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Sincerely,  
Darryl Hosford

Hosford Web Service  
919 Liberty St. Ext.  
Grove City, PA 16127

Email: [ptnotes@ptcentral.com](mailto:ptnotes@ptcentral.com)  
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### Embryology Class Notes

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# Embryology

PT 634 Fall 1995

Instructor: Dr. Simon Beeching

Notes Taken and Edited by Darryl Hosford

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## Gastrulation

Early in week three, the embryo begins the process of gastrulation, which is the formation of three primary (germ) layers. The ectoderm, mesoderm and the endoderm.

- I. Formation:
  - A. Formation of the primitive streak begins with a thickening of cells along the cranial - caudal axis.
  - B. Migration of cells to the caudal extent of the primitive streak in opposing waves of migrating cells.
  - C. Epiblast cells invaginate (flow over the edge) and ingress (migrate through the upper layer of cells to the area above the hypoblast.)
  - D. Ingressing cells displace the cells of the hypoblast.
  - E. Flow of cells into the primitive streak continues for 2 weeks.
  - F. Advance of the primitive streak cranially with the primitive groove and primitive node (Hensen's node) with the primitive pit at the base of the node.
  
- II. Structures and layers formed
  - A. The ingressing cells form three embryonic tissue types:
    1. mesenchyme - embryonic connective tissue
    2. embryonic mesoderm
    3. embryonic endoderm
  - B. Notochordal process (mesodermal) forms a cylindrical structure called the notochord. It functions as a basic organizer of the embryo.
  - C. Cranial extent of the notochord = the mouth
  - D. Caudal extent of the primitive streak = the anus

## Embryonic Tissue Layers

As the bilaminar disk develops via gastrulation, three primary tissue layers form the triploblastic embryo.

### I. Ectoderm

#### A. Surface ectodermal derivatives

1. epidermis made of stratified squamous epithelium
2. hair and nails (keratinized epidermal structures)
3. cutaneous glands
  - a) sweat glands
  - b) sebaceous glands (oil producing associated with hair follicle)
4. mammary glands
5. adenoypophysis (anterior pituitary)
6. tooth enamel (from ameloblast cells)
7. inner ear (organs of equilibrium)
8. lens of the eye

#### B. Neuro ectoderm

1. CNS
2. retina
3. pineal body (gland)
4. neurohypophysis (posterior pituitary)
5. neural crest cell derivatives
  - a) ganglia
  - b) medulla of adrenal gland (producing adrenaline which is:
    - (1) epinephrine
    - (2) norepinephrine
  - c) pigment cells (melanocytes)
  - d) branchial arch cartilage
  - e) head mesenchyme

### II. Mesoderm

#### A. Head mesoderm

1. skull
2. head muscles and facial connective tissue
3. dentine (layer of tooth deep to enamel)
  - a) hydroxyapatite matrix
  - b) acellular

#### B. Paraxial mesoderm

1. trunk musculature
2. skeletal elements
3. dermis
4. somatic connective tissues

C. Intermediate mesoderm

1. urogenital system

D. Lateral mesoderm

1. muscle and connective tissues of appendages
2. serous membranes of the body cavities
3. blood and lymph cells
4. circulatory system
5. spleen
6. cortex of the adrenal gland (produces steroids)

III. Endoderm

- A. Epithelium of the respiratory system
- B. Epithelium of the digestive system
- C. Thyroid gland
- D. Tympanic cavity (middle ear)
- E. Tonsils
- F. Parathyroid glands

## Extraembryonic Membranes

There are four primary extraembryonic membranes that surround cavities around the embryo.  
These are the amnion, the chorion, the yolk sac, and the allantois.

### I. Amnion formation

#### A. by day 10

1. epiblast derivatives
2. extraembryonic mesoderm surrounds the amnion

#### B. by day 12

1. extraembryonic mesoderm has given rise to a cavity called the coelom (extraembryonic coelom)

#### C. by week 3 the amnion is formed, when composed of:

1. epiblast derived cells surround the amniotic cavity
2. extraembryonic “somatic” mesoderm

### II. Chorion formation (also referred to as the serosa)

#### A. Made of:

1. syncytiotrophoblast cells
2. cytotrophoblast cells
3. extraembryonic “somatic” mesoderm

#### B. by end of week 2 the cytotrophoblast cells form columns of cells that project into the decidua, and are called 1° villi

### III. Yolk Sac

#### A. Made of:

1. extraembryonic endoderm (from the hypoblast)
2. extraembryonic “splanchnic” (meaning visceral) mesoderm

#### B. In humans, the yolk sac is considered partially vestigial

### IV. At day 16 the allantois diverticulum (meaning a blind pouch) forms

#### A. Functions in:

1. hematogenesis (blood formation)
2. formation of urinary bladder
3. formation of umbilical arteries and veins

#### B. Primitive functions

1. respiratory functions
2. storage site for metabolic wastes

## Placentation

### I. Problems with implantation site

- A. Atypical implantation in the uterus may be problematic
  - 1. Normal implantation occurs in the upper central portion posterior wall of the uterus.
  - 2. Implantation in the internal ostium (inner narrowing toward cervix) results in placenta previa. Since the placenta forms next to or over the internal opening of the uterus, fetal movement can cause bleeding. (This can sometimes be confused with normal menstrual flow.)
- B. Ectopic Pregnancy - less than 2% of all pregnancies
  - 1. Pregnancy and implantation outside of the uterus
  - 2. Fallopian tube implantation will burst the tube and endanger the life of the mother.

### II. Changes in the endometrium due to implantation.

Note that implantation is usually complete by the eleventh day. Diagram of 10-4-95 B.

Trophoblast implanted.

#### A. Endometrium

- 1. Changes in endometrium
  - a) Endometrial cells (called "pale cells") proximal to the syncytiotrophoblast enlarge.
  - b) This gravid endometrium is shed (called decidua) as afterbirth with the placenta.
- 2. Expansion of uterine glands which are invaginations from the surface into the functional layer of the endometrium.

#### B. Fetal tissue

Expanding syncytiotrophoblast erodes maternal blood vessels (spiral arteries) within the endometrium

- 1. This leads to lacunae filling with maternal blood
- 2. and serves as embryotroph by supplying nutrition for the embryo.

### III. Placental development

#### A. Villi development: (see diagram on p 117)

- 1. Primary villi are columns of cytotrophoblast cells that extend further into the endometrium
- 2. Secondary villi are primary villi that have been invaded by extraembryonic somatic mesoderm
- 3. During week 3 embryonic circulation is beginning to form, including vessel formation (angiogenesis)
- 4. Tertiary villi are chorionic villi that have blood vessels within themselves
- 5. Some mature villi form anchoring villi

#### B. By week 4 you see early embryonic circulation

- 1. Formation of chorionic blood vessels
- 2. Extraembryonic vessels can communicate with developing intraembryonic vessels via umbilical veins and arteries.
- 3. Umbilical vessels develop from the differentiation of the extraembryonic "splanchnic" mesoderm of the allantois.

#### IV. Placental characteristics

- A. The human placenta is a chorioallantoic placenta.
- B. The placenta forms within the decidua (see diagram on p 114)
  - 1. Decidua basalis is the area deep to the embryo. This is the area of placental development.
  - 2. Decidua capsularis is the superficial region of the endometrium that is stretched over the developing embryo.
  - 3. Decidua parietalis is the rest of the decidua of the uterus not directly around the embryo.
- C. The chorion becomes villous in the region of the decidua basalis.
- D. The developing placenta has two components:
  - 1. Maternal, derived from the decidua basalis
  - 2. Fetal, derived from the villous chorion
- E. Trophoblastic cells migrate and envelop the syncytiotrophoblast area.
  - 1. Intervillous space fills with maternal blood
  - 2. Blood enters under arterial pressure, spurting into the intervillous space, and is drained by maternal veins.
  - 3. There are 60 - 100 anchoring villi in a normal placenta.
  - 4. The nutrient flow to the fetus is maternal spiral artery  $\Rightarrow$  intervillous space  $\Rightarrow$  fetal umbilical vein. Wastes are removed through a similar diffusion pathway back to maternal blood.
- F. Chorionic villous sampling
  - 1. Snipping off of a piece of chorionic villous
  - 2. Used to detect birth defects
  - 3. Can be done in the second month

## Neurulation

During the third to the fourth week the embryo produces a downward fold of tissues on all sides with the end intent of closing in the gut with endoderm on the inside. The head and tail undergo a fold, and also the lateral fold forms.

- I. Gastrulation results in three embryonic tissue layers and three axis of symmetry.  
During cleavage, there is restricted gene expression which fates the presumptive ectoderm to one of three basic pathways
  - A. surface ectoderm
  - B. neural ectoderm
  - C. neural crest
  
- II. Neurulation is the formation of the neural tube and the subsequent overlaying of surface ectoderm.
  - A. The process is called neurula
  - B. Begins around 18th day and is complete during the fourth week (specifically complete with the closing of the cranial neuropore and the caudal neuropore.)
    1. Neural tube forms the CNS
    2. Neural tube formation is induced by the chorda mesoderm (a.k.a. the presumptive notochord). This is called primary induction.
  - C. Indications of neuralization
    1. Elongation of cells overlaying the notochord. As if they were becoming more columnar in appearance.
    2. Associated with microtubule assembly. (Colchicine can disrupt neural plate formation by halting the microtubule formation.)
    3. The ectoderm rises up in two folds side by side
      - a) possibly caused by apical constriction- where there is a widening of the base and a narrowing of the apex.
      - b) and / or poisson buckling- where tension along the cranial / caudal axis is thought to form a trough down the center line.
  - D. Fusion of the two folds along the dorsal midline
    1. As the neural folds approximate, the cells along their cresting margins are freed from the developing neural tube.
    2. The neural tube undergoes subsidence into the ectoderm layer.
    3. The neural crest band splits and cells migrate ventrolaterally. Many neural crest cells migrate throughout the embryonic body to form various tissues.
      - a) neuroglial cells of the PNS such as the Schwann cell
      - b) pia matter and arachnoid layer
      - c) pigment cells of the skin- melanocytes
      - d) adrenal medulla
      - e) head mesenchyme

- f) the cells remaining in the ventrolateral bands form:
  - (1) dorsal root ganglia
  - (2) cranial nerve ganglia associated with V the Trigeminal, VII the Facial, IX the Glossopharyngeal, and X the Vagus
- E. Early CNS development
  - 1. Takes place as a series of cranial expansions
  - 2. Craniocaudal sequence
    - a) Prosencephalon “forebrain”
      - (1) Telencephalon “chamber at the end”
      - (2) Diencephalon - composing all the “mus” structures
    - b) Mesencephalon “midbrain”
    - c) Rhombencephalon “hindbrain”
      - (1) Metencephalon - the pons and cerebellum
      - (2) Myelencephalon - the medulla oblongata
- F. Targeting of Nervous Tissue (How does it find its target?)
  - 1. Neurons develop by the formation of growth cones.
    - a) exhibit relatively dramatic pathfinding abilities as seen in early embryos
    - b) relatively few mistaken connections
  - 2. There are three suggestions as to a directional mechanism:
    - a) Haptotaxis: where the growth cones follow adhesive gradients. They seem to be attracted from less adhesive to more adhesive areas.
    - b) Chemotaxis: where orientation is due to a diffusible substance in the environment. Examples include NGF (neural growth factors) that are diffusible polypeptide chemoattractants. These bind selectively to membrane bound receptors of developing neurons as well as other embryonic tissues.
    - c) Contact inhibition: where new growth cones are sprouted in other directions once a growth cone contacts another cell. This inhibition tends to direct growth cones toward areas of low cell density.
- G. Neuromeres
  - 1. Formed by segmentation of the cranial neural tube
  - 2. First discovered in the late 19th century.
  - 3. In chicks, they appear in day 2, and disappear by day 14. They are well formed in the Rhombencephalon.
  - 4. They are probably organizational centers within the developing CNS.
- H. Neuromeres and Organization
  - 1. Studies of *Drosophila* have revealed how segmentation can provide organization in development.
  - 2. *Drosophila* larva consist of 14 segments which collectively give rise to the adult structures.
  - 3. Successive segments within the lateral body differentially express a cascade of homeotic selector genes.
    - a) Genes are activated in a craniocaudal direction as a chain of triggered events along the segments.
    - b) They are controllers of genes within the segments, which then activate sub genes within that cluster to allow further differentional pathways.

- c) Homeotic mutation in *Drosophila* causes a leg to form in the place of an antenna.
- 4. Homeobox
  - a) All of the above selector genes have a 180 base pair nucleotide sequence and it has been discovered as being well conserved.
  - b) Homeobox nucleotide sequences are converted to proteins. (DNA via transcription  $\Rightarrow$  mRNA which via translation  $\Rightarrow$  protein.) This 60 amino acid “blob” is found on all homeobox proteins and is called a homeodomain.
  - c) The homeodomain is a highly conserved DNA binding region, and all form transcription factors that effect the nucleus by turning on or turning off genes.
- 5. Connection to humans
  - a) Recent studies have examined neuromeres in light of *Drosophila* development
    - (1) Staining of mitotically active cells revealed that mitotic activity is intense within the neuromeres (also called rhombomeres). The activity is in the center but relatively rare at the edges. (therefore they are not artifacts.)
    - (2) Nerve cells associated with CN V Trigeminal only form in rhombomeres 2 and 3, CN VII only forms from Rhombomeres 4 and 5.
    - (3) Vital stain (which does not kill but marks the cell for migrational studies) shows that cells migrate within the Rhombencephalon freely up until the appearance of the neuromeres. After that time they do not move out of the rhombomere. It looks as if the cells are settling down for differentiation.
    - (4) Olaf Sundin (in 91-93 ?) discovered the sequence of the gene expressed only in the chick Rhombomere 4. This gene had a homeobox.

## Heart Formation

- I. Adult heart blood flow
  - A. superior and inferior vena cava return blood from systemic circulation to the right atria
  - B. blood passes through the tricuspid valve to the right ventricle
  - C. from the right ventricle through the semi lunar valve to the pulmonary trunk
  - D. the blood passes through the lungs
  - E. pulmonary veins empty blood into the left atria
  - F. blood passes through the bicuspid valve to the left ventricle
  - G. from the left ventricle through a semi lunar valve to the aorta and then the systemic circulation to start the loop over again.
  
- II. Early heart development
  - A. The yolk sac is the site of early hematopoiesis (early blood formation)
  - B. Early heart development is critical because the yolk sac is deplete in nutrients
  - C. By ~day 16, a crescent shaped region of mesoderm forms cephalic to the embryo cardiogenic plate.
  - D. Lateral folds, head folds and tail folds are raising the embryo (this will ultimately draw the heart from its cephalic location into the body cavity below the head.
  - E. Later in the third week, the developing heart becomes visible as the cardiac primordia
    1. This development is from paired cardiogenic cords (arms of the crescent formation) ventrolateral to the developing foregut.
    2. Paired primordia drawn together and develop into fused midline structures / organs.
    3. Each cord canalizes (to hollow out) to form paired endocardial tubes. The tubes have two regions:
      - a) inner endocardial primordium
      - b) outer epimyocardial primordium
    4. Lateral to the endocardial tubes, a split forms in the mesoderm. The cavity thus formed is the pericardial coelom (the cavity that will surround the heart).
    5. Fusion of the paired endocardial tubes form a single midline structure. A single tube heart with a series of swellings. (These structures are out of order, the bending of development will properly align the structures again.) In caudocranial sequence:
      - a) sinus venosus
      - b) atrium
      - c) ventricle
      - d) bulbus cordis
  - F. Formation of the cardiac loop
    1. At this time the heart is encased within the pericardial cavity. As the heart structure elongates within the pericardial cavity, yet being held within the cavity, it begins to bend and twist to position the ventricle in the caudal direction.
    2. This elongation causes the heart to undergo D-looping (with a bulge to the right).
    3. By the end of the 4th week the heart assumes an S-shape (shifting the atria superior to the ventricles).

4. The atrium is moving cranially relative to the ventricle.
5. The junction of sinus venosus and the atrium shifts from midline to the right (clearing space for the pulmonary veins on the left.)

### III. Development of the fetal heart

- A. Flow of fetal blood from caudal to cranial
  1. Atrium receiving blood from the sinus venosus
  2. Ventricle is represented by the bent portion formed by D-looping and subsequent expansion.
  3. Bulbus cordis remains undifferentiated (to form trunks)
- B. Ventricular medial furrow indicates future site of the interventricular septum.
- C. Atrium assumes a bilobed appearance- results from expansion on either side of the midline.
- D. Time line
  1. division of the chambers begins during week five
  2. at week 6 there is an influx of tissue (thickening pads called endocardial cushions) in the atrio-ventricular canal
  3. separation of the atria involves the sequential formation of partitions
    - a) Septum primum proceeds downward (like a dropping curtain) to divide the atria.
    - b) As this septum closes, the space under the "curtain" is called the interatrial foramen primum.
    - c) As the septum primum is closing, it perforates at the top, forming the interatrial foramen secundum.
    - d) A second septum, the septum secundum is appearing as the above is taking place. This septum begins to close in from all sides (like a camera aperture). It does not close all of the way, and the foramen is called the foramen of ovale (present at birth).
    - e) The septum primum flap below the perforation serves as a one-way valve allowing blood to flow transatria. It is called the valvula foramina ovalis. (This closes with the first breath by the decrease of pressure in the right atria. This flap soon heals closed.)
    - f) Fetal circulation persists like this till birth since the lungs are not functional. This foramina ovalis serves as a shunt to allow blood to pass around the pulmonary circuit.
  4. at week 5 you see the growth of the interventricular septum
  5. at week 8 this interventricular septum fuses with the AV cushion
  6. In later developmental stages the bulbus cordis elongates and becomes known as the truncus arteriosus.
    - a) Destined to give rise to the aorta and pulmonary trunk.
    - b) A septum forms dividing the truncus, called the septum aorticum or the aortopulmonary septum.

### IV. Congenital heart defects

- A. Interatrial septal defects
  1. most found at the foramen ovale
  2. resorption of septum primum

- a) may render the valvula foramen ovalis inadequate to cover the foramen ovalis at birth (typically coupled with the problem of having an oversized foramen ovalis)
  - b) failure of the septum primum flap to heal closed (not fusing with the AV canal cushion)
- B. Interventricular septal defects
- 1. the interventricular septum may not close properly. This occurrence is often coupled with an improper partitioning of the trunks.
  - 2. trabeculae are present (perforations of the interventricular septum)
    - a) usually not a life threatening problem as the ventricular contractions close these pores during systole
- C. Abnormality in trunk partitioning (from the time period of week 6)
- 1. failure of truncus partition to form is called a persistent truncus. This allows the free mix of systemic and aortic blood
    - a) usually fatal at birth
  - 2. transposition of the pulmonary artery and the aorta
    - a) usually a fatal condition
  - 3. aortic stenosis is a narrowed aorta
    - a) typically fatal
  - 4. pulmonary stenosis is a narrowing of the pulmonary trunk
    - a) usually not fatal
    - b) This is often related to a complex: the Tetralogy of Fallot (baby typically cyanotic at birth)
      - (1) pulmonary stenosis
      - (2) defective interventricular septum
      - (3) an oversized aorta
      - (4) abnormally thickened (hypertrophy) right ventricular wall
- D. Malfunction of the valves
- 1. partial fusion of the semilunar valves, also causing stenosis
  - 2. the atrioventricular valve could be malformed or missing cusps
  - 3. malformed chordae tendinae or papillary muscles for valve reinforcement
- E. Other congenital defects:
- 1. ectopia cordis, where the heart is outside of the body, and the sternum does not form properly
  - 2. dextrocardia, the reversal of the heart orientation

## Circulatory System Development

- I. General considerations:
  - A. The heart becomes contractile by the end of week 3
  - B. Blood and vessel formation occur, first extraembryonically and later within the embryo proper.
    1. Blood islands first appear on the splanchnopleure of the yolk sac. Splanchnopleure is:
      - a) extraembryonic endoderm
      - b) extraembryonic splanchnic mesoderm
    2. Next these islands appear on the allantois and then on the embryo.
    3. The blood islands begin to cavitate (hollow out). These hollow spaces fuse to adjacent spaces to make up the early vessels. Blood vessel precursors form from coalescing of the cavities within the blood islands.
    4. The inner cells differentiate as endothelium.
    5. Blood cells are also derived from blood islands.
- II. The early heart receives blood from caudal end and pumps it cranially to the aortic sac. From the aortic sac, blood enters a series of bilaterally paired vessels, the aortic arches.
  - A. coeliac artery - blood to the stomach
  - B. anterior mesenteric artery - blood to the intestines
  - C. posterior mesenteric artery -
  - D. Aortic arches fuse dorsally over the gut to form the dorsal aorta.
- III. Return of the blood to the heart
  1. Vitelline veins: the venous return of blood from the yolk sac through the yolk stalk is via the vitelline veins.
    - a) The right vitelline vein persists to function as a hepatic vein.
    - b) An anastomosis between the right and left vitelline veins will give rise to the hepatic portal vein.
  2. Umbilical veins: the venous return from the placenta through the area of the liver.
    - a) The right vein of the pair degenerates.
    - b) The left umbilical vein degenerates between the liver and the sinus venosus (the rest forms the umbilical vein.)
    - c) The ductus venosus develops as a shunt between the left umbilical vein and the inferior vena cava for blood passage due to the above degeneration. (b and c coincide and are functionally related.)
  3. Cardinal veins: these drain blood from the embryo proper.
    - a) in week 8 anterior cardinals join via anastomosis, and this joining forms the left brachiocephalic artery
    - b) the right anterior and common cardinals form the superior vena cava.
    - c) most of the posterior cardinals degenerate. The distal portions of the posterior cardinals are retained as common iliac vein.
    - d) inferior vena cava forms from several components including posterior cardinal anastomoses.

## Pharyngeal Arches

- I. In the 4th and 5th week a series of pharyngeal arches are forming.
  - A. Arch development:
    1. The first aortic arch degenerates to contribute to maxillary and external carotid arch arteries
    2. The second arch forms the stapedial arteries
    3. The third arch forms the carotid arteries
    4. The fourth arch forms the right subclavian artery, and the left part of the arch of the dorsal aorta
    5. The fifth often don't develop. If they do, they quickly degenerate.
    6. The sixth
      - a) left portion: forms the left pulmonary artery and the ductus arteriosus
      - b) right portion: forms the right pulmonary artery
  - B. Pharyngeal arches and pouches (the external clefts) are transitory.
    1. transitional structures in amniotes. (Amniotes produce a cleidoic egg in which extraembryonic membranes develop the yolk sac, amnion, and chorion.)
    2. pharyngeal grooves or clefts
      - a) the first groove forms the external auditory meatus
      - b) others degenerate
    3. pharyngeal arches
      - a) by week 6 there is an expansion of the 2nd pharyngeal arch. It begins to bulge and arch backward forming a cervical sinus
        - (1) ultimately covers all the external clefts, smoothing them out.
        - (2) remnant cervical vesicle thus produced is normally obliterated
      - b) in section, each arch contains
        - (1) an artery
        - (2) a nerve
        - (3) invading mesenchyme forming cartilage's, bone and muscle
    4. Nerves
      - a) Motor fibers associated with CN V - trigeminal, enervate developing muscles of pharyngeal arch I.
      - b) Motor fibers of CN VII - facial, enervate muscles of pharyngeal arch II.
      - c) Motor fibers of CN IX - glossopharyngeal, enervate muscles of pharyngeal arch III.
      - d) Sensory or afferent fiber pathways are not so restricted. Facial afferent returns through the CN V - trigeminal
    5. Connective tissues formed by the arches:
      - a) The first pharyngeal arch forms both the upper and lower jaw, the maxillae (maxillary processes) and the mandibulum (mandibular processes.)
      - b) The first and second arch gives rise to the ear ossicles
        - (1) first - malleus and incus
        - (2) second - stapes
      - c) The second and third arches give rise to the hyoid bone.

- d) The fourth and sixth give rise to the laryngeal cartilage's of the neck.
  - 6. Muscular tissues formed by the arches:
    - a) The first pharyngeal arch forms the muscles of mastication, including the masseters, temporalis and buccinator
    - b) The second arch gives rise to the muscles of expression
    - c) The third to sixth arch give rise to the muscles of the larynx, pharynx and neck.
    - d)
  - 7. Structures formed by pharyngeal pouches
    - a) first pharyngeal pouch
      - (1) eustachian tube (first closing plate forms)
      - (2) tympanic membrane
    - b) second pharyngeal pouch - forms the palatine tonsil
    - c) third pharyngeal pouch - contributes to two structures
      - (1) inferior III parathyroid glands
      - (2) thymus
    - d) fourth pharyngeal pouch - superior (IV) parathyroid glands
    - e) fifth pharyngeal pouch - forms rudimentary structures:
      - (1) ultimobranchial bodies
      - (2) form parafollicular cells (C-cells) of the thyroid. (C-cells are named because they produce a hormone called calcitonin which stimulates calcium deposition)
- C. Structure and organ development
1. Thyroid gland:
    - a) A thickening of cells in the pharynx producing a diverticulum.
    - b) Gives rise to a developing thyroid gland. The tube forms a thyroglossal duct and an orifice with the pharynx, the foramen cecum.
  2. The oropharyngeal membrane ruptures at day 25-26.
  3. The tongue forms anterior to the foregut
    - a) anterior 2/3 forms from the floor of the oral cavity
    - b) posterior 1/3 forms from floor of the pharynx
    - c) The tongue has foramen cecum
    - d) Invasion of nerve fibers into the tongue - This invasion induces the formation of taste buds on the tongue.
      - (1) anterior portion - CN V
      - (2) posterior portion - CN IX
      - (3) motor control of the tongue is supplied by XII - hypoglossal
  4. Salivary glands form from the endoderm of the oral cavity as a thickening of cells into a "rod shape group"
    - a) the secretory cells of the gland come from endoderm
    - b) the support cells of the gland come from mesenchyme from the neural crest

5. Facial development occurs primarily from weeks 4-8
  - a) forms from five facial primordia
    - (1) one frontonasal prominence
      - (a) later there is a thickening of cells called nasal placodes
      - (b) these invaginate to form the nasal pit
    - (2) two maxillary prominences
    - (3) two mandibular prominences
  - b) mandibular processes fuse to form the jaw
  - c) the left maxillary process fuses to the medial nasal prominence, then medial nasal prominence and the right maxillary process.