Inderbir Singh’s

HUMAN

EMBRYOLOGY

Edited by
V Subhadra Devi
Inderbir Singh’s

HUMAN EMBRYOLOGY

ELEVENTH EDITION

Edited by

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It gives me immense pleasure to read the edited chapter titled "Cardiovascular system" of Dr. I.B. Singh's Embryology book, a book which I have read as a student and since last 10 years as a teacher. The following additions I noticed in the new edition:

1. Nutrition of the embryo at various stages of development
2. Components of blood vascular system
3. Vasculogenesis and angiogenesis
4. Molecular regulation of angiogenesis and vasculogenesis
5. Cardiac progenitor cells and primary and secondary heart fields (Fig. 15.4 and 15.5)
6. Details of fate of sinus venosus are now mentioned in the beginning of development of atria which is helpful in clear understanding of the development of right atrium
7. Sinus venosus table with embryonic parts and adult derivatives
8. Development of the three parts of interventricular septum is now mentioned together
9. Some new diagrams in the development of heart and its exterior
10. Diagrams for the axis arteries of upper and lower limbs
11. Table of differences between 3 systems of veins
12. Fetal circulation peculiarities
13. Table 15.4 post natal occlusion of vessels, their remnants and reasons
14. Diagram for lymphatic system
15. Timetable for some events
16. Case Scenarios with diagrams

These significant changes will definitely contribute to a better understanding for the students. Congratulations to the editors to make it more interesting with all the above additions.

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This revised 11th edition of Inderbir Singh's Embryology is made very simple and student friendly by presenting the subject in an orderly manner and chronological order. Developmental events are highlighted by marking in bullet format. This helps the students to revise the subject easily. Highlights of this book are incorporation of flow charts and Embryological Basis for Clinical Conditions or Anatomical Observations. These features make this book an excellent choice not only to undergraduate students but also for those preparing for post graduate entrance examinations.

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How this Book is Useful?

Features

- Chronological organization of developmental events.
- Emphasis on Clinical importance of embryology.
- Gaps in the development of some of the structures eg. Individual bones, muscles are incorporated.
- Modification of existing figures, addition of new figures facilitates continuity of correlating with text.
- Tables and flow charts for easy understanding.
- Clinical images of various fetal anomalies including some rare variations.
- Incorporation of case scenarios with embryological explanation.
- Review questions for each chapter.
Preface to the Eleventh Edition

During the publication of my earlier book - “Basic Histology – A Color Atlas and Text” the publishers proposed to me to revise the embryology book written by late Prof Inderbir Singh. Notwithstanding 35 years of experience in teaching embryology and several publications in human developmental anatomy, I was skeptical because it is simply difficult for anyone to match the simplicity of expression and sheer elegance of images so diligently originated by Prof. Singh. With the encouragement provided by the publishers and colleagues, I have taken the proverbial plunge.

When I started my career as a medical teacher way back in 1981, I used to reproduce the diagrams from Prof. Inderbir Singh’s embryology on black board. With the evolution of technology, I have initially transcribed the figures on to OHP sheets and recently upgraded several of them into 3D images, some of which are included in the present edition of the book.

Like all its previous editions, this is also a one person effort which clearly offers scope for improvement. Suggestions from academics, students and professionals are welcome for incorporation in the coming editions.

I thank all my students who are my inspiration for revising this book. I am thankful to all staff and students in the Department of Anatomy, SV Medical College and Sri Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh, India, for their continuous support and constructive feedback at different stages while this book is evolving. I make a special mention of Mr. K Thyagaraju, Assistant Professor, for drawing and Photoshop editing several of the figures. Some of the figures in the present edition originated from the research carried out by the postgraduate students in my lab.

I am also thankful to Shri Jitendar P Vij (Group Chairman), Mr Ankit Vij (Group President) of M/s Jaypee Brothers Medical Publishers (P) Ltd, New Delhi, India, for kindly agreeing to publish this book, and the production team especially Ms. Ritu Sharma, Dr Madhu Chaudhary, Dr Pinky Chauhan and Ms. Samina Khan for their dedicated work.

V Subhadra Devi
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The process of attachment of developing embryo to the uterine endometrium is called **implantation**.
The type of implantation in the human beings is called **interstitial implantation** as the embryo gets buried in the substance of endometrium.
**Decidua** is the name given to the endometrium after implantation.
The placenta is formed partly from embryonic structures and partly from decidua. Placenta is responsible for transport of nutrients and oxygen to the fetus, and for removal of waste products.
The essential elements of the placenta are **chorionic villi**. The villi are surrounded by maternal blood. Fetal blood circulates through capillaries in villi. The maternal blood and the fetal blood are separated by a very thin placental membrane (or barrier). All substances passing from mother to fetus (and vice versa) traverse this membrane.
The placenta is attached to the upper part of the body of the uterus. A placenta attached lower down is called **placenta previa**. It can cause problems during childbirth.

## FORMATION OF PLACENTA

### Introduction
- The placenta is a fetomaternal organ. It connects growing embryo/fetus with the wall of pregnant uterus. It is an organ where there is intimate apposition or fusion of fetal organ to maternal tissue for the purpose of physiological exchange.
- **It is a circular or disc-shaped organ of 500 g weight. It has two surfaces and two structural components.**

#### Surfaces (Figs 6.1A and B):
- Maternal surface: It is irregular and is divided into 15–20 small lobules called maternal cotyledons.
- Fetal surface: It is smooth and covered with amnion, and umbilical cord is attached at or near the center of this surface.
• **Structural components:** It has structural components of fetal and maternal origin.
  - Maternal component is contributed by *decidua basalis* or *decidual plate*.
  - Fetal component is contributed by *chorion frondosum* or *chorionic plate*.

For proper understanding of the structure and function of placenta, knowledge on *implantation*, *decidua*, *trophoblast* and *chorion* are required.

**Implantation**

*Definition:* It is the process of attachment of blastocyst to uterine endometrium and subsequent invasion (embedding) of blastocyst (conceptus) into the uterine endometrium in placental animals.

**Implantation period:** It takes place between 6th and 12th days after fertilization.

**Process of implantation:** For understanding the sequence of events, the whole process of implantation can be considered as those occurring preliminary to implantation and those taking place (stages) in implantation. These are simplified in the Flowchart 6.1.

A. Processes preliminary to implantation (Fig. 6.2):

1. *Release and transport of ovum into the uterine tube:*
   The ovum with its surrounding zona pellucida and corona radiata cells is shed from the ovary at
ovulation. Later it travels through the fimbrial end of fallopian tube into the ampulla of uterine tube.

2. **Fertilization of ovum:** The ovum and sperm fuse in the ampulla of uterine tube. The process of fusion of male and female pronuclei is called fertilization. If fertilization occurs, segmentation of the ovum begins.

3. **Cleavage divisions of fertilized ovum and its migration into the fundus of uterus:** The fertilized ovum undergoes series of mitotic divisions and becomes *morula* (16-cell stage) at about 3rd day after fertilization. While cleaving it moves along the uterine tube and reaches the uterus. The morula is still surrounded by the zona pellucida, which prevents it from sticking to the wall of uterine tube/uterus during its journey.

4. **Blastocyst formation:** At about 4th/5th day after fertilization, the cleaving blastomeres reorganize into the central *inner cell mass/embryoblast* (8 cells) and peripheral *outer cell mass/trophoblast* (99 cells) with a central cavity, the blastocyst cavity. The cells of inner cell mass contribute for the formation of embryo proper. The cells of trophoblast have the property of attaching to any tissue with which it comes into contact.

5. **Differentiation of trophoblast cells:** The trophoblast differentiates into *polar trophoblast* (30 cells) and *mural trophoblast* (69 cells). The part of blastocystic trophoblast making contact with endometrium is the polar trophoblast and the remaining is called mural trophoblast (Fig. 4.9C).

B. **Processes (stages) at the time of implantation (Figs 6.2 and 6.3):**

- **Decidual reaction/changes in uterine endometrium:**
  - When the morula reaches the uterus, the endometrium is in the secretory phase of menstrual cycle.
  - The change in the endometrial stroma with implantation of blastocyst is called the *decidual reaction*.

- **Hatching of blastocyst:** The zona pellucida of the cleaving blastocyst that is rolling on the uterine wall gradually becomes thin on 5th day. This thinning is due to the production of trypsin like enzyme that causes dissolution of zona pellucida. By 6th day, the zona pellucida disappears (Fig. 4.8D).

- **Adhesion of polar trophoblast to columnar uterine epithelium:** The trophoblast has the tendency to stick to the structure with which it comes in contact. Once the zona pellucida disappears, the cells of the trophoblast stick to the uterine endometrium. This is called the beginning of the process of implantation.

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**Fig. 6.2:** Various processes before and during implantation: ovulation, fertilization, cleavage, blastocyst, trophoblast differentiation, decidual change, hatching of blastocyst, and penetration defect
and it takes place on 6th day after fertilization. The disappearance of zona pellucida initiates attachment of polar trophoblastic cells to the columnar uterine epithelium between the mouths of uterine glands.

- **Penetration of blastocyst through uterine epithelium:** The trophoblastic cells have got the penetrating/burrowing nature. The polar trophoblast cells situated over the embryoblast/inner cell mass start penetrating the uterine epithelium to provide passage for the blastocyst. Disarrangement and destruction of epithelial cells occurs due to the penetration of blastocyst.

- **Erosion of the uterine endometrium:** Erosion of stratum compactum and stratum spongiosum by cells of polar trophoblast occurs. This is due to the proteolytic enzymes secreted by both polar trophoblast and uterine epithelium. The blastocyst burrows deeper and deeper into the uterine mucosa till the whole of it comes to lie within the thickness of the endometrium.

- **Differentiation of trophoblast:** By about 8th day of development, the blastocyst has partially embedded into the uterine endometrial stroma. The polar trophoblast over the embryonic pole differentiates into two layers.
  - Cellular/Cytotrophoblast—Langhans layer: The inner layer of cells is cuboidal to low columnar, mononucleated and contains mitotic figures indicating their capacity to divide.
  - Syncytiotrophoblast—plasmodial layer: The outer layer of multinucleated cells without mitotic figures. These are formed by the dividing cells of cytotrophoblast that have migrated to the periphery and fused.

- **Closure of penetration defect in uterine epithelium:** Once passage of blastocyst through epithelial surface is completed, closure of penetration defect in surface epithelium takes place around 9th day after fertilization by a coagulum of tissue fluid and debris that forms a fibrin plug.
Completion of embedding of blastocyst and establishment of nutritive relationship with maternal blood vessels: By 12th day of fertilization, the blastocyst has completely embedded in the endometrium. Spaces appear in the syncytiotrophoblast that will fuse to form larger lacunae. The syncytiotrophoblast cells erode the maternal capillaries, which become congested and dilated to form sinusoids. This contact between syncytiotrophoblast and maternal sinusoids initiates nutritive relationship between fetus and mother. The lacunae in the syncytial trophoblast become continuous with maternal sinusoids.

Types of Implantation (Figs 6.4A to C):
1. Central implantation: Blastocyst is implanted in the uterine cavity, e.g. carnivores—cow.
2. Eccentric implantation: Blastocyst is implanted in the uterine crypt, e.g. mouse.
3. Interstitial implantation: Blastocyst is implanted in the endometrium of uterine wall. This is the type of implantation in guinea pig and human.

Normal and Abnormal Sites of Implantation
A. Normal site of implantation: The normal site of implantation is the upper part of body of uterus in mid-sagittal plane, in the posterior wall (55%) or in the anterior wall (45%) [Fig. 6.5 (1)].
B. Abnormal sites of implantation [Fig. 6.5 (2-6)]
- Uterine:
  - Lower uterine segment: If the implantation is in the lower uterine segment, it is called placenta previa [Fig. 6.5 (2)].
- Extraterine:
  - Tubal implantation: The most common extraterine implantation site is in the uterine tube. The various parts in the order of frequency are:
    - Interstitial [Fig. 6.5 (3)]
    - Ampulla [Fig. 6.5 (4)]
    - Isthmus of uterine tube
  - Abdominal implantation [Fig. 6.5 (5)]: It is also rare. Implantation can be:
    - Primary: If implantation takes place in relation to the mesentery, it is called primary abdominal implantation and is very rare.
    - Secondary: It is due to reimplantation of tubal or ovarian pregnancy. It usually results from ruptured tubal pregnancy.
  - Ovarian implantation: Fertilization and implantation take place in the ovary. It is rare [Fig. 6.5 (6)]. It can cause teratoma.

Implantation—Additional points
- The process of implantation is aided by proteolytic enzymes produced by the trophoblast. The uterine mucosa also aids the process.
- Implantation results due to the mutual interaction between trophoblast cells and endometrium. This interaction is mediated by receptors present on the uterine epithelium and by the secretion of L-selectin and integrins by trophoblastic cells.
- Carbohydrate-binding proteins on trophoblast cells and carbohydrate-binding sites on uterine epithelium facilitate attachment of blastocyst to the uterine wall.
- Interaction between integrin proteins of trophoblast cells and laminin and fibronectin molecules of intercellular stroma of endometrium facilitate invasion of blastocyst and its implantation.
- Principal mechanisms in implantation are:
  - Muscular
  - Adhesive—interaction between polar trophoblast and uterine epithelium—pentasaccharide, lacto-N-fucopentose-1
  - Invasive
  - Immunological.

Decidua
Definition: It is the functional stratum (stratum compactum) of uterine endometrium after the implantation of blastocyst (Fig. 6.2). The word decidua means falling off as this part of endometrium separates and falls off during childbirth.

Change in endometrium: After implantation, the features of the endometrium, which are seen during the secretory phase of the menstrual cycle, are maintained and intensified under the influence of the hormone the human chorionic gonadotropin (hCG) which is secreted by the cells of syncytiotrophoblast. On 17th or 18th day of menstrual cycle, i.e. 5th day after fertilization and at the time of implantation,
the uterine endometrium is highly modified, edematous and vascular.

Decidual reaction: Due to the higher levels of maternal progesterone and the hCG, the stromal cells enlarge, become vacuolated and filled with glycogen and lipids (decidual transformation). These cells are called decidual cells. The intercellular substance increases, and it gives edematous appearance. This change in the endometrial stroma is called the decidual reaction. The glycogen and lipids provide nutrition to the early embryo until the placenta takes over this function. The saw-toothed appearance of endometrial glands increases and the blood vessels of endometrium become more tortuous. The decidual reaction is a defensive mechanism to protect the endometrium.

Subdivisions of Decidua (Fig. 6.6 and Flowchart 6.2)

1. Decidua basalis/Serotina: The part that contributes for the maternal component of placenta. It is the part that lies deep to the developing blastocyst. The maternal blood vessels (spiral arteries) proliferate in the region of decidua basalis and are filled with blood and dilate to form sinusoids. The decidua basalis consists predominantly of large decidual cells that contain large amounts of lipids and glycogen (that presumably provide a source of nutrition for the embryo). The decidua basalis is also referred to as the decidual plate, and is firmly united to the chorion.

2. Decidua capsularis/Reflexa: The part of endometrium that surrounds the embryo like a capsule and separates it from the uterine cavity.

3. Decidua parietalis/Vera: The part of decidua that lines the rest of uterine cavity.

Fate of decidua: As the conceptus enlarges during development, the decidua capsularis enlarges into the uterine cavity and finally fuses with decidua parietalis during 3rd month of pregnancy thus obliterating the uterine cavity. At the end of pregnancy, the decidua is shed off, along with the placenta and membranes. It is this shedding off which gives the decidua its name (c.f. deciduous trees).

Clinical correlation

Placenta previa

- The normal attachment of placenta is in the upper uterine segment (Fig. 6.7). The attachment of placenta may extend partially or completely into the lower uterine segment. This condition is called placenta previa. This is due to the implantation of the blastocyst close to the internal os.

- Degrees of placenta previa (Figs 6.8A to D):
  - First degree: Attachment of placenta does not extend to internal os.
  - Second degree: Attachment of placenta extends up to internal os but does not cover it.
  - Third degree: Placental edge covers the internal os. With the dilatation of internal os at the time of childbirth, the placenta will not occlude the internal os.
  - Fourth degree: Placenta completely covers the internal os even when the internal os is completely dilated. This can cause severe bleeding during pregnancy or during parturition.

Ectopic pregnancy

- This results from abnormal sites of implantation, i.e. extraterine pregnancies.
- Ectopic pregnancies do not progress and usually result in death of the embryo. Rarely does this embryo develop to full term.
- The most common ectopic pregnancy is tubal pregnancy with a 95% incidence. Tubal pregnancies are terminated by medical intervention. If it is permitted to progress, it can result in rupture of uterine tube with severe internal bleeding.
- Other types of ectopic pregnancies are abdominal, ovarian.

Trophoblast

It is the first embryonic membrane. The trophoblast cells are the precursor cells of human placenta. At first the cells form
Placenta, Fetal Membranes and Twinning

**Flowchart 6.2: Components of decidua and chorion**

![Flowchart 6.2](image)

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a unilaminar fetal membrane. Later with the formation of blastocyst it becomes bilaminar.

**Differentiation of two layers of trophoblast:** This is essential for the formation of chorionic villi. The trophoblast is at first made up of a single layer of cells (Figs 6.9 and 6.10A). As these cells multiply, two distinct layers are formed (Fig. 6.10B):

- The cells that are nearest to the decidua (i.e. the most superficial cells) lose their cell boundaries. These cells form a layer of multiple cells without cell outlines and form one continuous sheet of cytoplasm containing many nuclei. Such a tissue is called a syncytium. Hence, this layer of the trophoblast is called the syncytiotrophoblast or plasmodiotrophoblast (Fig. 6.10B).

- Deep to the syncytium, the cells of the trophoblast retain their cell walls and form the second layer called the cytotrophoblast or Langhans’ layer that rests on extraembryonic mesoderm. This single layer of cuboidal cells with a clear outline is close to the extraembryonic mesoderm.

- All these elements (syncytium, cytotrophoblast and mesoderm) take part in forming chorionic villi.

**Chorion and Formation of Chorionic Villi (Flowchart 6.2)**

**Chorion**

*Definition:* The cellular, outermost extraembryonic membrane composed of trophoblast lined with extraembryonic somatopleuric mesoderm.

**Formation**

- The extraembryonic somatic mesoderm and the two layers of trophoblast (cytotrophoblast and syncytiotrophoblast) contribute for the formation of chorion all around the developing embryo (Fig. 6.9).

- The extraembryonic coelom is now called the chorionic cavity. Embryo and its amniotic and yolk sacs are suspended into it by connecting stalk. The amniotic sac with embryonic epiblast forms its floor and the yolk sac with embryonic hypoblast forms its roof.
Later blood vessels develop in the extraembryonic mesoderm which forms the chorionic vessels.

The chorionic villi develop from the chorion and cover the entire chorionic sac until the beginning of the 8th week. These become vascularized by allantoic vessels.

**Types of Chorion**

The chorionic villi are first formed all over the trophoblast and grow into the surrounding decidua (Fig. 6.10).

- **Chorion laeve**: The villi associated with decidua capsularis are transitory. As the gestational sac grows, they get compressed and their blood supply is reduced.
Because of reduced blood supply these villi soon degenerates producing an avascular bare area of smooth chorion called chorion laeve. It regresses in 3rd month of pregnancy.

- **Chorion frondosum**: The chorionic villi associated with decidua basalis retain the vascularity, undergo considerable development and form a bushy area called chorion frondosum. This contributes fetal part of placenta as the maternal part is contributed by decidua basalis.

**Stages in the Formation of Chorionic Villi**

The structural component of chorionic villus differs at different periods of embryonic development. Accordingly there are three types of chorionic villi.

1. **Primary villi**: They consist of a central core of cytotrophoblast covered by a layer of syncytiotrophoblast. Adjoining villi are separated by an intervillous space.

2. **Secondary villi**: These show three layers. Outer syncytiotrophoblast, an intermediate layer of cytotrophoblast, and an inner layer of extraembryonic mesoderm.

3. **Tertiary villi**: These are like secondary villi except that they have fetal blood capillaries in the mesoderm.

**Process of villus formation**: The various processes in the formation of villi are as follows:

- **Appearance of lacunae and trabeculae in syncytiotrophoblast**: The syncytiotrophoblast grows rapidly and becomes thick. Small cavities called lacunae appear in this layer (Fig. 6.11C). Gradually, the lacunae increase in size. At first they are irregularly arranged (Fig. 6.11D), but gradually, they come to lie radially (Figs 6.12A to C) around the blastocyst. The lacunae are separated from one another by partitions of syncytiotum, 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 (Figs 6.12A to C).

- **Erosion of maternal endometrium by syncytiotrophoblast and entry of maternal blood into the syncytial lacunae**: 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 (Figs 6.13A to C).

- **Formation of primary chorionic villi (Figs 6.14A to C):** Each trabeculus is, initially, made up entirely of syncytiotrophoblast and in cut section it is surrounded by lacunar space filled with maternal blood. Now the cells of the cytotrophoblast begin to multiply and grow into each trabeculus. The trabeculus thus comes to have a central core of cytotrophoblast covered by an outer layer of syncytium. It is surrounded by maternal blood, filling the lacunar space. The trabeculus is now called a primary villus and the lacunar space is now called the intervillous space.

- **Formation of secondary chorionic villi (Figs 6.15A to C):** Extraembryonic mesoderm invades the center of each primary villus. The villus now has a core of mesoderm covered by cytotrophoblast and by syncytium. This structure is called a secondary villus.

Figs 6.13A to C: (A) Radial arrangement of trabeculae and lacunae around the blastocyst with maternal blood vessels entering lacunar space; (B) Uterine blood vessels in the decidua open into the lacunar space and fill with maternal blood and trabecular filled with syncytiotrophoblast; (C) Transverse section through trabeculae containing syncytiotrophoblast surrounded by lacunar spaces filled with maternal blood.

Figs 6.14A to C: (A) Primary chorionic villi and lacunae around the blastocyst with maternal blood vessels entering lacunar space and extensions of cytotrophoblast cells in the center of syncytial trabeculae; (B) Primary villi with central cytotrophoblast cells surrounded by syncytiotrophoblast; (C) Transverse section of primary villi with central cytotrophoblast and peripheral syncytiotrophoblast in contact with maternal blood in intervillous space.
- **Formation of tertiary chorionic villi (Figs 6.16A to C):** 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.

- **Establishment of fetal blood circulation in tertiary villi:** 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 intervillous space.

- **Formation of cytotrophoblastic shell:** 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. 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. 6.17). The cells of this shell multiply rapidly and the placenta increases in size.

**Subdivisions of Villus (Fig. 6.18)**

- The villi that are first formed (as described above) and are attached on the fetal side to the extraembryonic mesoderm and on the maternal side to the cytotrophoblastic shell. They are, therefore, called anchoring villi.
- Each anchoring villus consists of a stem villus or truncus chorii.
- Each stem villus divides into a number of branches called rami chorii.

- The rami chorii in turn divide into finer branches called ramuli chorii. The ramuli chorii are attached to the cytotrophoblastic shell.
- The anchoring villi give off numerous branches that grow into the intervillous space as free/floating villi. New villi also sprout from the chorionic side of the intervillous space. Ultimately, almost the whole intervillous 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 presents two parts (fetal and maternal), two surfaces (fetal and maternal), two types of cotyledons and a peripheral margin.

- **Maternal part:** This is contributed by decidua basalis or decidua plate of endometrium.
- **Fetal part:** This is contributed by chorion frondosum or chorionic plate. This surface is covered by the fetal membrane amnion and the umbilical cord is attached near the center of this surface.

**Maternal surface:** The maternal surface is rough and irregular (Fig. 6.19A). It is subdivided into a number of lobes called maternal cotyledons. Septa that grow into the intervillous space from the maternal side (Fig. 6.18) divide this surface into 15–20 rough and irregular maternal cotyledons.
cotyledons. If the placenta is viewed from the maternal side, the bases of the septa are seen as grooves while the cotyledons appear as convex areas bounded by the grooves.

**Fetal surface:** This surface is smooth and is covered by amnion (Fig. 6.19B). The umbilical cord is attached close to the center of this surface. Umbilical vessels radiate from the umbilical cord beneath the amnion. The fetal part is contributed by chorionic frondosum that is seen as a plate called chorionic plate. From the chorionic plate 40–60 extensions (fetal cotyledons) arise and extend toward the decidua basalis. Each fetal cotyledon (Fig. 6.18) consists of a stem villus/trunus chorii that show ramifications into number of branches (ramus chorii), each further subdivides (ramuli chorii) like the branches of a tree. Their terminal ramifications look like fingers and are called chorionic villi. The villi that are attached to decidua basalis are called anchoring villi. Others float in the maternal blood that flows in between the villi and are called floating villi (Fig. 6.18).

**Maternal and fetal cotyledons:** There are 15–20 maternal cotyledons in placenta. Each maternal cotyledon contains 2–4 anchoring villi and their branches. One anchoring villus and its ramifications (ramus chorii, ramuli chorii and floating villi) constitute a fetal cotyledon.

**Peripheral margin of placenta:** It presents fetal membrane which is contributed from inside outward by decidua capsularis and parietalis, chorion laeve and amnion. After the birth of the child, the placenta is shed off along with the decidua.

**Measurements of placenta at full term:**
- Diameter: 15–20 cm
- Thickness: 3 cm
- Weight: 500 g.

**Structure of placenta (Fig. 6.20):**
- Maternal side—basal plate
  - Stratum spongiosum of decidua basalis containing maternal blood vessels
  - Outer layer of syncytiotrophoblast (Nitabuch’s layer)
  - Outer shell of cytotrophoblast
  - Inner layer of syncytiotrophoblast (Rohr’s fibrinoid stria).
- Fetal side—chorionic plate
  - Covered by amnion
  - Primary mesoderm with fetal blood vessels
  - Cytotrophoblast
  - Syncytiotrophoblast.
Between basal plate and chorionic plate
- Intervillous space
  - Volume—140 mL
  - Maternal blood passing through intervillous space—500 mL/minute
  - Volume of fetal blood flowing through fetal villi—400 mL/minute.
- Stem villi—primary, secondary, tertiary.

Description of human placenta based on certain criteria is presented in Table 6.1.

Placental Membrane/Barrier
- In the placenta, maternal blood circulates through the intervillous space and fetal blood circulates through blood vessels in the villi. Though the maternal and fetal bloods are flowing side by side and in opposite directions they do not mix with each other. They are separated by a membrane, made up of the layers of the wall of the villus.
- Tissues intervening between fetal blood in chorionic villi and maternal blood in intervillous space constitute the placental membrane or barrier. All interchanges of oxygen, nutrition and waste products take place through this membrane.
- The constituent structures forming the placental barrier or maternal fetal barrier extending from the maternal erythrocyte to fetal erythrocyte are as follows:
  - In the early part of pregnancy, the barrier presents the following layers (Fig. 6.21A)
    - Endothelium of fetal blood vessels, and its basement membrane
    - Surrounding mesoderm (connective tissue)
    - Cytotrophoblast and its basement membrane
    - Syncytiotrophoblast.
  - In the later part of pregnancy, the efficiency of the membrane is increased due to the reduction in its thickness (Fig. 6.21B) by
    - Disappearance of cytotrophoblast
    - Thinning of syncytiotrophoblast
    - Edematous stroma
    - Peripheral migration of fetal blood vessels
    - It presents endothelium of fetal capillaries resting on basement membrane and syncytiotrophoblast only.
- The total area of this membrane varies from 4 m² to 14 m². 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.
- This membrane, which is at first 0.025 mm thick, is reduced to 0.002 mm. However, toward the end of pregnancy, a fibrinoid deposit appears on the membrane, and this reduces its efficiency.

Functions of Placenta
It has several functions that facilitate growth of the fetus.
- It acts as a temporary organ that allows transport of oxygen, water, electrolytes and nutrients (in the form of carbohydrates, lipids, polypeptides, amino acids...
and vitamins) from maternal to fetal blood and thus maintains the nutrition of the fetus. 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 eliminates excretion of carbon dioxide, urea and other waste products produced by the fetus into the maternal blood.

- Maternal antibodies [immunoglobulin G (IgG), gamma globulins 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 poliomyelitis, 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 estrogens (e.g. diethylstilboestrol) 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 4th month (when the corpus luteum degenerates). Estrogens (mainly estriol) produced by the placenta reach maternal blood and promote uterine growth and development of the mammary gland.

### Classification of Placenta

1. Based on shape (Figs 6.22A to J):
   - Discoid—round or disc like (Fig. 6.22A)
   - Bidiscoidal—it consists of two discs (Fig. 6.22B)
   - Oval (Fig. 6.22C)
   - Triangular (Fig. 6.22D)
   - Irregular (Fig. 6.22E)
   - Lobed—it divides into lobes (Fig. 6.22F)
   - Diffuse/placenta membranacea (Fig. 6.22G)—chorionic villi persists all-round the blastocyst
   - Placenta succenturiata (Fig. 6.22H)—a small part of the placenta is separated from the rest of it
   - Fenestrated (Fig. 6.22I)—presence of hole or opening in the placenta
   - Circumvallate (Fig. 6.22J)—when peripheral edge of placenta is covered by a circular fold of decidua, it is called circumvallate.

2. According to attachment of umbilical cord (Figs 6.23A to D):
   - Normal—Central insertion (Fig. 6.23A)
   - Paracentral insertion of umbilical cord (Fig. 6.23B)
   - Marginal or battledore placenta (Fig. 6.23C)—Cord is attached to the margin of placenta
   - Velamentous (Fig. 6.23D)—Umbilical cord is attached to the fetal membrane close to the peripheral margin of placenta.

![Figs 6.22A to J: Types of placenta based on shape: (A) Discoid; (B) Bidiscoidal; (C) Oval; (D) Triangular; (E) Irregular; (F) Lobed—it divides into lobes; (G) Diffuse or placenta membranacea; (H) Placenta Succenturiata; (I) Fenestrated; (J) Circumvallate](image)
3. According to distribution of umbilical arteries:
   - Disperse type (Fig. 6.22C)—Umbilical arteries show dichotomous branching and show progressive reduction in size
   - Magistral type (Fig. 6.23C)—Arteries present uniform caliber up to the periphery of placenta
   - Furcate (Fig. 6.24)—Blood vessels divide before reaching the placenta.

4. Phylogenetic classification: According to tissues from maternal and fetal parts of placenta contributing for placental barrier (Fig. 6.25) (Table 6.2).

Clinical correlation
- **Human chorionic gonadotropin** 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.
- Human chorionic somatomammotropin (hCS) has an antiinsulin 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 (Fig. 6.26):
  - 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.
  - 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 15–20 seconds (i.e. three to four times per minute).

FETAL/EXTRAEMBRYONIC MEMBRANES

*Definition:* Tissues or structures that develop from the zygote but do not form part of embryo proper.
Amnion and Amniotic Fluid

- It is the fetal membrane that covers the embryo and forms the amniotic sac that is filled with amniotic fluid (Figs 6.27A and B). It appears in the 2nd week of development.

Formation and expansion of amniotic cavity: The amniotic cavity is lined by extension of cells of ectoderm from the inner cell mass and amniogenic cells from the trophoblast (Figs 6.3 and 6.9). The amniogenic cells line the roof and lateral wall of amniotic sac and its floor is formed by ectodermal cells. The amniotic cavity expands...
As pregnancy advances, the quantity of this fluid increases, till at full term it is about 1 L.
- There is constant exchange of water between the amniotic fluid and maternal blood, the water being completely replaced every 3 hours.
- Sometime in the 5th month the fetus begins to swallow amniotic fluid. This fluid is absorbed (through the gut) into fetal blood and is transferred through the placenta to maternal blood.
- When the fetal kidneys start working, the fetus passes urine into the amniotic fluid. This does not cause harm because fetal urine is made up mostly of water (metabolic wastes being removed from blood by the placenta and not through the kidneys).

**Umbilical Cord**

**Introduction:** It is one of the fetal membranes. Umbilical cord develops from yolk sac and contains its remnants. Umbilical cord is tubular in structure and is covered by amniotic membrane. It contains blood vessels, yolk sac remnants and embryonic connective tissue. One end of it is attached to the anterior abdominal wall of fetus and the other end is fixed to the center of fetal surface of placenta (Figs 6.1A and B). It is 50 cm in length and 2 cm in breadth at full term. If the cord is too long, it can wind round the neck of fetus resulting in strangulation or it can prolapse into the cervical canal. If the cord is too short, it can cause difficulty during delivery of the fetus.

**Function:** The umbilical vessels transport oxygen and nutrients from the placenta to the developing fetus and eliminate carbon dioxide from fetal circulation into the placenta.

**Formation of Umbilical Cord**
- During 2nd week of development with the appearance of extraembryonic coelom, the extraembryonic mesoderm is divided into somatopleuric and splanchnopleuric layers around the entire conceptus except at one area.
This unsplit area of extraembryonic mesoderm forms the connecting stalk (Fig. 6.9).

- The connecting stalk contains the primary mesoderm and suspends the developing bilaminar embryonic disc along with amniotic and yolk sac cavities in the blastocyst/chorionic cavity (Fig. 6.9).
- With the establishment of cephalocaudal axis of the embryo, the connecting stalk moves toward the caudal end of the embryo. An evagination from the caudal end of secondary yolk sac known as allantoic diverticulum extends into the primary mesoderm of connecting stalk during 3rd week of development (Figs 6.14 and 6.15).
- During 3rd week of development, extraembryonic blood vessels develop in the chorion and connecting stalk and are known as umbilical vessels (Fig. 6.16).
- During the 4th week of development with the formation of head fold, tail fold and lateral folds of the embryo, the connecting stalk with its constituent allantoic diverticulum moves to the ventral surface of the developing embryo. With the incorporation of yolk sac into the head and tail folds of the embryo, contributing for the foregut and hind gut respectively the midgut between the two is in communication with the extraembryonic part of yolk sac known as definitive yolk sac (Fig. 6.28). This communication between midgut and definitive yolk sac is known as vitellointestinal duct and lies close to the connecting stalk. Because of the formation of embryonic folds, the amniotic membrane forms a tubular investment enclosing the connecting stalk along with allantoic diverticulum, vitellointestinal duct and umbilical vessels forming the umbilical cord.

**Components:** Components of umbilical cord vary with gestational age of the fetus. They are:
- **Umbilical arteries:** Two umbilical arteries known as right and left umbilical arteries that are derived from ventral division of internal iliac arteries. These transport deoxygenated blood from the fetus to the chorionic villi of placenta.
- **Umbilical veins:** In the early part of gestation, two umbilical veins known as right and left umbilical veins are present. During later part of pregnancy, the right umbilical vein disappears leaving the left umbilical vein that conveys oxygenated blood from the placenta to fetus.
- **Allantoic diverticulum:** It is a ventral projection of hindgut into the connecting stalk. The proximal part of diverticulum gets incorporated into the apex of urinary bladder and its distal part undergoes fibrosis to form urachus.
- **Vitellointestinal duct:** It is the communication between the midgut and extraembryonic part of yolk sac. In late fetal life, it disappears.
- **Communication between intra- and extraembryonic coelom:** The coelomic cavity exists around the vitellointestinal duct at the fetal end of umbilical cord up to 10th week of development. During this period, there is herniation of U-shaped midgut loop into the extraembryonic coelom which is known as physiological hernia.

**Clinical correlation**

**Amniotic fluid**
- **Amniotic fluid:** It is a clear, watery fluid (98%) and contains 2% solids (inorganic salts, urea, proteins, sugars).
  - **Source:** Fetal/maternal/both
    - Amnion, fetal kidney, fetal lung, placenta
    - Amnio-fetomaternal exchange
  - **Amount**
    - 10th–20th week: 25–400 mL
    - Increases up to 6th month, then decreases. At 28 weeks, it is 800 mL and at term it is 400 mL
  - **Abnormal production**
    - Hydramnios—more than 2 L of amniotic fluid will be present. In some cases, hydramnios is associated with atresia of the esophagus, which prevents swallowing of amniotic fluid by the fetus
    - Oligoamnios—scanty amniotic fluid. It is sometimes associated with renal agenesis, as no urine is added to the amniotic fluid.
  - Both conditions can cause abnormalities in the fetus. They can also cause difficulties during childbirth.

**Clinical importance of amniotic fluid**

**Amniocentesis:** It is a technique to collect amniotic fluid. The fluid is collected either through cervix or anterior abdominal wall. This procedure is usually done during 15–20 weeks of pregnancy. There is risk of fetal injury or preterm delivery in performing this procedure.
The indications for this procedure are:

- Maternal age
- Bad obstetric history
- Cytogenetic analysis: Diagnosis of trisomy's, sex-linked disorders
- Biochemical analysis: Enzyme estimations—gross fetal anomalies—alpha-fetoproteins, surfactant
- Metabolic disorders:
  - Lipid—Tay-Sachs disease
  - Mucopolysacharides—Hurler's syndrome
  - Carbohydrate—Pompe's disease
  - Purine—Lesch-Nyhan syndrome
- Amniotic stem cells: Production of embryonic cells in stem cell therapy for defects of mesenchymal, hematopoietic, neural, epithelial or endothelial cell origin.

Amniotic bands

Tears in the amnion results in amniotic bands. These bands may encircle parts of fetus particularly the limbs. Amputation of limb, ring like constrictions of limb, other abnormalities including craniofacial malformations can occur. This condition results from infections or toxins affecting the fetus or fetal membranes or both.

Clinical correlation

Umbilical cord

- Single umbilical artery: Instead of normal two umbilical arteries a single umbilical artery will be present. Usually the left umbilical artery is absent. Its incidence is 1% and is associated with fetal anomalies.
- Cord blood therapies: Cord blood is the source of stem cells that are used for various disorders.
  - Hematopoietic stem cells
  - Cardiovascular diseases—myocardial infarction
  - Genetic diseases
  - Brain injury
  - Type 1 diabetes.
- Wharton's jelly: Mesenchymal stem cells—cartilage, bone.
- Umbilical cord cyst (Fig. 6.29)

Mutual Relationship of Amniotic Cavity, Extraembryonic 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 Figures 6.2, 6.3, 6.6 and 6.9 and then by studying Figures 6.30 to 6.32.

In Figure 6.30, we see three cavities, namely (1) the uterine cavity, (2) the extraembryonic coelom and (3) the amniotic cavity. The outer wall of the extraembryonic coelom is formed by chorion and the inner wall by amnion. As the amniotic cavity enlarges, the extraembryonic 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 Figure 6.31, it will be seen that the wall of the amniotic cavity is now formed by (1) amnion, (2) chorion and (3) 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 (Figs 6.32A and B).

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 causes these membranes to bulge into the cervical canal. This bulging helps to dilate this canal. The bulging membranes can be felt through the vagina and are referred to as the bag of waters. Ultimately the membranes rupture. Amniotic fluid flows out into the vagina. After the child is delivered, the placenta and the membranes, along with all parts of the decidua, separate from the wall of the uterus and are expelled from it.

**MULTIPLE BIRTHS AND TWINS**

*Multiple births*: If more than one fetus is carried to term in a single pregnancy. When a mother gives birth to two infants at the same time, they are called twins. Three (triplets), four (quadruplets) or even more infants are sometimes born simultaneously.

*Types of twinning*: Twins can be produced in two ways (Table 6.3):

- **Dizygotic twins**: Two ova may be shed simultaneously from the ovary. Each of them may be fertilized and may develop in the usual manner. This results in twins that are called *dizygotic* or *fraternal twins*. As each of them develops from a separate ovum, they have independent genetic constitutions. These twins, therefore, need not be of the same sex, nor do they resemble each other any more than children of the same parents that are born separately. Each fetus has its own chorionic and amniotic sacs (*bichorial, biamniotic*). Dizygotic twinning is more common in human beings than monozygotic twinning (Fig. 6.33A).

- **Monozygotic twins**: Twins can also arise from a single fertilized ovum. These are called *monozygotic* or *maternal twins*. The genetic constitution of the two twins is exactly the same. Hence they are of the same sex. They are also exactly alike in appearance. Monozygotic twins are produced in one of the following ways:
  - *Early blastomere separation*: The cells formed in the first few divisions of the zygote are totipotent, i.e. each cell is capable of developing into a complete embryo. The two cells formed by the first division may separate and develop independently. In such a case, the fetuses will have separate chorionic and amniotic sacs (*bichorial, biamniotic*) as in dizygotic twins. The percentage incidence is 25–30% and can result up to 3rd day after fertilization as separation takes place after the first cellular division (Fig. 6.33B).

**TABLE 6.3**: Differences in features between monozygotic and dizygotic twins

<table>
<thead>
<tr>
<th>Feature</th>
<th>Monozygotic twins</th>
<th>Dizygotic twins</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of ova fertilized</td>
<td>Fertilization of a single ovum</td>
<td>Fertilization of two separate ova</td>
</tr>
<tr>
<td>Incidence</td>
<td>More common</td>
<td>Less common</td>
</tr>
<tr>
<td>Sex of embryos/fetuses</td>
<td>Similar sex</td>
<td>Same or different sexes</td>
</tr>
<tr>
<td>Appearance</td>
<td>Identical in every way including the HLA genes</td>
<td>Unlike/fraternal twins</td>
</tr>
<tr>
<td>Genetic constitution</td>
<td>Identical genetic constitution</td>
<td>Genetically dissimilar</td>
</tr>
<tr>
<td>No. of amnion, chorion, placenta</td>
<td>Majority diamniotic, monochorionic</td>
<td>Two amnions, chorions and placentae</td>
</tr>
</tbody>
</table>
Figs 6.33A to D: Twinning: (A) Dizygotic twins resulting from fertilization of two different ova—bichorial, biamniotic; (B to D) Monozygotic twins: (B) Bichorial, biamniotic; (C) Monochorial, biamniotic; (D) Monochorial, monoamniotic

- **Duplication of inner cell mass**: The embryo may develop normally up to the stage of the morula. However, when the blastocyst is formed, two inner cell masses form within it and each develops into a complete fetus. In this case, the two fetuses have a common chorionic sac but each lies in an independent amniotic cavity (**monochorial, biamniotic**). The percentage incidence is 70–75%. Separation takes place a little later in the development but before the blastocyst has defined the roles of each cell, i.e. between 4th and 7th day after fertilization (Fig. 6.33C).

- **Duplication of embryonic disc**: The inner cell mass may split into two; or two embryonic axes may be established in one inner cell mass. By this we mean that two separate embryonic discs are formed within it, each with its own prochordal plate and primitive streak. In this case, the two fetuses share a common chorion as well as a common amniotic cavity (**monochorial, monoamniotic**). The percentage
incidence is 1–2%. Separation takes place at the stage when the amniotic bag is already being formed, i.e. between 8th and 12th day after fertilization (Fig. 6.33D).

Multiple births may occur by subdivision of one zygote into more than two parts, by the simultaneous fertilization of more than two ova, or by a combination of both these factors (Figs 6.34 and 6.35).

**Clinical correlation**

**Hazards of monochorionic monoamniotic twinning**

*Incomplete duplication of disc (Figs 6.36A to D):* This results in the formation of conjoined twins or double monsters or Siamese twins. Incomplete separation of monozygotic twins results in the birth of two infants that are joined together in some part of the body. In some cases, it is possible to separate them by operation, but most of them are born dead. Depending on the degree of incomplete separation or fusion, different types of conjoined twins result:
- Cranioptagus—twins united at head
- Thoracopagus—twins showing fusion of thorax
- Pygopagus—fusion at sacral region
- Cephalothoracopagus—fusion of thorax and head

**Acephalic, acardiac fetus:** Sometimes the two twins do not undergo equal development, possibly as a result of unequal blood supply (Fig. 6.37). The underdeveloped fetus may possess no heart of its own and may depend upon the other fetus for its blood supply. Unequal division of embryonic axis/unequal blood supply are responsible for this type of anomaly.

**Parasitic twins:** Sometimes the second conceptus may be represented as a mass attached to other fetus, or may be embedded within its body (Fig. 6.38). This results from cessation of development of one embryo/fetus which is called parasitic as it is incompletely developed and is wholly dependent on the complete embryo/fetus for its growth and development.

**EMBRYOLOGICAL BASIS FOR CLINICAL CONDITIONS OR ANATOMICAL OBSERVATIONS**

**Case Scenario 1**

A 28-year married woman with a history of regular menstrual cycles comes to the obstetrician with a history of amenorrhea of 2 months and a complaint of severe lower abdominal pain on right side. What is your explanation for her condition? What investigations you will suggest? What treatment you advice? Give the embryological explanation for the condition.

- Amenorrhea is absence of menstruation in a woman of reproductive age. The physiological cause of amenorrhea is pregnancy and lactation. In the present case, the cause for amenorrhea is pregnancy.
- The cause for severe pain in abdomen in the present case is most probably an ectopic pregnancy. Normal
site of implantation of blastocyst is in the upper uterine segment. The most common site of extrauterine implantation is in the uterine tube. It is a case of ectopic pregnancy with implantation of blastocyst in the right uterine tube.

- It is diagnosed by a pelvic examination for location of pain/mass in the abdomen. Ultrasound examination for confirmation of the embryo in right uterine tube.
- The treatment is surgical removal of right uterine tube with the implanted embryo and sending it for histopathological examination for confirmation. If the conceptus is removed intact it presents the embryo in closed gestational sac (Fig. 6.39A) and when it is removed with tube and subjected for examination by opening the tube the amniotic cavity and the attached conceptus can be identified (Fig. 6.39B).
- As the cleaving blastocyst is passing through the uterine tube for implantation in the uterus, it is prevented from adhering to tubal mucosa by the zona pellucida. The zona pellucida of the cleaving blastocyst that is rolling on the uterine wall gradually becomes thin on 5th day. By 6th day the zona pellucida disappears. If fertilized ovum cannot reach the uterus by 5th day of fertilization, the implantation of blastocyst takes place in the extrauterine site and in the present case in the uterine tube (Fig. 6.39C).
REVIEW QUESTIONS

1. What are the abnormal sites of implantation?
2. Explain the decidual reaction.
3. What are the different types of decidua?
4. What is chorion? What are the different types of chorion?
5. Explain the stages in the formation of chorionic villi.
6. Describe placental barrier.
7. Describe umbilical cord.
8. Write short notes on dizygotic twins.
9. Write short notes on monozygotic twins.