OBJECTIVES

The medical student will be able to answer the following questions after reading this lecture:

- Define decidua basalis, decidua capsularis, decidua parietalis, chorion laeve, chorion frondosum, placental membrane, placental septum, intervillous space, spiral artery.
- Mention the placental changes at the end of pregnancy.
- Describe in a few sentences the surfaces of delivered placenta.
- Mention the structures passing through primitive umbilical ring, primitive umbilical cord and umbilical cord.
- Cite the mechanisms of transfer of substances across the placental membrane.
- Enumerate the fetal membranes and mention their significance.
- Mention the differences between arrangement of fetal membranes in monozygotic and dizygotic twins.

The placenta is the primary site of nutrient and gas exchange between the mother and fetus. It is a fetomaternal organ that has two components:

- A fetal part that develops from the chorionic sac.
- A maternal part that is derived from the endometrium.

THE DECIDUA

It refers to the gravid endometrium, the functional layer of the endometrium in a pregnant woman that separates from the remainder of the uterus after parturition (childbirth).

DECIDUAL REACTION

The cellular and vascular changes occurring in the endometrium as the blastocyst implants constitute the decidual reaction.

- Thickness & vascularity of the mucous membrane greatly increased.
- Its glands are elongated & tortuous.
- Interglandular tissue is also increased and is crowded with decidual cells. These cells swell with accumulation of lipid & glycogen.
- These changes “decidua reaction” at 1st are confined to the area immediately surrounding the implantation site but soon occur throughout the endometrium.

DECIDUAL CELLS

In response to increasing progesterone levels in the maternal blood, the connective tissue cells of the decidua enlarge to form pale-staining decidual cells. These cells enlarge as glycogen and lipid accumulate in their cytoplasm. Decidual regions, clearly recognizable during ultrasonography, are important in diagnosing early pregnancy. The full significance of decidual cells is not understood, but it has also been suggested that they protect the maternal tissue against uncontrolled invasion by the syncytiotrophoblast and that they may be involved in hormone production.
The three regions of the decidua are named according to their relation to the implantation site

- The decidua basalis is the part of the decidua deep to the conceptus that forms the maternal part of the placenta.
- The decidua capsularis is the superficial part of the decidua overlying the conceptus.
- The decidua parietalis is all the remaining parts of the decidua.

**CHORION**

Outer – trophoblast (syncytiotrophoblast and cytotrophoblast)
Inner - somatic mesoderm

**CHANGES IN THE TROPHOBLAST**

At the beginning of the second month of development, the trophoblast is characterized by a great number of secondary and tertiary villi, which give it a radial appearance. At the embryonic pole, villi are numerous and well formed; at the abembryonic pole, they are few in number and poorly developed.

**CHORION**

- Chorion laeve: is the greater part of the chorion in contact with decidua capsularis and over this portion the villi undergo atrophy and by the 4th month scarcely a trace of villi is left. This part of the chorion becomes smooth.
- Chorion frondosum: is the part of the chorion which is in contact with decidua basalis and the villi over this part increase greatly in size and complexity.

Stem (anchoring) villi extend from the mesoderm of the chorionic plate to the cytotrophoblast shell.

The capillary system developing in the core of the villous stems soon comes in contact with capillaries of the chorionic plate and connecting stalk, thus giving rise to the extraembryonic vascular system.

**SPIRAL ARTERIES**

Maternal blood is delivered to the placenta by spiral arteries in the uterus. Erosion of these maternal vessels to release blood into intervillous spaces is accomplished by endovascular invasion by cytotrophoblast cells.

Cytotrophoblast cells, released from the ends of anchoring villi, invade the terminal ends of spiral arteries, where they replace maternal endothelial cells in the vessels’ walls, creating hybrid vessels containing both fetal and maternal cells. To accomplish this process, cytotrophoblast cells undergo an epithelial to endothelial transition.

Invasion of the spiral arteries by cytotrophoblast cells transforms these vessels from small-diameter, high-resistance vessels to larger-diameter, low-resistance vessels that can provide increased quantities of maternal blood to intervillous spaces.

**CLINICAL CORRELATES**

**PREECLAMPSIA**
is a condition characterized by maternal hypertension, proteinuria, and edema. It may begin suddenly anytime from about 20 weeks’ gestation to term and may result in fetal growth retardation, fetal death, or death of the mother.

The condition appears to be a trophoblastic disorder related to:
- failed or incomplete differentiation of cytotrophoblast cells,
- many of which do not undergo their normal epithelial to endothelial transformation

During the following months, numerous small extensions grow out from existing stem villi and extend as free villi into the surrounding lacunar or intervillous spaces.

Structure of the Placenta
By the beginning of the fourth month, the placenta has two components:
(a) a fetal portion, formed by the chorion frondosum and
(b) a maternal portion, formed by the decidua basalis

On the fetal side, the placenta is bordered by the chorionic plate
On the maternal side, the placenta is bordered the decidual plate

junctional zone: trophoblast and decidual cells intermingle. This zone
- is characterized by decidual and syncytial giant cells,
- is rich in amorphous extracellular material.

DECIDUAL SEPTA
During the fourth and fifth months, the decidua forms a number of decidual septa, which project into intervillous spaces. These septa have a core of maternal tissue, but their surface is covered by a layer of syncytiotrophoblast cells, so that at all times, a syncytial layer separates maternal blood in intervillous lakes from fetal tissue of the villi.

As a result of this septum formation, the placenta is divided into a number of compartments, or cotyledons. These septa do not reach the chorionic plate (contact between intervillous spaces in the various cotyledons is maintained).

Because the maternal blood in the intervillous spaces is separated from the fetal blood by a chorionic derivative, the human placenta is considered to be of the hemochorial type.

PLACENTAL SIZE
As a result of the continuous growth of the fetus and expansion of the uterus, the placenta also enlarges. Throughout pregnancy it covers approximately 15% to 30% of the internal surface of the uterus.

The increase in thickness of the placenta results from arborization of existing villi and is not caused by further penetration into maternal tissues.
- 1st trimester: Placenta > fetus
- 12-14 weeks: Placenta = fetus
- >14 weeks: Placenta < fetus
28 weeks: ratio 1:4
40 weeks: ratio 1:7

THE PLACENTAL MEMBRANE
was formerly called the placental barrier, an inappropriate term because there are only a few substances, endogenous or exogenous, that are unable to pass through the placental membrane in detectable amounts. acts as a barrier only when the molecule is of a certain size, configuration, and charge such as heparin and bacteria. Some metabolites, toxins, and hormones, although present in the maternal circulation, do not pass through the placental membrane in sufficient concentrations to affect the embryo/fetus.

**SYNCYTIAL KNOTS**
During the third trimester, numerous nuclei in the syncytiotrophoblast aggregate to form multinucleated protrusions called nuclear aggregations or syncytial knots. These aggregations continually break off and are carried from the intervillous space into the maternal circulation. Some knots lodge in capillaries of the maternal lung where they are rapidly destroyed by local enzyme action.

**PLACENTAL ABNORMALITIES**
- **Placenta Accreta**: Abnormal adherence, with absence of decidua basalis.
- **Placenta Increta**: Occurs when the placenta penetrates into the uterine muscle, but does not penetrate the uterine serosa.
- **Placenta Percreta**: Placental villi penetrate myometrium and through to uterine serosa.
- **placenta previa** occurs When the blastocyst implants close to or overlying the internal os of the uterus.

**SEPARATION OF THE PLACENTA**
The placenta is torn from the uterine wall and, approximately 30 minutes after birth of the child, is expelled from the uterine cavity. The expelled placenta is discoid with a diameter of 15 to 25 cm, is approximately 3 cm thick, and weighs about 500 to 600 g.
The fetal surface of the placenta (facing the fetus) has a shiny, smooth surface provided by the amniotic membrane that covers it. A number of large arteries and veins, the chorionic vessels, converge toward the umbilical cord. The attachment of the umbilical cord is usually eccentric. Maternal side of the placenta is textured and spongy looking. It is divided by a series of fissures into lobules or cotyledons. The fissures contain the remains of septae which extended between the maternal and fetal portions.

**EXAMINATION OF THE PLACENTA**
prenatally by ultrasonography or magnetic resonance imaging. Or postnatally by gross and microscopic study. It may provide clinical information about the causes of IUGR, placental dysfunction, fetal distress and death, and neonatal illness.
Placental studies can also determine whether the placenta is complete. Retention of a cotyledon or an accessory placenta in the uterus may cause severe uterine hemorrhage.

**PLACENTAL CHANGES AT THE END OF PREGNANCY**
At the end of pregnancy, a number of changes that occur in the placenta may indicate reduced exchange between the two circulations. These changes include:

(a) an increase in fibrous tissue in the core of the villus,
(b) thickening of basement membranes in fetal capillaries,
(c) obliterative changes in small capillaries of the villi, and
(d) deposition of fibrinoid on the surface of the villi in the junctional zone and in the chorionic plate. Excessive fibrinoid formation frequently causes infarction of an intervillous lake or sometimes of an entire cotyledon. The cotyledon then assumes a whitish appearance.

**FUNCTION OF THE PLACENTA**

Main functions of the placenta are:

(a) exchange of metabolic and gaseous products between maternal and fetal bloodstreams and
(b) production of hormones.

**PLACENTAL TRANSFER**

The transport of substances in both directions between the fetal and maternal blood is facilitated by:

1. the great surface area of the placental membrane.
2. free surface of syncytiotrophoblast has many microvilli, more than 1 billion/cm² at term

Almost all materials are transported across the placental membrane by one of the following four main transport mechanisms:

1. simple diffusion,
2. facilitated diffusion,
3. active transport, and
4. pinocytosis.

Other Placental Transport Mechanisms

- **red blood cells** may pass in either direction through very small defects in the placental membrane.
- **cells cross the placental membrane under their own power**, e.g., maternal leukocytes and *Treponema pallidum*, the organism that causes syphilis.
- **some bacteria and protozoa** such as *Toxoplasma gondii* infect the placenta by creating lesions and then **cross the placental membrane** through the defects that are created.

**TRANSPORT OF GASES AND NUTRIENTS**

- **Transfer of Gases** Oxygen, carbon dioxide, and carbon monoxide cross the placental membrane by simple diffusion.
- **Nutritional Substances**:
  1. **Water** is rapidly exchanged by simple diffusion and in increasing amounts as pregnancy advances.
  2. **Glucose** produced by the mother and placenta is quickly transferred to the embryo/fetus by facilitated diffusion.
3. There is little or no transfer of maternal cholesterol, triglycerides, or phospholipids. Although there is transport of free fatty acids, the amount transferred appears to be relatively small.

4. Amino acids are actively transported across the placental membrane and are essential for fetal growth.

5. Water-soluble vitamins cross the placental membrane more quickly than fat-soluble ones.

- **Hormones**
  - **Protein hormones** do not reach the embryo or fetus in significant amounts, except for a slow transfer of thyroxine and triiodothyronine.
  - **Unconjugated steroid hormones** cross the placental membrane rather freely.

- **Electrolytes**
  These compounds are freely exchanged across the placental membrane in significant quantities, each at its own rate.

**Transmission of Maternal Antibodies:**

- Immunological competence begins to develop late in the first trimester, by which time the fetus makes all of the components of complement.

- **Immunoglobulins**
  1. consist almost entirely of maternal immunoglobulin G (IgG), which are readily transported to the fetus by transcytosis at approximately 14 weeks. In this manner, the fetus gains passive immunity against various infectious diseases.
  2. Newborns begin to produce their own IgG, but adult levels are not attained until the age of 3 years

A maternal protein, **transferrin**, crosses the placental membrane and carries iron to the embryo or fetus. The placental surface contains special receptors for this protein.

- **Waste Products**
  - Urea and uric acid pass through the placental membrane by simple diffusion.
  - Conjugated bilirubin (which is fat soluble) is easily transported by the placenta for rapid clearance

- **Drugs and Drug Metabolites**
  Most drugs and drug metabolites cross the placenta by simple diffusion, the exception being those with a structural similarity to amino acids, such as methyldopa and antimetabolites.

Some drugs cause major congenital anomalies.

Fetal drug addiction may occur after maternal use of drugs such as heroin and 50% to 75% of these newborns experience withdrawal symptoms.

2. production of hormones

The placenta (syncytiotrophoblast) is classified as an endocrine organ. It produces both protein and steroid hormones

- human Chorionic Gonadotropin (hCG)
- estrogen
- Progestrone
- human Chorionic Somatomammotropin (hCS)

**human Chorionic Gonadotropin (hCG)**

Synthesis of this hormone begins before implantation and the presence of hCG in mother’s urine form the basis of pregnancy test. Its main function is to maintain the activity of the maternal corpus luteum. Production of hCG peaks at 8 weeks and then gradually declines.

**Estrogen**

The amount of estrogen secreted increase with time during pregnancy and the maximum point breaches just before labour. The synthesis of estrogen depend on the integrity of foetal adrenals and liver as well as the placenta. Estrogen stimulate uterine growth and development of the mammary glands.

**Progestrone**

Secretion of progestrone increase during pregnancy. The placenta can produce progestrone hormone independently from cholestrol precursors. In early pregnancy, progestrone inhibits the movement of the uterus. Its main function is to maintain the inner layer of the uterus.

**human Chorionic Somatomammotropin (hCS)**

Formly known as human placental lactogen (hPL). Similar to growth hormone, this protein hormone influencing:

1. the preparations of breasts for lactation and
2. lipid & CHO metabolism

**PRIMITIVE UMBILICAL RING**

Is the oval line of reflection between the amnion and embryonic ectoderm (amnio-ectodermal junction).

At the fifth week of development, the following structures pass through the ring:

(a) the connecting stalk, containing the allantois and the umbilical vessels, consisting of two arteries and one vein;
(b) the yolk stalk (Vitelline duct), accompanied by the vitelline vessels; and
(c) the canal connecting the intraembryonic and extraembryonic cavities

**THE PRIMITIVE UMBILICAL CORD**

The amniotic cavity enlarges rapidly at the expense of the chorionic cavity, and the amnion begins to envelop the connecting and yolk sac stalks, crowding them together and giving rise to the primitive umbilical cord.

Distally, the cord contains the yolk sac stalk and umbilical vessels. More proximally, it contains some intestinal loops and the remnant of the allantois.

When the allantosis and vitelline duct and its vessels are also obliterated, all that remains in the cord are the umbilical vessels surrounded by a jelly of wharton which function as a protective layer for the blood vessels.

**THE UMBILICAL CORD**

The attachment of the umbilical cord to the placenta is usually near the center of the fetal surface of this organ, but it may attach at any point.
For example, insertion of the umbilical cord at the placental margin produces a battledore placenta and its attachment to the fetal membranes is a velamentous insertion of the cord.

The umbilical cord is usually 1 to 2 cm in diameter and 30 to 90 cm in length (average, 55 cm). Because the umbilical vessels are longer than the cord, twisting and bending of the vessels (false Knots) are common.

Excessively long or short cords are uncommon. Long cords have a tendency to prolapse and/or to coil around the fetus. A very short cord may cause premature separation of the placenta from the wall of the uterus during delivery. The umbilical cord usually has two arteries and one vein that are surrounded by mucoid connective tissue (Wharton jelly). However a single umbilical artery is present and these babies have approximately a 20% chance of having cardiac and other vascular defects.

**FETAL MEMBRANES**

Thin layers or tissues which surround the embryo or foetus and provide for its nutrition, respiration, excretion and protection.

They are:

A. amnion
B. yolk sac;
C. allantosis;
D. chorion

**AMNION**

Is a transparent greyish membrane which lines the chorion. It covers the foetal surface of the placenta and the umbilical cord.

Amnionic membrane is two cell layers
1) epiblast derived extra embryonic ectodermal layer
2) thin non-vascular extra embryonic mesoderm

As the amnion enlarges it encompasses the embryo on the ventral side, merging around the umbilical cord. It forms the epithelial layer of the umbilical cord.

With embryo growth the amnion obliterates the chorionic cavity. The amniotic sac contains the foetus swimming in the liquor amni.

**AMNIOTIC FLUID (LIQUOR AMNI)**

**Nature**

Is a clear, pale, slightly alkaline pH 7.2 fluid.

The amount of fluid increases
30 mL at 10 weeks of gestation
50 mL at 12 weeks of gestation
450 mL at 20 weeks
800 to 1000 mL at 37 weeks. Then decreases later on to be scanty in post-term pregnancy.

**composition**

Water 98%-99%
Carbohydrates (glucose and fructose)
Proteins (albumin and globulin)
Lipids
Hormones (estrogen and progesterone)
Enzymes (alkaline phosphatase)
Minerals (sodium; potassium and chloride)
Suspended materials as vernix caseosa, lanugo hair, desquamated epithelial cells and meconium.

Circulation of amniotic fluid
The amniotic fluid is not in a static state but is in a continuous turnover. The volume of amnionic fluid is replaced every 3 hours.
amniotic fluid is produced in part by amniotic cells but is derived primarily from maternal blood
Uptake of amniotic fluid is by absorption through the amnion to the maternal circulation and by
Foetal swallowing
From the beginning of the fifth month,
(1) the fetus swallows its own amniotic fluid,
(2) Fetal urine is added daily to the amniotic fluid

Functions During pregnancy
- Protects the foetus against injury
- A medium for free foetal movement which permits musculoskeletal development
- Facilitate symmetric growth and development of the foetus
- Maintains the foetal temperature
- Source of oral fluid for the foetus
- A medium for foetal excretion

Function during labour
- The fore bag of water helps the dilatation of the cervix during labour
- It acts as an antiseptic for birth canal after rupture of the membranes

Clinical Correlates

Hydramnios or polyhydramnios
is the term used to describe an excess of amniotic fluid (1,500 to 2,000 mL).
Primary causes of hydramnios include
idiopathic causes (35%)
maternal diabetes (25%)
congenital malformations, including central nervous system disorders (e.g., anencephaly) and gastrointestinal defects (atresias, e.g., esophageal) that prevent the infant from swallowing the fluid.

oligohydramnios
refers to a decreased amount (less than 400 mL).
may result from renal agenesis.
May cause club foot or lung hypoplasia

Amniotic Bands
Occasionally, tears in the amnion result in amniotic bands that may encircle part of the fetus, particularly the limbs and digits.
May result in Amputations, ring constrictions, and other abnormalities, including Craniofacial deformations
Origin of the bands is unknown

Premature rupture of the membranes (PROM)
is the most common cause of preterm labor. It occurs in 10% of pregnancies.
Causes are unknown but risk factors include
Previous pregnancies affected by prematurity
Black race
Smoking
Infections
Severe polyhydramnios

**YOLK SAC**
It consists of 2 layers
- Inner endoderm +
- outer extraembryonic mesoderm

**Significance of the Yolk Sac**
- It has a role in the transfer of nutrients to the embryo during the second and third weeks when the utero-placental circulation is being established.
- Allantois develops from its posterior during 3rd week.
- Blood development first occurs in the well-vascularized extra-embryonic mesoderm covering the wall of the yolk sac
- the endoderm of the yolk sac is incorporated into the embryo as the primitive gut.
- Its endoderm, derived from epiblast, gives rise to the epithelium of the trachea, bronchi, lungs, digestive tract and the glands which open in gastro-intestinal tract and urinary bladder.
- Primordial germ cells appear in the endodermal lining of the wall of the yolk sac in the third week and subsequently migrate to the developing sex glands.

**FATE OF THE YOLK SAC**
- At 10 weeks the small yolk sac lies in the chorionic cavity between the amnion and chorionic sac.
- It atrophies as pregnancy advances

**ALLANTOIS**
During the third week allantosis appears as a sausage like diverticulum from the posterior wall of the yolk sac that extends into the connecting stalk.

As the folding proceeds, the allantosis elongates and has two parts:
- Intra-embryonic portion (shares in the formation of urinary bladder).
- Extra-embryonic portion (degenerates)

The intra-embryonic portion of the allantosis runs from the umbilicus to the urinary bladder. As the bladder enlarges, the allantosis involutes to form a thick tube, the urachus. After birth the urachus becomes a fibrous cord, the median umbilical ligament that extends from the apex of the urinary bladder to the umbilicus.

**Significance of Allantosis**
- Blood formation occurs around it during the third to fifth weeks. The allantosis induces the formation of the blood vascular system in the connecting stalk.
- Its blood vessels persist as the umbilical vein and arteries.
- The allantosis remains very small but it does contribute in development of urinary bladder.

**CHORION**
This the outer membrane. It forms a large portion of the connective tissue thickness of the placenta on its foetal side. It is the structure in and through which the major branching umbilical vessels travel on the surface of the placenta.

**FETAL MEMBRANES IN TWINS**

Arrangement of fetal membranes in twins, depending on the
a. type of twins
b. the time of separation of Monozygotic twins.

**DIZYGOTIC TWINS**

Normally, each embryo has its own amnion, chorion, and placenta but sometimes the placentas are fused.

Each embryo usually receives the appropriate amount of blood, but on occasion, large anastomoses shunt more blood to one of the partners than to the other.

**POSSIBLE RELATIONS OF FETAL MEMBRANES IN MONOZYGOTIC TWINS**

A. Splitting occurs at the two-cell stage, and each embryo has its own placenta, amniotic cavity, and chorionic cavity.

B. Splitting of the inner cell mass into two completely separated groups. The two embryos have a common placenta and a common chorionic sac but separate amniotic cavities.

C. The separation occurs at the bilaminar germ disc stage, just before the appearance of the primitive streak.

The embryos have a common placenta, a common amniotic cavity, and a common chorionic cavity.

In cases of conjoined twins, in which the fetuses are not entirely split from each other, there is one amnion, one chorion, and one placenta.

**PARTURITION (BIRTH)**

For the first 34 to 38 weeks of gestation, the uterine myometrium does not respond to signals for parturition (birth). However, during the last 2 to 4 weeks of pregnancy, this tissue undergoes a transitional phase in preparation for the onset of labor.

Labor itself is divided into three stages:

1. Effacement (thinning and shortening) and dilatation of the cervix (this stage ends when the cervix is fully dilated),
2. Delivery of the fetus, and
3. Delivery of the placenta and fetal membranes

**Factors initiating labor are not known and may involve**

1. “Retreat from maintenance of pregnancy,” in which pregnancy-supporting factors (e.g., hormones) are withdrawn, or
2. Active induction caused by stimulatory factors targeting the uterus.

Probably, components of both phenomena are involved.

**PRETERM BIRTH**

(delivery before 37 weeks)

is due to

- premature rupture of the membranes,
- premature onset of labor, or
- pregnancy complications requiring premature delivery.

Risk factors are

- Previous preterm birth
- Black race
- Multiple gestations
- Maternal infections such as periodontal disease and bacterial vaginosis,
- Low maternal body-mass index