Head and Neck development I: Pharyngeal apparatus and their derivatives

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Objectives

- Describe the components of pharyngeal apparatus
- Describe derivatives of the apparatus
- Describe the anatomical basis of malformations related to the apparatus

Pharyngeal Apparatus 1

- Pharyngeal arches are rod-like thickenings of mesoderm present in the wall of the foregut.
- The ventral ends of the arches of the right and left sides meet in the middle line in the floor of the pharynx.
- In the interval between any two arches, the endoderm (lining the pharynx) is pushed outwards to form a series of pouches - endodermal, or pharyngeal, pouches.
- They are evident in the head and neck region by 4th week
- Resemble fish gills (branchia) thus their earlier name - Branchial apparatus - derived from the Greek word branchia or gill
- They are derived from neural crest cells

Pharyngeal Apparatus 2

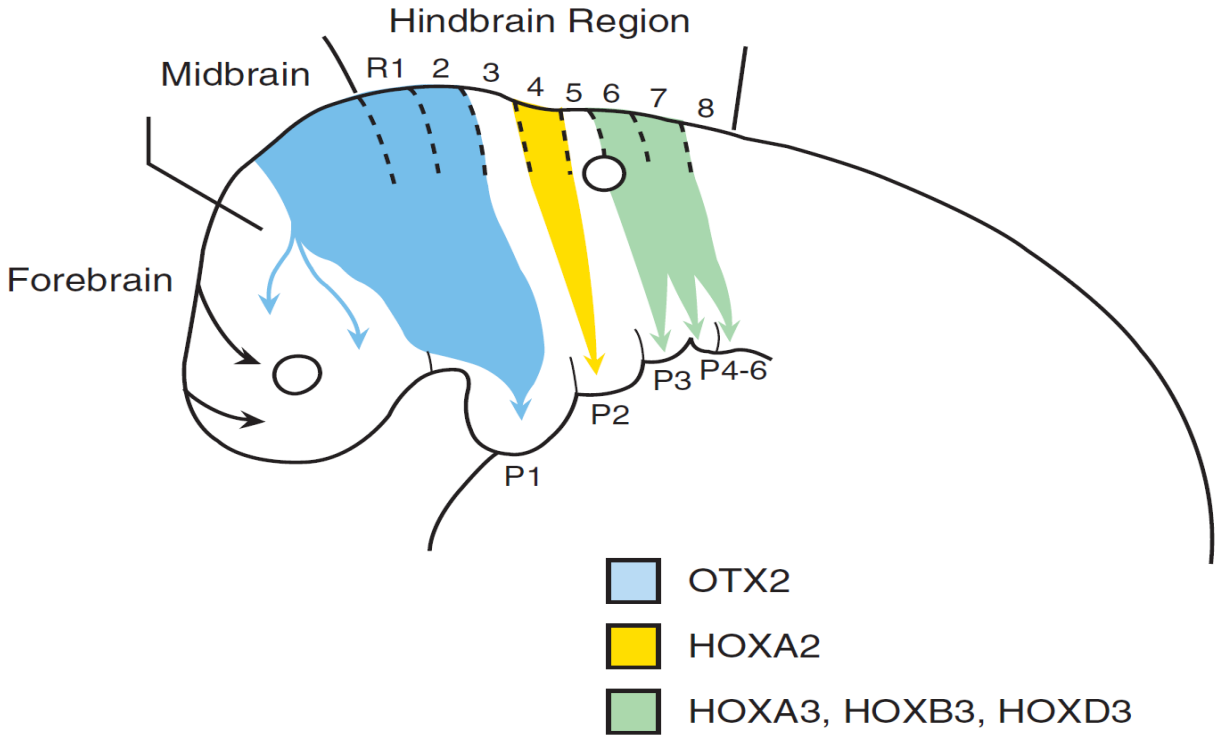
- Contribute to the formation of the neck as well as the face.
- The neural crest cells that populate the first arch are derived from:
  - rhombomeres 1 and 2
  - midbrain
- Mesenchyme arise from
  - Neural crest cells
  - mesoderm (somitomeres)

Pharyngeal apparatus consists of 4 components:

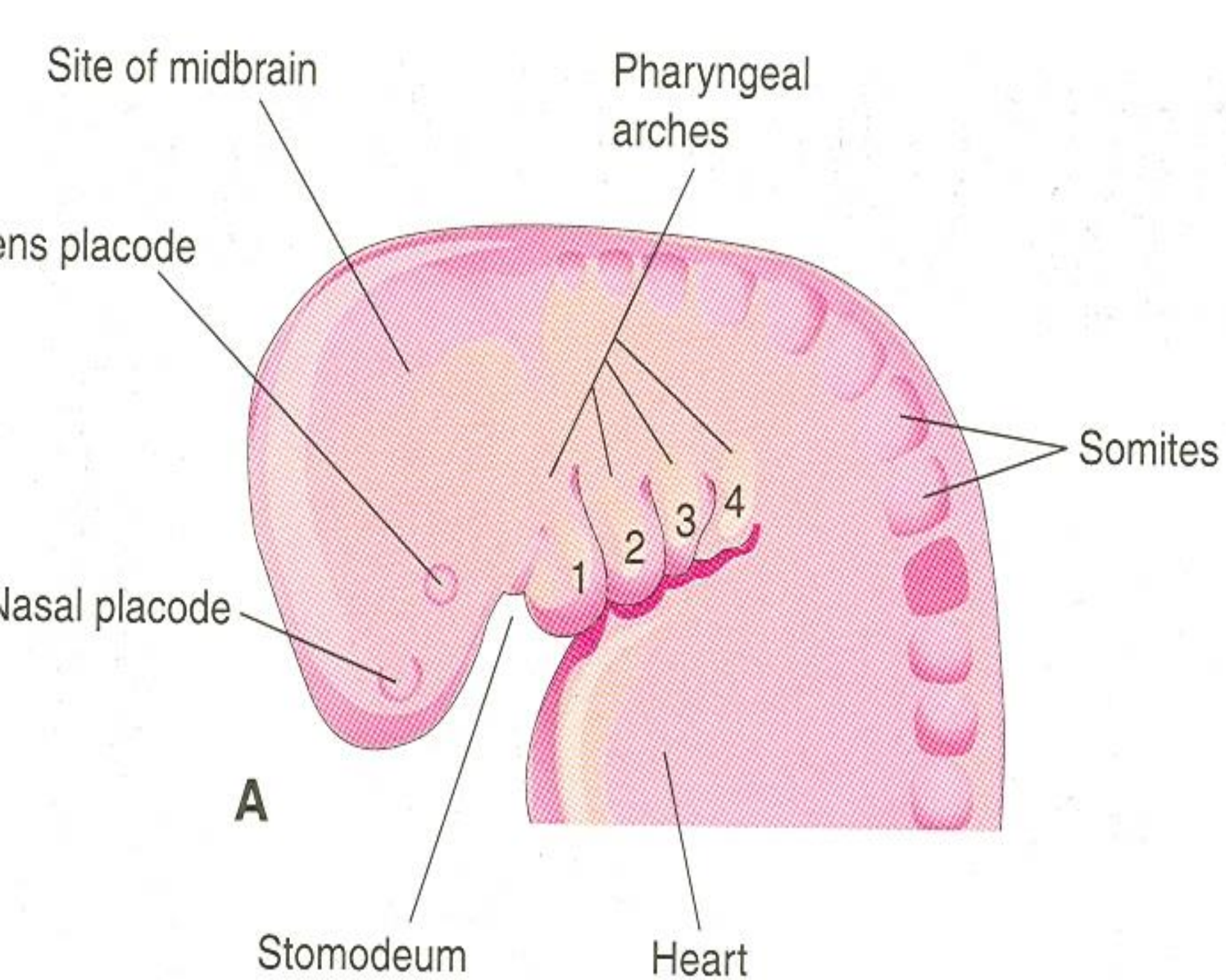
1. A central skeleton which is made of cartilage that has developed from the earlier mesenchymal cells.
2. A muscular component.
3. A vascular component which is derived from the aortic arch artery.
4. A nervous component, motor and sensory which grows into each arch from the hindbrain.

Pharyngeal Arches 3

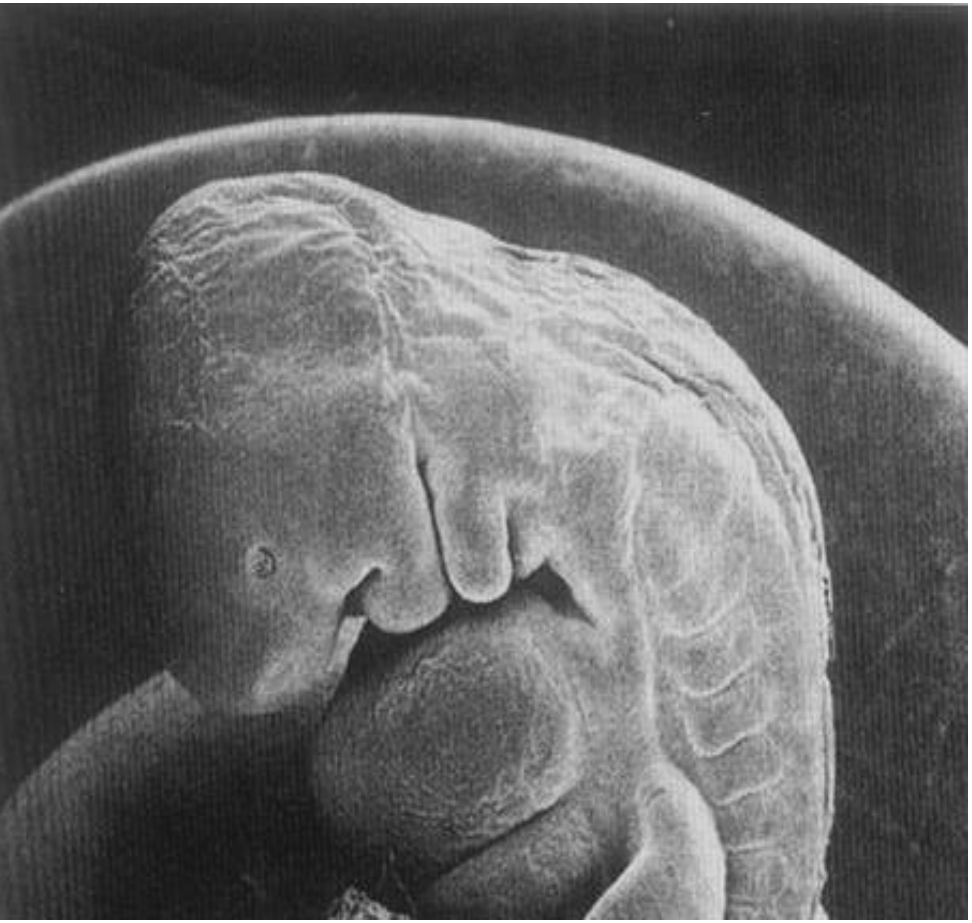
- 4th week neural crest cells migrate into the head and neck region – rhobomeres 1 & 2 and midbrain
- The first pair of pharyngeal arches - primordium of jaws, appears as a surface elevations lateral to the developing pharynx
- Soon other arches appear as obliquely disposed, rounded ridges on each side of the future head and neck regions



Drawing showing the pathways of neural crest cell migration from the cranial neural folds into the face and pharyngeal arches. From the hindbrain region, crest cells migrate from segments called rhombomeres. Rhombomeres express a specific pattern of HOX genes (the midbrain and rhombomeres 1 and 2 express the homeodomain-containing transcription factor OTX21), and neural crest cells carry these expression patterns into the pharyngeal arches. Also, notice that there are three streams of crest cells and that rhombomeres 3 and 5 do not contribute many (if any) cells to these streams. The three streams are important because they provide guidance cues for cranial nerves growing back from their ganglia to establish connections in the hindbrain.


Site of midbrain
Pharyngeal arches
ens placode
Somites
1
2
3
4
Nasal placode
A
Stomodeum
Heart

Pharyngeal Apparatus (weeks 4-5)

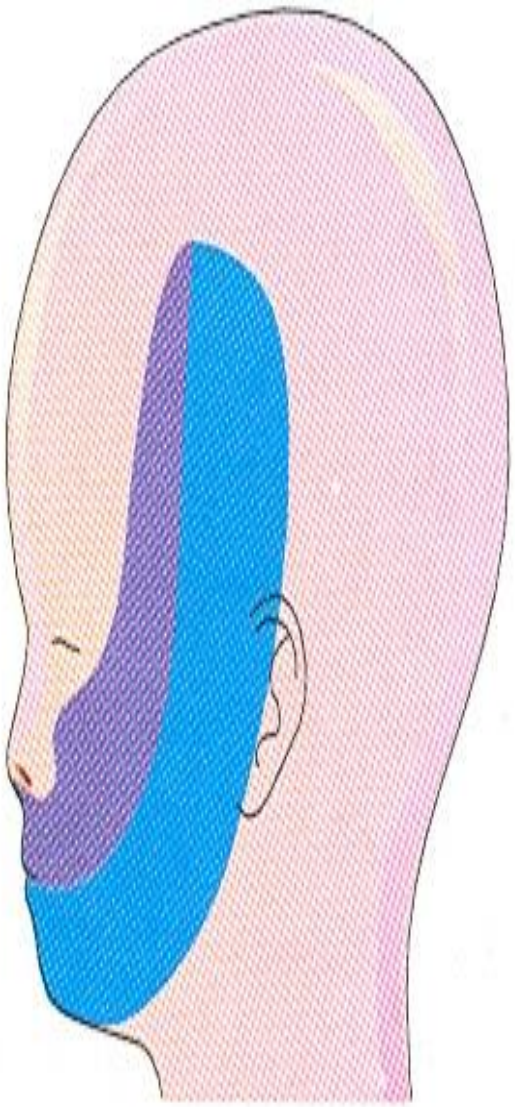


Pharyngeal Arches 4

- At first there are six arches.
- The 5^{th} and 6^{th} arches are rudimentary and are not visible on the surface of the embryo
- The pharyngeal arches are separated from each other by fissures called pharyngeal grooves
- They are numbered in craniocaudal sequence

Pharyngeal Arches 5

- The first pharyngeal arch (mandibular arch) develops:
  - maxillary and
  - mandibular prominences
- The first pair plays a major role in facial development
- The second pharyngeal arch (hyoid arch) contributes to the formation of hyoid bone



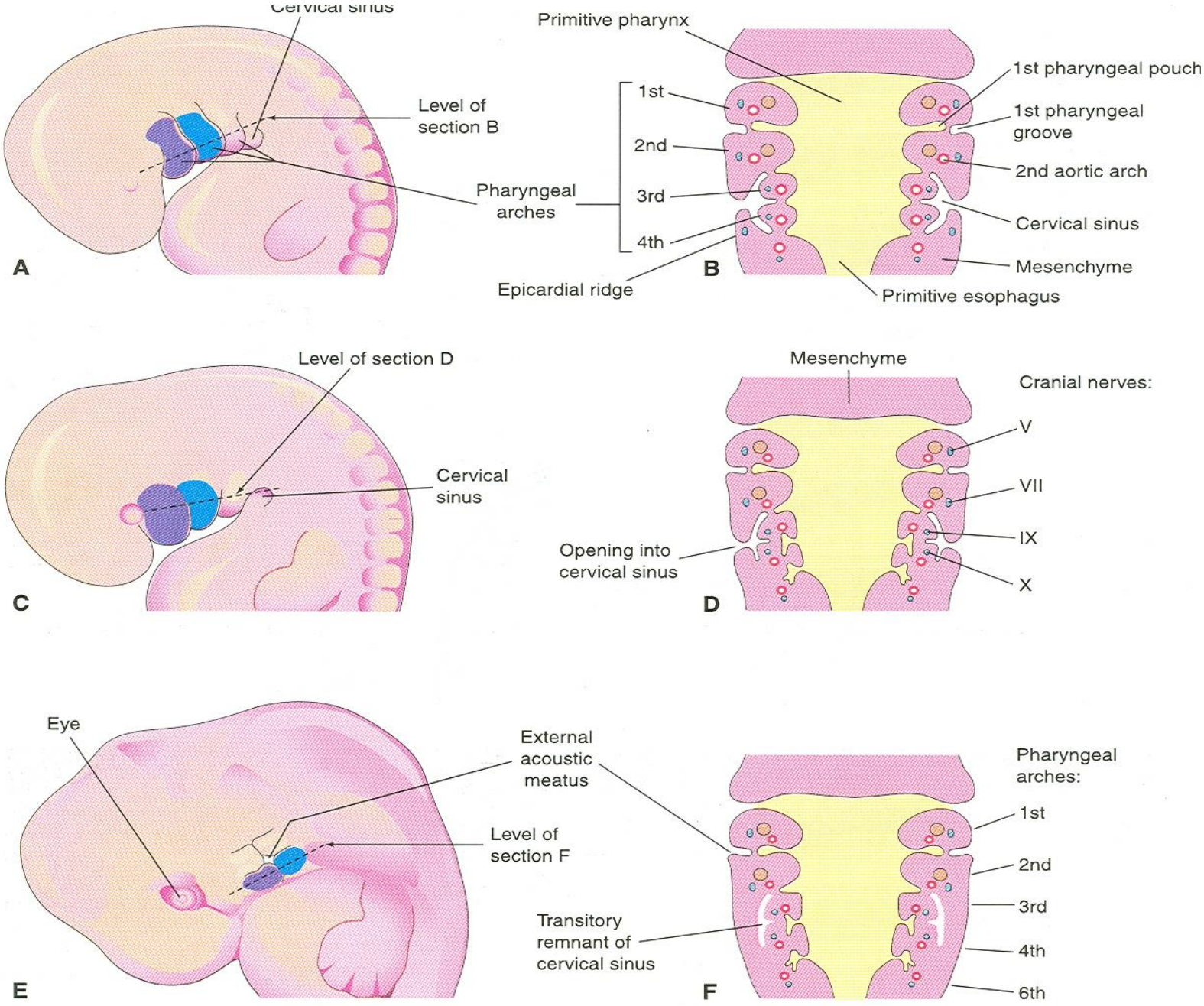
1st pharyngeal arch

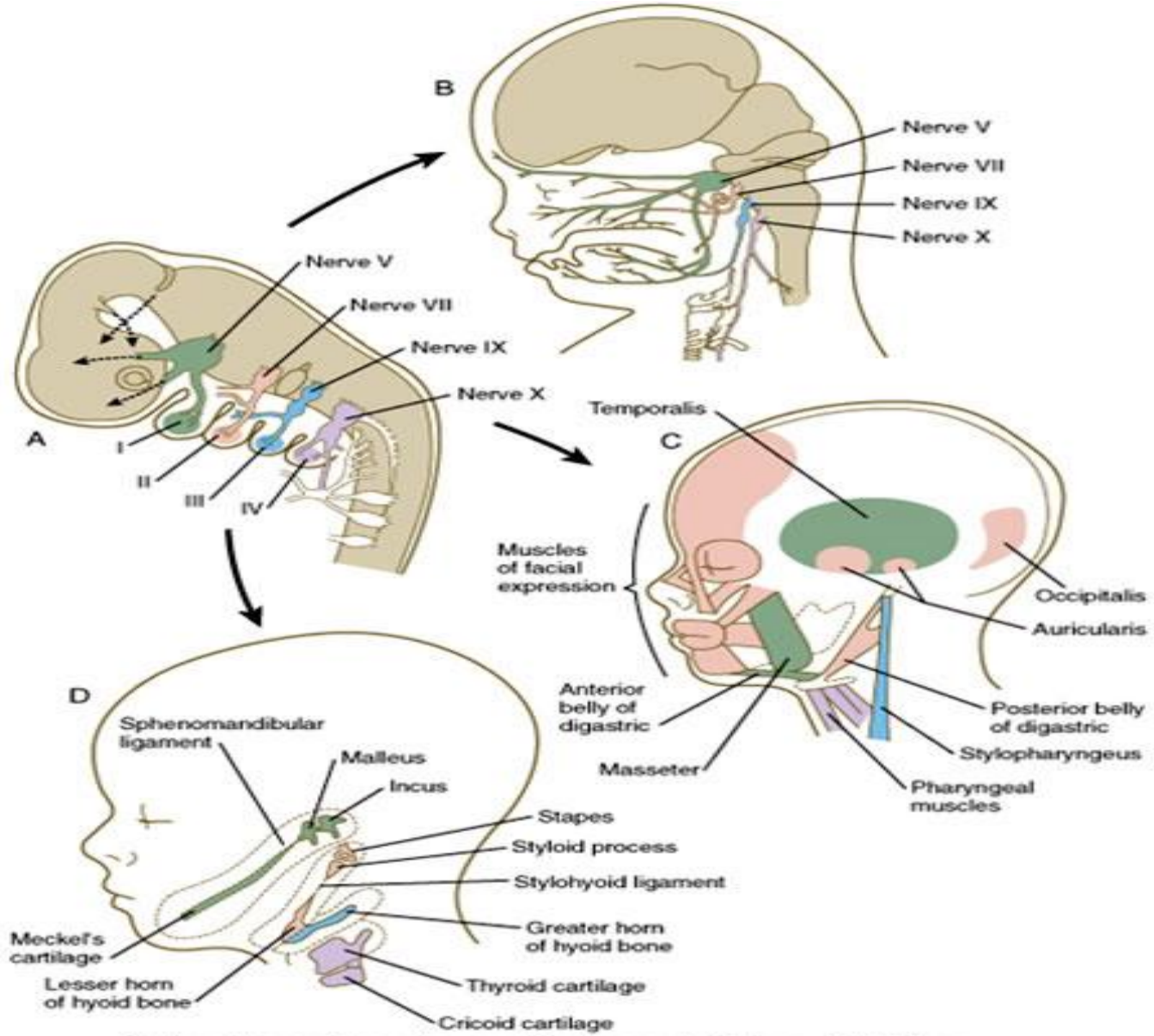
Maxillary prominence

Mandibular prominenc

Fate of Pharyngeal Arches 1

- The pharyngeal arches contribute exclusively to the formation of the:
  - face,
  - nasal cavities,
  - mouth,
  - larynx,
  - pharynx and
  - neck
- During the 5th week, the second pharyngeal arch enlarges and overgrows the third and fourth arches, forming the ectodermal depression called cervical sinus
- By the end of 7th week the second to fourth pharyngeal grooves and the cervical sinus have disappeared, giving the neck a smooth contour

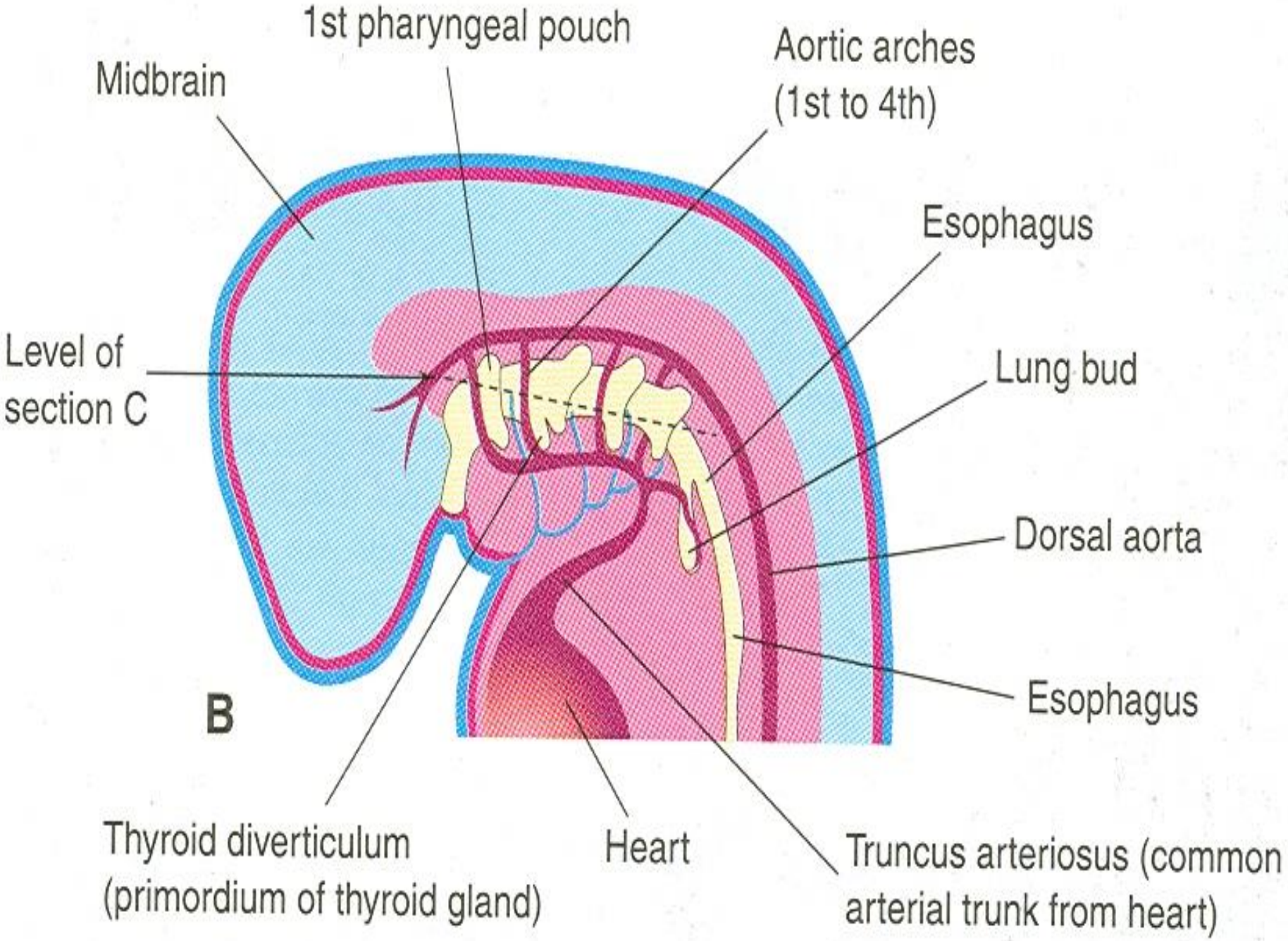

Cervical sinus
Level of section B
Pharyngeal arches
A
Primitive pharynx
1st
2nd
3rd
4th
Epicardial ridge
1st pharyngeal pouch
1st pharyngeal groove
2nd aortic arch
Cervical sinus
Mesenchyme
Primitive esophagus
B
Level of section D
Cervical sinus
C
Mesenchyme
Cranial nerves:
V
VII
IX
X
Opening into cervical sinus
D
Eye
External acoustic meatus
Level of section F
E
Pharyngeal arches:
1st
2nd
3rd
4th
6th
Transitory remnant of cervical sinus
F



Fate of Pharyngeal Arches 2

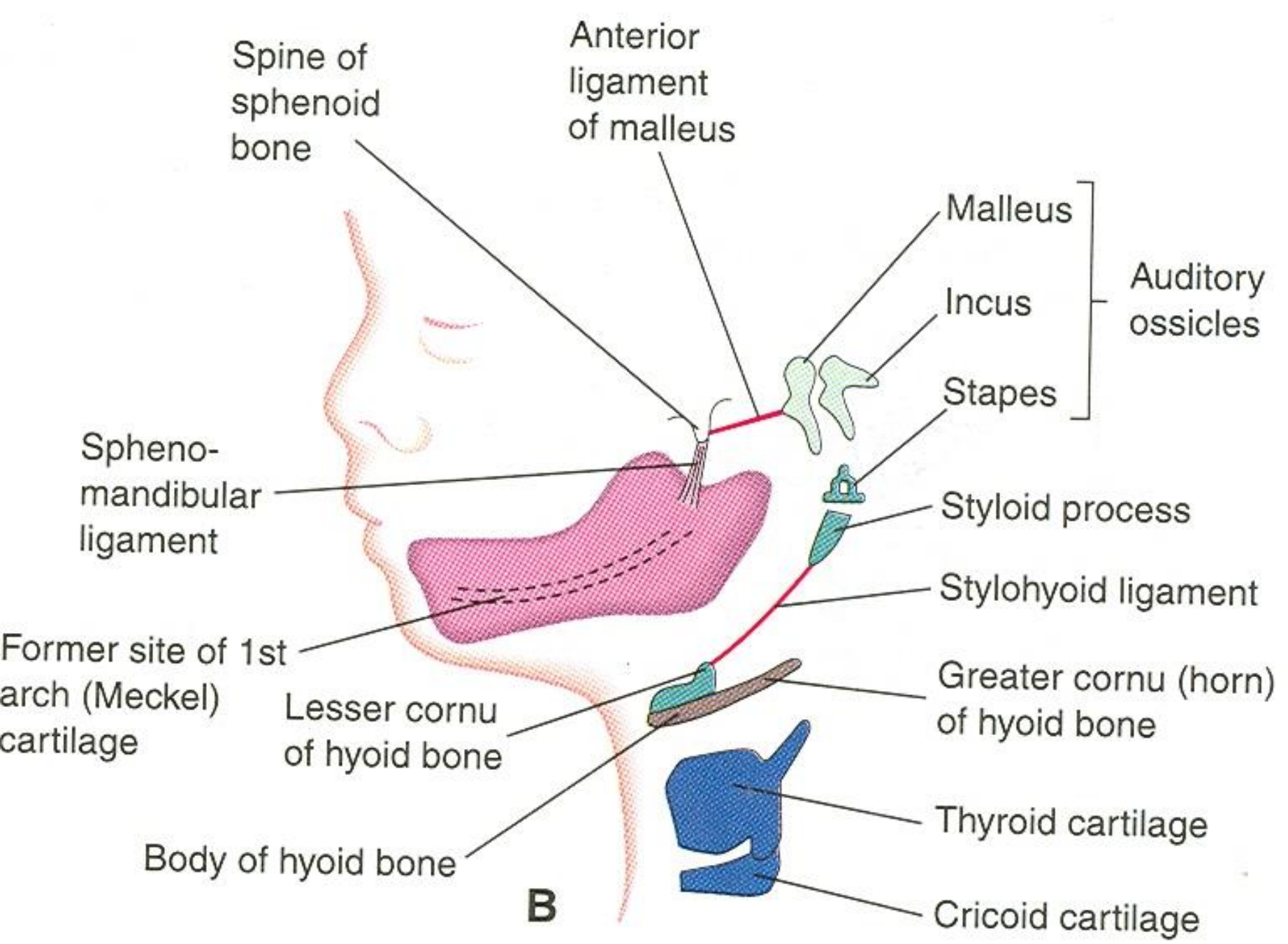
A typical pharyngeal arch contains:

- An aortic arch, an artery that arises from the truncus arteriosus of the primordial heart
- A cartilaginous rod that forms the skeleton of the arch
- A muscular component that differentiates into muscles in the head and neck
- A nerve that supplies the mucosa and muscles derived from the arch


1st pharyngeal pouch
Midbrain
Aortic arches
(1st to 4th)
Esophagus
Level of
section C
Lung bud
Dorsal aorta
B
Esophagus
Thyroid diverticulum
(primordium of thyroid gland)
Heart
Truncus arteriosus (common
arterial trunk from heart)

Derivatives of Pharyngeal Arch Cartilages: 1st arch

- The dorsal end of first arch cartilage (Meckel cartilage) ossifies to form malleus and incus
- The middle part of cartilage forms anterior ligament of malleus and sphenomandibular ligament
- Ventral part of the first arch cartilages form primordium of the mandible
- The cartilage disappears as mandible develops around it

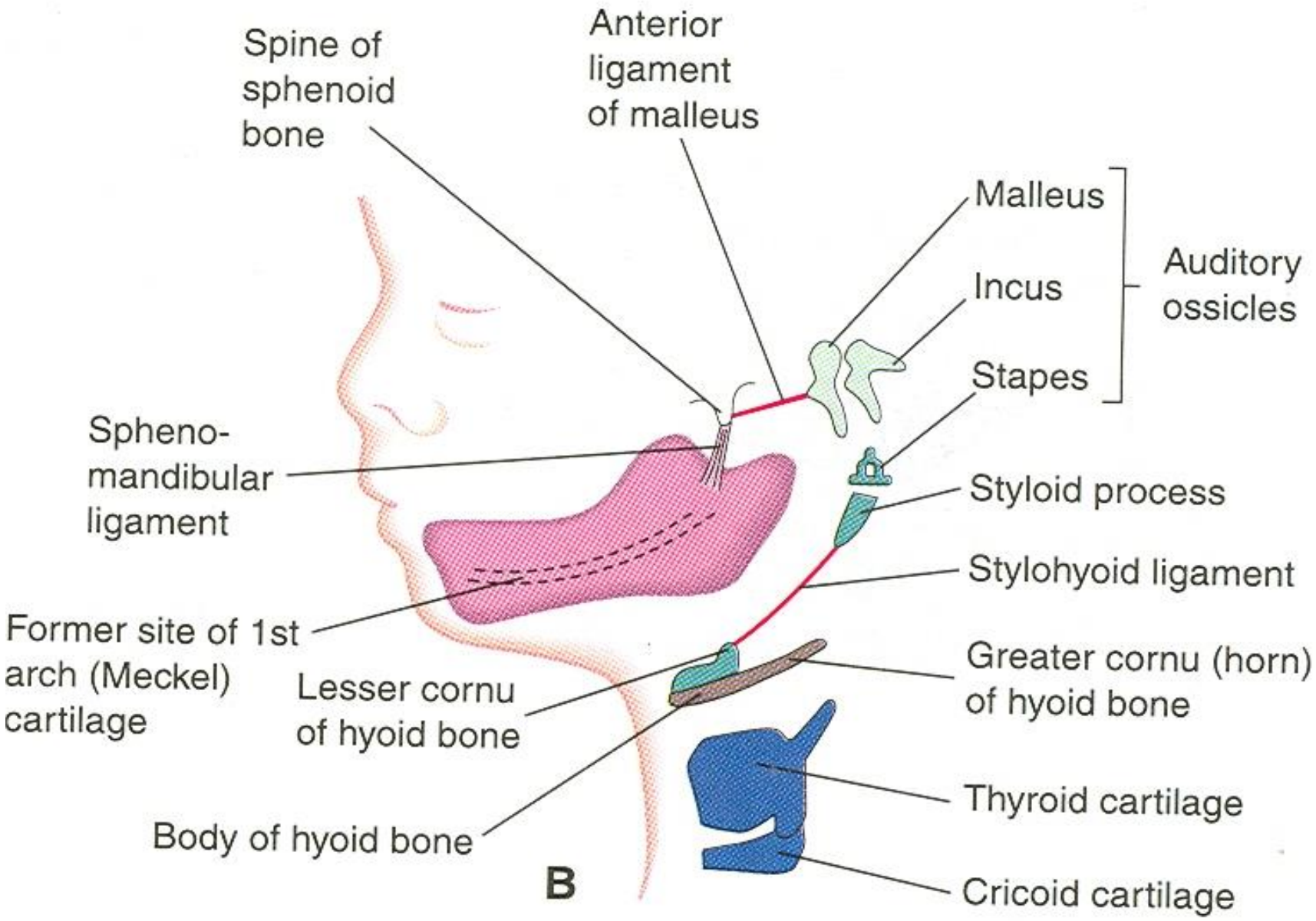

Spine of sphenoid bone
Anterior ligament of malleus
Malleus
Incus
Stapes
Auditory ossicles
Spheno-mandibular ligament
Styloid process
Stylohyoid ligament
Former site of 1st arch (Meckel) cartilage
Lesser cornu of hyoid bone
Greater cornu (horn) of hyoid bone
Thyroid cartilage
Body of hyoid bone
Cricoid cartilage
B

Derivatives of Pharyngeal Arch Cartilages: 2nd arch

- The dorsal end of second arch cartilage (Reichert cartilage) ossifies to form:
  - the stapes (ossicle) and
  - styloid process of the temporal bone
- The ventral end of second arch cartilage ossifies to form the:
  - lesser cornu and
  - superior part of the body of the hyoid bone
- Its perichondrium forms the stylohyoid ligament
- Patterning of the second pharyngeal arch is strongly influenced by the homeobox gene Hoxa2

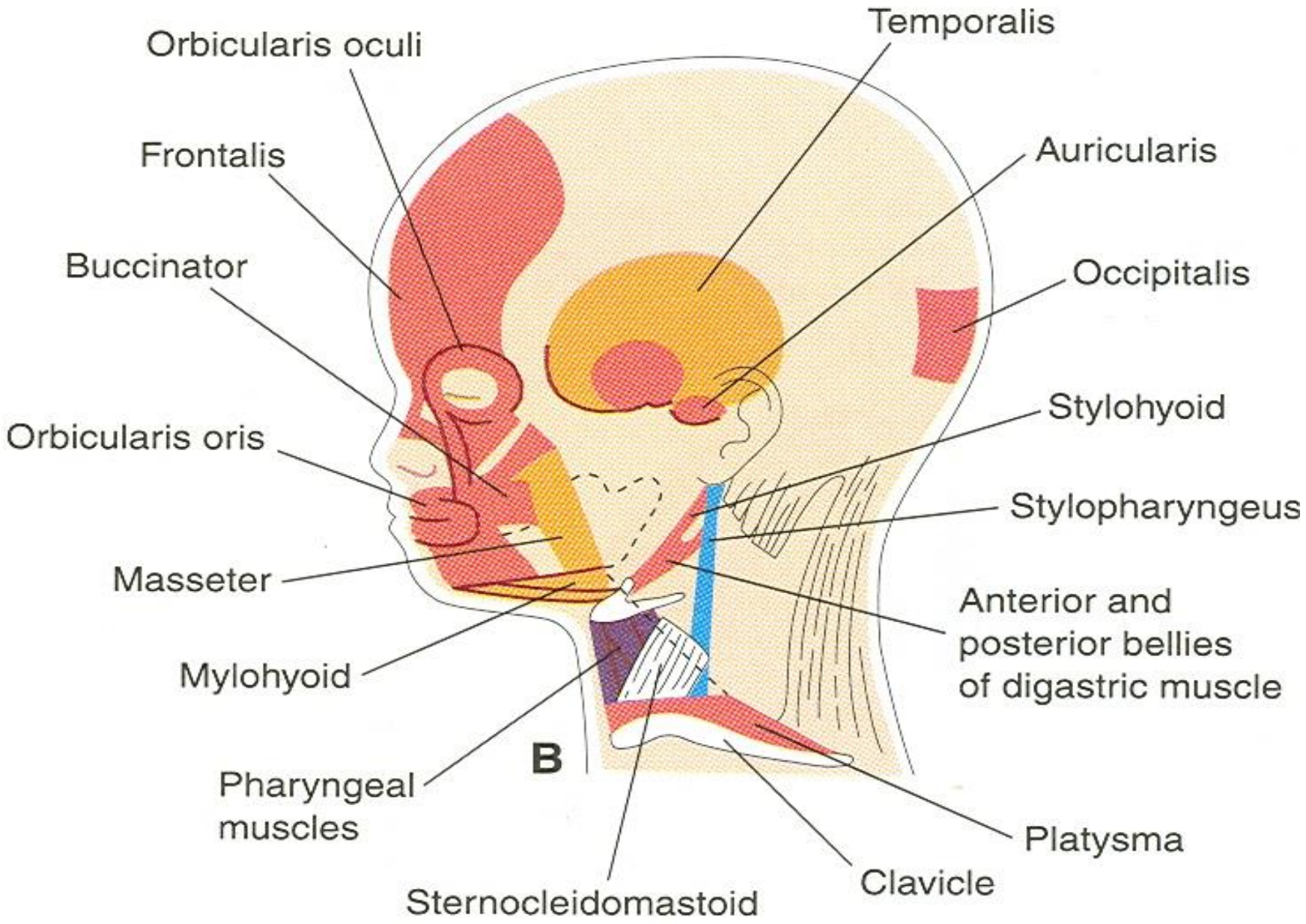
Derivatives of Pharyngeal Arch Cartilages: 3rd arch and others

- The 3rd arch cartilage ossifies to form:
  - the greater cornu and
  - the inferior part of the body of the hyoid bone
- The 4th and 6th arch cartilages fuse to form:
  - the laryngeal cartilages except
  - epiglottis which develops from hypopharyngeal eminence
- The 5th pharyngeal arch is rudimentary and has no derivatives


Spine of sphenoid bone
Anterior ligament of malleus
Malleus
Incus
Stapes
Auditory ossicles
Spheno-mandibular ligament
Styloid process
Stylohyoid ligament
Former site of 1st arch (Meckel) cartilage
Lesser cornu of hyoid bone
Greater cornu (horn) of hyoid bone
Thyroid cartilage
Body of hyoid bone
Cricoid cartilage
B

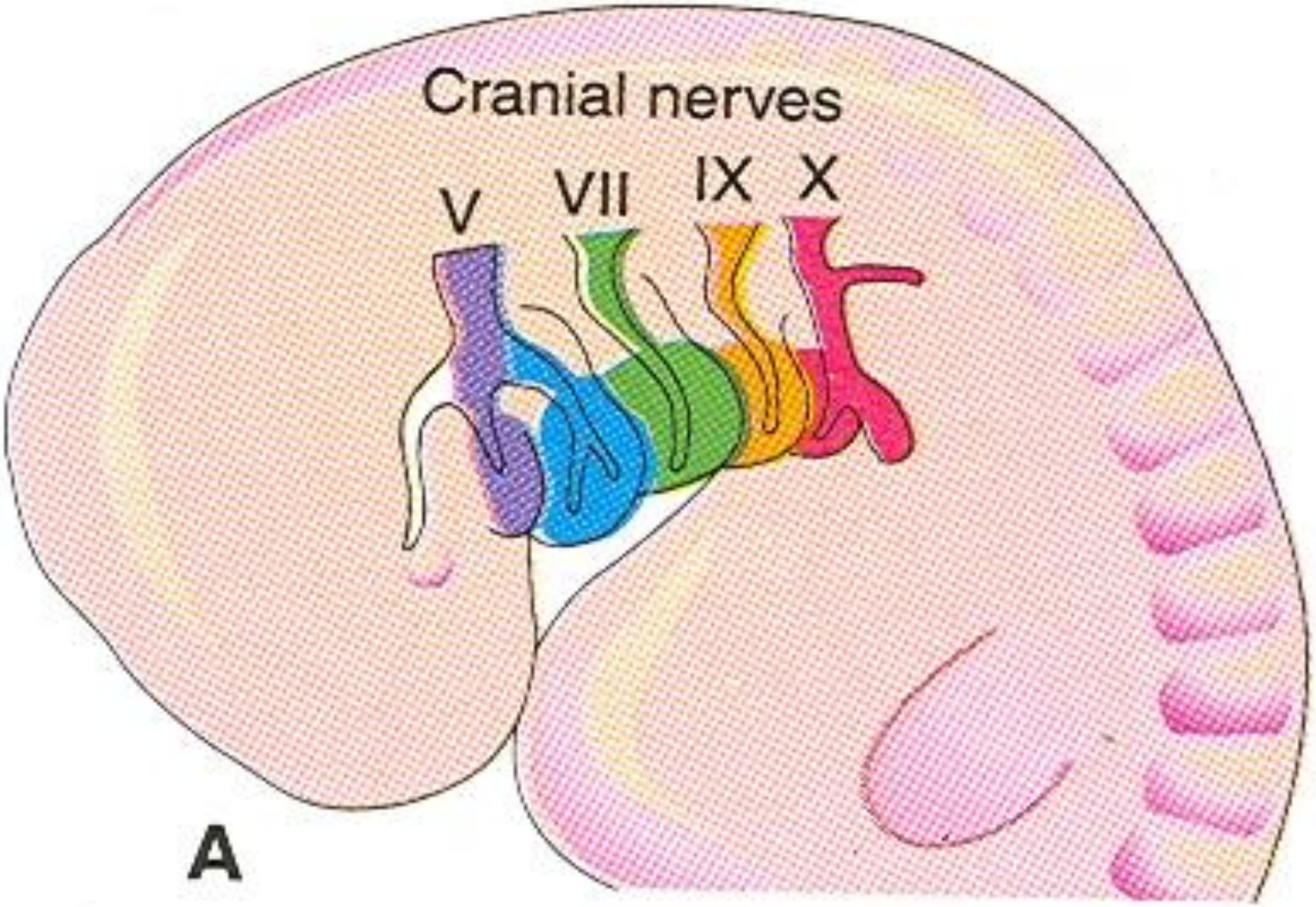
Derivatives of Pharyngeal Arch: Muscles

- The musculature of the first pharyngeal arch forms the muscles of mastication
- The 2nd pharyngeal arch forms the stapedius, stylohyoid, posterior belly of digastric, auricular and muscles of facial expression
- The 3rd arch forms the stylopharyngeus
- The 4th arch forms cricothyroid, levator veli palatini and constrictors of pharynx
- 6th pharyngeal arch forms the intrinsic muscles of the larynx


Orbicularis oculi
Temporalis
Frontalis
Auricularis
Buccinator
Occipitalis
Stylohyoid
Orbicularis oris
Stylopharyngeus
Masseter
Anterior and
posterior bellies
of digastric muscle
Mylohyoid
B
Pharyngeal
muscles
Platysma
Clavicle
Sternocleidomastoid

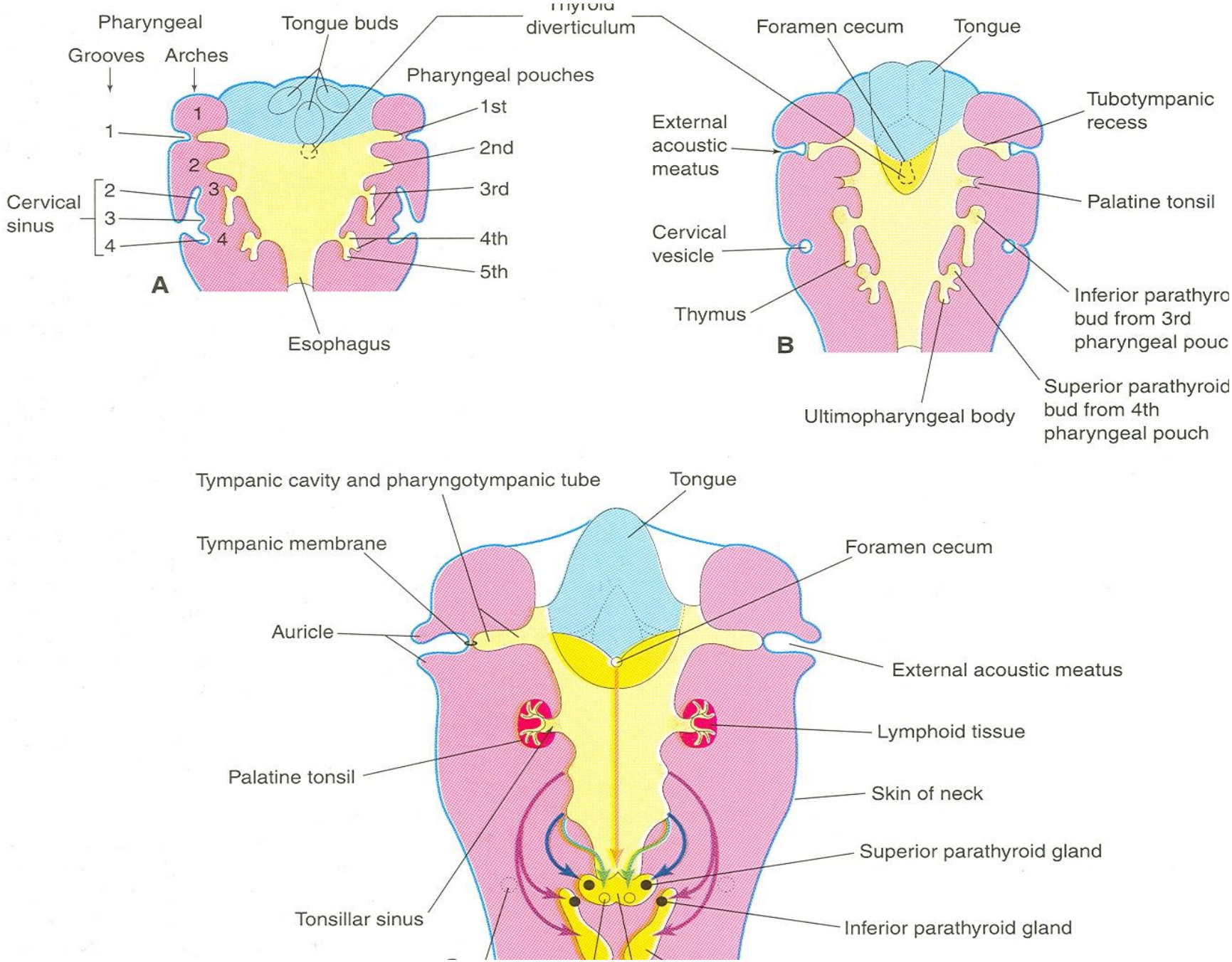
Derivatives of Pharyngeal Arch Nerves

- Caudal two branches of Trigeminal nerve (maxillary and mandibular) supply derivatives of the first pharyngeal arch
- The facial - second, glossopharyngeal - third and vagus nerves supply fourth to sixth arches
- The fourth arch is supplied by superior laryngeal branch of vagus nerve
- The sixth arch is supplied by its recurrent laryngeal branch


Cranial nerves
V
VII
IX
X
A

Pharyngeal Pouches 1

- The primordial pharynx, derived from the foregut, widens cranially where it joins the primordial mouth or stomodeum
- It narrows caudally where it joins the esophagus
- The endoderm of the pharynx lines the internal aspects of pharyngeal arches and passes into balloonlike diverticula called pharyngeal pouches


Pharyngeal
Grooves
Arches
Tongue buds
Thyroid diverticulum
Pharyngeal pouches
1st
2nd
3rd
4th
5th
1
2
3
4
Cervical sinus
A
Esophagus
Foramen cecum
Tongue
Tubotympanic recess
External acoustic meatus
Palatine tonsil
Cervical vesicle
Thymus
Inferior parathyro bud from 3rd pharyngeal pouc
Superior parathyroid bud from 4th pharyngeal pouch
Ultimopharyngeal body
B
Tympanic cavity and pharyngotympanic tube
Tongue
Tympanic membrane
Foramen cecum
Auricle
External acoustic meatus
Lymphoid tissue
Palatine tonsil
Skin of neck
Superior parathyroid gland
Tonsillar sinus
Inferior parathyroid gland

Pharyngeal Pouches 2

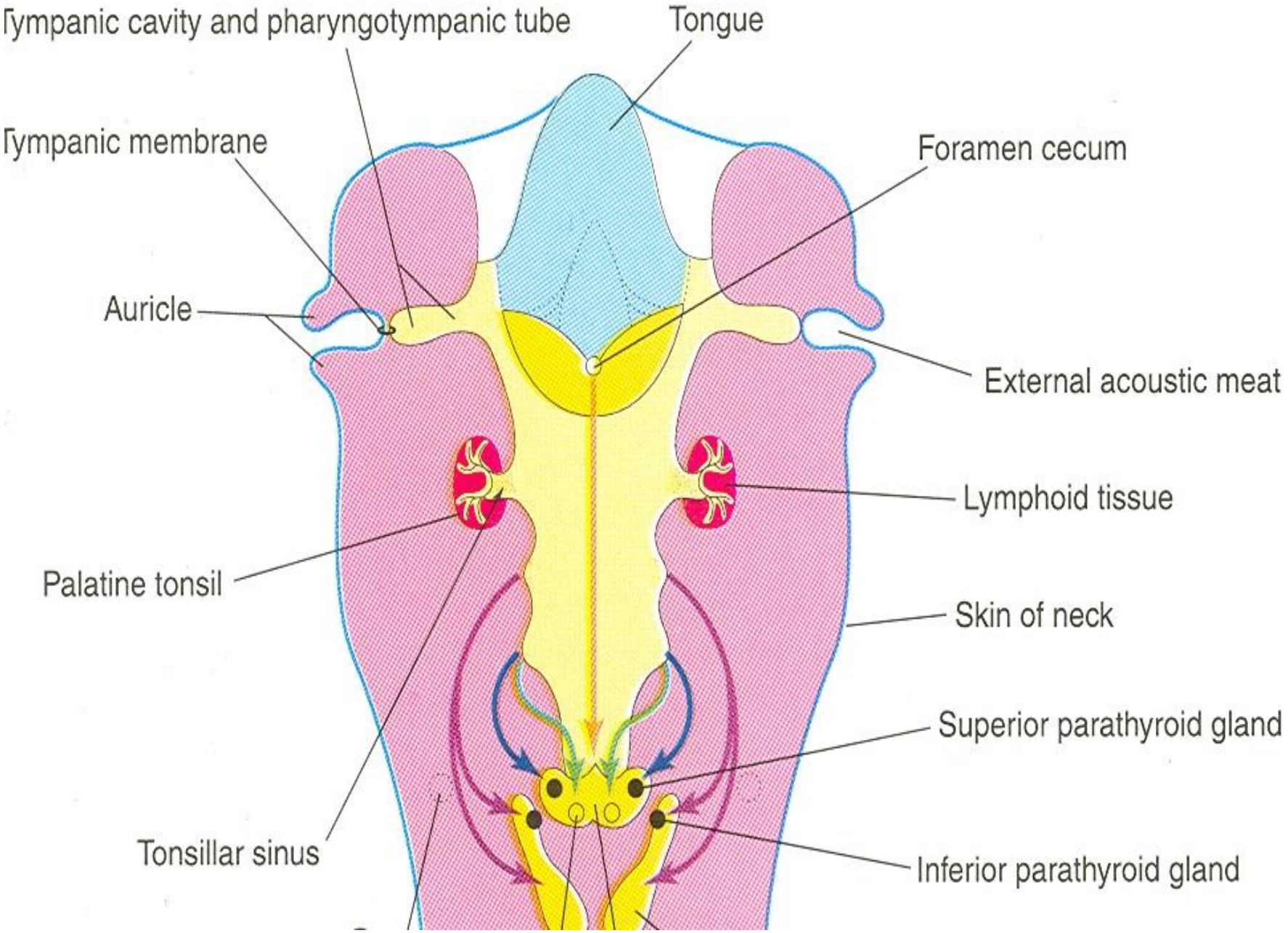
- The pairs of pouches develop in a craniocaudal sequence between the arches
- The first pair of pouches lies between the first and second pharyngeal arches
- There are four well defined pairs of pharyngeal pouches
- The fifth pair is absent or rudimentary

Pharyngeal Pouches 3

- The endoderm of the pouches contacts the ectoderm of the pharyngeal grooves and together they form the double layered pharyngeal membranes that separate the pharyngeal pouches from the pharyngeal grooves

Derivatives of First Pharyngeal Pouch

- The first pharyngeal pouch expands into an elongate tubotympanic recess
- The expanded distal part of this recess contacts the first pharyngeal groove, where it contributes to the formation of the tympanic membrane (eardrum)
- The cavity of the tubotympanic recess gives rise to the tympanic cavity and mastoid antrum

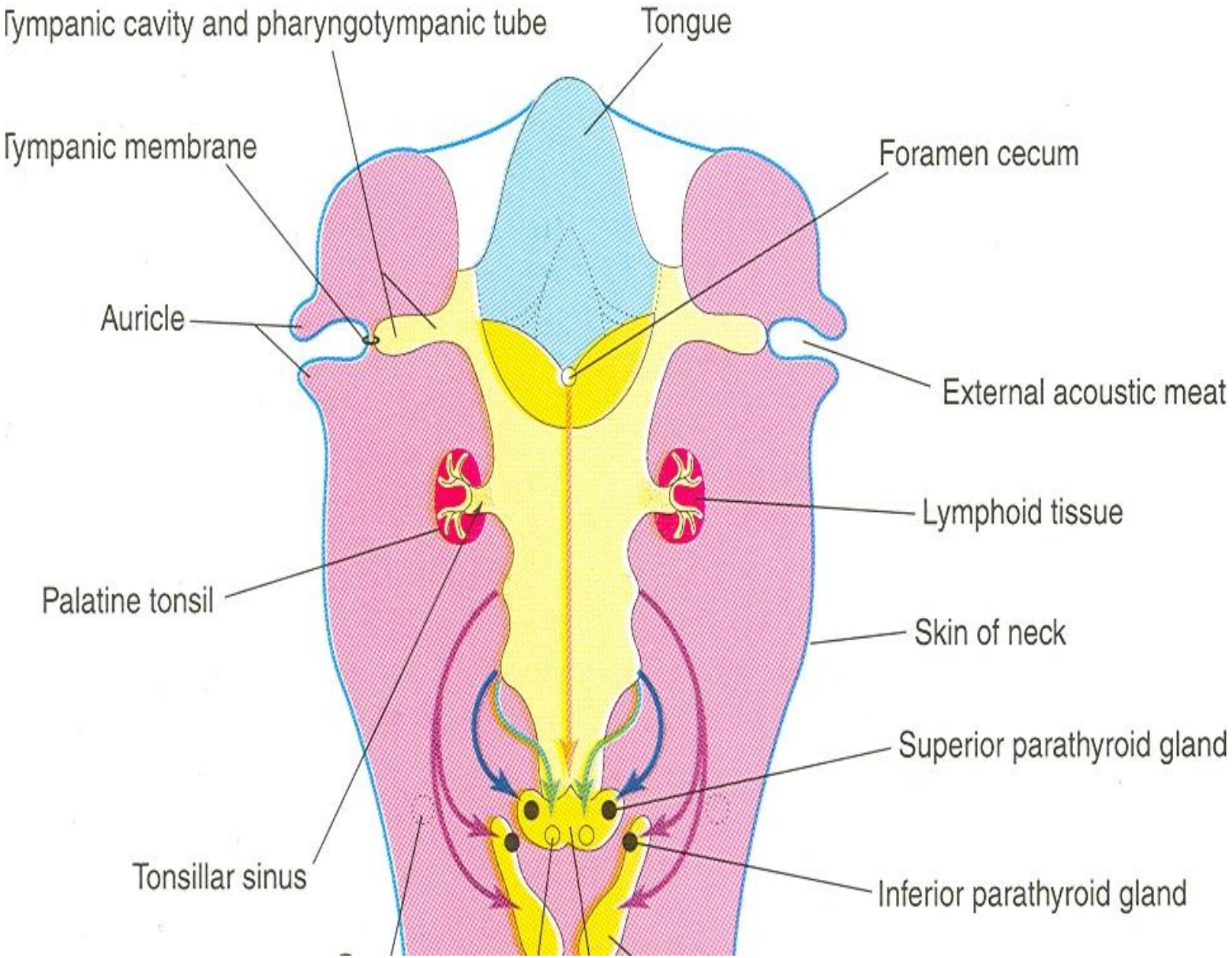

Tympanic cavity and pharyngotympanic tube
Tongue
Tympanic membrane
Foramen cecum
Auricle
External acoustic meat
Lymphoid tissue
Palatine tonsil
Skin of neck
Superior parathyroid gland
Tonsillar sinus
Inferior parathyroid gland

Derivatives of Second Pharyngeal Pouch 1

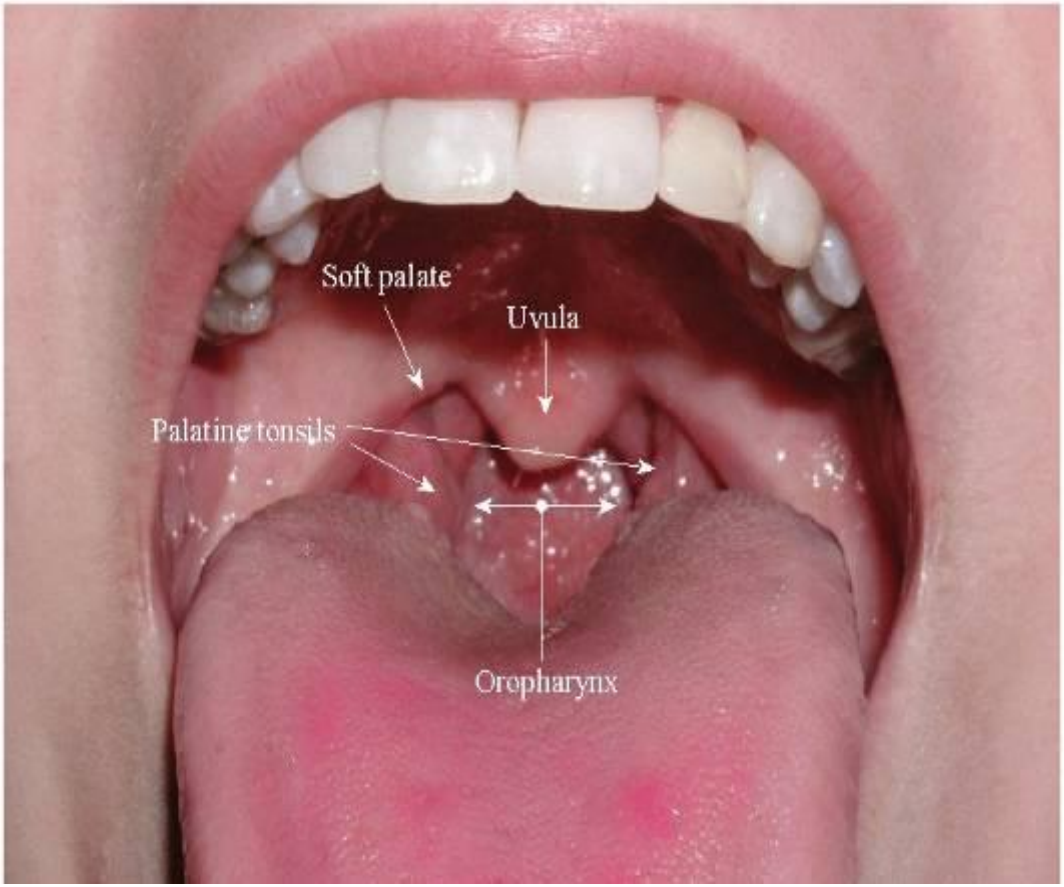
- The second pharyngeal pouch is largely obliterated as the palatine tonsils develop
- Part of the cavity of this pouch remains as the tonsillar sinus or fossa
- The endoderm of the pouch proliferates and grows into the underlying mesenchyme
- The central parts of these buds form crypts

Derivatives of Second Pharyngeal Pouch 2

- The pouch endoderm forms the surface epithelium and the lining of the tonsillar crypts
- At about 20 weeks the mesenchyme around the crypts differentiates into lymphoid tissue
- These tissues soon organize into the lymphatic nodules of the palatine tonsil


Tympanic cavity and pharyngotympanic tube
Tongue
Tympanic membrane
Foramen cecum
Auricle
External acoustic meat
Lymphoid tissue
Palatine tonsil
Skin of neck
Superior parathyroid gland
Tonsillar sinus
Inferior parathyroid gland

Second pharyngeal pouch



Derivatives of Third Pharyngeal Pouch 1

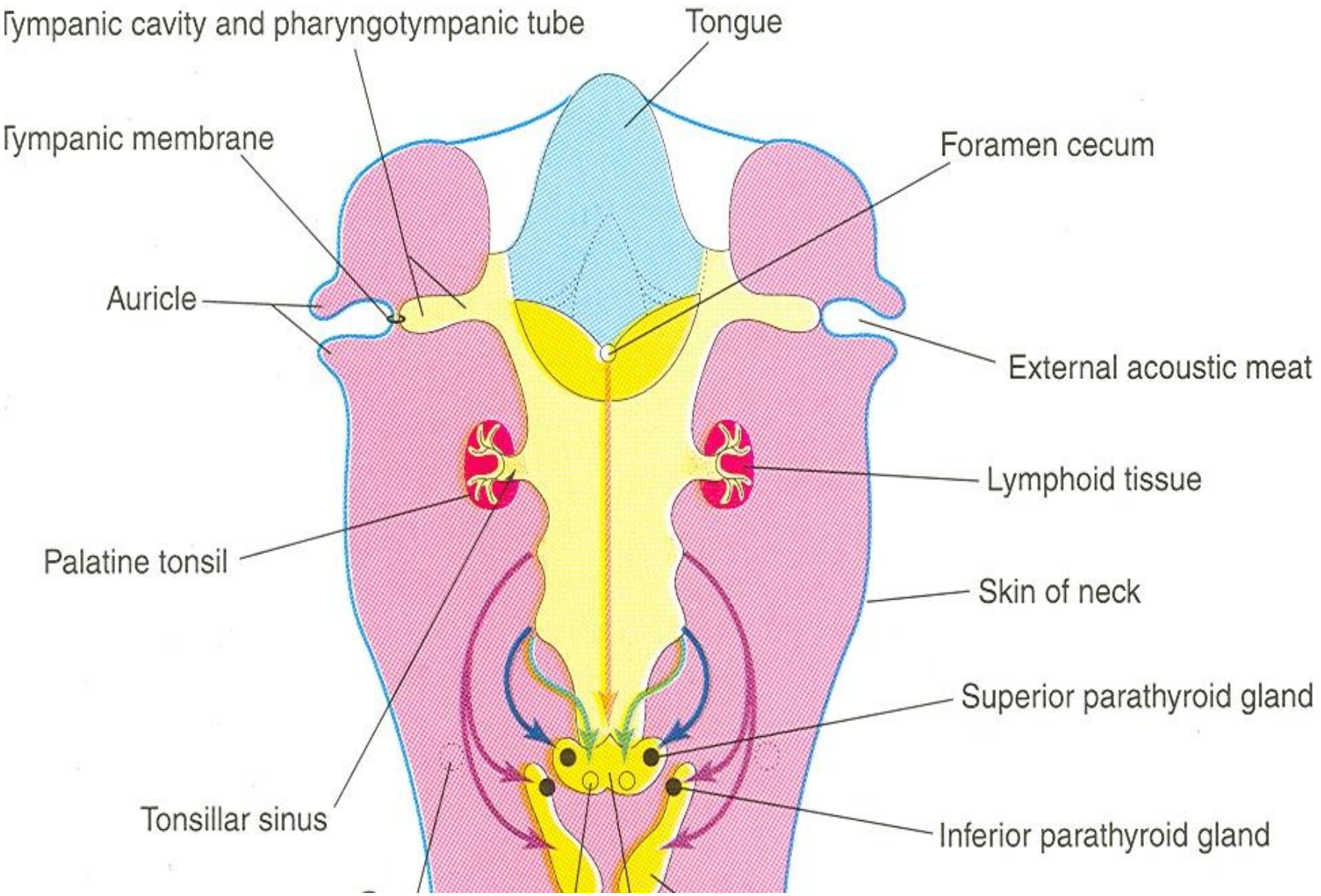
- The third pharyngeal pouch expands and develops a solid, dorsal bulbar part and a hollow elongate ventral part
- Its connection with the pharynx is reduced to a narrow duct that soon degenerates
- By the 6^{th} week the epithelium of each dorsal bulbar part begins to differentiate into inferior parathyroid gland

Derivatives of Third Pharyngeal Pouch 2

- The epithelium of the elongate ventral parts of third pharyngeal pouch proliferates and their cavities obliterate
- These bilateral primordia of thymus come together in the median plane to form thymus
- It descends into the superior mediastenum
- The bilobed form of thymus remains throughout life
- Discretely encapsulated and each lobe has its own blood supply, lymphatic drainage and nerve supply

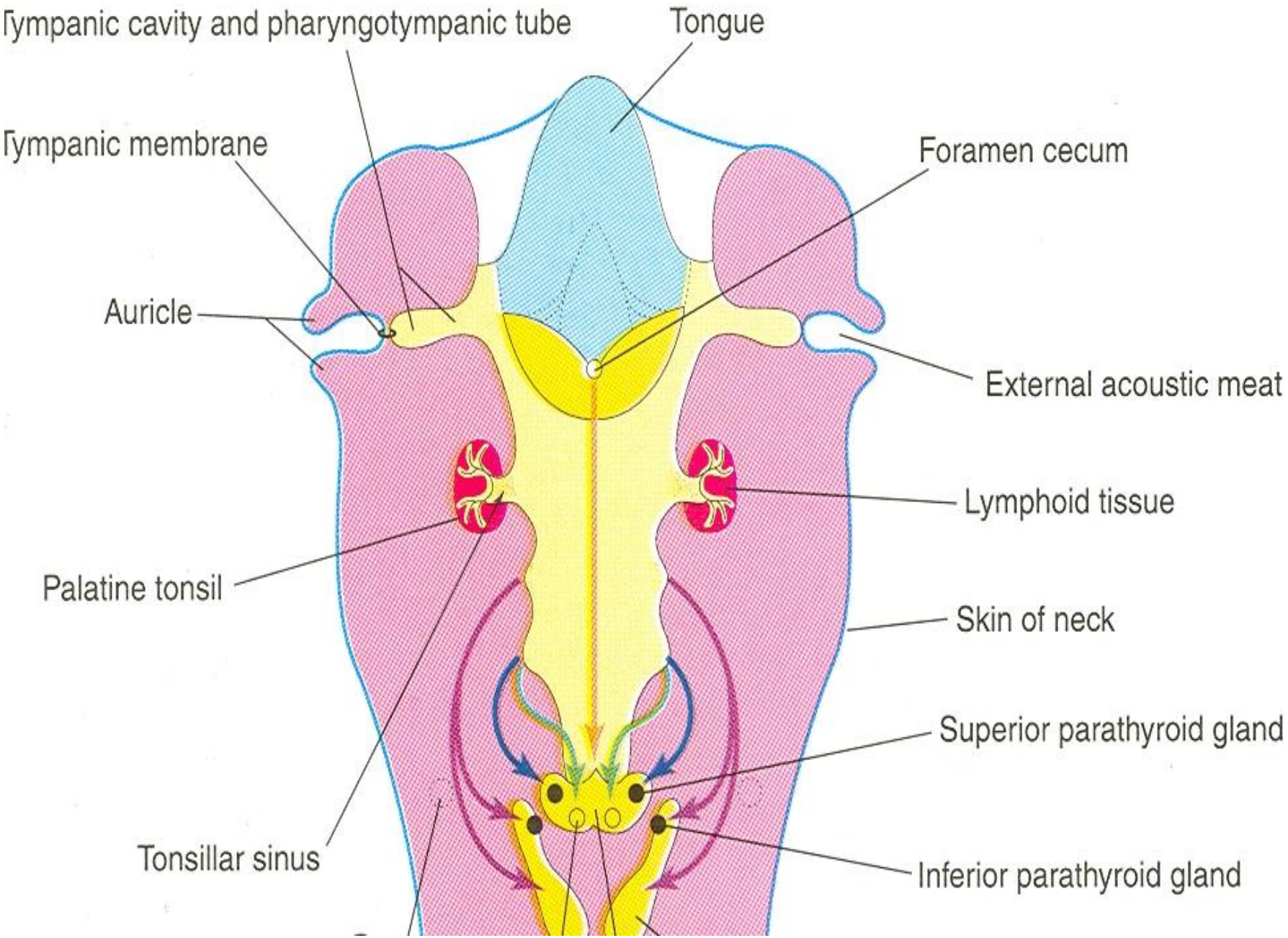
Derivatives of Third Pharyngeal Pouch 3

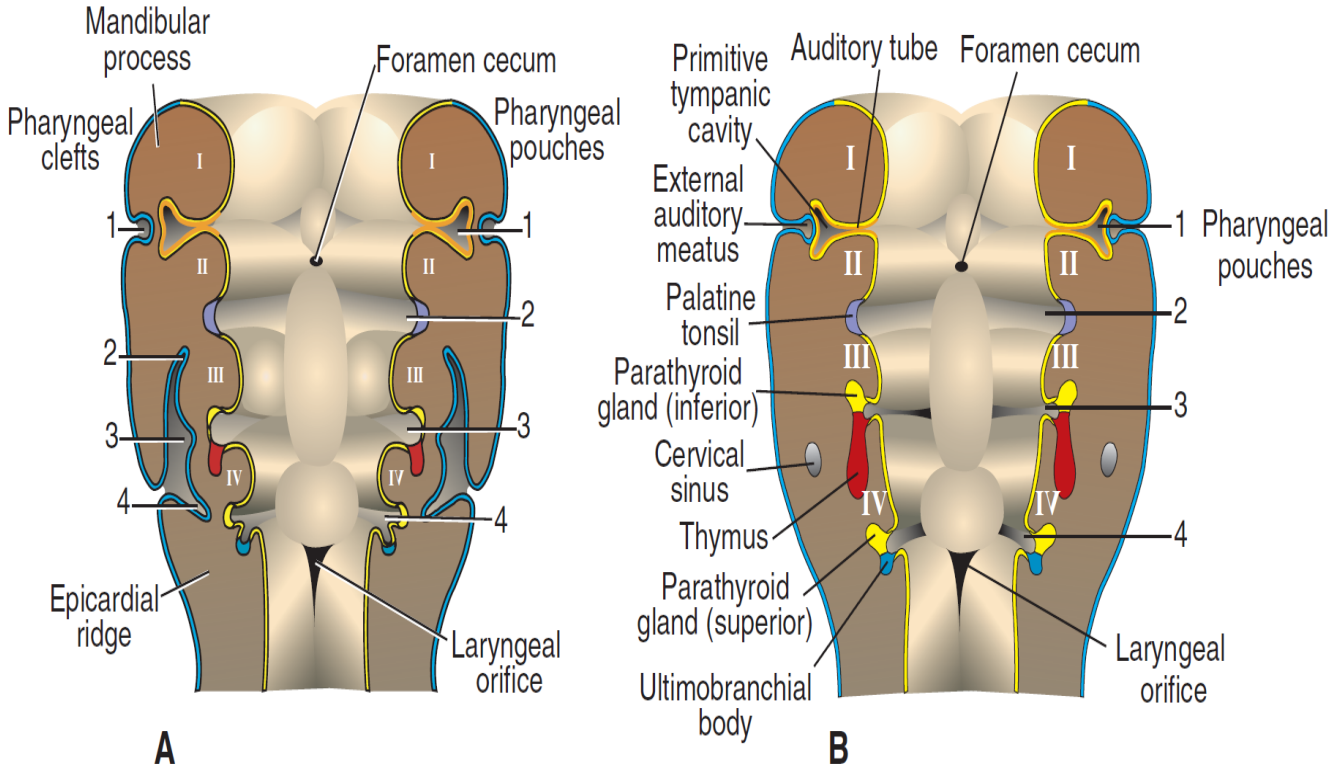
- The primordia of thymus and parathyroid glands lose their connections with the pharynx and migrate into the neck
- Later the parathyroid glands separate from the thymus and lie on the dorsal surface of the thyroid gland


Tympanic cavity and pharyngotympanic tube
Tongue
Tympanic membrane
Foramen cecum
Auricle
External acoustic meat
Lymphoid tissue
Palatine tonsil
Skin of neck
Superior parathyroid gland
Tonsillar sinus
Inferior parathyroid gland

Derivatives of Fourth Pharyngeal Pouch 1

- 4th pharyngeal pouch also expands into dorsal bulbar and elongate ventral parts
- Its connection with the pharynx is reduced to a narrow duct that soon degenerates
- By the 6th week, each dorsal part develops into a superior parathyroid gland
- It lies on the dorsal surface of the thyroid gland


Tympanic cavity and pharyngotympanic tube
Tongue
Tympanic membrane
Foramen cecum
Auricle
External acoustic meat
Lymphoid tissue
Palatine tonsil
Skin of neck
Superior parathyroid gland
Tonsillar sinus
Inferior parathyroid gland



Development of the pharyngeal clefts and pouches. The second arch grows over the third and fourth arches, burying the second, third, and fourth pharyngeal clefts. B. Remnants of the second, third, and fourth pharyngeal clefts form the cervical sinus, which is normally obliterated. Note the structures formed by the various pharyngeal pouches.

Derivatives of Fourth Pharyngeal Pouch 2

- The parathyroid glands derived from the third pouches descend with the thymus and are carried to a more inferior position than the parathyroid derived from the fourth pouches
- This explains why the parathyroid glands derived from the third pair of pouches are located inferior to those from the fourth pouches

Histogenesis of Parathyroid Gland

- The epithelium of the dorsal parts of the third and fourth pouches proliferates during the 5th week
- Forms small nodules on the dorsal aspect of each pouch
- Vascular mesenchyme soon grows into these nodules, forming capillary network
- The chief or principal cells differentiate during the embryonic period and regulate fetal calcium metabolism
- The oxiphil cells differentiate 5 to 7 years after birth

Histogenesis of Thyroid Gland

- The elongated ventral part of each fourth pouch develops into ultimopharyngeal body
- Its cells disseminate within the thyroid gland, giving rise to parafollicular cells
- They are also called “C” cells because they produce calcitonin that regulate normal calcium level in body fluids
- “C” cells differentiate from neural crest cells

The Fifth Pharyngeal Pouch

- When this develops, this rudimentary pouch becomes part of the fourth pharyngeal pouch and helps to form the ultimopharyngeal body

Pharyngeal Grooves

- These grooves separate the pharyngeal arches externally
- Only first pair persists as the external acoustic meatus
- The other grooves normally obliterated with the cervical sinus as the neck develops

Pharyngeal Membranes

- Pharyngeal membranes appear in the floor of the pharyngeal grooves
- These membranes form where the epithelia of the grooves and pouches approach each other
- The endoderm of the pouches and ectoderm of the grooves are soon separated by mesenchyme
- Only first pharyngeal membrane becomes the tympanic membrane, others obliterate

arch	nerve	muscles	skeletal structures	ligaments	arteries
1. mandibular (maxillary and mandibular process)	n. trigeminus	**muscles of mastication** (m. temporalis, m. masseter, m. pterygoideus medialis et lateralis) m. mylohyoideus, venter anterior m. digastrici m. tensor tympani m. tensor veli palatini	premaxilla, maxilla, os palatinum, os zygomaticum, squama ossis temporalis, Meckel´s cartilage, mandibula, malleus, incus	lig. mallei ant., lig. sphenomandibulare	a. maxillaris
2. hyoid	n. facialis	**muscles of facial expression** (m. buccinator, mm. auriculares, m. frontalis, platyzma, m. orbicularis oris et oculi) m. stapedius m. stylohyoideus, venter posterior m. digastrici	stapes, processus styloideus, cornua minora et corpus ossis hyoidis (upper part)	lig. stylohyoideum	a. stapedia
3. arch	n.glossopharyngeus	m. stylopharyngeus	cornua majora et corpus ossis hyoidis (lower part)		a. carotis communis a. carotis interna (proximal part of pars cervicalis)
4. left	n. laryngeus superior (n.X)	m. cricothyroideus, m. levator veli palatini, m. constrictor pharyngis med. et inf., intrinsic muscles of larynx striated muscles of the oesophagus	5th arch is missing cartilaginous parts of the 4th and 6th arch merge into a common base of the cartilages of the larynx cartilago thyroidea, cricoidea, arytenoidea, corniculata, cuneiformis		arcus ortae from a. carotis communis sin. to a. subclavia sin
right					prox. part of a.subclavia dx.
6. left	n. laryngeus recurrens (fibres from n. accessorius using n. vagus)				a.pulmonalis sin., ductus arteriosus
right					a.pulmonalis dx.

Derivatives of pharyngeal pouches

Pharyngeal Pouch	Derivatives
1	Tympanic (middle ear) cavity
	Auditory (eustachian) tube
2	Palatine tonsils
	Tonsillar fossa
3	Inferior parathyroid gland
	Thymus
4	Superior parathyroid gland ultimobranchial body (parafollicular [C] cells of the thyroid gland)

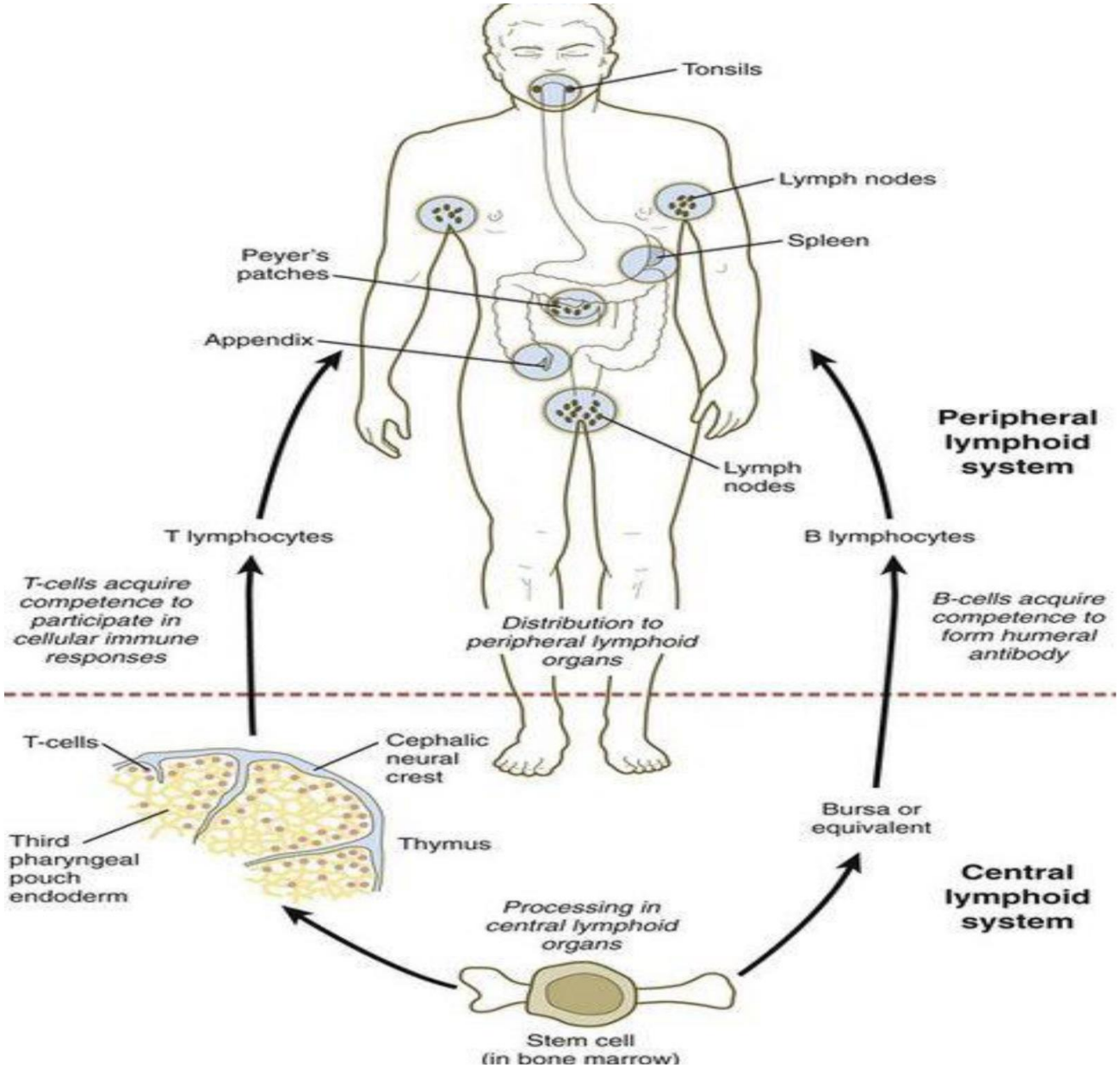
Thymus and Lymphoid Organs

- Paired endodermal thymic primordia begin to migrate from their third pharyngeal pouch origins during the 6th week.
- Their path of migration takes them through a substrate of mesenchymal cells until they reach the area of the future mediastinum behind the sternum.
- By the end of their migration, the two closely apposed thymic lobes are still epithelial structures.
- **Soon, however, they become invested with a capsule of neural crest–derived connective tissue, which also forms septa among the endodermal epithelial cords and contributes to the thymic vasculature.**
- In the absence of neural crest, the thymus fails to develop.
- An interaction between the neural crest and endodermal components of the thymic primordia conditions the latter for subsequent differentiation of thymic structure and function.

- At about 9 to 10 weeks' gestation, blood-borne thymocyte precursors (**prothymocytes**), which originate in the hematopoietic tissue, begin to invade the epithelial thymus, in response to the secretion of the **chemokine CC121** by the thymus.
- Just before the **prothymocytes** invade the thymus, the thymic epithelium begins to express the transcription factor **WHN**, which is necessary for colonization of the thymic epithelium by the prothymocytes.
- In homozygous *WHN* mutants, the absence of such colonization results in the absence of functional T cells, thus leaving the individual severely immunocompromised and unable to reject foreign cells and tissue.
- Within the thymus, the prothymocytes force apart the epithelial cells and cause them to form a spongy **epithelial reticulum**.
- Responding to signals from the thymic epithelium, the prothymocytes proliferate and become redistributed, forming the **cortical and medullary** regions of the thymus.

- By 14 to 15 weeks of gestation, blood vessels grow into the thymus, and a week later, some epithelial cells aggregate into small, spherical **Hassall's corpuscles**.
- Functionally, the action of various **thymic hormones** causes the thymus to condition or instruct the prothymocytes migrating into it to become competent members of the **T-lymphocyte** family.
- The T lymphocytes leave the thymus and populate other lymphoid organs (e.g., lymph nodes, spleen) as fully functional immune cells.
- The T lymphocytes are principally involved in **cellular immune responses**.
- Other population of lymphocytes from the bone marrow is instructed to become **B lymphocytes**, which are the mediators of **humoral immune responses**.

- B-lymphocyte precursors (**pro-B cells**) also must undergo conditioning to become fully functional, but their conditioning does not occur in the thymus.
- In birds, the pro-B cells pass through a cloacal lymphoid organ known as the **bursa of Fabricius**, where conditioning occurs.
- Humans do not possess a bursa, but its functional equivalent, although still undefined, is assumed to exist.
- B-lymphocyte conditioning is thought to occur in the bone marrow; in early embryos, conditioning possibly occurs in the liver.
- The thymus and the bursa or mammalian equivalent are commonly referred to as **central lymphoid organs**.
- The lymphoid structures that are seeded by B and T lymphocytes are called **peripheral lymphoid organs**.



Embryonic development of the lymphoid system

Derivatives of Pharyngeal Pouches

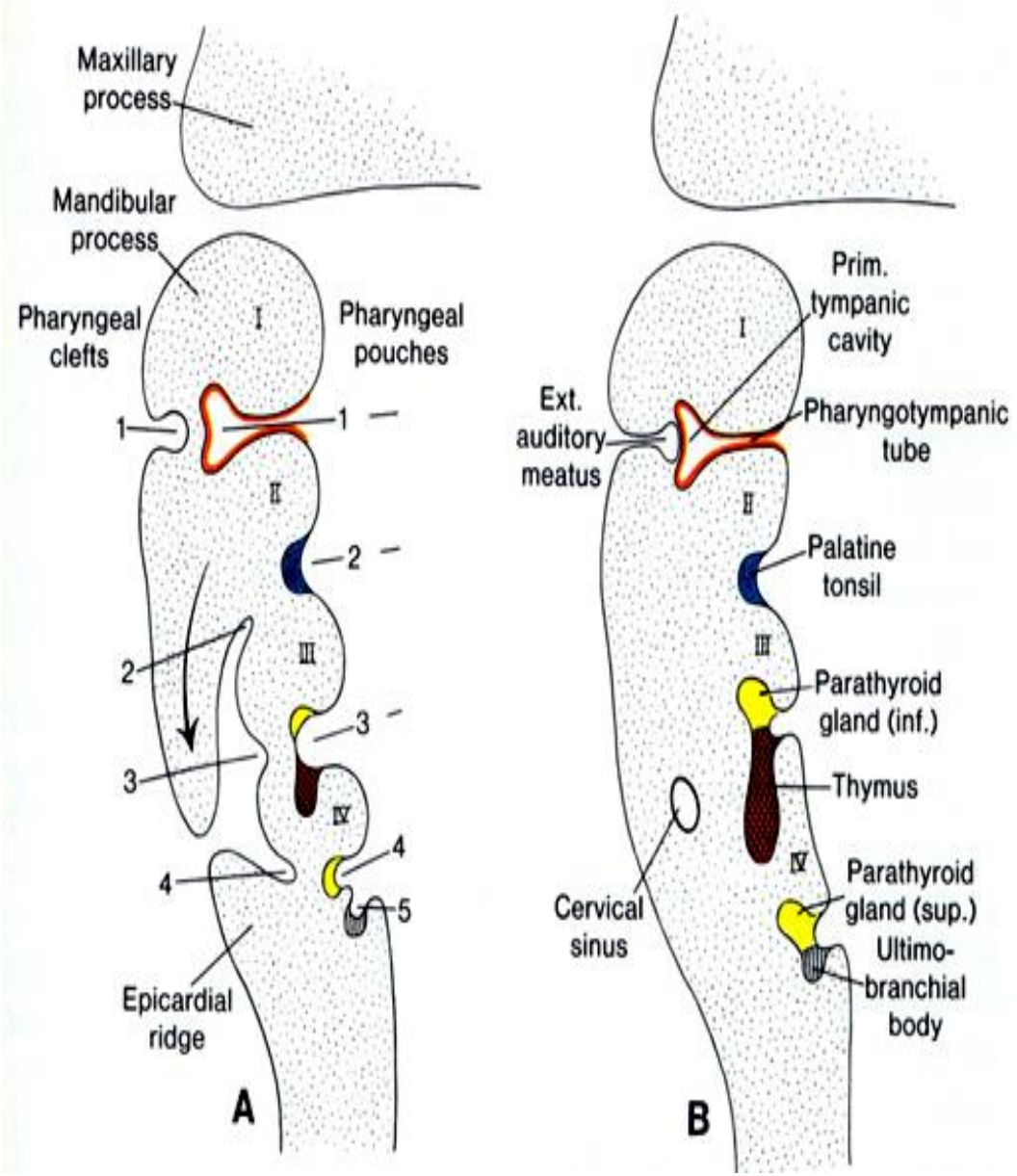
1st pouch

1) Lateral → tympanic cavity

Medial → pharyngotympanic tube

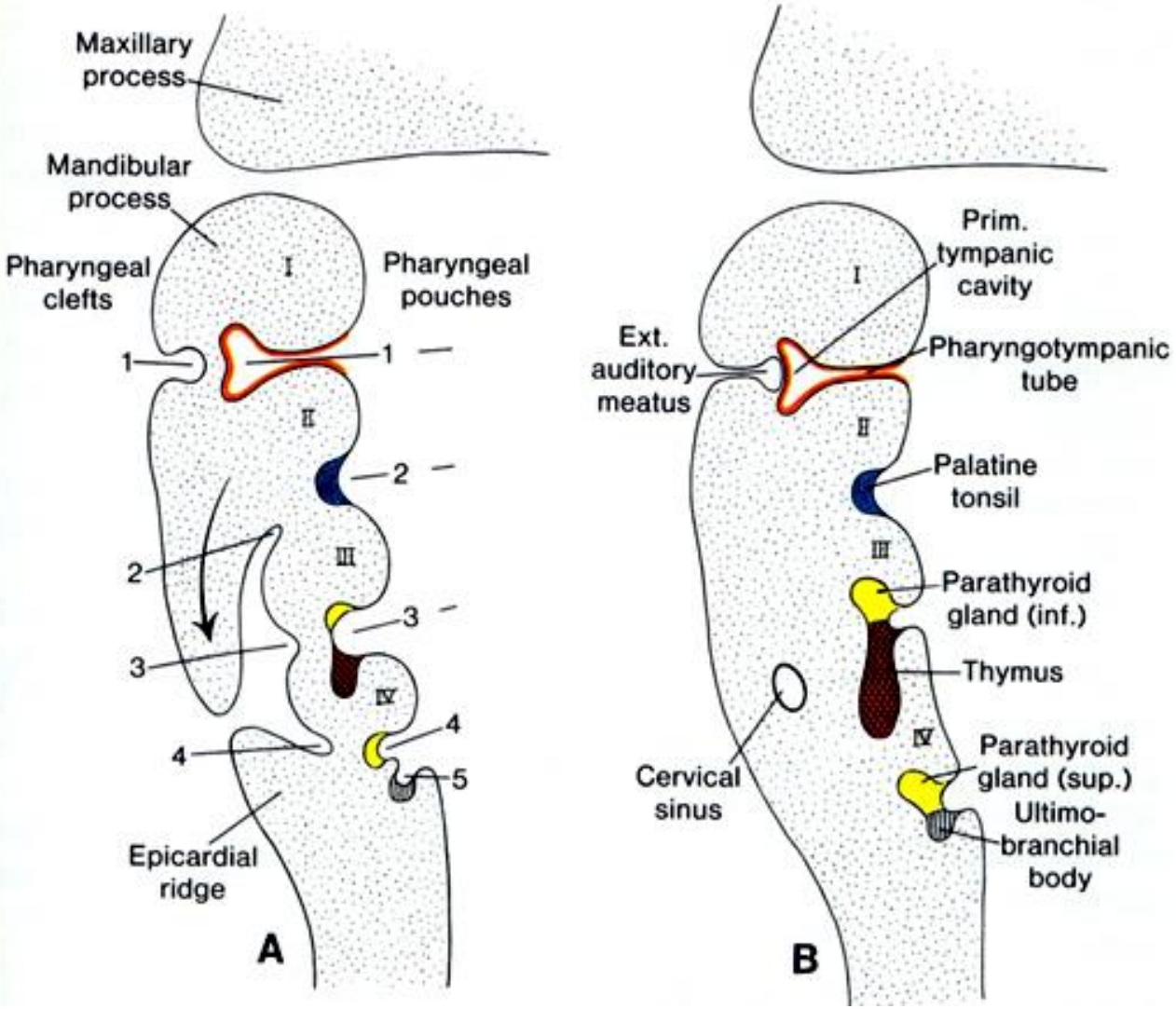
2) Branchial membrane → tympanic membrane

Branchial groove → external auditory meatus



2nd pouch

Medial → tonsillar fossa, surface epithelium of palatine tonsil; Lateral → degenerates



3rd pouch

Dorsal part → inferior parathyroids

Ventral part → thymus

Both migrate caudally.

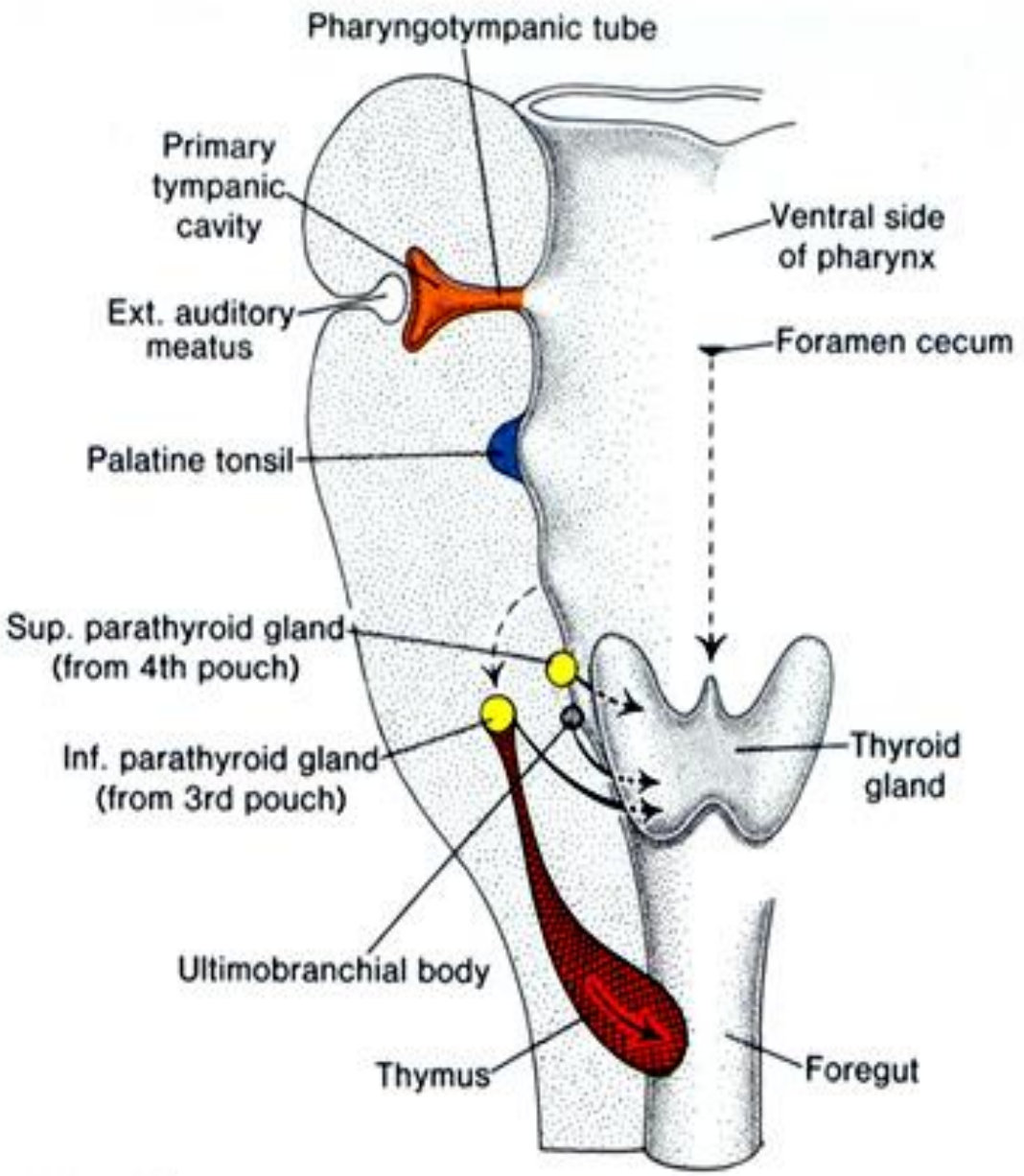
4th pouch

Dorsal → superior parathyroids

Ventral → degenerates

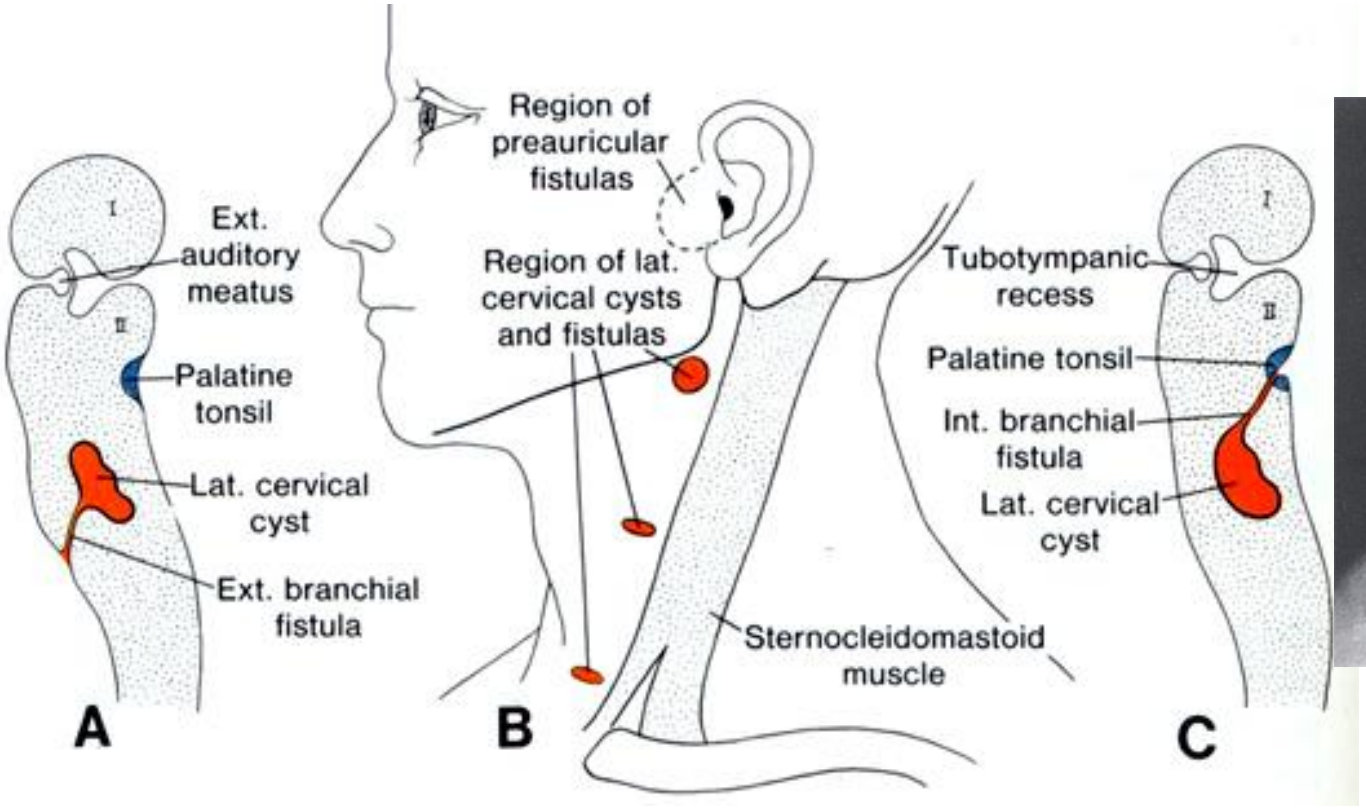
5th pouch → ultimobranchial body → (in thyroid)

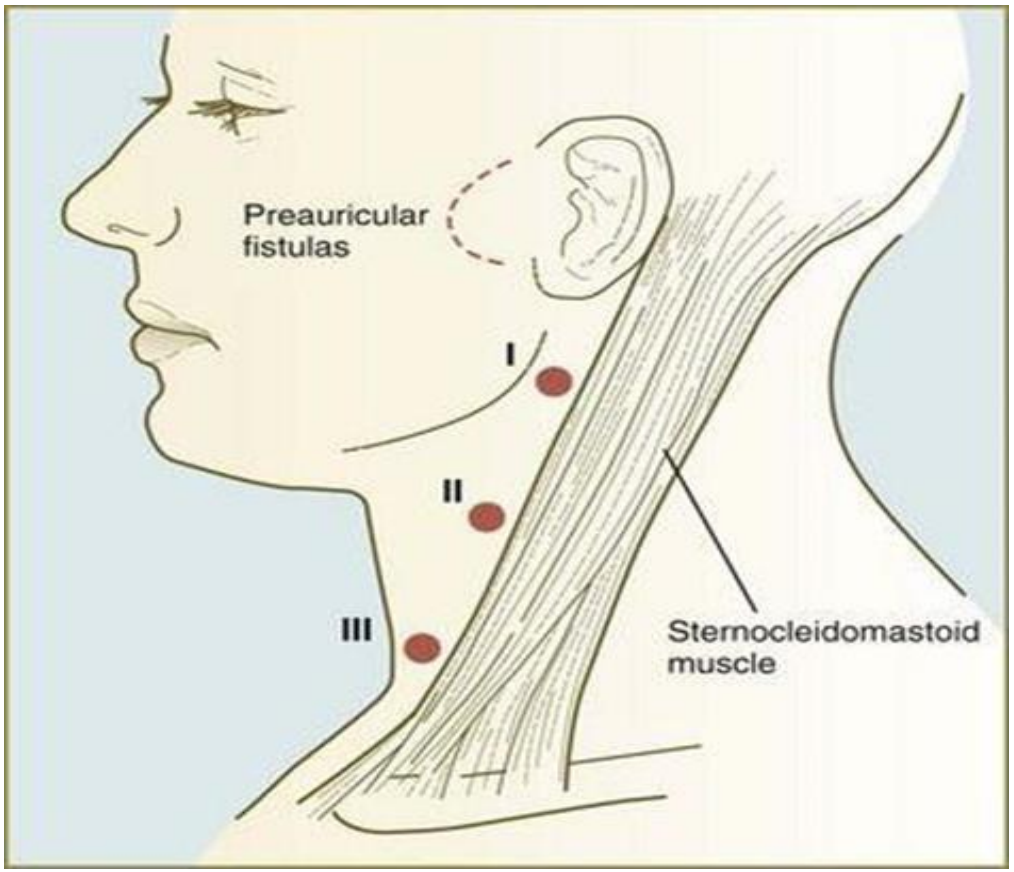
Neural crest cells → parafollicular cells



Cervical cyst and fistula

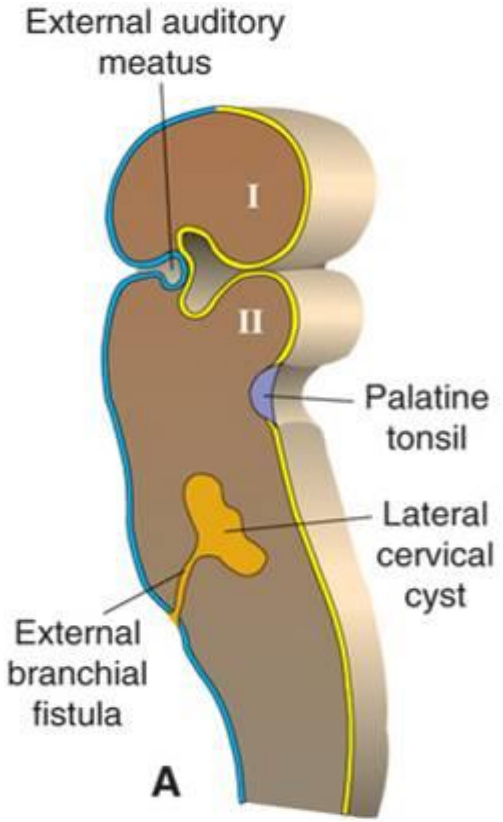
- Failure of closure of cervical sinus(cyst), may connect to surface or pharynx(fistula);
- Cyst on lateral side of neck along anterior border of sternocleidomastoid muscle.





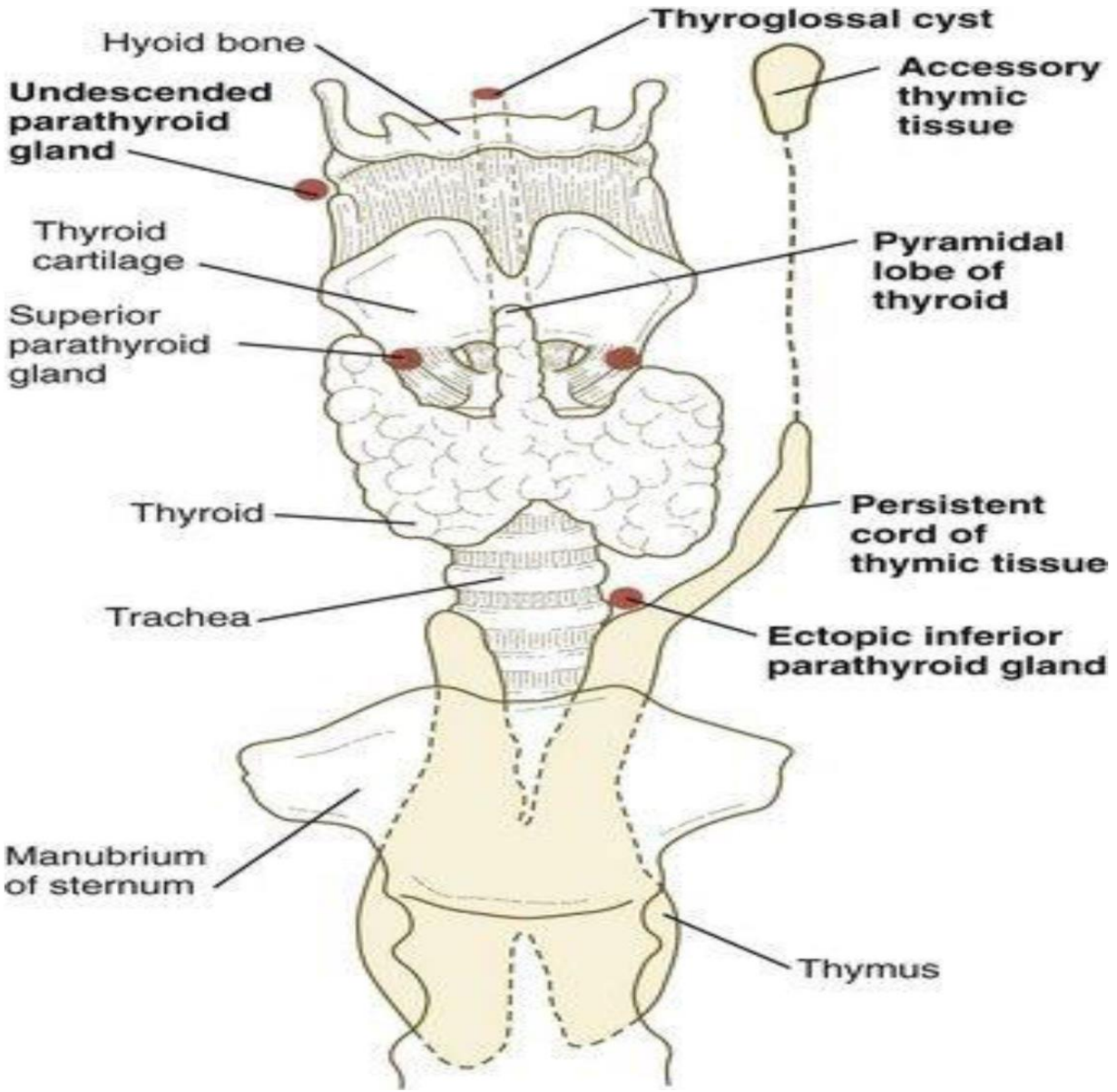
Common locations of lateral cervical (branchial) cysts and sinuses (red circles) and preauricular fistulas. Roman numerals refer to the cervical cleft origin of the cysts.

Lateral cervical fistula



8-4A Pharyngeal pouch defects: Cervical cysts and fistulas

Fig 1- Neck fistula in the right muscular space of the neck



Locations where abnormally positioned pharyngeal glands or portions of glands can be found.

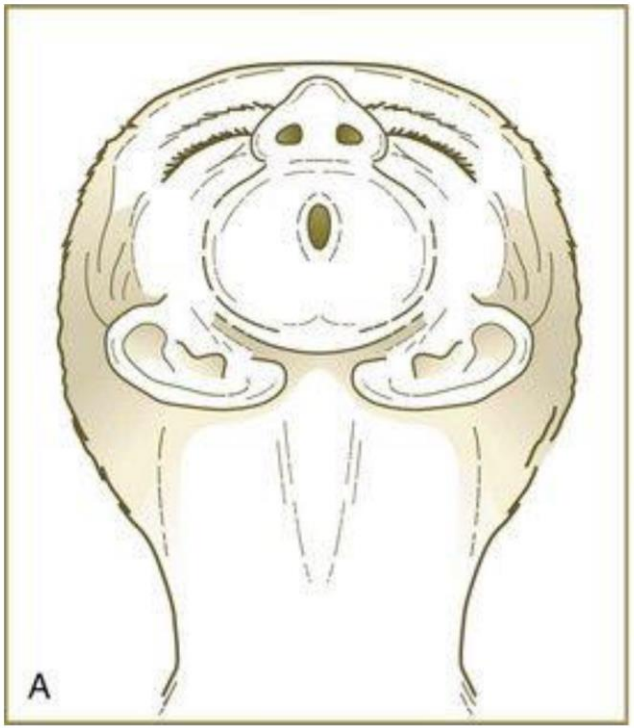
Syndromes Involving the First Pharyngeal Arch

- Several syndromes involve hypoplasia of the mandible and other structures arising from the first pharyngeal arch.
- Various mechanisms can account for these syndromes.
- Many have a genetic basis, and others result from exposure to environmental teratogens.
- With the fine balance of signaling molecules and transcription factors that are involved in the development of the pharyngeal arches, it is not surprising that disturbances in the function of single genes, whether through mutation or the action of teratogens, can result in a visible morphological anomaly.
- Hypoplasia of the lower face has been associated with the ingestion of isotretinoin (a vitamin A derivative used for the treatment of acne) during early pregnancy.

- **Pierre Robin syndrome** involves extreme **micrognathia** (small mandible), cleft palate, and associated defects of the ear.
  - An imbalance often exists between the size of the tongue and the very hypoplastic jaw, which can lead to respiratory distress caused by mechanical interference of the pharyngeal airway by the large tongue.
  - Although many cases of Pierre Robin syndrome are sporadic, others have a genetic basis.
- **Treacher Collins syndrome** (**mandibulofacial dysostosis**) is typically inherited as an autosomal dominant condition.
- The responsible gene, called *TCOF1*, has been identified.
- Operating through the **Treacle** protein, it affects the survival and proliferation of cranial neural crest cells.

- In mutations of this gene, neural crest cell migration is normal, but increased apoptosis and decreased proliferation result in a much reduced population of neural crest cells in the first pharyngeal arch.
- This syndrome includes various anomalies, not all of which are found in all patients.
- Common components of the syndrome include hypoplasia of the mandible and facial bones, malformations of the external and middle ears, high or cleft palate, faulty dentition, and coloboma-type defects of the lower eyelid.

- The most extreme form of first-arch hypoplasia is **agnathia**, in which the lower jaw basically fails to form.
- In severe agnathia, the external ears remain in the ventral cervical region and may join in the ventral midline.

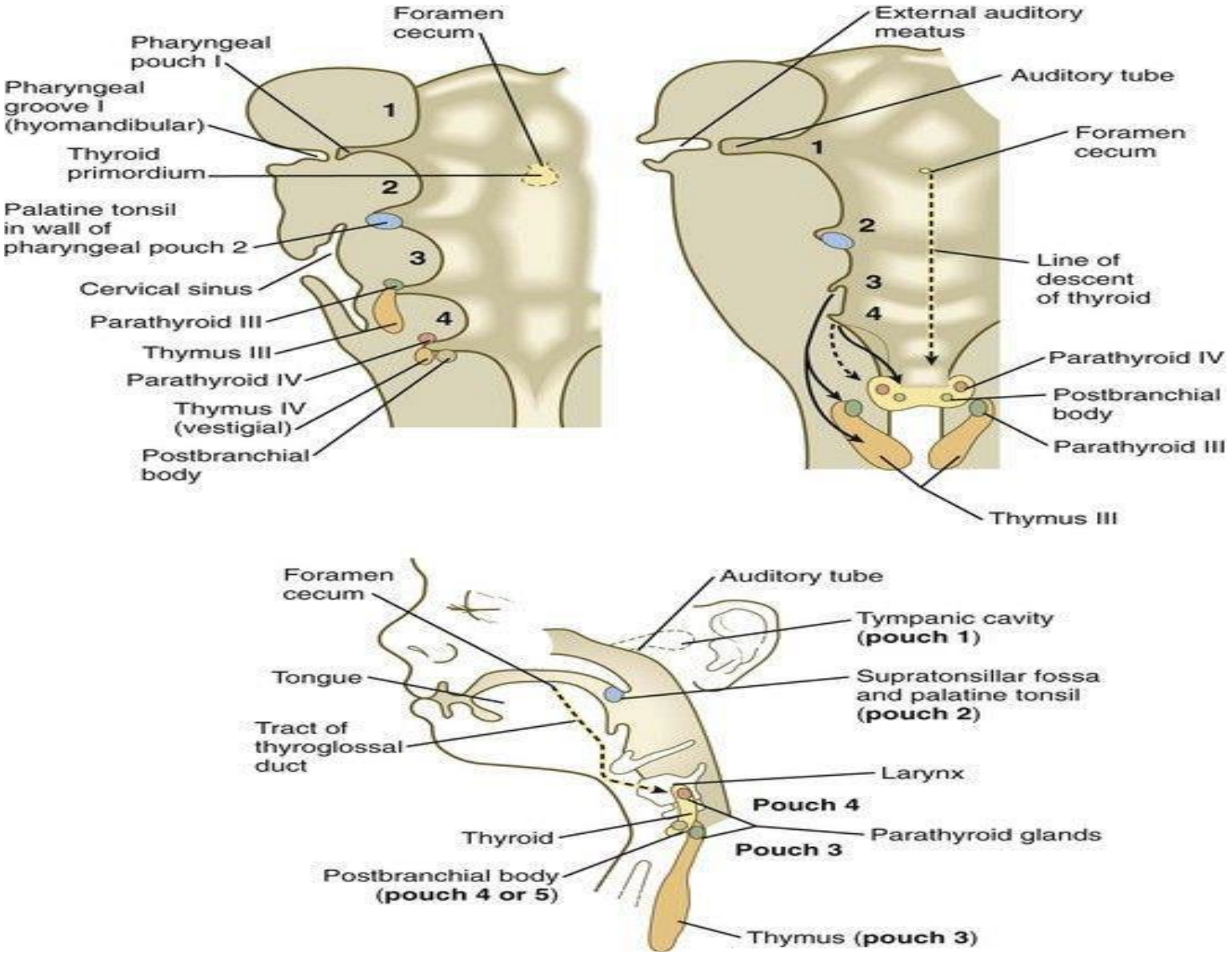


Development of the thyroid gland

- Development begins during the 4th week with local mesodermal inductive signals acting on the ventral endoderm of the foregut which results in specification of a small number of endodermal cells to be destined to a thyroid fate.
- These founder cells, the thyroid anlage, increase in number to form a thickened placode – thyroid bud that soon begins to extend into the surrounding mesodermal mesenchyme.
- The unpaired primordium - thyroid bud appears in the ventral midline of the pharynx between the first and second pouches just caudal to the median tongue bud (tuberculum impar).
- Thyroid bud becomes thyroid diverticulum.
- These cells are characterized by the expression of four transcription factors (Hhex, Nkx2-1, Pax-8, and Foxe-1), which operate together in a complex interacting pattern and all of which are required for further thyroid development.

- The pathway of caudal extension of the bilobed thyroid diverticulum is determined by the pattern of arteries in the neck and extension and continues during pharyngeal development.
- During its caudal migration, the tip of the thyroid diverticulum expands and bifurcates to form the thyroid gland itself, which consists of two main lobes connected by an isthmus.
- Progressive descent in front of hyoid bone and cartilages of larynx.
- For some time, the gland remains connected to its original site of origin by a narrow thyroglossal duct.
- By about the 7^{th} week, when the thyroid has reached its final location at the level of the second and third tracheal cartilages, the thyroglossal duct has largely regressed.

- In almost half the population, the distal portion of the thyroglossal duct persists as the pyramidal lobe of the thyroid.
- The original site of the thyroid primordium persists as the foramen cecum, a small blind pit at the base of the tongue.
- The thyroid gland undergoes histodifferentiation and begins functioning early in embryonic development.
- By 10 weeks of gestation, follicles containing some colloid material are evident, and a few weeks thereafter, the gland begins to synthesize noniodinated thyroglobulin.
- Secretion of triiodothyronine, one of the forms of thyroid hormone, is detectable by late in the fourth month.

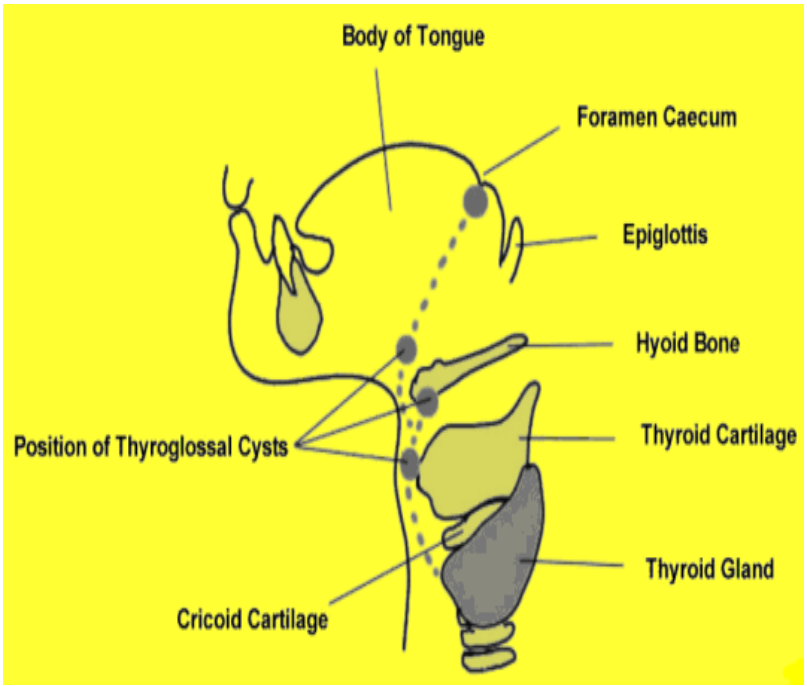


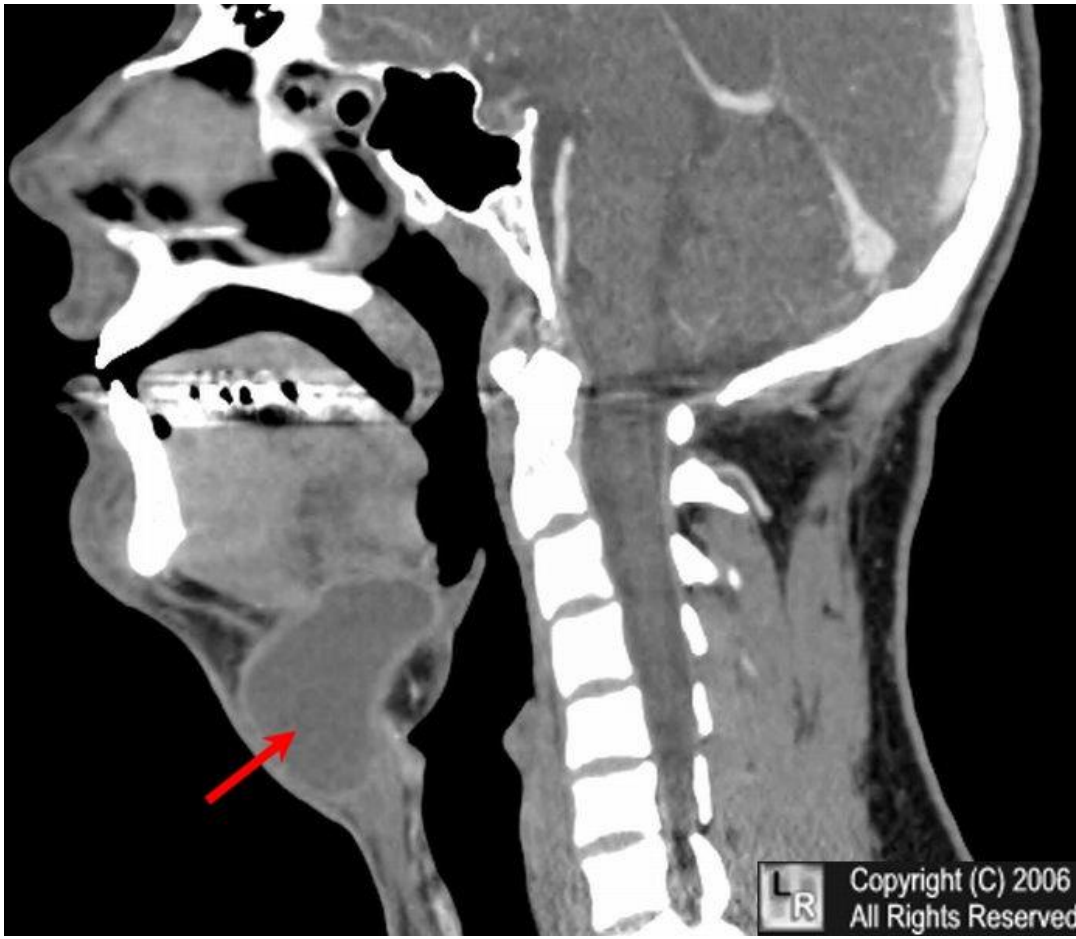
Embryonic origins and pathways of primordia of glands derived from the pharyngeal pouches and the floor of the pharynx

Congenital defects of thyroid gland

- Thyroglossal duct cysts
  - may develop anywhere along the course of descent of thyroid gland from the tongue
- Thyroglossal duct fistulae
  - communication of cysts with external space
- Ectopic thyroid gland
  - along the course of descent
  - most often at root of tongue
  - this tissue may be functional

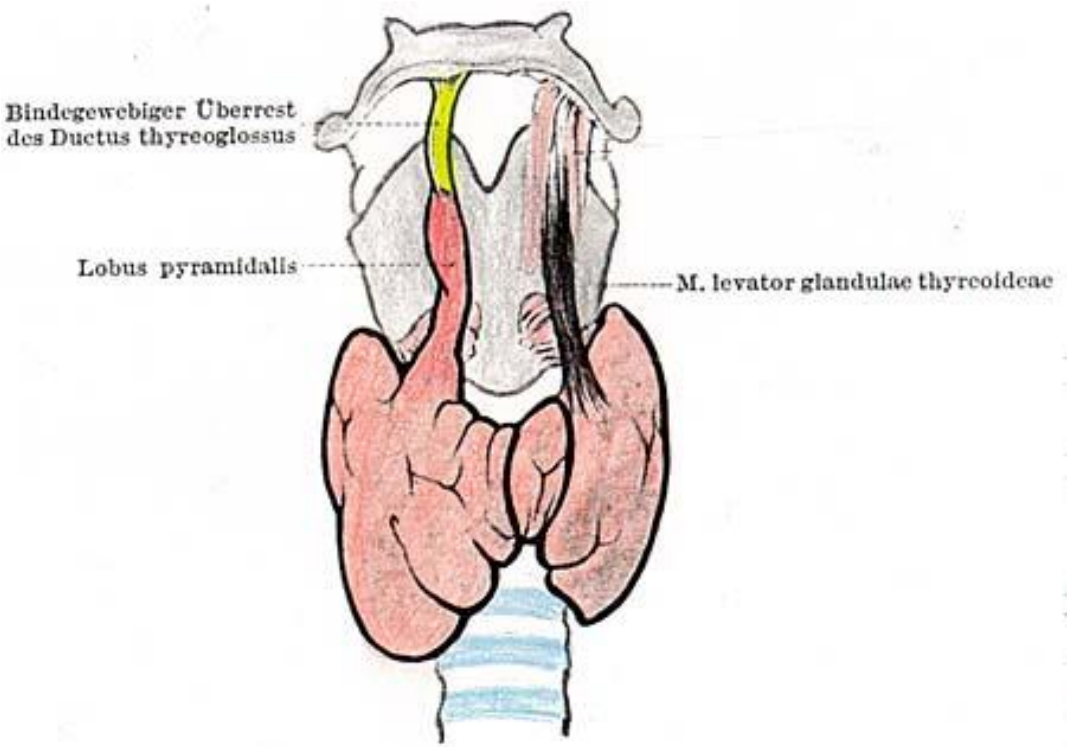
Thyroglossal duct cysts

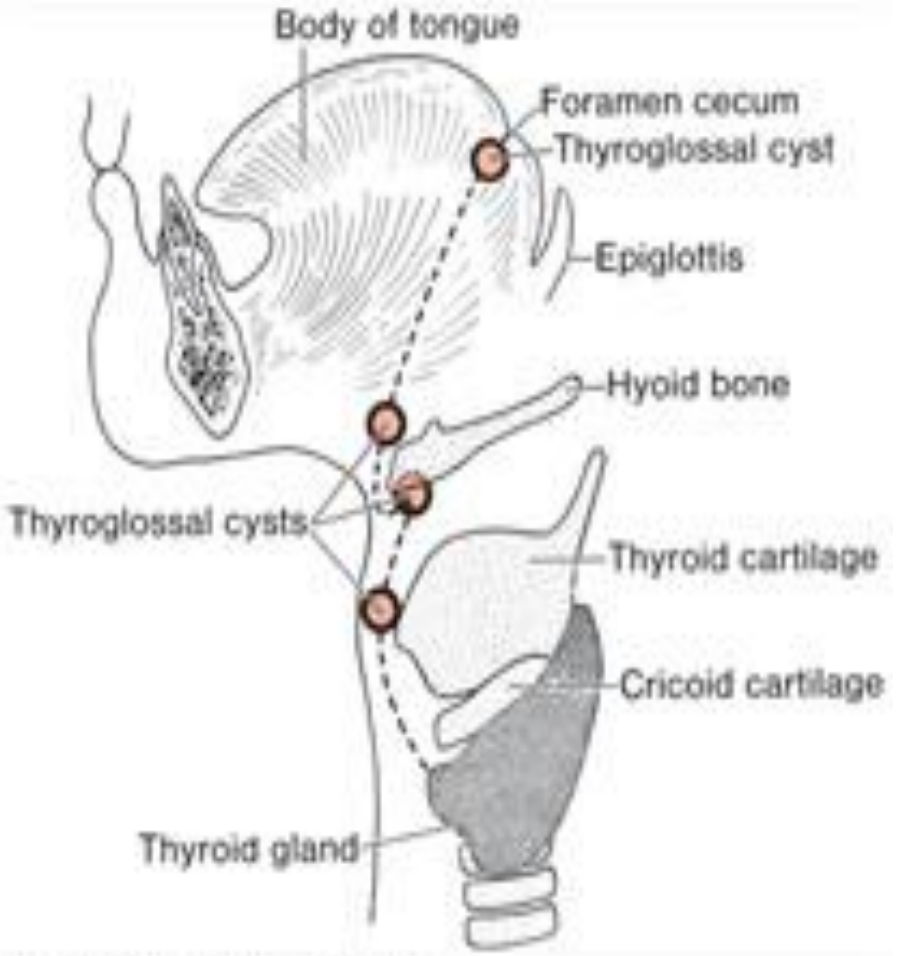




Processus pyramidalis glandulae thyroideae

- The most common congenital defect
- Along the course of the descent
- 40%




Body of tongue
Foramen cecum
Thyroglossal cyst
Epiglottis
Hyoid bone
Thyroglossal cysts
Thyroid cartilage
Cricoid cartilage
Thyroid gland

DiGeorge syndrome
Aplasia thymoparathyroidea

microdeletion 22q11.2

1:3000

DiGeorge Syndrome

=

Basal Ganglia and Periventricular Calcification

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Cardiac (tetralogy of Fallot)

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Abnormal facies

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Thymic aplasia

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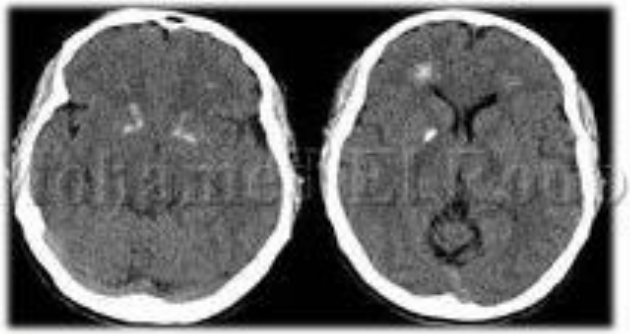
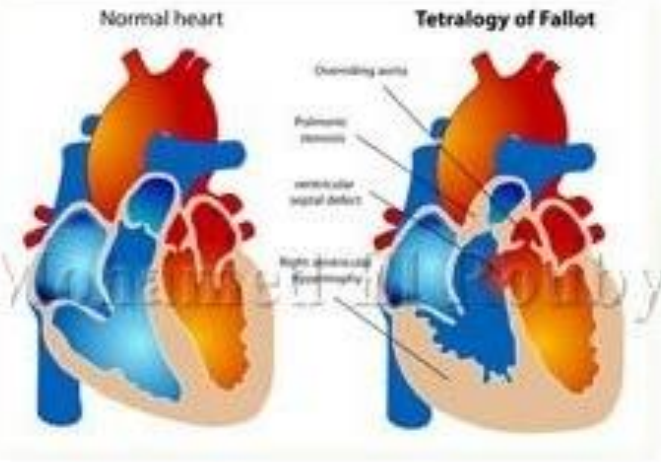
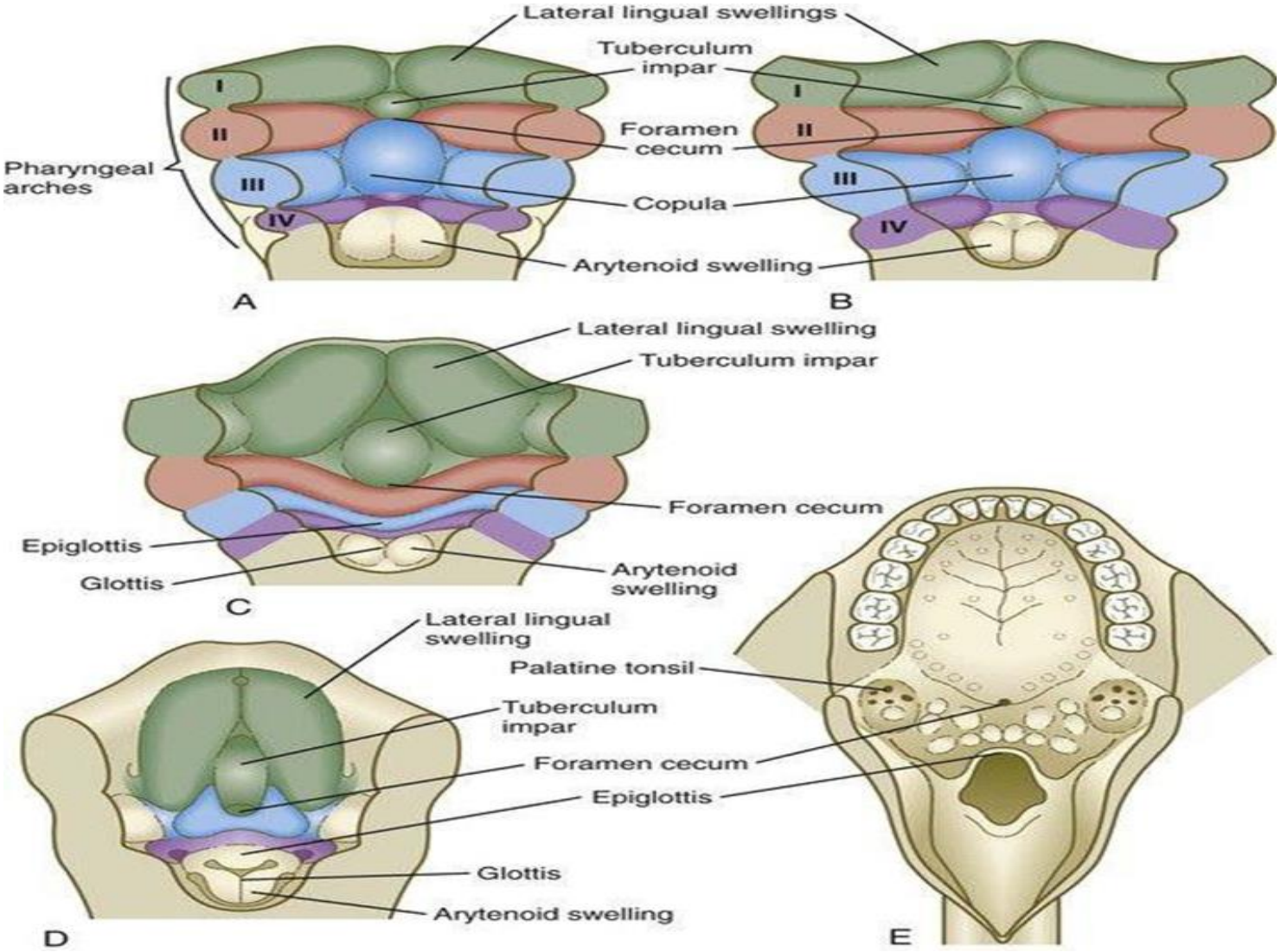
Cleft palate





Development of tongue

- The tongue develops during the 4th week in relation to pharyngeal arches in the floor of the developing mouth.
- The medial-most parts of the mandibular arches proliferate to form two ***lingual swellings***.
- Lingual swellings are partially separated from each other by another swelling that appears in the midline - median lingual swelling or **tuberculum impar**.
- The swellings arise on the ventral part of the mandibular arch.
- A blind pit called foramen caecum develops behind the medial swelling.
- This foramen marks the site of origin of the thyroid diverticulum.
- Another, midline swelling develops on the medial ends of the second, third and fourth arches - the ***hypobranchial eminence***.



Development of the tongue as seen from above. A, At 4 weeks. B, Late in the fifth week. C, Early in the sixth week. D, Middle of the seventh week. E, Adult.

- **Hypobranchial eminence** divides into a cranial part related to the second and third arches - the ***copula*** and a caudal part related to the 4th arch which forms part forms the epiglottis.
- The fused lateral lingual swelling and tuberculum impar to form the anterior two-thirds of the tongue (oral part).
- The posterior third of the tongue (pharyngeal part) develops from the cranial part of the hyobranchial eminence – the copula.
- The fusion of copula with other first arch lingual swellings results in burying of the second arch mesoderm.
- As a result, there is no sensory innervation of the tongue from facial (cranial 7) nerve.
- The third arch mesoderm grows over it to fuse with the mesoderm of the first arch.
- The posterior one-third of the tongue is thus formed by third arch mesoderm.

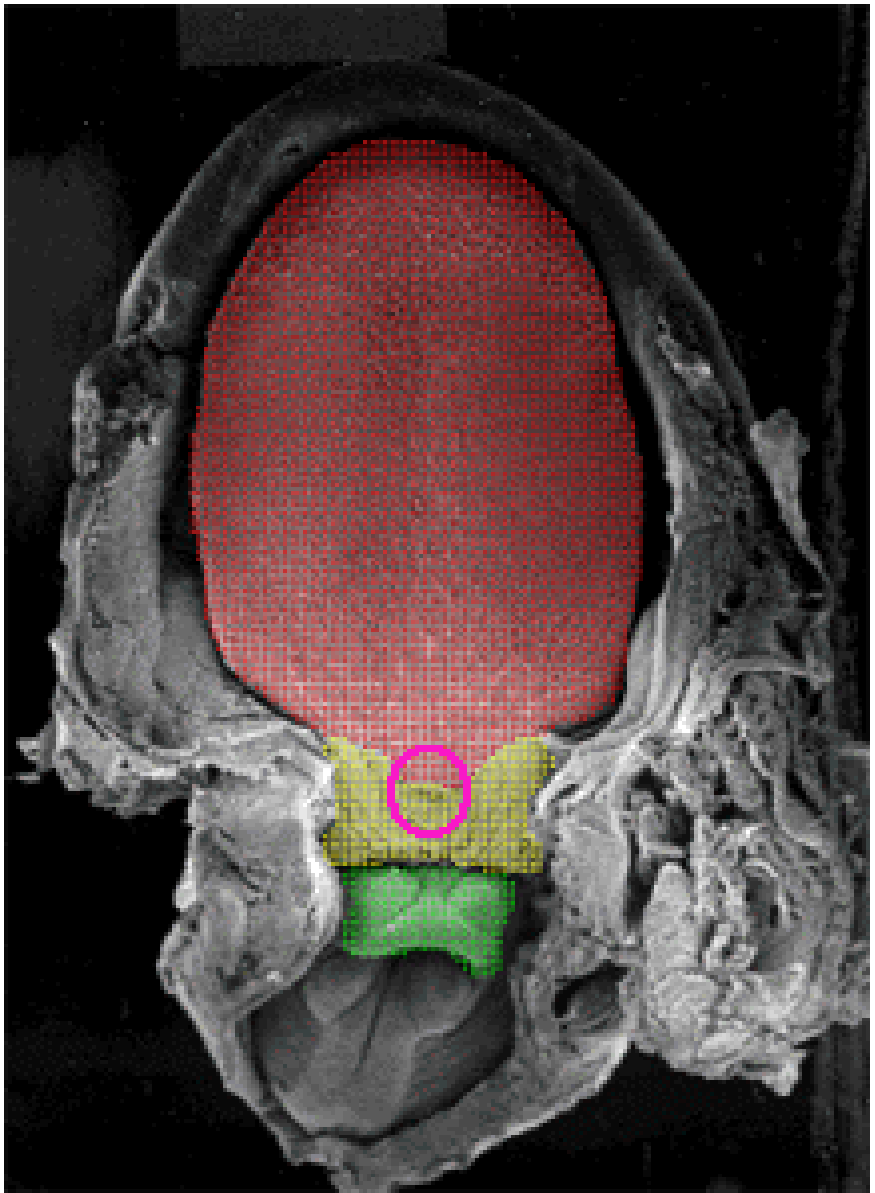
- The line of fusion between the oral (arch 1) and the pharyngeal part (mainly arch 3) of the tongue is marked in the adult by the sulcus terminalis whose apex is the foramen caecum.
- The endoderm differentiates into the stratified squamous epithelium of the tongue.
- The posterior-most part of the tongue is derived from the fourth arch.
- The dorsal surface of the tongue is covered with a large number of papillae.
- Development of the filiform papillae, follows a course that is similar to that of hair follicles.
- The large circumvallate papillae develop anterior to the sulcus terminalis at two to five months of intrauterine life.
- Filiform and fungiform papillae appear earlier on the dorsal mucosa of the tongue.

- Taste buds appear during the 7th week of gestation.
- In contrast to an earlier hypothesis that they are induced by fibers of the visceral afferent cranial nerves VII and IX, which innervate taste buds postnatally, more recent evidence suggests that taste bud formation is independent of cranial nerves.
- Considerable evidence indicates that the fetus is able to taste, and it has been postulated that the fetus uses the taste function to monitor its intra-amniotic environment.
- The various components of the tongue retain their initial nerve supply.
- Thus the contribution of the first arch is represented by the lingual nerve branch of the mandibular nerve, which is the post-trematic nerve of the first arch, and by the chorda tympani which is the pre-trematic nerve of the second arch which supplies sensory fibres to the anterior two-thirds of the tongue.
- The posterior one-third of the tongue is supplied by the glossopharyngeal nerve, which is the nerve of the third arch.
- The most posterior part of the tongue is supplied by the superior laryngeal nerve branch of vagus, which is the nerve of the fourth arch.
- Cranial nerves VII (facial) and IX innervate the taste buds.

- The origin of the muscles of the tongue is controversial.
- They form either in situ from the mesenchyme or from the occipital somites.
- Except for the palatoglossus which is innervated by the pharyngeal plexus, the muscles of the tongue are supplied by the hypoglossal nerve.
- Given that these muscles are innervated by hypoglossal nerve, it suggests that the musculature of the tongue migrates from a considerable distance (the occipital [postotic] myotomes).
- Growth of the body of the tongue is accomplished by a great expansion of the lateral lingual swellings, with a minor contribution by the tuberculum impar.
- The root of the tongue is derived from the copula, along with additional ventromedial tissue between the third and fourth pharyngeal arches.
- The length, breadth and thickness of the tongue double in dimension between birth and childhood.

Part of tongue	Embryonic part from which derived	General sensation	Nerve Supply	
			Taste	Motor
Epithelium over anterior two-thirds	First arch	Mandibular (lingual br.)	Facial (Chorda tympani)	
Epithelium over posterior two-thirds	Third arch	Glossopharyngeal	Glossopharyngeal	
Epithelium over posterior-most past	Fourth arch	Superior laryngea br. of vagus	Superior laryngea br. of vagus	
MUSCLE	Occipital myotomes			Hypoglossal

Development of tongue



Thomas W. Sadler, Langman´ Medical embryology, 10th edition

Congenital defects of tongue

- The tongue may be too large ***(macroglossia)*** as is observed in mongolism or too small (***microglossia).***
- Very rarely the tongue may be absent ***(aglossia).***
- The tongue may be bifid because of non-fusion of the two lingual swellings - Glossoschissis.
- The apical part of the tongue may be anchored to the floor of the mouth by an overdeveloped frenulum - ***ankyloglossia*** or tongue-tie.
- It interferes with free movement of the tongue and speech.
- Occasionally, the tongue may be adherent, to the palate ***(ankyloglossia superior).***

- A red, rhomboid-shaped smooth zone may be present on the tongue in front of the foramen caecum.
- It is considered to be the result of persistence of the tuberculum impar.
- Thyroid tissue may be present in the tongue either under the mucosa or within the muscles.
- Remnants of the thyroglossal duct may form cysts at the base of the tongue.
- The surface of the tongue may show fissures – furrowed tongue

Ankyloglossia

http://www.ghorayeb.com/TongueTie.html

Macroglossia - Microglossia

Furrowed tongue

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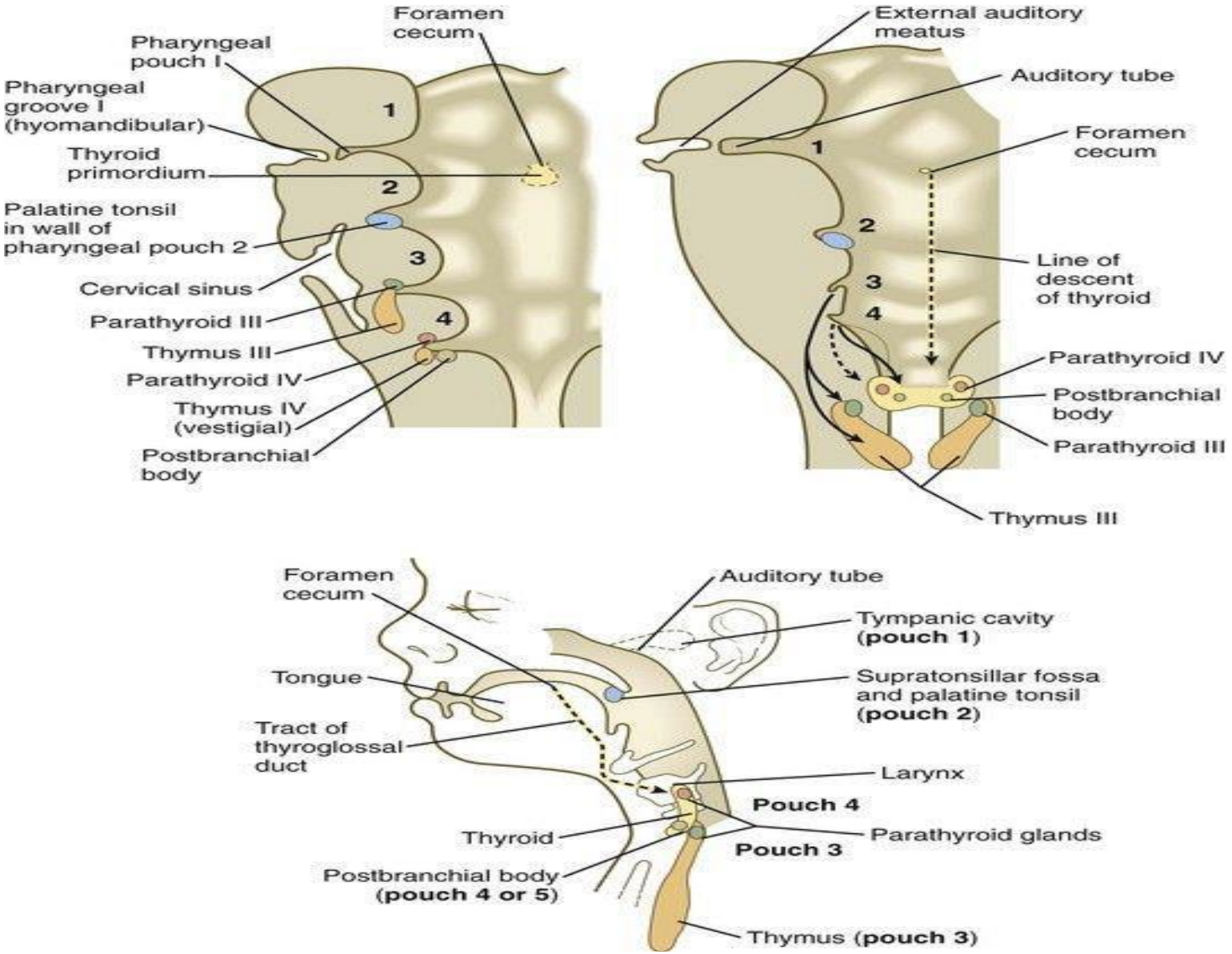

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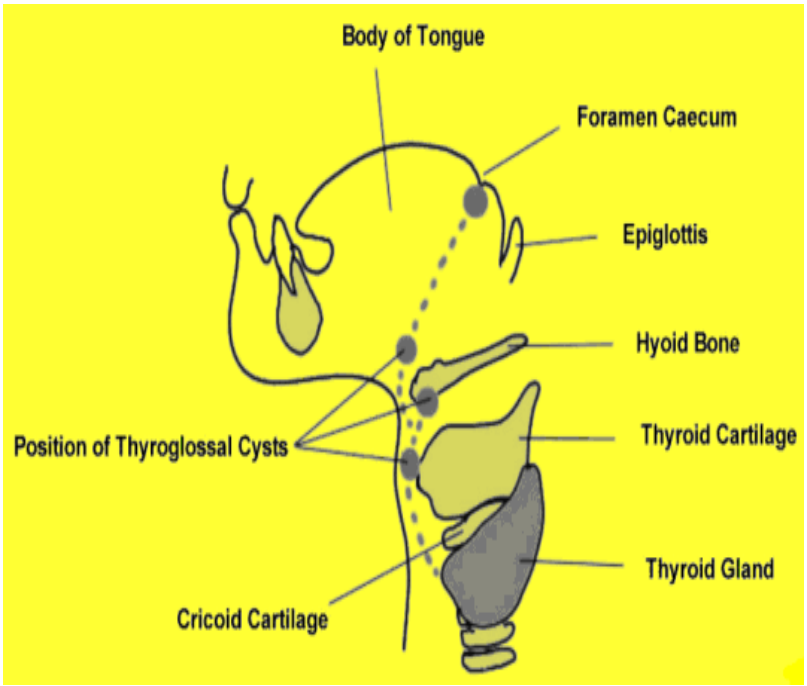

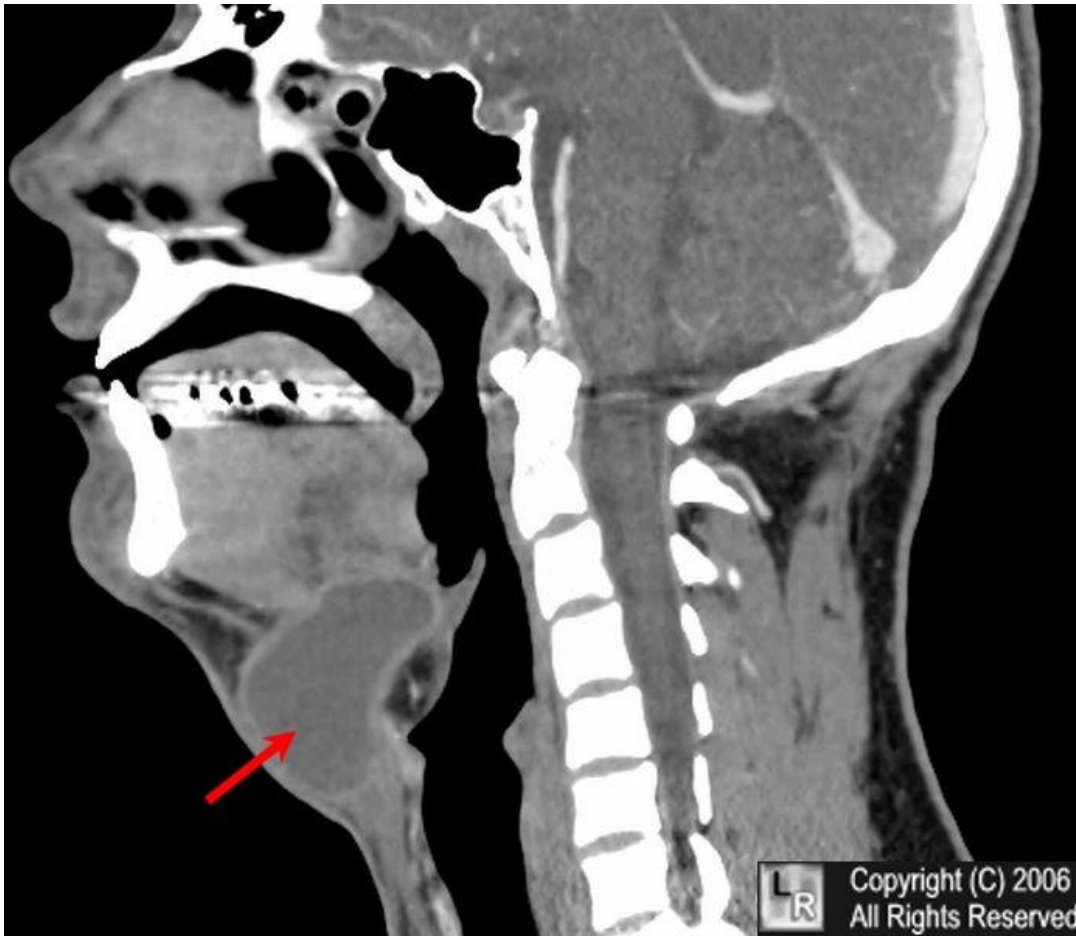

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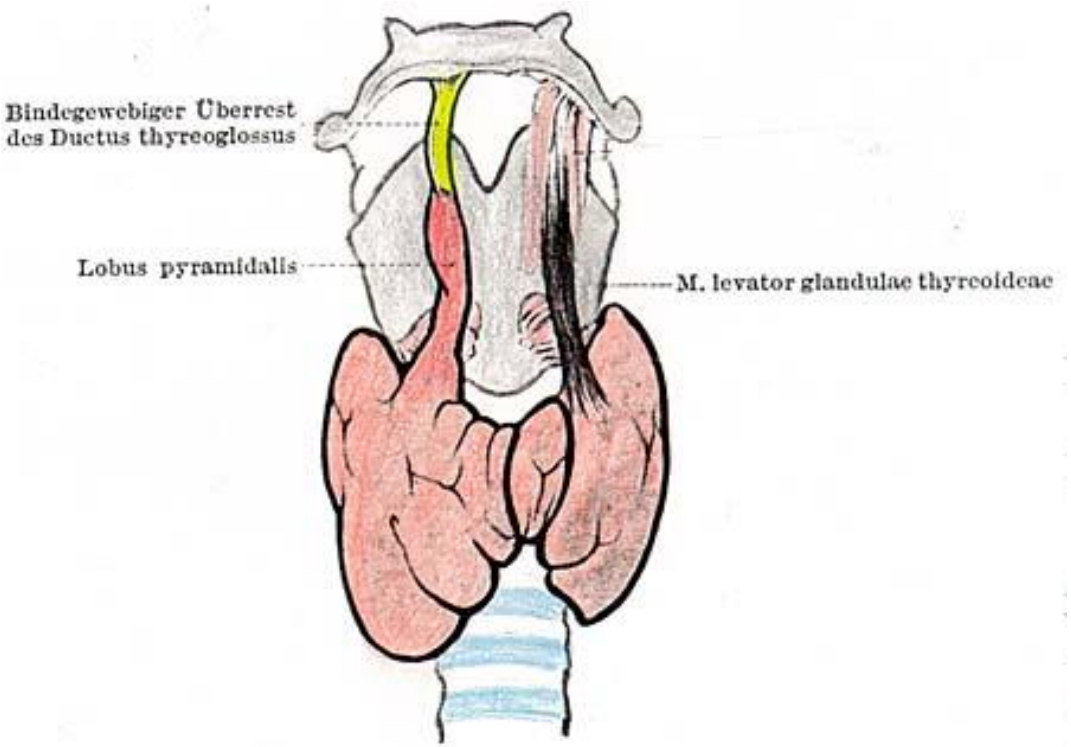

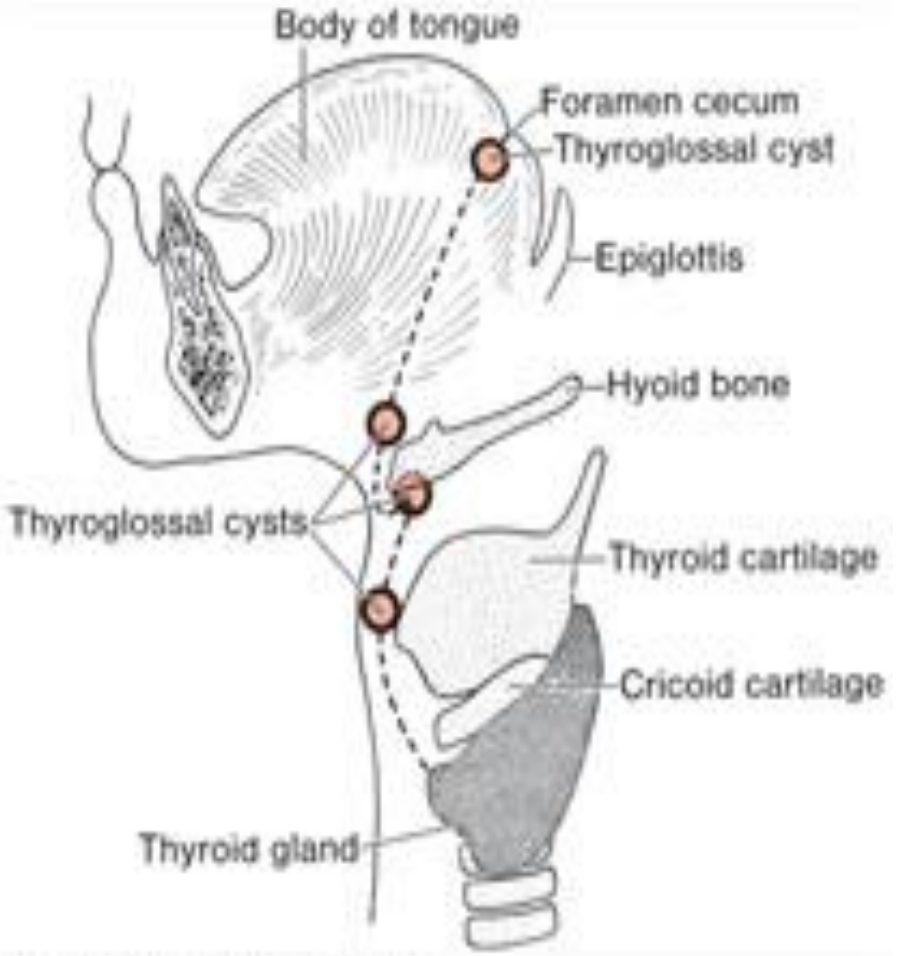
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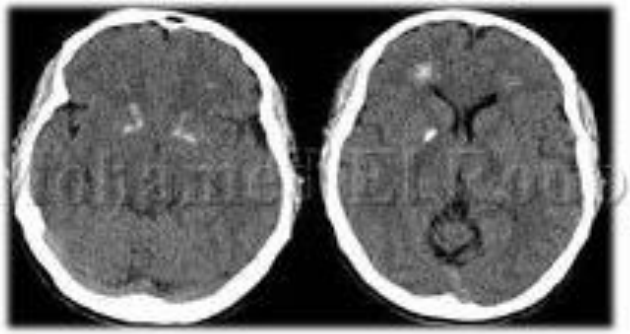

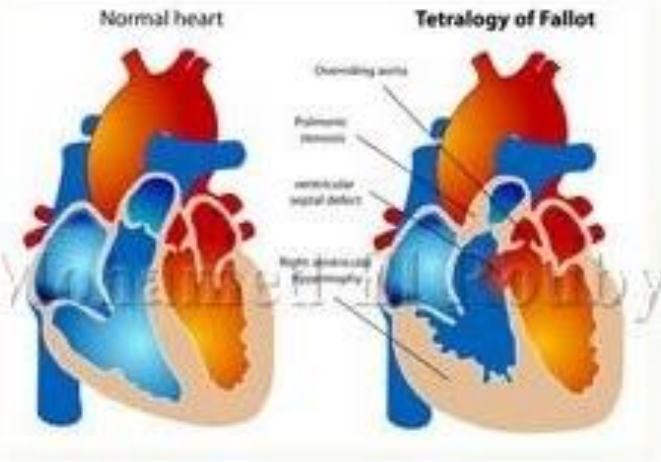

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