Embryology of the Head and Neck

Selected High-Yield Topics

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Overview

- Branchial arches, pouches, and clefts
- Ear development
- Nasal, lip, and facial development
- Thyroid development
- Laryngeal development
Derivatives of which embryonic structure gives rise to medullary thyroid cancer?

1. Foramen cecum
2. Third branchial pouch
3. Fourth branchial pouch
4. Fifth branchial pouch

(Answer on next slide)
Branchial Arches

- 5 arches present by 5 weeks gestation
- Fifth arch is sometimes called the sixth arch depending on the developmental naming theory followed

Figure source: Cummings Otolaryngology Head and Neck Surgery, 5th ed, 2010
Branchial Arches

- Each arch is composed of mesoderm
- Each arch is associated with
  - A cranial nerve
  - A group of muscles
  - An artery
  - Skeletal or cartilaginous derivatives

Figure source: Cummings Otolaryngology Head and Neck Surgery, 5th ed, 2010
Branchial Arches

- The connecting tissue between the arches form the branchial clefts and pouches.
- Clefts are composed of ectoderm.
- Pouches are composed of endoderm.

Figure source: Cummings Otolaryngology Head and Neck Surgery, 5th ed, 2010
First Arch (Mandibular Arch)

- Trigeminal nerve (CN V)
- Terminal branch of maxillary artery (degenerates)
- Muscles: muscles of mastication (temporalis, medial & lateral pterygoids, masseter), anterior belly of digastric, myelohyoid, tensor tympani, and tensor veli palatini
- Meckel’s cartilage
  - Upper part: malleus head & neck, incus body & short process
  - Lower: contributes to ramus of the mandible
Second Arch (Hyoid Arch)

- Facial nerve (CN VII)
- Stapedial artery (degenerates)
- Muscles: muscles of facial expression, posterior belly of the digastric, stylohyoid, stapedius
- Reichert’s cartilage: manubrium of the malleus, long and lenticular processes of the incus, stapes superstructure, styloid process and stylohyoid ligament, lesser cornu and upper body of the hyoid
Third Arch

- Glossopharyngeal nerve (CN IX)
- Common and internal carotid arteries
- Only one muscle: stylopharyngeus
- Cartilage derivatives: greater cornu and lower body of the hyoid
Fourth Arch

- Superior laryngeal nerve (CN X)
- Aortic arch (left) and proximal subclavian artery (right)
- Muscles: cricothyroid, cricopharyngeus, inferior constrictor
- Cartilage derivatives: Thyroid cartilage and cuneiform cartilage
Fifth (Sixth) Arch

- Recurrent laryngeal nerve (CN X)
- Pulmonary artery (bilateral) and ductus arteriosus (left only)
- Muscles: intrinsic muscle of the larynx
- Cartilage derivatives: cricoid, arytenoid, corniculate
Branchial Pouches

- First pouch: incorporated in the temporal bone to form the lining of the middle ear space and the medial surface of the tympanic membrane (endoderm)

Figure source: Cummings Otolaryngology Head and Neck Surgery, 5th ed, 2010
Branchial Pouches

- Second pouch: palatine tonsil
- Third pouch: inferior parathyroid gland and thymus
- Fourth pouch: superior parathyroid gland

Figure source: Cummings Otolaryngology Head and Neck Surgery, 5th ed, 2010
Branchial Pouches

- Fifth (sixth) pouch: ultimobranchial body
  - Infiltrated by neural crest cells, then detaches and migrates to the dorsal thyroid, where it forms the parafollicular C cells (source of calcitonin and medullary thyroid cancer)

Figure source: Cummings Otolaryngology Head and Neck Surgery, 5th ed, 2010
Branchial Clefts

- First cleft forms the external auditory canal and the outer layer of the tympanic membrane
- Remaining clefts obliterate

Figure source: Cummings Otolaryngology Head and Neck Surgery, 5th ed, 2010
Branchial Cleft Anomalies

• Cyst: a mucosa or epithelium-lined structure with no external opening
• Sinus: a tract, with or without a cyst, that communicates with the pharynx or skin
• Fistula: a tract connecting the pharynx and skin
• For sinuses and fistulae, the tract runs deep to its arch and superficial to more distal arches
• All tracts run anterior to the sternocleidomastoid muscle and superficial to CN XII
First Branchial Cleft Cyst

- Work type I: duplication of the membranous external canal; ectoderm only; no communication with the external canal; passes lateral to facial nerve
- Work type II: ectoderm and mesoderm; communicates with the external canal; passes medial to the facial nerve

Figure source: Neuroimaging Clin N Am 2000;10:75-93
Second Branchial Cleft Cyst

- Most common type
- Passes superficial to CN IX and CN XII
- Passes between external and internal carotid arteries
- Pierces middle constrictor
- Opens into tonsillar fossa

Figure source: Otolaryngol Clin North Am 1981;14:175-86
Third Branchial Cleft Cyst

- Passes deep to CN IX and superficial CN XII
- Passes posterior to the internal carotid artery
- Pierces thyrohyoid membrane
- Opens into piriform sinus

Figure source: Otolaryngol Clin North Am 1981;14:175-86
Fourth Branchial Cleft Cyst

• Very rare
• Tract descends along the carotid sheath, passes around the subclavian artery (right) or aortic arch (left), and ascends back into the neck to open into the piriform sinus
• Majority occur on the left
• Can present as suppurative thyroiditis or thyroid abscess = Direct laryngoscopy with focus on the piriform sinus for these patients
EAR DEVELOPMENT
What is the most common cochlear aplasia?

1. Alexander aplasia
2. Michel aplasia
3. Mondini aplasia
4. Scheibe aplasia

(Answer on next slide)
Development of the Auricle

- At 4 to 6 weeks gestation, 6 mesenchymal condensations (hillocks of His) appear around the future external canal.
- The hillocks fuse by 8 to 9 weeks; by 28 weeks the adult structures are evident.
- Hillocks 1-3 arise from the first branchial arch and give rise to the tragus, helical root, and helical crus.
- Hillocks 4-6 arise from the second branchial arch and give rise to the antihelix, antitragus, and lobule.

Figure source: Ballenger’s Otorhinolaryngology Head and Neck Surgery, 17th ed, 2009
External Canal, Tympanic Membrane, and Middle Ear

- Tympanic ring (first arch derivative) at 9 weeks develops around the medial first branchial cleft and begins diving deeper into the temporal bone.
- Meanwhile, the first branchial pouch is expanding to form the tubotympanic recess.
- As the first cleft and pouch meet to form the tympanic membrane, a thin layer of first arch mesoderm remains, forming the fibrous layer of the tympanic membrane.

Figure source: Ballenger's Otorhinolaryngology Head and Neck Surgery, 17th ed, 2009
External Canal, Tympanic Membrane, and Middle Ear

- A meatal plug fills the external canal until 21 weeks; at that point resorption begins and is complete by 28 weeks
- Failure of resorption of the plug results in congenital aural atresia
- Residual rests of epithelial cells within the tympanic membrane or tympanic cavity can give rise to congenital cholesteatoma

Figure source: Ballenger’s Otorhinolaryngology Head and Neck Surgery, 17th ed, 2009
Notable Anomalies of the External and Middle Ear

• Fissures of Santorini (cartilaginous EAC) and foramina of Huschke (bony EAC)
  — Connect the EAC to the parotid gland
  — Can lead to spread of infection/tumor from one location to the other

• Hyrtl fissure
  — Connects the middle ear space to the meninges; possible route for intracranial spread of otitis media

• Dehiscent facial nerve
  — Tympanic segment
  — 30 to 50% of patients
  — Increases the likelihood for facial paralysis from otitis media or middle ear surgery
Inner ear development

- Bony labyrinth (mesoderm)
- Membranous labyrinth (ectoderm)
  - Otic placode forms at 3 weeks; by 4 weeks, the edges come together to form the otic vesicle

Figure source: Ballenger’s Otorhinolaryngology Head and Neck Surgery, 17th ed, 2009
Otic vesicle rapidly undergoes extensive development, such that the membranous labyrinth is nearly mature by the 8th week of gestation.

Superior portion of the otic vesicle gives rise to the 3 semicircular ducts and utricle
- Superior duct is formed first, posterior second, and horizontal last

Inferior portion of the otic vesicle gives rise to the saccule and cochlea
- Cochlea has 1.5 turns by the 8th week, 2 turns by the 10th week, and the normal 2.5 turns by the 25th week
Inner Ear Malformations

• Michel aplasia
  – Complete agenesis of the petrous portion of the temporal bone; no cochlear structures present

• Mondini aplasia
  – Deformed cochlea with only the basal turn clearly identifiable; usually 1.5 turns present
  – Associated syndromes: Pendred, Waardenburg, Treacher Collins, Wildervanck, and CHARGE (which includes absent semicircular canals)

• Scheibe aplasia (pars inferior dysplasia)
  – Most common inner ear aplasia
  – Normal bony labyrinth and superior membranous labyrinth
  – Deformed tectorial membrane and collapsed Reissner’s membrane
  – Associated syndromes: Usher, Refsum, Waardenburg, Jervell and Lange-Nielsen, and congenital rubella

• Alexander aplasia
  – Basal turn of the cochlear duct is poorly developed
  – Bony and membranous labyrinth are otherwise normal
  – Results in high-frequency hearing loss
NASAL, LIP, AND FACIAL DEVELOPMENT
A newborn is discovered to have a unilateral cleft lip. This was caused by failure of fusion of which of the following pairs of embryonic structures?

1. Medial nasal process and maxillary prominence
2. Lateral nasal process and maxillary prominence
3. Medial nasal process and lateral nasal process
4. Palatine shelf and medial nasal process

(Answer on next slide)
Development of the Midface

- Basic morphology is formed in weeks 4 through 10 by five prominences:
  - Frontonasal prominence (1)
  - Maxillary swellings (2)
  - Mandibular swellings (2)

Figure source: Langman’s Medical Embryology, 6th ed, 1990
Development of the Midface

- At week 5, a pair of ectodermal thickenings, the nasal placodes, appear on the frontonasal process and begin to enlarge.
- At week 6, a nasal pit forms in the center of each placode and invaginates.
- The pit divides the placode into a medial and lateral nasal process.
- The nasolacrimal groove lies between the lateral nasal process and maxillary swelling; it invaginates in week 7 to form the nasolacrimal duct.

Figure source: Langman's Medical Embryology, 6th ed, 1990
Development of the Midface

- During week 6, the medial nasal processes fuse to form the future nasal dorsum, septum, and columella.
- The inferior portion of the fused medial processes forms the intermaxillary process, which gives rise to the premaxilla and philtrum; this process fuses bilaterally with the maxillary prominences to form the upper lip.
- The lateral nasal processes give rise to the nasal alae.
Midline Nasal Defects

- The foramen cecum is a defect in the anterior skull base at the apex of the prenasal space.
- During weeks 3 through 8, dura projects through the foramen cecum into the prenasal space to reach the ectoderm of the developing nasal bones; normally, dura regresses and the foramen closes.
- If the dura captures ectoderm and brings it back along its path of regression, a dermoid cyst, sinus, or fistula can occur.
- Premature closure of the foramen can result in isolated heterotropic glial tissue (nasal glioma).
- Failure of the foramen to close can result in an open connection to the central nervous system (meningocele or encephalocele).

Figure source: Cummings Otolaryngology Head and Neck Surgery, 5th ed, 2010
Cleft Lip and Palate

- Palatogenesis occurs during weeks 5 through 12
- Medial nasal processes fuse → intermaxillary segment → premaxilla (primary palate)
- Failure of the intermaxillary segment to fuse with the ipsilateral maxillary prominence results in unilateral cleft lip with or without a primary palate cleft; bilateral failure of fusion results in a bilateral cleft

Figure source: Langman's Medical Embryology, 6th ed, 1990
Cleft Lip and Palate

- Secondary palate is formed by the palatine shelves, which arise as outgrowths of the maxillary prominences.
- At week 6, the shelves are angled obliquely downward.

Figure source: Langman's Medical Embryology, 6th ed, 1990
Cleft Lip and Palate

- By week 7, the palatine shelves migrate to lie horizontally above the tongue.
- From this point, the shelves fuse medially to form the secondary palate.

Figure source: Langman’s Medical Embryology, 6th ed, 1990
Secondary palatal fusion occurs from anterior to posterior, beginning at the incisive foramen at week 8 and finishing at week 12 with uvular fusion.
Cleft Lip and Palate

- Unilateral cleft lip nasal deformity
  - Nasal tip is deflected toward the cleft side
  - Short medial crus and longer lateral crus on the cleft side
  - Lateral crus is caudally displaced
  - Columella and nasal septum are deflected to the non-cleft side from the pull of the orbicularis oris
  - Nostril on the cleft side is horizontally oriented (rather than normal vertical)
  - Alar base on the cleft side is displaced laterally, inferiorly, and posteriorly

Figure source: Cummings Otolaryngology Head and Neck Surgery, 5th ed, 2010
Cleft Lip and Palate

- Bilateral cleft lip nasal deformity
  - Columellar length is too short—one of the major challenges of bilateral cleft repair
  - Premaxilla is displaced anteriorly and superiorly
  - Alae are laterally displaced, resulting in horizontally oriented nostrils
Congenital Nasal Pyriform Aperture Stenosis

- Caused by bony overgrowth of the nasal process of the maxilla
- Can be associated with holoprosencephaly and a central mega-incisor (which is caused by dysgenesis of the premaxilla)

Figure source: Cummings Otolaryngology Head and Neck Surgery, 5th ed, 2010
Nasolacrimal Duct Cysts

- NLD obstruction occurs to some degree in 30% of all neonates, but very few develop symptomatic cysts in the inferior meatus
- Can cause respiratory distress, especially if bilateral
- Symptomatic cysts can be marsupialized endoscopically

Figure source: Cummings Otolaryngology Head and Neck Surgery, 5th ed, 2010
Choanal Atresia

- The nasal pits deepen to form nasal pouches that lie above the buccal cavity; these pouches remain separated from the primitive nasopharynx by the nasobuccal membrane
- Failure of the nasobuccal membrane to rupture in week 5 or 6 results in choanal atresia
- Alternative theory is that the atresia is caused by abnormal neural crest cell migration
- Two thirds are unilateral
- More common on the right
- 70% are mixed bony/membranous; 30% are pure bony

Figure source: Cummings Otolaryngology Head and Neck Surgery, 5th ed, 2010
The most common site of congenital ectopic thyroid tissue is:

1. Anterior neck
2. Mediastinum
3. Tongue
4. Thyroglossal duct cyst

(Answer on next slide)
Thyroid Development

- Between weeks 3 to 4, the median thyroid anlage arises at the foramen cecum at the junction of the anterior two-thirds and posterior one-third of the tongue; this gives rise to the majority of the future thyroid gland.

- Between weeks 5 to 7, the gland descends in the neck to its normal position in the neck, passing close to the hyoid, usually anterior, but sometimes intra-hyoid or posterior to the hyoid.

- The lateral thyroid anlages consist of the ultimobranchial bodies (paired), which become incorporated into the median anlage during week 5.

Figure source: Surgery of the Thyroid and Parathyroid Glands, 2nd ed., 2013.
Ectopic thyroid tissue can occur anywhere from the foramen cecum to the mediastinum.

Most common sites are the tongue base (lingual thyroid, 90%) and the anterior neck (10%).

Figure source: Surgery of the Thyroid and Parathyroid Glands, 2nd ed., 2013.
Lingual Thyroid

- Failure of descent of the thyroid from the foramen cecum
- Contains the only functioning thyroid tissue in the majority of cases
- Diagnosis can be confirmed with a radioiodine scan ➔ uptake in the base of tongue and none in the normal thyroid position
- Many patients are hypothyroid ➔ gland enlargement ➔ dysphagia; this can often be treated with thyroid hormone replacement

Bottom figure source: Cummings Otolaryngology Head and Neck Surgery, 5th ed, 2010
Thyroglossal Duct Cyst

- Caused by failure of obliteration of the tract of descent of the thyroid from the foramen cecum
- Most common congenital neck mass (3 times more common than a branchial cleft cyst)
- Midline mass (only 1% occur lateral of midline)
- Anchored to the hyoid and moves with tongue protrusion
- Infections are common, are often the first time the cyst is noticed, and can sometimes lead to a cutaneous fistula
- 1% develop thyroid carcinoma (usually papillary)
- Sistrunk procedure is the operation of choice, which includes removal of the central portion of the hyoid bone

Important to remember ectopic thyroid in the differential diagnosis ➔ pre-op ultrasound or radioiodine scan to confirm the thyroid is present in the normal position

Figure source: Cummings Otolaryngology Head and Neck Surgery, 5th ed, 2010
LARYNGEAL DEVELOPMENT
What is the correct order, from most frequent to least frequent, for causes of stridor in an infant?

1. Laryngomalacia, subglottic stenosis, vocal fold paralysis, laryngeal web
2. Vocal fold paralysis, laryngomalacia, subglottic stenosis, laryngeal web
3. Subglottic stenosis, laryngomalacia, laryngeal web, vocal fold paralysis
4. Laryngomalacia, vocal fold paralysis, subglottic stenosis, laryngeal web
5. Laryngomalacia, laryngeal web, subglottic stenosis, vocal fold paralysis

(Answer on next slide)
Development of the Larynx

- The lower respiratory system begins as a diverticulum in the primitive pharynx in week 4.
- Bronchopulmonary buds form as the diverticulum lengthens, and give rise to the lungs.
- The tracheal cartilages form from mesenchyme that surrounds the diverticulum.
- The laryngeal cartilages and muscles are formed from the fourth and fifth branchial arches.
- The endoderm of the diverticulum forms the epithelium of the larynx, trachea, and lungs.

Figure source: Ballenger's Otorhinolaryngology Head and Neck Surgery, 17th ed, 2009
Development of the Larynx

- The laryngotracheal opening is initially a sagittal slit between the 4th and 5th arches that becomes T-shaped as the hypobranchial eminence and arytenoid swellings develop.
- Hypobranchial eminence gives rise to the epiglottis.
- As these masses grow during weeks 5 to 7, the laryngeal lumen is obliterated.
- In week 9, recanalization occurs and forms an oval lumen.
- The arytenoids are initially separated by an interarytenoid notch, which is later obliterated.

Figure source: Skandalakis' Surgical Anatomy: The Embryologic and Anatomic Basis of Modern Surgery, 2004.
Laryngomalacia

- Most common cause of stridor in an infant and most common congenital laryngeal anomaly
- Precise etiology has not been determined
  - Immature neuromuscular control (favored)
  - Immature cartilage structures

Figure source: Cummings Otolaryngology Head and Neck Surgery, 5th ed, 2010
Laryngomalacia

• Findings:
  – Prolapse of arytenoid tissue into the airway (57%)
  – Shortened aryepiglottic folds (15%)
  – Posterior collapse of the epiglottis (12%)
  – Combination of the above (15%)

• Majority of patients can be observed, with supraglottoplasty reserved for those with feeding difficulties, failure to thrive, apneas, cyanosis, or pectus excavatum

• Median age of resolution of stridor is 9 months; stridor is resolved in 75% of patients by 18 months of age

• Reflux is frequently associated with laryngomalacia and can exacerbate symptoms; it should be treated if present

Figure source: Cummings Otolaryngology Head and Neck Surgery, 5th ed, 2010
Laryngeal Clefts

- Caused by failure of the posterior cricoid lamina to fuse and incomplete development of the tracheoesophageal septum
- Numerous classification systems; Benjamin-Inglis is shown to the left
- Presenting symptoms:
  - Feeding difficulties/aspiration
  - Stridor
  - Recurrent pneumonias
  - Chronic cough

Figure source: Cummings Otolaryngology Head and Neck Surgery, 5th ed, 2010
Laryngeal Clefts

- Mild clefts can be subtle, with only interarytenoid fullness or no apparent abnormality on flexible endoscopy; direct laryngoscopy with palpation is essential for the diagnosis.
- Treatment ranges from reflux medication only for the very mildest clefts, to endoscopic repair for Type 1 and some Type 2 clefts, to anterior laryngofissure and median sternotomy for Type 4 clefts.

Figure source: Cummings Otolaryngology Head and Neck Surgery, 5th ed, 2010
Congenital Laryngeal Stenosis and Webs

- Caused by incomplete recanalization after obliteration of the laryngeal lumen during development
- Degree of recanalization dictates the type of lesion: complete atresia vs stenosis vs webbing
- Cricoid is often abnormal
- 65% of patients with an anterior glottic web will have a chromosome 22q11.2 deletion (velocardiofacial syndrome); all patients with such a web should undergo fluorescent in-situ hybridization genetic analysis for the deletion
- Treatment usually requires an open approach
  - Laryngotracheal reconstruction
  - Anterior laryngofissure with keel placement
Congenital Subglottic Stenosis

- Third most common cause of stridor in an infant (2nd is vocal fold paralysis)
- Membranous
  - most common, pictured left
  - fibrous tissue in the subglottis
- Cartilaginous
  - Elliptical or otherwise malformed cricoid
- Patient has no history of intubation (which causes 90% of acquired subglottic stenoses)
- Congenital form predisposes to the acquired form
- Treatment options
  - Endoscopic dilation/laser treatment
  - Anterior cricoid split
  - Laryngotraceal reconstruction
  - Cricotracheal reconstruction
Conclusions

• This is just the tip of the iceberg—head and neck development from embryo to birth is intricately complex.

• Anomalies during development—including lack of fusion of two structures, persistence of a structure that should regress, trapping of one tissue within another, or failure of a vital structure to form—underlie the majority of the congenital lesions in the head and neck.

• Knowledge of the normal developmental pathways and the manner in which anomalies arise is essential for any surgical treatment of congenital lesions.
References


