Head and Neck

Thursday, August 21, 2025 4:07 PM

Embryology - Head and Neck

1. Sources of Mesenchyme for Head Formation

Mesenchyme in the head comes from four main sources:

- Paraxial Mesoderm (Somites + Somitomeres)
 - Forms:
 - \circ Neurocranium \rightarrow large portion (membranous + cartilaginous components of skull)
 - Voluntary muscles of craniofacial region
 - O Dermis & connective tissue of dorsal head region
 - o Meninges (caudal to prosencephalon)
- ♦ Lateral Plate Mesoderm
 - Forms:
 - Laryngeal cartilages (arytenoid, cricoid)
 - Connective tissue in laryngeal region
- Neural Crest Cells (NCCs)

- ullet Origin o Neuroectoderm of forebrain, midbrain, hindbrain
- Migration \rightarrow Ventral into pharyngeal arches & rostrally around forebrain/optic cup \rightarrow facial region
- Derivatives:
 - Entire viscerocranium (face)
 - Part of neurocranium (membranous + cartilaginous)
 - Other tissues: cartilage, bone, dentin, tendon, dermis, pia & arachnoid, sensory neurons, glandular connective tissue
- - ullet With NCCs o form sensory neurons of cranial ganglia:
 - CN V (Trigeminal)
 - o CN VII (Facial)
 - CN IX (Glossopharyngeal)
 - CN X (Vagus)
- 2. Pharyngeal Arches

- ullet Definition: Bars of mesenchymal tissue ullet separated by pharyngeal clefts
- Appearance: 4th-5th week of development
- Associated structures:
 - Pharyngeal clefts (external ectodermal invaginations)
 - \circ Pharyngeal pouches (endodermal outpocketings from pharynx wall \rightarrow do not open externally)
- Resemblance: Fish/amphibian gills (branchia), but no real gills in humans → hence "pharyngeal" is preferred over "branchial."
- 3. Role of Pharyngeal Arches
 - · Contribute to formation of neck and face
 - · End of 4th week:
 - O Stomodeum (primitive mouth) forms center of face
 - Surrounded by 1st pharyngeal arch
 - By 42 days (6th week) \rightarrow 5 prominences visible:

- \circ Mandibular prominences (from 1st arch) \rightarrow caudal to stomodeum
- \circ Maxillary prominences (dorsal 1st arch) \rightarrow lateral to stomodeum
- \circ Frontonasal prominence o cranial to stomodeum
- Later: Nasal prominences develop

4. Key Concept - Epithelial-Mesenchymal Interactions

- All differentiation of arches, pouches, clefts, prominences depends on reciprocal signaling between epithelium and mesenchyme.
- Disruption \rightarrow congenital anomalies (e.g., craniofacial malformations).

Exam Points

- ullet Paraxial mesoderm o skull, muscles, meninges
- Neural crest \rightarrow face (viscerocranium), sensory ganglia, connective tissue
- ullet Lateral plate mesoderm o laryngeal cartilages

- ullet Placodes + NCCs o cranial sensory ganglia
- Pharyngeal arches appear in 4th-5th week \rightarrow essential for face + neck
- 5 prominences by 42 days: mandibular, maxillary, frontonasal, nasal

Pharyngeal Arches

- 1. General Structure of a Pharyngeal Arch
 - Each arch has:
 - Core → mesenchymal tissue (from paraxial + lateral plate mesoderm + neural crest cells)
 - \circ Outer covering \rightarrow surface ectoderm
 - \circ Inner lining \rightarrow endodermal epithelium
 - Neural crest cells → skeletal elements of face
 - Mesodermal core → musculature of face & neck
 - Each arch has:
 - \circ Muscles \rightarrow with its own cranial nerve

Artery (aortic arch component)

F Key principle: Muscles may migrate away, but nerve supply remains from the arch of origin (basis of exam trick questions).

- 2. Individual Pharyngeal Arches & Their Derivatives
- First Arch (Mandibular Arch)
 - Processes:
 - Maxillary process (dorsal) → Premaxilla, maxilla, zygomatic bone, part of temporal bone (via membranous ossification)
 - \circ Mandibular process (ventral) \rightarrow contains Meckel's cartilage
 - Mostly disappears
 - lacktriangleright Dorsal remnants ightarrow malleus, incus
 - Surrounding mesenchyme → mandible (via membranous ossification)

Muscles:

 Muscles of mastication: temporalis, masseter, medial & lateral pterygoids

- o Mylohyoid
- Anterior belly of digastric
- Tensor tympani
- Tensor palatini
- Nerve: Trigeminal (CN V) \rightarrow Mandibular division (V3)
- Extra: Sensory supply to face via ophthalmic (VI), maxillary (V2), mandibular (V3)
- Second Arch (Hyoid Arch)
 - ullet Cartilage: Reichert's cartilage ightarrow
 - Stapes (middle ear ossicle)
 - Styloid process of temporal bone
 - Stylohyoid ligament
 - · Lesser horn + upper body of hyoid
 - Muscles:
 - Muscles of facial expression (buccinator, auricularis, frontalis, platysma, orbicularis oris, orbicularis oculi)
 - o Posterior belly of digastric
 - · Stylohyoid

- Stapedius
- Nerve: Facial nerve (CN VII)
- Third Arch
 - Cartilage: Greater horn + lower body of hyoid
 - Muscle: Stylopharyngeus
 - Nerve: Glossopharyngeal (CN IX)
- Fourth and Sixth Arches
 - ullet Cartilage: Fuse o laryngeal cartilages (thyroid, cricoid, arytenoid, corniculate, cuneiform)
 - Muscles:
 - 4th arch: Cricothyroid, levator veli palatini, pharyngeal constrictors
 - 6th arch: Intrinsic muscles of larynx (except cricothyroid)
 - Nerve: Vagus (CN X)
 - 4th arch → Superior laryngeal branch
 - 6th arch → Recurrent laryngeal branch

3. High-Yield Derivatives Table

Arch	Nerve	Muscles	Skeletal Derivatives
Ist (Mandib ular)	CN V (Mandibular div.)	Mastication (temporalis, masseter, pterygoids), mylohyoid, anterior belly of digastric, tensor tympani, tensor palatini	Maxilla, zygomatic, part of temporal, mandible (from mesenchyme), malleus, incus, sphenomandi bular ligament
2nd (Hyoid)	CN VII (Facial)	Facial expression, stapedius, stylohyoid, posterior belly digastric	Stapes, styloid process, stylohyoid ligament, lesser horn + upper hyoid body

3rd	CN IX (Glossophary ngeal)	Stylopharyngeus	Greater horn + lower hyoid body
44h	CN X (Superior laryngeal branch)	Cricothyroid, levator veli palatini, pharyngeal constrictors	Part of laryngeal cartilages
6th	CN X (Recurrent laryngeal branch)	Intrinsic laryngeal muscles (except cricothyroid)	Part of laryngeal cartilages

4. Exam Pointers

- Meckel's cartilage \rightarrow malleus + incus (NOT mandible itself; mandible from surrounding mesenchyme).
- Reichert's cartilage → stapes + styloid process + stylohyoid ligament + upper hyoid.
- ullet Muscles migrate but nerve supply doesn't change ullet basis for cranial nerve distribution in adult anatomy.
- ullet Only one muscle from 3rd arch o Stylopharyngeus

(CN IX).

 Vagus nerve split: superior laryngeal (4th arch) vs recurrent laryngeal (6th arch).

Pharyngeal Pouches

1. Overview

- Human embryo \rightarrow 4 well-defined pairs of pharyngeal pouches (5th is rudimentary).
- · Lined by endodermal epithelium.
- Each pouch gives rise to important head, neck, and endocrine structures.
- 2. Individual Pouches & Their Derivatives
- First Pharyngeal Pouch
 - ullet Forms a tubotympanic recess ullet contacts 1st pharyngeal cleft (external auditory meatus).
 - Derivatives:
 - \circ Distal part \to Primitive tympanic cavity (middle ear

cavity)

- \circ Proximal narrow part \rightarrow Auditory (Eustachian) tube
- \circ Lining \rightarrow contributes to tympanic membrane (eardrum)

Second Pharyngeal Pouch

- Epithelium proliferates \rightarrow buds \rightarrow invaded by mesoderm \rightarrow primordium of palatine tonsils.
- During 3rd-5th month \rightarrow infiltration by lymphatic tissue.
- ullet Adult remnant o Tonsillar fossa.
- Third Pharyngeal Pouch
 - Each pouch has dorsal wing + ventral wing.
 - ullet Dorsal wing o Inferior parathyroid glands
 - ullet Ventral wing o Thymus
 - Developmental changes:
 - \circ Thymus detaches, migrates caudally + medially ightarrow

- to anterior mediastinum (thorax), fuses with opposite side.
- Inferior parathyroids are "dragged down" with thymus → final position on dorsal thyroid surface.
- Thymus grows until puberty, then involutes (replaced by fat).
- Occasionally, accessory thymic tissue may persist in neck or thyroid.

Fourth Pharyngeal Pouch

- ullet Dorsal wing o Superior parathyroid glands (attach to dorsal thyroid).
- Ventral wing \rightarrow Ultimobranchial body \rightarrow incorporated into thyroid \rightarrow gives parafollicular (C cells).
- Function of C cells: secrete calcitonin \rightarrow lowers blood calcium (antagonizes parathyroid hormone).
- 3. High-Yield Derivatives Table

Pharyngeal Derivatives
Pouch

Ist Tympanic (middle ear) cavity, Auditory (Eustachian) tube, Contributes to tympanic membrane

2nd Palatine tonsil primordium, Tonsillar fossa

3rd Inferior parathyroid glands (dorsal wing),
Thymus (ventral wing)

4th Superior parathyroid glands (dorsal wing),
Ultimobranchial body → C cells of thyroid
(calcitonin)

4. Exam Tips

- Mnemonic for parathyroids:
 - \circ "3 goes Low, 4 goes High" \to 3rd pouch \to inferior parathyroids, 4th pouch \to superior parathyroids.
- · Clinical correlation:
 - DiGeorge Syndrome (22qII.2 deletion): failure of 3rd
 & 4th pouch development → absent thymus & parathyroids → T-cell deficiency + hypocalcemia.

- Accessory thymic tissue can be found in neck or thyroid gland.
- Ultimobranchial body origin of C cells is a frequent viva question.

Pharyngeal Clefts (Grooves)

1. General Features

- At 5 weeks \rightarrow embryo shows 4 pharyngeal clefts (ectodermal invaginations).
- Only the 1st cleft contributes to definitive structures.
- Others (2nd-4th) are normally obliterated.

2. Fate of Individual Clefts

- First pharyngeal cleft
 - Dorsal part deepens → forms external auditory meatus.
 - \circ Lining at bottom \rightarrow contributes to tympanic membrane (eardrum) (with 1st pouch & mesoderm).

- · Second, third, and fourth clefts
 - Overgrown by proliferating tissue of 2nd arch, which fuses with the epicardial ridge.
 - \circ Lose external contact \rightarrow form a cervical sinus (lined by ectoderm).
 - Normally, the cervical sinus disappears.

3. Clinical Correlates

- Ectopic Thymic & Parathyroid Tissue
 - Due to migration of glands from pouches.
 - Accessory glands or remnants may persist.
 - Inferior parathyroids → highly variable (can be found near carotid bifurcation).
 - Thymic tissue may persist in neck or thyroid.
- Branchial Fistula
 - Cause: Failure of 2nd arch to overgrow 3rd & 4th arches \rightarrow persistence of clefts.

- Remnants form a canal (fistula) that connects cervical sinus to the surface.
- Location: Lateral neck, anterior to sternocleidomastoid muscle.
- Usually opens externally → drains a lateral cervical cyst.

4. Exam Essentials

- Only 1st cleft is normal \rightarrow external ear canal.
- 2nd-4th clefts normally obliterated \rightarrow if not \rightarrow cysts, fistulas, sinuses.
- Cervical cysts/fistulas \rightarrow always on lateral neck (contrast with thyroglossal cyst \rightarrow midline).
- Tympanic membrane has 3 germ layer contributions:
 - · Ectoderm (from cleft),
 - Endoderm (from pouch),
 - Mesoderm (intervening connective tissue).

5. Quick Table - Derivatives of Pharyngeal Clefts

Pharyngeal Cleft Fate / Derivative

1st cleft External auditory meatus, contributes

to tympanic membrane

2nd, 3rd, 4th Normally obliterated \rightarrow transient

clefts cervical sinus (disappears)

Abnormality Persistence → Branchial cysts/fistulas

Branchial Cysts & Fistulas + Neural Crest Cell Defects

I. Lateral Cervical Cysts

- Origin \rightarrow Remnants of cervical sinus (2nd-4th clefts fail to regress).
- Common site \rightarrow Just below angle of the jaw, along anterior border of sternocleidomastoid.
- ullet Often not visible at birth ullet enlarge in childhood.

2. Branchial Fistulas

- External fistula \rightarrow Persistence of cleft canal \rightarrow opens on lateral neck (anterior to SCM).
- Internal fistula (rare):
 - o Cervical sinus connects with pharyngeal lumen.
 - Opening usually in tonsillar region (2nd cleft-pouch membrane ruptures).

Exam point:

- ullet Lateral cervical cyst/fistula o lateral neck.
- ullet Thyroglossal cyst/fistula o midline neck.

Neural Crest Cells & Craniofacial Defects

Role of Neural Crest Cells

- Essential for:
 - Craniofacial skeleton & connective tissue.
 - Conotruncal endocardial cushions (heart outflow tract).
 - Regulation of secondary heart field.

Hence, craniofacial anomalies often associated with congenital heart defects.

 Common cardiac anomalies: Persistent truncus arteriosus, TOF, Transposition of great vessels.

Key Syndromes

- 1. Treacher Collins Syndrome (Mandibulofacial dysostosis)
 - Cause: Mutation in TCOFI gene \rightarrow defective treacle protein \rightarrow impaired neural crest differentiation.
 - Inheritance: Autosomal dominant (60% new mutations).
 - Features:
 - O Malar hypoplasia (zygomatic bone underdeveloped)
 - Mandibular hypoplasia
 - Down-slanting palpebral fissures
 - Lower eyelid colobomas
 - Malformed external ear
 - Mimicked by: Retinoic acid teratogenicity.
- 2. Robin Sequence

- Defect: Mandibular hypoplasia (first arch).
- Triad:
 - Micrognathia
 - Glossoptosis (posterior tongue)
 - Cleft palate (palatal shelves fail to fuse).
- Causes: Genetic, environmental (e.g., oligohydramnios
 → chin compressed on chest).
- Incidence: ~ 1 in 8,500 births.
- 3. 22q11.2 Deletion Syndrome
- (= DiGeorge syndrome / Velo-cardio-facial syndrome / Conotruncal anomaly face syndrome)
 - Cause: Microdeletion on chromosome 22911.2.
 - Incidence: ~ 1 in 4,000 births.
 - Features:
 - Congenital heart defects (esp. conotruncal

anomalies)

- \circ Thymic hypoplasia/aplasia $\rightarrow \downarrow$ T-cell immunity \rightarrow recurrent infections
- \circ Hypocalcemia \rightarrow seizures (due to abnormal parathyroid development)
- Mild facial dysmorphology
- Learning disabilities
- Pathogenesis: Failure of neural crest cell contribution to mesenchyme → defective epithelial-mesenchymal interaction.

4. Oculoauriculovertebral Spectrum (Goldenhar Syndrome / Hemifacial Microsomia)

- Incidence: ~ 1 in 5,600 births.
- Features:
 - Craniofacial asymmetry (65%)
 - Maxillary, temporal, zygomatic bones small/flat
 - Ear defects → microtia, anotia
 - \circ Eye defects \rightarrow epibulbar dermoids, tumors
 - Vertebral anomalies → hemivertebrae, fused vertebrae, spina bifida

- Associated anomalies: Cardiac defects (TOF, VSD) in ~
 50%.
- Cause: Unknown.

Exam-Oriented Pearls

- Treacher Collins \rightarrow 1st arch + TCOF1 mutation.
- ullet Robin sequence o micrognathia o glossoptosis o cleft palate.
- 22qII deletion \rightarrow "CATCH-22" mnemonic:
 - C → Cardiac defects
 - \circ A \rightarrow Abnormal facies
 - \circ T \rightarrow Thymic hypoplasia
 - \circ C \rightarrow Cleft palate
 - \circ H \rightarrow Hypocalcemia
- Goldenhar → oculo-auriculo-vertebral defects + hemifacial microsomia.

Development of the Tongue

Embryonic Origin

Week 4

- Appears as swellings in the floor of the pharynx.
- 1. Anterior 2/3 (Body of Tongue)
 - Derived from 1st pharyngeal arch:
 - Tuberculum impar (median swelling).
 - Two lateral lingual swellings \rightarrow enlarge, overgrow tuberculum impar \rightarrow fuse.
 - Separated from posterior part by terminal sulcus (V-shaped groove).
- 2. Posterior 1/3 (Root of Tongue)
 - From 2nd, 3rd, and part of 4th arches.
 - 3rd arch overgrows 2nd arch, explaining innervation by CN IX (not CN VII).
- 3. Epiglottis & Extreme Posterior Tongue
 - Derived from posterior part of 4th arch (hypobranchial eminence).
 - Related to laryngeal orifice & arytenoid swellings.

4. Muscles of Tongue

- From occipital somites (myoblasts).
- Nerve: Hypoglossal nerve (CN XII).

Innervation of Tongue

Arr Key principle: Mucosa Arr from pharyngeal arches Arr supplied by their respective cranial nerves.

 \longrightarrow Muscles \longrightarrow from occipital somites \longrightarrow CN XII.

- 1. Anterior 2/3 (Body of Tongue)
 - Pharyngeal Arch Origin: 1st arch (tuberculum impar + lateral lingual swellings)
 - Muscle Origin: Occipital somites
 - General Sensation: CN V3 (lingual nerve)
 - Taste (Special Sensory): CN VII (chorda tympani)
 - Motor Innervation: CN XII (hypoglossal)

2. Posterior 1/3 (Root of Tongue)

- Pharyngeal Arch Origin: 3rd arch (overgrows 2nd) + part of 4th arch
- Muscle Origin: Occipital somites

- General Sensation: CN IX (glossopharyngeal)
- Taste (Special Sensory): CN IX
- Motor Innervation: CN XII

3. Epiglottis & Extreme Posterior Tongue

- Pharyngeal Arch Origin: 4th arch
- Muscle Origin: Occipital somites
- General Sensation: CN X (superior laryngeal branch)
- Taste (Special Sensory): CN X
- Motor Innervation: CN XII

Clinical Correlate

- Ankyloglossia (Tongue-tie)
 - Cause: Frenulum abnormally short, extends to tip of tongue.
 - \circ Embryology: Normally, degeneration of cells frees tongue from floor \rightarrow only frenulum remains.
 - Effect: Restricts tongue movement; may interfere with speech/feeding.

Exam Pearls

- Development: Body (Ist arch), Root (3rd arch),
 Epiglottis (4th arch).
- Innervation: CN V3, VII, IX, X for mucosa; CN XII for muscles.
- Taste vs. sensation \rightarrow classic MCQ:
 - Ant. 2/3 taste = CN VII.
 - Ant. 2/3 sensation = CN V3.
- Tongue-tie = frenulum persistence.

Thyroid Gland Development

Origin

- Appears as epithelial proliferation in the floor of pharynx:
 - Between tuberculum impar and copula
 - o Marked later by the foramen cecum

Descent

Moves anterior to pharyngeal gut as a bilobed diverticulum

- ullet Connected temporarily to tongue by thyroglossal duct ullet later disappears
- Descends in front of hyoid bone and laryngeal cartilages
- Reaches final position in front of trachea by 7th week
- Forms median isthmus + two lateral lobes

Function

- Begins at end of 3rd month
- Formation of thyroid follicles containing colloid:
 - \circ Follicular cells \rightarrow thyroxine (T4) & triiodothyronine (T3)
 - \circ Parafollicular (C) cells \to from ultimobranchial body \to secrete calcitonin

Clinical Correlates

- 1. Thyroglossal Duct Cyst
 - o Midline neck cyst anywhere along thyroid's

migratory path

- 0 ~50% located just below hyoid bone
- \circ Can be connected to skin \rightarrow thyroglossal fistula

2. Ectopic Thyroid Tissue

- Commonly at base of tongue (lingual thyroid)
- o Can develop same diseases as normal thyroid

Facial Development

Timeline

- End of 4th week: facial prominences appear, mainly neural crest-derived mesenchyme.
 - \circ Maxillary prominences \rightarrow lateral to stomodeum
 - \circ Mandibular prominences \rightarrow caudal to stomodeum
 - \circ Frontonasal prominence \rightarrow above stomodeum (forms upper border)
 - Nasal (olfactory) placodes form on frontonasal prominence under forebrain influence

Nasal Prominences

ullet Week S: nasal placodes invaginate o nasal pits

- Medial nasal prominences → inner edge
- Lateral nasal prominences → outer edge
- Weeks 6-7: maxillary prominences grow medially \rightarrow fuse with medial nasal prominences
 - Cleft between them disappears
 - Forms upper lip:
 - Medial nasal prominences (2) + maxillary prominences (2)
 - Lower lip & jaw → mandibular prominences merge

Nasolacrimal Duct Formation

- Initially: nasolacrimal groove between maxillary & lateral nasal prominences
- Ectoderm in floor \rightarrow solid epithelial cord \rightarrow canalizes \rightarrow nasolacrimal duct
- ullet Lacrimal sac o upper widehed end
- ullet Final position: medial corner of eye ullet inferior meatus of nasal cavity
- Maxillary prominences \rightarrow form cheeks & maxillae

Summary Table: Prominences & Structures

Prominence Structures Formed

Frontonasal Forehead, bridge of nose, medial &

(unpaired) lateral nasal prominences

Medial nasal Philtrum, crest & tip of nose

Lateral nasal Ala of nose

Maxillary Cheeks, lateral upper lip

Mandibular Lower lip, jaw

Mnemonic for nose formation:

"5 Fingers for Nose" \rightarrow 1 frontonasal, 2 medial nasal, 2 lateral nasal prominences

- Exam Points
 - \bullet Foramen cecum \rightarrow thyroid origin

- ullet Thyroglossal duct cyst o midline neck, below hyoid
- Lingual thyroid \rightarrow base of tongue
- Upper lip = 2 medial nasal + 2 maxillary prominences
- Lower lip/jaw = mandibular prominences
- Nasolacrimal duct ightarrow nasolacrimal groove ightarrow canalization

Intermaxillary Segment (IMS)

Formation

- Formed by medial growth and deep fusion of two medial nasal prominences
- Composed of three components:
 - 1. Labial component -> Philtrum of upper lip
 - 2. Upper jaw component \rightarrow carries 4 incisor teeth
 - 3. Palatal component \rightarrow forms triangular primary palate

 Continuous with rostral nasal septum (from frontonasal prominence)

Mnemonic: "Phil In Palate" \rightarrow Philtrum, Incisors, Palate = Intermaxillary segment

Palate Development

Primary Palate

- · Derived from intermaxillary segment
- Forms triangular portion anterior to incisive foramen

Secondary Palate

- Formed by palatine shelves (shelf-like outgrowths of maxillary prominences)
- · Timeline:
 - Week 6: palatine shelves grow downward beside tongue
 - \circ Week 7: shelves ascend above tongue, fuse in midline \rightarrow secondary palate
- Fusion:

- \circ Anterior: with primary palate \rightarrow incisive foramen marks boundary
- Superior: nasal septum grows down and fuses with secondary palate
- 3. Clinical Correlates: Facial Clefts

Cleft Lip & Palate

ullet Incisive foramen o dividing landmark between anterior & posterior clefts

Anterior Clefts (anterior to incisive foramen)

- Structures involved: maxillary prominence + medial nasal prominence
- Examples:
 - Cleft lip
 - Cleff upper jaw
 - Cleft between primary & secondary palate
- ullet Severity: from minor vermilion defect ullet entire maxilla split between lateral incisor & canine

 Epidemiology: ~1/700 births, more common in males (65%)

Posterior Clefts (posterior to incisive foramen)

- Structures involved: palatine shelves
- Examples:
 - Cleft secondary palate
 - · Cleft uvula
- Causes:
 - o Small or underdeveloped palatine shelves
 - o Failure of shelves to elevate
 - Tongue obstructing fusion (micrognathia)
- Epidemiology: ~1/1,500 births, more common in females (55%)

Combination Clefts

- Involve both anterior & posterior regions
- Can affect lip, jaw, primary & secondary palate

Oblique Facial Clefts

- Failure of maxillary prominence to merge with lateral nasal prominence
- · Nasolacrimal duct may be exposed

Median (Midline) Cleft Lip

- Rare
- Caused by incomplete fusion of two medial nasal prominences
- Often associated with cognitive impairment & brain midline defects
- ullet Severe cases ullet holoprosencephaly (fusion of lateral ventricles)
- Induced very early: Days 9-21, during neurulation
- 4. Etiology of Clefts
 - · Multifactorial
 - Types:

- 1. Syndromic \rightarrow associated with genetic syndromes
- 2. Nonsyndromic \rightarrow isolated; may involve IRF6, MSXI
- 3. Teratogenic exposures:
 - Anticonvulsants (e.g., valproic acid)
 - Cigarette smoking during pregnancy

High Points

- Intermaxillary segment \rightarrow philtrum, 4 incisors, primary palate
- ullet Secondary palate o palatine shelves from maxillary prominences
- ullet Incisive foramen o landmark separating anterior & posterior clefts
- Anterior cleft \rightarrow failure of maxillary + medial nasal fusion
- ullet Posterior cleft o failure of palatine shelf fusion
- ullet Oblique cleft o failure of maxillary + lateral nasal

fusion

- ullet Midline cleft o failure of medial nasal prominences, possible holoprosencephaly
- Epidemiology:
 - Cleft lip ± palate → males > females
 - \circ Isolated cleft palate \rightarrow females > males

Nasal Cavities

1. Development of Nasal Cavities

Stage 1: Formation of Nasal Pits

- Week $6 \rightarrow$ nasal pits deepen due to:
 - 1. Growth of surrounding nasal prominences
 - 2. Penetration into underlying mesenchyme

Stage 2: Primitive Nasal Cavities

Initially separated from oral cavity by oronasal membrane

- ullet Breakdown of membrane o formation of primitive choanae
 - Location: behind the primary palate, on either side of midline

Stage 3: Definitive Nasal Cavities

- ullet With secondary palate formation ullet primitive nasal chambers expand
- Definitive choanae shift posteriorly:
 - Final position: junction of nasal cavity & pharynx

2. Paranasal Sinuses

- Develop as diverticula of the lateral nasal wall
- Extend into surrounding bones:
 - Maxilla
 - · Ethmoid
 - Frontal
 - Sphenoid

- ullet Growth: small in childhood \to reach maximum size at puberty
- Function: contribute to final shape of the face

3. Exam Points

- ullet Oronasal membrane o separates nasal pits from oral cavity early
- Primitive choanae → lie behind primary palate
- ullet Definitive choanae o after secondary palate formation, at nasopharyngeal junction
- ullet Paranasal sinuses o develop late, enlarge at puberty
- ullet Clinical importance: their growth ullet contributes to facial contour