These lectures are supported by web resources:

DB3 lectures on mammalian morphogenesis.

Index:

- Lecture slides for lecture 1 in open document format
- Lecture slides for lecture 2 in open document format
- Lecture slides for lecture 3 in open document format
- Pdf copies of Handouts
- **Movies** supporting the lecture material (these are external links)
  - Human neurulation
  - Somite derivatives
  - Crest migration
  - Chris Armit's film *Morphogenesis*
  - Primordial Germ Cell Migration
  - Retinotectal pathfinding
  - Growth cone turning at boundary
  - Growth cone collapse
- **Podcasts** supporting the lecture material. These five 15-minute podcasts are on human development, and were developed for my lectures to first-year medical students on human development. The material here overlaps strongly with the DB3 course, and you may find some or all of these podcasts helpful in helping you to understand mammalian embryology. It is, though, presented in 'Medical School' style.

  In ogg format:

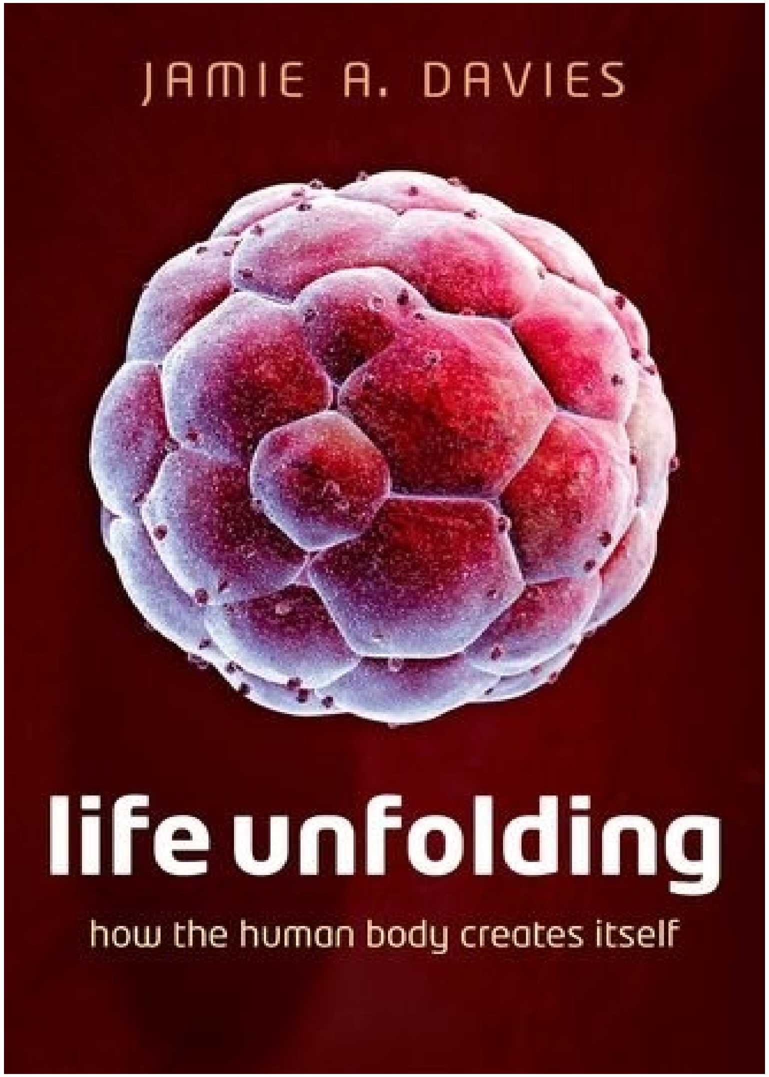
  - Podcast 1 (gametogenesis - not v. relevant to DB3)
  - Podcast 2 (fertilization to blastocyst)
  - Podcast 3 (gastrulation)
  - Podcast 4 (neurulation, neural crest migration)
  - Podcast 5 (growth control)
  - Podcast 6 (sex determination)

  In mp3 Format:

  - Podcast 1 (gametogenesis - not v. relevant to DB3)
  - Podcast 2 (fertilization to blastocyst)
  - Podcast 3 (gastrulation)
  - Podcast 4 (neurulation, neural crest migration)
  - Podcast 5 (growth control)
  - Podcast 6 (sex determination)

  You can contact me at jamie.davies@ed.ac.uk.

You may also find this useful (publication date: 27 Feb 2014).



Oxf Univ Press

Morphogenesis:

the making of mice (and men)

(but this is a fish: movie by 'CarolineZebrafish' on YouTube)

Morpho | genesis

shape

creation

Road map of these three lectures:

1 – Morphogenesis of mice and men, from anatomy to an overview of a set of basic mechanisms

2 – Morphogenesis by cell migration

3 – Morphogenesis by folding and fusion

Core text: Davies JA (2013) *Mechanisms of Morphogenesis* (Darwin Liby)

Road map of these three lectures:

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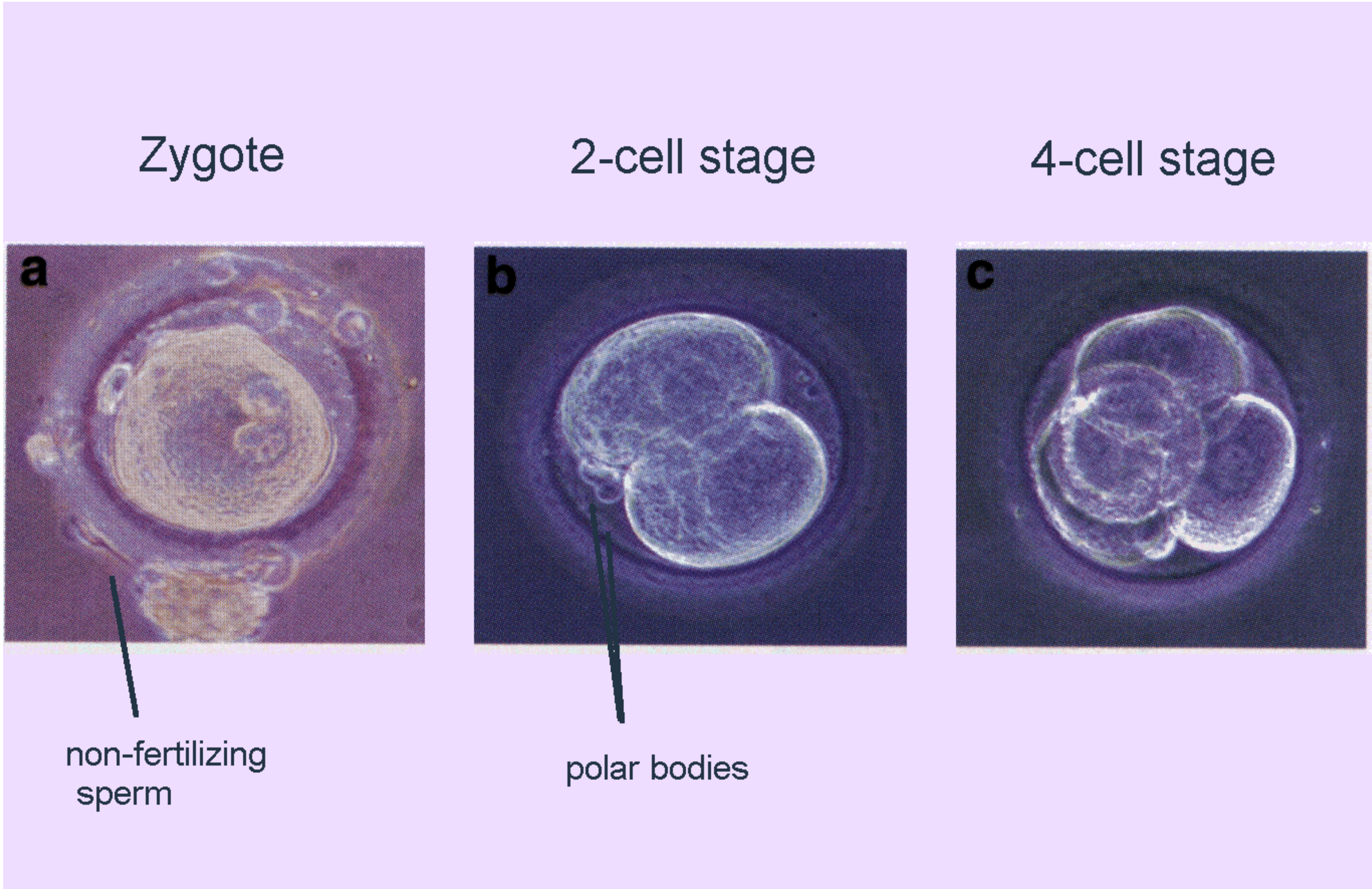
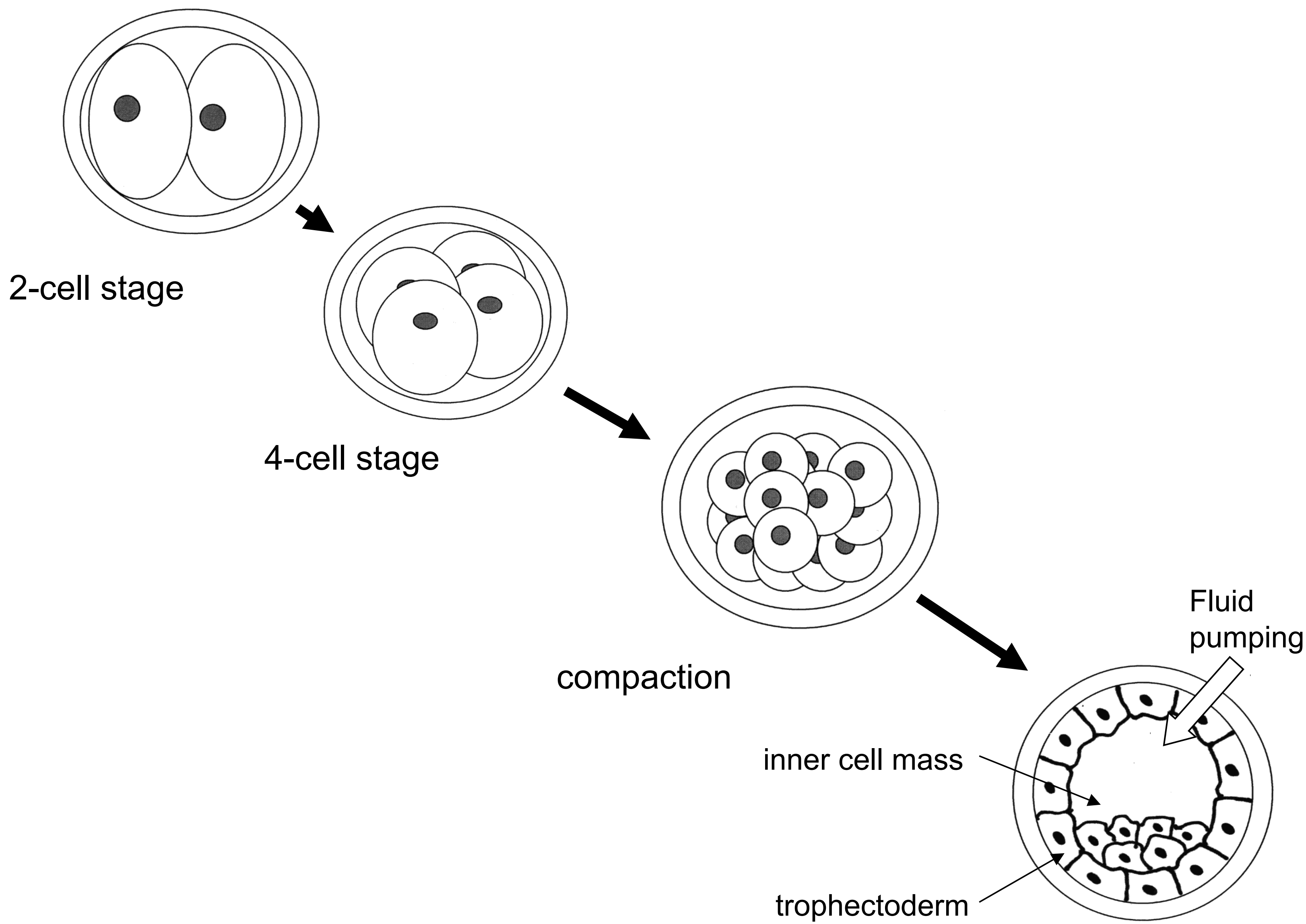
Ex ovo omnia:

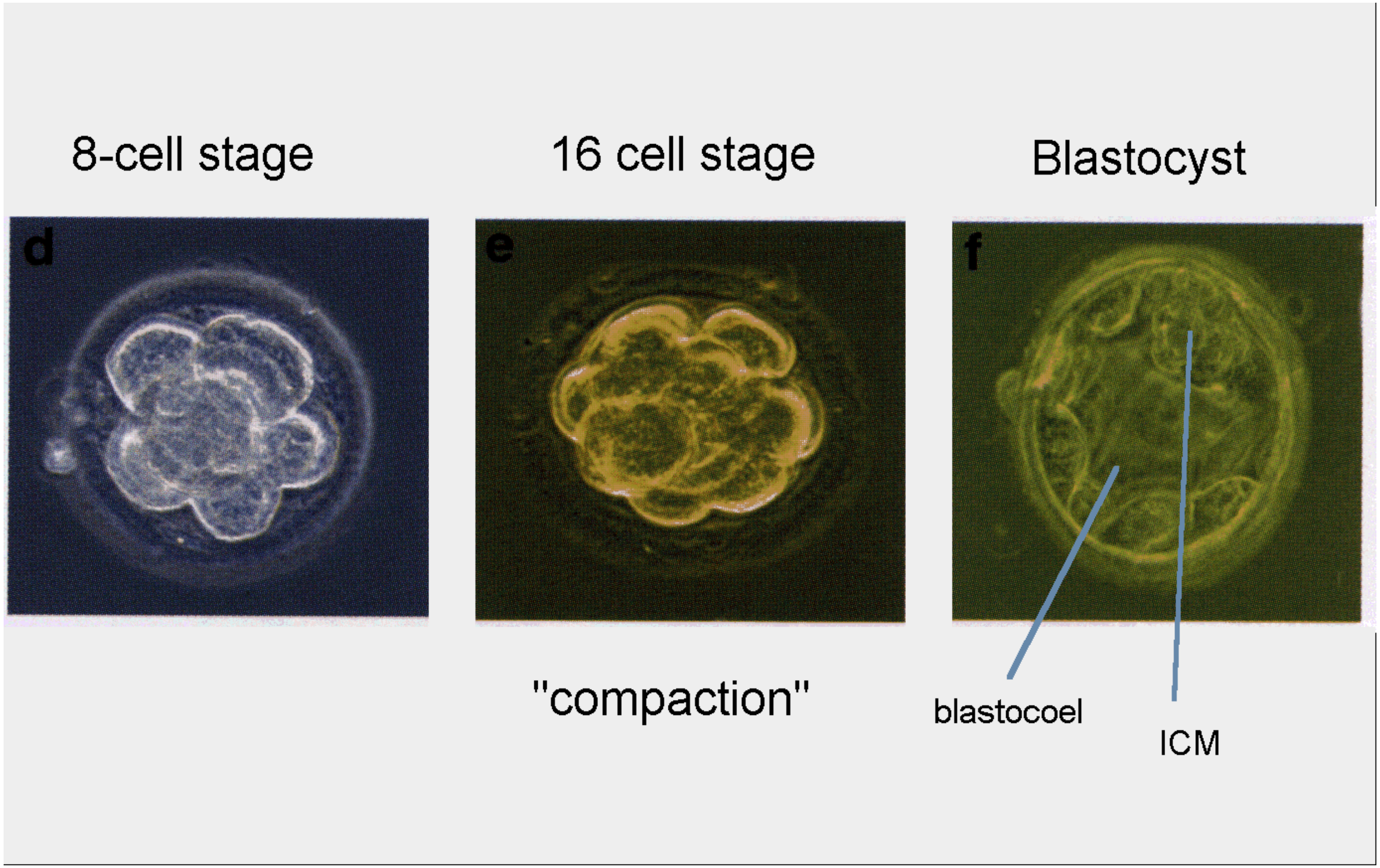
First steps: cleavage (mitosis with no growth)



Pic: Johnson & Everitt "Essential Reproduction"

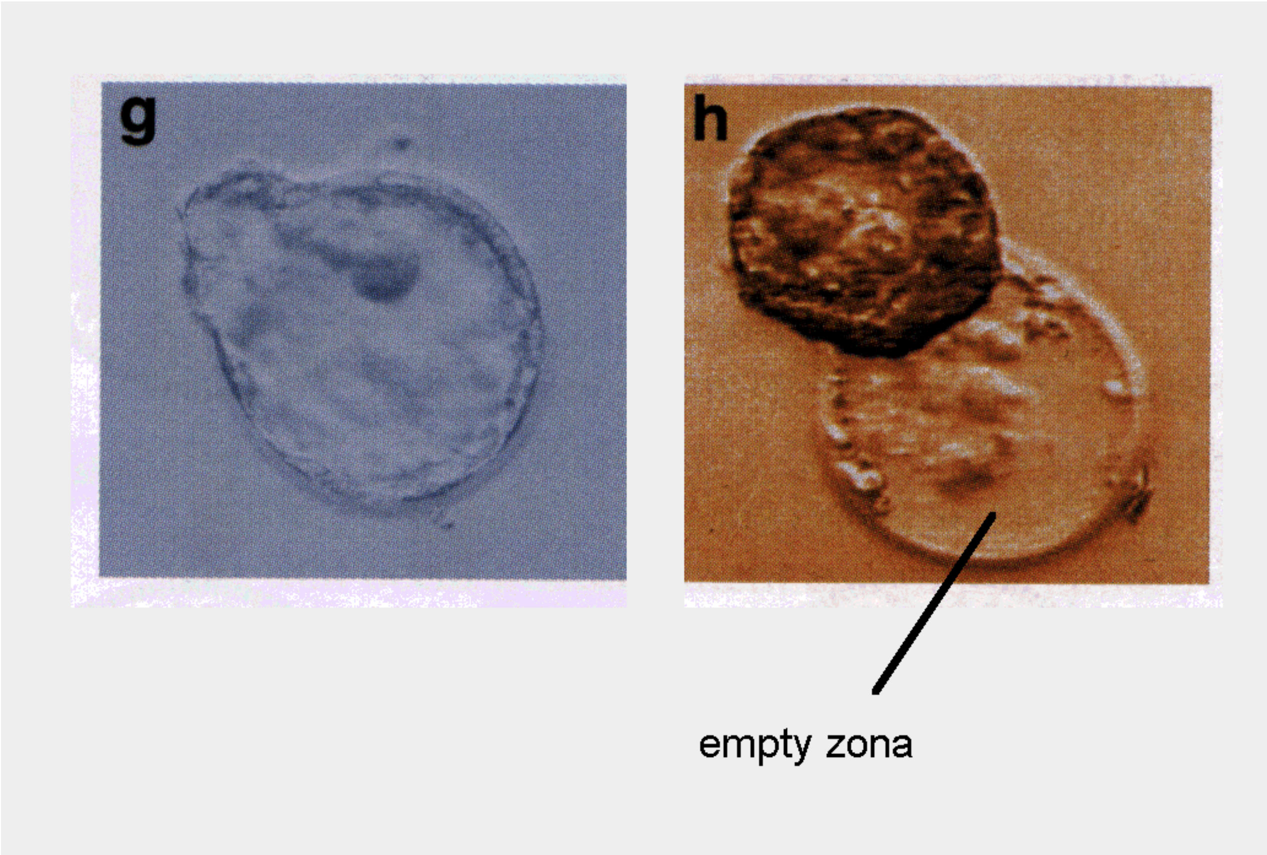

2-cell stage
4-cell stage
compaction
Fluid pumping
inner cell mass
trophectoderm

(Pictures of the real thing;)

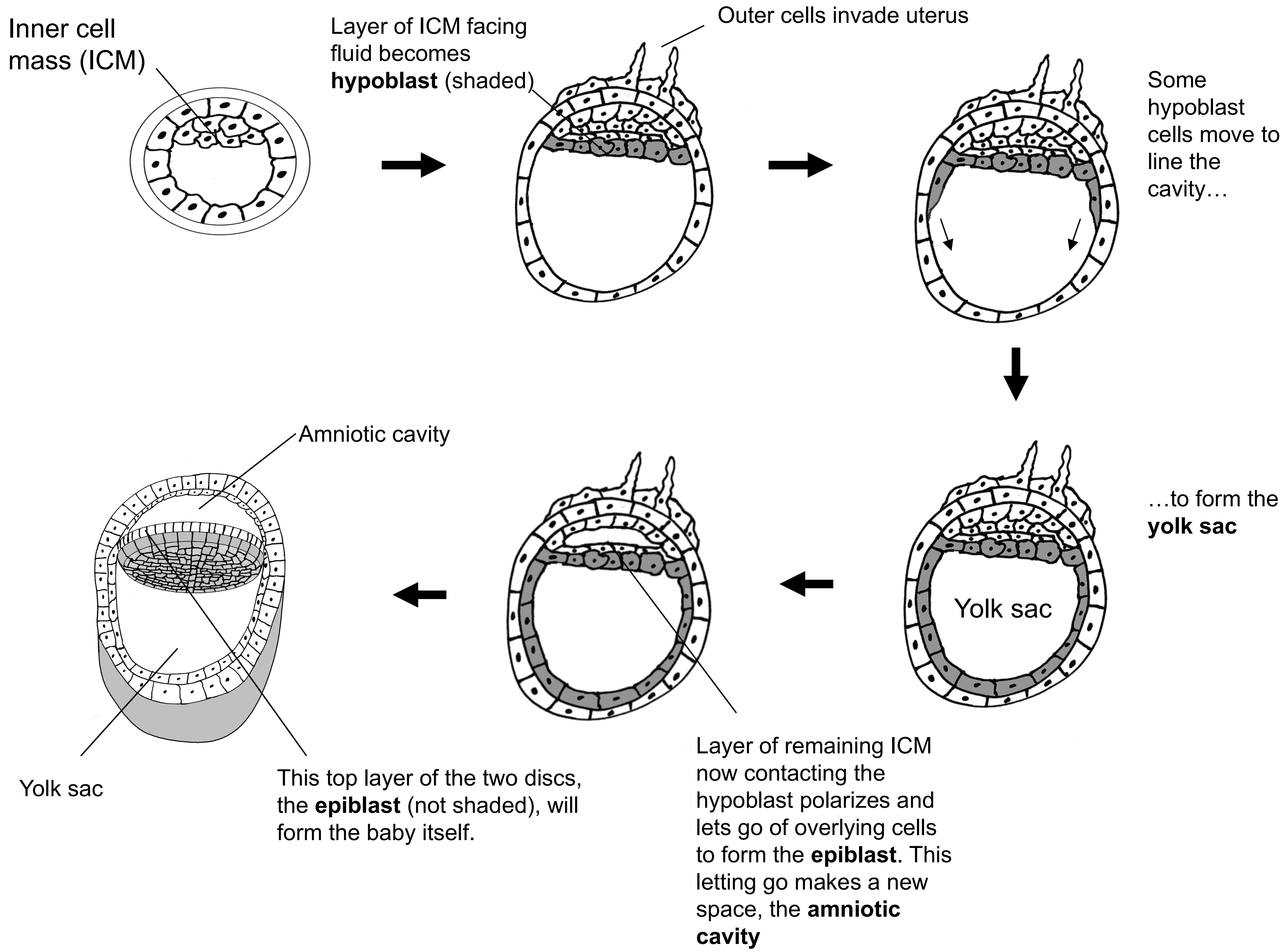


Pic: Johnson & Everitt "Essential Reproduction"

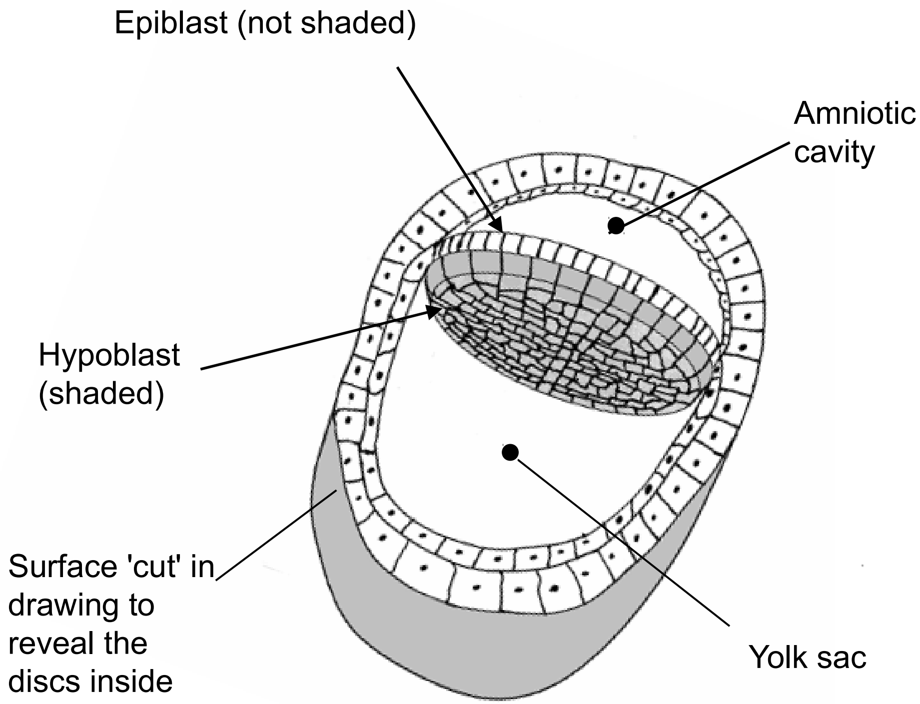
The blastocyst ‘hatches’ through Zona Pellucida;



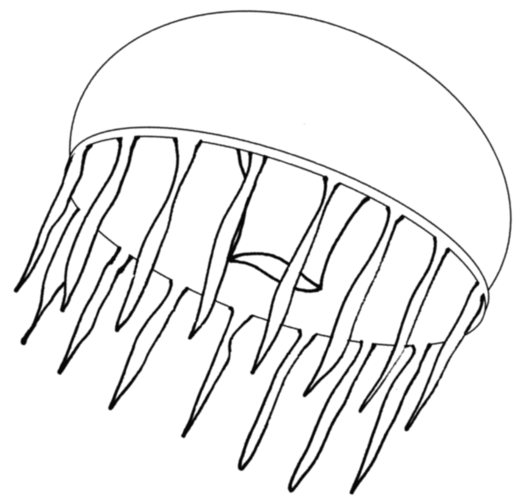
Pic: Johnson & Everitt "Essential Reproduction"



Inner cell mass (ICM)
Layer of ICM facing fluid becomes **hypoblast** (shaded)
Outer cells invade uterus
Some hypoblast cells move to line the cavity…
…to form the **yolk sac**
Yolk sac
Layer of remaining ICM now contacting the hypoblast polarizes and lets go of overlying cells to form the **epiblast**. This letting go makes a new space, the **amniotic cavity**
Amniotic cavity
Yolk sac
This top layer of the two discs, the **epiblast** (not shaded), will form the baby itself.



Human embryo at 9 days



Jellyfish (for comparison of symmetry)

Most 'errors' at this stage are lethal, but some subtle and rare 'errors' are tolerable by the embryo, and result in identical (monozygotic) twins;

Photo credit: Linda & Terri Jamison, Wikimedia Commons

Monozygotic Twinning (1) – cells separate inside Z.P.

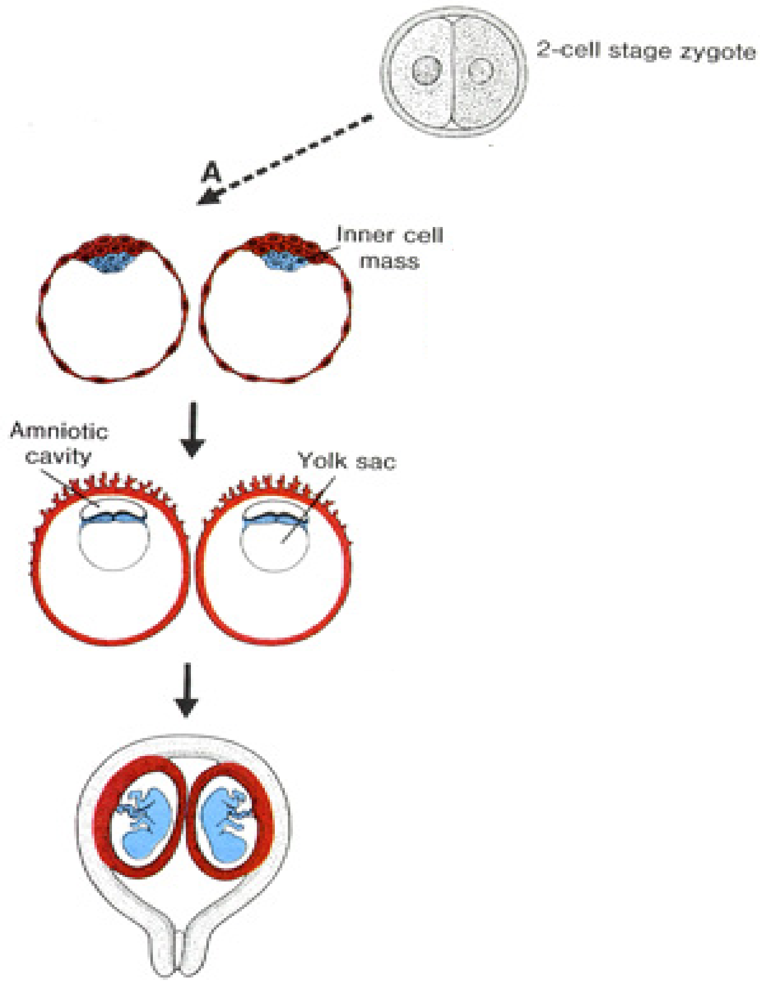


Image Credit: Harvey Kliman, Yale

Monozygotic Twinning (2) – Two Inner Cell Masses form

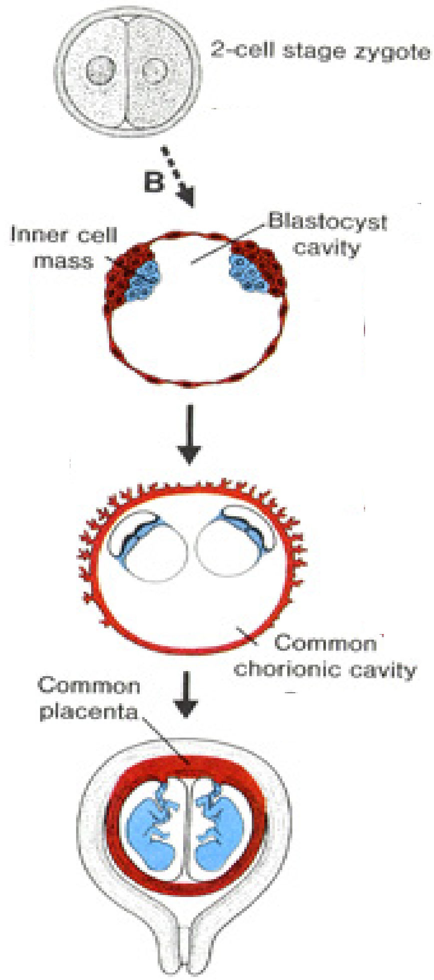
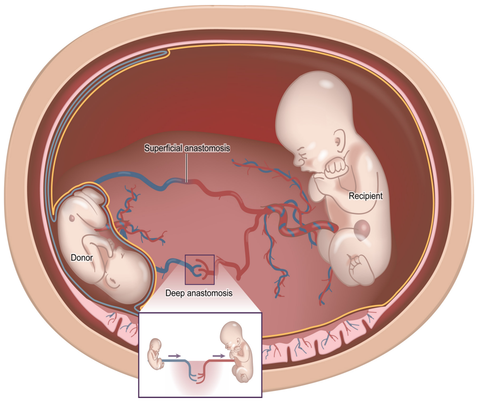


Image Credit: Harvey Kliman, Yale

Monozygotic Twinning (2) – Two Inner Cell Masses form

Danger of foetal transfusion syndrome ('twin-to-twin transfusion syndrome)



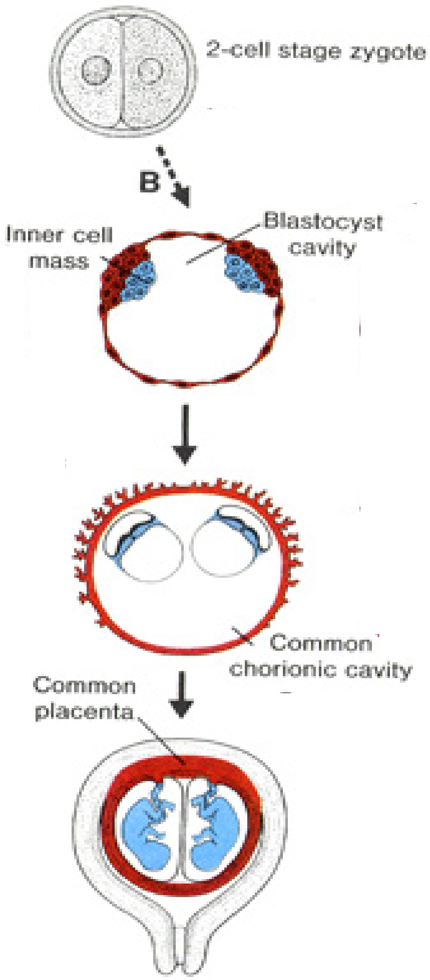
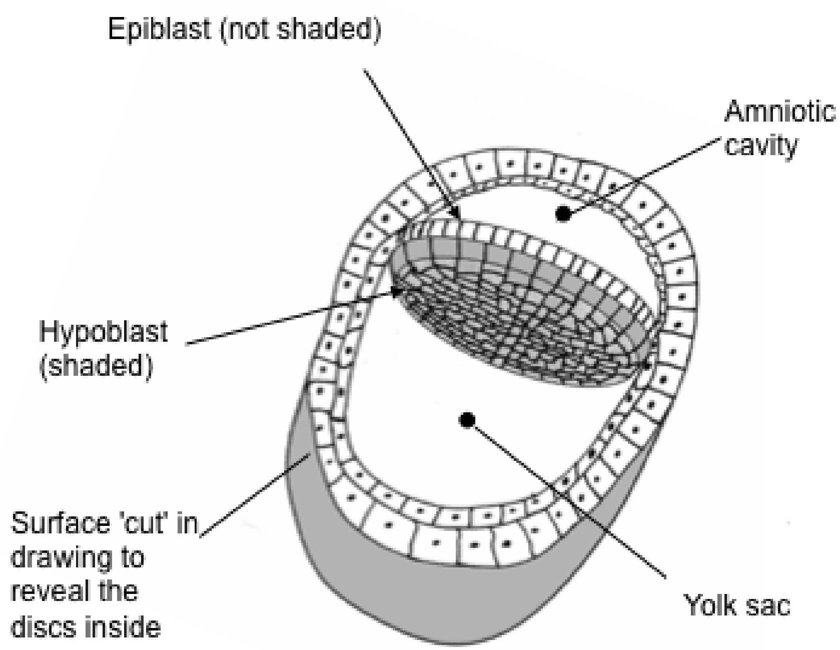
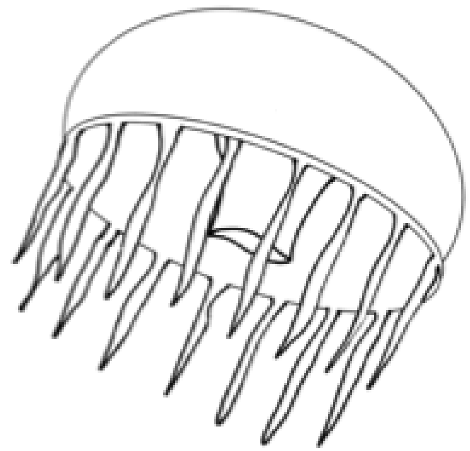


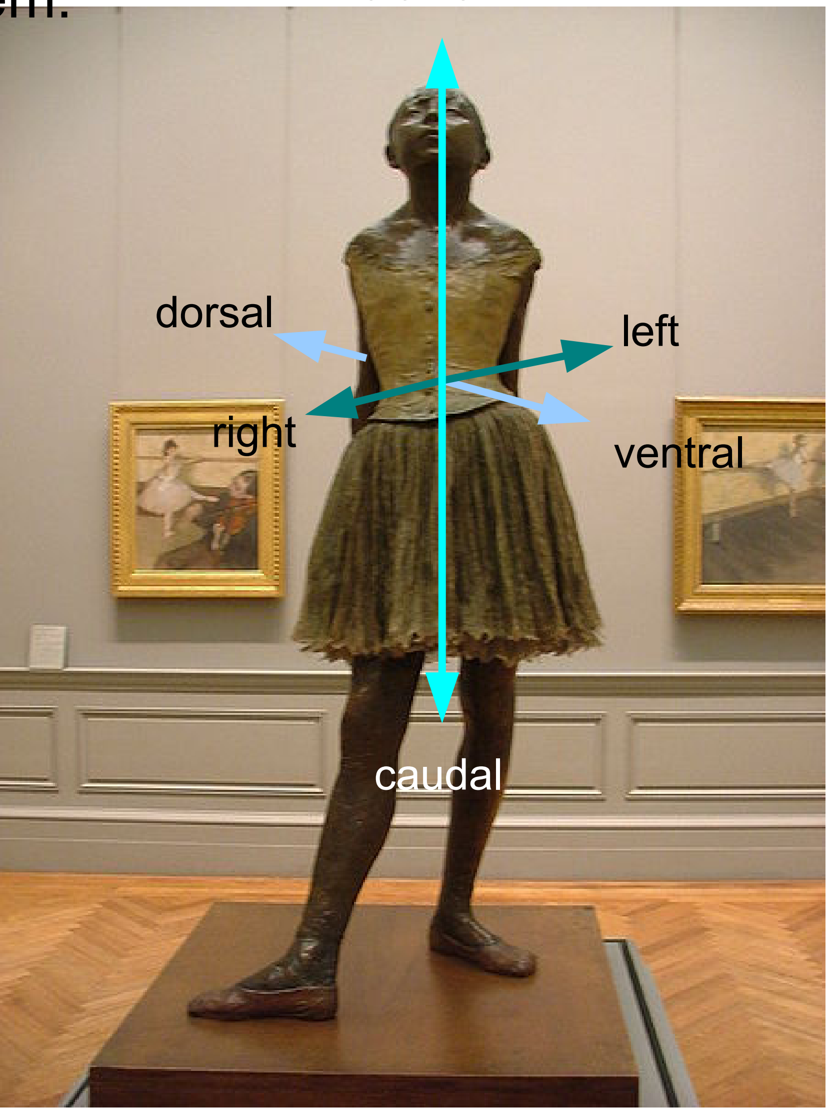
Image Credit: Harvey Kliman, Yale

The symmetry properties of this early embryo are radial, rather like a jellyfish





This give the embryo a mathematical problem:

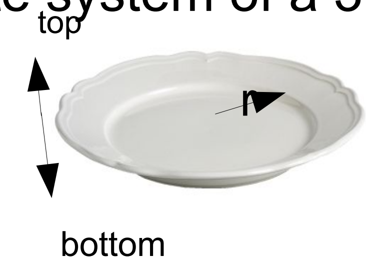


Disc: 2 axes

Human: 3 orthogonal axes

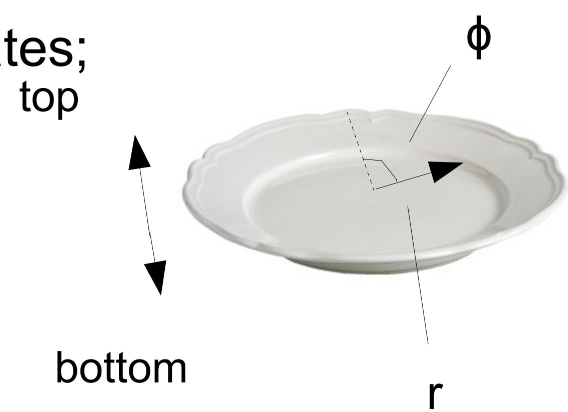
Sculpture: Degas

There is no way to transform the 2-coordinate system of a disc to a 3-coordinate system of a 3-D object.

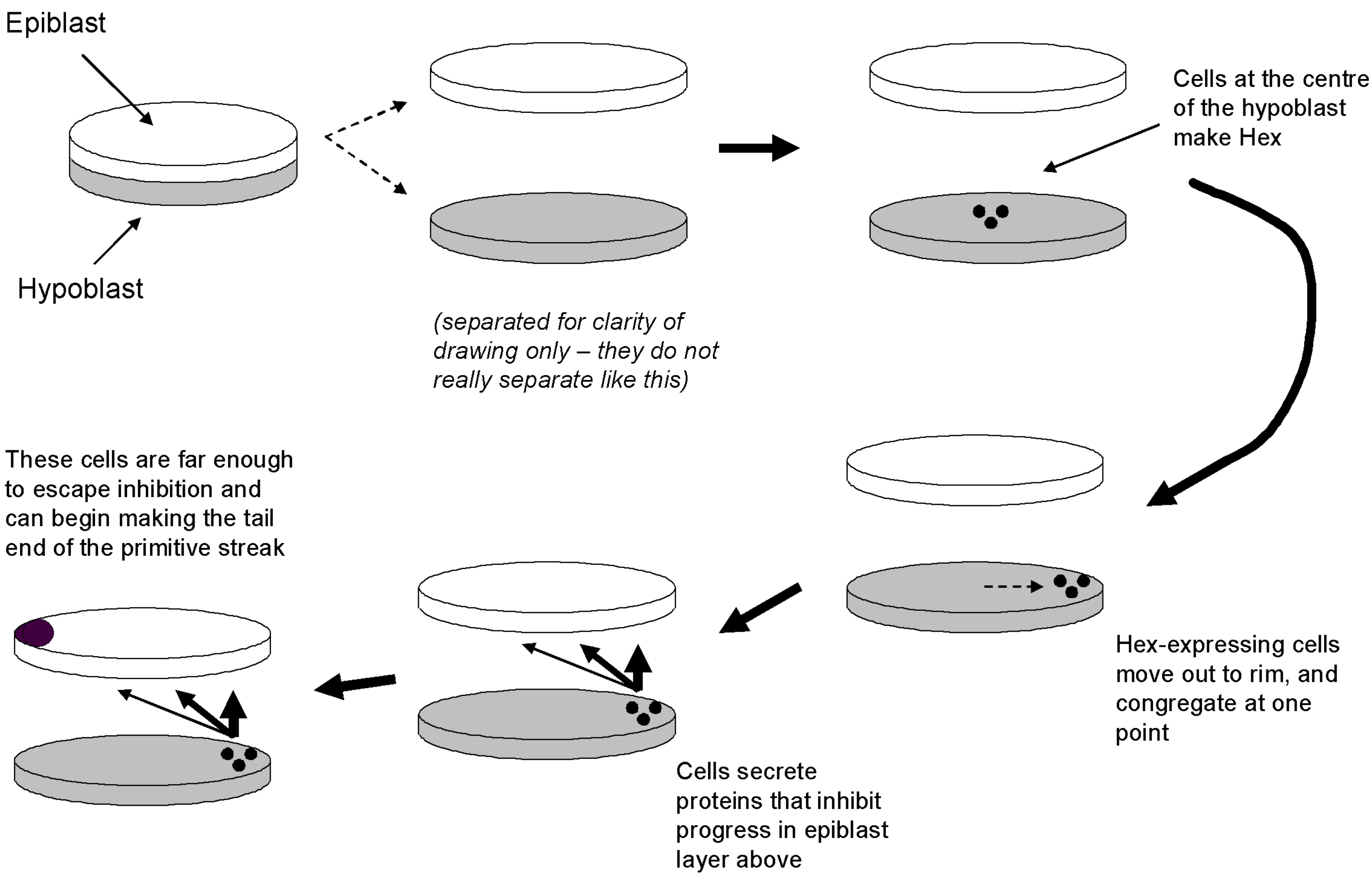


There is no way to transform the 2-coordinate system of a disc to a 3-coordinate system of a 3-D object.

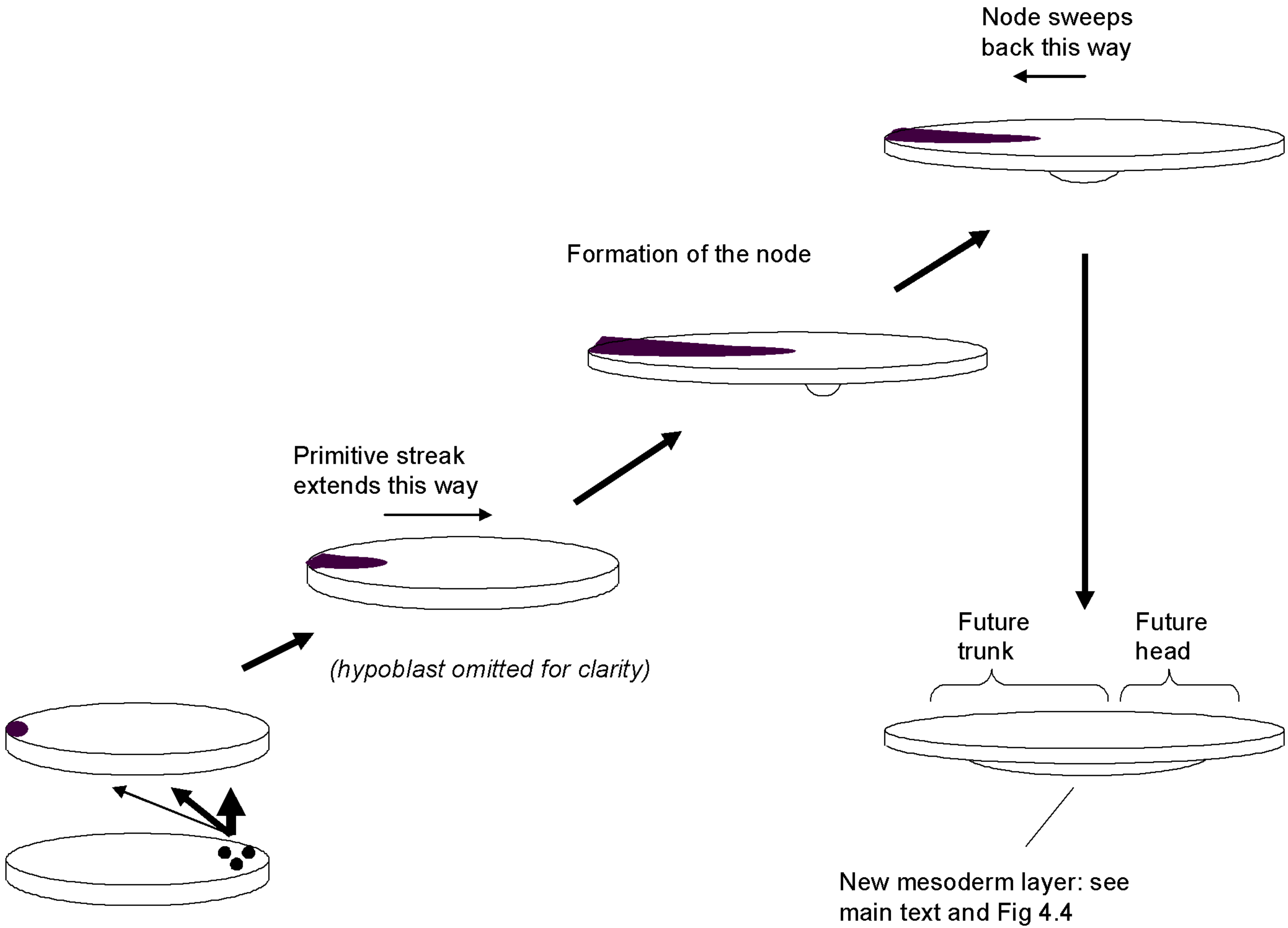
BUT, if the embryo can somehow make one part of the edge of the disc differe ock', then it can have 3 coordinates;



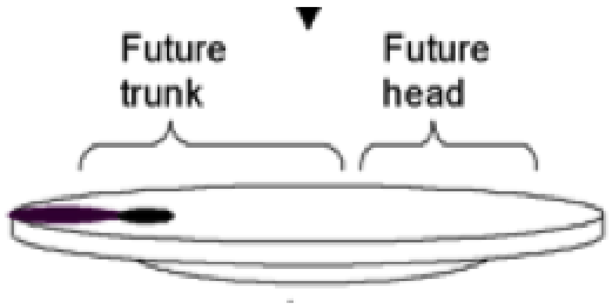
… and these can be transformed, with some cleverness, into the body axes.



Epiblast
Hypoblast
(separated for clarity of drawing only – they do not really separate like this)
Cells at the centre of the hypoblast make Hex
Hex-expressing cells move out to rim, and congregate at one point
Cells secrete proteins that inhibit progress in epiblast layer above
These cells are far enough to escape inhibition and can begin making the tail end of the primitive streak



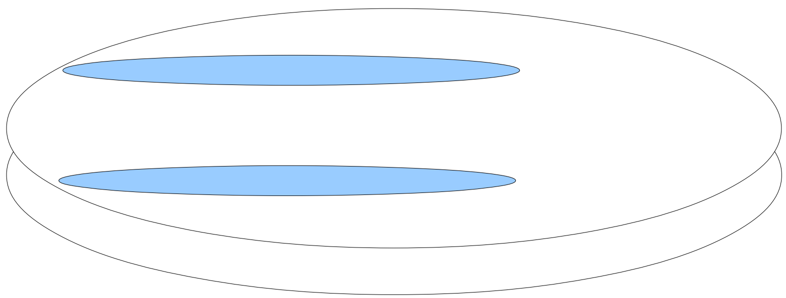
This is the end-point of Fig 4.2



Eventually, these coordinate systems will correspond to the body thus:

The formation of one body axis depends on the Hex-expressing cells being in one point on the rim of the hypoblast:

If there are two distinct sites, then two heads will form and maybe two primitive streaks:



This gets us to the third, very rare, form of monozygotic twinning.

Monozygotic Twinning (3) – Two Primitive Streaks form

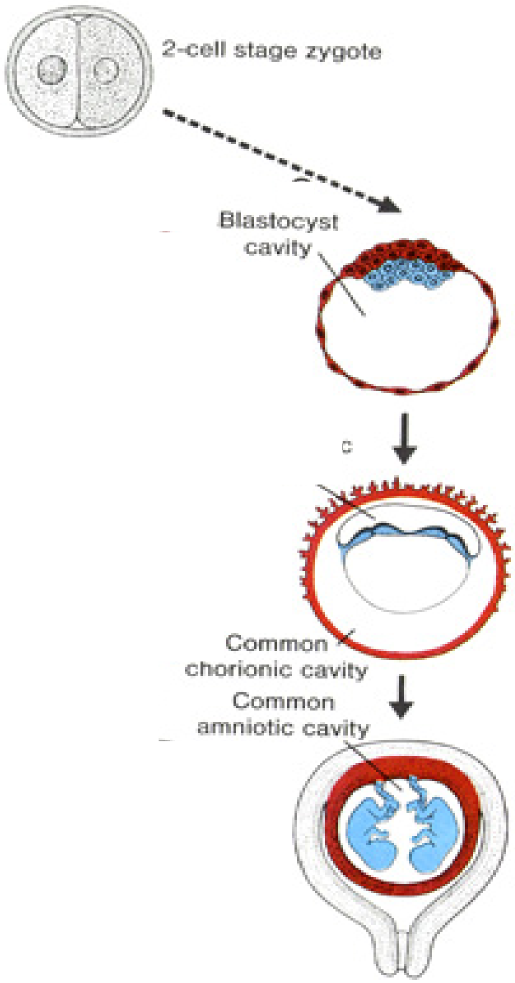


Image Credit: Harvey Kliman, Yale

All of the twinning types compared.

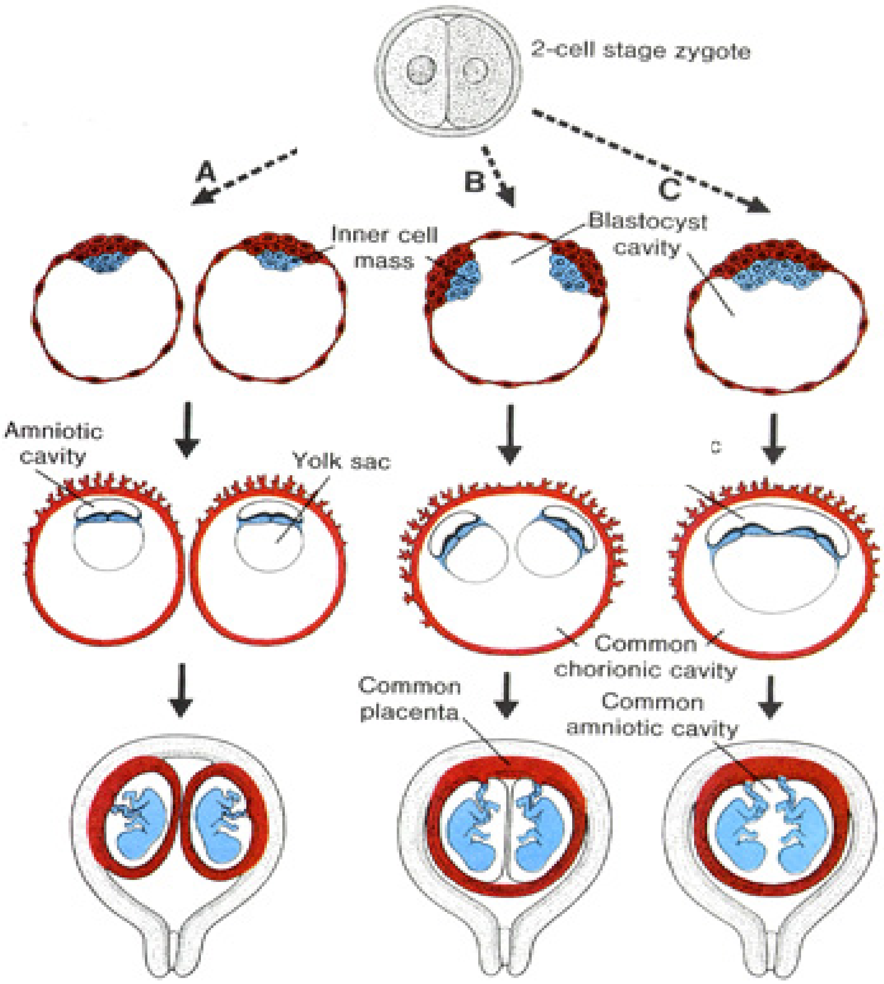
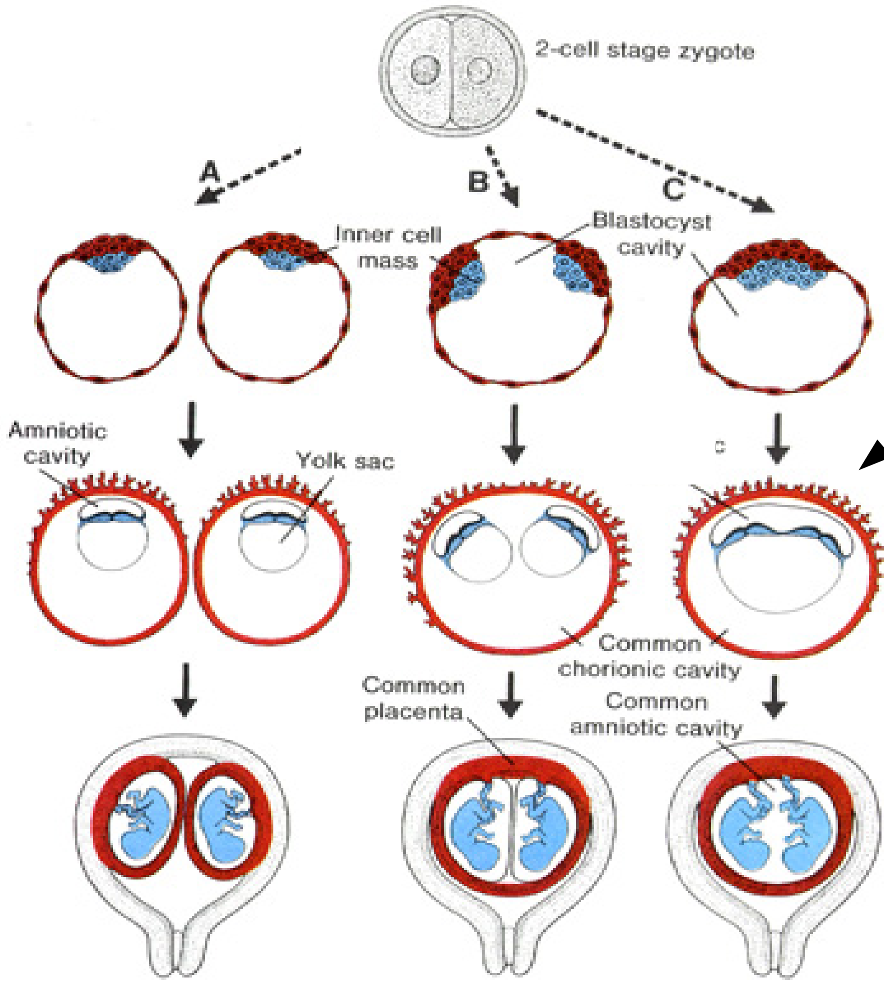


Image Credit: Harvey Kliman, Yale

All of the twinning types compared.



This is rather dangerous, because there is nothing definite (such as a membrane) to separate the two embryos.

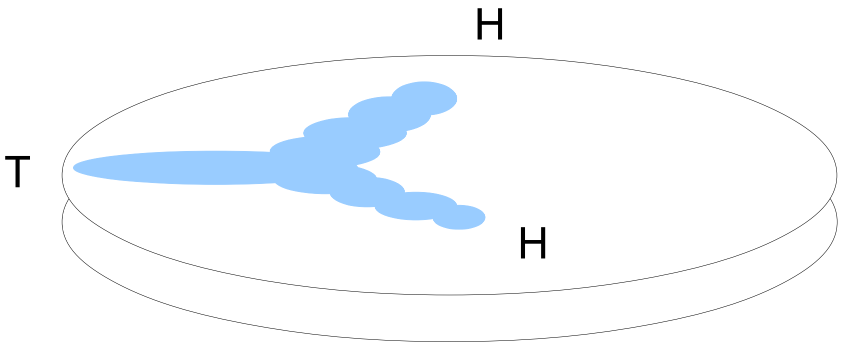
Image Credit: Harvey Kliman, Yale

Conjoined twins:

Chang & Eng Bunker, the Original “Siamese Twins” (as they called themselves for their stage act in PT Barnum's circus)

Partial axis duplications:

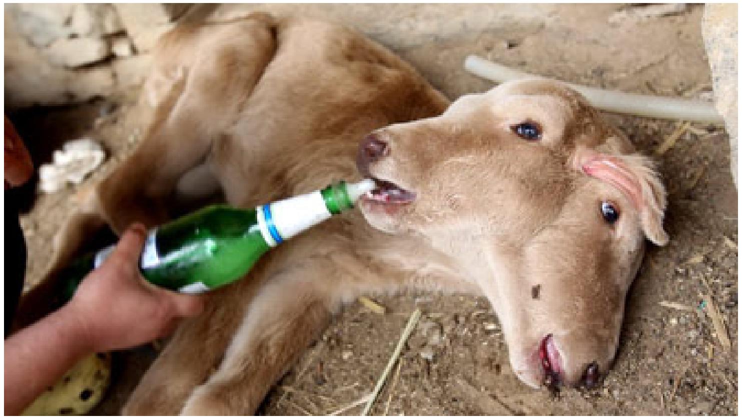
Things can get even more complicated if the two head organizing areas still agree on one site for the tail:



This gets us to the third, very rare, form of monozygotic twinning.

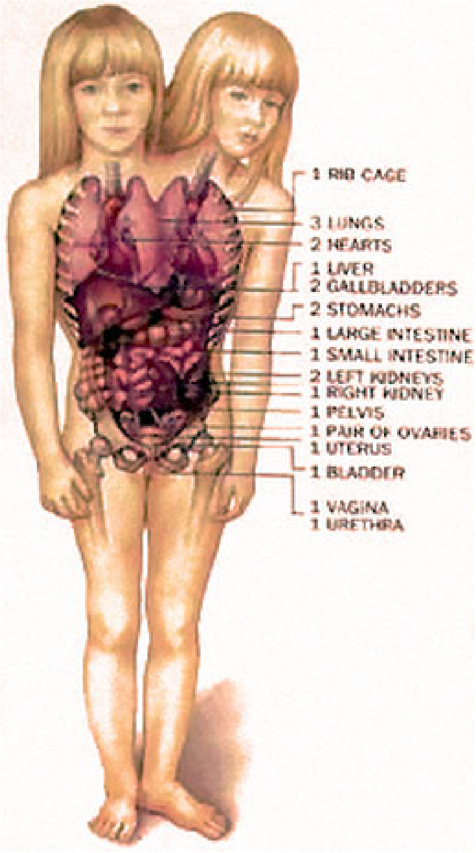
This has been seen many times in reptiles

… occasionally in domestic animals



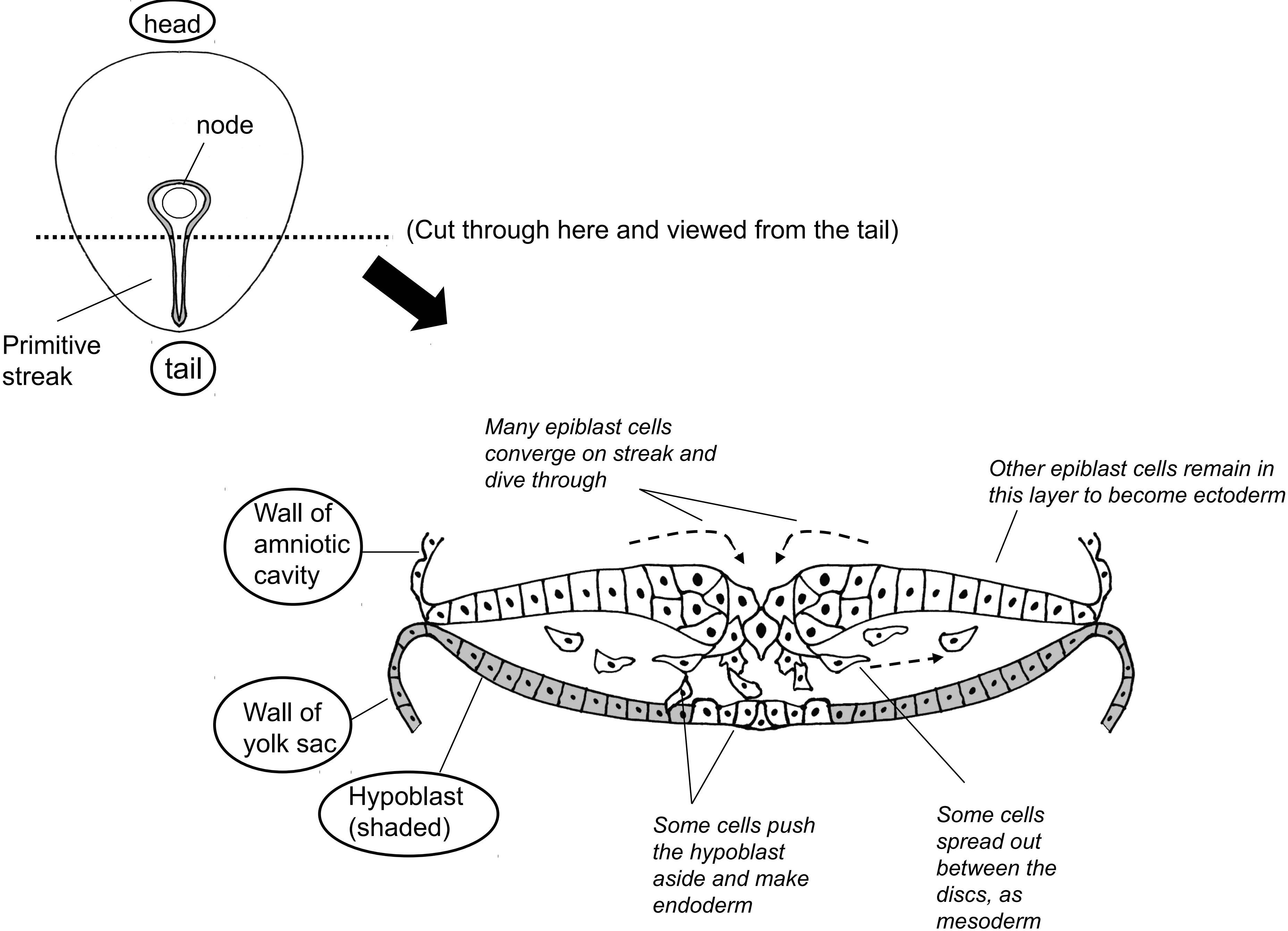
And in humans, where it is normally lethal pre- or peri-natally.

But not always: Abigail and Brittany Hensel

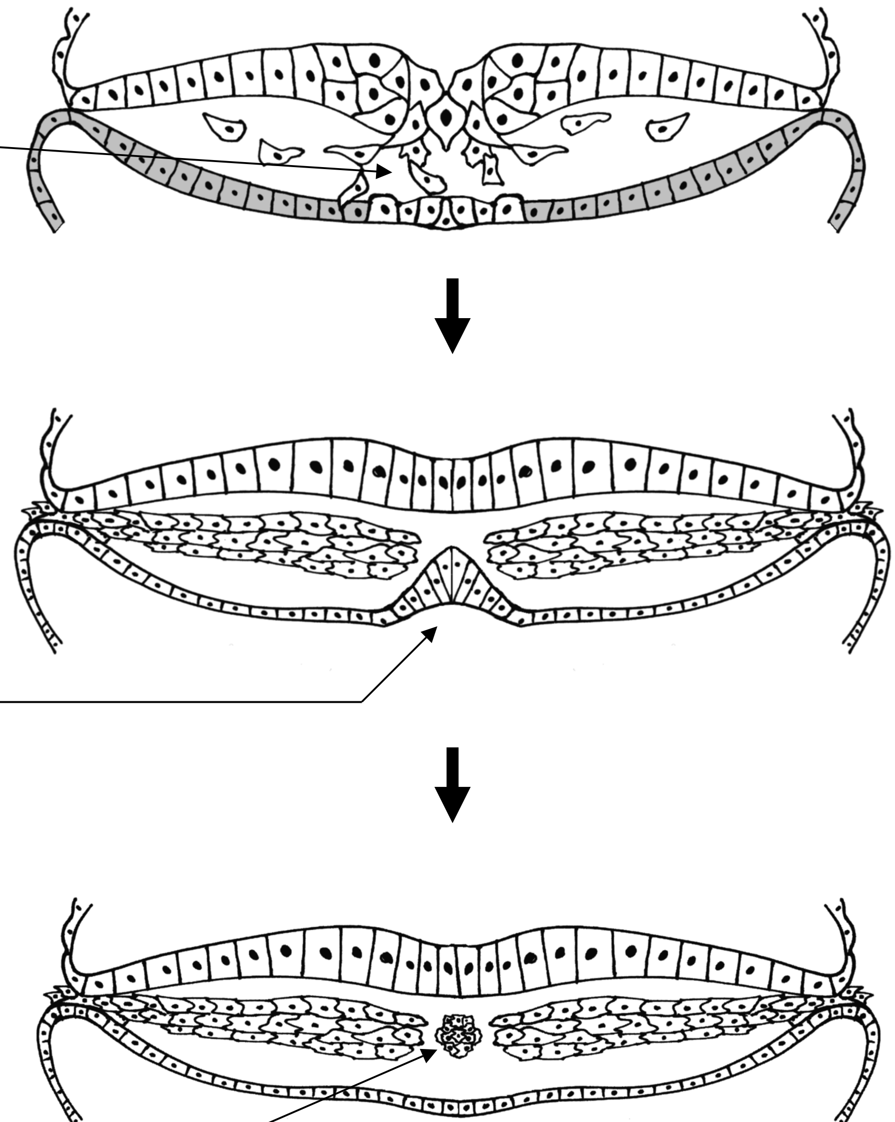


(a 3rd, rudimentary arm, was amputated in infancy)

Abigail and Brittany Hensel, about your age

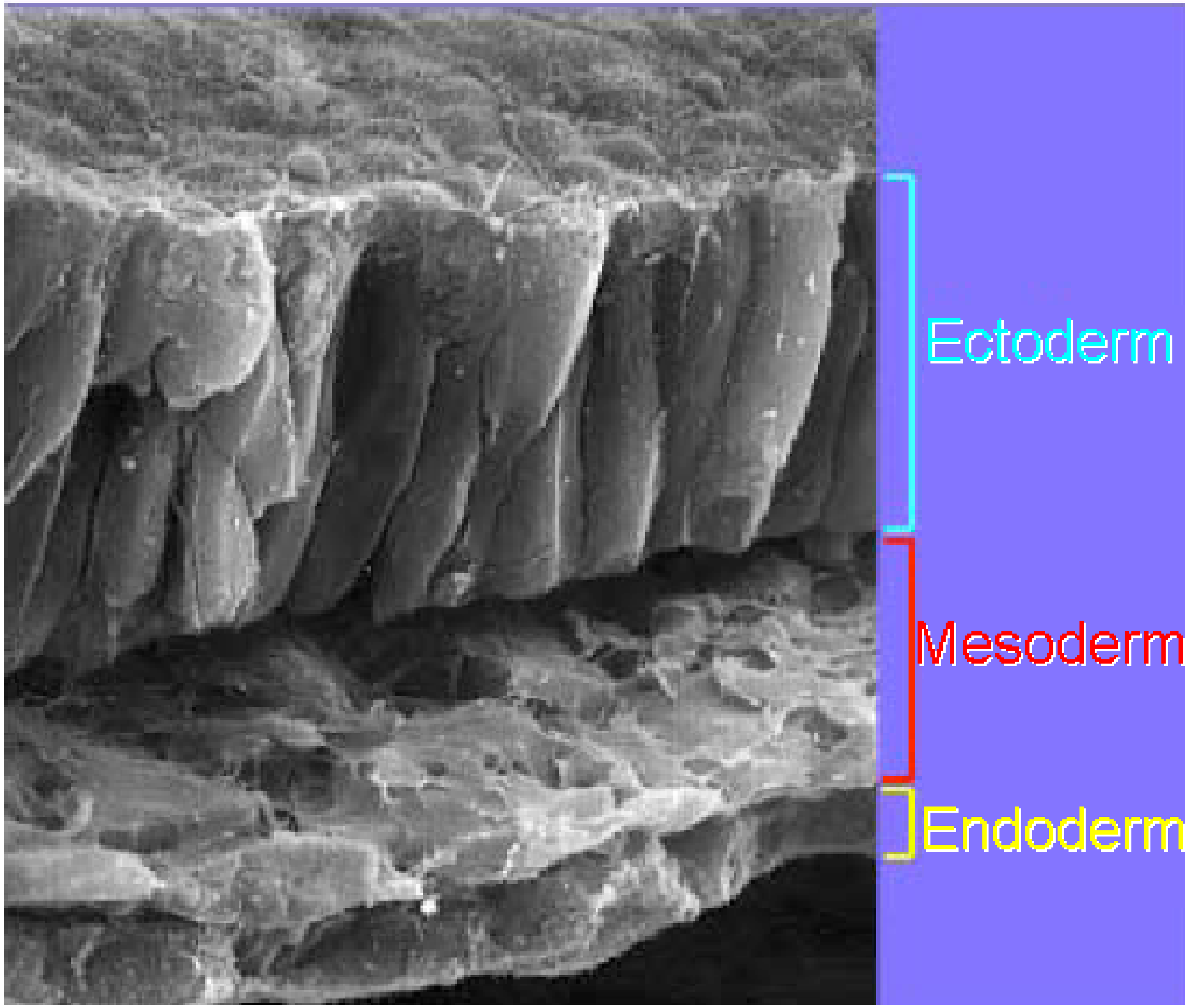

head
node
(Cut through here and viewed from the tail)
Primitive streak
tail
Many epiblast cells converge on streak and dive through
Other epiblast cells remain in this layer to become ectoderm
Wall of amniotic cavity
Wall of yolk sac
Hypoblast (shaded)
Some cells push the hypoblast aside and make endoderm
Some cells spread out between the discs, as mesoderm

The embryo's endoderm forms from cells diving through streak (this is the same image as in the last figure, shown again here for continuity)



Middle part of new endoderm rises to make notochord plate…

…and detaches to become the notochord



Pic: http://www.utm.utoronto.ca/~w3bio380/lecture12.htm#section6 ,

http://embryology.med.unsw.edu.au/Sections/anat2300/2004/ANAT2300L6Mesoderms1.pdf

Gastrulation (3):

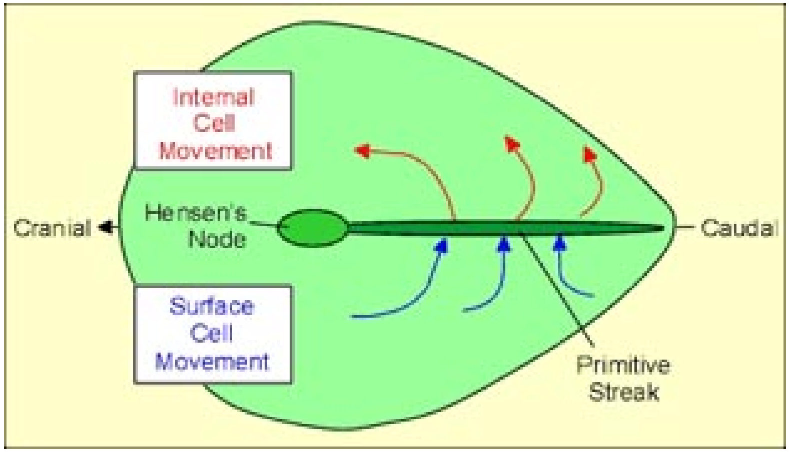
The fates of the cells depend on where and when they dived down:

Cells that never dive down remain on the surface and make ectoderm (-> CNS and epidermis).

Cells that dive down first, right through the node, become endoderm and then form the notochord.

Cells that dive down early but not directly through the node become endoderm (-> gut and most abdominal organs)

Cells that dive down later become mesoderm (-> muscles, connective tissue, urogenital system).



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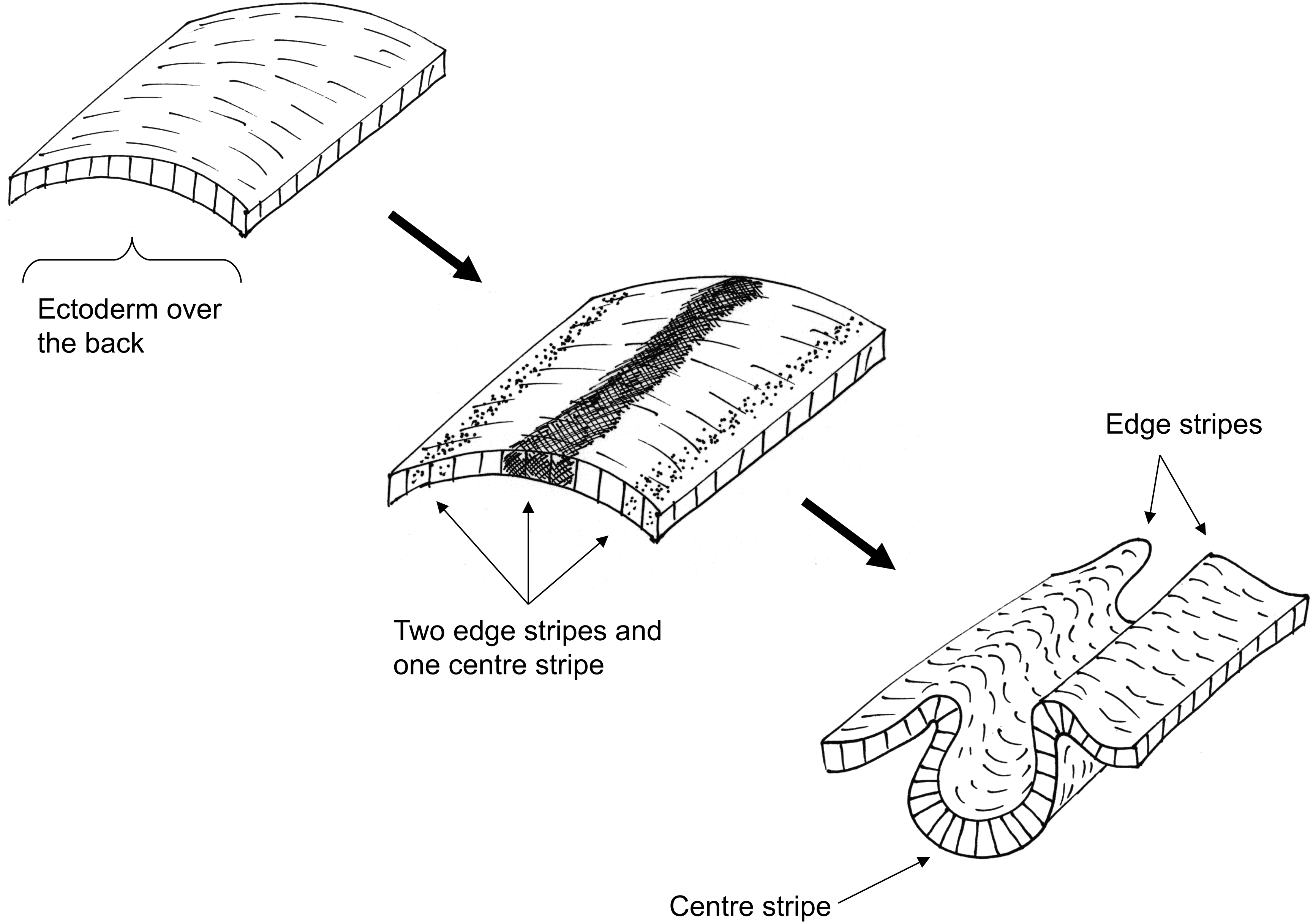
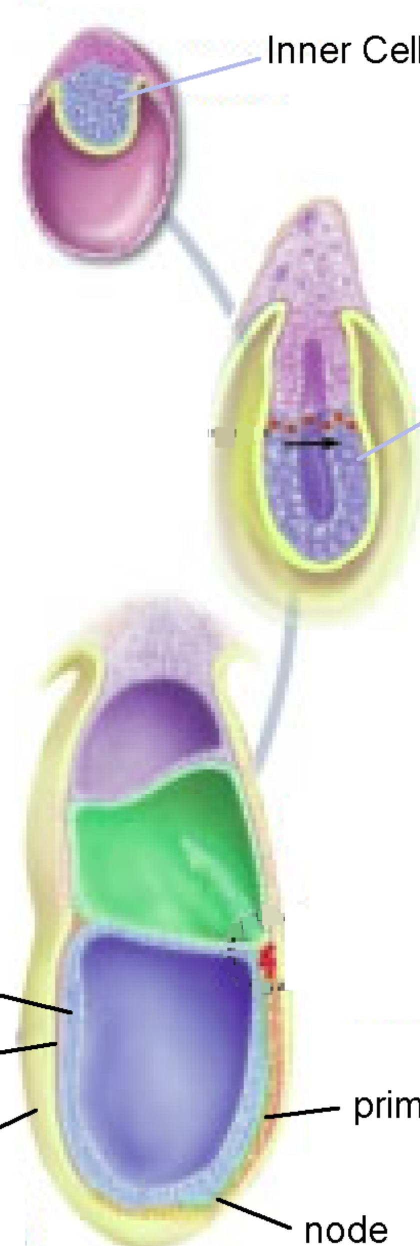
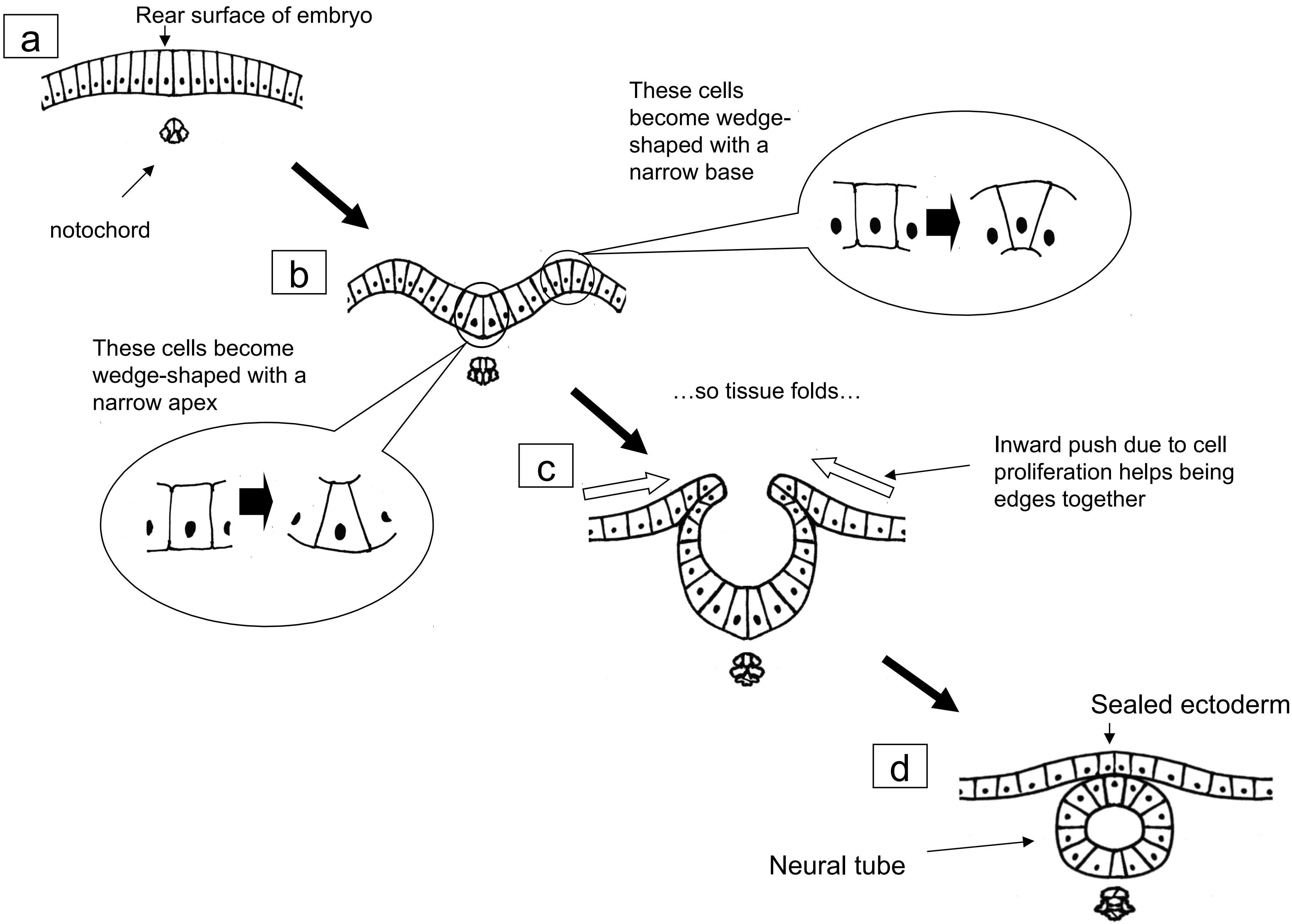


Ectoderm over the back
Two edge stripes and one centre stripe
Edge stripes
Centre stripe

Mice are really annoying in that they make a 'cup' shape rather than staying flat, and the 'cup' is arranged 'inside-out':

like this, sort of

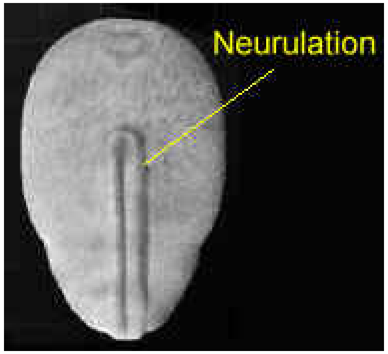




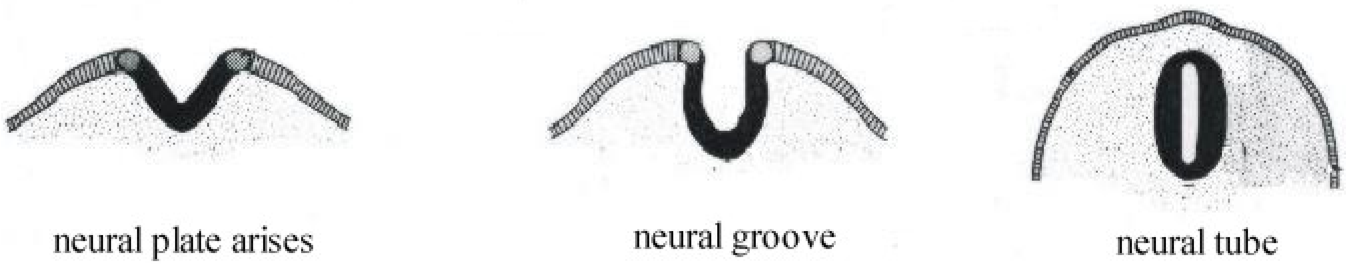
a
Rear surface of embryo
notochord
b
These cells become wedge-shaped with a narrow base
These cells become wedge-shaped with a narrow apex
…so tissue folds…
c
Inward push due to cell proliferation helps being edges together
d
Sealed ectoderm
Neural tube

Neurulation:

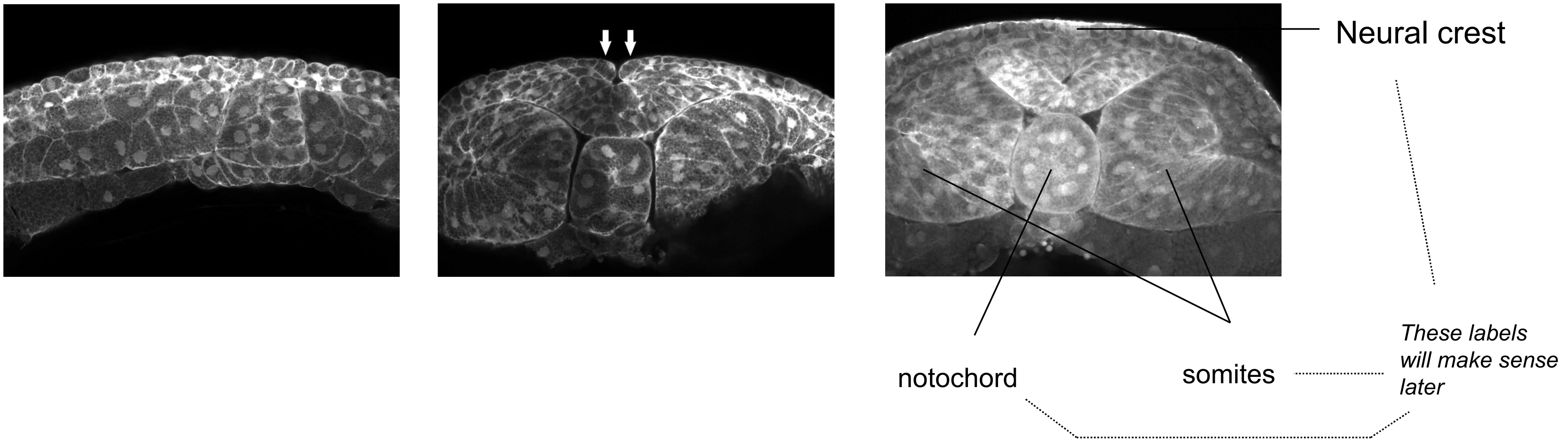
The neural tube comes from invagination of the mid-line of the ectoderm:



http://cas.bellarmine.edu/tietjen/Ecol&Evol/ComparativeEmbryology/comparative_embryology.htm



Pic: http://www.anencephalie-info.org/medical.htm



Neurulation

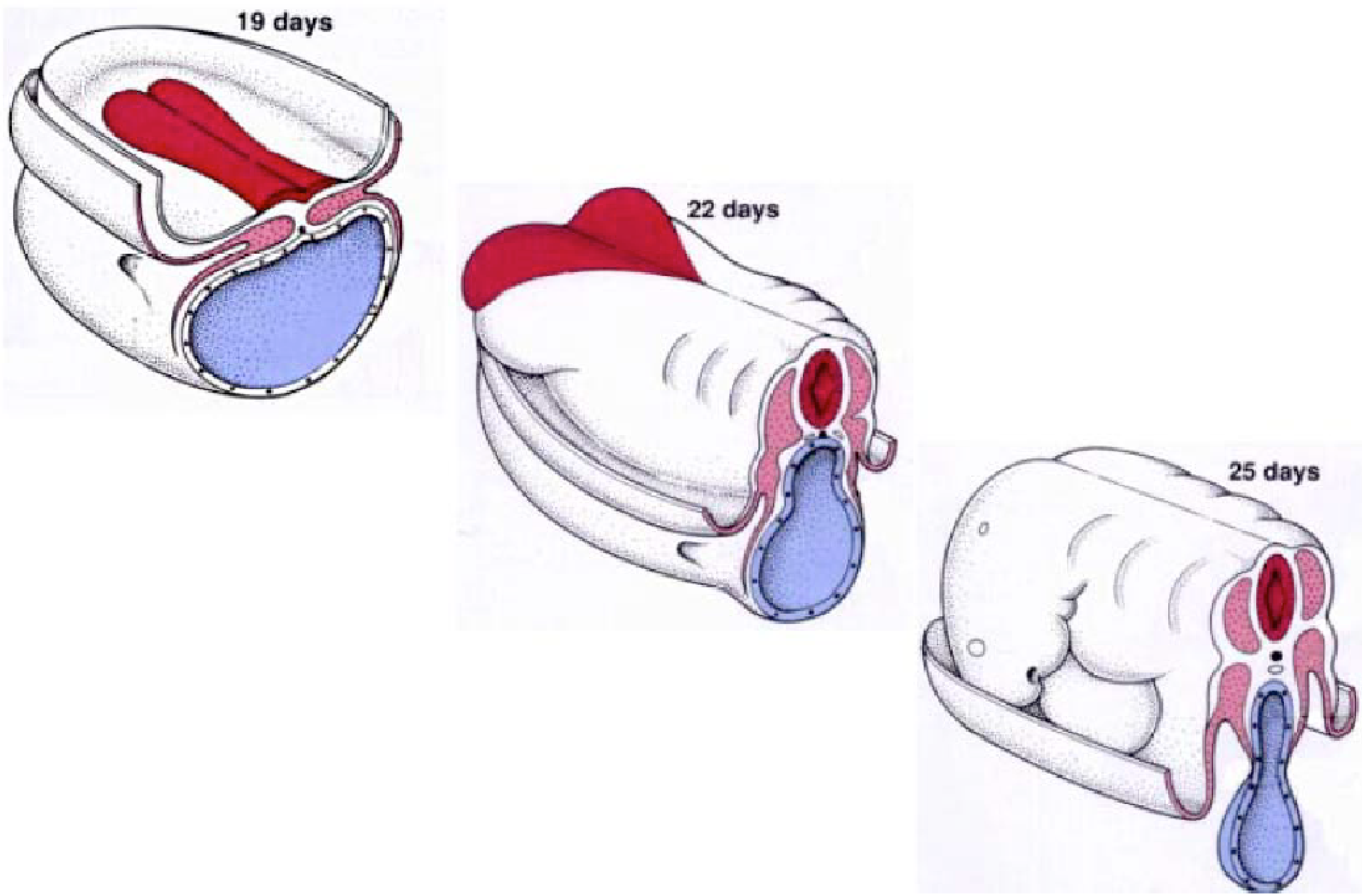
This is not a mouse, which is why it is not curled back on itself

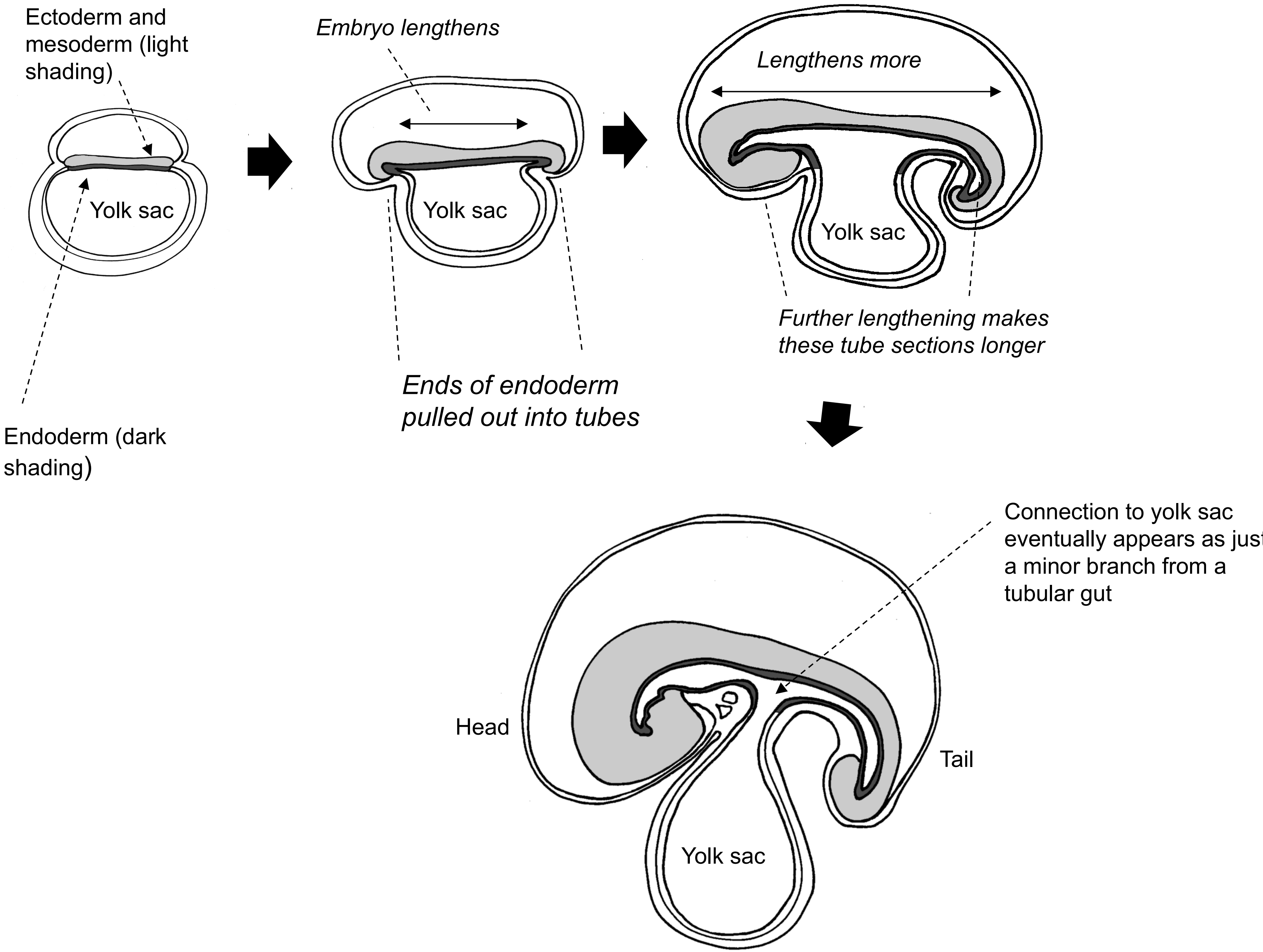
Movie from http://embryology.med.unsw.edu.au/Movies/Humemb.htm

MEDICAL IMAGE WARNING
(next 2 slides)

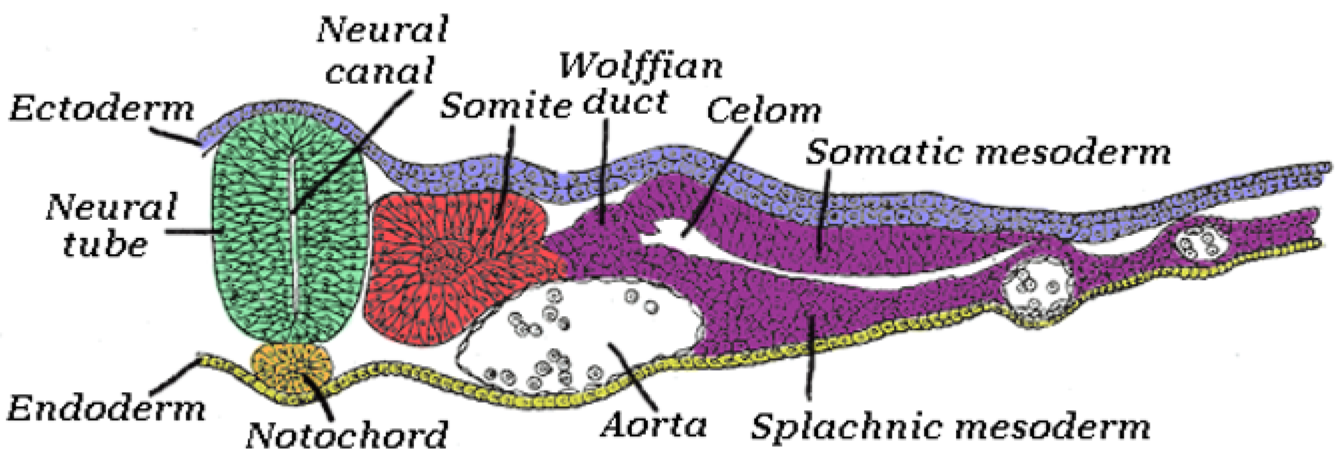
Failure of fusion during neurulation: spina bifida of various types.

Mesoderm development:

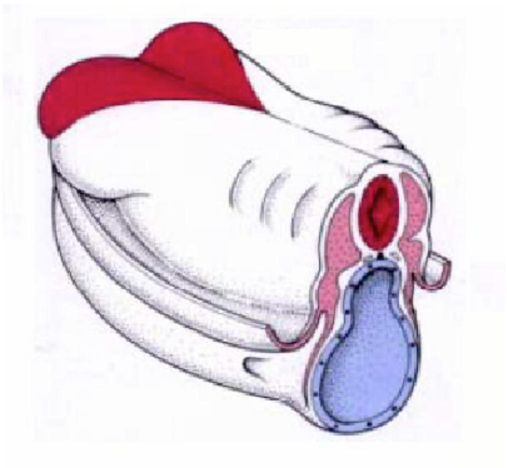


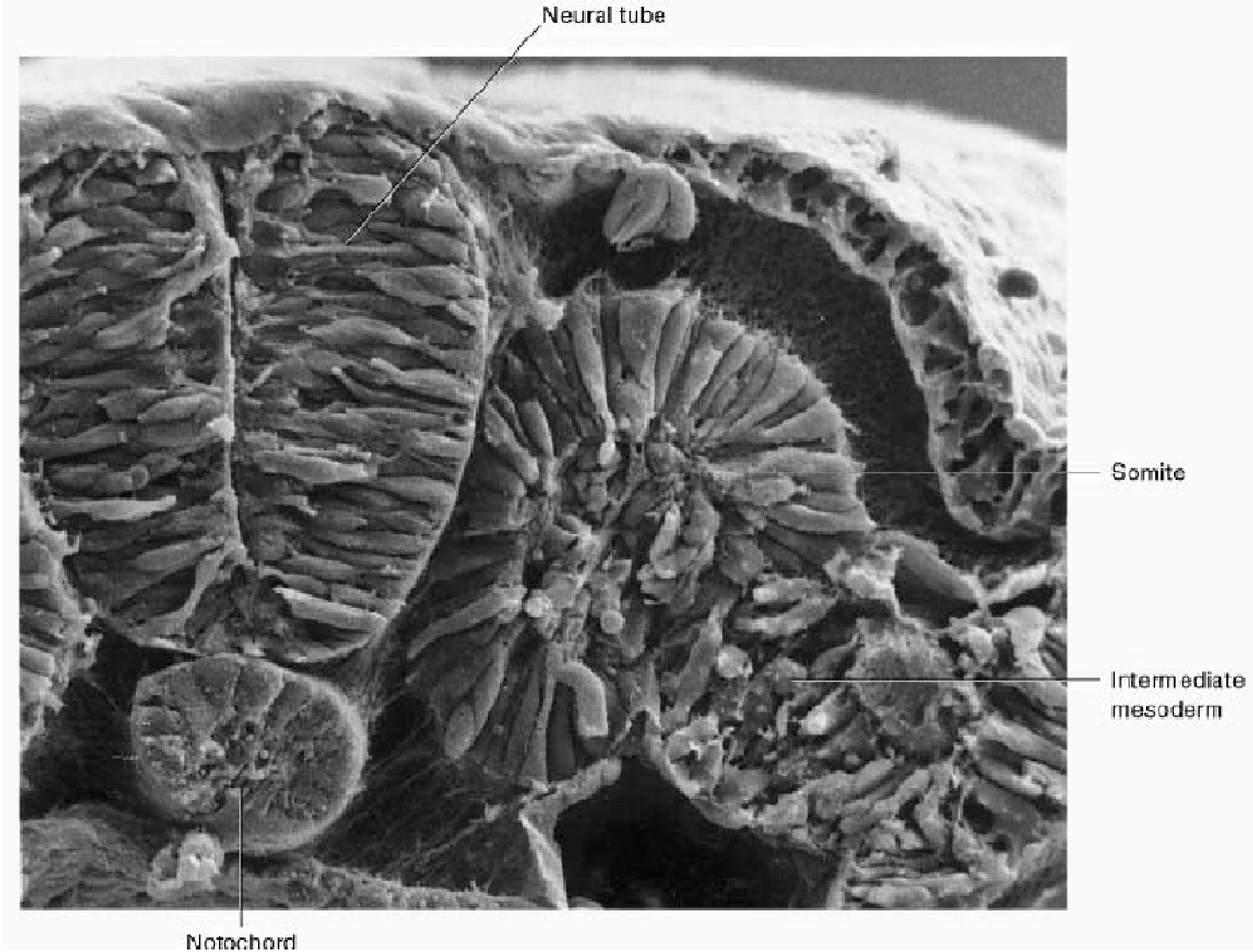

Ectoderm and mesoderm (light shading)
Endoderm (dark shading)
Yolk sac
Embryo lengthens
Yolk sac
Ends of endoderm pulled out into tubes
Lengthens more
Yolk sac
Further lengthening makes these tube sections longer
Connection to yolk sac eventually appears as just a minor branch from a tubular gut
Head
Tail
Yolk sac

Development of the mesoderm:



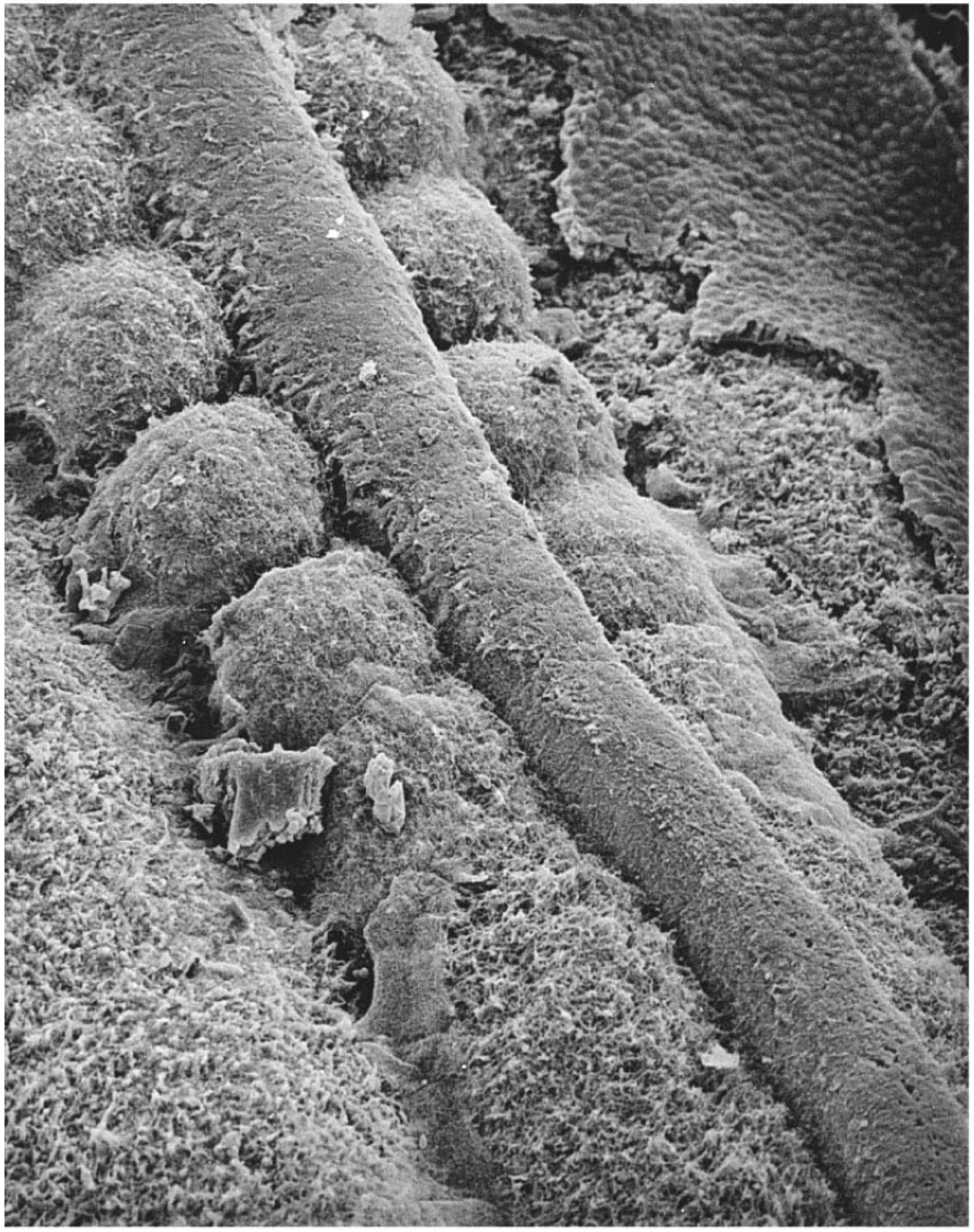
This is a chick embryo – like mouse but flattened out (so easier to see). The mouse looks like this:





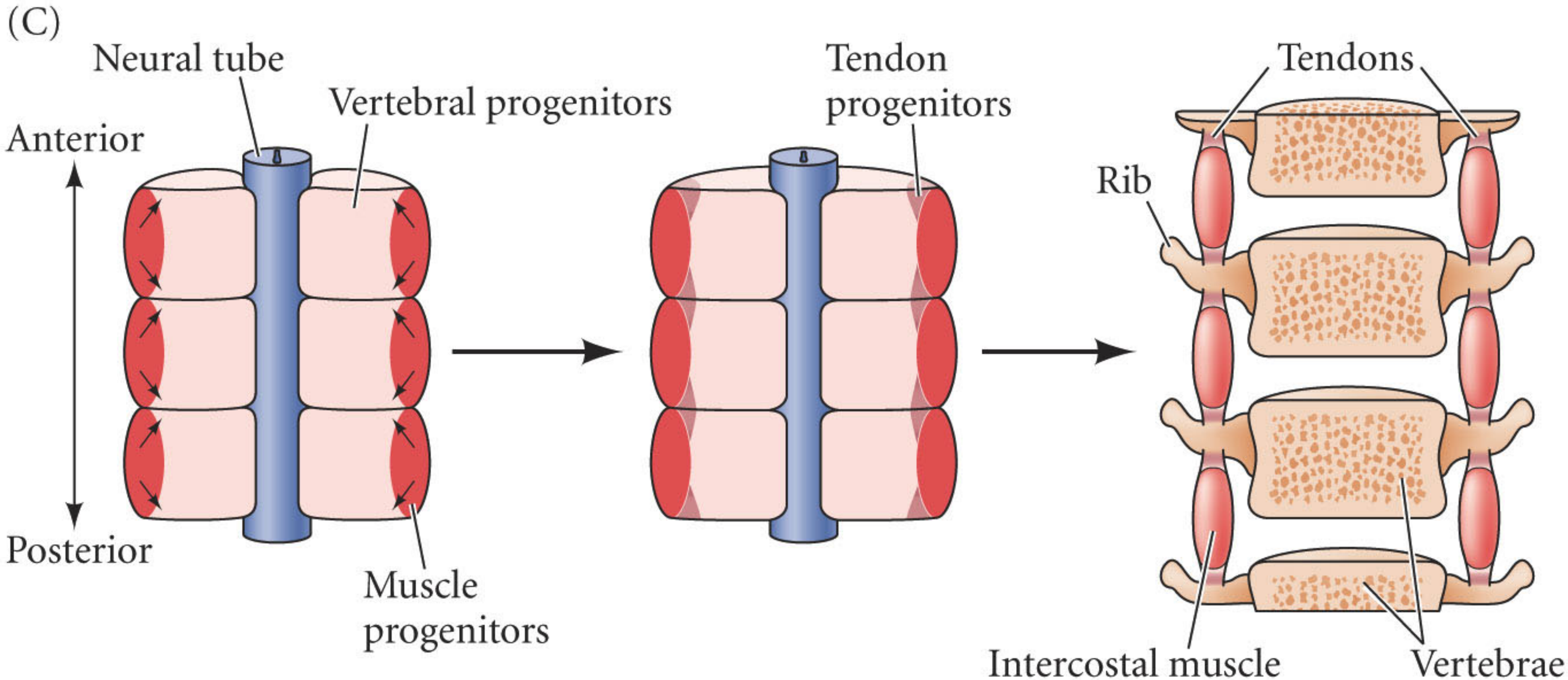
Pic: Mark Hill

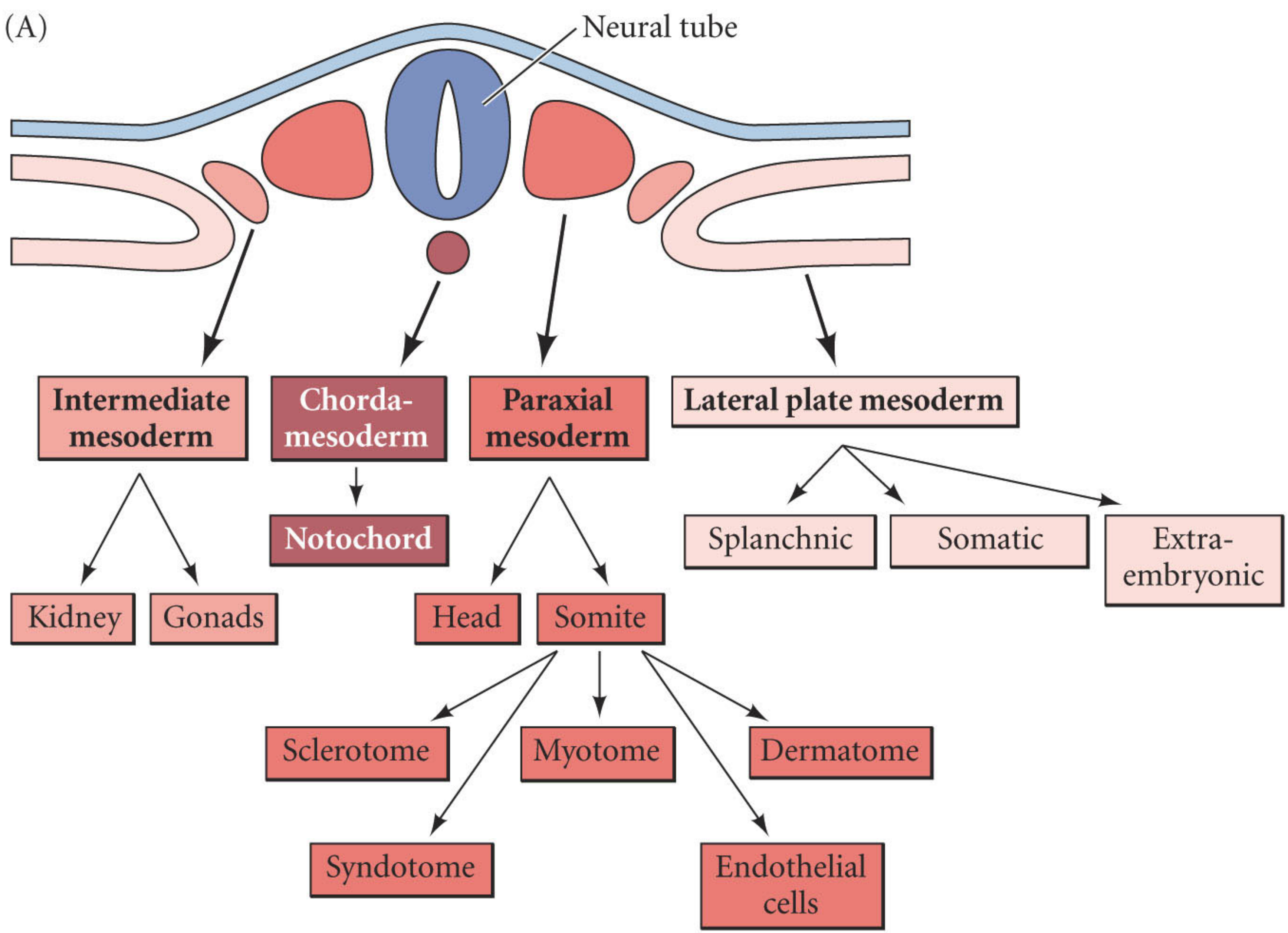
Somites
(ectoderm
removed)



Somites scatter cells and reform to make vertebrae, ribs, muscles and dermis:

Movie from http://embryology.med.unsw.edu.au/Movies/Humemb.htm


(C)
Neural tube
Vertebral progenitors
Anterior
Posterior
Muscle progenitors
Tendon progenitors
Tendons
Rib
Intercostal muscle
Vertebrae


(A)
Neural tube
Intermediate mesoderm
Chorda-mesoderm
Paraxial mesoderm
Lateral plate mesoderm
Notochord
Splanchnic
Somatic
Extra-embryonic
Kidney
Gonads
Head
Somite
Sclerotome
Myotome
Dermatome
Syndotome
Endothelial cells

The neural crest:

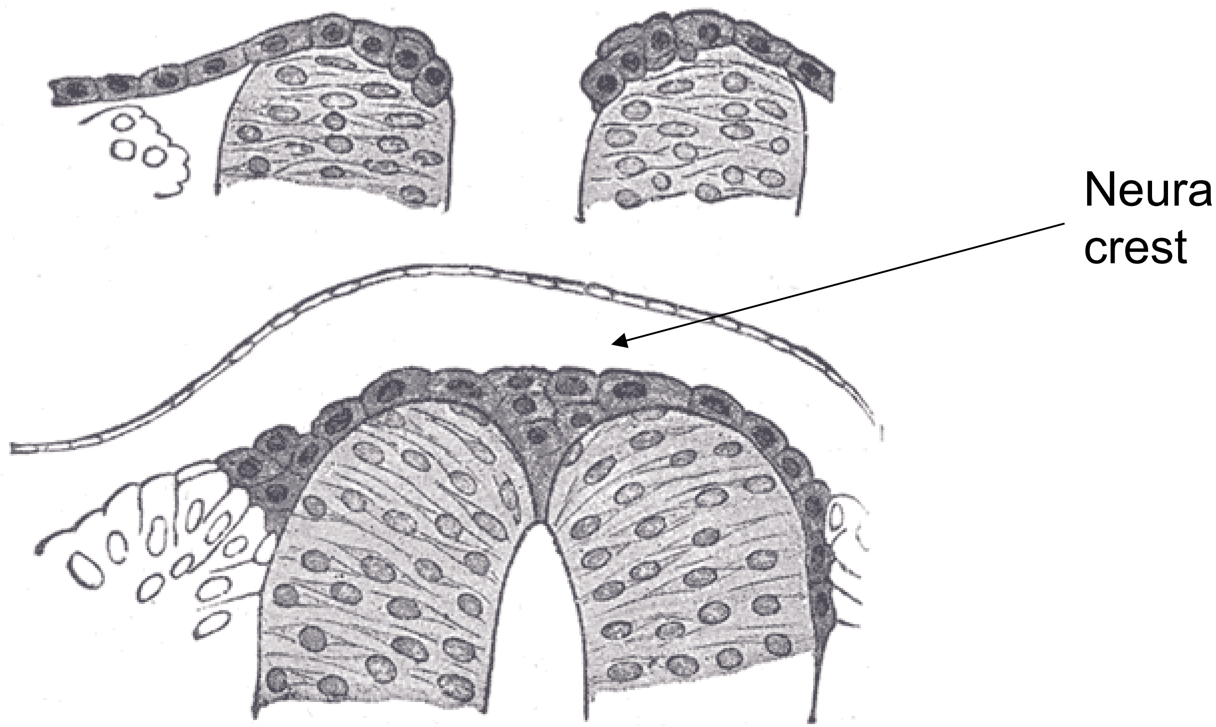


Image: wikipedia

Migration of the neural crest

Peripheral nervous system (PNS):

•Neurons, including sensory ganglia, sympathetic and parasympathetic ganglia, and plexuses, Schwann cells cells

Endocrine and paraendocrine derivatives:

•Adrenal medulla calcitonin-secreting cells, Carotid body type I cells

Pigment cells:

•Epidermal pigment cells

Facial cartilage and bone:

•Facial and anterior ventral skull cartilage and bones

Connective tissue:

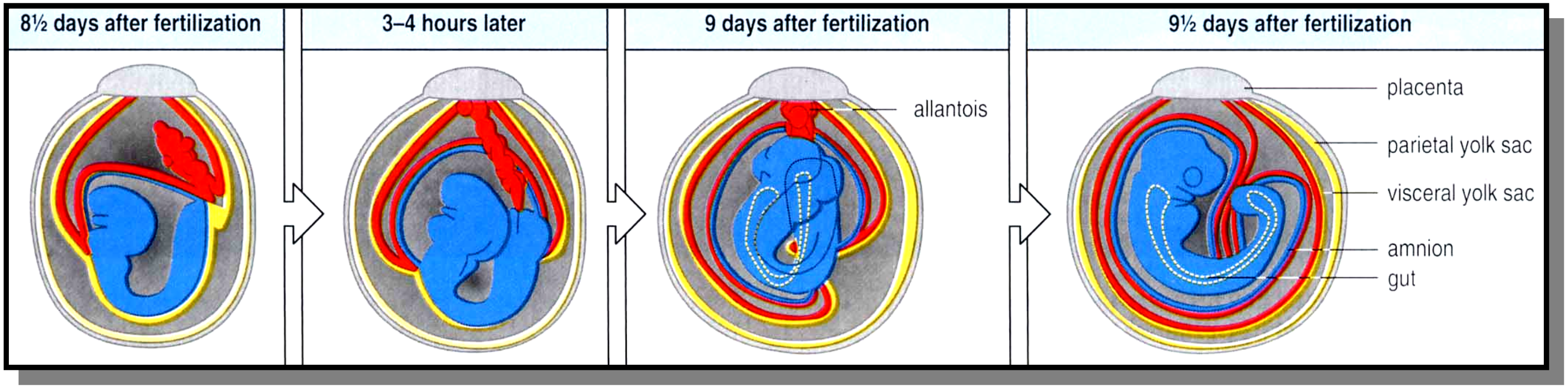
•Corneal endothelium and stroma, Tooth papillae, smooth muscle and adipose tissue of skin of head and neck, connective tissue of salivary, lachrymal, thymus, thyroid, and pituitary glands, connective tissue and smooth muscle in arteries of aortic arch origin

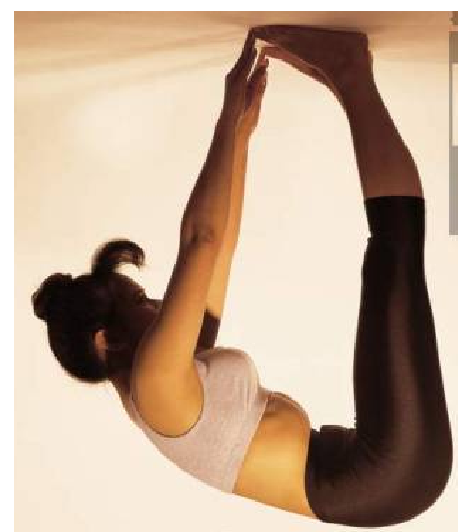
Movie from http://embryology.med.unsw.edu.au/Movies/Humemb.htm

Migration of the neural crest

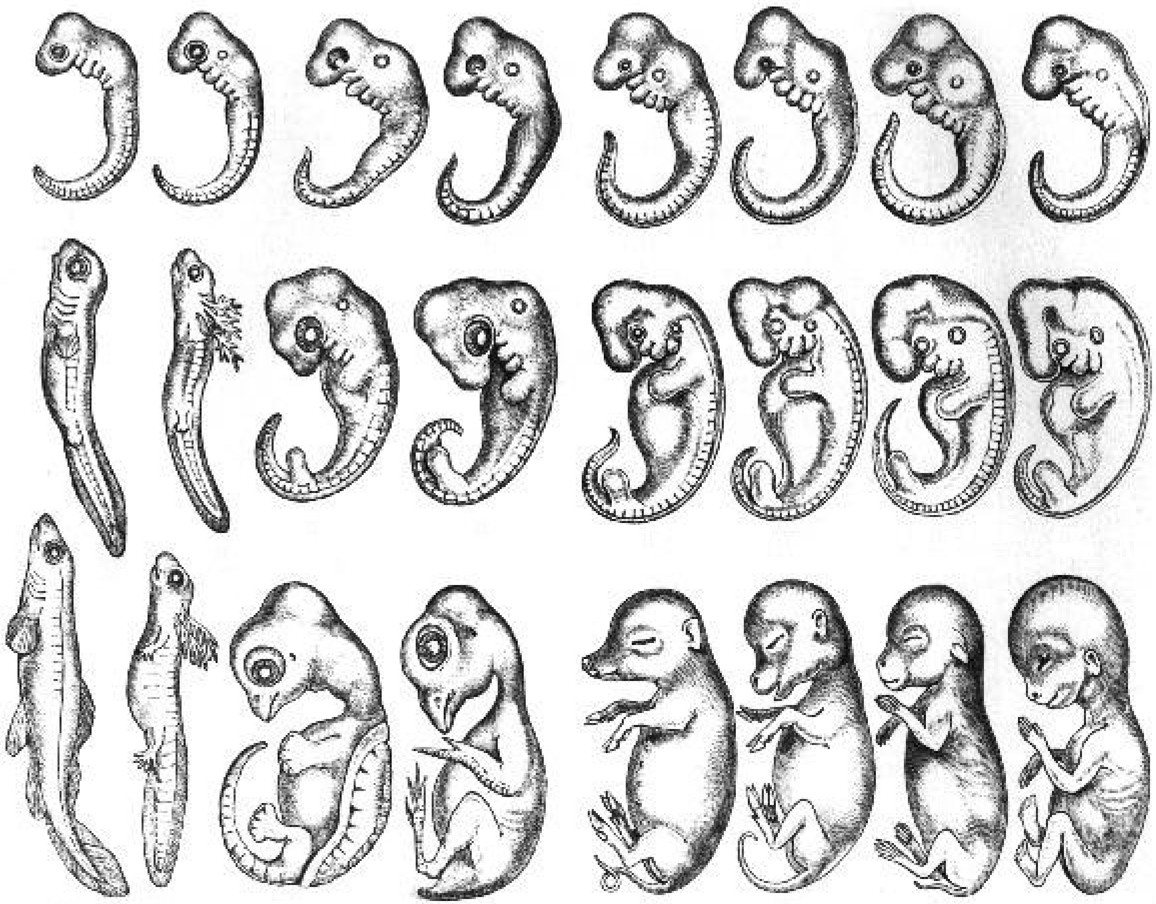
Movie from http://embryology.med.unsw.edu.au/Movies/Humemb.htm

At about E9, the embryo 'turns' (=twists) to end up bent the normal way:





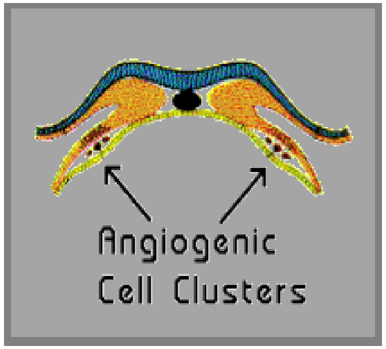
The phylotypic stage:

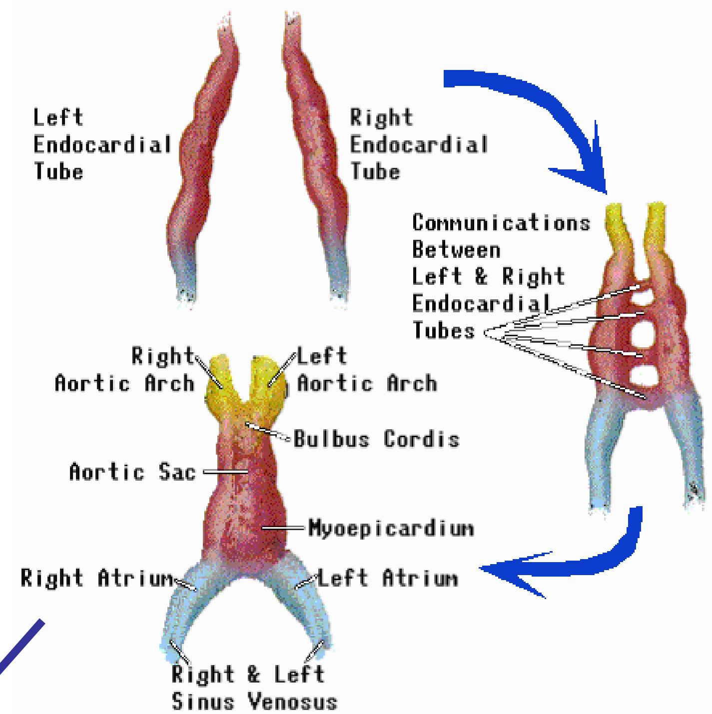


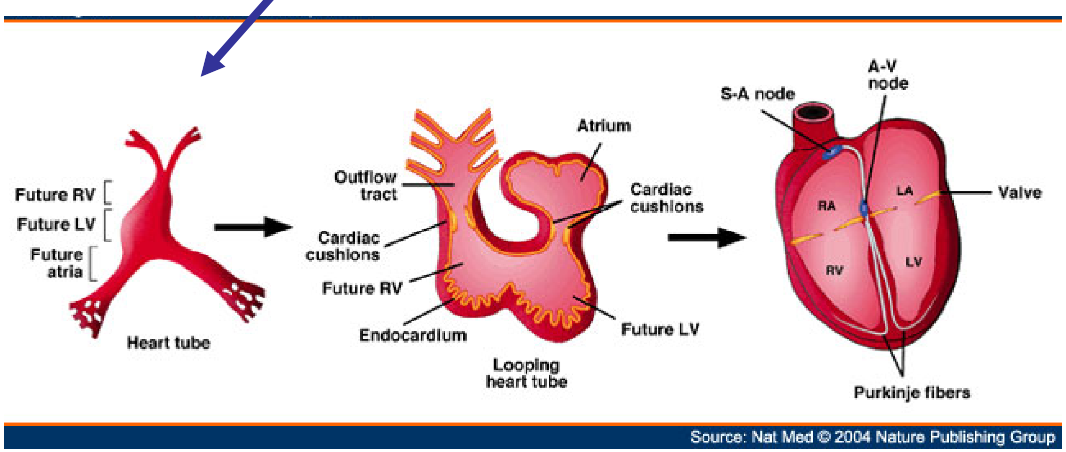
Pic: Von Baer

The circulation

Pic: http://user.gru.net/clawrence/vccl/chpt1/fetal.HTM





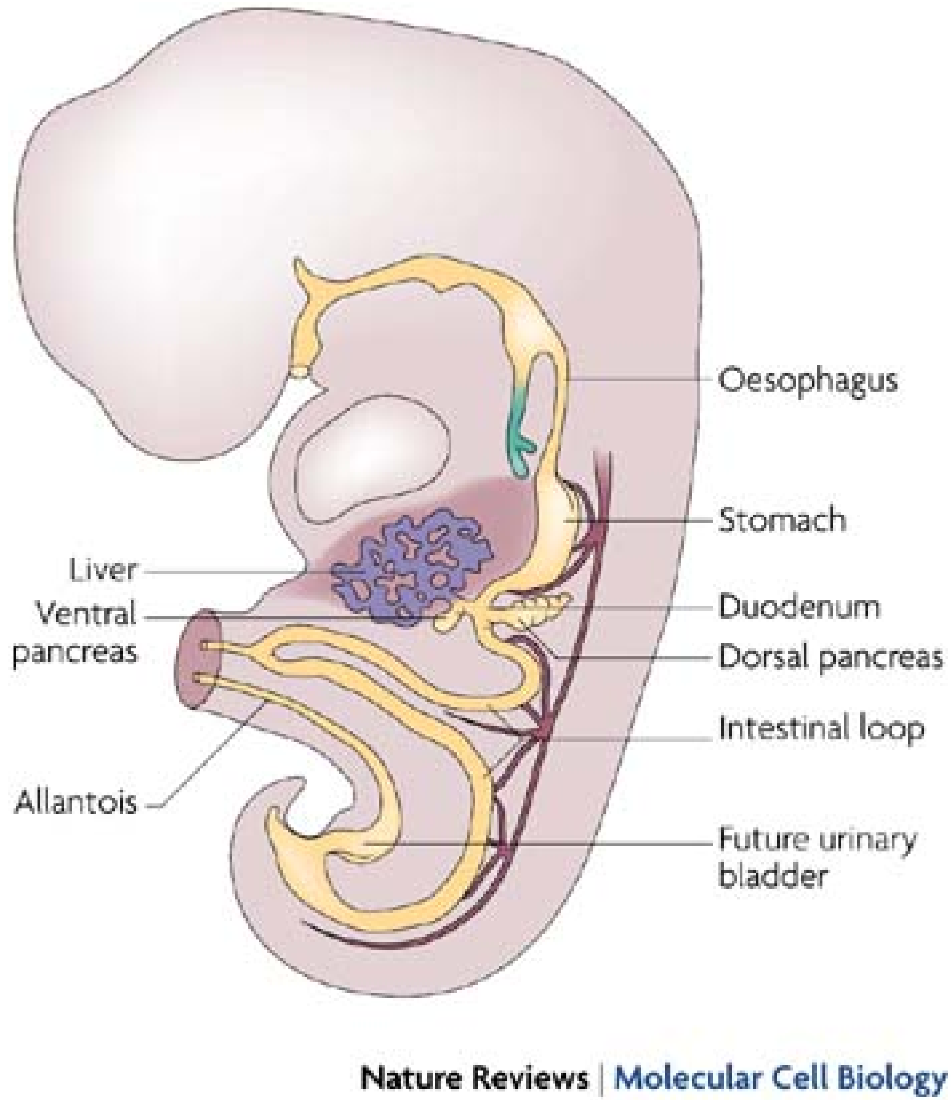


(Lots of folding)

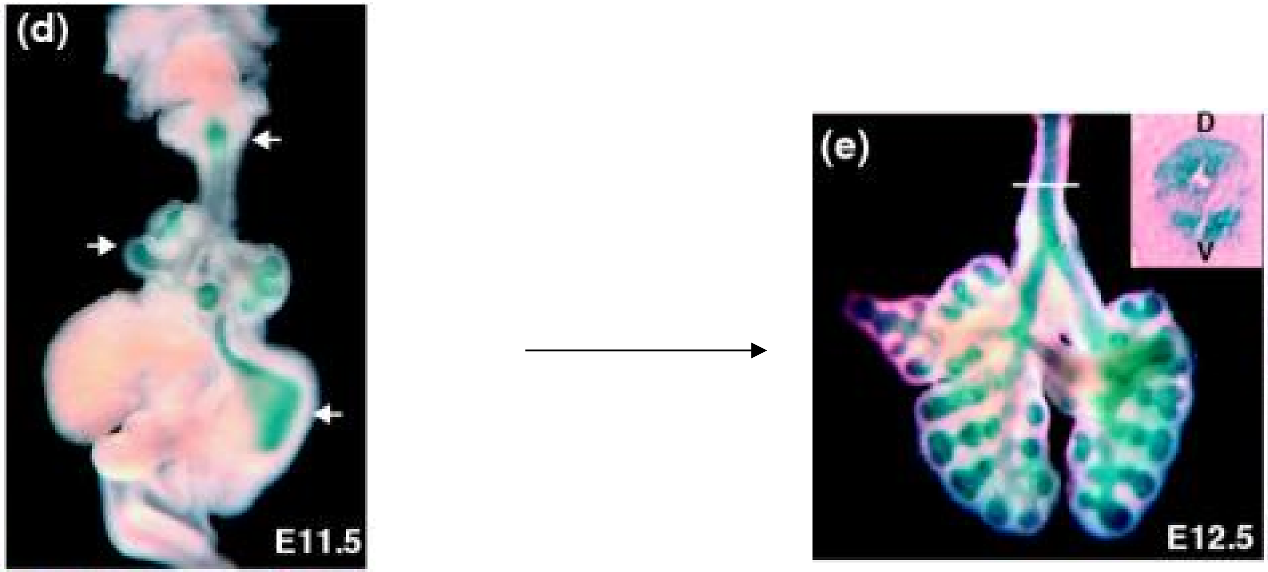
E12 onwards – mostly organogenesis

The endoderm makes a tube:

- Gut
- Lungs
- Liver
- Pancreas

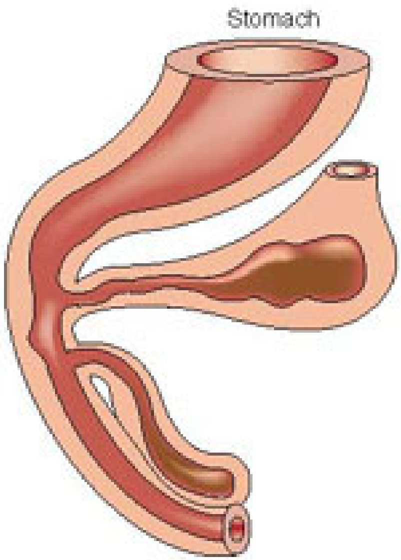


Gut diverticula: lungs

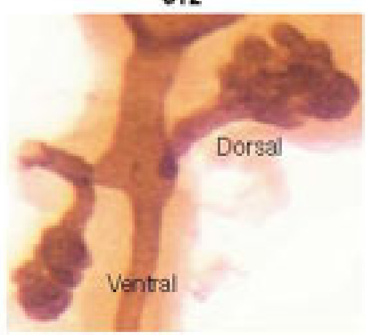


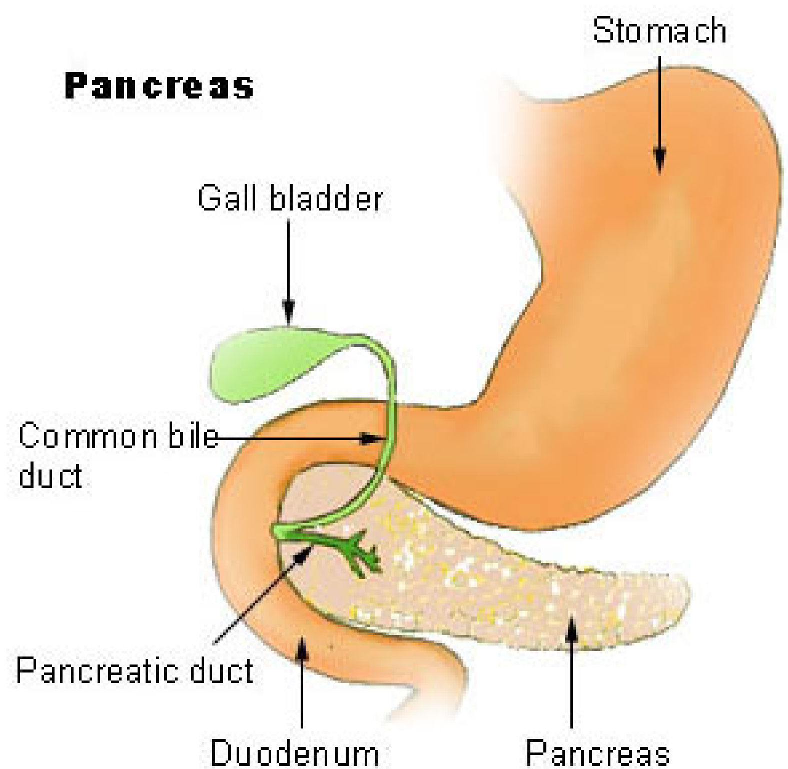
Okubo and Hogan *Journal of Biology* 2004 **3**:11 doi:10.1186/jbiol3

Gut diverticula: pancreas



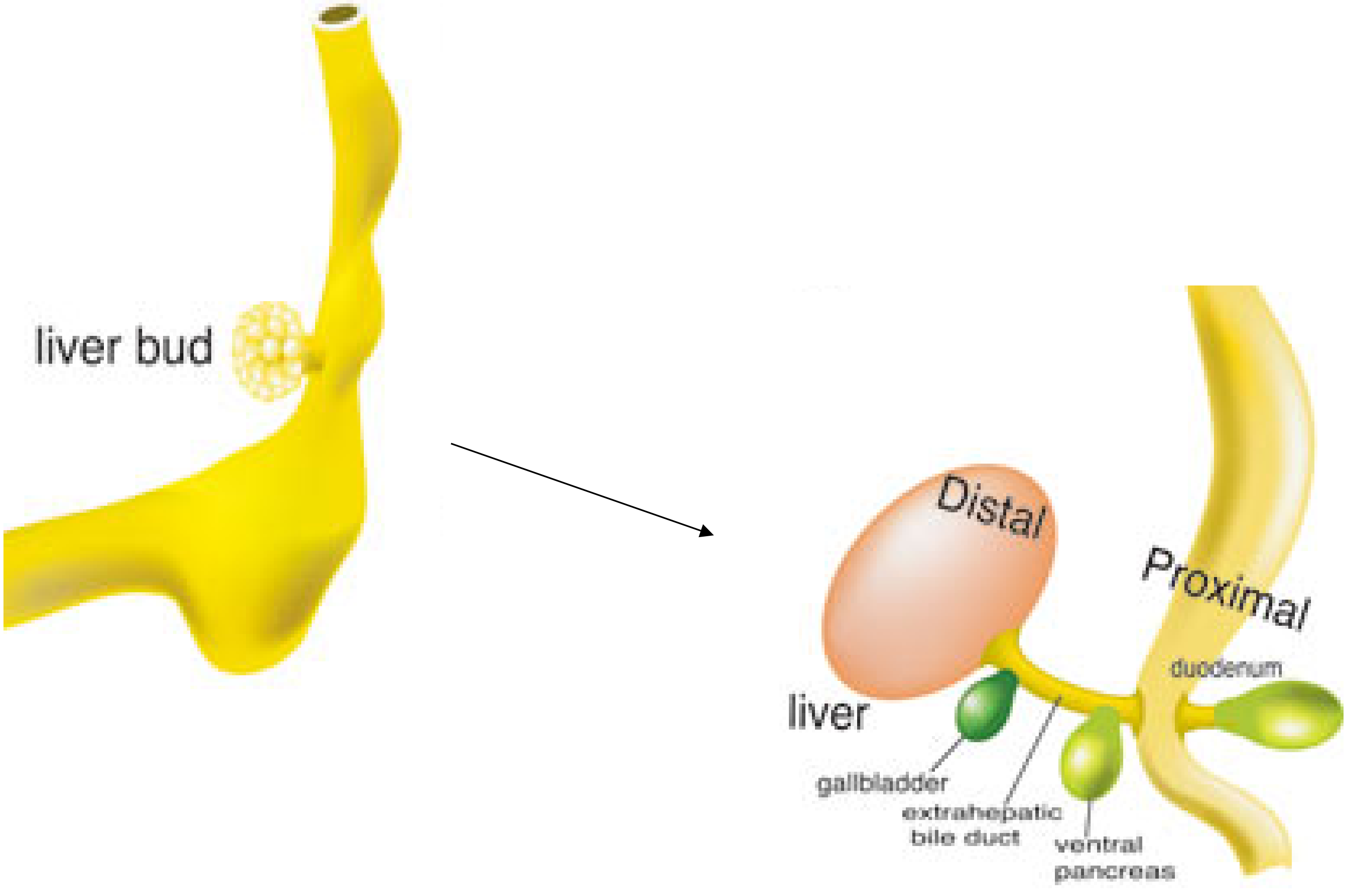
e12

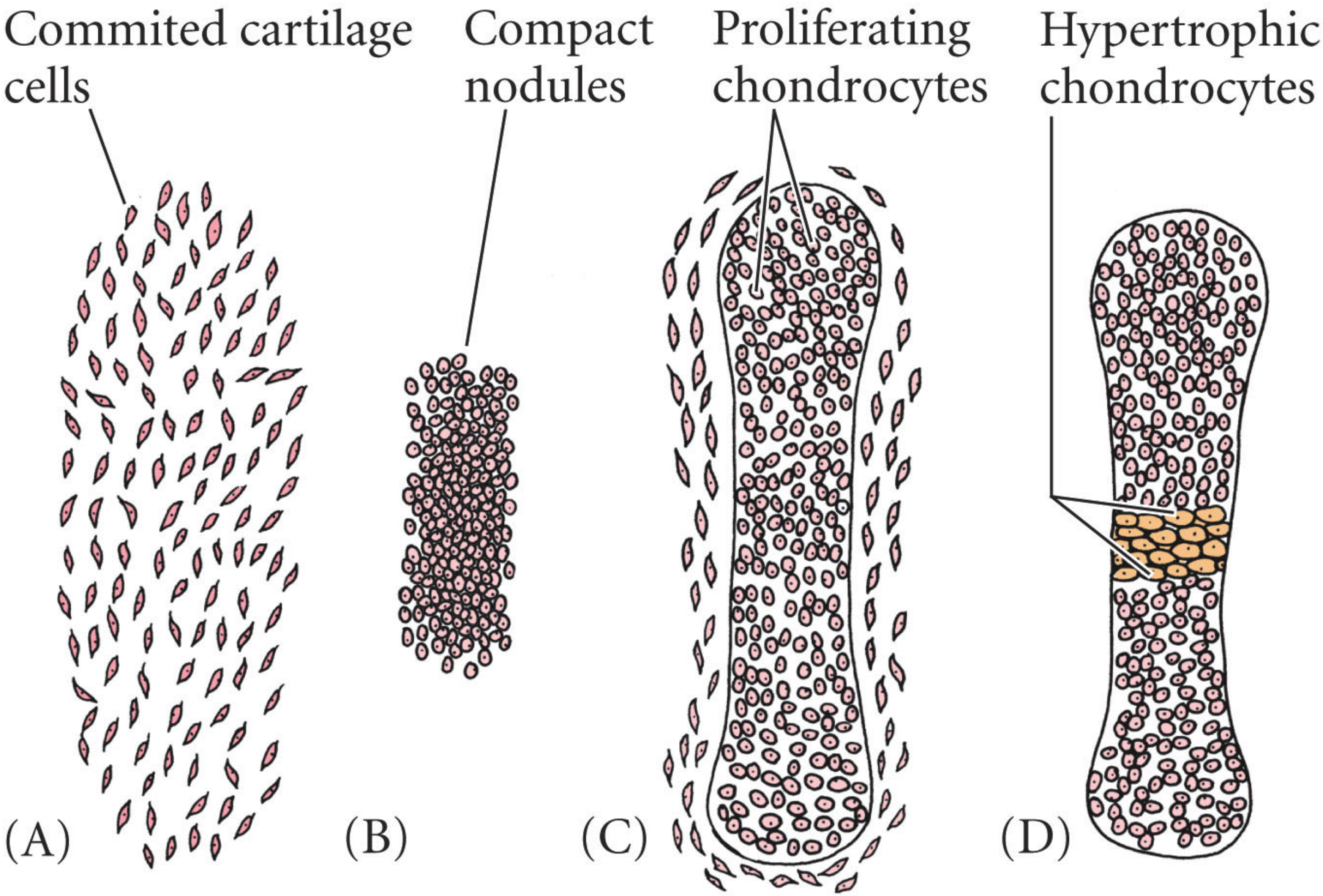




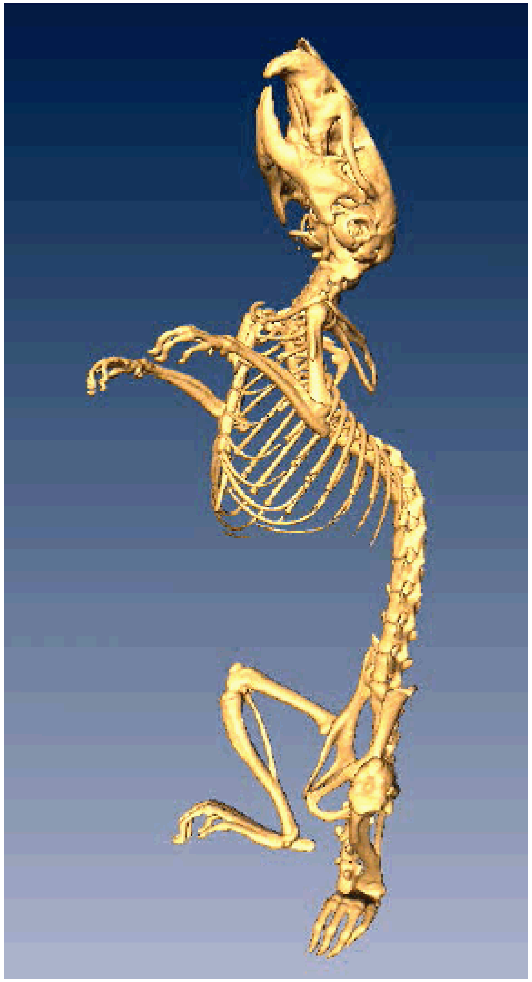
http://ucmm.cs.it-norr.com/default.asp%3Fid%3D1267%26PTID%3D%26refid%3D1042&h=378&w=591&sz=46&hl=en&start=5&tbnid=nFDYPgoj43WsOM:&tbnh=86&tbnw=135&prev=/images%3Fq%3Dpancreas%2Bdevelopment%26gbv%3D2%26ndsp%3D21%26hl%3Den%26safe%3Doff%26sa%3DN

Gut diverticula: liver




Commited cartilage cells
Compact nodules
Proliferating chondrocytes
Hypertrophic chondrocytes
(A)
(B)
(C)
(D)

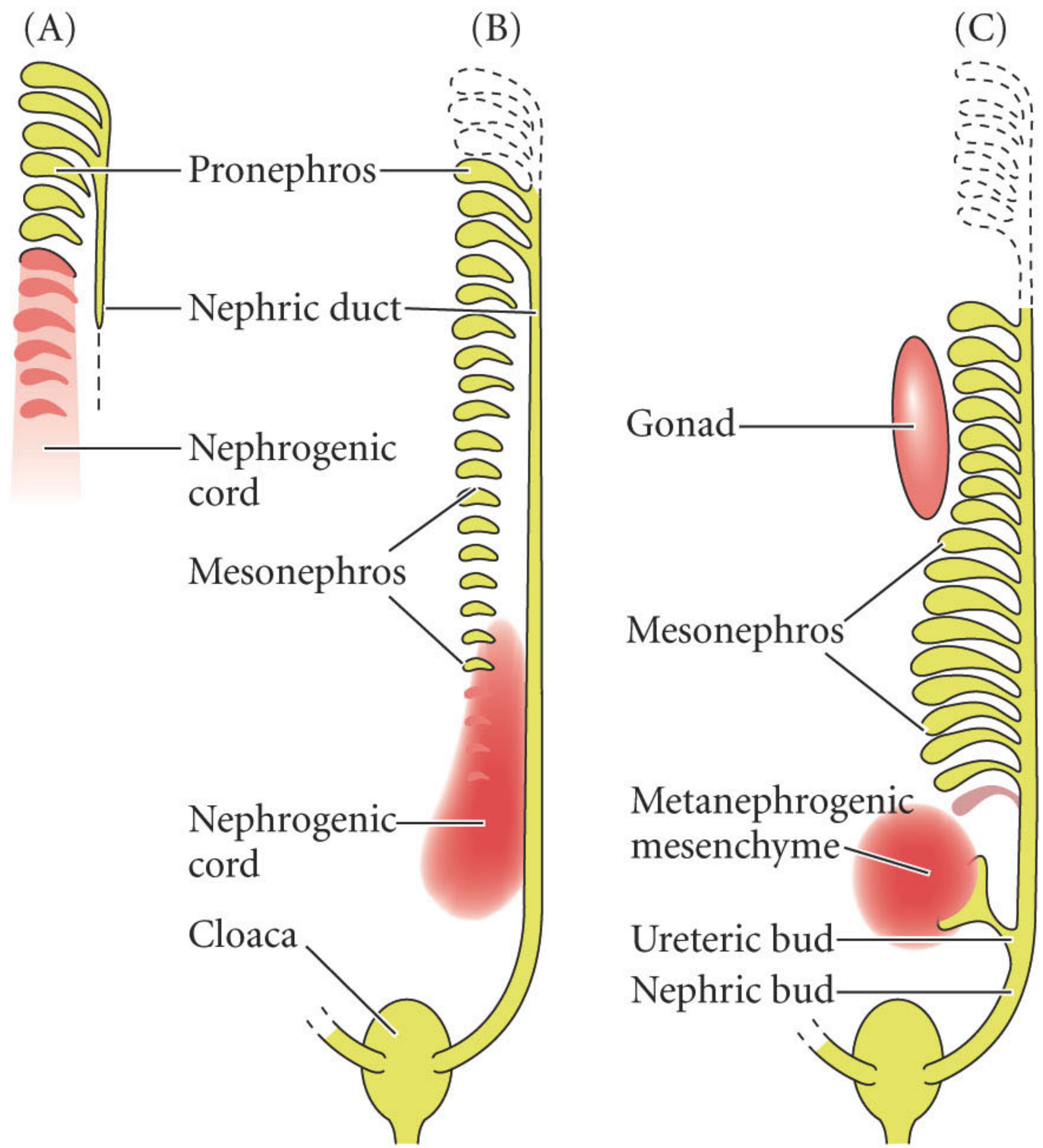
Pics: Richard Harland



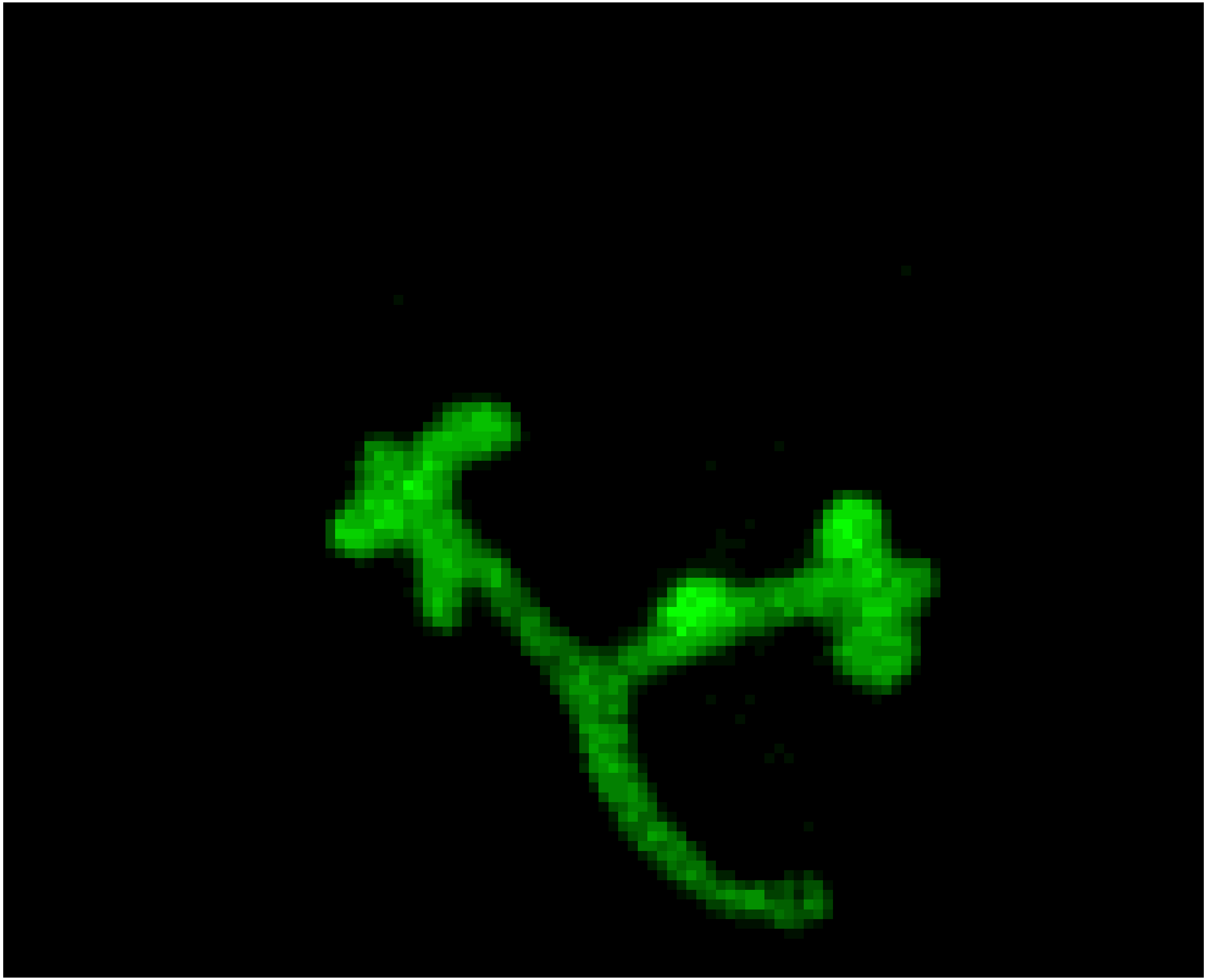
Pic:
www.biospace.fr/popup/ct_mouse_skeleton.html

And the human version…

The intermediate mesoderm: organogenesis



Morphogenesis of urine collecting ducts in a kidney

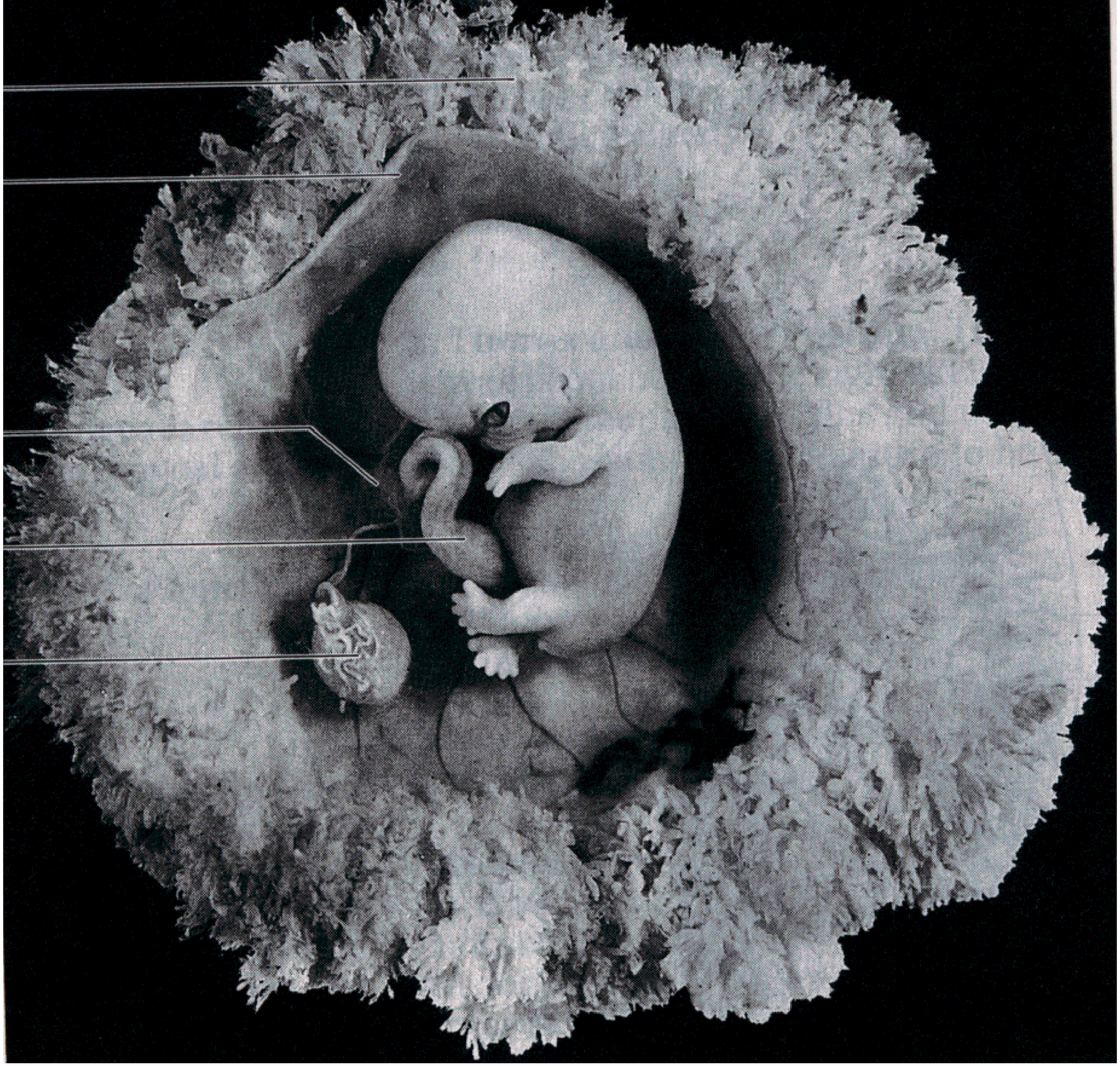


The finished collecting duct.

Dr Chris Armit

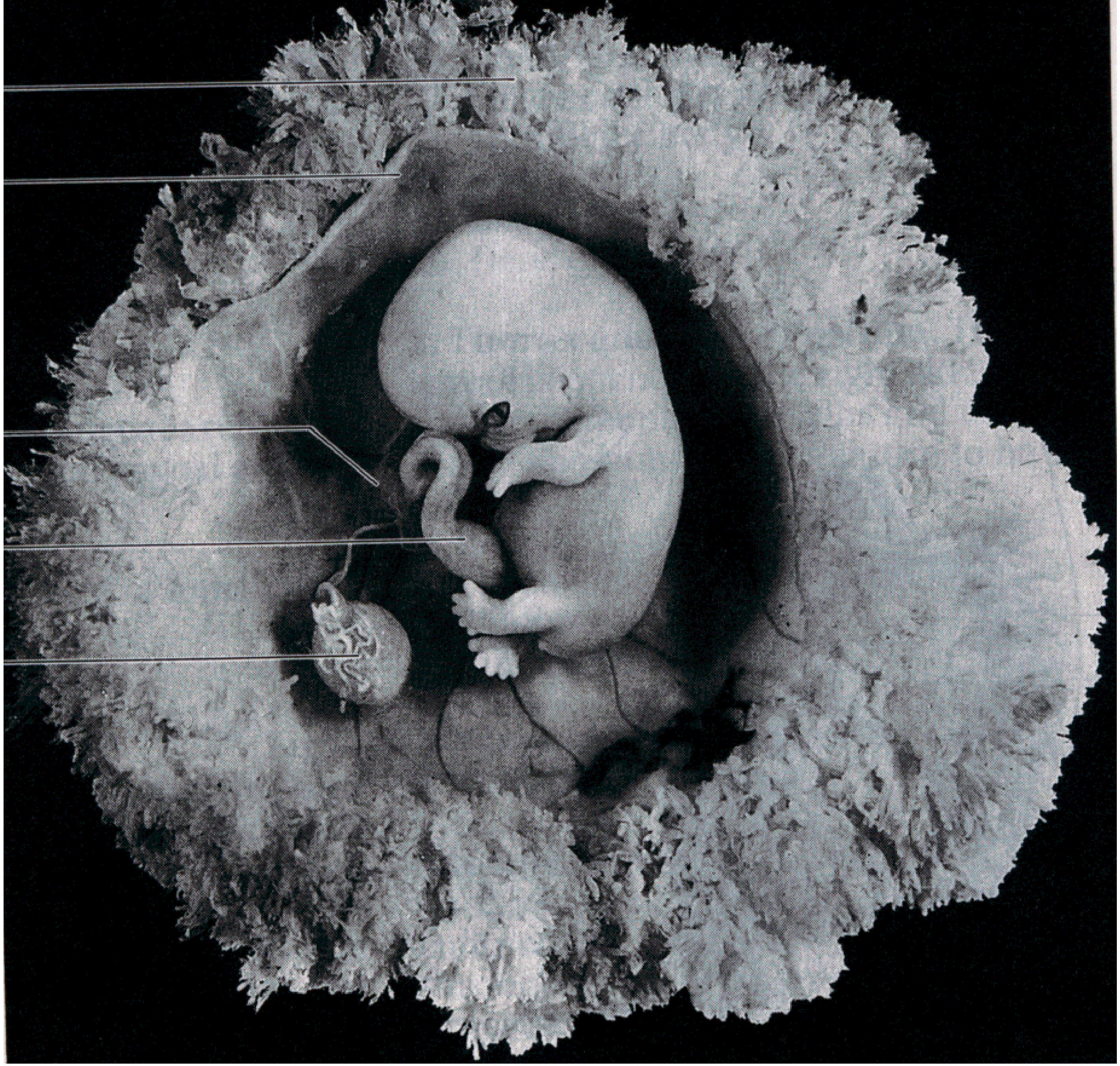
10th week of development

(= 8 weeks)



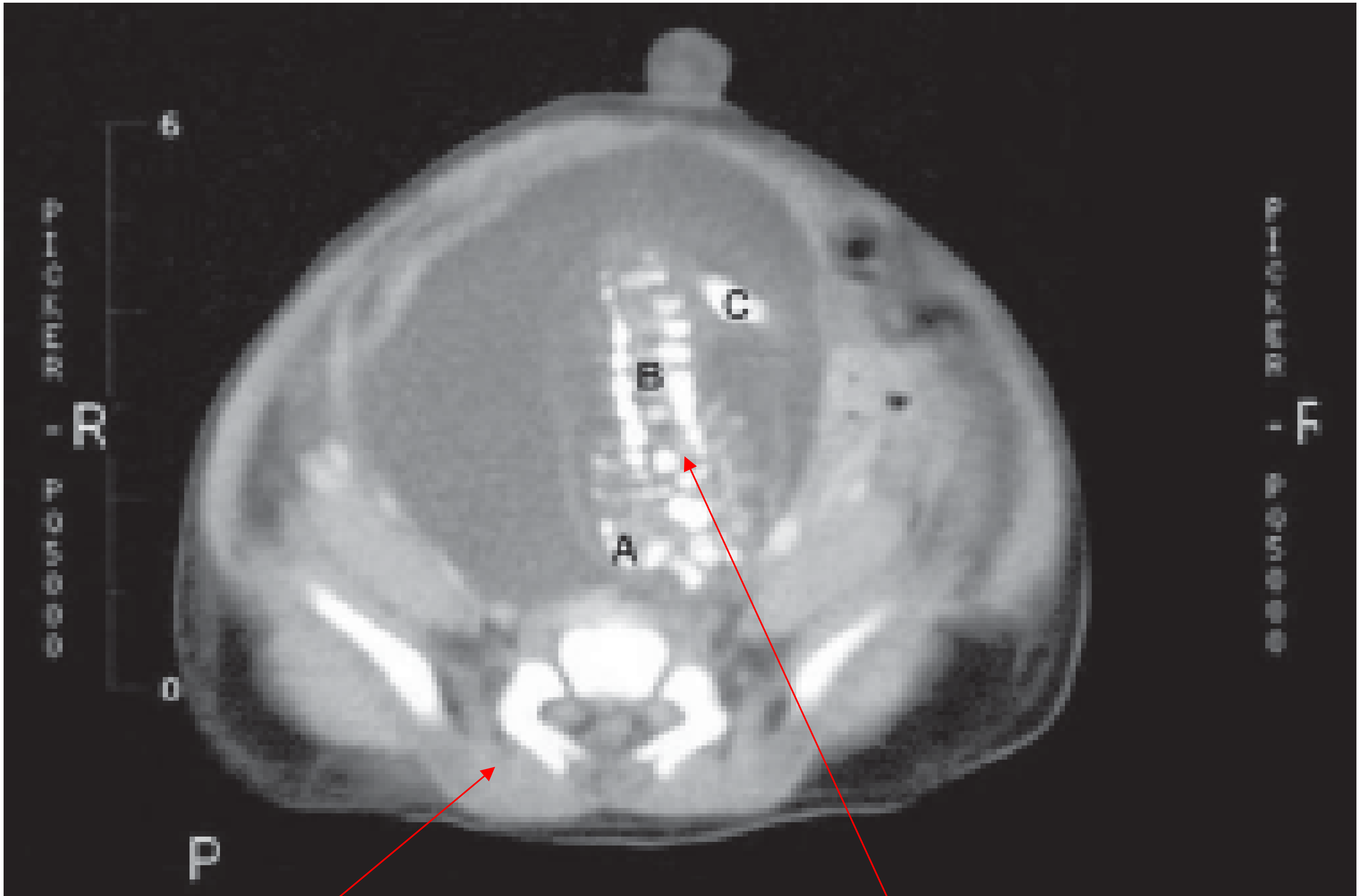
10th week of development

(= 8 weeks)



16th week of development

Foetus in fetu (human)



This is the main foetus' pelvis

This is the vertebrae of the foetus in fetu

Ten basic mechanisms of animal morphogenesis: