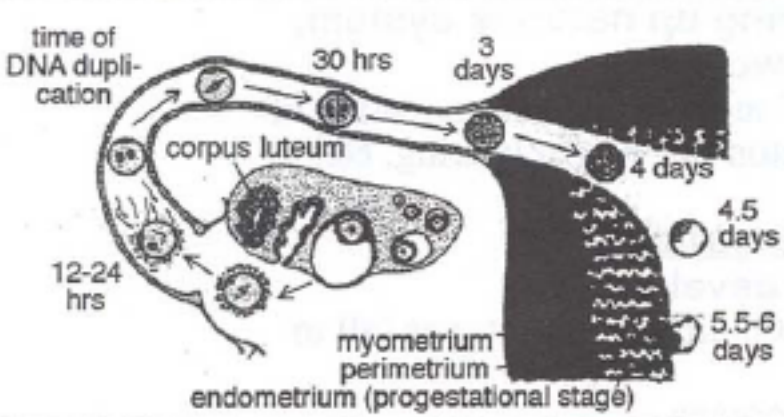
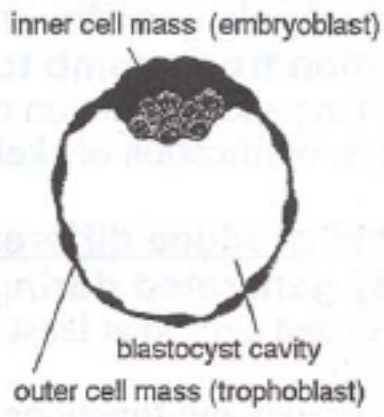
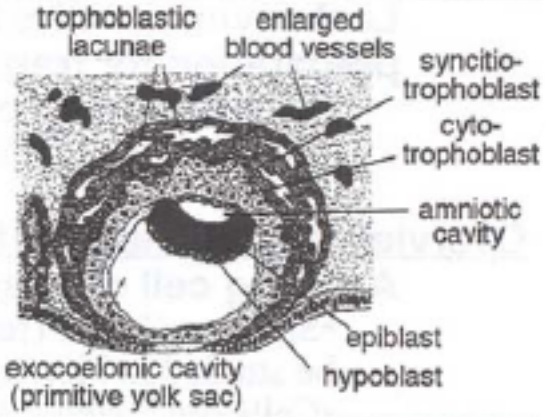
Lecture 4: Gastrulation

Seung K. Kim
Dept. of Developmental Biology
DB201 Development & Disease Mechanisms

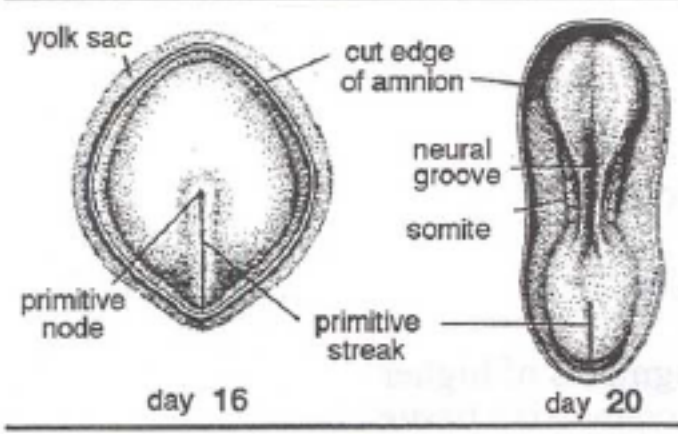


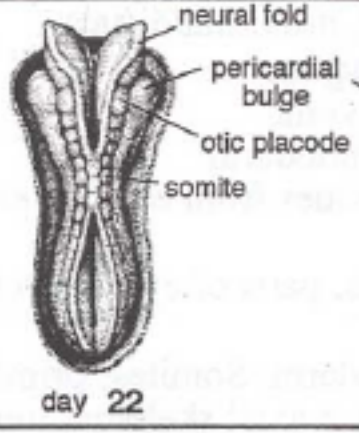


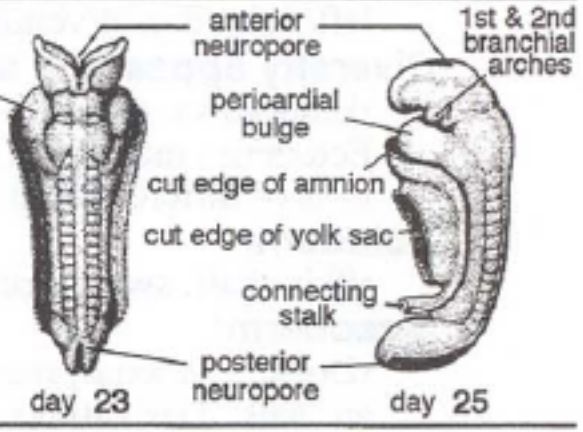


Week 1

Week 2



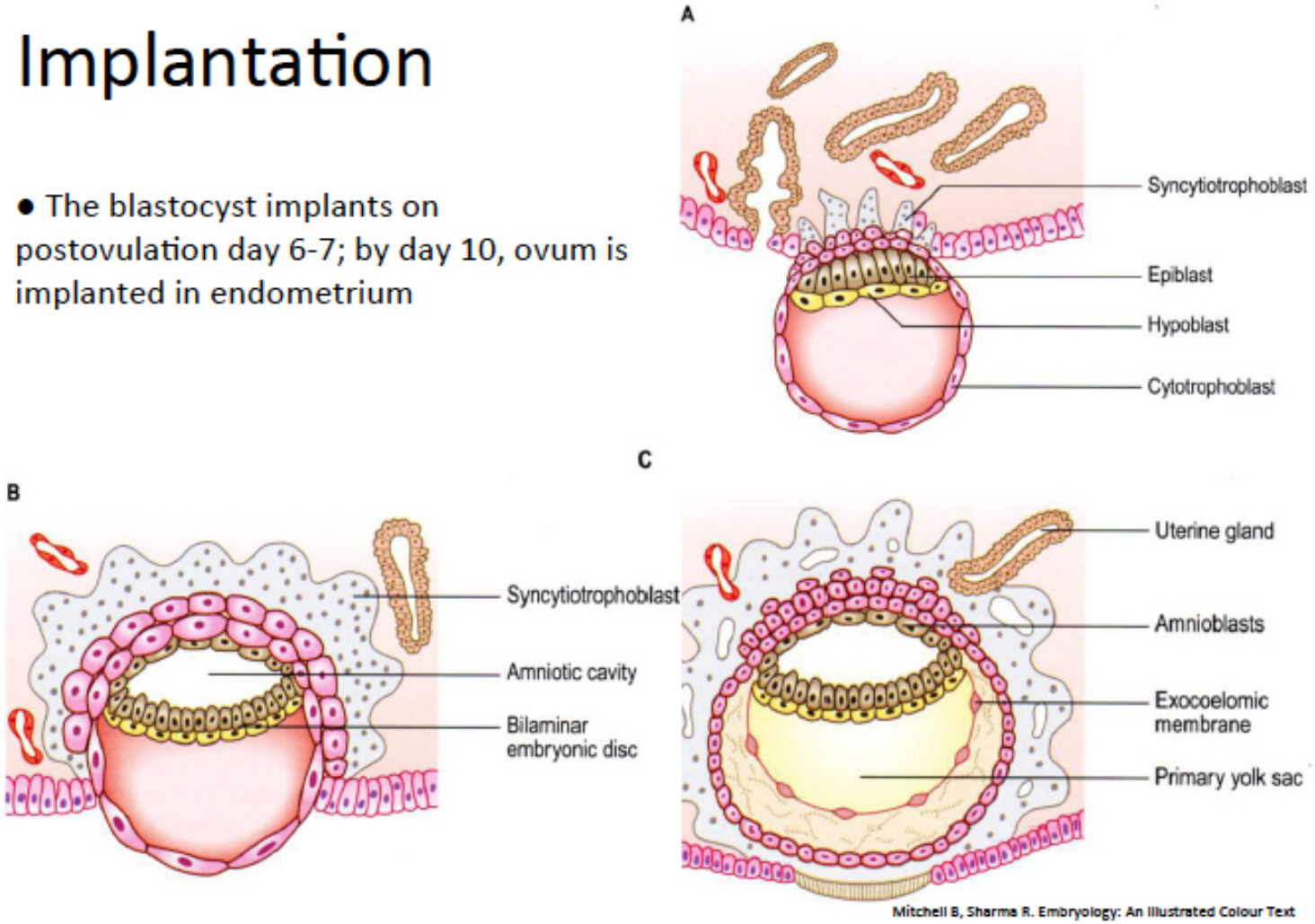




Week 3

Implantation

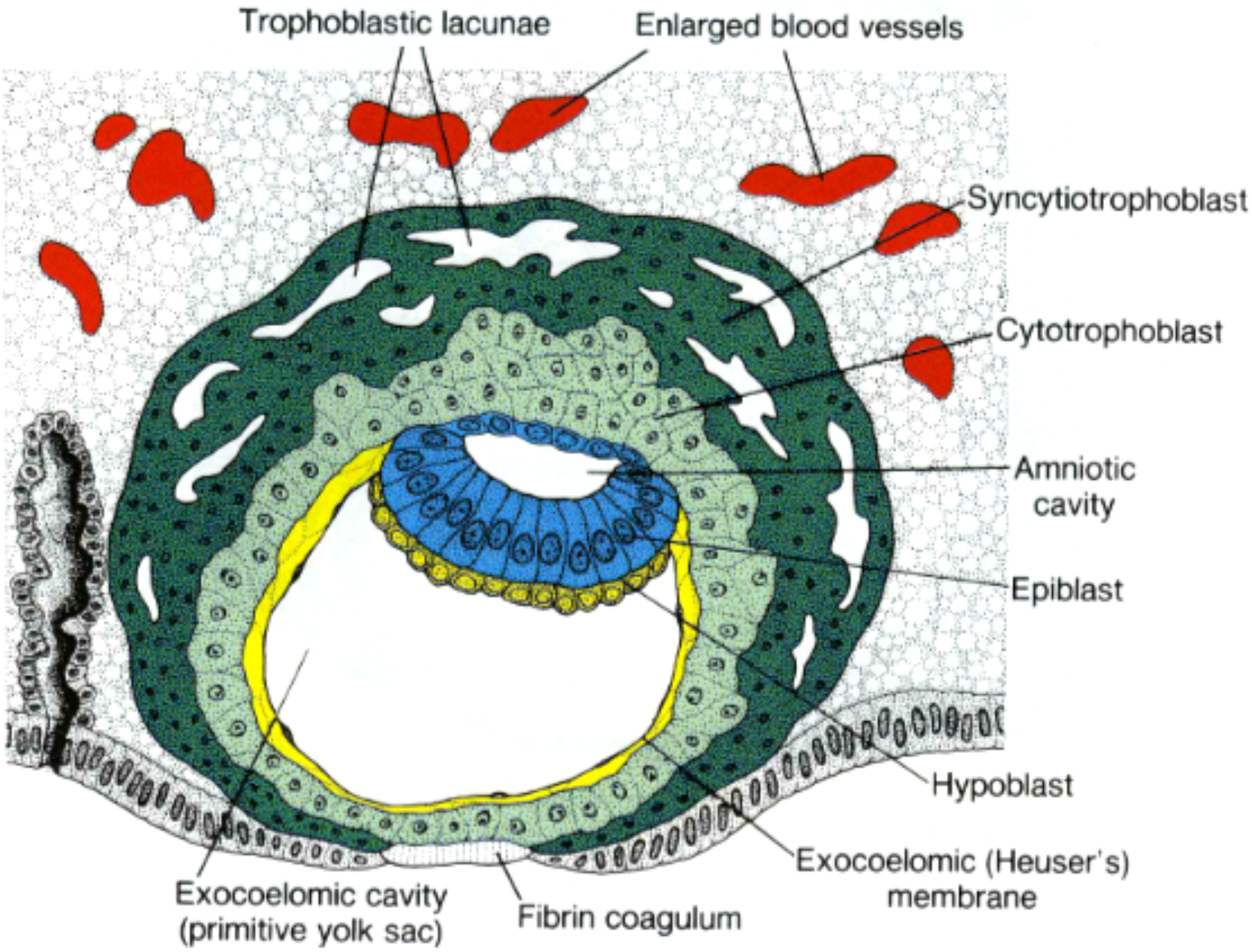
- The blastocyst implants on postovulation day 6-7; by day 10, ovum is implanted in endometrium



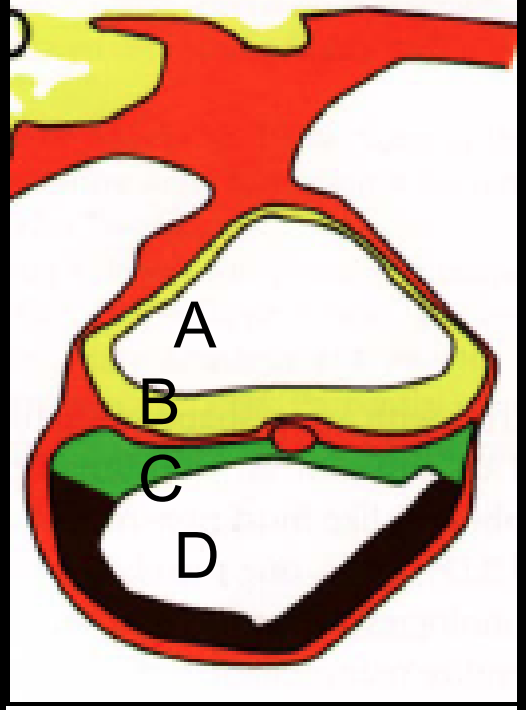
Trophoblasts produce a protein called L-selectin that is thought to mediate binding to the endometrial cells. Later, L-selectin may also mediate ‘homing’ of the syncytiotrophoblasts to maternal spiral arteries.

Syncytiotrophblasts formation may be mediated by a protein called syncytin. Blood megakaryocytes are another example of multinucleated cells in humans.

Beginning of week 3: gastrulation



Sadler, T.W. (2006) Langman's Medical Embryology



Human bilaminar disc at ~16 days

Eakin and Behringer, Gastrulation in Other Mammals and Humans, 2004

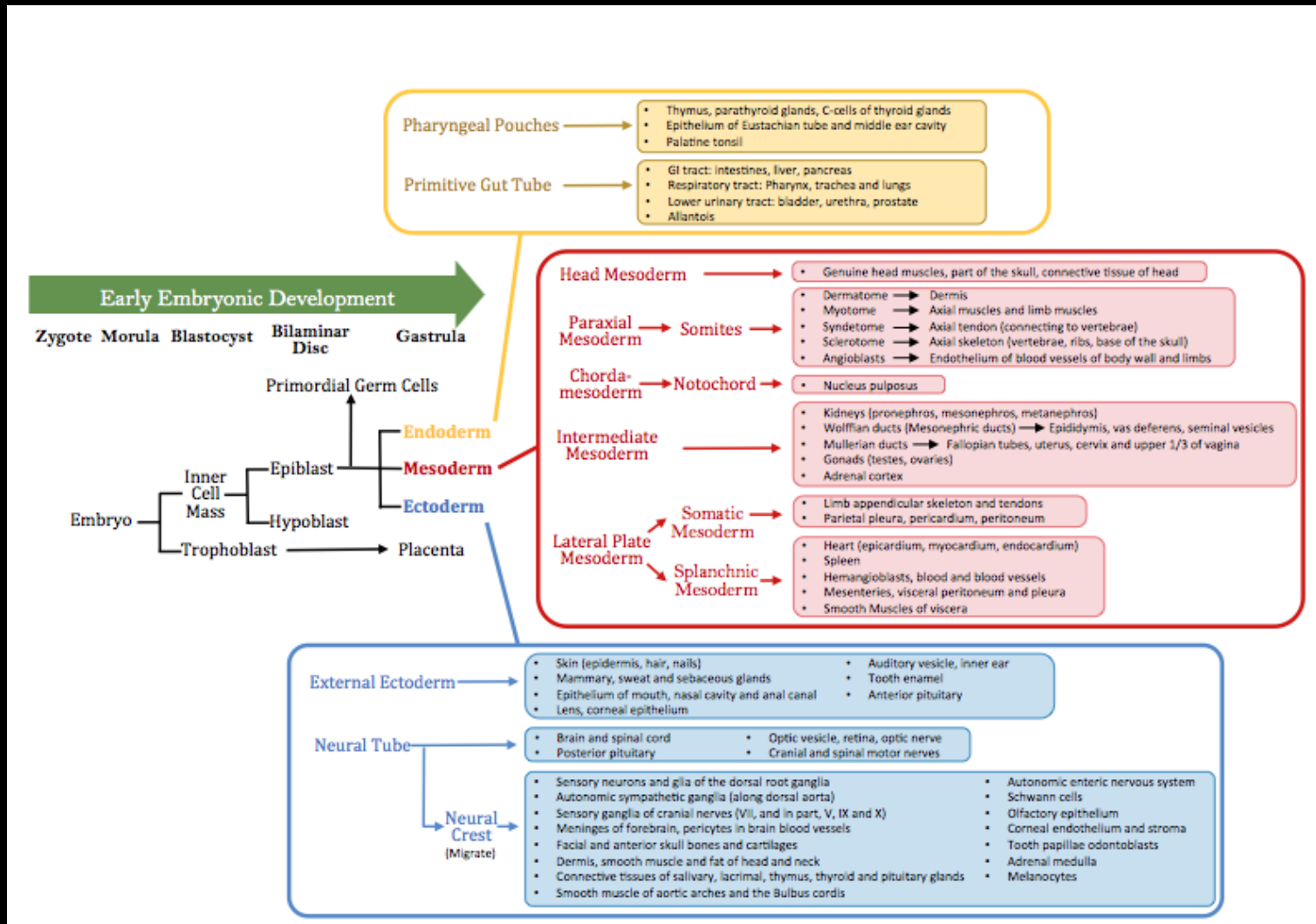
“It is not birth, marriage, or death, but gastrulation, which is truly the most important time in your life.”

Lewis Wolpert (1986)

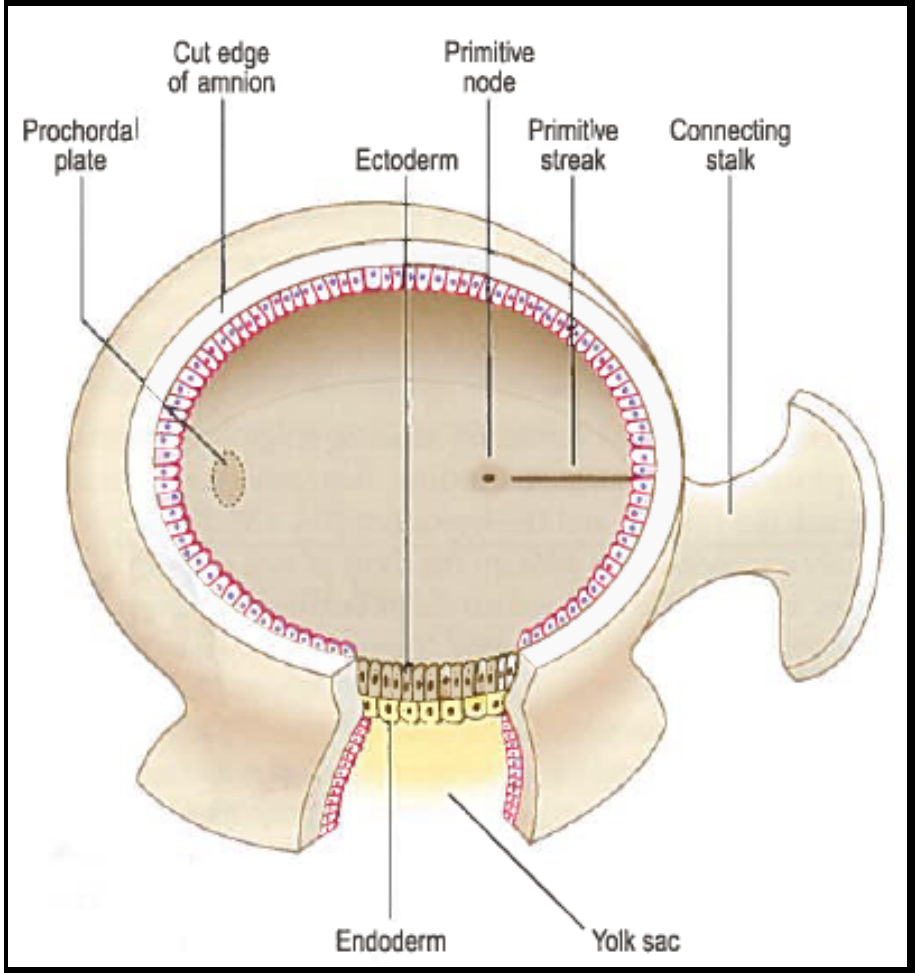
Gastrulation

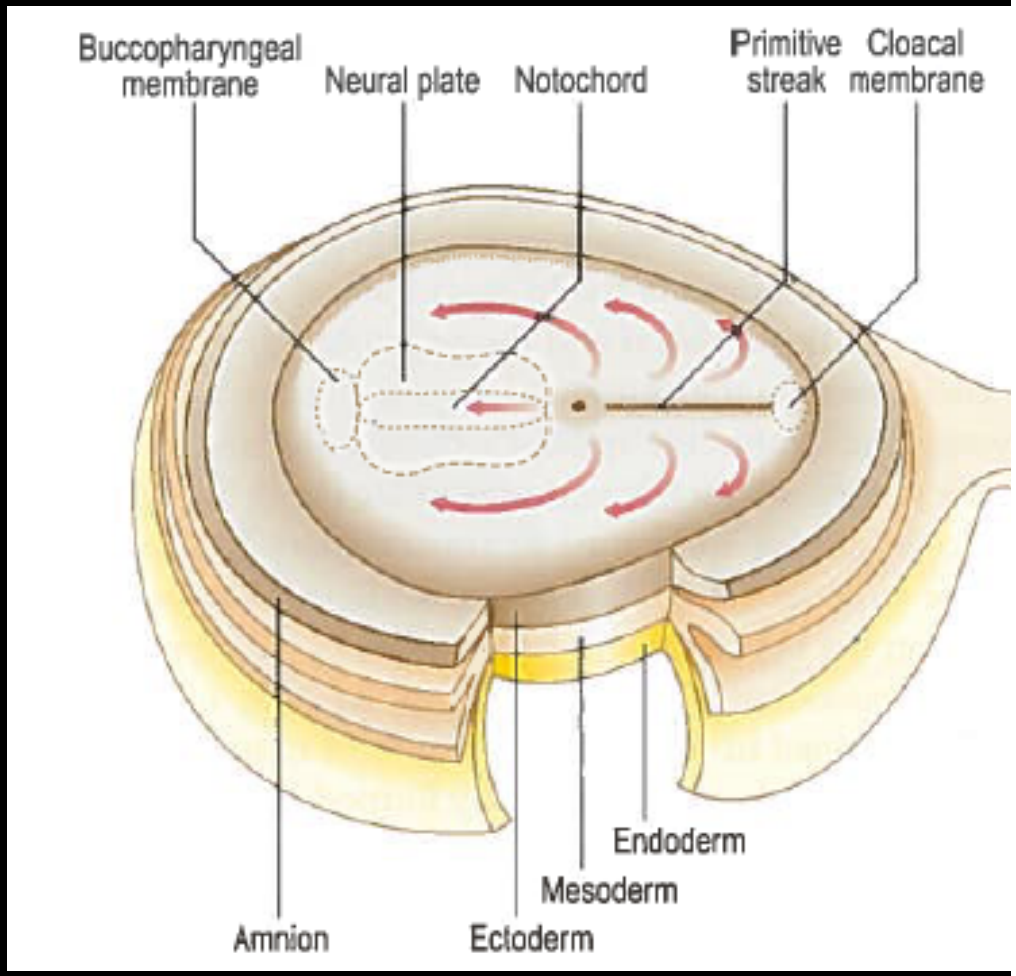
- Generate primary ‘germ layers’ endoderm, mesoderm, ectoderm
- Generate crucial signaling centers coordinating tissue development (‘organizers’) including the primitive streak, node and anterior visceral endoderm (AVE).
- Break axial symmetry along A-P, D-V and L-R axes
- Generate primordial germ cells

Do I need to know this?



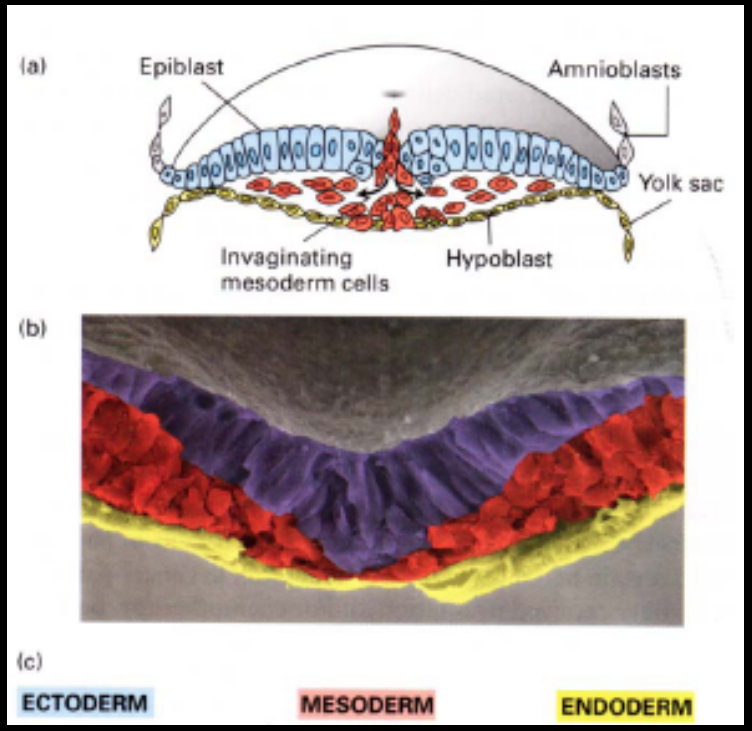
Summary of cell movements in gastrulation





Mitchell and Sharma, Embryology, An Illustrated Colour Text 2005)

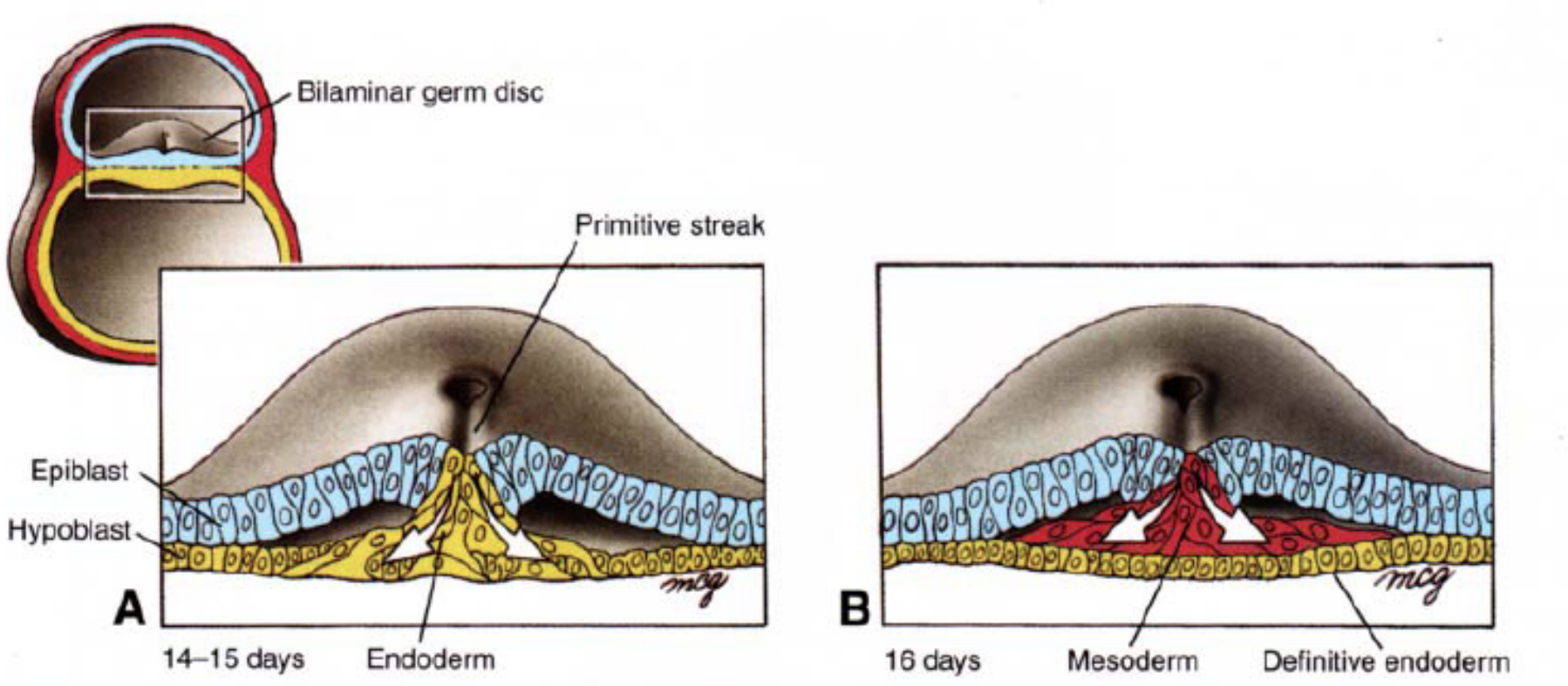
Formation of the primitive streak



Lodish, *Molecular Cell Biology* 2006

- Establishing bilateral symmetry
- Beginning of A-P axis
- Initiating formation of endoderm and mesoderm and ectoderm

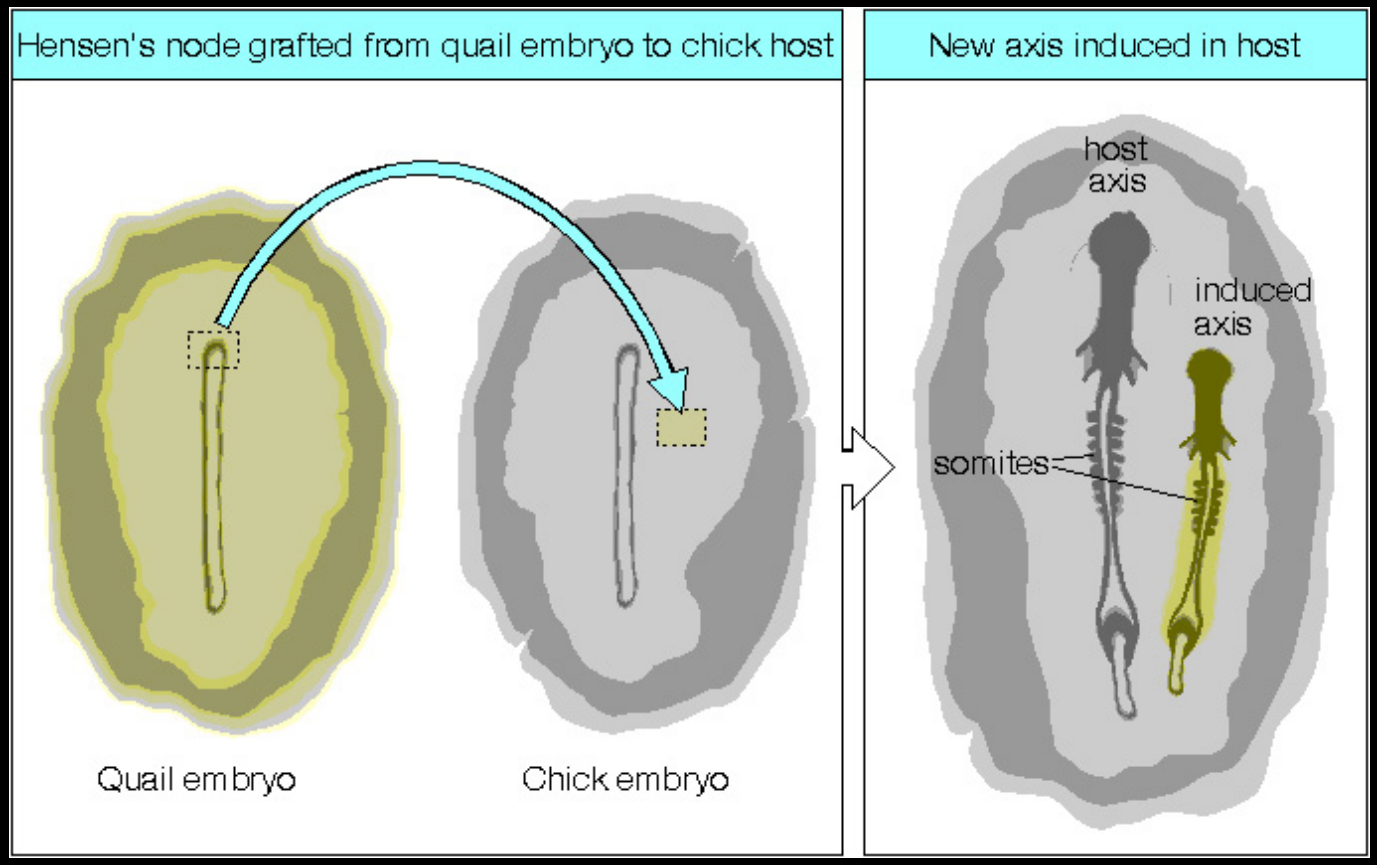
Definitive endoderm and mesoderm development



Epithelial mesenchymal transition (EMT)

- Fibroblast growth factor (FGF) >> Snail (Zn finger transcription factor)

The node as organizer of embryonic development



Wolpert Principles of Development. 2006

- The node determines and patterns the anterior-posterior axis of the embryo
- The node develops into notochord, directs the development of somites, and induces neural tube.
- The node produces signals like nodal, noggin, chordin, and follistatin

The Mangold and Spemann ‘Organizer’ experiment, 1922-26.

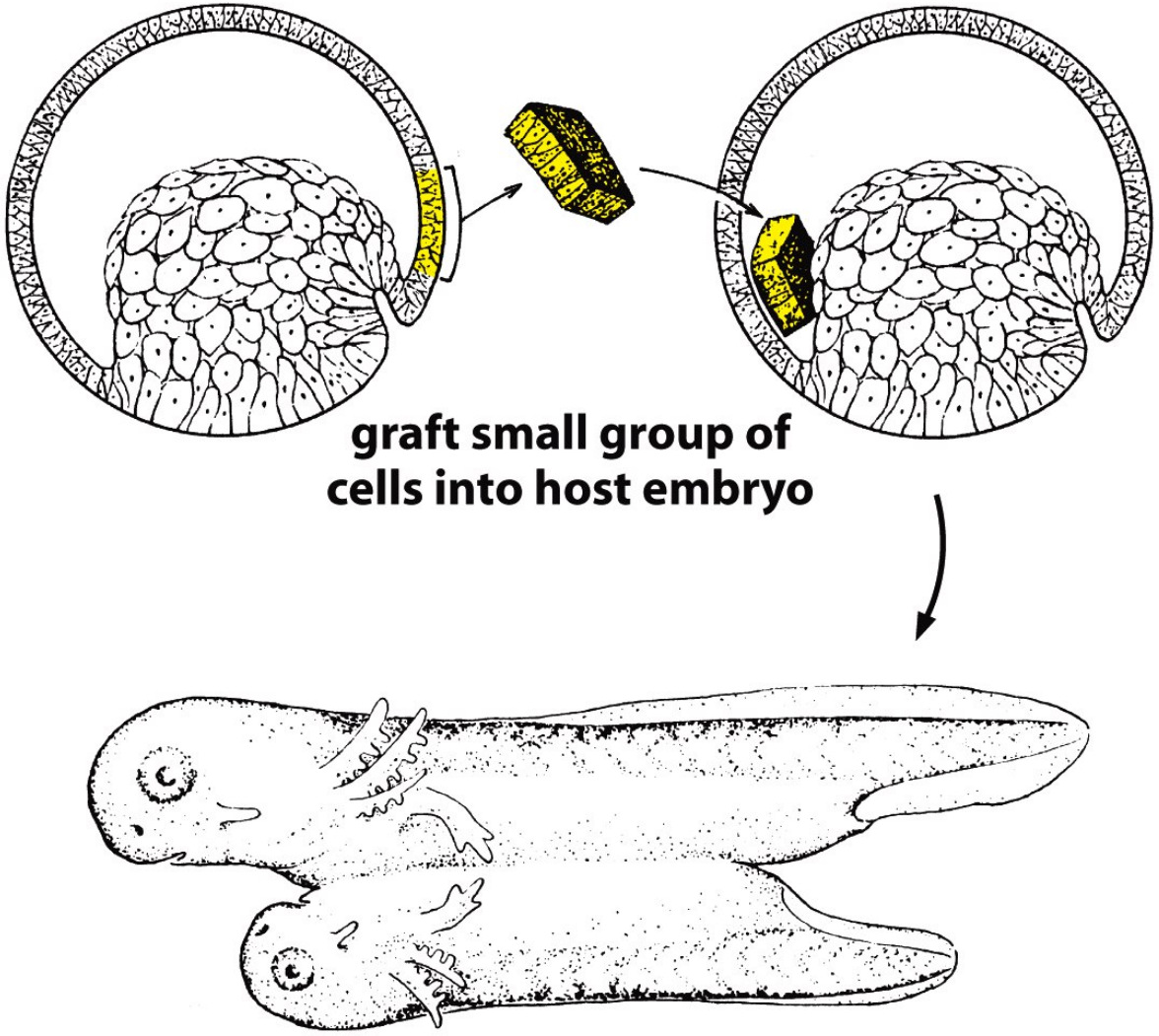
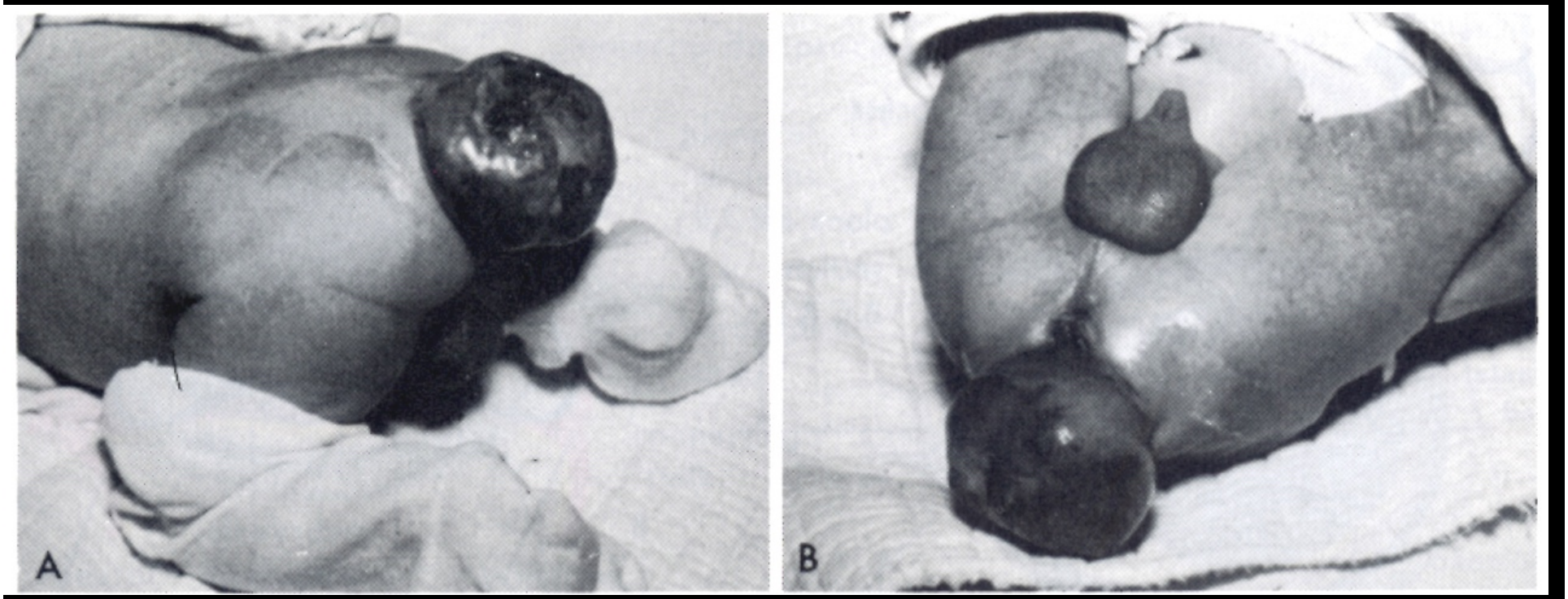


Figure 22-6b *Molecular Biology of the Cell* (© Garland Science 2008)

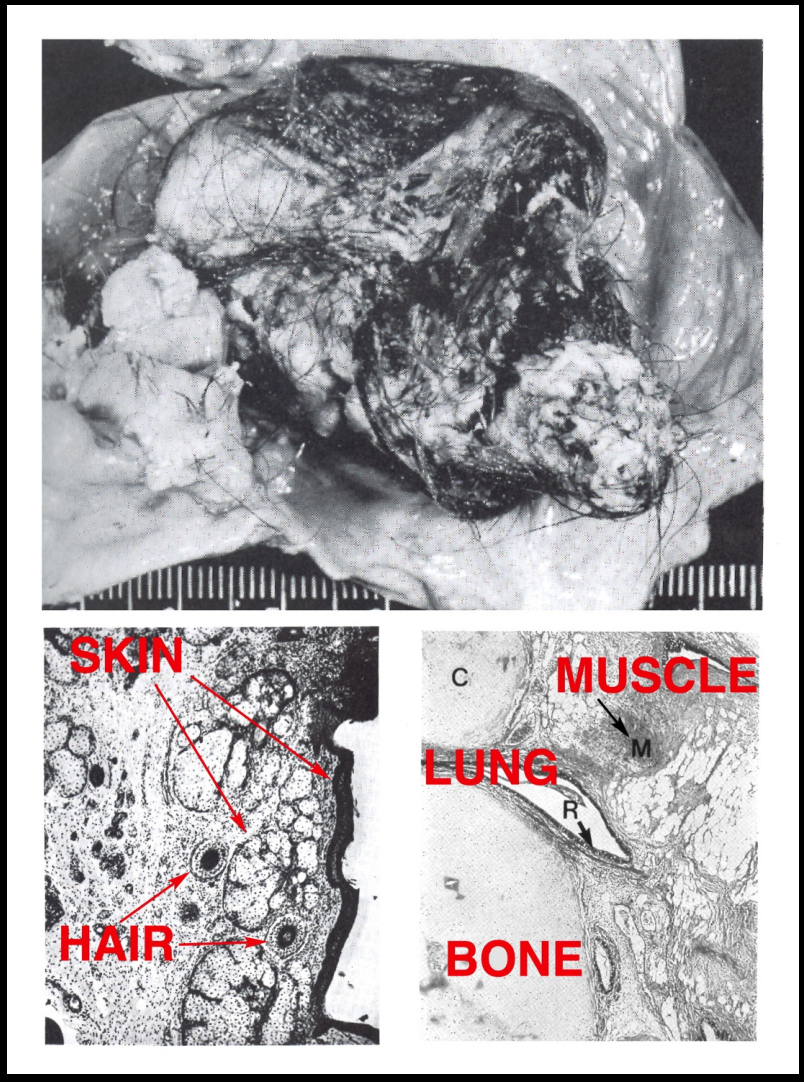
Modern reproduction of Spemann and Mangold organizer transplant

Spemann's organizer and self-regulation in amphibian embryos Edward M. De Robertis. Nature Reviews Molecular Cell Biology 7, 296-302

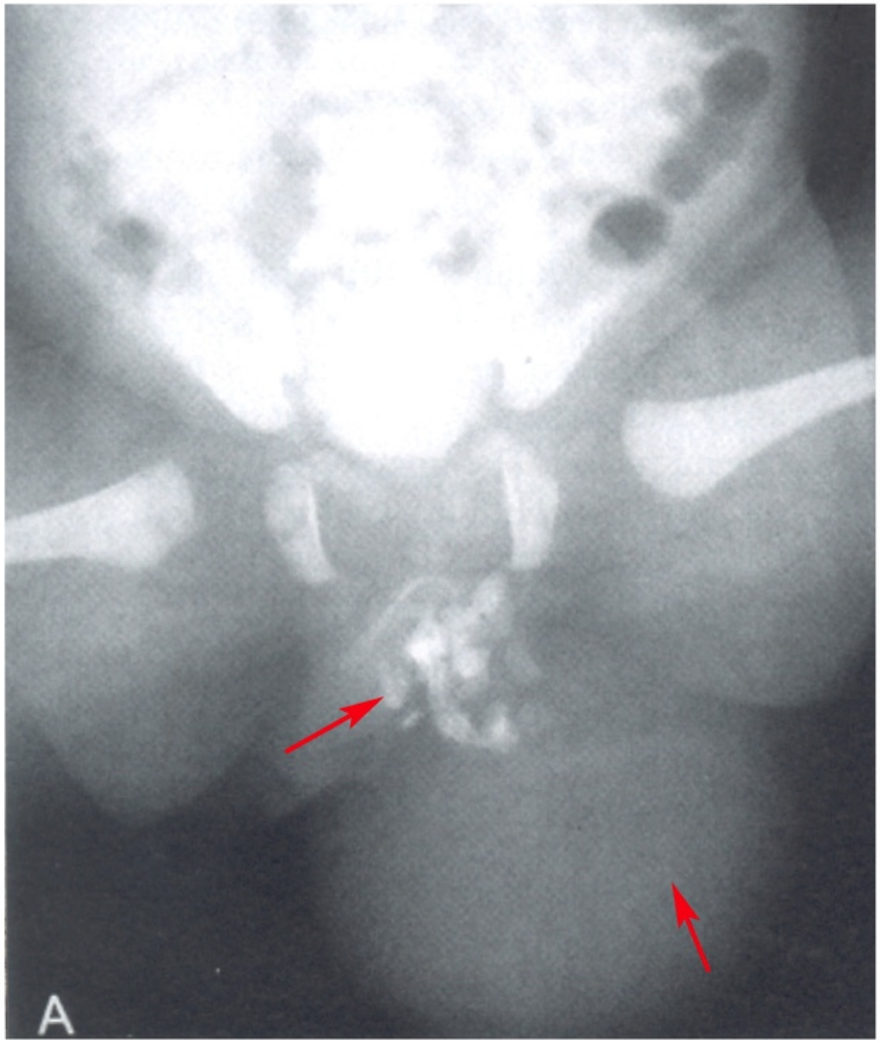
Sacrococcygeal teratoma: can develop from disrupted gastrulation



Teratoma histology reflects origins from three principal germ layers



Radiography may reveal bone and teeth in teratomas

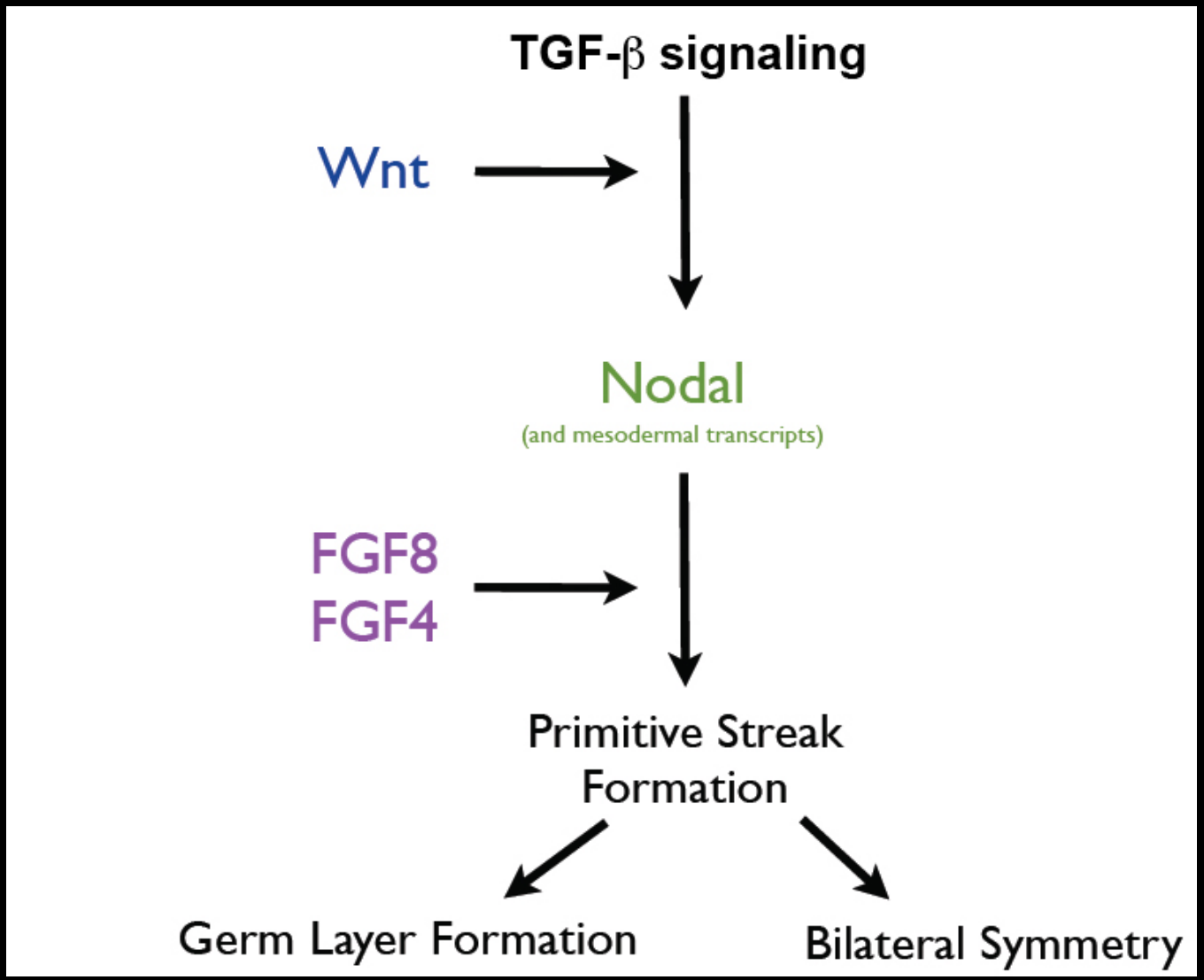


Laboratory tests or Diagnostic evaluations
"Plain" film X-ray study. Up to 60% of saccrococcygeal teratomas have calcifications, often forming ectopic bone or teeth. Seeing these "clinches" the diagnosis. If fatty density is seen within the mass, lipomatous tissue is likely present, and makes the diagnosis of teratoma likely.

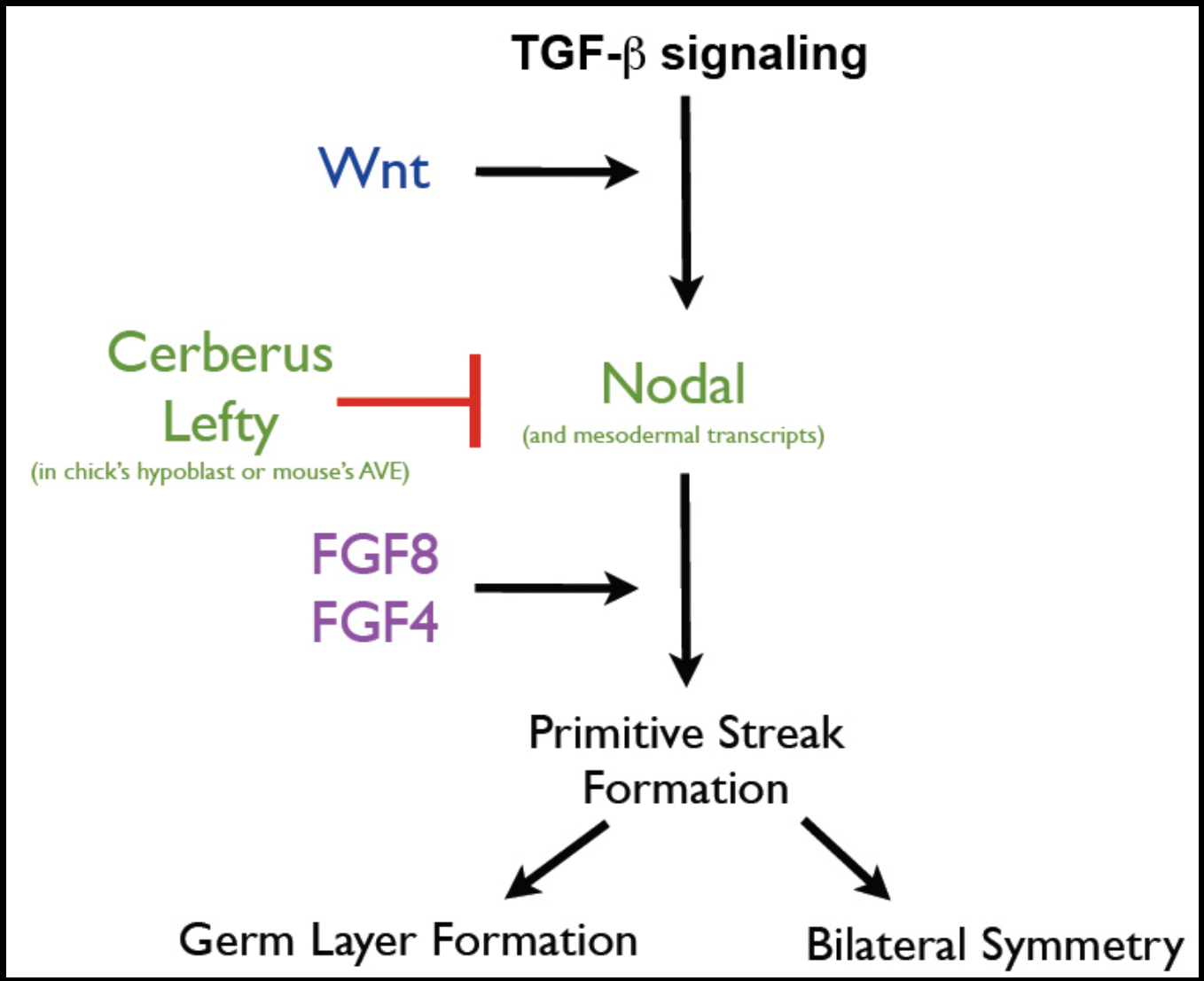
Chest X-ray is important to assess the possibility of pulmonary metastases. CT scan of the abdomen and pelvis may determine if primary surgery is feasible

Serum alpha feto-protein (AFP) and ß-human chorionic gonadotropin (ß-HCG) are two "tumor markers" that can be elevated in malignant teratoma. A high AFP level (mean= 50,000 U/mililiter) is found in the normal newborn with gradual fall to adult levels (<10 U/mililiter). AFP is often grossly elevated (> several million U/mililiter) in malignant teratoma, but normal in benign tumors. Serial measurements are required, to plot the rate of fall and compare it to that expected based on the half life of AFP (5 days). Failure to fall at the expected rate after surgery, or a subsequent rise, indicates residual malignant cells, or development of metastases. In about 10% of cases, these markers are not elevated.

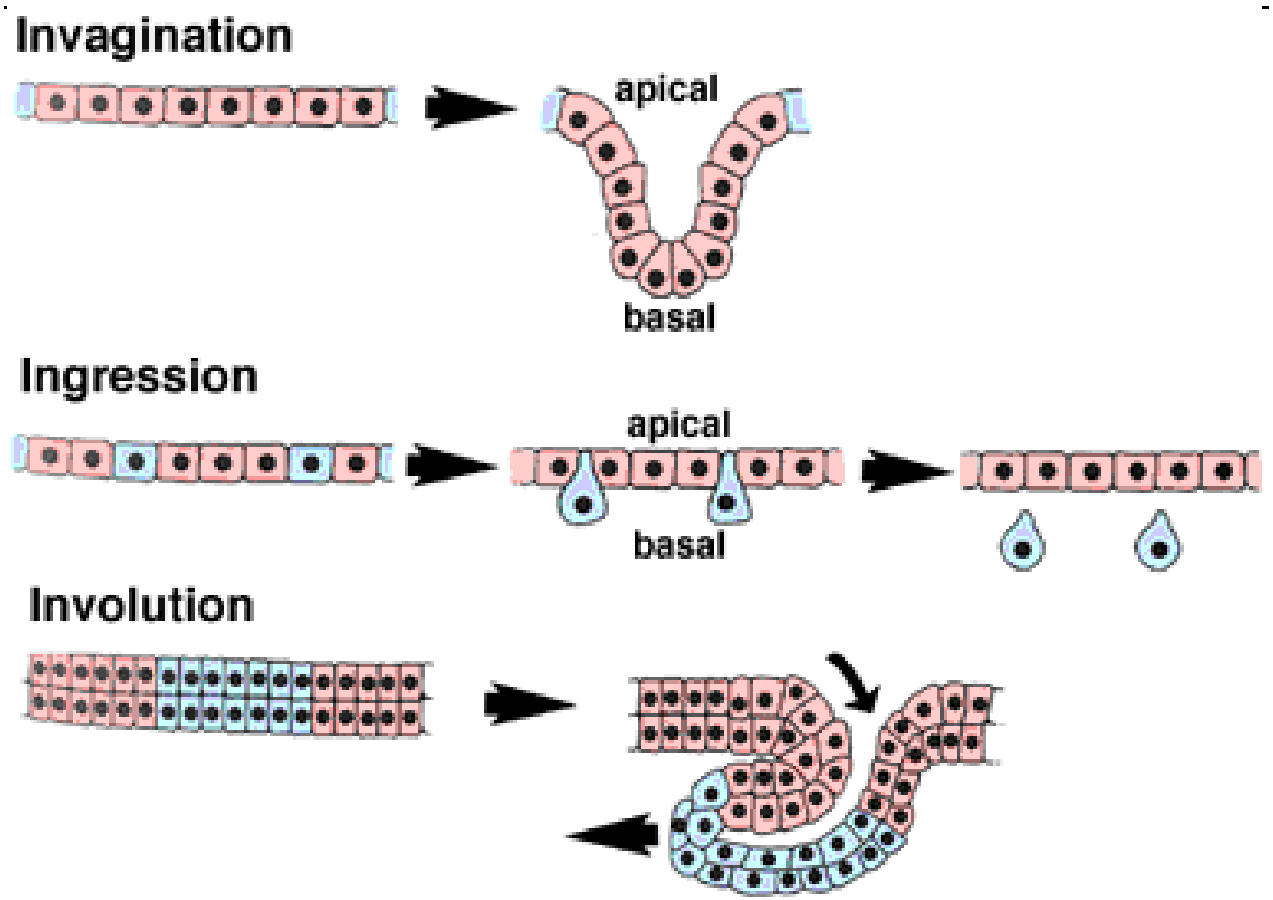
Signaling regulation of primitive streak development



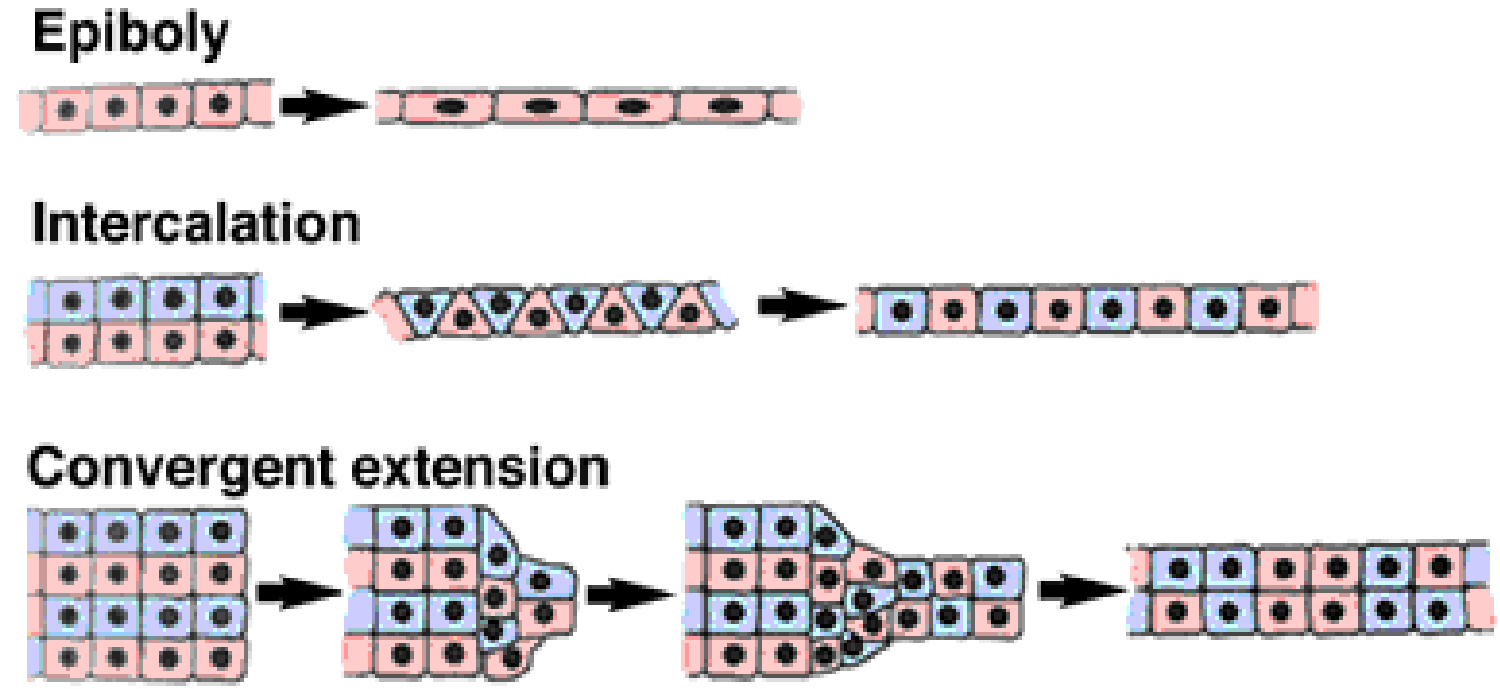
Signaling restriction of primitive streak development



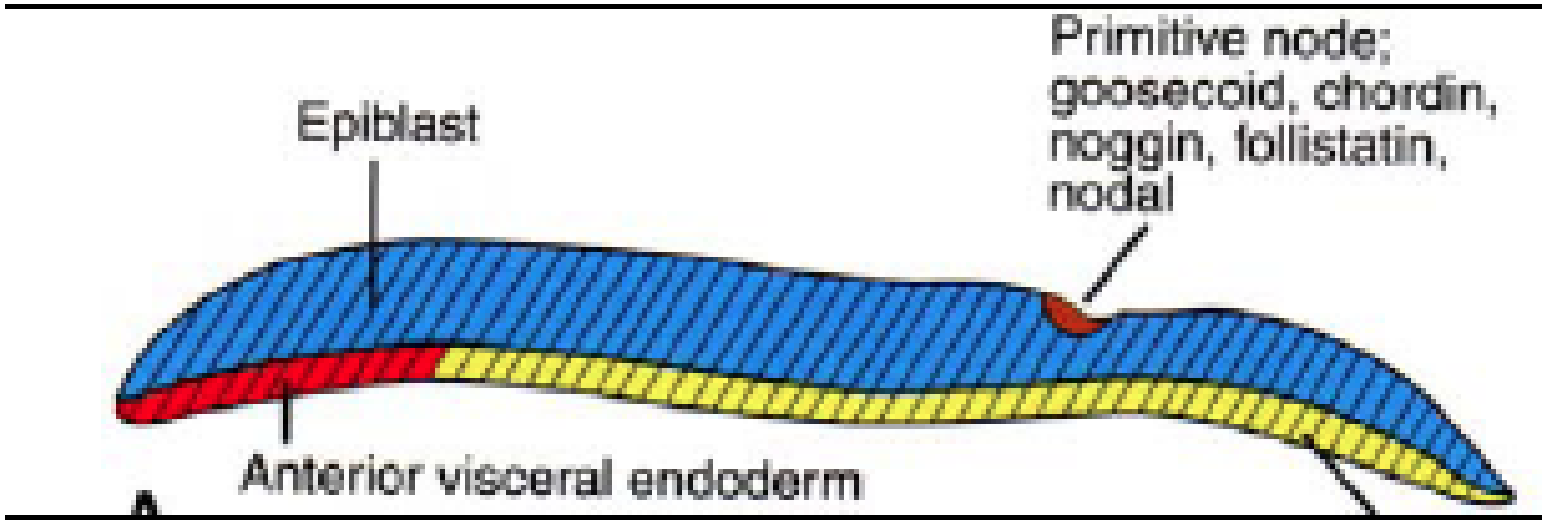
Examples of cell movement or remodeling in gastrulation



Examples of cell movement or remodeling in gastrulation

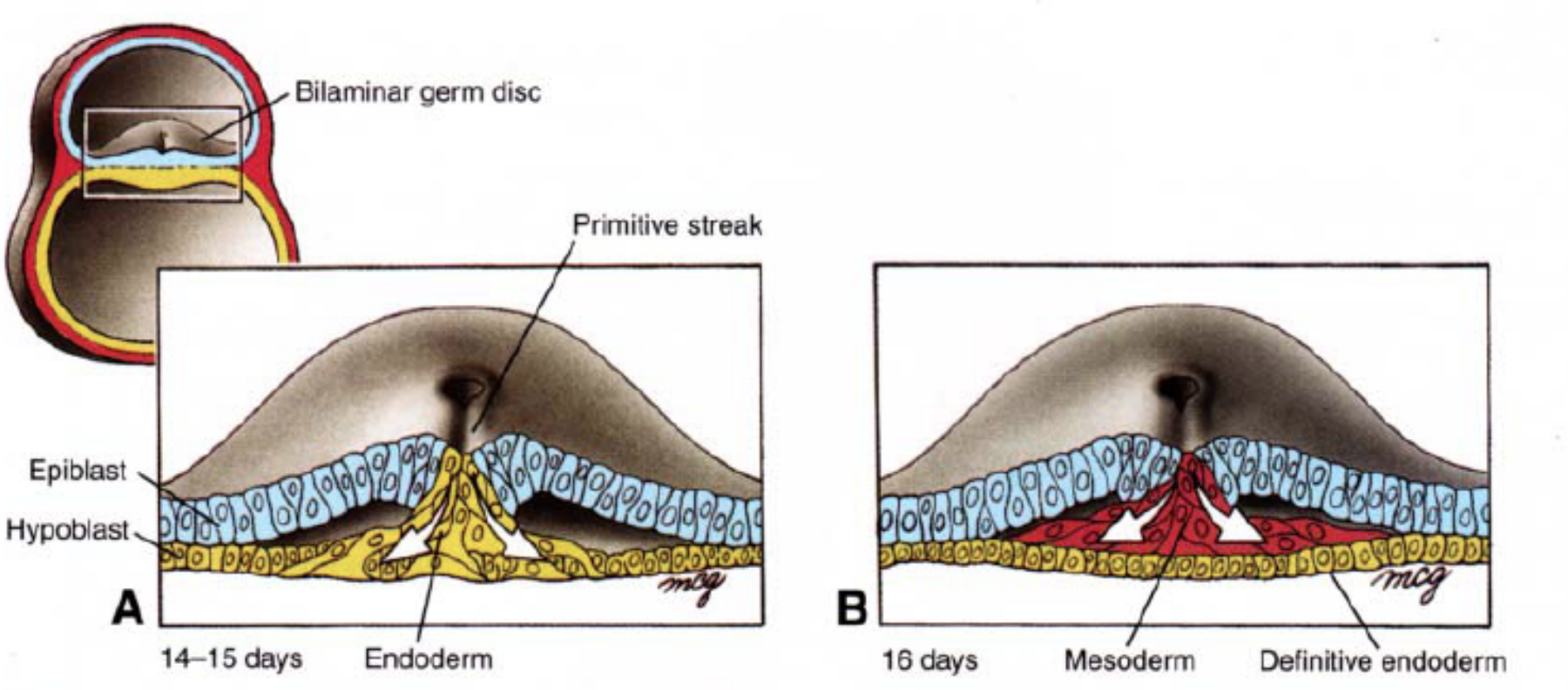


Sagittal schematic of human gastrula



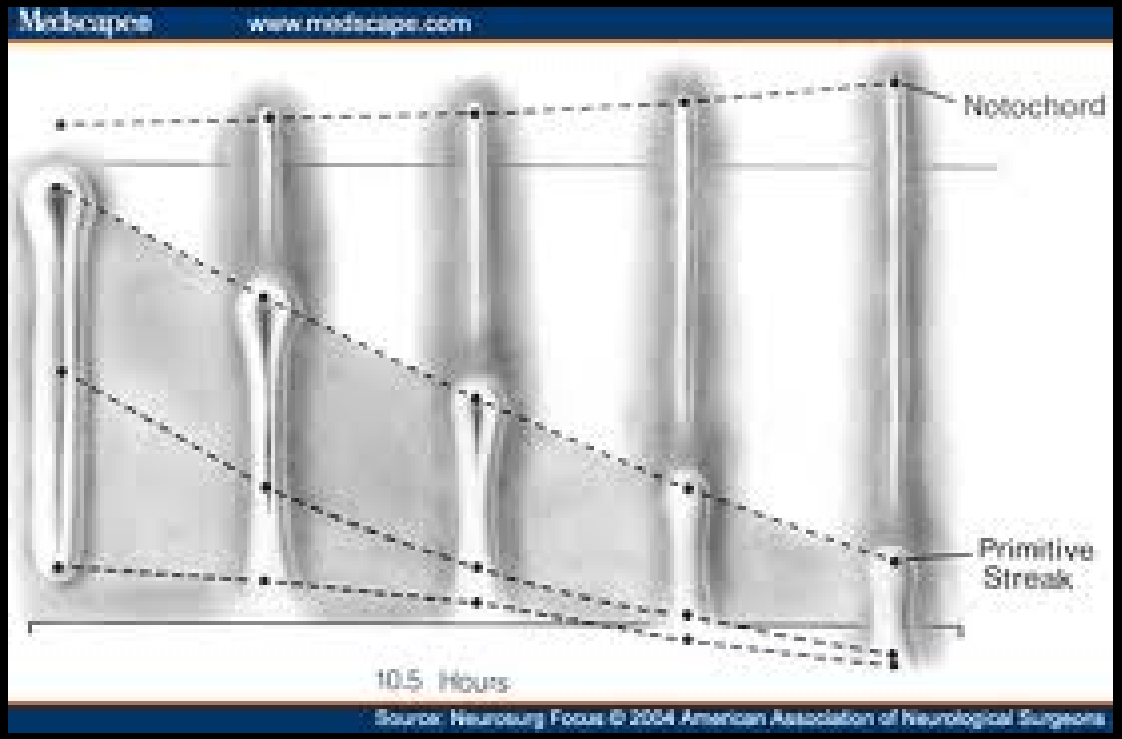
Langman's Medical Embryology 11th Edition

Overview of mesoderm development and differentiation



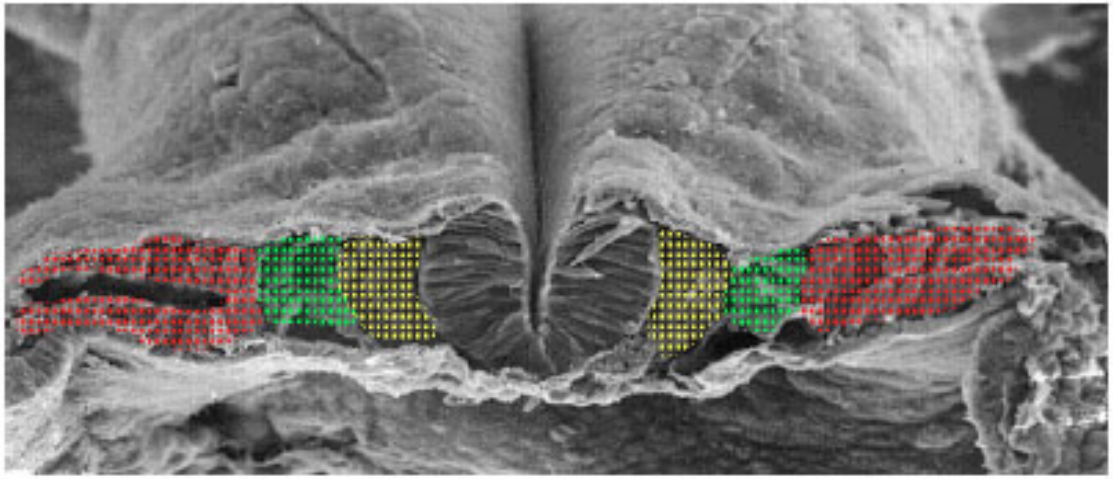
Mesoderm fates are distinct along a medial-lateral axis

Primitive streak regression and notochord growth



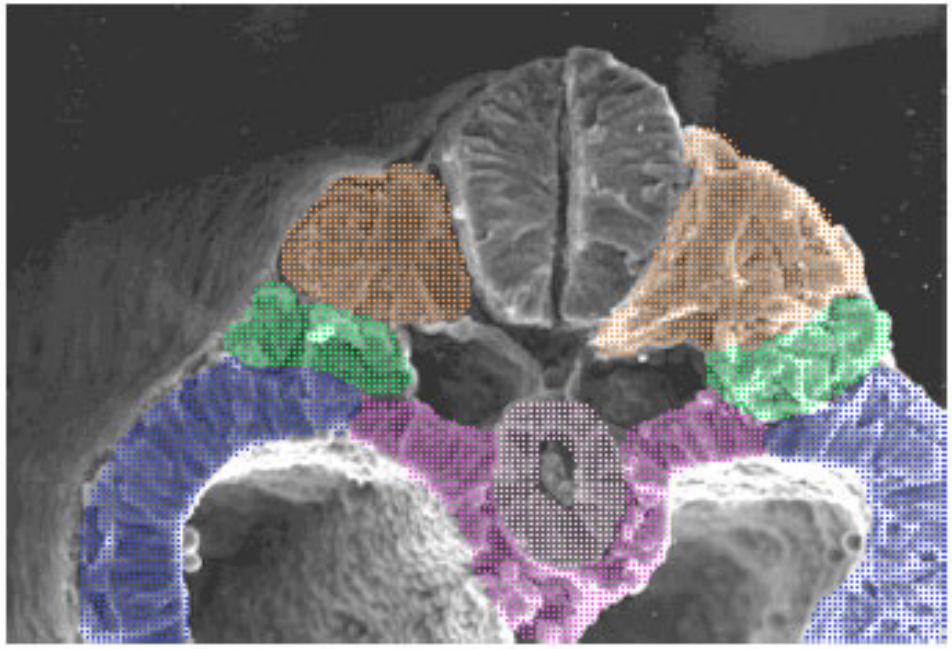
Distinct mesoderm divisions with different later fates

~ Day 22, human



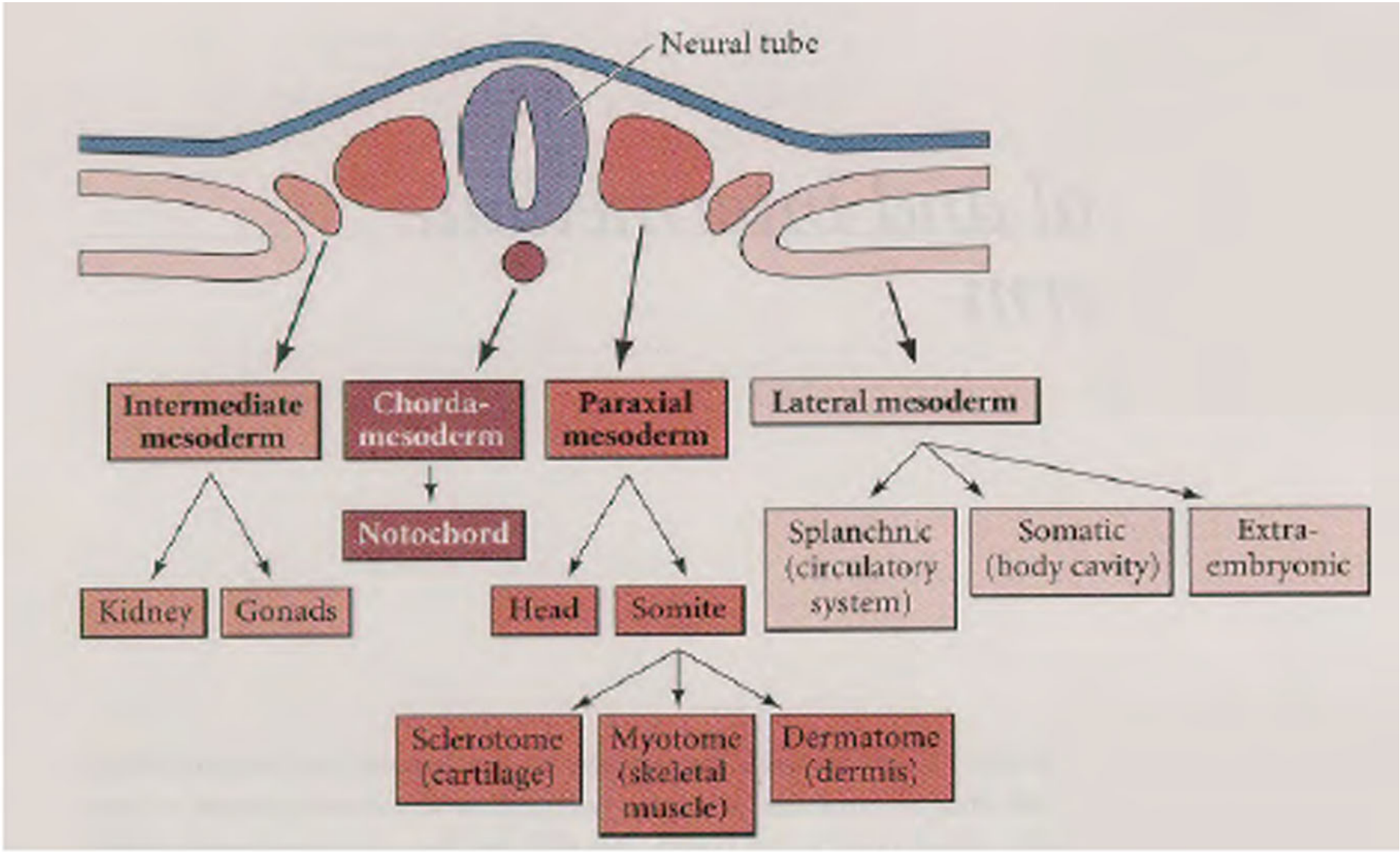
After gastrulation, mesoderm from medial to lateral has different features and fates. Paraxial (yellow), intermediate (green), and lateral (red).

~ Day 26, human

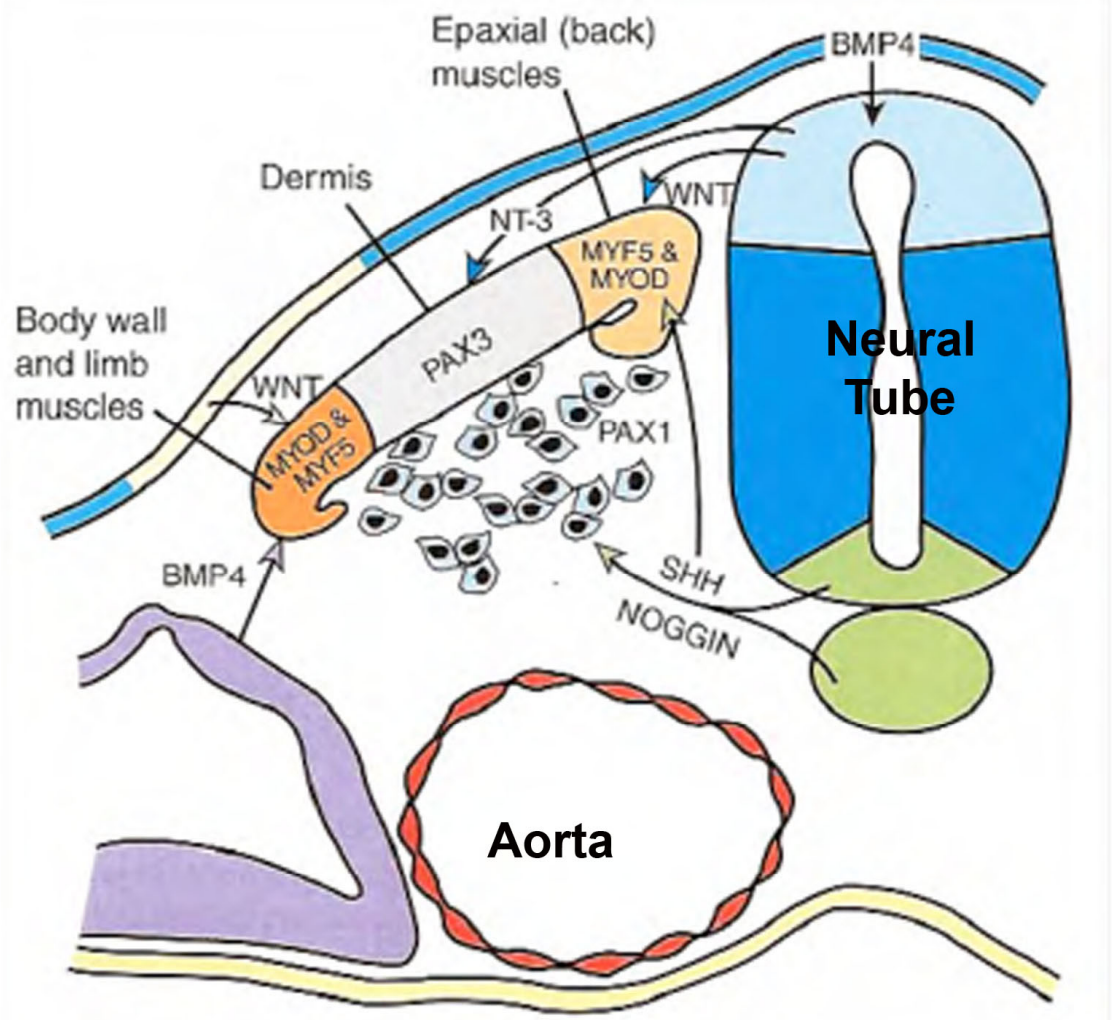


Within a few days, these mesoderm precursor cells have further sub-divided into additional types:
somatic (blue)
splanchnic (purple) surrounding endoderm (light purple),
intermediate (green) and
paraxial (tan).

Fates of different mesoderm subdivisions



Signals regulating mesoderm development along the dorsal-ventral axis



Regulation of somite differentiation along the dorsal ventral axis. Arrows show known signals controlling somite cell fates, including Sonic hedgehog (Shh) and neurotrophin 3 (NT-3) and Wnt from the ‘roof plate’ of the neural tube. The later fates of subsets of some somite cells are also shown.

We will see in the next lecture how the notochord is an organizer of neural development.

Inductive tissue interactions organize tissue development

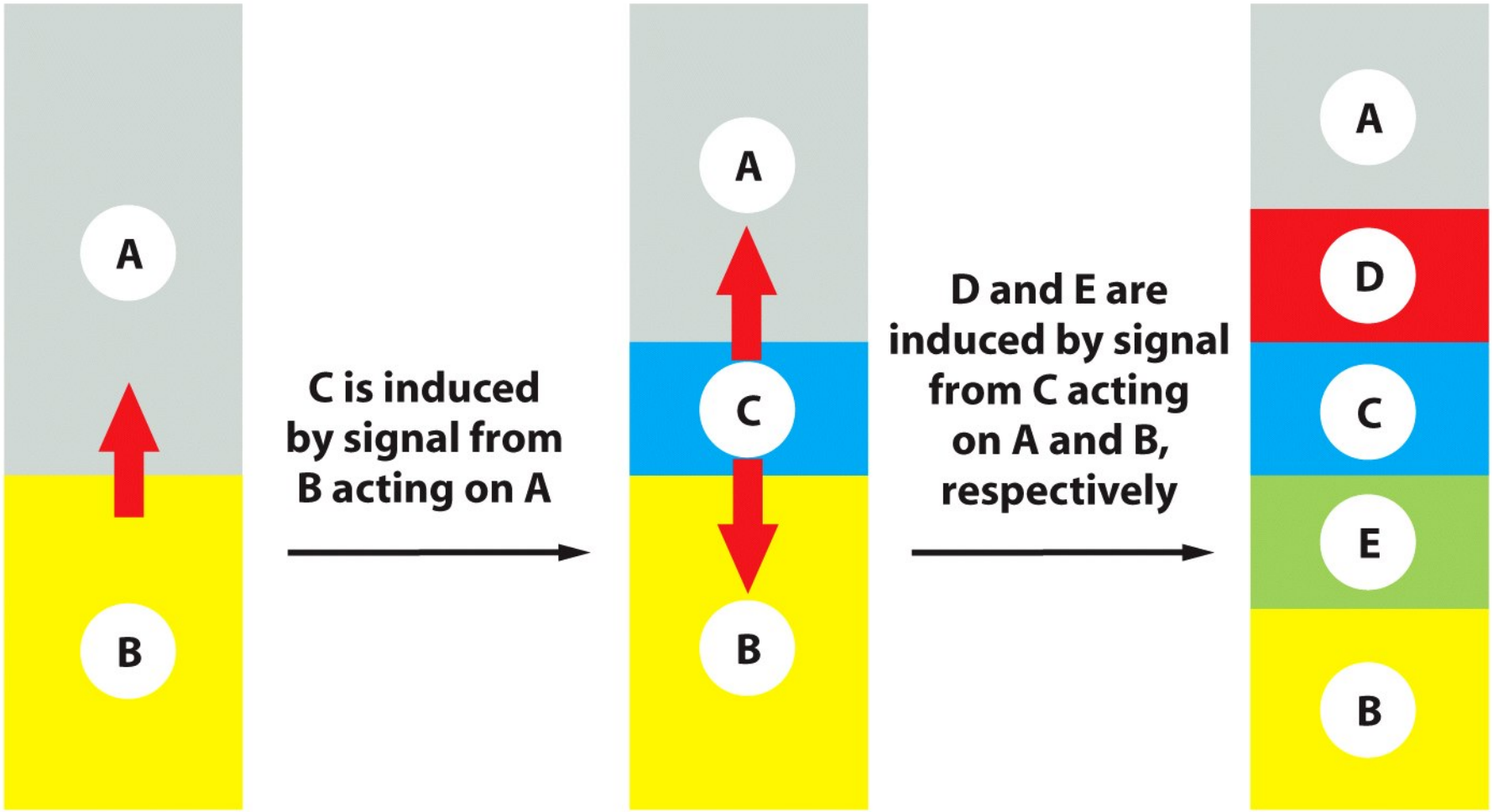
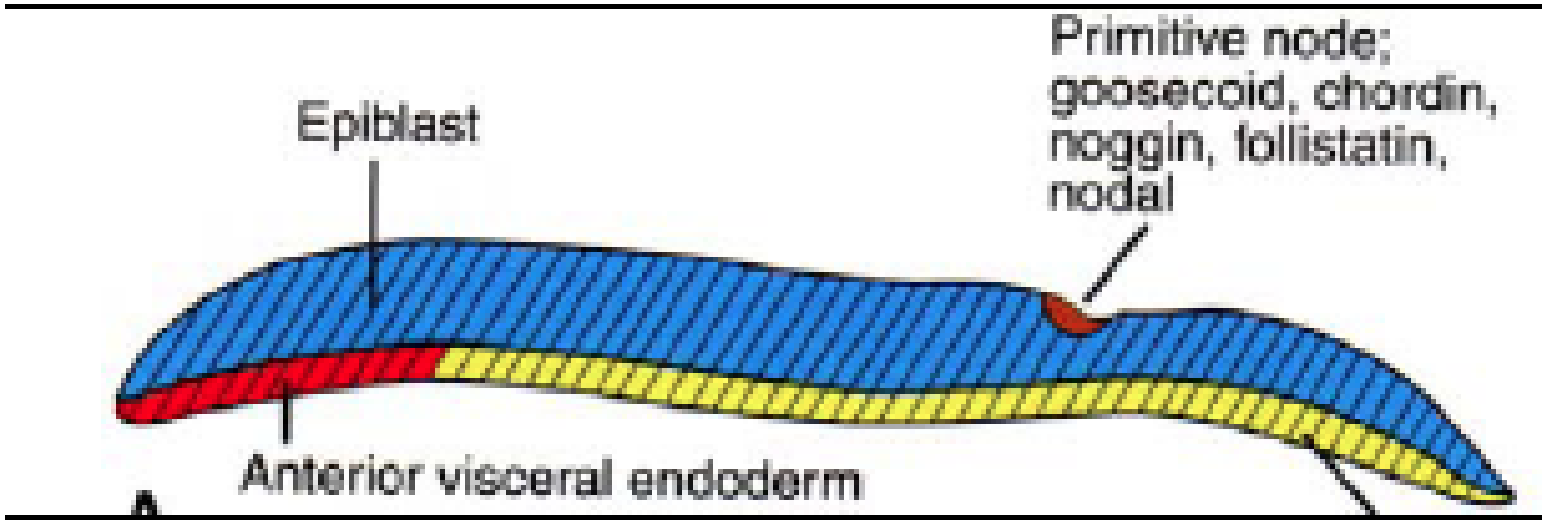


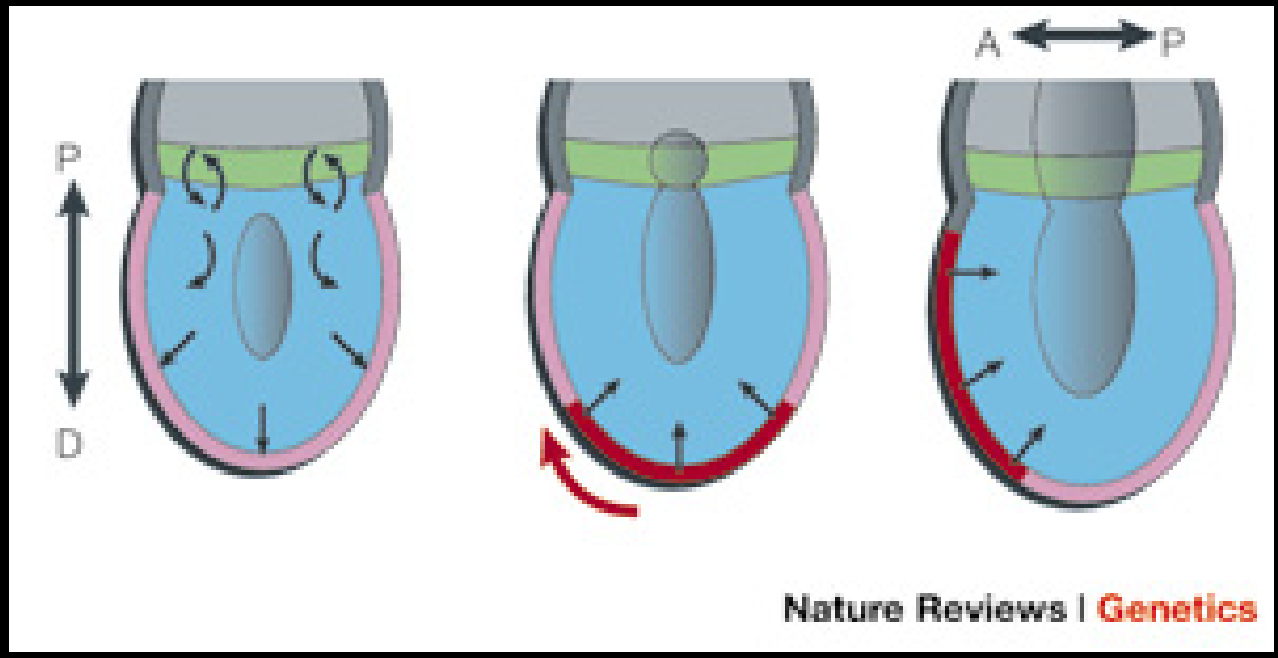
Figure 22-16 *Molecular Biology of the Cell* (© Garland Science 2008)

Sagittal schematic of human gastrula



Langman's Medical Embryology 11th Edition

Gastrulation in mice to generate the anterior visceral endoderm (AVE) signaling center

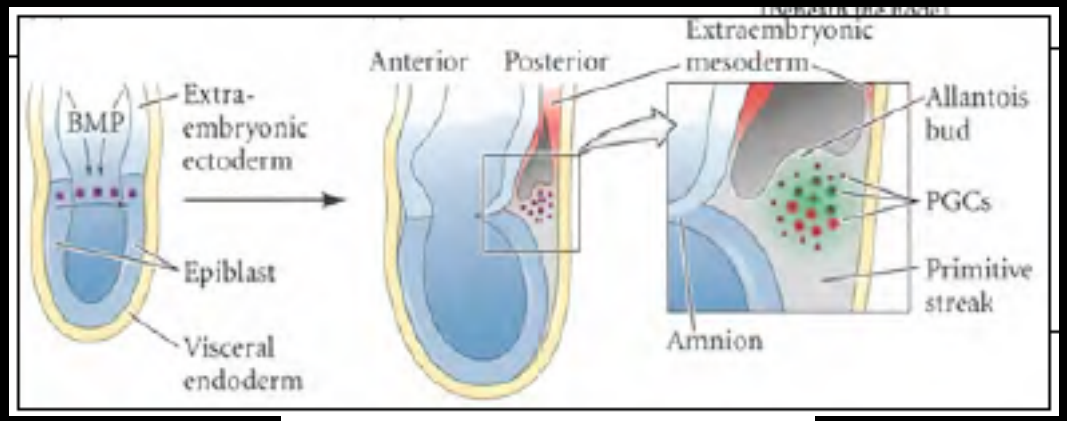


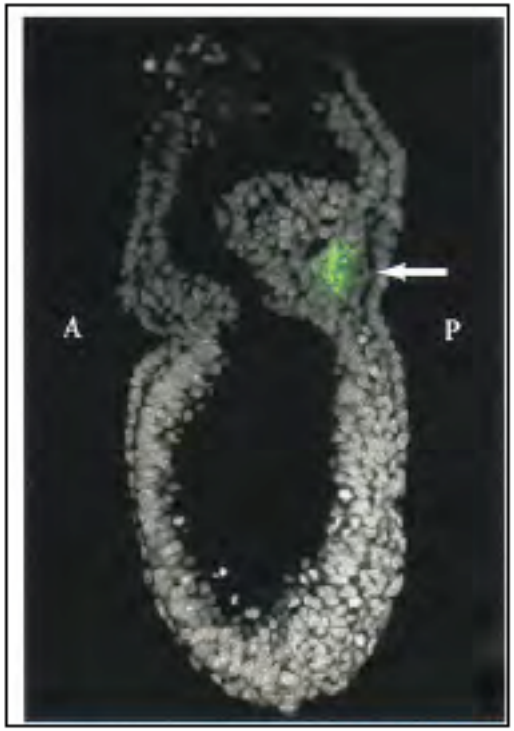
Inner cell mass expression of Oct4 a marker and regulator of pluripotent cells

Other markers: Sox2, Nanog

Other outcomes: “Embryonic stem cells”

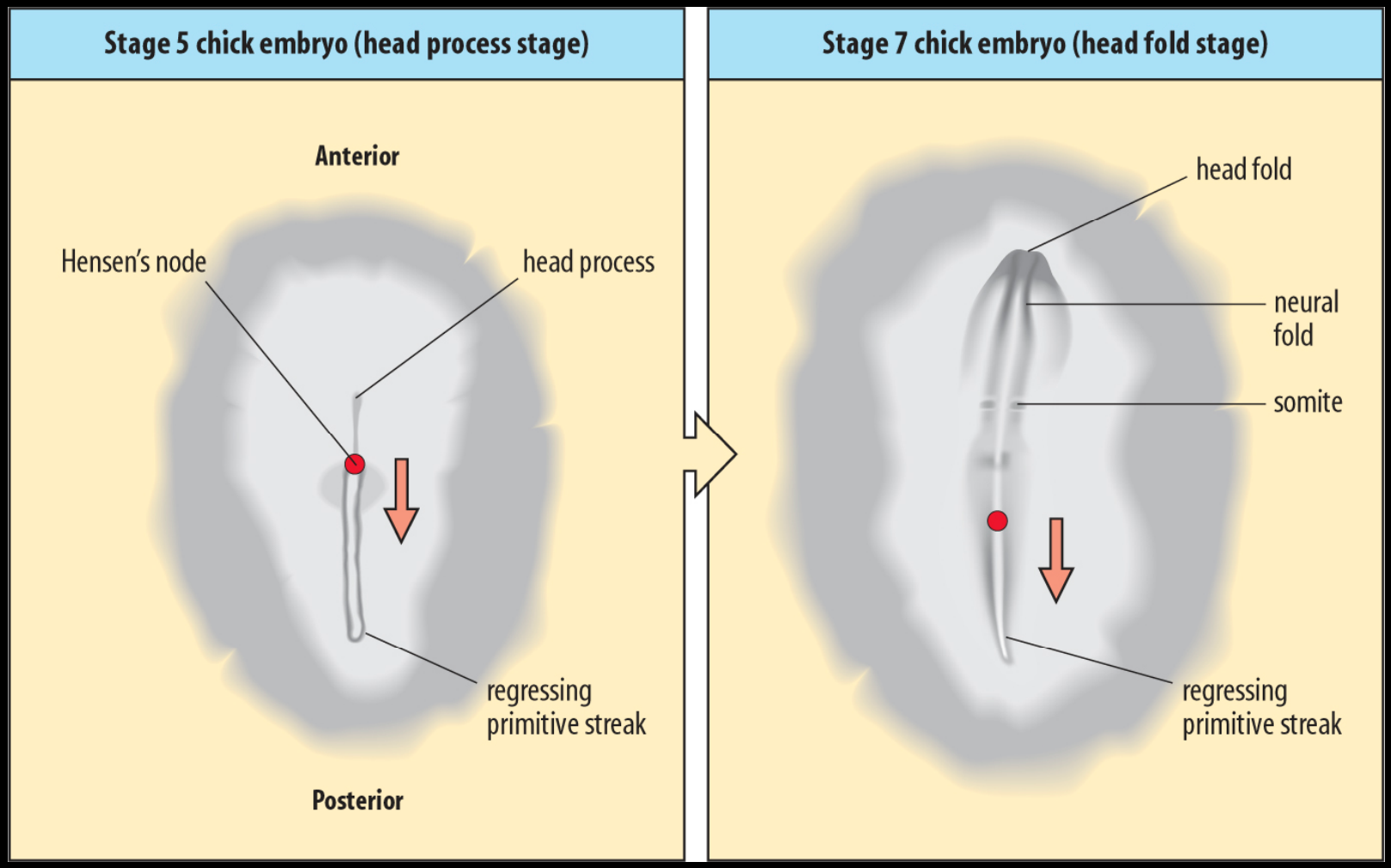
Primordial germ cells are set aside early in gastrulation





Gilbert *Developmental Biology* 2010

Contrasting morphogenesis anterior and posterior of the node



The node breaks bilateral symmetry to form the L-R axis

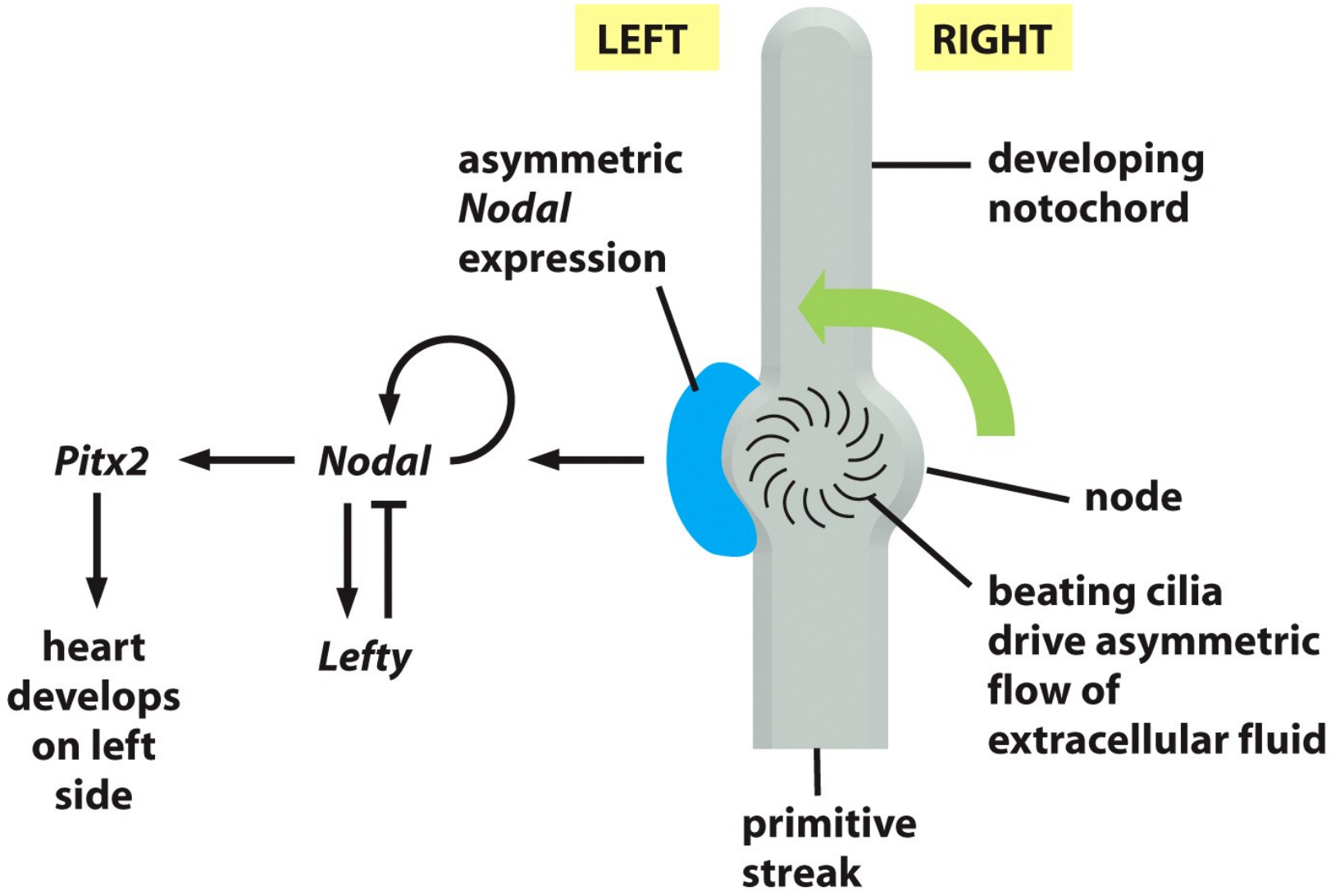
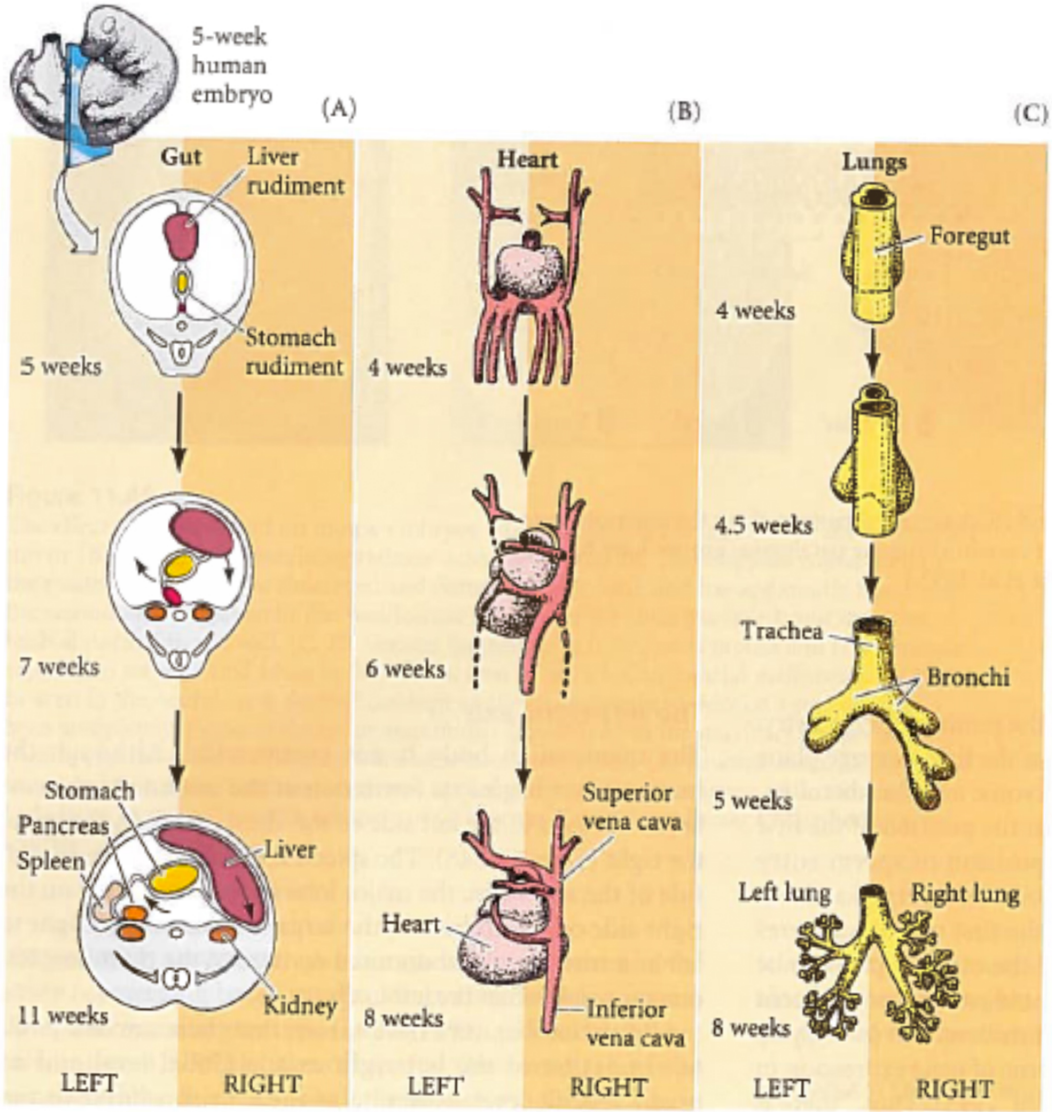


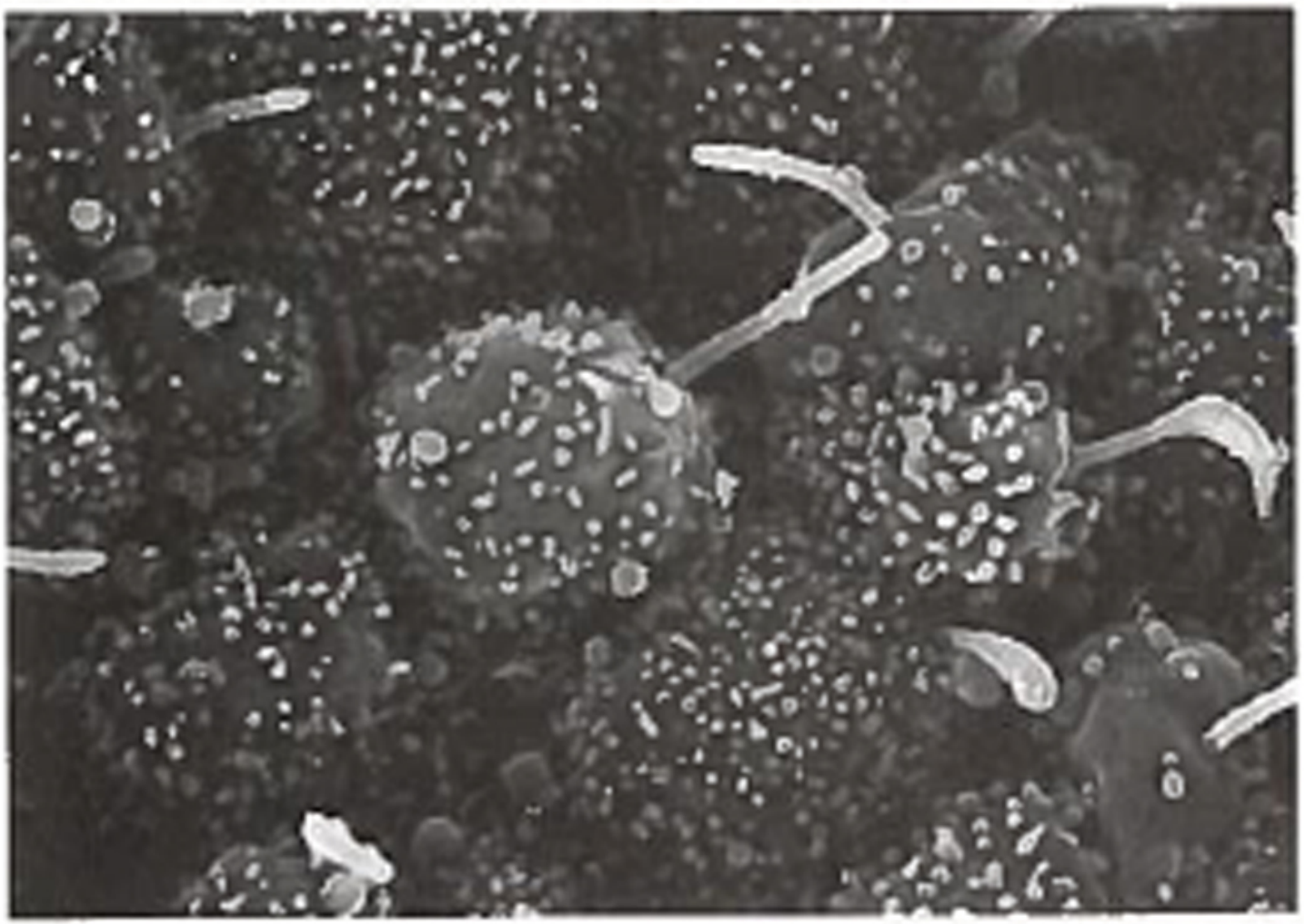
Figure 22-87a *Molecular Biology of the Cell* (© Garland Science 2008)

Stereotyped L-R axial patterning of organ systems

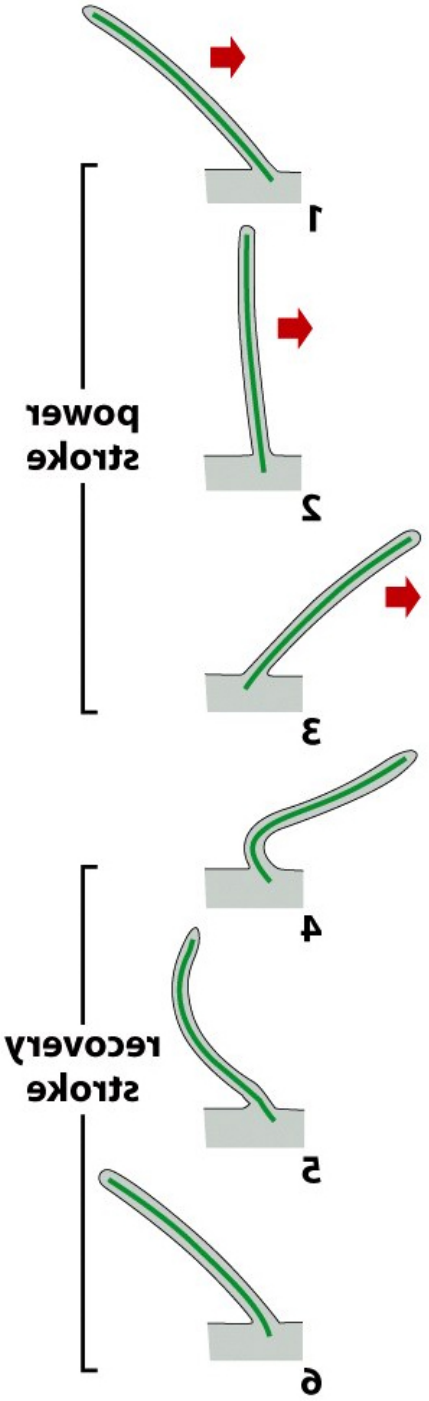


Gilbert, *Developmental Biology*, 2010.

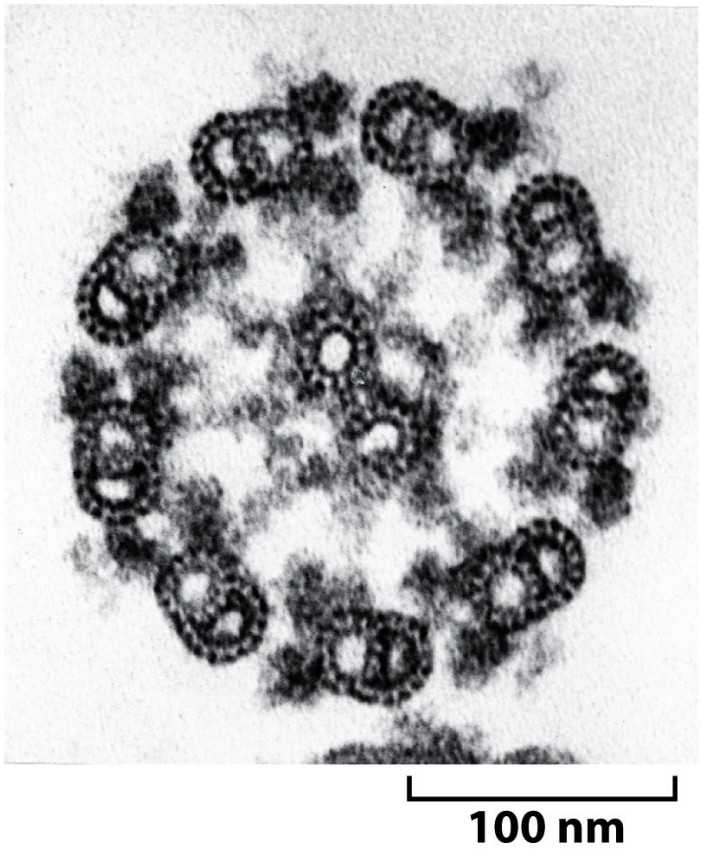
Node cells have motile cilia



Alberts, Molecular Biology of the Cell 5th ed.



Motile cilia ultrastructure: ~250 protein components



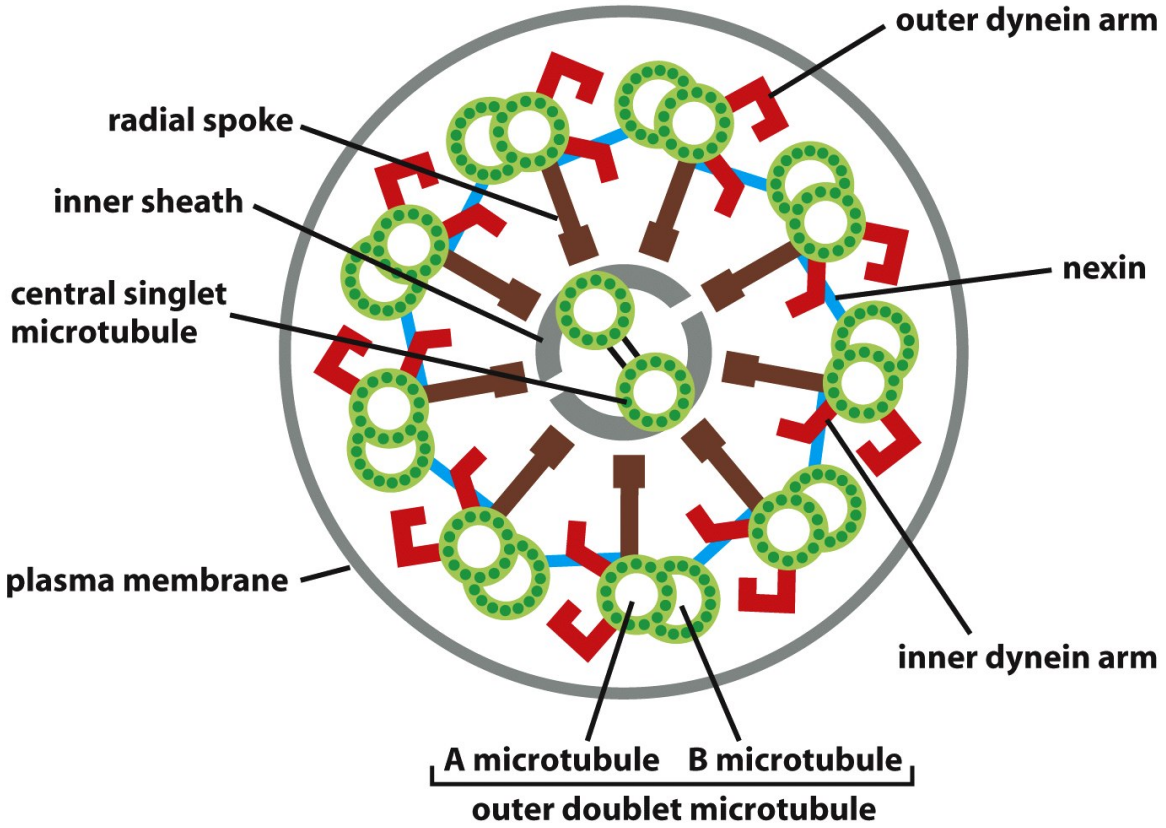


Figure 16-81a *Molecular Biology of the Cell* (© Garland Science 2008)

The node breaks bilateral symmetry to form the L-R axis

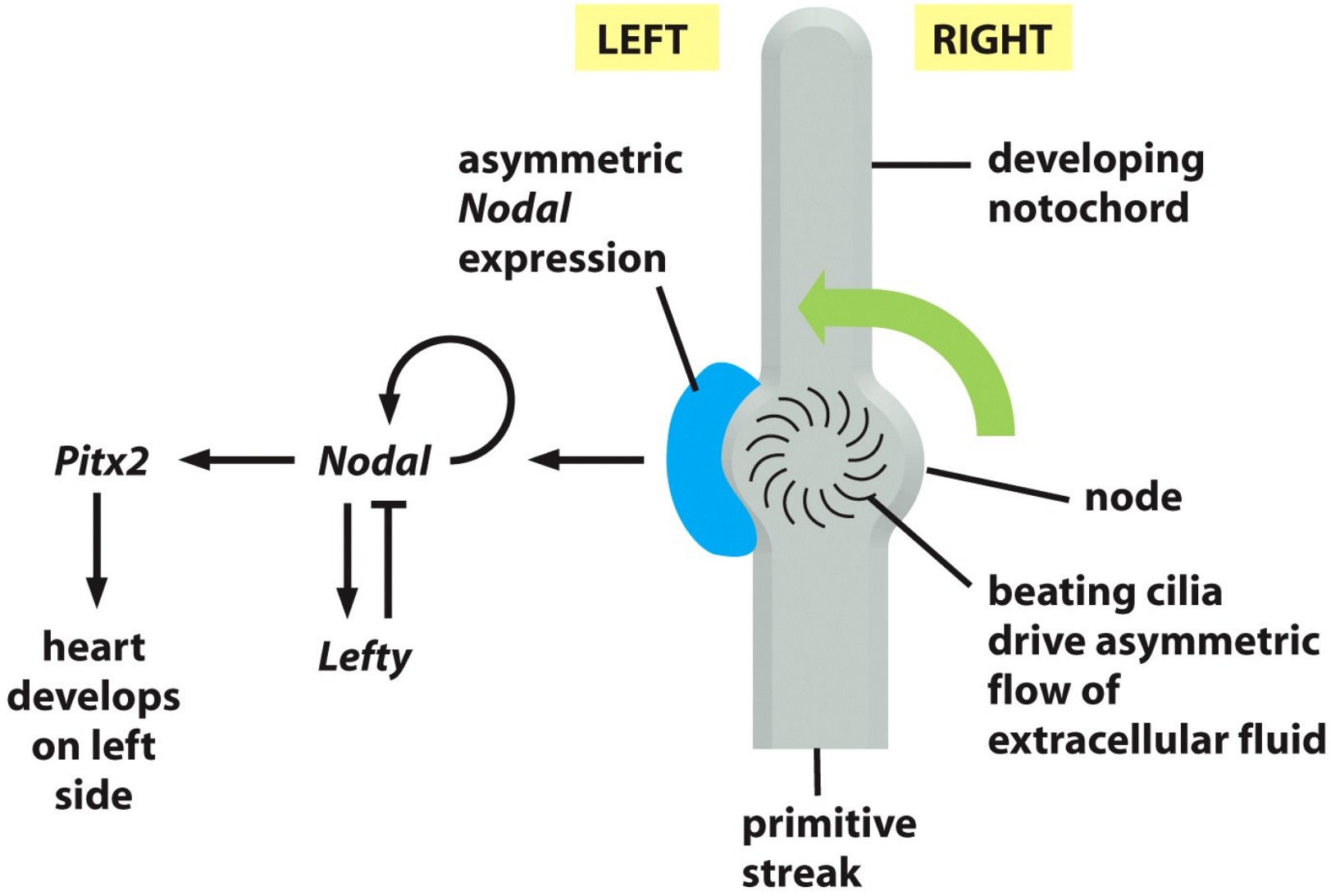
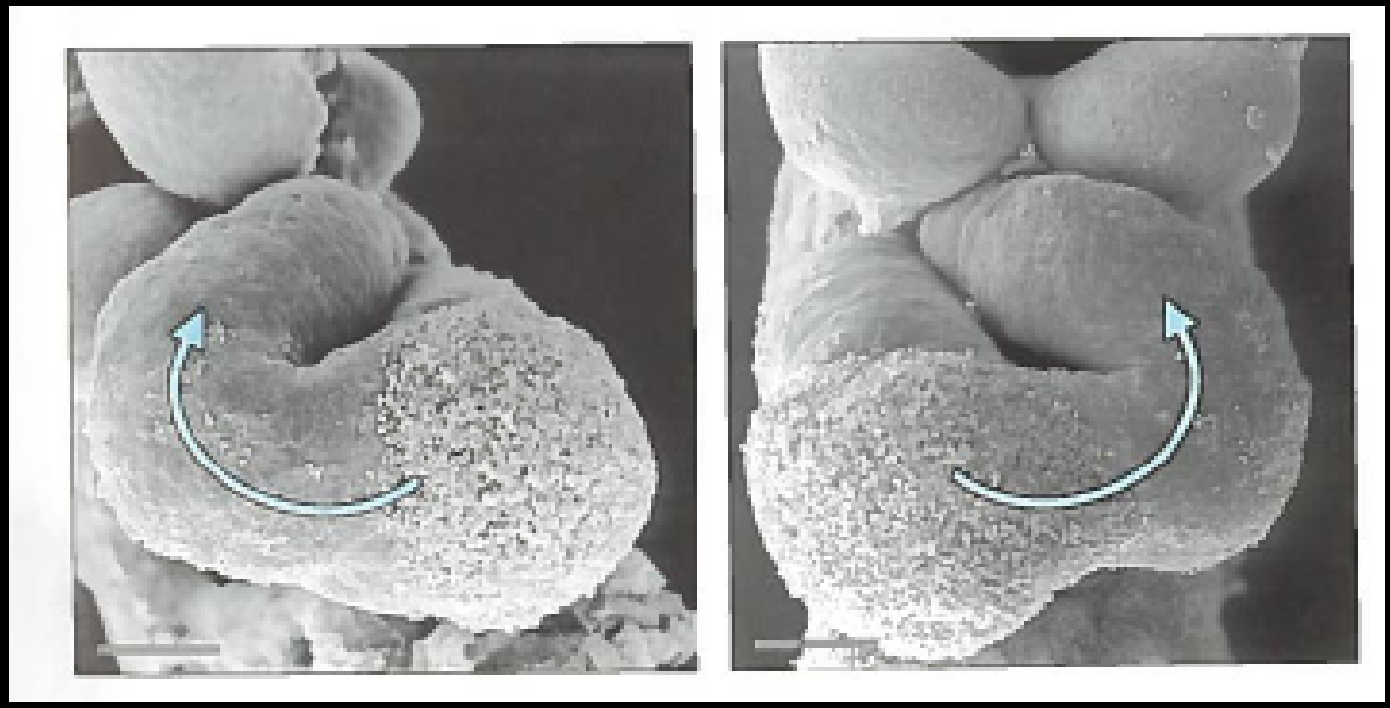


Figure 22-87a *Molecular Biology of the Cell* (© Garland Science 2008)

Asymmetric (left-sided) Nodal expression in gastrulation

Figure 22-87b *Molecular Biology of the Cell* (© Garland Science 2008)

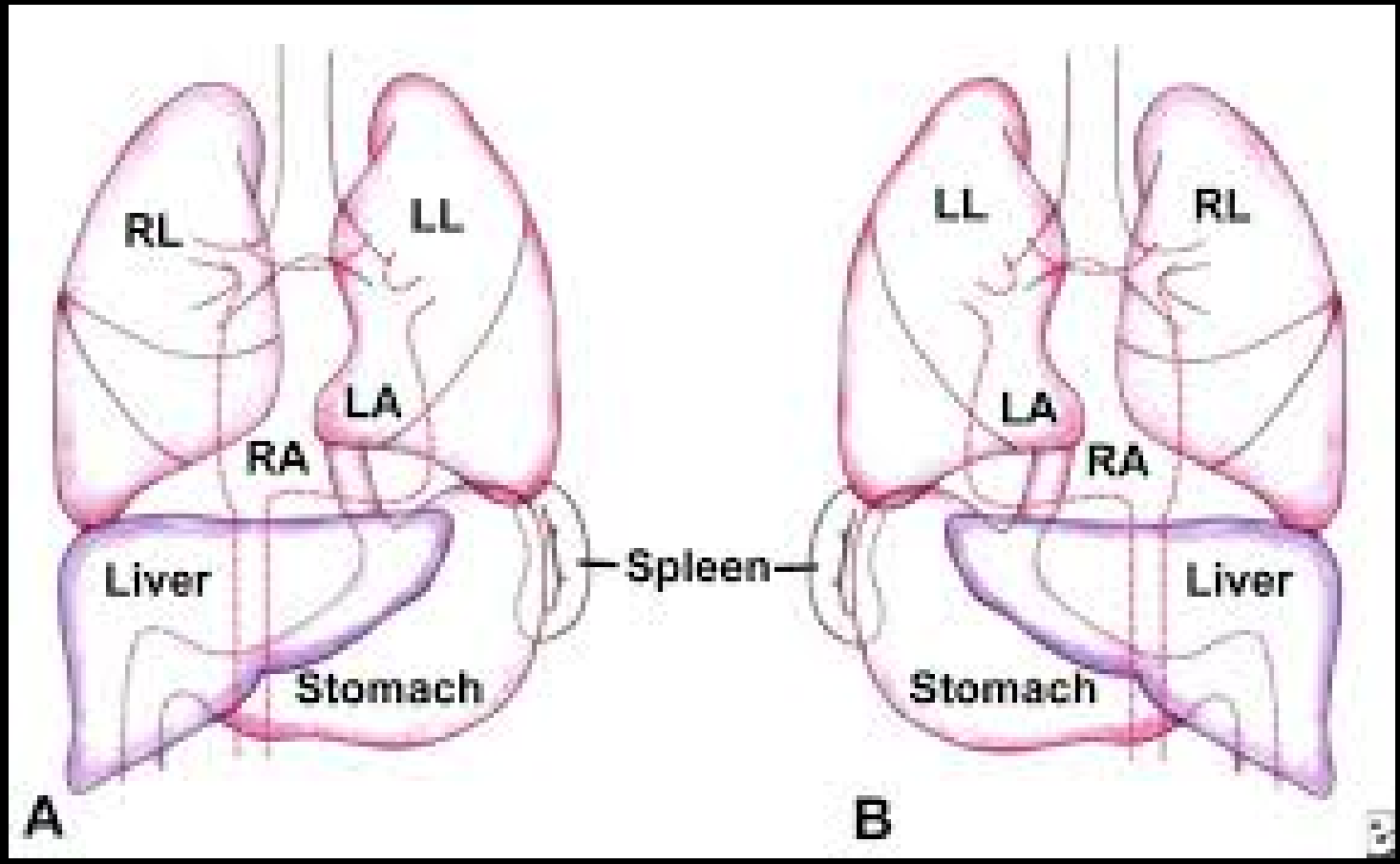
Heart ‘looping’ is an early morphological sign of L-R asymmetry

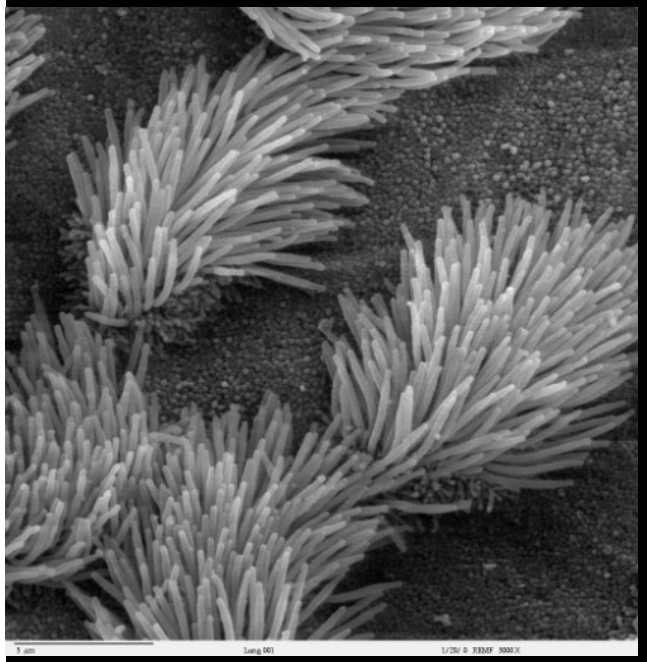


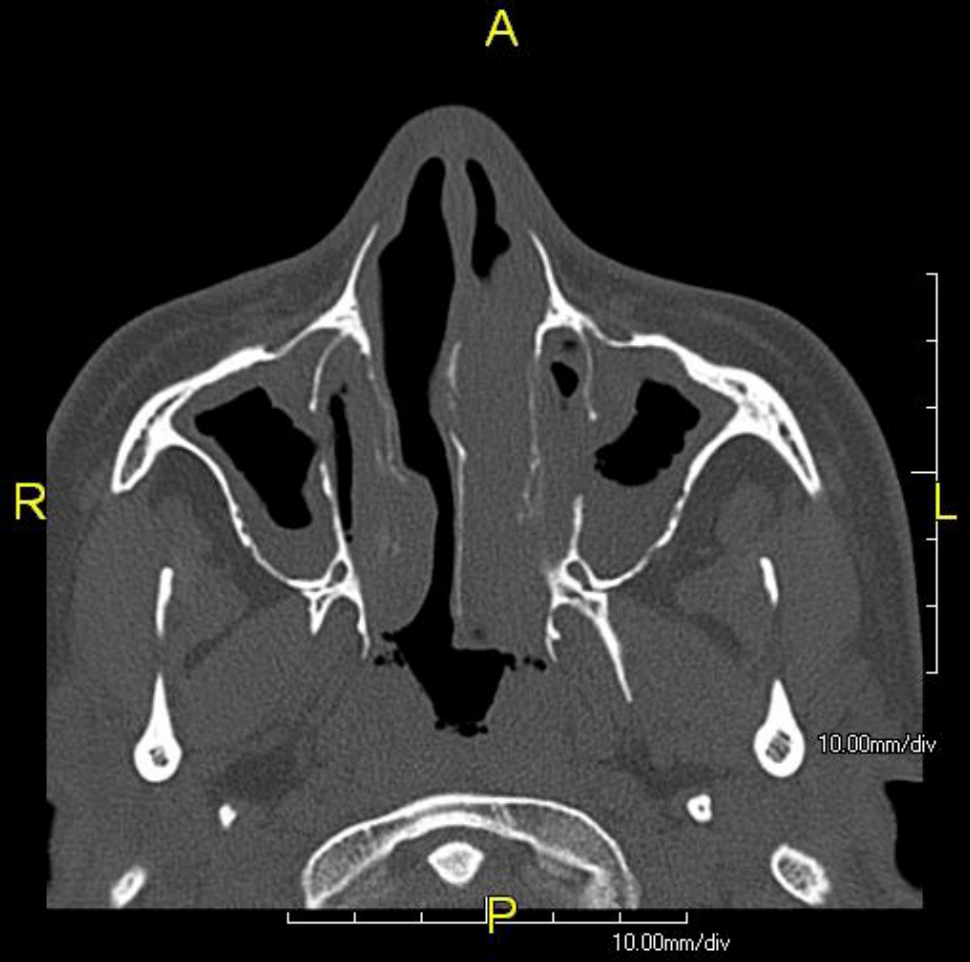
Case history

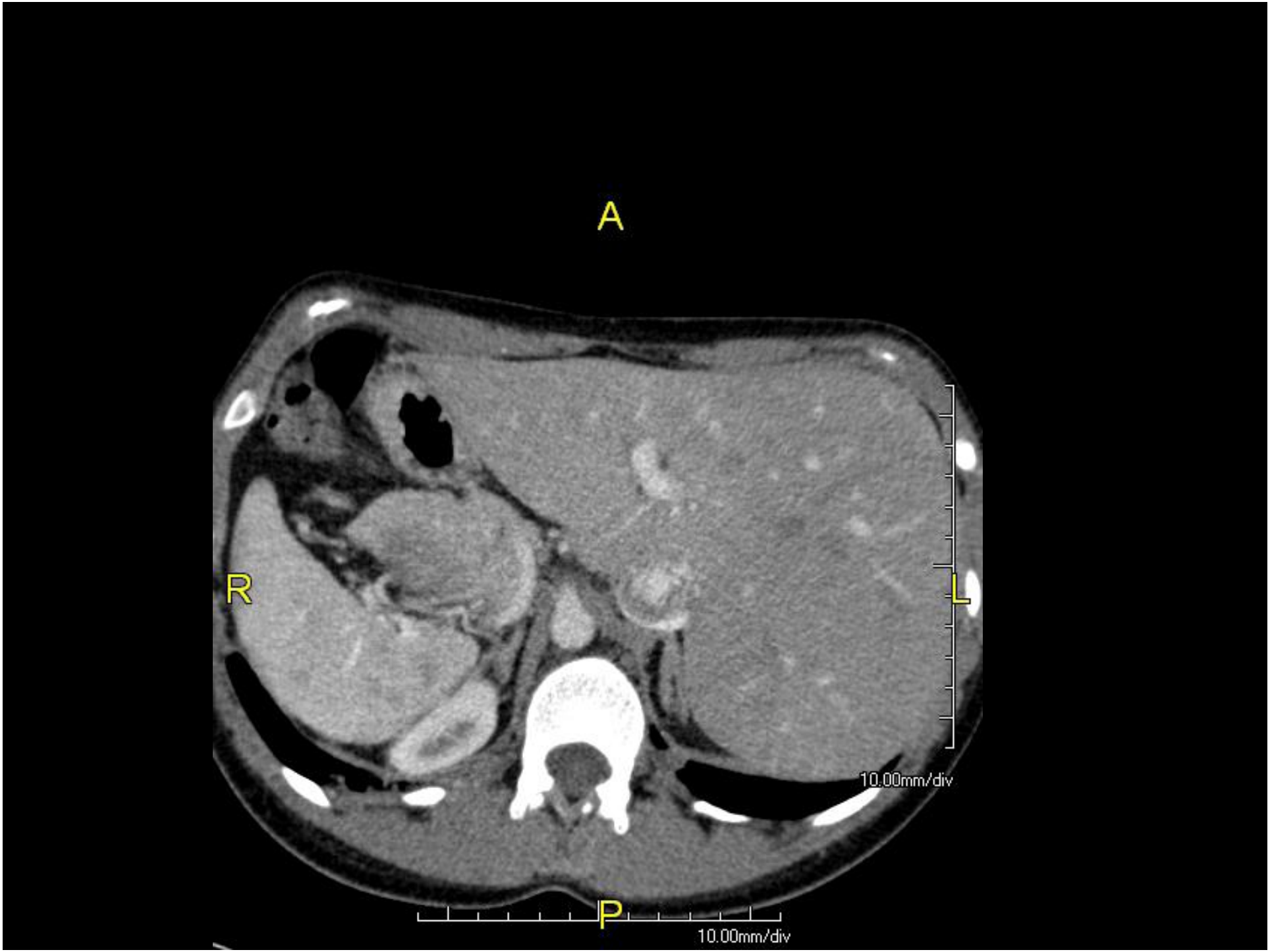
You are rotating at a Swedish infertility clinic.

A 42 y.o. male postal worker presents with a history of infertility that on work up shows immotile sperm. He has a history of chronic bronchitis and sinus infections (sinusitis) treated with antibiotics and respiratory therapy. You note on chest X-ray that there is situs inversus.


RL
LL
LA
RA
Liver
Stomach
A
Spleen
LL
RL
LA
RA
Liver
Stomach
B

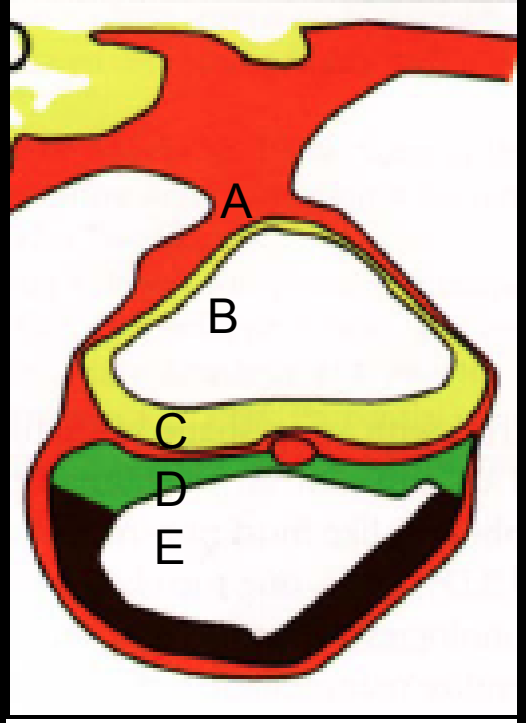



A
R
L
P
10.00mm/div
10.00mm/div


A
R
L
10.00mm/div
P
10.00mm/div

Summary

- Generate primary ‘germ layers’ endoderm, mesoderm, ectoderm
- Generate crucial signaling centers coordinating tissue development (‘organizers’) including the primitive streak, node and anterior visceral endoderm (AVE)
- Break axial symmetry along A-P, D-V and L-R axes
- Generate primordial germ cells



Polling questions

Eakin and Behringer, Gastrulation in Other Mammals and Humans, 2004

Polling questions

A. Node
B. Notochord
C. Primitive Streak
D. Anterior visceral endoderm