

6. Embryology, Epidemiology, Classification

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PART I: EMBRIOLOGY OF THE HEAD AND NECK

Prenatal life

Embryonic period (weeks 1-8)

1. Most organ systems established
2. Most congenital anomalies appear
3. Major features of body form recognizable

Fetal period (weeks 9-40)

Week 1:

Single cell progresses to a multicelled, hollow blastocyst embedded in endometrial stroma. First stages of segmentation of fertilized ovum.

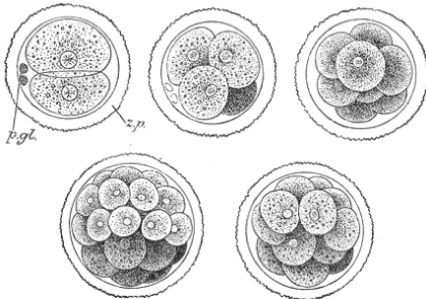


Figure 6-1. First stages of division of mammalian embryo. Henry Vandyke Carter – Henry Gray (1918) *Anatomy of the Human Body*. Bartleby.com: Gray's Anatomy, Plate 9.

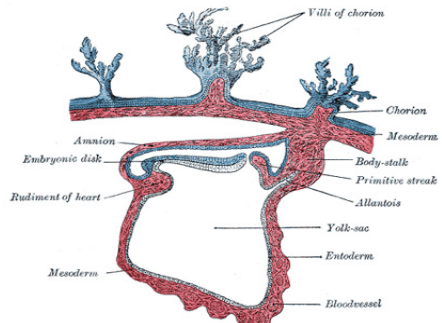


Figure 6-2. Cross section of human embryo. Henry Vandyke Carter – Henry Gray (1918) *Anatomy of the Human Body*. Bartleby.com: Gray's Anatomy, Plate 21.

Week 2:

Bilaminar germ disc is formed with ectoderm and endoderm.

- Anterior and posterior ends
- Dorsal and ventral surfaces

Week 3:

Folding of the Trilaminar Embryonic Germ Disc: Ectoderm, Mesoderm, Endoderm

Ectoderm - Nervous System, Skin, Neural Crest Cells

Mesoderm - Bone, Cartilage, Muscles, Connective Tissue, Dura, Cardiovascular System

Endoderm - Gastrointestinal and Respiratory Lining, Digestive Organs

Notochord - Formed from invaginating cells

Neural folds - Develop above the notochord, fuse to form the neural tube.

Neural crest cells - Form intermediate layer between neural tube and surface ectoderm.

Week 4:

Neural crest cells in the head infiltrate developing pharyngeal (branchial) arch structures, proliferate extensively, and differentiate into mesenchyme, forming the majority of the facial structures.

28 days: 4 well-developed pairs of arches

Pharyngeal arch - Artery, nerve, cartilage, muscle

Pharyngeal cleft - External groove below each arch

Pharyngeal pouch - Internal out-pouching of primitive pharynx

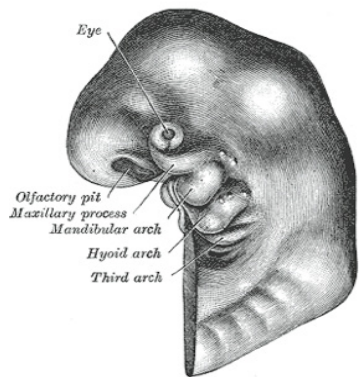


Figure 6-3. Head end of human embryo, end of fourth week. Henry Vandyke Carter – Henry Gray (1918) Anatomy of the Human Body. Bartleby.com: Gray's Anatomy, Plate 41.

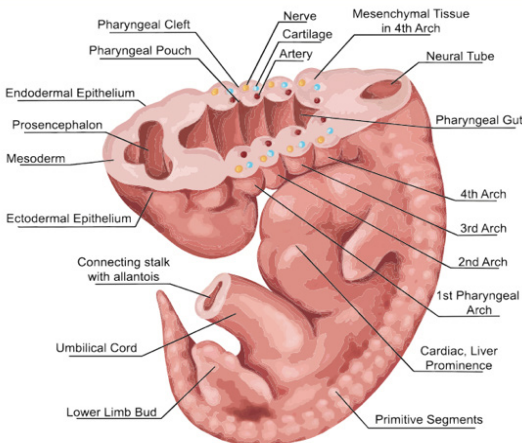


Figure 6-4. Formation of the branchial (pharyngeal) arches in human embryo at five weeks. Medical illustrator stihil / Shutterstock.com

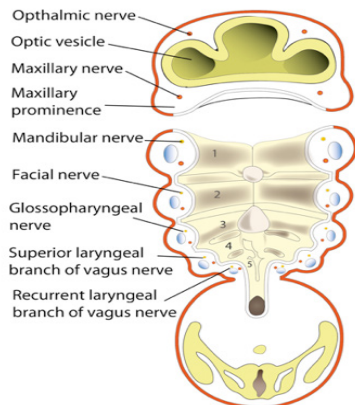


Figure 6-5. Schematic diagram of the pharyngeal arches. © 2017 A Campbell, C Restrepo

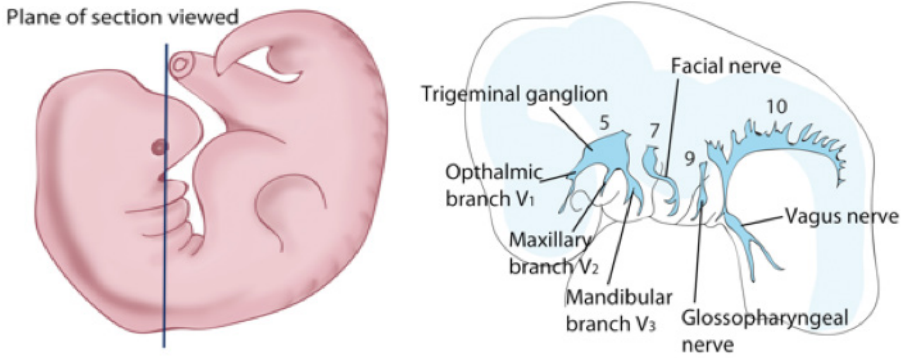


Figure 6-6. Cranial nerves of the (pharyngeal) arches. © 2017 A Campbell, C Restrepo.

BRANCHIAL ARCHES AND THEIR DERIVATIONS IN THE HEAD AND NECK

BRANCIAL ARCH	CRANIAL NERVE	MUSCLES	SKELETAL STRUCTURES
First	V(Mandibular branch)	Muscles of mastication (temporal, masseter, medial and lateral, pterygoid), mylohyoid and anterior belly of digastric; tensor muscle of tympanic membrane and palatine curtain.	Meckel's cartilage, malleus and incus, mandible, sphenomandibular ligament, Reichert's cartilage.
Second	VII	Muscles of facial expressions (cheek, occipitofrontal, auricular, occipitofrontal, platysma, orbicular), stapedius, stylohyoid, posterior belly of digastric).	Stapes, styloid process, lesser cornu of hyoid, upper part of body of hyoid bone, Stylohyoid ligament.
Third	IX	Stylopharyngeal and upper pharyngeal.	Greater cornu of hyoid, lower part of body of hyoid bone Thyroid, arytenoid, corniculate, and cuneiform cartilages.
Fourth, fifth, and sixth	X (superior laryngeal and recurrent laryngeal branch.	Pharyngeal and laryngeal	Thyroid, arytenoid, corniculate, and cuneiform cartilages

Table 6-1. Branchial (pharyngeal) arches with associated nerves, muscles, skeletal derivatives.

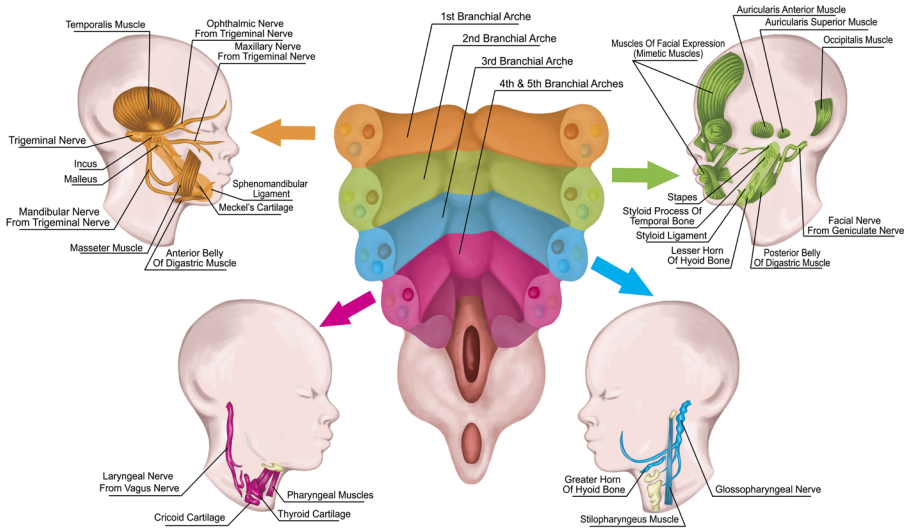


Figure 6-7. The system of branchial (pharyngeal) arches with associated nerves, muscles, skeletal derivatives.
 Medical illustrator stihii / Shutterstock.com

Weeks 4-7: Development of the Face

Prominences

Frontonasal prominence

1. Frontal prominence
 2. Medial nasal prominences
 3. Lateral nasal prominences
- Maxillary prominences (paired)
 Mandibular prominences (paired)

Formation of the Maxilla

Medial nasal prominence of frontonasal prominence fuses with maxillary prominence to form the nasal tip and columella, philtrum, lip, alveolus, and primary palate.
 Lateral nasal prominences of frontonasal prominence become the ala, and are separated from the maxillary prominence by the nasolacrimal groove, which becomes nasolacrimal duct.
 Nasal pits enlarge dorsally to become nasal cavities

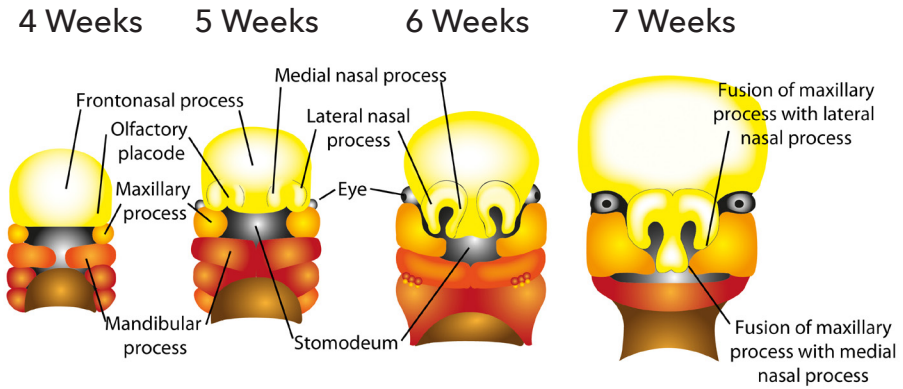


Figure 6-8. Development of the human face. © 2017 A Campbell, C Restrepo

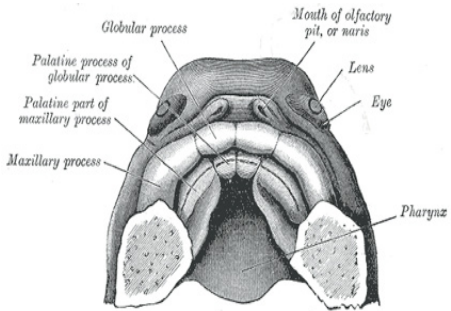


Figure 6-9. Figure 6-9. The roof of the mouth of a human embryo, aged about two and a half months, showing the mode of formation of the palate. Henry Vandyke Carter – Henry Gray (1918) Anatomy of the Human Body. Bartleby.com: Gray's Anatomy, Plate 50.

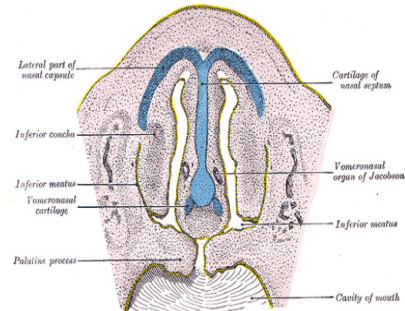


Figure 6-10. Frontal section of nasal cavities of a human embryo 28 mm long. Henry Vandyke Carter – Henry Gray (1918) Anatomy of the Human Body. Bartleby.com: Gray's Anatomy, Plate 51.

Weeks 5-6:

The primary palate (palate anterior to the incisive foramen) forms from the fusion of the medial nasal prominence of frontonasal prominence with the maxillary prominence.

Weeks 9-12:

The secondary palate (hard and soft palate posterior to the incisive foramen) develops from internal projections of the bilateral maxillary prominences called lateral palatine processes. As the mandible develops the tongue drops and the palatine processes grow medially to fuse in the midline. They also fuse with the nasal septum and the primary palate. The nasal cavity becomes divided by a vertical sep-

tum, which extends downward and unites below with the palatine processes.

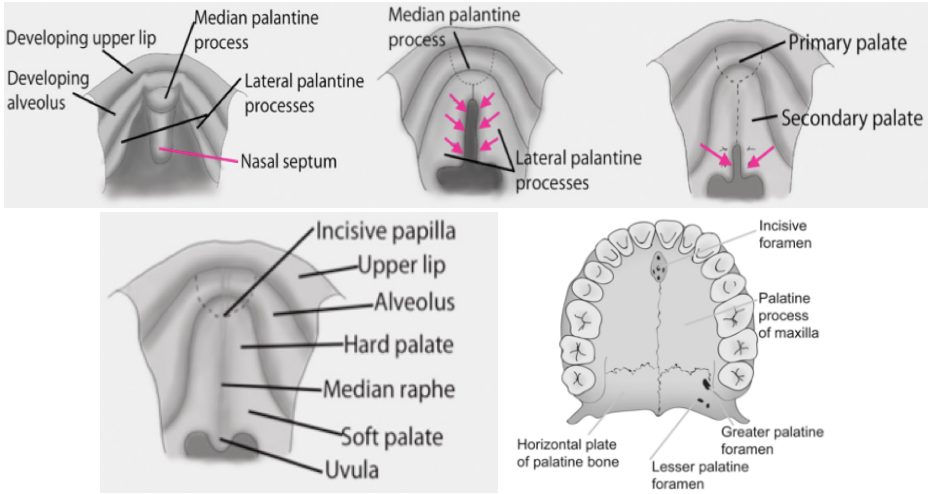


Figure 6-11. Development of the human palate. © 2017 A Campbell, C Restrepo

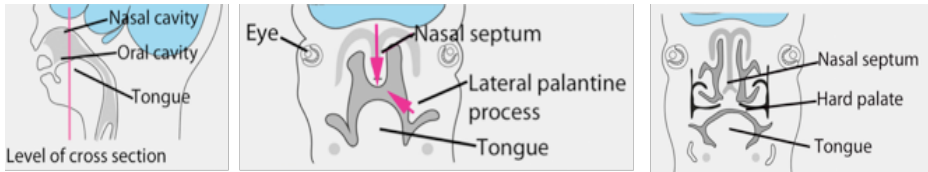


Figure 6-12. The nasal cavity becomes divided by a vertical septum that unites with the palatine processes below. © 2017 A Campbell, C Restrepo

Prominence Derivatives

Frontonasal Prominence

- Forehead
- Apex of Nose

Medial Nasal Prominences

- Primary Palate
- Mid-maxilla
- Mid-lip
- Philtrum
- Central Nose
- Septum

Lateral Nasal Prominences

- Nasal Alae

Maxillary Prominences

- Secondary Palate
- Lateral Maxilla
- Lateral Lip

Mandibular Prominences

- Mandible
- Lower Lip
- Lower Face

FAILURE OF DEVELOPMENT

UNILATERAL CLEFT LIP

- Failure of fusion of the medial nasal process and the maxillary process.

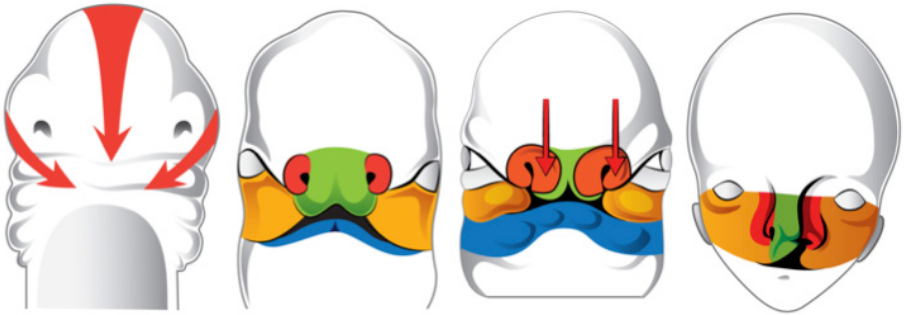


Figure 6-13. A unilateral cleft lip is caused by the failure of fusion of the medial nasal process and the maxillary process on the affected side.

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- Full thickness defect of skin, muscle, mucosa, and bone.

Abnormal Surface Anatomy

- Poorly defined philtral ridge
- Vertical shortness
- Thinning of vermillion

Abnormal Surface Anatomy

- Poorly defined philtral ridge
- Vertical shortness
- Thinning of vermillion
- White roll discontinuous
- Hypoplastic musculature



Figure 6-14. Incomplete unilateral cleft lip.

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Orbicularis Oris Muscle

- Cleft side: Abnormal insertion into alar base
- Noncleft side: Abnormal insertion into nasal spine

Osseous Deformities

- Projection and outward rotation of premaxilla with retropositioning of the lateral maxillary segment

Orbicularis Oris

- Cleft side: Abnormal insertion into alar base
- Noncleft side: Abnormal insertion into nasal spine

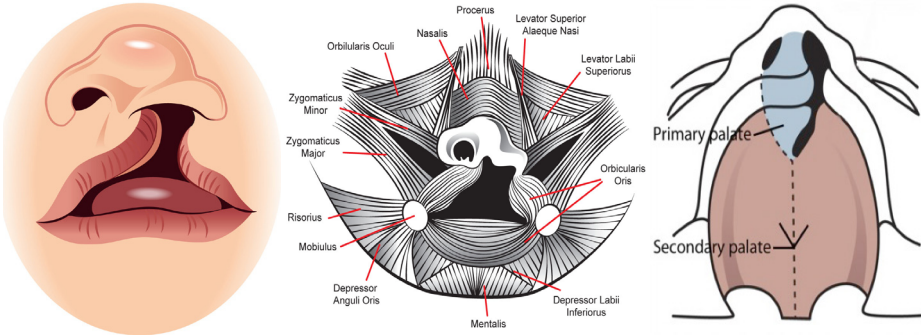


Figure 6-15. A complete unilateral cleft lip involves a full thickness defect of skin/mucosa (A), orbicularis oris muscle (B), and maxillary bone (C) of the anterior cleft palate (anterior to incisive foramen) when palatine shelves fail to fuse with primary palate. © 2017 A Campbell, C Restrepo

Nasal Deformity

- Caudal septum deviated to noncleft side
- Posterior septum convex on cleft side, impinging airway
- Columella shortened, and base deviated to noncleft side
- Nasal tip deviated to noncleft side, dome depressed on cleft side
- LLC attenuated and caudally displaced
 - Medial crura separated at dome from noncleft side
 - Lateral crura flattened and spans cleft in obtuse angle
- Loss of overlap ULC and LLC
- Inferior displacement and hooding of alar rim
- Alar base outwardly rotated, flared, posteriorly displaced, and farther from midline than noncleft side
- Hypoplastic maxilla and posterior displaced piriform margin on cleft side
- Weak or absent alar-facial groove on cleft side
- Widened nostril floor on cleft side
- Vestibular lining deficient on cleft side

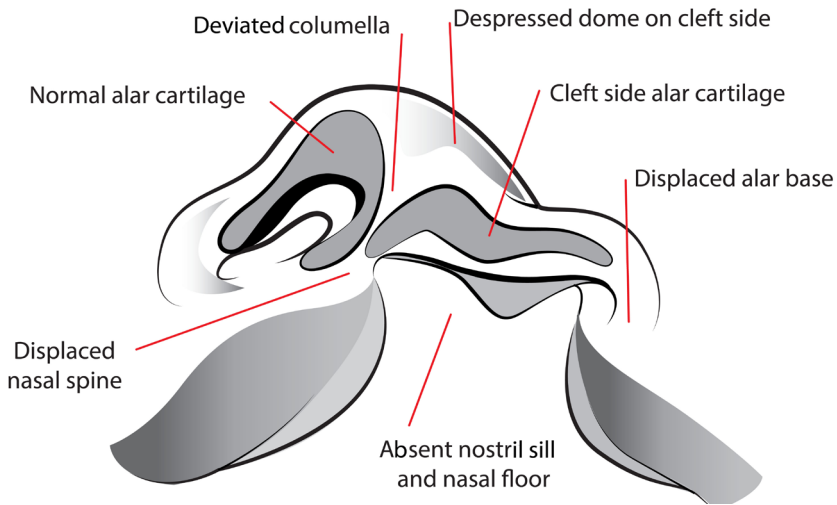


Figure 6-16. Nasal deformity associated with unilateral cleft lip. © 2017 A Campbell, C Restrepo

BILATERAL CLEFT LIP

- Failure of maxillary processes to meet and unite with medial nasal processes with on both sides.

Bilateral Cleft Lip Anatomy

- Bilateral cleft lip deformity
- Orbicularis inserts into alar base bilaterally.
- Paucity of tissue of the central lip element
- Absent muscle in central lip element
- Inadequate or diminutive columella
- Limited blood supply to the prolabium
- Osseous Deformities
- Premaxilla outwardly rotated / projecting



Figure 6-17. Complete bilateral cleft lip.
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- Lateral maxillary elements retro-positioned and collapsed medially

CLEFT PALATE

- Failure of fusion of the palatal processes of the two maxillary processes

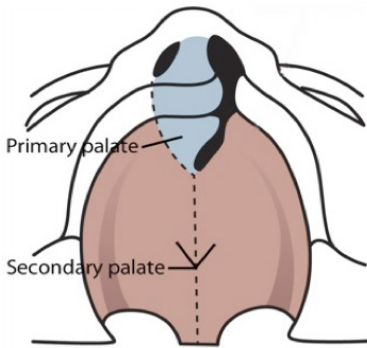


Figure 6-18. Complete cleft of primary palate.

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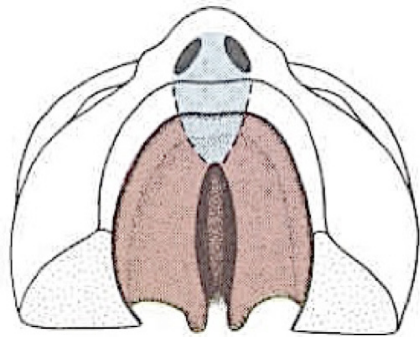


Figure 6-19. Complete cleft of secondary palate.

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Primary Palate Clefts

- Can involve lip, nostril sill, alveolus, and/or hard palate anterior to incisive foramen
- Complete vs Incomplete
- Unilateral vs Bilateral
- Submucous Cleft

Secondary Palate Clefts

- Hard palate posterior to incisive foramen and/or soft palate
- Complete vs Incomplete
- Cleft Velum

PART II: EPIDEMIOLOGY OF CLEFT LIP AND PALATE

Epidemiology

Overall incidence around 1 in 700 live births; varies by racial group

- 1 in 1,000 births in whites
- 1 in 500 births in Asians and Native Americans
- 1 in 2,400 to 2,500 births in people of African descent

Cleft Lip & Palate - 46%; M:F 2:1

Isolated Cleft Palate - 33%; M:F 2:1

Isolated Cleft Lip - 21%

6:3:1 - Unilateral Left CL : Unilateral Right CL : Bilateral CL

Predisposing Factors

- Prenatal Nutrition (folic acid)
- Smoking (2x)
- Alcohol
- Social Class
- Parental age > 30
- Altitude

- Anticonvulsants (10x)
- Retinoic acids
- Infections (rubella, toxo)
- Oligohydramnios
- GH deficiency
- Pituitary insufficiency

Genetic Models

- Multifactorial Model: genetic susceptibility governed by many genes and their interaction with environmental variables
- Cleft lip (with or without cleft palate) is an embryologically, anatomically, and genetically distinct entity from isolated cleft palate.

Malformations Associated with Cleft Lip and Cleft Palate

- Incidence in CL/CP (14%)
- Incidence in isolated CP (42%)
- Central nervous system, club foot, cardiac anomalies

Syndromes

- 3% associated with síndrome
- More common with isolated CP than CL/CP
- > 154 syndromes
- Stickler syndrome (17.5%) most commonly recognized

Van der Woude's Syndrome

- Autosomal dominant (risk 50%)
- Lower lip pits, CL+/- P, absent 2nd molars
- 70-80% penetrance

PART III: CLASSIFICATION OF CLEFT LIP AND PALATE

Classification of Cleft Lip

1. Lip
2. Alveolus
3. Hard palate
4. Soft palate

Unilateral vs Bilateral
Incomplete vs Complete
Cleft Lip +/- Cleft Palate

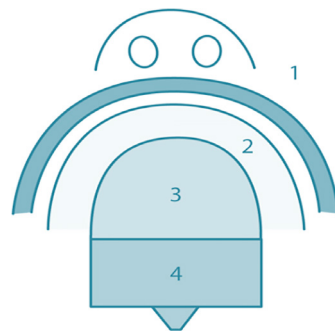


Figure 6-20. Classification schematic of cleft lip and cleft palate, which can involve the lip (1), alveolus (2), hard palate (3), and soft palate (4). © 2017 A Campbell, C Restrepo

MICROFORM (FORME FRUSTE) CLEFT LIP

- Mild Incomplete Cleft
- Vertical furrow extending from vermillion to nasal floor
- Notch in vermillion border
- Varying degrees of vertical lip shortness
- + / - Alar deformity

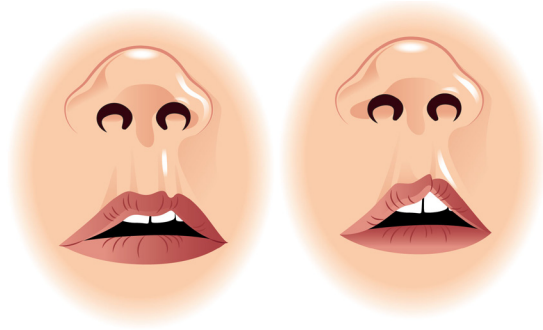


Figure 6-21. Micrform cleft lip. © 2017 A Campbell, C Restrepo

UNILATERAL INCOMPLETE CLEFT LIP

UNILATERAL COMPLETE CLEFT LIP

UNILATERAL COMPLETE CLEFT LIP AND CLEFT PALATE

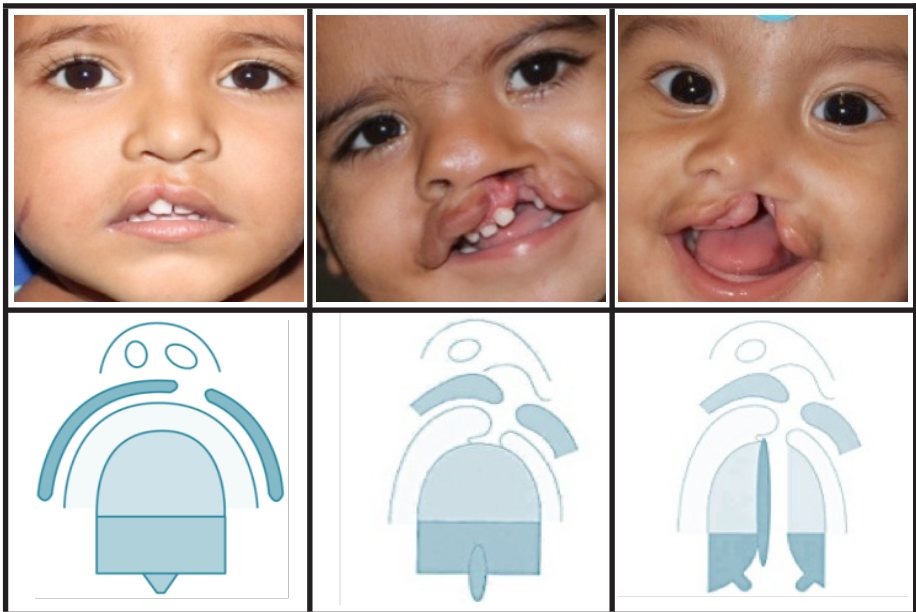


Figure 6-22. Unilateral incomplete cleft lip involving skin, muscle, and mucosa. © 2017 A Campbell, C Restrepo

Figure 6-23. Unilateral complete cleft lip involving skin, muscle, mucosa, alveolus, and primary palate. © 2017 A Campbell, C Restrepo

Figure 6-24. Unilateral complete cleft lip involving skin, muscle, mucosa, primary palate, and secondary palate. © 2017 A Campbell, C Restrepo

**BILATERAL INCOMPLETE
CLEFT LIP**

BILATERAL COMPLETE CLEFT LIP

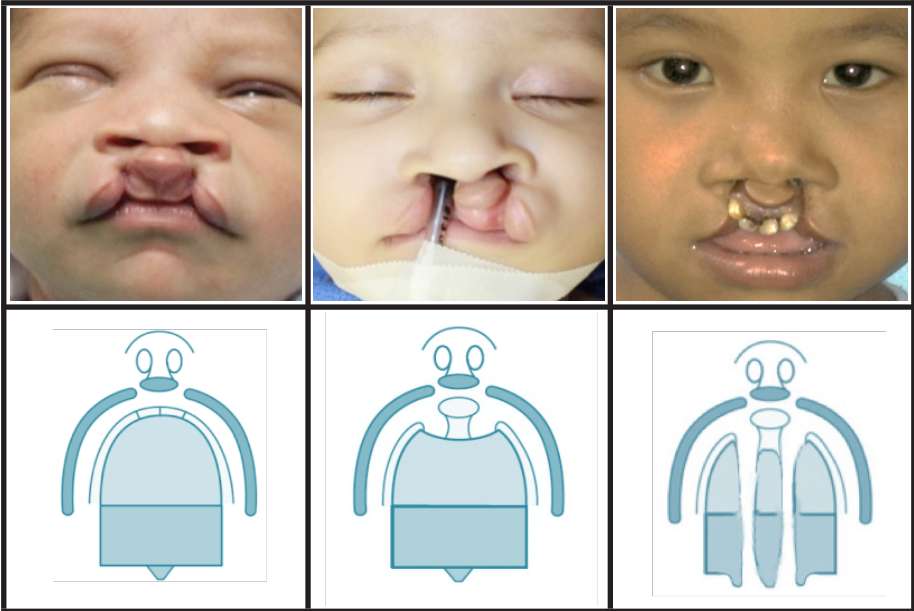


Figure 6-25. Bilateral incomplete cleft lip involving skin, muscle, mucosa, and alveolus.
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Figure 6-26. Bilateral complete (asymmetric) cleft lip involving skin, muscle, mucosa, and alveolus.

Figure 6-27. Bilateral complete cleft lip involving skin, muscle, mucosa, alveolus, primary and secondary palate, with protrusive premaxilla.
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1 Normal Lip

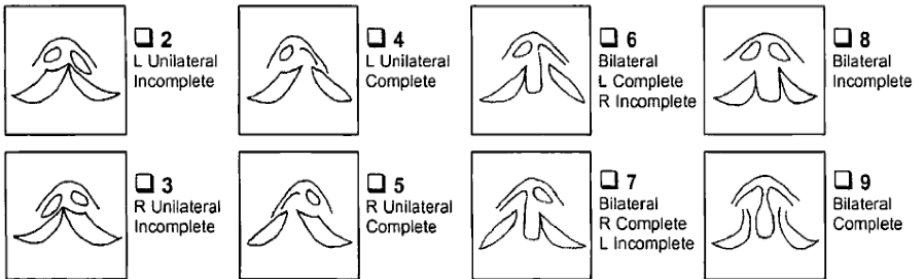


Figure 6-28. Operation Smile classification system cleft lip. Adapted from the Operation Smile Medical Record.

Classification of Cleft Palate

Veau Classification	
CLASS	SITE INVOLVED
I	Soft palate
II	Soft palate and hard palate
III	Soft palate and hard palate and unilateral cleft of primary palate
IV	Soft palate and hard palate and bilateral cleft of primary palate

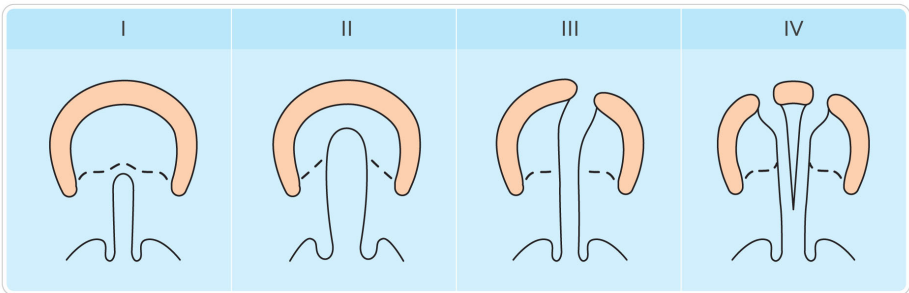


Figure 6-29. Veau classification of cleft palate. © 2017 A Campbell, C Restrepo

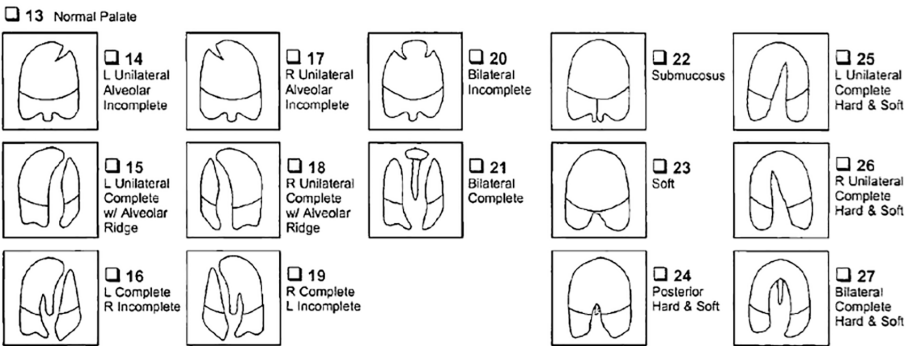


Figure 6-30. Operation Smile classification system cleft palate. Adapted from the Operation Smile Medical Record.

KEY READING

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3. Embryology. In Grey H and Lewis W: Grey's Anatomy 12th Edition. Philadelphia: Lea & Febiger, 1918. New York, Bartleby.com, 2000. Available at: <http://www.bartleby.com/107/>