



Volgograd state medical university

Department of histology, embryology, cytology

Implantation.

Blastula, gastrula, neurula.

for the 1st course

English medium students

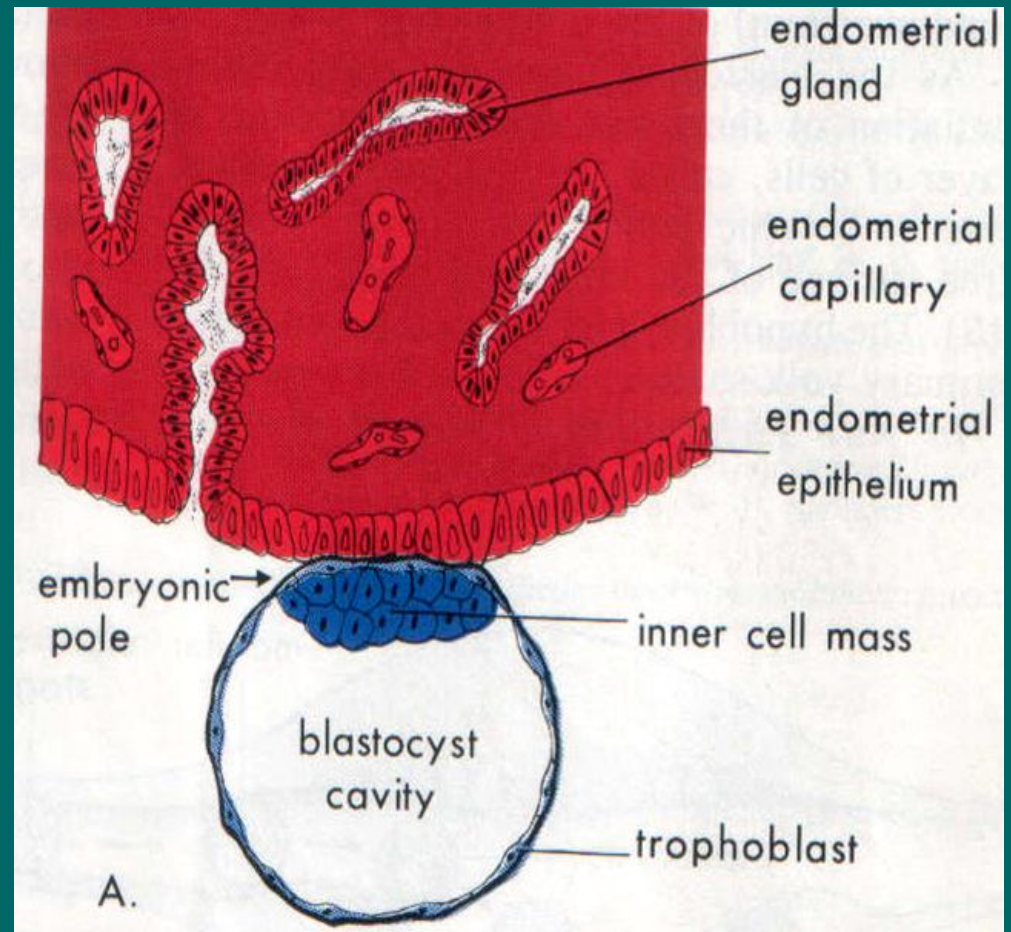
Objectives

- To demonstrate the formation of blastocyst and its implantation in the endometrium at the end of the 1st week of prenatal life.
- To explain the development of the bilaminar and trilaminar germ disc during the 2nd and the 3rd week of prenatal development.
- To assess the significance of neurulation in the human embryo.

Developmental periods (Prenatal life)

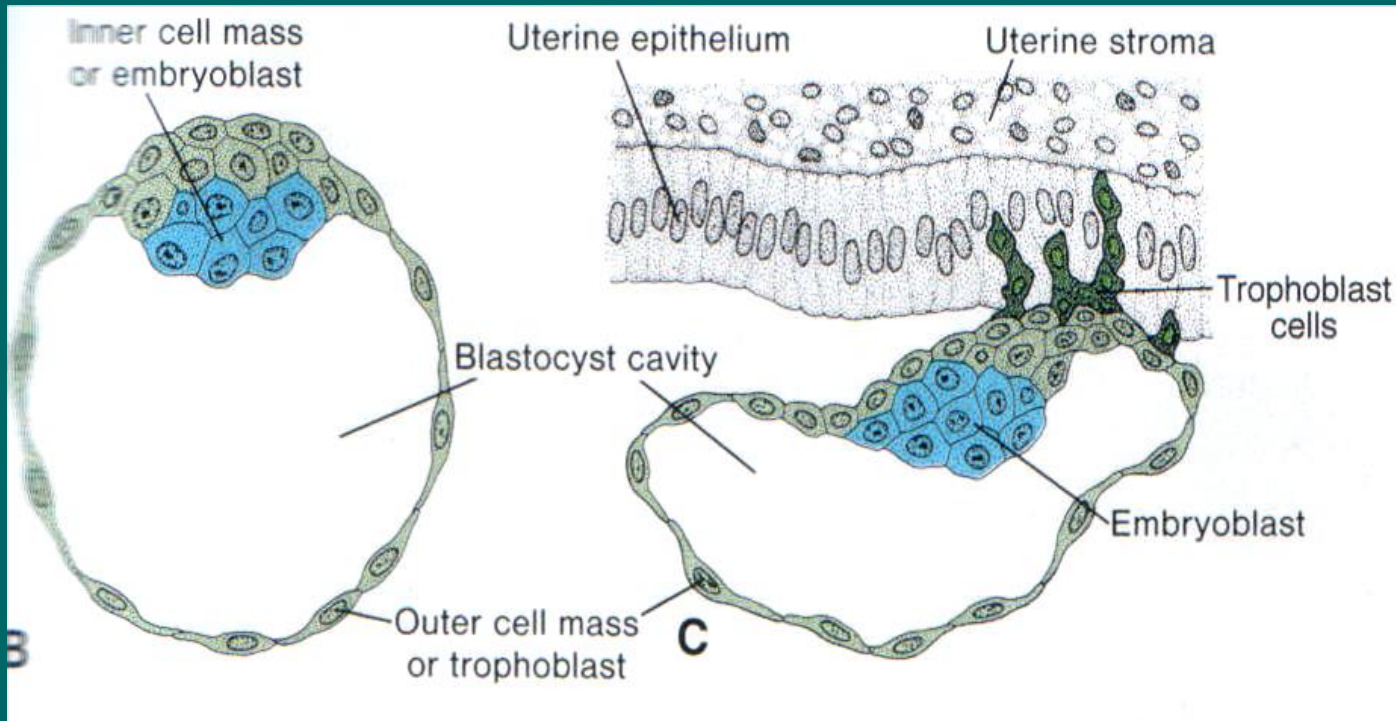
- ✦ Pre-embryonic period or germinal period: from time of fertilization to end of 3rd week – cleavage, morula, blastula, gastrulation, differentiation of the germ layers.**
- ✦ Embryonic period: 4th to 8th week inclusive - (histogenesis, organogenesis).**
- ✦ Fetal period: 9th week to birth - further differentiation of organs and tissues.**

Early stage of implantation (the 6th day). The trophoblast is attached to the endometrial epithelium at the embryonic pole of the blastocyst.



By the 4th day the fluid-filled spaces fuse to form a single large space known as blastocyst cavity or blastocele. This converts morula into a blastocyst. The inner cell mass (future embryo) projects into the blastocyst cavity and the trophoblast forms the wall of the blastocyst. The blastocyst lies free in the uterine secretion for about 2 days. On about 5th day zona pellucida disappears and the blastocyst attaches to the maternal uterine epithelium on about 6th day.

IMPLANTATION

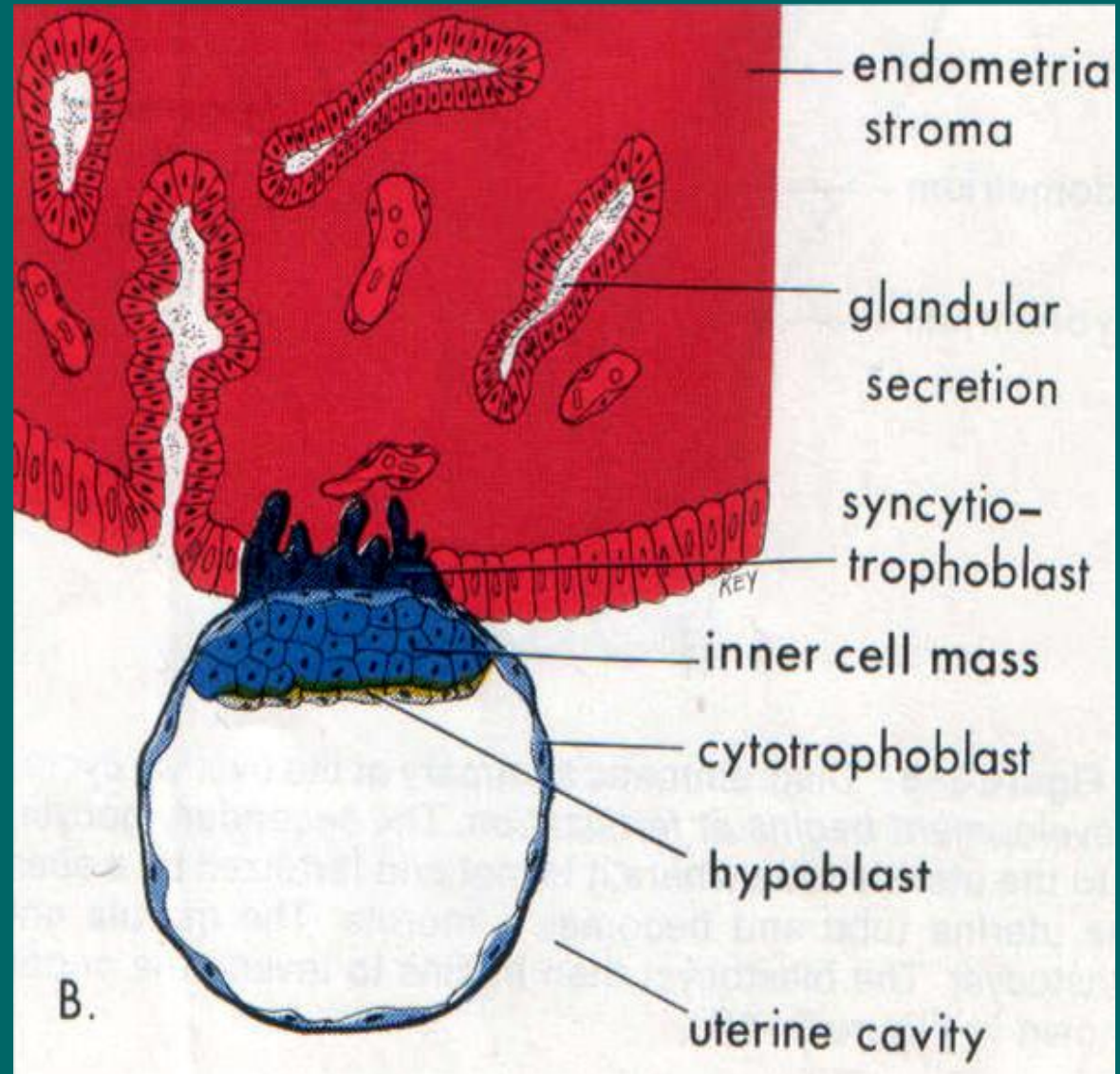


In humans trophoblastic cells over the embryoblast pole begin to penetrate between the epithelial cells of the uterine mucosa about the 6th day. Attachment and invasion of the trophoblast involves integrins expressed by the trophoblast, and the extracellular matrix molecules laminin and fibronectin. These molecules also interact along signal transduction pathways to regulate trophoblast differentiation so that implantation is the result of mutual trophoblastic and endometrial action.

Early Stage of Implantation (7th day).

As invasion of the trophoblast proceeds, two cell layers form in it: an inner cytotrophoblast (cellular) and an outer syncytio-trophoblast (syncytial multinucleated mass).

The finger-like processes of syncytiotrophoblast penetrate the endometrial epithelium, begin to destroy adjacent endometrial cells and invade endometrial stroma. By the end of the 1st week the blastocyst is superficially implanted in the endometrium.

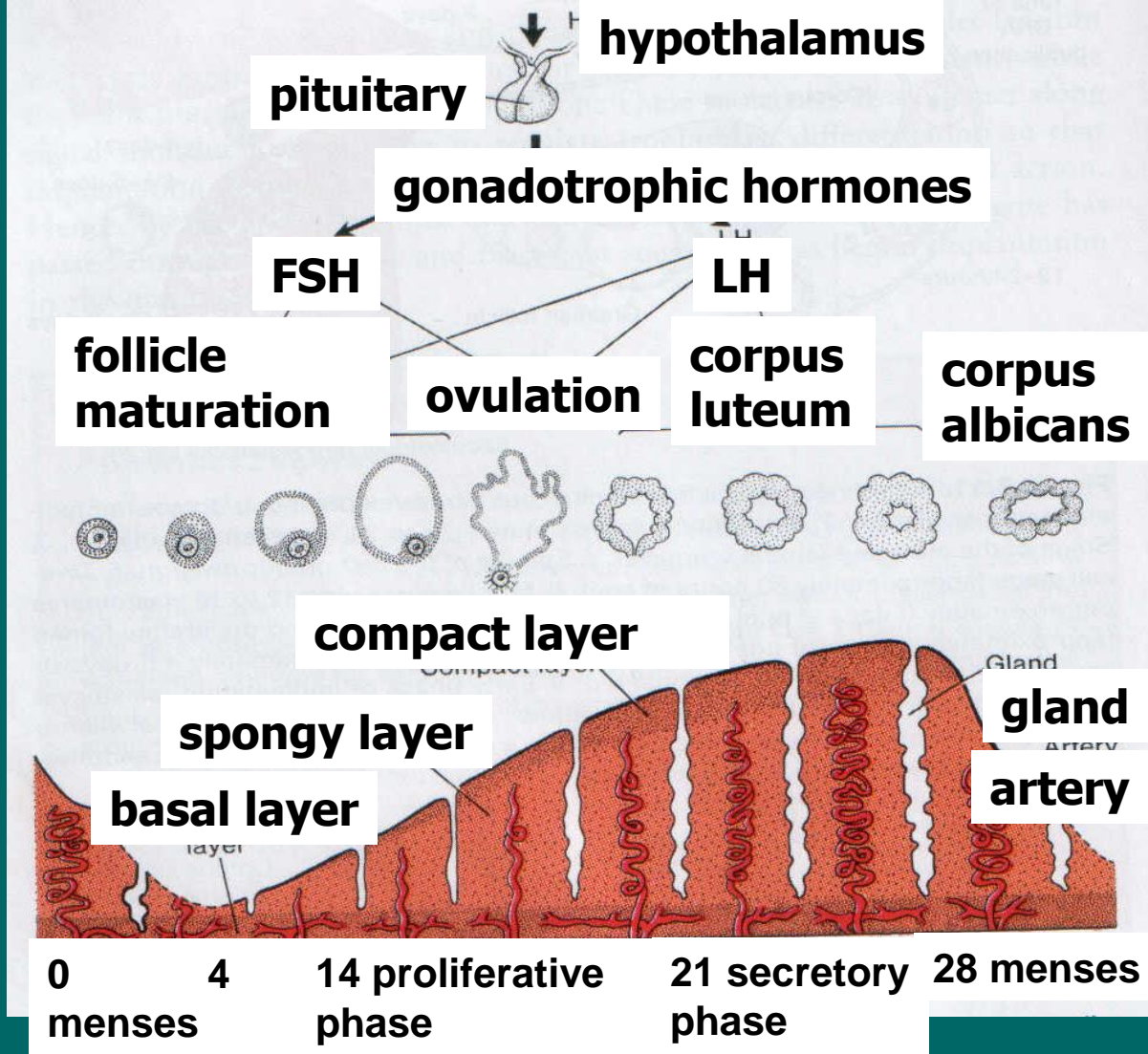


By the end of the 1st week:

- ✿ **the human zygote has passed through the morula and blastocyst stages,**
- ✿ **the blastocyst has begun implantation in the uterine mucosa.**

From puberty (11-13 years old) until menopause (45-50 years), the endometrium undergoes changes in a menstrual cycle of approximately 28 days under hormonal control of the ovary passing through 3 stages: menstrual, proliferative & secretory phases.

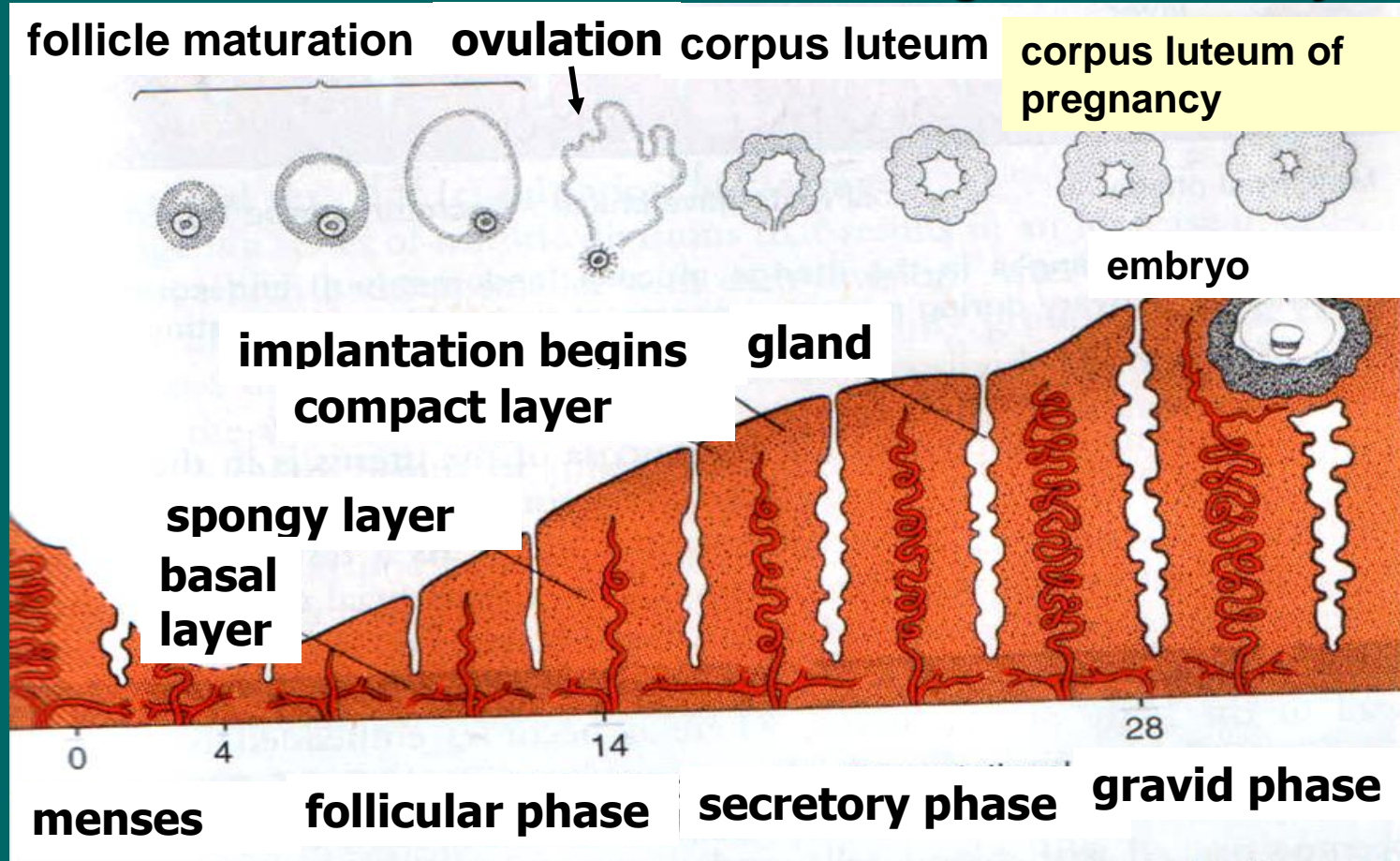
Changes in the Endometrium Correlated with Changes in the Ovary.



The secretory phase begins 2-3 days after ovulation in response to progesterone secreted by the corpus luteum in the ovary. If fertilization does not occur, shedding of the endometrium (compact and spongy layer) marks the beginning of the menstrual phase.

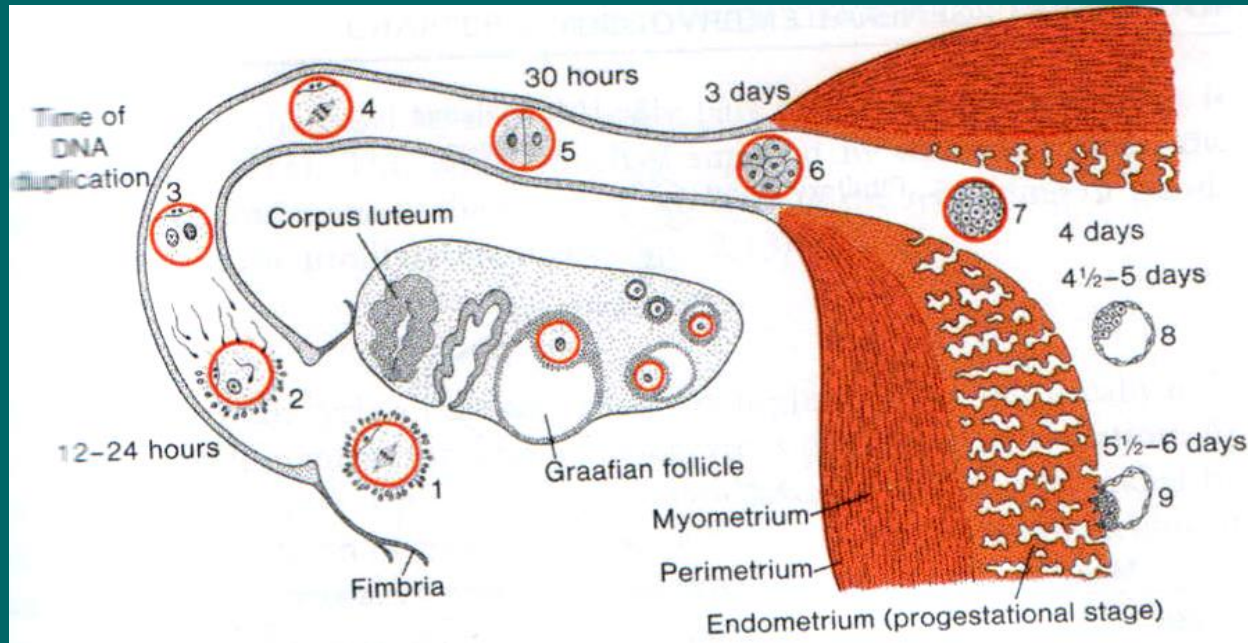
Changes in the Endometrium Correlated with Changes in the Ovary.

If fertilization does occur, the endometrium assists in implantation and contributes to the formation of placenta. At the time of implantation, the mucosa of the uterus is in the secretory phase.



During secretory phase uterine glands and arteries become coiled and the tissue becomes succulent. As a result, three distinct layers can be recognized in the endometrium: a superficial compact layer, an intermediate spongy layer and a thin basal layer. Implantation of the blastocyst has caused a development of a large corpus luteum of pregnancy. Secretory activity of the endometrium increases gradually as a result of large amounts of progesterone produced by the corpus luteum of pregnancy.

Normally the human blastocyst implants in the in the uterus along the posterior or anterior wall of the body of the uterus where it becomes embedded between the opening of the glands.



The 1st week of human development: 1- oocyte immediately after ovulation, 2 – fertilization (12-24 hours after ovulation), 3- stage of the male and female pronuclei, 4 – spindle of the 1st mitotic division, 5 – 2-cell stage (30 hours of age), 6 – morula with 12-16 blastomeres, 7 – advanced morula stage reaching the uterine lumen (4 days of age), 8 – early blastocyst (4.5 days of age), 9 – implantation (blastocyst of 6 days of age). The ovary shows stages of transformation from the primary follicle through Graafian follicle to a corpus luteus. The endometrium is shown in a secretory phase.

SUMMARY:

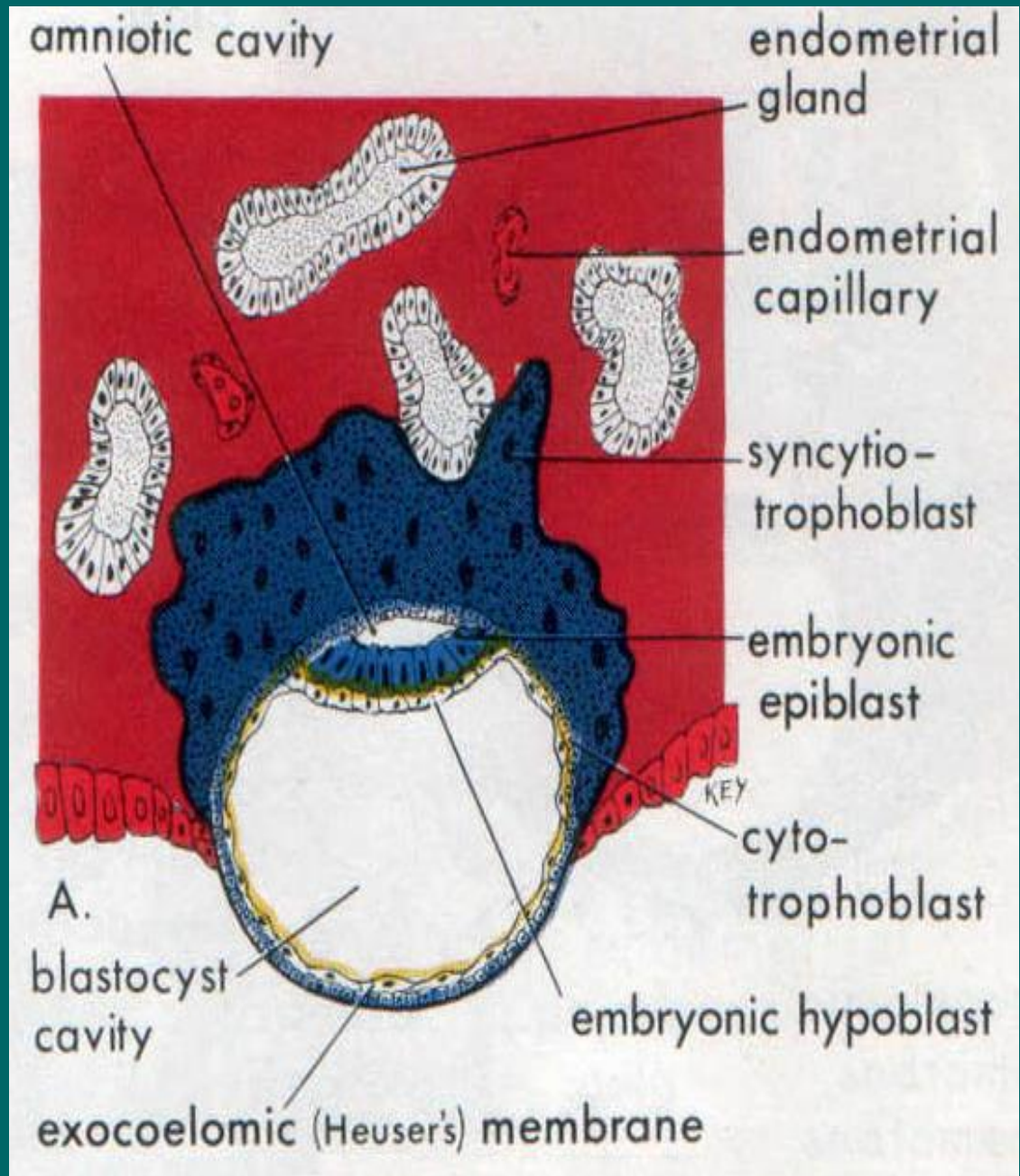
- 1) The results of fertilization are:**
 - ✦ Restoration of the diploid number of chromosomes,**
 - ✦ Determination of chromosomal sex,**
 - ✦ Initiation of cleavage.**
- 2) Cleavage is a series of mitotic divisions that result in an increase in cells, blastomeres, which become smaller with each division.**
- 3) After 3 divisions blastomeres undergo compaction to become a tightly grouped ball of cells with inner and outer layer. Compacted blastomeres divide to form a 16-cell morula.**
- 4) As the morula enters the uterus on the 3rd-4th day after fertilization, a cavity begins to appear, and the blastocyst forms.**
- 5) The inner cell mass, which formed at the time of compaction and will develop into the embryo proper, is at one pole of blastocyst. The outer cell mass, which surrounds the inner cells and blastocyst cavity, will form the trophoblast.**

Clinical correlations:

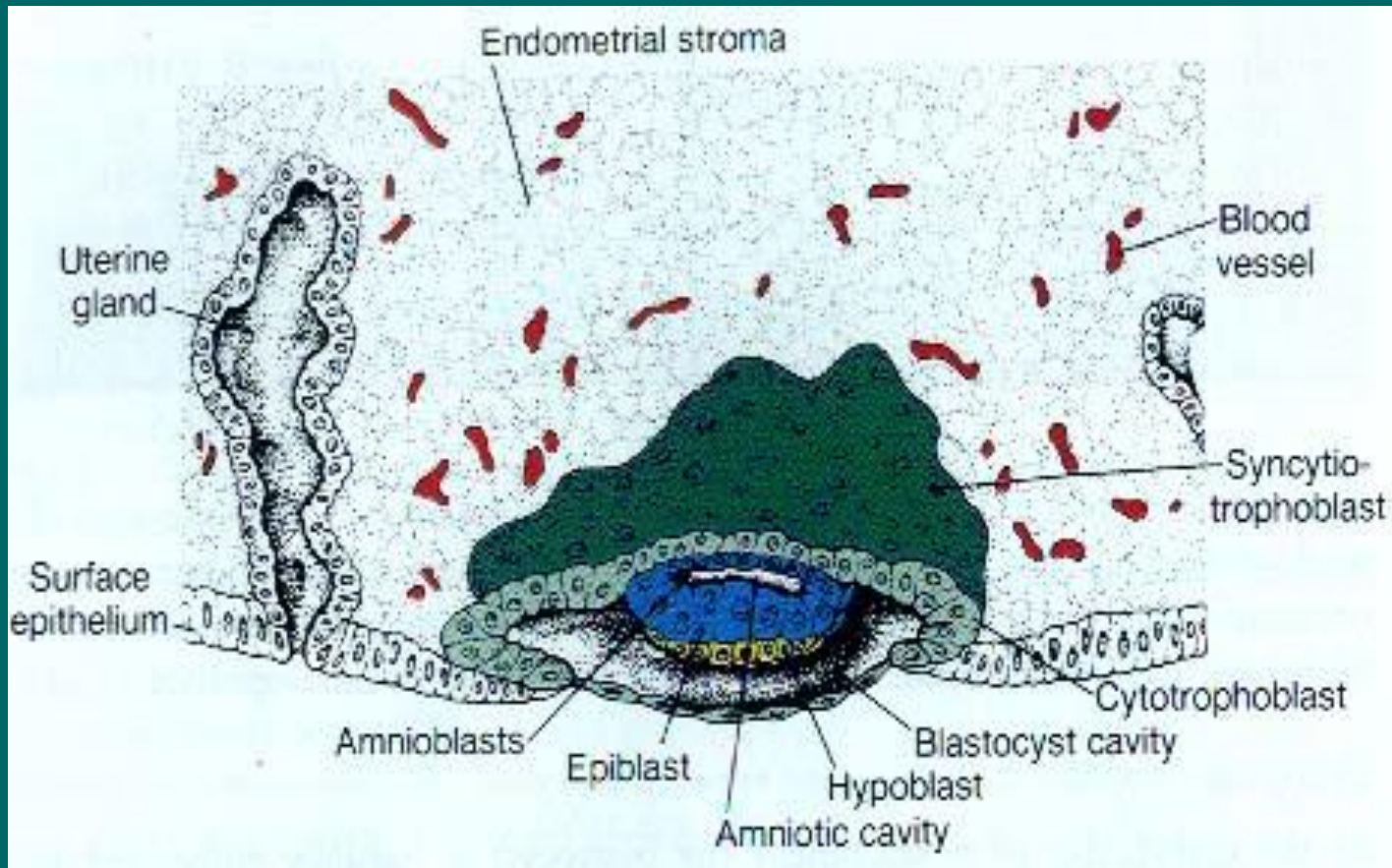
- 1) In vitro fertilization of human ova and cleavage of the zygote have been achieved.**
- 2) It is done in infertile women with occluded uterine tubes with intention of establishing pregnancy by transferring a morula, cultured in vitro, in the uterus.**
- 3) The major problem of this technique is to synchronize the endometrium and the cleavage stage of the zygote, because in vitro development is 20-30% retarded in the development as compared with normal in vivo development.**
- 4) About 15% of all zygotes result in detectable spontaneous abortion, but this estimate is undoubtedly low because the loss of zygotes during the 1st week is thought to be high.**
- 5) The actual rate is unknown as the women do not know they are pregnant at this early stage. Clinicians often have a patient who states that the last menstruation period was delayed by 1 or 2 weeks and then the menstrual flow was unusually profuse. Very likely such a patient has an early spontaneous abortion.**
- 6) Early abortion occurs for a variety of reasons, one being the presence of chromosomal abnormalities in the zygote. This early loss of zygotes, once called pregnancy wastage, appears to represent a disposal of abnormal conceptuses that could not develop normally, i.e. a natural prenatal screening of embryos.**

Week 2. Day 8. Size of the conceptus – 0.1 mm

At the 8th day the blastocyst is partially embedded in the endometrial stroma. Cells of the cytotrophoblast divide and migrate into syncytio-trophoblast where they fuse and lose their individual cell membranes. Small spaces appear between the cells of the inner cell mass (embryoblast), these spaces soon coalesce to form a slit-like amniotic cavity.



Blastocyst partially embedded at 8th day, showing embryoblast and trophoblast



As amniotic cavity forms, changes occur in the embryoblast resulting in the formation of the flattened, essentially circular, embryonic disk. Cells of the embryoblast also differentiate into two layers: a layer of small cuboidal cells adjacent to the blastocyst cavity known as hypoblast; and the layer of high columnar cells adjacent to the amniotic cavity, the epiblast. Cells of both layers form a flat disk and together are known as bilaminar germ disk.

Formation of bilaminar germ disc:

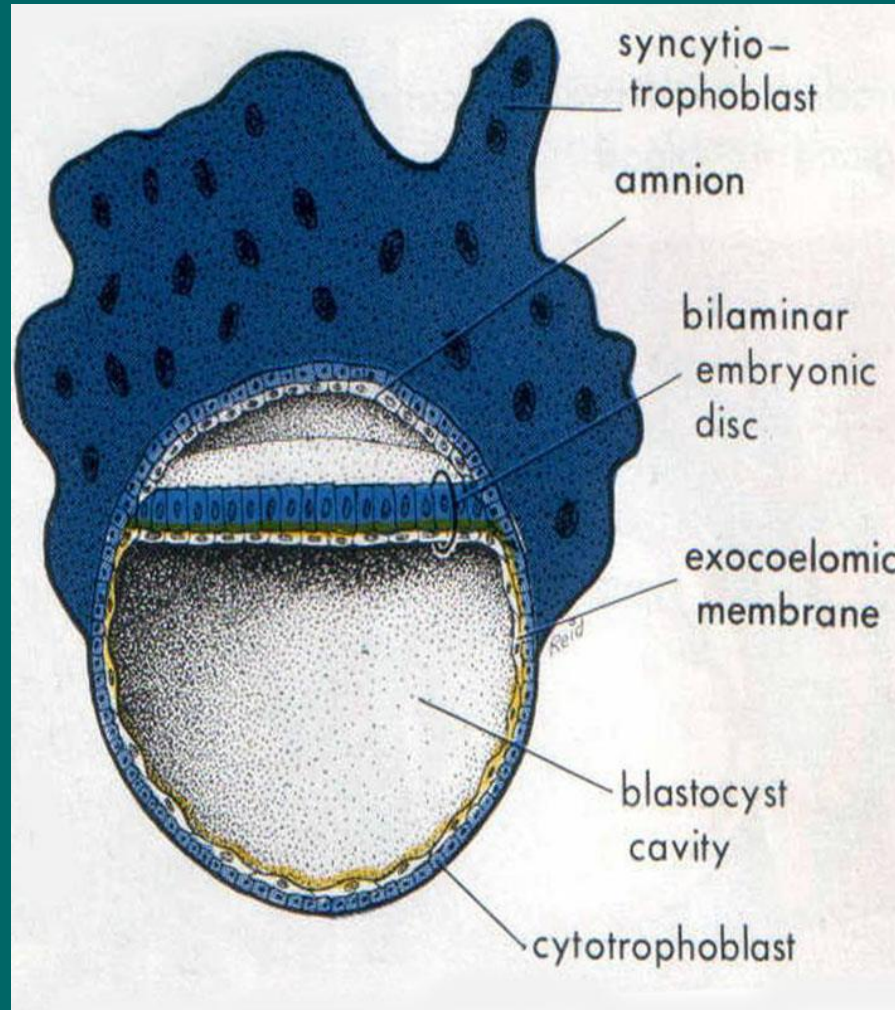
Beginning of 2nd week

✿ Further embedding of blastocyst

✿ Inner cell mass → epiblast
→ hypoblast

✿ Outer cell mass → cytotrophoblast
→ syncytiotrophoblast

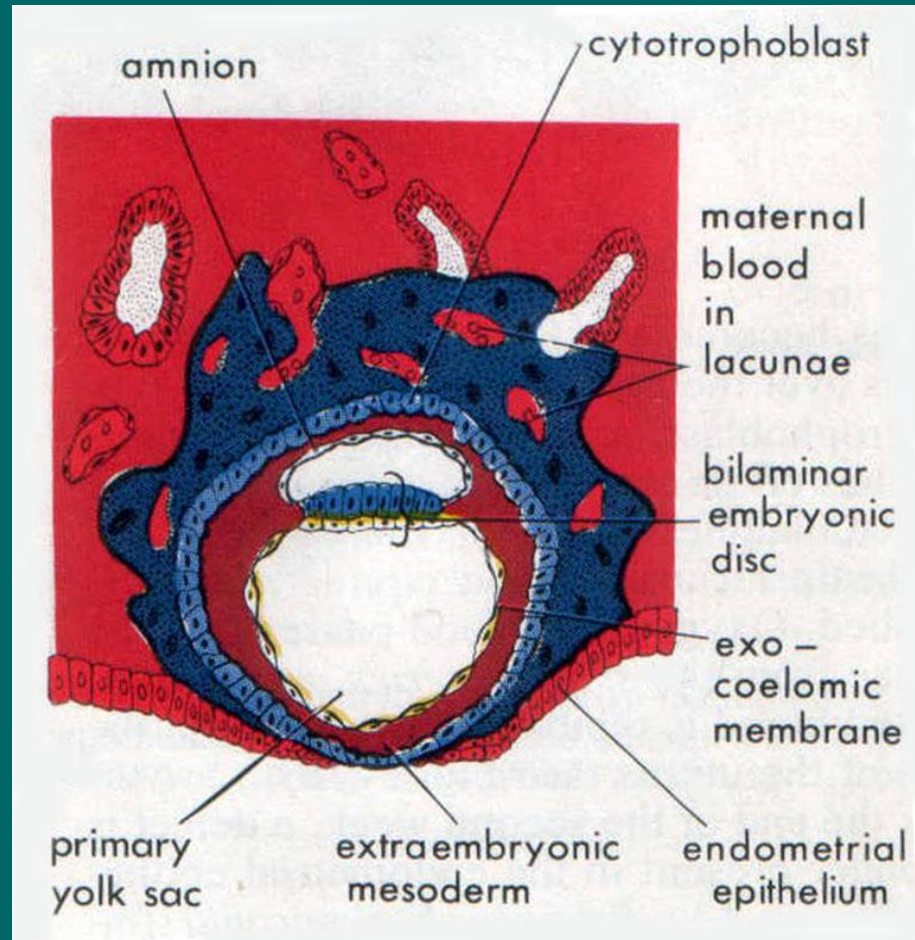
Human blastocyst. Day 8.



As the amniotic cavity enlarges, a thin epithelial roof, the amnion, forms from the cytotrophoblastic cells. The epiblast forms the floor of the amniotic cavity and is continuous peripherally with the amnion.

Human Blastocyst. Day 9.

The spaces or lacunae appear in the syncytiotrophoblast. They soon begin to communicate with the endometrial blood vessels and glands.



Epiblast cells adjacent to the cytotrophoblast are called amnioblasts. Together with the rest of the epiblast they line the amniotic cavity.

Concurrently other cells probably originating from hypoblast form a thin exocoelomic membrane (Heuser's membrane) which encloses, together with the hypoblast, a cavity known as the primary (primitive) yolk sac¹⁷ or exocoelomic cavity.

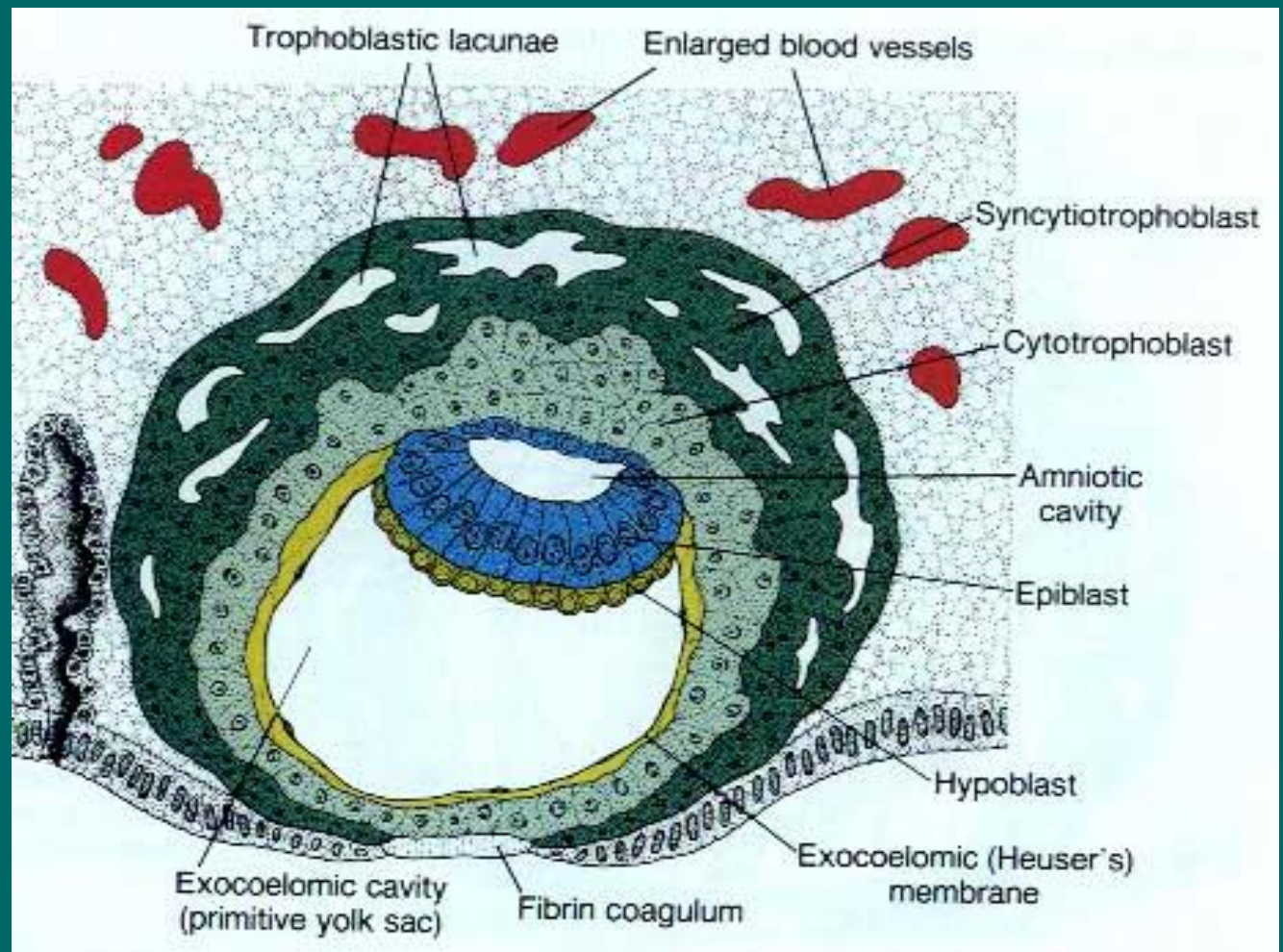
Amniotic cavity & amnion (9th day)

- ✿ **Small cavity within epiblast**
- ✿ **Lined by epiblast and amnioblast cells**

Primary yolk sac (exocoelomic cavity)

- ✿ **Cavity facing hypoblast**
- ✿ **Lined by Heuser's membrane from hypoblast.**

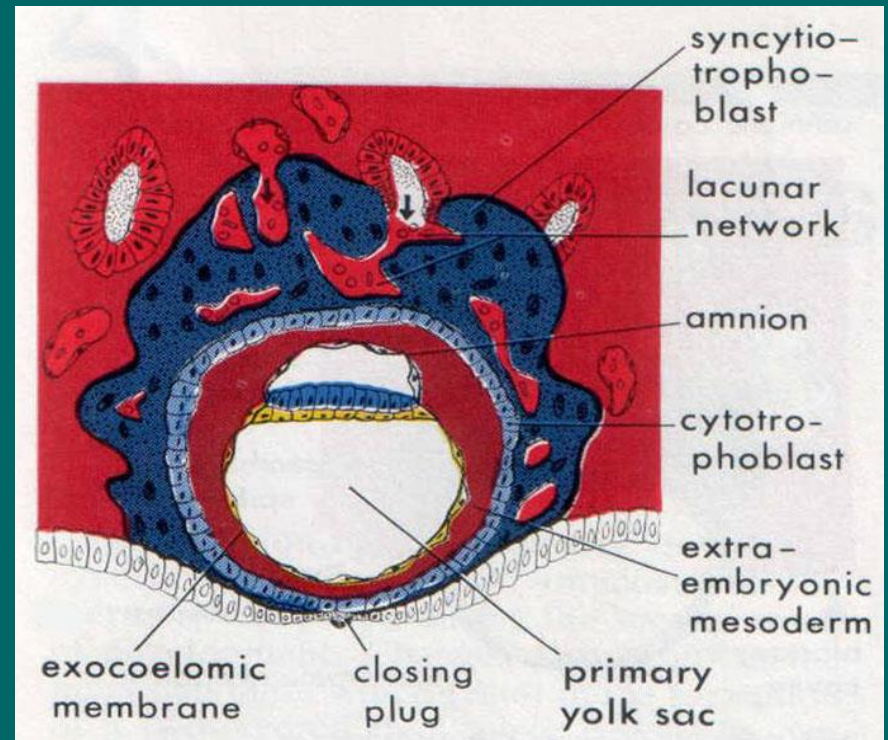
The Human Blastocyst, 9th day. Bilaminar germ disk in the lacunar stage.



The blastocyst is more deeply embedded in the endometrium, and the penetration defect in the surface epithelium is closed by a fibrin coagulum. The trophoblast shows considerable progress in development, particularly at the embryonic pole, where vacuoles appear in the syncytium. When these vacuoles fuse, they form large lacunae, and this phase of trophoblast development is known as the lacunar stage. The lacunar networks are the primordia of the intervillous spaces of the placenta.

Implanted human blastocyst. 10 days.

Trophoblastic lacunae at the embryonic pole are in open connection with maternal sinusoids in the endometrial stroma.

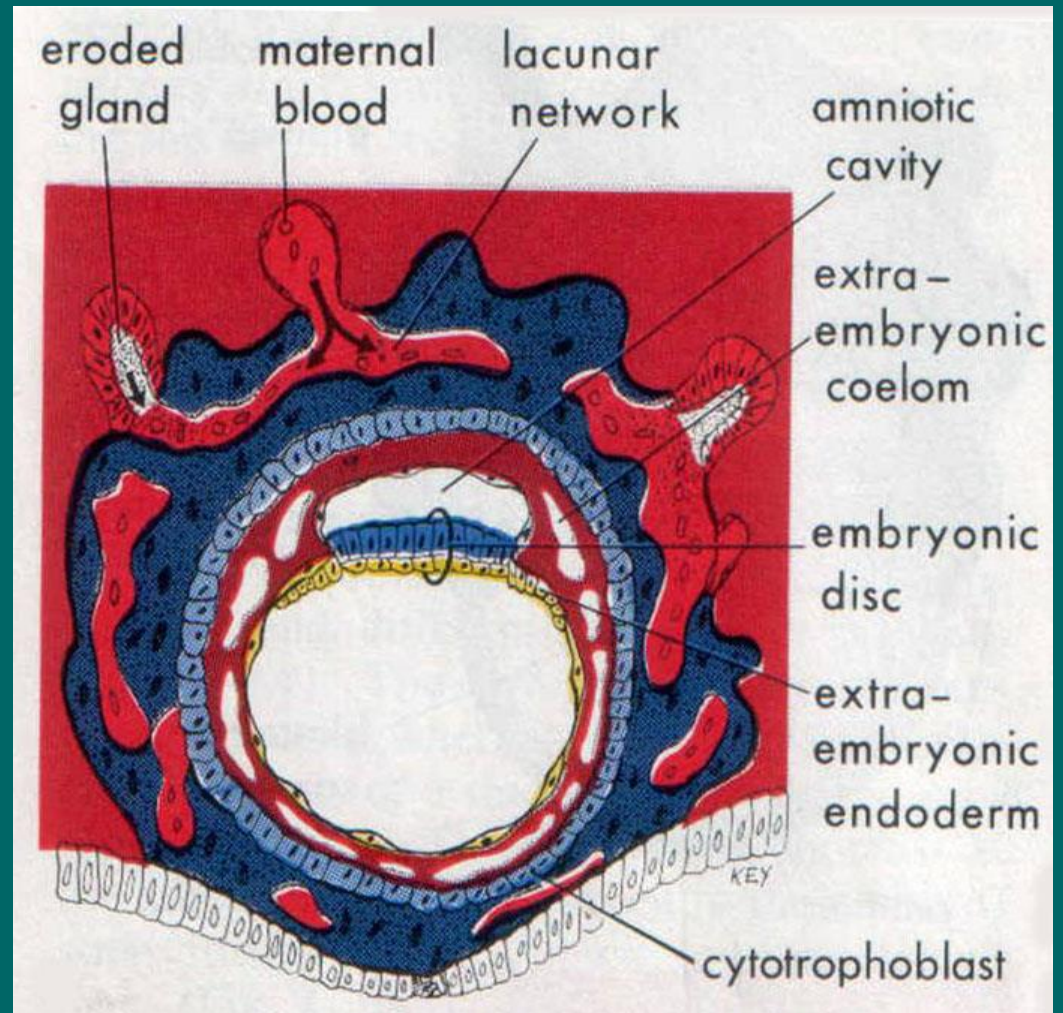


The endometrial capillaries around the implanted embryo become dilated to form sinusoids and some of them become eroded by syncytiotrophoblast. Maternal blood now seeps into the lacunar networks and soon begins to flow slowly through the lacunar system, establishing a primitive uteroplacental circulation. When maternal blood flows into the syncytiotrophoblastic lacunae, its nutrients become available to the embryonic tissues over the very large surface of the syncytiotrophoblast. As both arterial and venous vessels come into communication with the syncytiotrophoblastic lacunae, blood circulation is established.

A new population of cells appears between the inner surface of the cytotrophoblast and the outer surface of the exocoelomic cavity. These cells, derived from the yolk sac cells, form a fine loose connective tissue, the extraembryonic mesoderm.

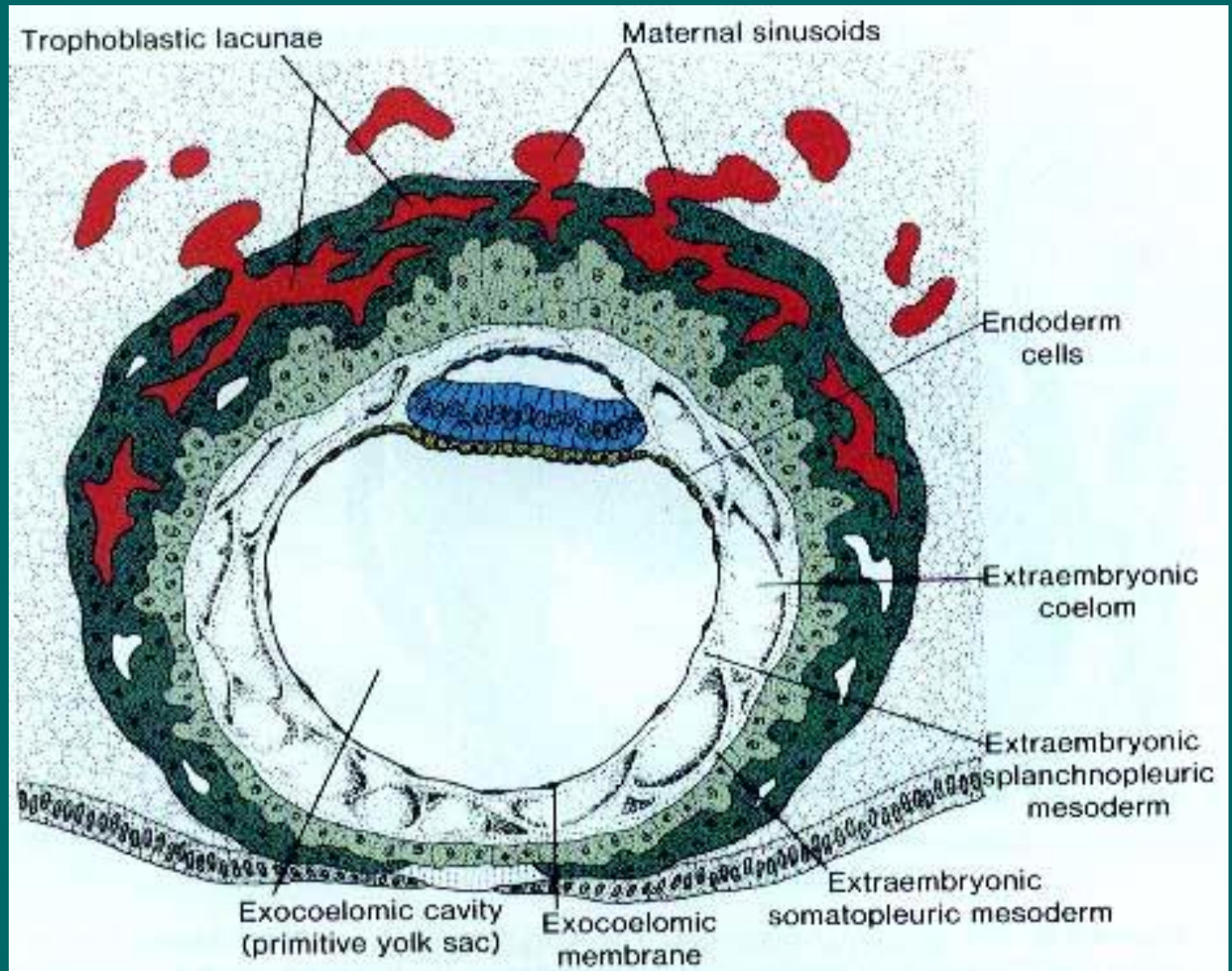
Implanted human blastocyst. 12 days.

A defect is no longer present in the endometrial epithelium: the blastocyst is completely embedded in the endometrial stroma. The blastocyst now produces a slight protrusion into the lumen of the uterus.



Extraembryonic mesoderm eventually fills all the space between the trophoblast externally and the amnion and exocoelomic membrane internally. Soon large cavities appear in it, and when these become confluent, they form a new space known as extraembryonic coelom or chorionic cavity.

Formation of primary or extraembryonic mesoderm between Heuser's membrane and cytotrophoblast at 12th day.



The extraembryonic mesoderm lining the cytotrophoblast and amnion is called the extraembryonic somatopleuric mesoderm; that covering the yolk sac is called extraembryonic splanchnopleuric mesoderm.

Chorion & chorionic cavity

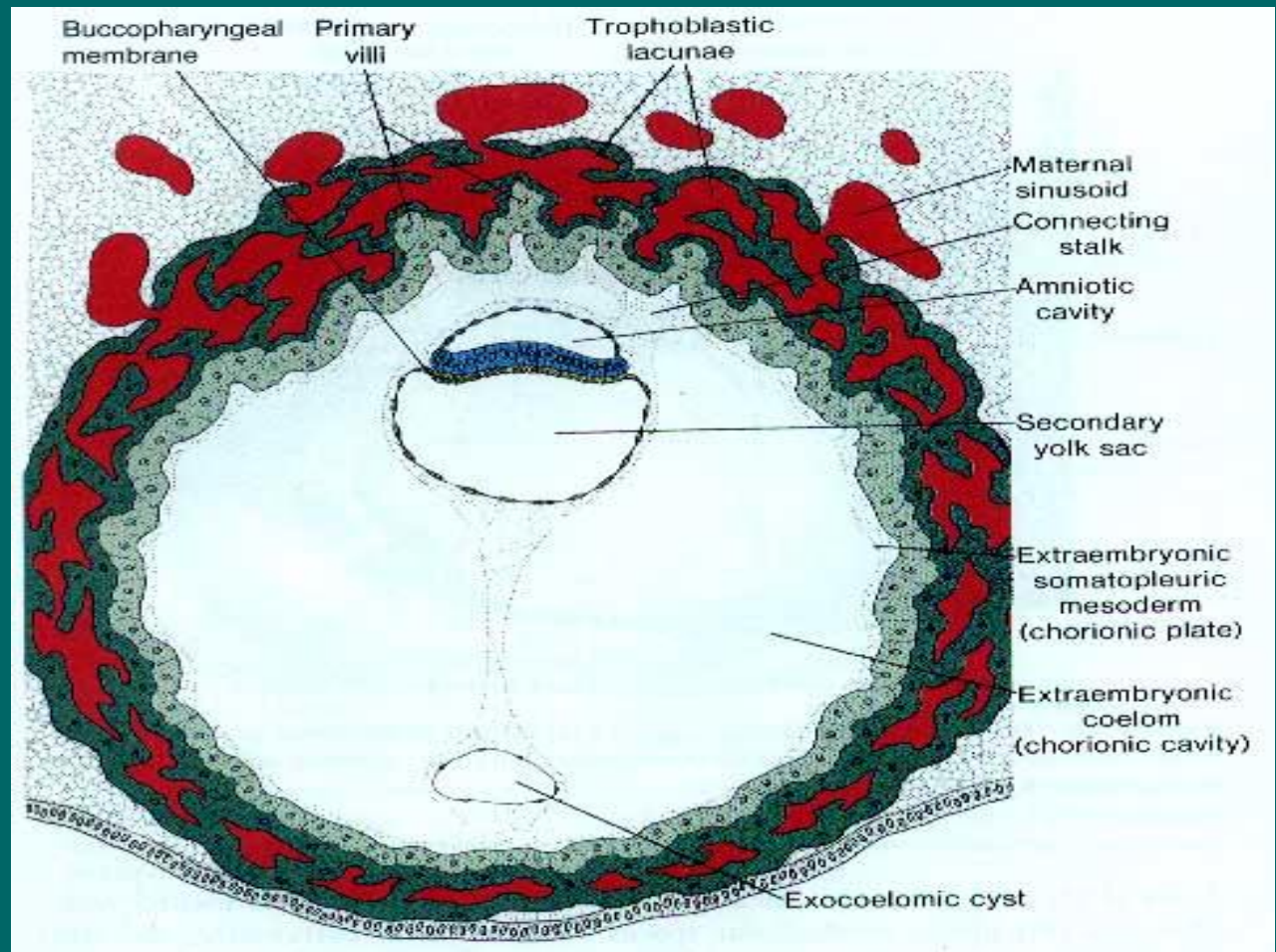
Formation of :

- ✦ **Extraembryonic mesoderm**
- ✦ **Extraembryonic coelom (chorionic cavity)**
- ✦ **Extraembryonic somatopleuric mesoderm**
- ✦ **Extraembryonic splanchnopleuric mesoderm**
- ✦ **Chorion plate**
- ✦ **Connecting stalk**

Clinical Correlations:

- ✿ **By the 13th day of development the surface defect in the endometrium has usually healed.**
- ✿ **Occasionally bleeding occurs at the implantation site as a result of increased blood flow into the lacunar space.**
- ✿ **Since this bleeding occurs near the 28th day of the menstrual cycle, it may be confused with normal menstrual bleeding and so cause inaccuracy in determining the expected delivery date.**

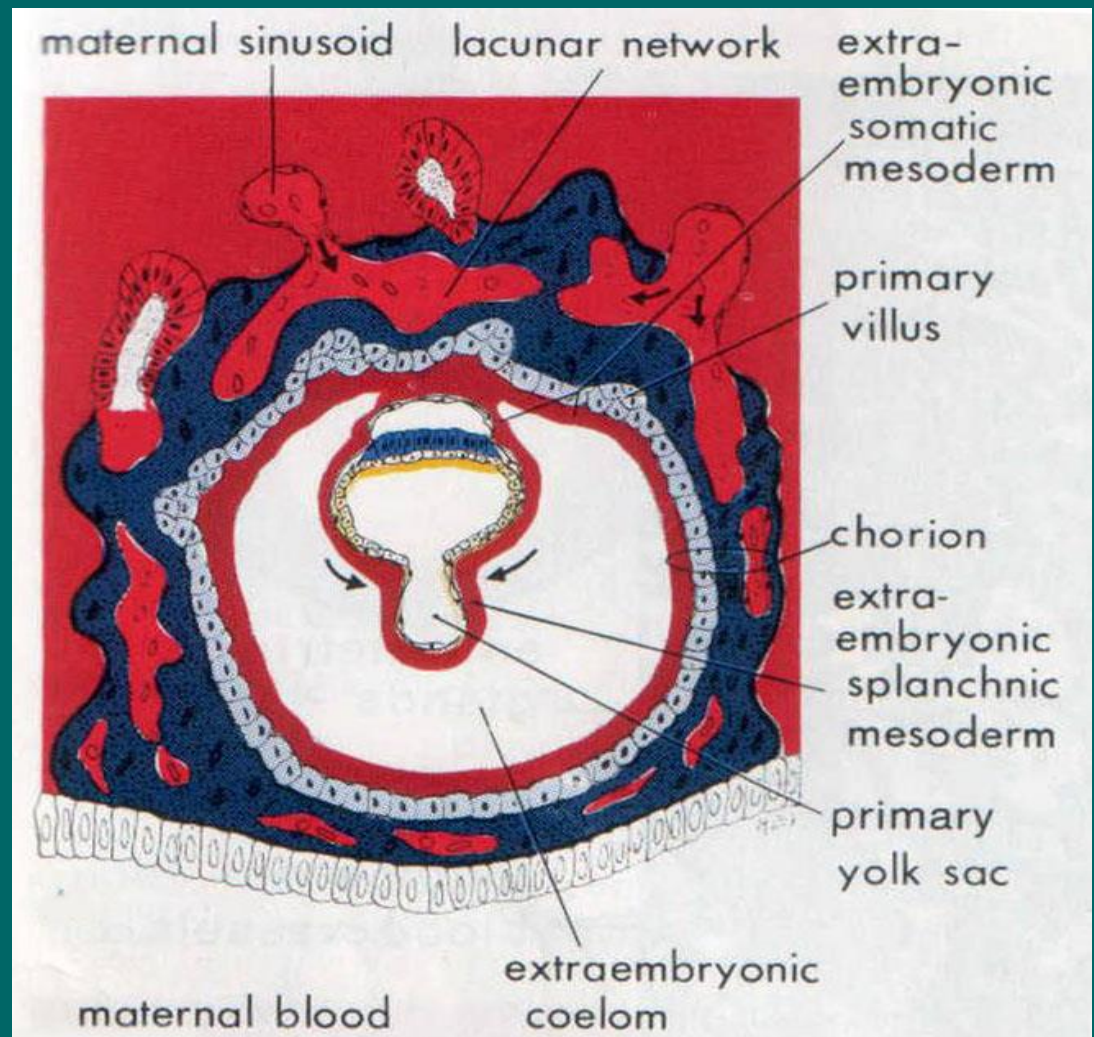
Blastocyst of 13 days showing chorionic cavity and endoderm lined secondary yolk sac



The trophoblast is characterized by villous structure. Cells of cytotrophoblast proliferate locally and penetrate into the syncytiotrophoblast, forming cellular columns surrounded by syncytium. Cellular columns with the syncytial covering are known as primary villi.

Extraembryonic coelom surrounds the primitive yolk sac and amniotic cavity except where the germ disc is connected to a trophoblast by the connecting stalk.

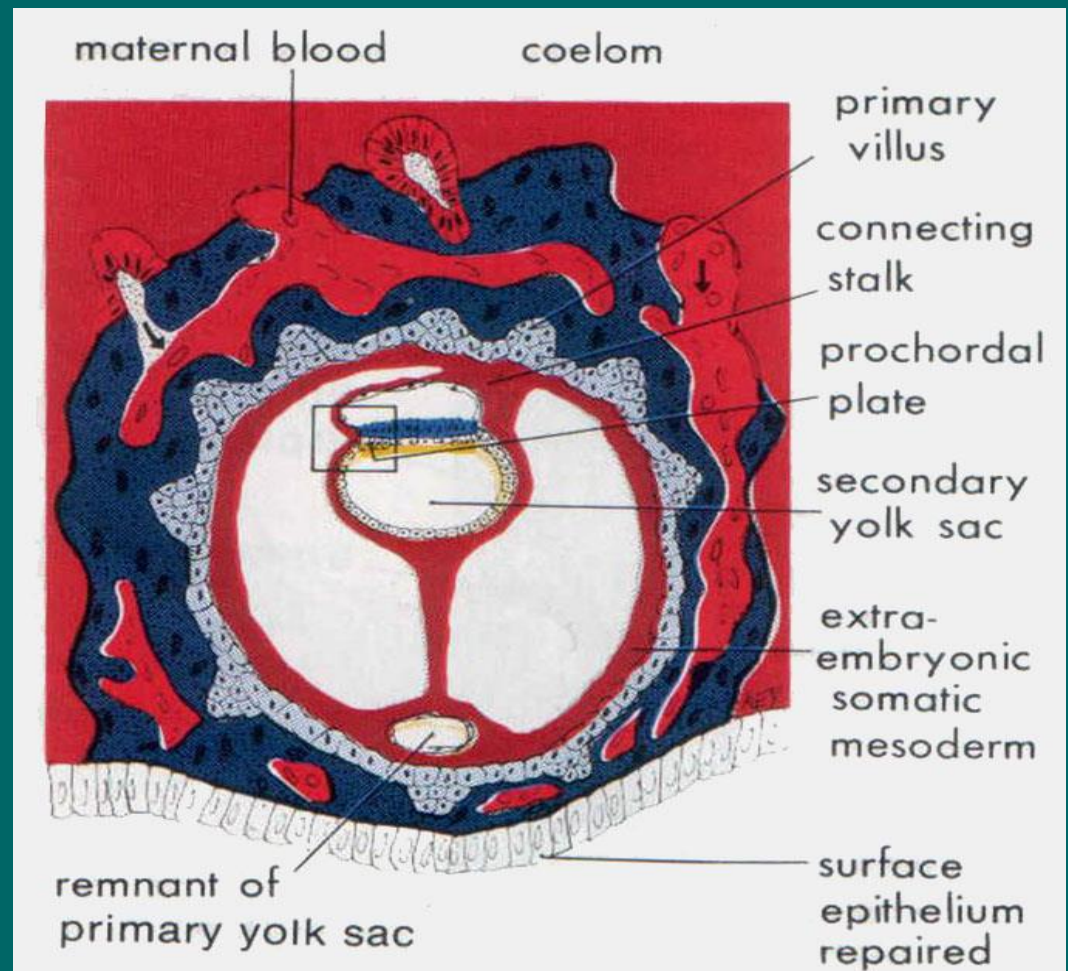
Human embryo, 13 days old.



The extraembryonic somatic mesoderm and the trophoblast together constitute the chorion. Extraembryonic mesoderm lining the inside of the trophoblast is known as chorionic plate.

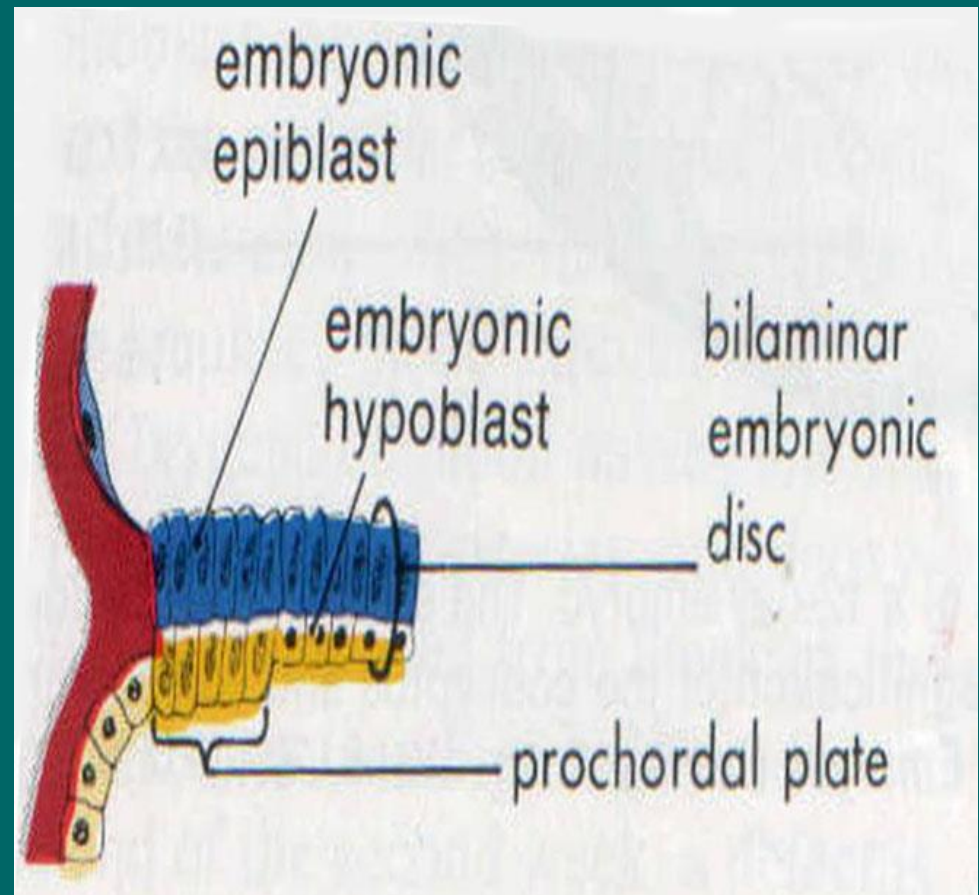
A small secondary yolk sac has formed inside the primitive yolk sac as it is pinched off thus decreasing the primitive yolk sac.

Human embryo, 14 days old.



The definite yolk sac is much smaller than the primitive yolk sac or original exocoelomic cavity. During its formation large portions of the exocoelomic cavity are pinched off. These portions are represented by exocoelomic cysts, which are often found in the extraembryonic coelom or chorionic cavity.

Human Embryo, 14 days old. Detail.



By the end of the 2nd week the germ disc is represented by two opposed cells discs: the epiblast which forms the floor of the continuously expanding amniotic cavity, and the hypoblast, which forms the roof of the secondary yolk sac. In its cephalic region the hypoblastic disc shows a slight thickening known as buccopharyngeal membrane. This area of columnar cells that are firmly attached to the overlying epiblastic disc.

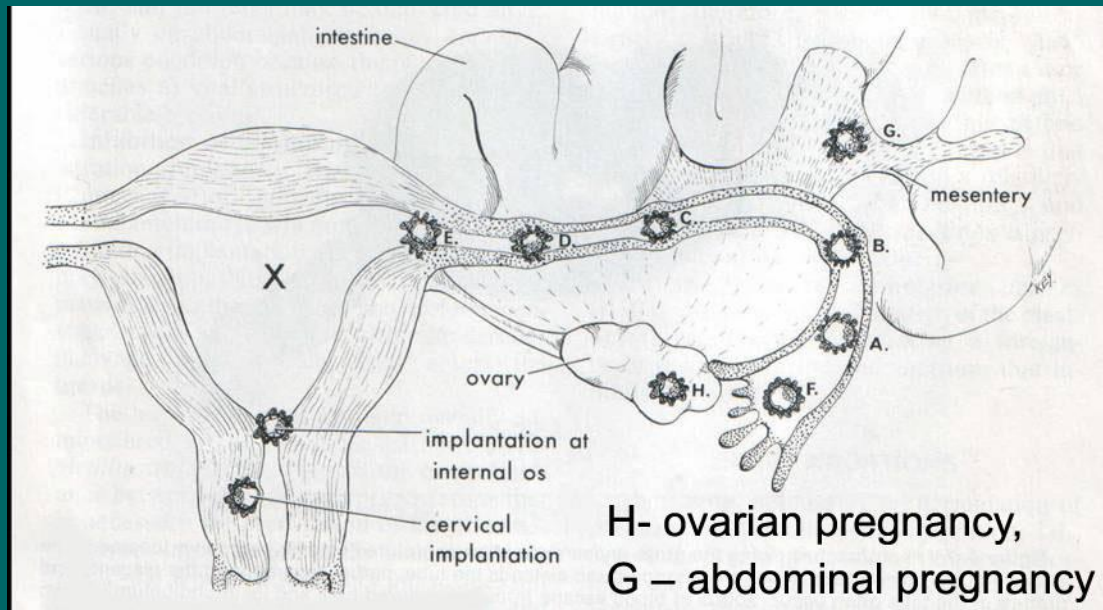
Summary.

The 2nd week of development is known as the week of twos:

- ✿ the trophoblast differentiates into 2 layers: cytotrophoblast and syncytiotrophoblast,
- ✿ the embryoblast forms the two layers: the epiblast and the hypoblast,
- ✿ the extraembryonic mesoderm splits into two layers: somatopleure and splanchnopleure,
- ✿ the two cavities form in the conceptus: amniotic sac and yolk sac.

CLINICAL CORRELATIONS.

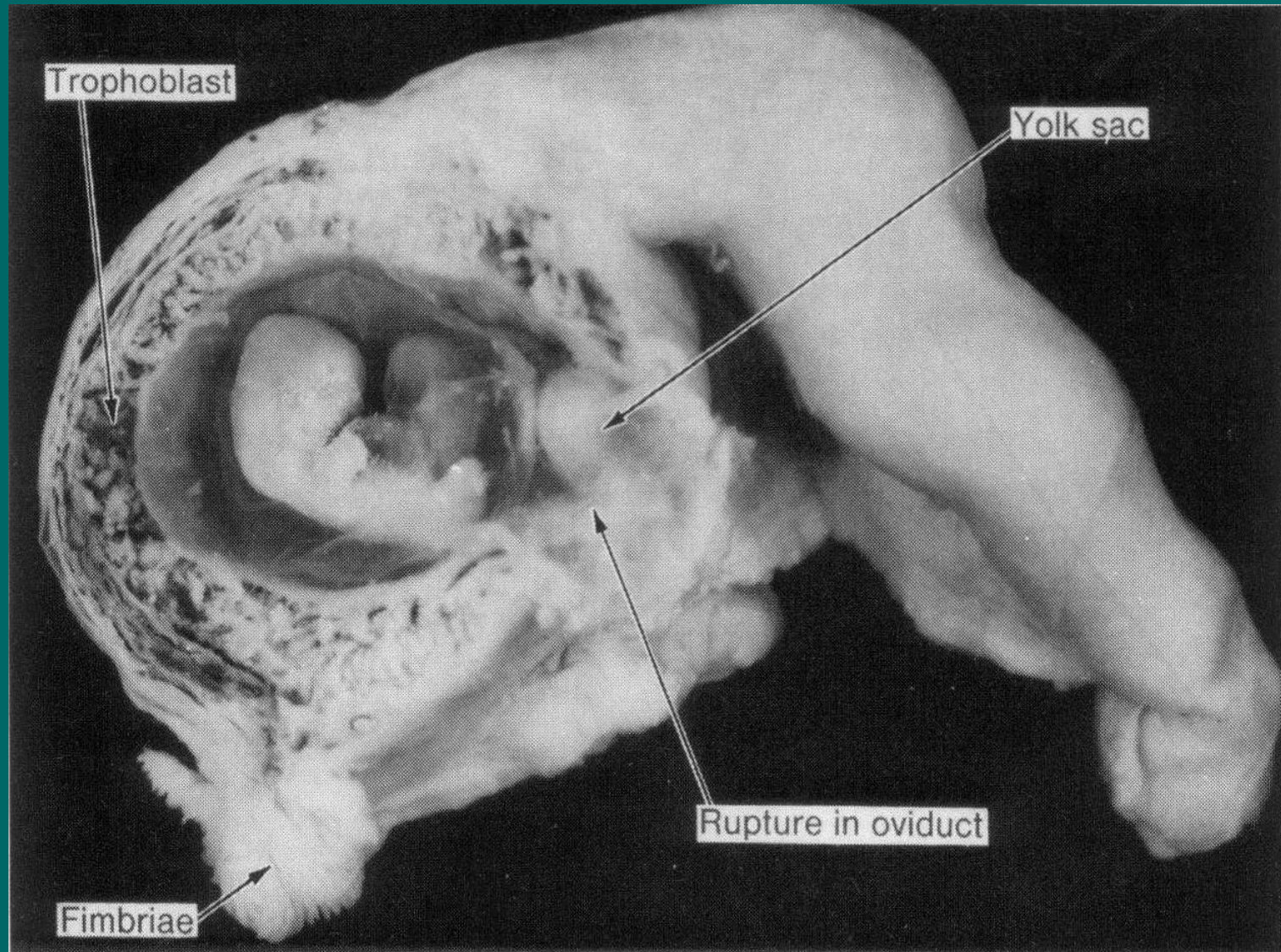
1. The syncytiotrophoblast is responsible for hormone production including human chorionic gonadotropin (HCG). By the end of the 2nd week quantities of this hormone are sufficient to be detected by pregnancy testing.
2. Normally the human blastocyst implants along the posterior or anterior wall of the body of the uterus. Occasionally the blastocyst implants close to the internal os of the cervix so that a future placenta will cover the internal ostium. This condition is called placenta previa and may result in severe life-threatening bleeding during the 2nd part of pregnancy and delivery.
3. Implantation often occurs outside the cavity of the uterus. It includes tubal, cervical and interstitial types. More than 90% of ectopic implantations occur in the uterine tube (1 in 80 to 1 in 250 pregnancies).



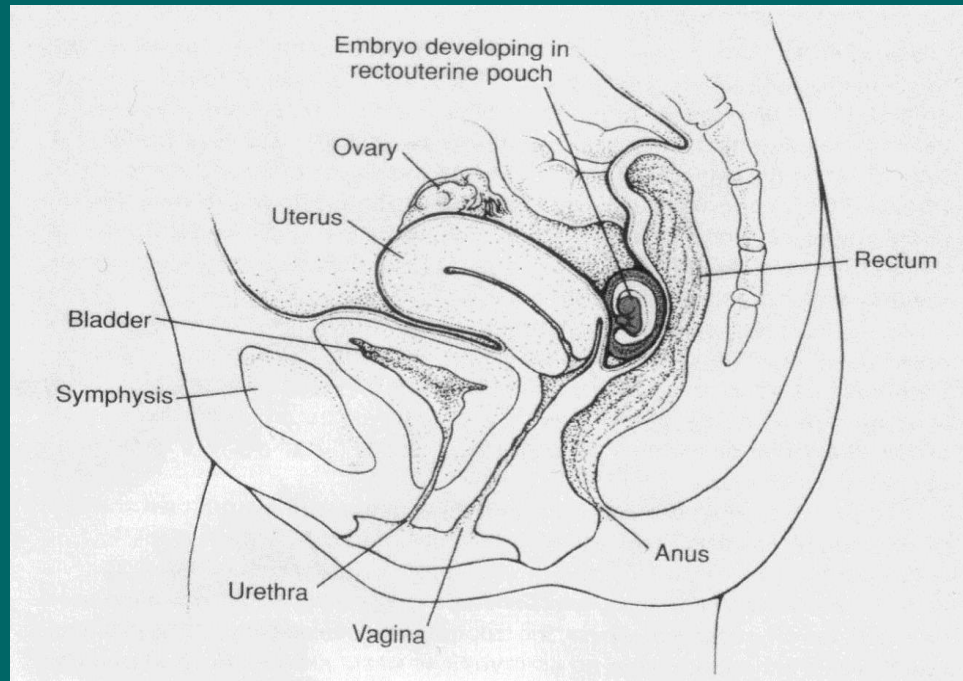
Tubal pregnancy:

- ✿ **Most of them are in ampulla,**
- ✿ **The cause is usually related to factors that delay or prevent transport of dividing zygote to the uterus (tubal infection causing adhesion of the mucosal folds; pelvic inflammatory disease, etc).**
- ✿ **Ectopic tubal pregnancy usually results in rupture of the uterine tube and hemorrhage during the first eight weeks followed by the death of the embryo.**
- ✿ **The affected tube and embryo need to be surgically removed.**
- ✿ **Tubal rupture and hemorrhage constitute a threat to mother's life and so are of major clinical importance.**

Tubal Pregnancy



Midline section of bladder, uterus, and rectum to show an abdominal pregnancy in the rectouterine (Douglas') pouch.



Ovarian and abdominal (in the rectouterine cavity) pregnancies are rare. In exceptional cases an abdominal pregnancy may progress to a full term and the fetus may be delivered alive. Usually abdominal pregnancy creates a serious condition as the placenta often attaches to vital structures causing serious bleeding.

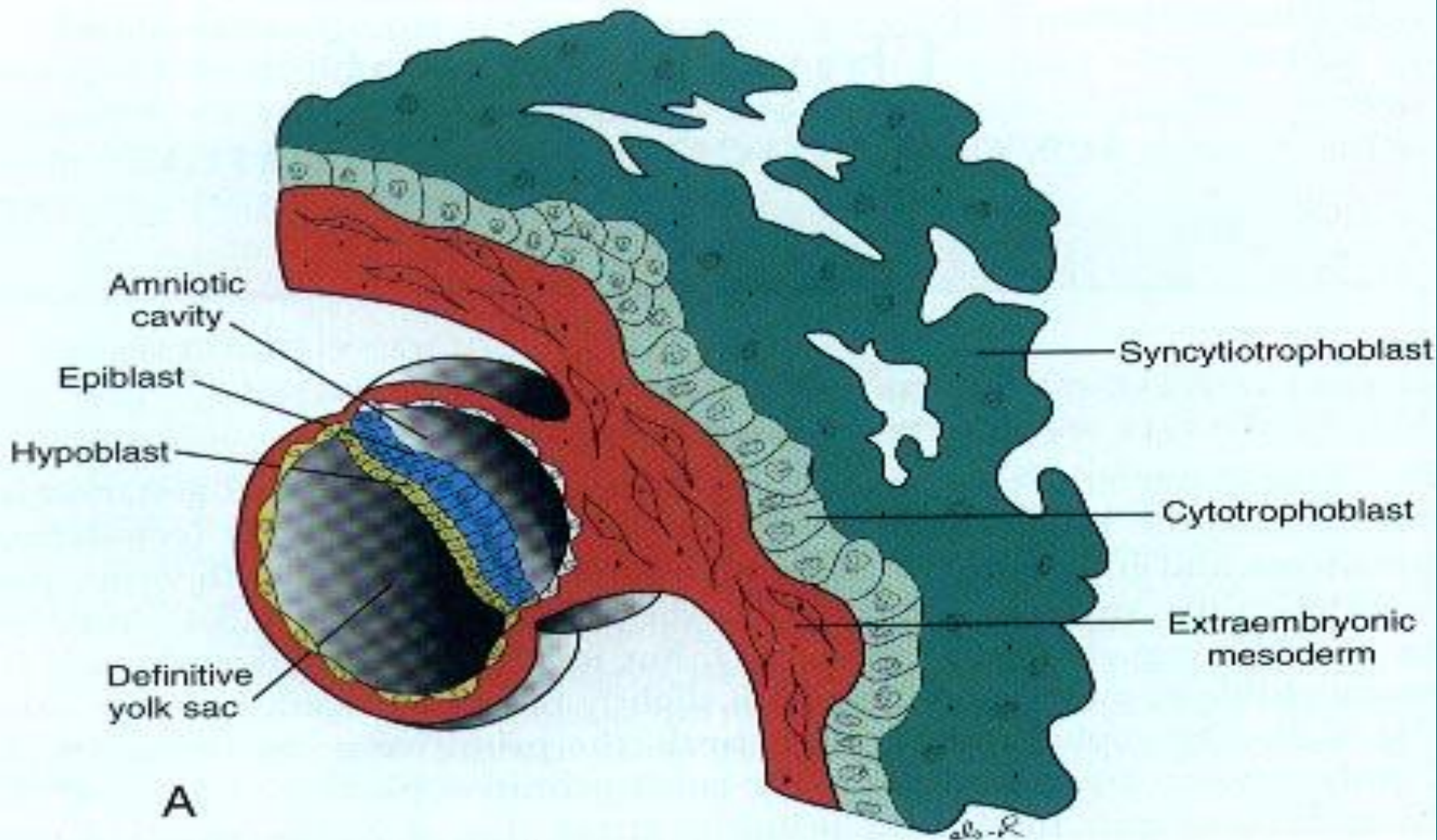
Clinical Correlations

4. Inhibition of Implantation.

- ✦ The administration of relatively large doses of estrogens (“mor ning-after” pills) for several days after sexual intercourse will prevent pregnancy by inhibition of implantation of the blastocyst that may develop.
- ✦ Normally the endometrium progresses to the secretory phase of the menstrual cycle as the zygote forms, undergoes cleavage, and the blastocyst enters the uterus.
- ✦ The large amount of estrogen, usually administered as the synthetic estrogen DES (diethylstilbestrol), disturbs the normal balance between estrogen and progesterone that is necessary for preparation of the endometrium for implantation of the blastocyst. When the secretory phase does not occur, implantation cannot take place, and the blastocyst soon dies.
- ✦ Various types of intrauterine devices (IUDs) also prevent implantation of blastocyst, presumably by inducing a foreign-body response in the edometrium that inhibits implantation.
- ✦ Contraception is preferable to contraimplantation.

The 2nd week of development

- ☀ Completion of Implantation**
- ☀ Differentiation of trophoblast**
- ☀ Formation of bilaminar embryonic disc**
- ☀ Formation of amniotic cavity & amnion**
- ☀ Formation of primary and secondary yolk sacs**
- ☀ Appearance of primary mesoderm**
- ☀ Development of chorion & chorionic cavity**
- ☀ Formation of the connecting stalk**



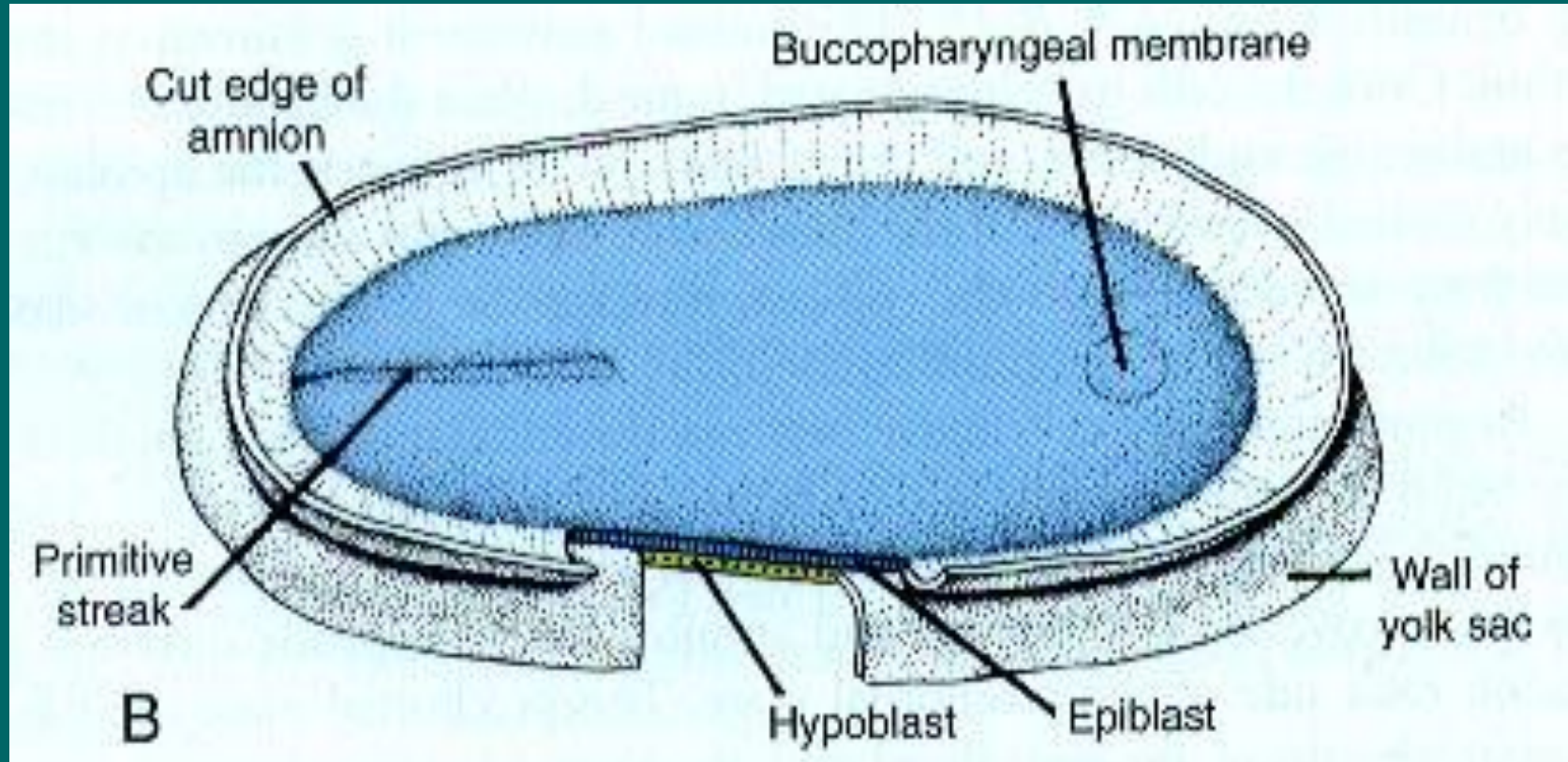
Human Embryo, 14 days old. Bilaminar germ disc lined with tall columnar ectoderm cells and cuboidal endoderm cells.³⁶

Beginning of 3rd week of development.

By process of gastrulation formation of:

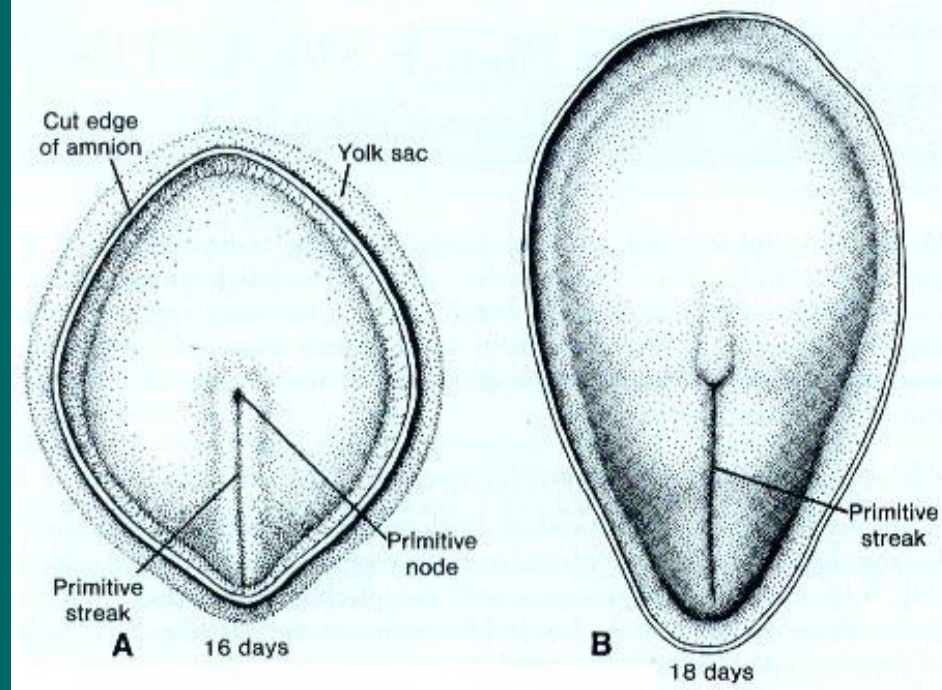
- ☀ Primitive streak & primitive pit**
- ☀ Primitive node (Hensen's node)**
- ☀ Secondary mesoderm & trilaminar germ disc**
- ☀ Buccopharyngeal & cloacal membrane and**
- ☀ Establishment of body axis**
- ☀ Growth of embryonic disc**

Beginning of 3rd week. Formation of primitive streak in the caudal region of the embryo (dorsal aspect).



Gastrulation begins with formation of the primitive streak – a thick linear band on the surface of the epiblast. Initially the primitive streak is vaguely defined.

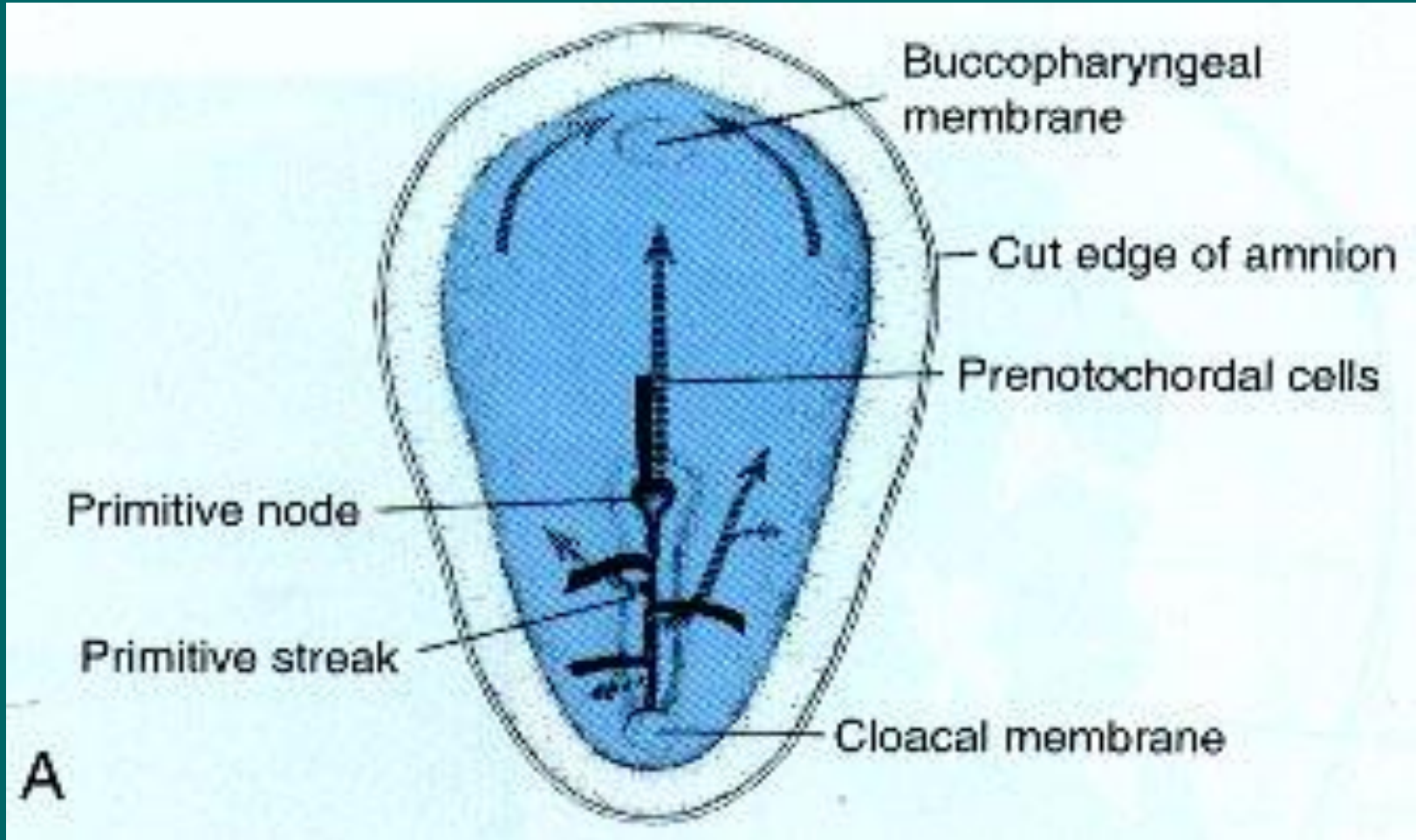
Dorsal aspect of pear-shaped embryo with primitive streak and node (16 & 18 days).



**Length
is
1.25mm**

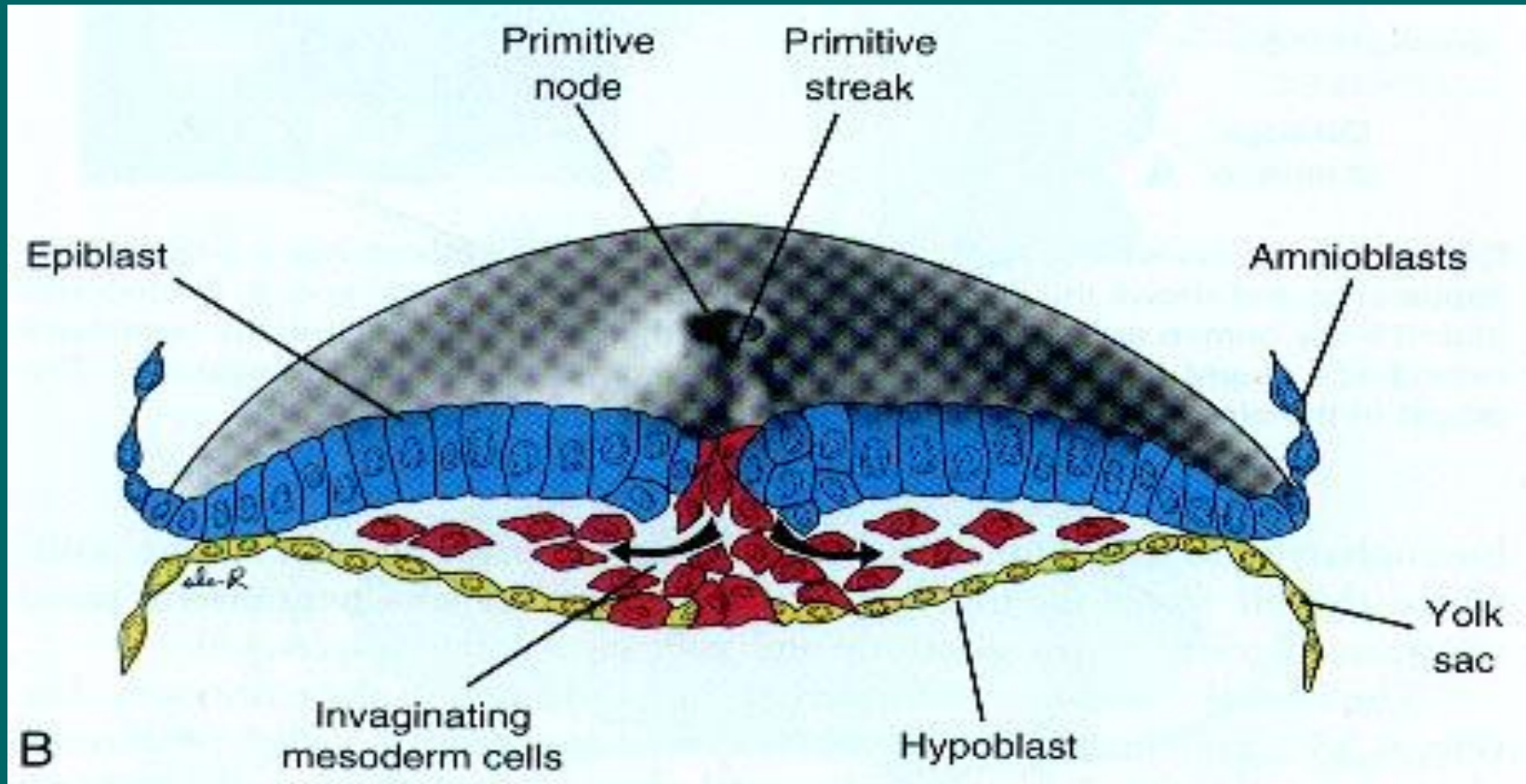
In the 16th day old embryo the primitive streak is clearly visible as a narrow groove with slightly bulging regions on either side. The cephalic end of the streak, the primitive node (knot), consists of a slightly elevated area surrounding the small primitive pit. As the primitive streak elongates by addition of cells to its caudal end, its cranial end thickens. The primitive streak gives rise to mesenchymal cells which form loose embryonic CT, often called mesoblast.

Germ disk of a 16-day embryo indicating the movement of surface epiblast cells through primitive streak and primitive node.



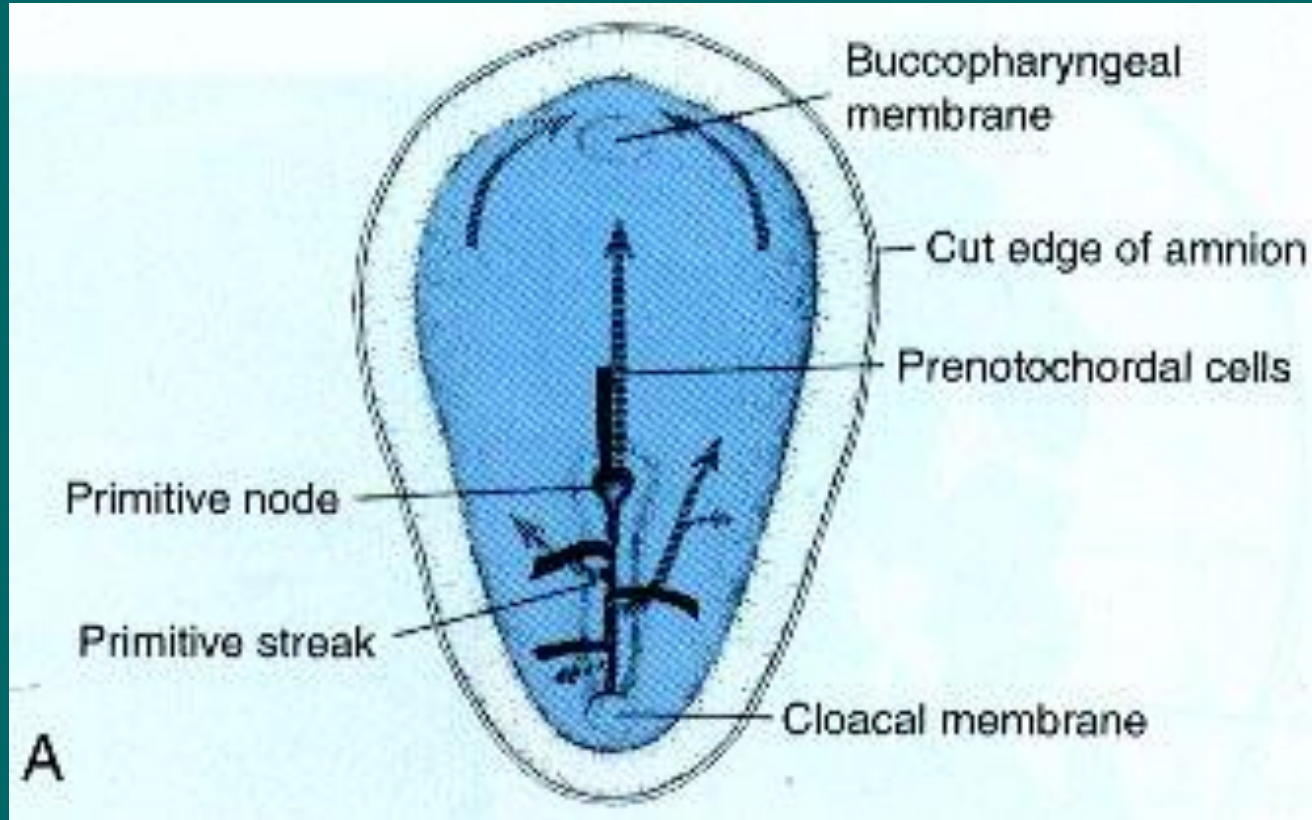
Cells of epiblast migrate towards the primitive streak (black solid lines).

Cross section at cranial region of streak - Invagination of epiblast cells. Formation of definitive endoderm and secondary mesoderm.



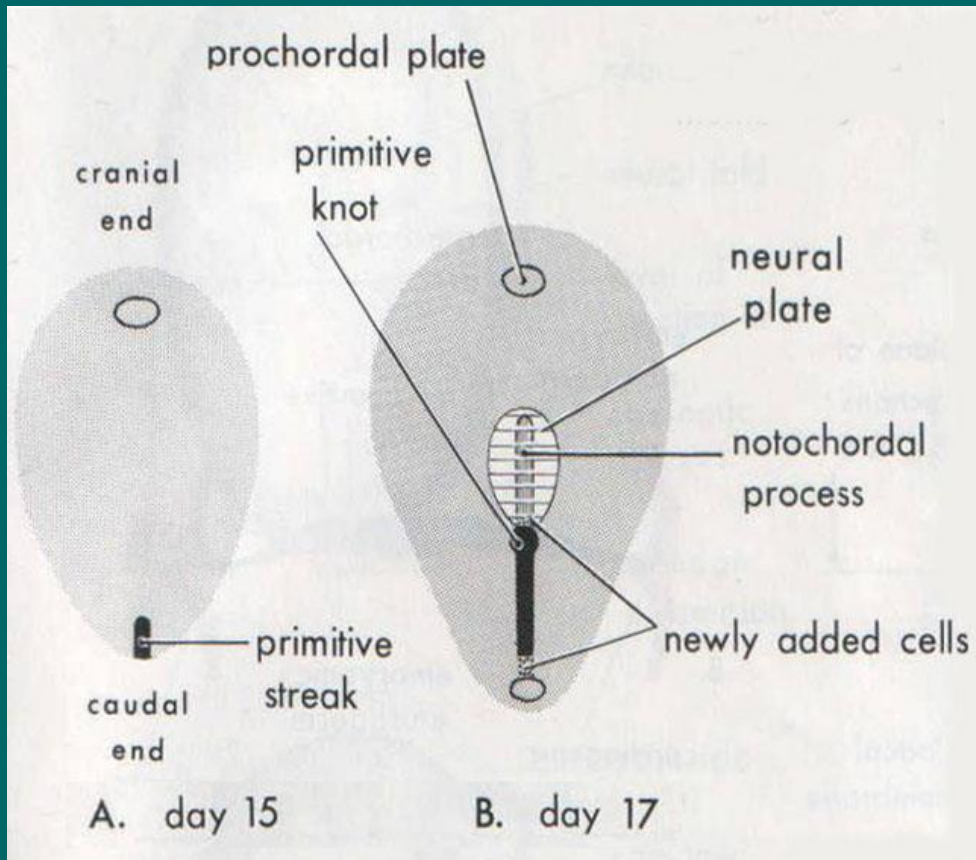
On the arrival of the epiblast cells in the zone of the primitive streak they become flask-shaped, detach from epiblast, and slip beneath it. This movement is known as invagination. Once the cells have invaginated, some displace the hypoblast, creating embryonic endoderm, and others come to lie between the epiblast and newly created endoderm to form mesoderm. Cells remaining in the epiblast then form ectoderm. Thus the epiblast, through the process of gastrulation, is the source of all the germ layers in the embryo.

Germ disk of a 16-day embryo indicating the movement of surface epiblast cells through primitive streak and primitive node.



Broken lines show the subsequent migration of cells between the hypoblast and epiblast. Initially embryonic disc is flat and essentially circular, but it soon becomes pear-shaped. Much of the growth and elongation of the embryonic disc result from the continuous migration of mesenchymal cells from the primitive streak.

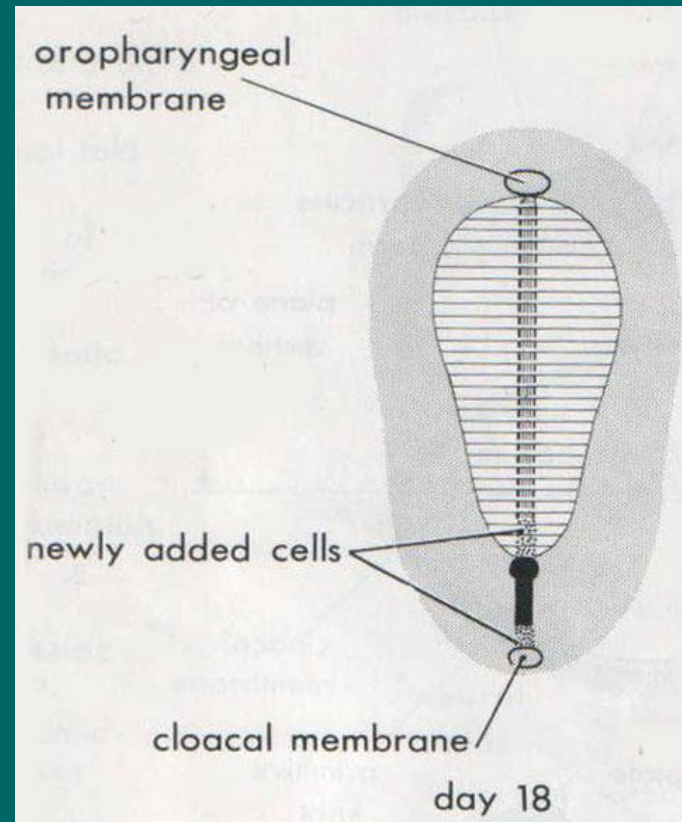
Cells migrate cranially from the primitive knot and form a midline cord known as the notochordal process. This cord grows between ectoderm and endoderm until it reaches the prochordal plate, which indicates the future site of the mouth.



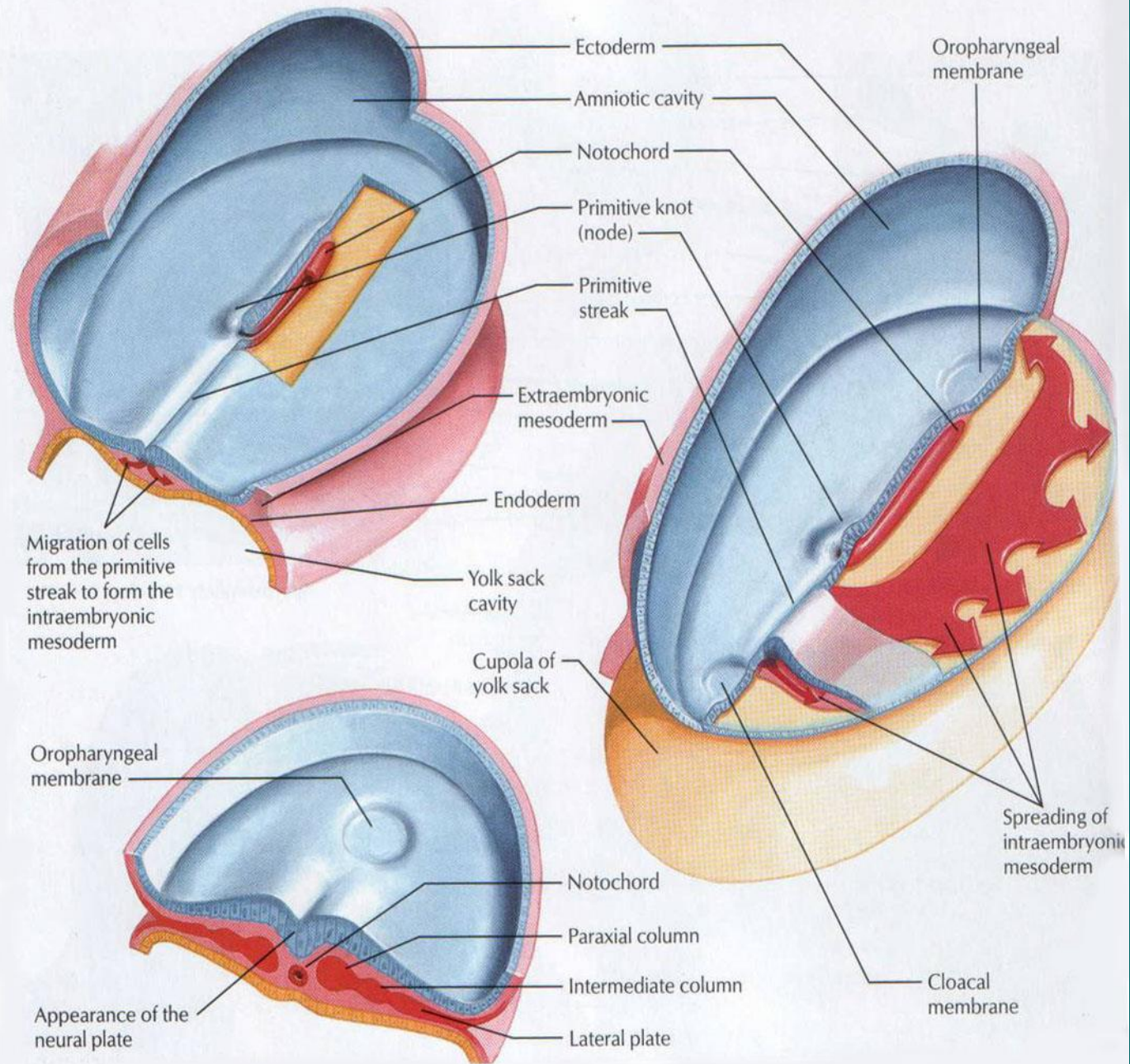
Formation of the Notochord

The notochordal process can extend no further because the prechordal plate is firmly attached to the overlying ectoderm, forming oropharyngeal membrane. Caudal to the primitive streak a circular area is formed known as cloacal membrane. The embryonic disc remains bilaminar here also because the ectoderm and endoderm are fused.

Formation of the Notochord

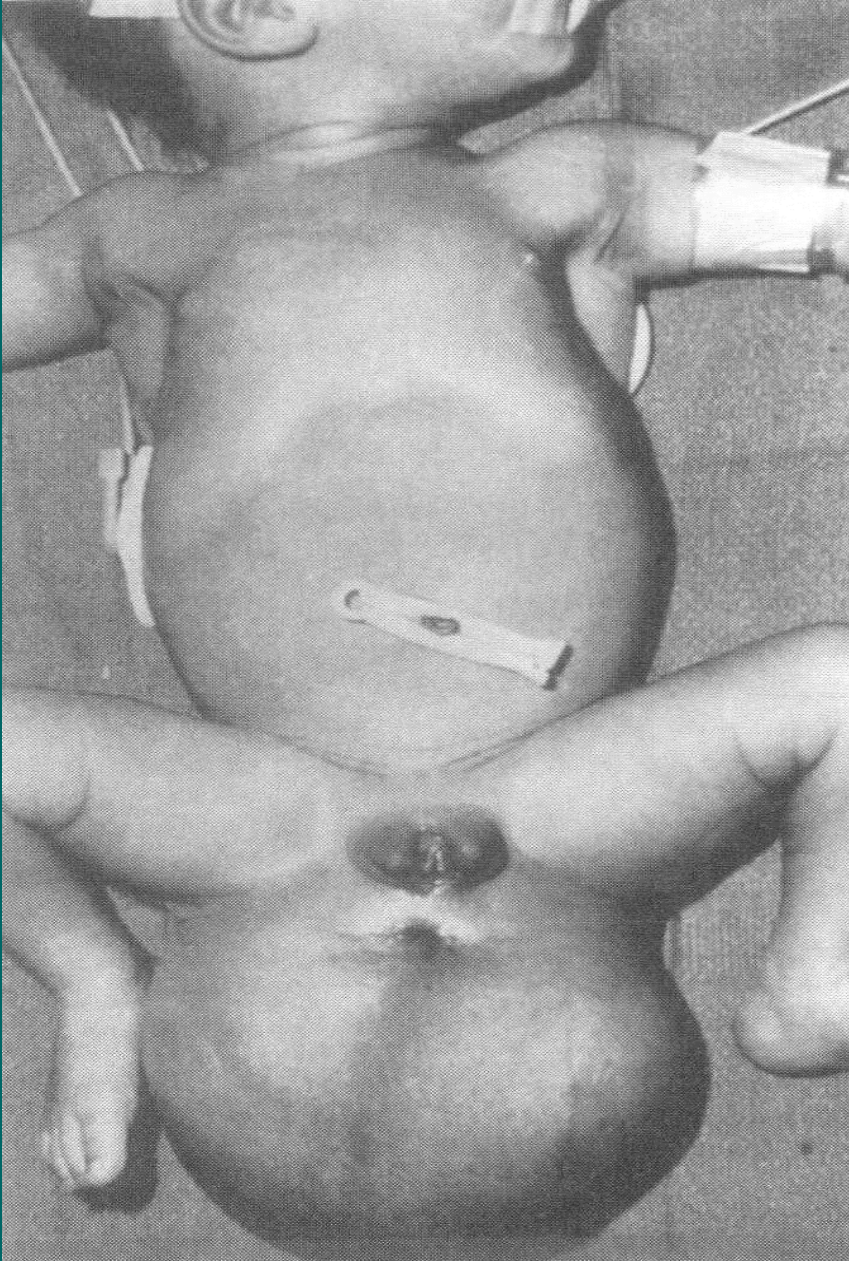


Formation of Intraembryonic Mesoderm from the Primitive Streak and Node (Knot)



Clinical Correlates.

- 1. The primitive streak continues to form mesenchyme until about the end of the 4th week.**
- 2. Thereafter, mesenchyme production from this source slows down.**
- 3. The primitive streak quickly diminishes in relative size and becomes insignificant structure in the sacro-coccygeal region of the embryo.**
- 4. Normally it undergoes degenerative changes and disappears, but primitive streak remnants may persist and give rise to a tumor known as a sacrococcygeal teratoma.**



Sacrococcygeal teratoma resulting from remnants of the primitive streak. These tumors may become malignant and are most common in females.

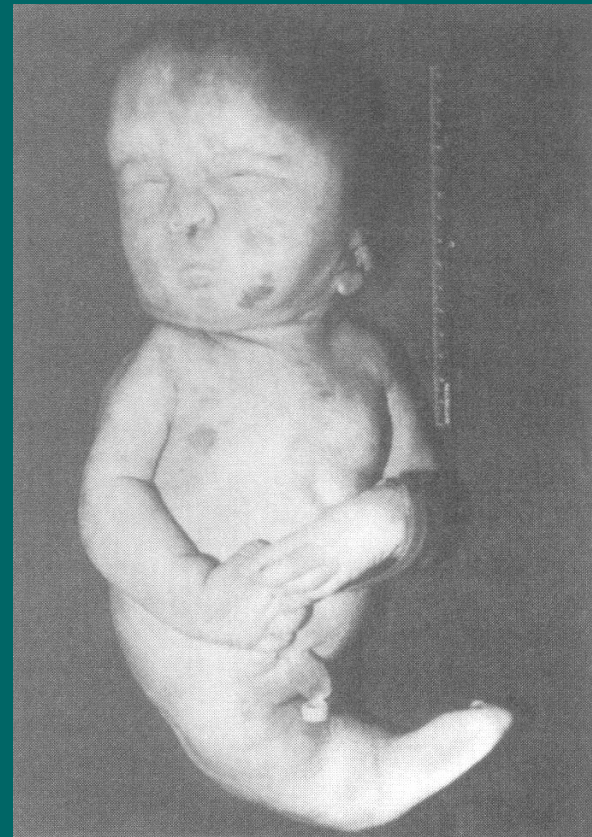
Primitive Streak (3rd week of Intrauterine Life)

- ✦ **Appears at caudal end of embryonic disc as a linear thickening of epiblast cells**
- ✦ **Involves invagination of epiblast cells as flask-shaped mesenchyme cells**
- ✦ **Spreads in all directions between epiblast and hypoblast layers with exception of buccopharyngeal and cloacal membranes**
- ✦ **Provides formation of intraembryonic mesoderm and endoderm**

Clinical Correlations:

Gastrulation itself may be disrupted by genetic and teratogenic causes. In caudal dysgenesis (sirenomelia) insufficient mesoderm is formed in the caudalmost region of the embryo. Since this mesoderm contributes to the formation of the lower limbs, urogenital system and lumbosacral vertebrae, abnormalities in these structures ensue.

Sirenomelia (caudal disgenesis). Loss of mesoderm in the lumbosacral region has resulted in fusion of the limb buds and other defects.



Affected individuals exhibit a variable range of defects, including hypoplasia and fusion of the lower limbs, vertebral anomalies, renal agenesis, imperforate anus, and anomalies of the genital organs. In humans this condition is associated with maternal diabetes and other causes.

Formation of the Notochord

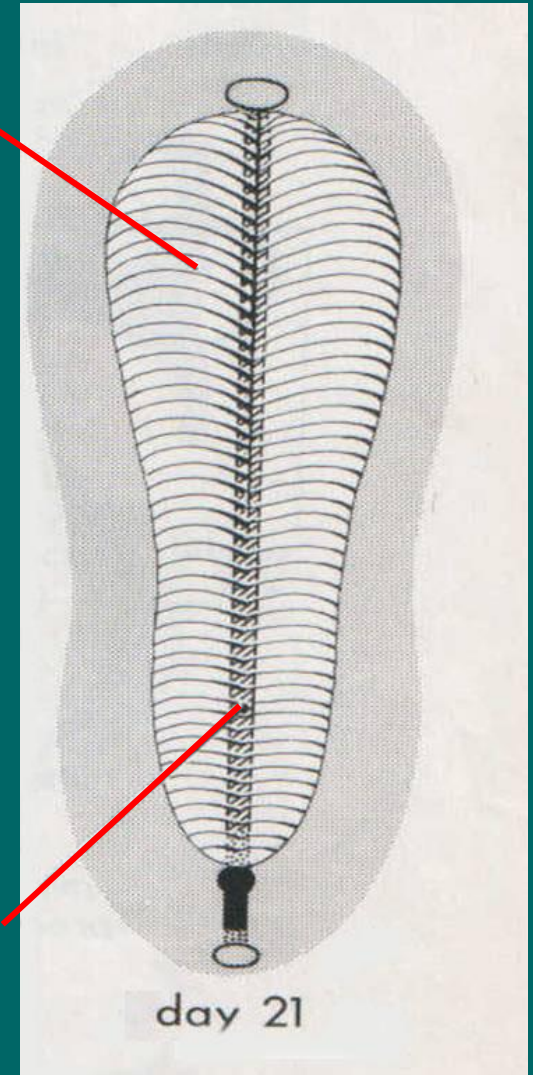
The notochord is a cellular rod that develops from the notochordal process and defines the primitive axis of the embryo.

In lower chordate it forms the skeleton of a grown animal. In human embryo it forms a midline axis and the basis of the axial skeleton (vertebral column, ribs, sternum and the skull).

By the end of the 4th week the notochord is almost completely formed and extends from the oropharyngeal membrane cranially to the primitive node caudally.

neural
plate

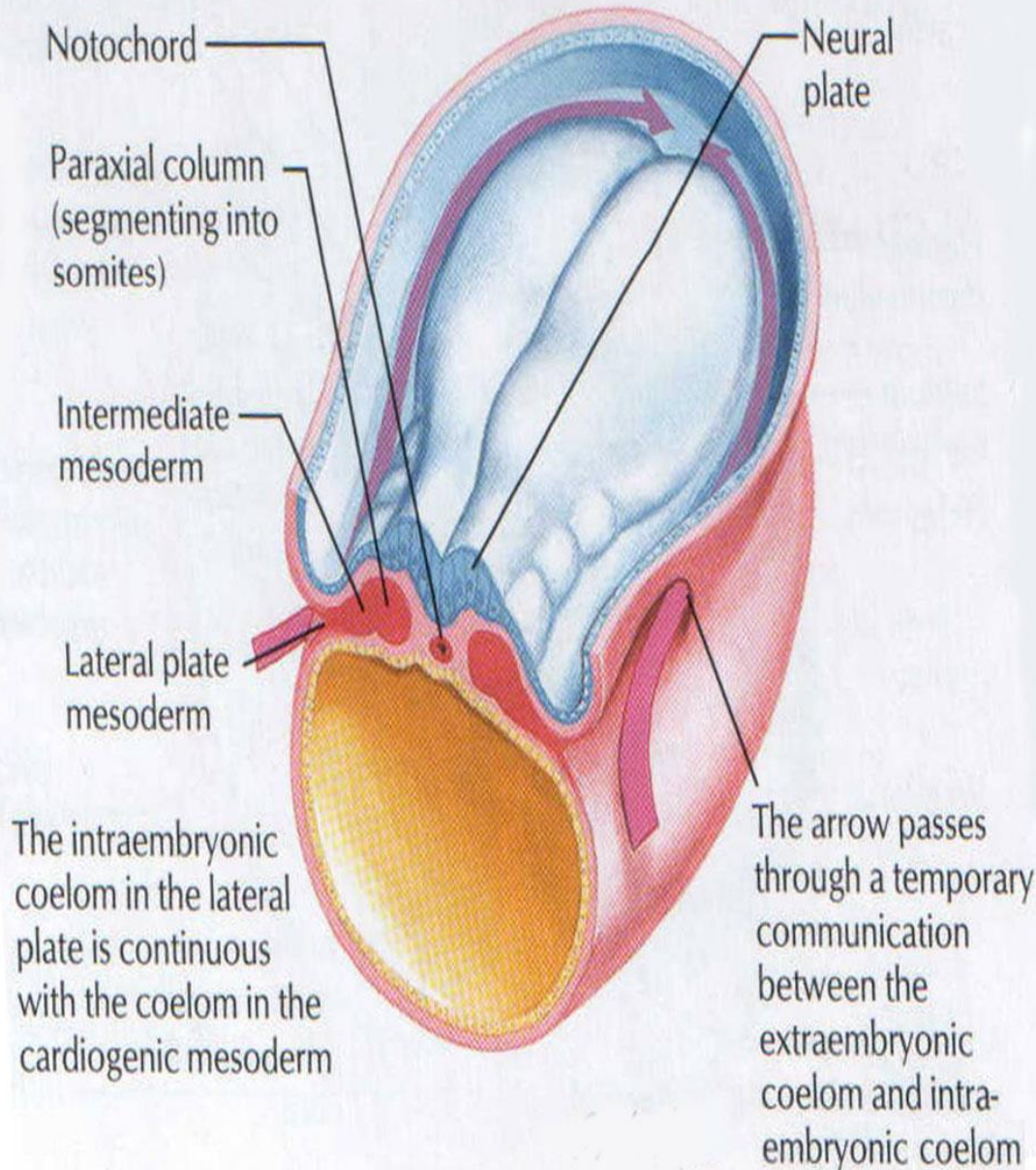
notochord



The Embryonic Period: 3rd to 8th weeks.

1. During the embryonic period or the period of organogenesis, each of the three germ layers gives rise to a number of specific tissues and organs.
2. By the end of the embryonic period the main organ systems have been established, rendering the major features of the external body form recognizable by the end of the 2nd month.

Cross section of embryo



Neurulation

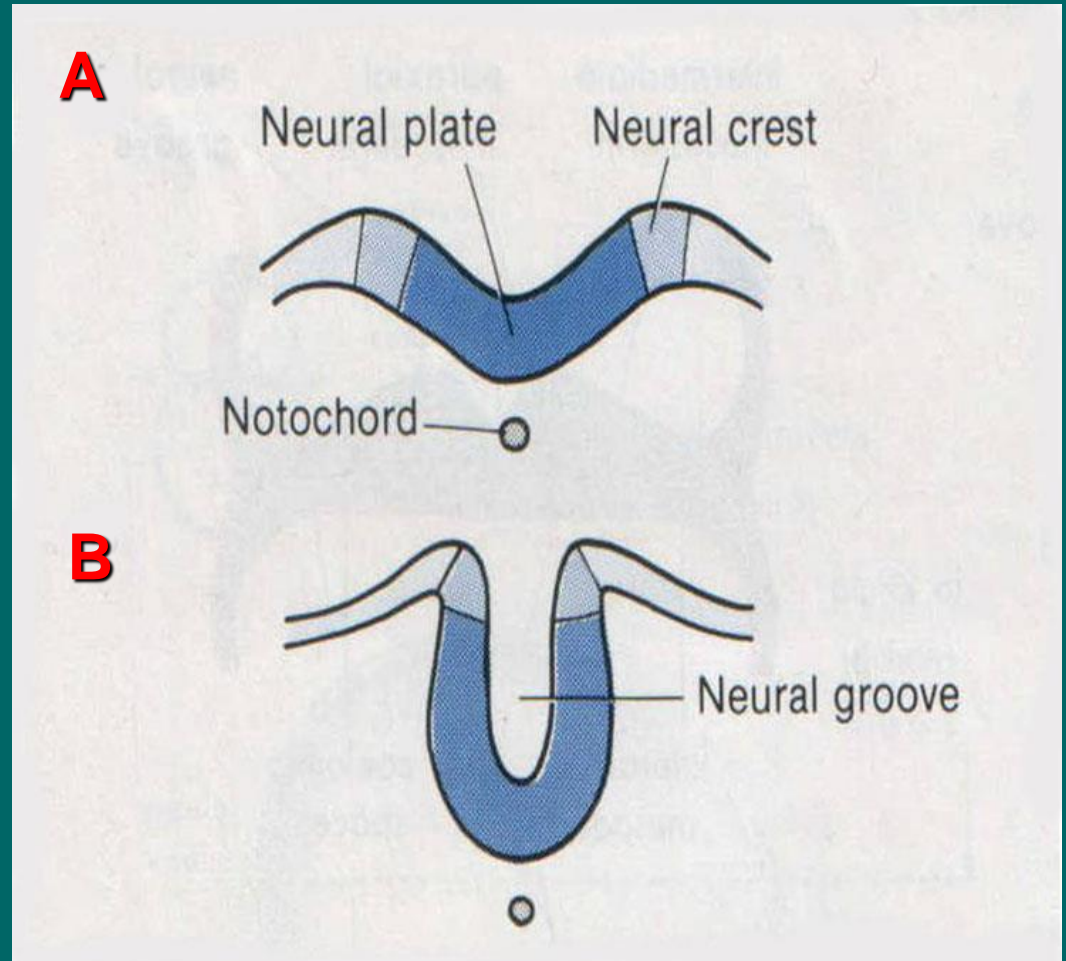
The notochord is a structure around which the vertebral column forms. It degenerates and disappears where it is surrounded by the vertebral bodies, but persists as the nucleus pulposus of each intervertebral disc.

The notochord also induces the overlying ectoderm to form the neural plate, the primodium of the CNS.

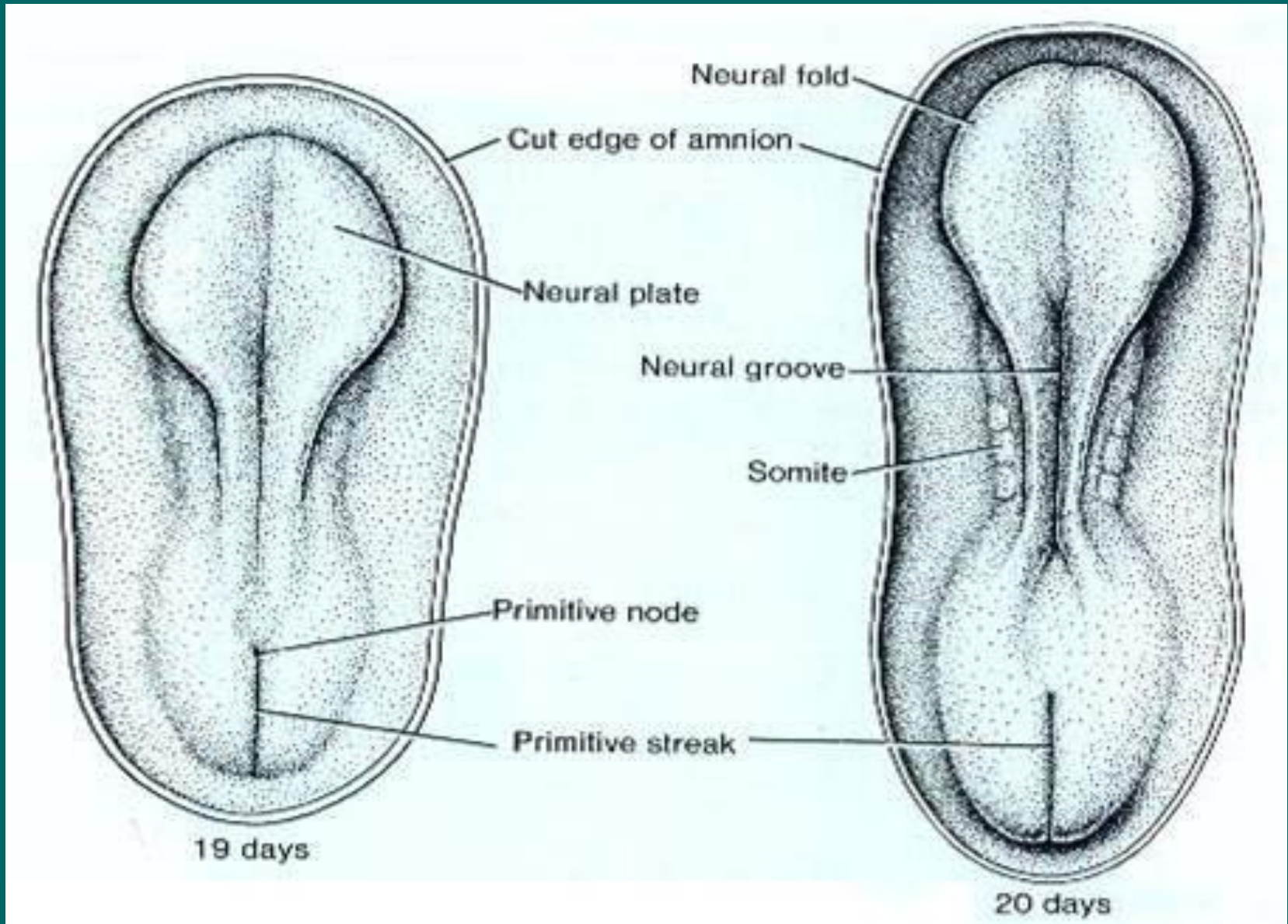
Derivatives of the Ectodermal Germ Layer. NEURULATION

A – day 17, as the notochord develops, the embryonic ectoderm over it thickens to form the neural plate giving rise to the CNS.

B – day 18, the neural plate invaginates along its central axis to form a neural groove with neural folds on both sides.



Concurrent with gastrulation are the 1st steps in the formation of the nervous system.

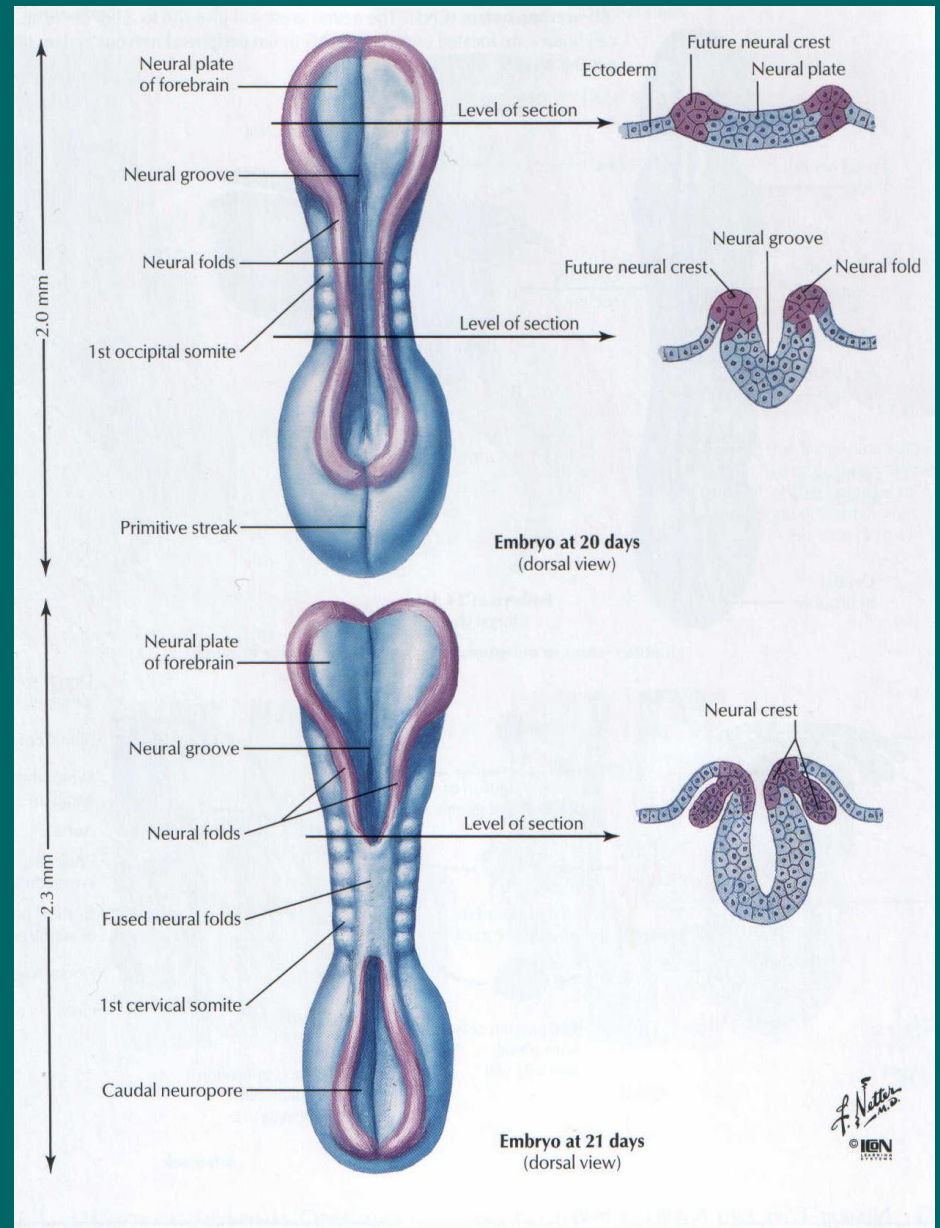


19-20 days embryo: formation of neural plate from ectoderm cranial to primitive node

NEURULATION

In response to induction by the notochord and paraxial mesoderm, the surface ectoderm thickens and begins to sink and fold in on itself near the junction of the future brain and spinal cord in the middle of the embryo.

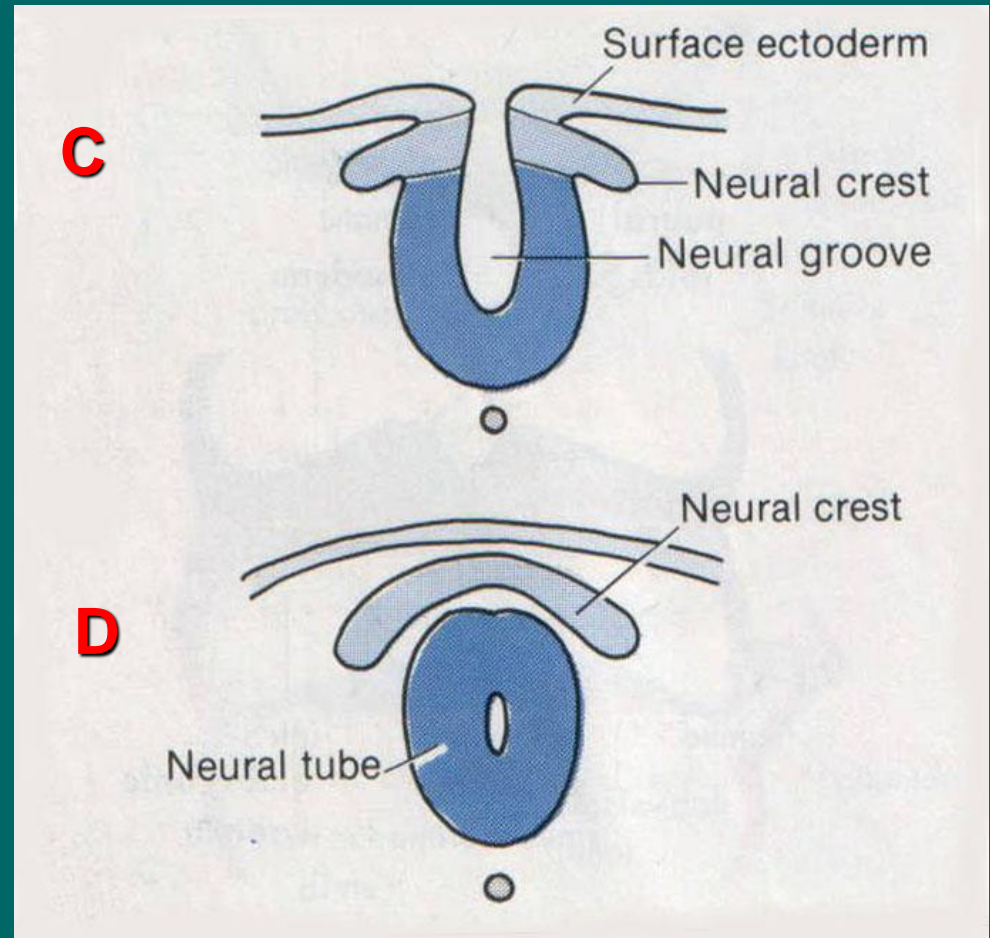
The ectodermal neural crests on each side approach each other and fuse as the tube sinks below the surface. Some of these cells will pinch off and migrate to form ganglia throughout the trunk and a variety of other tissues in the head and neck. Neurulation advances both cranially and caudally.



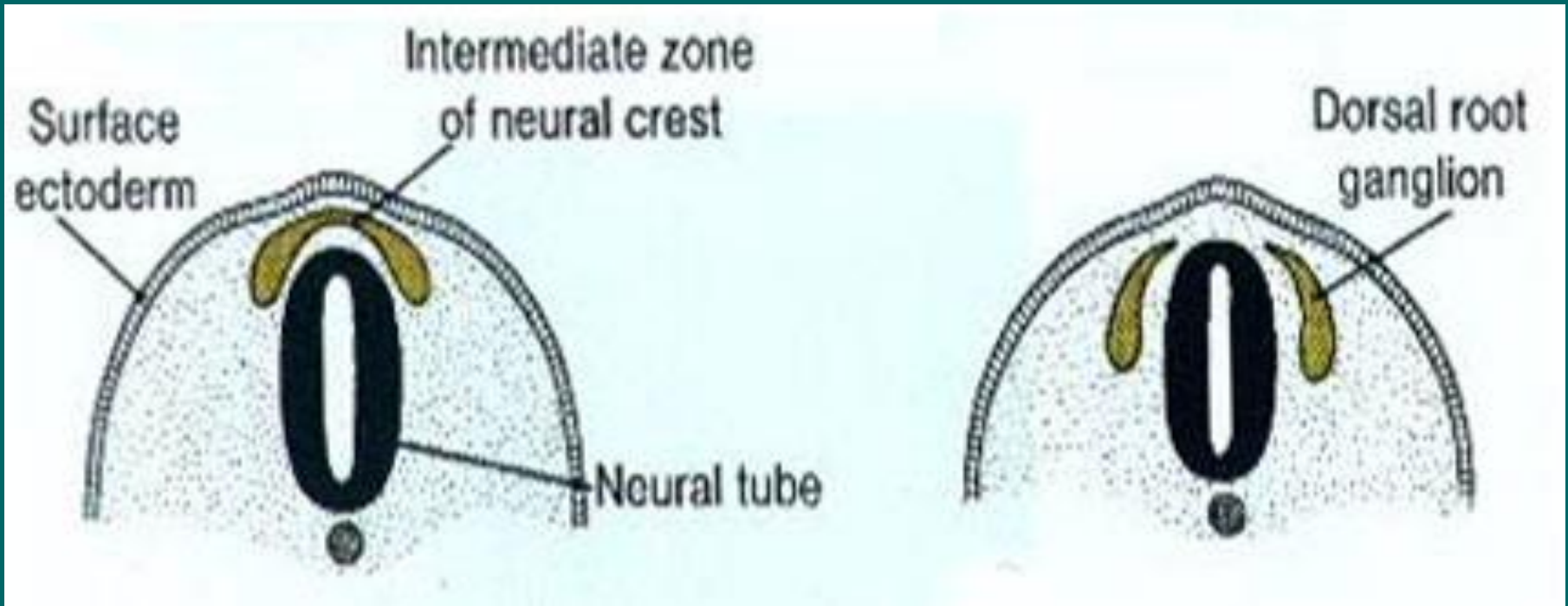
NEURULATION

C, D – by the end of the 3rd week the neural folds at the middle of the embryo have moved together and fused, converting the neural plate into a neural tube.

As the neural tube separates from the surface ectoderm, these neural crest cells migrate inwardly and invade mesoblast on each side of the neural tube. They form the irregular flattened mass called the neural crest between the neural tube and overlying surface ectoderm.



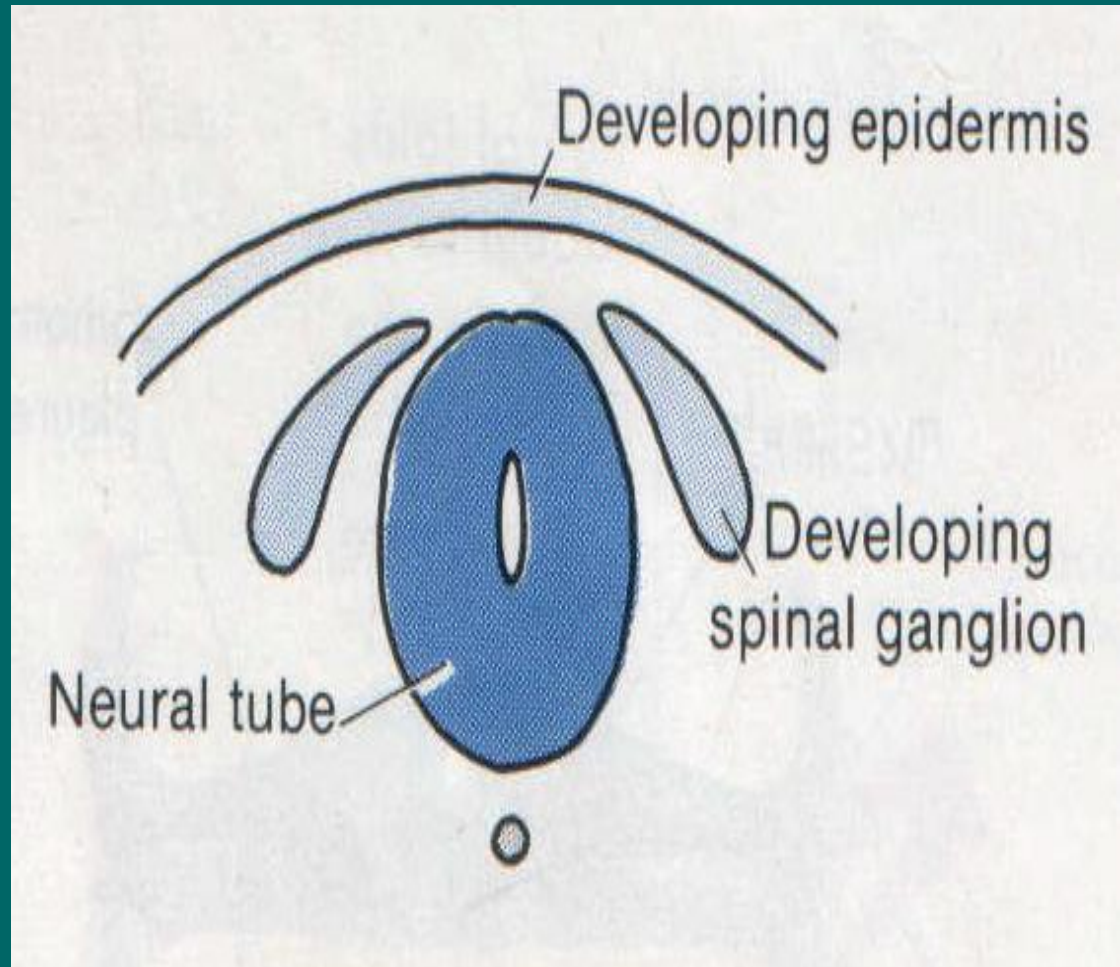
Initially continuous across the midline, the neural crest soon separates into right and left parts. The two parts of the neural crest migrate to the dorsolateral aspect of the neural tube, where they give rise to the sensory ganglia of the spinal and cranial nerves.



NEURULATION

Neural crest cells give rise to the spinal ganglia and the ganglia of the autonomous nervous system. The ganglia of the cranial nerves (V, VII, IX and X) are also partly derived from the neural crest.

They also form Schwann cells, meningeal covering of the brain and the spinal cord, contribute to the formation of the pigment cells, adrenal medulla, and several skeletal and muscular components in the head.

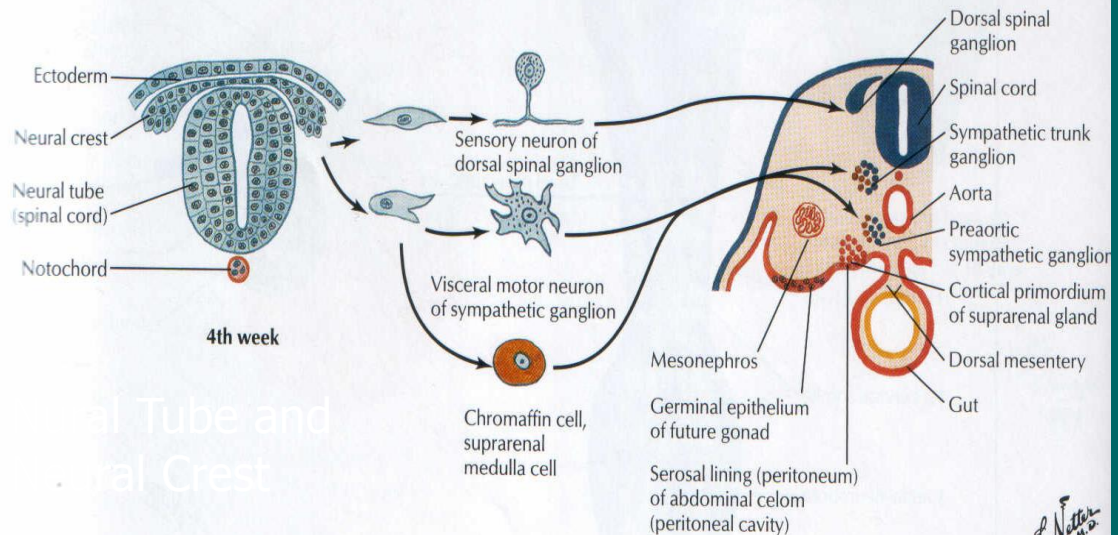
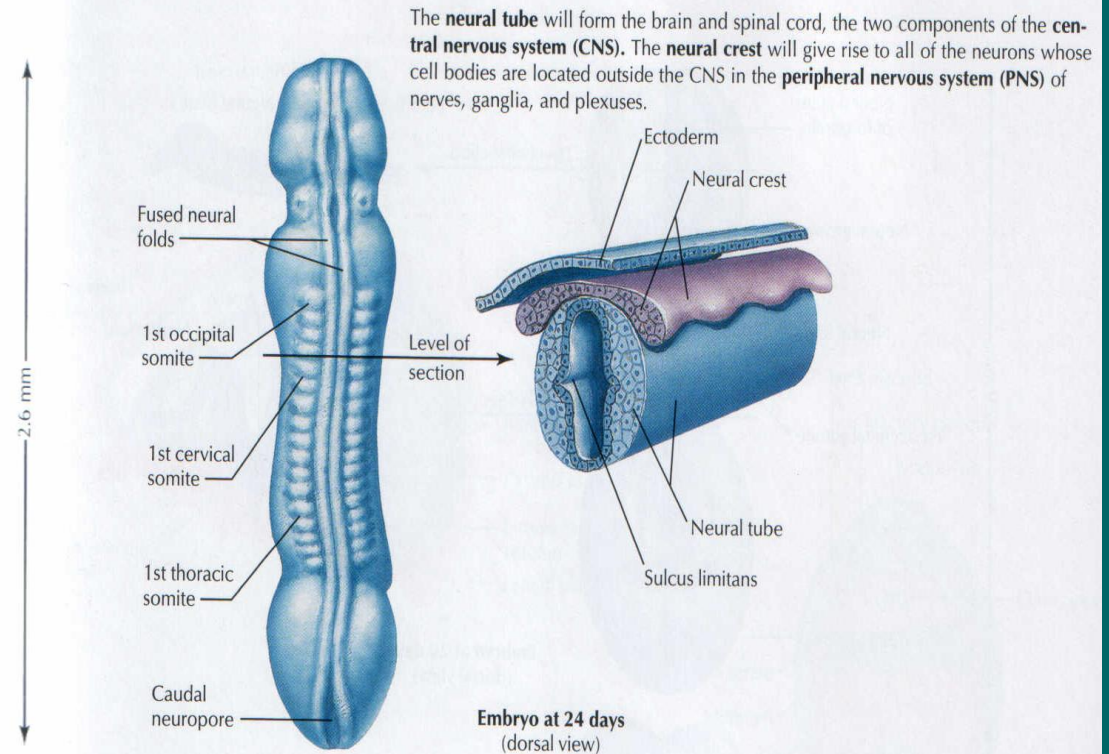


Derivatives of the neural tube include:

- Supporting cells of the CNS
- Somatomotor neurons of the PNS
- Neurons of the CNS
- Presynaptic autonomous neurons of PNS.

Derivatives of the neural crest include:

- Sensory neurons in the PNS,
- Postsynaptic autonomic neurons,
- Schwann cells,
- Adrenal medulla cells,
- Head mesenchyme,
- Melanocytes in the skin,
- Arachnoid and pia mater of meninges (dura mater from mesoderm).



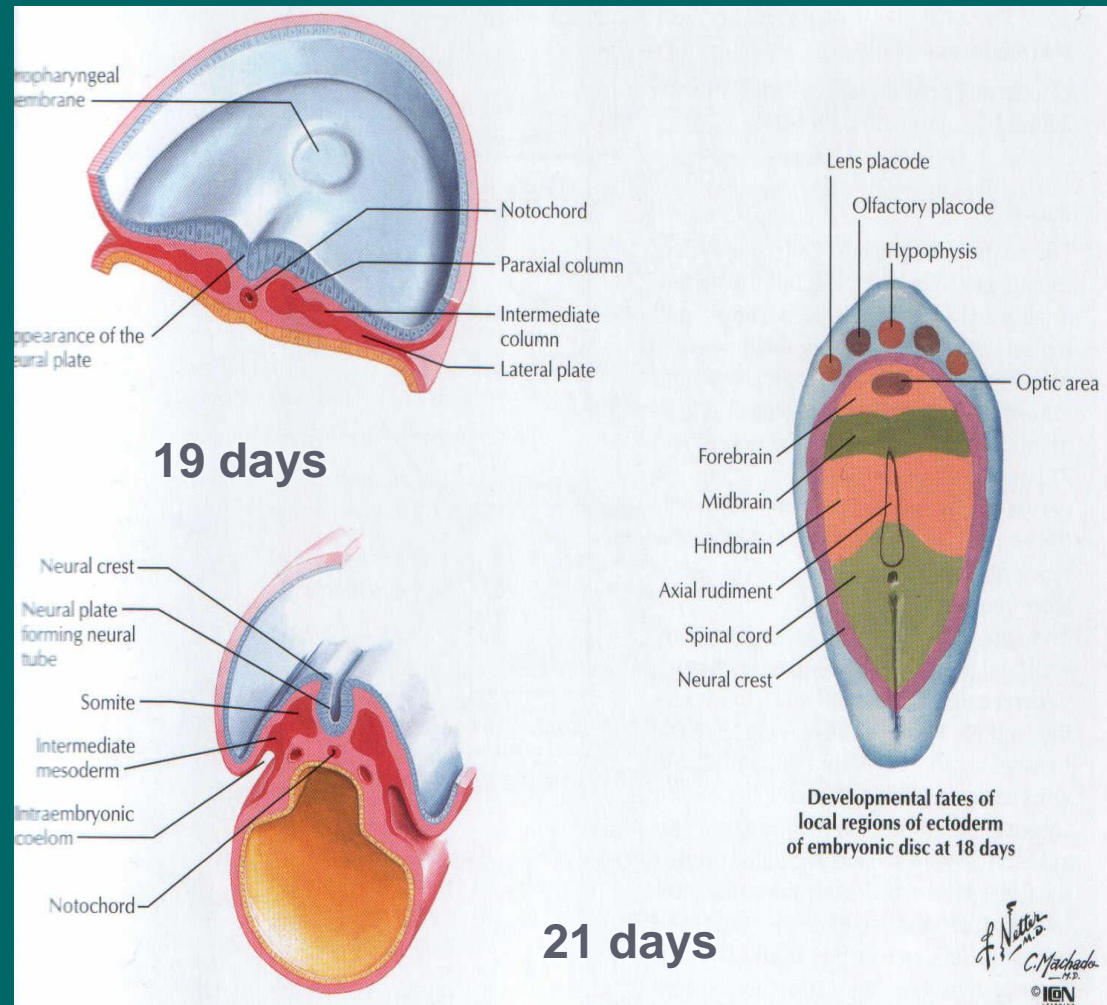
Completion of neurulation by 4th week

- ✦ **Closure of neuropores**
- ✦ **Neural tube presented by :**
 - ✦ **Narrow caudal part → spinal cord**
 - ✦ **Broader cephalic part → brain vesicles**
- ✦ **Separation of neural crest cells**
- ✦ **Appearance of otic and lens placodes**

Summary of the Formation of the Neural Plate

As primitive streak recedes toward the tail of the embryo near the end of gastrulation the mesodermal notochord and paraxial columns begin to induce the formation of the neural plate, a thickening of the overlying surface ectoderm cranial to the primitive streak.

Contributions of the neural ectoderm to the future brain, spinal cord, and neural crest are shown at the picture. Because of the way the neural plate invaginates to form the neural tube, the dorsal sensory component are lateral on the plate, and the ventral, motor component of the tube are medial.



Summary.

1. The notochord develops from the notochordal process and forms the primitive skeletal support of the embryo around which the axial skeleton later forms.
2. The neural plate appears as a midline thickening of the embryonic ectoderm, cranial to the primitive knot. A longitudinal neural groove develops which is flanked by neural folds. These folds meet and fuse to form the neural tube.
3. As this process occurs, some cells migrate ventrolaterally to form the neural crest.
4. The neurulation is completed by the 4th week of the prenatal development.