

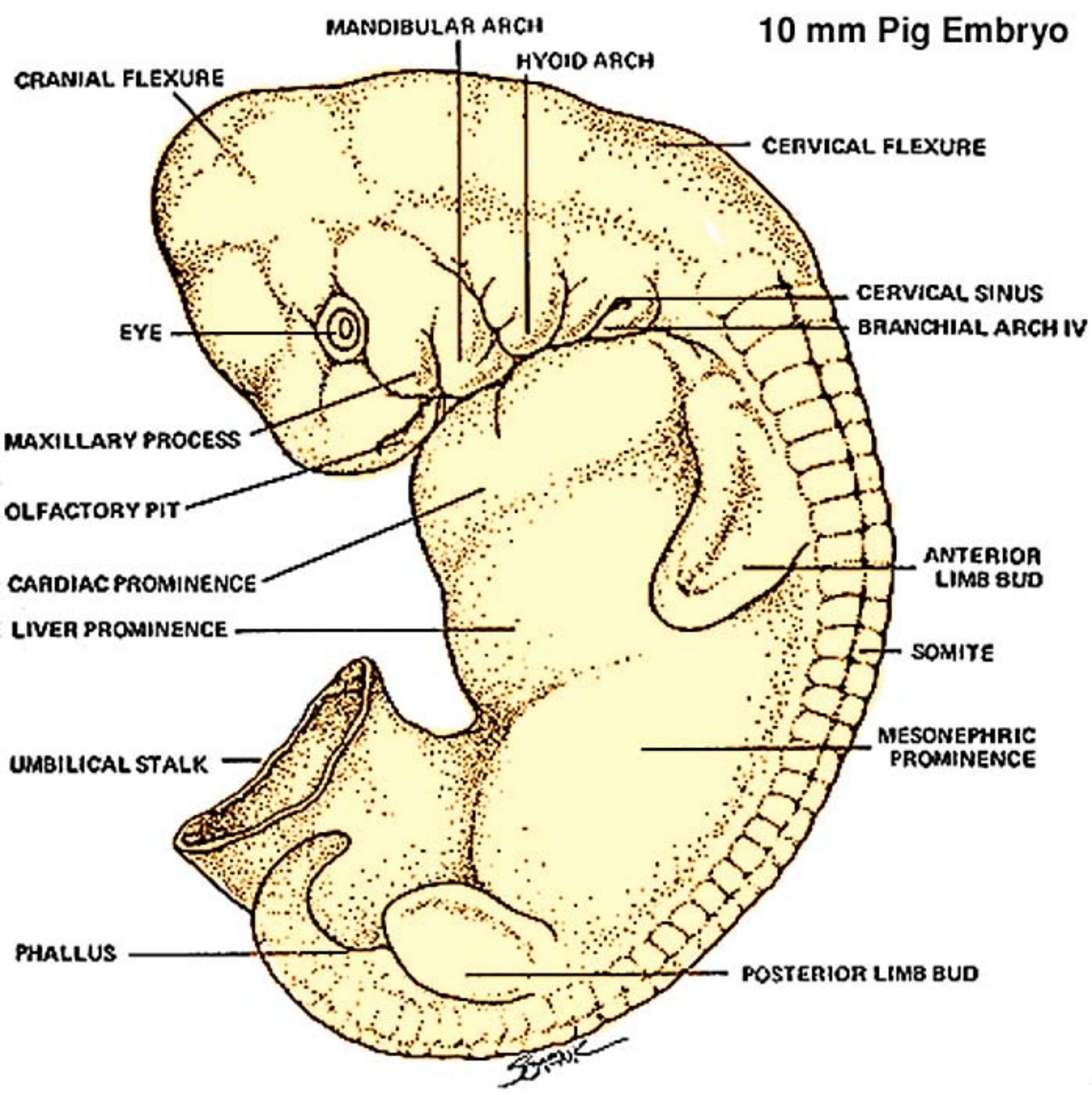
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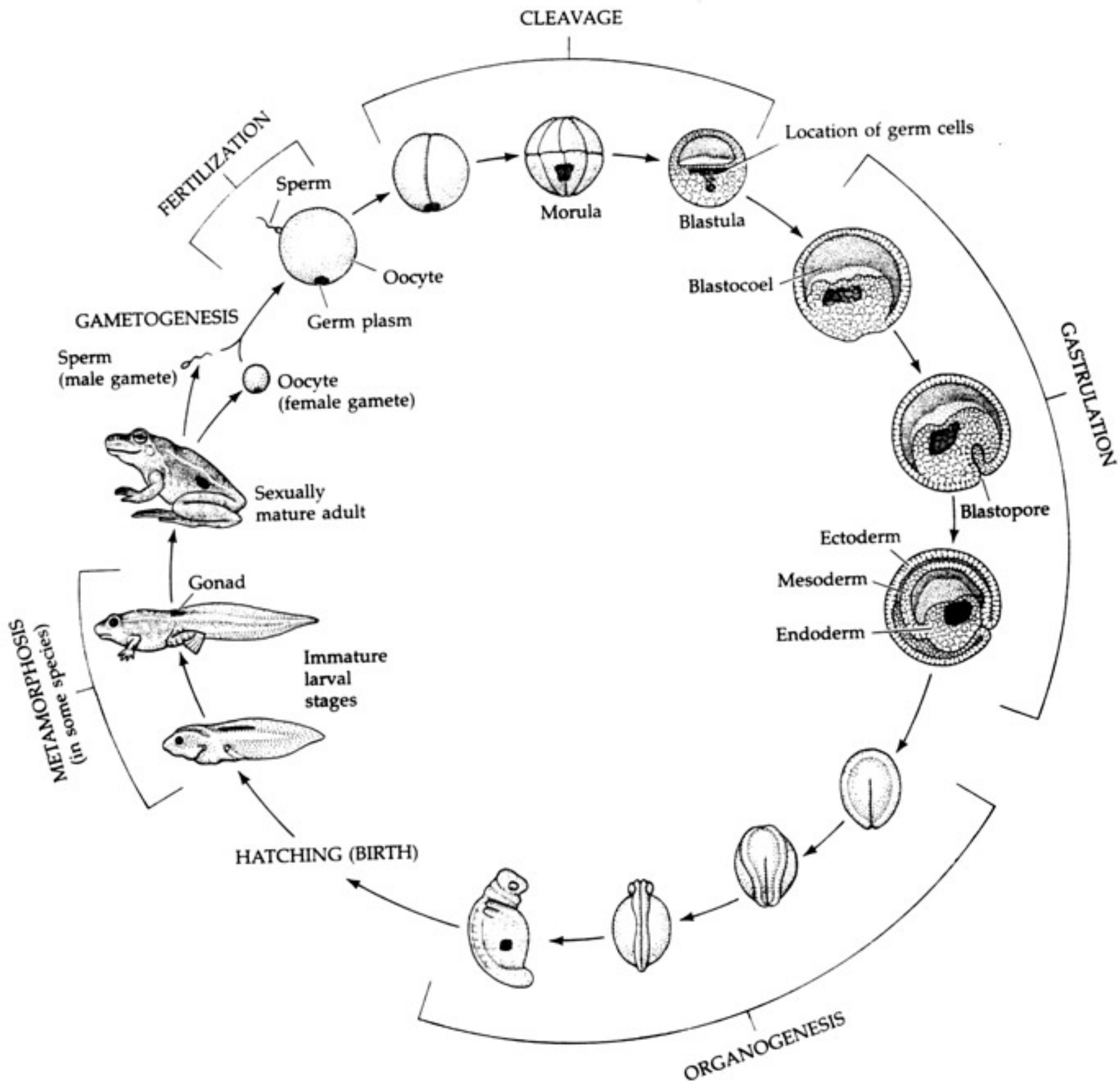
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## Why is embryology in the veterinary curriculum?

- A]** facilitates understanding of clinical developmental anomalies
- B]** developmental anatomy reinforces your knowledge of anatomy
- C]** inherently interesting (progression from a single cell to a fetus)
- D]** provides the kind of foundation knowledge that distinguishes a doctor from a technician (whose knowledge is a black box)
- E]** all of the above

# 10 mm Pig Embryo





# Embryology vs Developmental Anatomy

## Embryology Issues

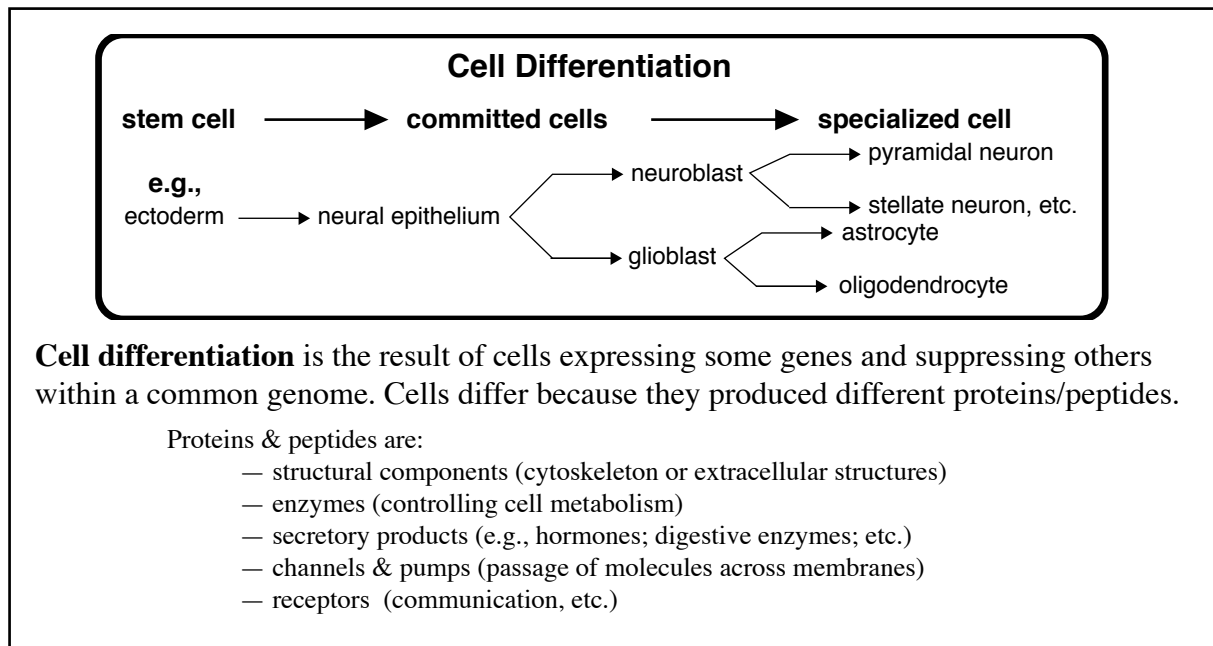
- which genes are active during development
- what proteins/peptides are produced/released to . . .
  - regulate cell adhesion
  - modify the cellular cytoskeleton
  - establish chemical gradients to induce/ modify cell migration
- what cell receptors react to what chemical agents to . . .
  - regulate gene activity

## Developmental Anatomy

Stages of Development (snapshots of a “movie” sequence)

# Early Embryogenesis

**Embryogenesis**, the formation of body structures & organs (organogenesis), requires cell division (proliferation) and cell differentiation (specialization) to produce the great variety of cell types and extracellular products found in the body. Gene expression (and the resultant protein production) is the ultimate explanation for the process of cell differentiation and embryogenesis. The genetic expression of a particular cell depends on its previous genetic history (commitment) and its current cellular environment (intercellular communication).



**Embryonic Period** — defined as the time from fertilization to the earliest (primordial) stages of organ development (about 30 days in dog, cat, sheep, pig; almost 60 days in horse, cattle, human).

**Fetal Period** — the time between the embryonic period and parturition (the end of gestation), during which organs grow and begin to function.

## Fertilization:

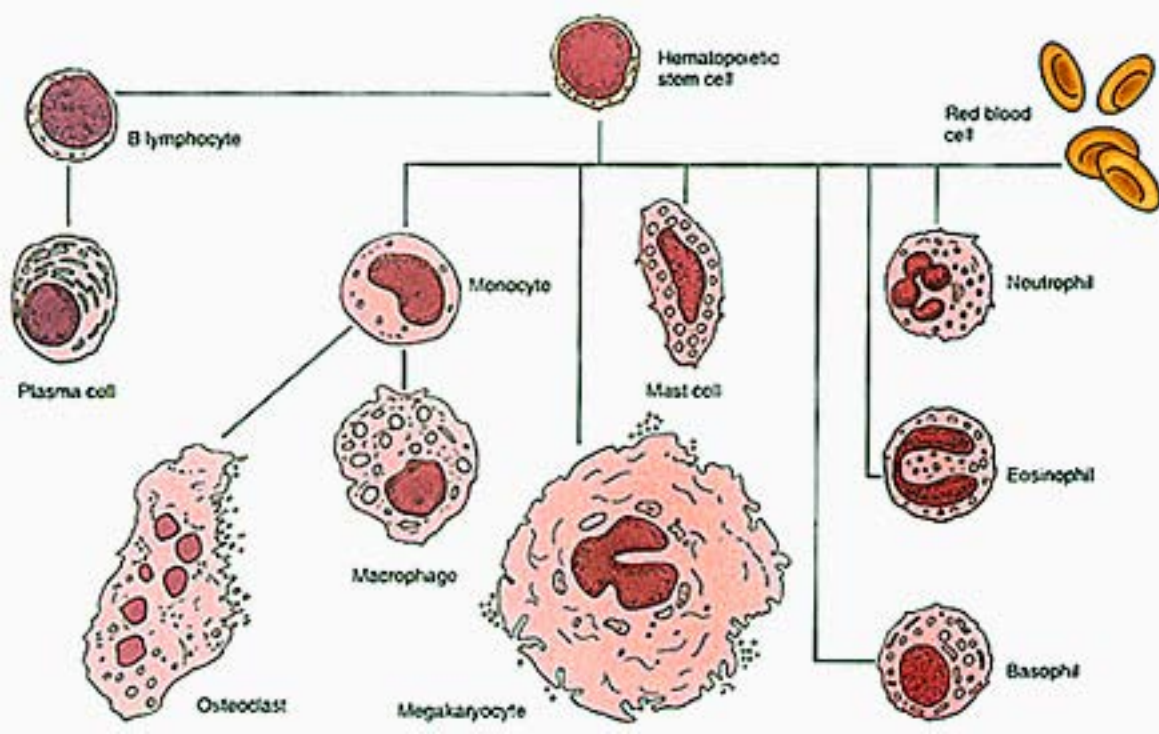
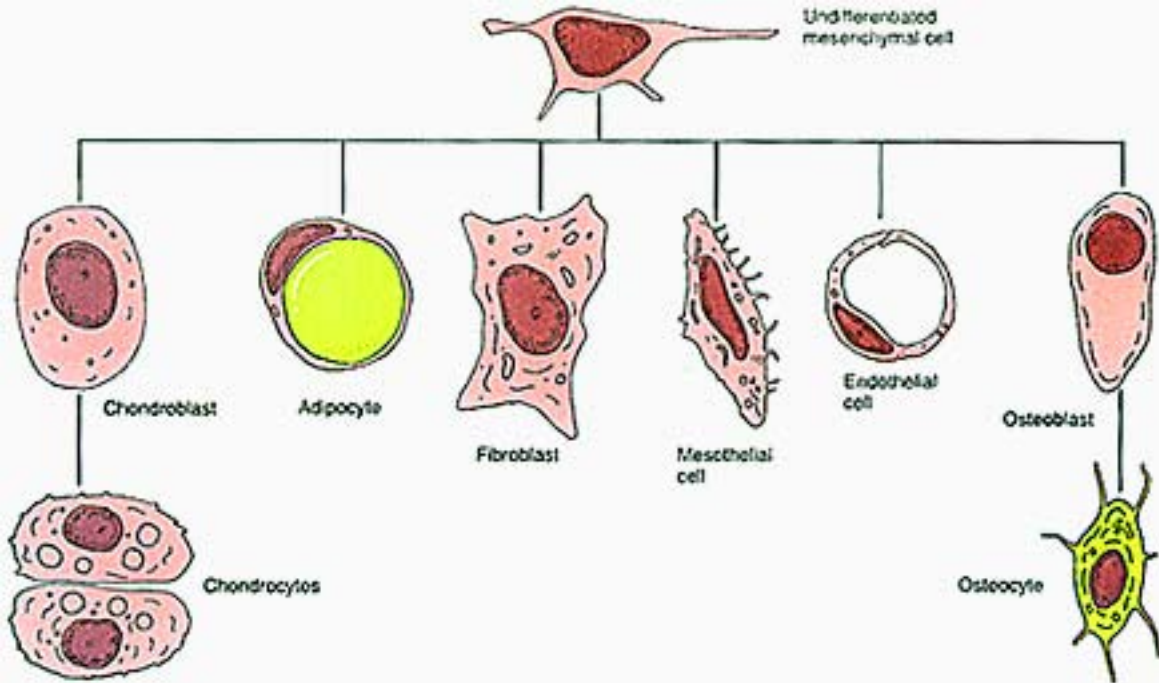
Refers to the union of a haploid oocyte with a haploid spermatozoon to produce a diploid zygote (a single cell capable of developing into a new individual)

**Oocyte** (enveloped by a zona pellucida (glycoprotein membrane) and corona radiata (granulosa cells) at ovulation)

- selective follicles mature at each cycle (in response to circulating FSH hormone from the pituitary)
- primary oocytes resume meiosis following ovulation (having been suspended in Meiosis I since before birth by inhibitory secretion of follicle granulosa cells)
- secondary oocytes complete meiosis (Meiosis II) following fertilization (if unfertilized they degenerate).

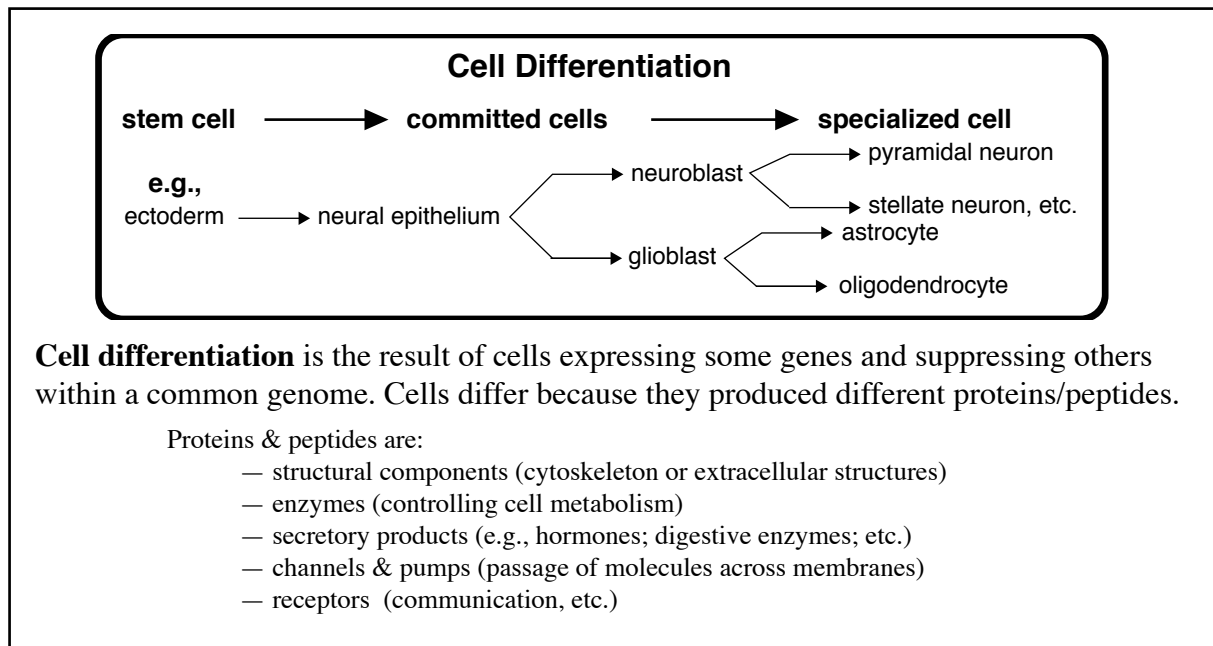
**Spermatozoa** (several hundred million per ejaculate)

- propelled from vagina to uterine tube by contraction of female genital tract
- undergo capacitation (removal of surface proteins that impede making contact with oocyte)
- undergo acrosomal reaction (enzyme release) after binding to zona pellucida (binding triggers release of acrosomal enzymes that denature zona pellucida proteins to facilitate penetration by the reactive sperm).



# Early Embryogenesis

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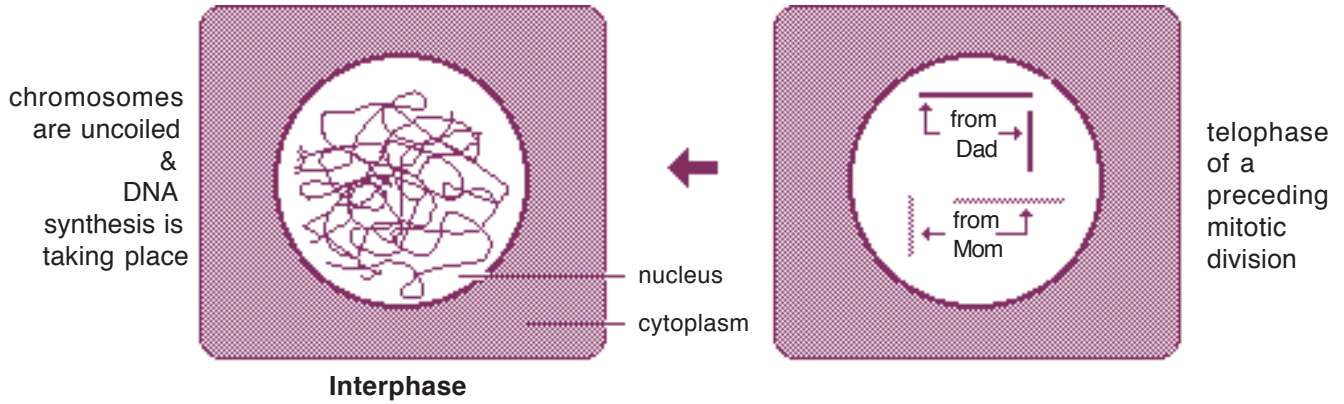
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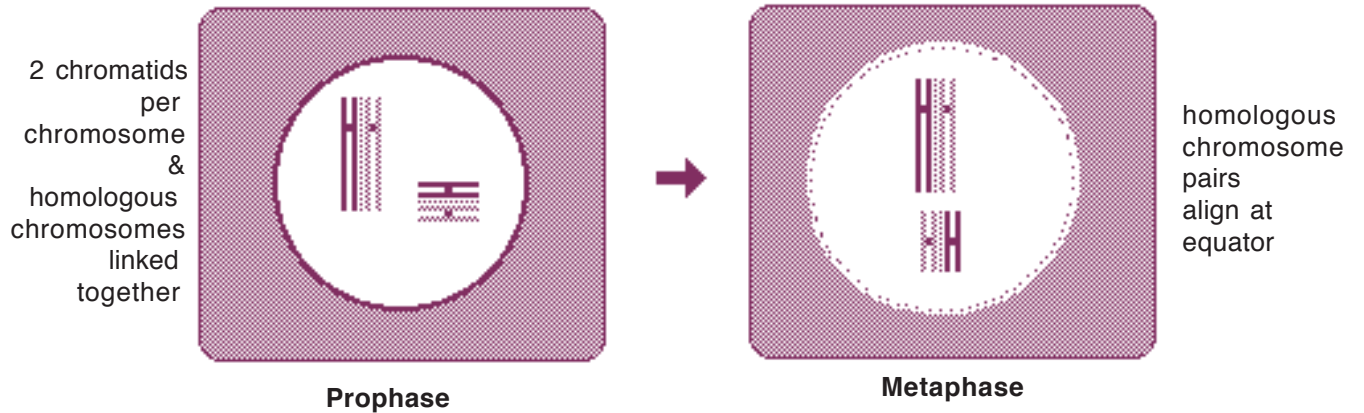
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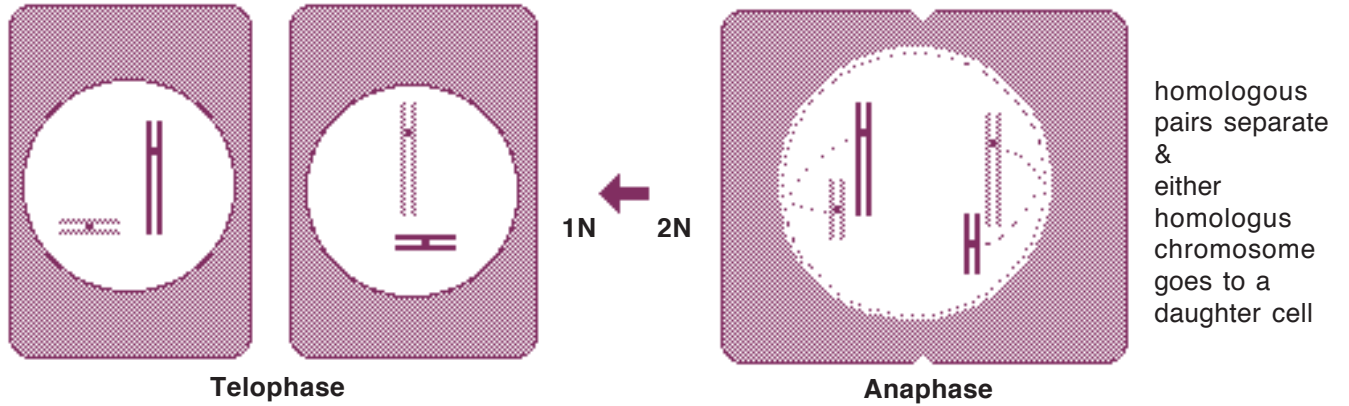
# Primary spermatocyte or oocyte (diploid germ cell)



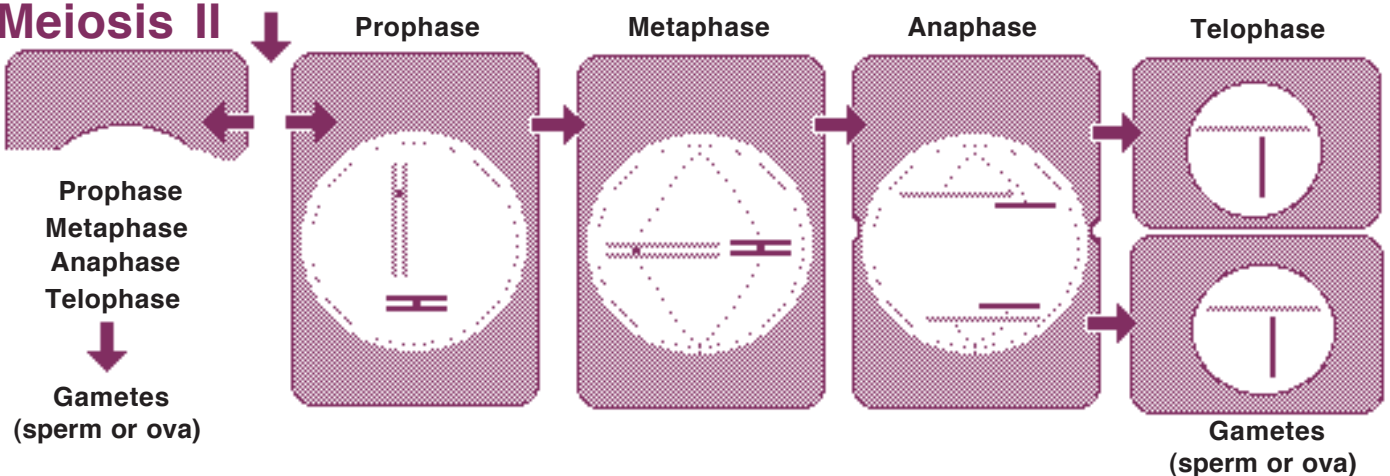
## Meiosis I



### Secondary spermatocytes or oocytes (haploid)



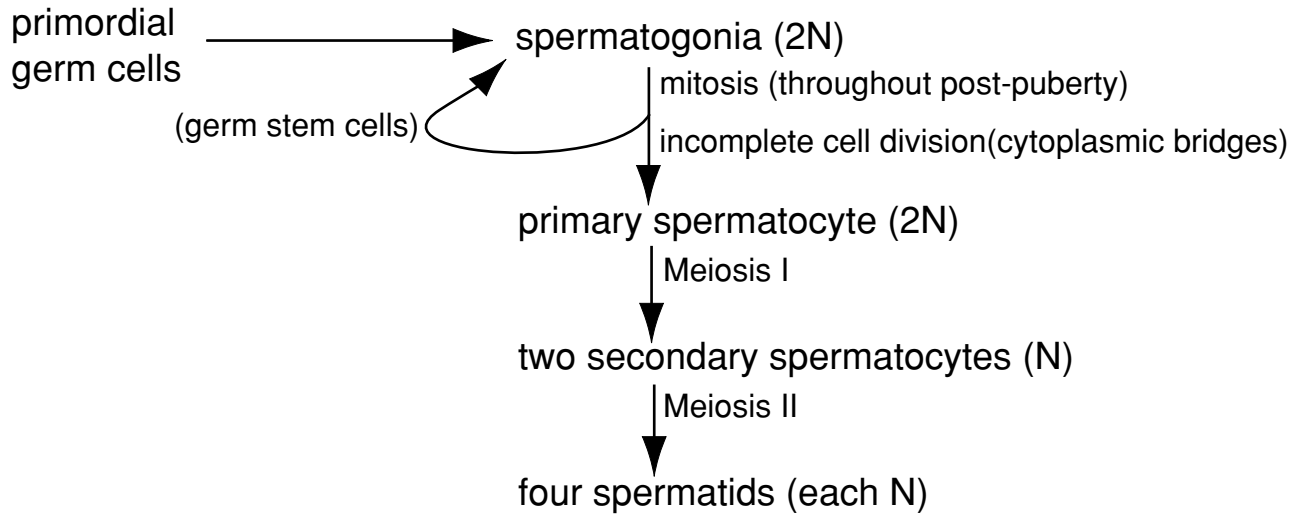
## Meiosis II



# Gametogenesis

## Spermatogenesis (formation of spermatozoa)

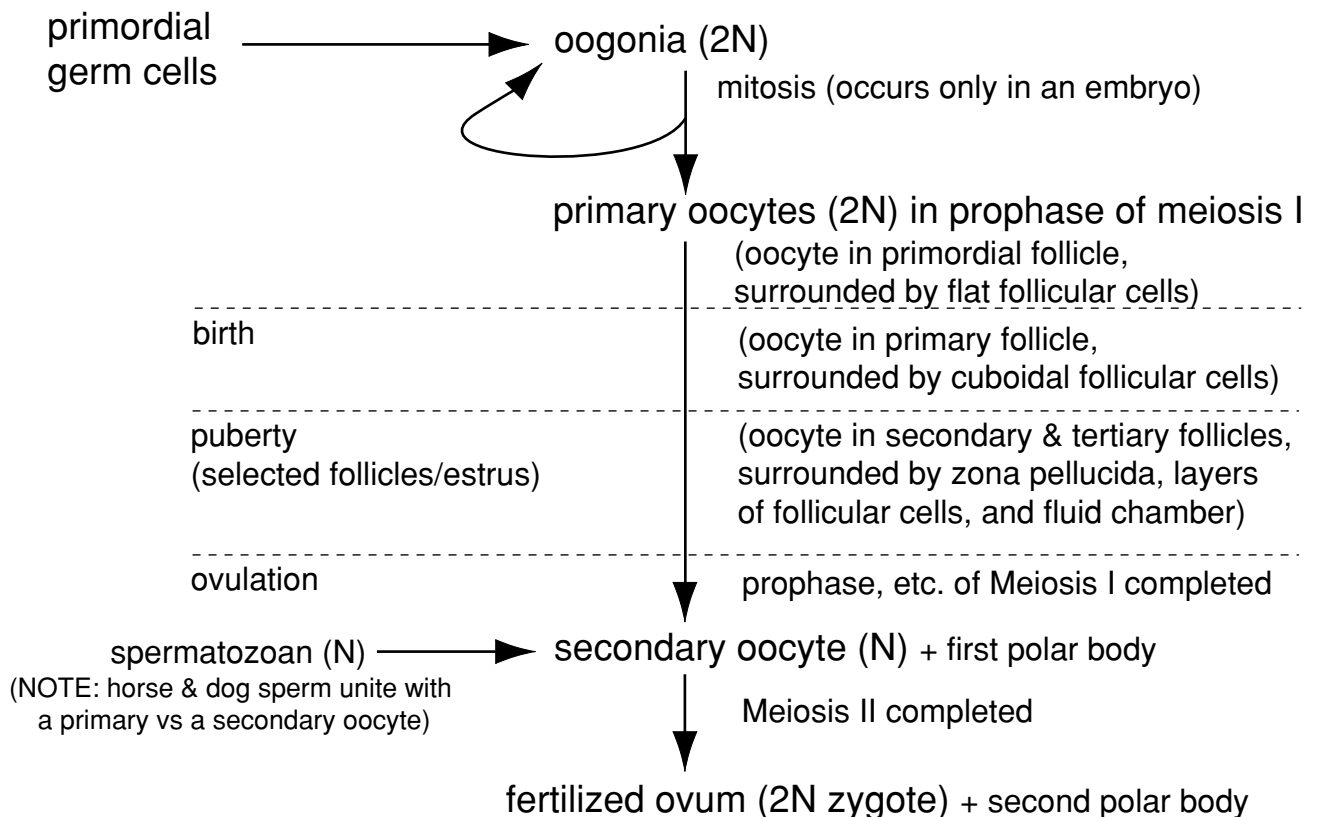
### A] Spermatocytogenesis (formation of spermatids in seminiferous tubules)



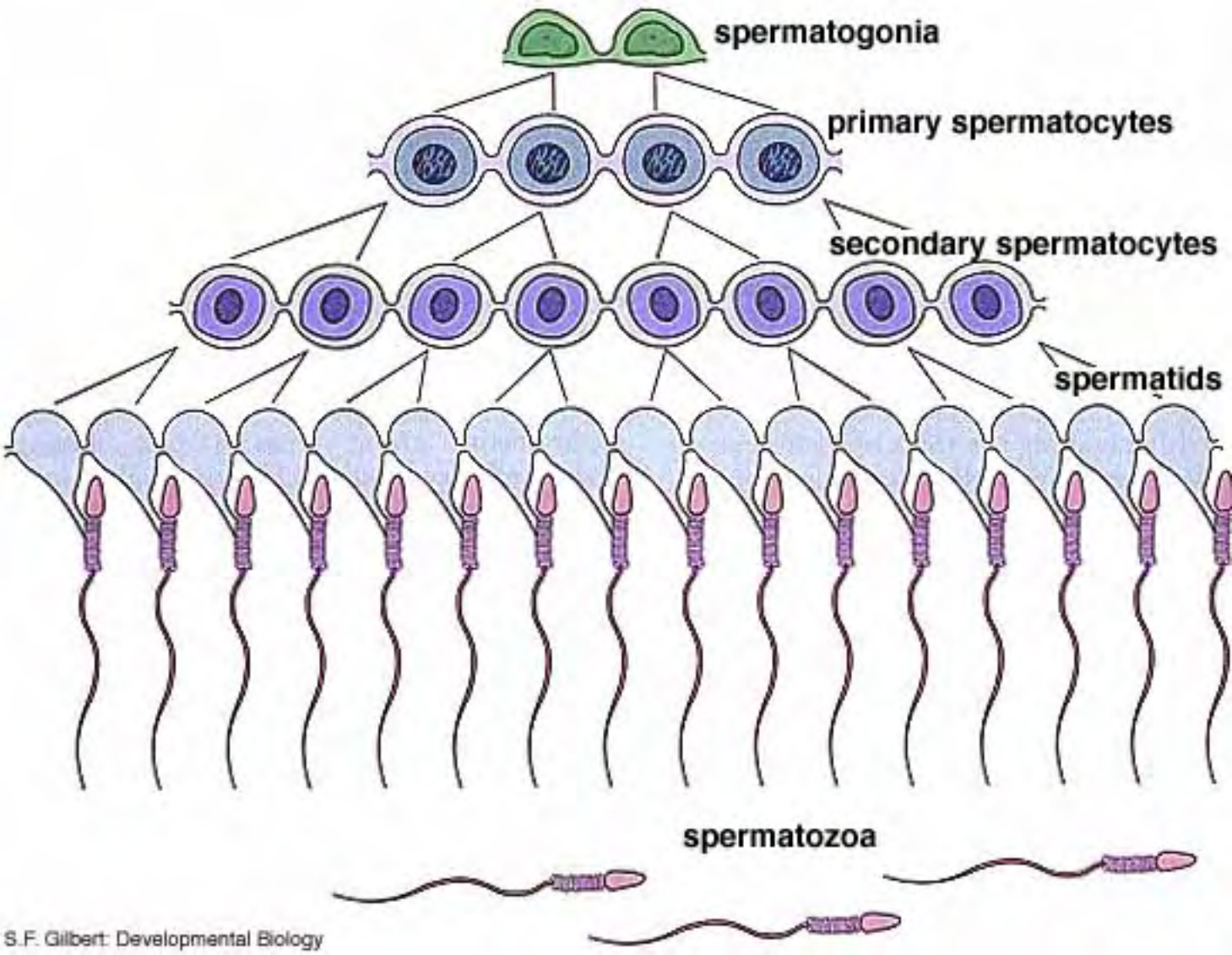
### B] Spermiogenesis (transformation of spermatids to spermatozoa)

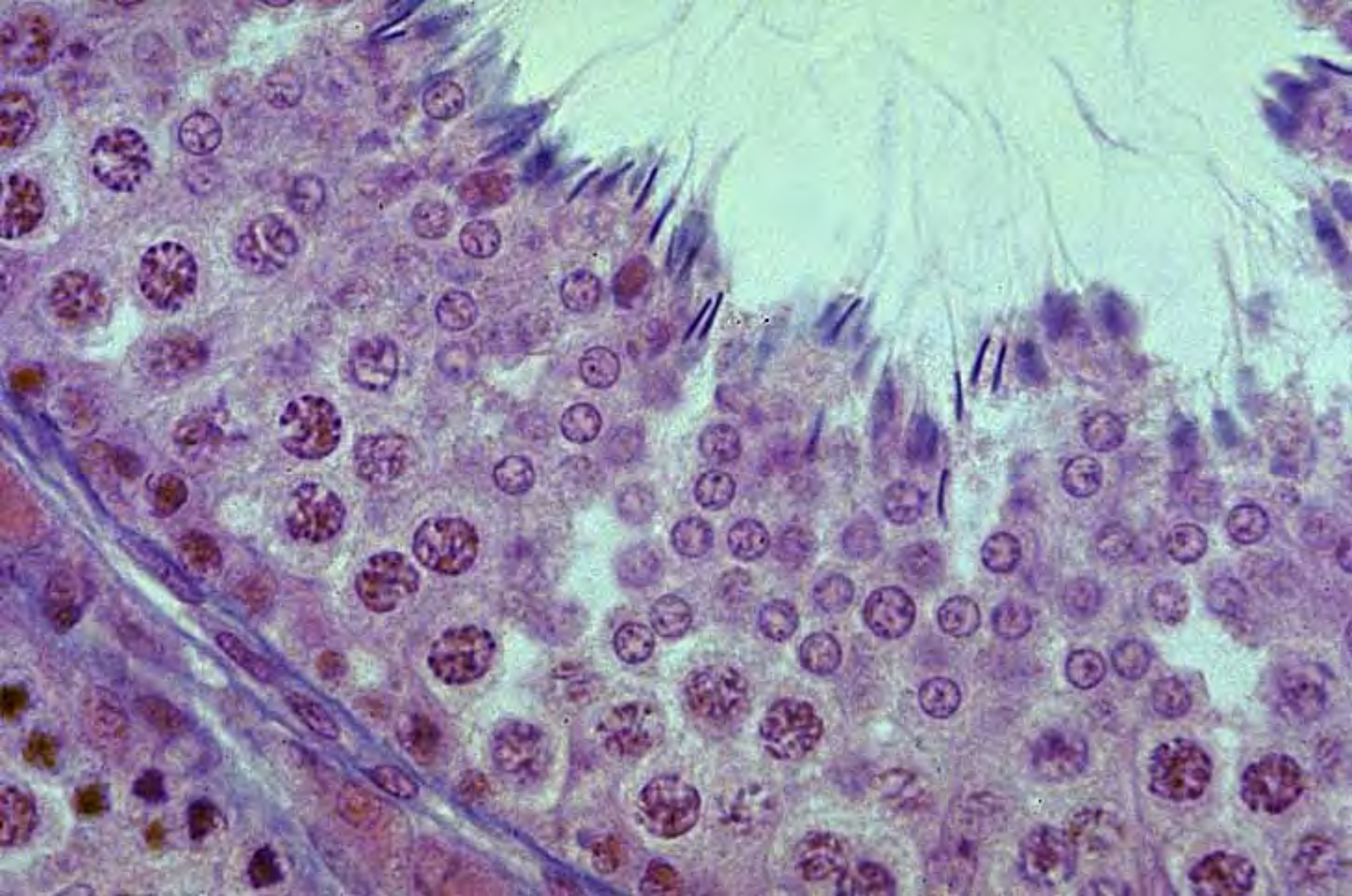
- elongate nucleus, loss of cytoplasm & cytoplasmic bridges, formation of acrosome & tail
- transformation occurs while linked to a Sertoli cell
- spermatozoa are released into lumen of seminiferous tubule

## Oogenesis (formation of an ovum)

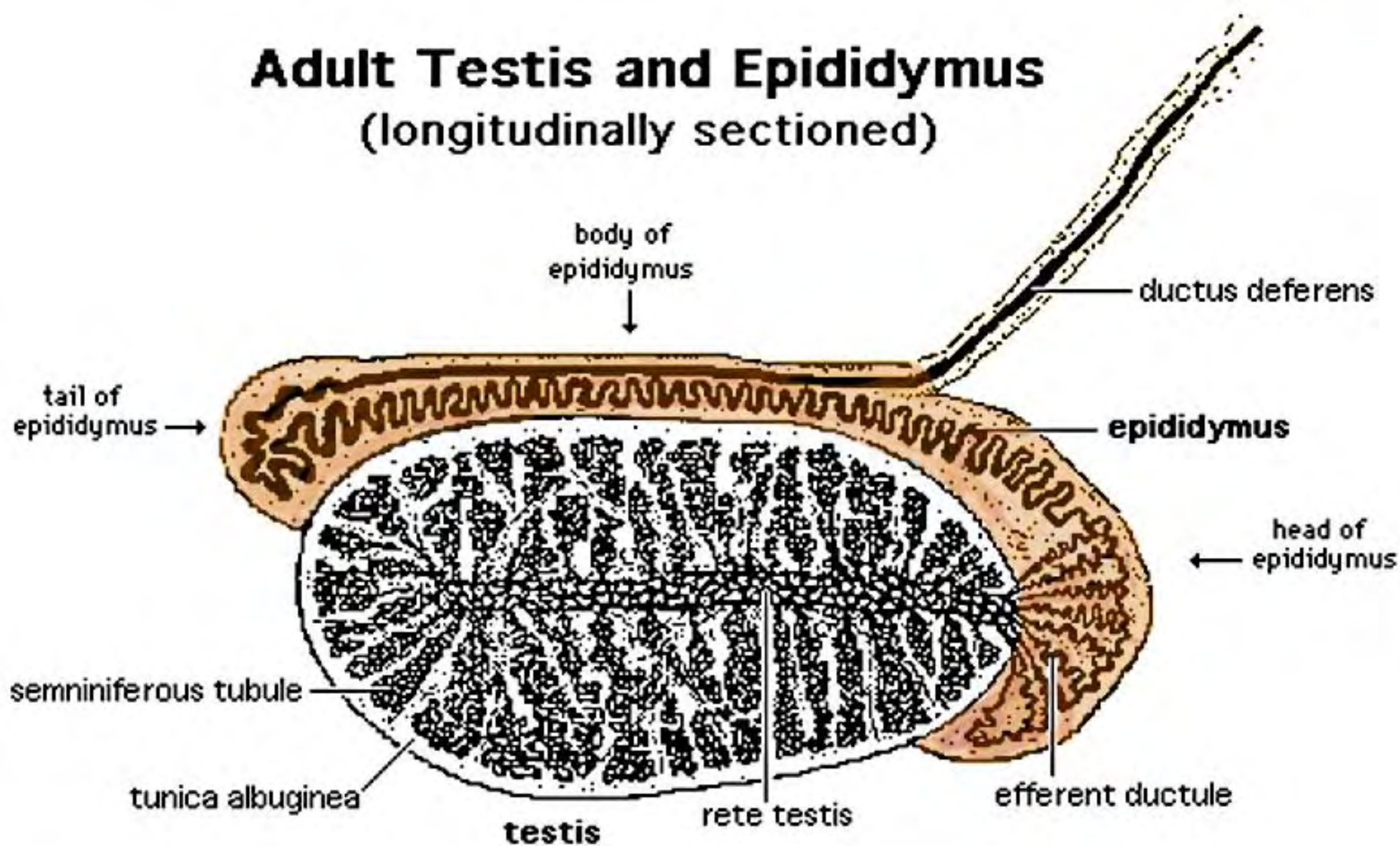


**Note:** Fertilization begins with union of male and female gametes and ends with the start of zygote cell division (cleavage).

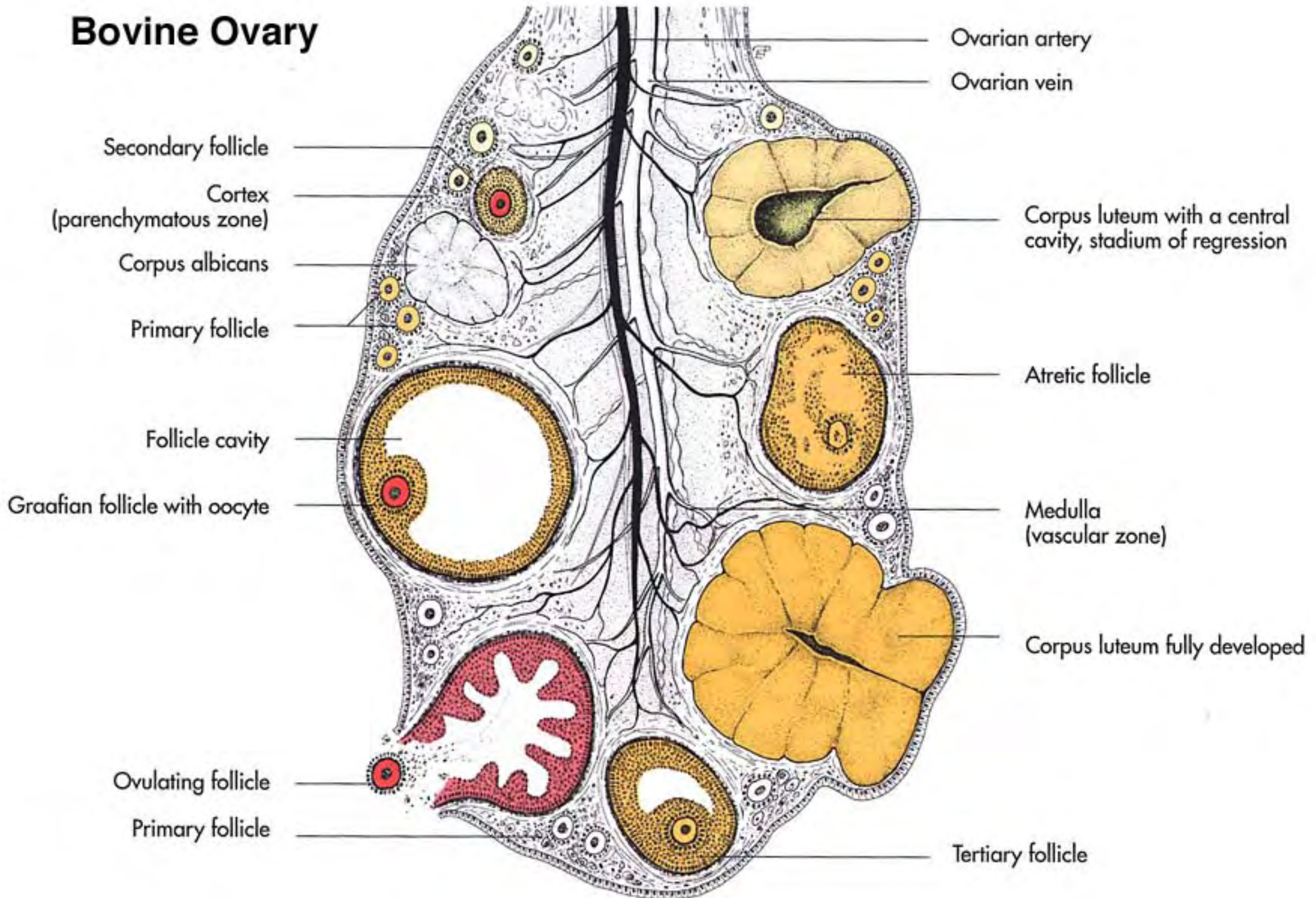


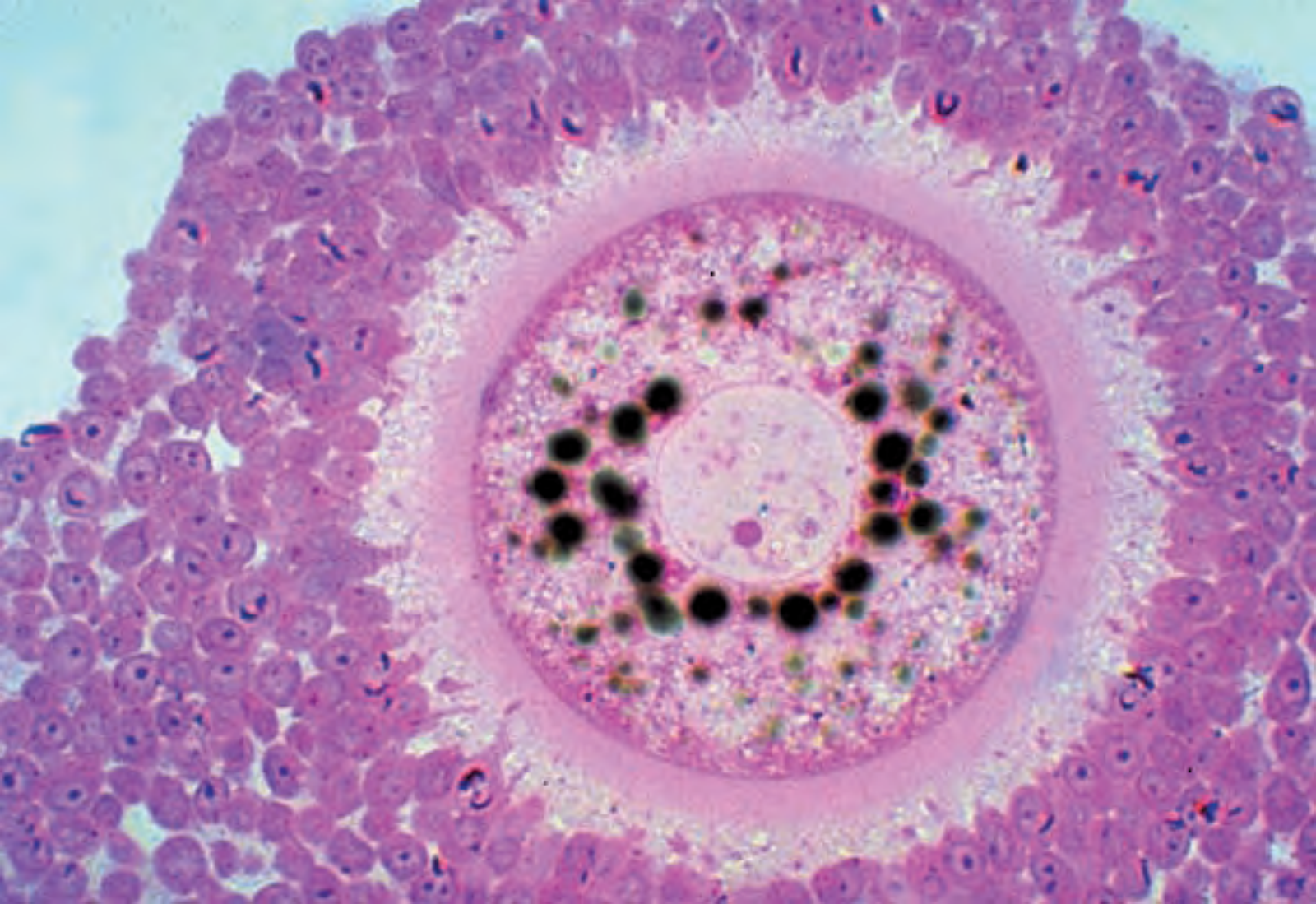


# Adult Testis and Epididymus (longitudinally sectioned)



# Bovine Ovary









**Fertilization of one ovum by multiple sperm is ...**

**A]** impossible

**B]** possible

**C]** sexy

**D]** fatal

**E]** creates a chimera

## Fertilization details:

Fertilization begins with gamete fusion (zygote formation). The fusion of a spermatozoon with a secondary oocyte takes place in the uterine tube, near the ovary:

- to begin, a spermatozoon binds to a specific glycoprotein on the zona pellucida that surrounds the oocyte [this recognition process precludes union with foreign sperm];
- the spermatozoon releases degradative enzymes (acrosomal reaction) that allows the sperm cell to penetrate the zona pellucida;
- spermatozoon and oocyte plasma membranes fuse (the secondary oocyte completes meiosis);
- the oocyte precludes fusion with other sperm by immediately canceling its membrane potential (via  $\text{Ca}^{++}$  influx) and then by denaturing its zona pellucida (via enzymes released by exocytosis from oocyte cytoplasmic granules);
- male & female haploid pronuclei make contact, lose their nuclear membranes, and begin mitosis (mitosis begins 12 hours after sperm fusion; DNA synthesis takes place before mitosis)

Fertilization ends with the initiation of zygote cell division (the start of cleavage)

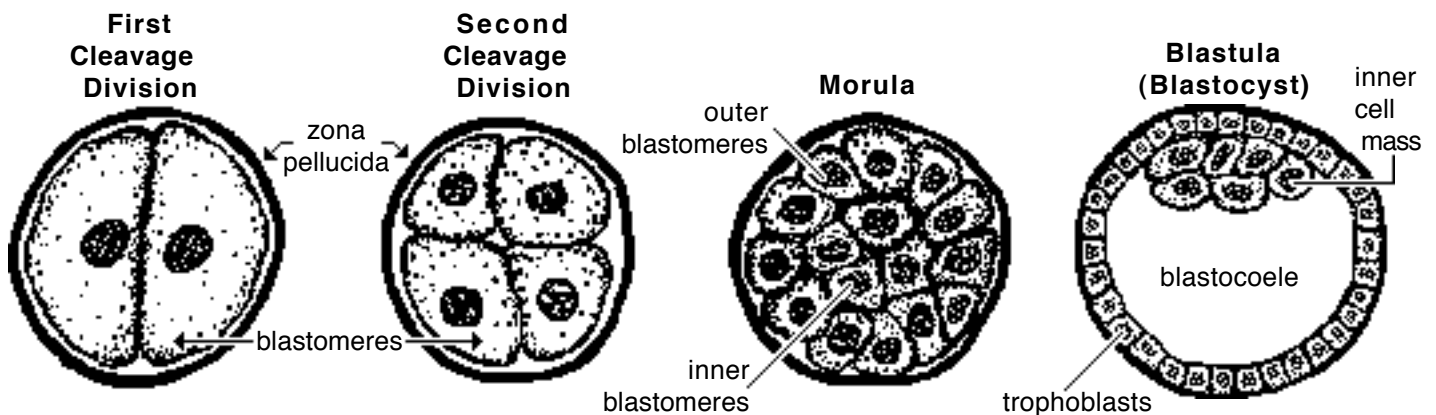
## Cleavage:

This term refers to the series of mitotic divisions by which the large zygote is fractionated into numerous “normal size” cells. Each daughter cell of the cleavage process is termed a *blastomere*.

- cleavage begins with a *zygote*, progresses through compaction to a *morula* stage and terminates at the start of the *blastocyst* (blastula) stage
- the first eight blastomeres are undifferentiated and have identical potential in domestic mammals; thereafter, blastomeres differentiate into inner & outer cells with different missions

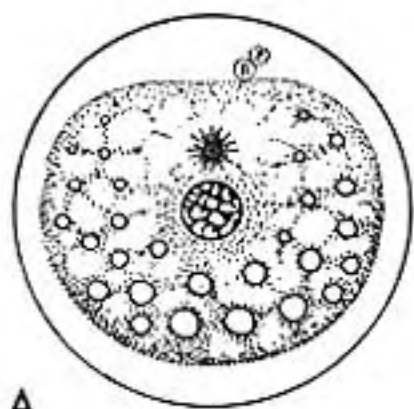
**Note:** The first cleavage division occurs 1 to 5 days following ovulation (depending on species), thereafter cells divide about once every 12 hours;

As many as eight generations of mitoses may occur without intervening cell growth (cytoplasmic increase). Thus, e.g., one 150 micron diameter zygote can become a collection of 256 cells, each about 7 microns in diameter.

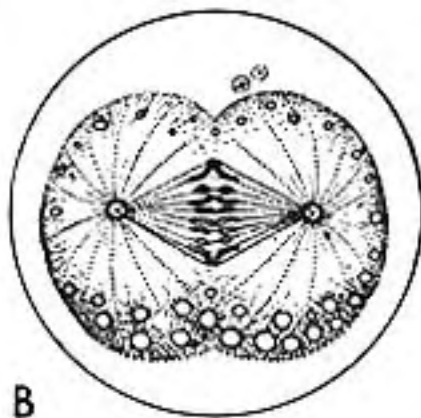


A **morula** [L.= small mulberry] is a solid ball of blastomeres, within a zona pellucida. A morula typically consists of 16 to 64 blastomeres = four to six cell divisions. Blastomeres become compacted; cells packed on the inside differentiate from those along the surface of the morula:

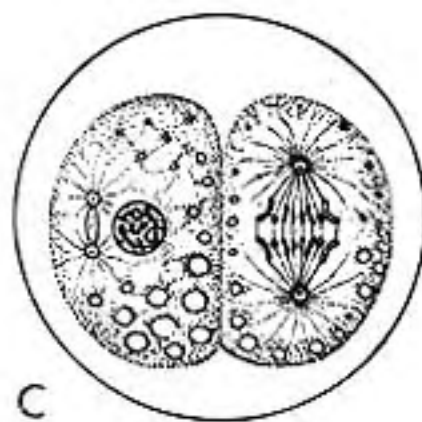
- *outer blastomeres* become flattened and form tight junctions (resulting in reduced permeability to fluids); they develop the capacity to secrete fluid (internally); they are destined to become *trophoblasts* which form the chorion & amnion (fetal membranes);
- *inner blastomeres* form gap junctions to maximize intercellular communication; they are destined to become *inner cell mass* which forms the embryo (plus two fetal membranes).



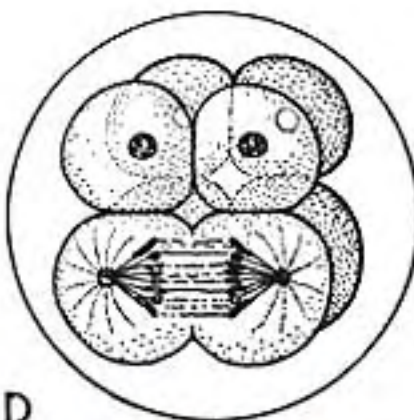
A



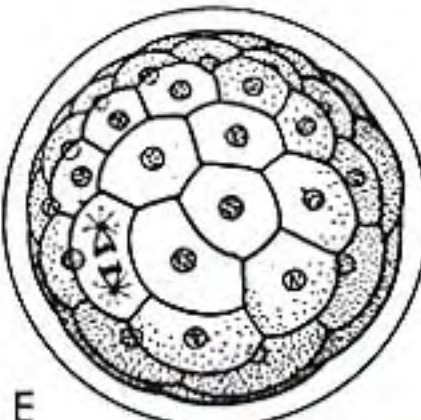
B



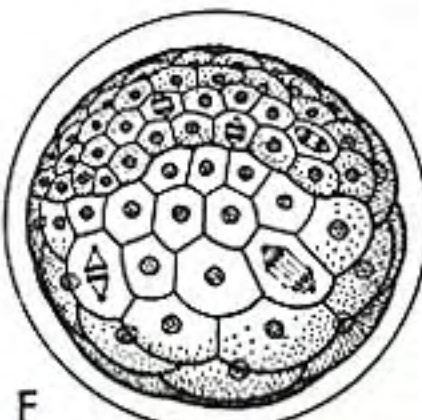
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D



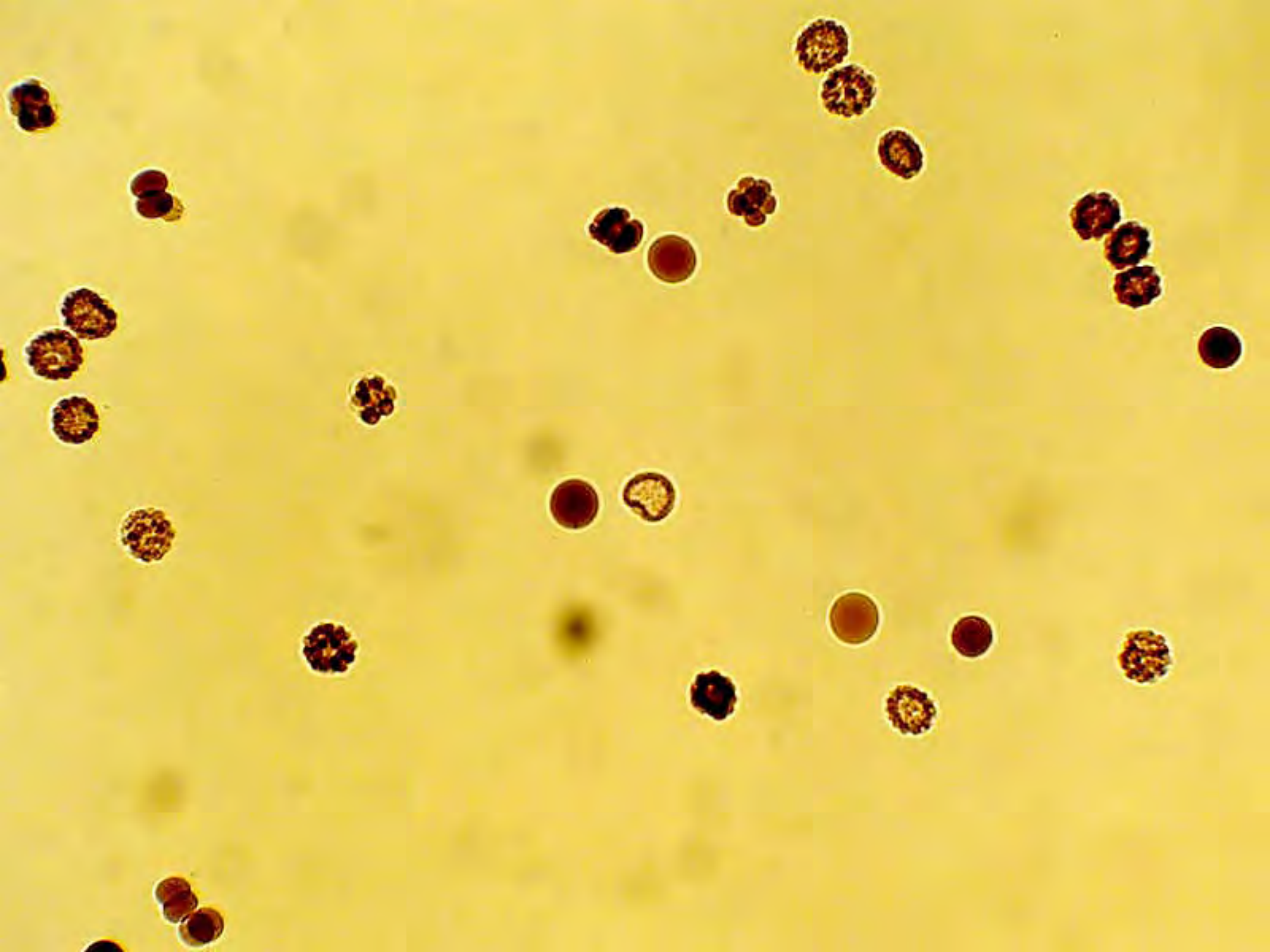
E

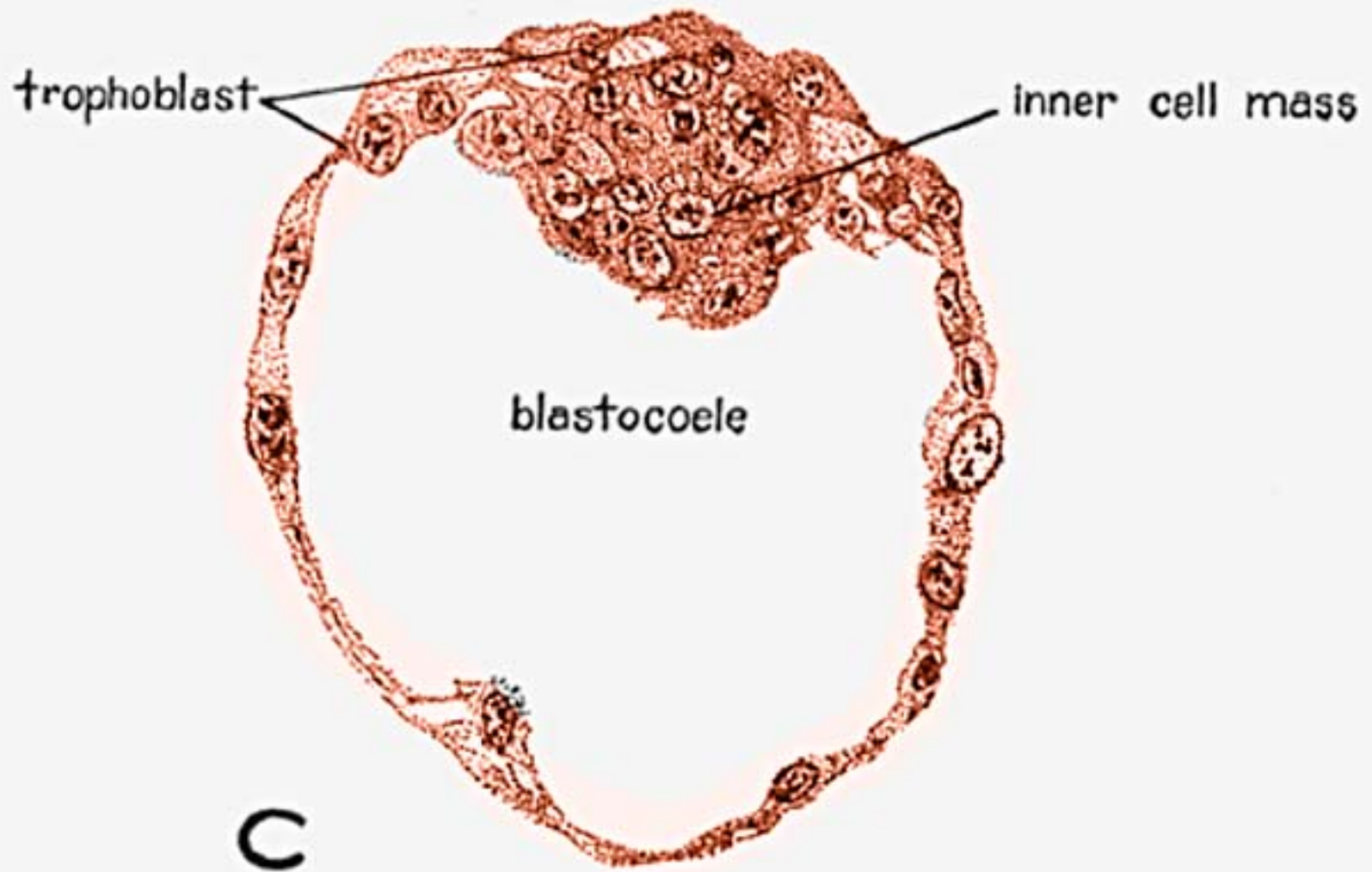
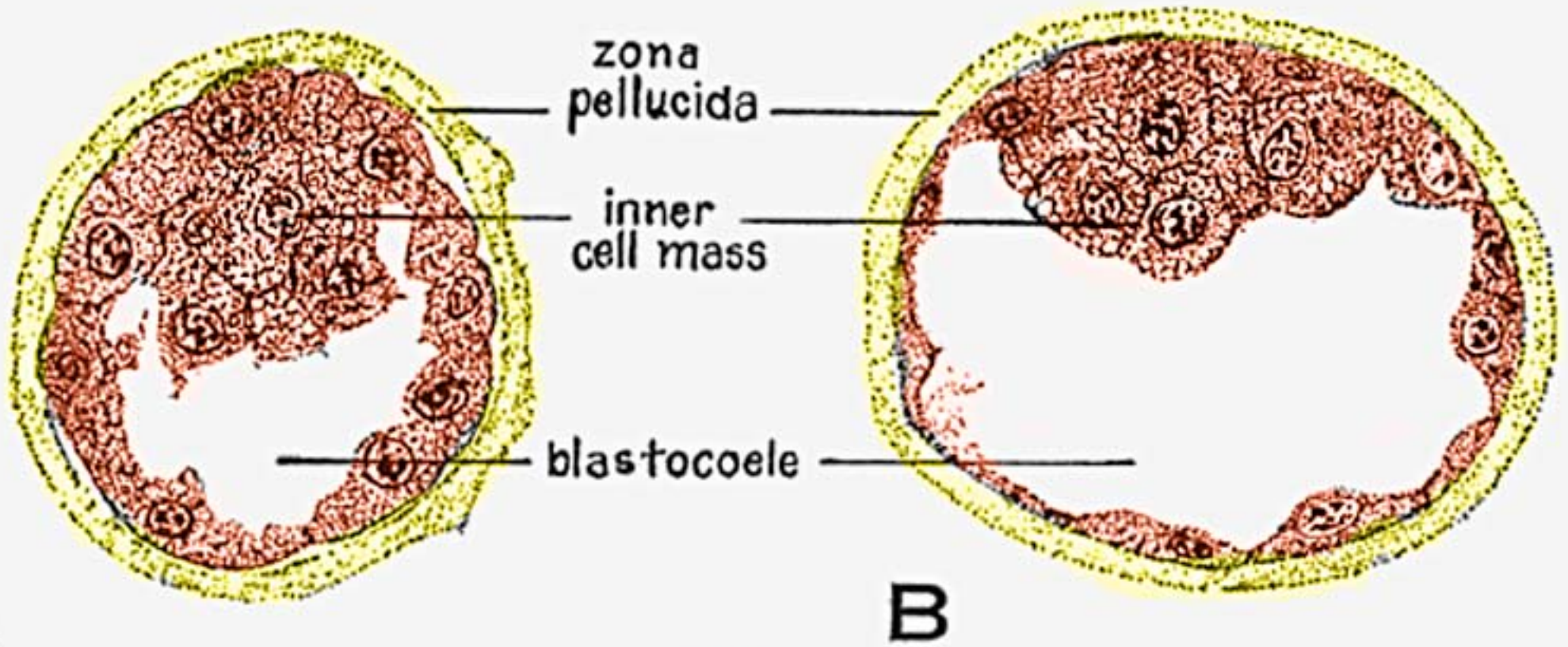


F









- Note:**
- As few as three inner blastomeres are sufficient to produce an entire embryo (and adult).
  - When a morula leaves the uterine tube and enters the uterus (uterine horn) it is at about the 16-cell stage, around 4 to 7 days after fertilization (depending on species).
  - The 32-cell stage morula (5-7 days post ovulation) is ideal for embryo transfer in cattle.

A **blastocyst** (or blastula) develops during week two following rupture of the zona pellucida. It consists of a large number of blastomeres arranged to form a hollow (fluid filled) sphere/cylinder containing an **inner cell mass** (embryoblast), a collection of cells localized inside one pole (end) of the blastula. The surface cells of the blastocyst are designated **trophoblasts**, and the fluid cavity is called a **blastocoele**. Eventually the blastocyst attaches to the uterine wall (implantation).

#### **Cleavage in fish, reptiles, and birds:**

Large quantities of yolk impede cell division during cleavage. Thus a *blastodisc* (rather than a spherical or elliptical blastocyst) is formed at the animal pole of the egg.

A *telolecithal ovum* (egg with large amounts of asymmetrically distributed yolk) has its nucleus displaced to one end (pole). Such an ovum has an *animal pole* where the nucleus is located and an opposite *vegetal pole* where yolk is concentrated. Cleavage is partial (meroblastic): cells divide more rapidly (completely) at the animal pole than at the vegetal pole. The result is many, small blastomeres (micromeres) at the animal pole and few, large macromeres at the vegetal pole. (Cleavage is completed and gastrulation is underway and the conceptus is composed of about 60,000 cells by the time a chicken egg is laid.)

In contrast, mammalian ova have meager amounts of yolk (oligolecithal ova) which is uniformly distributed (isolecithal). Cleavage is holoblastic (total): each blastomere division produces two equal-size daughter cells. Thus animal and vegetal poles are not evident in mammalian ova.

#### **TWINS**

*Monozygotic*: identical (same genetic composition) twins can result from either:

- 1] separation of early blastomeres (up to the 8-cell stage)—each separate blastomere(s) develops into an independent conceptus [conceptus = embryo and placental membranes]; or
- 2] separation of inner blastomeres within a single morula—each separate blastomere(s) develops into an independent embryo and the two embryos share a common placenta (this is less common than the first possibility).

Note: Diplopagus (Conjoined; Siamese) twins, as well as double heads, etc. types of anomalies are the result of separations later in embryonic development.

*Dizygotic*: fraternal twins result when two (or more) zygotes develop “independently” during the same pregnancy (independence can be compromised by fusion of fetal membranes and blood supplies). It is possible for fraternal blastomeres to merge and produce a single conceptus that has two different genotypes represented among its population of cells (a chimera).

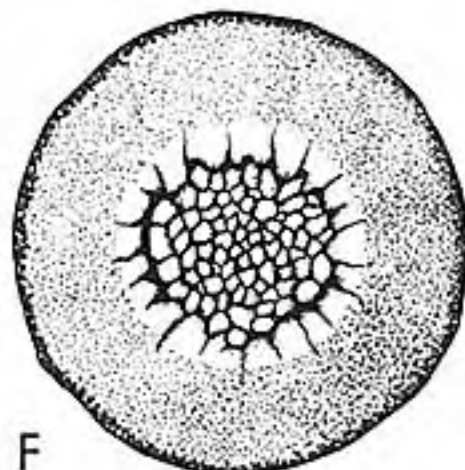
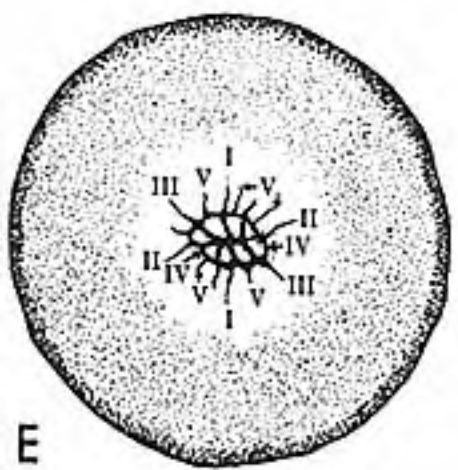
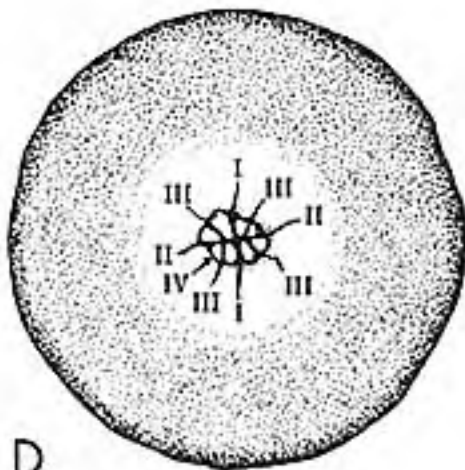
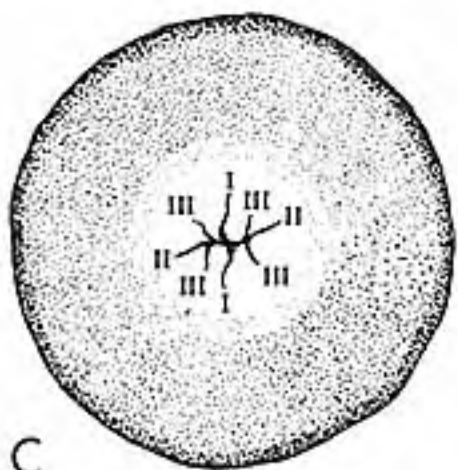
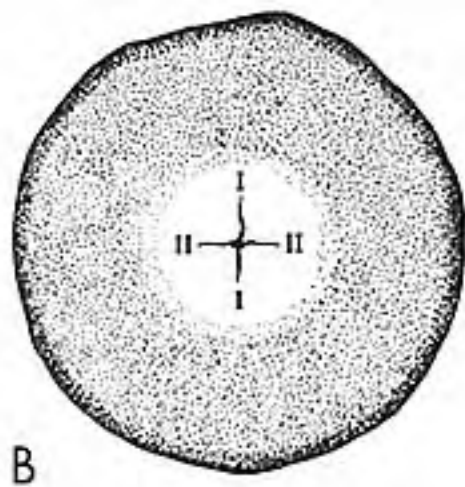
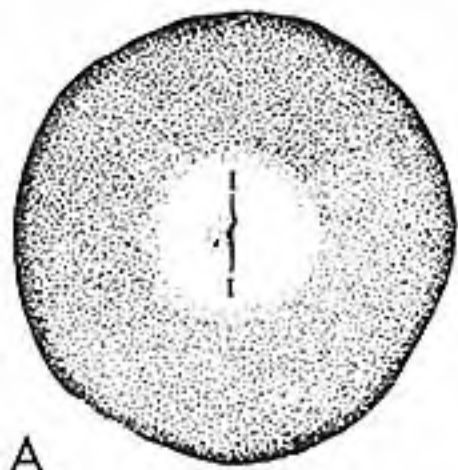
#### **GERM LAYERS are formed during gastrulation:**

**Ectoderm**, **mesoderm** and **endoderm** are designated *primary germ layers* because origins of all organs can be traced back to these three layers.

Ectoderm forms epidermis of the skin, epithelium of the oral and nasal cavities, and the nervous system and sense organs.

Mesoderm forms muscle and connective tissue, including bone, and components of the circulatory, urinary and genital systems.

Endoderm forms mucosal epithelium and glands of respiratory and digestive systems.







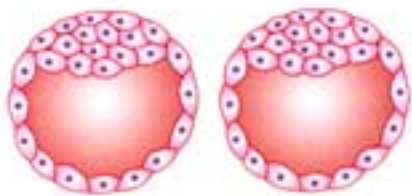
Two cell stage



Two cell stage



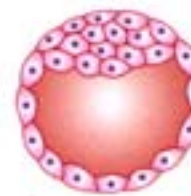
Two cell stage



Two blastocysts



Two inner cell masses



One blastocyst



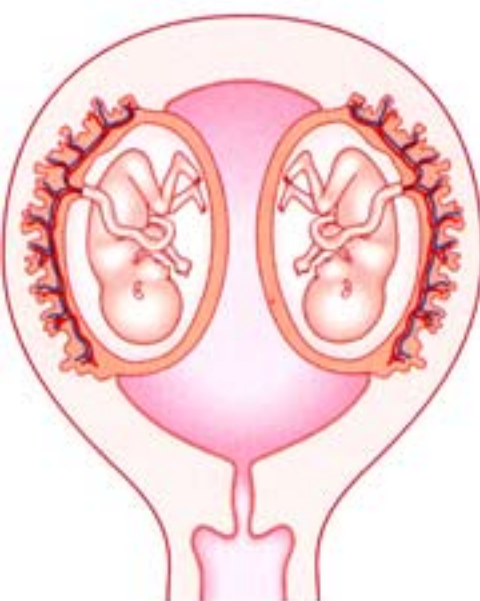
Two implanted blastocysts



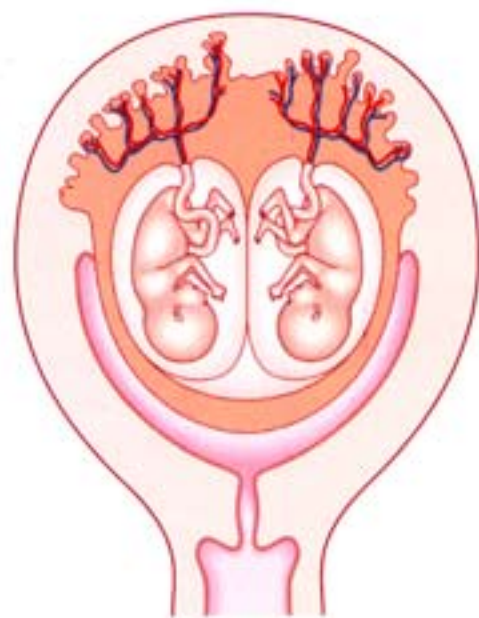
Implanted blastocyst



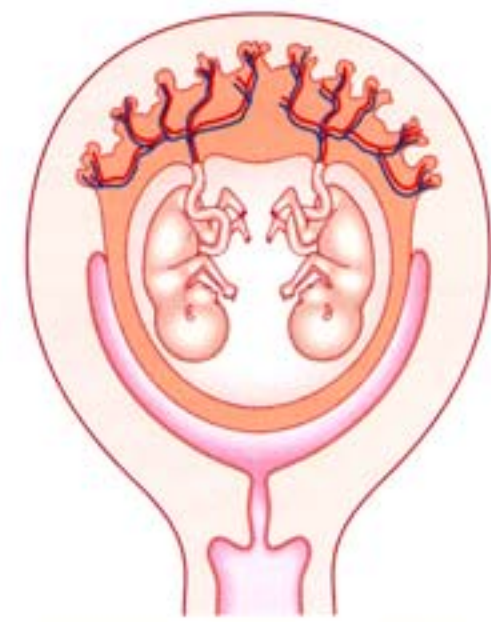
Division of the embryonic disc



Two chorions, amniotic sacs  
and placentae



Two amniotic sacs,  
common placenta



Single amniotic and chorionic sacs,  
common placenta

**(A) Dizygotic**

**(B) Monozygotic**

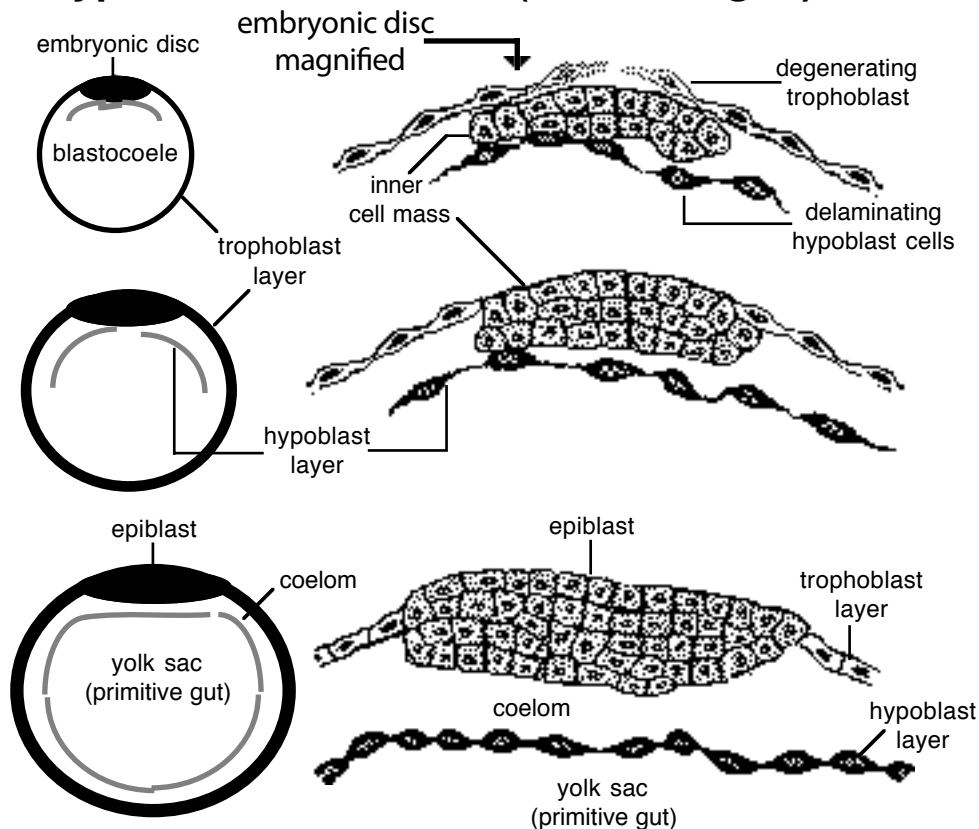
**(C) Monozygotic**

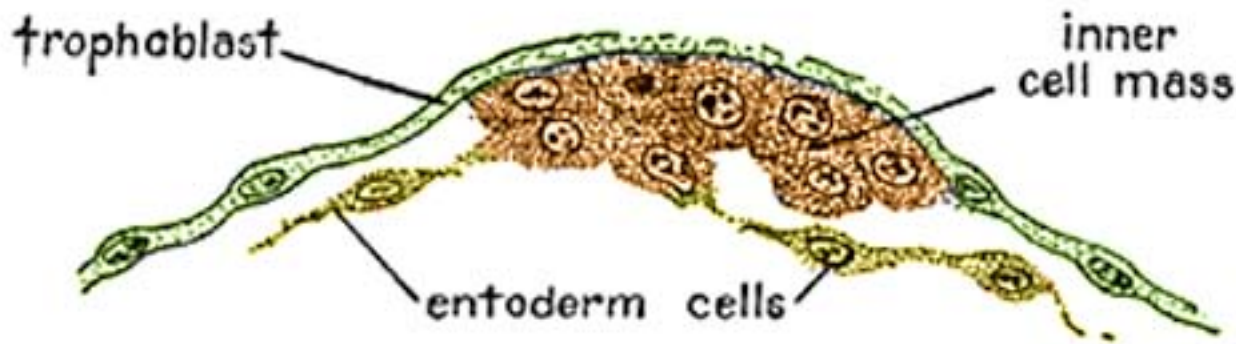
## Gastrulation:

Gastrulation is the morphogenic process that gives rise to three germ layers: **ectoderm**, **mesoderm**, and **endoderm**. (In a *gastrula* [Gr.= little stomach] one can see evidence of primitive gut formation.) Gastrulation includes the following sequence, beginning with a blastocyst:

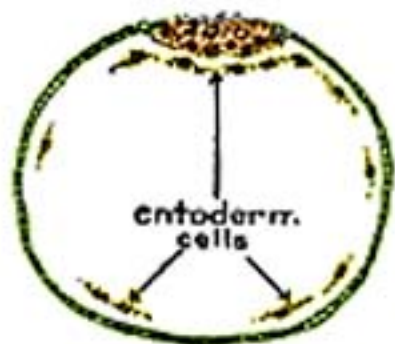
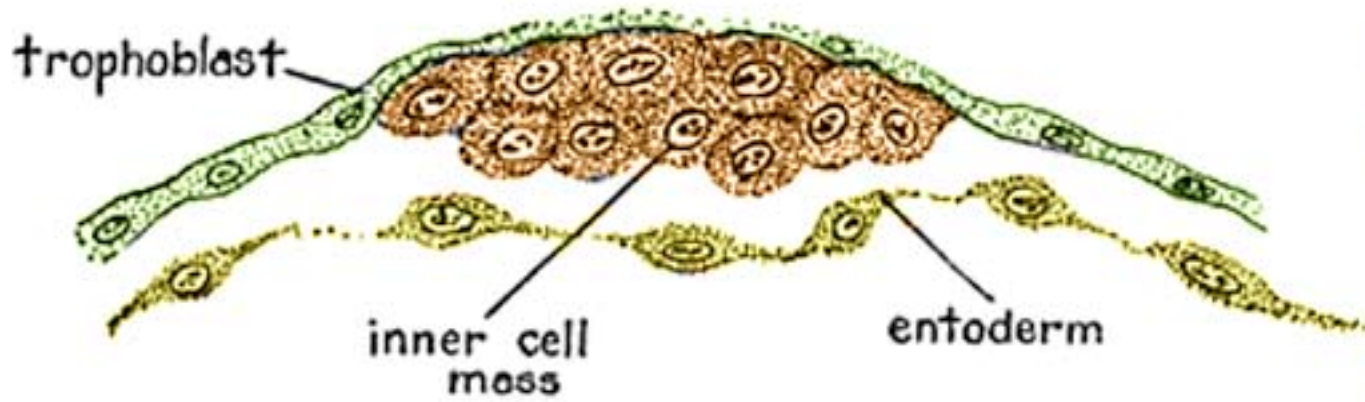
- A thickened embryonic disc becomes evident at the blastocyst surface, due to cell proliferation of the inner cell mass cells. Trophoblast cells overlaying the inner cell mass degenerate in domestic mammals (in some mammals, e.g., mouse and human, trophoblast cells overlaying the inner cell mass separate and, instead of degenerating, become amnionic wall.)
- From the inner cell mass, cells proliferate, break loose (delaminate), and migrate to form a new cell layer inside the trophoblast layer. The new layer of cells is called the *hypoblast*; it forms a yolk sac. The remaining inner cell mass may henceforth be called *epiblast*.
- On the epiblast surface, a **primitive streak** forms as differential cell growth generates a pair of ridges separated by a depression. [NOTE: The primitive streak defines the longitudinal axis of the embryo and indicates the start of germ layer formation.]
- The separation of the hypoblast layer from the epiblast establishes a space (**coelom/celom**) deep to the primitive streak. Subsequently, the coelom is temporarily filled by mesoderm that undergoes cavitation to reestablish the coelom that gives rise to body cavities.
- Epiblast cell proliferation along primitive streak ridges becomes the source of a cellular migration through the streak depression. The migrating cells form endoderm & mesoderm layers.

### Hypoblast Formation (three stages)

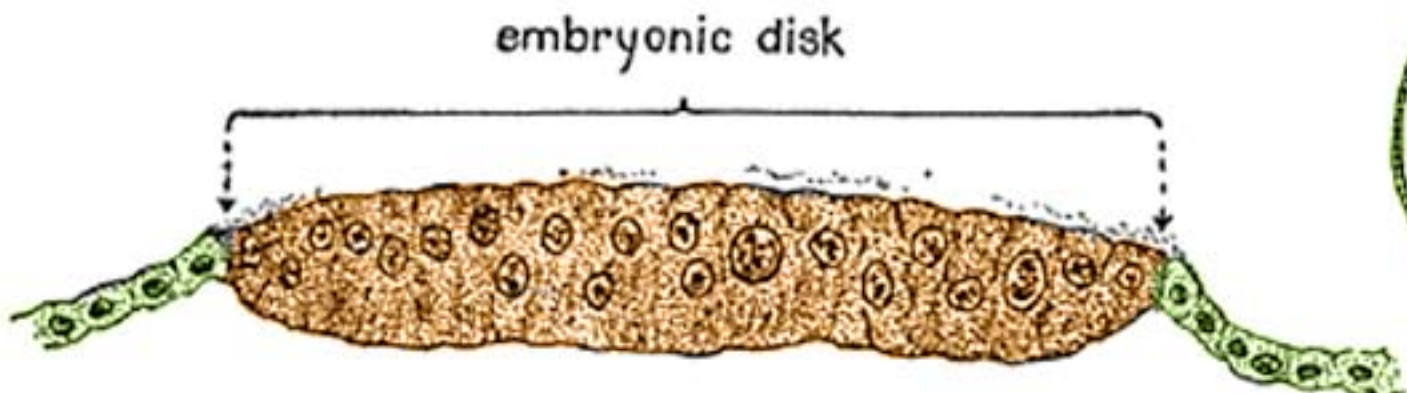




A

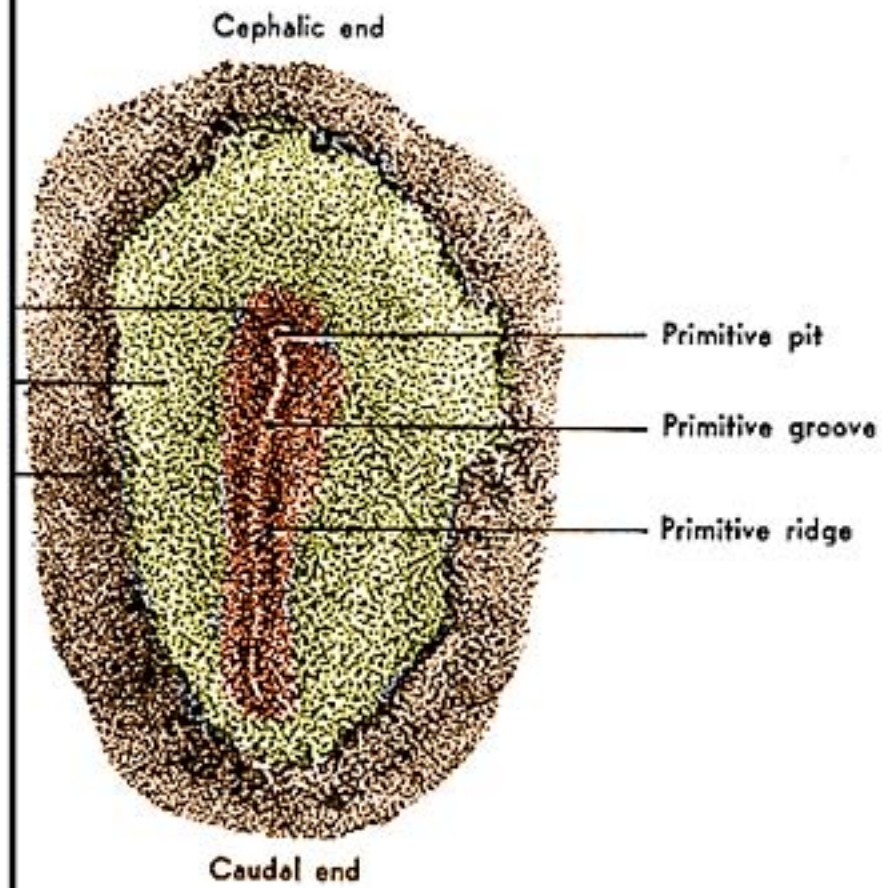
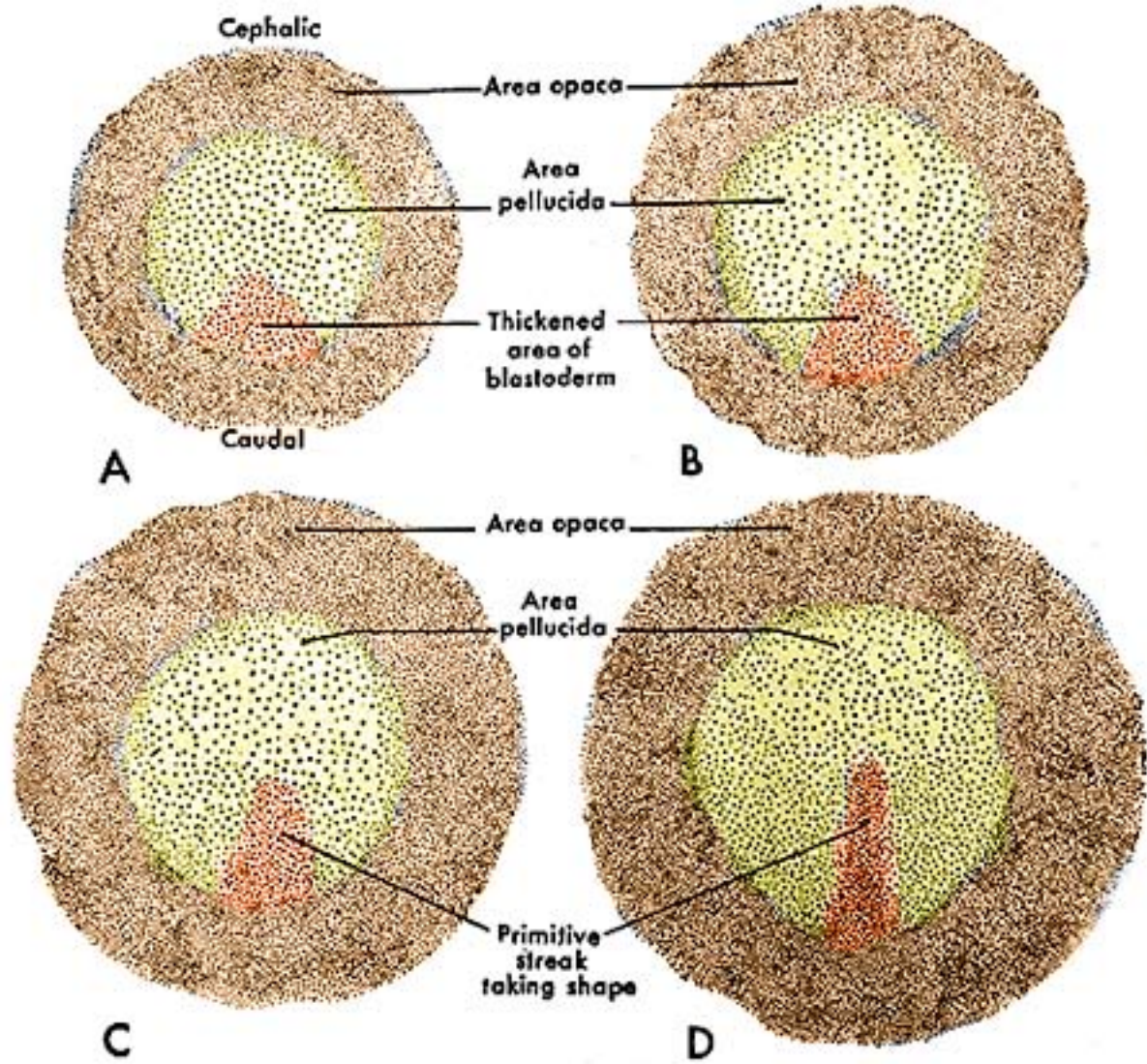


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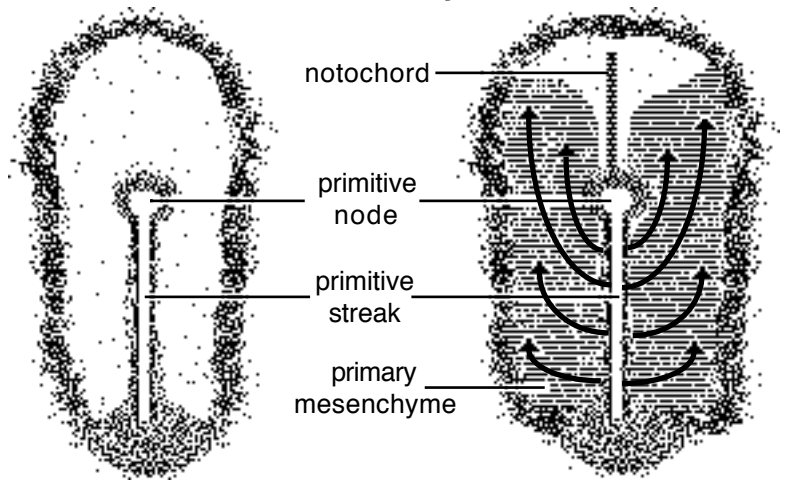
C

trophoblast  
entoderm



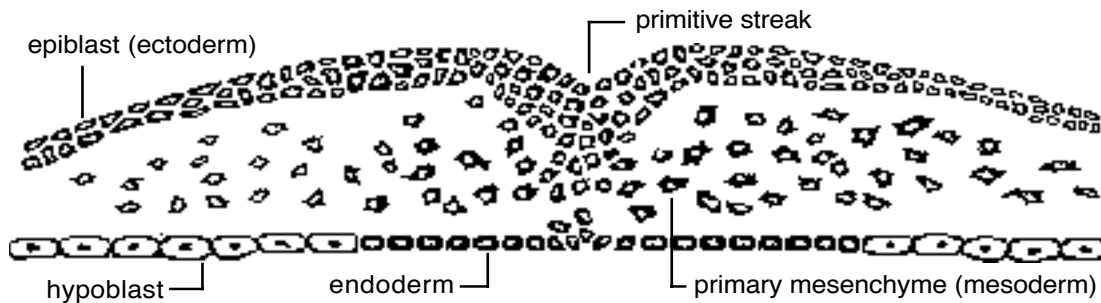
- Initial migrating cells join the hypoblast layer, forming embryonic **endoderm**. (The hypoblast constitutes yolk sac endoderm.)
- The majority of migrating cells enter the coelom as primary mesenchyme and become **mesoderm**. The primary mesenchyme migrates laterally and cranially (but not along the midline region directly cranial to the primitive streak where notochord will form). Note: Mesoderm divides into: paraxial, intermediate, and lateral mesodermal regions.

### Dorsal View of Embryonic Disc



NOTE: Arrows indicate the spread of primary mesenchyme through the primitive streak and between the epiblast and hypoblast

- Cavitation re-establishes a coelom (horseshoe-shaped) within the lateral mesoderm. The mesoderm splits into two layers bordering the coelom—*somatic mesoderm* is attached to the ectoderm and *splanchnic mesoderm* is joined to endoderm.
- The remaining epiblast becomes **ectoderm** which forms skin epidermis & nervous system.



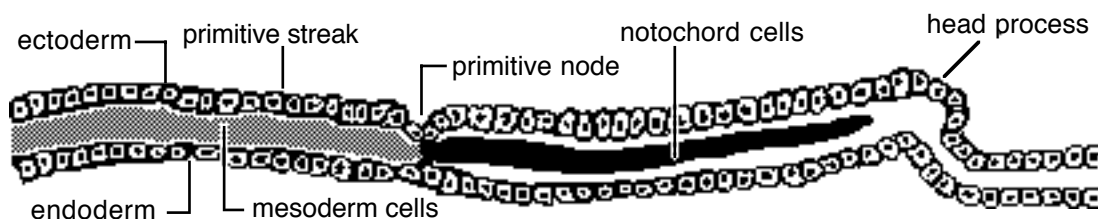
### Formation of the notochord:

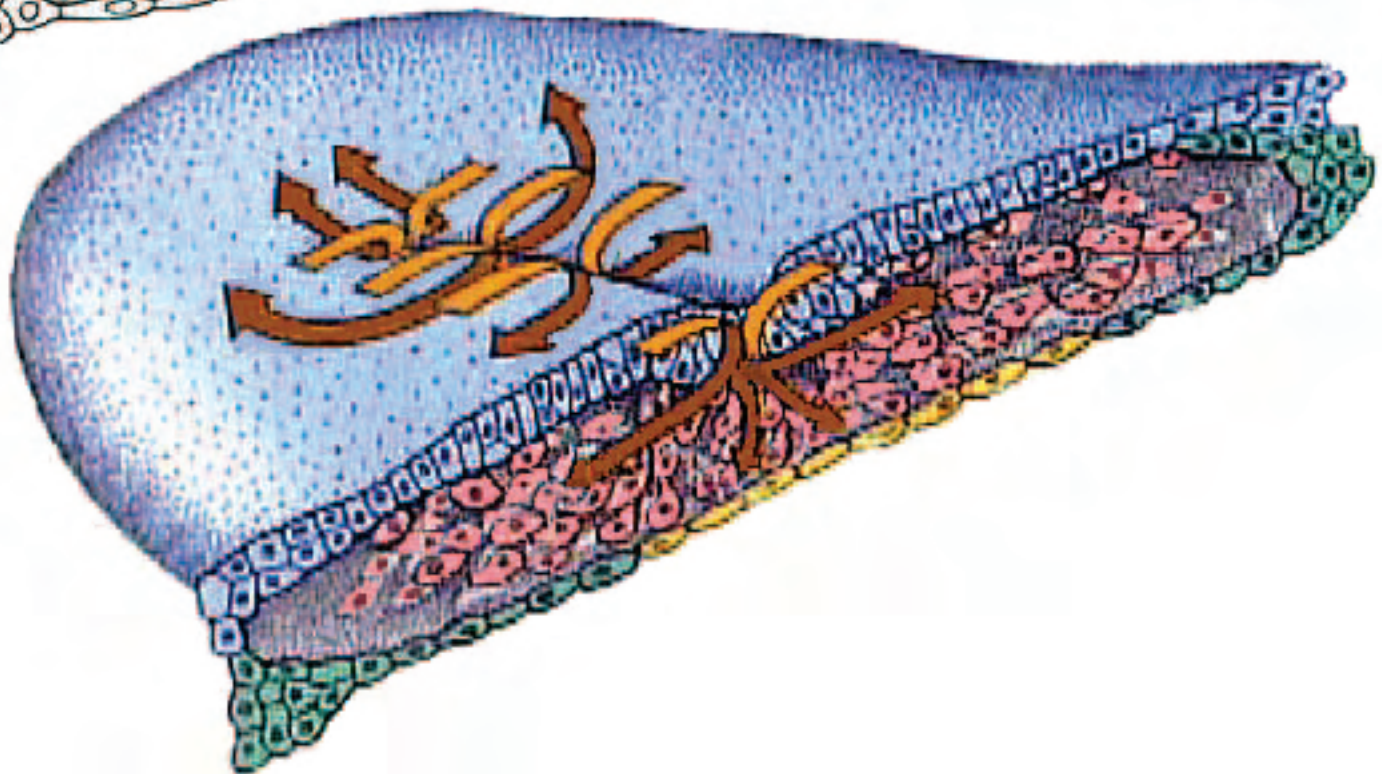
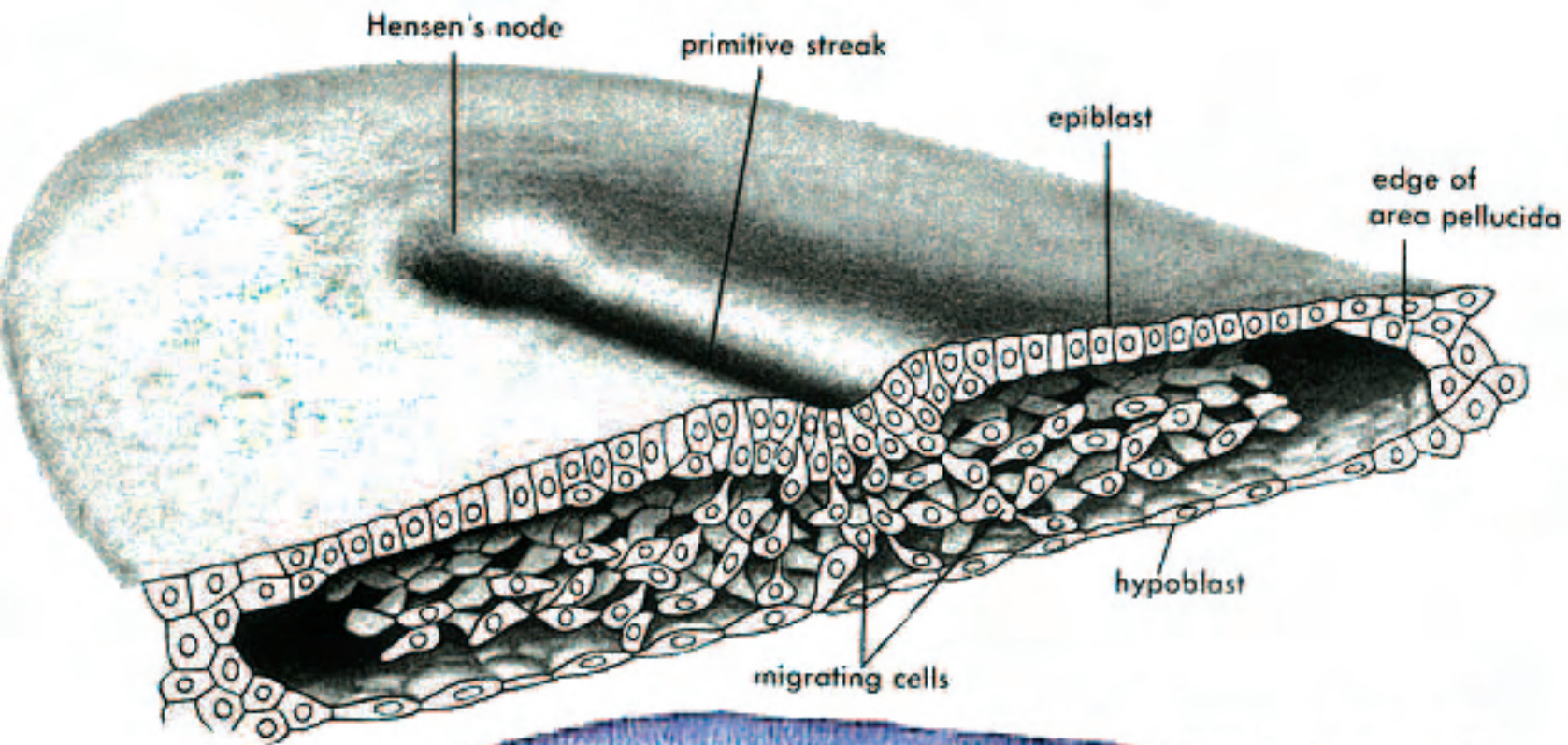
The **notochord** is a rod-shaped aggregate of cells located cranial to the primitive streak of the embryo. It occupies the midline coelomic space between ectoderm and endoderm that was not invaded by migrating primary mesenchyme.

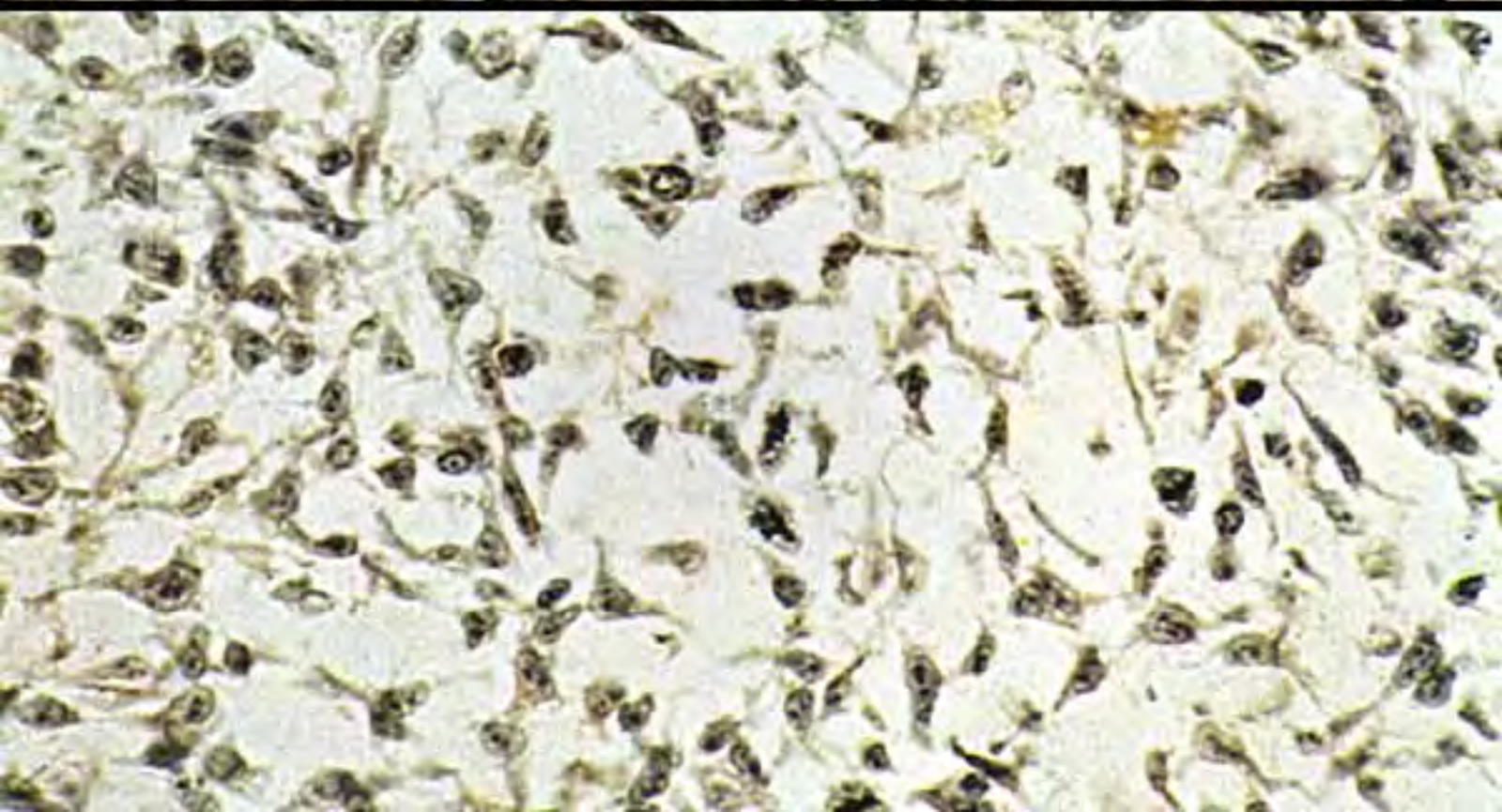
The notochord is important because it induces formation of the head, nervous system development, and somite formation. It marks the future location of the vertebral column and the base of the cranium. Its ultimate fate is to become the nucleus pulposus of intervertebral discs.

The notochord develops from the *primitive node* located at the cranial end of the primitive streak. From the node, mesoderm-forming cells proliferate and migrate forward into the future head region where they become the rod-shaped notochord.

### Longitudinal Section Through Primitive Node and Notochord







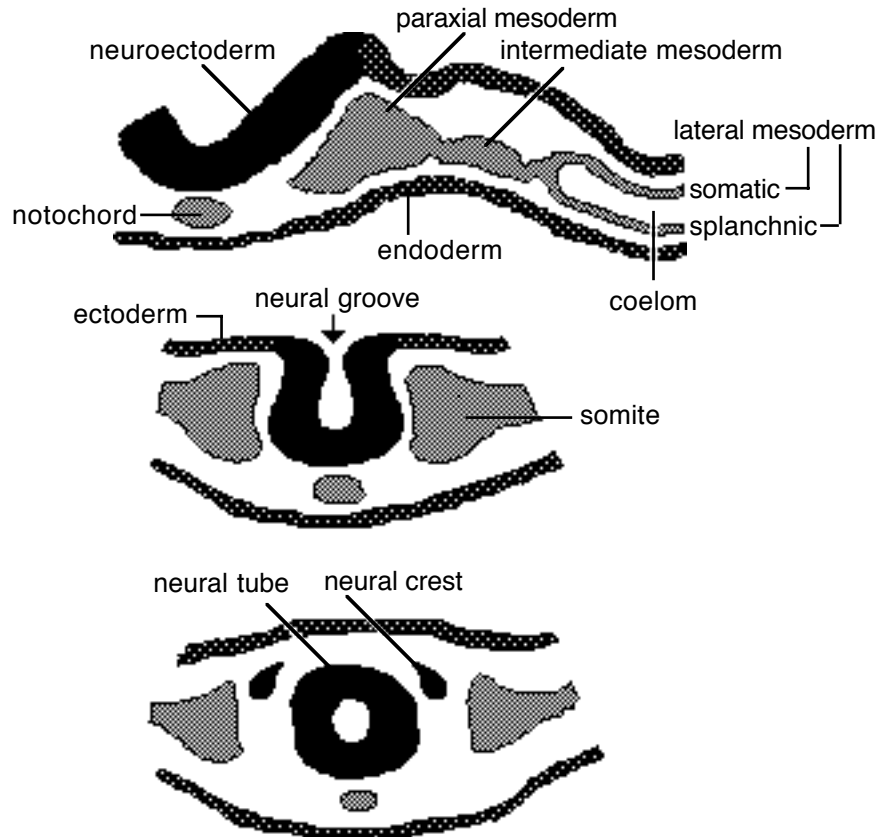
## Early Formation of the Nervous System (Neurulation):

*Neurulation* refers to notochord-induced transformation of ectoderm into nervous tissue. The process begins during the third week in the region of the future brain and then progresses caudally into the region of the future spinal cord.

The following steps are involved in neurulation:

- ectodermal cells overlaying the notochord become tall columnar (neuroectoderm); they form a thickened area designated the *neural plate*. Other ectodermal epithelium is flattened.
- a *neural groove* is formed as edges of the neural plate become raised on each side of a midline depression. (Apical ends of individual neuroectodermal cells constrict.)
- a *neural tube* then forms as the neural groove undergoes midline merger of its dorsal edges. The tube separates from non-neural ectoderm which unites dorsal to it. (Tube formation begins in the cranial cervical region of the central nervous system and progresses cranially and caudally until *anterior* and *posterior neuropores*, the last openings, finally close.)
- bilaterally, where the neural groove is joined to non-neural ectoderm, cells detach as the neural groove closes; the cells proliferate and assume a position dorsolateral to the neural tube—forming *neural crest*.

## Neurulation



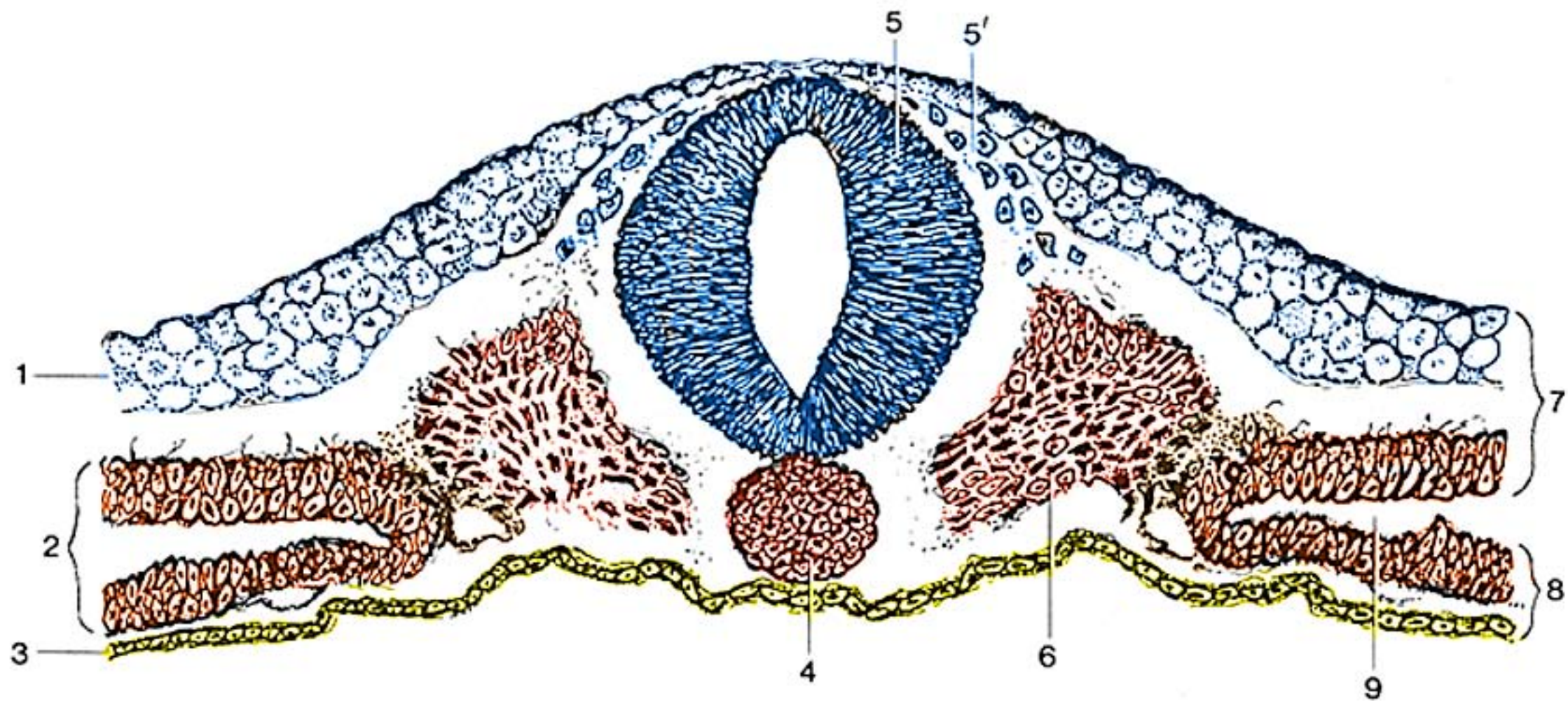
### NOTE:

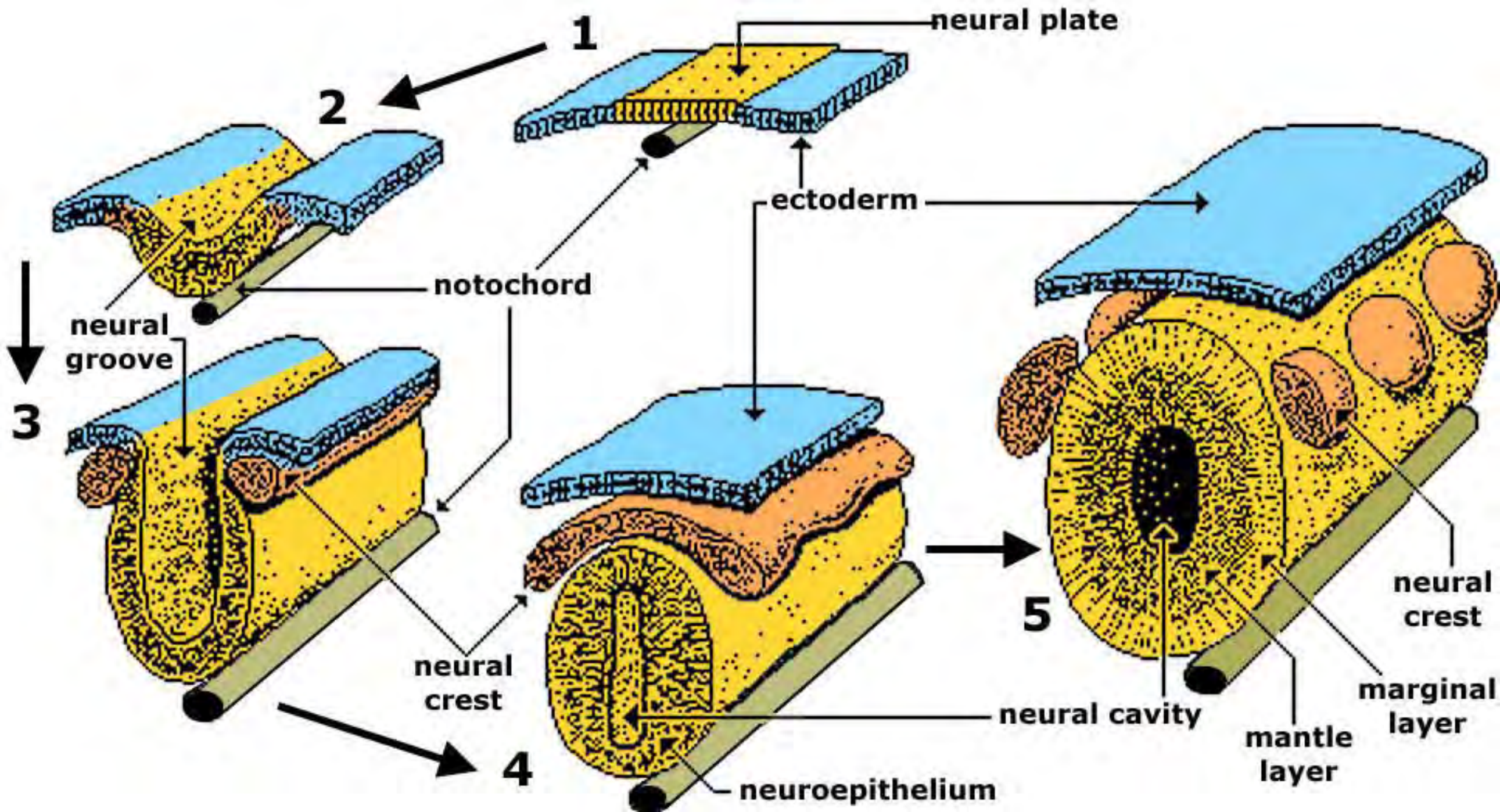
Neural tube becomes the central nervous system, i.e., the brain and spinal cord.

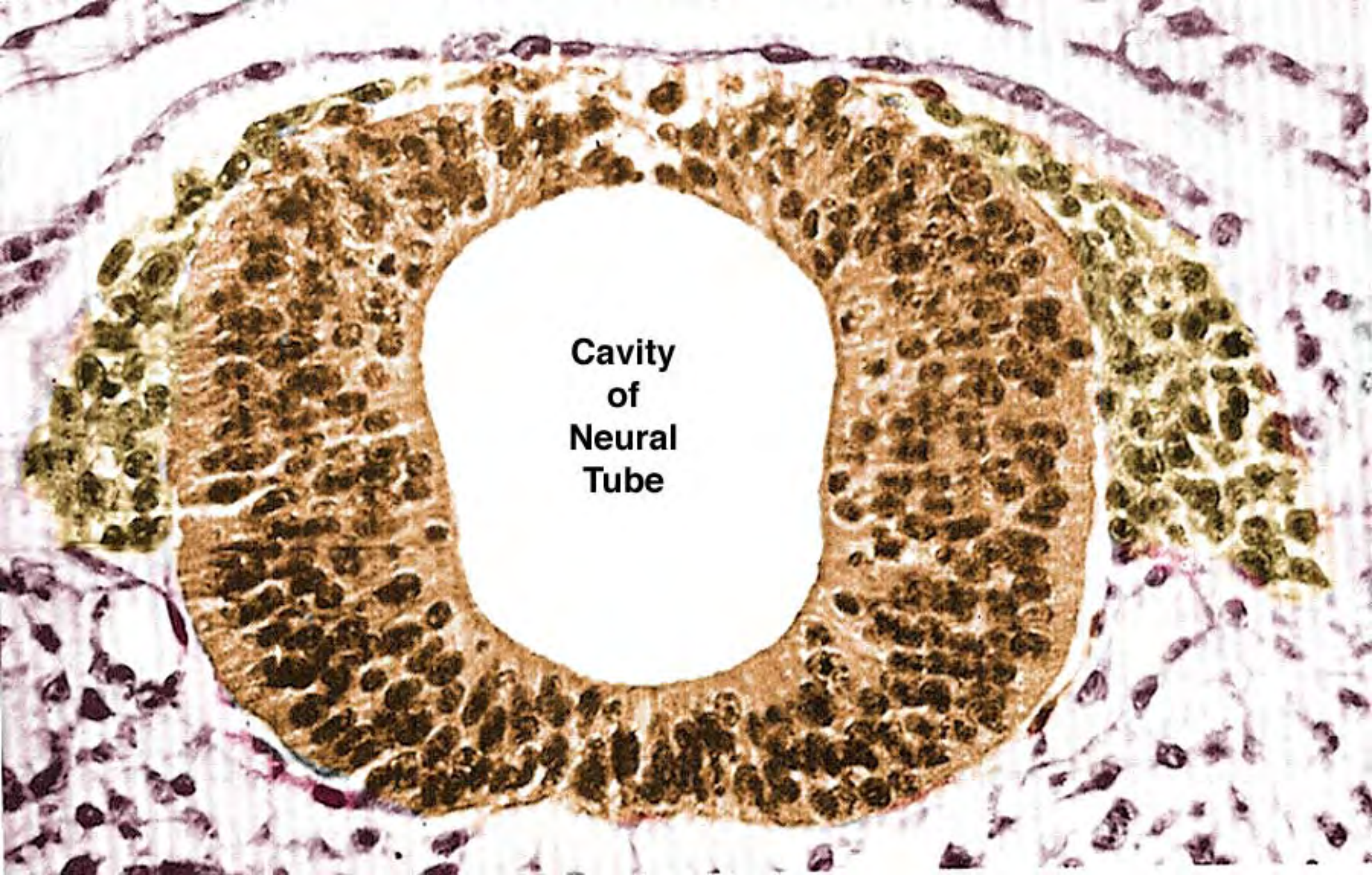
Neural crest cells are remarkable for the range of structures they form. Some cells migrate dorsally and become pigment cells in skin. Other cells migrate ventrally and become neurons and glial cells of the peripheral nervous system, or adrenal medulla cells. In the head, neural crest forms mesenchyme (ectomesenchyme) which becomes meninges, bone, fascia, and teeth.

**Note:** Each organ system has a critical period during development when it is most sensitive to external agents (teratogens) that produce birth defects.



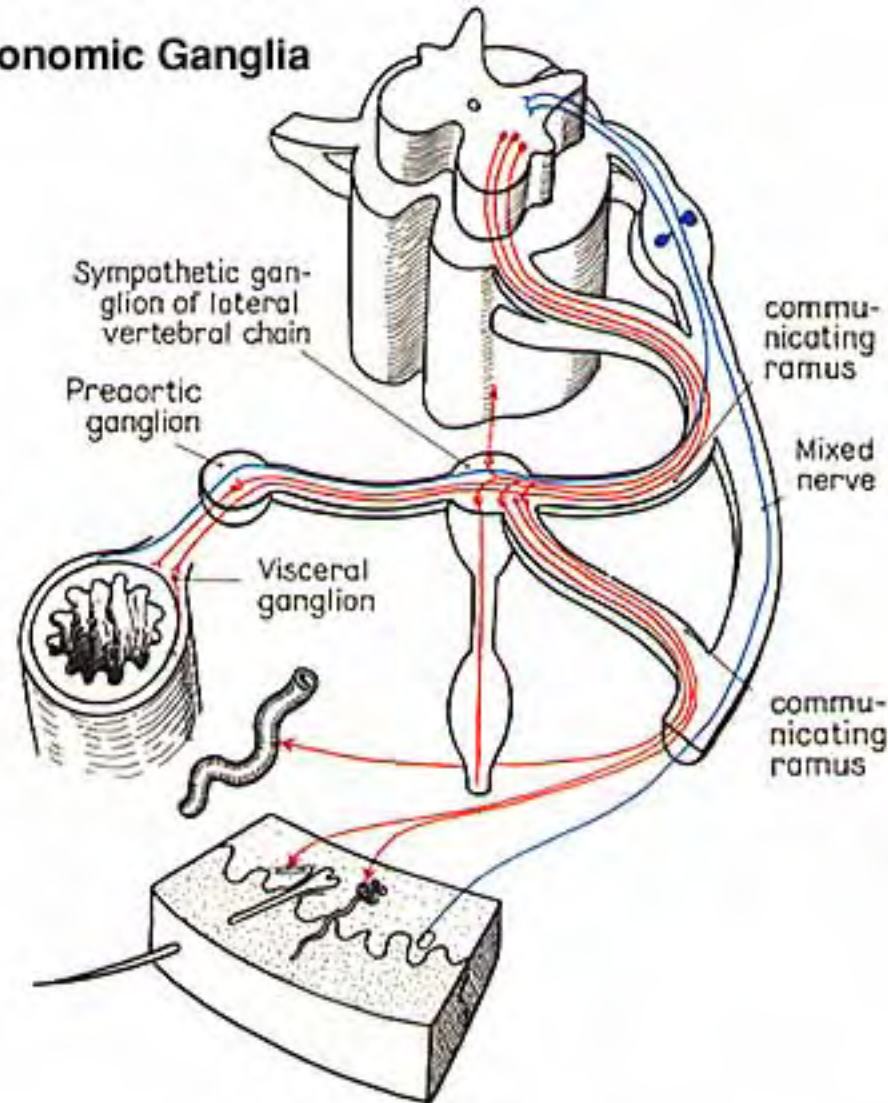
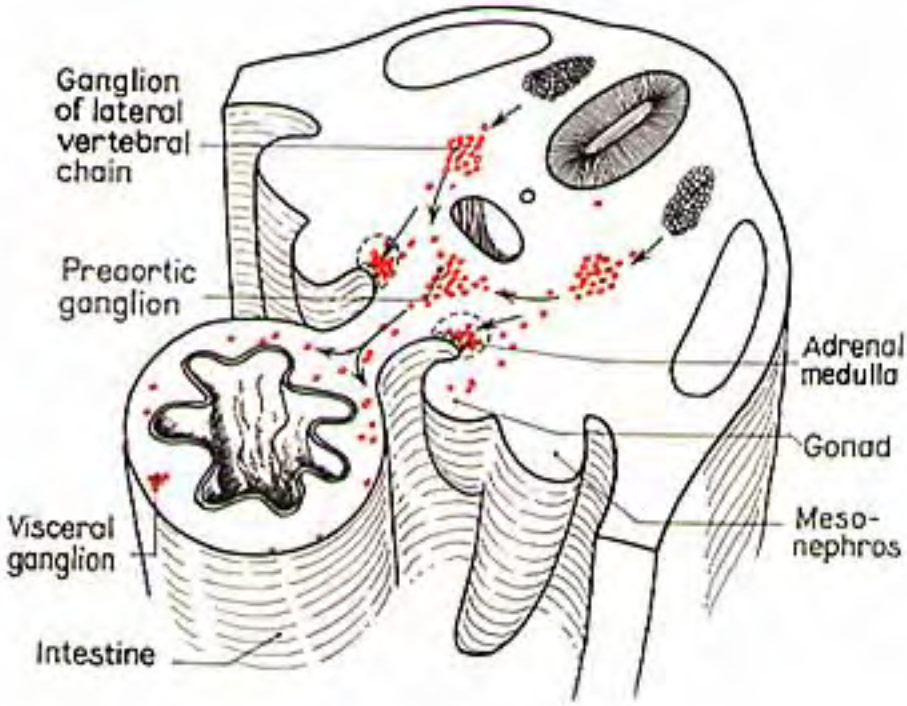


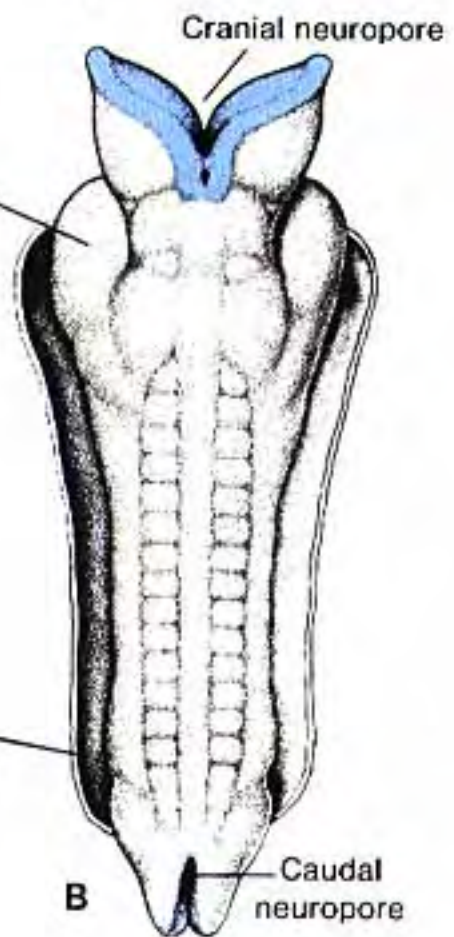
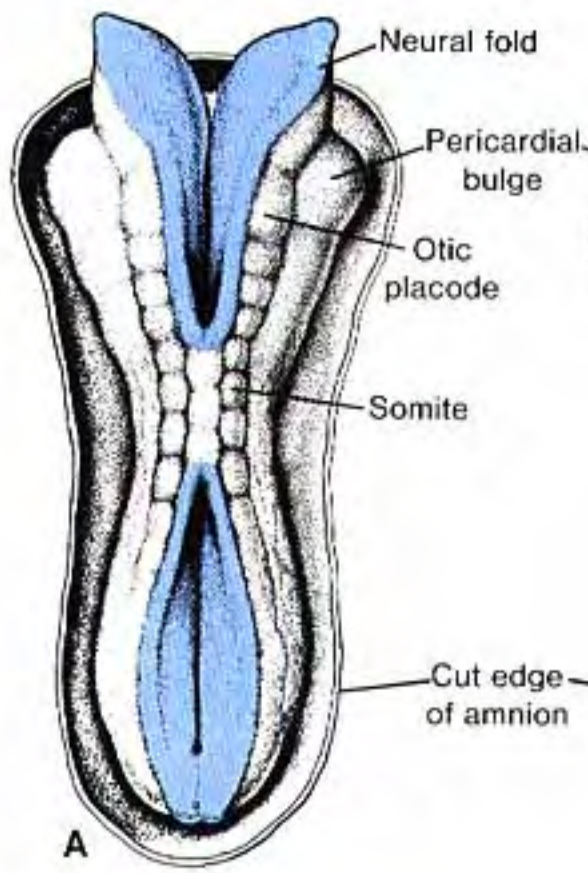
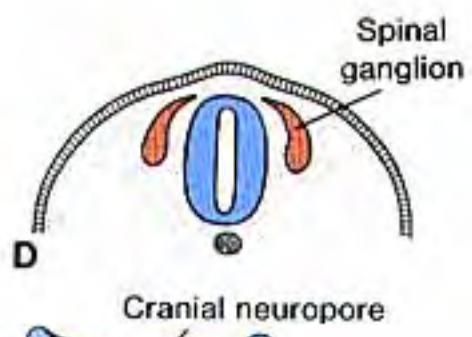
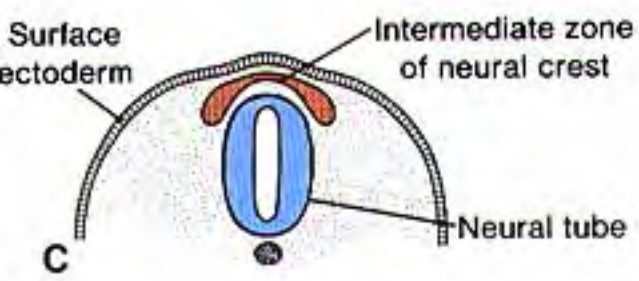
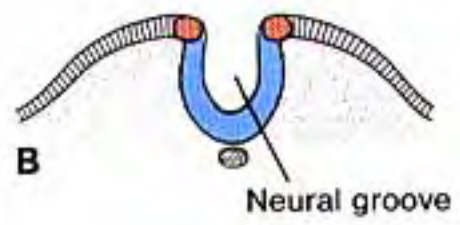
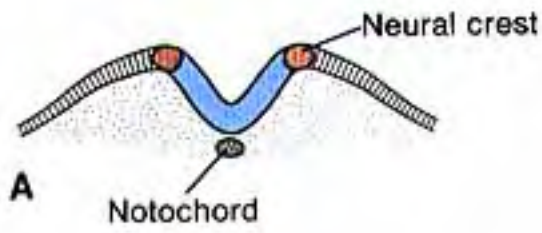




**Cavity  
of  
Neural  
Tube**

# Neural Crest Migration to form Spinal and Autonomic Ganglia





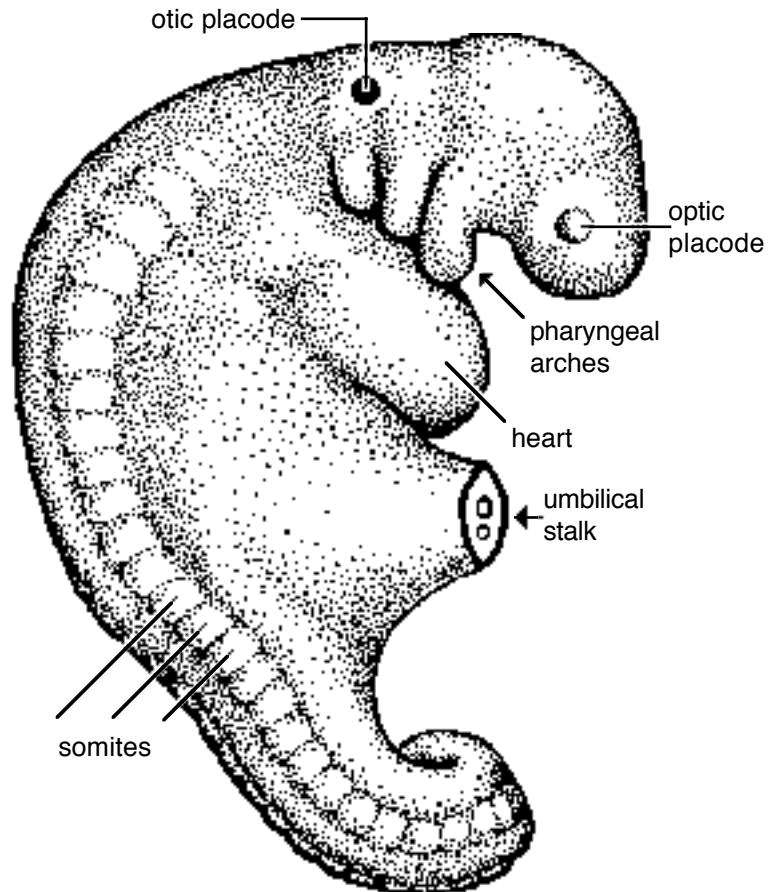
## Somite formation:

**Somites** are blocks of mesoderm located just lateral to the notochord. Generally, there are a pair of somites for every vertebra and a half dozen somite pairs in the head. The number of somites in an embryo is indicative of age because somites develop chronologically, in craniocaudal order.

**Note:** The ventromedial portion of a somite develops into a *sclerotome* (which forms vertebrae, ribs, & basal bones of the skull), the lateral portion becomes a *dermatome* (skin dermis), and the rest of the somite forms a *myotome* (skeletal muscle).

Somites develop as follows:

- mesoderm accumulates on each side of the notochord; this medially positioned mesoderm is designated *paraxial mesoderm*
- progressing from rostral to caudal over time, transverse fissures divide the paraxial mesoderm into blocks
- each block is a **somite** (epithelioid cells within a somite block re-orient 90°, from transverse to the notochord to longitudinal)
- head (occipital) somites develop from proliferation of local mesenchyme lateral to the cranial end of the notochord
- rostral to the notochord, mesenchyme forms less-developed somites, called *somitomeres*, which migrate into pharyngeal arches and form muscles of the jaw, face, pharynx, & larynx.



### NOTE:

Mesoderm can exist in two morphologic forms: mesenchyme and epithelioid:

**Mesenchyme** features aggregates of stellate cells within an abundant extracellular matrix composed of fluid and macromolecules (polymers).

**Epithelioid** refers to organized cells having distinct apical and basal surfaces; the latter commonly rests on a basal lamina produced by epithelioid secretion.

Mesoderm can transform from a mesenchyme to epithelioid and vice versa: The

mesoderm that streams through the primitive streak is *primary mesenchyme*.

Somatic, splanchnic, and somite mesoderm can be temporarily epithelioid.

The temporary epithelioid transforms to a *secondary mesenchyme* which ultimately forms muscle and connective tissue (including cartilage, bone, ligaments, tendons, dermis, fascia, and adipose tissue).

Thus, the term “mesenchyme” refers to the morphologic appearance of embryonic tissue. Although most mesenchyme is mesoderm, the other germ layers can also form mesenchyme, e.g., ectomesenchyme from neural crest ectoderm.

# 10 mm Pig Embryo

