomes heaped up with the result that the anal membrane comes to lie at the bottom of a pit called the anal pit, or proctodeum. The anal pit contributes to the formation of the anal canal.

**Derivatives of Foregut**

- Part of the floor of the mouth, including the tongue.
- Pharynx.
- Various derivatives of the pharyngeal pouches, and the thyroid.
- Oesophagus.
- Stomach.
- Duodenum: Whole of the superior (first) part and upper half of the descending (second) part (up to the major duodenal papilla).
- Liver and extra-hepatic biliary system.
- Pancreas.
- Respiratory system.
**Derivatives of Midgut**

- Duodenum: Descending (second) part distal to the major papilla; horizontal (third) and ascending (fourth) parts.
- Jejunum.
- Ileum.
- Caecum and appendix.
- Ascending colon.
- Right two-thirds of transverse colon.

**Derivatives of Hindgut**

- Left one-third of transverse colon.
- Descending and pelvic colon.
- Rectum.
- Upper part of anal canal.
- Parts of the urogenital system derived from the primitive urogenital sinus.
Chapter 13 – Alimentary System—II. Gastrointestinal Tract

At this stage, it may be noted that endoderm of the foregut, midgut and hindgut gives rise only to the epithelial lining of the intestinal tract. The smooth muscle, connective tissue and peritoneum are derived from splanchnopleural mesoderm (Fig. 13.6).

**Arteries of the Gut**

The *coeliac artery* is the artery of the foregut. It supplies the gut from the lower part of the oesophagus to the middle of the duodenum.

The *superior mesenteric artery* is the artery of the midgut.

The *inferior mesenteric artery* is the artery of the hindgut.

At this stage, it might be noted that the endoderm of the foregut, midgut and hindgut gives rise only to the epithelial lining of the intestinal tract. Smooth muscle, connective tissue and peritoneum are derived from splanchnic mesoderm (Fig. 13.6).

**DERIVATION OF INDIVIDUAL PARTS OF ALIMENTARY TRACT**

**Oesophagus**

The oesophagus is developed from the part of the foregut between the pharynx and the stomach. It is at first short but elongates with the formation of the neck, with the descent of the diaphragm, and with the enlargement of the pleural cavities.

The musculature of the oesophagus is derived from mesenchyme surrounding the foregut. Around the upper two-thirds of the oesophagus, the mesenchyme forms striated muscle. Around the lower one-third, the muscle formed is smooth (as over the rest of the gut).

**Stomach**

The stomach is first seen as a fusiform dilatation of the foregut just distal to the oesophagus. Its dorsal border is attached to the posterior abdominal wall by a fold of peritoneum called the *dorsal mesogastrium*. Its ventral border is attached to the septum transversum by another fold of peritoneum called the *ventral mesogastrium* (Figs. 13.7A, B).
Fig. 13.7: (A) Side view of stomach showing the dorsal and ventral mesogasticums. (B) Transverse section through 'A' showing that the ventral mesogastrium connects the stomach to the septum transversum. (C) The most important remnant of the ventral mesogastrium is the lesser omentum. It passes from the stomach to the liver (which develops in the septum transversum). The spleen is formed in relation to the dorsal mesogastrium. Its formation divides this part of the dorsal mesogastrium into the gastroplenic ligament and the lienorenal ligament.

Subsequently, the liver and the diaphragm are formed in the substance of the septum transversum. The ventral mesogastrium now passes from the stomach to the liver, and from the liver to the diaphragm and anterior abdominal wall (Fig. 13.7C). The part of the ventral mesogastrium between the liver and the stomach becomes the lesser omentum, while the part between the liver and the diaphragm (and anterior abdominal wall) gives rise to the coronary, and falciform ligaments.

Similarly, the dorsal mesogastrium is divided by the development of the spleen into a part between stomach and spleen (gastroplenic ligament) and a part between spleen and posterior abdominal wall called the lienorenal ligament (Fig. 13.7C).

The stomach undergoes differential growth resulting in considerable alteration in its shape and orientation. The original ventral border comes to face upward and to the left and becomes the lesser curvature. The dorsal border now points downwards and to the right and becomes the greater curvature. The original left surface becomes its anterior surface and the original right surface becomes the posterior surface.