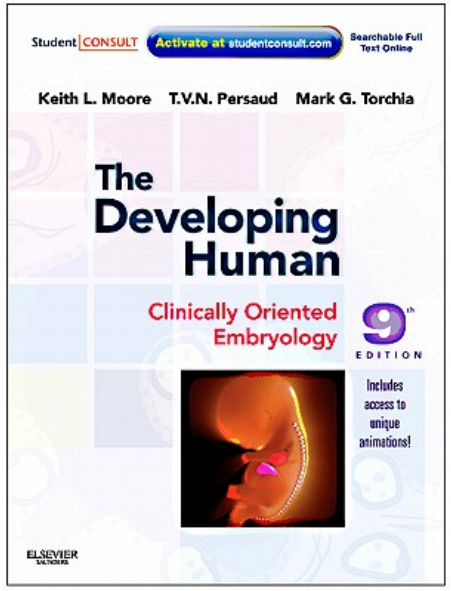
**Mesoderm** – *Middle Skin*

During embryogenesis, mesodermal cell groups are often called **mesenchymal** – meaning the cells are loosely organised in a non-epithelial fashion. They migrate easily and can differentiate into many different cell types.

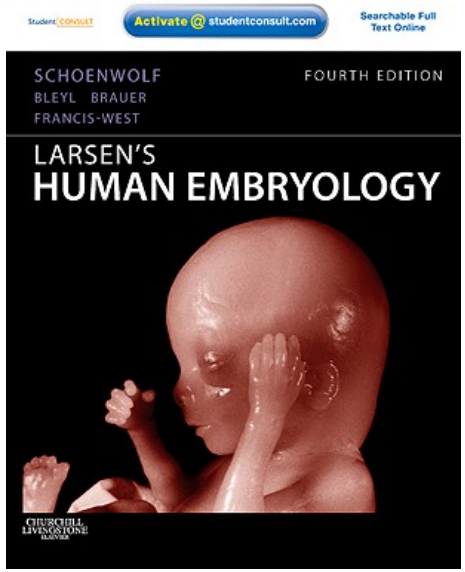
However, mesenchyme is not the same thing as mesoderm. Neural crest-derived cells can also be **mesenchymal**

## Objectives

- Understanding of events during the third week of development
- Understanding of notochord formation
- Understanding the process of early somite development
- Understanding the process of body cavity formation
- Brief understanding of the future fate of mesoderm components
- Brief understanding of early heart formation



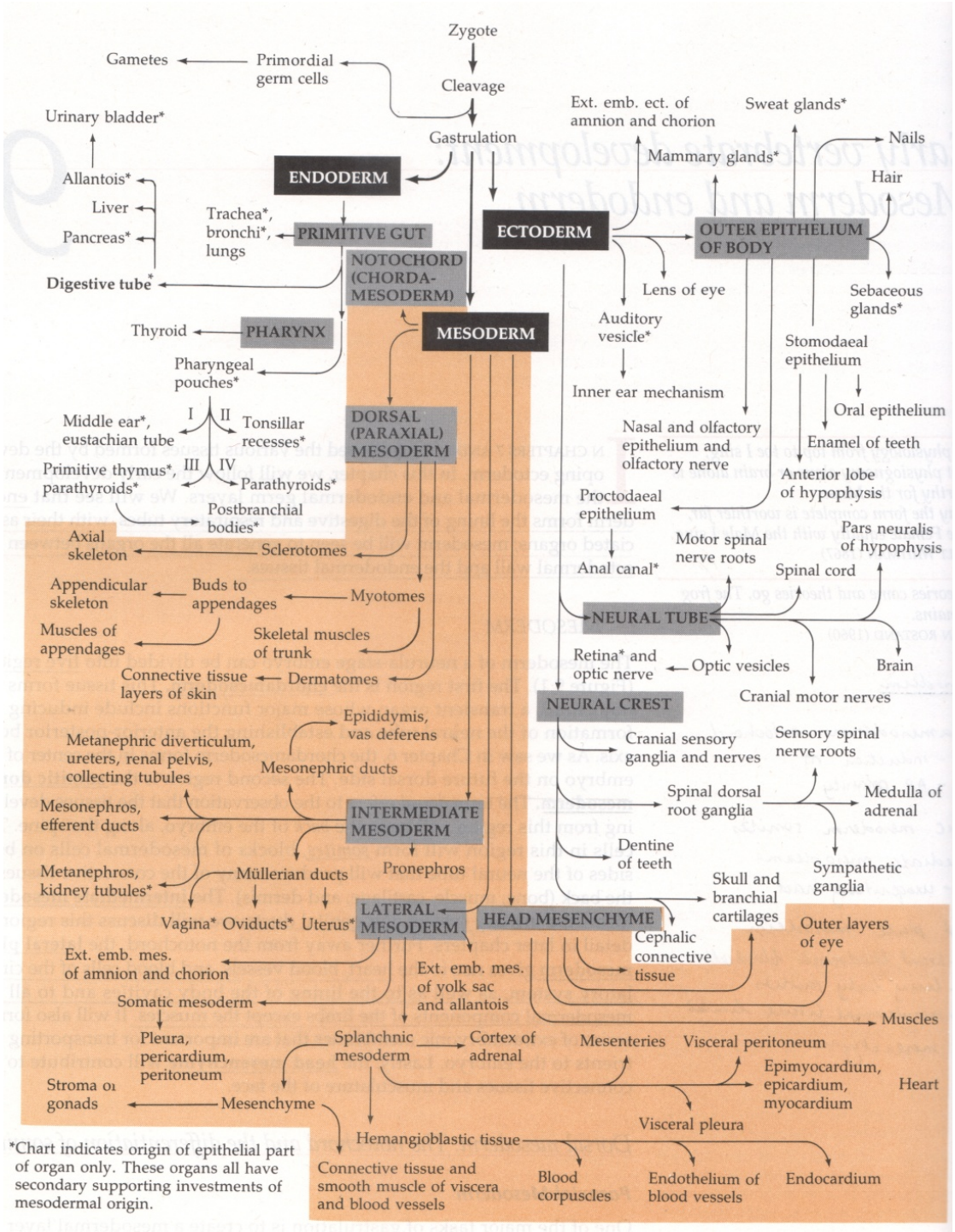

**Citation:** The Developing Human: clinically oriented embryology 9th ed. Keith L. Moore, T.V.N. Persaud, Mark G. Torchia. Philadelphia, PA: Saunders, 2011.
Chapter 4 – Third Week of Human Development
Chapter 5 – Fourth to Eighth Weeks of Human Development
Chapter 15 - Muscular System



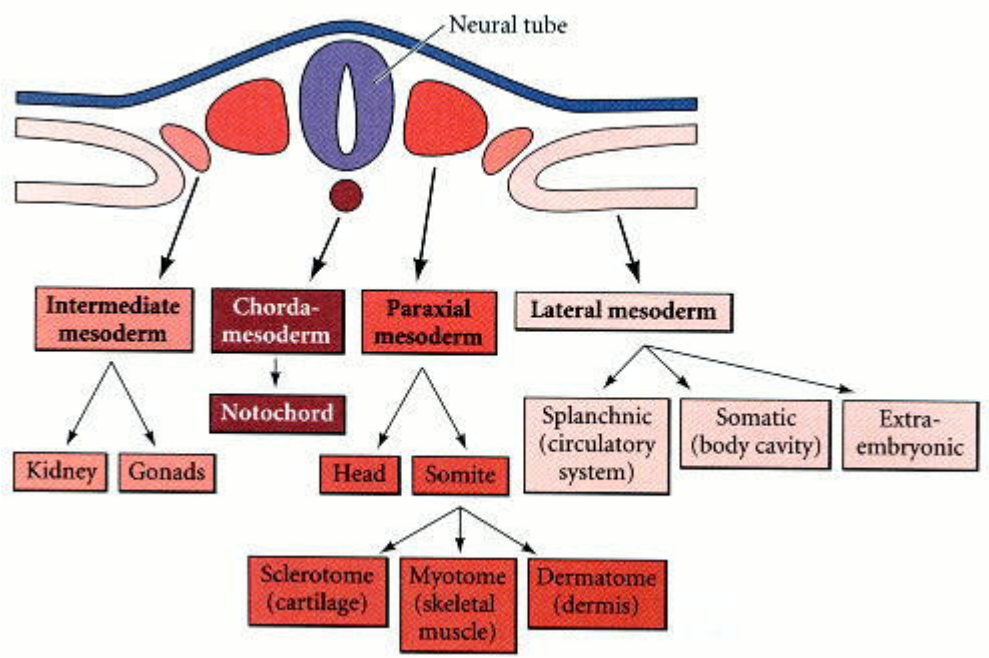

**Citation:** Larsen's human embryology 4th ed. Schoenwolf, Gary C; Larsen, William J, (William James). Philadelphia, PA : Elsevier/Churchill Livingstone, c2009.
Chapter 3 - Third Week: Becoming Trilaminar and Establishing Body Axes
Chapter 4 - Fourth Week: Forming the Embryo
Chapter 8 - Development of the Musculoskeletal System

**What tissues does mesoderm make?**
**Lineage mapping**

Most of the skeleton
Most of the skeletal muscle tissue
Underlying dermis of the skin
Kidneys
Gonads
Linings of the body cavities
Connective tissues
Blood vessels
Most of the heart
Cortex of the adrenal gland
blood

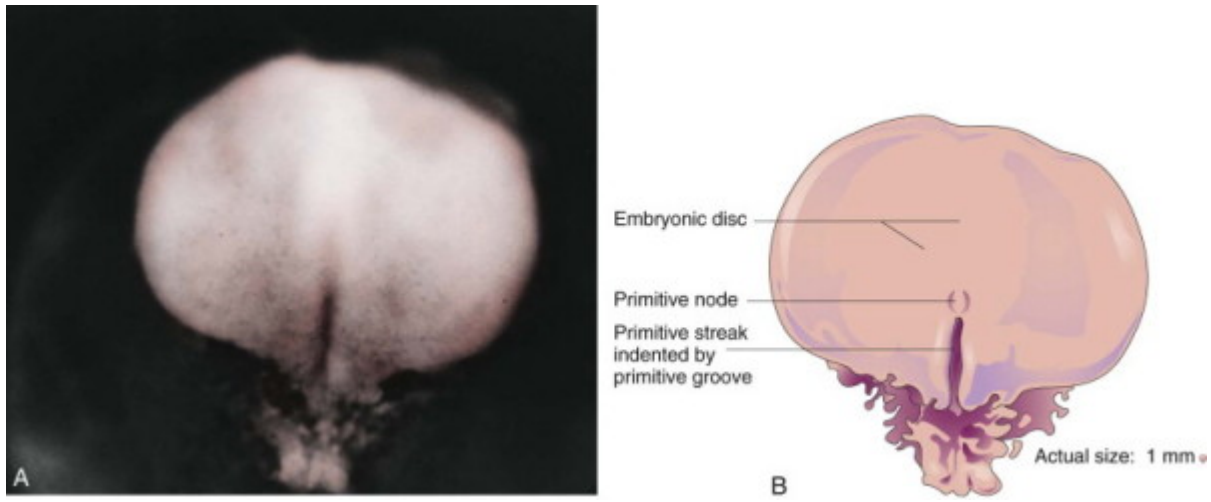


Lineage mapping and **subdivisions of the mesoderm**



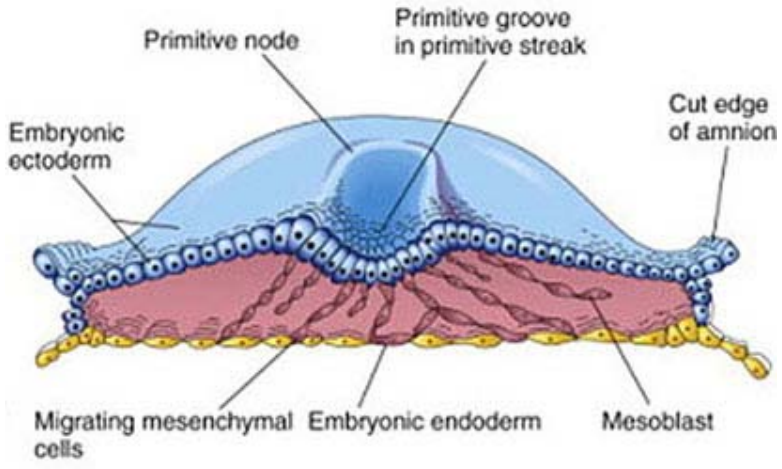

Developmental Biology. 6th edition.
Gilbert SF.
Sunderland (MA): Sinauer Associates; 2000.

Review gastrulation week 3 and the formation of the mesoderm
Looking down on the epiblast




*From Moore KL, Persaud TVN, Shiota K: Color Atlas of Clinical Embryology, 2nd ed. Philadelphia, WB Saunders, 2000.*

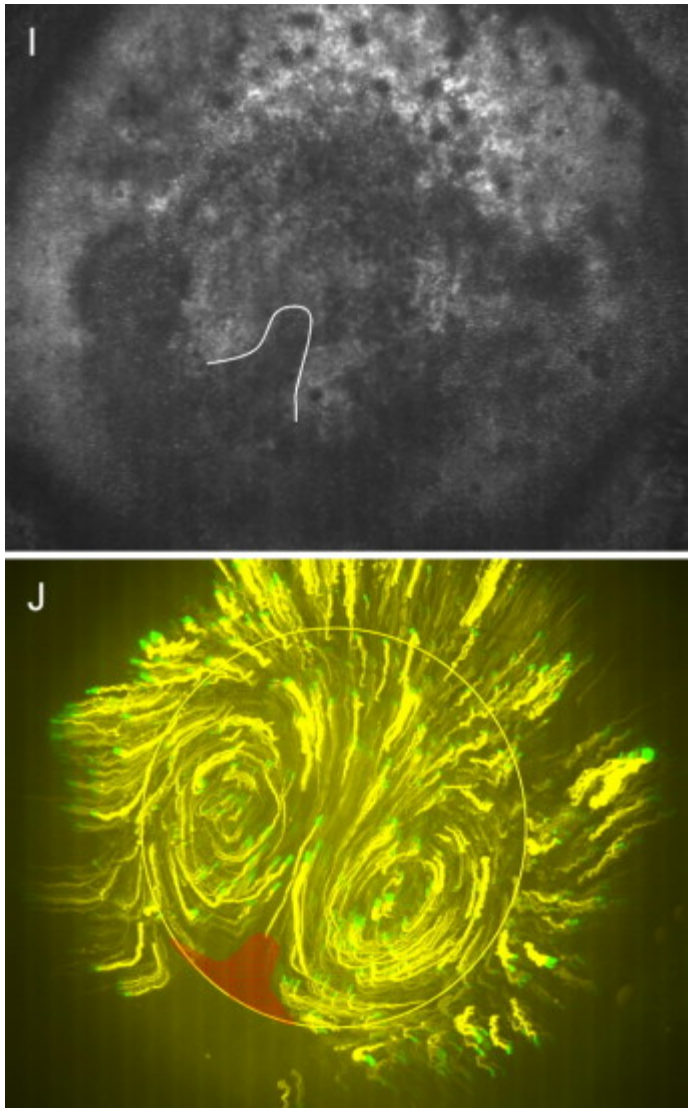
The primitive streak forms mesoderm by the ingression of cells until the early part of the 4th week then mesoderm formation slows. The primitive streak diminishes and becomes an insignificant structure in the sacrococcygeal region, degenerates and disappears by the end of the 4th week.




*From Moore KL, Persaud TVN, Shiota K: Color Atlas of Clinical Embryology, 2nd ed. Philadelphia, WB Saunders, 2000.*

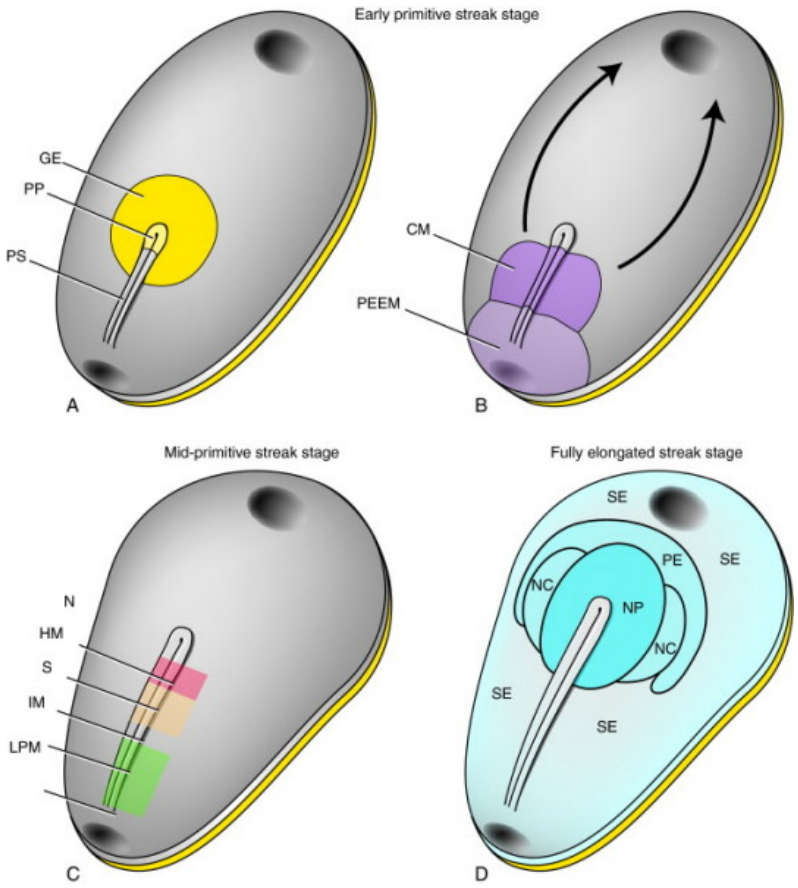
**Gastrulation movements involve the whole embryo**

Cell movements in a 5 hour time window marked by GFP and time lapse microscopy




**The Mechanisms Underlying Primitive Streak Formation in the Chick Embryo**

*Manli Chuai and Cornelis J. Weijer*
Division of Cell and Developmental Biology, Wellcome Trust Biocentre,
College of Life Sciences, University of Dundee, Dundee DD1 5EH, United Kingdom

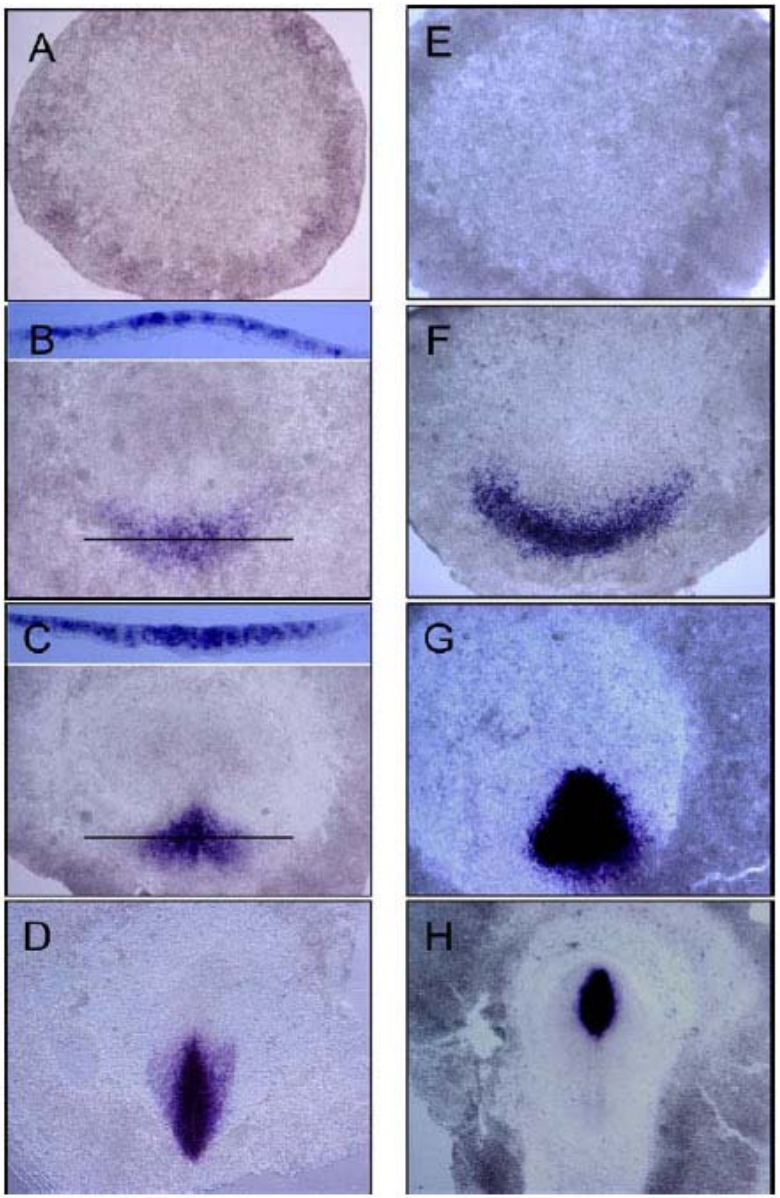



**Where do the endoderm and mesoderm cells come from?**

**Figure 3-10** Prospective fate maps of the epiblast (based on data obtained from both chick and mouse embryos), showing the regions of epiblast that ingress through the primitive streak and form the major subdivisions of the trilaminar embryonic disc. *A*, Early primitive streak stage showing locations of prospective gut endoderm (GE) in epiblast and prospective prechordal plate (PP) in the cranial end of the primitive streak (PS; dark outline in subsequent figures). Oval at the cranial end of the epiblast (in all figures) indicates the location of the future oropharyngeal membrane; caudal oval indicates future clavical membrane. *B*, Early primitive streak stage showing locations of prospective cardiogenic mesoderm (CM) and prospective extraembryonic mesoderm (PEEM) in epiblast and primitive streak. Arrows indicate the directions of migration of the cardiogenic mesoderm. *C*, Midprimitive streak stage showing locations of prospective mesoderm in epiblast and primitive streak. These include prospective notochord (N), head mesoderm (HM), somites (S), intermediate mesoderm (IM), and lateral plate mesoderm (LPM). *D*, Fully elongated primitive streak stage showing locations of the neural plate (NP), surface ectoderm (SE), neural crest cells (NC), and placodal ectoderm (PE) after cells in the cranial half of the embryonic disc have completed their ingression into the primitive streak. Some epiblast still remains caudally at this stage, where cells are still moving into and ingressing through the primitive streak.

**Mesoderm markers**

Wnt8C Chordin

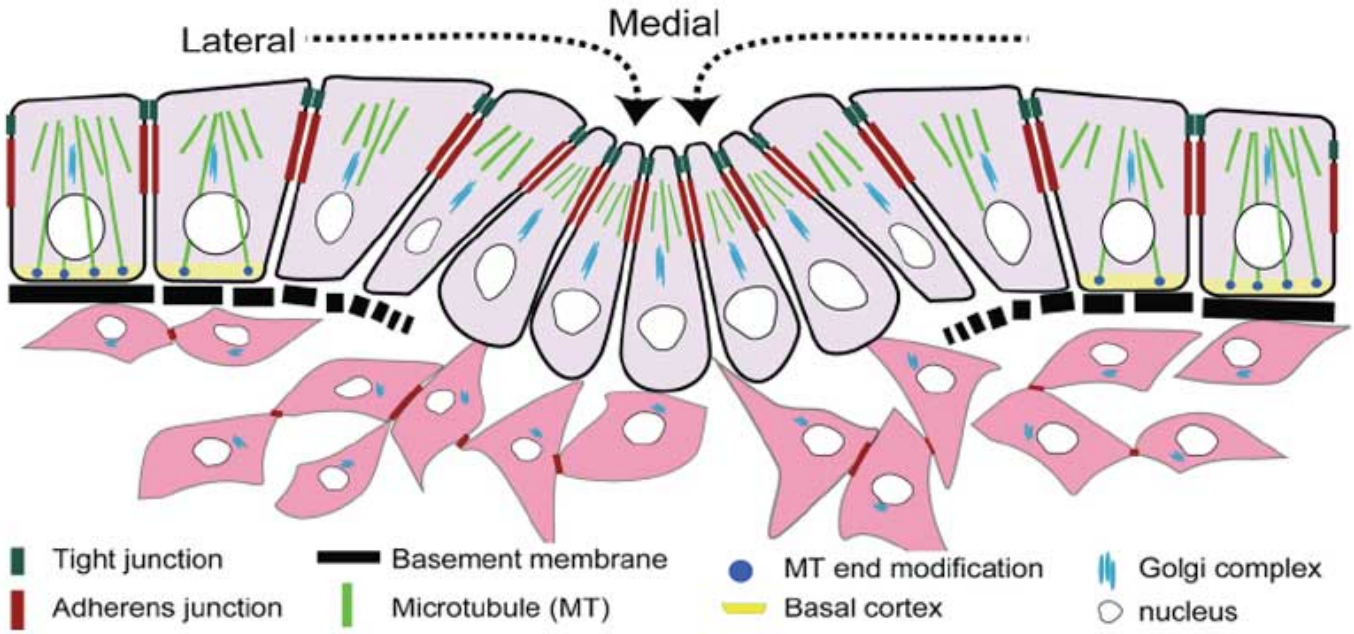



Gastrulation is dependent on the expression of mesoderm specific genes and the successful differentiation of mesoderm

**The Mechanisms Underlying Primitive Streak Formation in the Chick Embryo**

*Manli Chuai and Cornelis J. Weijer*
Division of Cell and Developmental Biology, Wellcome Trust Biocentre,
College of Life Sciences, University of Dundee, Dundee DD1 5EH, United Kingdom

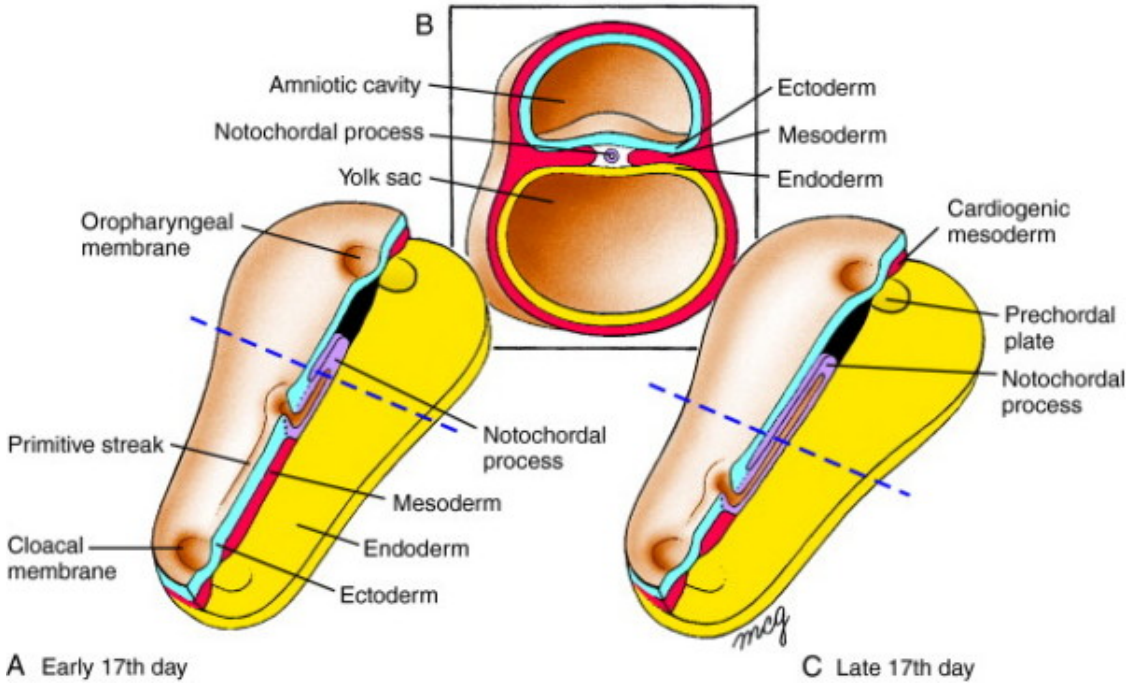
Gastrulation involves a process of **epithelial to mesenchymal transition (EMT). Basement membrane** breakdown follows the expression of mesoderm markers and before **tight junction** disruption




**Chicken Gastrulation**

**An amicable separation: Chick's way of doing EMT. Nakaya Y, Sheng G. Cell Adh Migr. 2009 Apr;3(2):160-3. Epub 2009 Apr 10. PMID: 19262172**

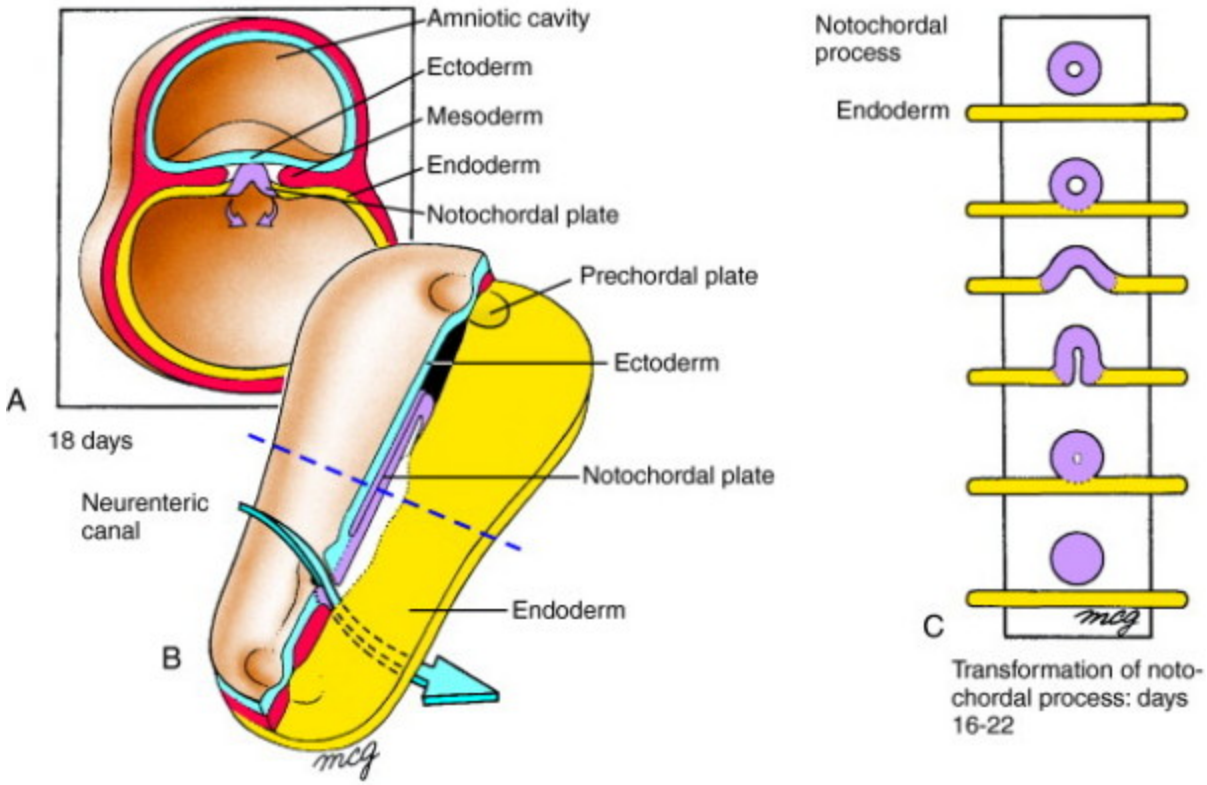
**The axial mesoderm - Notochord formation –** one of the main regulators of notochord formation is the DNA-binding protein **Brachyury** encode by the *T* gene.




Formation of the notochord begins with cranial midline extension from the primitive node of a hollow tube, the **notochordal process**. This tube grows in length as primitive node cells are added to its proximal end, concomitant with regression of the primitive streak

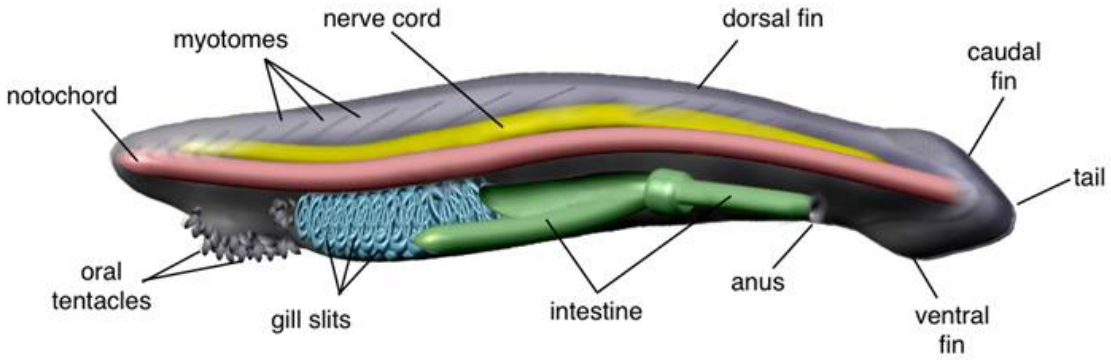
**Schoenwolf: Larsen's Human Embryology, 4th ed.**

**Later formation of the notochord** *chord = string, noton (Gk) = back. Coined by English anatomist Sir Richard Owen (1804-1892)*

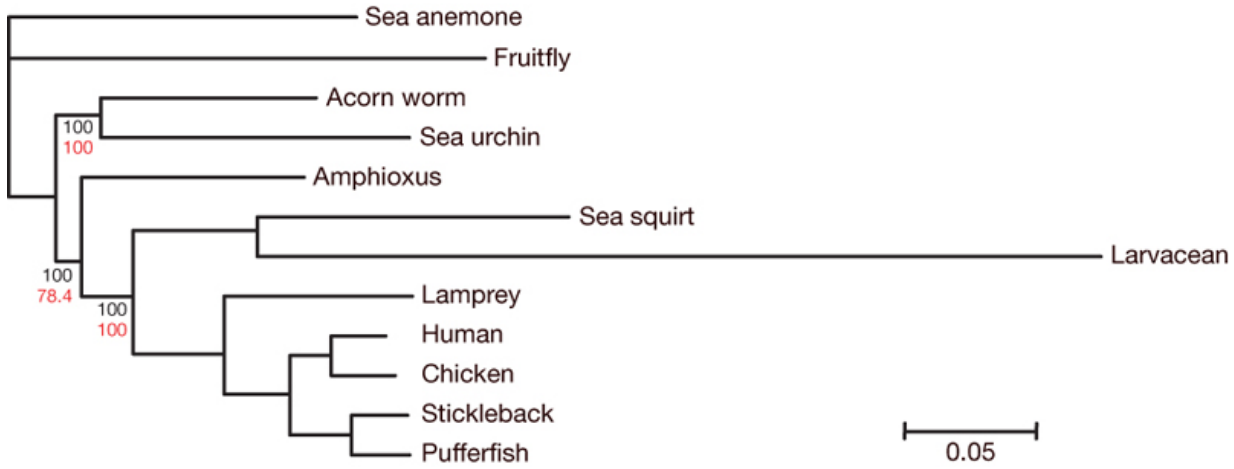



The process by which the hollow notochordal process is transformed into a solid notochord between days 16 and 22. First, the ventral wall of the notochordal process fuses with the endoderm and the two layers break down, leaving behind the flattened notochordal plate. An open neurenteric canal is briefly created between the amniotic cavity and the yolk sac cavity. *C*, Series of events by which the notochordal process becomes the notochordal plate and then the notochord.

The notochord is a transient structure in vertebrates but it is an evolutionary remnant that still functions as the main “backbone” in amphioxus and sea squirts.

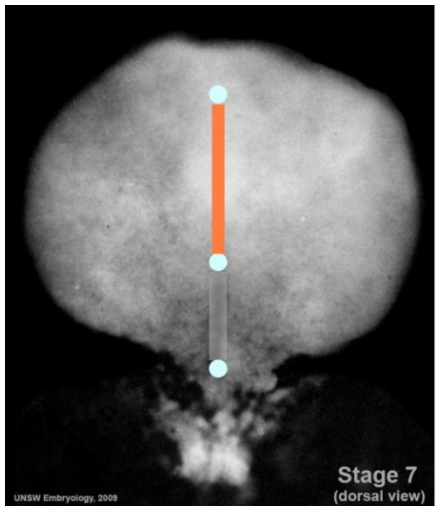



Amphioxus

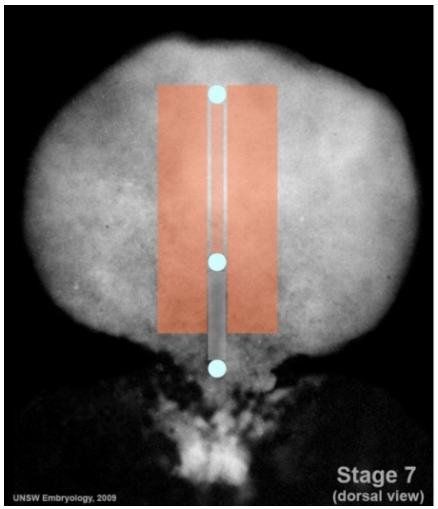


## Stage 7 (Early wk 3) human embryo subdivisions of the mesoderm other than the notochord

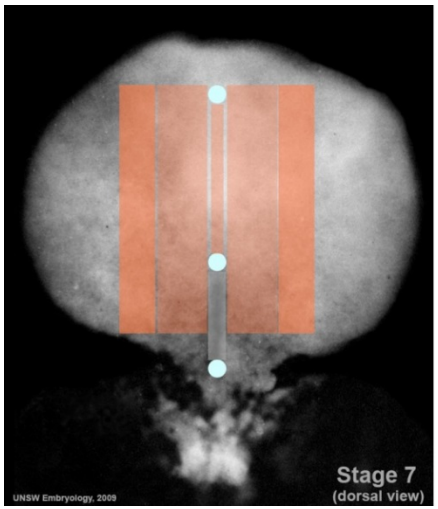
Notochord or axial mesoderm



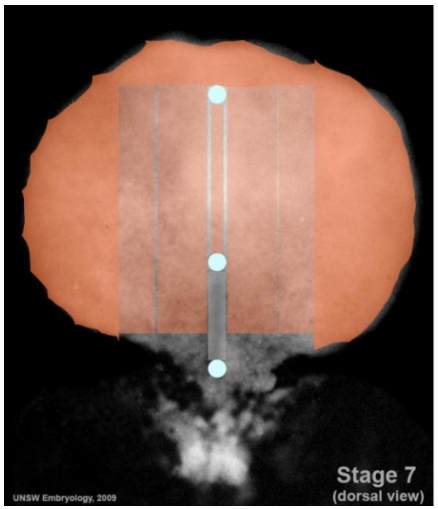

Paraxial mesoderm



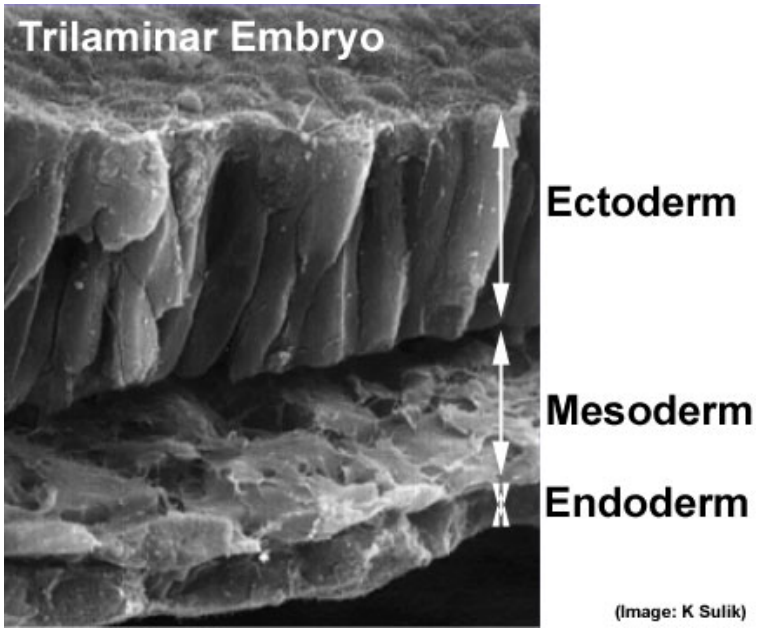

Intermediate mesoderm



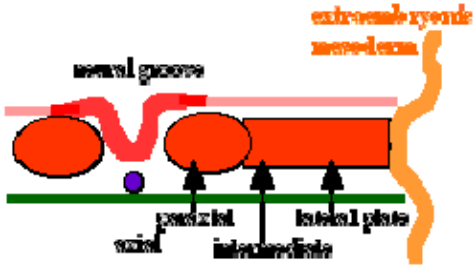

Lateral plate mesoderm

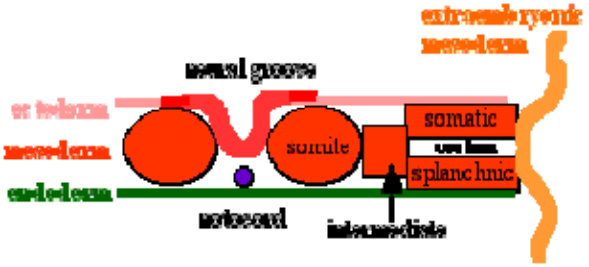


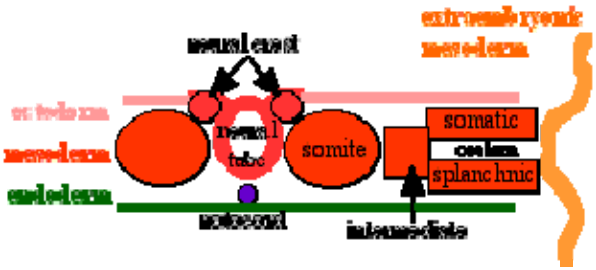
## In transverse section - starting point before appearance of subdivisons

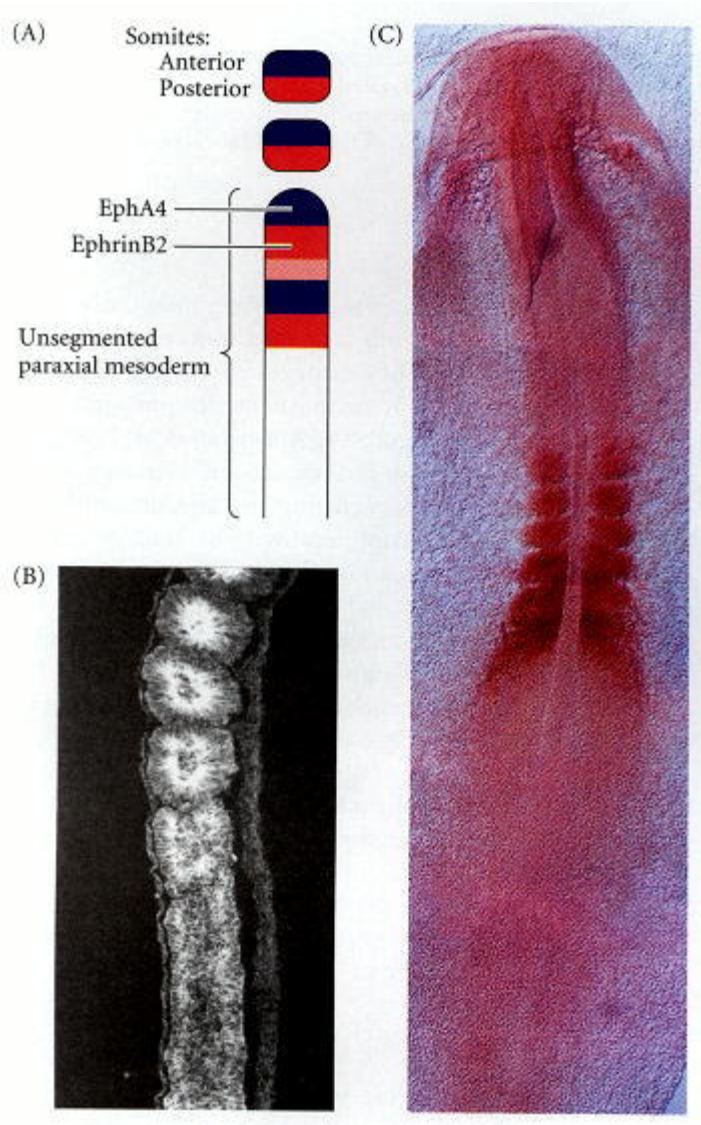
**In simple schematic form – subdivisions of the mesoderm**
**Somitogenesis in the paraxial mesoderm and creation of the coelom in the lateral plate to form somatic and splanchnic mesoderm**



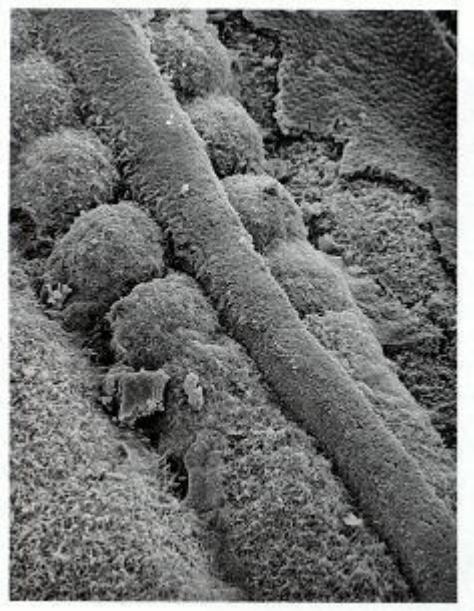



# Somitogenesis - molecular events precede appearance of somites

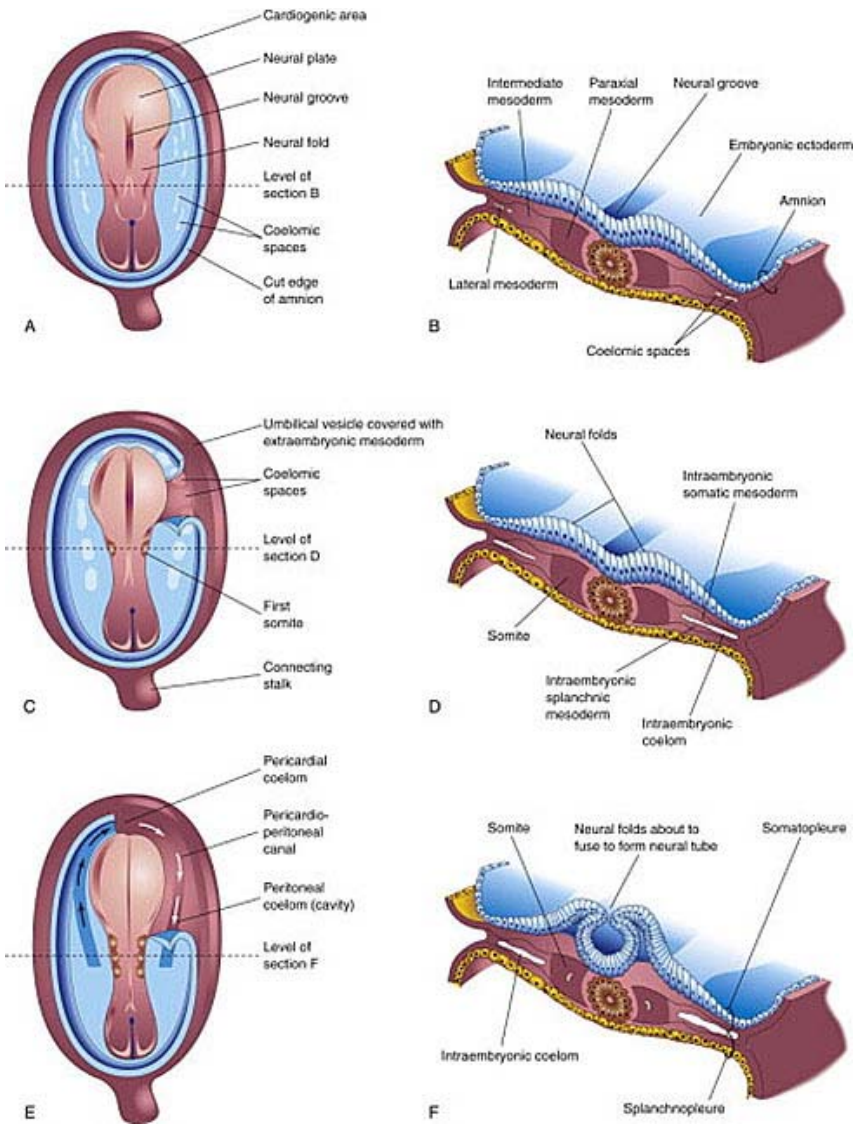



Transition from somitomere to somite. (A) Expression pattern of receptor tyrosine kinase EphA4 (blue) and its ligand, ephrinB2 (red) as somites develop. The somite boundary forms at the junction between the region of ephrin expression on the posterior of the last formed somite and the region of Eph expression on the anterior of the next somite to form. In the presomitic mesoderm, the pattern is created anew as each somite buds off. The posteriormost region of the next somite to form does not express ephrin until that somite is ready to separate.



Developmental Biology. 6th edition.
Gilbert SF.
Sunderland (MA): Sinauer Associates; 2000.

Mesoderm has a different fate depending on where it is on the A/P axis and the mediolateral axis



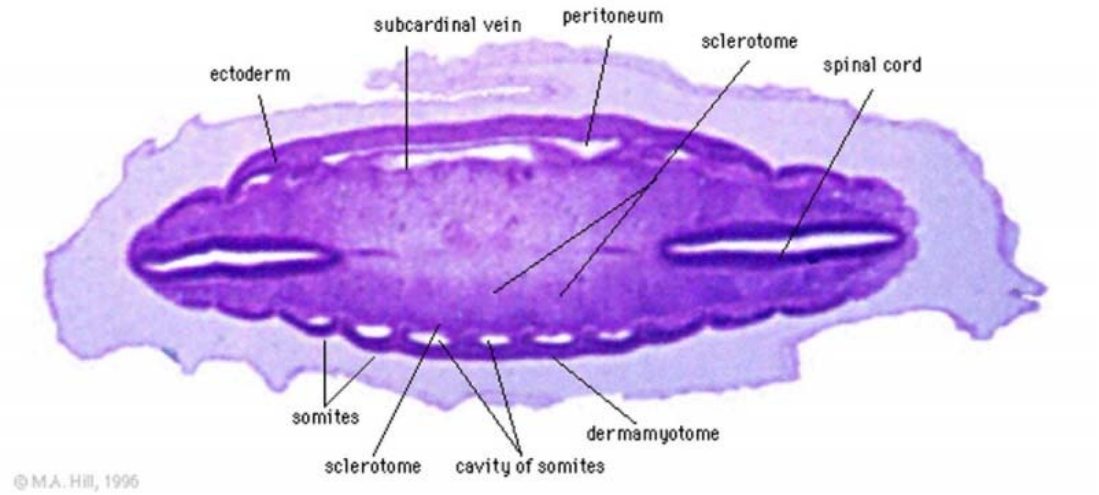

The head paraxial mesoderm is unsegmented. Neural crest cells invade into the head mesoderm and both contribute to head formation

The trunk paraxial mesoderm segments into **somites** that are thought to form by a **clock-wavefront** model. Starting from the cranial end of the embryo, the pairs of somites start to form at regular time intervals either side of the midline.

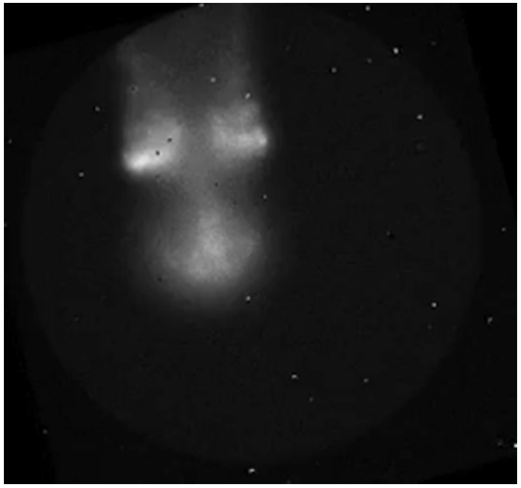
In the lateral plate mesoderm, spaces start to form at several locations which then join to form one continuous cavity called the coelom

*From Moore KL, Persaud TVN, Shiota K: Color Atlas of Clinical Embryology, 2nd ed. Philadelphia, WB Saunders, 2000.*

## Section through human embryo





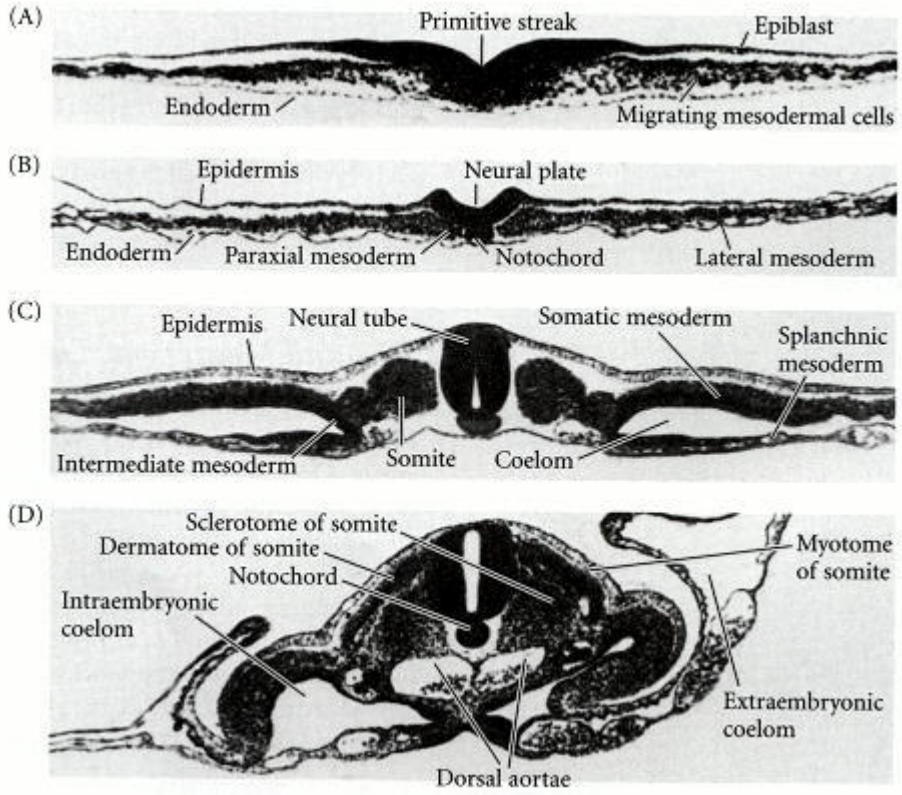


## Clock-wavefront

Transcription factor Hes1 (Hairy and enhancer of split – 1) in presomitic mesoderm

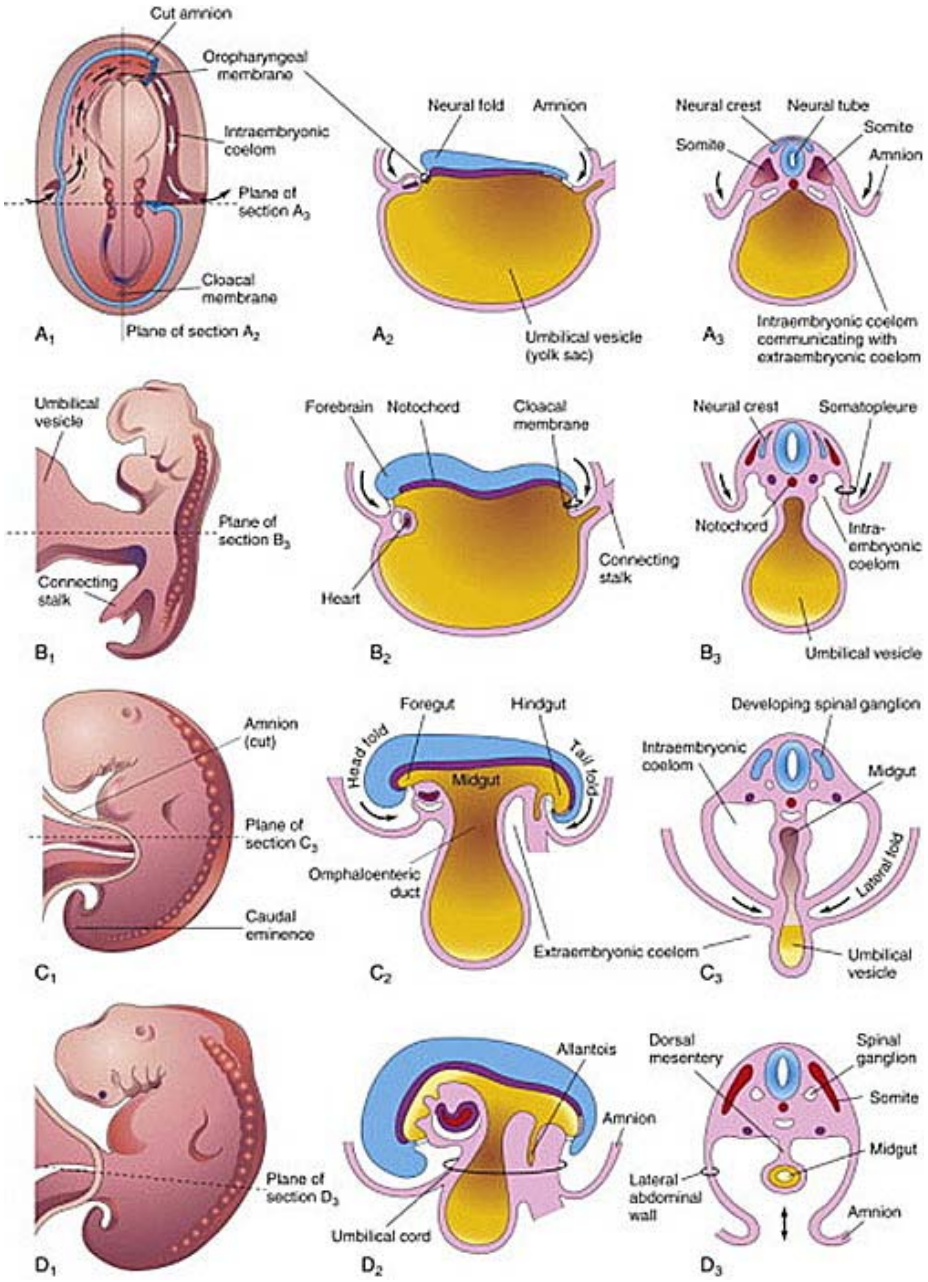
Expression of Hes1 in presomitic mesoderm (PSM) in the mouse embryo. Embryonic day E10.5 Hes1-Ub1-Luc embryo. Images were taken by 20-min exposure and binning of pixels 4 × 4 over a period of 15 h. Oscillation was propagated from the caudal end to S0 in the PSM.

# Real transverse sections of the chick embryo




Gastrulation and neurulation in the chick embryo, focusing on the mesodermal component. (A) Primitive streak region, showing migrating mesodermal and endodermal precursors. (B) Formation of the notochord and paraxial mesoderm. (C, D) Differentiation of the somites, coelom, and the two aortae (which will eventually fuse). A-C, 24-hour embryos; D, 48-hour embryo

Developmental Biology. 6th edition.
Gilbert SF.
Sunderland (MA): Sinauer Associates; 2000.

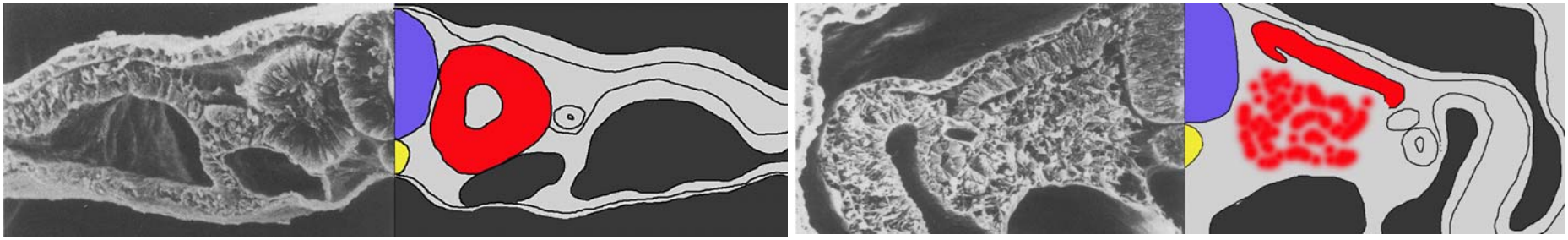


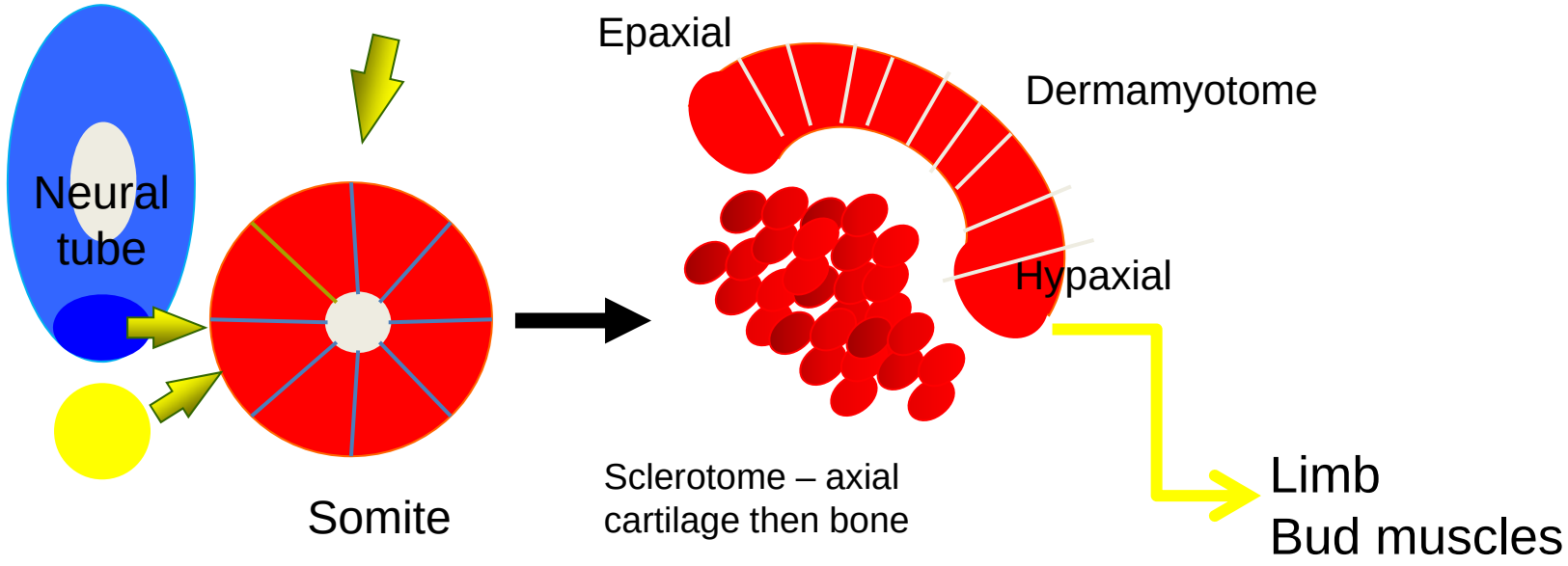

Change in shape from week 3 to week 4

**Embryonic folding**. Endoderm encloses the forming gut and the mesoderm comes round with it.

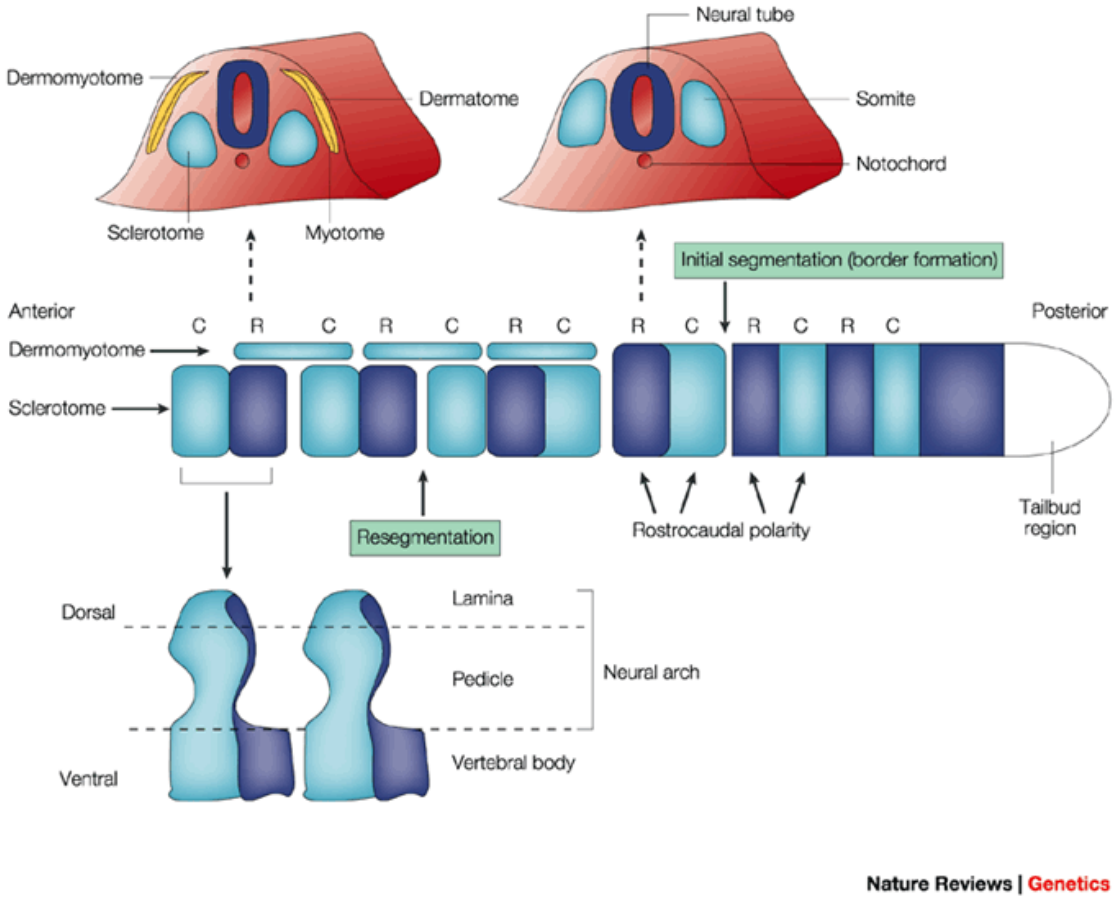
*From Moore KL, Persaud TVN, Shiota K: Color Atlas of Clinical Embryology, 2nd ed. Philadelphia, WB Saunders, 2000.*

## Somite differentiation in the chick embryo



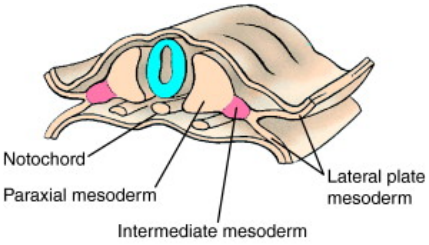


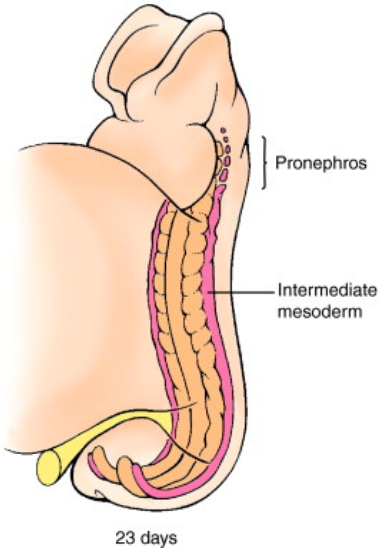
**Metameric segmentation** – somites form muscle blocks, vertebrae and determines exit points of spinal nerves

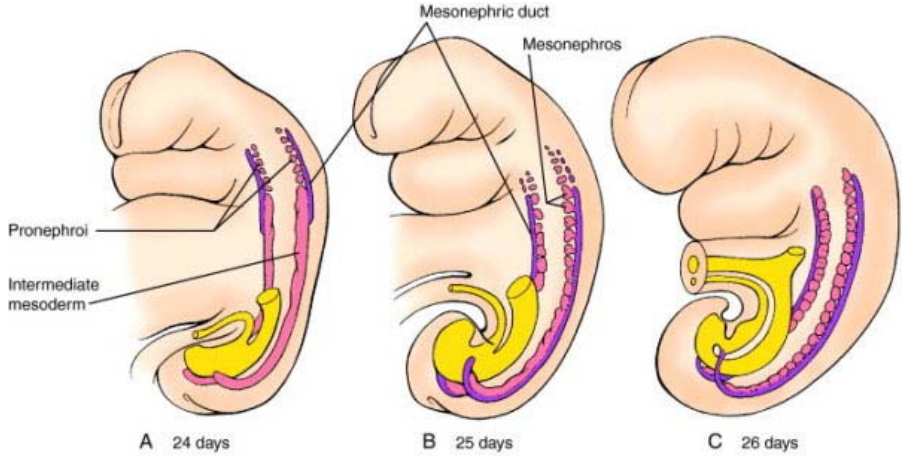



The making of the somite: molecular events in vertebrate segmentation
Yumiko Saga & Hiroyuki Takeda
Nature Reviews Genetics 2, 835-845 (November 2001)

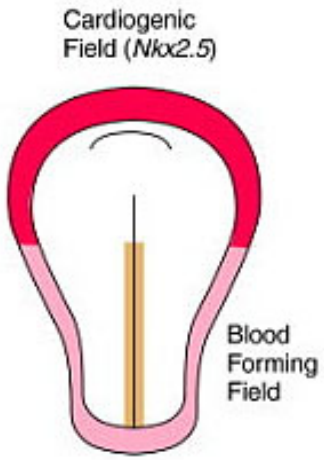
The **intermediate mesoderm** forms the **urogenital system**
Kidneys and gonads – pronephros, mesonephros and metanephros

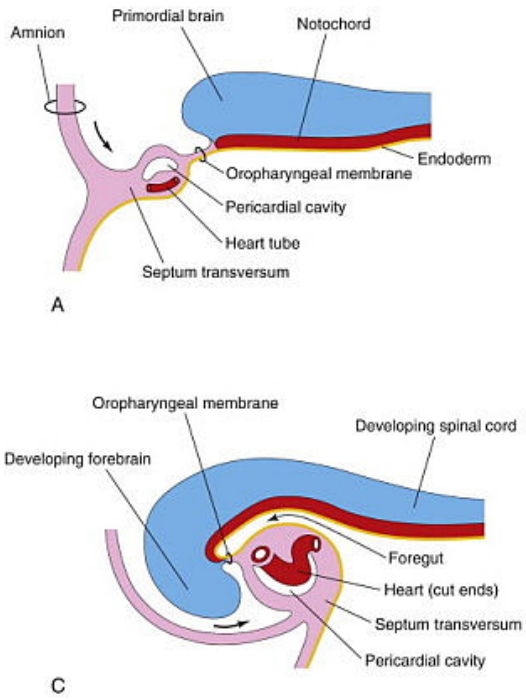


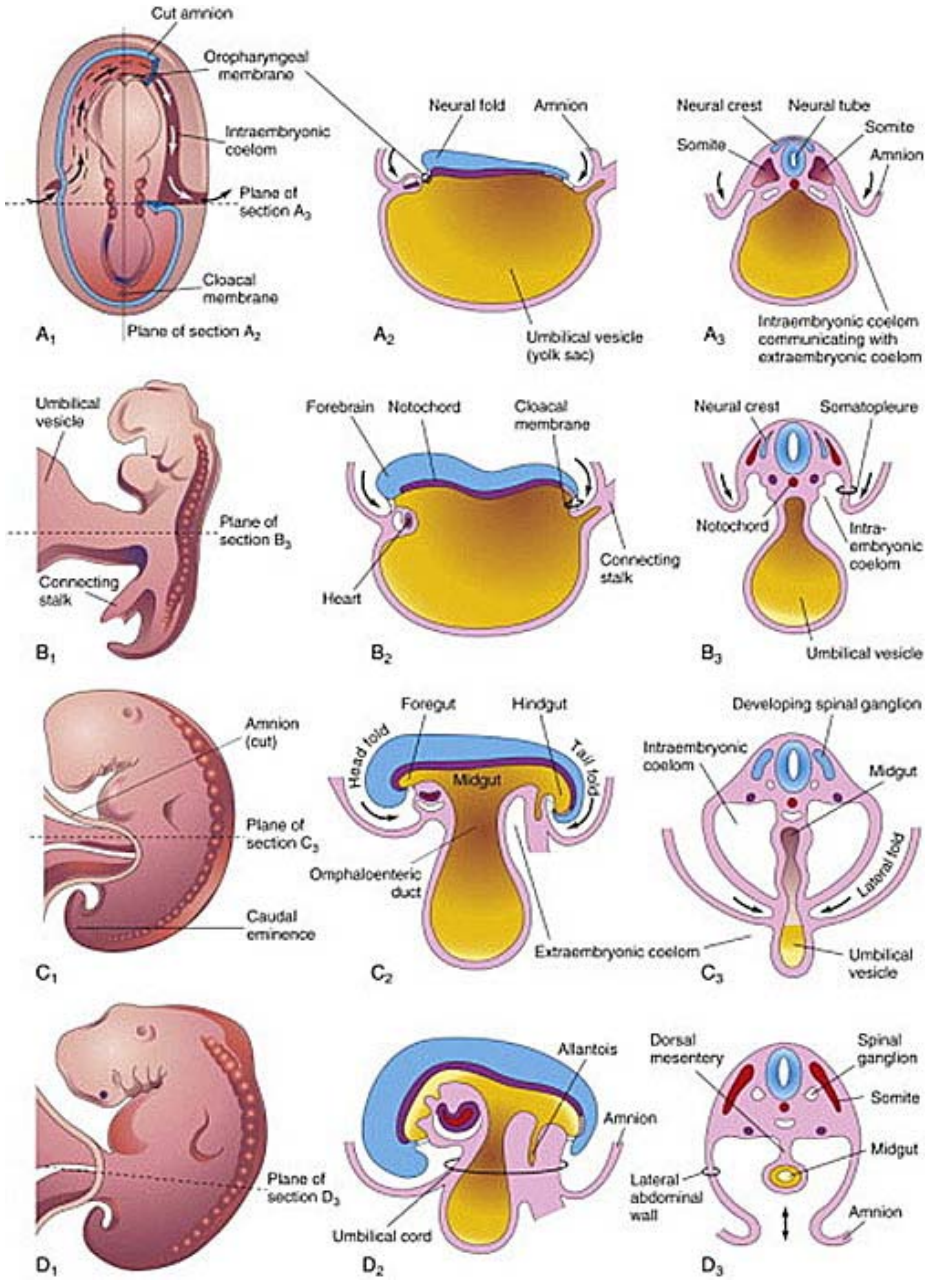
The heart forms from a horseshoe shaped **cardiogenic region** of mesoderm in the most anterior region of the embryo which folds into its final position on the ventral region of the thorax.




**Schoenwolf: Larsen's Human Embryology, 4th ed.**


*From Moore KL, Persaud TVN, Shiota K: Color Atlas of Clinical Embryology, 2nd ed. Philadelphia, WB Saunders, 2000.*




**Lateral plate mesoderm** forms the tissue surrounding the coelomic cavities.

At the level of the abdomen – peritoneal,
at the level of the thorax – pleural,
at the level of the heart field - pericardial

*From Moore KL, Persaud TVN, Shiota K: Color Atlas of Clinical Embryology, 2nd ed. Philadelphia, WB Saunders, 2000.*

Don’t forget to revise lecture content from last week for tomorrow’s test – ONLY **week 3 of development** only 5 questions