DEVELOPMENT OF THE PHARYNGEAL (BRANCHIAL) ARCHES


OBJECTIVES: Following lecture and assigned reading, students should be able to:

- Explain the phylogenetic relationship between the "branchial apparatus" and the "pharyngeal apparatus."
- List the components of the pharyngeal arches and, using labeled sketches, illustrate their relationships with each other.
- List the origins and derivatives of pharyngeal arch cartilages; define Meckel's and Reichert's cartilages.
- Describe the cervical sinus and its normal fate.
- Describe the innervations and fate of pharyngeal arch muscles.
- List the derivatives(s) of each pharyngeal pouch, groove, and membrane.
- Discriminate between malformations known as cyst, sinus and fistula – give examples.
- Describe the development of the tongue, differentiating between ectodermally and endodermally derived portions of it. Explain the overgrowth of the tuberculum impar and copula by the lateral lingual swellings and hypobranchial eminence.
- Describe common malformations of the tongue.
- Understand which parts of the tongue are innervated by PA cranial nerves.
- Discuss the development of the thyroid gland and the embryological basis of ectopic thyroid tissue and thyroglossal duct cysts.

Helpful Definitions:

Mesenchyme - undifferentiated cells with the capacity to differentiate into various cell types. Usually of mesodermal or neural crest origin.

Primitive Pharynx – the cranial portion of the foregut.

Cranio-caudal from the front of the embryo (cranio) to the back of the embryo (caudal).

Diverticulum – an outpocketing.
01. **Pharyngeal arches** are homologous with the **branchial arch** system of fish and larval amphibians.

- In these non-mammalian species, the **branchial apparatus** (arches and contained structures) forms a system for combined respiratory exchange and feeding called **gills**.
- Branchial arches provide structural support for the gills.
- Water w/dissolved gases and food moves into the **pharynx** through the mouth, is filtered and leaves the body through the gill slits on either side of the pharynx.
- A branchial apparatus develops during mammalian embryonic development, but true gills are not formed. The mammalian branchial arches are transformed during development and we refer to the structure as the **pharyngeal apparatus**.

02. The pharyngeal arch system contributes greatly to head and neck development.

- The arches appear in the 4th week. They are best appreciated on the external surface of the embryo.

- By the end of the 4th week, 4 pairs of arches are visible. The 5th and 6th are not visible on the surface of the embryo, however there are 6th arch structures within the embryo. The 5th arch is rudimentary in humans.
- Each arch initially consists of a **mesenchyme** core derived from **paraxial** and **lateral plate mesoderm** with an external surface layer of ectoderm and an internal lining of endoderm.
- During the 4th week, **neural crest cells** migrate into the region from the neural folds that will form the fore-, mid- and hindbrain. Migration and proliferation of neural crest cells in the arch **mesenchyme** make the arches more prominent.
- Arches are paired structures, right and left at each level. They are numbered cranial-to-caudal.
- Between successive arches are prominent **pharyngeal clefts** or **grooves**, also numbered in a **cranio-caudal** sequence.
• The 1st arch develops lateral to the patent stomodeum (primitive mouth). The oropharyngeal (buccopharyngeal) membrane ruptures around day 26.
• The 1st arch is also called the mandibular arch.
• It will develop 2 prominences, an upper maxillary prominence and lower mandibular prominence. These play roles in jaw and face formation.
• The 2nd arch is also called the hyoid arch.

The initial role of the pharyngeal arches is simply to support the lateral walls of the cranial foregut (the primitive pharynx) and keep the tube open.

03. Components of the pharyngeal arches.

A typical pharyngeal arch contains within its mesenchyme the following 4 things:

a) an aortic arch that courses from the aortic sac around the pharynx to the dorsal aorta;
b) a piece of cartilage, derived from neural crest, that forms the skeleton of the arch;
c) muscular tissue, derived from the original arch mesoderm. Forms muscles of head and neck;
d) a specific cranial nerve that supplies structures which develop from the arch.

Remembering which arch is paired with which cranial nerve will be very helpful in figuring out the embryological origins of a structure, and vice versa.

<table>
<thead>
<tr>
<th>Arch</th>
<th>CN</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>V (V2 and V3)</td>
</tr>
<tr>
<td>2</td>
<td>VII</td>
</tr>
<tr>
<td>3</td>
<td>IX</td>
</tr>
<tr>
<td>4</td>
<td>X (superior laryngeal branch)</td>
</tr>
<tr>
<td>6</td>
<td>X (recurrent laryngeal branch)</td>
</tr>
</tbody>
</table>

04. Structure of the pharyngeal arches.

An understanding of the transformation of the pharyngeal arches requires a clear picture of early arch structure and organization, both externally and internally.

Think of the pharynx as a tube, around which the arches are placed. Imagine rings of tissue being built around the tube.
Instead of the rings being entirely isolated, they are internally connected with "continuous mesenchyme".

- A single cell layer of **ectoderm** lines the outside of the arches.
- A single cell layer of **endoderm** lines the inside of the arches.
- These single cell layers also line the invaginations between the arches on surfaces.

- The invaginations between arches on the external surface are **pharyngeal** lined by ectoderm.
- The invaginations between arches on the internal surface are **pharyngeal pouches**. They are lined by endoderm.
- The endoderm layer and ectoderm layer meet and juxtapose between the arches to form the 2 layered **pharyngeal membranes**. Except for the first membrane, these 2 layers are soon separated by ingrowth of mesenchyme.
- In fish, the pouches and grooves breakthrough to each other, forming gill slits! (See arrows in photomicrograph below)

- Pouches, grooves and membranes take the number of the arch immediately cranial to them. For this reason, there are 5 arches (1-4 and 6) but only 4 grooves, pouches and membranes (1-4). The pouch, groove and membrane are rudimentary for the 6th arch.
- Remember that all of these structures, like the arches, are paired.

- As shown in the diagram above, **pharyngeal arches** are the swellings or outpocketings of tissue formed when mesenchyme is pushed aside by formation of the pouches and grooves.
05. Pharyngeal arch components are transformed during embryonic development.

Table 1: Synopsis of Pharyngeal Arch Transformations

<table>
<thead>
<tr>
<th>Artery</th>
<th>Cartilage</th>
<th>Muscles</th>
<th>Nerve</th>
<th>Groove</th>
<th>Pouch</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Mandibular)</td>
<td>Incus;</td>
<td>Muscles of mastication</td>
<td>V2 &amp; V3 (trigeminal - maxillary &amp; mandibular branches)</td>
<td>External auditory meatus</td>
<td>Tympanic cavity</td>
</tr>
<tr>
<td>2 (Hyoid)</td>
<td>Stapes</td>
<td>Stylohyoid ligament</td>
<td>IX (glossopharyngeal)</td>
<td>INCORPORATED INTO CERVICAL</td>
<td>Tonsillar cleft for</td>
</tr>
<tr>
<td></td>
<td>Greater horn &amp; lower body of hyoid bone</td>
<td>Ant. body of digastic</td>
<td>X (superior laryngeal branch of vagus)</td>
<td>SINUS ~~~~~~~~~</td>
<td>Dorsal: Inf Parathy</td>
</tr>
<tr>
<td></td>
<td>Cartilage of larynx</td>
<td>Cricothyroid</td>
<td>X (recurrent laryngeal branch of vagus)</td>
<td>~~~~~~~~~</td>
<td>Dorsal: Sup Parathy</td>
</tr>
<tr>
<td></td>
<td>Cartilage of larynx</td>
<td>Striated muscles of upper esophagus</td>
<td></td>
<td></td>
<td>Rudimentary</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Eustachian Tube</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Palatine tonsil</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ventral: Thymus</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Ventral: Thyroid C cells (Ultimo-branchial body)</td>
</tr>
</tbody>
</table>
D. Grooves.

• The only groove which has an adult derivative is groove 1. This groove forms in the area of the **otic placode**. Tissues from groove 1, the otic placode, arches 1 & 2, and membrane 1 will form external and middle ear structures.

• As common sense suggests, the external groove in the area of the developing ear will form the **external auditory meatus**. It will be lined by ectoderm, since it is formed by a pharyngeal groove.

• Grooves 2, 3 & 4 are obliterated by external overgrowth of arches 2 and 6. As tissue from arches 2 & 6 grow towards each other, they pinch off the other 3 grooves as an ectodermally lined **cervical sinus**. The cervical sinus normally obliterates.

• The external surface of the pharyngeal arches, which was pocketed by the grooves, now is smoothed.

• The overgrowth of 2nd arch tissue mimics what happens in fish where more modest growth of this tissue creates the **operculum**, or gill cover.
E. Pouches and Membranes. These change shape, are pinched off, and/or move around within the embryo during transformation to adult structures. Structures derived from pharyngeal pouches are derived from endoderm.

• Pouch 1: This invaginating pouch associated with the outer ear forms the tubotympanic recess. The inner part of this pouch widens to become the tympanic cavity, while the narrower portion leading from the surface of the pharynx elongates to form the auditory (eustachian) tube.
• The membrane where pouch 1 and groove 1 meet forms the tympanic membrane (eardrum). It does NOT remain a 2 layer structure. Still a membrane, but strengthened by mesenchyme cells migrating between the layers.

• Pouch 2: Located behind the 2nd arch. Invaginates further to form the fossa for the palatine tonsil (tonsils of the oropharynx).
• Pouch 3: Has at least 2 parts. The upper forms the inferior parathyroids, also referred to as the PT3 glands because of their derivation from the 3rd pouch. The lower part forms thymus gland.
• Movement of the PT3 are driven by the movement of thymic tissue, which drags the more superior part of pouch 3 with it.
• Although there are 2 inferior parathyroid glands in the adult, there is only 1 thymus gland. The right and left primordial thymuses move into a medial position where they fuse into a single gland.
• Pouch 4: Also has at least 2 parts. The upper forms the superior parathyroids (PT4). The lower forms the ultimobranchial body of the thyroid gland. This initially discrete set of cells fuses with the thyroid and breaks up within it to form areas of C cells which secrete calcitonin.** (Although some texts say that a 5th pouch gives rise to the ultimobranchial body after being incorporated into the 4th pouch).
• The inferior parathyroids start out from a superior location, but end up lower than the PT4 because they migrate further. The parathyroids were named from their adult position.
06. Common anomalies: Cysts, sinuses, and fistulas.

- Cysts, sinuses and fistulas are all remnants of ducts that should have obliterated.
- **Cysts** are small pieces of ducts that are pinched off anywhere along the length. Often fluid-filled.
  - EX: *auricular cysts* are remnants of the 1st groove forming the external auditory meatus.
- **Sinuses** result when a pouch or groove leaves an opening from its surface into central tissues
  - EX: *external branchial sinus* due to an abnormal opening from a persistant cervical sinus.
- **Fistulas** result from a persistant duct that fails to close at both ends OR breakthrough of a pharyngeal membrane if mesenchyme fails to reinforce it, OR from persistance of an adjacent pouch and groove.
  - EX: Fistula from side of neck to tonsillar fossa (persistant 2nd pouch & groove)
07. The tongue derives from a series of swellings on the floor of the pharynx

- All of these swellings are associated with particular pharyngeal arches. They appear at the end of the 4th week as a result of proliferation of underlying mesenchyme.
- Some swellings remain to form adult structures. Others regress,
- 1st arch tissue forms a median swelling, the **median tongue bud** or **tuberculum impar**. It is the initial site of tongue formation.
- 2 swellings appear on either side of the tuberculum impar. These are the **lateral lingual swellings**. They are also derived from PA 1. Will overgrow and obliterate the tuberculum impar.
- The **copula** develops from PA 2 tissue immediately behind the tuberculum impar. Mostly lost during development, although residual pieces are important in innervation patterns.
- A final swelling, the **hypobranchial eminence** develops behind the copula. Comprised of 3rd and 4th arch tissue. The eminence will overgrow the copula.

Persistant structures:
- a) Lateral lingual swellings:
  - form anterior 2/3 tongue -PA 1 (CN ??)
- b) Hypobranchial eminence
  - form posterior 1/3 tongue -PA 3/4 (CN ??)
- c) Piece of copula
  - function to induce taste buds -PA 2 (CN??)
• Merging of the tongue prominences result in 2 superficial landmarks, the median sulcus and terminal sulcus.
• Another important landmark is the foramen cecum, visible at the point where the two sulci intersect. This is site of invagination of the thyroid gland.
• General sensory innervation of the tongue reflects its pharyngeal arch derivations. Thus, the anterior 2/3 of the tongue is innervated by CN V3 from PA 1. Sensory innervation of the posterior 1/3 of the tongue is from CN IX (PA 3) with a small component of CN X (PA 4).

Specialized sensory organs called **taste buds** develop mostly on the dorsal surface of the tongue during weeks 11-13. Taste innervation to the anterior 2/3 of the tongue is by CN VII via remnants of tissue from copula. Taste innervation to the posterior tongue is mostly by CN IX (some posterior by CN X).

• Intrinsic tongue muscles are innervated by **CN XII**, reflecting their derivation from migrating **occipital somite myoblasts** rather than from pharyngeal arch tissues.

• Malformations of tongue development include:
  A) **Ankyloglossia** (tied-tongue) - A malformation of the frenulum. Failure of developmental cell death leaves the tongue anchored to the floor of the pharynx.
  B) **Bifid tongue** - A failure of the lateral lingual swellings to merge completely.
  C) **Macro-** or **microglossia** - Enlarged or reduced tongue size. Due to abnormal proliferation of mesenchymal tissues within prominences.

08. **Formation of the thyroid gland**

The thyroid gland is derived from tissue in the floor of the pharynx.
• Late in the 4th week, a mass of endoderm begins to proliferate on the floor of the pharynx at the site of the **foramen cecum** (sulci interception point). This is the **thyroid primordium**.
• Continued growth of the thyroid primordium causes a small outpocketing, the **thyroid diverticulum**. For a while the developing gland tissue descends at the base of the opening it has created, the **thyroglossal duct**. The duct connects the thyroid to the tongue at its opening, the foramen cecum.
• The duct normally solidifies and obliterates by the 5th week, although part or all of it may persist to form a **thyroglossal cyst or sinus**.
• The thyroid continues to descend through tissues of the neck until about week 7. The gland can be active as early as the 10th week in utero.
SAMPLE QUESTIONS PHARYNX

1. All of the following take place within each pharyngeal arch, EXCEPT:
   A. An artery (aortic arch) develops from mesodermal mesenchyme.
   B. Striated muscle develops from mesodermal mesenchyme.
   C. Intramembranous ossification forms a supporting bar-like structure.
   D. Supporting cartilaginous structures develop from neural crest, in pharyngeal arches #I –III but not IV & VI.
   E. Nerves grow from the CNS and cranial nerve ganglia.

2. A young patient presents with a swelling on the anteriolateral aspect of the neck along the border of the sternocleidomastoid muscle. There is a small opening slightly inferior to the swelling and a slight discharge from the opening. Of the following, which is the most likely diagnosis?
   A. Cervical cyst, formed from a persistent pharyngeal pouch I.
   B. Cervical cyst, resulting from a persistent cervical sinus and complete fusion of the hyoid arch with the future neck region.
   C. External branchial fistula: persistent cervical sinus and incomplete fusion of the hyoid arch with the future neck region.
   D. Internal branchial fistula: persistent cervical sinus and breakdown of the closing membrane between a pharyngeal pouch and cleft.

3. All of the following are true statements regarding the arterial vasculature of the pharyngeal region, EXCEPT.
   A. Pharyngeal arch arteries are called aortic arches.
   B. Arteries in each arch initially terminate in paired dorsal aortae.
   C. Aortic arches form sequentially and are never all present at the same time.
   D. Arteries in each arch are transitory structures, none of which persist, even in part, in the adult.
   E. Portions of certain arteries of the pharyngeal arches persist as components of adult arteries.

4. The orbicularis oculi muscles are derived from which pharyngeal arch and innervated by which cranial nerve?
   A. I; V
   B. I; VII
   C. II; V
   D. II; VII
   E. III; IX

5. Which of the following pair of items is incorrectly associated?
   A. Pharyngeal arch I; muscles of mastication
   B. Pharyngeal arch IV; rudimentary or entirely absent
   C. Pharyngeal III; cranial nerve IX
   D. Pharyngeal arch II; orbicularis oris muscle

6. Which of the following are true statements regarding the supporting cartilages of the pharyngeal arches?
   1. The first pharyngeal arch is supported by maxillary and mandibular (Meckel’s) cartilages.
   2. Meckel’s cartilage is a transitory structure that supports the lower jaw until the mandible later is formed.
   3. Meckel’s cartilage undergoes endochondral ossification to form the entire mandible.
   4. The dorsal end of the maxillary cartilage undergoes endochondral ossification and forms the stapes of the middle ear.
5. Bone of the mental symphysis and mandibular condyle form by endochondral ossification.

7. Pharyngeal arch muscles:

1. Are derived from mesenchymal cells of somitomeres that migrate into the pharyngeal arches.
2. Initially are confined to an “arch of origin” where muscle-nerve relationships are established.
3. Are smooth muscles, like most of the muscles of the gut.
4. Change their muscle-nerve relationships once muscle primordia migrate away from the pharyngeal arches.
5. Migrate from the first pharyngeal arch to form, among others, the muscles of mastication.

ANSWERS:
1 = C;
2 = C;
3 = D;
4 = D
5 = B
6) 1 = T; 2 = T; 3 = F; 4 = F; 5 = T
7) 1 = T; 2 = T; 3 = F; 4 = F; 5 = T