K. J. Lee: Essential Otolaryngology and Head and Neck Surgery (IIIrd Ed)

Chapter 11: Embryology of the Clefts and Pouches

Correlation between Age and Size of Embryo

2.5 weeks	=	1.5 mm
3.5 weeks	=	2.5 mm
4 weeks	=	5 mm
5 weeks	=	8 mm
6 weeks	=	12 mm
7 weeks	=	17 mm
8 weeks	=	23 mm
10 weeks	=	40 mm
12 weeks	=	56 mm
16 weeks	=	112 mm
5-10 months	=	160-350 mm

Development of the Branchial Arches

1. The first 8 weeks constitutes the period of greatest embryonic development of the head and neck. There are five arches named *pharyngeal or branchial arches.* Between these arches are the grooves or clefts externally and the pouches internally. Each pouch has a ventral or dorsal wing. The derivatives of arches are usually of mesoderm origin. The groove is lined by ectoderm while the pouch is lined by entoderm (se Fig. 11-1).

Each arch has an artery, nerve, and cartilage bar. These nerves are anterior to their respective arteries except in the fifth arch where the nerve is posterior to the artery. Embryologically, the arch after the fourth is called the fifth or sixth arch depending on the theory one follows. For simplicity in this synopsis, it will be referred to as the fifth arch. Caudal to all the arches lies the XII nerve. The sternocleidomastoid muscle is derived from the cervical somites posterior and inferior to the above arches.

2. There are two ventral and two dorsal aortas in early embryonic life. The two ventral ones fuse completely while the two dorsal ones fuse caudally only (Fig. 11-2a). In the course of embryonic development, the first and second arch arteries degenerate. The second arch artery has an upper branch which passes through a mass of mesoderm which later chondrifies and ossifies as the stapes. This stapedial artery degenerates in late fetal life. The third arch artery is the precursor of the carotid artery in both left and right sides. The left fourth arch artery becomes the arch of the aorta. The right fourth arch artery becomes the proximal subclavian. The rest of the right subclavian and the left subclavian are derivatives of the seventh segmental arteries. The left fifth arch artery becomes the pulmonary artery and ductus arteriosus. The right fifth arch artery becomes the pulmonary artery with degeneration of the rest of this arch vessel (Fig. 11-2b).

3. (a) Should the right fourth arch artery degenerate and the right subclavian arise from the dorsal aorta instead as shown in Fig. 11-2c, the right subclavian would become posterior to the esophagus, thus causing a constriction of the esophagus without any effect on the

trachea (dysphagia lusoria). (b) The innominate artery arises ventrally. Hence, when it arises too far from the left, an anterior compression of the trachea results.

4. The fifth arch nerve is posterior and caudal to the artery. As the connection on the right side between the fifth arch artery (pulmonary) and the dorsal aorta degenerates, the nerve (recurrent laryngeal nerve) loops around the fourth arch artery which subsequently becomes the subclavian. On the left side, the nerve loops around the ductus arteriosus and the aorta.

Table 11-1. The Branchial Arches and Their Derivatives

First arch: Semilunar ganglion. V. Mandible. Head, neck, manubrium of malleus. Body and short process of incus. Anterior malleal ligament. Sphenomandibular ligament. Tensor tympani. Mastication muscles. Anterior belly of digastric muscle. Tensor palati muscle.

Second arch: Geniculate ganglion. VII. Manubrium of malleus. Long process of incus. All of stapes except vestibular portion of footplate and annular ligament. Styloid process. Stylohyoid ligament. Lesser cornu of hyoid. Part of body of hyoid. Stapedius muscle. Facial muscles. Buccinator, posterior belly of digastric muscles. Styloid muscle. Part of pyramidal eminence. Lower part of facial canal.

Third arch: IX. Greater cornu of hyoid and rest of hyoid. Stylopharyngeus muscle.

Fourth arch: Superior laryngeal nerve. Thyroid cartilage, cuneiform, inferior pharyngeal constrictor, cricopharyngeus, cricothyroid muscles.

Fifth arch (Often called the sixth arch from the standpoint of evolution and comparative anatomy): Recurrent laryngeal nerve. Cricoid, arytenoids, corniculate, trachea, intrinsic laryngeal muscles.

Derivatives of the Pouches

1. Each pouch has a ventral and a dorsal wing. The fourth pouch has an additional accessory wing. The entodermal lining of the pouches proliferates into glandular organs.

First pouch: Dorsal and ventral: Middle ear cavity.

Second pouch: Dorsal: Middle ear cavity. Ventral: Tonsillar fossa and palatine tonsil.

Third pouch: Dorsal: Parathyroid 3. Ventral: Thymus.

Fourth pouch: Dorsal: Parathyroid 4. Ventral: ? Accessory: Ultimobranchial body.

2. During embryonic development, the thymus descends caudally pulling with it parathyroid 3. Consequently, parathyroid 3 is inferior to parathyroid 4 in the adult.

3. The fate of the ultimobranchial body is unknown.

4. As these "out-pocketing" pouches develop into glandular elements, their connections with the pharyngeal lumen referred to as pharyngobranchial ducts become obliterated. Should obliteration fail to occur, a branchial sinus (cyst) is said to have resulted.

The second pharyngobranchial duct (between the second and third arches) is believed to open into the tonsillar fossa, while the third pharyngobranchial duct opens into the pyriform sinus and the fourth opens into the lower part of the pyriform sinus or larynx. An alternative school of thought believes that branchial sinuses and cysts are not remnants of patent pharyngobranchial ducts, but are rather remnants of the cervical sinus of His (Davies J: Embryology of the Head and Neck in Relation to the Practice of Otolaryngology, A Manual, AAOO, 1965).

5. The cutaneous openings of branchial sinuses, if present, are always anterior to the anterior border of the sternocleidomastoid muscle. The tract always lies deep to the platysma muscle which is derived from the second arch (Fig. 11-3).

The course of a third arch branchial cyst:

a. Deep to second arch derivatives and superficial to third arch derivatives.

b. Superficial to the XII nerve and anterior to the sternocleidomastoid.

c. In close relationship with the carotid sheath but superficial to it.

d. Superficial to the IX nerve, pierces middle constrictor, deep to stylohyoid ligament, opens into tonsillar fossa.

The course of a second arch branchial cyst:

a. Again, it is subplatysmal and opens externally anterior to the sternocleidomastoid muscle.

b. Superficial to the XII nerve, deep to the internal carotid artery and the ninth nerve.

c. Pierces the thyrohyoid membrane above the internal branch of the superior laryngeal nerve and opens into the pyriform fossa,.

The course of a fourth arch branchial cyst:

Right:

a. The tract lies low in the neck beneath the platysma and anterior to the sternocleidomastoid muscle.

b. It loops around the subclavian and deep to it, deep to the carotid, lateral to the XII nerve, inferior to the superior laryngeal nerve, and opens into the lower part of the pyriform sinus or into the larynx.

Left:

a. Since the fourth arch vessel is the adult aorta, the cyst may be intrathoracic, medial to the ligament arteriosus and the arch of aorta.

b. Lateral to the XII, inferior to the superior laryngeal nerve.

c. Opens into the lower pyriform sinus or into the larynx.

First Arch (Mandibular Arch)

Meckel's cartilage: Upper part: Malleus, head and neck; incus body, short process.

Meckel's cartilage: Intermediate: Anterior malleal ligament; sphenomandibular ligament.

Meckel's cartilage: Lower part: Mandible.

Mesoderm: Tensor tympani, masticator muscles, anterior belly of digastric, tensor palati.

Nerve: V. Semilunar ganglion.

Artery: "Degenerates".

Second Arch (Hyoid Arch)

Recihert's cartilage: Manubrium of malleus, long process of incus, lenticular process, stapes (except vestibular part of footplate), styloid process, pyramidal eminence, stylohyoid ligament, lesser cornu of the hyoid, part of body of the hyoid, lower half of facial canal.

Mesoderm: Platysma, stapedius muscle and tendon, facial muscles, auricular muscles, posterior belly, stylohyoid muscle.

Nerve: VII. Geniculate ganglion.

Artery: "Degenerates" (stapedial artery).

Third Arch

Cartilage bar: Greater cornu of the hyoid, part of body of the hyoid.

Mesoderm: Stylopharyngeus muscle.

Nerve: IX. Superior and inferior ganglia.

Artery: Common and internal carotids.

Fourth Arch

Cartilage bar: Thyroid cartilage, cuneiform cartilage.

Mesoderm: Inferior pharyngeal constrictor, cricothyroid and cricopharyngeus muscle.

Nerve: Superior laryngeal nerve. Jugular and nodose ganglion.

Artery: Left: Aorta. Right: Proximal subclavian (the rest derived from seventh segmental artery).

Fifth Arch (? Sixth)

Cartilage bar: Cricoid, arytenoid, corniculate.

Mesoderm: Intrinsic muscles of larynx (except cricothyroid), trachea.

Artery: Left: Pulmonary, ductus arteriosus. Right: Pulmonary.

Nerve: Recurrent laryngeal nerve.

Embryology of the Thyroid Gland

On a 4-week-old embryo, a ventral (thyroid) diverticulum of endodermal origin can be identified between the first and second arches on the floor of the pharynx. It also is situated between the tuberculum impar and the copula. The tuberculum impar together with the lingual swellings becomes the anterior two-thirds of the tongue while the copula is the precursor of the posterior one-third of the tongue. The ventral diverticulum develops into the thyroid gland. During development, it descends caudally within the mesodermal tissues. At 4.5 weeks, the connection between the thyroid diverticulum and the floor of the pharynx begins to disappear. By the sixth week, it should be obliterated and atrophied. Should it persist through the time of birth or thereafter, a thyroglossal duct cyst is present. This tract travels through the hyoid and reaches the foramen cecum (Fig. 11-4).

Embryology of the Tongue

The tongue is derived from ectodermal origin (anterior two-thirds) and entodermal origin (posteriorly). At the fourth week, two lingual swellings are noted at the first arch and a swelling, the tuberculum impar, appears between the first and the second arches. These three prominences develop into the anterior two-thirds of the tongue. Meanwhile, another swelling is noted between the second and third arches, called the copula. It develops into the posterior one-third of the tongue. On the seventh week the somites from the high cervical areas differentiate into voluntary muscle of the tongue. The circumvallate papillae develop between the eight and twentieth week while filiform and fungiform papillae develop at the eleventh week (Table 11-2).

Table 11-2. Embryonic Development of the Tongue

Fourth week: Tuberculum impar. Lingual swellings. Copula.

Seventh week: Voluntary muscles. Nerve XII. Papillae. Tonsillar tissues.

Eight to twentieth week: Circumballate papillae.

Eleventh week: Filiform and fungiform papillae.

Embryology of the Tonsils and Adenoids

1. Palatine tonsil (8 weeks old) from second pouch (ventral or dorsal).

2. Lingual tonsil (6.5 weeks old) from between second and third arches ventrally.

3. Adenoids (16 weeks old) develop as a subepithelial infiltration of lymphocytes.

Embryology of the Salivary Glands

1. Parotid (5.5 weeks old). Ectodermal origin. First pouch.

2. Submaxillary (6 weeks old). Ectodermal origin. First pouch.

3. Sublingual (8 weeks old). Ectodermal origin. First pouch.

Embryology of the Nose

The nasal placode is of ectodermal origin and appears between the middle of the third and fourth week of gestation (Fig. 11-5A). It is of interest to note that, at this stage, the eyes are laterally placed, the auricular precursors lie below the mandibular process, and the primitive mouth is wide. Hence, abnormal embryonic development at this stage may result in these characteristics in postnatal life.

On the fifth week the placodes become depressed below the surface and appear as invaginated pits. The nasal pit extends backward into the oral cavity but is separated from it by the bucconasal membrane (Fig. 11-5B). This membrane ruptures at the seventh to eight week of gestation to form the posterior nares. Failure in this step of development results in choanal atresia. While the nasal pit extends backward, it also extends upward toward the forebrain area. Epithelium around the forebrain thickens to become specialized olfactory sensory cells.

Anteriorly, the maxillary process fuses with the lateral and medial nasal processes to form the anterior nares. The fustion between the maxillary process and the lateral nasal process also creates a groove called the nasolacrimal groove. The epithelium over the groove is subsequently buried, and when the epithelium is resorbed the nasolacrimal duct is formed, opening into the anterior aspect of the inferior meatus. This duct is fully developed at birth.

The frontonasal process (mesoderm) is the precursor of the nasal septum (Fig. 11-6a, b). The primitive palate (premaxilla) located anteriorly is also a derivative of the frontonasal process (mesoderm). Posteriorly (Fig. 11-7a, b), the septum lies directly over the oral cavity until the ninth week at which time the palatal shelves of the maxilla grow medially to fuse with each other and with the septum to form the secondary palate. The hard palate is formed by the eight to ninth week (Fig. 11-8) while the soft palate and the uvula are completed by the eleventh to twelfth week.

From the eight week to the 24th week of embryonic life, the nostrils are occluded by an epithelial plug. Failure to resorb this epithelium results in atresia or stenosis of the anterior nares.

Along the lateral wall of the nasal precursor, the maxilloturbinal is the first to appear. This is followed by the development of five ethmoturbinals and one nasoturbinal. Table 11-3 gives the derivatives of each embryonic anlage, and Table 11-4 gives a timetable of their development.

Table 11-3. Embryonic Anlagen and Their Derivatives

Maxilloturbinal	Inferior concha
First ethmoturbinal	Middle concha
Second and third ethmoturbinal	Superior concha
Fourth and fifth ethmoturbinal	Supreme concha
Nasoturbinal	Agger nasi area.

Table 11-4. Timetable of Nasal Development

Inferior concha formed - 7th week.
Middle concha formed - 7th week.
Uncinate process formed - 7th week.
Superior concha formed - 8th week.
Cartilage laid down - 10th week.
Vomer formed and calcified - 12th week.
Ethmoid bone calcified - 20th week.
Cribriform plate calcifies - 28th week.
Perpendicular plate, crista galli calcifies - After birth.

Table 11-5 outlines the development of the paranasal sinuses.

Table 11-5. Development of Paranasal Sinuses

Maxillary sinus: Arises as a prolongation of the ethmoid infundibulum. At 12 weeks. Pneumatizes at birth. Reaches stable size at 18 years old.

Frontal sinus: Arises from the upper anterior area of the middle meatus. Starts at late fetal life or even after birth. Pneumatizes after 1 year. Full size at 20 years old.

Sphenoid sinus: Arises from the epithelial outgrowth of the upper posterior region of the nasal cavity in close relation with the sphenoid bone. Starts at 3rd fetal month. Pneumatization during childhood. Full size at 15 years old.

Ethmoid sinus: Arises from the evagination of the nasal mucosa into the lateral ethmoid mass at 6th fetal month. Pneumatization completed at 7 years old. Full size at 12 years old.

Embryology of the Larynx

Figure 11-9a, b, c, d depicts the embryonic development of the larynx between the eight and 28th week of fetal life.

The entire respiratory system is an outgrowth of the primitive pharynx. At 3.5 weeks, a groove called the laryngotracheal groove develops in the embryo at the ventral aspect of the foregut. This groove is just posterior to the hypobranchial eminence and is located closer to the fourth arch than to the third arch. In embryonic development, when a single tubal structure is to later become two tubal structures the original tube is first obliterated by a proliferation of lining epithelium, then, as resorption of the epithelium takes place, the second tube is formed and the first tube is recannulized. Hence, any malformation will involve both tubes. This process of growth accounts for the fact that more than 90% of traheoesophageal fistulae are associated with esophageal atresia. During development, the mesenchyme of the foregut grows medially form the sides, "pinching off" this groove to crease a separate opening. With further maturation, two separate tubes are formed: the esophagus and the laryngotracheal apparatus.

This laryngotracheal opening is the primitive laryngeal aditus and lies between the fourth and fifth arches. The sagittal slit opening is altered to become a T-shaped opening by the growth of three tissue masses:

1. The hypobranchial eminence which first appears on the third week. This mesodermal structure gives rise to the furcula which later develops into the epiglottis.

2. The two arytenoid masses which appear on the fifth week. Later, each arytenoid swelling shows two additional swellings which eventually mature into the cuneiform and corniculate cartilages.

As these masses grow betweent the fifth and seventh week, the laryngeal lumen is obliterated. On the ninth week the oval shape lumen is reestablished. Failure to recannulize may result in atresia or stenosis of the larynx. The true and false cords are formed between the eight and tenth week. The ventricles are formed at the twelfth week.

The two arytenoid masses are separated by an "interarytenoid notch" which later becomes obliterated. Failure of this obliteration to occur would result in a posterior cleft up to the cricoid cartilage and opening into the esophagus, the culprit of severe aspiration in the newborn.

The laryngeal muscles are derivatives from the mesoderm of the fourth and fifth

arches and hence are innervated by the tenth nerve.

The infant larynx is situated at a level between the second and third cervical vertebrae. In the adult, it lies opposite the body of the fifth cervical vertebra.

Table 11-6 illustrates the muscular and cartilaginous development of the larynx.

Table 11-6. Laryngeal Muscular and Cartilaginous Development with Embryonic Age.

Muscular

4 weeks old: Inferior pharyngeal constrictor and cricothyroid muscles are formed.

5.5 weeks old: Interarytenoid and postcricoarytenoid muscles are formed.

6 weeks old: Lateral cricoarytenoid muscle is formed.

Cartilage

3 weeks old: Development of epiglottis takes place (hypobranchial eminence).

5 weeks old: Thyroid cartilage (fourth arch) and cricoid cartilage (fifth arch) appear.

7 weeks old: Chondrification of these two cartilages begins.

12 weeks old: Development and chondrification of arytenoid (fifth arch) and corniculate (fifth arch) takes place. Vocal process is the last to develop.

20 weeks old: Chondrification of the epiglottis occurs.

28 weeks old: Development of the cuneiform cartilage (fourth arch) occurs.

Ossification of Laryngeal Skeleton

Hyoid: Ossification from six centers. Starts at birth. Completed by 2 years old.

Thyroid: Starts at 20-23 years old. Starts at inferior margin. Extends posteriorly at each ala. Superior margin never ossify.

Cricoid: Starts at 25-30 years old. Incomplete. Starts at inferior margin.

Arytenoids: Starts at 25-30 years old.

Middle Ear

Cartilage is retained at the incudo-stapedial joint, the malleal-incudal joint, the stapedial base, the medial aspect of short crus of incus, and certain parts of manubrium of malleus. Remodelling of bone continues in postnatal life in malleus and incus but not in

stapes.