GESTATIONAL PHYSIOLOGY

(PRENATAL DEVELOPMENT AND GROWTH)

- Pregnancy begins by the process of fertilization and continues to the parturition.

Oviductal migration

- Fertilization of the potential ovum by the sperm takes place at the ampullary-isthmic junction **(AIJ)** in the fallopian tube.
- The zygote will migrate through the oviduct to reach the uterus at:
  - The 32-cell stage (morula) at 3 to 4 days after fertilization in cows and after 4 to 8 days in bitch and queen.
  - The 8-cell stage at day 3 in ewe.
  - The 4 to 8-cell stage at day 2 in sow.
  - The blastocysts stage at 5-6 days in mare.
- This tubal migration of the zygote varies in duration depending on:
  - Degree of ciliary movements
  - Degree of muscular contractions
  - Degree of muscular constriction at the AIJ or that at the tubo-uterine junction.
- Such factors are governed by the variable concentrations of ovarian steroids and local prostaglandins.

Spacing of embryos and trans-uterine migration

- In polytocous species, the blastocysts arrange themselves in the uterus in a manner to utilize effectively the uterine space.
- The trans-uterine migration occurs before nidation, after the arrival to the uterus.

- The embryo during this period floats freely in the uterine lumen and feeds on the uterine milk (histotroph).
- The result of this migration might be that a fetus may be found in the right uterine horn, while the functioning corpus luteum of pregnancy is in the left ovary.

The process of placentation (Nidation)

Time of occurrence

- Twelve to 20 days in sow, 18-20 days in ewe, 30-35 days in cow and 56-60 days in mare.

Mechanism

It occurs in three phases, pre-contact phase, apposition phase and adhesive phase.

A. **Pre-contact phase**

- Begins on day 17 with the formation of the chorion (single layer of flat or cubic cells) which lies in close apposition with the unaltered uterine epithelium.

B. **Apposition phase**

- Commences on day 18.
- The double-layered chorion begins to unit - by microvilli – to the altered uterine epithelium (polynucleated cells).

C. **Adhesive phase**

- Begins on the 22nd day.
- The trophoblast, consisting of several cell layers and the uterine epithelium is double layer of mono or polynuclear cells.

- ☆ By the beginning of the second month, the trophoblastic cells over the chorion – overlying the caruncles- produce visible localized thickenings which are the forerunner cotyledons.
- ☆ By the 33rd day, each cone of trophoblastic cells has enlarged to form a single villus which penetrates into a crypt in the submucosal of the caruncle.
- ☆ A more intimate and firmer union occurs when numerous finger-like villi extend deeper into the caruncles and produce lateral branches.

N.B

- ❖ Placentation, in rare occasions, occurs in the intercaruncular region especially in the body of the uterus near the internal cervical os.
- ❖ The embryo feeds on stored nutrients during its presence inside the oviduct.

Stages of a normal gestation

I. Cellular (cleavage or germinal) stage

- A fertilization process results in one cell stage (zygote).
- Division of the zygote and its redivision will yield 2 cell satge, 4 cell, 8 cell, 16 cell and 32 cell stage.
- The 32 cell stage is the morula (the stage at which it reaches the uterus in cows) is at about 4-6 days.
- Then the zona pellucida allows water to enter inside this cellular mass to collect centrally forming a structure known as the blastocysts (7-12 days).
- At 12-14 days, zona pellucid cracks and weaken and the blastocyst hatches from it, thus begins to elongate.

- During this stage, there is no increase in size or weight of the embryo and only some trace elements and vitamins are required for this stage.
- It is a stage of series of mitotic divisions which end by the hatched blastocyst.
- Any prolonged cleavage period denoted bad embryo health and also the highest embryonic losses occur during this period.

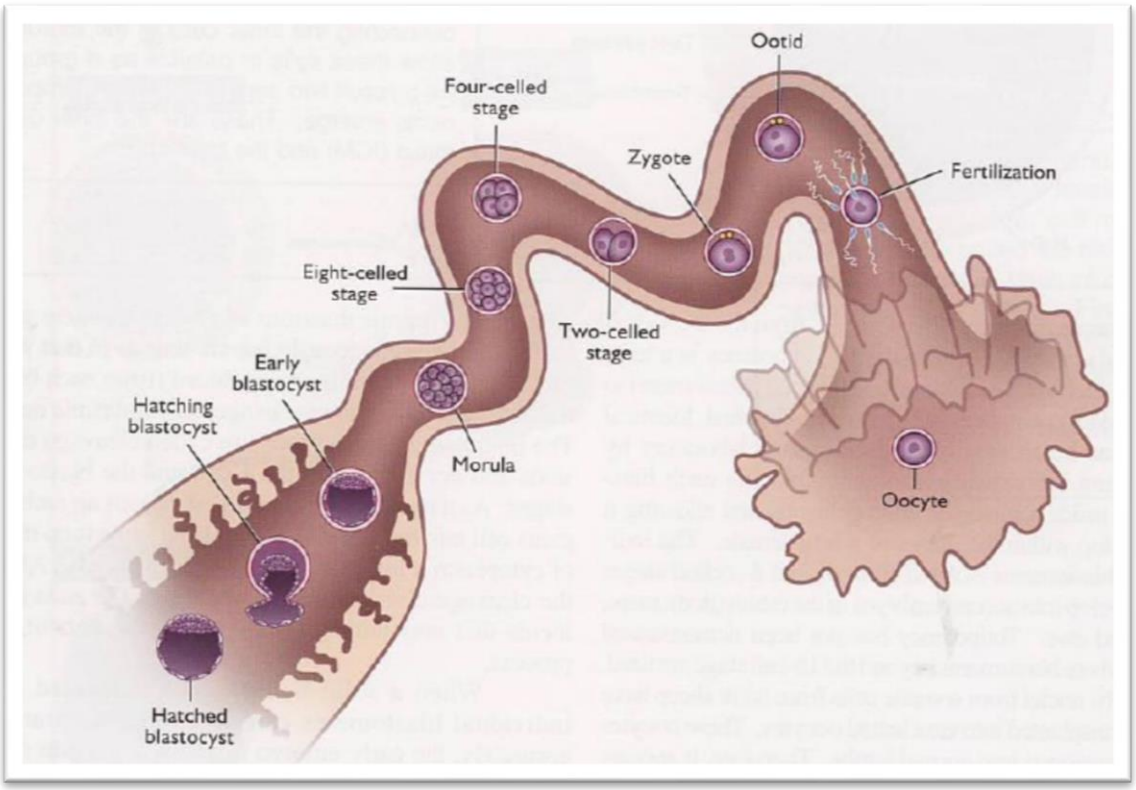


Figure 1. schematic illustration of pre-attachment embryo development

II. Embryonic (differentiation) stage

Definition

It is that period during which cells form tissues and organs of the body.

Duration

Between 14 and 45 days of pregnancy.

This period involves three periods.

A. Formation of the three primitive germinal layers.
- The three germinal layers include the ectoderm, the mesoderm and the endoderm.
- This period extends from 14 to 16 days post-fertilization.

B. Formation of the extra-embryonic membranes.
- The extra-embryonic membranes include the yolk sac, the chorion, the allantois and the amnion.
- This period extends between 17 and 22 days post-fertilization.

C. Formation of the various organs and tissues.
- This process ends at about 45 days of pregnancy.

A. Formation of the three germinal layers
   I. Formation of the endoderm
      - Large cubic cells arrange in the inner surface of the inner cell mass and extends toward the blastoderm forming the endoderm.
   II. Formation of the mesoderm
      - Mesenchymal cells arrange arrange between the endoderm and the blastoderm to give the mesoderm.
   III. The ectoderm
      - This layer arises from the blastoderm.

B. Formation of the extra-embryonic membranes
   I. Formation of the amnion
      - Time: the amnion appears between the 18^{th} and 20^{th} day post-conception.

- Mechanism:
  - Arises by circumferential folding of the somatopleur. So that a crescentic fold is formed and its edges become united together forming the amnion.

II. Formation of the yolk sac

- Time: begins at 14 days and reaches maximum size on 23rd day after which it regresses and only vestiges remain after one week.
- Mechanism:
  - The mid-gut extends to form a clear sac (yolk sac) which acts as a transient nutritive source for the embryo till placentation.
  - Yolk sac regresses at 35 days in bovine feti and regresses at 56-60 days in equine feti.

III. Formation of the allantois

- Time: 20th to 22nd day of pregnancy.
- Mechanism
  - Appears as an invagination of the hind-gut from the splanchnopleur.
  - By the end of the first month, it completely fills the gravid horn and takes one week to penetrate into the non-gravid horn.
  - Fusion of the allantois with the chorion forms the **Chorioallantoic membrane.**
  - Fusion of the allantois with the amnion forms the **Amniochorion.**

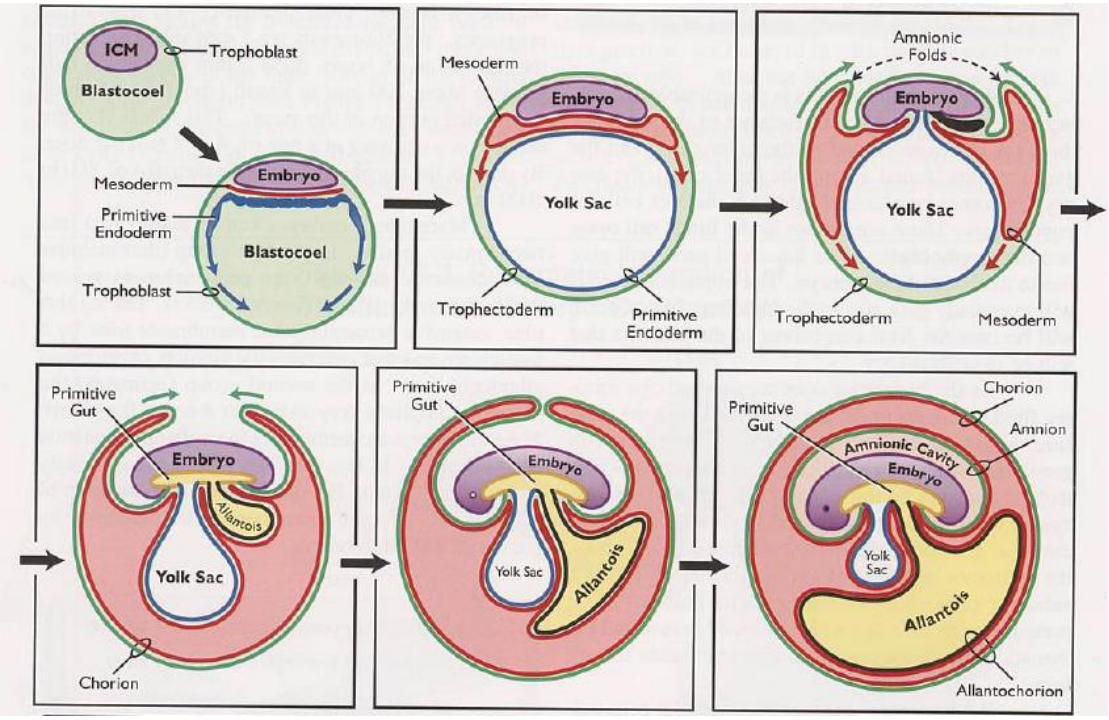


Figure 2: Development of the extra-embryonic membranes in mammals

C. Formation of different tissues and organs

Germ layer	Endoderm	Mesoderm	Ectoderm
Organs	-Digestive system -Liver -Pancreas -Thyroid gland -Lung	-Musculo-skeletal system -Cardio-vascular system -Uro-genital system (except the primordial germ cells)	-Mammary gland -Central nervous system -Sense organs -Skin -Hair -Hooves

Table1: Different body systems related to their embryonic origin in cows

N.B.

Any teratogenic drug or agent introduced during the embryonic period will lead to congenital malformations of the embryo.

Tissue	Days of pregnancy
Neural plate	20th day
Heart and allantoic sac	22nd day
Fore limb bud	25th day
Hind limb bud	28th day
Eye	35th day
Sexual differentiation in male	37th day
Sexual differentiation in female	43rd day
Facial features of the embryo	45th day

Table 2: Chronology of different fetal features during the embryonic period in cows

III. Fetal (growth) stage.

- Time: from the end of the embryonic stage at 45 days pregnancy till full term.
- Features

a. Some growth, development and transformation of certain organs

- Bone calcification: begins on day 70 and is completed by 180 days.
- Teeth eruption at 110 days.
- Hairing and hair distribution:
  - Begins at the end of the fifth month, starting at the front, eye lashes, lips, anterior and dorsal aspects of the fore limbs.
  - Then -after three weeks- it involves the midline of the dorsum.
  - Complete hairing occurs ate 230 days in cows and at about 280 days in mares.

- Testicular descent occurs at mid-gestation in cow feti and just before parturition in equine feti.

b. Growth of the fetus

- Fetal growth during the fetal stage is not steady.
- The actual weight gain during the early fetal period is low, but the relative weight gain is very high.
- During late pregnancy, particularly the last month, the relative weight gain decreases, but the actual or absolute weight gain increases.
- The last two months of gestation are so criticial and high nutrient intake by the dam must be ensured to allow her to face the nutrient requirements of the rapidly growing fetus.

How to calculate the absolute and the relative weight gains of bovine feti?

Relative weight gain (R.W.G.)=

Future weight – initial weight/initial weight X 100

Absolute weight gain (A.W.G.) = future weight – initial weight

Age (days)	Weight (gm)	A.W.G.	R.W.G.
30	<1	19 gm	1900%
60	20		
210	14000	12 Kg	85%
240	26000		

Table 3: A.W.G. and R.W.G. of the bovine fetus during early and late gestation

CLINICAL CHANGES IN THE DAM DURING PREGNANCY

- The clinical changes occurring in the pregnant dam are classified into internal changes and external changes.

A. Internal changes in the pregnant dam

a. Cessation of cyclical ovarian activity and persistence of the corpus luteum.
b. Cervical seal and formation of the cervical pluge which is thick tenacieous and visid mucus.
c. Obvious inequality of the consistence and size of the uterine horns.
d. Changes in the weight of the uterus from 1-2 kg in the non-gravid stage to 10-15 kg in late pregnancy.
e. Changes in the site of the pregnant uterus where it can not be reached at mid-pregnancy and at some cases, the uterus grows over the cervix, in late pregnancy, forming a supra-vaginal pouch.
f. A changes in the tension and the arrangement of the broad ligaments
    i. They loss their horizontal features and become more anterio-ventrally directed.
    ii. This change, together with the anterio-ventral displacement of the cervix, is a useful sign of mid or late pregnancy (but not confirmatory).
g. An increase in the size of the middle uterine artery supplying the pregnant horn starts at 3rd month and a characteristic **fermitus, buzz, whirring or thrilling** becomes noted.
h. Appearance of the placentomes (caruncle-cotyledon complexes) at the 3rd month but can be detected rectally by

the 4th month. Such structures increase in size with advancement of gestation.

B. External changes in the pregnant dam

- Changes in the animal behavior
  - The pregnant animal becomes quite and tends to increase in weight.
  - The increase in weight is due to the increased appetite and reduced muscular activities associated with estrus and also increased efficiency of feed conversion **(Preg-anabolism).**
- Detection of the fetal movements
  - From mid to late pregnancy, the fetus can be detected by ballottement of the right ventral abdomen.
  - The detection can be performed more accurately in late pregnancy and easily performed in less obese cows when the fetus lies close to the right abdominal wall.
- Mammary gland development
  - Occurs on two phases, the first phase is the growth and development of the alveolar and duct system.
  - The second phase comprises secretory activities.
  - This development begins at the sixth month in heifers and in last month in cows.
  - Some pregnant cows do not show external mammary enlargement except during the last few days of pregnancy.
- Changes in the vulva
  - In late pregnancy - even early in mid pregnancy – the heavy weight of the pregnant uterus pulls the genitalia forward and

s a result the vulva tilts and become slightly more dorsally located.

N.B.

By the end of gestation period in cows, the average weight of the uterus is 10-15 kg, the fetal membranes reach 4-5 kg, the fetal fluids account for 15-20 liters, two thirds of which are allantoic fluid and one third is amniotic fluid.

Factors affecting the gestation period

1- Genetic factors

a. Species

- The length of the gestation period varies among different species (see table 4).

b. Breed

- The gestation period varies even among breeds within the same species (see table 4).

c. Individual variations

- Within cows, the gestation period is 9 months±10 days.

2- Environmental factors

2.1- Internal environmental factors

A. Age/parity.

- The duration of pregnancy may be shorter in heifers than older cows as the uterus is incapable of accommodating further fetal growth.

B. Sex of the fetus

- Dams carrying male feti usually have longer gestation periods than those pregnant in female feti.
- Male feti are usually born heavier than female feti of the same breed.

C. Littersize

- Higher littersize in polyparous species is associated with shorter duration of the gestation period and smaller size of the newborn.

D. Pathologies

- Pathological affections particularly of the endocrine system affect the length of the gestation period.

2.2- External environmental factors

A. Season

- ……

B. Management

- **…….**

C. Poisonous plants

- **……..**

D. Diseases causing abortion

THE FETAL MEMBRANES AND THE FETAL FLUIDS

The fetal membranes

1. Changes in size and weight

- Initially, there is a slow and steady increase due to formation and gradual extension of the membranes throughout the uterus.
- Later, the increase in weight is due to increase of size and/or volume of the existing structures.
- During the first month of gestation, the weight of the fetal membranes exceeds that of any intrauterine structure.
- Then the weight of the fetal membranes becomes intermediate between that of the fetus and the intrauterine liquids for the ensuing two months.
- After three months, it decreases to become the lightest structure present (5% of the total weight of the gravid uterus).

2. Changes in extension

- The allantoic membrane grows very rapidly and extends in the pregnant horn, then the body and extends also to the non-pregnant horn.

3. Arrangement in multiple pregnancies

- In twin pregnancies, unicornual twin pregnancy is associated with only an increased size of the placentomes (double the size in singletons).
- In a bicornual twin pregnancy, the number and size of placentomes on each pregnant horn resemble these found in singletons.
- The chorio-allantoic membranes usually fuse together in twin pregnancies. Blood exchange occurs between the twins and may be associated with a sterile female (co-twined by a male one), known as the free-martin condition.
- In some cases, this female twin is born fertile due to:
    - Failure of fusion of the two chorio-allantoic membranes.
    - Another cause may be presence of a distinct structure line at the point of contact preventing blood exchange.

- The incidence of free-martinism is lower in pigs, sheep and equines due to the late anastomosis of the two chorio-allantoic membranes.

Functions of the fetal membranes

1. **Nutritive function**

- Transfer of nutrients from the dam to the fetus through the chorio-allantoic membrane.

2. **Selective permeability**

- For certain essential minerals and vitamins.

3. **Storage function**

- The fetal membranes can store glycogen and fats.

4. **Immunological function**

- The feto-maternal barrier protects the fetus against large-sized molecules including harmful agents.
- However, it does not protect against specific infectious and non-infectious causes of abortion.
- RH factor is prevented in first pregnancy to provoke deleterious effects to the fetus, but mixing of dam and fetal blood leads to antibody formation against fetal RH factor causing serious problems in the subsequent pregnancies.

5. **Secretory function**

- The placenta of mare, ewe and humans secrete progesterone, in late pregnancy, which is able to mentian pregnancy without luteal progesterone.

6. **Gaseous exchange**

- Oxygen and carbon dioxide exchange together with the removal of the fetal metabolic waste products.

TYPES OF PLACENTA

- Placenta is the ultimate connection between the mother and the fetus.
- Formed by the chorio-allantoic membrane from the fetal side and the endometrium from the maternal side.

A. Types of placenta according to the manner of villar distribution on the chorio-allantoic membrane (ANATOMICAL CLASSIFICATION).

1. Simple diffuse type

- The villi are evenly distributed on the surface of the chorio-allantoic membrane.
- Examples: mare and sow

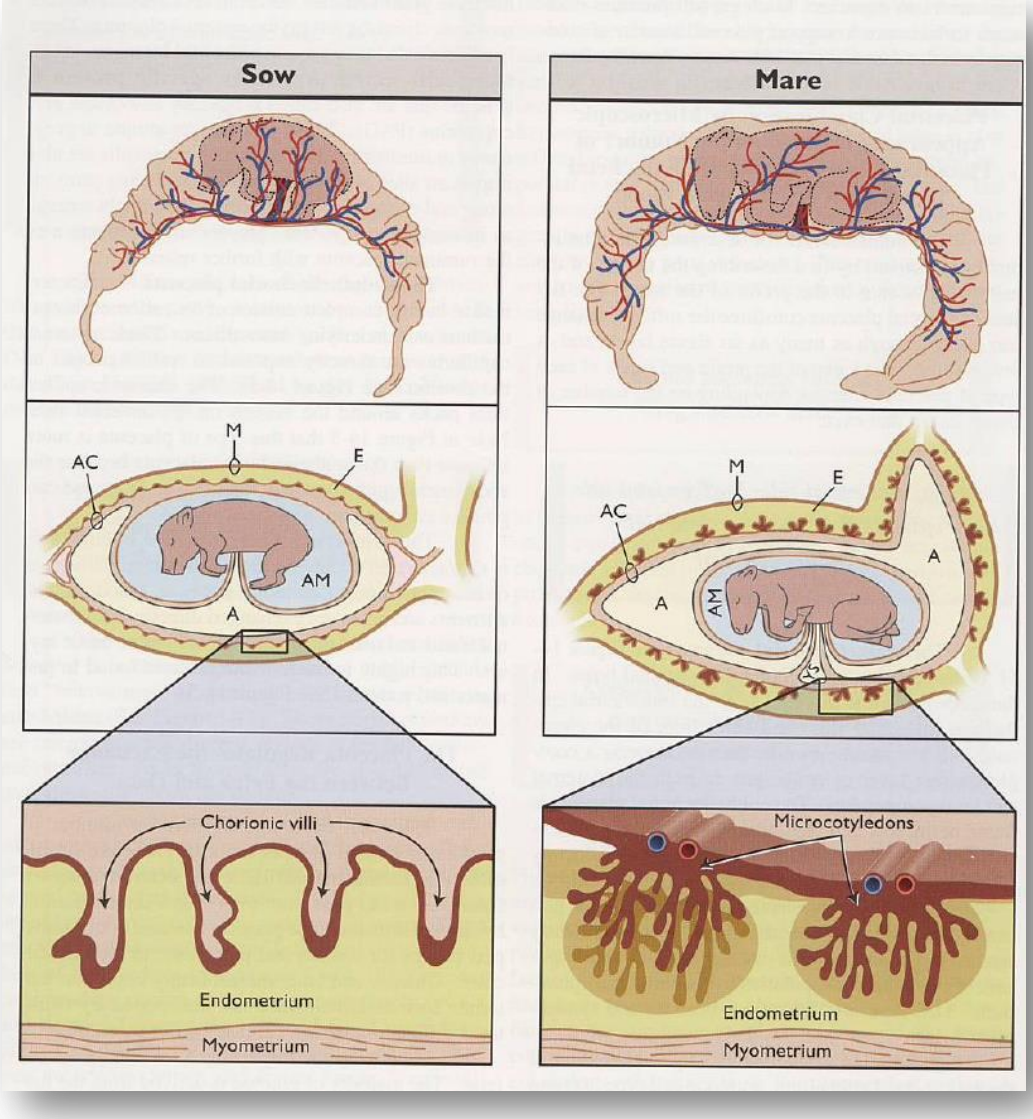


Figure : Simple diffuse placenta

2. Cotyledonary type

- The villi are restricted only into circumscribed areas on the chorio-allantoic membrane called cotyledons.
- Examples: large and small ruminants

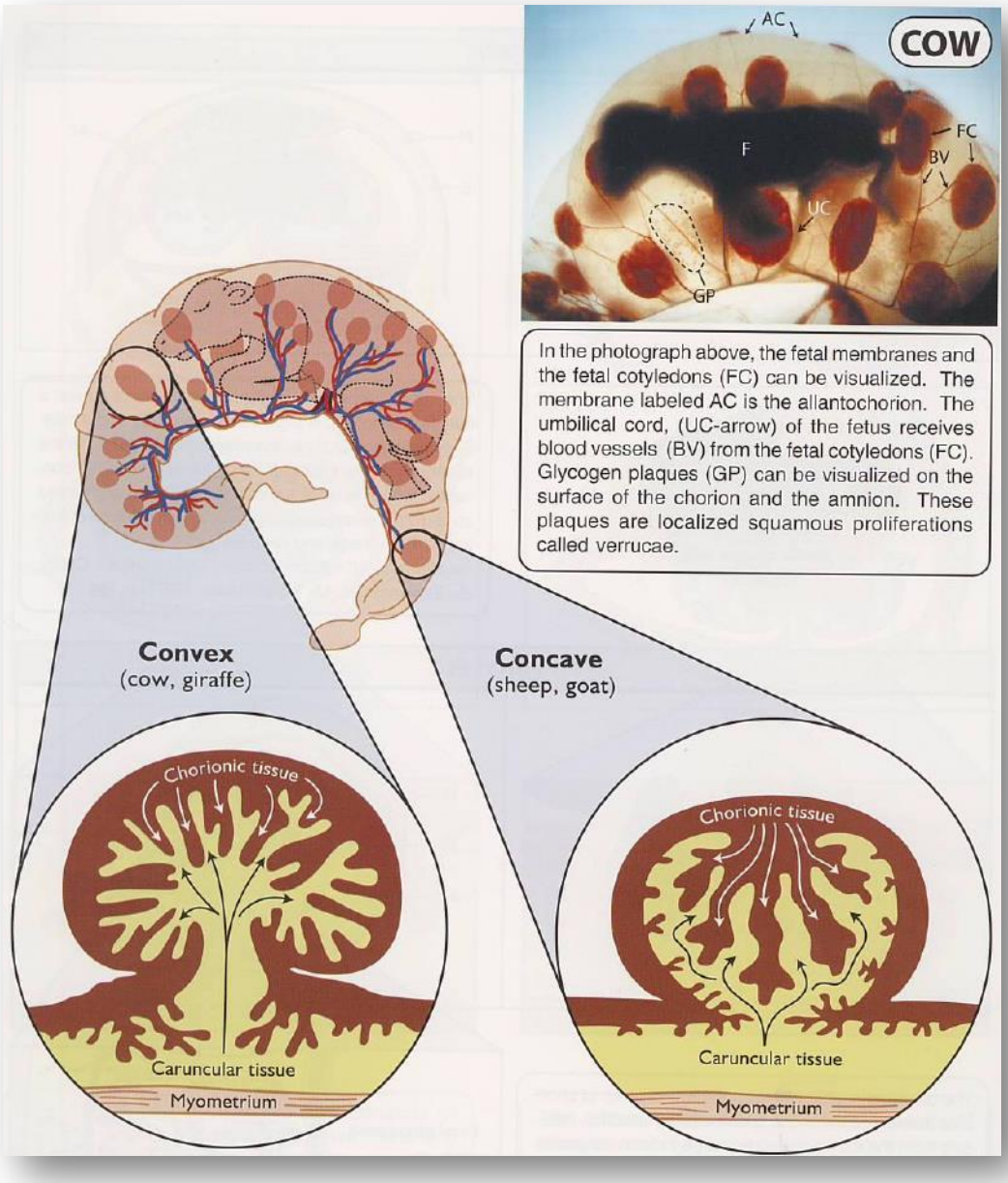


Figure : Cotyledonary placenta

3. Zonary type

- The villi are distributed in the form of a broad encircling belt around the fetal compartment.
- Examples: Bitch and queen

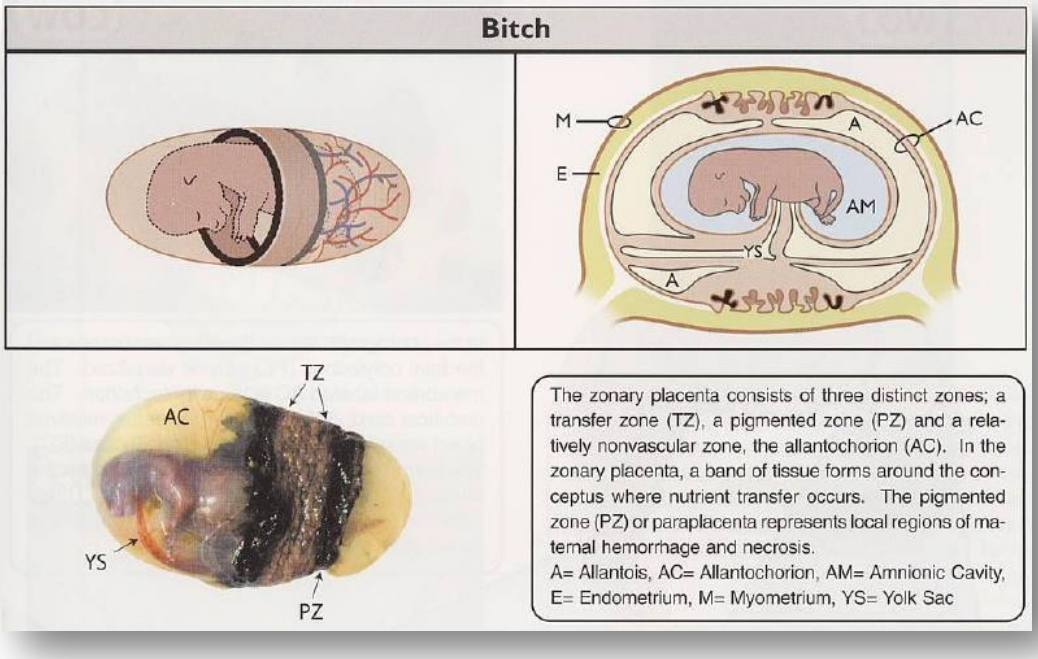


Figure : Zonary placenta

4. Discoidal type

- Villar growth is in the form of one or two discs.
- Examples: primates and rodents

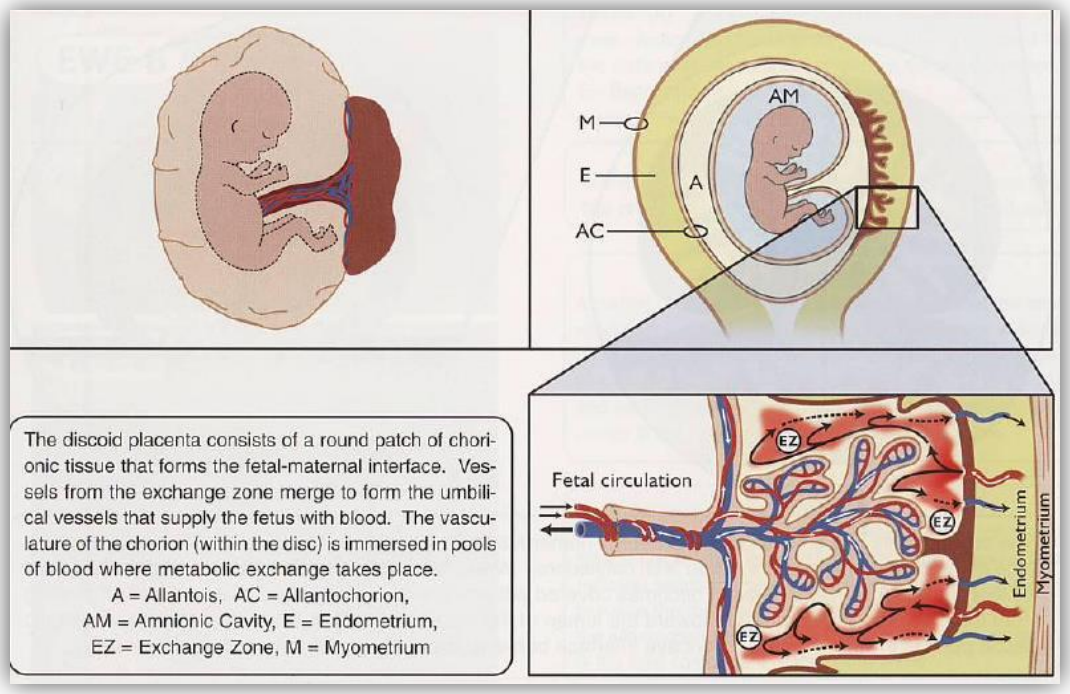
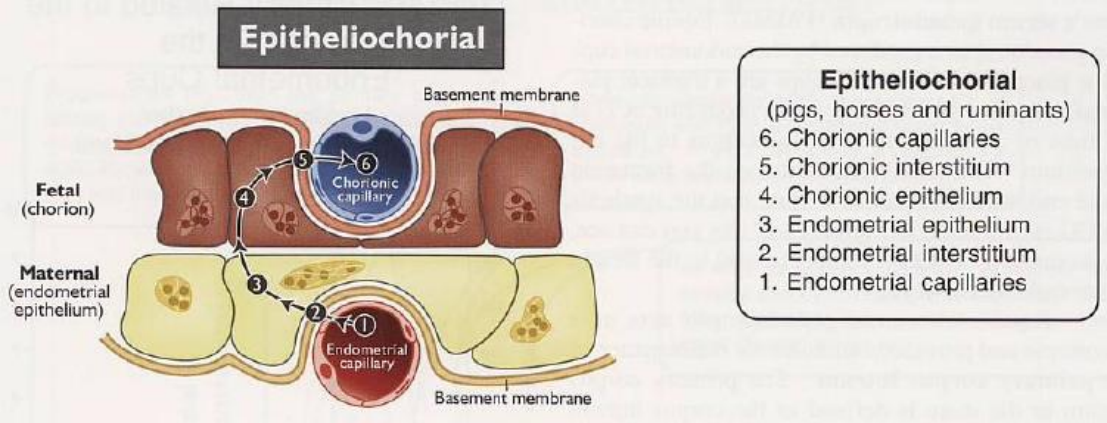


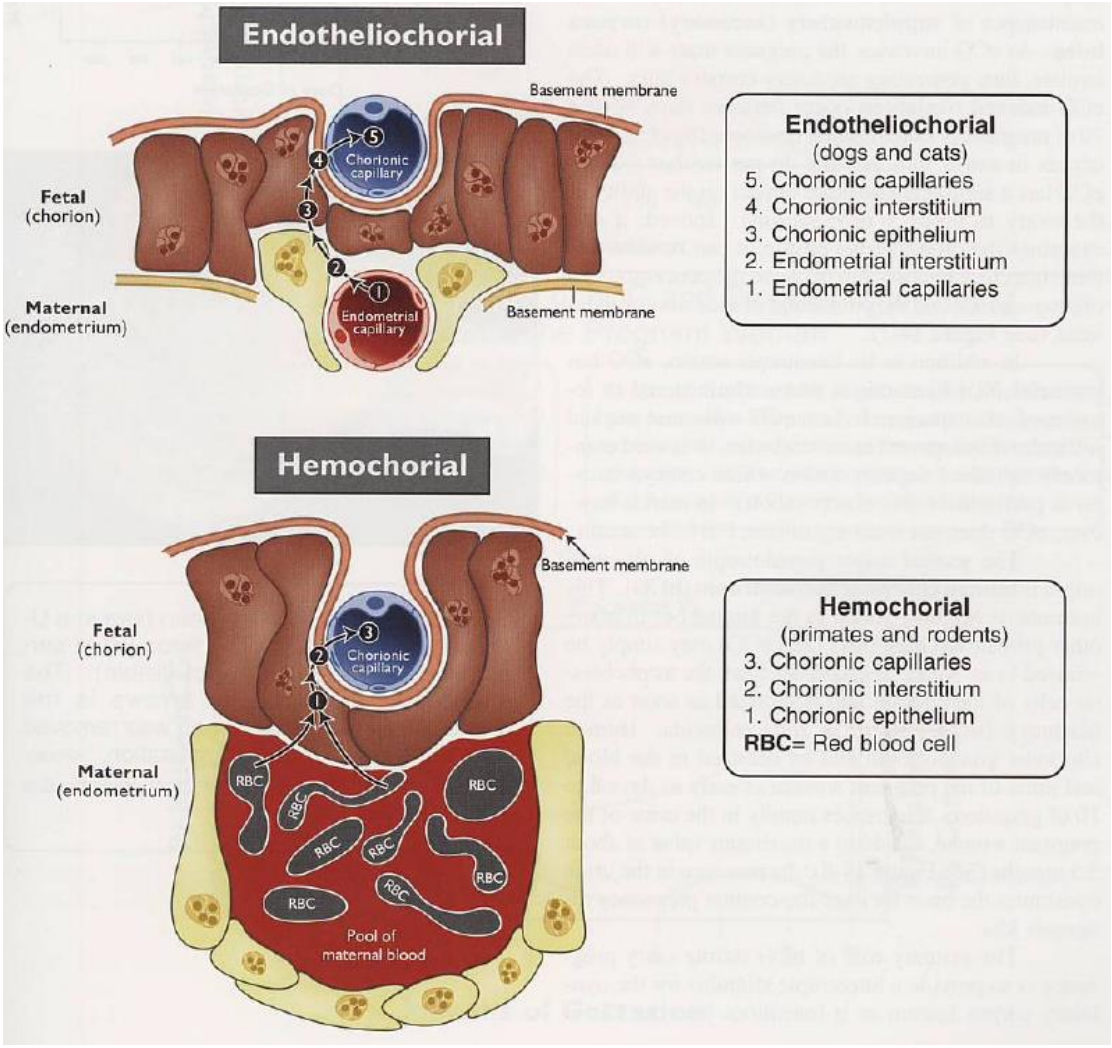
Figure : Discoidal placenta

B. <u>According to the phagocytic activity of the trophoblast</u> (The layer of maternal side facing another of the fetal side, number of layers separating between the fetal and the maternal blood) (HISTOLOGICAL CLASSIFICATION)

1. **Epithelio-chorial**
   - There are six layers separate the fetal and the maternal blood.
   - The trophoblast has no phagocytic activity.
   - Example: Mare, sow, she-camel



2. **Syndesmochorial**
   - Loss of the endometrial epithelium.
   - It is thought to be a physiological condition or pathological due to inflammation.
   - Example: cow, buffalo cow, ewe and doe.
3. **Haemochorial**
   - No layers of the maternal side are found.
   - The trophoblast faces the maternal blood.
   - Example: primates and rodents.
4. **Endotheliochorial**
   - Endothelium of the maternal side faces the chorion of the fetal side.
   - Example: bitch and queen.
5. **Haemo-endothelial**
   - The blood of the maternal side is separated from that of the fetal side by the endothelium of the trophoblastic core.
   - Example: some rodents as Guinea pig.



THE FETAL FLUIDS

- The fetal fluids in pregnant dams include the allantoic fluid and the amniotic fluid.
- The allantoic fluid is watery and pale yellow in color, while the amniotic fluid is bluish and has lubricant properties.

Functions of the fetal fluids

1. Act as a hydrostatic anti-concussion bag which protects the fetus against the external pressure and trauma.
2. Protects the fetus against hyperthermia.
3. Provides an opportunity for even fetal growth from both extremities.

4. Allows free movement of the fetus inside the uterus so allows it to maintain normal presentation, position and posture at parturition.
5. The allantoic fluid has antiseptic characters, while the amniotic fluid acts as a lubricant during parturition.

Characters of the fetal fluids during gestation

A. Changes in amount

- Throughout gestation, there is a progressive increase in the amount of the intrauterine liquid with more rapid increase occurring on three phases:
  - First at two months after conception.
  - Second at mid gestation.
  - Third at end of second or beginning of third trimester of gestation.
- The allantoic fluid increases at the first and the last trimester, while the amniotic fluid increases during the intervening period.
- At about the 5^{th} month of gestation, there is about 5 liters of fetal fluids in the uterus which increases to reach 20 liters at term. Two thirds of this amount is allantoic fluid and the other third is amniotic.
- At term, the weight of the fetal fluids accounts for 25% of the total weight of the gravid uterus.

B. Changes in constituents and appearance

- Both, the allantoic and the amniotic fluids are similar in appearance in the first half of gestation being clear, watery colorless liquids initially then acquire pale straw yellow color.
  - The yellow color is due to the urinary excretions of the fetal kidneys which reach the allantoic cavity via the urachus and the amniotic cavity via the urethra.
- During the later half of gestation, little changes occur:
  - The yellow color of the allantoic fluid intensifies and it acquires the urinepherous odor due to accumulation of nitrogenous waste products.

- The amniotic liquid becomes turbid grayish white in late gestation and is high in protein content.

- The volume of the amniotic liquid is steady in late gestation due to fetal drinking activity.
- The origin of the amniotic fluid is the amniotic sac, fetal skin, nasopharynx and digestive tract. The swallowed amniotic fluid forms the meconium.

Hippomans (foal bread)

- These are rubber-like, semisolid irregular shaped masses floating in the allantoic fluid.
- These masses are thought to be fetal hairs, meconium and sloughed uterine material coated by some salts.

Summary of hormonal regulation of gestation

1. **Pituitary gland**

- Hypophysectomy in early pregnancy causes termination of pregnancy (ACTIVITY, NET SEARCH).
- Hypophysectomy in late pregnancy causes failure of lactation after parturition (ACTIVITY, NET SEARCH).

2. **Ovaries**

- In most animal species, the corpus luteum secrets progesterone which maintains pregnancy for up to parturition except in mare and ewe.
- In ewe, the placenta takes the role of progesterone secretion as early as day 50 of pregnancy.
- Lutectomy in cows is followed by abortion even in the 8^{th} month of gestation.

3. **The placenta**

- Generally the placenta secrets substances that can:
    - Stimulate ovarian function
    - Maintain pregnancy
    - Influence fetal growth
    - Stimulate mammary function

  - Assist in parturition
- The placenta secrets estrogens, progesterone and in mare and woman secrets pituitary-like gonadotropins, humane chorionic gonadotropin "hCG" and pregnant mare serum gonadotropin "PMSG" which has another name, equine chorionic gonadotropin "eCG".
- The placenta in animals like ewe, cow, mouse and rat secrets a substance called "placental lactogens or Somatomammotropin" which is believed to be similar to growth hormone.
  - The placental lactogens may stimulate fetal growth or may enhance development and secretory activity of the mammary gland of the pregnant dam.
  - A possible sire effect is proposed to govern the degree at which the fetus can produce placental lactogen.

The umbilical cord

- It is a cord arising from the connecting stalk towards the lesser curvature of uterus.
- It is formed of mesodermal cells which will be transformed to a jelly-like substance called "wharton's jelly".
- It is covered by a layer of the aminon and contains blood vessels.
- Its length is about 10 cm in ewe, 35 cm in cow and 70-100 cm in mare.
- The cord is severed naturally as the fetus is delivered in cow, but the dam severs it in bitch and queen.
- In mare, the cord is separated only from the newborn foal when the dam gets up after foaling.
- Due to the long cord in mare, it is possible for the cord to be twisted around the neck of the freely swimming fetus in the amniotic fluid. If the twist is severe, the fetus may die.