




CRANIOFACIAL DEVELOPMENT

DR. NITIN AWASTHI



General embryology

- Introduction
 - Prenatal development
 - Induction competence differentiation
 - Formation of three layered embryo
 - Formation of neural tube
 - The neural crest cells
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Craniofacial embryology

- Formation of head
- Branchial arches
- Fate of branchial grooves and pouches
- Anatomy of the arch
- Formation of face
- Formation of secondary palate
- Formation of tongue
- Development of maxilla and mandible

WHAT IS GROWTH?

- **“Developmental increase in mass.” - Stewart.(1982)**
- **“An increase in size or number.” - Profitt. (1986)**
- **“Normal changes in amount of living substance.” - Moyers(1988)**
- **“Growth signifies an increase, expansion or extension of any given tissue.” - Pinkham.(1994)**

WHAT IS DEVELOPMENT?

“Development is a progress towards maturity” – Todd(1931)

“Development connotes a maturational process involving progressive differentiation at the cellular and tissue levels” – Enlow.

Theories Of Growth

- Genetic theory
- Sutural theory
- Cartilagenous theory
- Functional matrix theory
- van Limborgh's theory
- Enlow's expanding 'V' principle
- Enlow's counterpart principle
- Neurotrophic process in orofacial growth

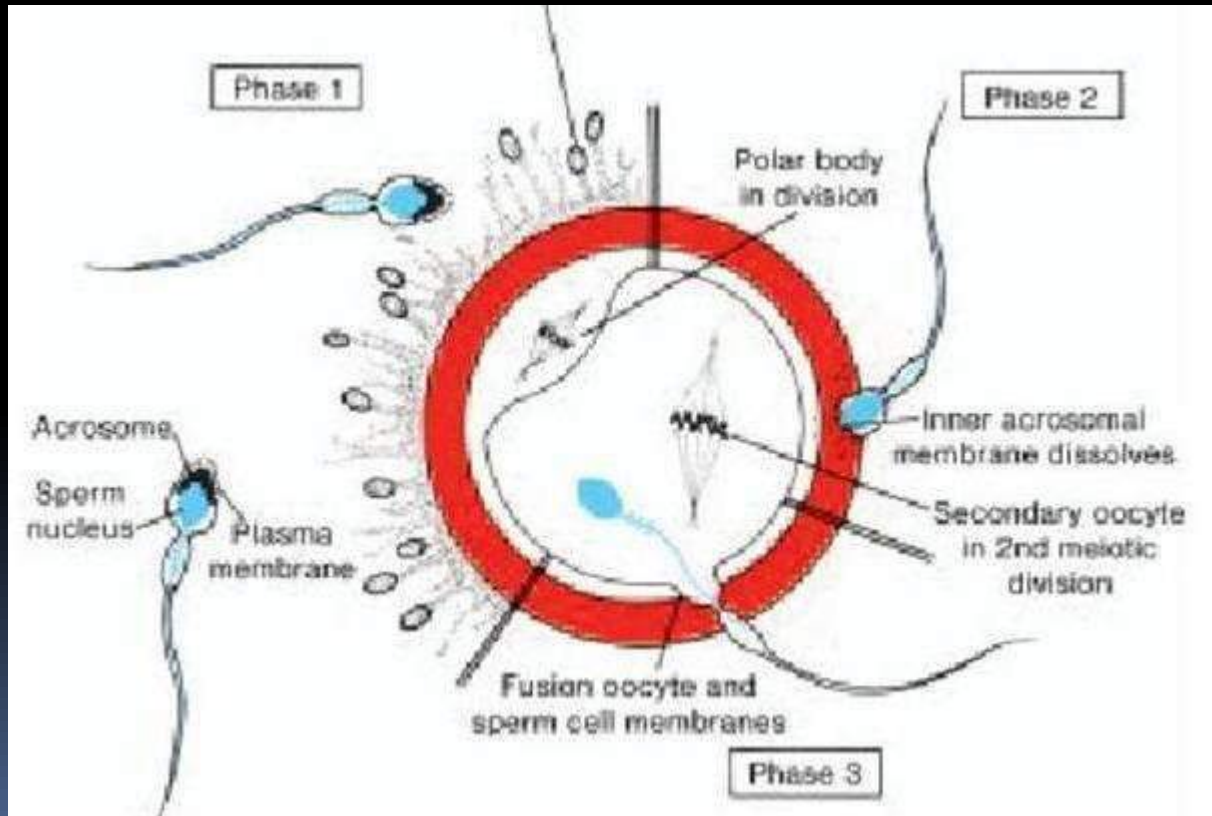
INTRODUCTION

- The human somatic cell contains 46 chromosomes, called as the diploid number. Out of which 44 are autosomes and the remaining 2 are sex chromosomes, designated as X and Y.
- The sex chromosomes in females are XX and in males are XY.
- There are two series of division of somatic cells- MITOSIS and MEIOSIS.

- MITOSIS produces the same number of chromosomes in the resulting daughter cell while MEIOSIS produces half the number i.e. 23 designated as haploid, with resultant formation of gametes .
- Development begins with FERTILIZATION, the process in which the male gamete- the sperm, and the female gamete- the oocyte, unite to form a ZYGOTE.

THE PROCESS OF FERTILIZATION

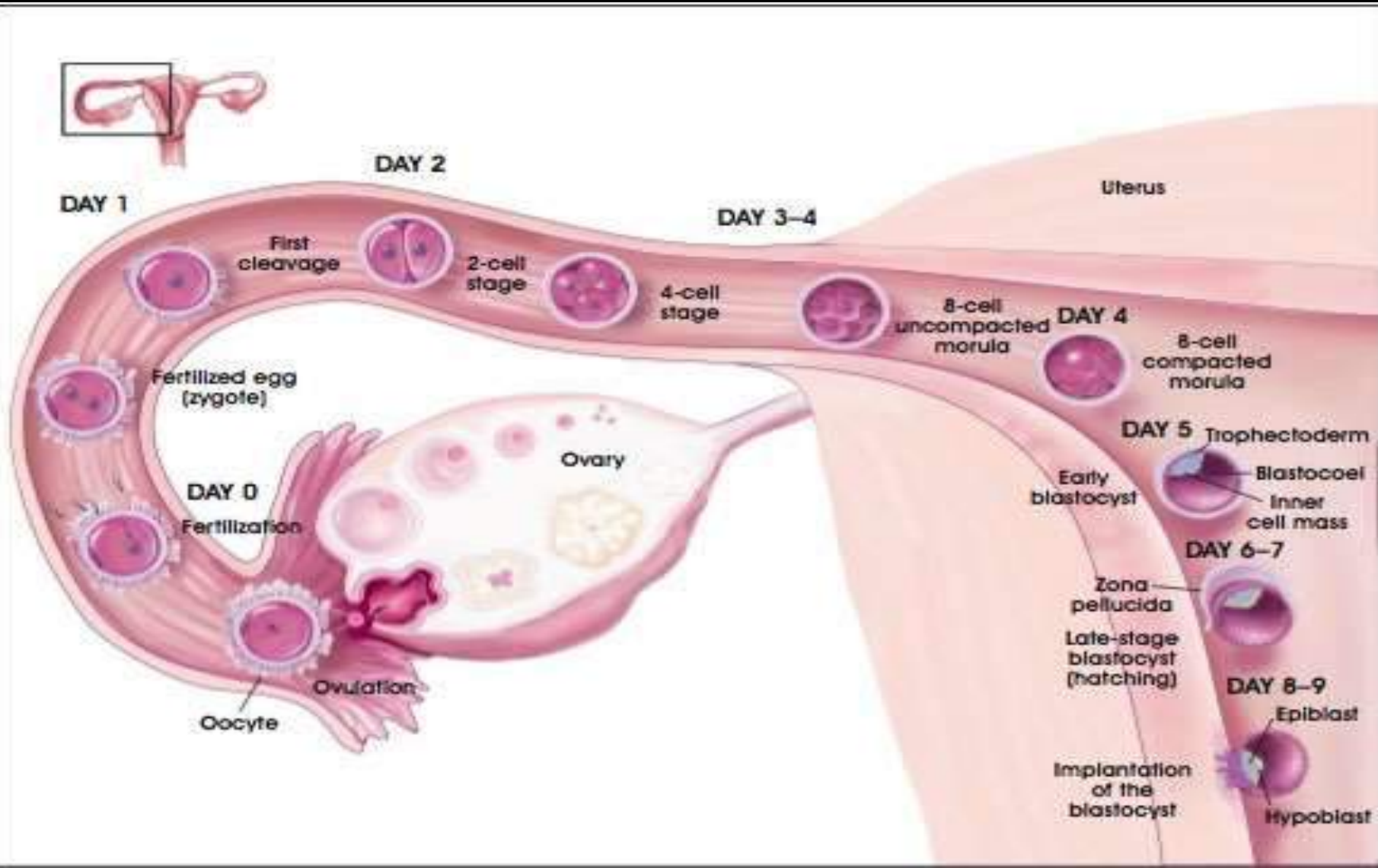
THE MALE GAMETE (SPERM) FUSES WITH THE FEMALE GAMETE (OVUM)



Prenatal development

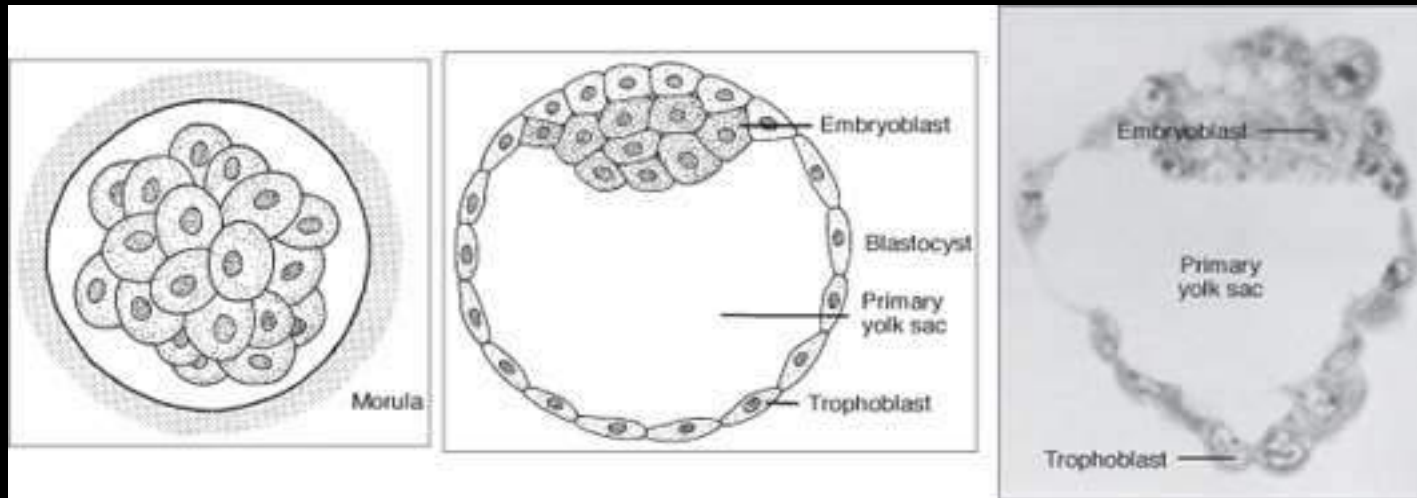
- Divided into three phases
 - First and second phase: Embryonic
 - Third phase: Foetal
- First phase- Cellular proliferation and migration
- Second phase- Morphogenesis
- Third phase- Growth and maturation

First week development



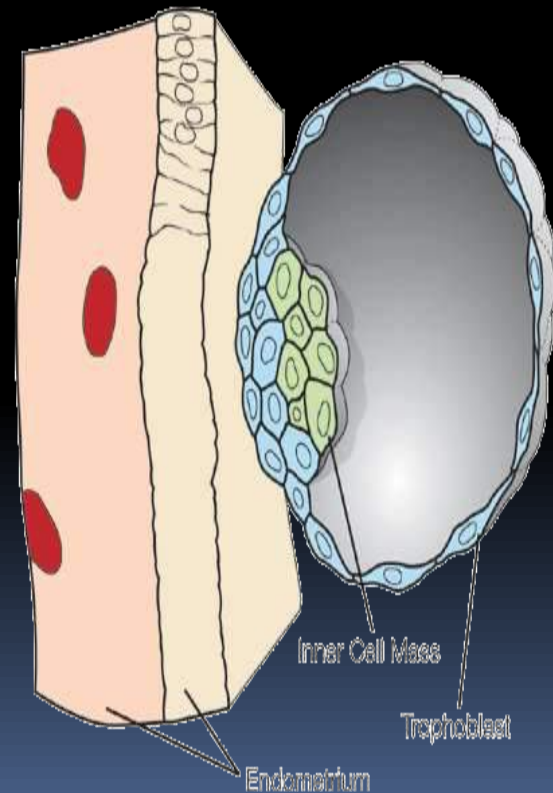
- After two cell stage, cells undergo mitotic division
- Until 8 cells cells loosely arranged
- 16 cell stage is called morula
- Outer layer- outer cell mass
- Inner layer – inner cell mass
-





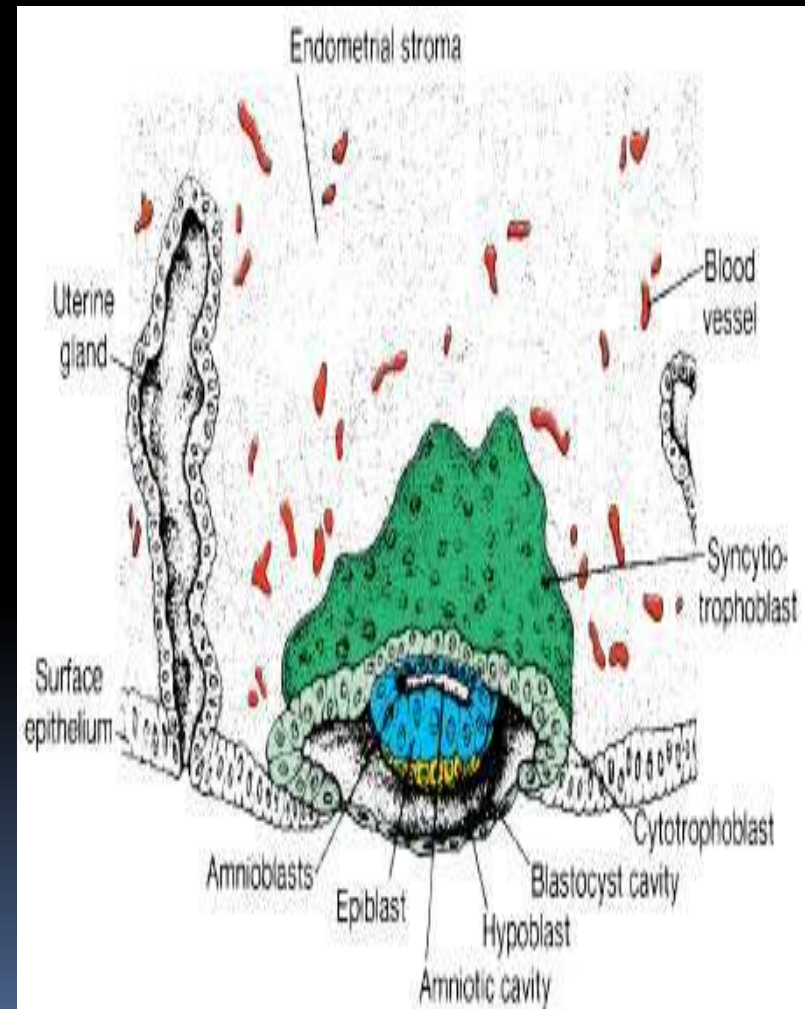
Fluid seeps into morula to form two cell population embryoblast and trophoblast- blastocyst


- Trophoblast adjacent to embryoblast will adhere to endometrial lining by means of laminins, integrins and fibronectins



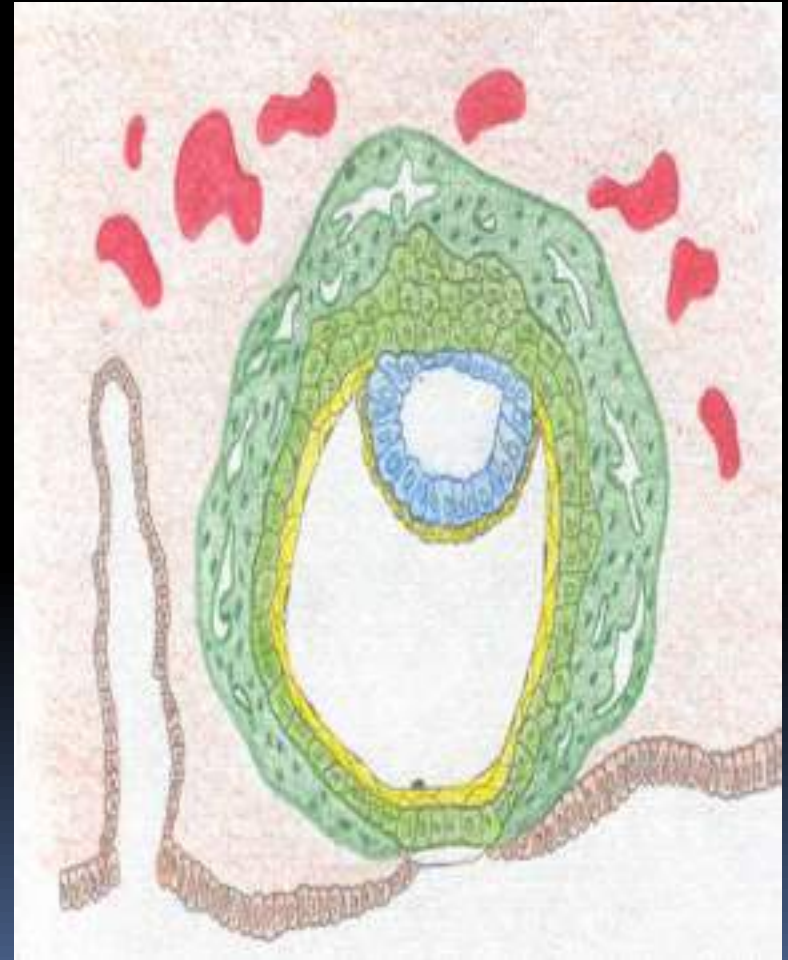
2nd week development

- Day 8th , trophoblast forms 2 layers. Syntical and cytotrophoblast
- Blastocyst partially embedded
- Formation of bilaminar germ disc
- Epiblast and hypoblast



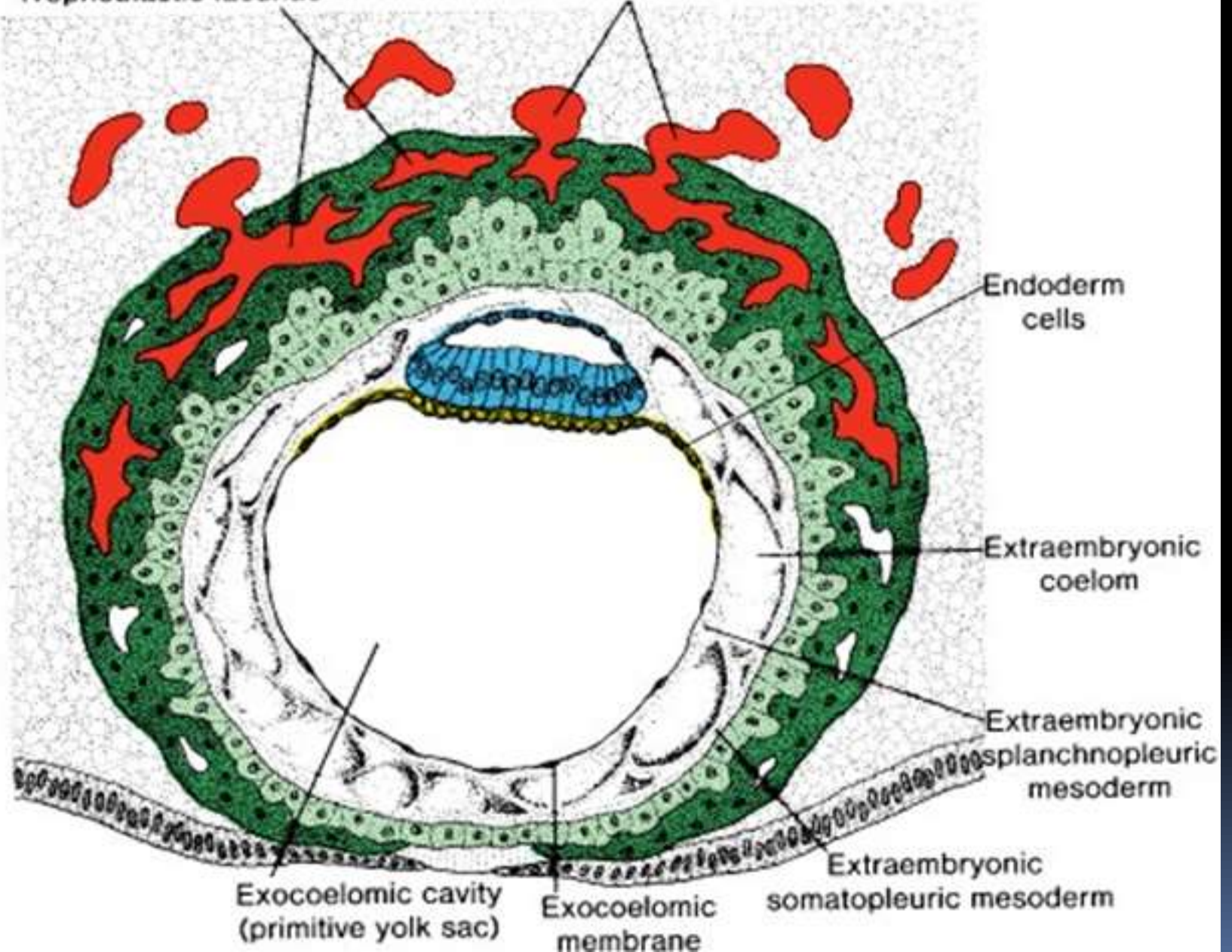
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- Day 9, there is formation of lacunar spaces in syncytial trophoblast.
 - Blastocyst embedd more into endometrium
 - Implantation site closed with fibrin coagulam



- Day 11 and 12, implantation site covered with surface epithelium.
- Formation of maternal sinusoids that forms uteroplacental



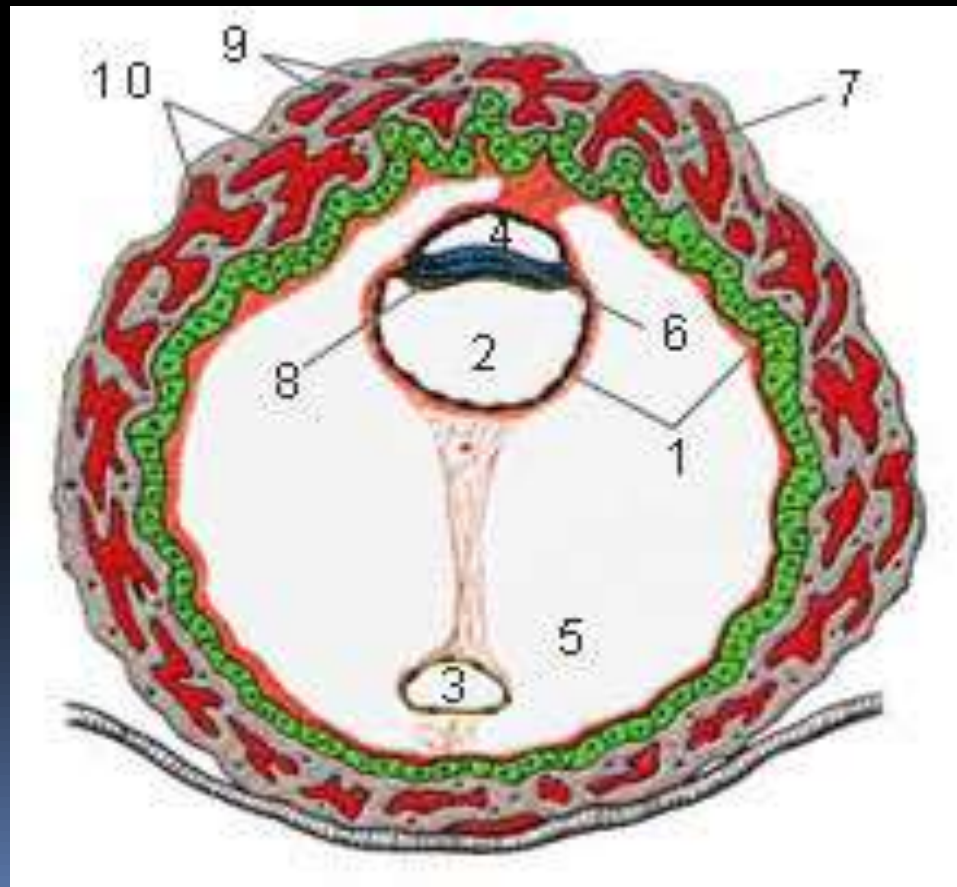
Trophoblastic lacunae

Maternal sinusoids



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- Cells derived from the yolk sac cell will form **extraembryonic mesoderm**.
 - Extraembryonic mesoderm between cytotrophoblast and primitive yolk sac – **extraembryonic somatopleuric mesoderm**
 - Extraembryonic mesoderm between amniotic cavity and cytotrophoblast- **extraembryonic splanchnopleuric mesoderm**
- 

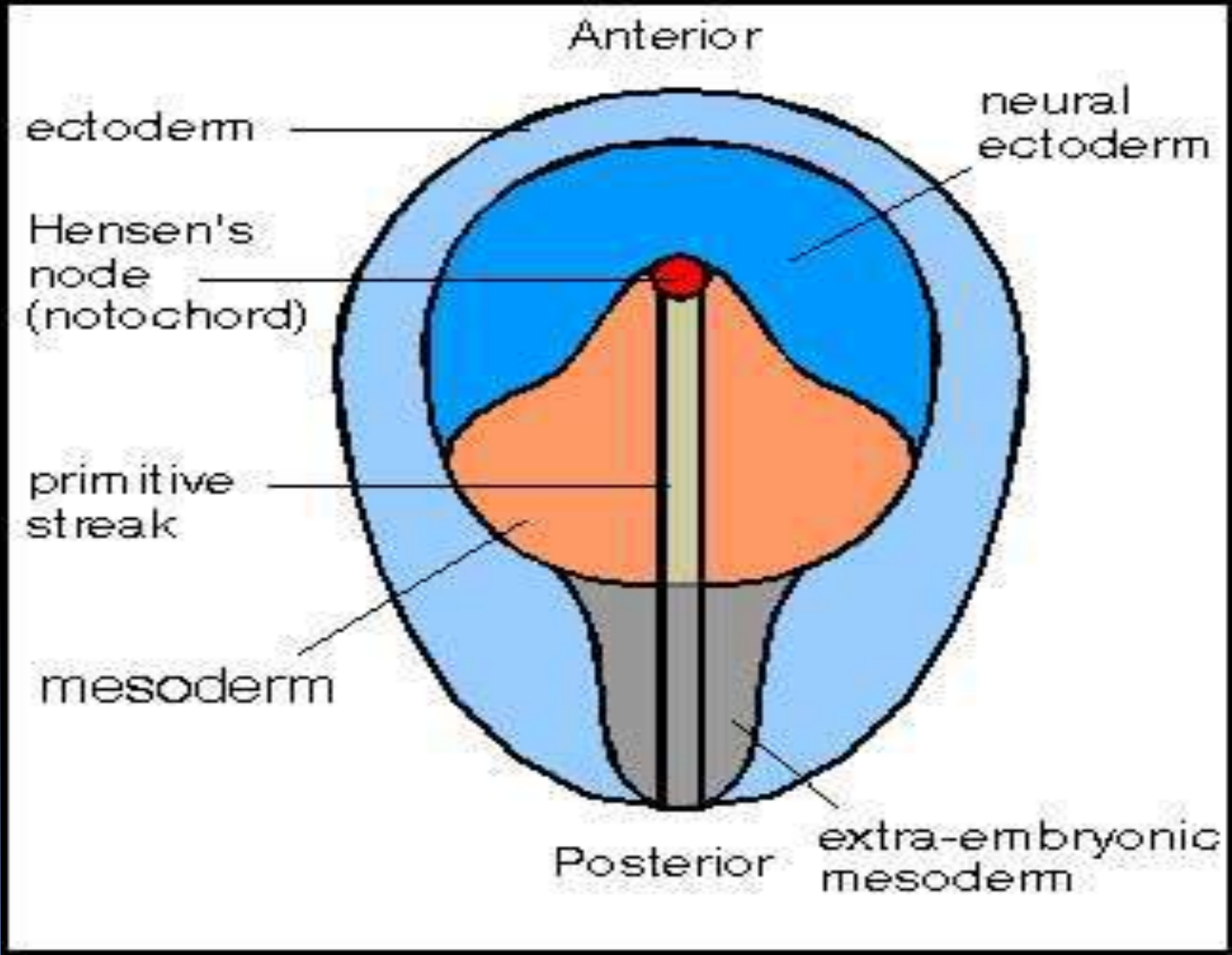
- Day 13, formation of secondary yolk sac from cells of hypoblast
- Connecting stalk forms umbilical cord.
- Large portion of exocoelomic cavity is pinched off- exocoelomic cyst



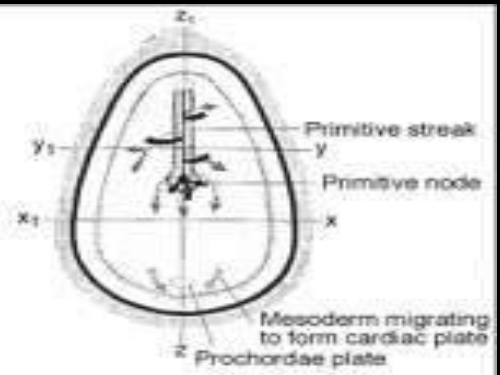
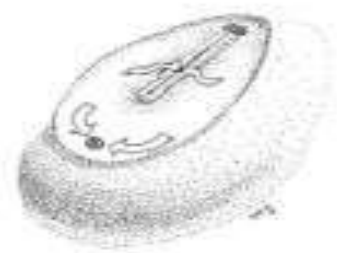
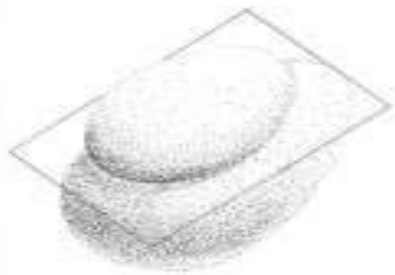
Formation Of Three Layered Embryo

- Fertilized egg
- Morula
- Blastocyst
(Trophoblast Embryoblast)
- Bilaminar germ disc
(Ectodermal and Endodermal cells)
- Prochordal plates
- Trilaminar germ disc
(Primitive streak, Primitive node)
- Notochord
- Ectodermal cell divide and migrate towards streak, invaginate and spread laterally giving rise to mesoderm
- Ectodermal cells move forward anterior to prochordal plate – cardiac plate

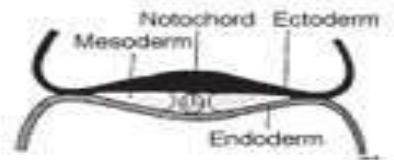
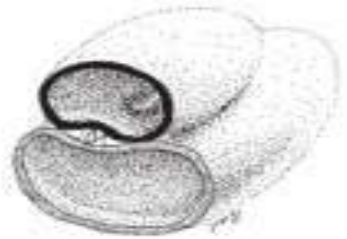
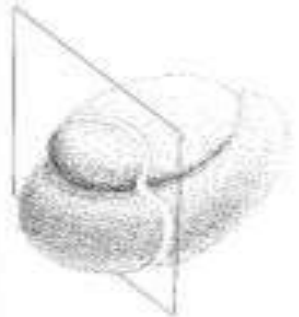
Primitive Streak



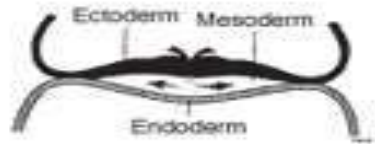
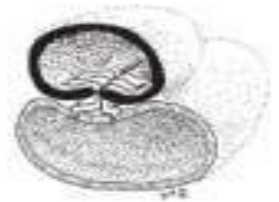
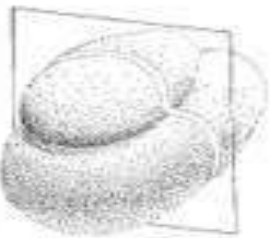
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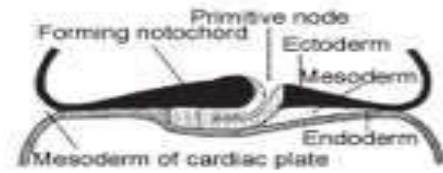
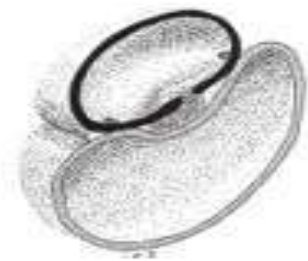
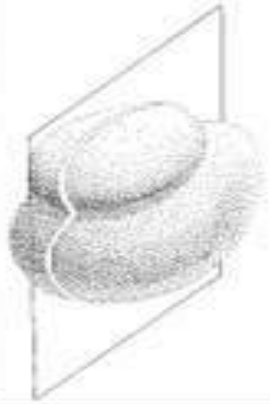
B




C



D



- 
- Notochord
 - Ectodermal cells divide and migrate towards streak, invaginate and spread laterally giving rise to mesoderm
 - Ectodermal cells move forward anterior to prochordal plate – cardiac plate

Formation of neural tube



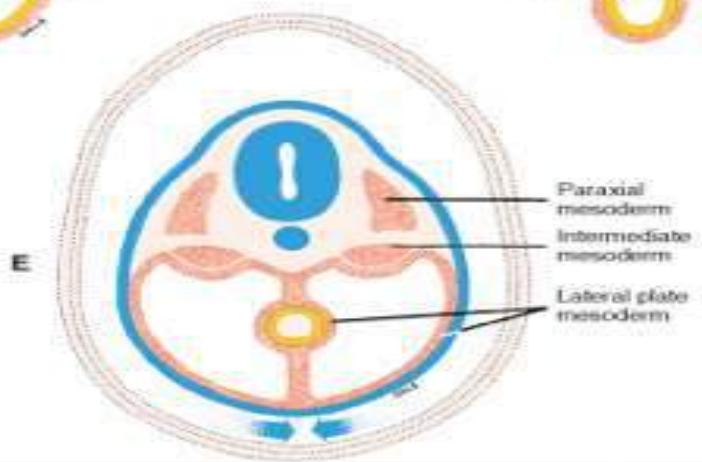
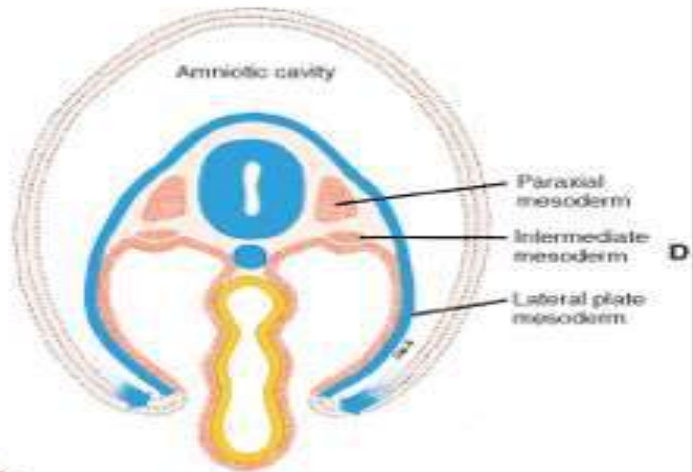
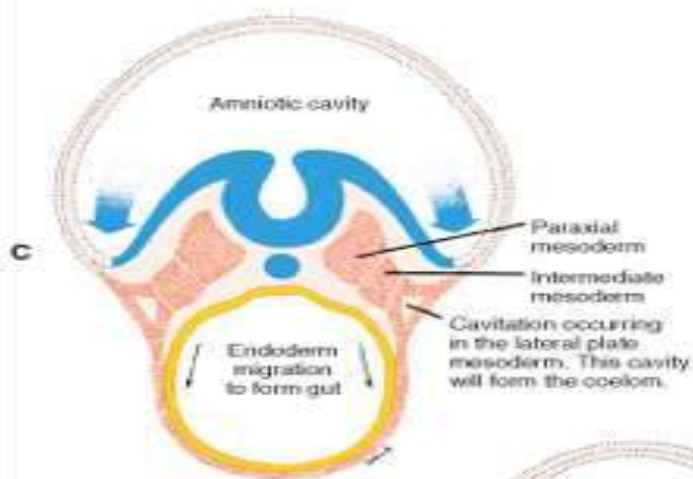
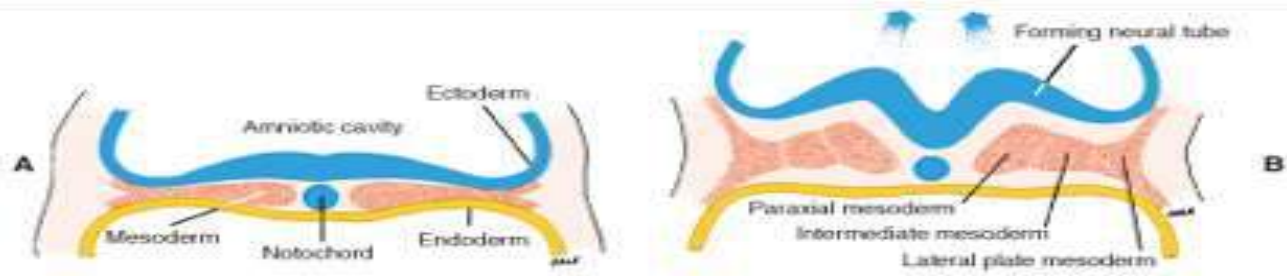
- Next 3-4 months of development – major tissues and organs differentiate from triploblastic embryo
- Nervous system develop as:

Thickening within ectodermal layer
(Neural Plates)

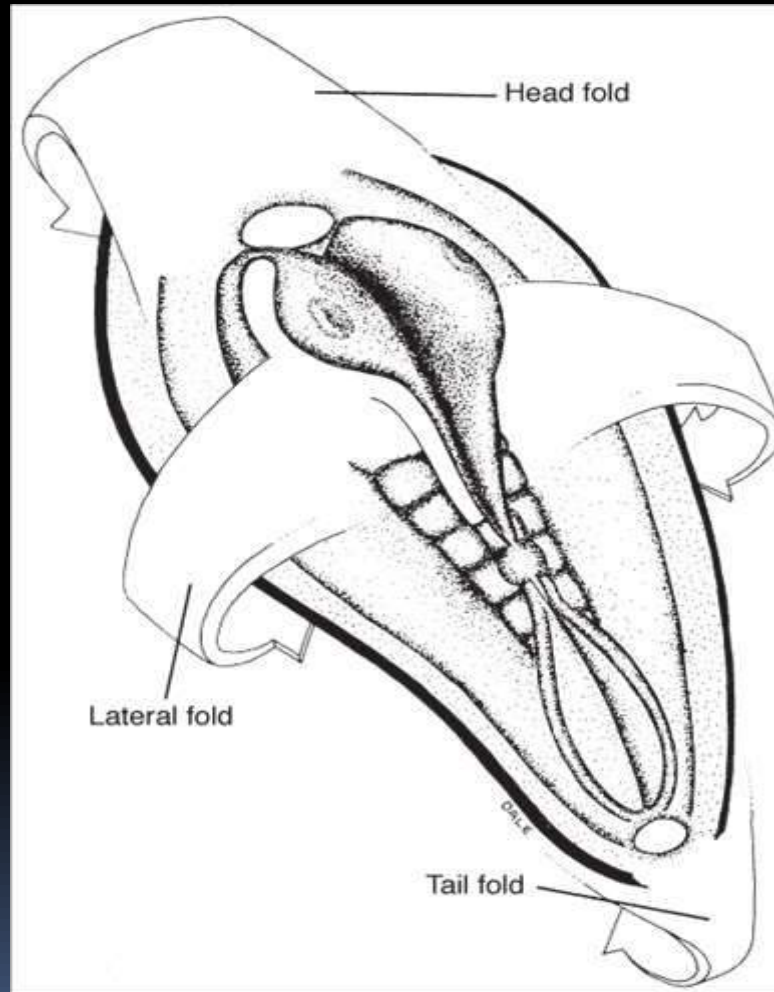
Raised margins: neural folds

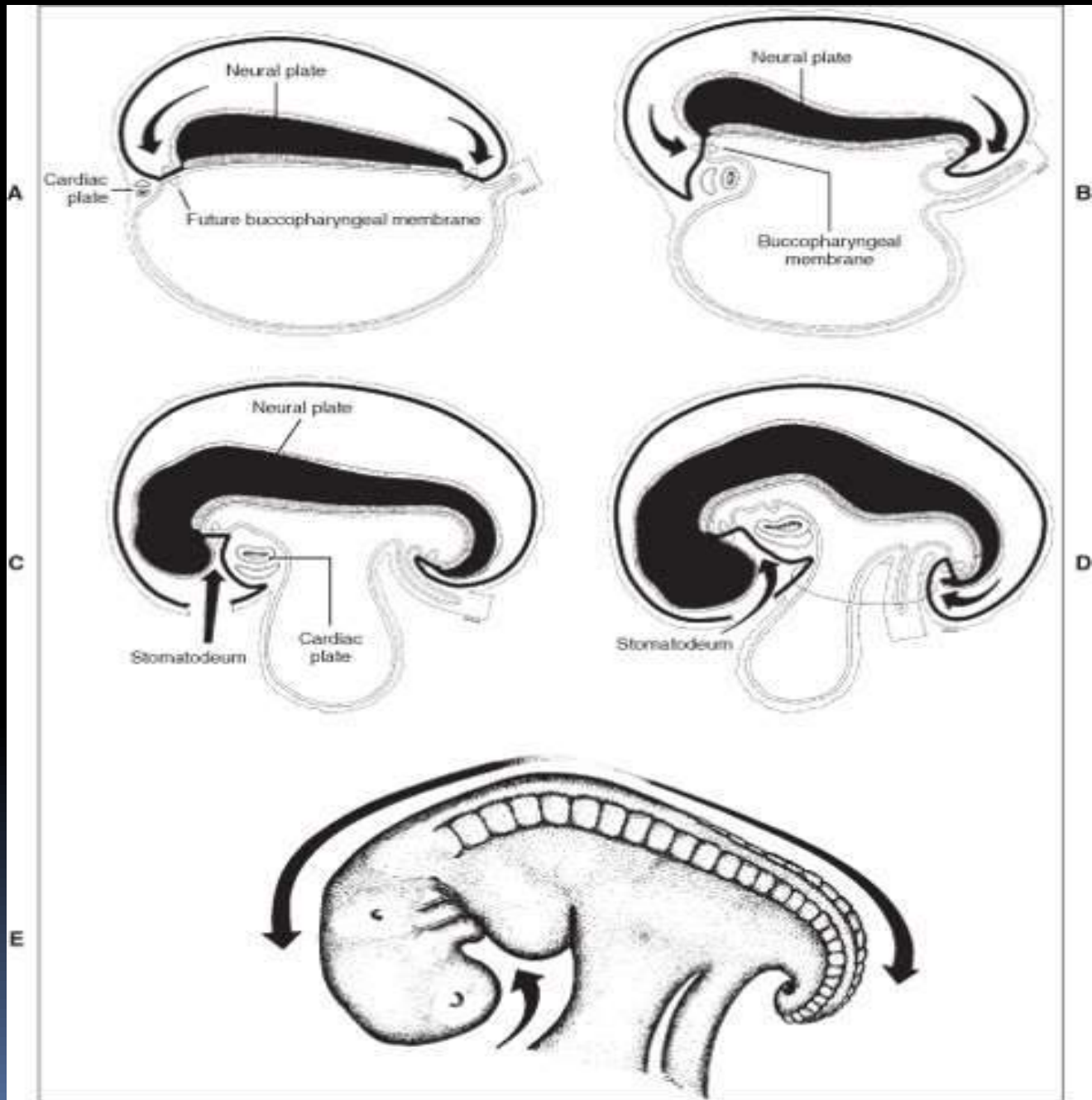
Midline depression: neural groove

These three give rise to neural tube



Folding of embryo

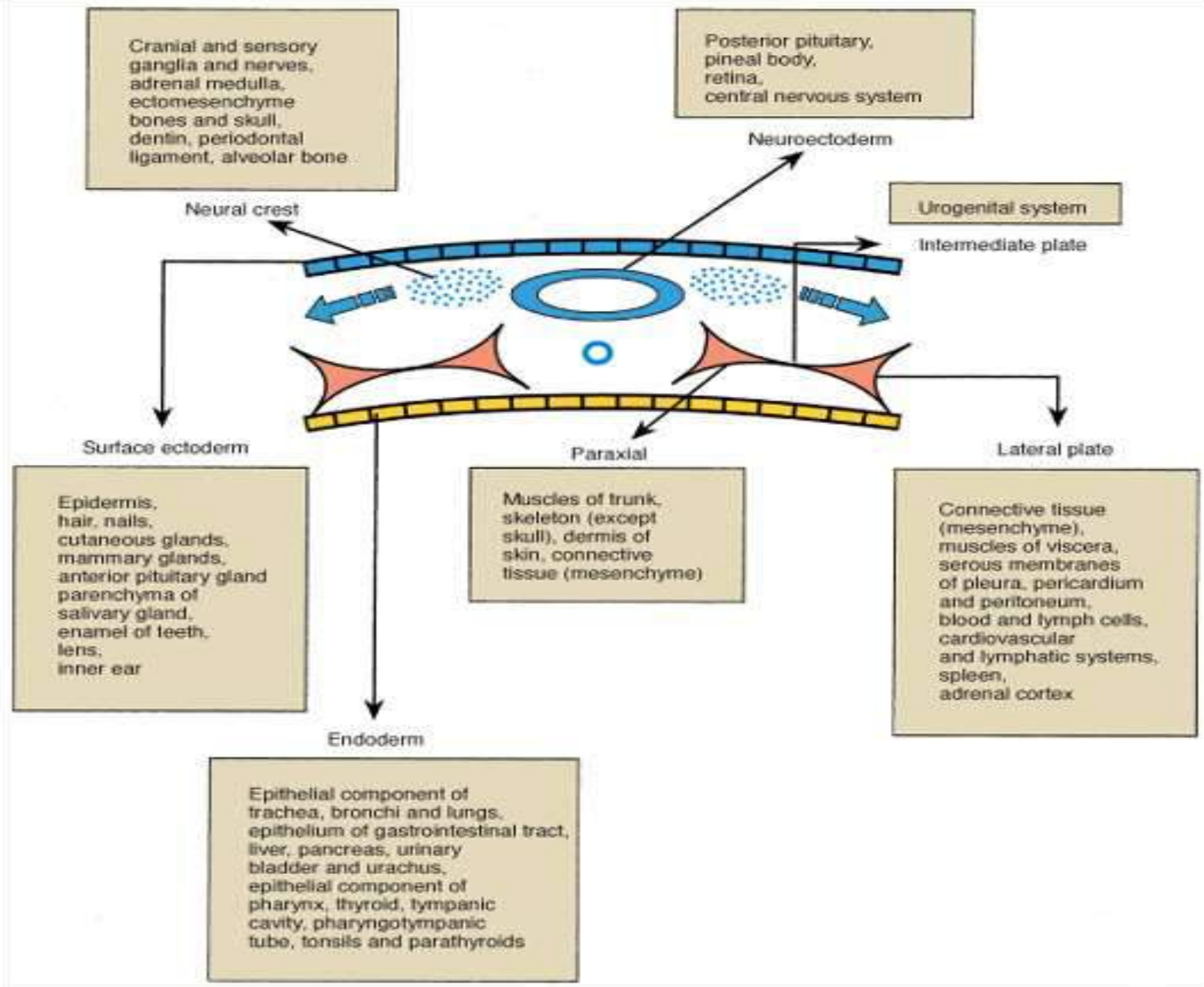




Fate of germ layers

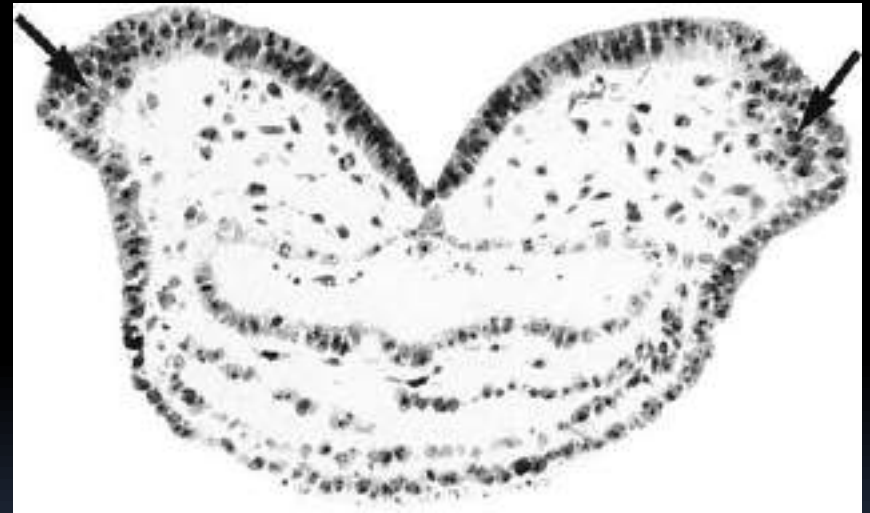
- As neural tube forms, mesoderm differentiate to
 - a. Paraxial mesoderm
 1. Somites: sclerotome, myotome, dermatome
 2. Somatomeres: head musculature
 - b. Intermediate mesoderm
 - c. Lateral plate mesoderm



Somitomere 1 & 2	muscles supplied by oculomotor nerve
Somitomere 3	superior oblique muscle supplied by trochlear nerve
Somitomere 4	muscles of 1 st pharyngeal arch supplied by mandibular nerve
Somitomere 5	lateral rectus muscle supplied by abducent nerve
Somitomere 6	muscles of 2 nd pharyngeal arch supplied by facial nerve
Somitomere 7	stylopharyngeus (3 rd arch) supplied by glossopharyngeal nerve
Occipital somites 1 and 2	laryngeal muscles (4 th to 6 th arches) supplied by vagus nerve
Occipital somites 3 – 5	muscles of tongue supplied by hypoglossal nerve




Neural crest

- As neural tube forms group of cells separate from neuroectoderm.
- Capacity to migrate and differentiate extensively.
- They separate from lateral aspect from neural plate.
- Expresses SNAIL ZINC FINGER TRANSCRIPTION FACTOR



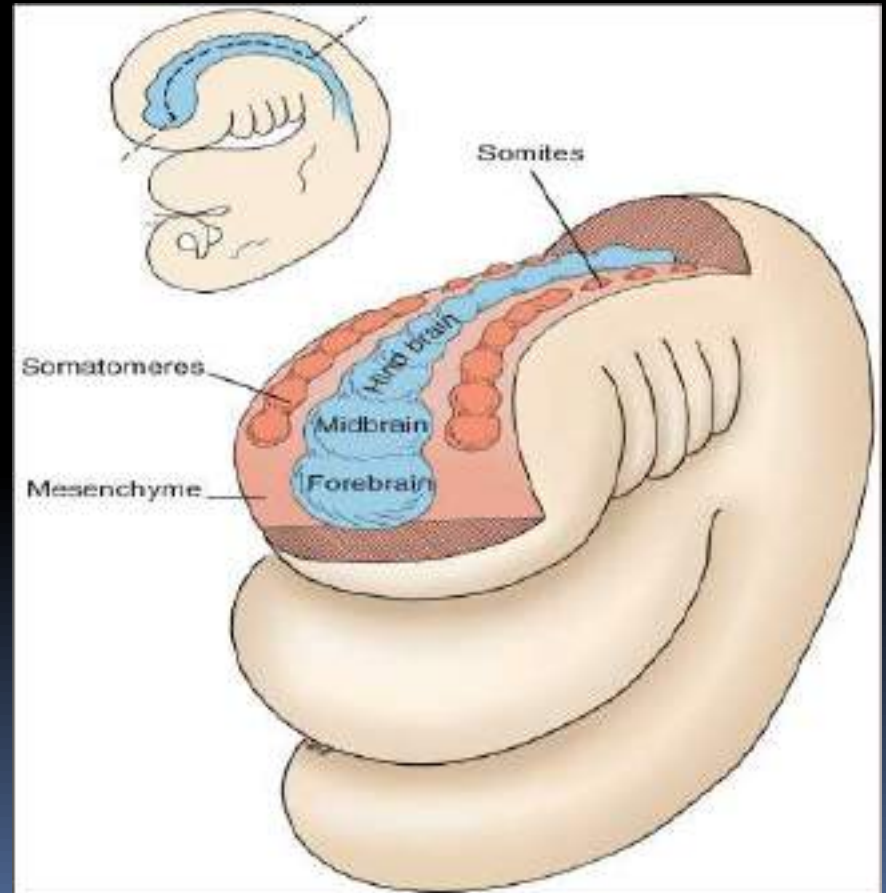
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- Neural crest cells forms connective tissue of head, hence called ectomesenchyme.
 - While rest of the connective tissue of the body derived from mesoderm, hence called mesenchyme.
- 




Craniofacial Embryology

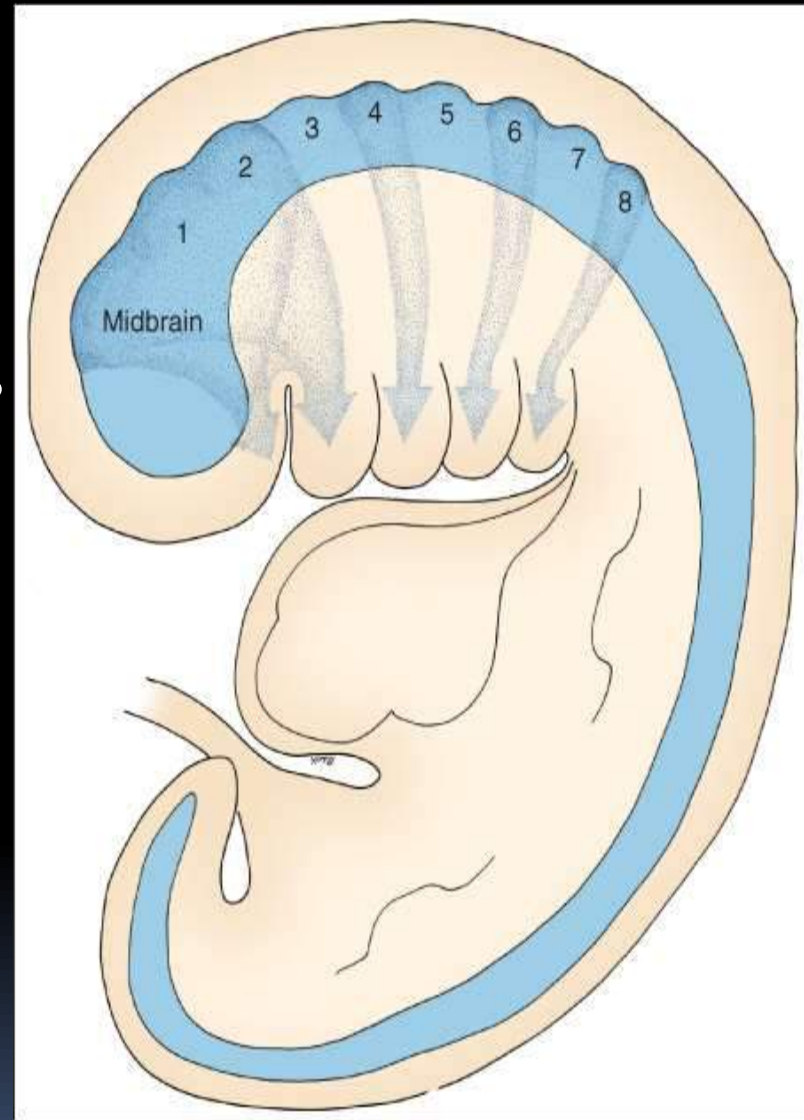
Formation of head

- Anterior portion of neural tube forms
 1. Forebrain
 2. Midbrain
 3. Hindbrain



- 
- Hindbrain develops series of eight bulges
 - Rhombomeres
 - Lateral to neural tube, paraxial mesoderm partially segments rostrally- form 7 somatomeres and fully segmented caudally somites.

- Neural crest cells arise from midbrain and rhombomeres in the form of streams.
- The first two rhombomeres express *Msx*, *Dlx* and *Barx* genes.
- Common signaling pathways such as Sonic hedgehog (*Shh*), *Fgf* and *BMP*.




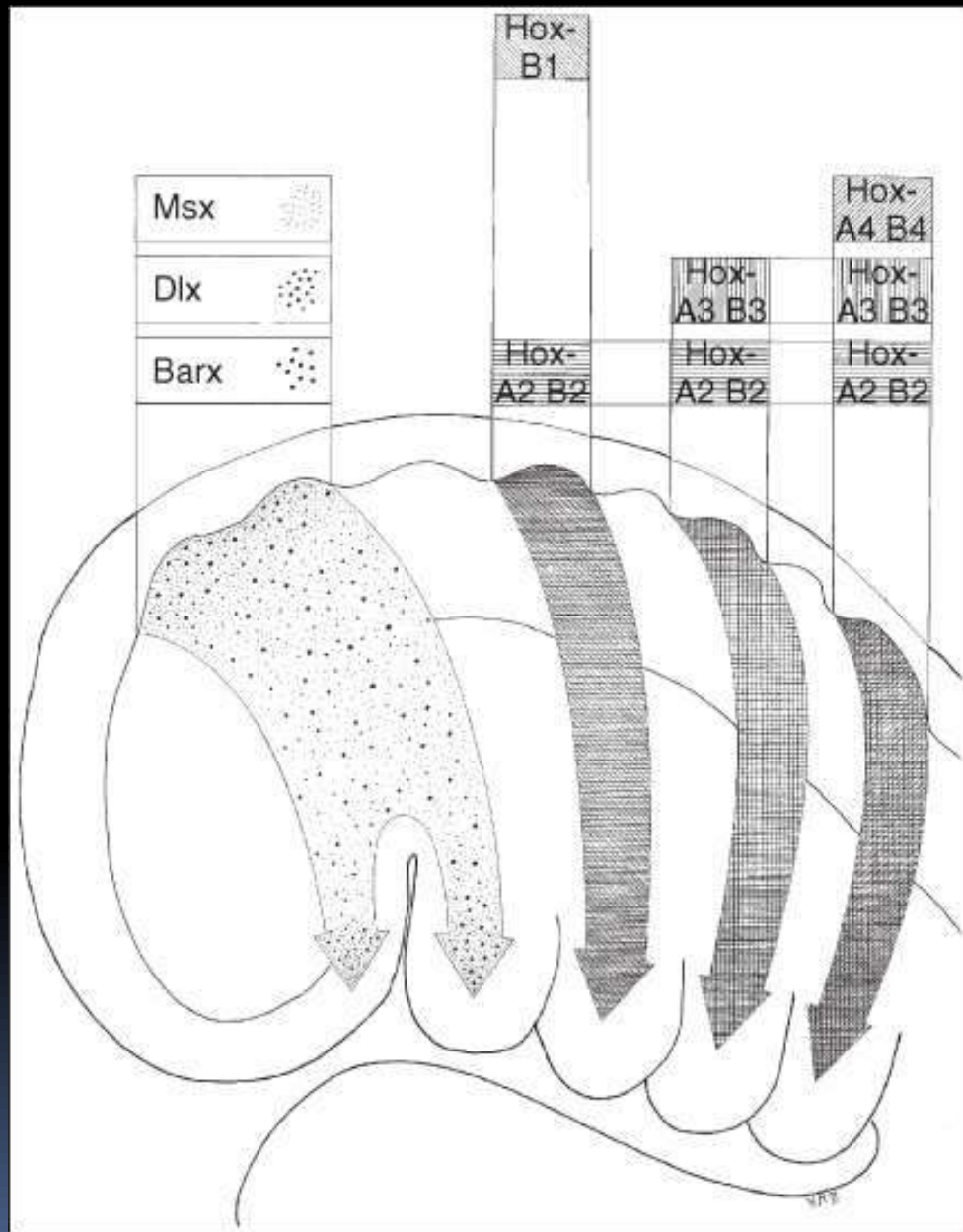
Molecular regulation of facial development

- Neural crest cells arise from edge of neural fold.
- **BMP** and **WNT1** expression cause neural cells go undergo EMT and migrate into underlying mesenchyme.
- Crest cells migrate in three streams.

- From R1 & R2; R4, R6 & R7
- Streams provide axonal guidance
- Neural crest cells populate pharyngeal arches to form skeletal component which is controlled by signals from endodermal pouches.
- These pouches express **BMP7**, **Fgf8** and **Shh** gene.
- The response of mesenchyme to endodermal signals is dependent on transcription factors.

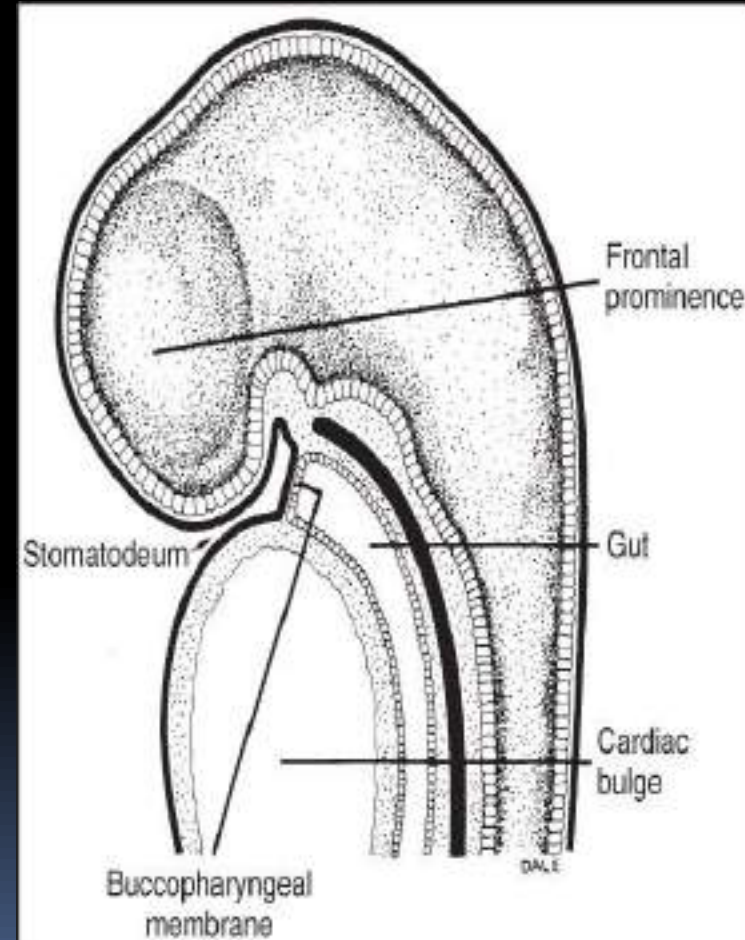
- 1st arch : **HOX** negative but expresses **Msx**, **Dlx** & **Barx** genes
- 2nd arch : **HOXA2**
- 3 to 6 arch : **HOXA3**, **HOXB3** & **HOXD3**
- Transcription factors allows mesenchyme of each arch to respond differently to signals emanating from pouch endoderm, such that 1st arch forms maxilla & mandible, 2nd arch the hyoid bone.

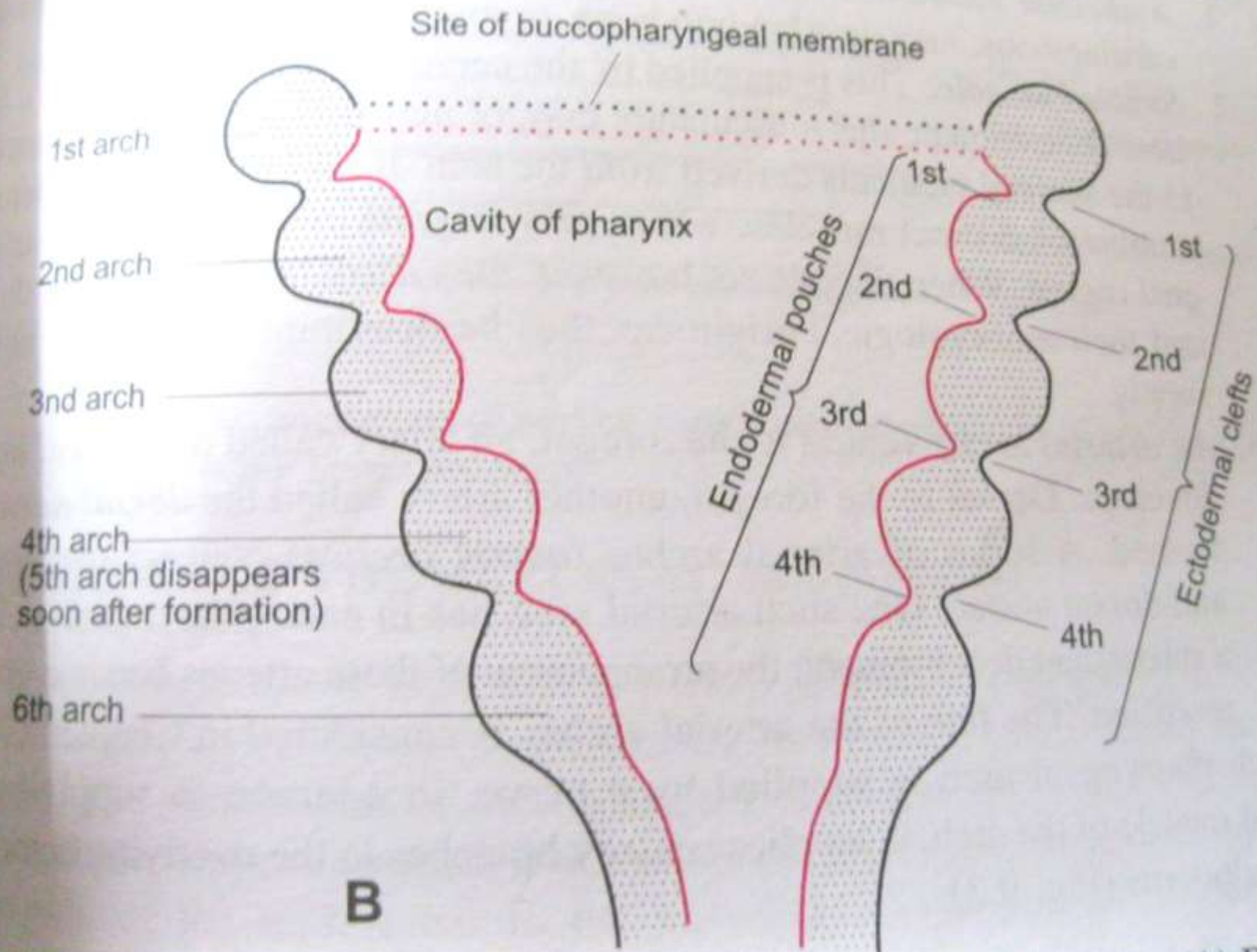
- 
- Remainder of facial skeleton, mid and upper facial region, derived from neural crest cells that migrate into frontal prominence.
 - Signals emanating from surface ectoderm and underlying neuroepithelium dictate fate of mesenchyme.
 - Shh & Fgf8 play major roles.




Branchial (Pharyngeal) Arches

- Stomatodeum bounded by
 - Rostrally- Frontal prominence
 - Caudally- Cardiac bulge
 - Laterally- 1st pharyngeal arch
- Buccopharyngeal membrane separated from foregut.
- Branchial arches forms pharyngeal wall from lateral plate mesoderm.

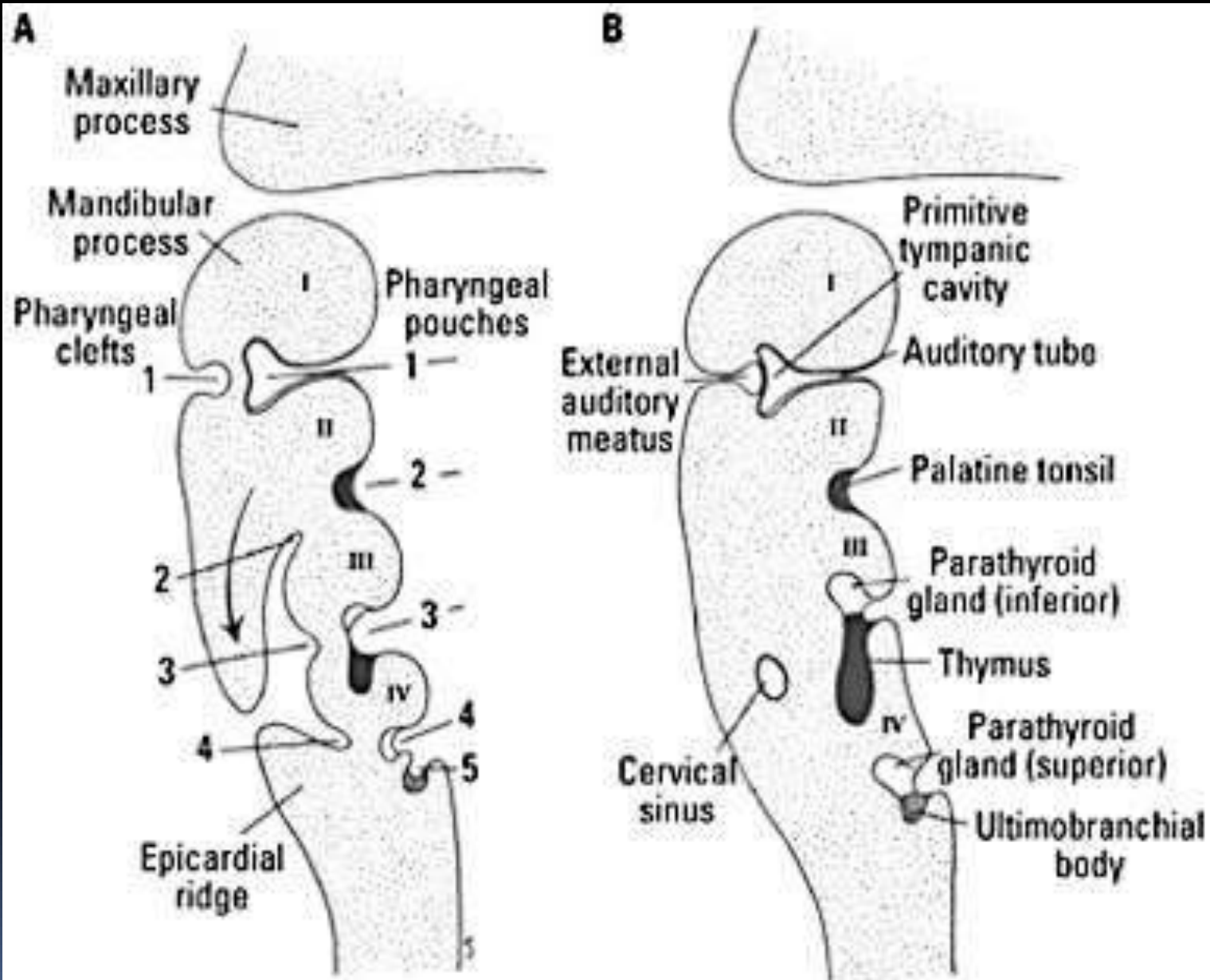


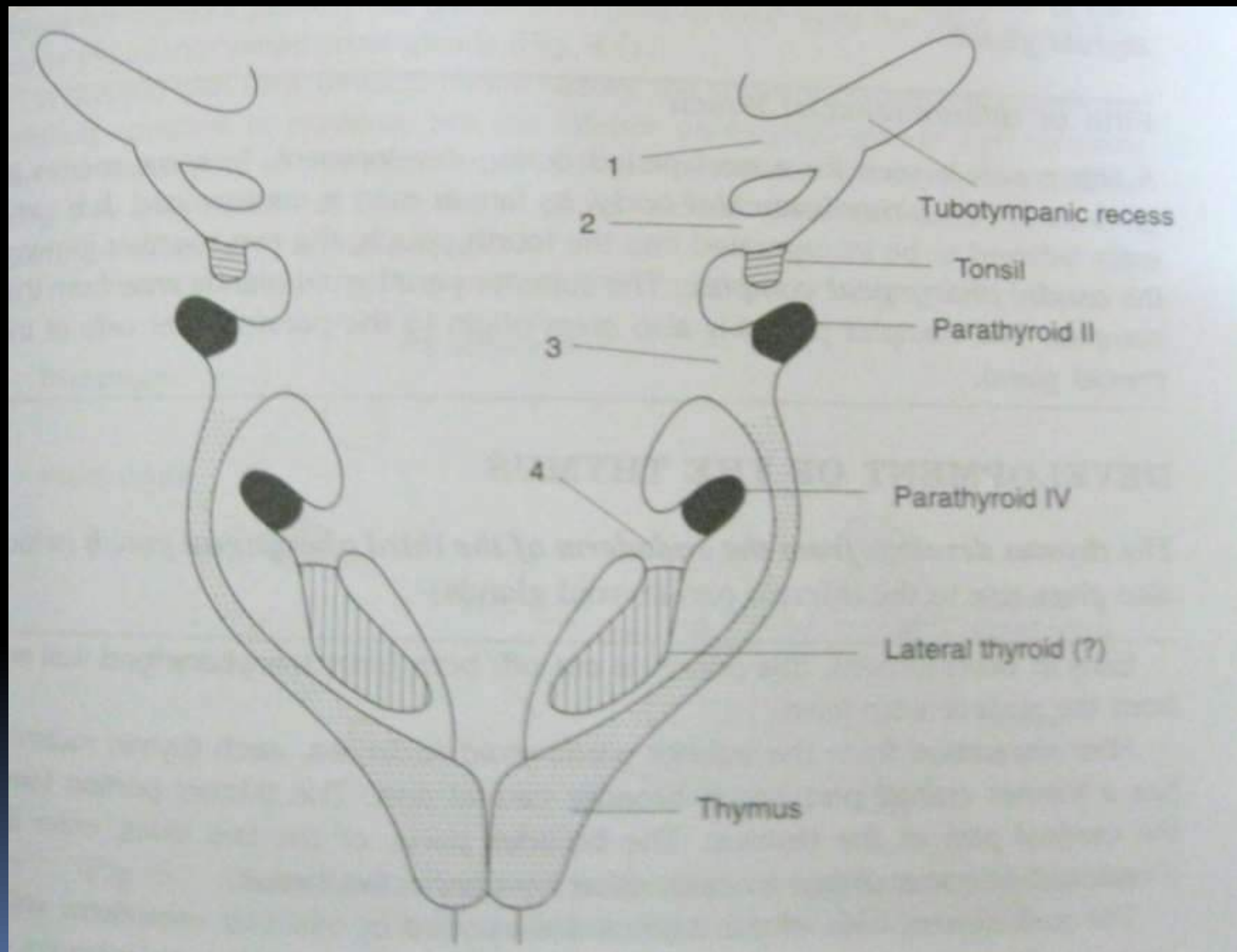


- 
- Arches seen clearly as bulges on the lateral aspect of embryo separated by
 - externally- pharyngeal grooves
 - internally- pharyngeal clefts

Derivatives of the Branchial arch system


	ARCH	GROOVE	POUCH
First	<ol style="list-style-type: none"> 1. Mandible and Maxilla 2. Meckel's cartilage <ol style="list-style-type: none"> a. Incus and Malleus of inner ear b. Sphenomalleolar ligament c. Sphenomandibular ligament 	<ol style="list-style-type: none"> 1. External auditory meatus 	<ol style="list-style-type: none"> 1. Tympanic membrane 2. Tympanic cavity 3. Mastoid antrum 4. Eustachian tube
Second	<ol style="list-style-type: none"> 1. Reichert's cartilage <ol style="list-style-type: none"> a. Styloid process of temporal b. Stylohyoid ligament c. Lesser horns of hyoid d. Upper part of body of hyoid 	Obliterated by down growth of second arch	<ol style="list-style-type: none"> 1. Largely obliterated 2. Contributes to tonsil
Third	<ol style="list-style-type: none"> 1. Lower part of body of hyoid 2. Greater horns of hyoid 		Inferior parathyroid gland Thymus
Fourth	<ol style="list-style-type: none"> 1. Cartilage of larynx 		Superior parathyroid gland Ultimobranchial body
Fifth	Rudimentary		Rudimentary
Sixth			






Anatomy of the arch

- Inner aspect- covered by endoderm
- Outer aspect- covered by ectoderm
- Central core- consist of mesenchyme from lateral plate mesoderm
- Each arch consist of
 - ❖ Skeletal component
 1. 1st arch cartilage- Meckel's cartilage
 2. 2nd arch cartilage- Reichert's cartilage



3. 3rd arch cartilage- body and greater horns of hyoid

4. 4th arch cartilage- cartilage of larynx

- ❖ Muscular component
 - ❖ Cranial nerve component
 - ❖ Arterial component
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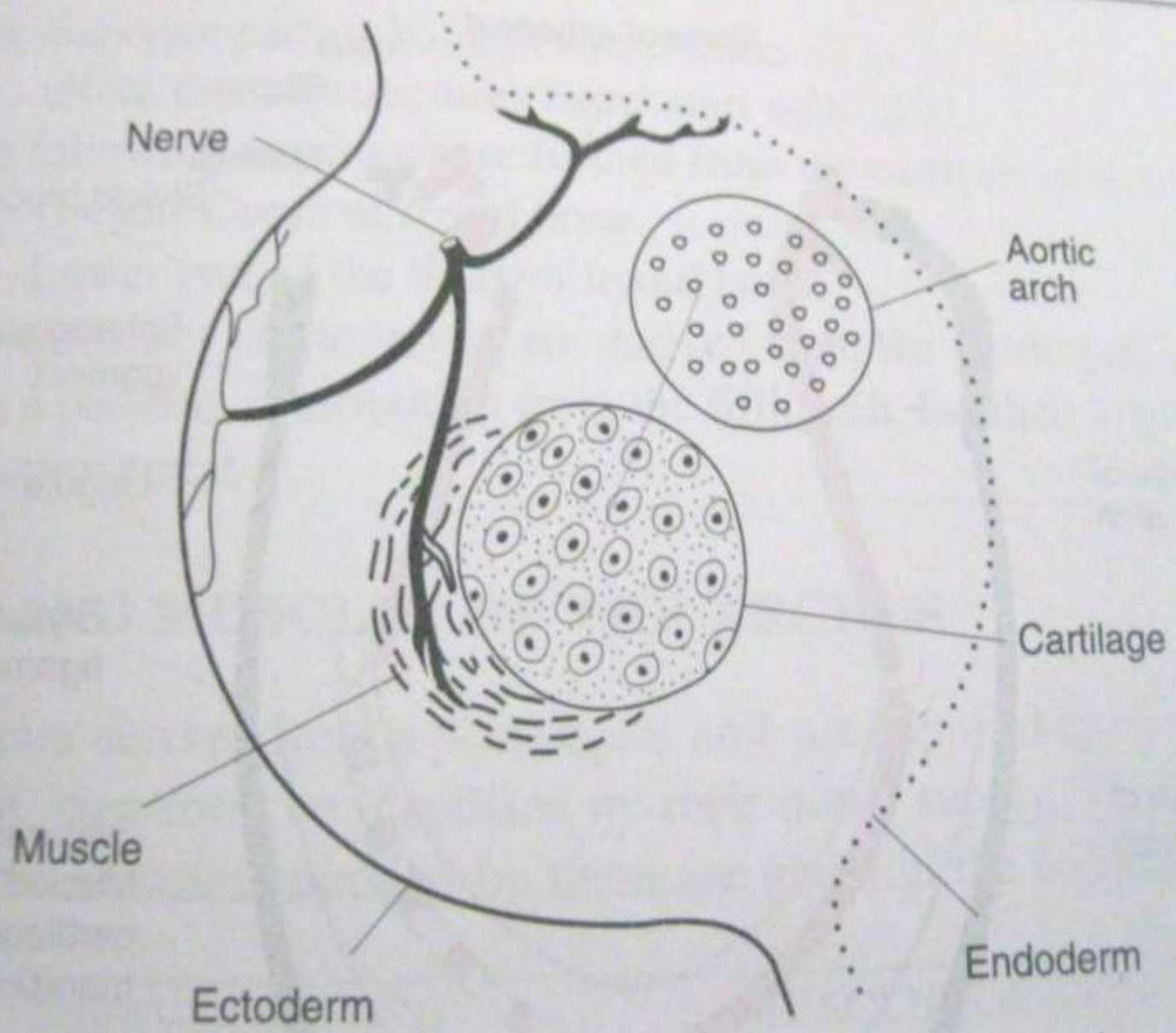
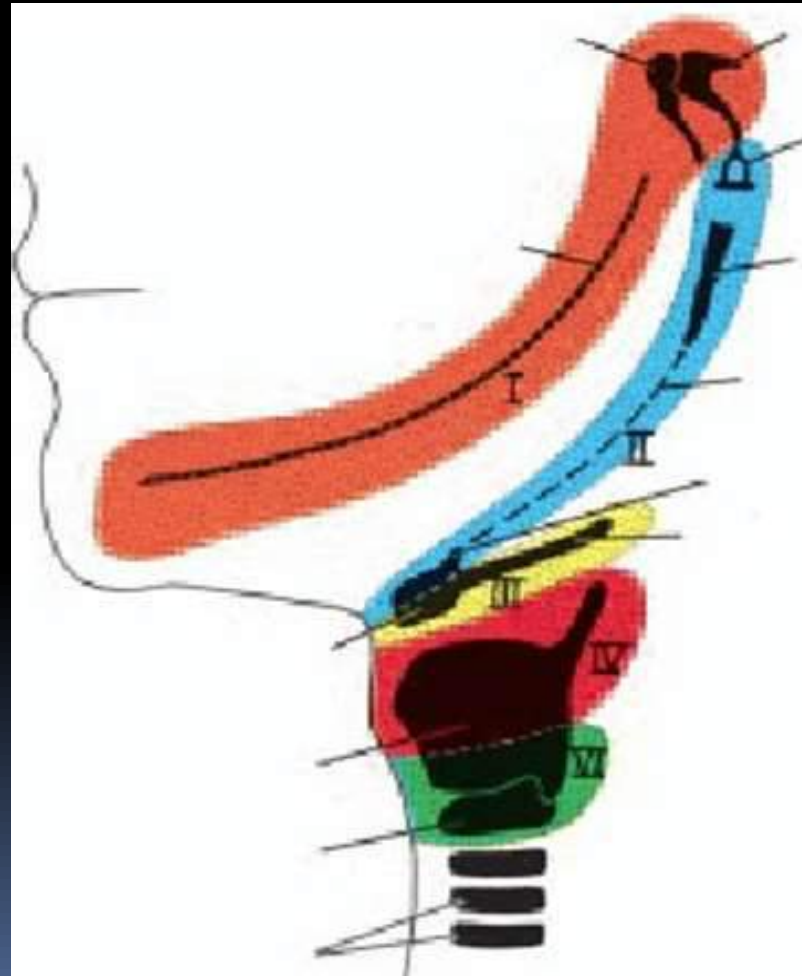


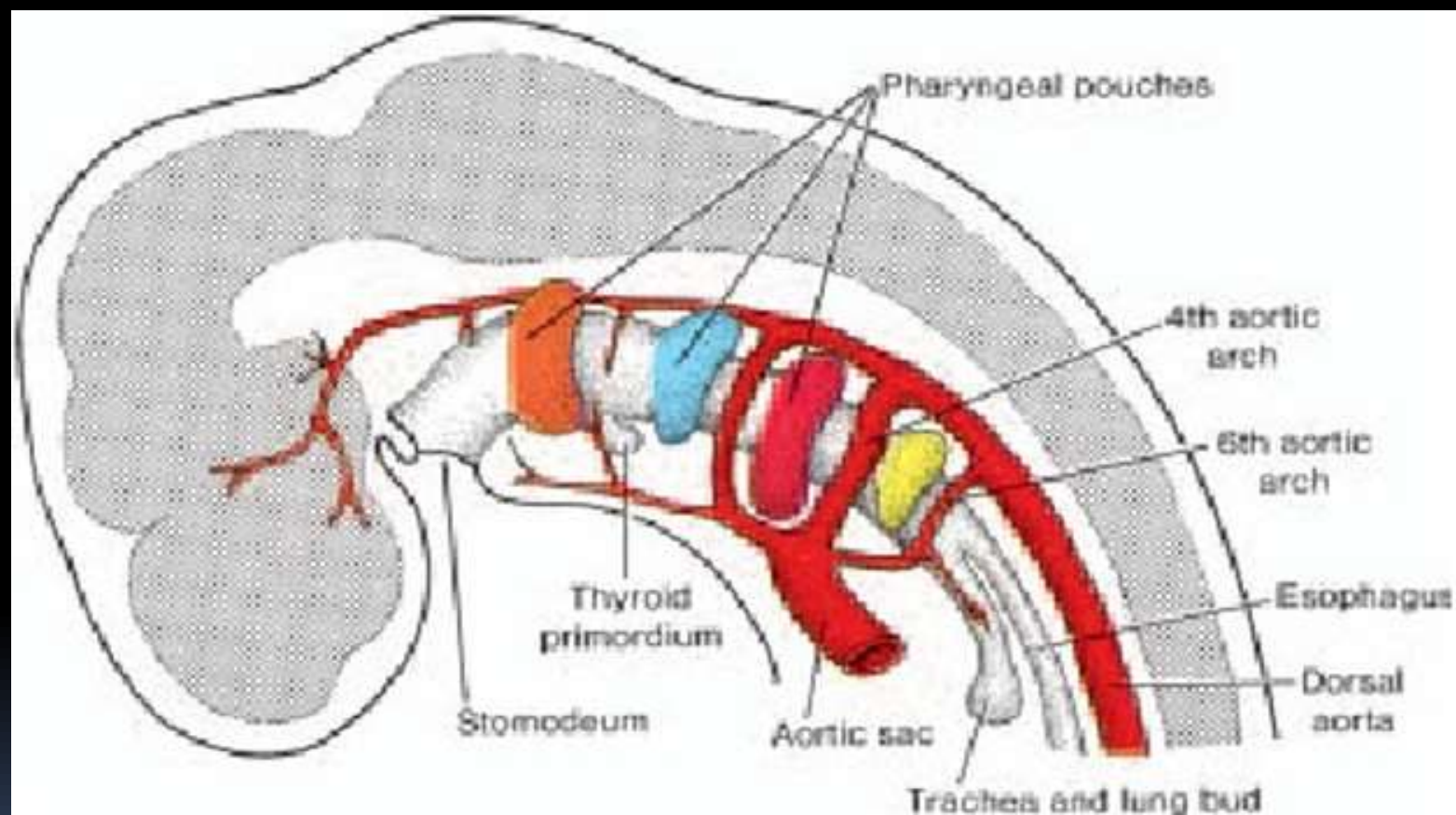
Fig 9.2 Structures to be seen in a pharyngeal arch


Development of Branchial Arch Cartilages




Innervation and Vascularization of pharyngeal arches

Arch	Blood Vessel	Nerve
First	First aortic arch	Trigeminal nerve
Second	Second aortic arch	Facial nerve
Third	Third aortic arch	Glossopharyngeal nerve
Fourth	Fourth aortic arch	Vagus nerve



- 
- The anterior right and left aortic arches develop first and, after a week, begin to disappear as more posterior arches develop.
 - The most caudal arch vessels then enlarge and mature.
 - The 5th arch vessels disappear next.
 - The 3rd, 4th and 6th arch vessels do not disappear but are important in later functions.
 - The 3rd arch vessels become the common carotid arteries which supply the neck, face and brain.

- The 4th arch vessels become the dorsal aorta which supplies blood to the entire body.
- The vessels of the 6th arch supply blood to the lungs as pulmonary circulation.
- In an embryo at 4 weeks, the heart is ventral to the arches, and the blood passes dorsally to the brain and body.
- By the 5th week, the 1st and 2nd branchial arch vessels have disappeared, and then the blood supply to the face is carried out by the 3rd branchial artery which becomes the carotid artery.

- 
- The 7th week is an important period of rapid growth expansion and fusion of the facial processes. The lip and palate are undergoing maximal developmental changes during this time.
 - Thus, a vascular deficiency at this time may result in oxygen and nutritional deficiency which could result in cleft lip, cleft palate or both.

Clinical Correlates

- Birth defects involving the pharyngeal region.
 1. Ectopic thymic and parathyroid tissue remnants of thymic tissue remains in the neck.

The inferior parathyroids more variable in position than the superior ones.



2.Branchial fistulas

2nd pharyngeal arch fails to grow caudally over
3rd and 4th arches.





- Neural crest cells and craniofacial defects


1. Treacher Collins syndrome


2. Robins sequence

Alters 1st arch structures

3. DiGeorge anomaly

4. Hemifacial microsomia(oculoauriculovertebral spectrum, Goldenhar syndrome)





DEVELOPMENT OF FACE, ORAL CAVITY AND TONGUE

PRESENTED BY:

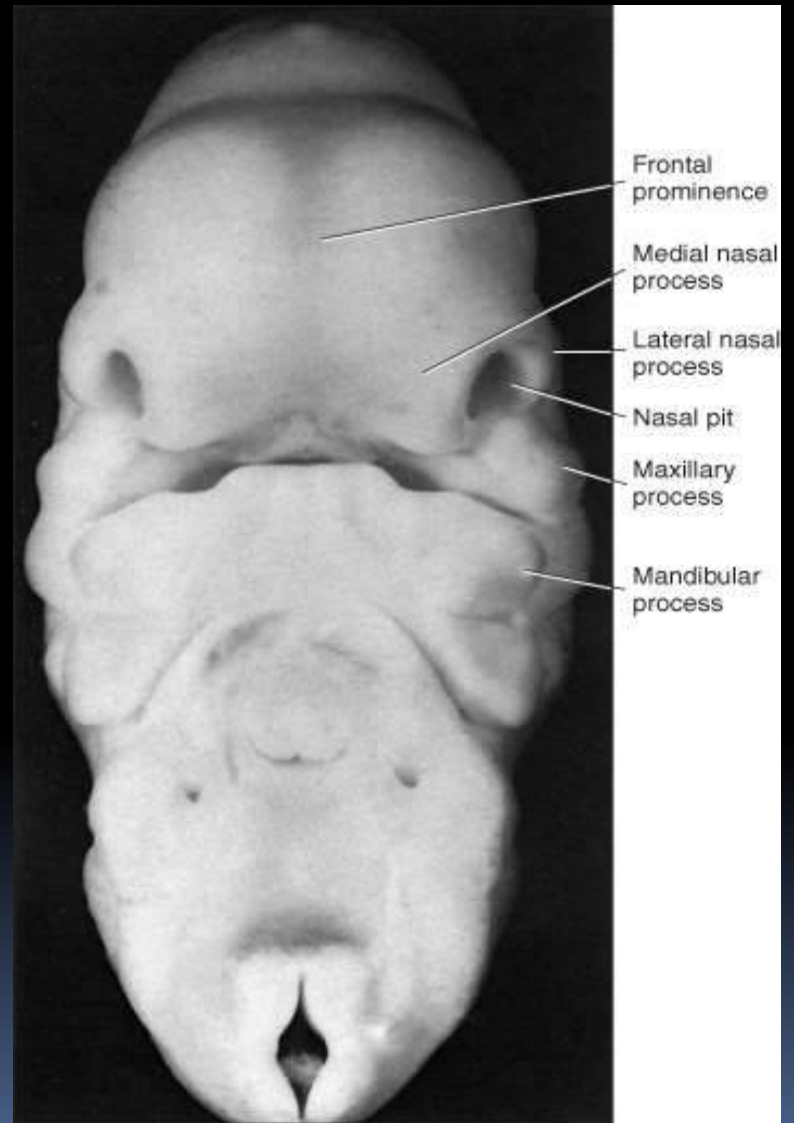
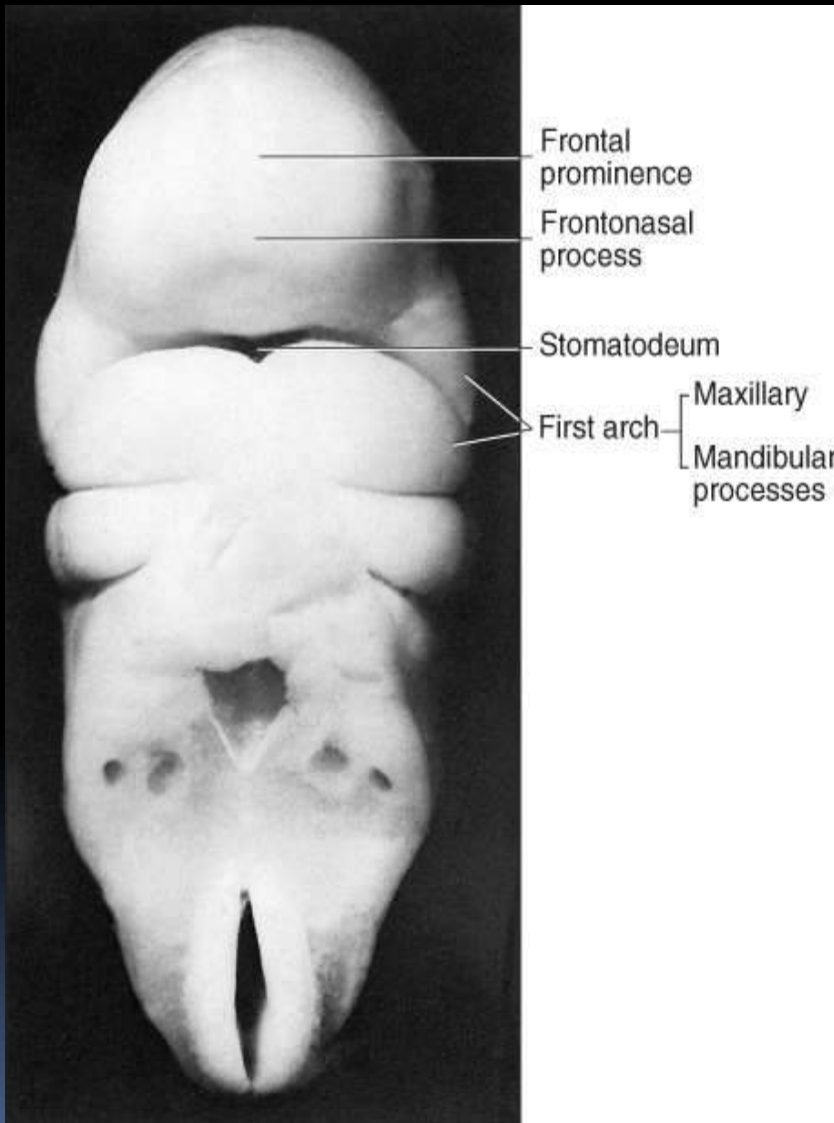
NITIN AWASTHI

MDS 1ST YEAR

Formation of face



Structures contributing to formation of face


Prominence	Structures formed
Frontonasal	Forehead, bridge of nose, medial & lateral nasal prominences
Maxillary	Cheeks, lateral portion of upper lip
Median nasal	Philtrum of upper lip, Crest & tip of nose
Lateral nasal	Alae of nose
Mandibular	Lower lip

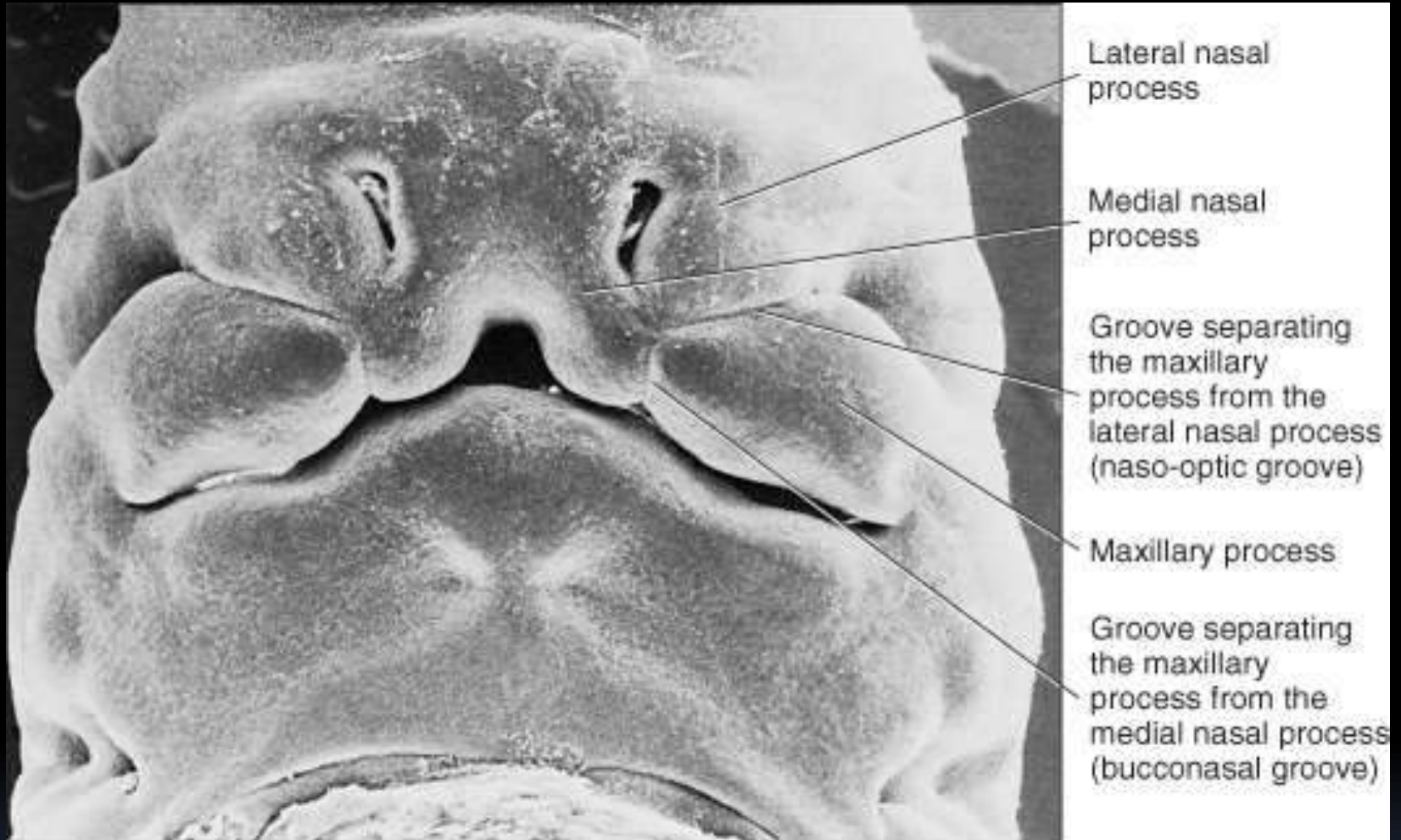


Formation of the face


- At about 28 days, localized thickening develops on frontal prominence called as olfactory placodes.
- Rapid proliferation of mesenchyme around placodes form lateral and medial nasal process.
- Changes occur in the region of frontal prominence known as frontal process

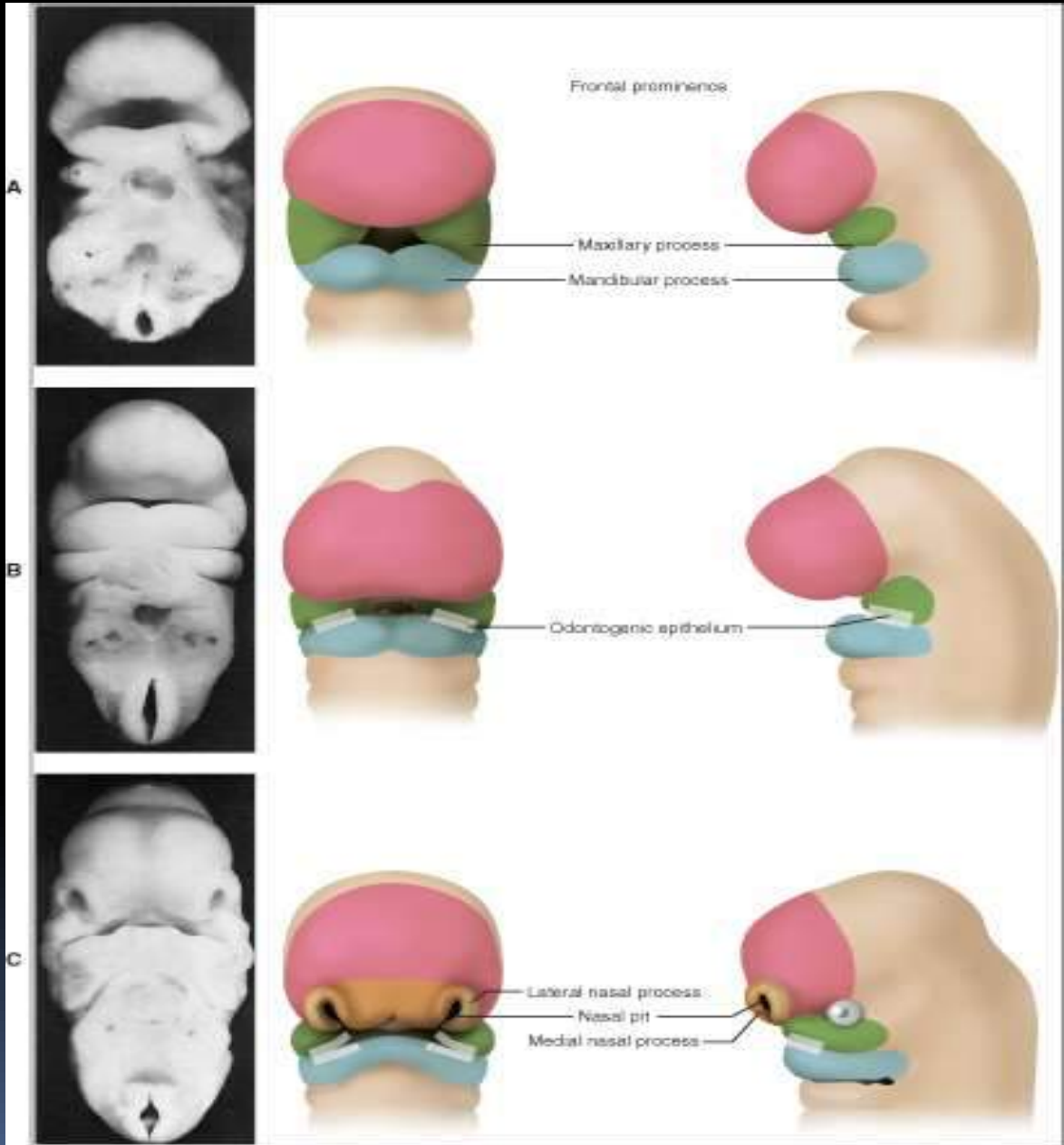
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- Medial nasal process forms
 1. Mid portion of the nose
 2. Mid portion of upper lip
 3. Anterior portion of maxilla
 4. Primary palate
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- Maxillary process grows medially and approaches lateral and medial nasal process and are separated by 2 grooves naso-optic and bucconasal groove.
 - Maxillary process and lateral nasal process separated by naso optic furrow.

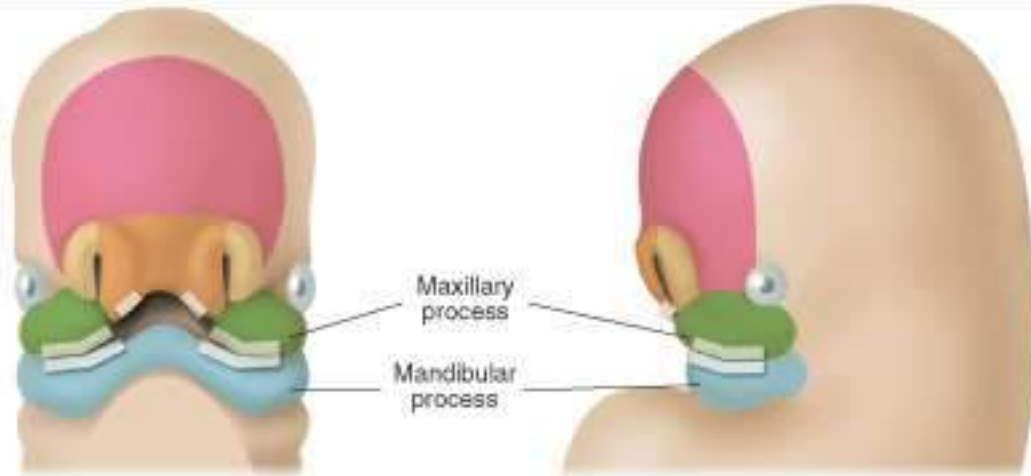


- Tencates

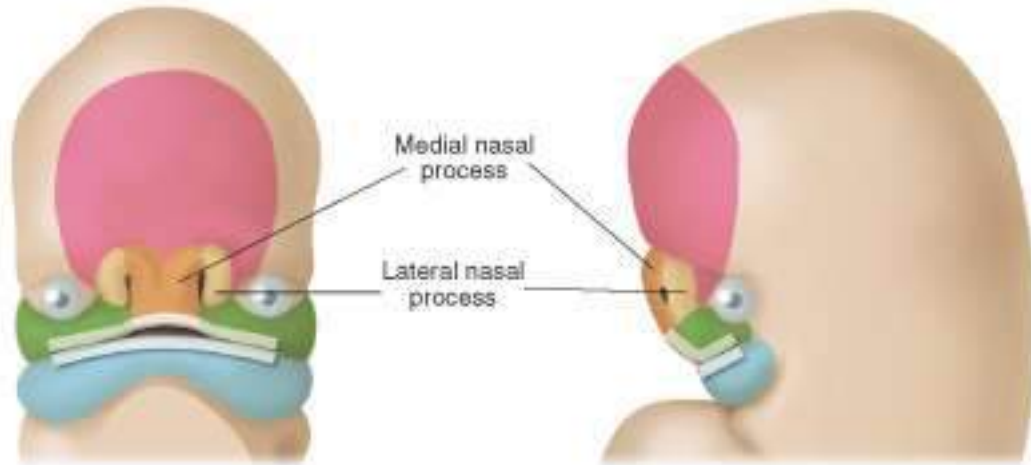
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- From nasolacrimal groove- forms the nasolacrimal duct
 - On inferior surface of maxillary process and superior surface of mandibular process epithelial thickening develops known as primary epithelial band.



D



E



Development of Nose

- Complex contribution from frontal prominence, medial nasal and lateral nasal prominence and cartilagenous nasal capsule.
 - Internal and external nasal regions develops from :
 1. deep capsular field
 2. superficial alar field
- .blind sac – nasal pit seperated from stomatodeum by oronasal membrane

- Cartilagenous nasal capsule form around the primary nasal pits forms the

1. mesethemoid

2. ectethemoid

Mesethmoid form nasal septum

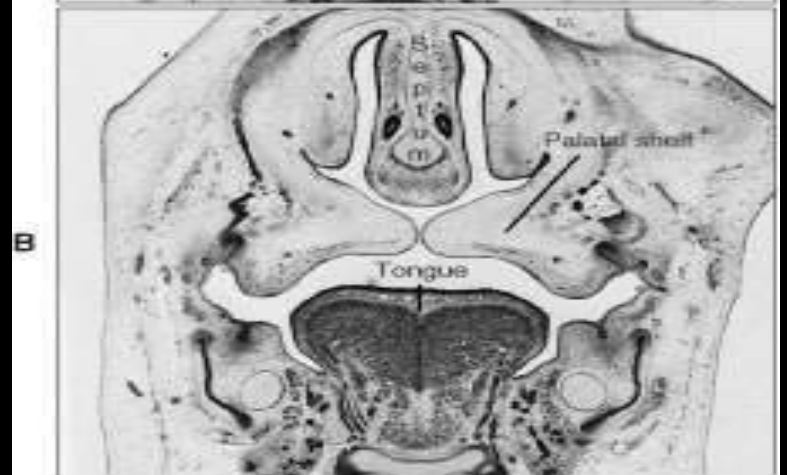
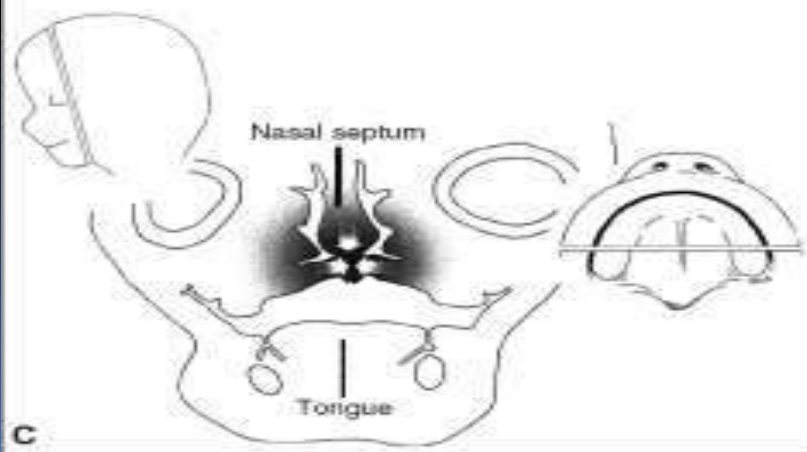
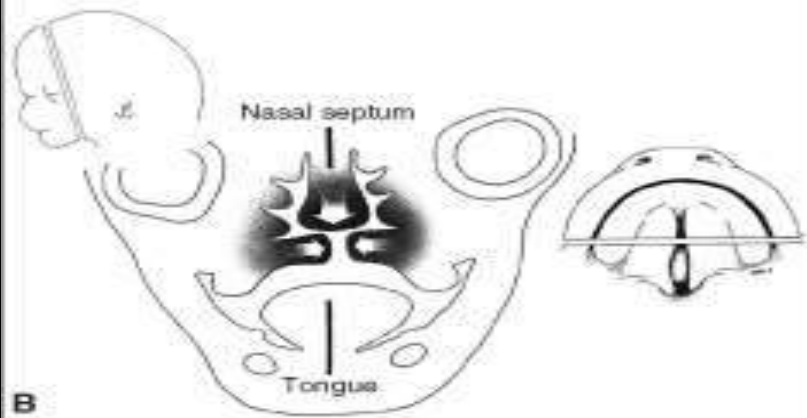
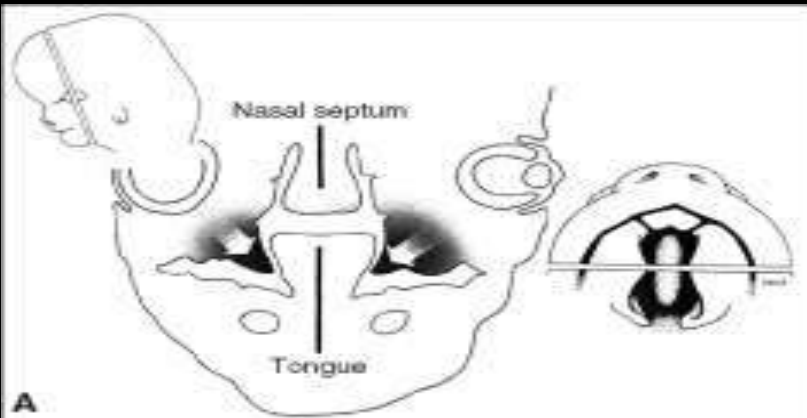
Ectethemoid forms alar cartilage and nasal choncae

Development of Cheek

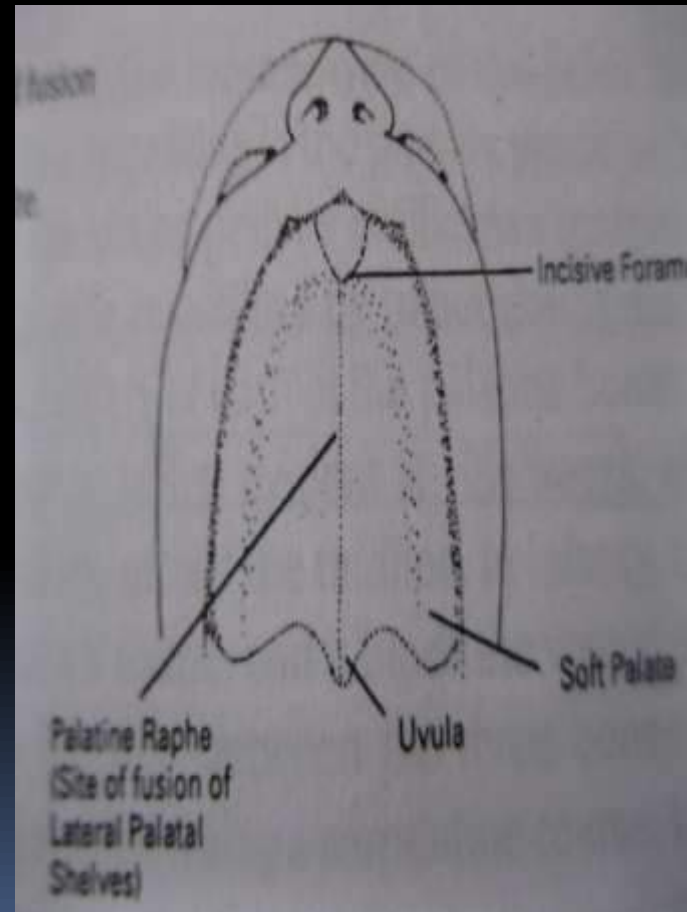
- After formation of upper and lower lips, primitive mouth is very broad.
- On lateral aspect, bounded above by maxillary process and below by mandibular process.
- These processes fuse to form cheeks.


Secondary palate

- Formation between 7-8 weeks and completion around 3rd month of gestation.
- Formed by nasal septum and two palatal shelves.
- Nasal septum grows downwards and palatal shelves towards midline and they fuse together.



- Merging of two palatal shelves marked by- mid palatal suture
- Palatal shelves merge with primary palate. Junction is marked by incisive foramen
- Superficial- median raphe and incisive papilla



- 
- During 6-7th week tongue is placed between the palatal shelves- causing the vertical orientation of palatal shelves
 - By the 9th week, upper facial complex has lifted away from thorax permitting downward displacement of tongue and permit growth of lower jaw.



- Mechanisms responsible for elevation of palate are

1. biochemical transformation in physical consistency of connective tissues
2. sudden increase in tissue turgor and rapid differential mitotic growth
3. intrinsic shelf elevating process by hydration of connective tissue.
4. Alignment of mesenchymal cells- act as elevating force
5. Downward movement of tongue
6. Prognathic movement of mandible



- **Fusion of process**

- epithelium overlying thee shelves merges to form epithelial seam

- merging start from anterior region of hard palate to posterior region

- Merging followed by epithelial adherence

- Medial edge epithelium – decline in epidermal growth factor receptor- apoptotic cell death

- Basal layer – epithelial mesenchymal transformation
- Epithelial cells that persist – epithelial pearls





- MOLECULAR REGULATION OF PALATOGENESIS

- Palatogenesis is an ordered sequence mediated by multiple signaling molecules

- 6th week- development of palatal primordia vertically oriented

- 9th week elevation and fusion

- Firstly fusion of epithelial covering to form midline epithelial seam(MES)
- 



- Fate of MES:

1. apoptotic cell death
2. migration to oral and nasal side
3. EMT

Palatal fusion completes around 12th week

After fusion – ossification of ant two third – hard
palate



- Secreted proteins

1. TGFb1- transformation growth factor

TGFB3-palatal fusion

TGFB1&2-mesenchymal proliferation

2. During elevation- type III collagen

fibronectins and hyaluronate- replaced by type I collagen

3. Proteoglycans – hydration and compressibility of connective tissue

4. SHH and WNT1 – cellular proliferation and survival



5. Tenascin c- determine the fate of MES

6. E-cadherins- apical basal polarity

7. nectins- epithelial junctions



■ ANOMALIES OF PALATE

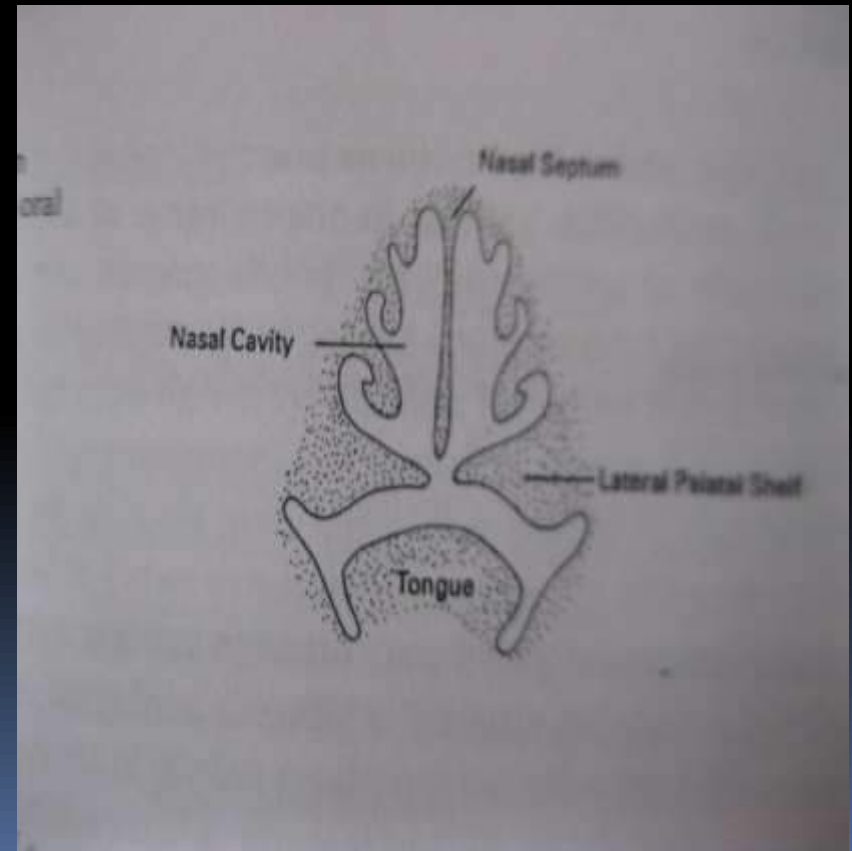
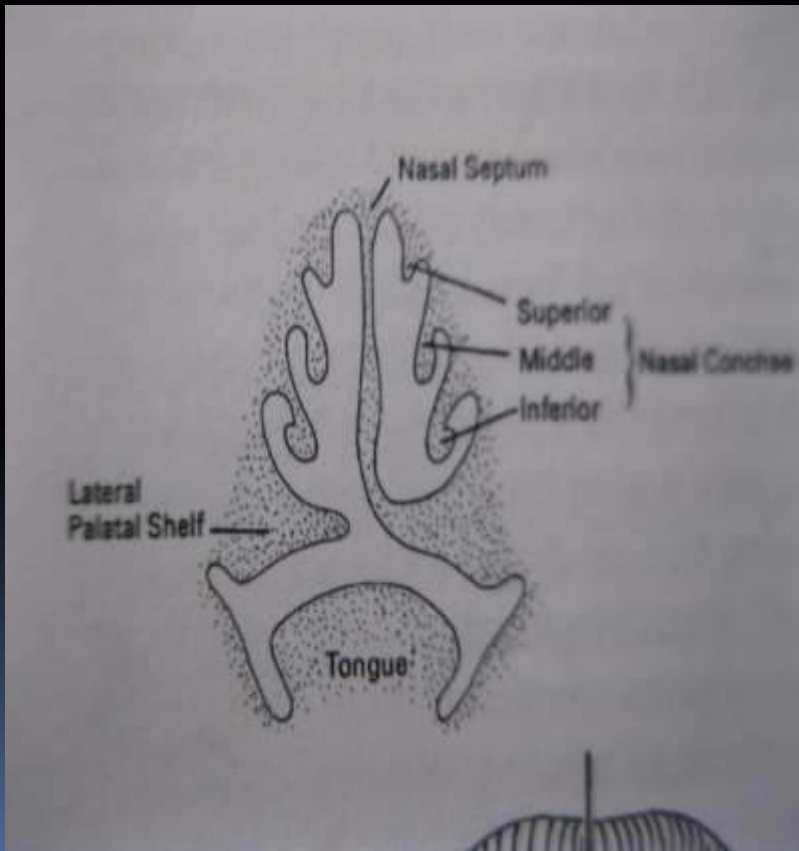
- Mis-timing of any of these critical events by environmental factors or genetic predisposition- CLEFTS
- Entrapment of epithelial pearls- median palatal rest cyst. Superficial expression – EPSTEIN PEARLS
- Delayed elevation – widened gap between palatal shelves


Causes of clefts

- Speech difficulty
- Spillage of food

- Unilateral clefts

- Bilateral clefts



- 
- Syndromes associated
 1. Treachers collin
 2. Pierre robins
 3. Down syndrome
 4. Marfans syndrome
 5. Crousos syndrome

Torus palatinus- localised midpalatal overgrowth

Clinical Correlates

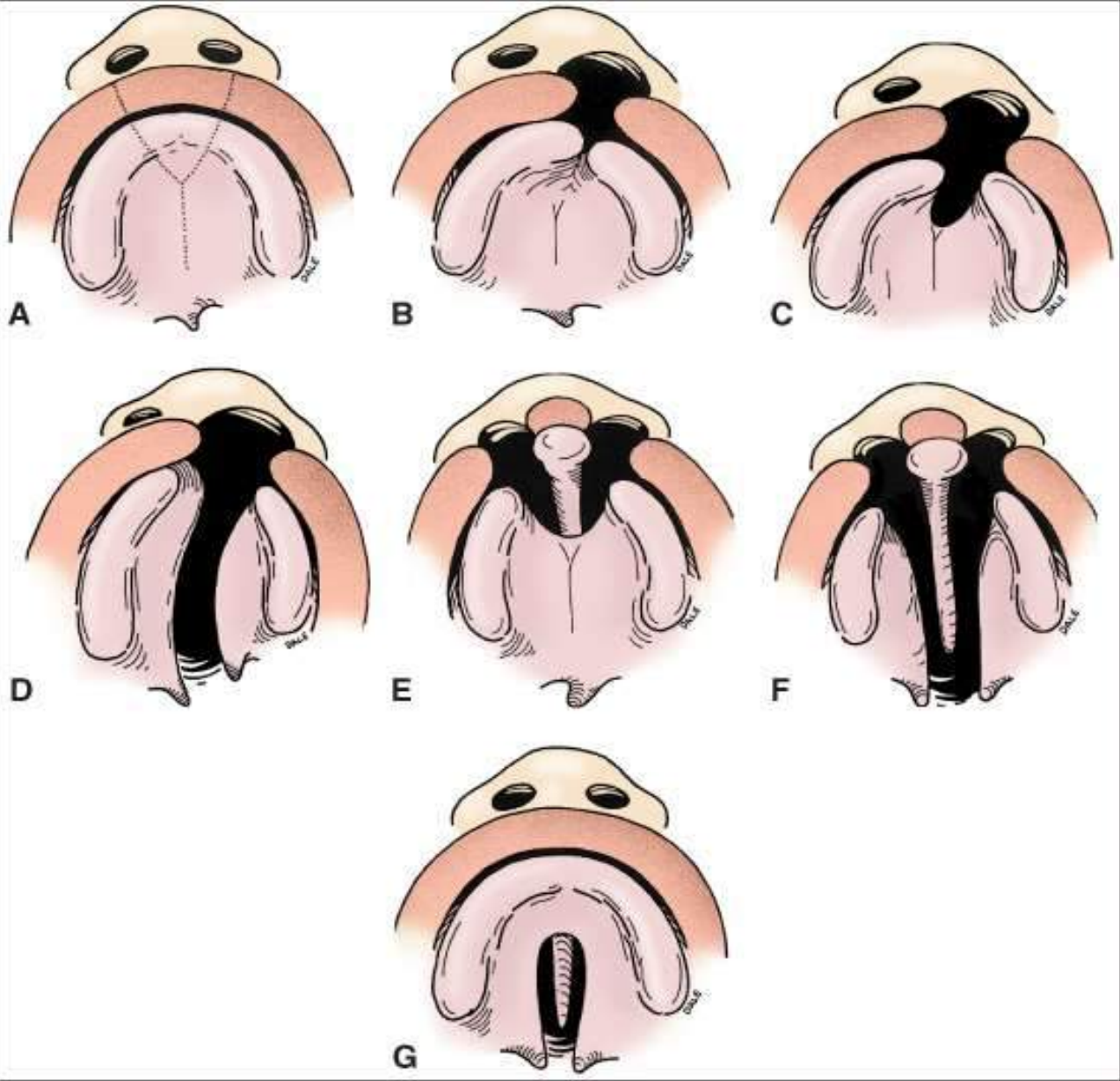
- Facial clefts

- Cleft lip and Cleft palate:

partial or complete lack of fusion of maxillary prominence with medial nasal prominence.



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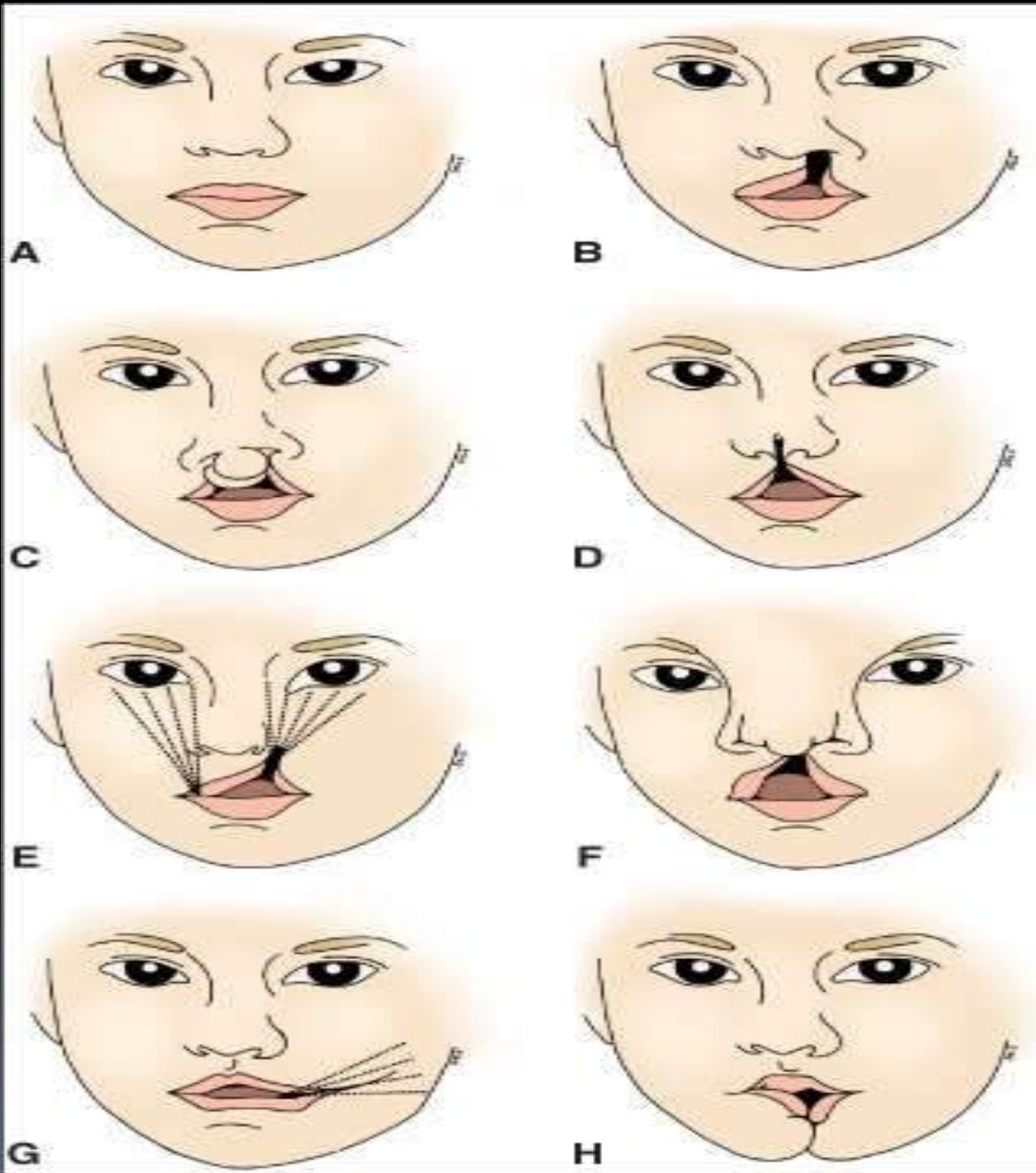
- Oblique facial clefts:

Failure of maxillary prominence to merge with lateral nasal prominence.

- Median cleft lip:

incomplete merging of two medial nasal prominences in midline.





- **Reasons for failure of fusion**

1. Glossoptosis

2. Failure of fusion due to presence of epithelial covering

- 3 . Rupture after fusion of shelves

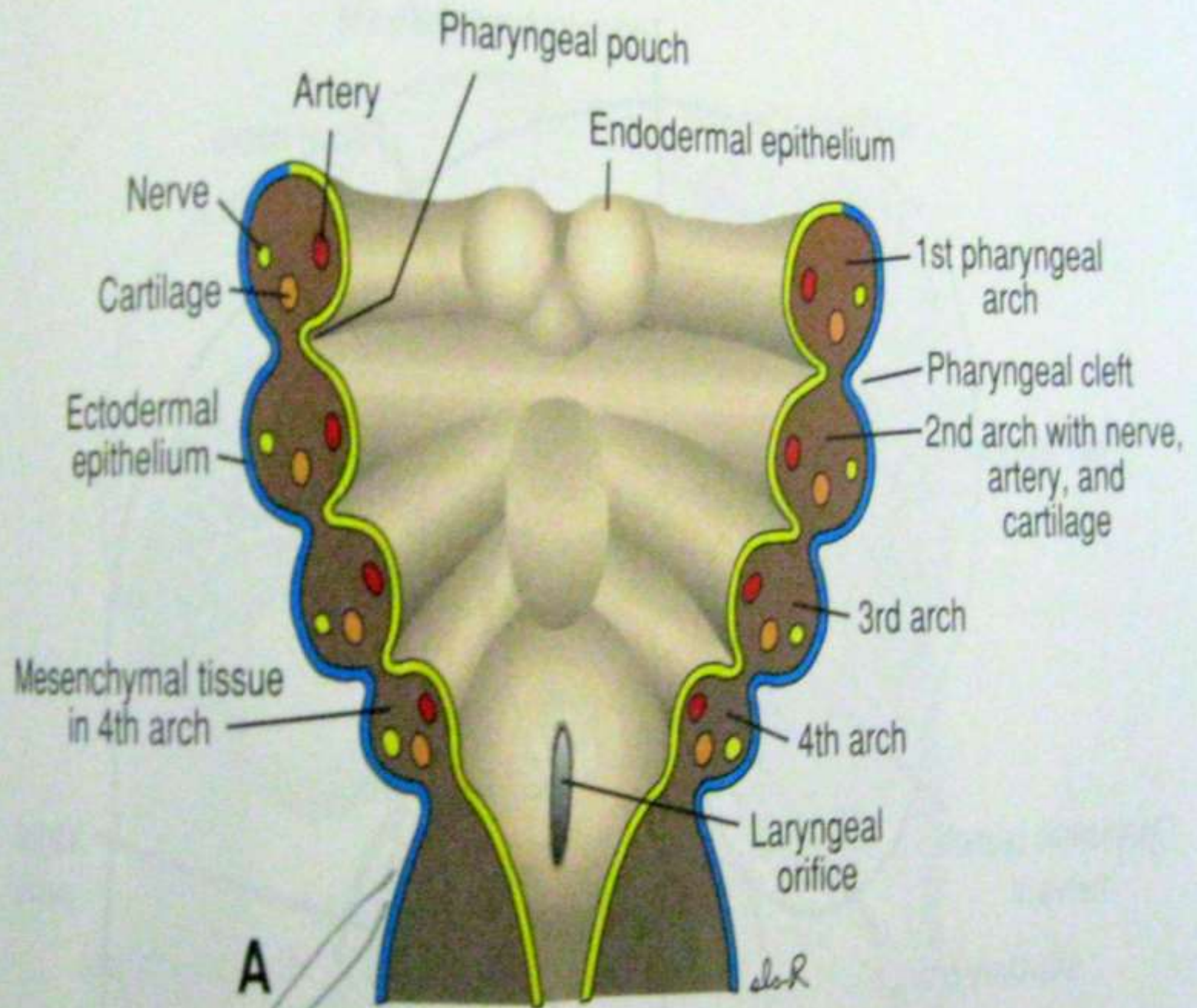
4. Defective merging of mesenchyme

- **Environmental factors**

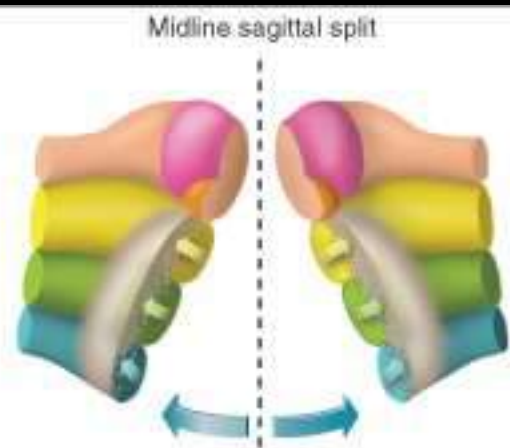
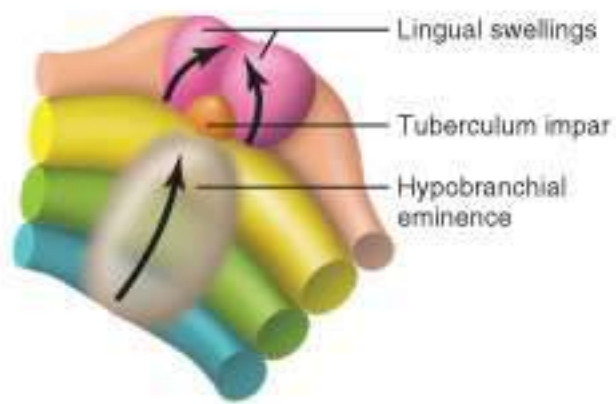
1. Infections
2. X-ray radiation
3. Drugs
4. Hormones
5. Nutritional deficiency

Formation of tongue

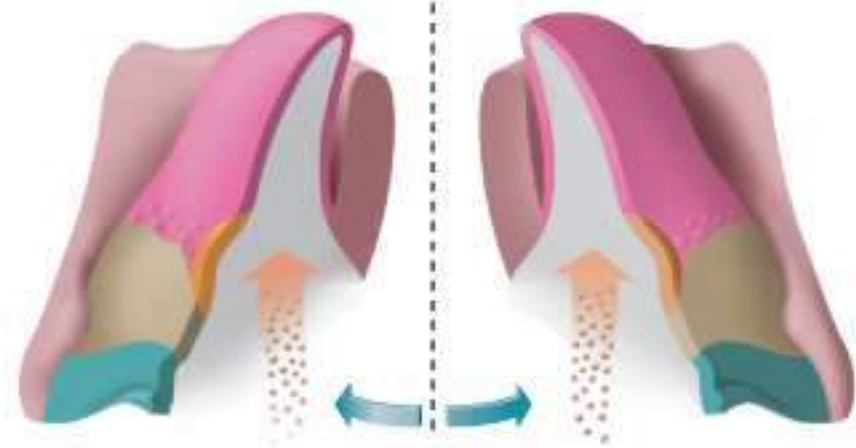
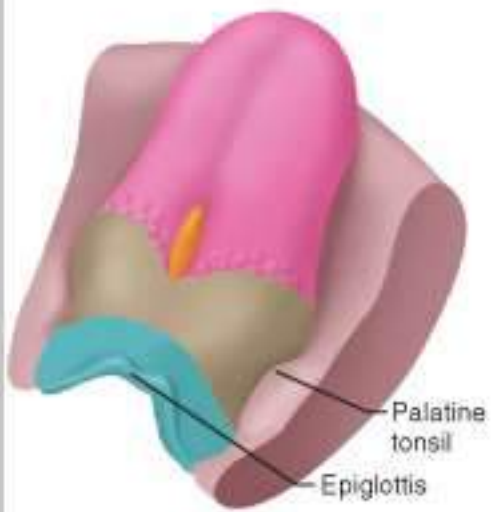
- The tongue begins to develop at about 4 weeks.
- Pharyngeal arches meet in the midline beneath the primitive mouth.
- Local proliferation of mesenchyme give rise to swellings in the floor of the mouth.
 1. Tuberculum impar
 2. Lingual swellings
 3. Copula
 4. Hypobranchial eminence



A



B



- Arch 1
- Arch 2
- Arch 3
- Arch 4

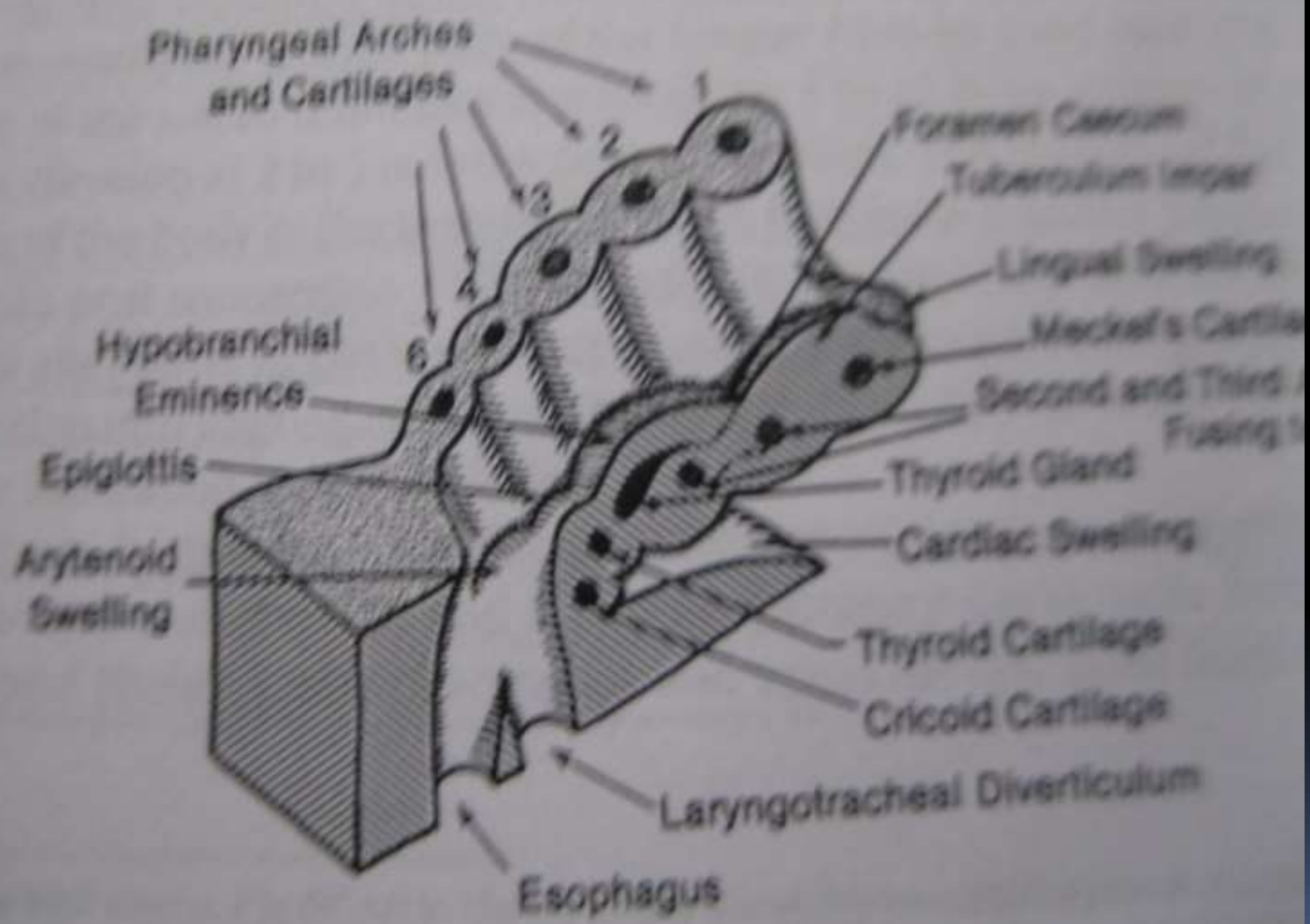
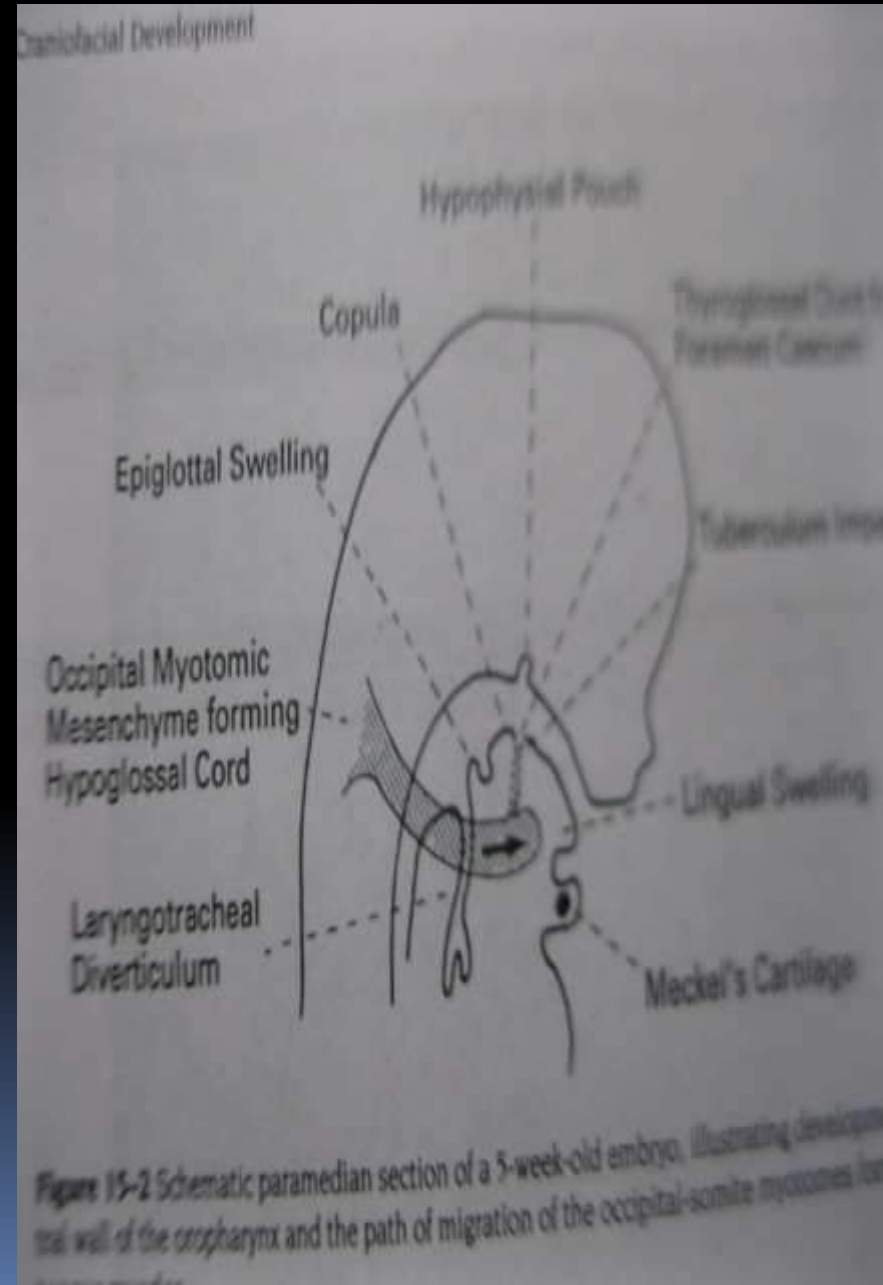


Figure 15-1 Tongue primordia arising in the ventral wall of the pharynx of a 4-week

- Caudally to tuberculum impar, a blind pit known as foramen caecum.
- Marks the origin of thyroid diverticulum
- Ventral to pharynx, continues as thyroglossal duct ends in thyroid gland




- Proliferation of epithelial cells beneath the mesenchyme, separate the body of tongue from floor
- Fungiform papillae develops on dorsal surface by 11th week
- Body of tongue separated from the root by sulcus terminalis
- Taste bud develops by inductive interactions
- Occipital somites form the muscles of the tongue. Migrates to tongue through hypoglossal cord

- Muscles of tongue originate from occipital somites carrying **hypoglossal nerve**.
- Mucosa of anterior 2/3rd : 1st arch; **trigeminal nerve**
- Mucosa of posterior 1/3rd : 3rd arch; **glossopharyngeal nerve**
- Posterior part of hypobranchial eminence forms the **epiglottis**.
- Cartilage differentiate within the epiglottis by 15th week
- Epiglottis full develop by 21st week and contact the soft palate by 23st week.

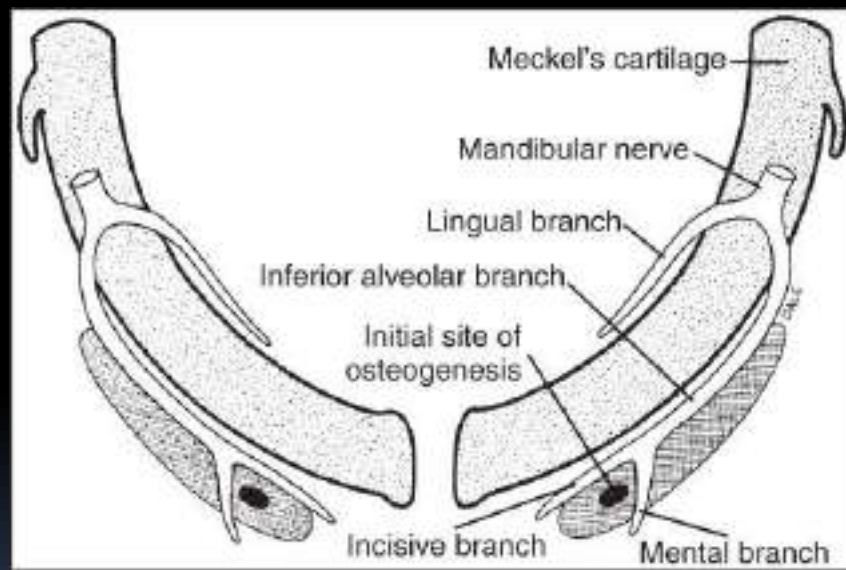
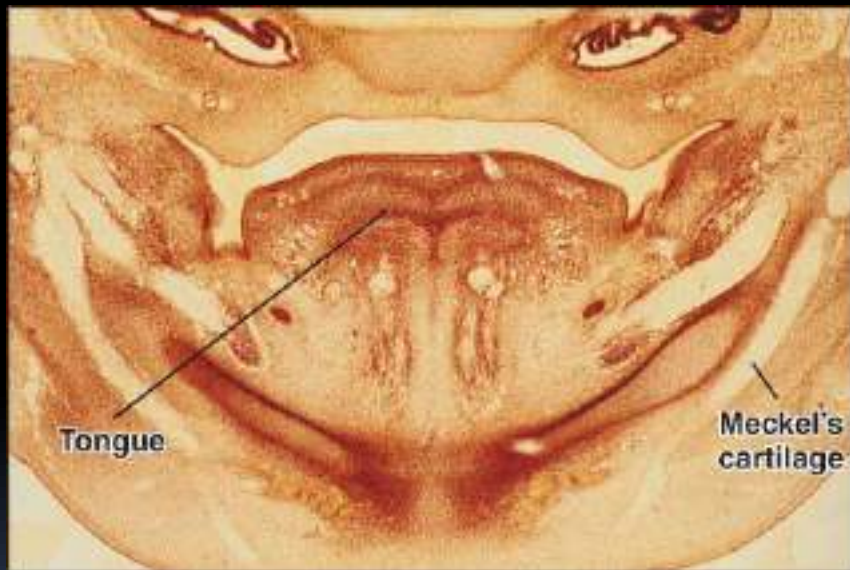


Clinical correlates

- Macroglossia and microglossia
 - Bifid tongue
 - Ankyloglossia
 - Lingual thyroid
 - Remnants of thyroglossal duct
 - Fissured tongue
 - CHARGE syndrome
- 

Development of Mandible

- Forms from 1st arch (Meckel's cartilage)
- By the 6th week cartilage extends as cartilagenous rod.
- On the lateral aspect of Meckel's cartilage condensation of mesenchyme occurs.
- At 7 weeks, intramembranous ossification begins in condensation, forming 1st bone of mandible.

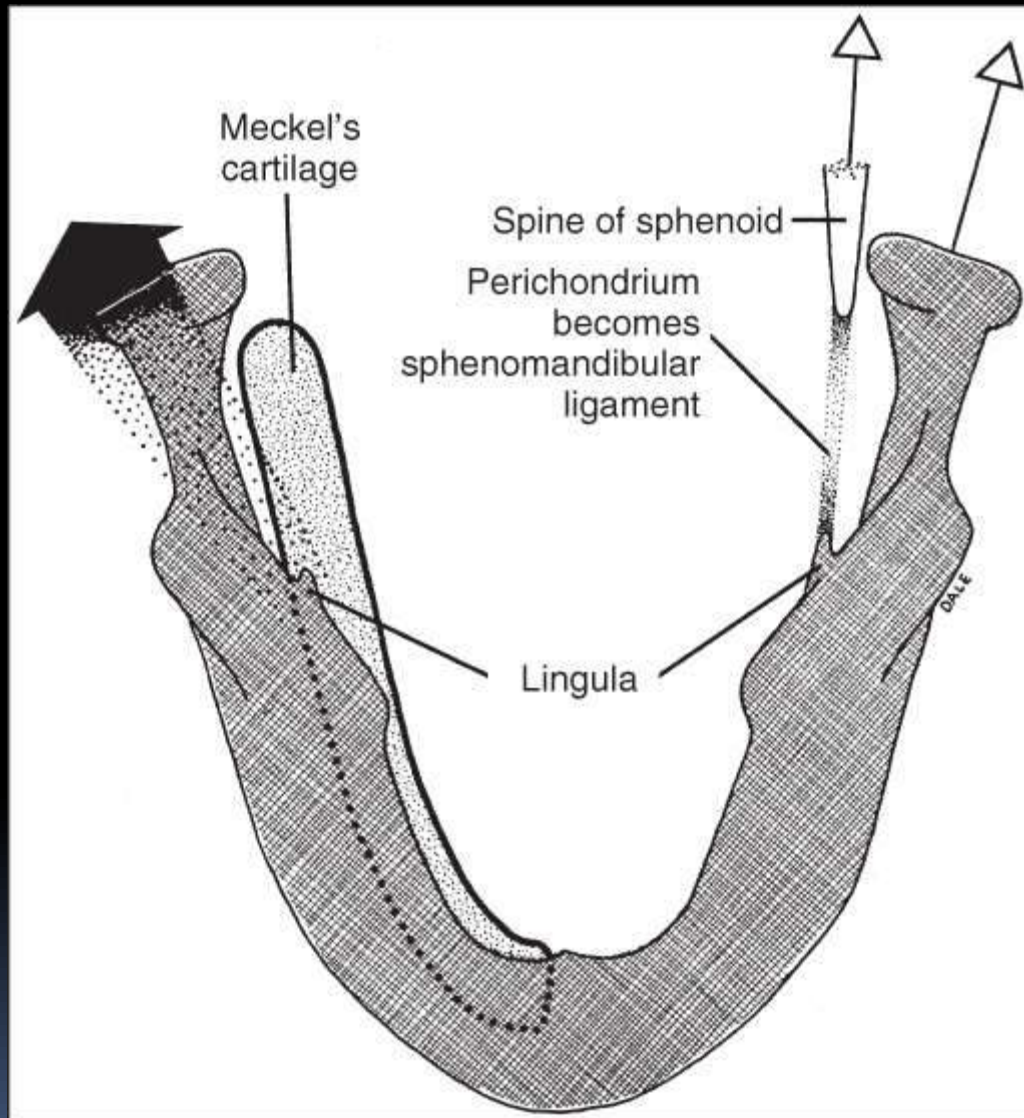


- 
- From this center of ossification, bone formation spreads anteriorly and posteriorly.

- ❖ Ramus:


develops by rapid spread of ossification posteriorly.





■ Fate of meckel's cartilage

1. The most posterior proximity forms incus and malleus of inner ear and sphenomalleolar ligament
2. From sphenoid to division of mandibular nerve cartilage is totally lost, but fibrocellular capsule persists sphenomandibular ligament
3. From lingula to division of inferior alveolar nerve, cartilage degenerates
4. Forward from this point cartilage ossifies by endochondral ossification

- 
- By 10 weeks rudimentary mandible forms.
 - Until birth, growth is influenced by 3 secondary cartilages:

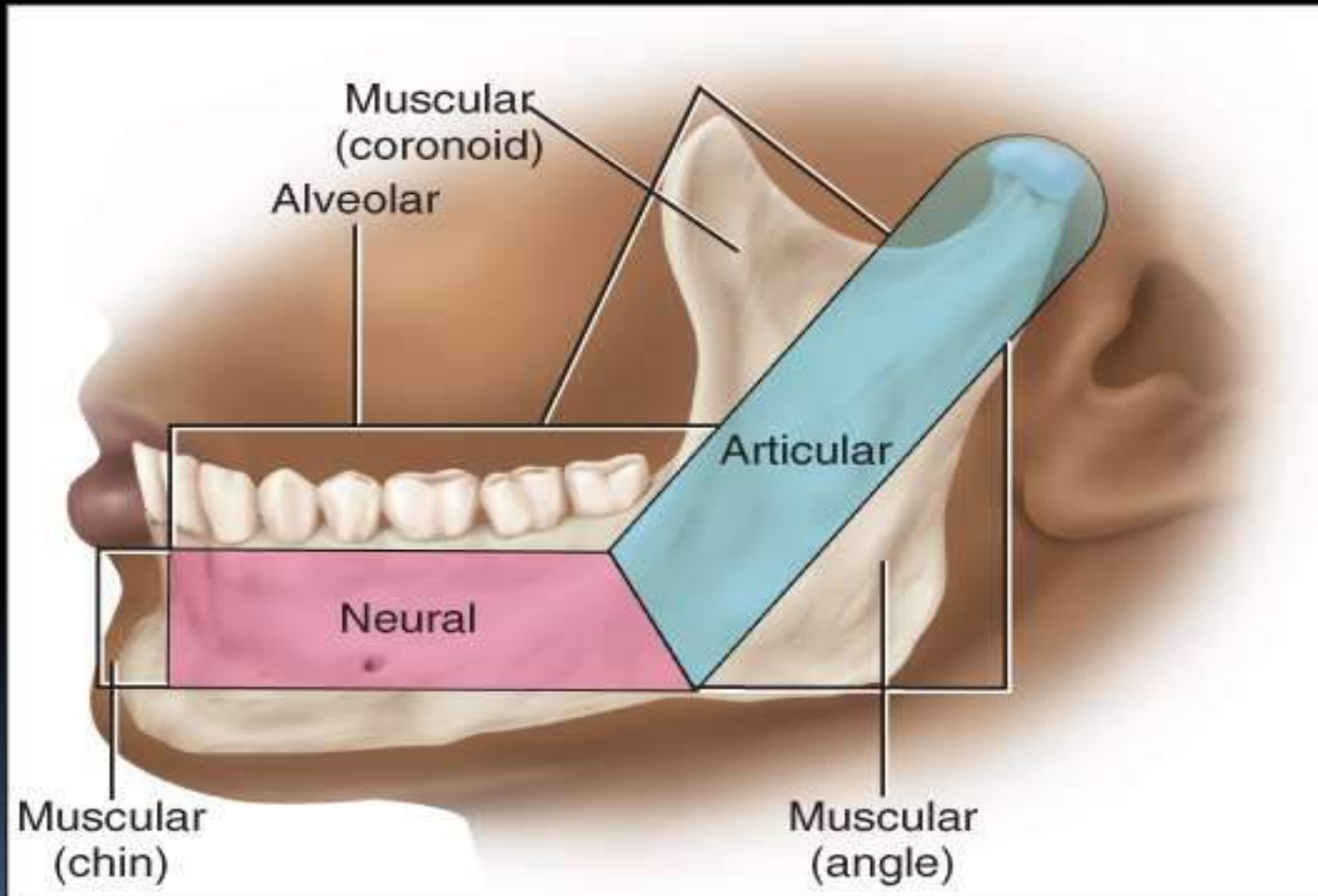
Condylar cartilage

Coronoid cartilage

Symphyseal cartilage






Different developmental blocks for the mandible



Development of Maxilla

- No primary cartilage exists in maxillary process.
- Center of ossification closely associated with cartilage of nasal capsule.
- Center of ossification present at division of anterosuperior dental nerve given off from the inferior orbital nerve.

- 
- From center bone formation spreads
posteriorly below orbit
anteriorly incisor region
superiorly frontal process of maxilla
 - Ossification forms hard palate, medial alveolar plate and main body of maxilla.

- 
- Secondary cartilage: zygomatic or malar cartilage appears in developing zygomatic process.
 - Maxillary sinus forms during 16th week.
At birth sinus is still rudimentary.
- 

DEVELOPMENT OF SKULL

- Skull forms from :
 1. NEUROCRANIUM
 2. VISROCRANIUM

NEUROCRANIUM

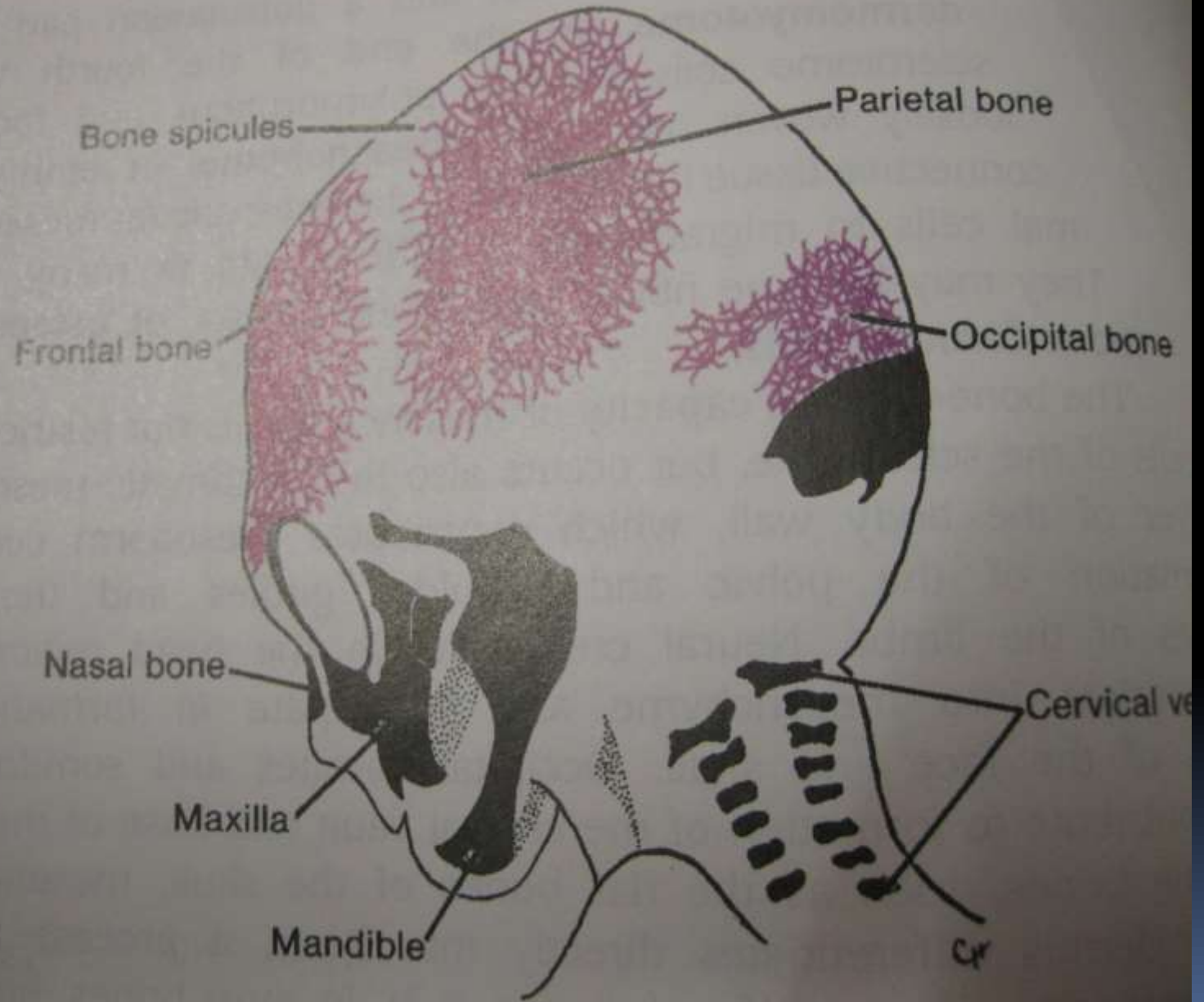
A. membranous part

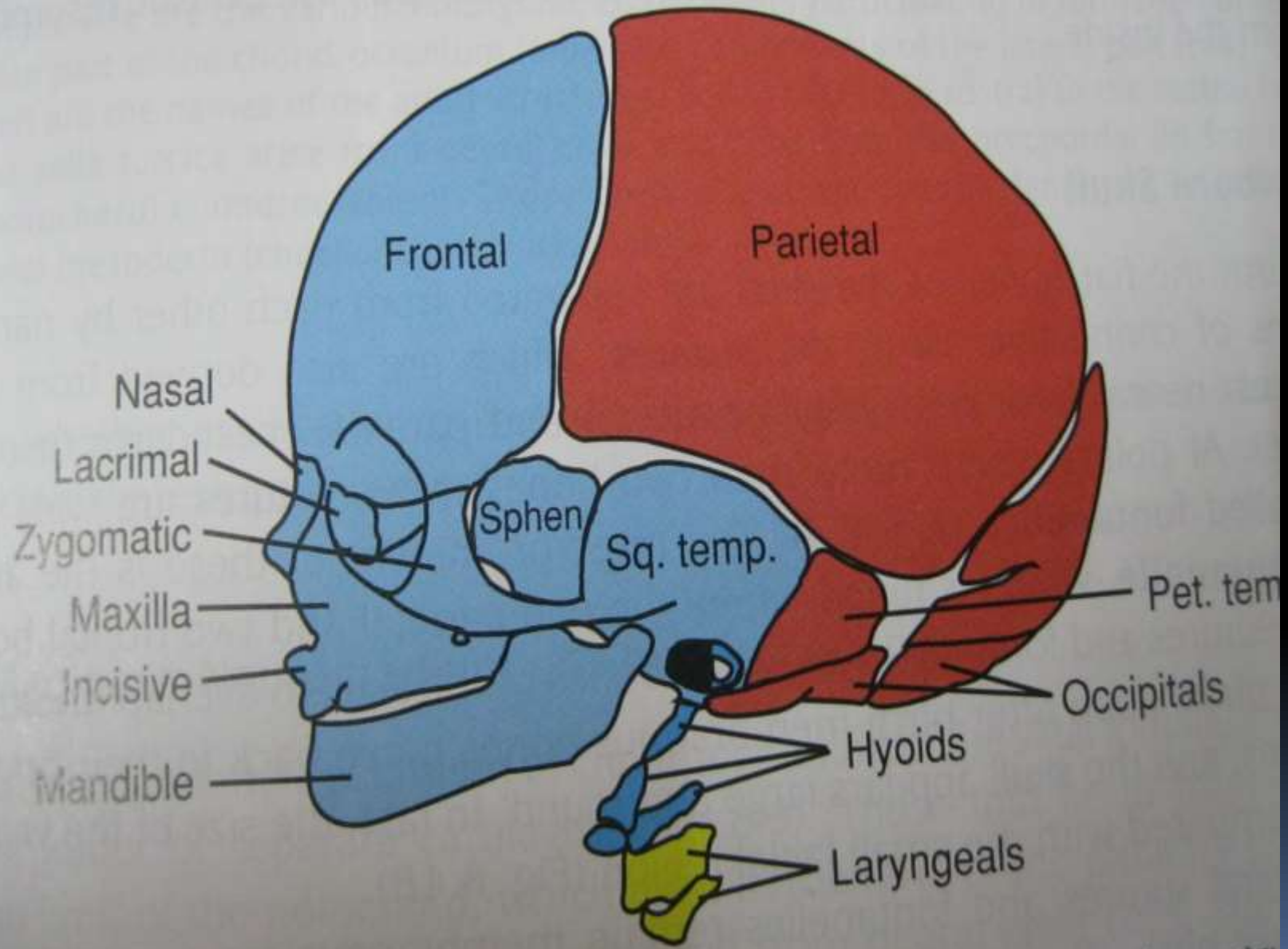
B. cartilagenous part

- MEMBRANOUS NEUROCRANIUM
derived from neural crest cell and paraxial mesoderm
- Ossifies by membranous ossification

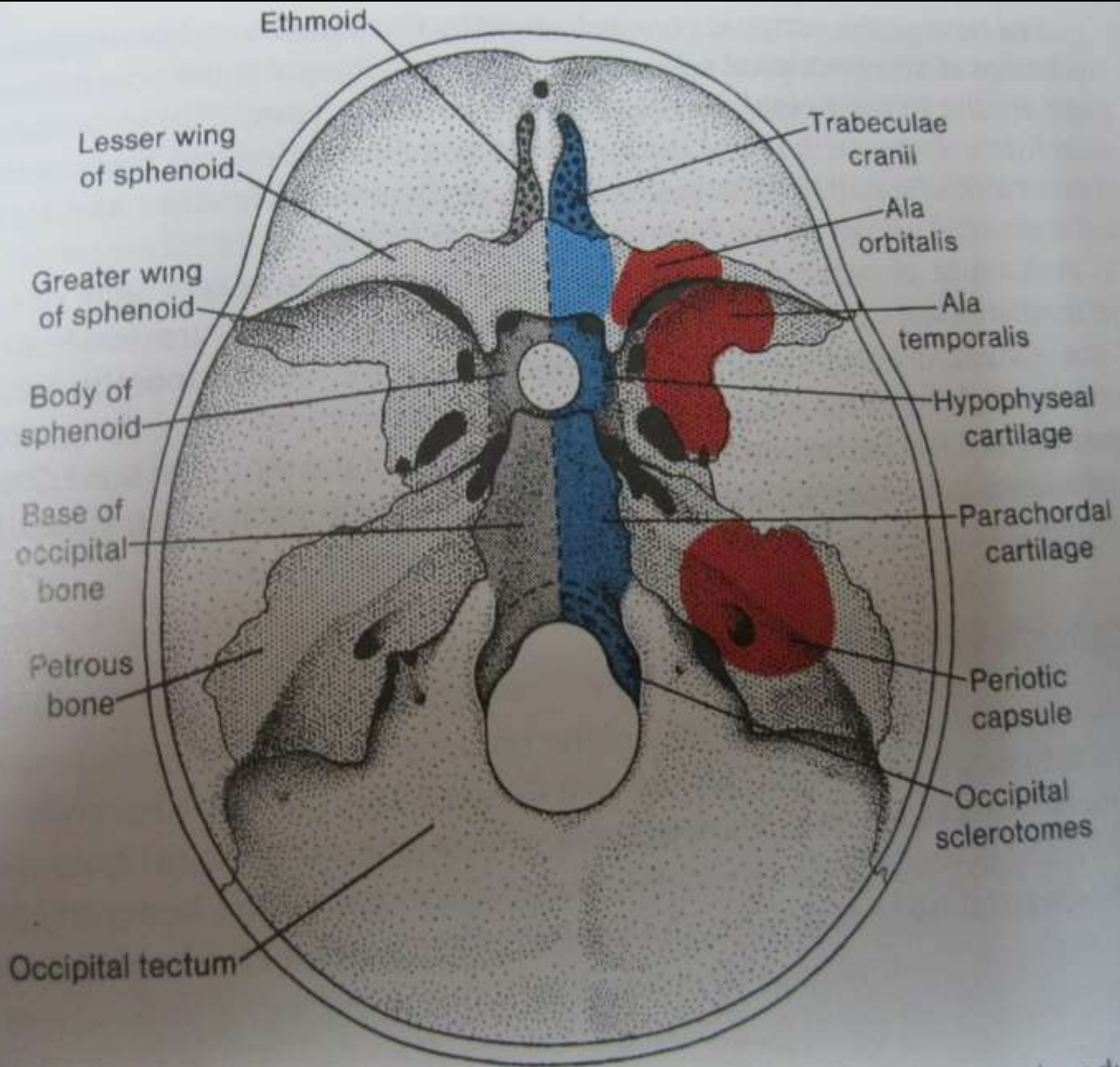
CARTILAGENOUS NEUROCRANIUM

- Prechordal chondrocranium
- Chordal chondrocranium
- Ossifies by endochondral ossification





See these STRL



■ **VISROCRANIUM**

Form the bones of the face

Mainly from 1st and 2nd pharyngeal arches

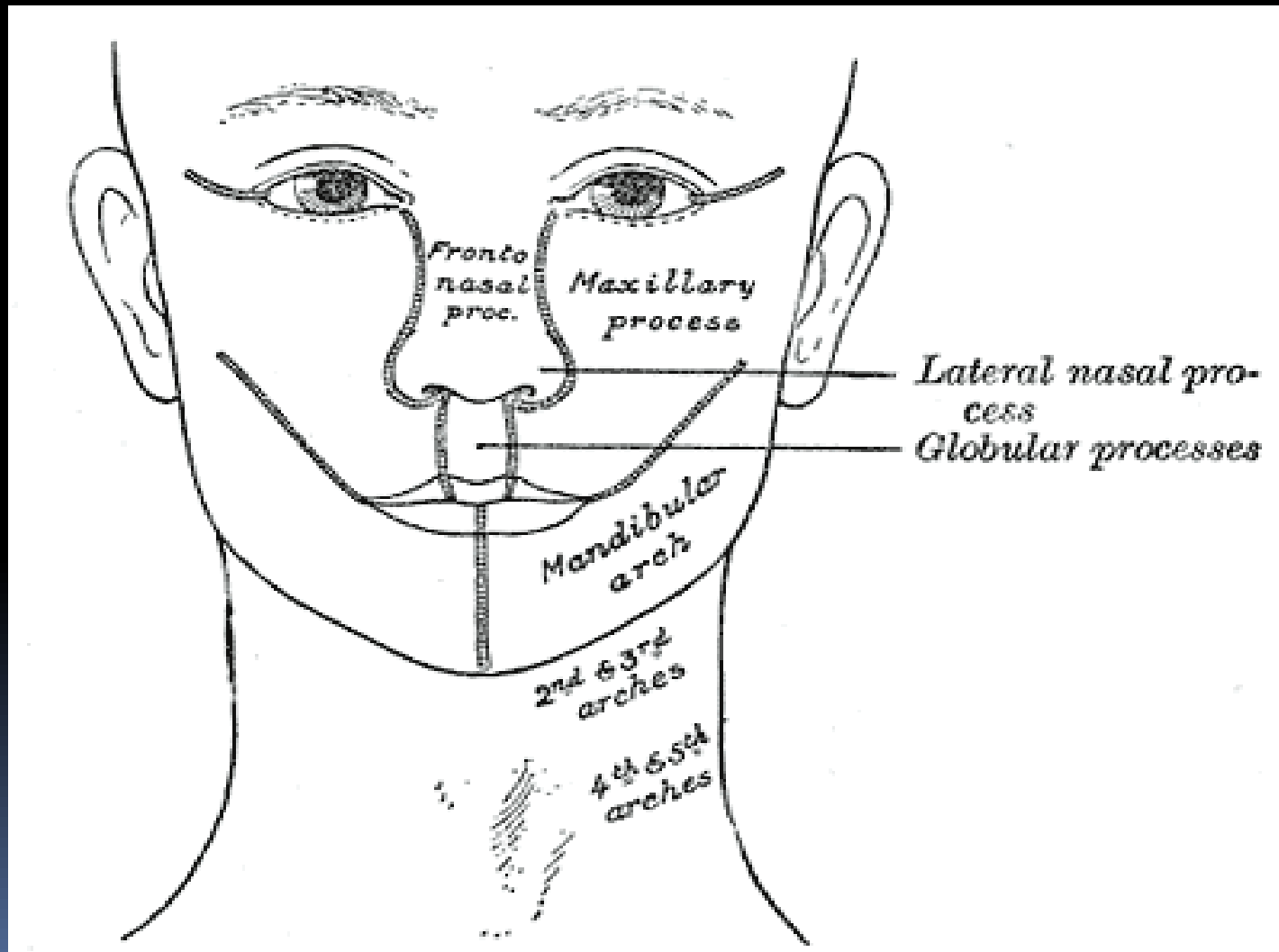
➤ **Maxillary process**

➤ **Mandibular process**

Dorsal tip of mandibular process along with 2nd pharyngeal arches form incus , malleous and stapes

> **Mesenchyme for formation of face derived from neural crest cells.**

OVERALL SUMMARY OF DEVELOPMENT OF FACE



- *I will praise thee: for I am fearfully and wonderfully made.*

-Psalm CXXXIX 14

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THANK

YOU