BGDA Lecture - Development of the Embryo/Fetus 2

ExpandEmbryology - 12 May 2019 Expand to Translate
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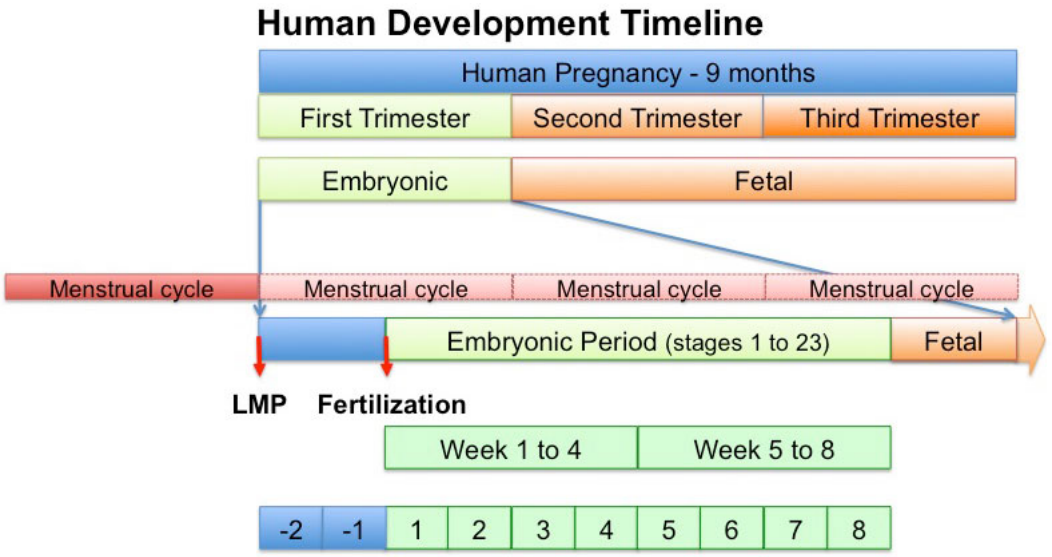
Introduction



This lecture covers the period of Embryonic development, in Humans from week 3 to week 8 (**GA** week 5-10) and is divided into 23 Carnegie stages of embryonic development. There will also be a brief introduction to fetal development. Note, the period from week 9 to week 38 is considered Fetal development and will be covered in detail in the Laboratory 12.

2018 Lecture PDF (to be updated for 2019 - notice removed when completed)

Lecture Objectives

- Understand key structures and events in embryonic development.
- Understanding of the dynamic changes internal and external structures.
- Brief understanding of organ and system formation (functional / not functional).
- Brief understanding of critical periods of development.

1 Minute Embryology | UNSW theBox

ExpandLecture Archive
[Media:2018 BGDA Lecture - Development of the Embryo-Fetus 2.pdf 2018 PDF] | 2017 | 2017 PDF | 2016 | 2015 | 2014 | 2014 PDF | 2013 | 2012 | 2010 | Practical 6 Embryonic Development | Practical 12 Fetal Development

ExpandTextbooks

UNSW Embryology

Hill, M.A. (2019). *UNSW Embryology* (19th ed.) Retrieved May 12, 2019, from https://embryology.med.unsw.edu.au

- human timeline | first trimester timeline
- Week 3 | Week 4 | Week 5 | Week 6 | Week 7 | Week 8
- fetal
- abnormal development | birth | neonatal | Neonatal Diagnosis

Diagnosis Links: Prenatal Diagnosis | Pregnancy Test | Amniocentesis | Chorionic villus sampling | Ultrasound | Alpha-Fetoprotein | Pregnancy-associated plasma protein-A | Fetal Blood Sampling | Magnetic Resonance Imaging | Computed Tomography | Non-Invasive Prenatal Testing | Fetal Cells in Maternal Blood | Preimplantation Genetic Screening | Comparative Genomic Hybridization | Genome Sequencing | Neonatal Diagnosis | Category:Prenatal Diagnosis | Fetal Surgery | Classification of Diseases | Category:Neonatal Diagnosis

The Developing Human: Clinically Oriented Embryology

Moore, K.L., Persaud, T.V.N. & Torchia, M.G. (2015). *The developing human: clinically oriented embryology* (10th ed.). Philadelphia: Saunders. (links only function with UNSW connection)

Chapter 5 Fourth to Eighth Weeks of Human Development

Chapter 6 Fetal Period

Chapter 20 Human Birth Defects

ExpandThe Developing Human: Clinically Oriented Embryology (10th edn)

UNSW Students have online access to the current 10th edn. through the UNSW Library subscription (with student Zpass log-in).

APA Citation: Moore, K.L., Persaud, T.V.N. & Torchia, M.G. (2015). *The developing human: clinically oriented embryology* (10th ed.). Philadelphia: Saunders.

Links: PermaLink | UNSW Embryology Textbooks | Embryology Textbooks | UNSW Library

1. Introduction to the Developing Human
2. First Week of Human Development
3. Second Week of Human Development
4. Third Week of Human Development
5. Fourth to Eighth Weeks of Human Development
6. Fetal Period
7. Placenta and Fetal Membranes
8. Body Cavities and Diaphragm
9. Pharyngeal Apparatus, Face, and Neck
10. Respiratory System
11. Alimentary System
12. Urogenital System
13. Cardiovascular System
14. Skeletal System
15. Muscular System
16. Development of Limbs
17. Nervous System
18. Development of Eyes and Ears
19. Integumentary System
20. Human Birth Defects
21. Common Signaling Pathways Used During Development
22. Appendix : Discussion of Clinically Oriented Problems

Larsen's Human Embryology

Schoenwolf, G.C., Bleyl, S.B., Brauer, P.R., Francis-West, P.H. & Philippa H. (2015). *Larsen's human embryology* (5th ed.). New York; Edinburgh: Churchill Livingstone.(links only function with UNSW connection)

Chapter 4 Fourth Week: Forming the Embryo

Chapter 6 Fetal Development and the Fetus as Patient

ExpandLarsen's Human Embryology (5th edn)

UNSW students have full access to this textbook edition through UNSW Library subscription (with student Zpass log-in).

APA Citation: Schoenwolf, G.C., Bleyl, S.B., Brauer, P.R., Francis-West, P.H. & Philippa H. (2015). *Larsen's human embryology* (5th ed.). New York; Edinburgh: Churchill Livingstone.

Links: PermaLink | UNSW Embryology Textbooks | Embryology Textbooks | UNSW Library

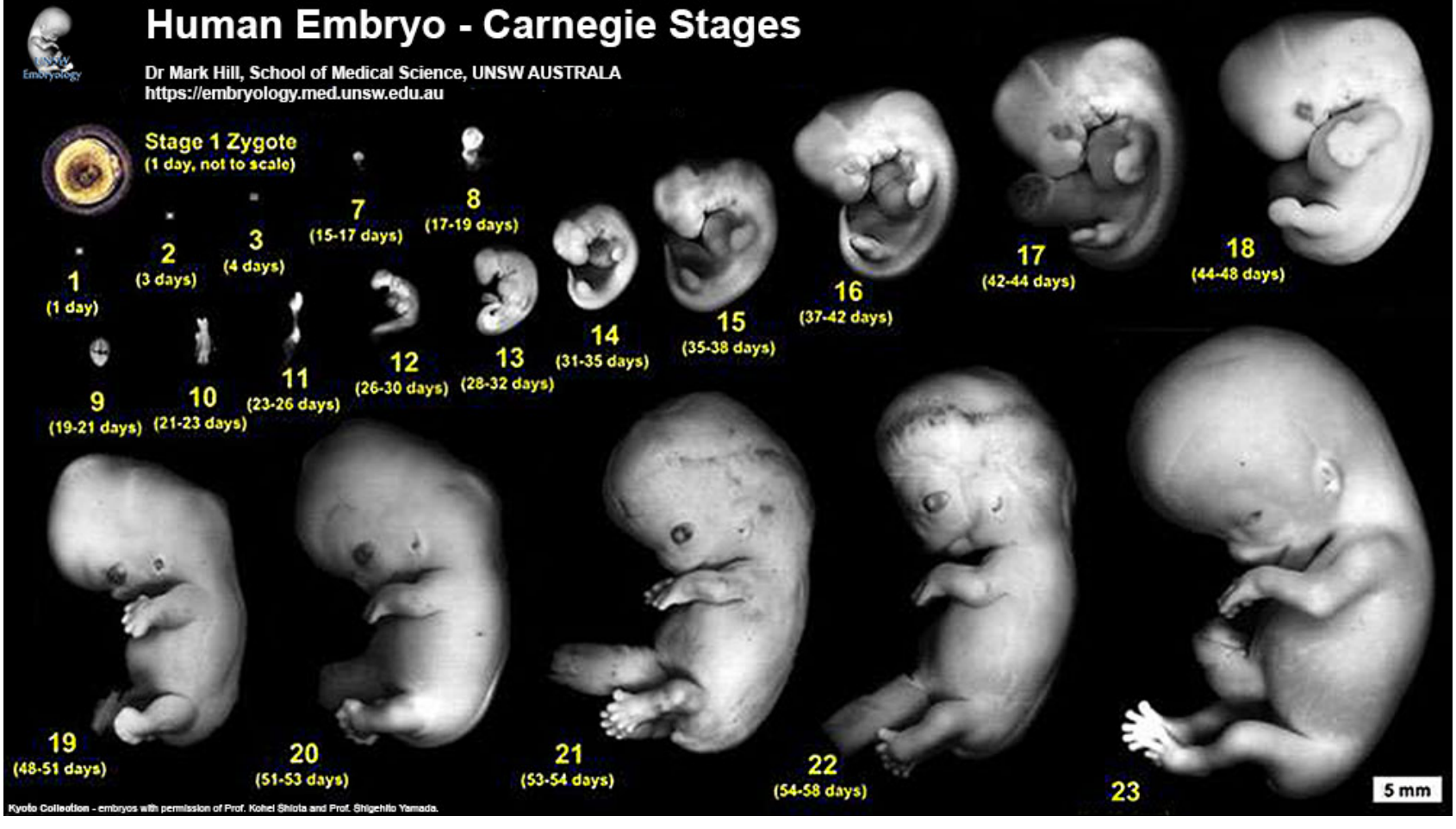
1. Gametogenesis, Fertilization, and First Week
2. Second Week: Becoming Bilaminar and Fully Implanting
3. Third Week: Becoming Trilaminar and Establishing Body Axes
4. Fourth Week: Forming the Embryo
5. Principles and Mechanisms of Morphogenesis and Dysmorphogenesis
6. Fetal Development and the Fetus as Patient
7. Development of the Skin and Its Derivatives
8. Development of the Musculoskeletal System
9. Development of the Central Nervous System
10. Development of the Peripheral Nervous System
11. Development of the Respiratory System and Body Cavities
12. Development of the Heart
13. Development of the Vasculature
14. Development of the Gastrointestinal Tract
15. Development of the Urinary System
16. Development of the Reproductive System
17. Development of the Pharyngeal Apparatus and Face
18. Development of the Ears
19. Development of the Eyes
20. Development of the Limbs

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	

First 8 Weeks

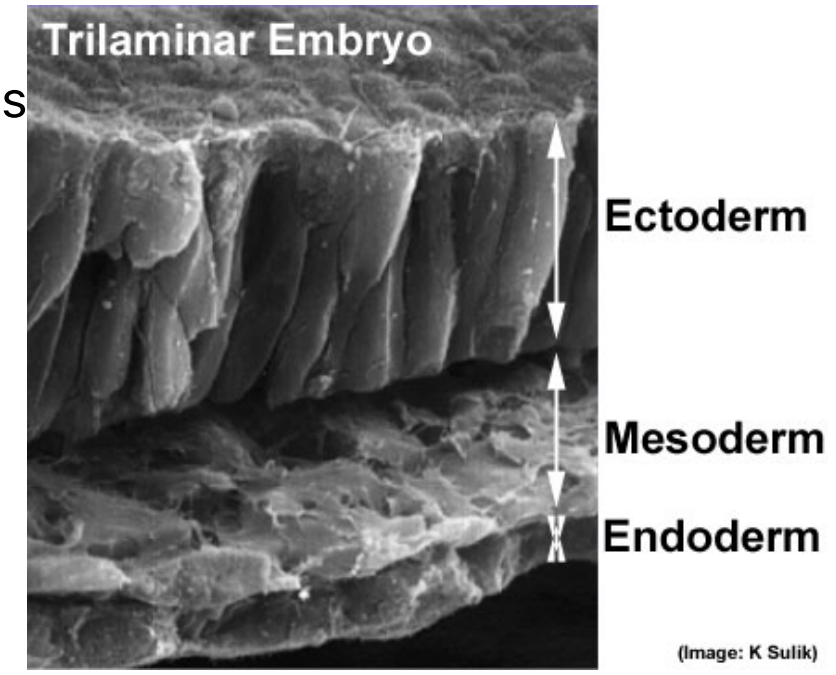


The Carnegie stages of the first 8 week of human development.

Week 3

Mesoderm means the "middle layer" and it is from this layer that the body's connective tissues are derived (note that the head neural crest ectoderm also forms connective tissues)

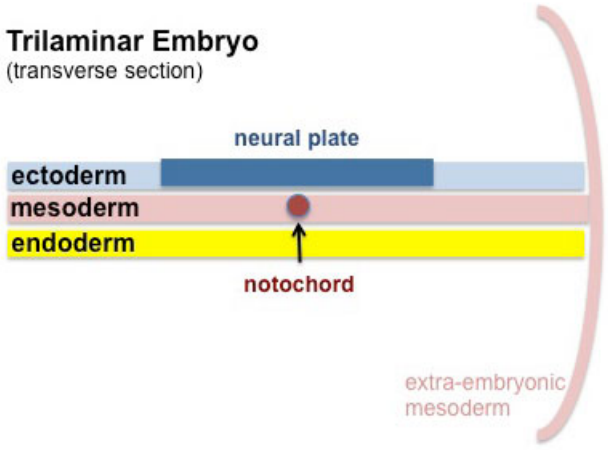
In early mesoderm development a number of transient structures will form and then be lost as tissue structure is patterned and organised.



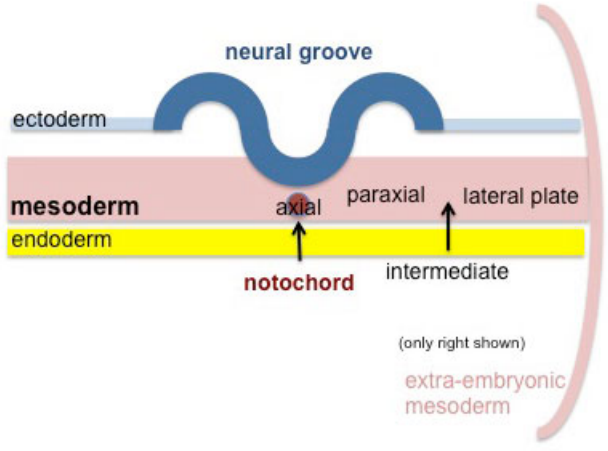
Week 3 - Gastrulation

Humans as vertebrates have a "backbone" and the first mesoderm structure we will see form after the notochord will be somites.

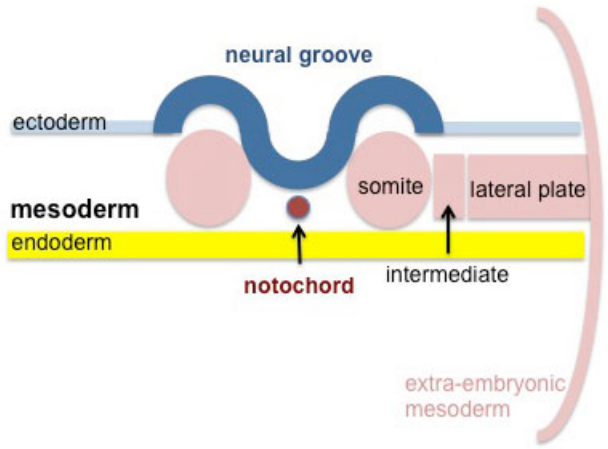
- **Mesoderm and Ectoderm Cartoons**



- Trilaminar Embryo



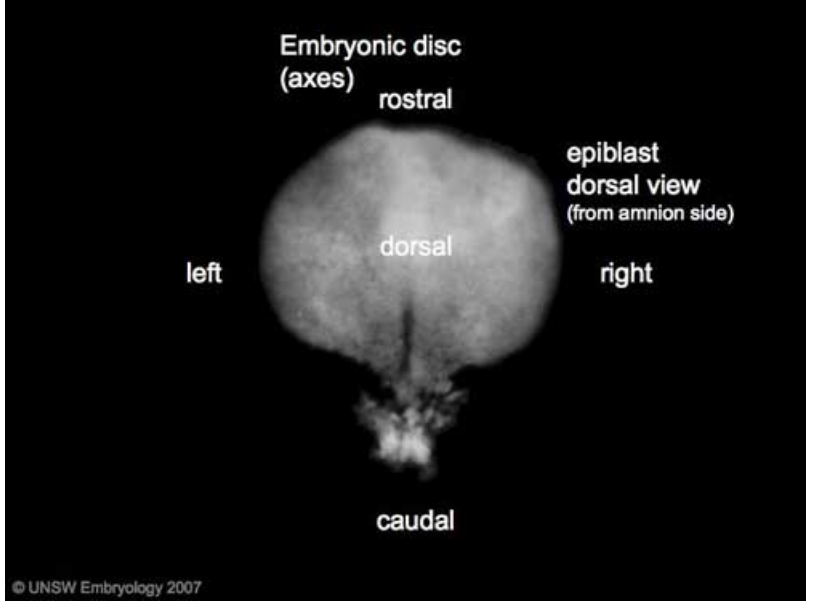
- Paraxial and Lateral Plate



- somites
- Somatic and Splanchnic

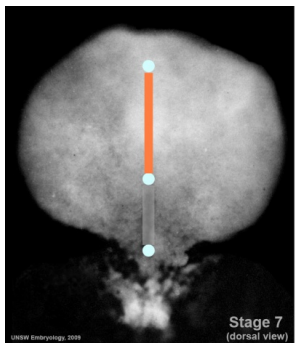
Mesoderm organization: (left to right)

lateral plate - intermediate mesoderm - paraxial mesoderm - **axial mesoderm** - paraxial mesoderm - intermediate mesoderm - lateral plate



- axial mesoderm
- Stage 7 paraxial mesoderm
- Stage 7 intermediate mesoderm
- Stage 7 lateral plate

Axial Mesoderm



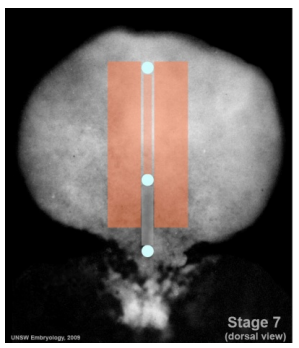
- Axial Mesoderm = notochord

1. mechanical role in embryonic disc folding
2. molecular role in patterning surrounding tissues

Adult - contributes to the nucleus pulposis of the intervertebral disc

- Stage 7 primitive-streak-node
- Stage 7 cloacal-oral-membranes

Paraxial Mesoderm

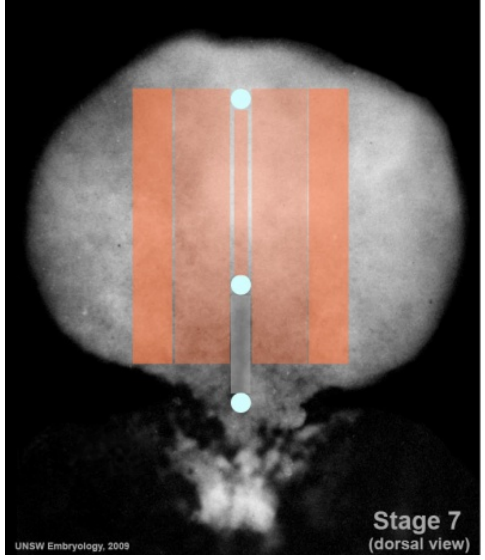


- differentiates rostro-caudally (head to tail)
- head region - remains unsegmented
- body region - segments to form pairs of **somites** along the length of the embryo.

Adult - contributes vertebral column (vertebra and IVD), dermis of the skin, skeletal muscle of body and limbs

Intermediate Mesoderm

- named by position (between paraxial and lateral plate)
- differentiates rostro-caudally (head to tail)

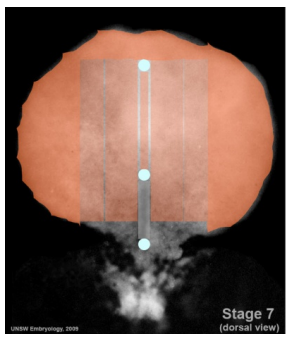


- renal forms 3 sets of "kidneys" in sequence

1. pronephros
2. mesonephros
3. metanephros

Adult - metanephros forms the renal kidney

Lateral Plate Mesoderm



- at edge of embryonic disc
- "horseshoe shaped" space forms in the middle, dividing this region
  - somatic mesoderm - closest to ectoderm
  - intra-embryonic coelom - single space forms the 3 major body cavities (pericardial, pleural, peritoneal)
  - splanchnic mesoderm - closest to endoderm

Adult - body connective tissues, gastrointestinal tract (connective tissues, muscle, organs), heart

Week 4

Somite Development

- Stage 10 (early)
- Stage 10 (late)
- Stage 10 (labeled)
- Stage 11
- Stage 11

Somite initially forms 2 main components

- ventromedial- sclerotome forms vertebral body and intervertebral

disc

- dorsolateral - dermomyotome forms dermis and skeletal muscle
- paraxial mesoderm
- early somite
- sclerotome and dermomyotome
- dermatome and myotome
- epaxial and hypaxial muscles

<table>
<tr><th>Sclerotome</th><th>Dermatome</th></tr>
<tr><td>

- sclerotome later becomes subdivided
  - rostral and caudal halves separated laterally by von Ebner's fissure
- half somites contribute to a single vertebral level body
- other half intervertebral disc
- therefore final vertebral segmentation “shifts”

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- connective tissue underlying epidermis
- begins as a dorsal thickening
- spreads throughout the body

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<tr><td></td><th>Myotome</th></tr>
<tr><td></td><td>

- Body - epaxial and hypaxial muscles
- Limbs - flexor and extensor muscles

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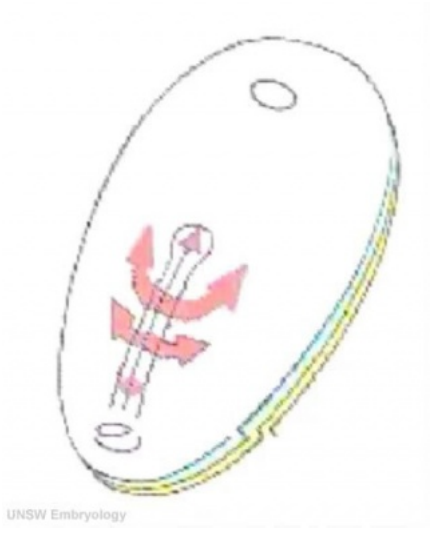

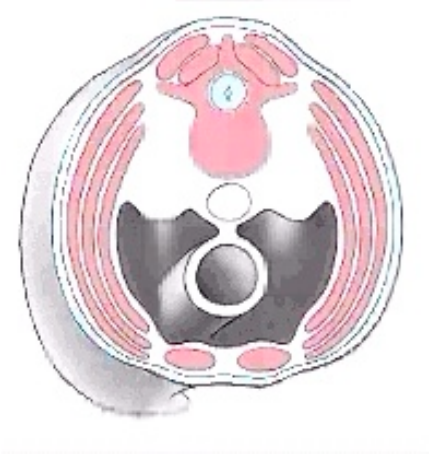

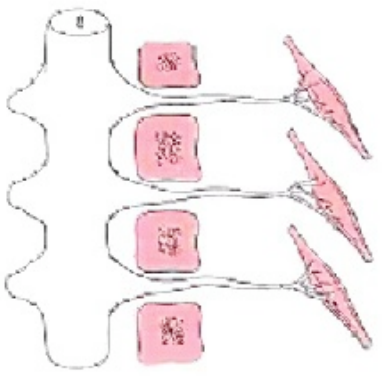

Heart

ExpandHeart Development Movies				
Week 3	**Heart Looping**	**Heart Realign**	**Atrial Septation**	**Outflow Septation**
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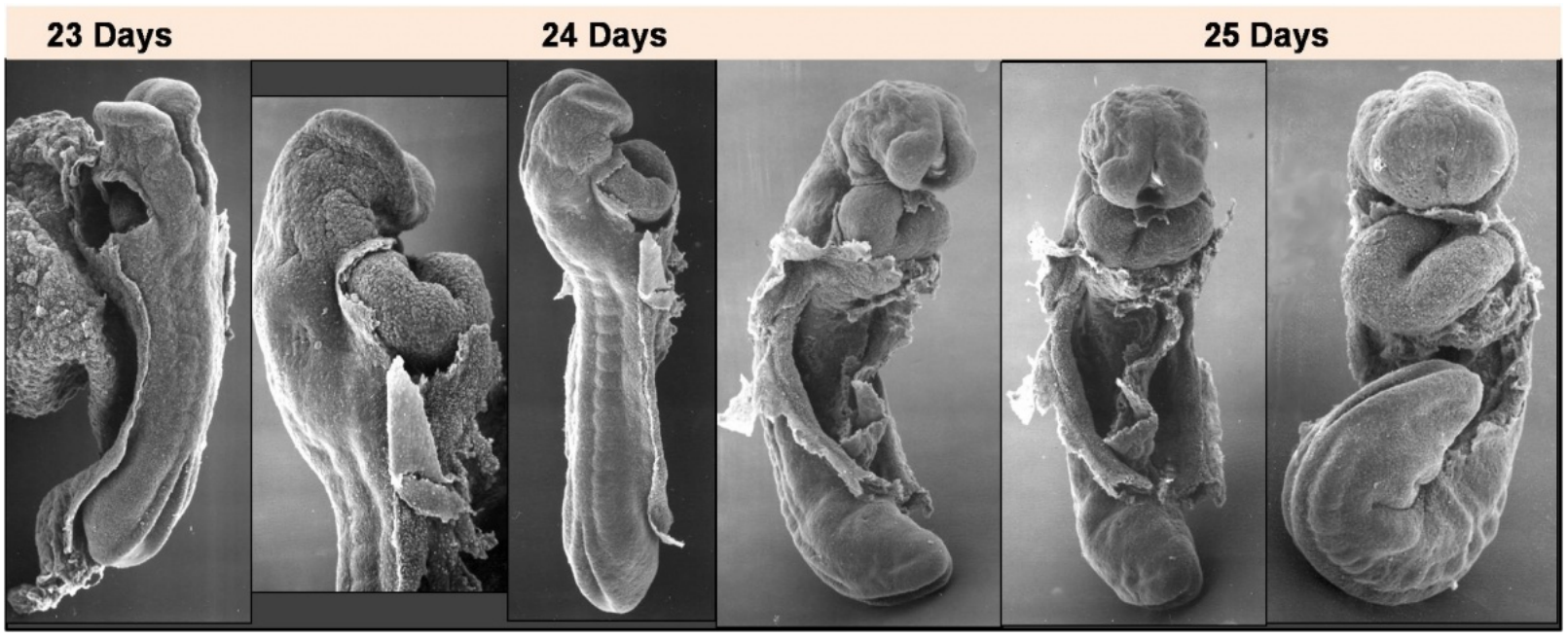
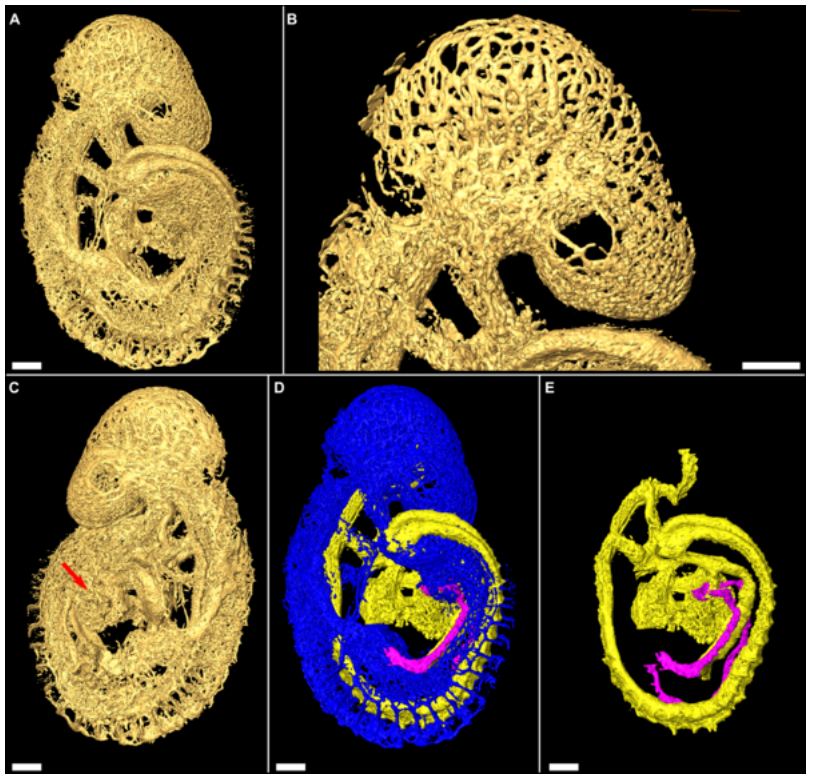


- forms initially in splanchnic mesoderm of prechordal plate region - **cardiogenic region**
    - growth and folding of the embryo moves heart ventrallly and downward into anatomical position
- week 3 begins as paired heart tubes that fuse to form single heart

tube
- begins to beat in Humans- day 22-23
- heart tube connects to blood vessels forming in splanchnic and extraembryonic mesoderm



Mesoderm vascular development

Week 2-3 pair of thin-walled tubes

Week 3 tubes fused, truncus arteriosus outflow, heart contracting

Week 4 heart tube continues to elongate, curving to form S shape

Week 5 Septation starts, atrial and ventricular

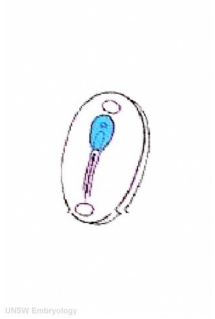
Links: Cardiac Embryology

Neural

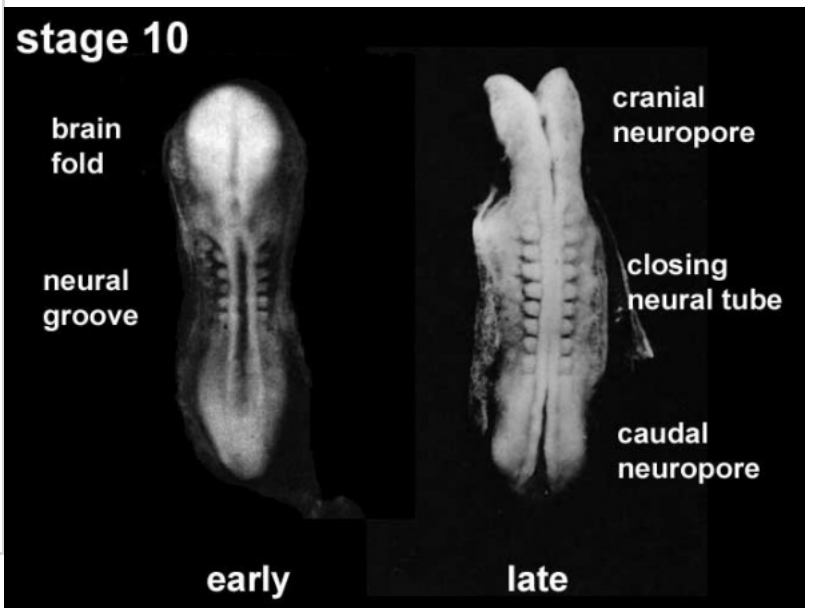
- **Mesoderm and Ectoderm Cartoons**
- Trilaminar Embryo
- Paraxial and Lateral Plate
- somites
- Somatic and Splanchnic

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



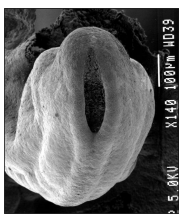
Stage 10 Week 4, 22 - 23 days

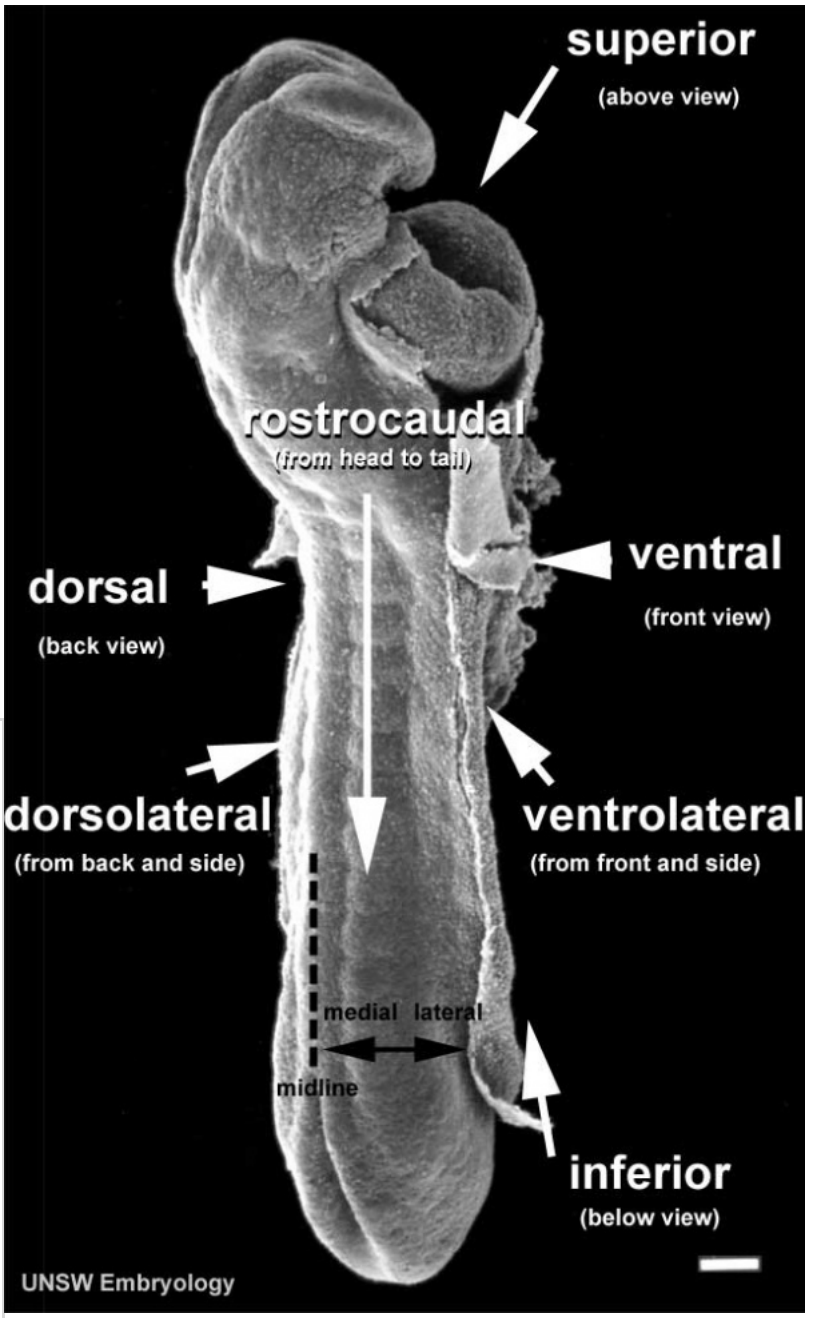
Neural Groove

- forms in the midline of the neural plate (day 18-19)
- either side of which are the neural folds which continues to deepen until about week 4
- neural folds begins to fuse, beginning at 4th somite level

Neural Tube

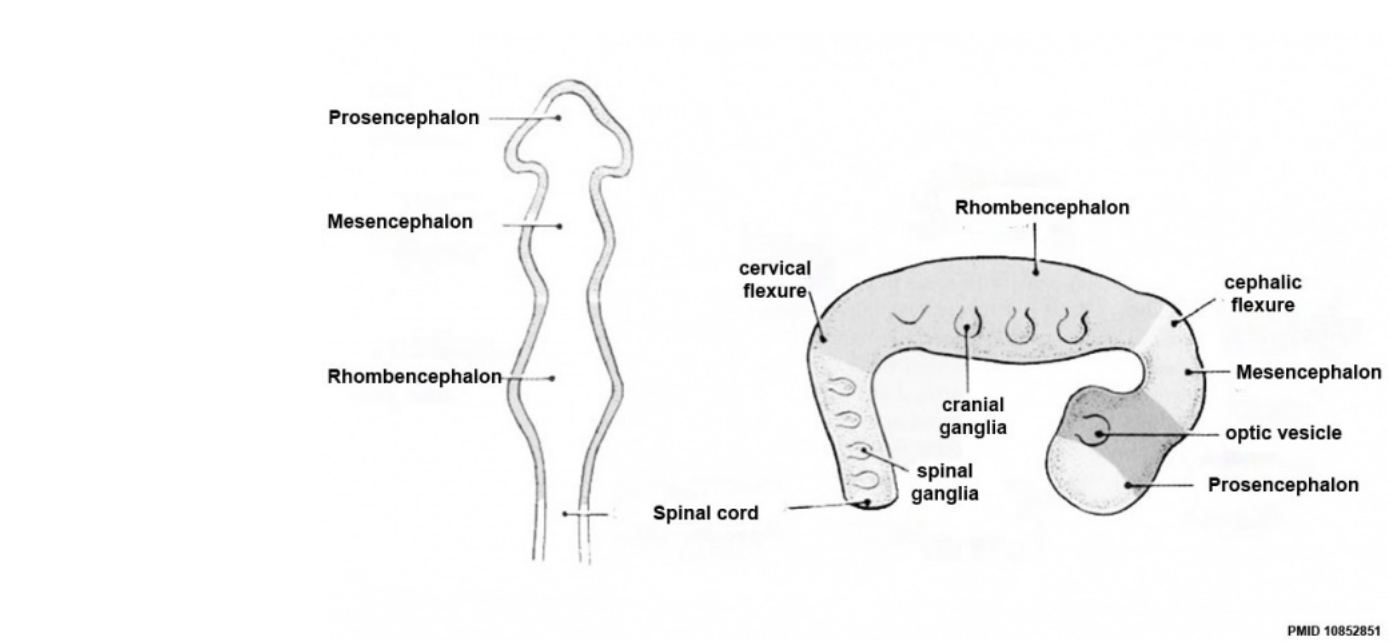
- the neural tube forms the brain and spinal cord
- fusion of neural groove extends rostrally and caudally
- begins at the level of 4th somite
- closes neural groove "zips up" in some species.
  - humans appear to close at multiple points along the





Stage 11 neural groove to tube

	tube. • leaves 2 openings at either end - **Neuropores** ◦ cranial neuropore closes before caudal Failure for the neural tube to close correctly or completely results in a **neural tube defect**.	



Neural - 3 primary vesicles

Neural Crest

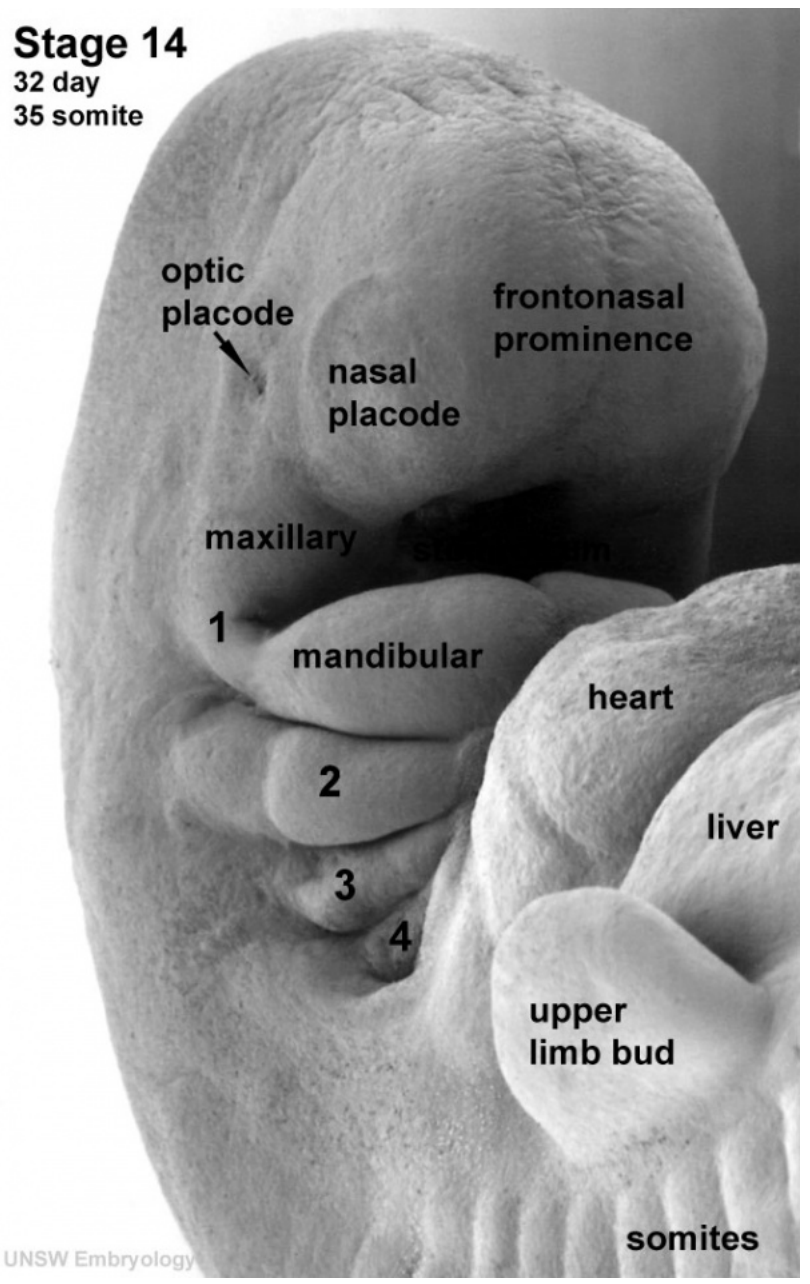
- population of cells at the edge of the neural plate that lie dorsally when the neural tube fuses
- dorsal to the neural tube, as a pair of streaks
- pluripotential, forms many different types of cells
- cells migrate throughout the embryo

Neural Crest Derivatives: dorsal root ganglia, autonomic ganglia, adrenal medulla, drg sheath cells, glia, pia-arachnoid sheath, skin melanocytes, connective tissue of cardiac outflow, thyroid parafollicular

cells, craniofacial skeleton, teeth odontoblasts

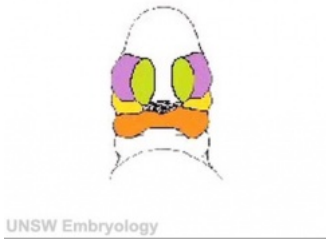
Head

- branchial arch (Gk. *branchia*= gill)
- arch consists of all 3 trilaminar embryo layers (ectoderm- outside, mesoderm - core of mesenchyme, endoderm - inside)
-
-
-



Stage 14 pharyngeal arches

- Humans have 5 arches - 1, 2, 3, 4, 6 (Arch 5 does not form or regresses rapidly)
- from in rostro-caudal sequence, Arch 1 to 6 from week 4 onwards
- arch 1 and 2 appear at time of closure of cranial neuropore
- Face - mainly arch 1 and 2
- Neck components - arch 3 and 4 (arch 4 and 6 fuse)



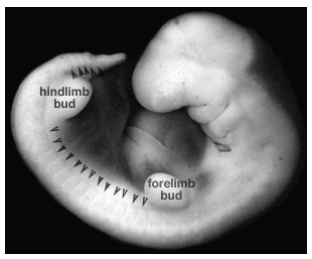
Sensory Placodes

- During week 4 a series of thickened surface ectodermal patches form in pairs rostro-caudally in the head region.

- These sensory placodes will later contribute key components of each of our special senses (vision, hearing and smell).
- Note that their initial postion on the developing head is significantly different to their final position in the future sensory system

- **Otic placode** - istage 13/14 embryo the otic placode sunk from the surface ectoderm to form a hollow epithelial ball, the **otocyst**, which now lies beneath the surface surrounded by mesenchyme (mesoderm). The epithelia of this ball varies in thickness and has begun to distort, it will eventually form the inner ear membranous labyrinth.
- **Lens placode** - lies on the surface, adjacent to the outpocketing of the nervous system (which will for the retina) and will form the lens.
- **Nasal placode** - has 2 components (medial and lateral) and will form the nose olefactory epithelium.

Upper and Lower Limb



- Limb development occurs at different times for forelimbs and hindlimbs.
- mid-4th week human upper limb buds first
- lower limbs about 2 days later
- The limbs form at vertebra segmental levels C5-C8 (upper limbs) L3-L5 (lower limbs).
- Limbs are initially undifferentiated mesenchyme (mesoderm) with an epithelial (ectoderm) covering.
- Blood vessels then begin forming, the largest (marginal vein) is adjacent to tip of the bud.
- Myotome invade the bud.

Gastrointestinal Tract

- Begins at buccopharyngeal membrane
- Ends at cloacal membrane
- 3 distinct portions (fore-, mid- and hind-gut)
- liver earliest forming organ

Germ layer contributions

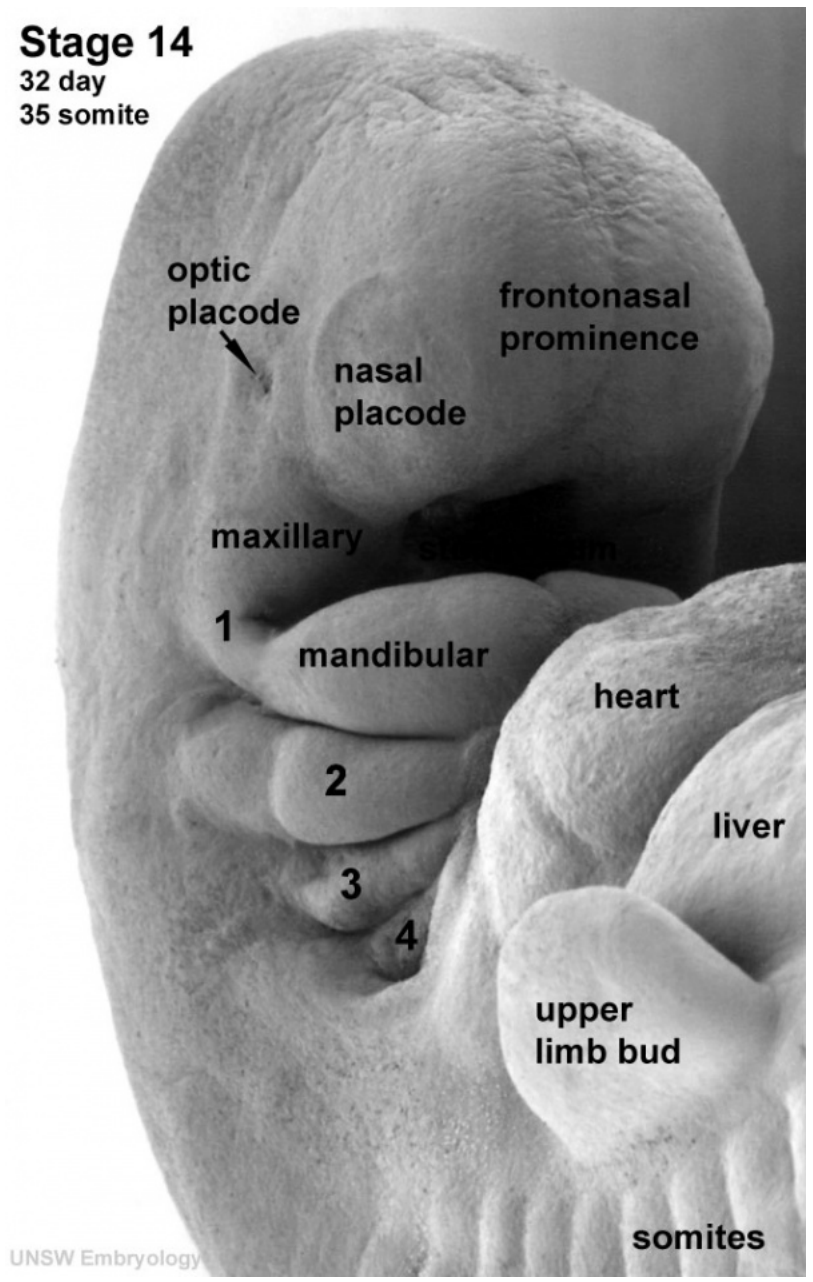
- **Endoderm** - epithelium and associated glands
- **Mesoderm** (splanchnic) - mesentry, connective tissues, smooth muscle, blood vessels
- **Ectoderm** (neural crest) - enteric nervous system

Both endoderm and mesoderm will contribute to associated organs.

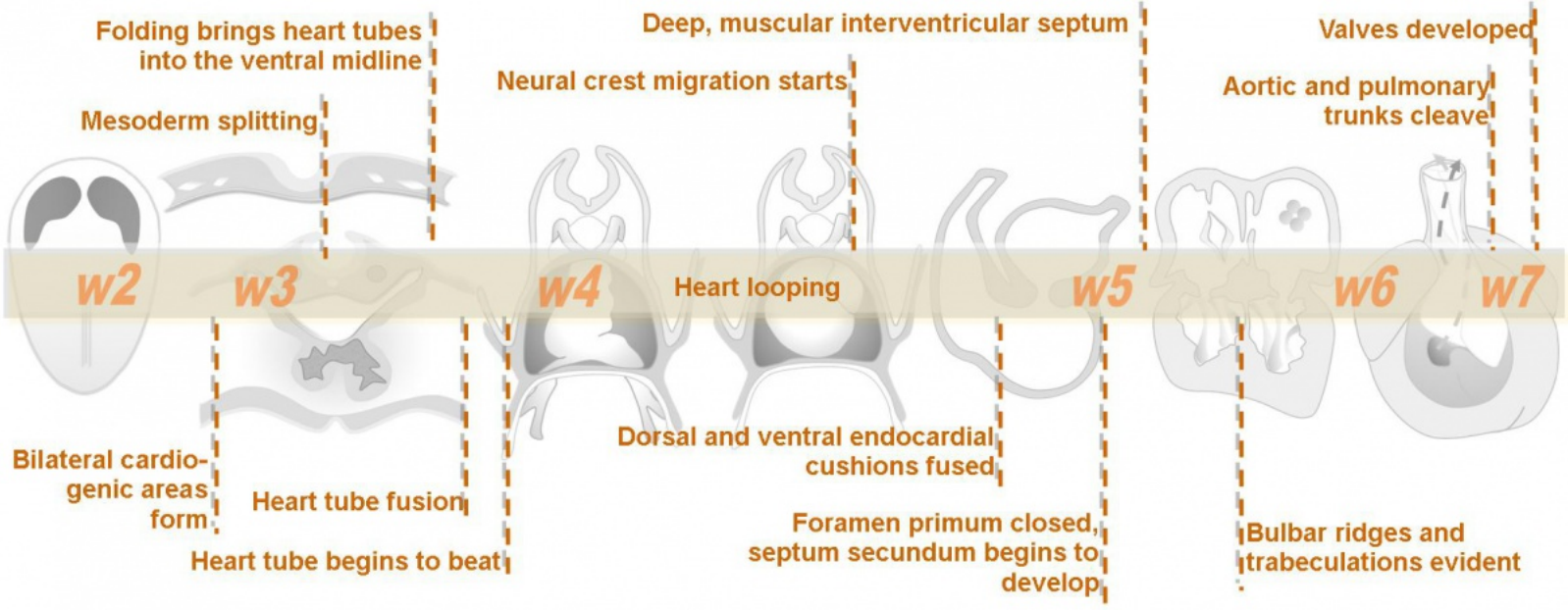
- Gastrointestinal Tract

Week 5

- Stage 14
- Stage 15
- Respiratory Tract
- Neural - 5 secondary vesicles
- Heart - septation starts, atrial and ventricular
- Vascular - 3 vascular systems (systemic, placental, vitelline) extensively remodelled
- Respiratory - left and right lung buds push into the pericardioperitoneal canals (primordia of pleural cavity)
- Sense - Hearing cochlear part of otic vesicle elongates (humans 2.5 turns)



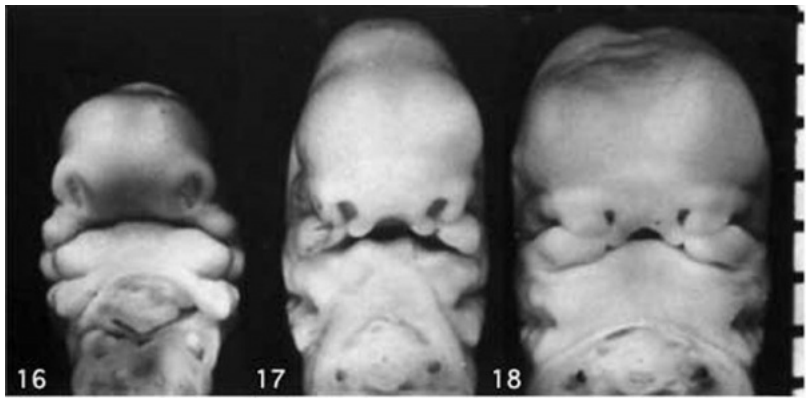
Stage 14 pharyngeal arches



Atrial septa remains open, foramen ovale, septation continues (week 5-7),

Week 6

- Stage 16
- Stage 17
- Endocrine development
    - pituitary - connecting stalk between pouch and oral



Week 6 Face Development

cavity degenerates
    - parathyroid - diverticulum elongate, hollow then solid, dorsal cell proliferation
    - thymus - diverticulum elongate, hollow then solid, ventral cell proliferation
    - adrenal - fetal cortex forms from mesothelium adjacent to dorsal mesentery, medulla neural crest cells from adjacent sympathetic ganglia

Week 7

- Stage 18
- Stage 19
- pancreas - Week 7 to 20 pancreatic hormones secretion begins and increases, small amount maternal insulin
- limb bones form by endochondrial ossification and throughout embryo replacement of cartilage with bone (week 5 onward).
- Endochondral ossification in limb
- Endochondral ossification
- Head Intramembranous ossification
- Intramembranous ossification

Human week 7

Week 8

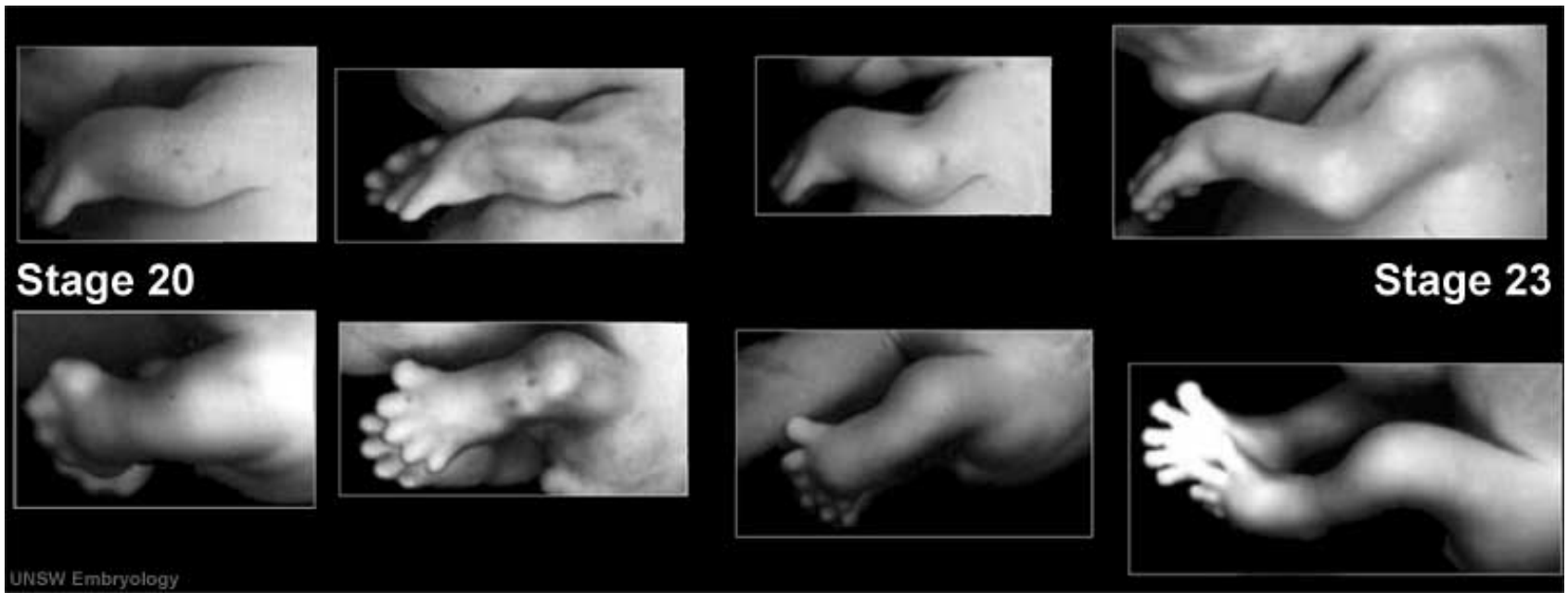
- Neural - secondary vesicles

- Neural - early developing cortex
- Gastrointestinal tract herniation

Sagittal GIT

Page | Play

- Limb - upper and lower limbs rotate in different directions (upper limb dorsally, lower limb ventrally)



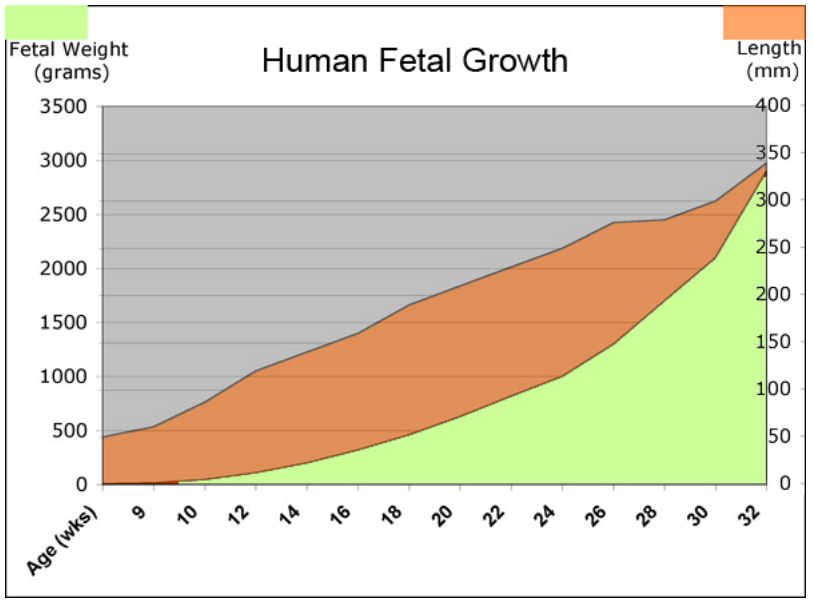
Links: Embryonic Development | Timeline human development

Fetal

Note - Fetal development topic will be covered in detail in practical 12 - Fetal. Information below is only a brief summary and may not be covered in this lecture.

- First Trimester (1 - 12 weeks) - embryonic and early fetal
- Second Trimester (13 - 24 weeks) - organ development, function,

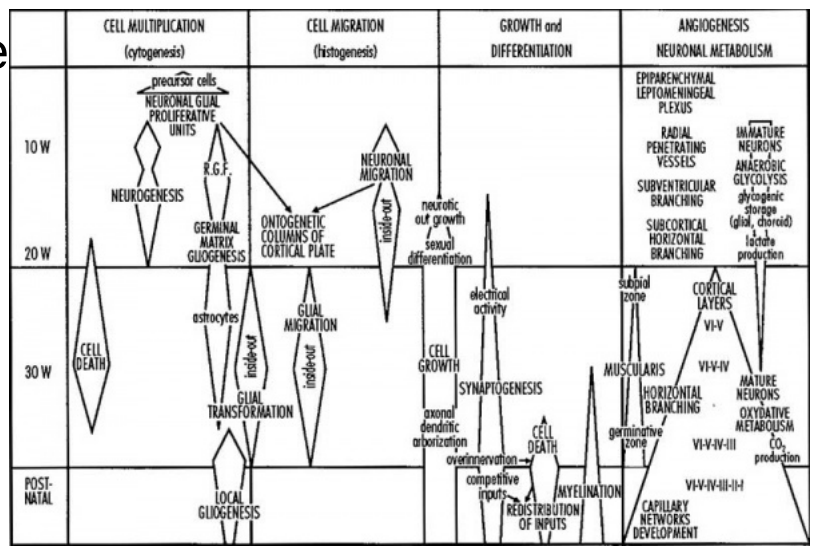
and growth (length)
- Third Trimester (25 - 40 weeks) - organ function and rapid growth (weight)



Fetal length and weight changes

Fetal Neural

- During the fetal period there is ongoing growth in size, weight and surface area of the brain and spinal cord. Microscopically there is ongoing: cell migration, extension of processes, cell death and glial cell development.
- Brain - folding of the initially smooth surface (insular cortex, gyral and culcal development)
- Neural development will continue after birth with substantial growth, death and reorganization occuring during the postnatal period



Timeline of events in Human Neural Development

Links: neural | BGDA Lecture - Nervous System

Lung Stages

respiratory

- week 4 - 5 embryonic
- week 5 - 17 pseudoglandular
- week 16 - 25 canalicular
- week 24 - 40 terminal sac
- late fetal - 8 years alveolar

Links: respiratory | SH Lecture - Respiratory

Fetal Genital

genital

- Gonad - ovary and testis development
- Internal genital tract - uterus and ductus deferens
- External genital tract - genital folds development
- Testis descent

  Links: genital | BGDB Lecture - Genital

Fetal Renal

renal

- week 32-34 nephron development completed
- term birth nephron number per kidney about 1 million (300,000 to 2 million)

  Links: renal

Fetal Endocrine

endocrine

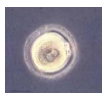
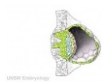
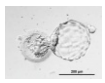
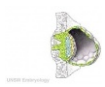
- Many endocrine organs begin to function in the early fetal period.
- Pituitary hormones - HPA axis established by week 20, pituitary functional throughout fetal development
- Thyroid hormone - important for neural development, required for metabolic activity, also in the newborn

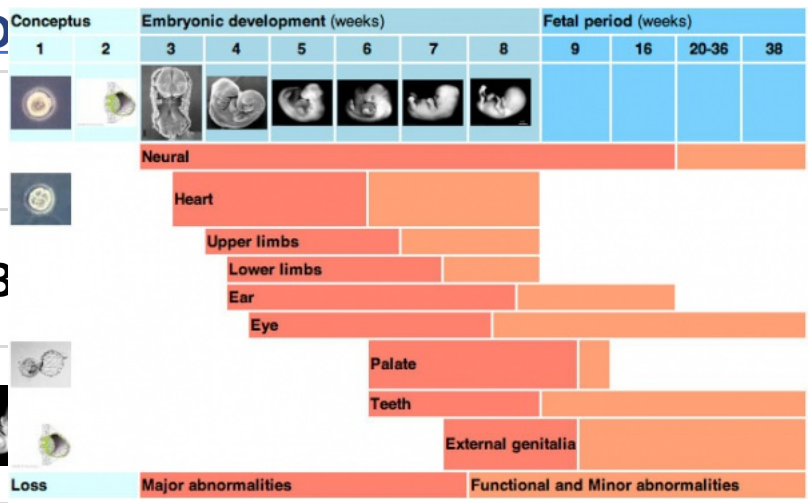
Remember that the Placenta also has important endocrine functions during development.

  Links: endocrine | placenta

Critical Periods

The term "Critical Periods" refers to periods of development when specific systems are more sensitive to teratogen exposure or developmental insults.

Critical Periods of Human D							
Conceptus		**Embryonic development** (weeks)					
1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
							
		Neural					
			**Heart**				
				Upper limbs			
					Lower limbs		
					Ear		
							Eye
							**Palate**
							Teeth
							**Ext ger**
Loss		**Major abnormalities**					**Fu ab**



Additional Information

See the associated BGDA Practical 6 class.

Links: human timeline | first trimester timeline | second trimester timeline | third trimester timeline | fetal | Template:Movies

Abnormality Links: abnormal development | abnormal genetic | abnormal environmental | Unknown | teratogens | ectopic pregnancy | cardiovascular abnormalities | coelom abnormalities | endocrine abnormalities |

gastrointestinal abnormalities | genital abnormalities | head abnormalities | integumentary abnormalities | musculoskeletal abnormalities | limb abnormalities | neural abnormalities | neural crest abnormalities | renal abnormalities | respiratory abnormalities | placenta abnormalities | hearing abnormalities | vision abnormalities | twinning | Developmental Origins of Health and Disease | **ICD-11**

ExpandHistoric Embryology

1915 Congenital Cardiac Disease | 1917 Frequency of Anomalies in Human Embryos | 1920 Hydatiform Degeneration Tubal Pregnancy | 1921 Anencephalic Embryo | 1921 Rat and Man | 1966 Congenital Malformations

ExpandFirst Trimester Timeline

Embryonic Weeks/Stages

Week:	1	2	3	4	5	6	7	8
Carnegie stage:	1 2 3 4	5 6	7 8 9	10 11 12 13	14 15	16 17	18 19	20 21 22 23

First Trimester Timeline

Links: human timeline | first trimester timeline | second trimester timeline | third trimester timeline

Gestational Day GA	**Stage**	**Event**
1	Menstrual Phase	menstrual cycle changes: uterus endometrium (loss), ovary (follicle development)
2		
3		
4		
5	Proliferative Phase	menstrual cycle changes: uterus endometrium (proliferation), ovary (Follicle Development)
6		
7		
8	Proliferative Phase	
9		menstrual cycle - Mid proliferative
10		
11		
12		
13		menstrual cycle - Late Proliferative
14	ovulation Capacitation	
Fertilization		

Day	Stage	Event
1	Secretory Phase **Stage 1**	fertilization, zygote, Secretory Phase
2	**Stage 2**	morula, Blastula
3		blastocyst
4	**Stage 3**	blastocyst Hatching (zona pellucida lost)
5		Late Secretory, blastocyst (free floating)
6	**Stage 4**	Adplantation
7	**Stage 5**	
8		implantation
9		
10		
11		
12		
13	**Stage 6**	Chorionic Cavity
14		
Day	**Stage**	**Event**
15		
16	**Stage 7**	
17		
18	**Stage 8**	neural neurogenesis, neural groove and folds are first seen
19		
20	**Stage 9**	Musculoskeletal somitogenesis, first somites form and continue to be added in sequence caudally (1 - 3 somite pairs). neural the three main divisions of the brain, which are not cerebral vesicles, can be distinguished while the neural groove is still completely open Neural Crest mesencephalic neural crest is visible[1]
21		heart cardiogenesis, week 3 begins as paired heart tubes.
Day	**Stage**	**Event**
		Neural Crest differentiation at spinal cord level from day 22 until day 26 neural folds begin to fuse near the junction between brain and spinal cord, when Neural Crest cells are

22	**Stage 10**	arising mainly from the neural ectoderm Neural Crest trigeminal, facial, and postotic ganglia components visible[1] Neural Crest migration of vagal level neural crest cells begins (7-10 somite stage) neural rostral neural tube forms 3 primary brain vesicles (week 4) respiratory Week 4 - laryngotracheal groove forms on floor foregut.
23		heart begins to beat in Humans by day 22-23, first functioning embryonic organ formed.
24	Stage 11	thyroid - thyroid median endodermal thickening in the floor of pharynx neural rostral (or cephalic) neuropore closes within a few hours; closure is bidirectional, it takes place from the dorsal and terminal lips and may occur in two areas simultaneously. The two lips, however, behave differently. ventricular Optic ventricle appears and the neural groove/tube space is initially filled with amniotic fluid. [2]
25	Stage 12	pituitary Week 4 hypophysial pouch, Rathke's pouch, diverticulum from roof liver septum transversum forming liver stroma and hepatic diverticulum forming hepatic trabeculae[3] neural caudal neuropore takes a day to close (closure is approximately at future somitic pair 31/sacral vertebra 2) neural secondary neurulation begins ventricular onset of the ventricular system and separates the ependymal from the amniotic fluid.[2] neural crest cardiac crest, neural crest from rhombomeres 6 and 7 that migrates to pharyngeal arch 3 and from there the truncus arteriosus[1] neural crest vagal neural crest enter the foregut (20-25 somite stage)
26		
27		
		neural the neural tube is normally completely closed, ventricular system now separated from amniotic fluid.

28	Stage 13	Neural crest at spinal level is segregating, and spinal ganglia are in series with the somites. Spinal cord ventral roots beginning to develop.[4] telencephalon cavity appears Neural - Vascular Development - hindbrain is supplied by two parallel neural arteries (or channels) that obtain their blood supply from carotid-vertebrobasilar anastomoses given by the pharyngeal arch arteries; trigeminal artery, the otic artery, hypoglossal artery, and the proatlantal artery.[5] liver epithelial cord proliferation enmeshing stromal capillaries[3] smell Crest comes from the nasal plates[6] integumentary 4 weeks - simple ectoderm epithelium over mesenchyme integumentary 1-3 months ectoderm- germinative (basal) cell repeated division of generates stratified epithelium; mesoderm- differentiates into connective tissue and blood vessels vision Optic vesicle lies close to the surface ectoderm. The surface ectoderm overlying the optic vesicle, in response to this contact, has thickened to form the lens placode.[7] Diaphragm - pleuroperitoneal fold (PPF) first discernible in human embryos (CRL 6mm).[8]
29		pituitary Week 5 elongation, contacts infundibulum, diverticulum of diencephalon heart Week 5 septation starts, atrial and ventricular respiratory Week 5 left and right lung buds push into the pericardioperitoneal canals (primordia of pleural cavity) Respiratory Week 5 to 17 lung histology - pseudoglandular hearing Week 5 cochlear part of otic vesicle elongates (humans 2.5 turns)
30		
31		
		Placodes sensory placodes, lens pit, otocyst, nasal placode, primary/secondary vesicles, fourth ventricle of brain

32	Stage 14	Template:Somite continued segmentation of paraxial mesoderm (somite pairs), heart prominence head 1st, 2nd and 3rd pharyngeal arch, forebrain, site of lens placode, site of otic placode, stomodeum **Body -** heart, liver, umbilical cord, mesonephric ridge visible externally as bulges. limb upper and lower limb buds growing. Abdominal Wall mesoderm of the primary body wall coalesced in the ventral midline to create the abdominal cavity.[9] neural first appearance of the future cerebral hemispheres. Cerebellar plate differentiated to an intermediate layer, and future rhombic lip identifiable[10] Neural - Vascular Development - basilar artery forms from the consolidation of the neural arteries.[5] ventricular Subarachnoid space initially as irregular spaces on the ventral surface of the spinal cord.[11] liver hepatic gland and its vascular channels enlarge, hematopoietic function appears[3] vision lens placode is indented by the lens pit.[7]
33	Stage 15	neural cranial nerves (except olfactory and optic) are identifiable in more advanced embryos[12] Neural - Vascular Development - vertebral arteries form from transverse anastomoses between cervical intersegmental arteries, beginning with the proatlantal artery and proceeding downward to the 6th intersegmental artery,[5] vision lens pit is closed. The lens vesicle and optic cup lie close to the surface ectoderm and appear to press against the surface.[7]
34		
35		vision 35 to 37 days retinal pigment present
		pituitary Week 6 - connecting stalk between pouch and oral cavity degenerates parathyroid Week 6 - diverticulum elongate, hollow then solid, dorsal cell proliferation thymus Week 6 - diverticulum elongate, hollow then solid, ventral cell proliferation

36		adrenal Week 6 - fetal cortex forms from mesothelium adjacent to dorsal mesentery, medulla neural crest cells from adjacent sympathetic ganglia respiratory Week 6 - descent of heart and lungs into thorax. Pleuroperitoneal foramen closes tongue Week 6 - gustatory papilla, caudal midline near the foramen caecum (week 6 to 7 - nerve fibers approach the lingual epithelium)
37	Stage 16	Neural first parasympathetic ganglia, submandibular and ciliary, are identifiable[13] Neural - Vascular Development - development of the middle cerebral artery is first identified as small buds originating proximal to the anterior cerebral artery on the anterior division of the primitive internal carotid artery.[5] limb upper limb bud **nerves** median nerve, radial nerve and ulnar nerve entered into hand plate, **myoblasts** spindle shaped and oriented parallel to limb bud axis. Abdominal Wall muscle cell migration about 25% of the hemicircumference of the abdominal cavity, the lateral plate mesoderm has become more condensed and thicker in the area around the myoblasts.[9] heart outflow tract elliptical configuration with four cushions, the two larger fusing at this stage. Semilunar valve leaflets form at the downstream end of the cushions head lip and palate components of the upper lip, medial nasal prominence and maxillary process present, median palatine process appears. Eyelid prior to the development of the eyelids, one small sulcus or groove forms above the eye (eyelid groove) and another below it.[7]
38		
39		
40		
		• neural ◦ telencephalon areas of the future archicortex, paleocortex, and neocortex, visible. Beginning of future choroid plexus[14] ◦ ventricular primordium of the epidural space appears first on the ventral part of the vertebral canal and develops rostro-

		caudally[15] • smell olfactory nerve fibres enter the brain[6] • Eyelid sulcus (groove) above and below eye deepen and eyelid folds develop (below first and then above)[7] • Diaphragm - pleuroperitoneal fold (PPF) no longer separated from the diaphragm (CRL 14mm)[8] • Abdominal Wall muscle cells now migrated approximately 50% of the distance to the ventral midline, inner and outer layers were not discernible yet.[9]
41	Stage 17	
42		heart separation of common cardiac outflow (aortic arch and pulmonary aorta)
Day	**Stage**	**Event**
43		pancreas Week 7 to 20 pancreatic hormones secretion increases, small amount maternal insulin respiratory Week 7 - enlargement of liver stops descent of heart and lungs
44	Stage 18	limb bone forms by endochondrial ossification and throughout embryo replacement of cartilage with bone (week 5-12). neural smell vomeronasal fibres and nervus terminalis[6] liverobturation due to epithelial proliferation, bile ducts became reorganized, continuity between liver cells and gut[3] ventricular duramater appears and spaces surround the circumference of the spinal cord, which coalesce and contain many blood vessels.[15] Female uterus opening of the paramesonephric (Müllerian) duct to the coelomic cavity formed as an invagination of the coelomic epithelium[16] Abdominal Wall separation of the myoblasts into distinct inner and outer layers, with unidirectional orientation. Abdominal wall thicker in the region where secondary structures were forming compared with the primary body wall region, dorsally outermost layer of connective tissue approximately half of this thickness.[9]
45		liver (stage 18 to 23) biliary ductules developed in periportal connective tissue

		produces ductal plates that receive biliary capillaries[3]
46		
47		
48	Stage 19	• vision - (stage 19 -22) eyelid folds develop into the eyelids and cover more of the eye as the palpebral fissure takes shape. The upper and the lower eyelids meet at the outer canthus in Stage 19.[7] • cardiovascular ◦ arterial system[17] Chapter 18 fig. 447). ◦ aortic arches [18] stages 11–19 (figs. 29–40). ◦ heart fusion of aortic and mitral endocardial cushion material[19] • Respiratory - first generation of subsegmental bronchi now complete, see bronchial tree reconstruction[20] (plates 3 and 4). • gastrointestinal tract - anal membrane defined. • renal - Cloacal membrane ruptures from urinary pressure at stage 18 or stage 19, • genital ◦ testis - Rete testis develops from the seminiferous cords at stages 19–23, and tunica albuginea forms.[21]. ◦ ovary - Rete ovarii cords are developing.[22] ◦ uterus Müllerian duct grows independently from the invagination of the coelomic epithelium during stages 19-23[16] • musculoskeletal ◦ Sternum right and left sternal bars are present.[23] (figs. 7-17 and 7-22) ◦ Abdominal Wall segregation of the myoblasts into four distinct muscle groups with unidirectional orientation of myoblasts. Myoblast migrated over half of the distance to the ventral midline, abdominal wall thickest where the muscles migrated and the outermost layer of connective tissue comprises approximately half of the total thickness of the abdominal wall. Rectus muscle completely separated after migrating over half the distance to the midline.[9] • neural ◦ rhombencephalon migration for olivary and arcuate nuclei begins. ◦ choroid plexus of the fourth ventricle present.

		◦ stria medullaris thalami reaches the habenular nuclei. ◦ habenular commissure begins to develop. ◦ accessory olivary nucleus appears[24] ◦ Neural - Vascular Development - middle cerebral artery becomes more prominent, the plexi fuse into a single artery and further branches pierce the cerebral hemisphere.[5]
49		
50	Stage 20	Head scalp vascular plexus visible limb upper limbs begin to rotate ventrally neural amygdaloid body has at least four individual nuclei[24] oculomotor nerve shows a dorsolateral and a ventromedial portion rhombic lip (rhombencephalon) formation of the cerebellum (intermediate layer) and of the cochlear nuclei cerebellum cell layer (future Purkinje cells) develops choroid plexuses of the fourth and lateral ventricles Eyelid the inner canthus is established.[7]
51		gastrointestinal tract anal membrane perforates
52	Stage 21	neural cortical plate appears in the area of future insula[25] Neural - Vascular Development - formation of the anterior communicating artery.[5] limb upper and lower limbs rotate Intraembryonic Coelom pericardioperitoneal canals close Abdominal Wall Myoblasts have reached the ventral midline and myotubes were present and oriented uniformly within all muscle groups. The rectus abdominis formed distinct bundles of muscle. Connective tissue layers comprised the majority of the thickness of the abdominal wall, outermost layer of connective tissue accounted for the majority of this thickness.[9]
53		
		neural neocortical fibres project to epithalamus, to

54	Stage 22	dorsal thalamus, and to mesencephalon[25] limb fingers and toes lengthen smell Stage 22 to early fetal period - migratory streams of neurons from the subventricular zone of the olfactory bulb towards the future claustrum[6] Uterus Vagina fused duct (uterovaginal canal) bifurcated at the caudal portion at Carnegie stages 22 and 23[16]
55		Genital 8 Weeks Testis - mesenchyme, interstitial cells (of Leydig) secrete testosterone, androstenedione Genital 8 to 12 Weeks - hCG stimulates testosterone production Tongue Week 8 - nerves penetrate epitheilai basal lamina and synapse with undifferentiated, elongated, epithelial cells (taste bud progenitor cell)[26]
56	Stage 23	Stage 23 defines the end of the embryonic (organogenesis) period Mesoderm heart prominence, ossification continues Head nose, eye, external acoustic meatus, eyelids, external ears, rounded head **Body** - straightening of trunk, umbilical cord, intestines herniated at umbilicus limb upper limbs longer and bent at elbow, hands and feet turned inward, foot with separated digits, wrist, hand with separated digits Extraembryonic Coelom chorionic cavity is now lost by fusion with the expanding amniotic cavity neural rhombencephalon, pyramidal decussation present, nuclei and tracts similar to those present in the newborn cerebellum present as only a plate connected to midbrain and hindbrain through fibre bundles[27] Axial Skeleton vertebral column 33 or 34 cartilaginous vertebrae (20-33 mm in total length), vertebral pedicles, articular and transverse processes identifiable (no spinous processes)[28] Abdominal Wall Rectus muscle forms 2 or 3 distinct layers with myotube orientation uniform in all muscles. The external oblique and internal oblique started to expand in thickness, transversus a thin

		layer of muscle.[9]
	Week 8	Stomach Week 8 - Gastrin containing cells in stomach antrum. Somatostatin cells in both the antrum and the fundus. Genital - Female Development paired paramesonephric (Müllerian) ducts contact each other and are fused into a single tube that separates again and returns to the mesonephric (Wolffian) ducts. The paramesonephric ducts have not yet reached the urogenital sinus.[16]
57-63	Week 9	Beginning of Fetal Development Historic Embryology - In 1949 the embryologist George Streeter[29] used the replacement of cartilage within the humerus by bone marrow as an arbitrary definition of the embryo to fetus transition. "*If the onset can be recognized in a given specimen, that specimen is straightway classed as a fetus.*" CRL 43 mm, femur length 6 mm 9 weeks CRL 50 mm - genital genitalia in both sexes look identical[30] uterus - paramesonephric ducts come into apposition with the urorectal septum and begin to fuse
Day	**Stage**	**Event**
64		Gastrointestinal Tract Week 10 intestines in abdomen Pituitary growth hormone and ACTH detectable Pancreas Week 10 glucagon (alpha) differentiate first, somatostatin (delta), insulin (beta) cells differentiate, insulin secretion begins Tongue Week 10 shallow grooves above the taste bud primordium Stomach Week 10 - Glucagon containing cells in stomach fundus. Nail Development fingernails appear outer ear Week 10 - Meatal plug extends in a disc-like fashion, the meatus is boot-shaped with a narrow neck and the sole of the meatal plug spreading widely to form the future tympanic membrane medially. Proximal portion of the neck starts to be resorbed. inner ear Week 10 - neural-crest-derived

		melanocytes migrate into the cochlea. They penetrate the basement membrane of the lateral wall epithelium and develop into the intermediate cells of the stria vascularis.[31]
65		
66		
67		
68		
69		
70		Week 10 - CRL 55 mm, femur length 9 mm, biparietal diameter 17 mm
Day	**Stage**	**Event** neural - Cerebrum appearance of the first sulcus (week 11-15, **GA** 13-17 weeks)[32]
71		Thyroid colloid appearance in thyroid follicles, iodine and thyroid hormone (TH) synthesis Stomach Week 11 - Serotonin containing cells in both the antrum and the fundus.
72		
73		
74		
75		
76		
77		Week 11 - CRL 68 mm, femur length 12 mm, biparietal diameter 20 mm
	ExpandSystems **Systems:** bone timeline | eye neural crest timeline | heart abnormality timeline | hearing EAM timeline | muscle timeline | ovary timeline | placental villi timeline | shoulder timeline | smell timeline | spleen timeline | ventricular timeline	

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Glossary Links

Glossary: 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 | Term Link

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