10. *Pharyngeal Arches Revisited and the* PHARYNGEAL POUCHES

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READING ASSIGNMENT: Larsen 3rd edition: p.352; pp. 371-378; pp. 393 bottom-398

SUMMARY:

The transient structures that are known as pharyngeal grooves and pharyngeal pouches disappear toward the end of the embryonic period. The first pharyngeal groove will give rise to the external auditory meatus of the adult ear. The other three grooves will disappear without having any further role in the development of adult structures.

The pharyngeal pouches develop into a series of structures that include the pharyngotympanic tube, middle ear cavity, palatine tonsil, thymus, the four parathyroid glands, and the ultimobranchial bodies of the thyroid gland. The related development of the external ear by contributions of the first and second pharyngeal arches is reviewed, as is the development of the tongue, which is formed by contributions from the first through fourth arches. Finally, the development of the thyroid gland, which is spatially related to the derivatives of the third and fourth pharyngeal pouches, is discussed briefly.

LEARNING OBJECTIVES

You should be able to:
a. List the derivatives of the first pharyngeal groove and describe the pattern of obliteration of pharyngeal grooves 2-4.
b. List the derivatives of the different pharyngeal pouches.
c. Describe briefly the development of the external and middle ear.
d. List the different swellings and explain the process of merging of these swellings in the development of external ear and tongue. You should be able to list the pharyngeal arches that contribute to these swellings.
e. Describe the sequence of events that lead to the development of the palatine tonsil.
f. Describe the initial development of the thyroid gland, list the initial site of development and describe the pathway of the growing gland. Describe the thyroglossal duct.
g. Describe the origin and developmental movements of the thymus gland and explain how the parathyroid glands, which develop from the third pouch become "inferior" while those that develop from the fourth pouch become "superior".

GLOSSARY:

Auricle. External ear, derived from three swellings (hillocks) on the first arch and three swellings on the apposing surface of the second arch.

Copula. A median swelling on the pharyngeal surface of the second pharyngeal arches. Is obliterated during further tongue development.

Hyoid operculum. A large outgrowth of the second pharyngeal arch, which obliterates the second, third and fourth pharyngeal grooves.

Hypobranchial eminence. A combined median swelling on the pharyngeal surface of the combined third and fourth pharyngeal arches. This swelling will give rise to the posterior third of the tongue and the epiglottic apparatus.

Thyroglossal duct. The duct that initially runs between the developing thyroid gland and the surface of the tongue, where it opens at the foramen cecum. The duct soon loses its lumen and becomes a solid cord: the thyroglossal tract.

Thyroglossal tract. See: Thyroglossal duct.

Tonsillar crypts. Epithelially lined depressions that extend into the underlying tonsillar stroma.

Tonsillar fossa. A small recess of the ventral second pharyngeal pouch.

Tonsillar stroma. Subepithelial connective tissue, which is infiltrated by lymphoid tissue.

Tuberculum impar. Median swelling on the pharyngeal surface of the first pharyngeal arches. Participates in the formation of the anterior 2/3 of the tongue.

TEXT:

As was seen before, the pharyngeal arches are bilateral/paired swellings that surround the foregut of the embryo and develop in **a rostral to caudal sequence**, in the fourth and fifth week of development. They are wedged between the developing heart and brain. On the ectodermal (future skin) surface, the depressions between the pharyngeal arches are called **pharyngeal grooves**. On the endodermal (future pharyngeal) surface the depressions between the pharyngeal arches are called **pharyngeal pouches**.

The ectodermally lined **pharyngeal grooves** are transient in nature and of limited significance. Only the *first pharyngeal groove* gives rise to a permanent structure: the ear canal or *external auditory meatus*. The developmental sequence will be described below. The *second, third and fourth* grooves are rapidly covered by a large outgrowth of the second pharyngeal arch, the *hyoid operculum*, and obliterated (Fig.10-1).

In contrast, the endodermally lined **pharyngeal pouches**, while also transient in nature, *all give rise to important structures*. In reviewing the derivatives of the pharyngeal pouches you must keep in mind that each pouch has a dorsal and a ventral part (Fig.10-2):

pouch 1	ventral	obliterated: no derivative
	dorsal	***pharyngotympanic tube and middle ear cavity***
pouch 2	ventral	***palatine tonsil***, partially obliterated by endoderm
	dorsal	contributes to pharyngotympanic tube
pouch 3	ventral	***thymus***
	dorsal	**inferior** ***parathyroid gland***
pouch 4	ventral	***ultimobranchial bodies*** (C-cells of thyroid gland)
	dorsal	**superior** ***parathyroid gland***

By the middle of the eighth week all pharyngeal pouch derivatives have reached the neck.
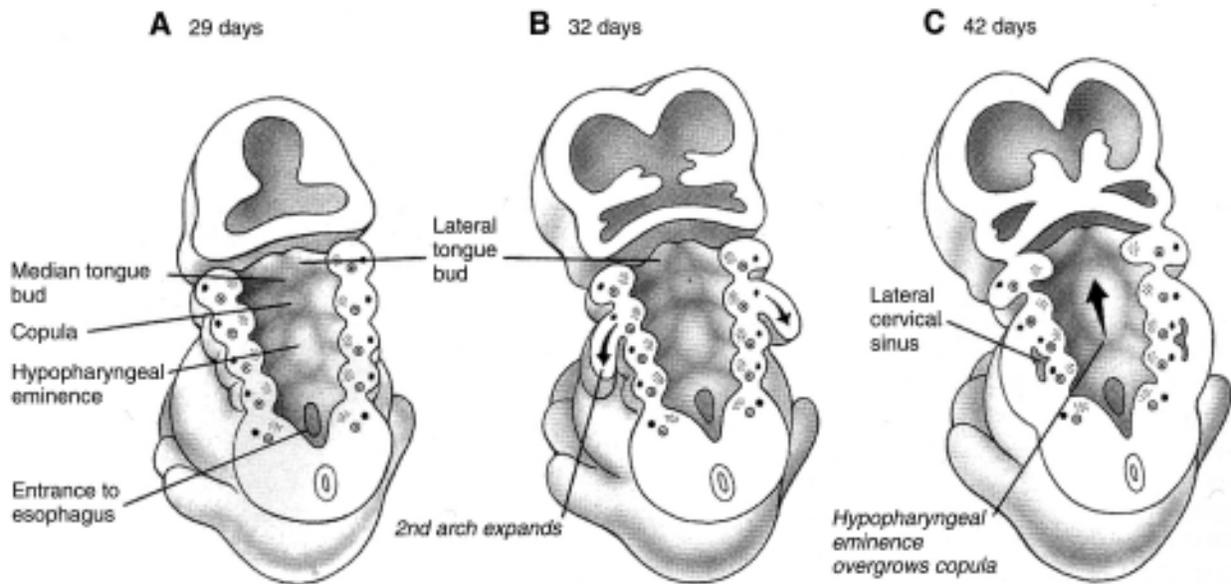
Fig.10-1. Fate of the pharyngeal grooves. The first pharyngeal groove forms the external auditory meatus. The second pharyngeal arch expands and fuses with the cardiac eminence to cover the remaining pharyngeal grooves, which form the transient lateral cervical sinus.
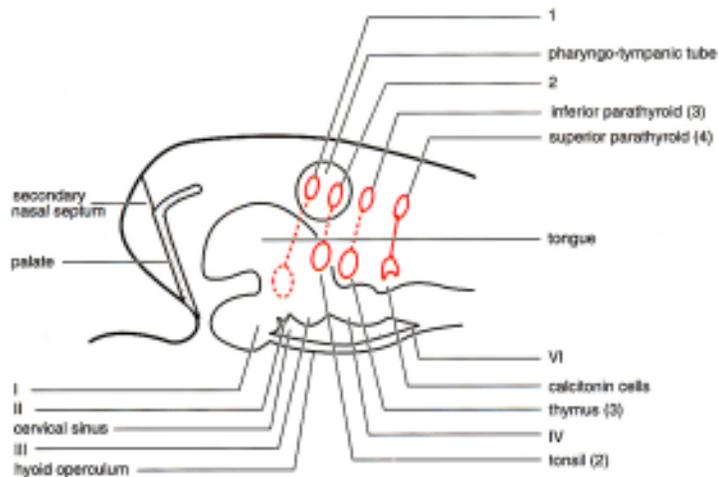

Fig. 10-2.

THE ROLE OF FIRST PHARYNGEAL POUCH AND GROOVE IN EAR DEVELOPMENT (Fig. 10-3)

We distinguish external, middle and internal ear. The development of the internal ear from the otic placode will be discussed in lecture 21.

The development of the **external ear** involves contributions of pharyngeal arches 1 and 2 to form the **auricle**, and the first pharyngeal groove to form the external auditory meatus. The auricle is derived from three swellings (hillocks) on the first arch and three swellings on the opposing surface of the second. The developing external auditory meatus lies in between. The swellings gradually are molded together (by merging) to form the characteristic shape of the auricle (Fig.10-4). The external ear can be a useful diagnostic tool: if it is severely malformed, you should anticipate problems in the other derivatives of the first and second arches.

The development of the **middle ear** involves skeletal elements of pharyngeal arches 1 and 2 that form the three ossicles of the middle ear: **incus, malleus and stapes**, and the first pharyngeal pouch to form the lining of the middle ear cavity. The auditory ossicles begin forming during the 7th week. The dorsal

first pharyngeal pouch elongates further dorsally to form a tubotympanic recess, which becomes the **pharyngotympanic tube** and the middle ear cavity (**tympanic cavity**). In this cavity the first pharyngeal pouch epithelium extends to surround the ossicles. Where the first pharyngeal pouch epithelium meets the epithelium of the first pharyngeal groove, the **tympanic membrane** or eardrum develops.
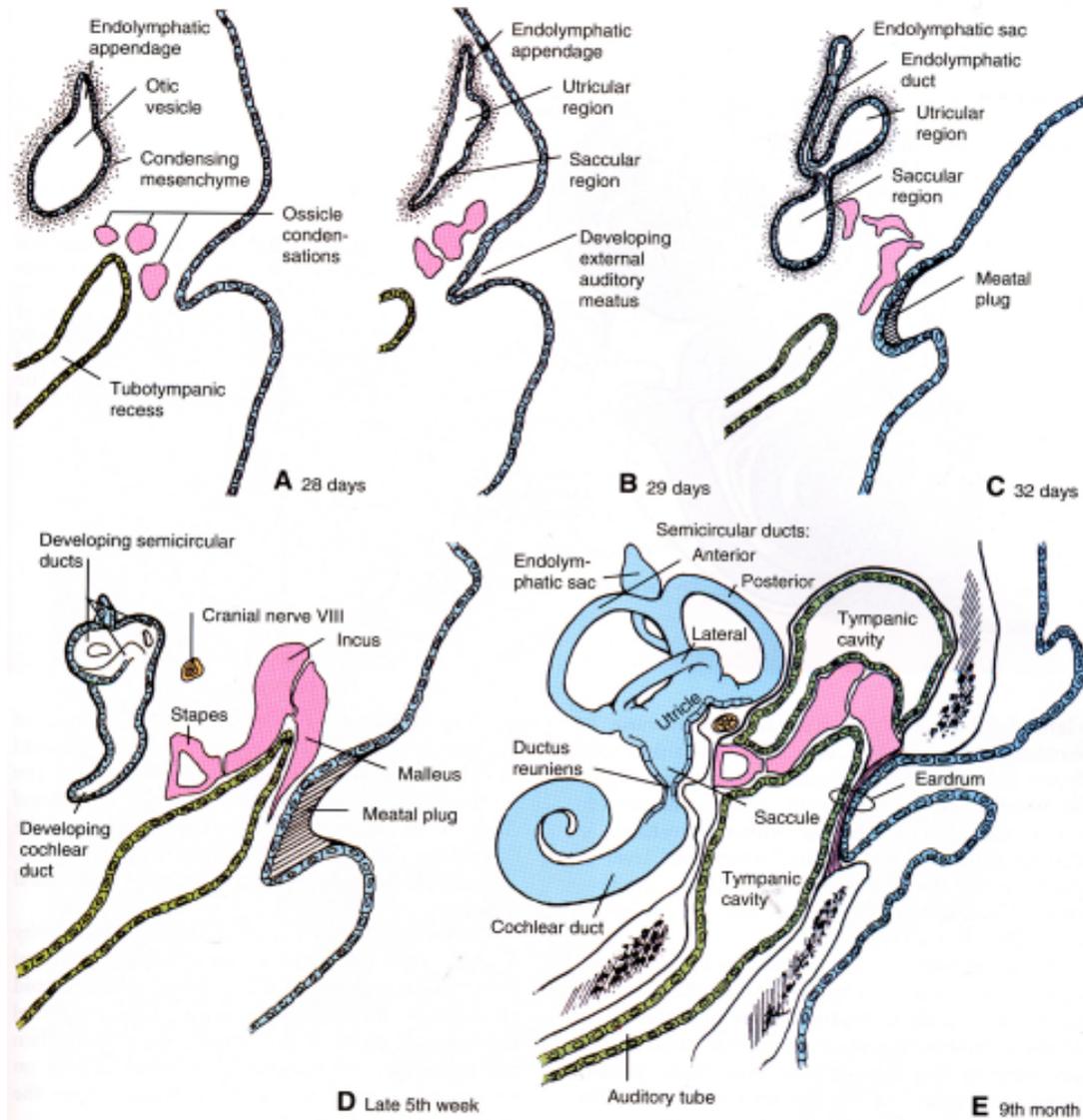

Fig. 10-3. Development of the ear. The components of the inner, middle, and outer ears arise in coordination from several embryonic structures. The otic vesicle gives rise to the membranous labyrinth of the inner ear and to the eighth nerve ganglia. *A, B,* The superior end of the otic vesicle forms an endolymphatic appendage, and the body of the vesicle then differentiates into utricular and saccular regions. *C, D,* The endolymphatic appendage elongates to form the endo-lymphatic sac and duct; the utricle gives rise to the three semicircular ducts; and the inferior end of the saccule elongates and coils to form the cochlear duct. Simultaneously, the three auditory ossicles arise from mesenchymal condensations formed by the first and second pharyngeal arches; the first pharyngeal pouch enlarges to form the tubotympanic recess (the future middle ear cavity), and the first pharyngeal cleft (the future external auditory meatus) becomes filled with a transient meatal plug of ectodermal cells. *C,* Finally, in the ninth month, the tubotympanic cavity expands to enclose the auditory ossicles, forming the functional middle ear cavity. The definitive eardrum represents the first pharyngeal membrane and is thus a three-layered structure comprising ectoderm, mesoderm, and endoderm.
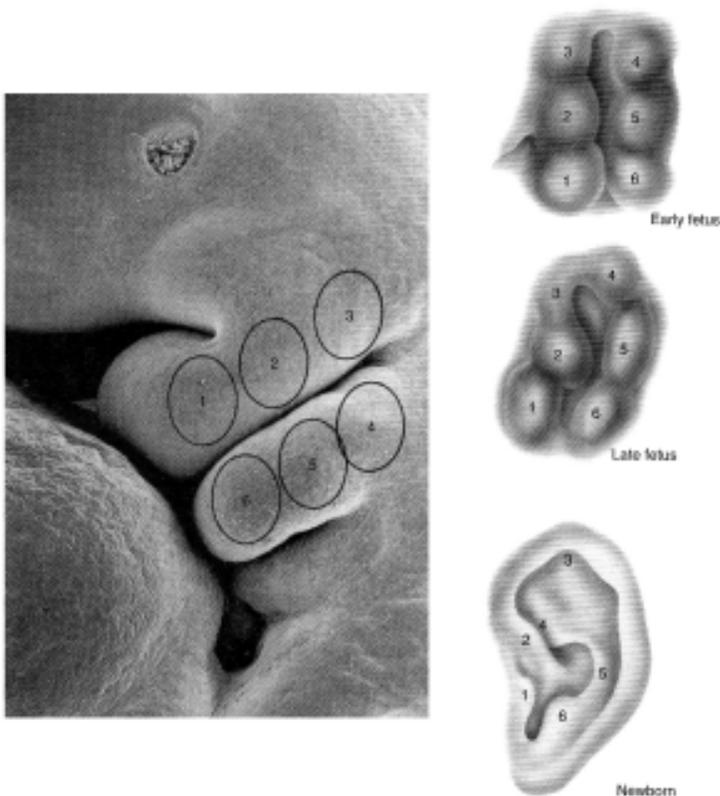
Fig. 10-4. Differentiation of the auricle. The auricle develops from six aricular hillocks, which arise on the apposed surfaces of the first and second pharyngeal arches. (A, Photo courtesy of Dr. Arnold Tamarin.)

SECOND PHARYNGEAL POUCH

The **tonsil** forms in a small persisting recess - the **tonsillar fossa** - of the *ventral pharyngeal pouch*, which is almost completely obliterated by the proliferation of the endodermal lining. The palatine tonsil - "the tonsil"- develops during the third month as a subepithelial infiltration of lymphoid tissue: **tonsillar stroma**. Solid cellular strands from the overlying epithelium subsequently extend into this stroma. The endothelium and associated mesenchymal stroma constitute the primordium of the tonsil. The cellular strands gradually open up to form **tonsillar crypts**. At about the fifth month lymphatic aggregates, coming from the blood stream, appear in the tonsillar stroma. During the last trimester recognizable lymphatic follicles develop around the crypts, which continue to branch deeper.

The development of tonsillar tissue is not unique to the second pharyngeal pouch. Other tonsils: pharyngeal and lingual form in similar fashion in non-pouch areas. A "tubal" tonsil may form around the pharyngotympanic tube, derived from the first pouch.

The *dorsal pharyngeal pouch* may contribute to the development of the tubotympanic recess and thus to the pharyngotympanic tube.

DEVELOPMENT OF THE TONGUE

In order to understand the development of the third and fourth pouch derivatives, we must first review the sequence of events leading to the development of the tongue. The tongue forms on the ventral surface of the foregut. The endodermal covering and underlying mesenchyme of the *first four pharyngeal arches* contribute to the developing tongue (Fig.10-5).

A series of swellings are visible in the fifth week of development:
a) on the **first arch**
   • *two distal swellings* (buds) and
   • *one median swelling (tuberculum impar)*
      These swellings will merge to become the **anterior two-thirds of the tongue**.

b) on the **second arch**
- a *median swelling (copula)*

  This swelling will be *overgrown* by contributions from third and fourth arches and does not contribute to the external surface of the tongue.

c) on the **third and fourth arches**
- a combined *median swelling (hypobranchial eminence)*

  This swelling will give rise to the **posterior third of the tongue and the epiglottic apparatus**.

The complex innervation of the tongue makes sense when you consider its origin from multiple arches. The anterior two-thirds receives sensory innervation from **CN V**, the nerve of the first arch; taste innervation to this region comes from **CN VII**, the pretrematic branch of the nerve of the second arch. The posterior third of the tongue receives sensory and taste sensation from **CN IX**, the nerve of the third arch. Finally, the mesoderm that gives rise to the intrinsic muscles of the tongue comes from the occipital myotomes, and carries with it its own motor innervation from **CN XII**.
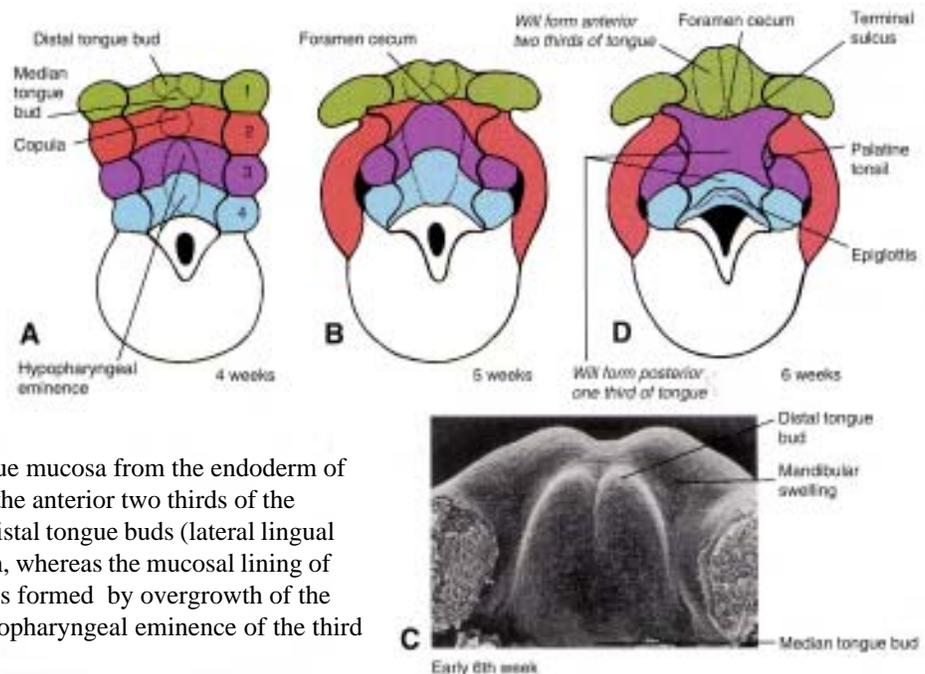

Fig. 10-5. Development of the tongue mucosa from the endoderm of the pharyngeal floor. The mucosa of the anterior two thirds of the tongue develops primarily from the distal tongue buds (lateral lingual swellings) of the first pharyngeal arch, whereas the mucosal lining of the posterior one third of the tongue is formed by overgrowth of the copula of the second arch by the hypopharyngeal eminence of the third and fourth arches.

DEVELOPMENT OF THE THYROID GLAND

Immediately behind the **tuberculum impar**, at the boundary of the anterior two-thirds and the posterior third of the tongue, is the site of initial development of the **thyroid gland**. It begins during the sixth week as an epithelial thickening, which grows rapidly into the underlying mesenchyme. The epithelium gradually assumes the shape of a bi-lobed flask, still connected to the tongue surface by a *thyroglossal duct*. The duct soon loses its lumen and becomes a solid cord (**thyroglossal tract**). It subsequently ruptures at its midpoint. Its point of origin remains as a small depression (**foramen cecum**) on the adult tongue surface (Fig.10-6).

The thyroid gland mass is now free to move down to its final destination, further caudal, anterior to the larynx. Along its path of descent remnants of the thyroglossal tract frequently remain present for some time during early childhood. In a limited number of instances a complete thyroglossal tract may remain ventral to the hyoid bone. The developing gland itself at first is a solid mass of endothelial cells. Soon 1-2-cell thick branches are formed, which become **isolated cords** as the cell mass breaks up during the ingrowth of
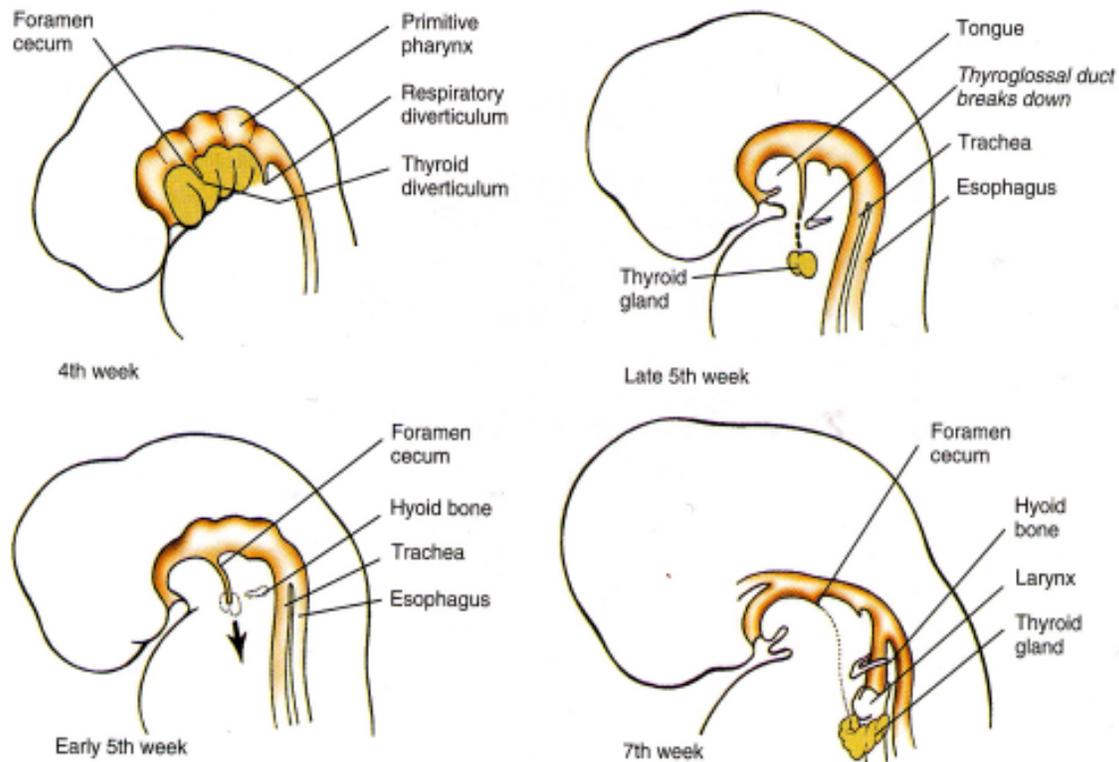
Fig. 10-6. The thyroid originates as an endodermal proliferation at the tip of the foramen cecum of the developing tongue and migrates inferiorly to its final site anterior and inferior to the larynx. Until the fifth week, the thyroid remains connected to the foramen cecum by the thyroglossal duct. The gland reaches its final site in the seventh week.

connective tissue and blood vessels. The cords are the future follicles. Colloid first appears in these during the second trimester.

THIRD AND FOURTH PHARYNGEAL POUCHES

The *ventral third pouches* form the primordia of the **thymus** bilaterally late in the 4th week. The thymus initially comprises a pair of hollow tubes, which invade the underlying mesenchyme. By the early 5th week, the thymic primordia are elongated, but still attached to the pharyngeal pouches and closely associated with the buds of the inferior parathyroid glands that are derived from the dorsal third pouches.

The rapid downward (caudal) growth of the thymic primordia coincides with a loss of their tubal lumina and an increase in bulk as a result of the transformation of their endothelium into solid branching cords that form the primordia of the **thymic lobules**. This initially densely packed epithelial mass later becomes more loosely arranged to form a reticulum in which lymphocytes soon appear. Further histogenesis leading to the development of a well-defined cortex and medulla has occurred by the 12th week. Hassall's corpuscles within the medulla are ectodermally derived structures, probably from the third pharyngeal groove, that have become incorporated in the thymus.

The tips of the thymic primordia swing toward the midline where they meet and fuse, below the sternum by the 6th week (Figs. 10-7, 10-8).

The *dorsal third pouches* give rise to the **inferior parathyroid glands**. The primordia of these glands initially are closely associated with the thymic primordia, as they both detach from the pharyngeal wall and together descend rapidly to a lower position. For a while the inferior parathyroid bud is even encased in thymic tissue.
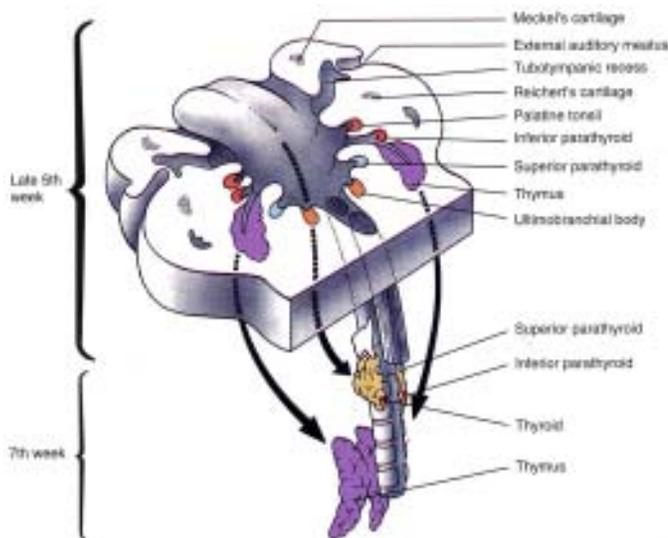
Fig. 10-7. Development of the pharyngeal pouch derivatives. All of the pharyngeal pouches give rise to adult structures. These are the tubotympanic recess (pouch 1), the palatine tonsils (pouch 2), the inferior parathyroid glands and thymus (pouch 3), the superior parathyroid glands (pouch 4), and the ultimobranchial (telopharyngeal) body (inferior part of pouch 4 or a hypothetical pouch 5). The parathyroids, thymus primordia, and ultimobranchial bodies separate from the lining of the pharynx and migrate to their definitive locations within the neck and thorax.
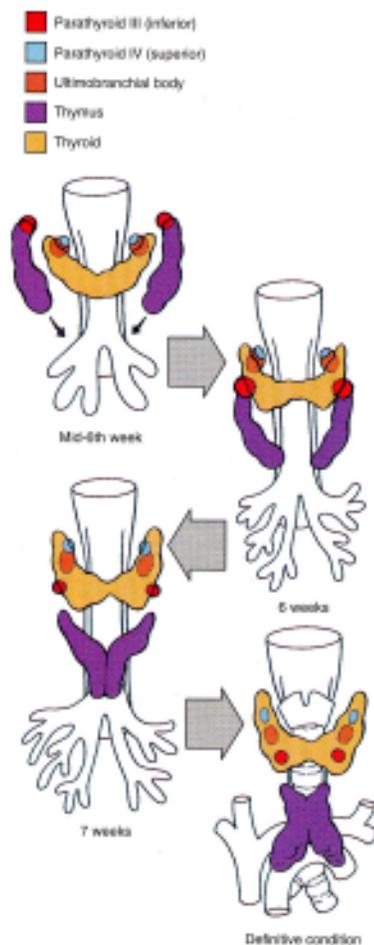

When the thymic primordia migrate past the thyroid gland , the inferior parathyroids become separated from the thymus and, by the 7th week, they come to lie on the infero-posterior surfaces of the thyroid lobes. After the separation of inferior parathyroids and thymic primordia the latter two descend further separately to their final position ventral and inferior to the thyroid.

The *ventral fourth pouches* (which may have incorporated a 5th "ultimobranchial" pouch) give rise to **ultimobranchial bodies** which become the C-cells (parafollicular cells) of the thyroid.

The *dorsal fourth pouches* give rise to the primordia of the **superior parathyroid glands**.

The two sets of derivatives of the fourth pouches arise in close association with each other and very near the supero-posterior surfaces of the lateral lobes of the thyroid gland which is developing nearby. They are readily attached to or even embedded in the thyroid parenchyma.

Developing parathyroid glands, both superior and inferior, initially remain connected with the pharyngeal wall via a small duct : the ductus pharyngo-branchialis III and IV, which gradually becomes solid and then breaks. This frees the glandular primordia and allows them to move away from the pharyngeal wall (Figs. 10-7 and 10-8).

Fig. 10-8. Migration of pharyngeal pouch derivatives. The parathyroid glands and the ultimobranchial bodies migrate inferiorly to become embedded in the posterior wall of the thyroid gland. The two parathyroids exchange position as they migrate: parathyroid III becomes the inferior parathyroid, whereas parathyroid IV becomes the superior parathyroid.