

BGDA Lecture - Development of the Embryo/Fetus 1

From Embryology

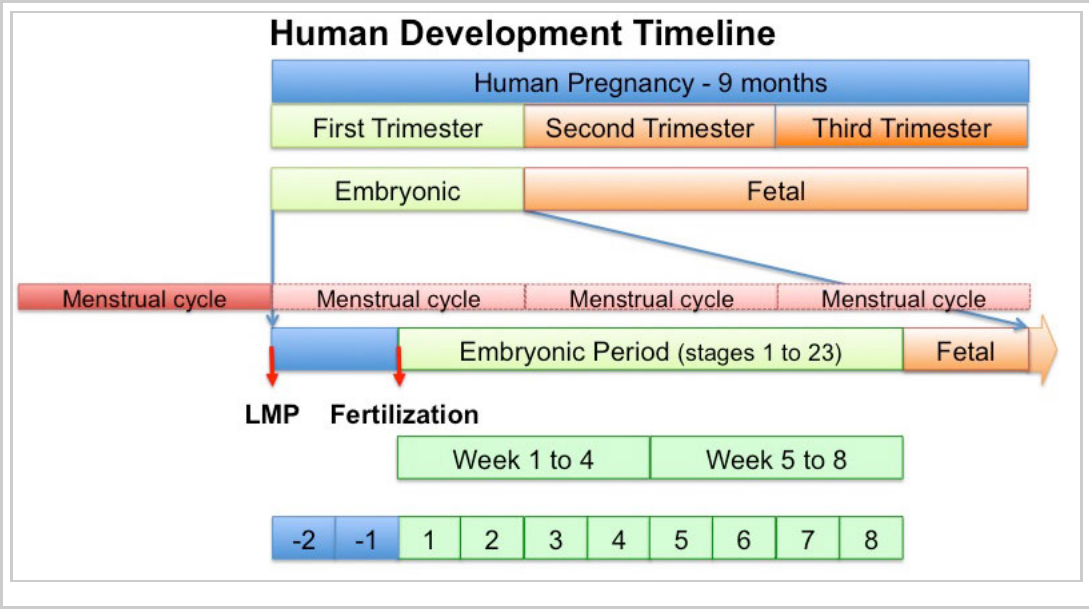


Introduction

In medicine foundations you were given a broad overview of human development. Now in BGDA we will be working through the human development process in more detail, focussing on key events.

- Begin by reviewing the recent Foundations Lecture and Practical.
- This BGDA lecture covers conceptus development from fertilization to implantation to trilaminar embryo formation.
 - Note that fertilization and week 1 concepts have already been covered in an earlier BGDA lecture.
- The lecture will also introduce early fetal membranes and placentation.

Lecture Archive[Expand]



Textbooks

[Collapse]



UNSW Embryology

Hill, M.A. (2015). *UNSW Embryology* (15th ed.) Retrieved May 7, 2015, from <https://embryology.med.unsw.edu.au>

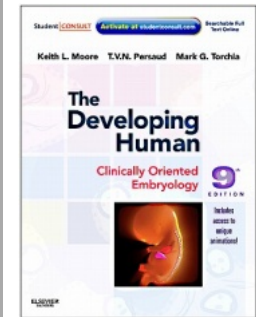


- BGDA Practical 3 - Fertilization to Implantation
- Menstrual Cycle | Oocyte | Spermatozoa | Meiosis | Mitosis
- Fertilization | Zygote | Morula | Blastocyst | Implantation
- Gastrulation | Somitogenesis
- Week 1 | Week 2 | Week 3
- Lecture - Fertilization | Lecture - Week 1 and 2

Links: More Embryology Textbooks

The Developing Human: Clinically Oriented Embryology

Citation: The Developing Human: Clinically Oriented Embryology 8th ed. Moore, Keith L; Persaud, T V N; Torchia, Mark G Philadelphia, PA : Saunders/Elsevier, c2011. (links only function with UNSW connection)



1. Introduction to the Developing Human (<http://er.library.unsw.edu.au/er/cgi-bin/eraccess.cgi?url=http://www.unsw.eblib.com.wwwproxy0.library.unsw.edu.au/patron/Read.aspx?p=1430154&pg=23>)
2. First Week of Human Development (<http://www.unsw.eblib.com.wwwproxy0.library.unsw.edu.au/patron/Read.aspx?p=1430154&pg=35>)
3. Second Week of Human Development (<http://www.unsw.eblib.com.wwwproxy0.library.unsw.edu.au/patron/Read.aspx?p=1430154&pg=63>)
4. Third Week of Human Development (<http://www.unsw.eblib.com.wwwproxy0.library.unsw.edu.au/patron/Read.aspx?p=1430154&pg=75>)

More Textbooks?

BGDA Practical Classes

Practical 3 - Fertilization to Implantation	Practical 6 - Implantation to 8 Weeks	Practical 12 - Fetal Period
	Practical 14 - Placenta and Fetal Membranes	

Human Reproductive Cycle

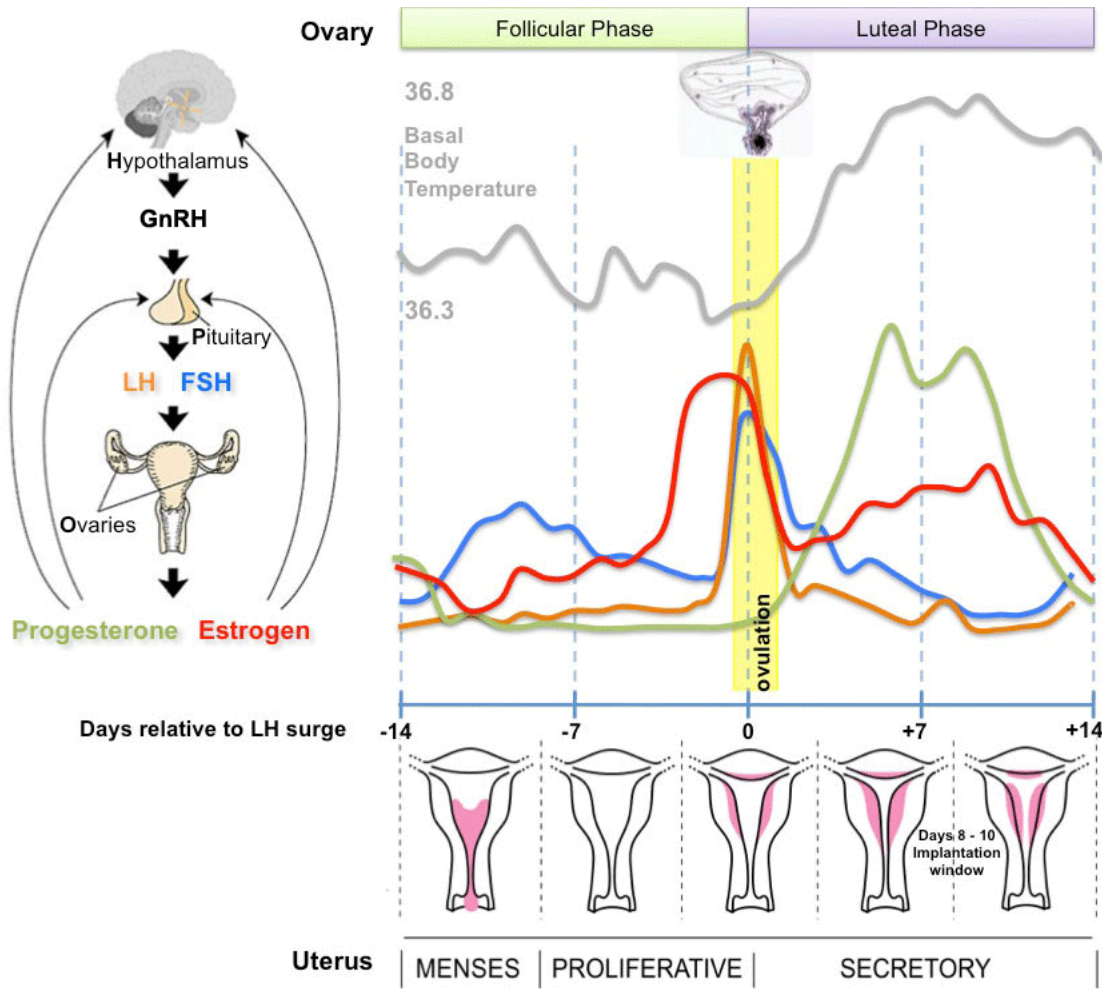
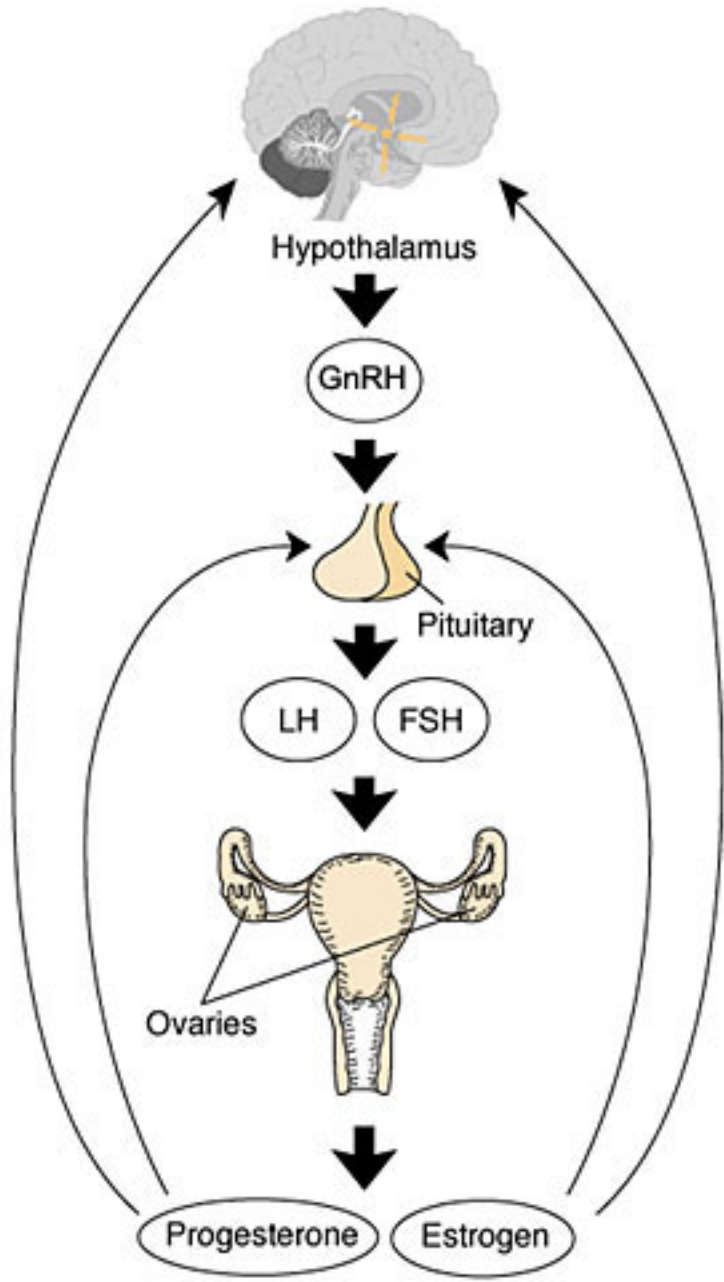
- Meiosis in gonad produces haploid gametes (egg and sperm)

Female

- Menstrual Cycle a regular cycle of reproduction (28 days)
- begins at puberty, release of 1 egg (oocyte) every cycle
- Endocrine controlled (HPG axis) **H**ypothalamus - **P**ituitary - **G**onad

Male

- continuous production of sperm (spermatozoa)
- begins at puberty, release millions of spermatozoa
- Endocrine controlled (HPG axis) **H**ypothalamus - **P**ituitary - **G**onad

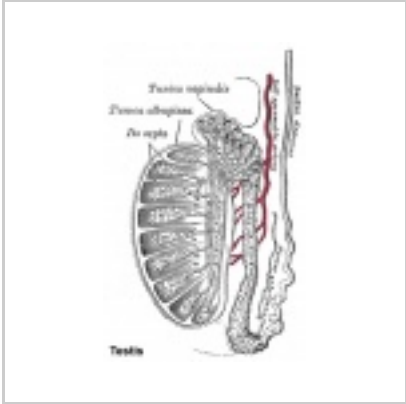


Gametogenesis

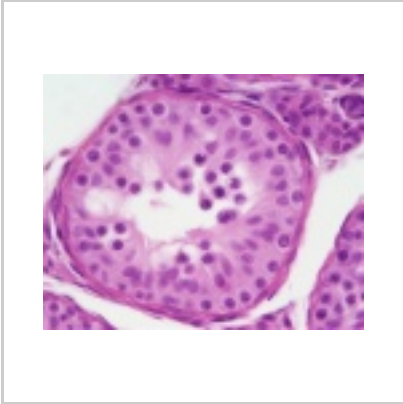
Male

The testes have two functions.

1. produce the male gametes or **spermatozoa**
2. produce male sexual hormone, **testosterone** (internal and external genitalia, sex characteristics)



Historic testis drawing



Child Seminiferous tubule



Adult Seminiferous tubule showing spermatozoa developmental stages



Seminiferous tubule cross-section and supporting cells



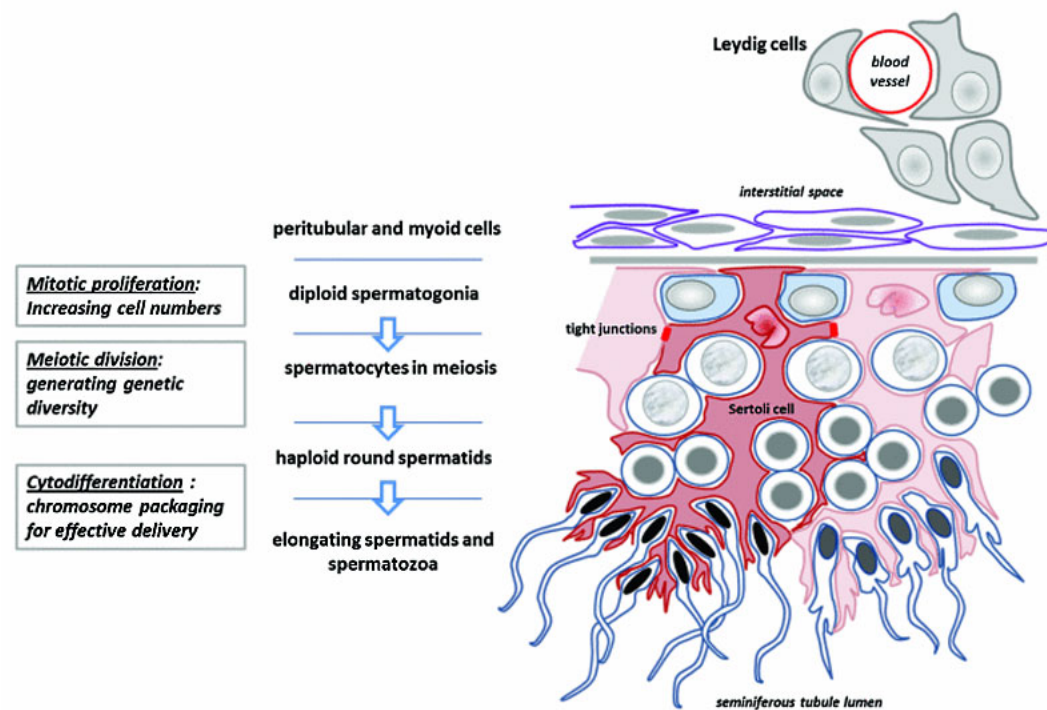
Human spermatozoa

Human spermatozoa take about **48 days** from entering meiosis until morphologically mature spermatozoa.

- Spermatogonia - are the first cells of spermatogenesis
- Primary spermatocytes - large, enter the prophase of the first meiotic division
- Secondary spermatocytes - small, complete the second meiotic division
- Spermatid - immature spermatozoa
- Spermatozoa - differentiated gamete

Spermatozoa development: primordial germ cell - spermatogonia - primary spermatocyte - secondary spermatocytes - spermatid - spermatozoa

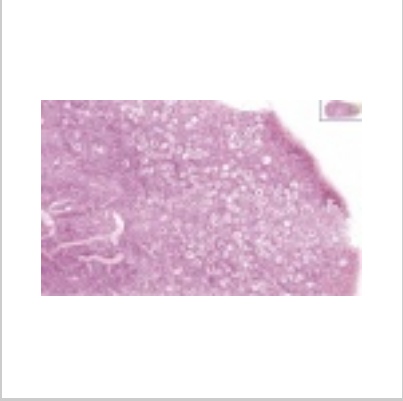
Sertoli cells (support cells) **Interstitial cells** or **Leydig cells** (produce hormone)



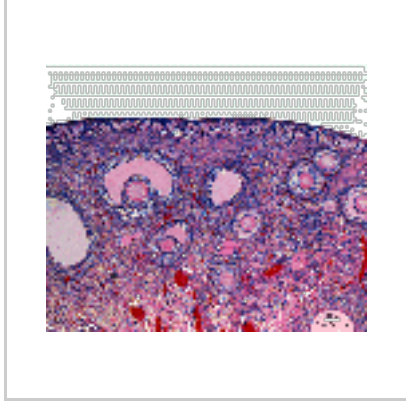
Female

The ovaries have two functions.

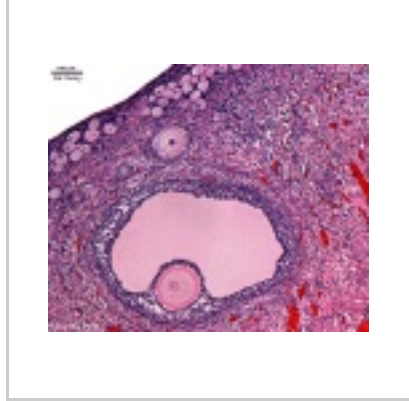
1. produce the female gametes or **oocytes**
2. produce female hormones, estrogen and progesterone (secondary sex characteristics, menstrual cycle)



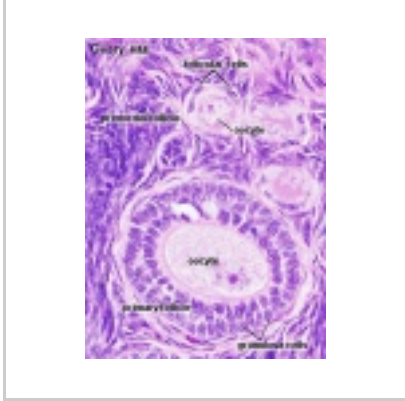
infant ovary



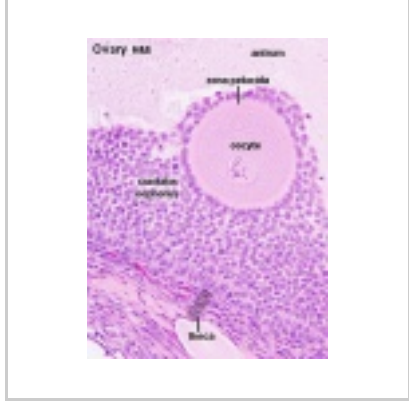
overview of ovary



three stages of follicle development

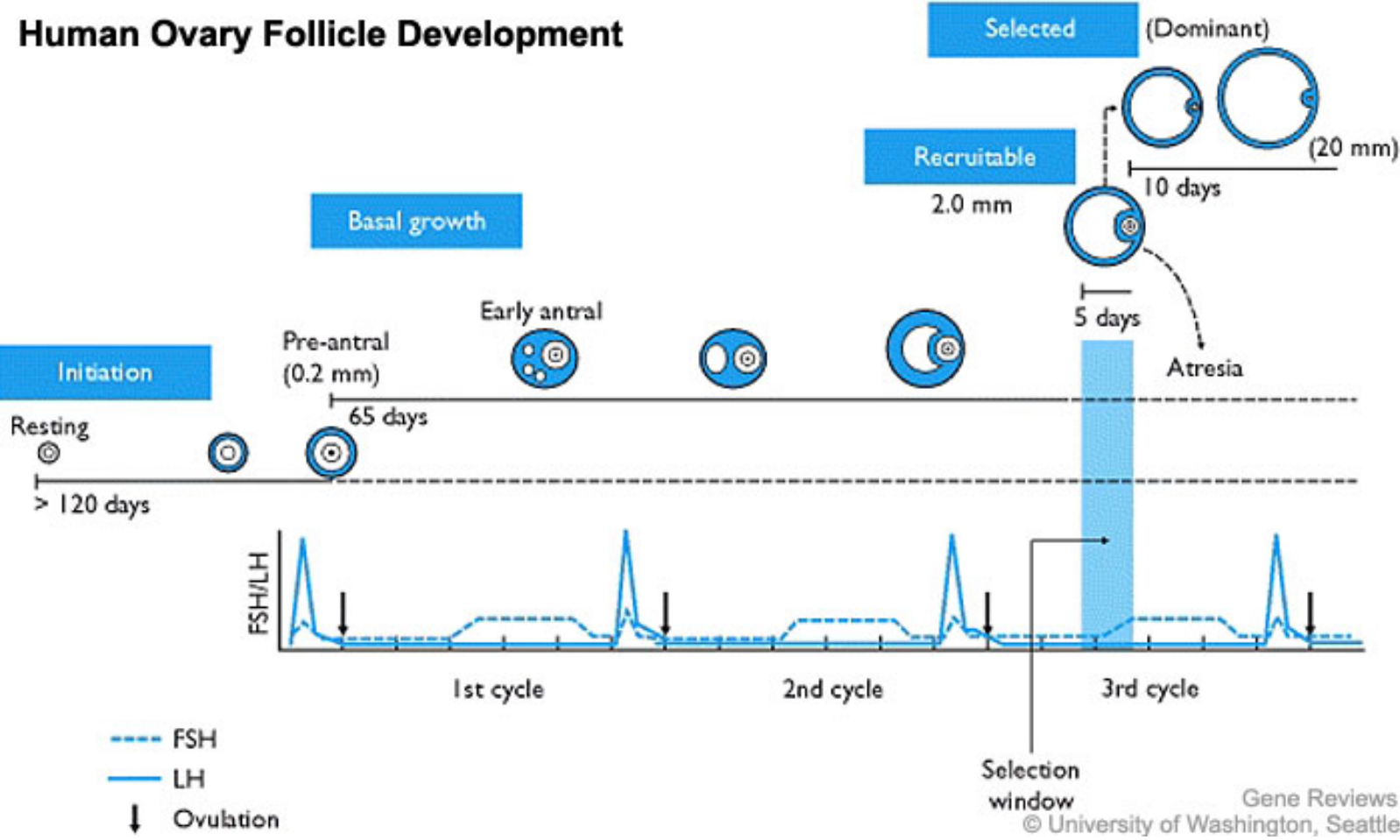


primary follicle



tertiary follicle

In an adult human female the development of a primordial follicle containing an oocyte to a preovulatory follicle takes in excess of **120 days**.



Human ovary follicle development

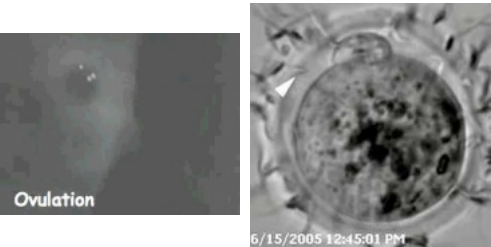
Ovarian Follicle Stages: primordial follicle - primary follicle - secondary follicle - tertiary follicle - preovulatory follicle

Follicle cells (support cells) **Theca cells** (produce hormone)

Links: Spermatozoa Development | Oocyte Development | MBoC - Figure 20-18. Influence of Sry on gonad development (<http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=mboc4.figgrp.3716>) | Endocrinology - Comparative anatomy of male and female reproductive tracts (<http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=endocrin&part=A972&rendertype=box&id=A1230>)

Fertilization

- Oogenesis - 1 gamete produced/meiosis + 3 polar bodies, meiosis is slow, 1 egg produced and released at ovulation
- Spermatogenesis - 4 gametes produced/meiosis, meiosis is fast, 200-600 million sperm released at ejaculation

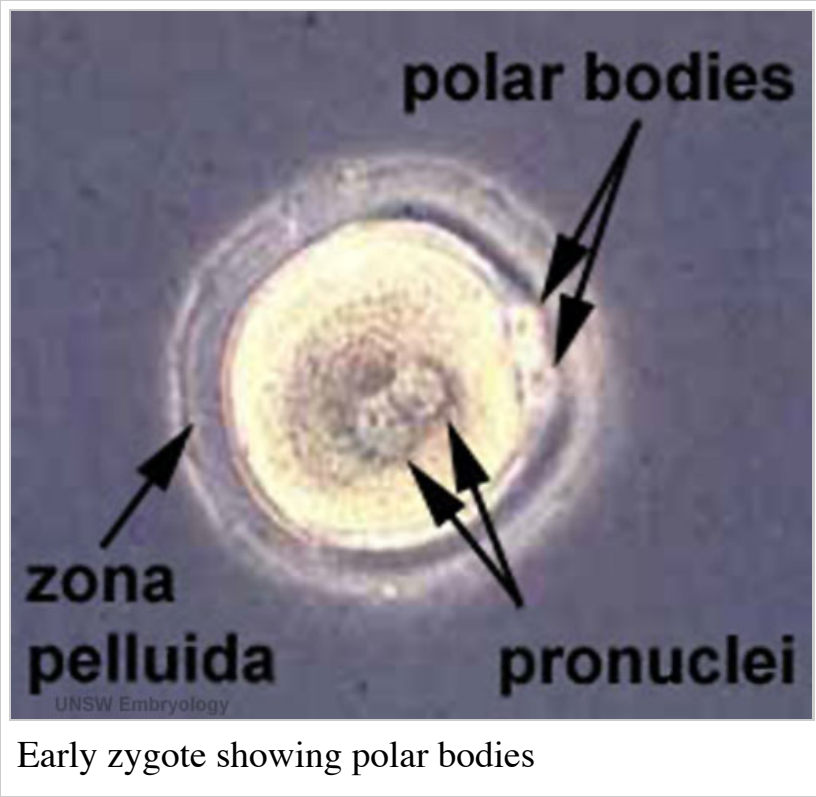


Fertilization Site

- Fertilization usually occurs in first 1/3 of uterine tube (oviduct, Fallopian tube)
- Fertilization can also occur outside uterine tube associated with Assisted Reproductive Technologies (IVF, GIFT, ZIFT...) and ectopic pregnancy
- The majority of fertilized eggs do not go on to form an embryo

Fertilization - Spermatozoa

- **Capacitation** - alteration of the spermatozoa metabolism and surface proteins
- **Sperm Binding** - zona pellucida protein ZP3 acts as receptor for sperm
- **Acrosome Reaction** - exocytosis of acrosome contents (Calcium mediated) MBoC - Figure 20-31. The acrosome reaction that occurs when a mammalian sperm fertilizes an egg (<http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=mboc4.figgrp.3741>)
 - enzymes to digest the zona pellucida
 - exposes sperm surface proteins to bind ZP2
- **Membrane Fusion** - between sperm and egg, allows sperm nuclei passage into egg cytoplasm



Approximate Timing of Early Human Events (in vitro)



20 min - components



28 min - spermatozoa penetrates zone pellucida



31 min - spermatozoa penetrates oocyte - fertilization

See also clock in lower righthand corner for the approximate timing of events.

Links: Human Fertilization Detail Movie | Human Fertilization Movie

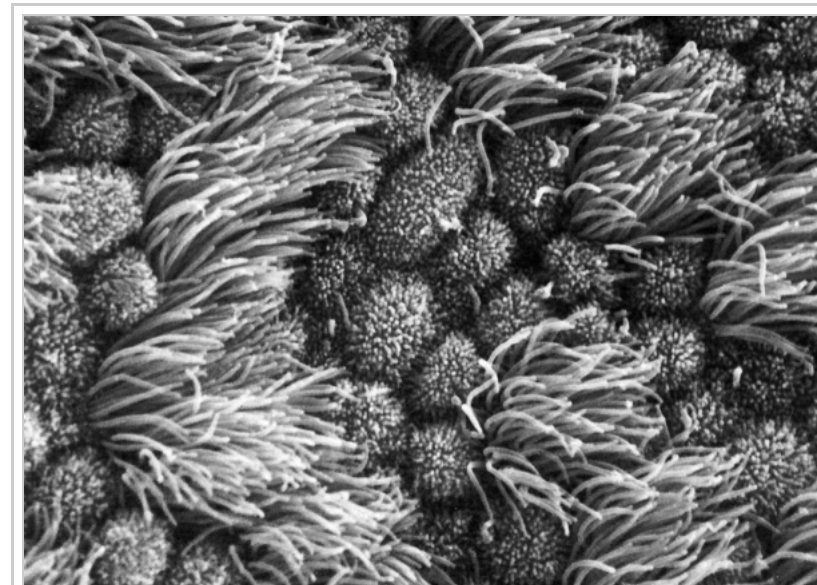
Reference: PMID 22695746 J Assist Reprod Genet.
(<http://link.springer.com/article/10.1007%2Fs10815-012-9815-x>)

Fertilization - Oocyte

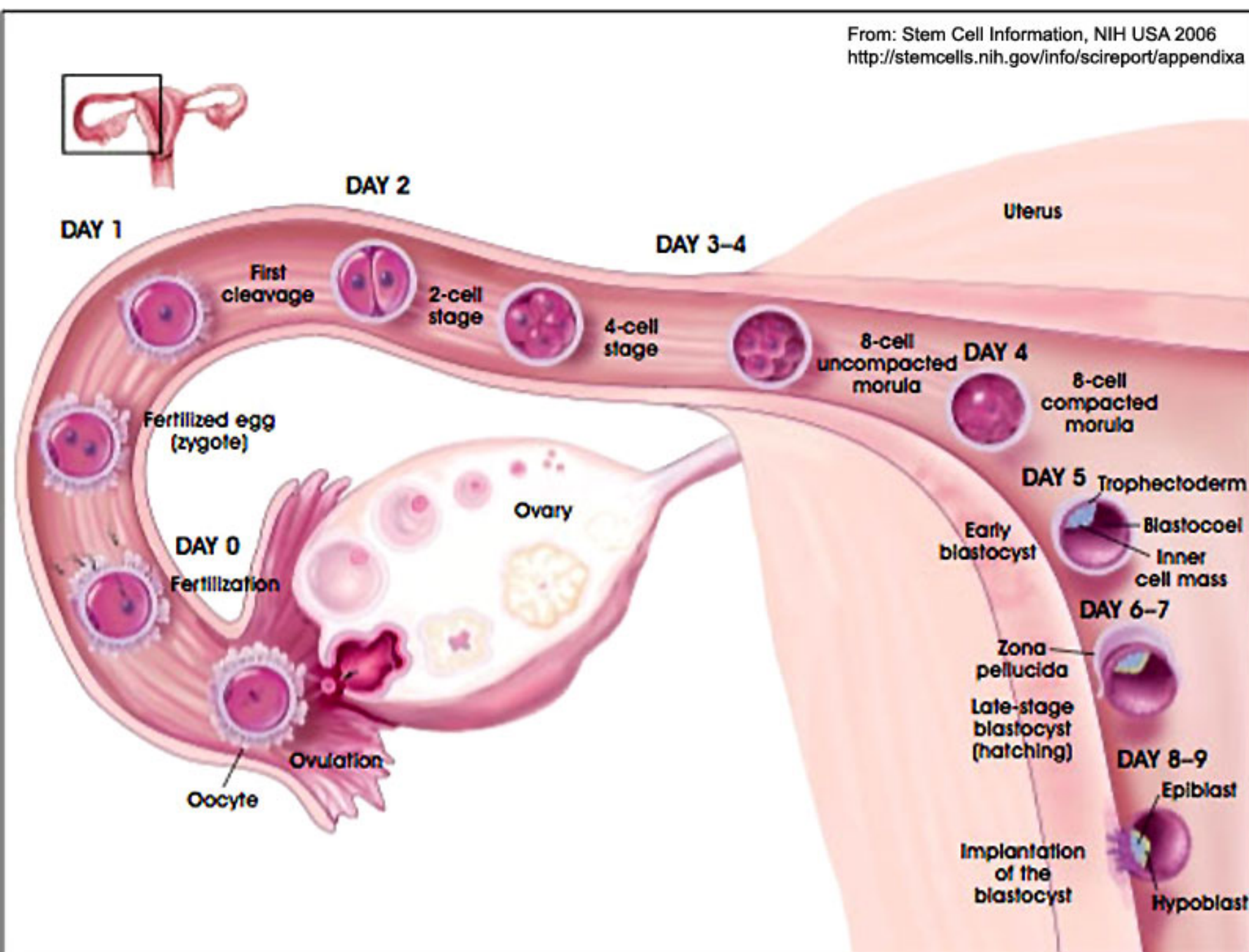
- **Membrane Depolarization** - caused by sperm membrane fusion, primary block to polyspermy
- **Cortical Reaction** - IP₃ pathway elevates intracellular Calcium, exocytosis of cortical granules MBoC - Figure 20-32. How the cortical reaction in a mouse egg is thought to prevent additional sperm from entering the egg (<http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=mboc4.figgrp.3743>)
 - enzyme alters ZP3 so it will no longer bind sperm plasma membrane
- **Meiosis 2** - completion of 2nd meiotic division
 - forms second polar body (a third polar body may be formed by meiotic division of the first polar body)

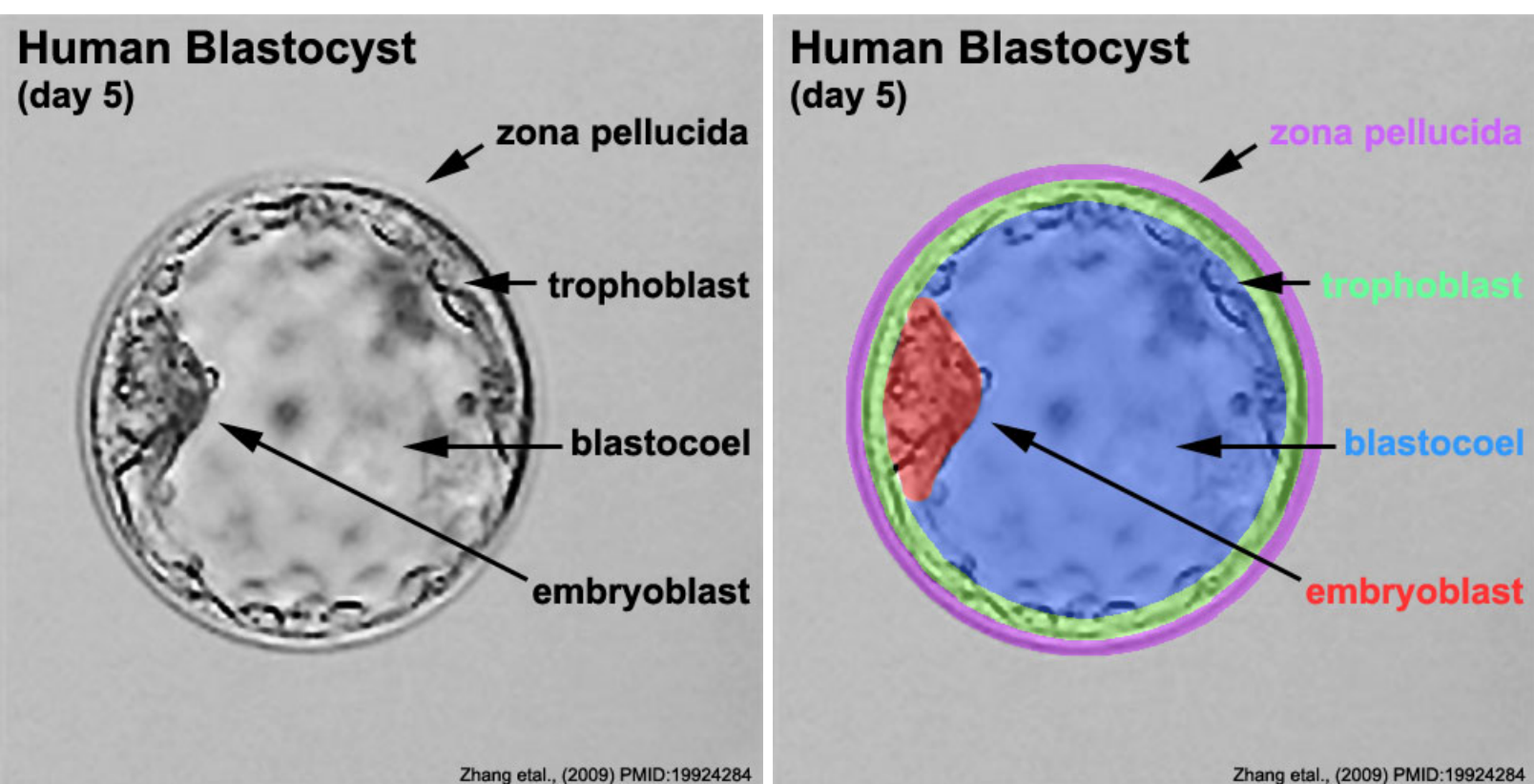
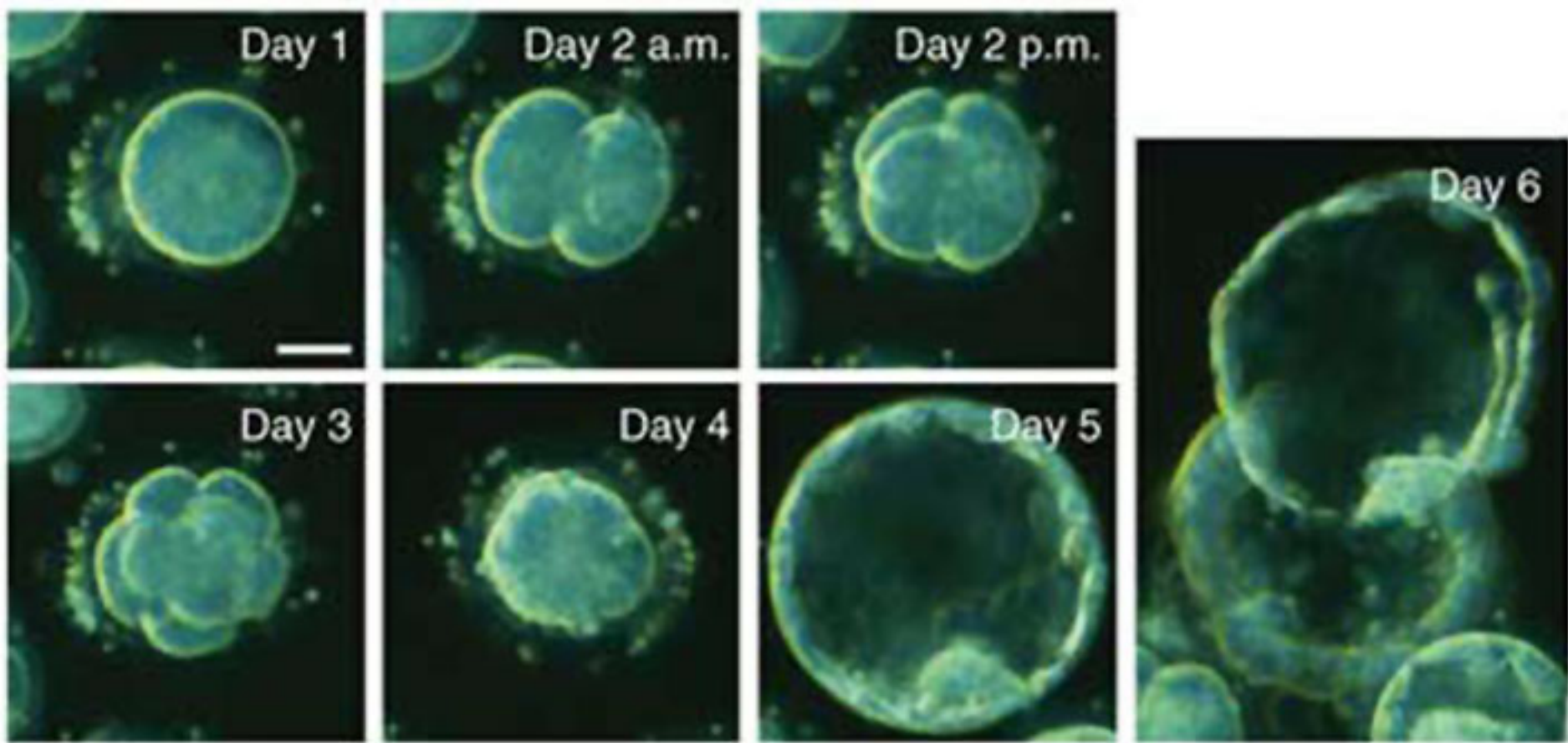


Week 1 and 2

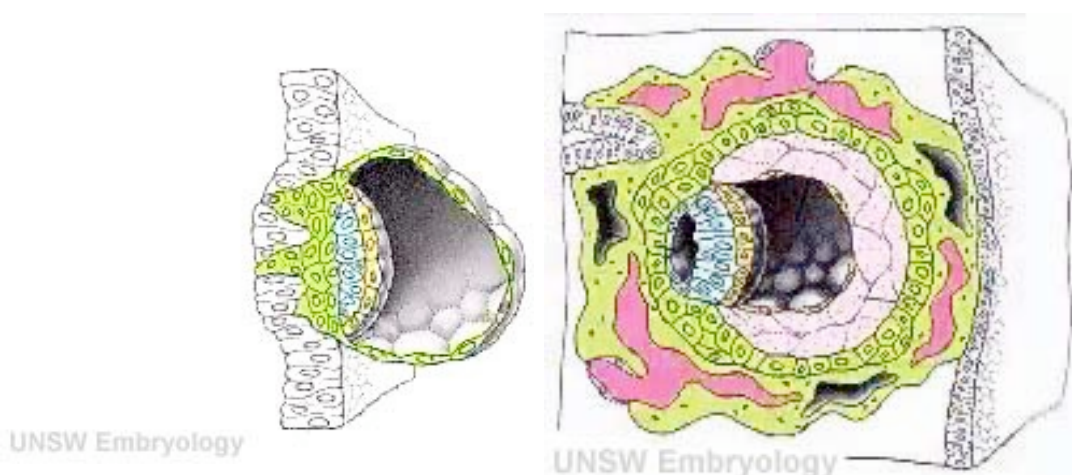


Human uterine tube ciliated epithelium (SEM)





Week 2 Implantation



Normal Implantation

- Uterine body
 - posterior, anterior, superior, lateral (most common posterior)
 - inferior implantation - placenta overlies internal os of uterus **Placenta Previa**

Abnormal Implantation

- Ectopic Sites
 - external surface of uterus, ovary, bowel, gastrointestinal tract, mesentery, peritoneal wall
 - If not spontaneous then, embryo has to be removed surgically
- Uterine - tubal pregnancy (most common ectopic)

Early Placenta



- interaction between implanting conceptus and uterine wall

- (endometrium)
- The uterine lining following implantation (Decidua)
 - forms 3 distinct regions, at approx 3 weeks
 - **Decidua Basalis** - implantation site
 - **Decidua Capsularis** - enclosing the conceptus
 - **Decidua Parietalis** - remainder of uterus
- uterine cavity is lost by 12 weeks

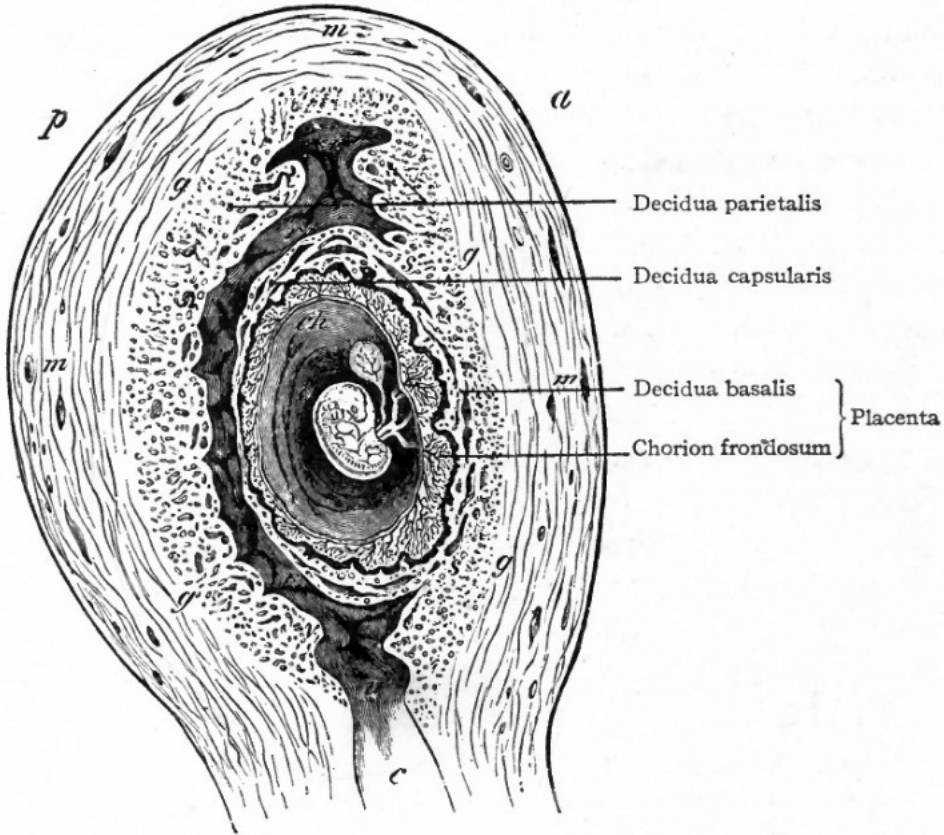
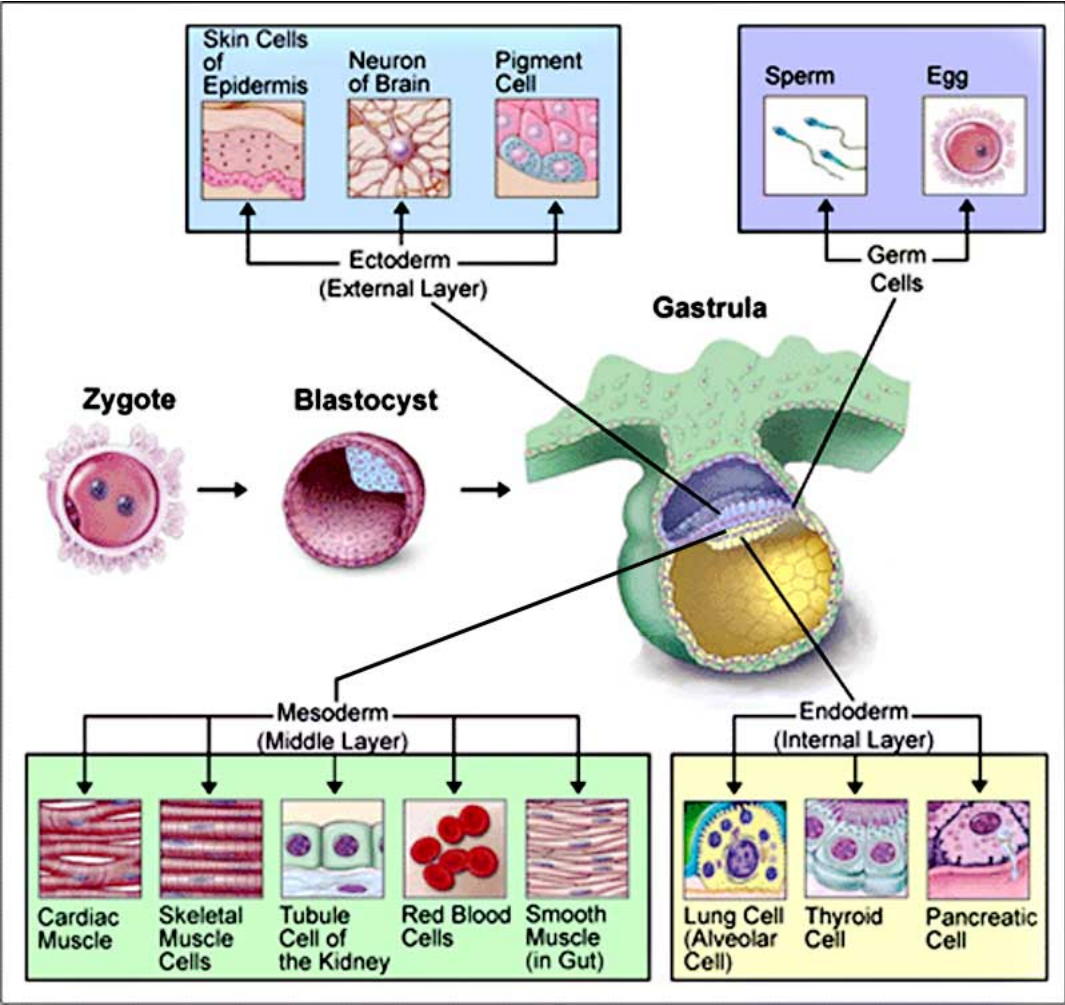


FIG. 494.—Semidiagrammatic sagittal section of human uterus containing an embryo of about five weeks. *Allen Thompson.*

Week 3 Gastrulation

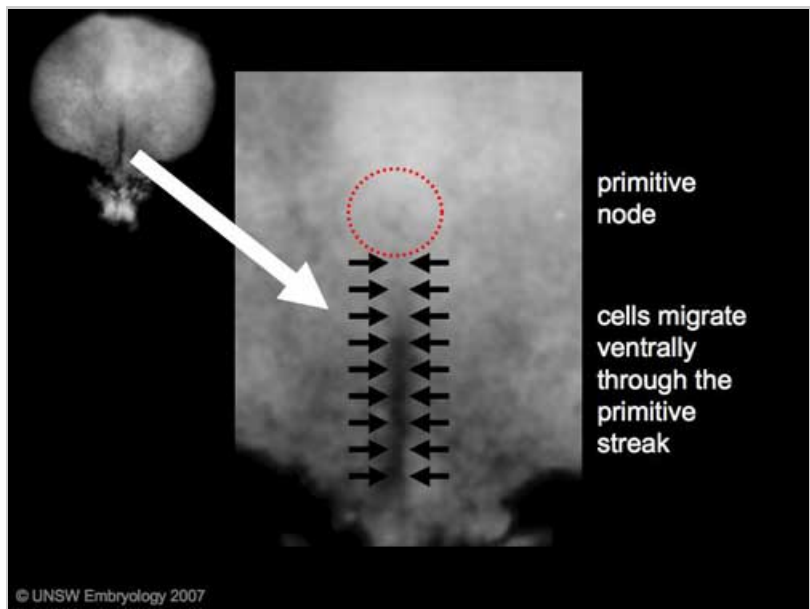
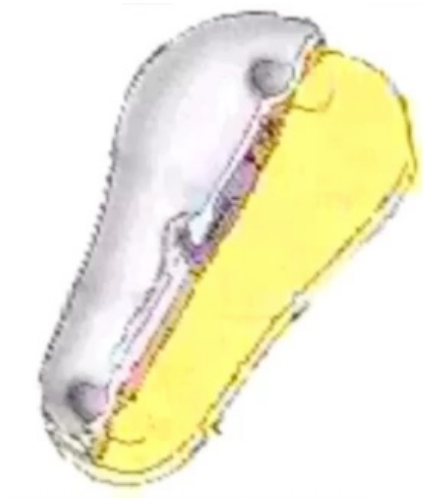
Gastrulation, (Greek = belly) means the formation of gut, but has been used in a more looser sense to to describe the formation of the trilaminar embryo. The epiblast layer, consisting of totipotential cells, derives all 3 embryo layers:endoderm, mesoderm and ectoderm. The primitive streak is the visible feature which represents the site of cell migration to form the additional layers. Historically, gastrulation was one of the earliest observable morphological event occurring in the frog embryo.

- primitive node - region in the middle of the early embryonic disc epiblast from which the primitive streak extends caudally (tail)
 - nodal cilia establish the embryo left/right axis
 - axial process extends from the nodal epiblast
- primitive streak - region of cell migration from the epiblast layer forming sequentially the two germ cell layers (endoderm and mesoderm)

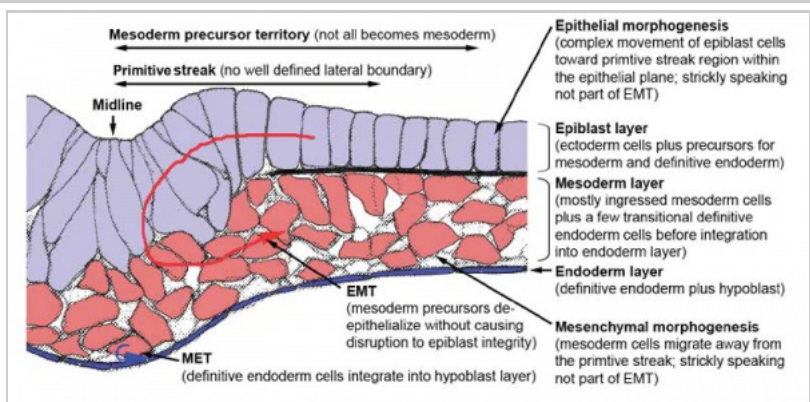


Notochord

The notochord is a structure which has an early **mechanical role** in embryonic disc folding and a major **signaling role** in patterning surrounding embryonic tissue development. This signaling role patterns many different tissues (neural plate, neural tube, somites, endodermal organs). It has its own sequence of development from a primitive axial process and is a developmental feature not present in the adult anatomy.

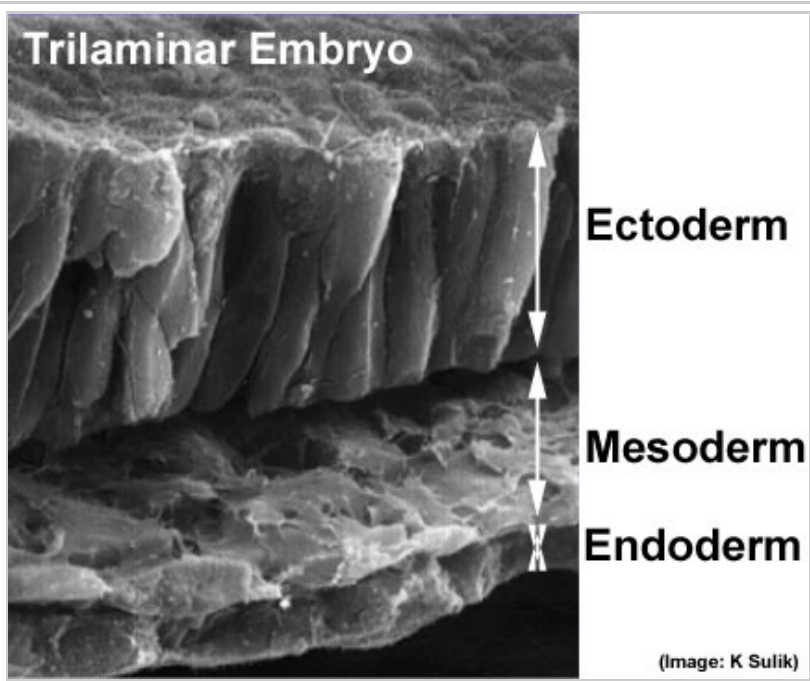


Stage7 primitive streak

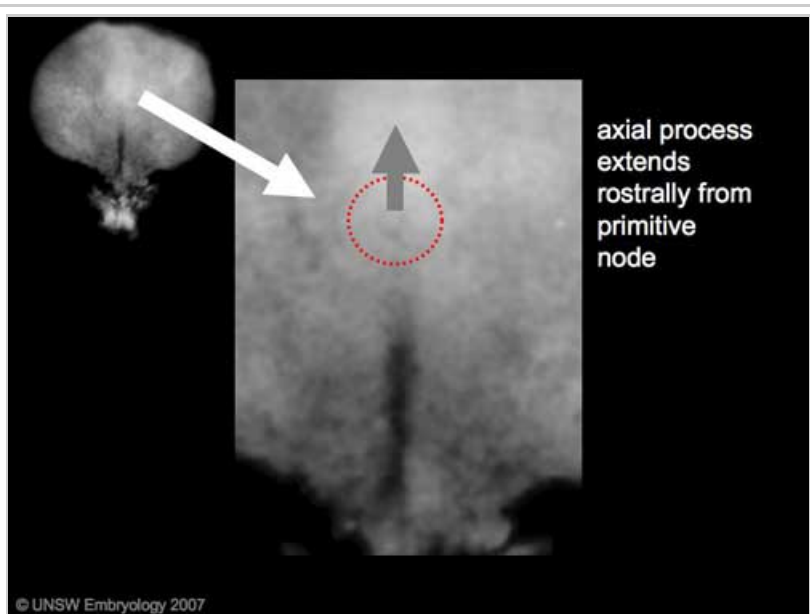


Chicken Gastrulation An amicable separation: Chick's way of doing EMT. Nakaya Y, Sheng G. Cell Adh Migr. 2009 Apr;3(2):160-3. Epub 2009 Apr 10. PMID: 19262172

gastrulation



Trilaminar embryo SEM



Stage7 axial process

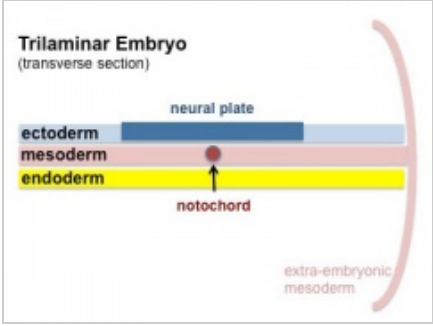
- **axial process** an initial epiblast hollow epithelial tube which extends in the midline from the primitive pit, cranially in the embryonic disc (toward the oral membrane).
- **neuroenteric canal** is a transient communication between the amnionic cavity and the yolk sac cavity formed by the axial process.
- **notochordal plate** forms from the axial process merging with the endoderm layer.
- **notochord** forms from the notochordal plate which then separates back into the mesoderm layer as a solid column of cells lying in the midline of the embryonic disc and running rostro-caudally (head to tail).
 - An alternate name for the notochord is "axial mesoderm".

Somitogenesis

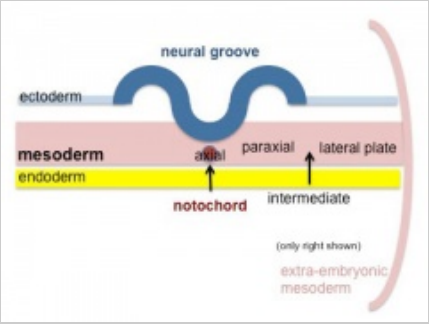
Mesoderm means the "middle layer" and it is from this layer that nearly all the bodies connective tissues are derived. In early mesoderm development a number of transient structures will form and then be lost as tissue structure is patterned and organised. Humans are vertebrates, with a "backbone", and the first mesoderm structure we will see form after the notochord will be **somites**.

Coelom, meaning "cavity", and major fluid-filled cavities can be seen to form both within the embryo (intraembryonic coelom) and outside the embryo (extraembryonic coelom). The **intraembryonic coelom** is the single primitive cavity that lies within the mesoderm layer that will eventually form the 3 major anatomical body cavities (**pericardial, pleural, peritoneal**).

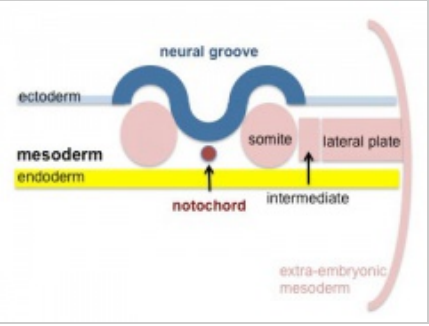
Mesoderm and Ectoderm Cartoons



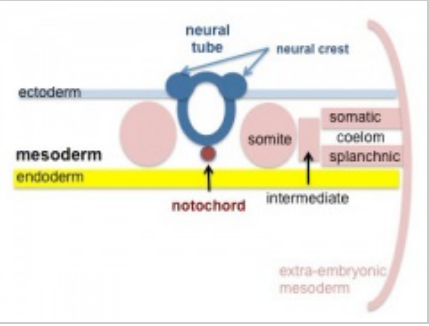
Trilaminar Embryo



Paraxial and Lateral Plate



Somites



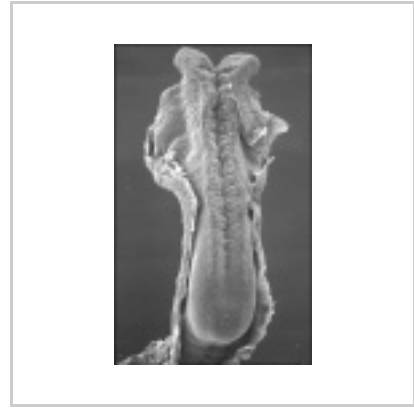
Somatic and Splanchnic

Somite initially forms 2 main components

- ventromedial- sclerotome forms vertebral body and intervertebral disc
- dorsolateral - dermomyotome forms dermis and skeletal muscle



Week 4 Neuralation



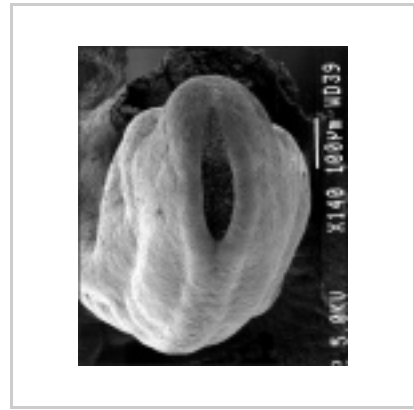
Stage 10 (22 - 23 days)



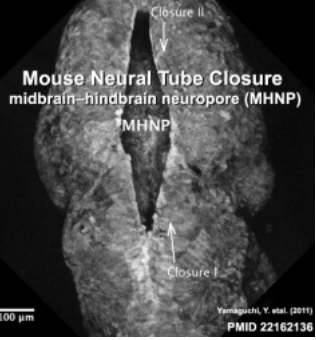
Stage 10 (22 - 23 days)



Stage 11 (23 - 26 days)



Stage 11 (26 - 30 days)

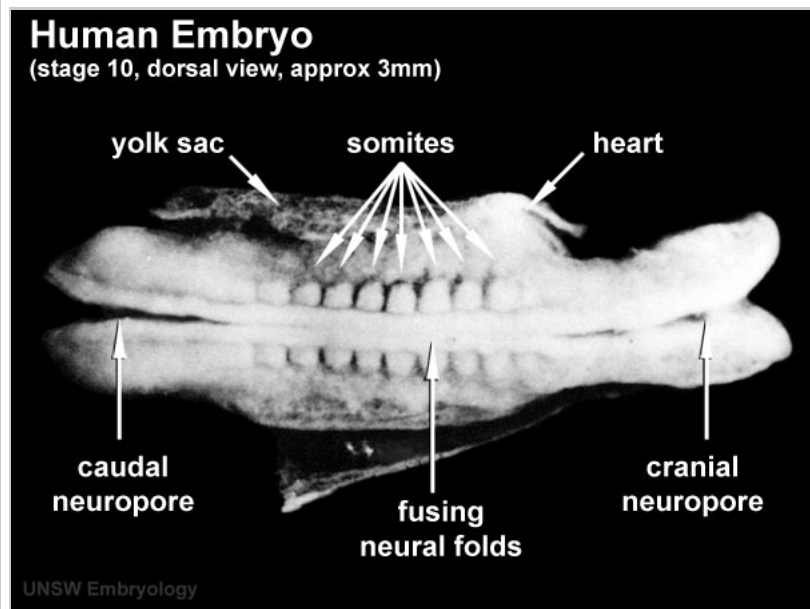


Neural Tube Close

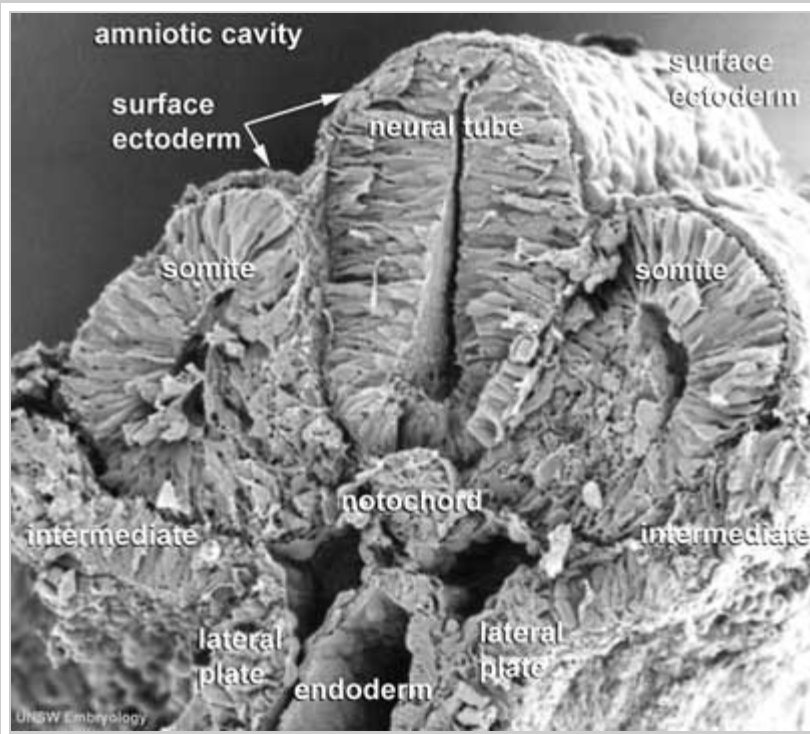
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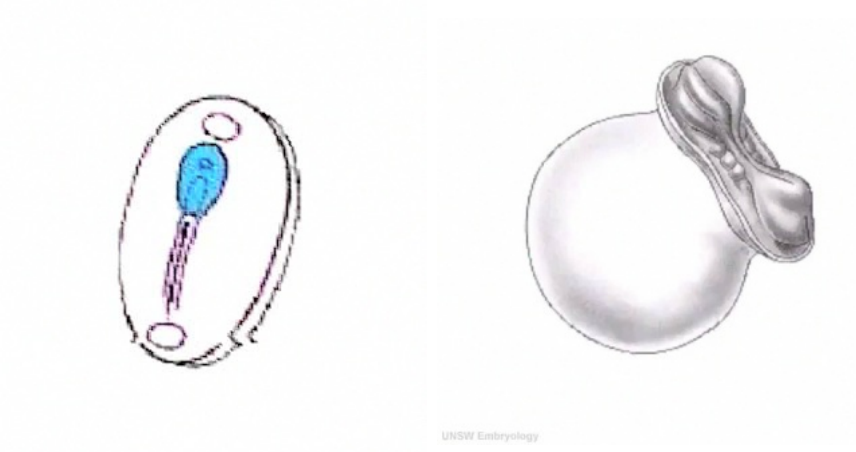
stage 9 Embryo



stage 10 Embryo



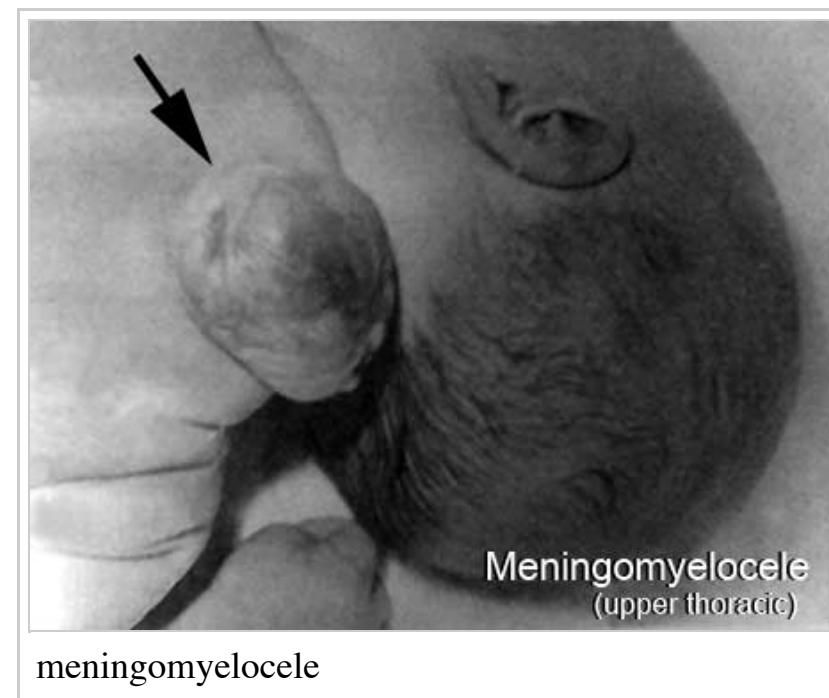
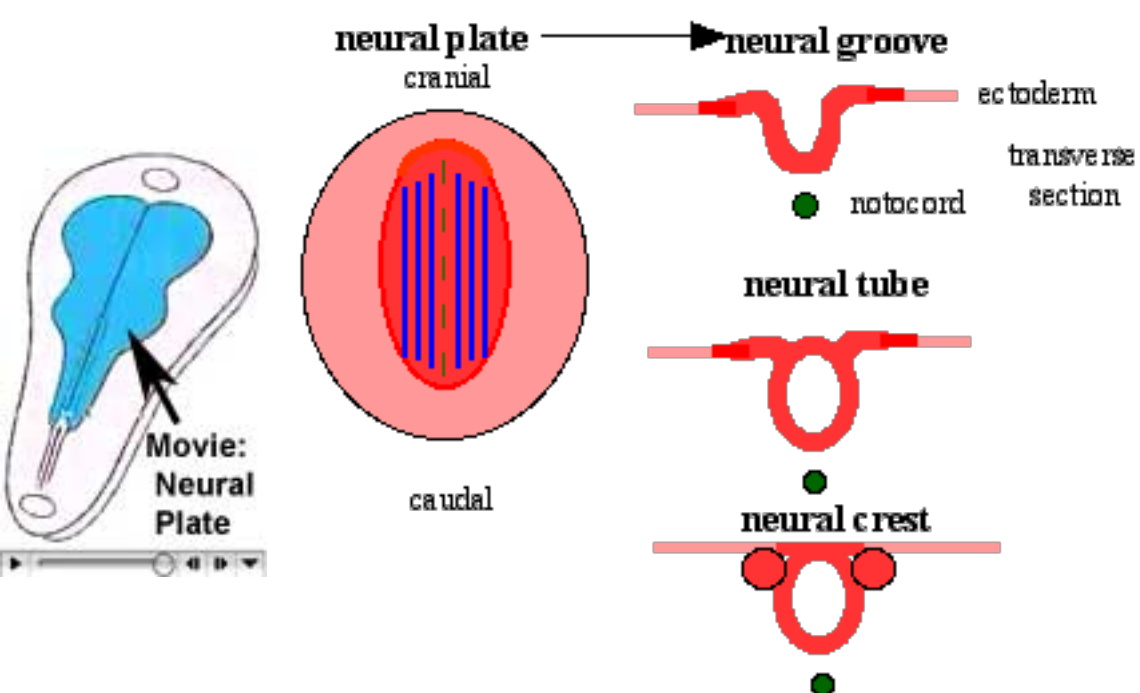
stage 11 Embryo



Ectoderm - 2 parts

- midline neural plate (columnar cells)
- lateral surface ectoderm (cuboidal cells)
 - sensory placodes
 - epidermis of skin, hair, glands, anterior pituitary, teeth enamel

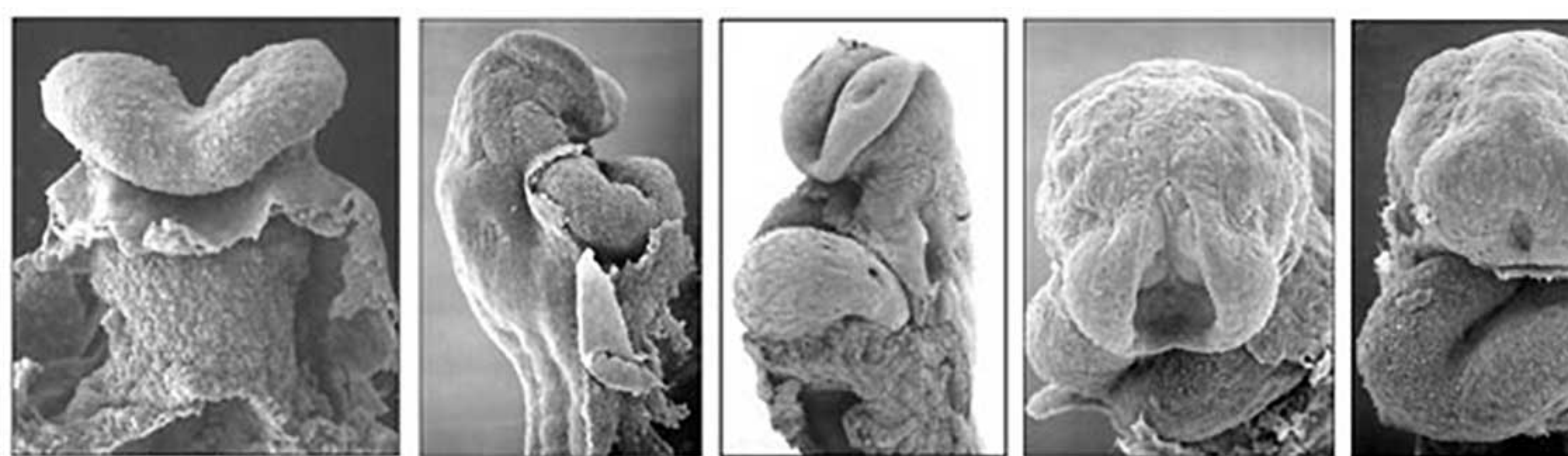
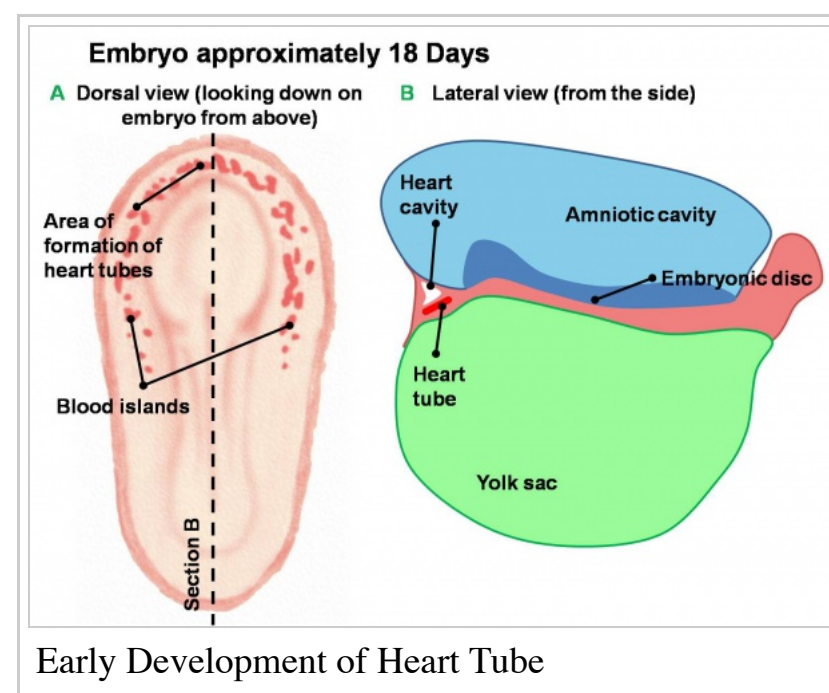
Neural Plate



- extends from buccopharyngeal membrane to primitive node
- forms above notochord and paraxial mesoderm
- neuroectodermal cells
 - broad brain plate
 - narrower spinal cord
- 3 components form: floor plate, neural plate, neural crest

Links: Neural System - Abnormalities | Folic Acid and Neural Tube Defects

Cardiogenesis



The Human Heart from day 10 to 25 (scanning electron micrograph)

- forms initially in splanchnic mesoderm of prechordal plate region - **cardiogenic region**
 - growth and folding of the embryo moves heart ventrally and downward into anatomical position
- week 3 begins as paired heart tubes that fuse to form single heart tube
- begins to beat in Humans- day 22-23

Blood Islands

- 2 populations of cells
 - peripheral- form endothelial cells that form the lining of all blood vessels
 - core- form blood cells (haemocytoblasts)

- all vessels (arteries and veins) appear initially the same

Blood Formation

- blood formation from stem cells occurs initially in the extraembryonic mesoderm of the yolk sac
- then later (week 5) throughout embryonic mesenchyme
- blood stem cells then migrate into the liver
 - then spleen, bone marrow, lymph nodes

Red Blood Cells

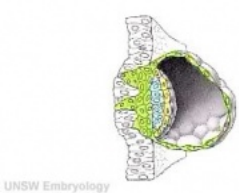
The only cells in the blood are nearly entirely fetal red blood cells (RBC).

These red blood cells differ from adult red blood cells in.

- often remaining nucleated
- contain fetal haemoglobin - has different oxygen and carbon dioxide binding characteristics

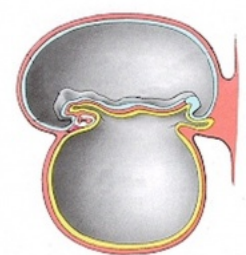
Links: Basic Cardiac Embryology

Early Placentation



The trophoblast layer has now differentiated into two morphologically distinct cellular layers.

- **Syncytiotrophoblasts** - form a multinucleated cytoplasmic mass by cytotrophoblast cell fusion and both invade the decidua and secrete hCG
- **Cytotrophoblasts** - form a cellular layer around the blastocyst, proliferates and extends behind syncytiotrophoblasts



Early Utero-Placental exchange - transfer of nutrition from maternal lacunae filled with secretions from uterine glands and maternal blood from blood vessels. The development of trophoblast villi extending into the uterine decidua.

There are three stages of villi development:

1. **Primary Villi** - cytotrophoblast
2. **Secondary Villi** - cytotrophoblast + extraembryonic mesoderm
3. **Tertiary Villi** - cytotrophoblast + extraembryonic mesoderm + blood vessels



Primary chorionic villi	Tertiary chorionic villi	Placenta anchoring villi
		

There are two main types of early villi:

- Anchoring villi - attached to decidua
- Floating villi - not attached to decidua, floating in maternal lacunae.

BGDA: Lecture 1 | Lecture 2 | Practical 3 | Practical 6 | Practical 12 | Practical 14 | *Histology Support* - Female | Male | Tutorial 2014

Glossary Links

A|B|C|D|E|F|G|H|I|J|K|L|M|N|O|P|Q|R|S|T|U|V|W|X|Y|Z|Numbers|Symbols

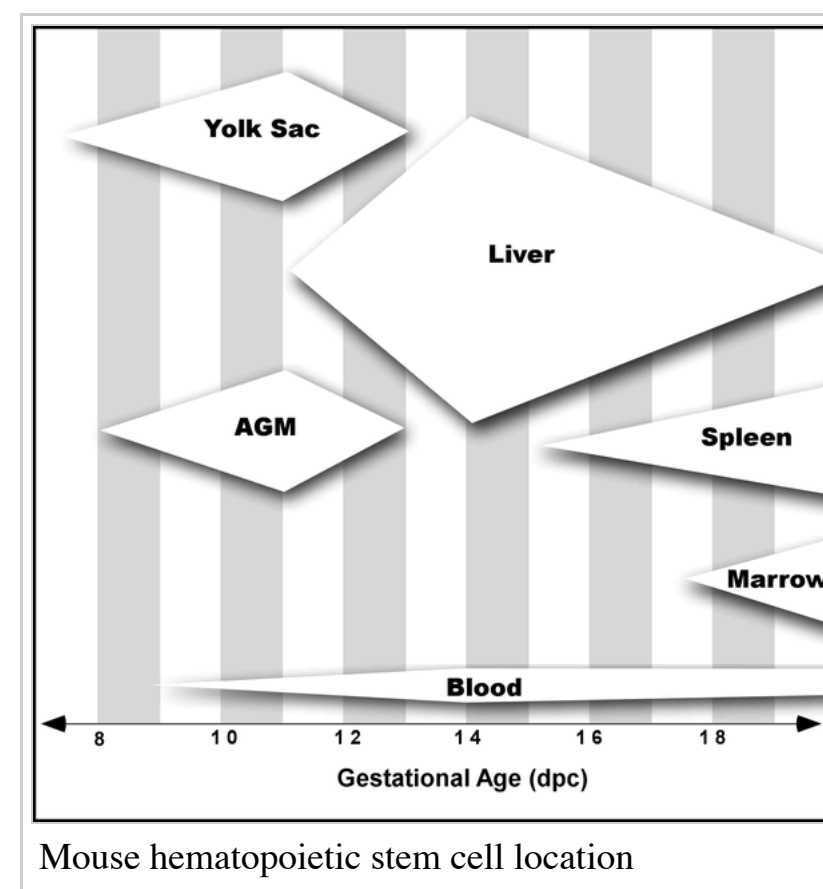
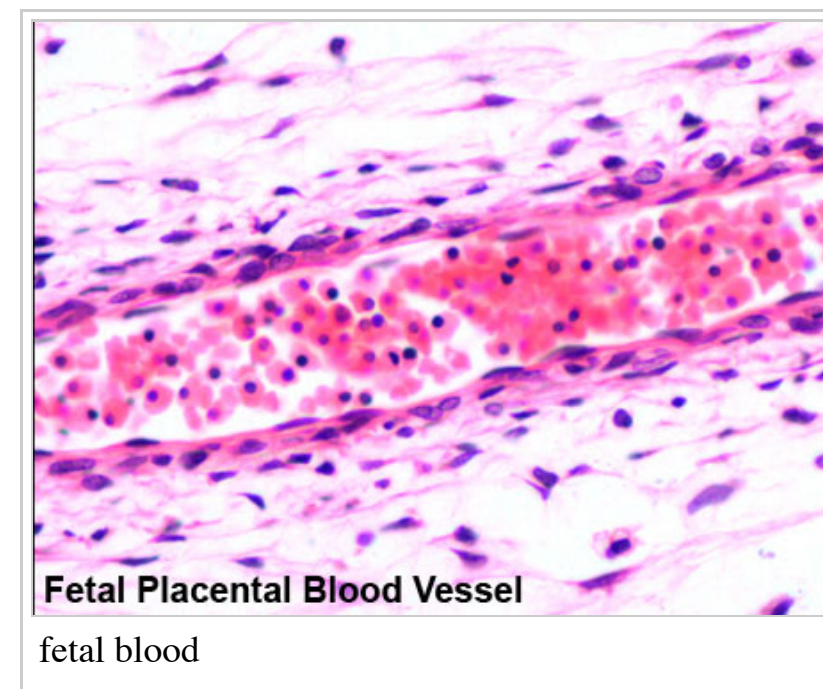
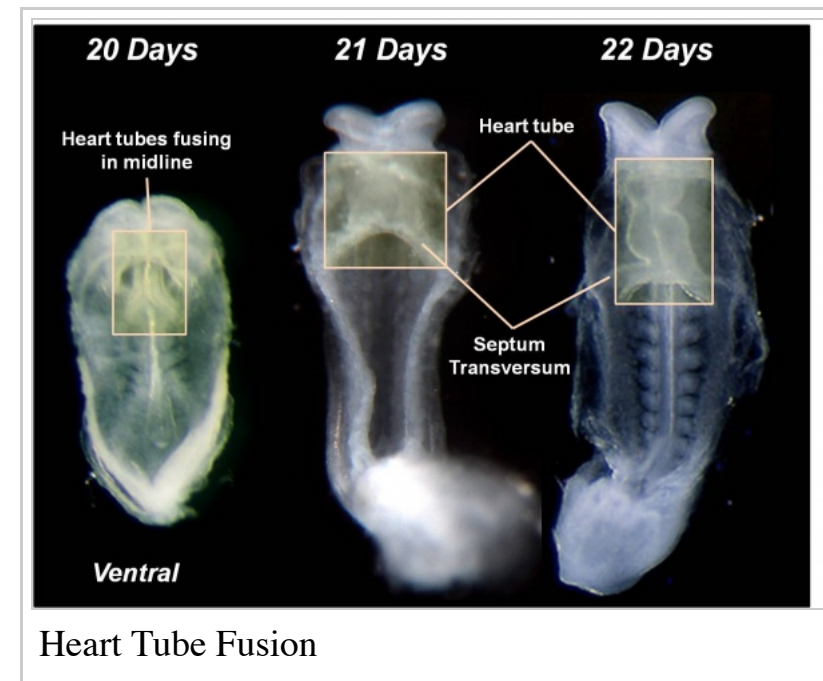
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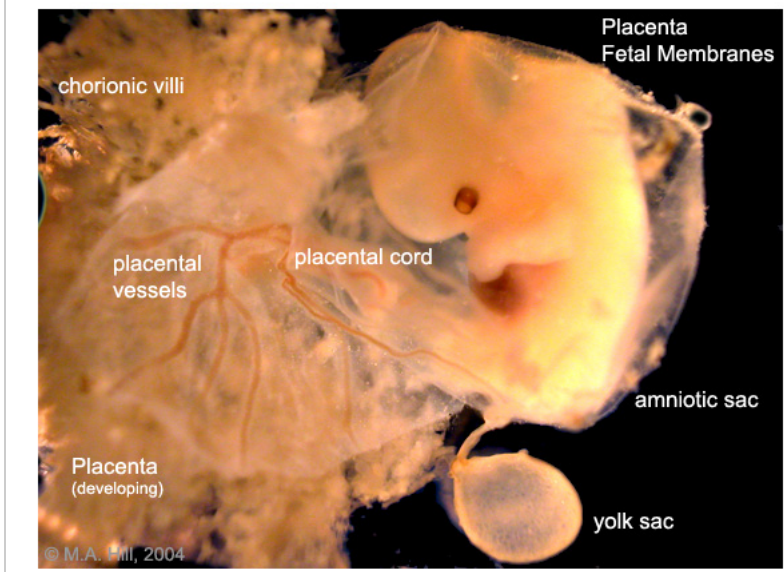
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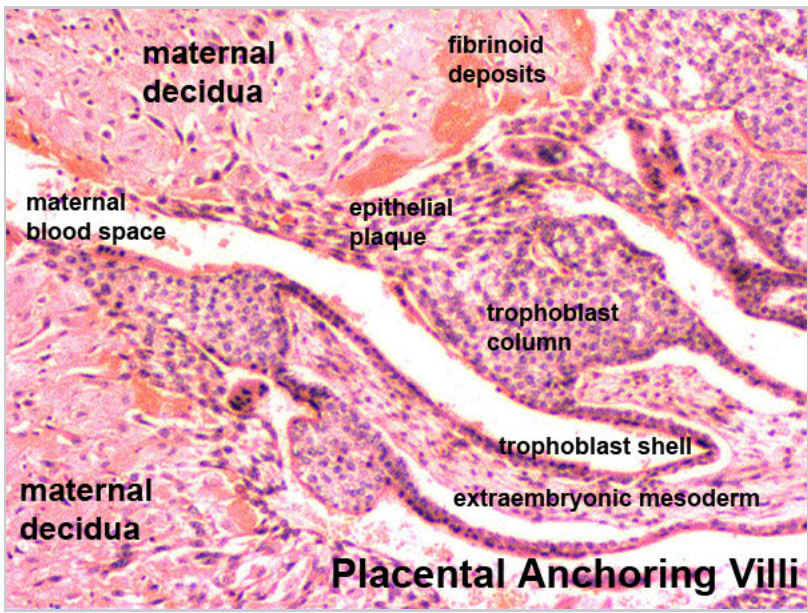
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Placenta and placental membranes



Placenta anchoring villi