Pharyngeal arches
Tongue and Salivary glands development

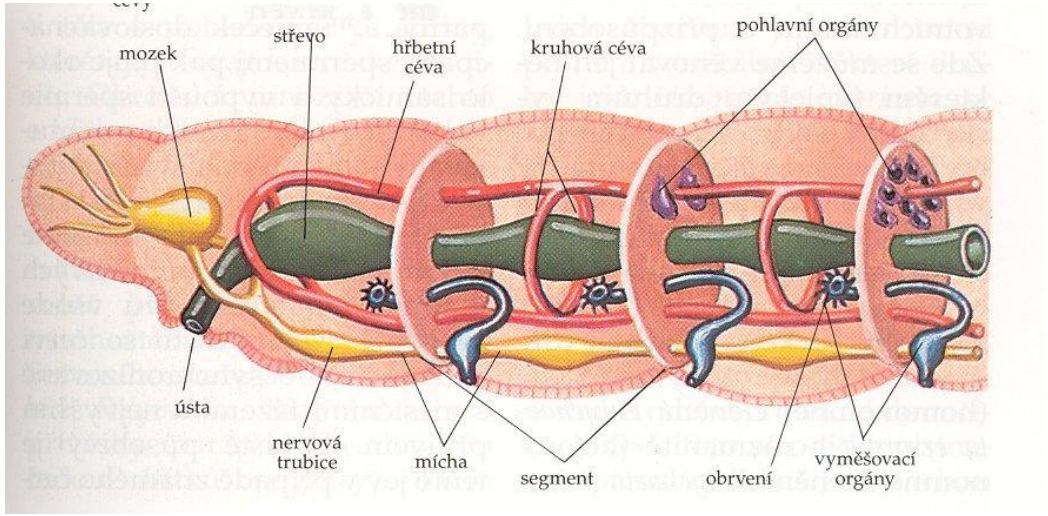
Face development and defects

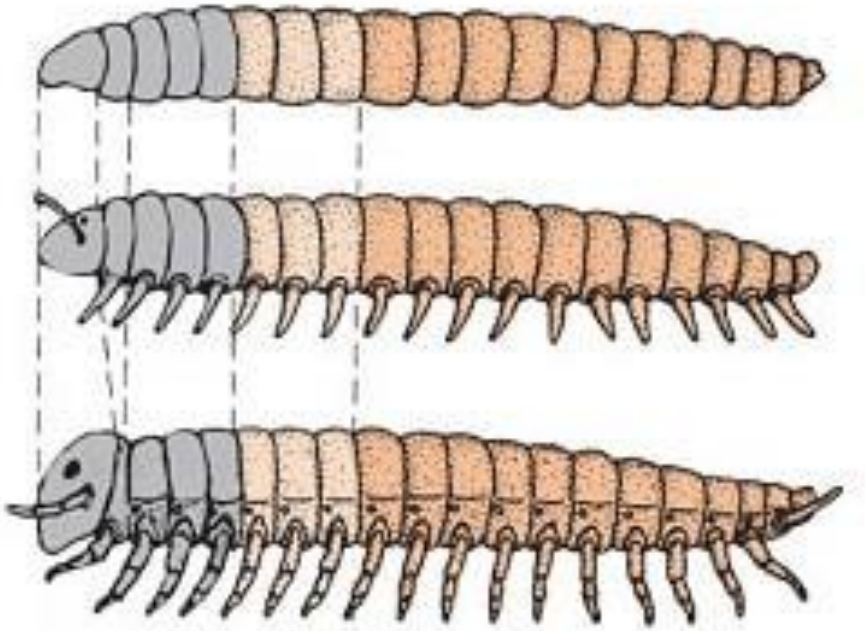
(face, jaws, palates, nose)

5. 5. 2022

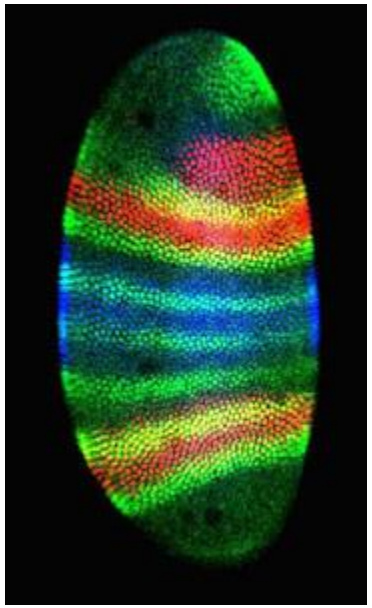
Jan Křivánek

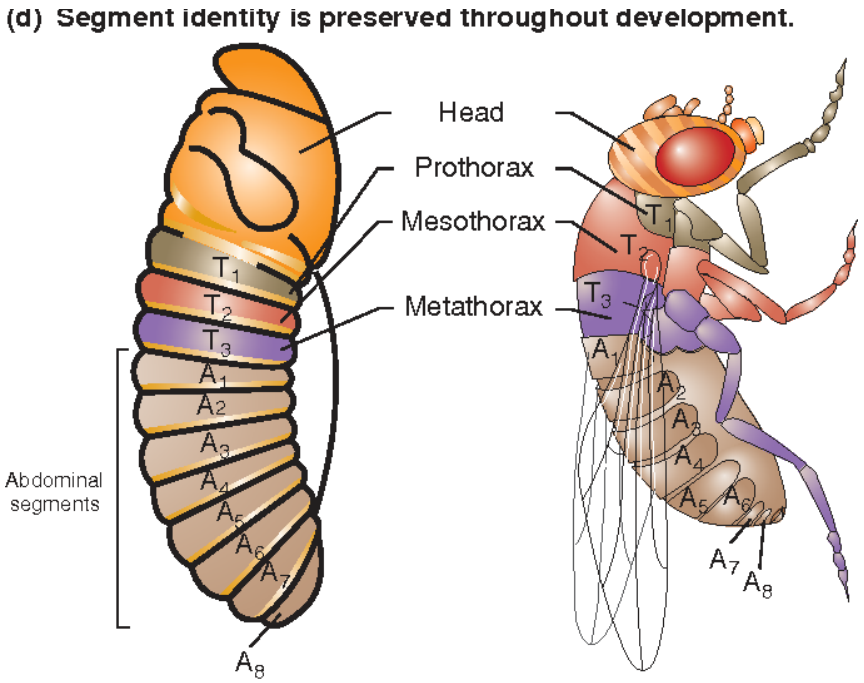
Body segmentation

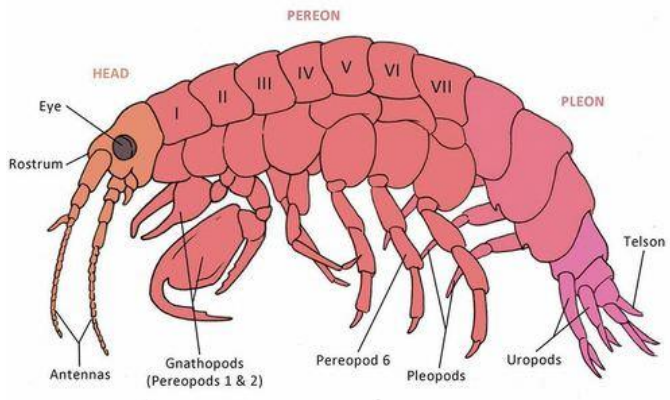


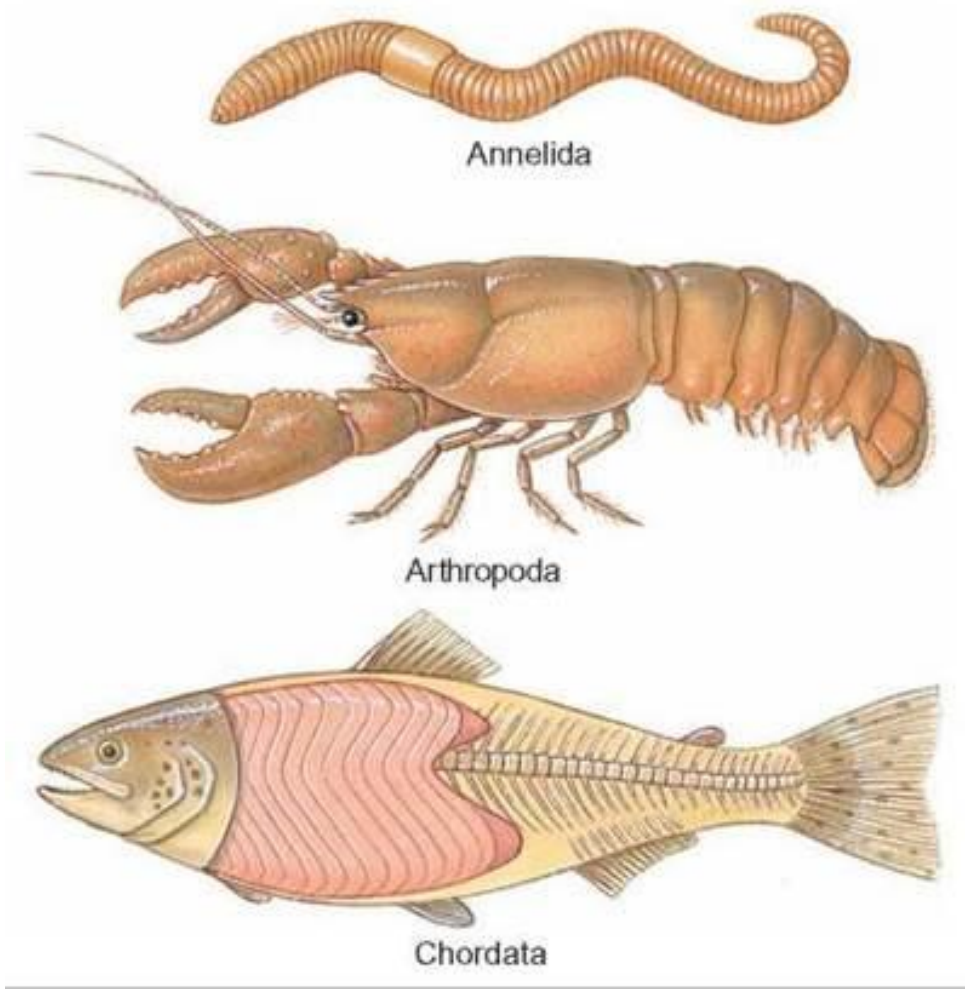


Body segmentation

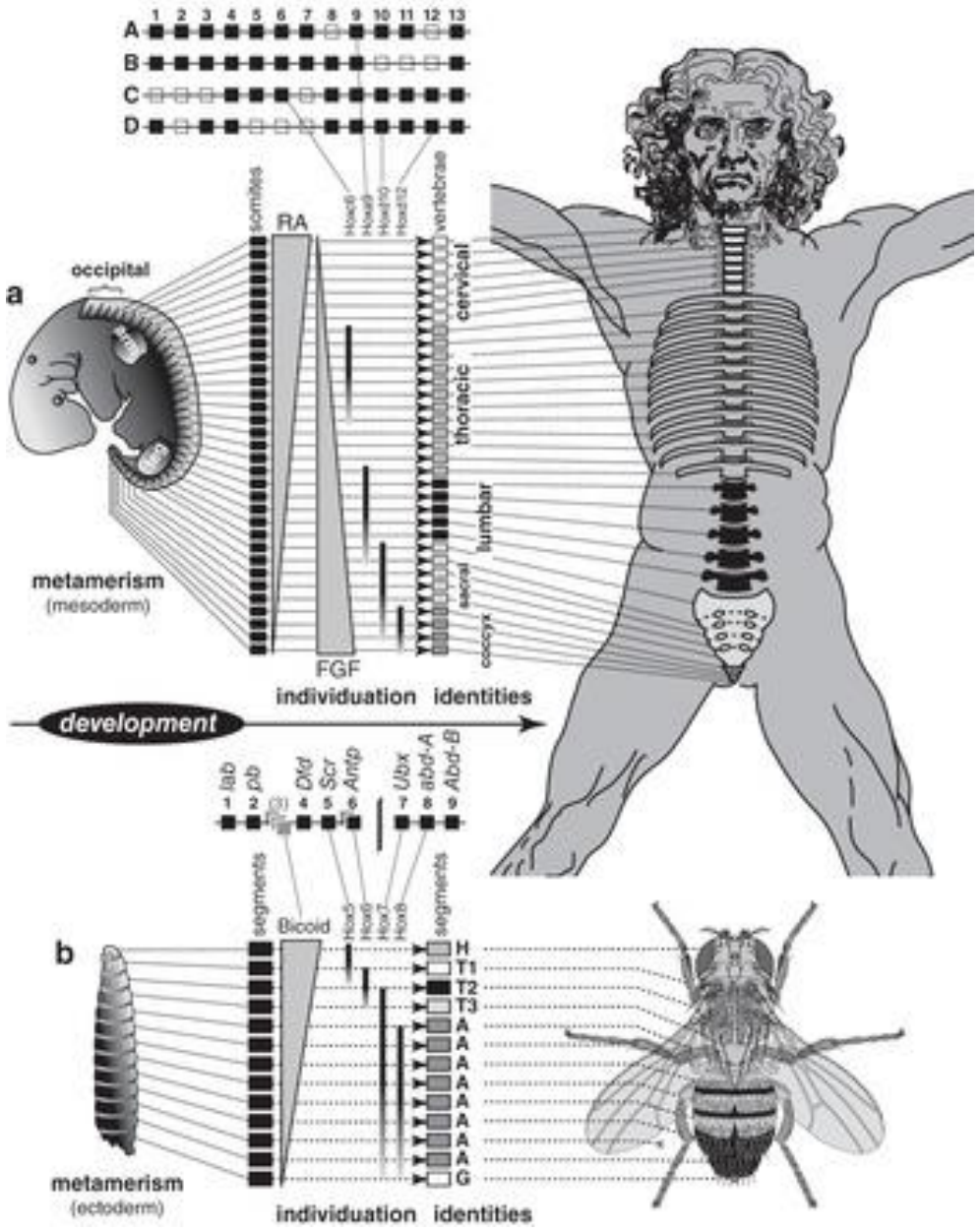








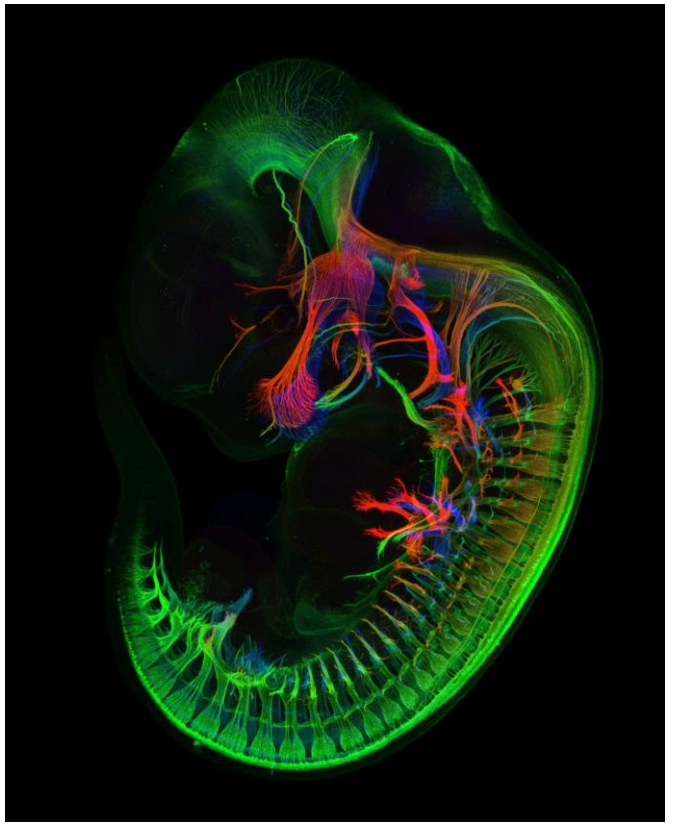
Body segmentation – is a human body segmented?



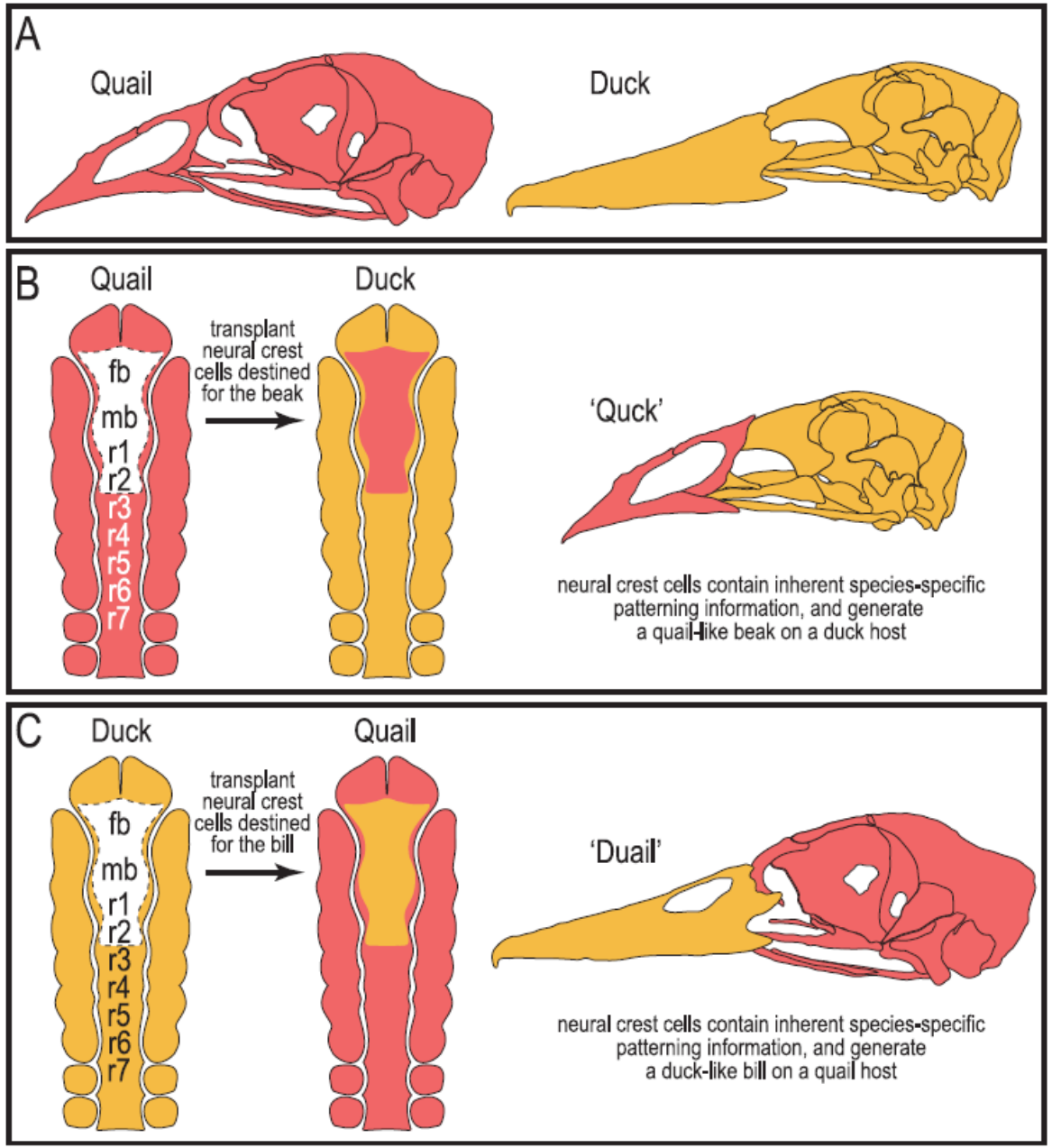
The same segmentation pattern as in a primitive species

The same signalling pathways

We are the result of minor changes in signalling pathways and its final tuning



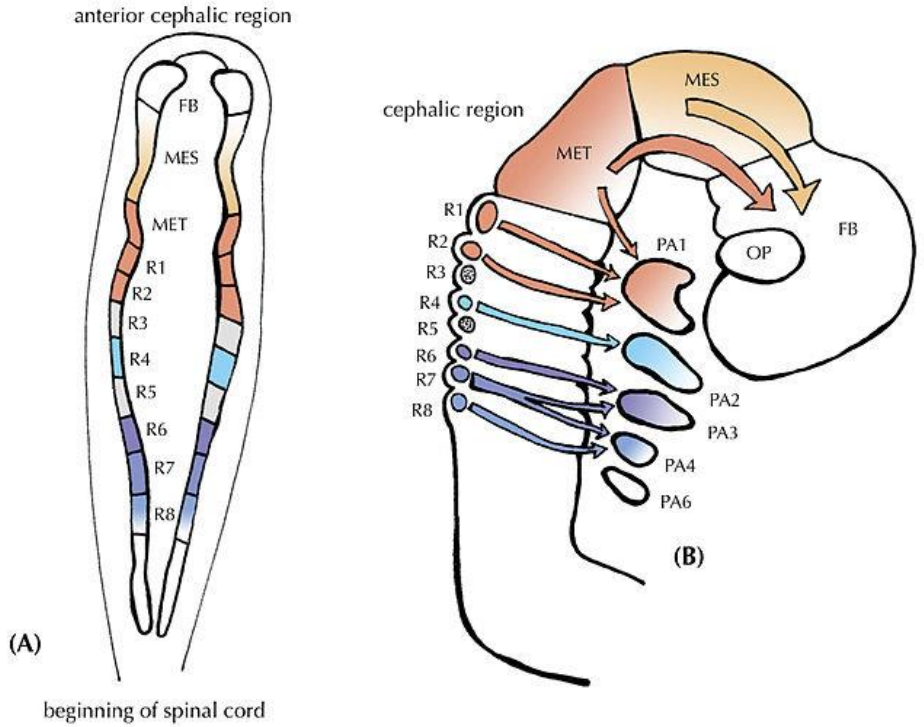
Face development – Neural crest

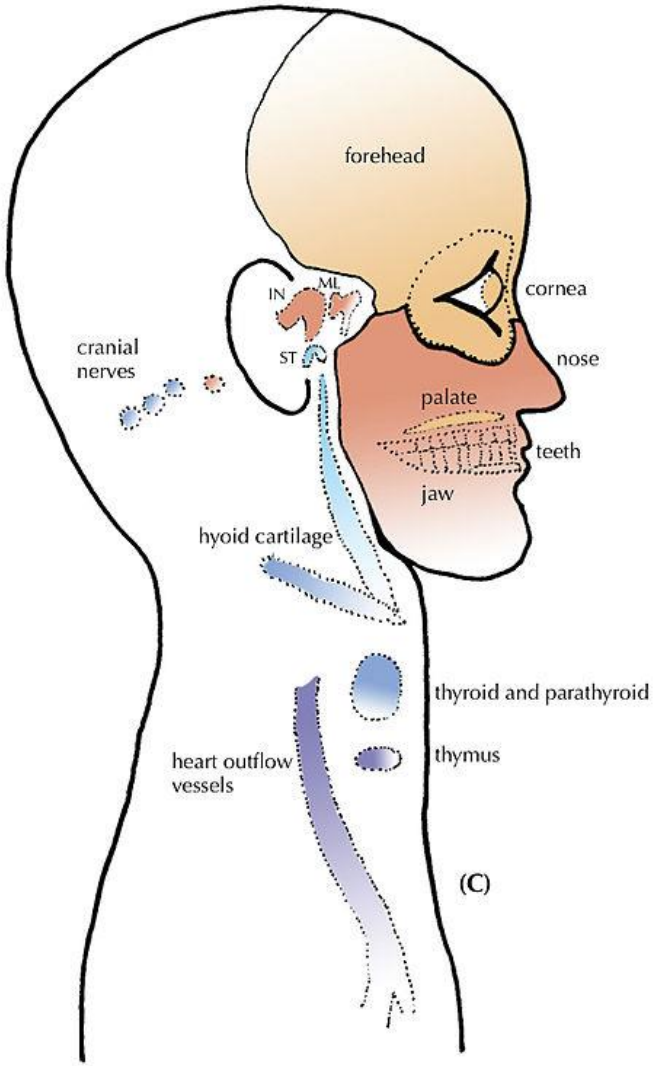


Doc. Petr Vaňhara

Neural crest

Figure 1. The sites of origin, migration, and arrival of cranial neural crest cells. (A) Embryonic neural tube showing the mesencephalon, metencephalon, and rhombomeres, with the dorsal face of tube coloured to show the location of neural crest before migration. (B) Sagittal view of embryo, showing paths of migration of cranial crest cells. (C) Sagittal view of adult human, showing the origins of various cranial crest derivatives.





MES mesencephalon
MET metencephalon
FB forebrain
OP optic vesicle
R1 rhombomere 1
R2 rhombomere 2
R3 rhombomere 3
R4 rhombomere 4
R5 rhombomere 5
R6 rhombomere 6
R7 rhombomere 7
R8 rhombomere 8
PA1 first pharyngeal arch
PA2 second pharyngeal arch
PA3 third pharyngeal arch
PA4 fourth pharyngeal arch
PA6 sixth pharyngeal arch
IN incus
ML malleus
ST stapes

Origin of structures in adult organism

- Frontonasal process
- First pharyngeal arch
- Second pharyngeal arch
- Third pharyngeal arch
- Fourth pharyngeal arch

Development from zygote

https://www.youtube.com/watch?v=1zpV5rzWXMA&ab_channel=GetAnimatedMedical

Face development

https://www.youtube.com/watch?v=FhhWG3XzARY&ab_channel=FacultyofDentistry%2CUniversityofToronto

https://www.youtube.com/watch?v=iLbqzTlZ6yA&ab_channel=Osmosis

Pharyngeal arches

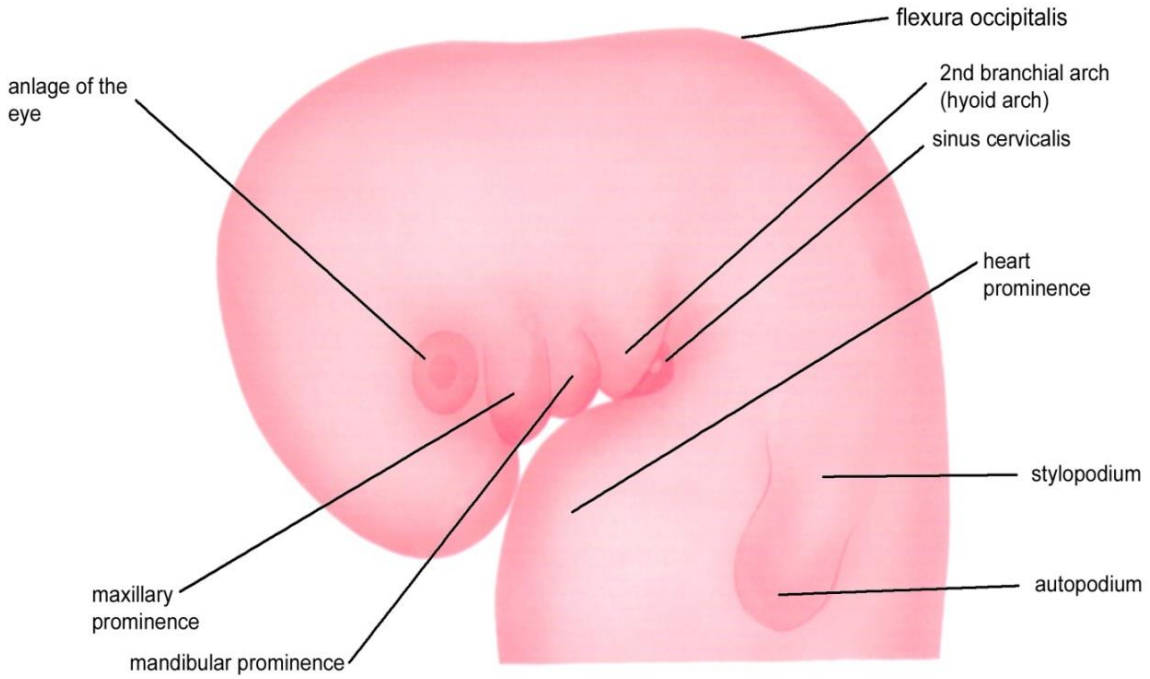
https://www.youtube.com/watch?v=oP1-ejJdZyc

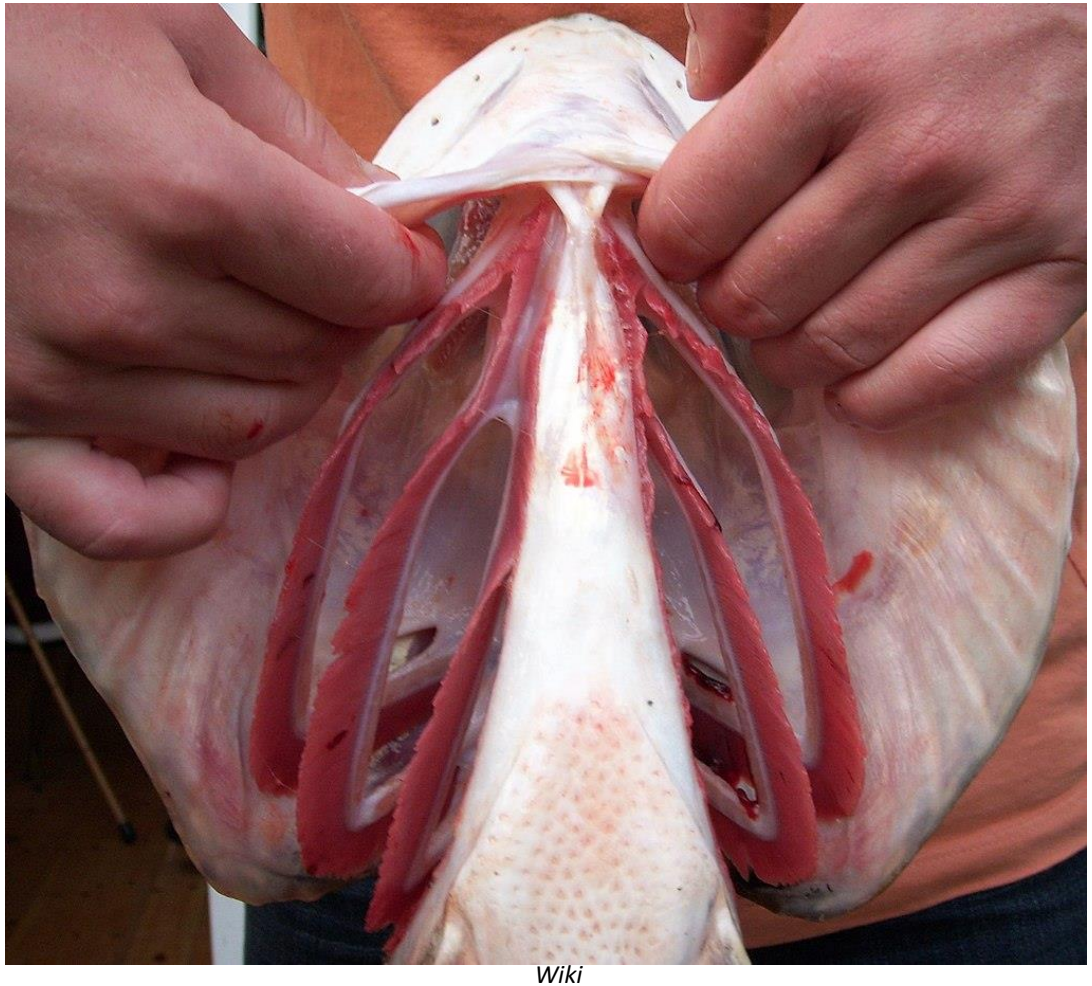
Pharyngeal arches

Phylogenetically conserved organ, serves as a carrier for gills (which work as a respiratory organ)

First appears in sharks, around the pharyngeal gut

In vertebrates, transforms and forms the basis of important organs - branchiogenic organs





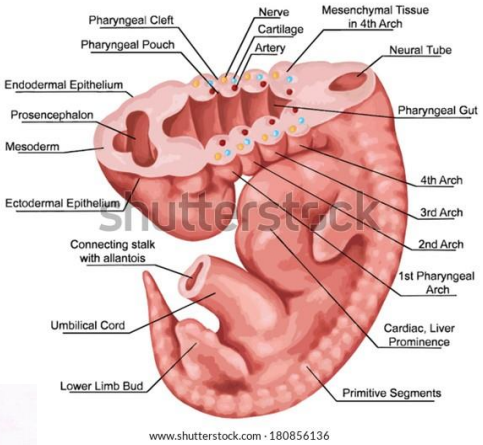
Wiki

Pharyngeal arches

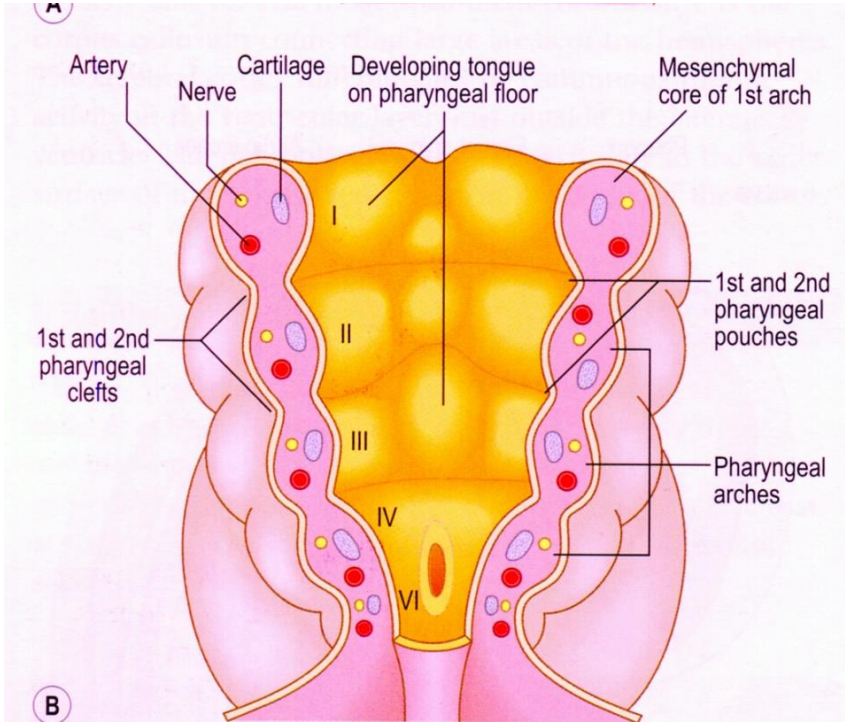
The pharyngeal apparatus starts to develop in human embryos in the neck region behind the frontal (frontonasal) prominence in the second half of the 4th week

Pharyngeal arches	6
Pharyngeal pouches (entodermal)	5
Pharyngeal clefts (grooves) (ectodermal)	4
Membranae obturantes	4

All structures are paired



Derivates of pharyngeal folds	Arch number	Aortic arch	Cranial nerv	Examples of branchiomeric muscles	Skeletal derivates	Derivates of pharyngeal pouch
external auditory meatus	I mandibular	maxillary artery	V trigeminal	muscles of mastication etc.	malleus,incus spheno-mandibular lig. Meckel cart.	I middle ear auditory tube
	II hyoid	hyoid, stapedia artery	VII facial	muscles of facial expression etc.	stapes, styl. proc., stylohyoid lig., part of hyoid cart.	II supra-tonsillar fossa
neck	III	internal carotid artery	IX glosso-pharyng.	m. stylopha-ryngeus	parts of hyoid cart.	III thymus, parathyr. gland
	IV	right subclavian artery, aorta	X vagus	pharyngeal and laryngeal musculature	laryngeal cart.	IV thymus parathyr. gland ultimobranch. body

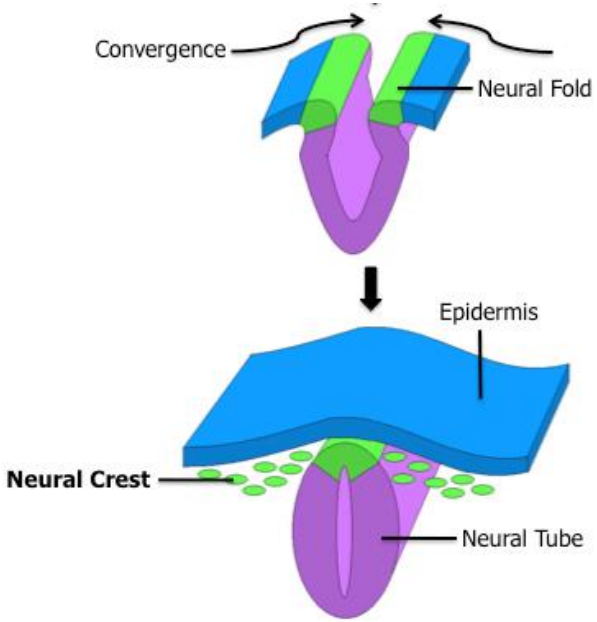


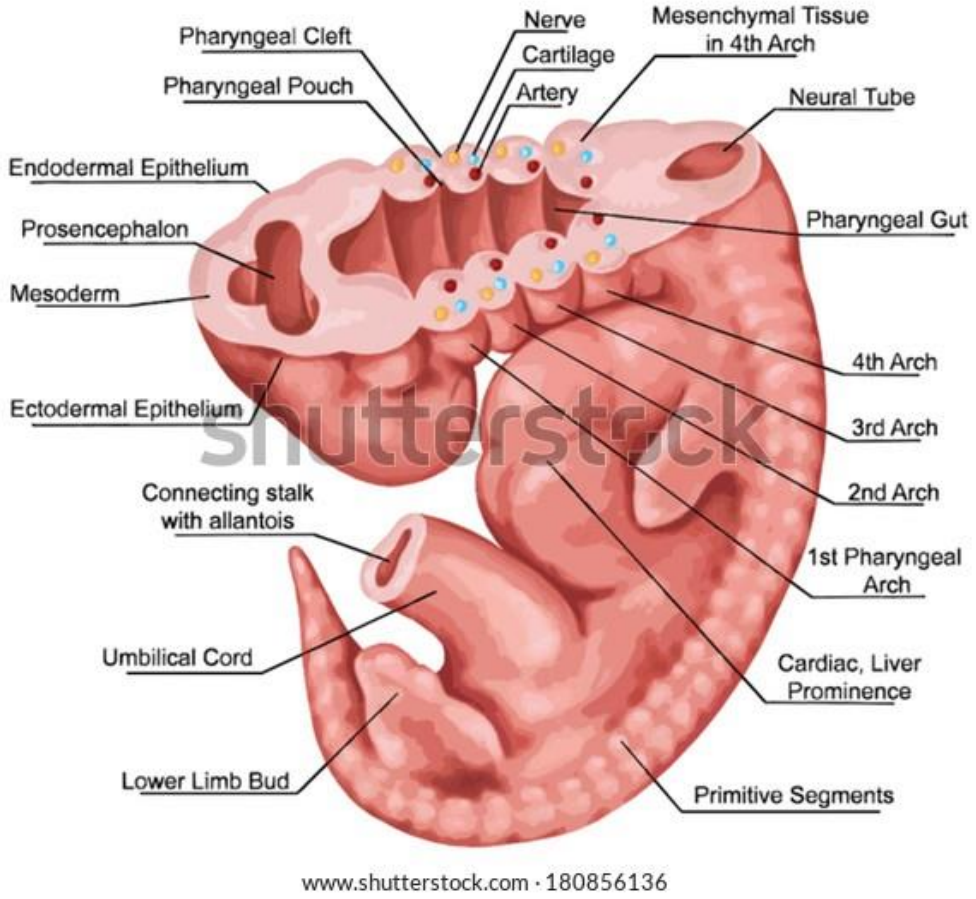
Pharyngeal (branchial) arches (6)

The first four - cause a obvious segmented structure of the neck (5th and 6th are rudimentary)

Cells of the **mesencephalic and rhombencephalic part of neural crest migrate** into the paraaxial mesoderm of the first cervical somites and contribute to formation on arches and subsequently organs

The formation of pharyngeal arches is controlled by the endoderm of the pharyngeal arches



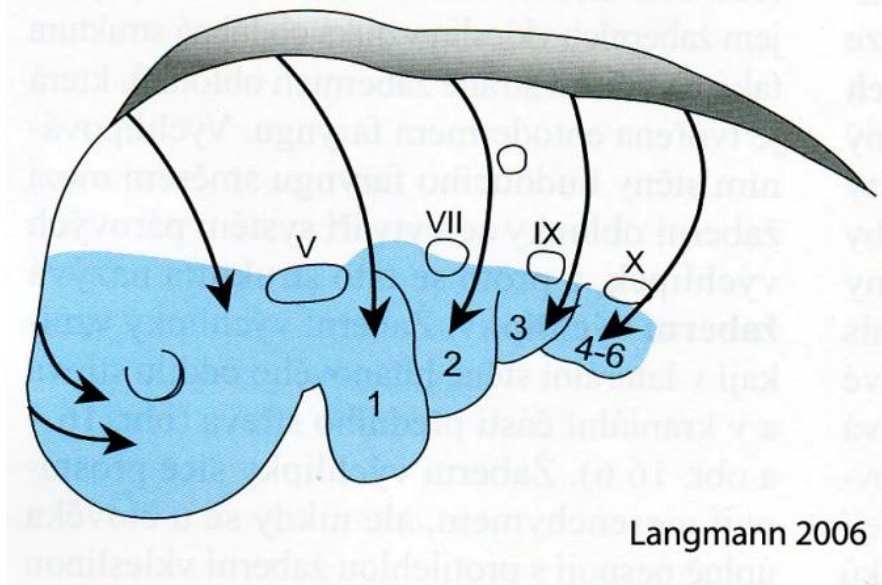


Ectomesenchymal derivatives: ligaments, cartilages, bones

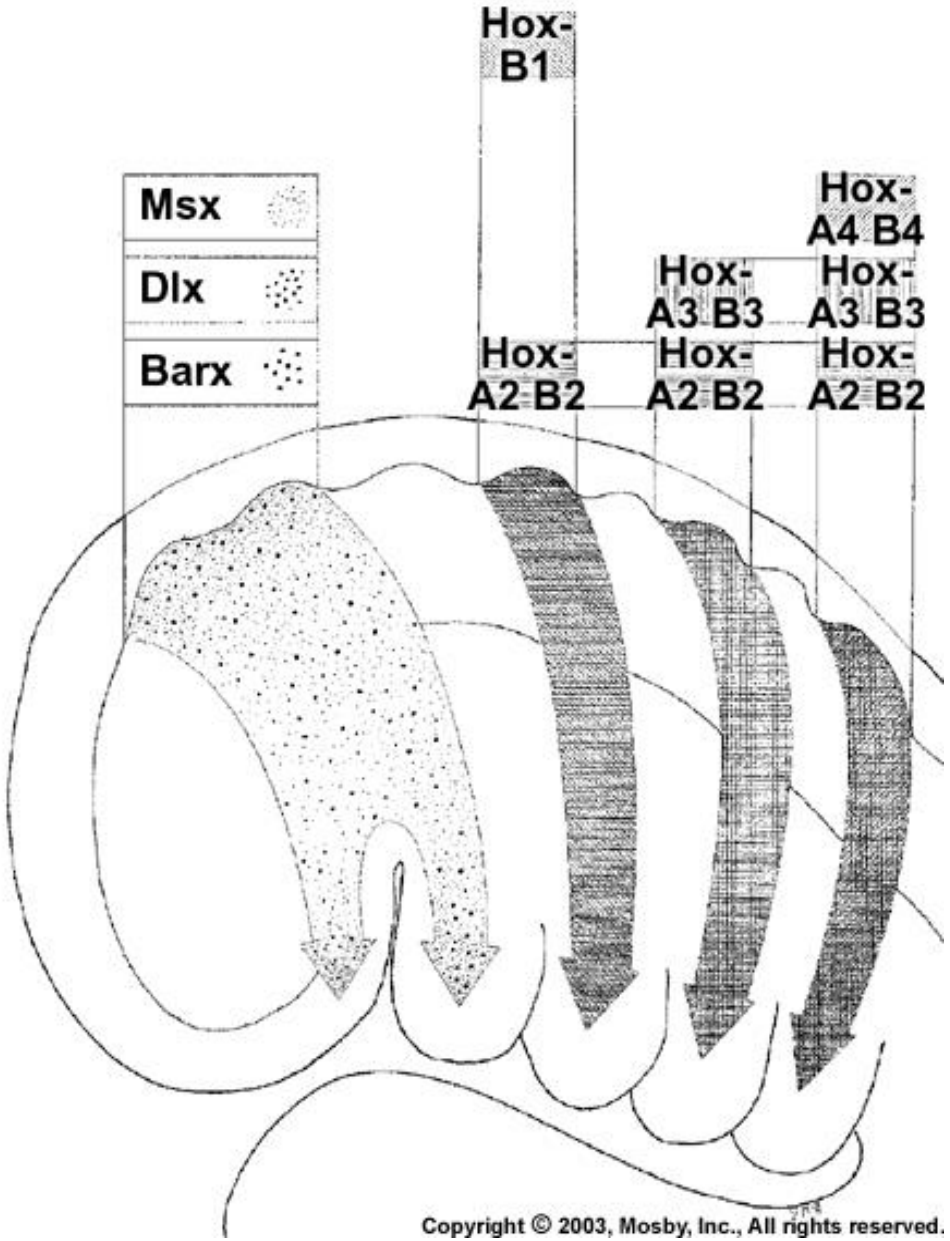
Paraaxial mesoderm derivatives: muscles of pharyngeal arches and branchial arteries

Migration of neural crest (ectomesenchyme) in several migratory pathways

Controled by **Hox genes** which regulate expression of transcription factors with effectory function



Langmann 2006

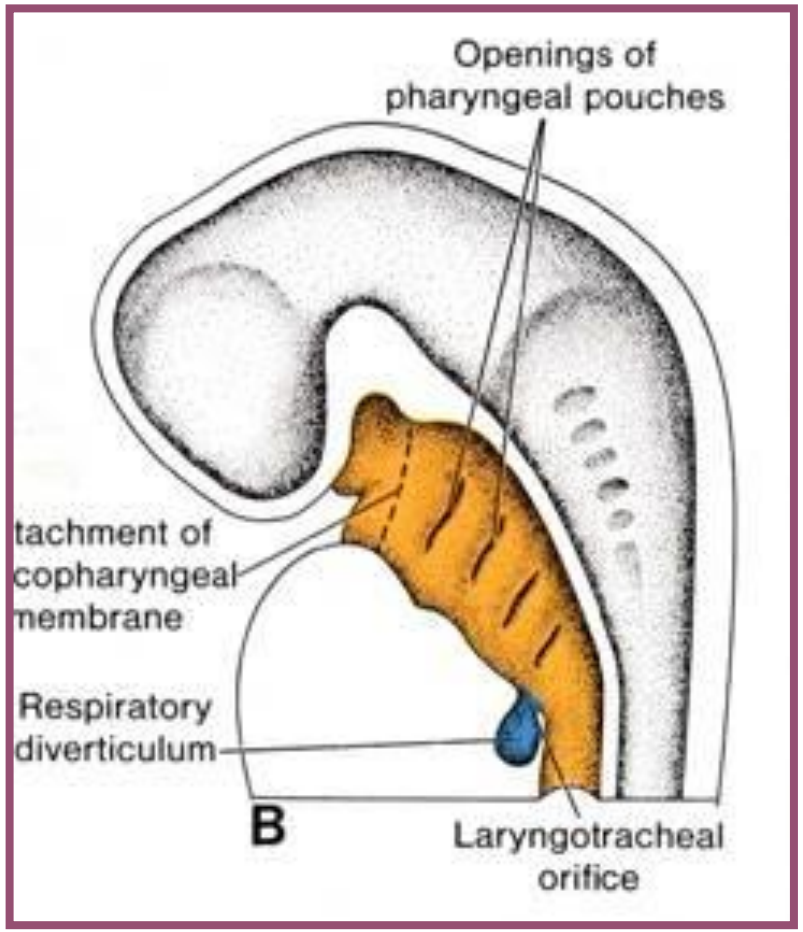


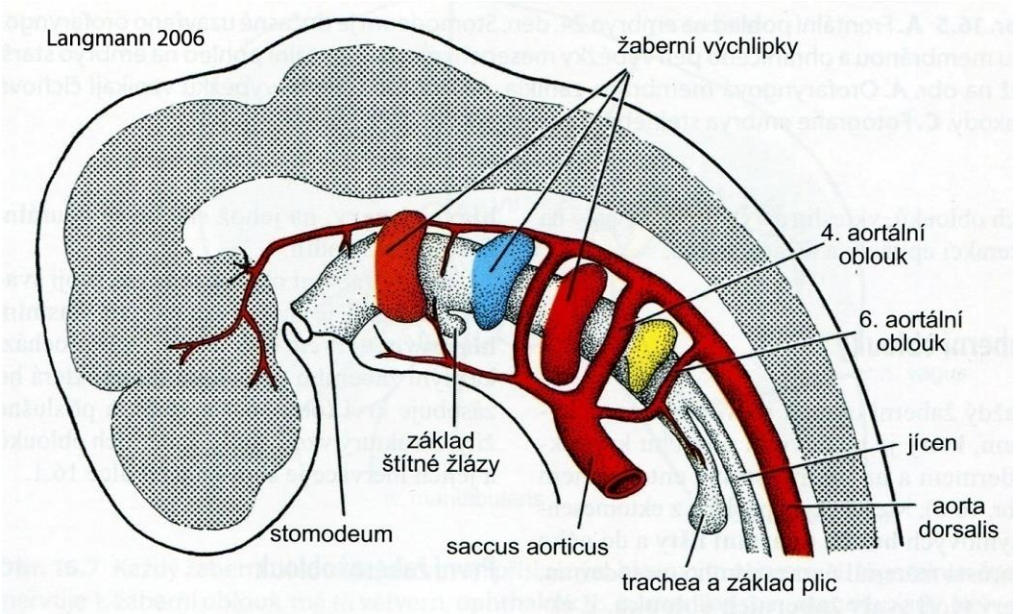
Pharyngeal pouches - 5

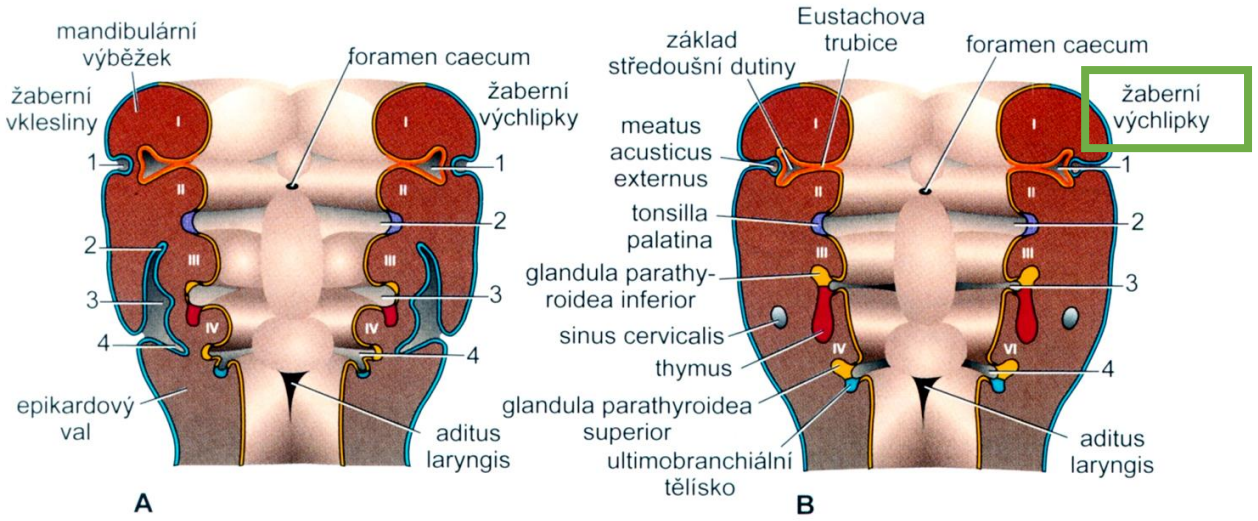
The first starts to develop on the stage of 5 somites

The 5th is rudimentary and develops as a part of the fourth pouch at end of the 1st month

Endodermal origin







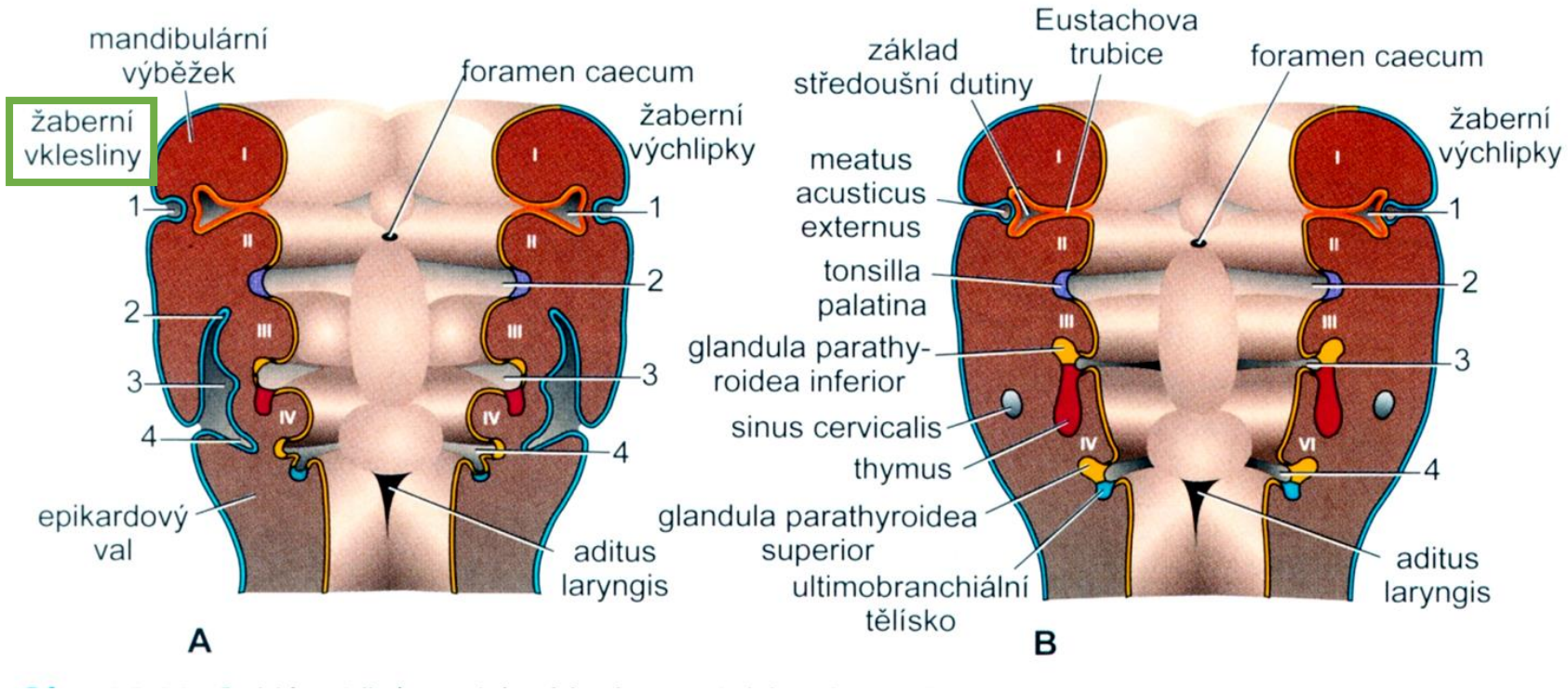
Pharyngeal clefts - 4

They have the form of shallow grooves

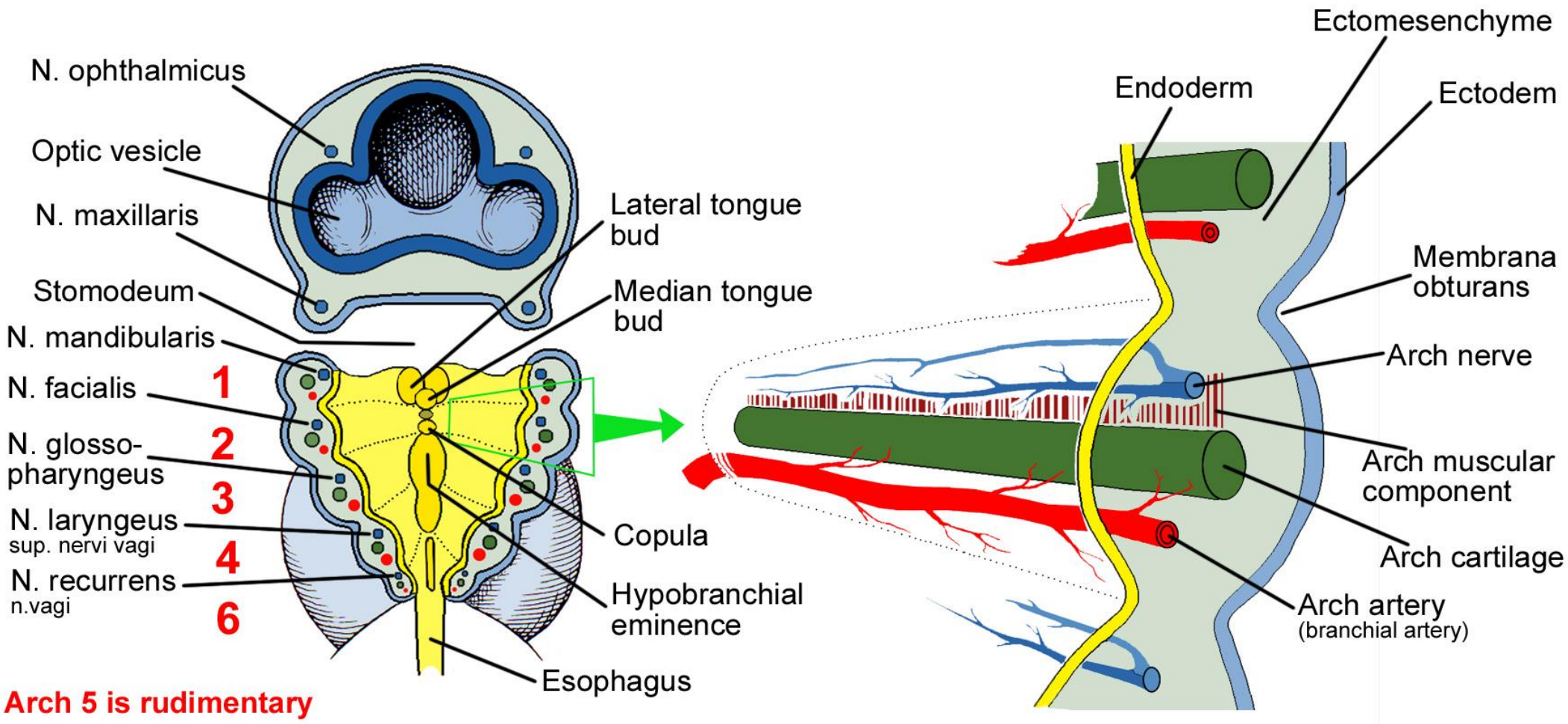
ectoderm origin

Membranae obturantes - 4

Two-layer memranes that separate each ectoderm and entoderm groove (physiologically do not perforate in humans)



Frontal section through apparatus and branchial arch components



In each arch is:

Cartilage

Skeletal muscle basis (mezoderm)

Arch artery

Branchial arch nerve

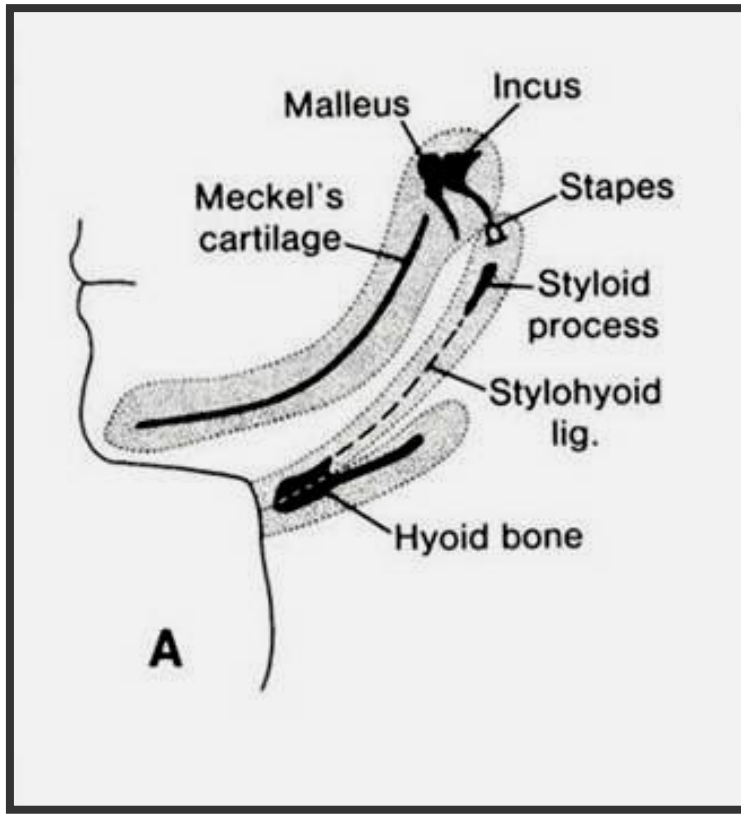
1. Pharyngeal arch (mandibular)

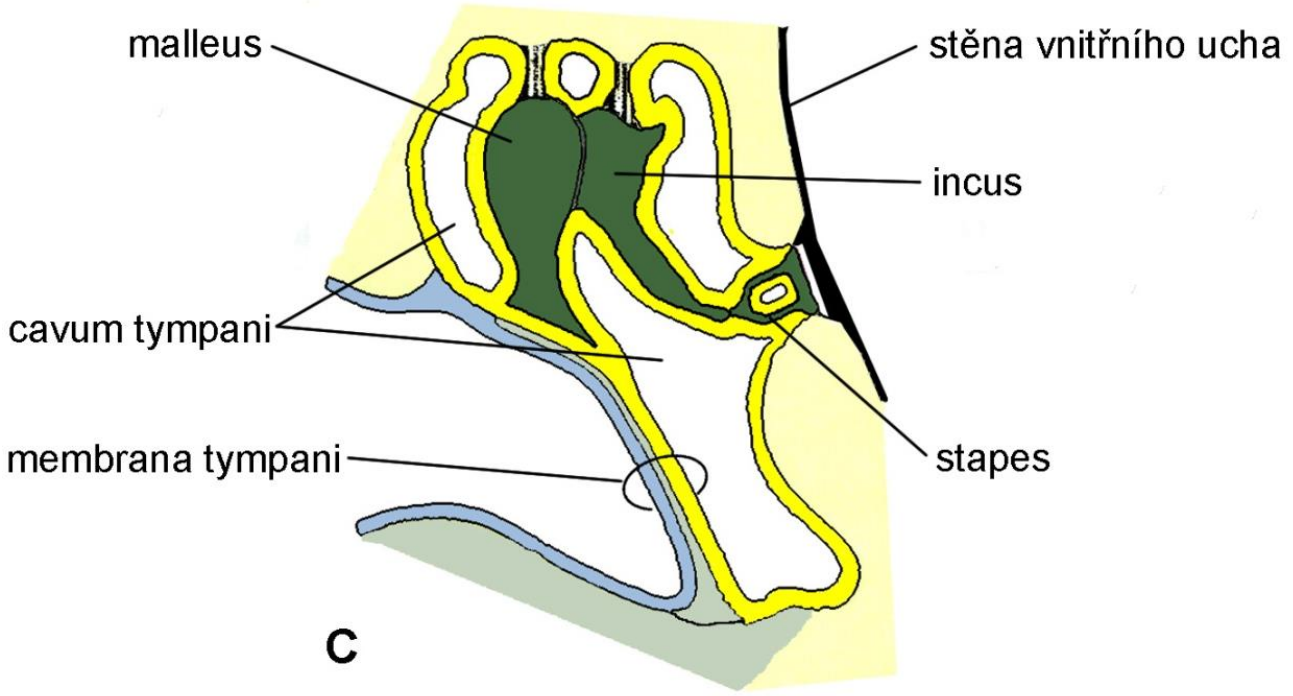
arch cartilage (Meckel´s cartilage) - malleus, incus, lig. mallei ant., sphenomandibulare lig.

muscles of mastication, mylohyoid and anterior belly of digastric, tensor tympani, tensor veli palatini

the 1st aortic arch - disappears (a small portion may persist and form maxillary artery)

the 1st branchial nerve - trigeminal





2. Pharyngeal arch (hyoid):

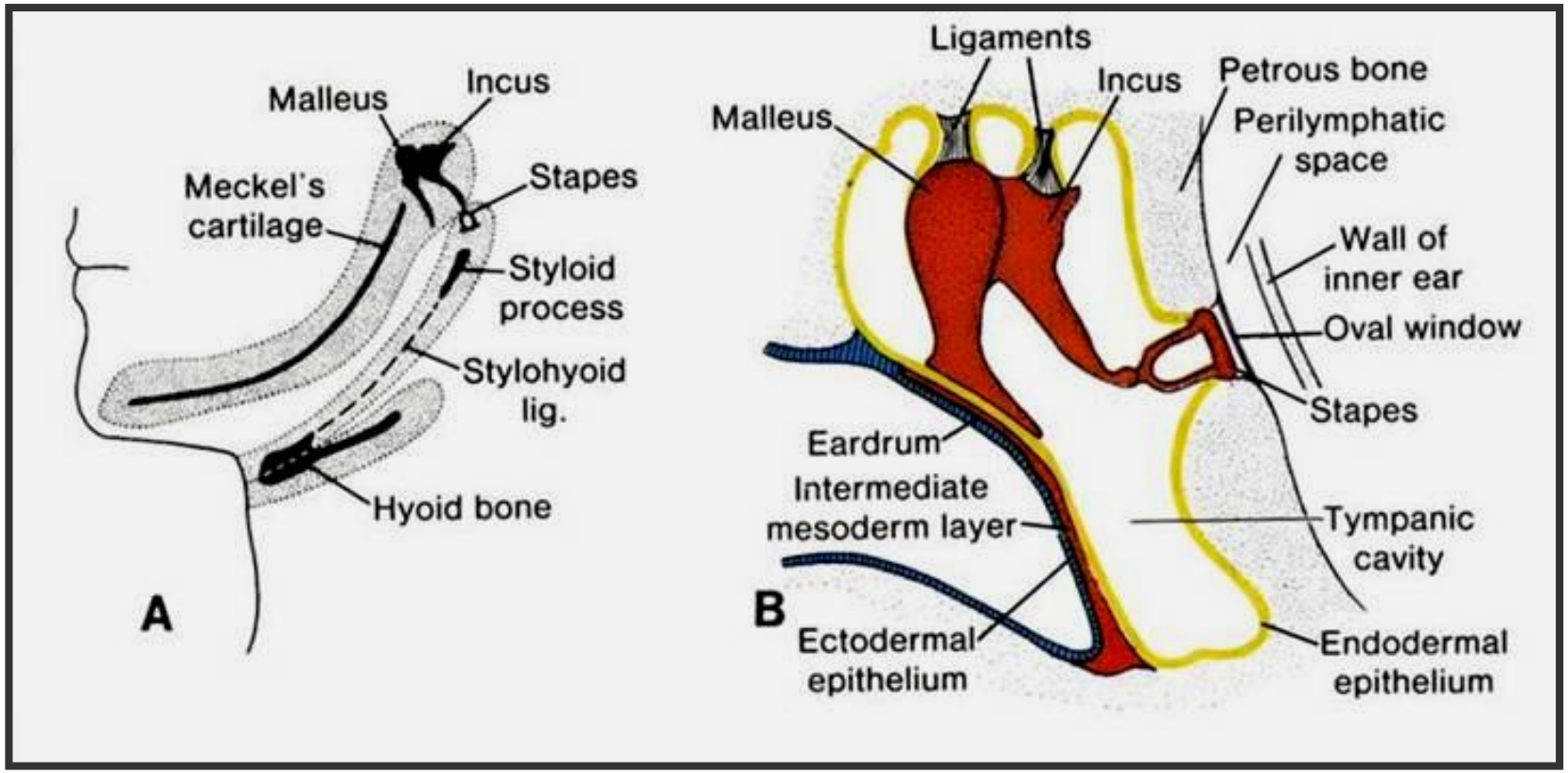
Derivatives of pharyngeal arches

arch cartilage (Reichert´s cartilage) - stapes, styloid process, lesser cornu of hyoid, upper part of body of the hyoid bone

muscles of facial expressions, stapedial and stylohyoid muscle, posterior belly of digastric

the 2nd aortic arch - disappears (small portions of this arch contributes to the hyoid and stapedial arteries)

the 2nd branchial nerve - facial



3. Pharyngeal arch

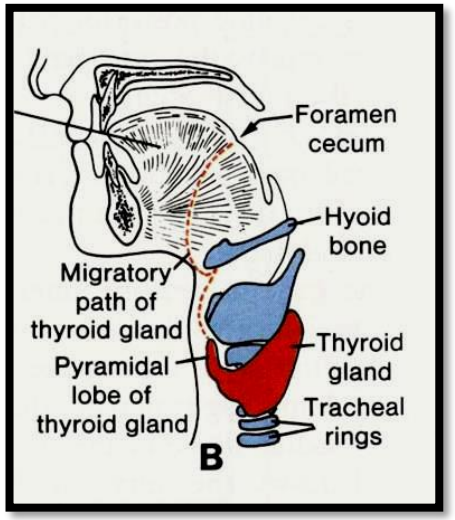
arch cartilage - greater cornu of hyoid, lower part of body of the hyoid cartilage

stylopharyngeus muscle

the 3rd aortic arch - has the same fate on the right and left sides and forms the **first part**

of the internal carotid artery

the 3rd branchial nerve - glossopharyngeal



Derivatives of pharyngeal arches

4. - 6. Pharyngeal arch

arch cartilages - laryngeal cartilages and tracheal rings

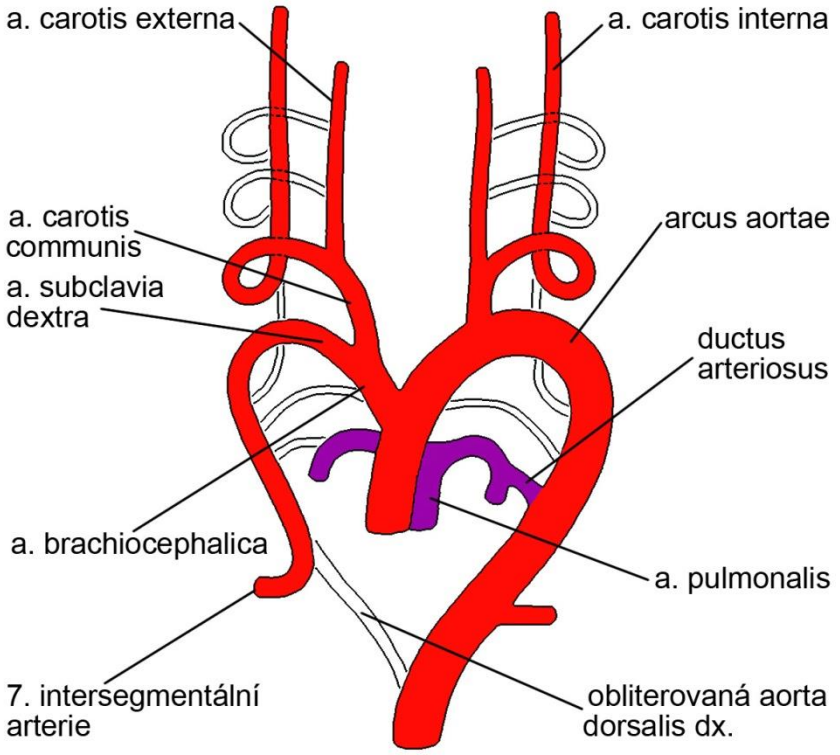
cricothyroid, levator veli palatini, constrictors of pharynx, intrinsic muscle of larynx

the 4th aortic arch - gives rise on left**: a part of the aortic arch** between left common carotid a left subclavian arteries; on the right: **the proximal segment of the subclavian artery**

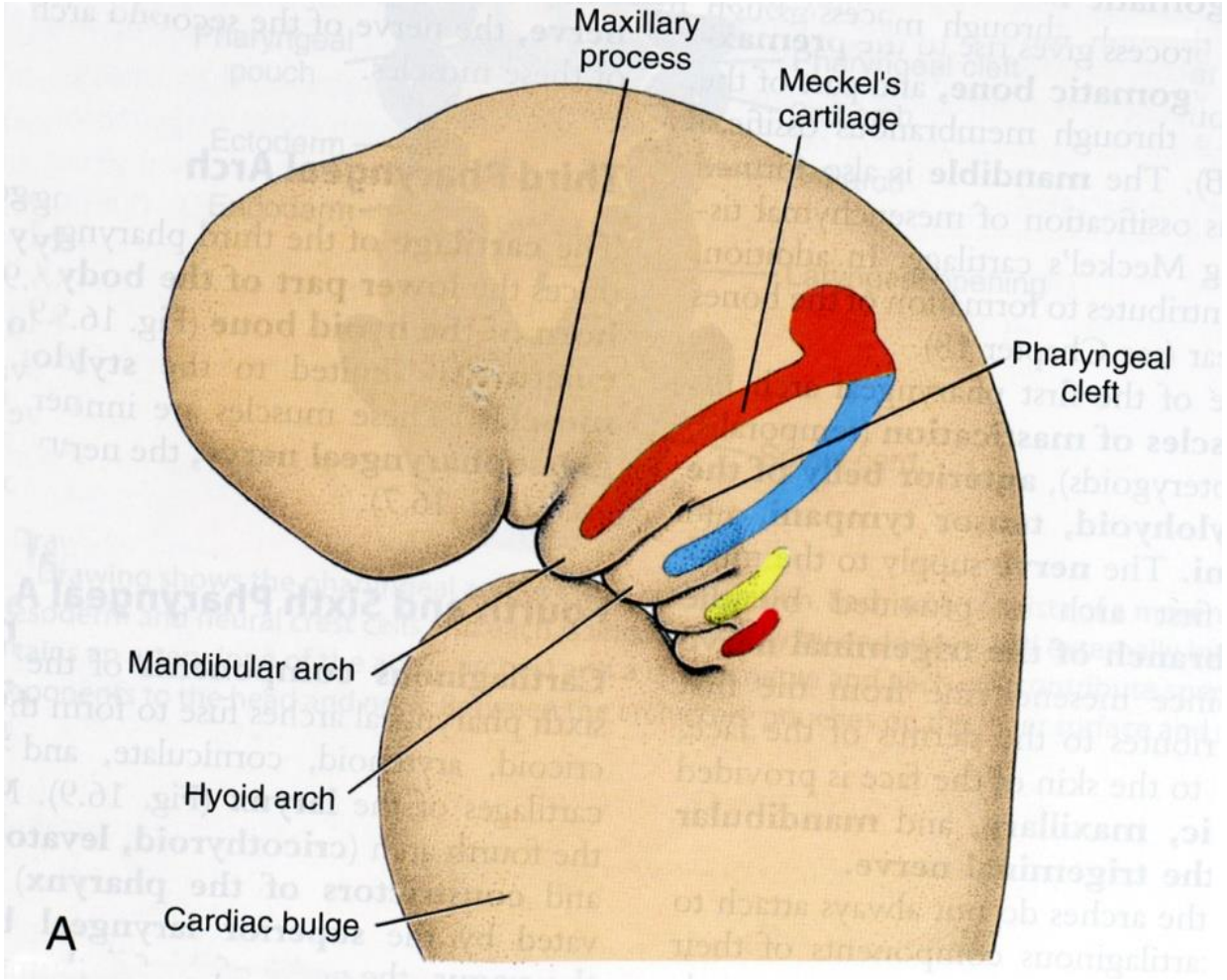
the 5th aortic arch - transient and **obliterates**

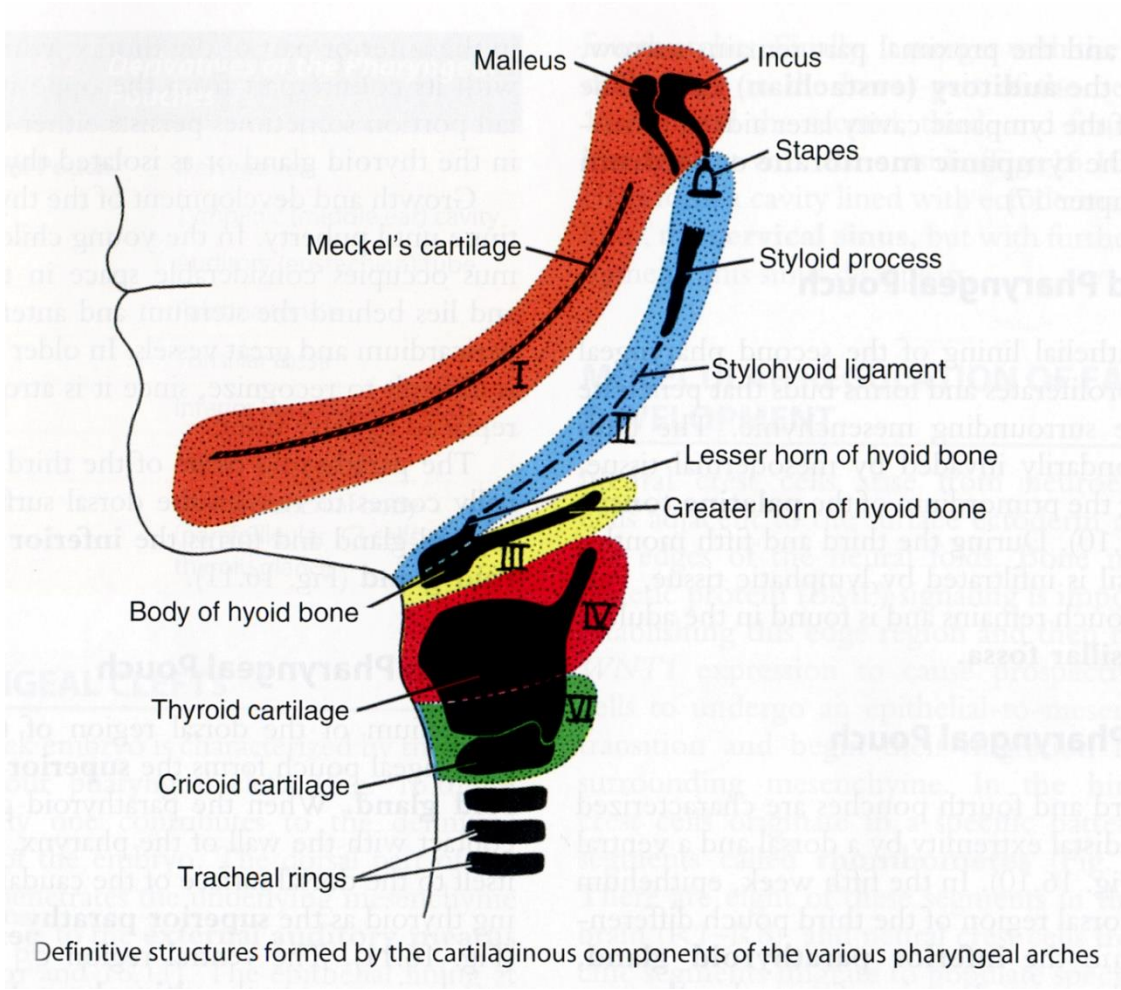
the 6th aortic arch - transformed into the **pulmonary artery** (their branches)

branchial nerves - vagus nerve /superior laryngeal, branch of vagus (from the 4th), recurrent laryngeal branch of vagus (from the 6th)



Transformation of cartilages of pharyngeal arches (summary)





Definitive structures formed by the cartilaginous components of the various pharyngeal arches

Transformations of aortic arches (summary)

the 1st aortic arch – **disappears** (a small portion can persist to form short piece of the maxillary artery)

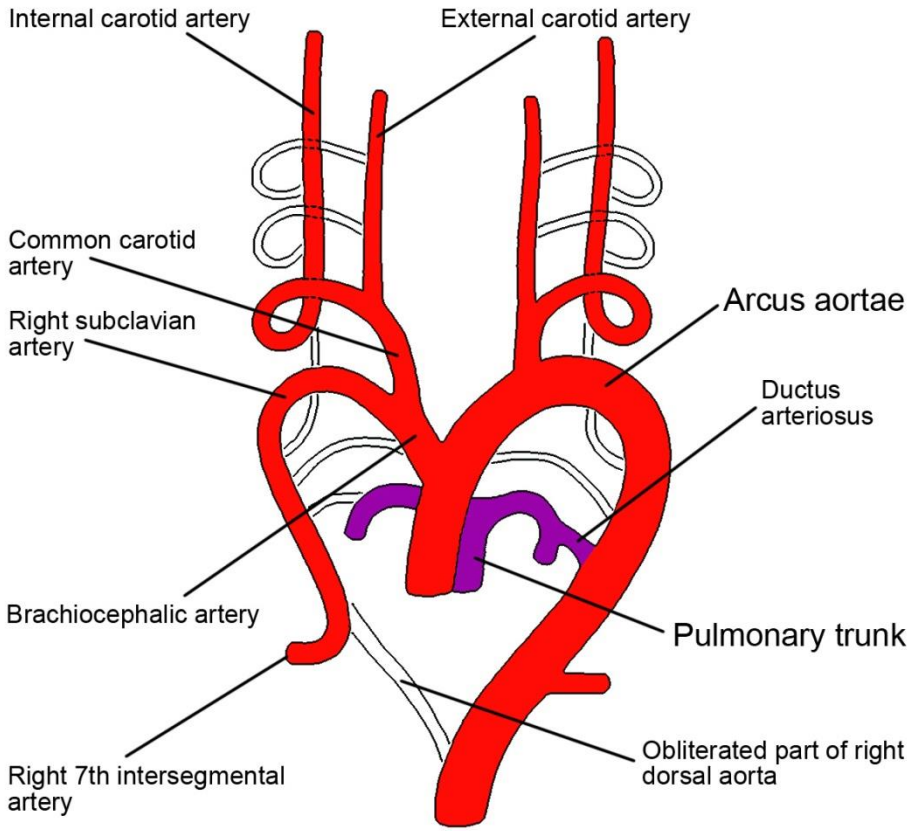
the 2nd aortic arch – **disappears** (small portions of this arch contributes to the hyoid and stapedial arteries)

the 3rd aortic arch – has the same development on the right and left side, it gives rise to the initial portion of **the internal carotid artery**

(the continuation of its trunk is formed by the cranial portion of the dorsal aorta + primitive internal carotid)

the external carotid derives from the cranial portion of the ventral aorta

the common carotid corresponds to a portion of the ventral aorta between exits of the third and fourth arches

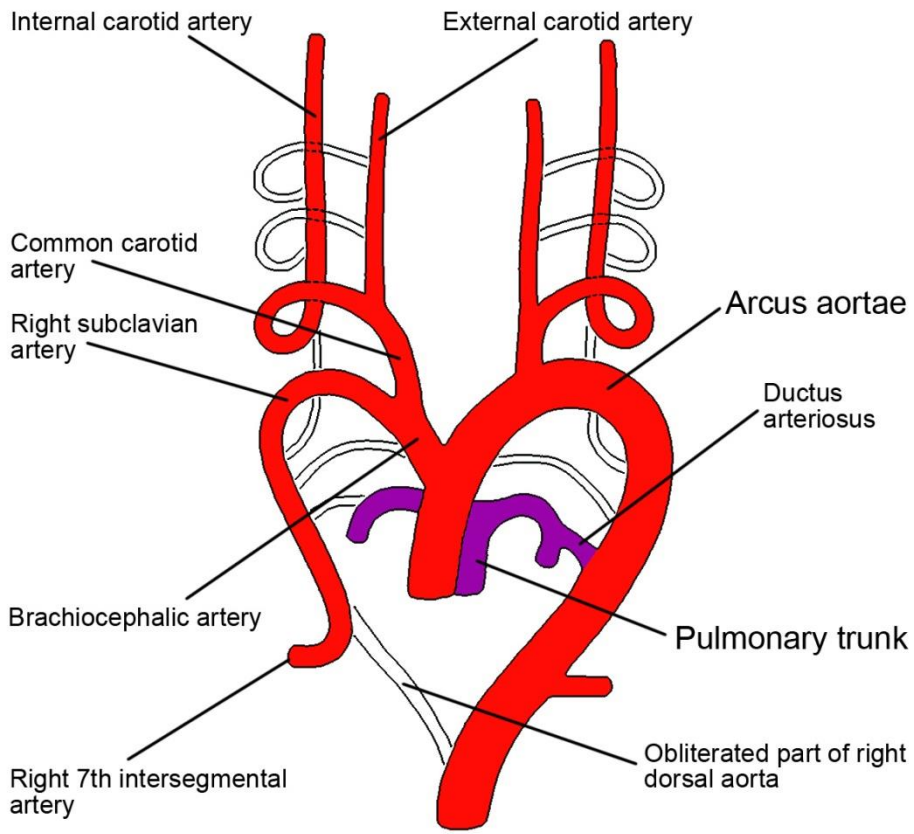


the 4th aortic arch - has ultimate fate different on the right and left side:

Left: forms **part of the arch of the aorta** between left common carotid and left subclavian artery

Right: forms the proximal segment of the **right subclavian artery**

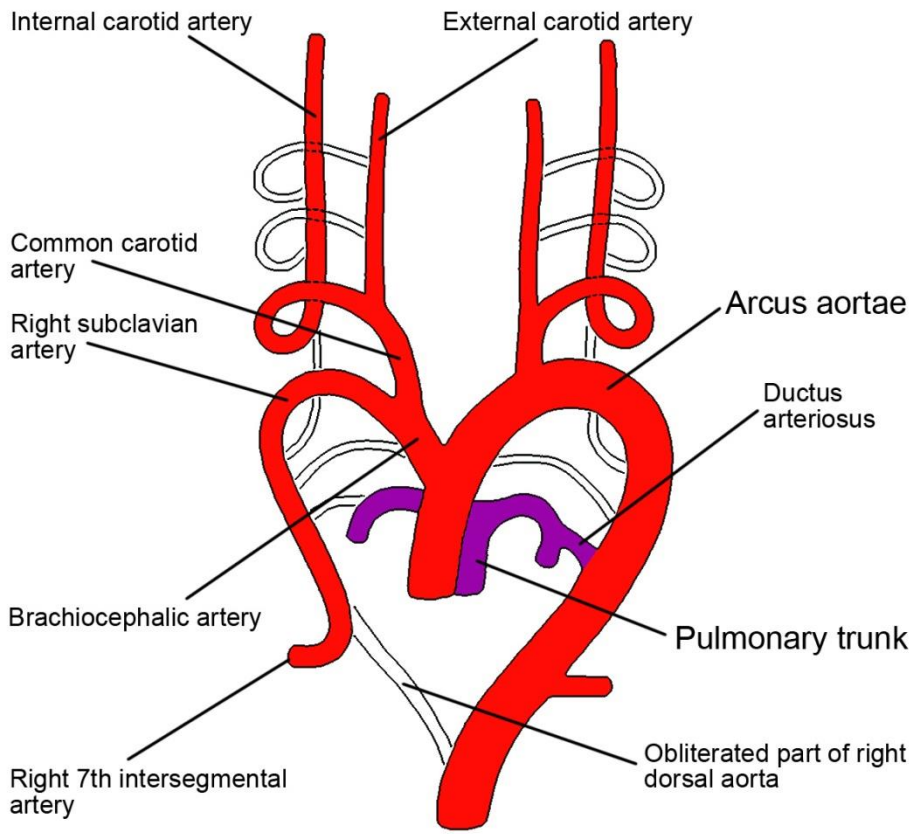
the 5th aortic arch - is transient and soon obliterates

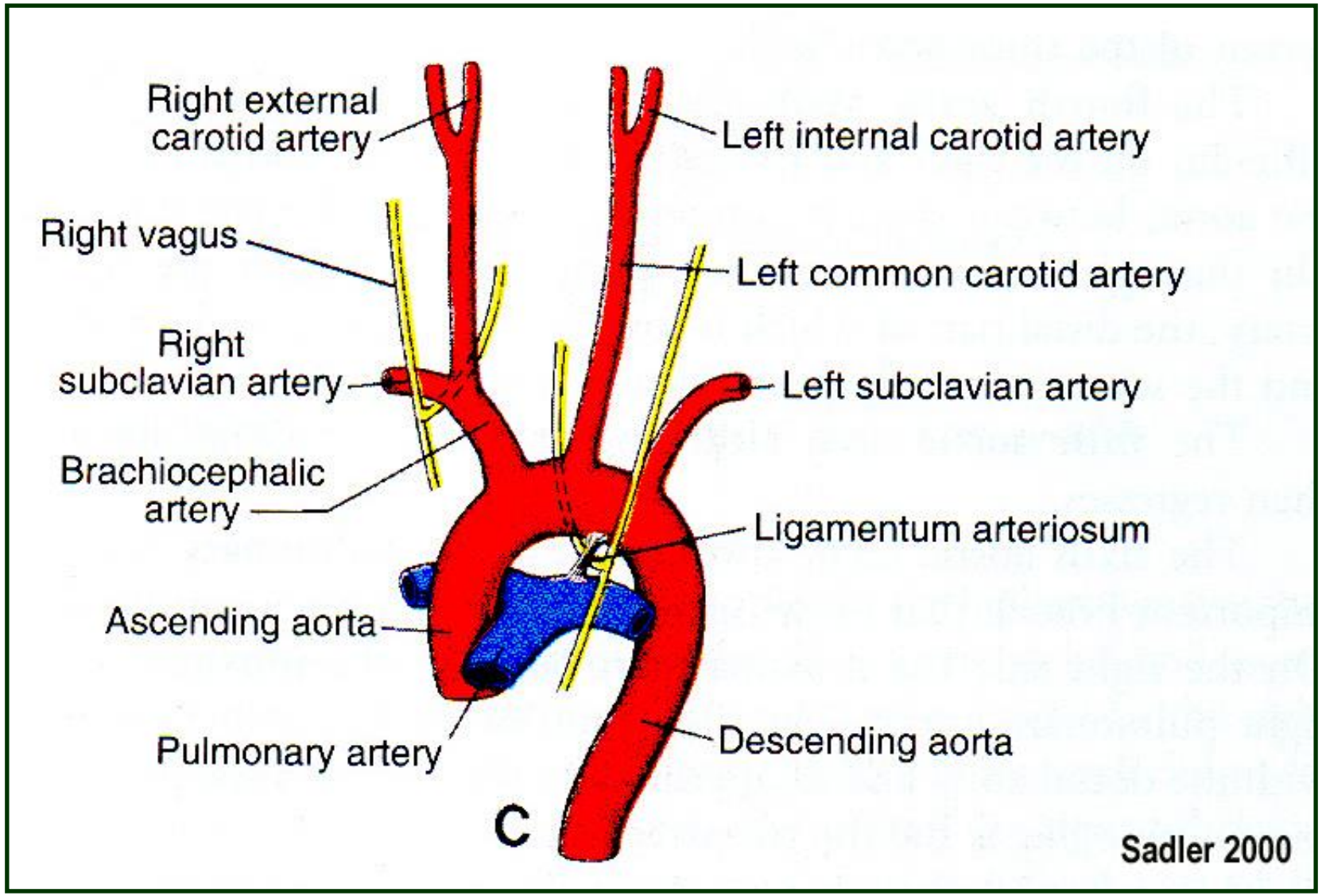


the 6th aortic arch - **pulmonary arch** - the proximal part transforms into the right branch of the pulmonary artery and the distal part disappears

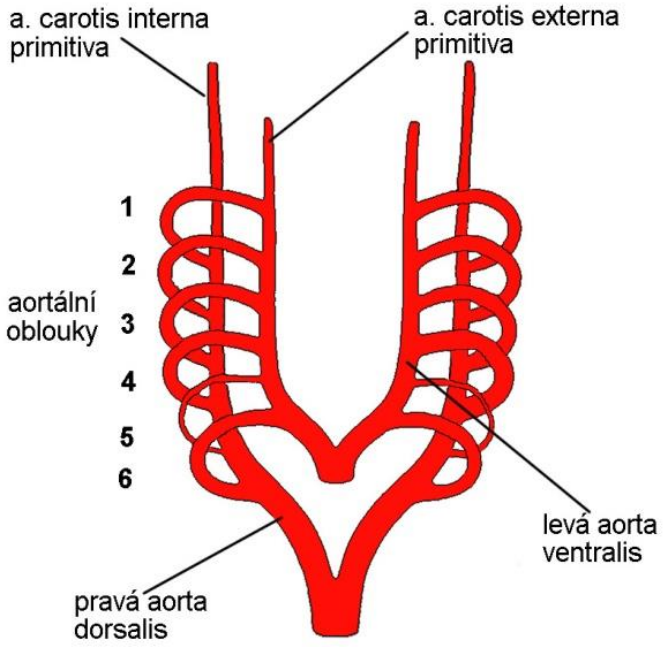
On the left side, the distal part persists as the **ductus arteriosus** during intrauterine life

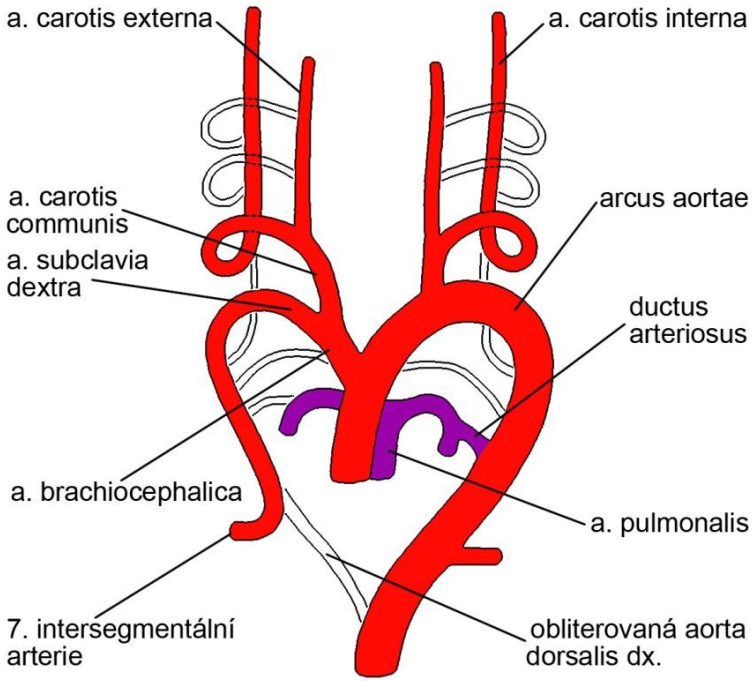
The proximal part gives rise to the left branch of the pulmonary artery

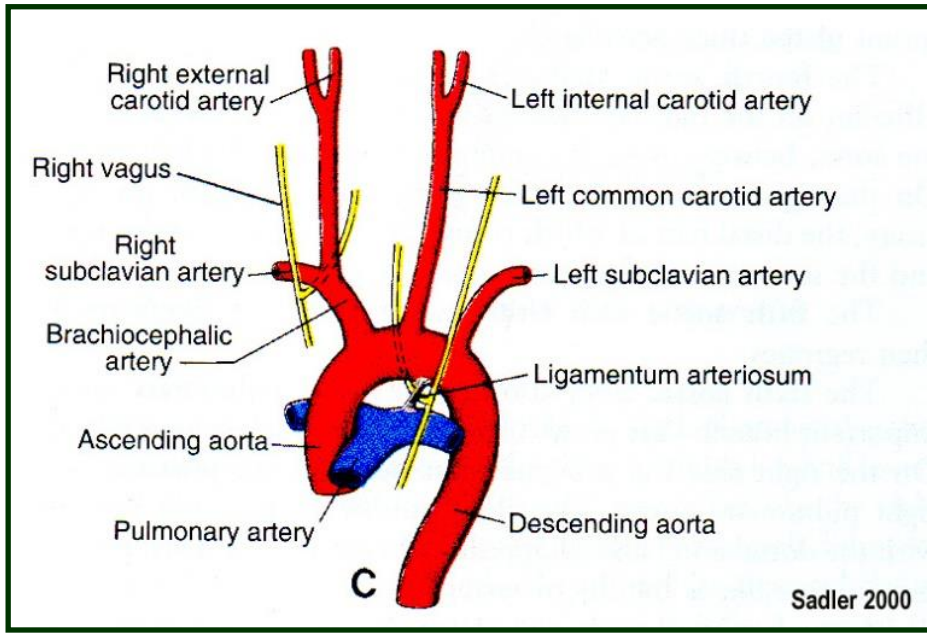



Right external carotid artery
Left internal carotid artery
Right vagus
Left common carotid artery
Right subclavian artery
Left subclavian artery
Brachiocephalic artery
Ligamentum arteriosum
Ascending aorta
Pulmonary artery
Descending aorta
C
Sadler 2000

Summary


a. carotis interna primitiva
a. carotis externa primitiva
1
2
aortální oblouky
3
4
5
6
levá aorta ventralis
pravá aorta dorsalis


a. carotis externa
a. carotis interna
a. carotis communis
arcus aortae
a. subclavia dextra
ductus arteriosus
a. brachiocephalica
a. pulmonalis
7. intersegmentální arterie
obliterovaná aorta dorsalis dx.


Right external carotid artery
Left internal carotid artery
Right vagus
Left common carotid artery
Right subclavian artery
Left subclavian artery
Brachiocephalic artery
Ligamentum arteriosum
Ascending aorta
Pulmonary artery
Descending aorta
C
Sadler 2000

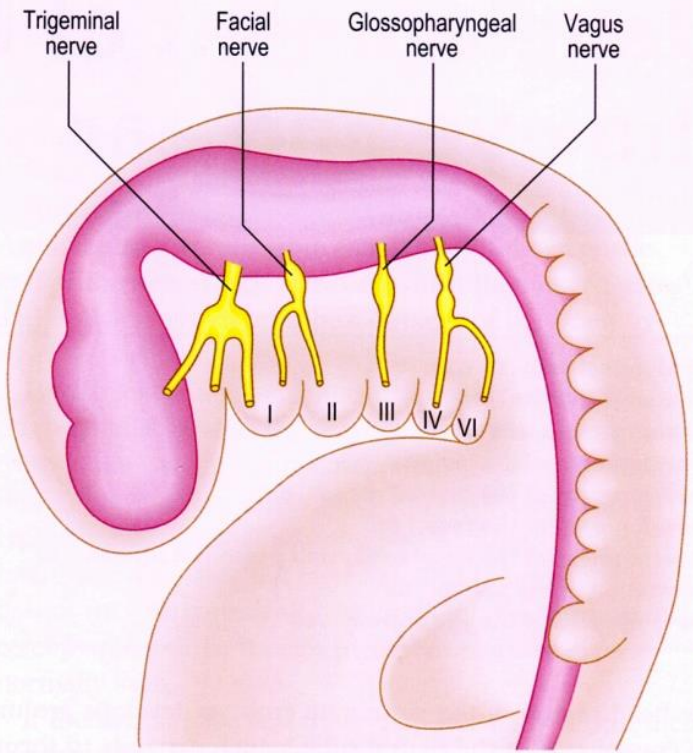
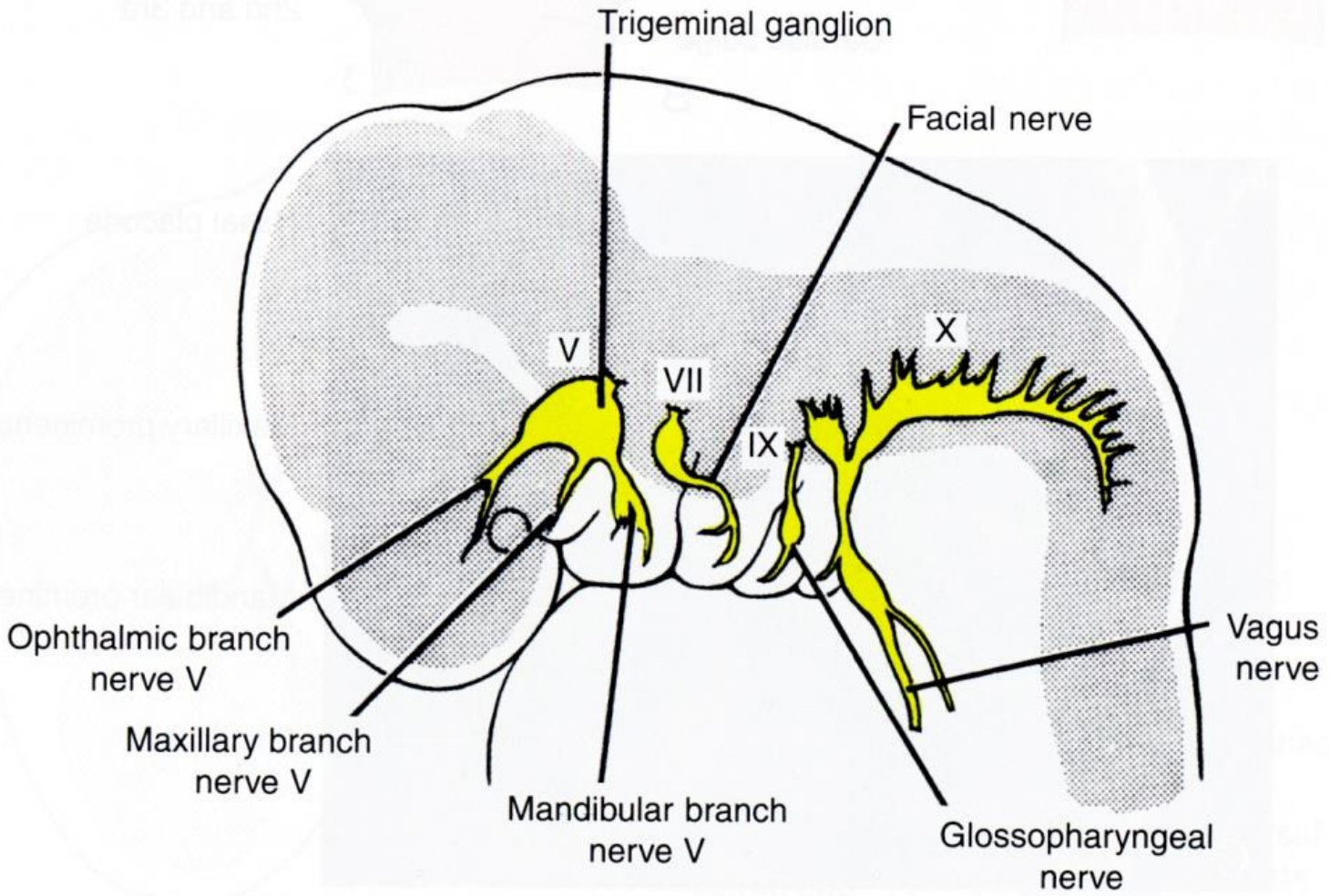


Fig. 11.3 **Sagittal section of a 5-week-old embryo indicating the cranial nerves supplying the pharyngeal arches.**

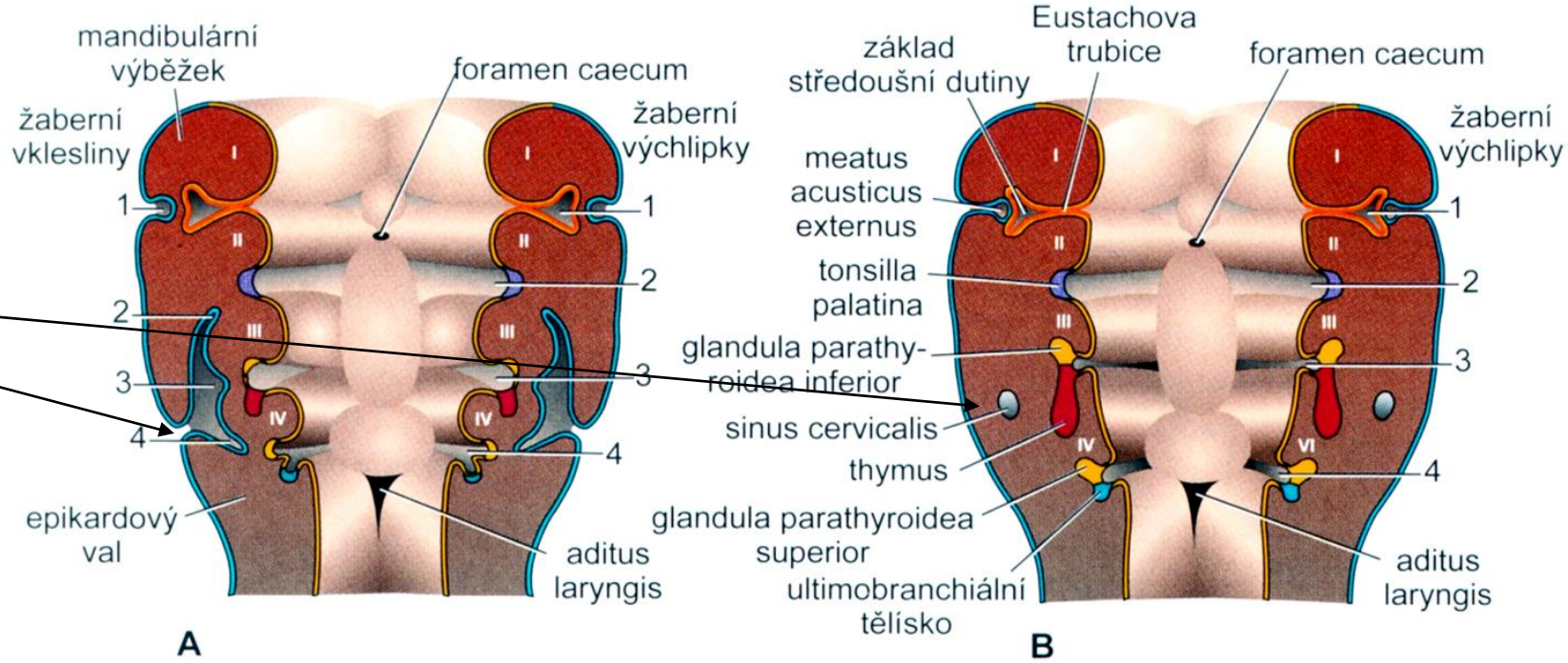


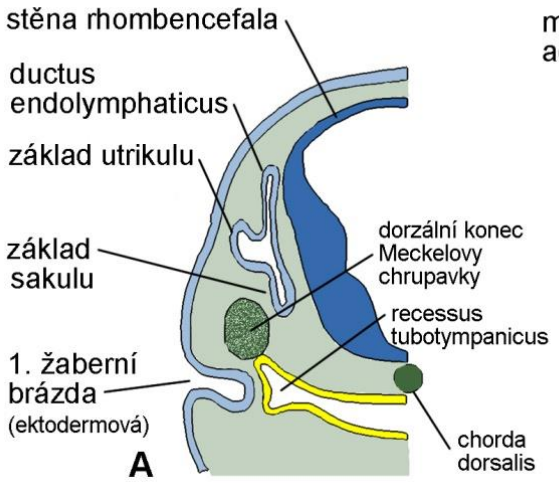
igure 16.7 Each pharyngeal arch is supplied by its own cranial nerve. The trigeminal nerve supplying the first pharyngeal arch has three branches: the ophthalmic, maxillary, and mandibular. The nerve of the second arch is the facial nerve; that of the third is the glossopharyngeal nerve. The musculature of the fourth arch is supplied by the superior laryngeal branch of the vagus nerve, and that of the sixth arch, by the recurrent branch of the vagus nerve.

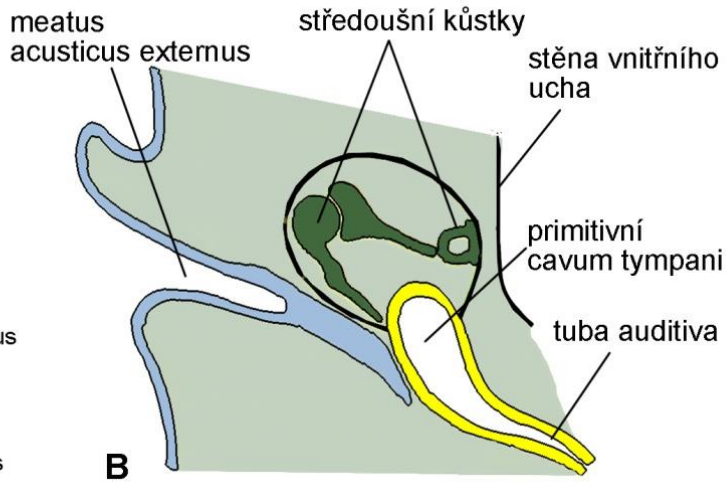
Pharyngeal clefts (ectodermal)

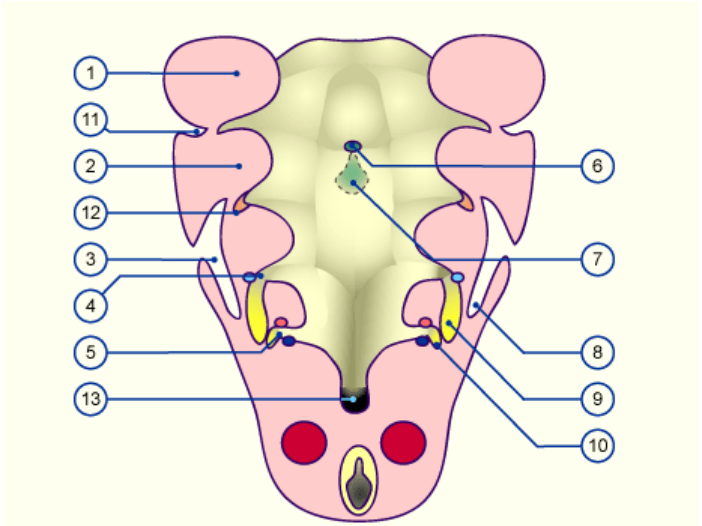
Functional future has only the
1. pouch

2. - 4. obliterates and form a sinus cervicalis



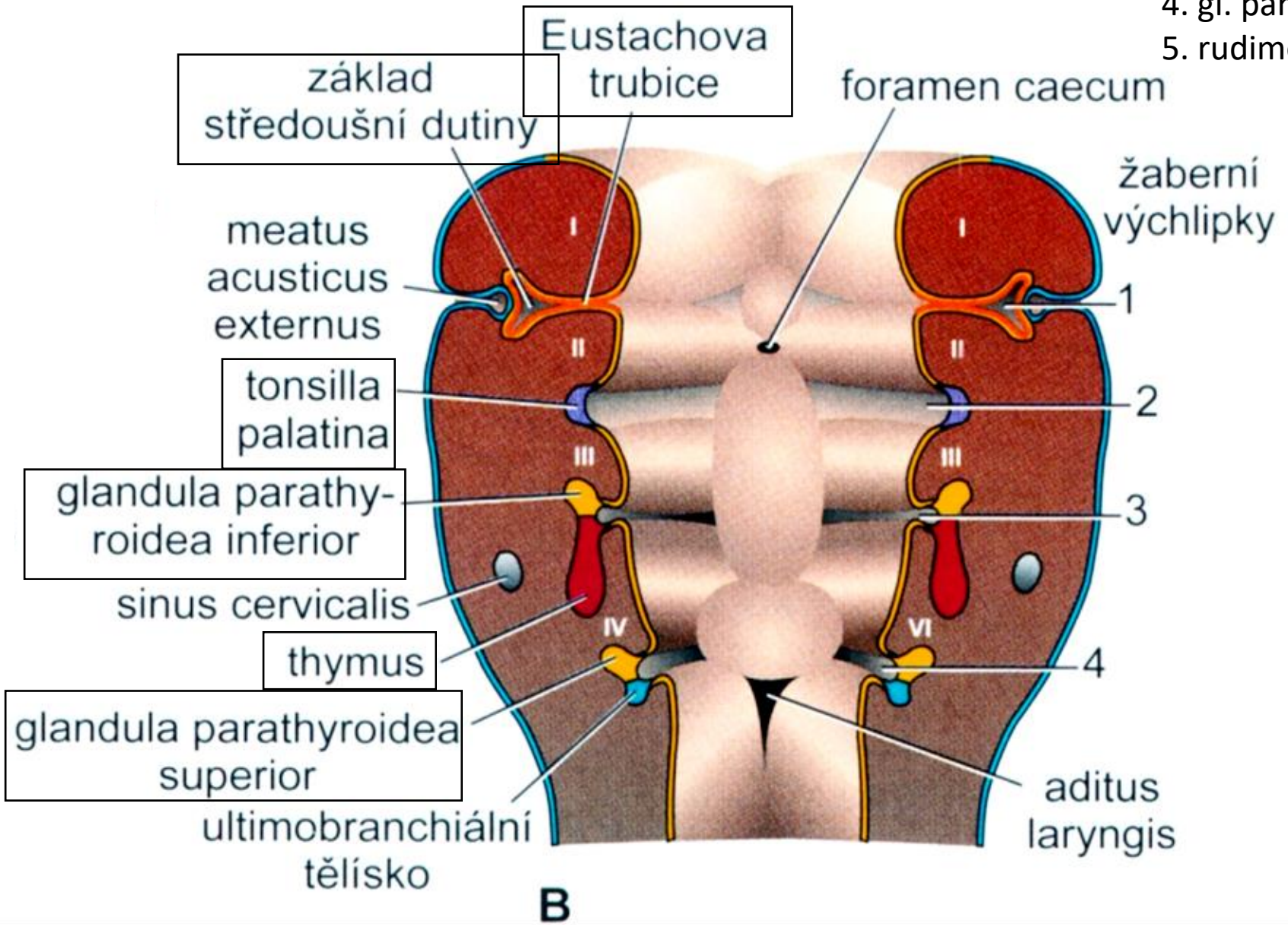


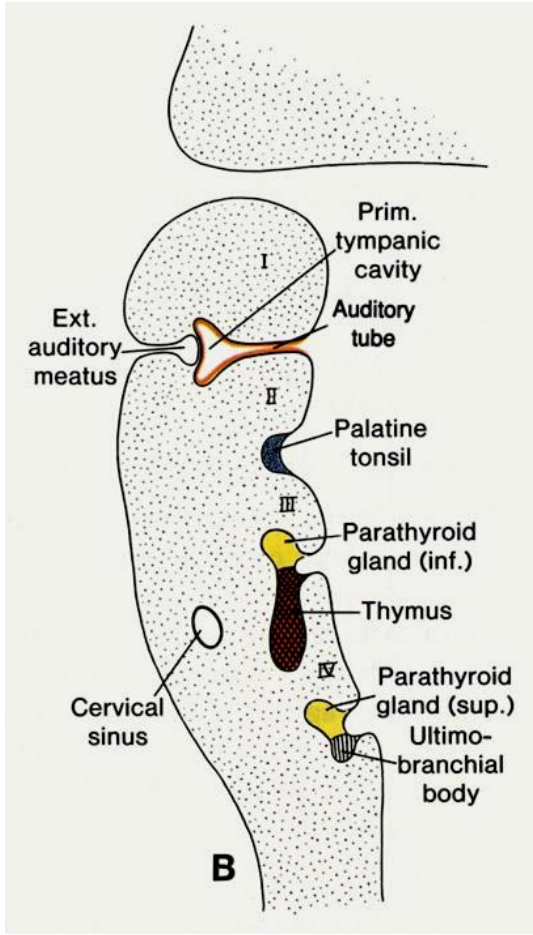




Derivatives of pharyngeal pouches

1. Cavum tympani and Eustachian tube
2. Fossa tonsilaris
3. Epithelial reticulum of thymus and gl. parathyr. inf.
4. gl. parathyroidea sup. + ultimobranchial body
5. rudimentary





Defects caused by maldifferentiation of the pharyngeal apparatus

1. **Branchial (cervical) cysts**
2. **Branchial (cervical) fistulae**
3. Branchial (cervical) vestiges (rudiments of branchial arches)
4. Preauricular cysts a fistulae
5. **Syndrome of the 1. branchial arch**
6. **DiGeorge syndrome**
7. Ectopia of thymus

Branchial cysts (lateral neck cysts)

Origin from persisting sinus cervicalis, positioned under angulus mandibulae

Subcutaneously or deep around the pharynx (possibly larynx)

When a cyst ruptures, communication occurs with the body surface or pharynx

Lined with stratified squamous epithelium

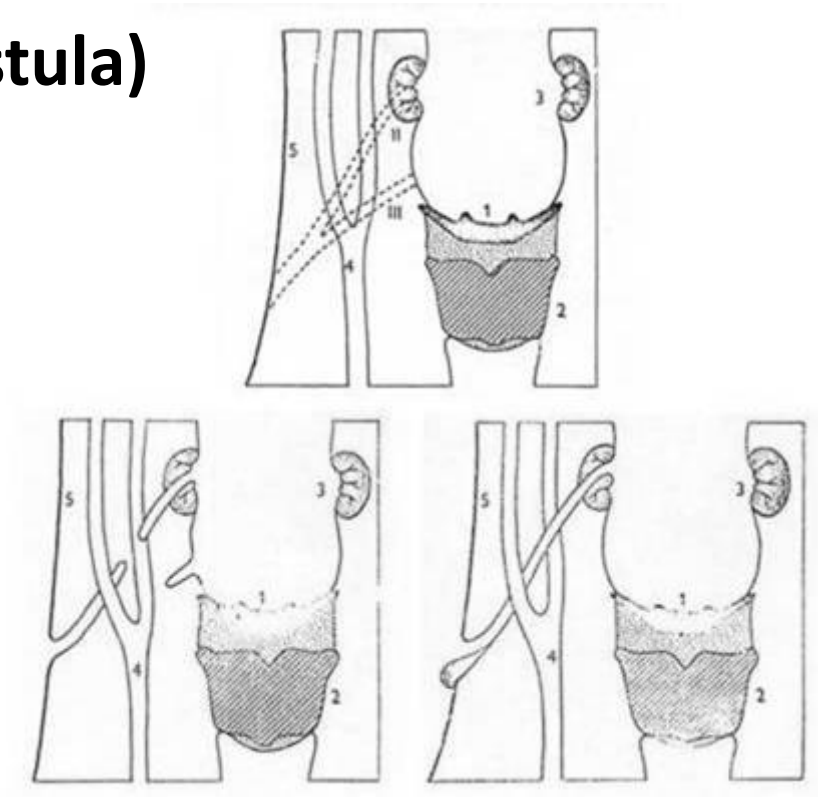
They may contain a liquid content with cholesterol crystals

Usually clinically not important

Figure 1 Branchial cleft cyst in the neck

https://subent.com/removal-of-branchial-cleft-cyst

Branchial fistula (lateral cervical fistula)



Abnormal communication of the pharyngeal cavity with the body surface

They arise when the membranae obturantes obliterate

Between 2. pouch and cleft

(fossa tonsillaris - sternocleidomatoideus muscle)

Between 3. pouch and cleft

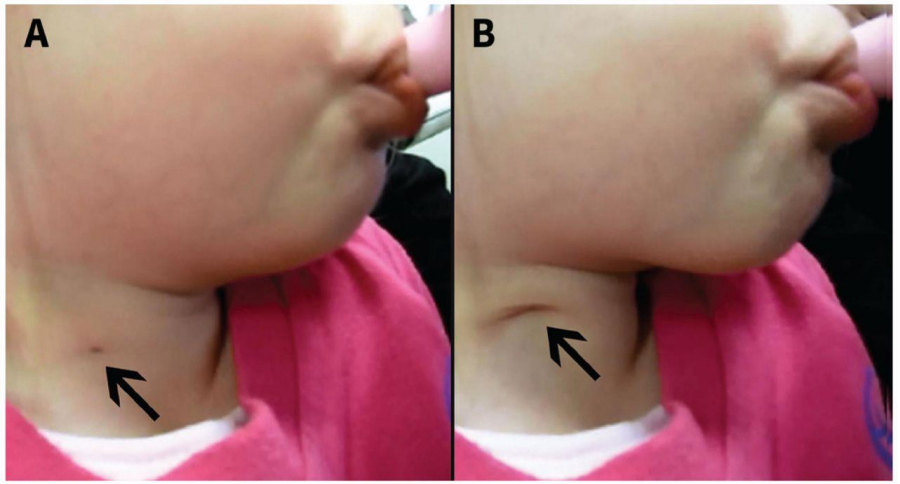
(tongue - art. sternoclavicularis)

Complete

at the outlet on the skin

Incomplete

external, internal



Koltsidopoulos et Skoulakis, CMAJ, 2018

Branchial vestiges (rudiments of branchial arches)

Residues of some components of the pharyngeal arches, usually cartilage.

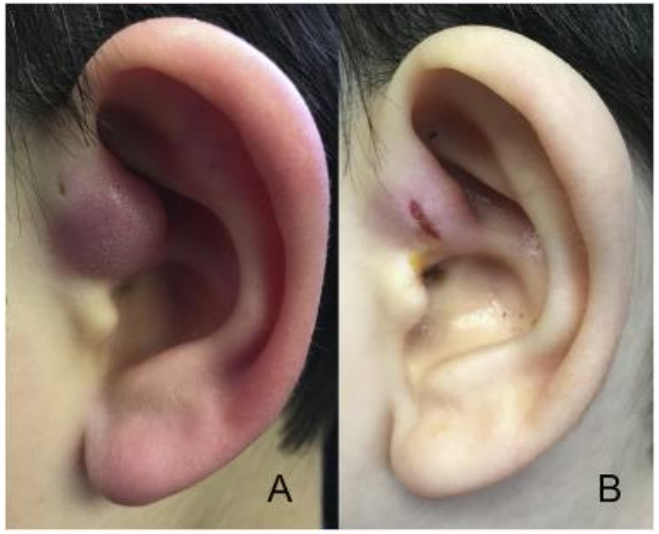
Occurrence: in the subcutaneous ligament of the neck above the lower 1/3 m.sternocleidomastoid

Rare

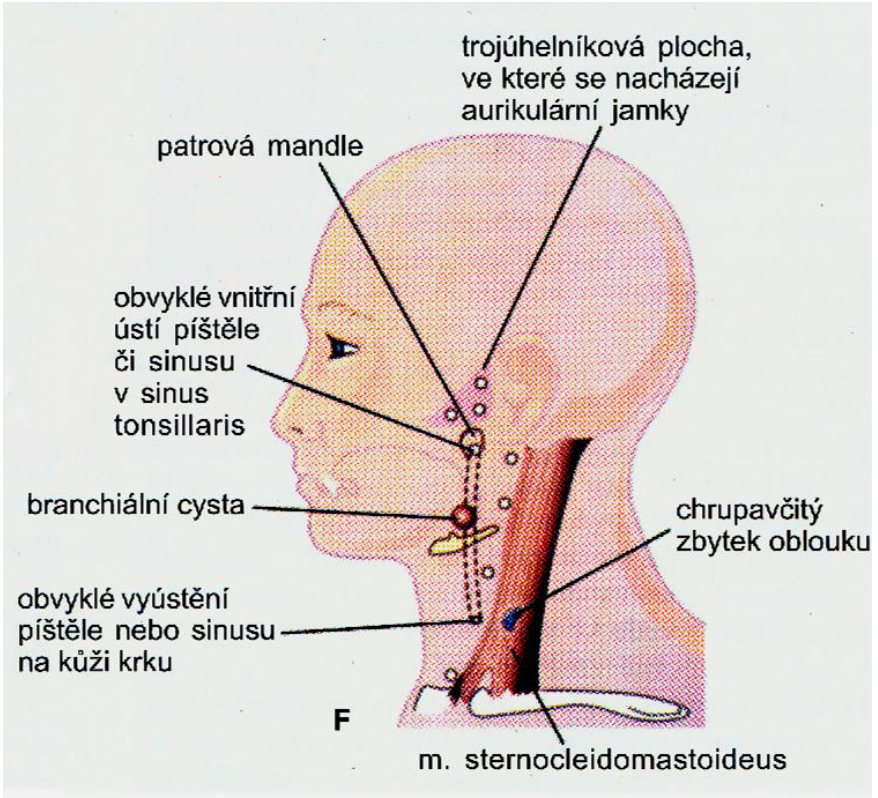
Preauricular cysts and fistulae

Small grooves, pits or cysts in skin in triangular area anteriorly to the pinna (auricle)

Origin: by persistence of sulci separating auricular hillocks



Isaacson, IJPO, 2019



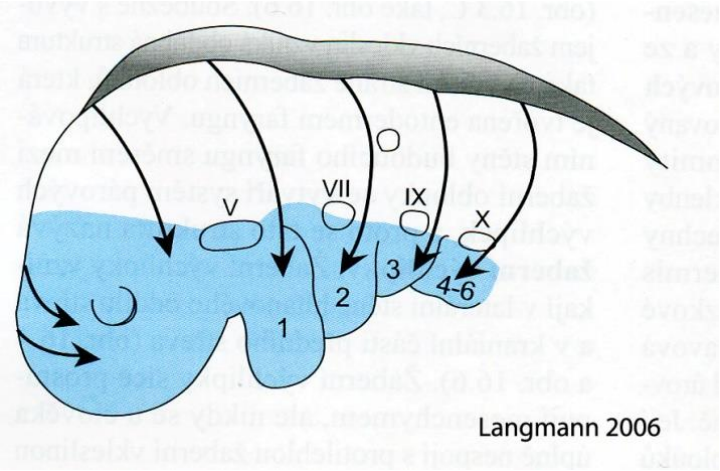
The First pharyngeal arch syndrome

Complex malformation of the skeleton of the face (both jaws, palate), eye and ear, **caused by delay or non-migration of crista neuralis** into the 1st pharyngeal arch

Types:

1) **<u>Treacher-Collins syndrome</u>** - dysostosis mandibulofacialis – autosomal dominant hereditary malformation

anatomically: hypoplasia to aplasia of zygomatic bones, hypoplasia of the upper and lower jaw, macrostomy, gothic floor, hypoplastic and sparse teeth, malocclusion - the face shows a characteristic physiognomy



2) Pierre-Robin syndrom

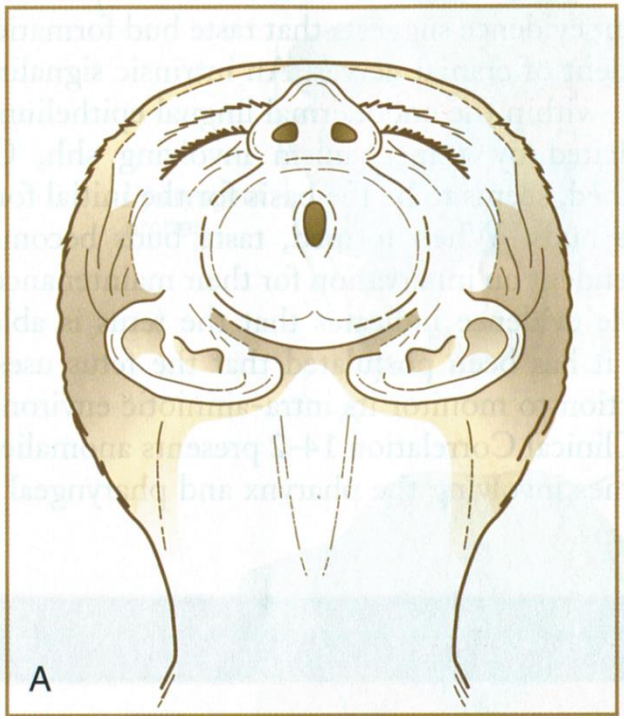
Hypoplasia of the mandible, gothic floor or posterior cleft palate, glossoptosis, ear defects

Autosomal recessive inheritance, X chromosome - linked

The intellect of individuals is not affected

Symptoms: due to the shortened base of the oral cavity, individuals after birth have difficulty feeding and breathing (stridor - caused by a disproportion between the lower jaw and the tongue)

Agnathia



Resnick et at, 2019

DiGeorge syndrome

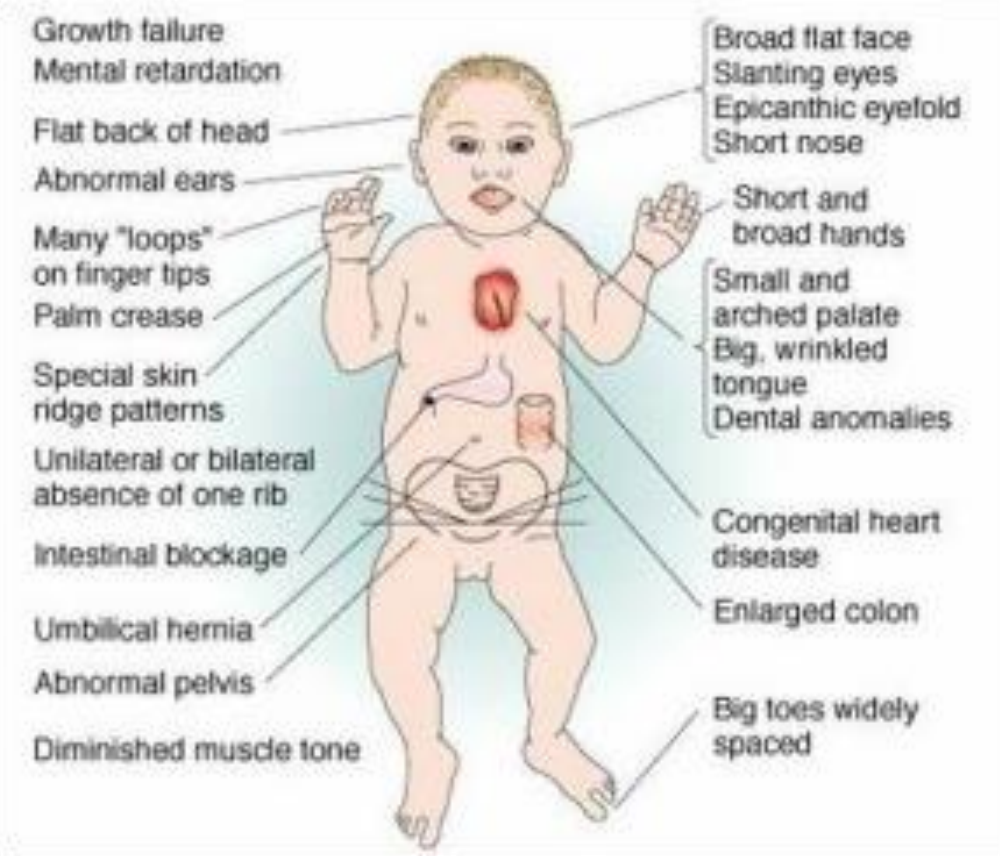
Incorrect development of the 1st pharyngeal arch. **Caused by improper migration of neural crest cells.**

Anatomically: hypoplasia of the mandible, shortened philtrum - nasal hypoplasia, congenital aplasia of the thymus and parathyroid glands, hypoplasia of the thyroid gland, defects of the heart and large vessels (right aortic arch), external ear defects

Clinically: hypoparathyroidism (hypocalcemic seizures), absence of cellular immunity, manifestations of heart defect

Incidence 1: 50 000

Etiology: Most frequently deletion on chromosome 22 - (22q11)



Thymus ectopia

Ectopia = correctly developer organ/structure in incorrect place

When thymus fails to descent: Cervical thymus - near the lower pair of parathyroid glands

Accessory thymus

Tongue development

The development of the tongue begins in the **5th week** at the interface of the stomodeum and the beginning of the primitive pharynx

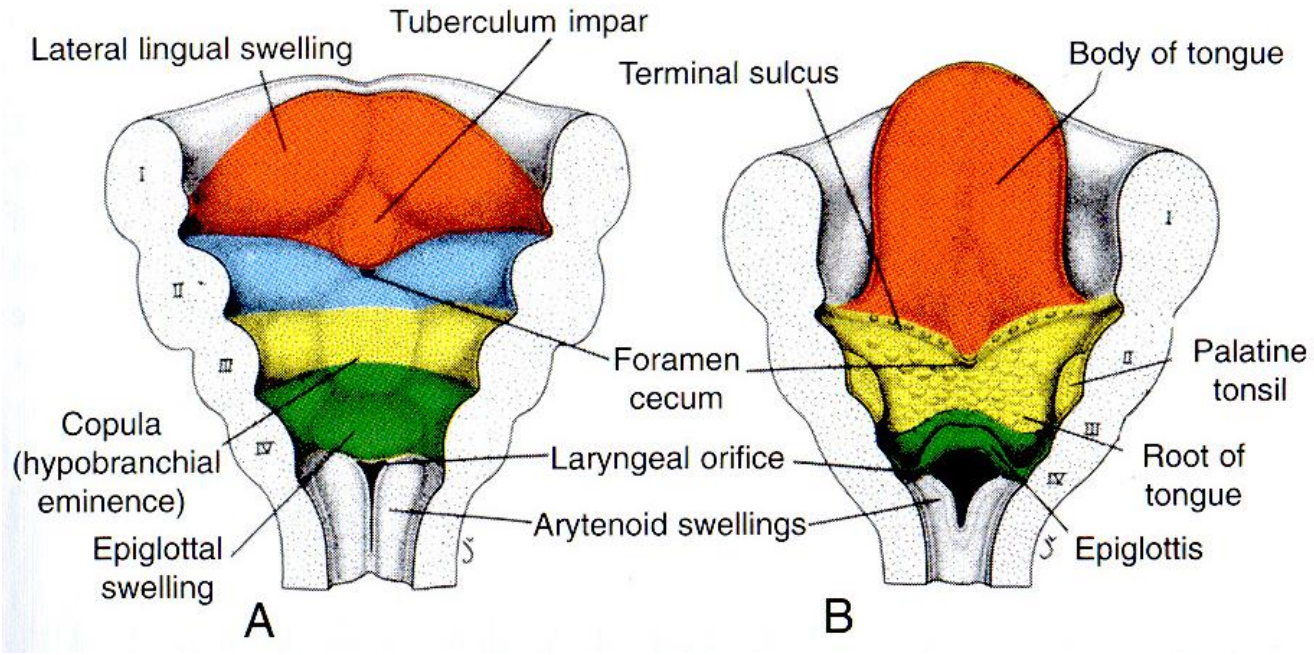
Anterior 2/3 of the tongue	Apex and corpus linguae	Formed from the mandibular process of the 1st pharyngeal arch
Posterior 1/3 of the tongue	Radix linguae	Formed from the 3rd and 4th pharyngeal arch

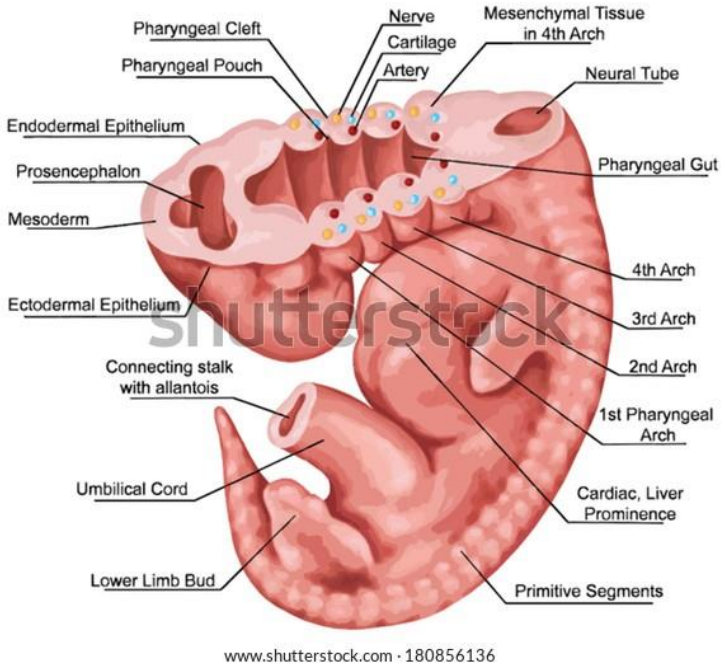
<u>Apex and corpus</u>

On the mandibular prominence are 3 mesenchymal protrusions covered with **ectoderm**:

Paired **tuberculum linguale laterale** (dx et sin) - distal lingual protrusion

Middle unpaired **tuberculum impar** (tuberculum linguale mediale) - middle tongue protrusion - more caudally





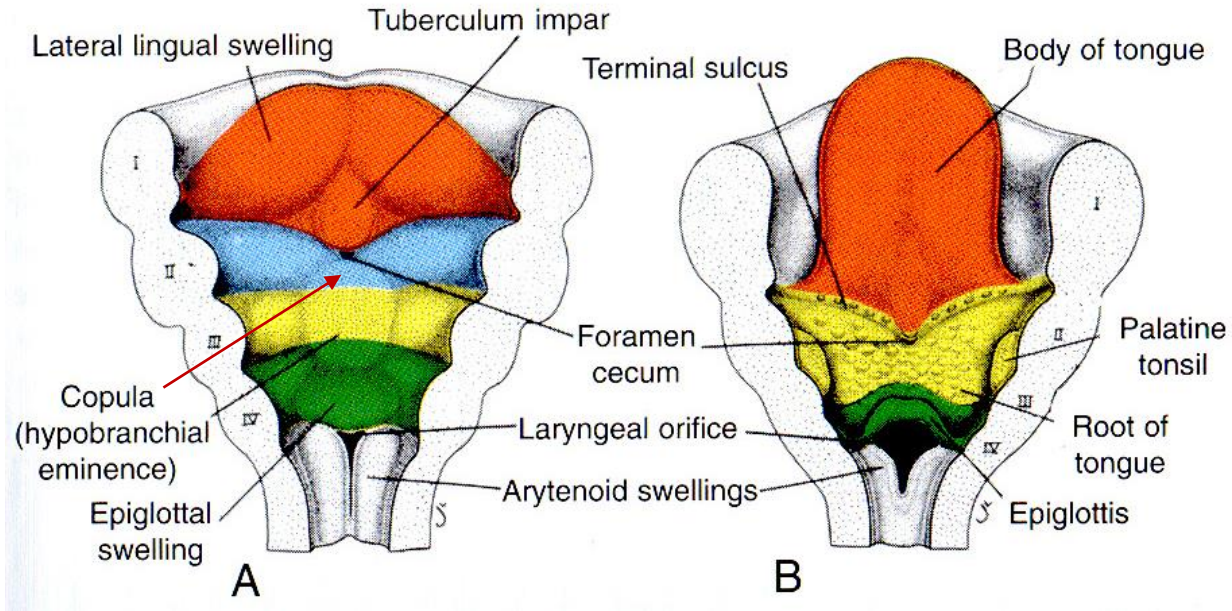
Radix linguae

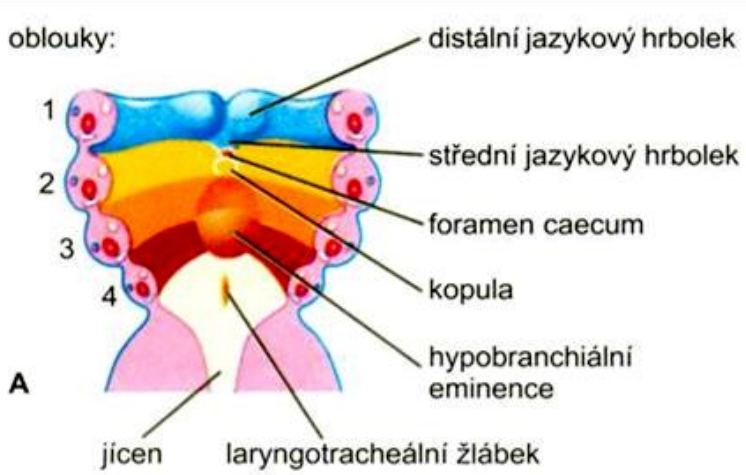
2 foundations: **copula** - fused ectomezenchyme of the ventral ends of the hyoid arch

eminentia hypobranchialis - formed by fusion of ventral ends of 3rd and 4th pharyngeal arch

both the copula and the hypobranchial eminence are covered by the **endoderm**

Endoderm between the tuberculum impar and the dome very intensively proliferates and grows caudally, its luminization creates a ductus thyreoglossus (see thyroid gland)



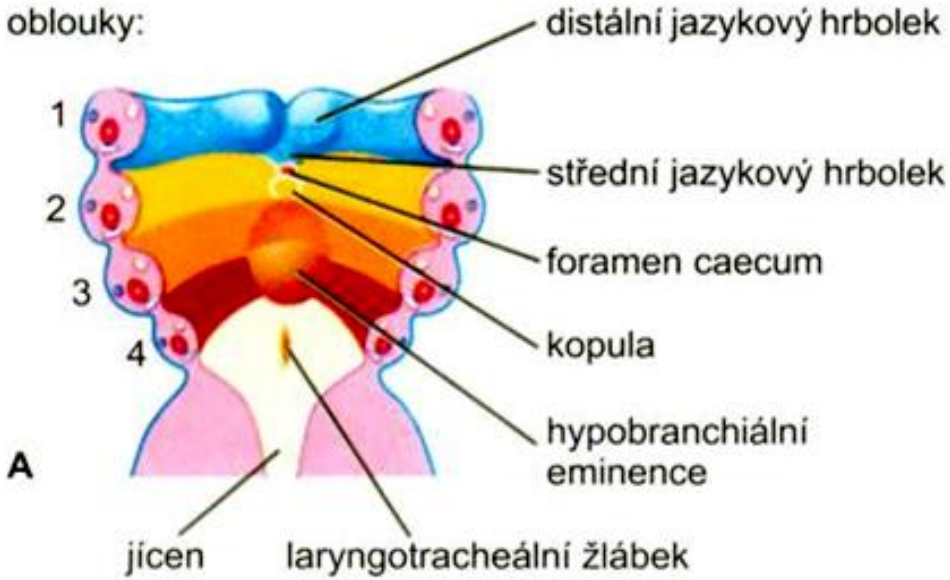


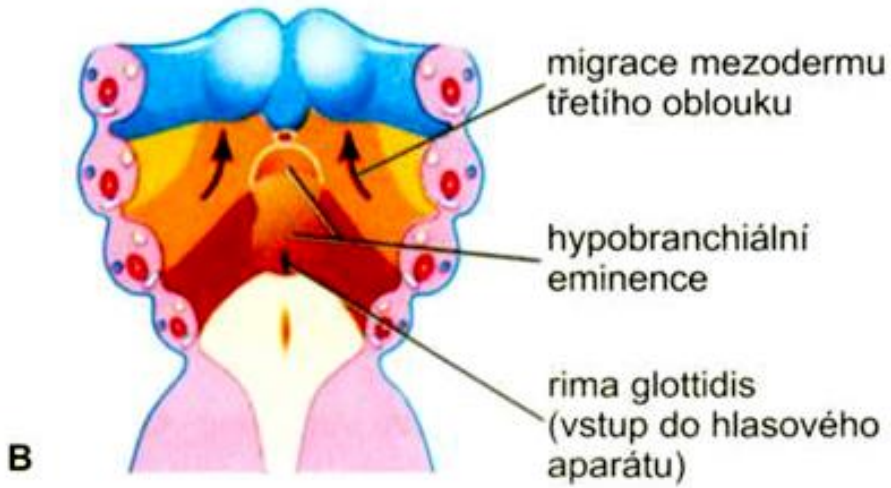
During the **6th week**, the protrusions begin to fuse together

Lateral protrusions enwrap the unpaired **tuberculum impar** - a uniform apex and corpus linguae is formed

In definitive proportions, it resembles the original symmetrical origin of the tip and body of the tongue **sulcus medianus linguae** (+septum linguae)

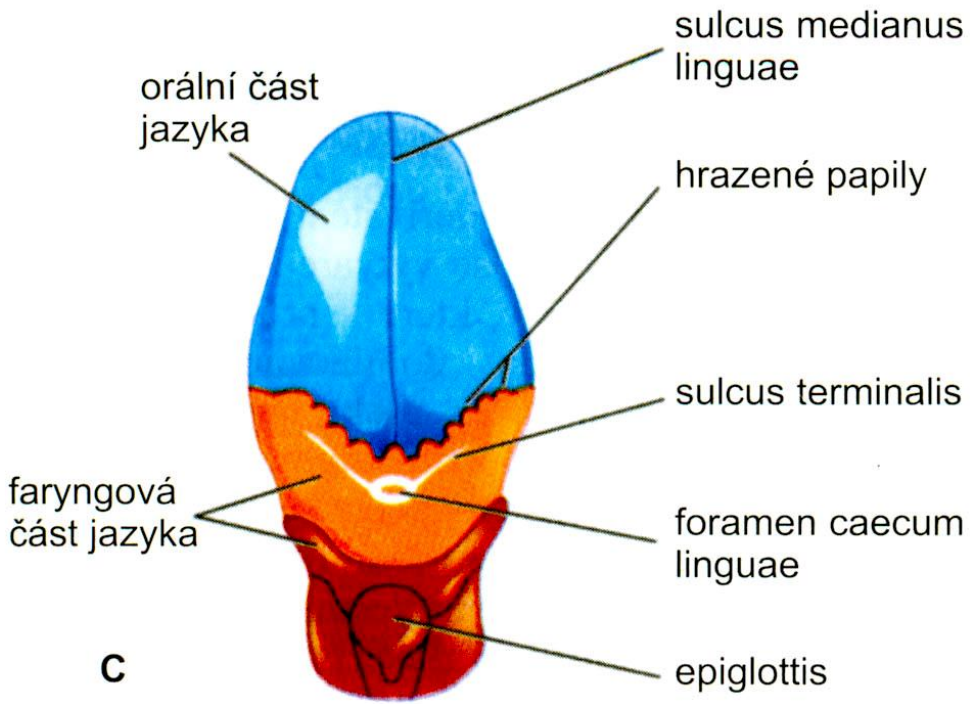
Only a small part of the body near the root of the tongue comes from the tuberculum impar)

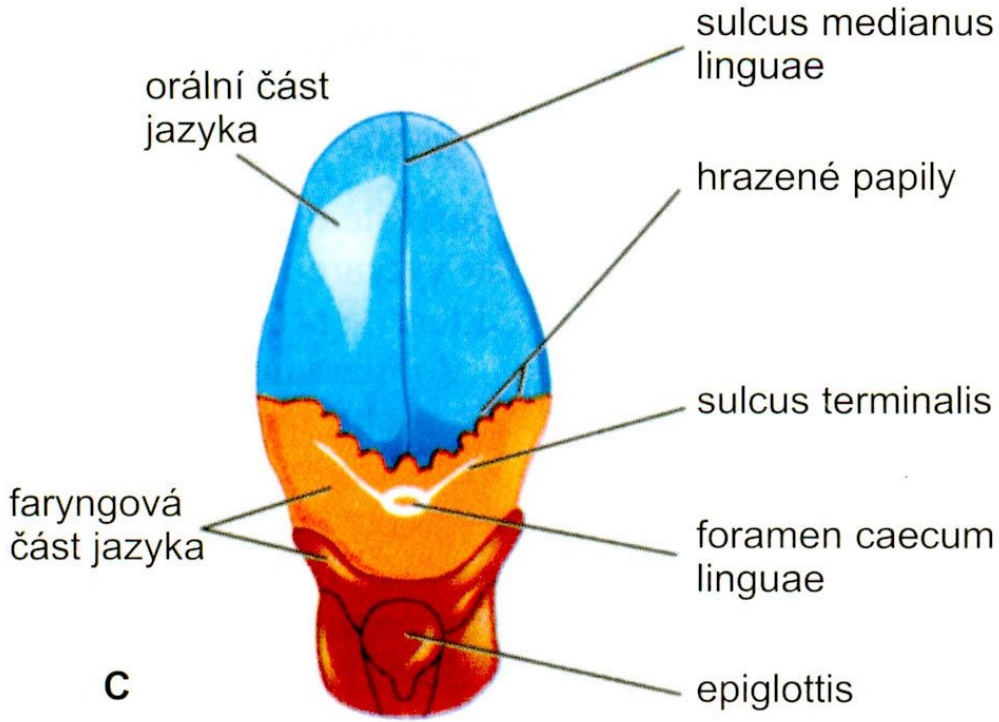




The hypobranchial process merges with copula and moves forward - approaching the base of the corpus with which it merges

Radix - Pharyngeal part of the tongue





Deriváty faryngových oblouků obsažené v jazyku

1. faryngový oblouk (CN V – ramus mandibularis)
2. faryngový oblouk (CN VII – chorda tympani)
3. faryngový oblouk (CN IX – glossopharyngeus)
4. faryngový oblouk (CN X – vagus)

The fusion line is visible until adulthood as a shallow "V" - shaped groove - **Sulcus terminalis**

At the top of the "V" is a short channel: **Foramen caecum**, remnant of the proximal end of the **ductus thyreoglossus**

Tongue development

The ectoderm and entoderm of the common base of the tongue differentiate into stratified squamous epithelium, taste bud cells, and secretory compartments and ducts of the tongue glands

From ectomezenchyme of fused protrusions, the ligament of the tongue, blood and lymph vessels develop, incl. lymphatic tissue of the root of the tongue

Muscles of the tongue come from the occipital myotoms, which move to its base and merge together.

During the fusion of myotomes, their motor nerves also merge (segmental arrangement) - the **hypoglossus nerve** is formed

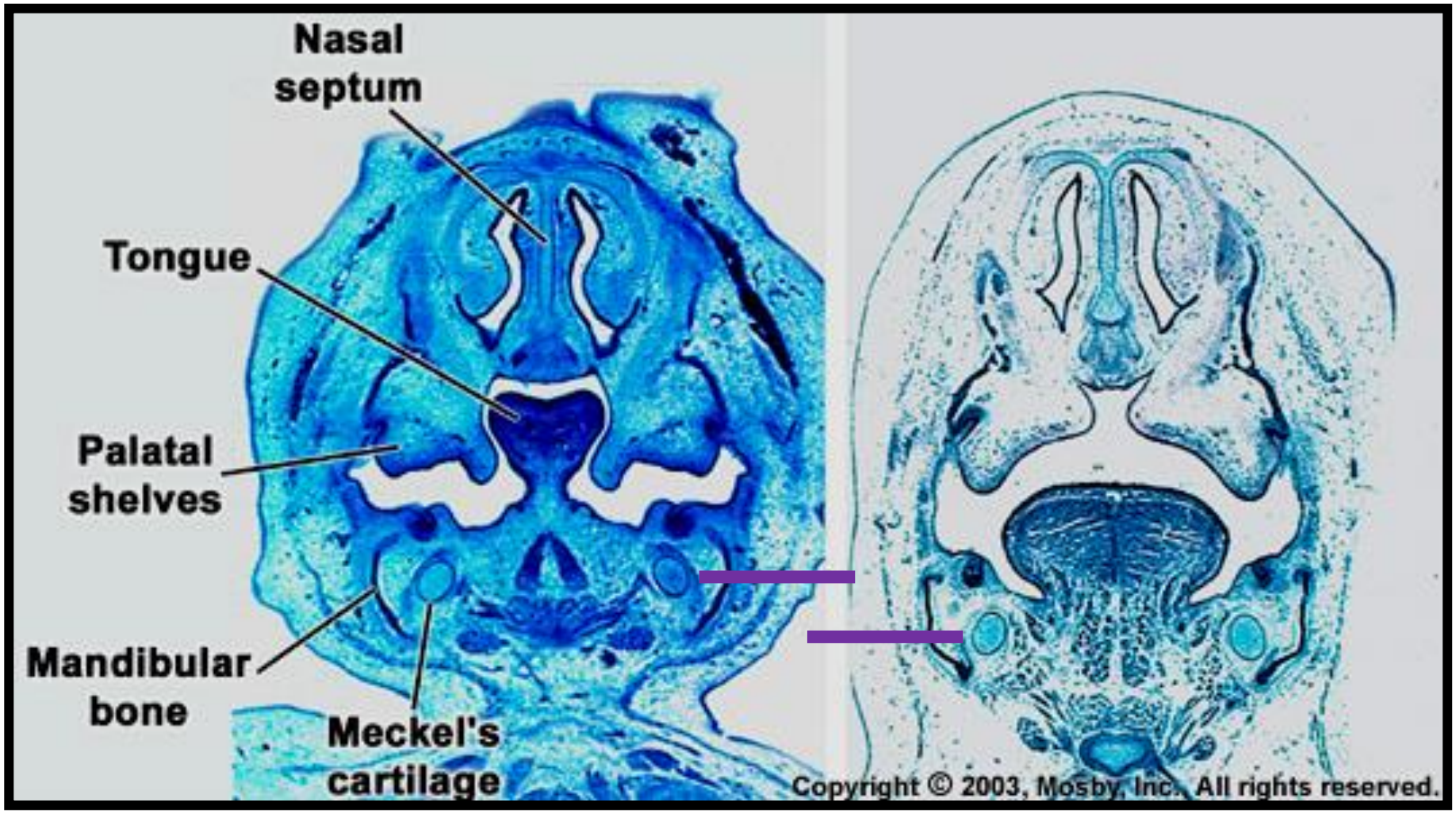
Development of tongue papillae - in the 8th week – firstly papillae vallatae, foliatae (near the branches of the n. IX.), fungiformes (branches of the n. Lingualis), filiformes (the 11th-12th week)

Taste buds - weeks 11-13

Sensitive innervation: **Apex and corpus - trigeminal nerve** (n. mandibularis)
Radix - n. Glossopharyngeus

Innervation of taste buds:

- Taste buds in papillae fungiformes fungal **- n. facialis** - chorda tympani
- Taste buds in papillae foliatae and circumvallatae - **n. glossopharyngeus**
- Taste buds in another location (radix lingue, isthmus faucium) - **n. vagus**



At birth: the tongue occupies the oral cavity

Postnatally: the root of the tongue descends into the pharynx – process finished at the 4th year of life

Overview of tongue development defects

Ankyloglossia (lingua accreta) - short frenulum, limited mobility of the tip of the tongue, it is not possible to stick out the tongue (difficulty breastfeeding), 1: 300 births. The frenulum usually lengthens spontaneously (surgery is not needed)

Congenital lingual cysts and fistulas - persistence of ductus thyreoglossus – clinically usually non important, causes problems only when enlarged (discomfort in the pharynx or dysphagia)

Macroglossia - a rare, abnormally large tongue (associated with some syndromes, e.g. Down sy.)

Microglossia - a rare, abnormally small tongue (mostly associated with micrognathia; microglossia in combination with limb defects - Hanhart's syndrome)

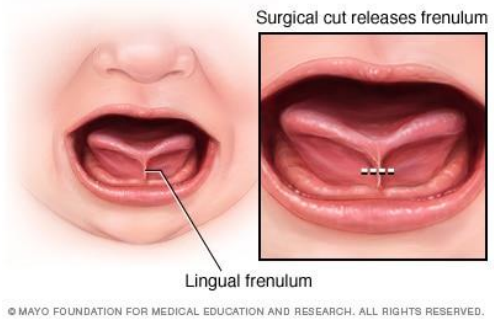
Glossoptosis - displacement of the tongue dorsally. Pushes on the epiglottis, narrowing of the pharynx.

Lingua bifida (lingua fissa, glossoschisis) - a very rare anomaly, incomplete fusion of the tubercula lingualia lateralia

complete cleft - including the tip of the tongue (associated with the cleft of the lower lip and jaw)

partial cleft - deep longitudinal groove (groove) in the body of the tongue

Aglossia – tongue not developed



Development of salivary glands

Salivary glands as derivatives of the lining of the stomodea or other structures: the oral side of the palate, the tip (ectoderm) and the root of tongue and the oral base (entoderm)

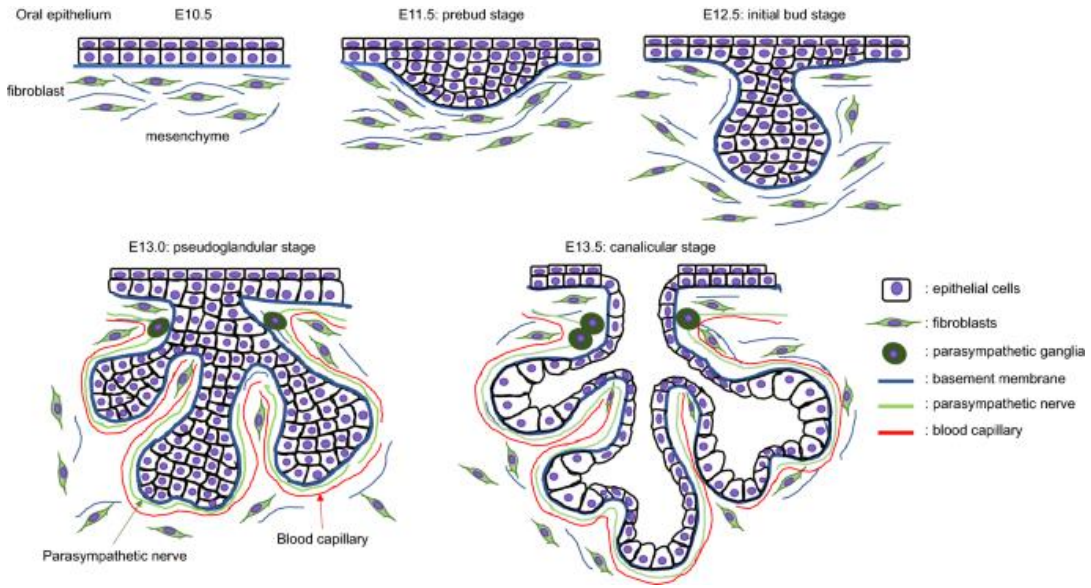
ectoderm: small salivary glands of lips and face, palate, gl. apicis lingue and parotid gland

entoderm: Weber's and Ebner's glands of the tongue, gl. submandibularis and gl. sublingualis

They all develop in a similar way:

From the epithelium (ecto- or entoderm) at the site of the future gland(s): cells begin to proliferate against adjacent ectomezenchyme

They lengthen and branch - the basis for the glandular duct system is created, the last 6th generation form **terminal branches**



Development of salivary glands

At the ends of the terminal branches (6th-7th generation) clusters of small spherical clusters of cells are subsequently formed - singular acins

The secretion starts during the **5th month** of development, followed by gradual lumen formation during the **6th month** of development

During this period, the division of the parenchyma into lobules begins, and thin septa are formed in glandular parenchyma from the superficial mesenchyme.

Lobulization continues until birth when glands become fully functional and begin to excrete saliva

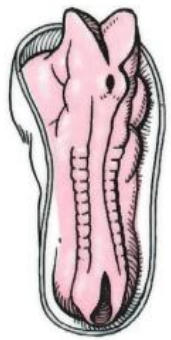
Basis for gl. parotis **4th - 6th week**, at the upper edge of both corners of the mouth; after narrowing of the rima oris, the ductus parotideus opens into the vestibule on the buccal side

Basis for gl. submandibularis **6th week**

Basis for gl. sublingualis **8th week**

Small salivary glands **during 3rd month** of development

Face development and defects



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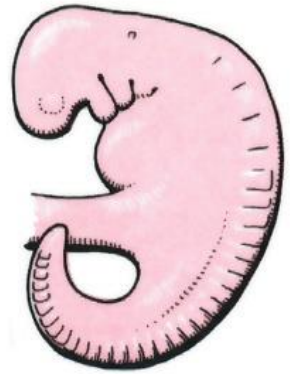
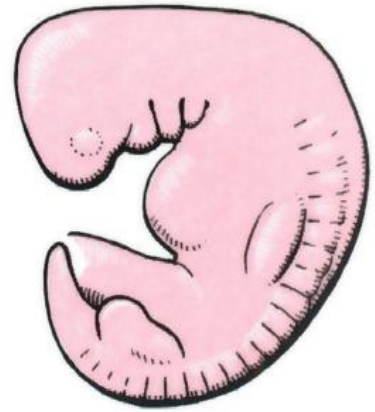
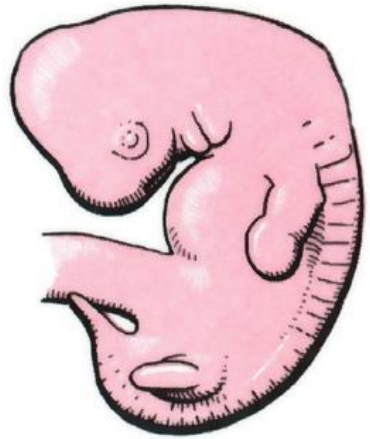


konec 4.týdne



polovina 5. týdne



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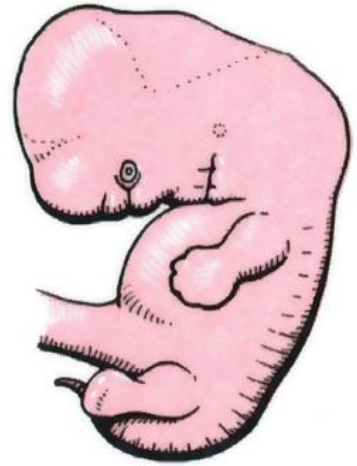
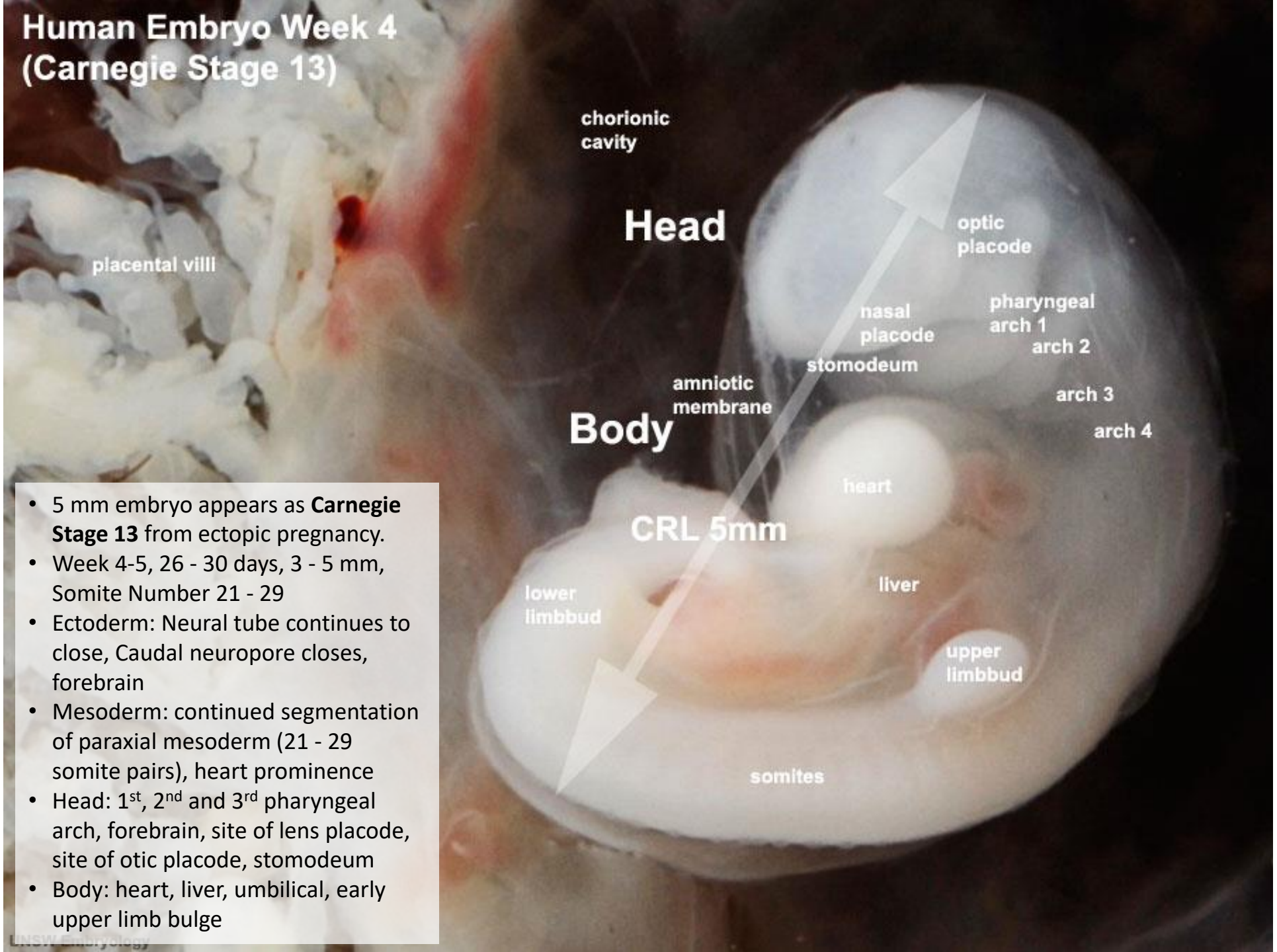


polovina 7. týdne

konec 8. týdne



- 5 mm embryo appears as **Carnegie Stage 13** from ectopic pregnancy.
- Week 4-5, 26 - 30 days, 3 - 5 mm, Somite Number 21 - 29
- Ectoderm: Neural tube continues to close, Caudal neuropore closes, forebrain
- Mesoderm: continued segmentation of paraxial mesoderm (21 - 29 somite pairs), heart prominence
- Head: 1st, 2nd and 3rd pharyngeal arch, forebrain, site of lens placode, site of otic placode, stomodeum
- Body: heart, liver, umbilical, early upper limb bulge

Human fetus at the end of 1st month of development

By the end of 1st month, the embryo has a form of short tube C-shaped curved dorsal side of embryo is convex and adjacent to amnion, cephalic end of the embryo is more advanced in development than caudal one

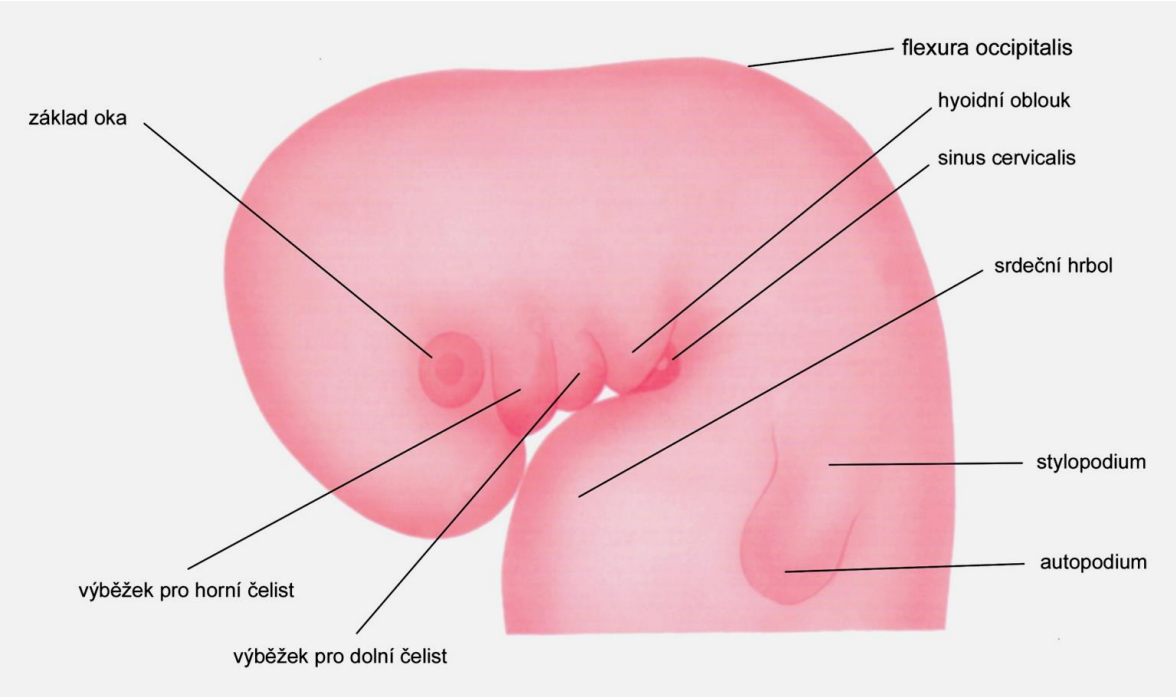
Body parts: head, neck, body and tail

Length of the embryo is 8 -10 mm

Frontal prominence with prosencephalon

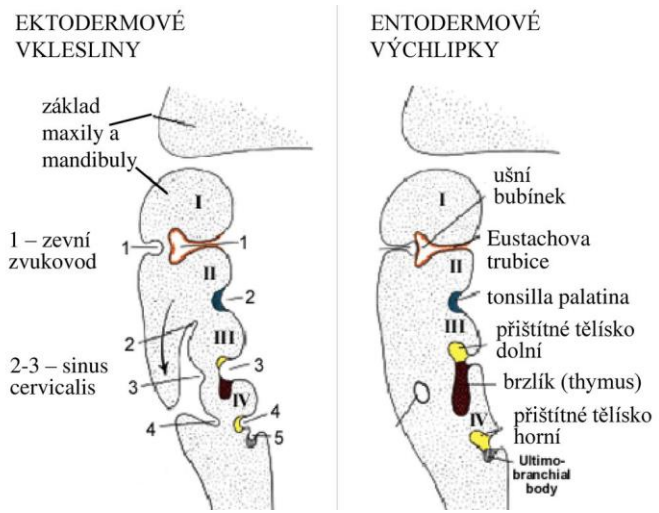
Mesencephalic prominence with mesencephalon - flexura cephalica

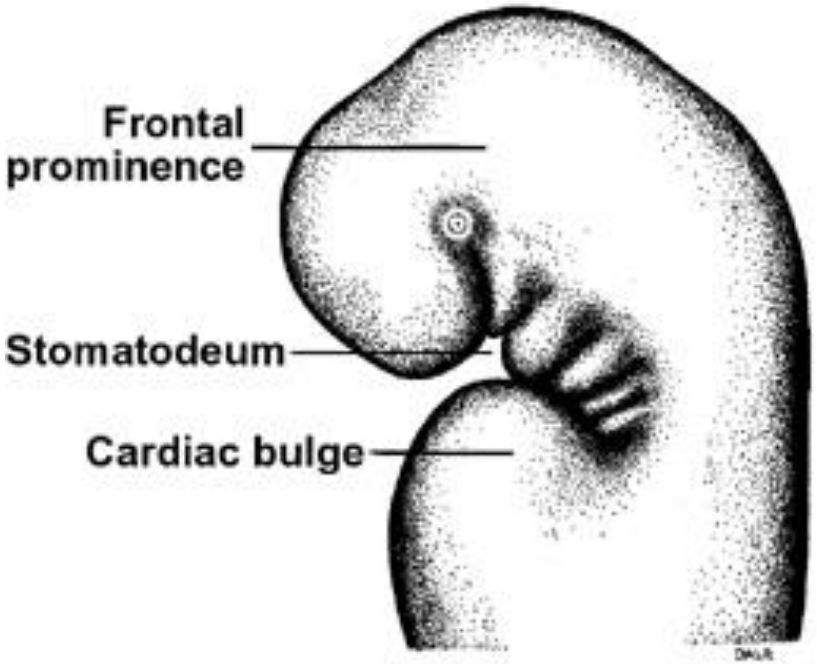
Occipital prominence with rhombencephalon - flexura occipitalis

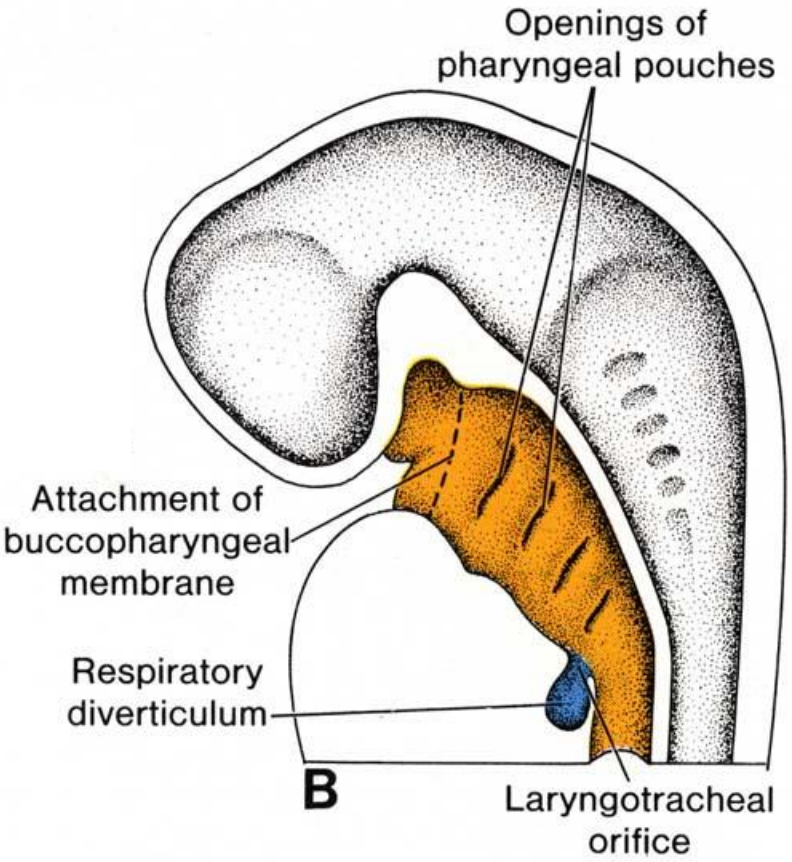


Human fetus at the end of 1st month of development

Pharyngeal (branchial) aparatus:
6 Branchial arches
4 Branchial clefts (grooves) (ectodermal)
5 Branchial pouches (entodermal) Separated by **membranae obturantes**

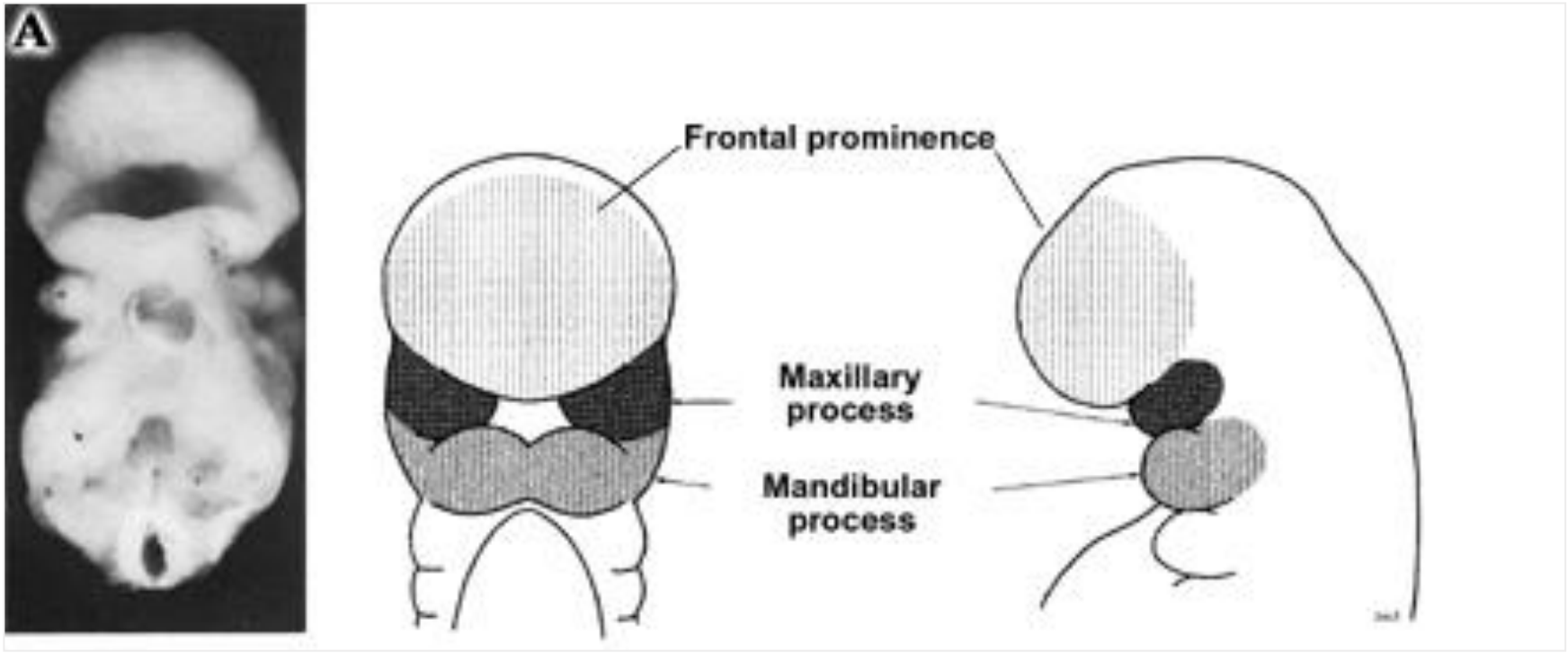




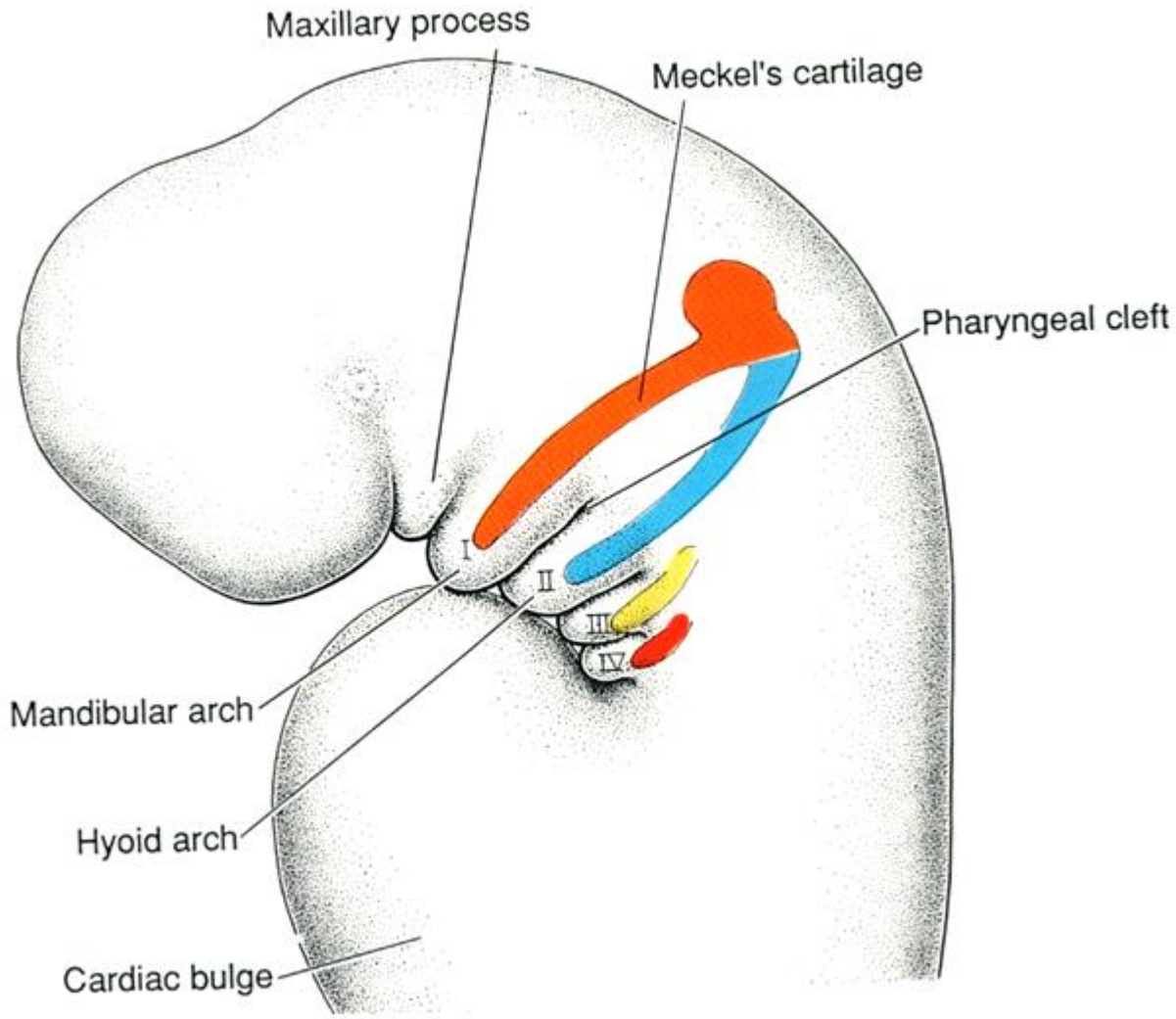


<u>1. Pharyngeal arch</u> (mandibular) is divided into :

- **Processus maxillaris**
- **Processus mandibularis**



Branchial aparatus



Face development

By the end of 4th week of development the face development is initiated around the primitive mouth opening: **stomodeum**

The oral cavity develops from the stomodeum or primitive mouth

Bottom of the stomodeum is constituted by oropharyngeal membrane (membrana oropharyngea)

Development is organized by 2 centers:
- **Prosencephalic**
- **Rhombencephalic**

5 processes limit the stomodeum:
- **Frontonasal** prominence
- Paired **maxillary** prominences (processus maxillares)
- Paired **mandibular** prominences (processus mandibulares)

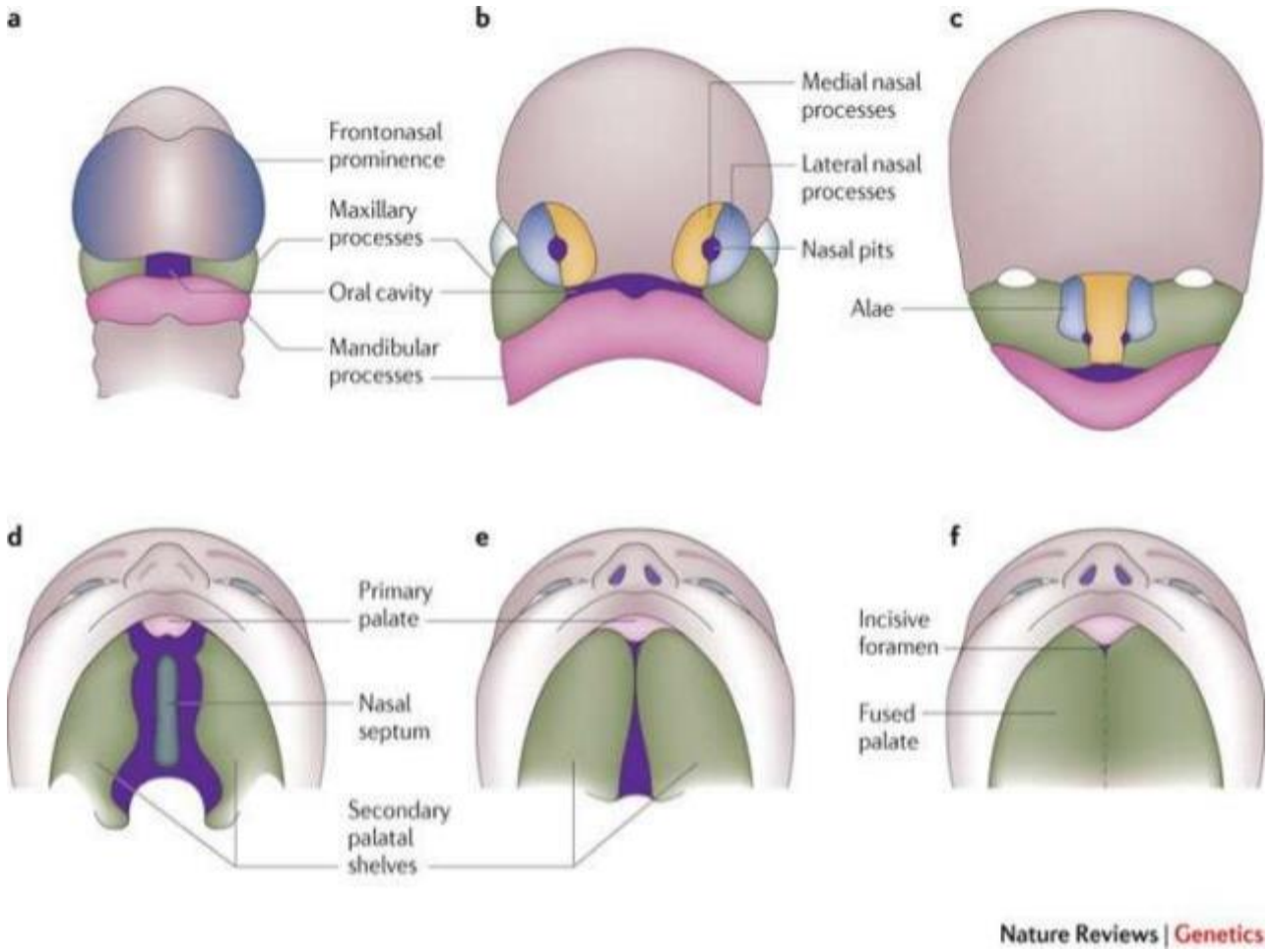
The base of the prominences is formed by an **ectomesenchyme**, which populated them from the lower mesencephalic and upper rhombencephalic section of the neural crest.

The surface of the prominences is covered by an **ectoderm**, which also lines the stomodeum.

Prominences are initially separated from each other by deep grooves. It is a dynamic process - it starts at the end of the 4th and beginning of 5th week of development and ends at about the 8th week. It depends on the proliferation of the ectoderm and ectomezenchyme of the prominences and their further divisions, movements and different growth rates.

It is terminated by the fusion of the protrusions.

Face development



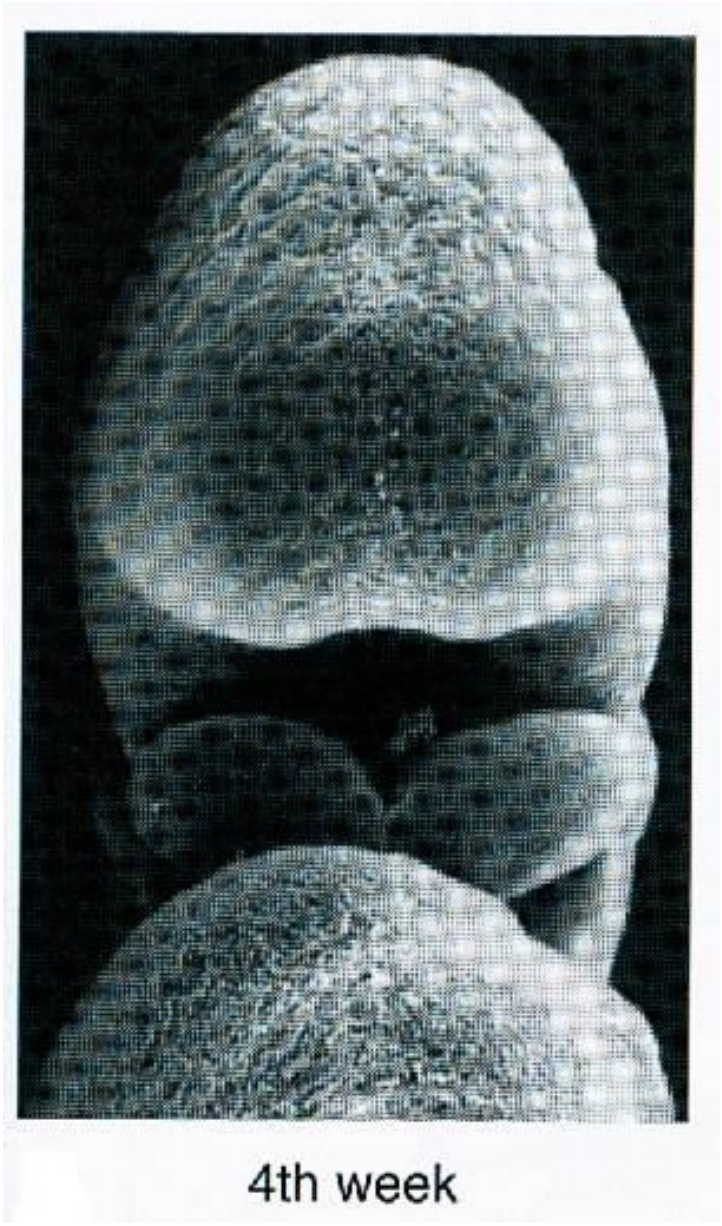
Face development

Initiation

Frontonasal prominence (processus frontonasalis)

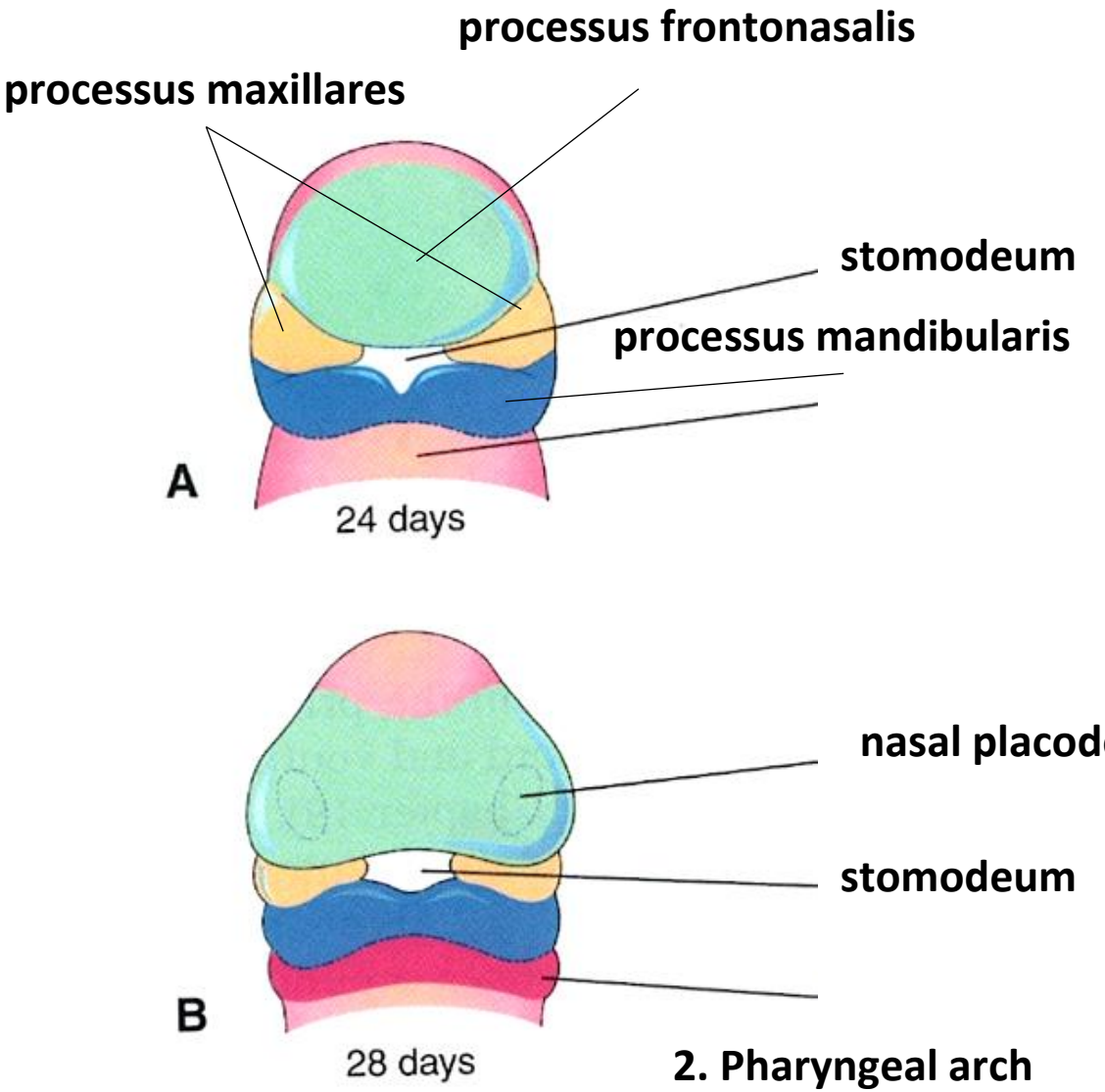
Paired prominences for upper jaw (processus maxillares)

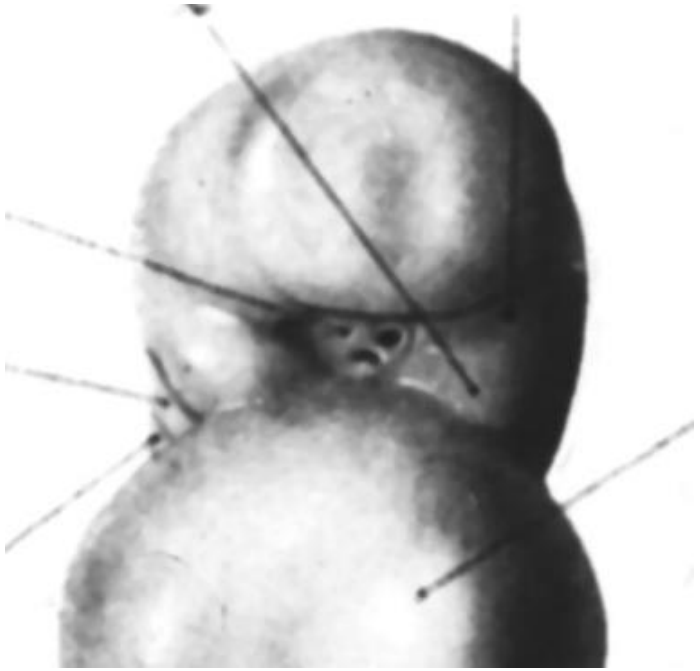
Paired prominences for lower jaw (processus mandibulares)



4th week

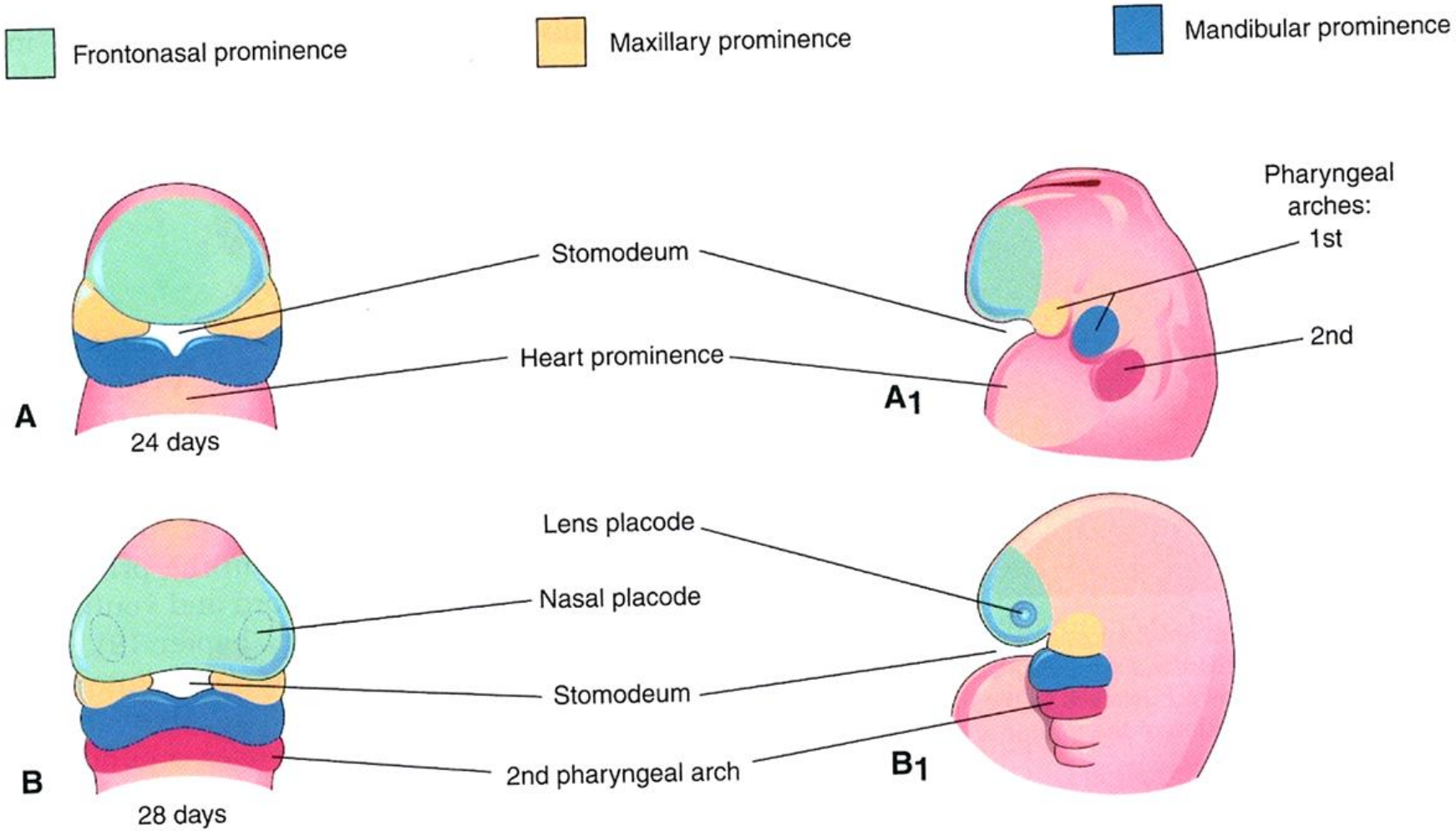
Face development





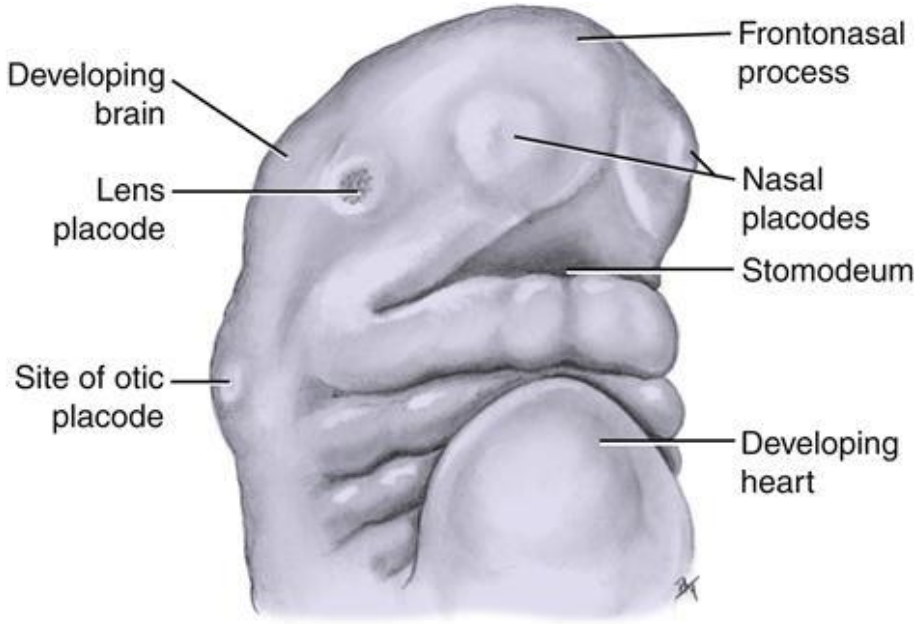
2. Pharyngeal arch

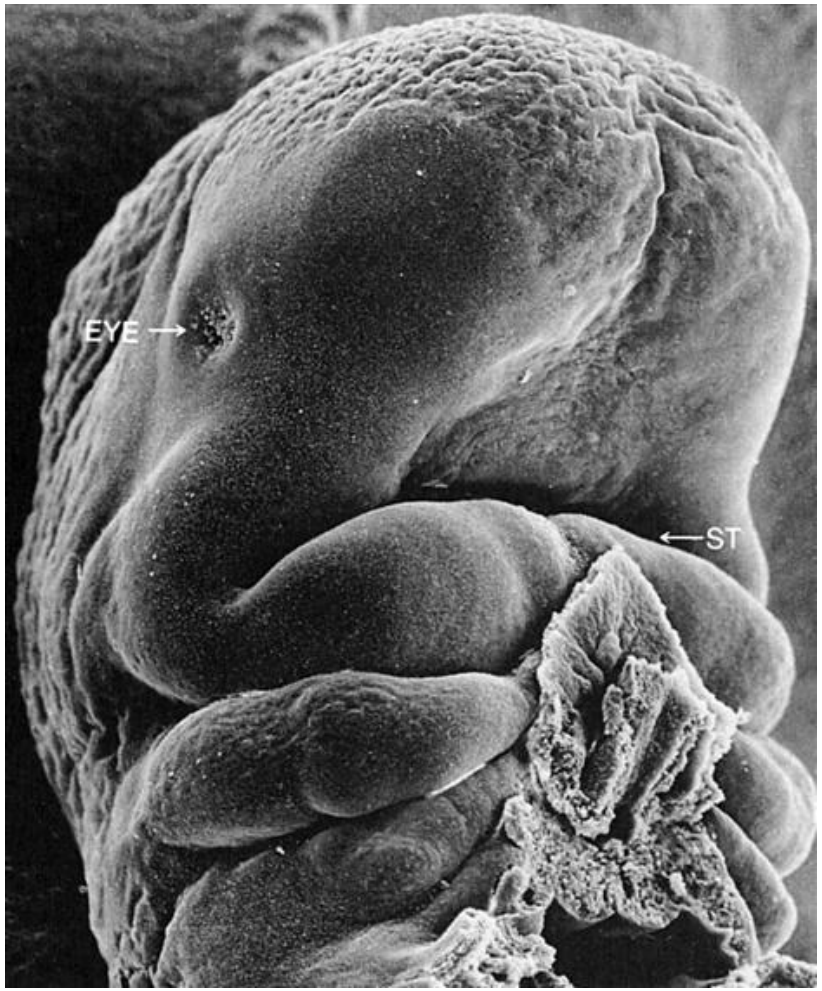
Face development



Face development

4th week





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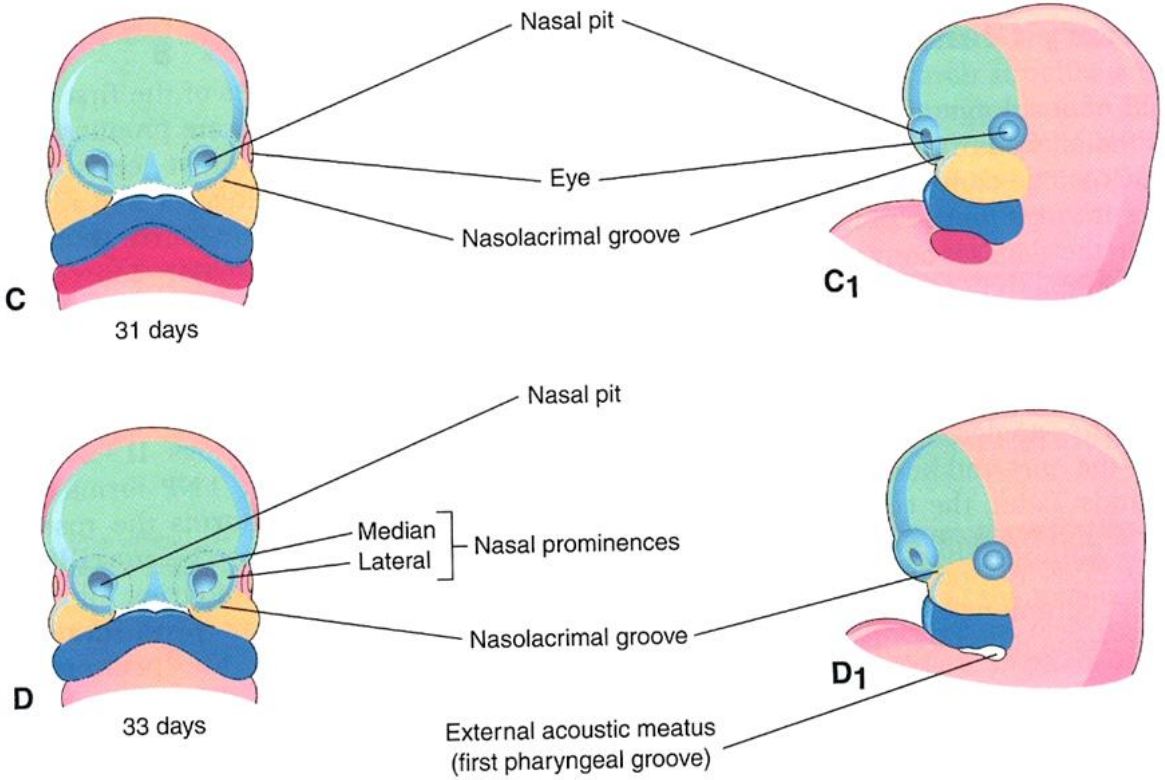
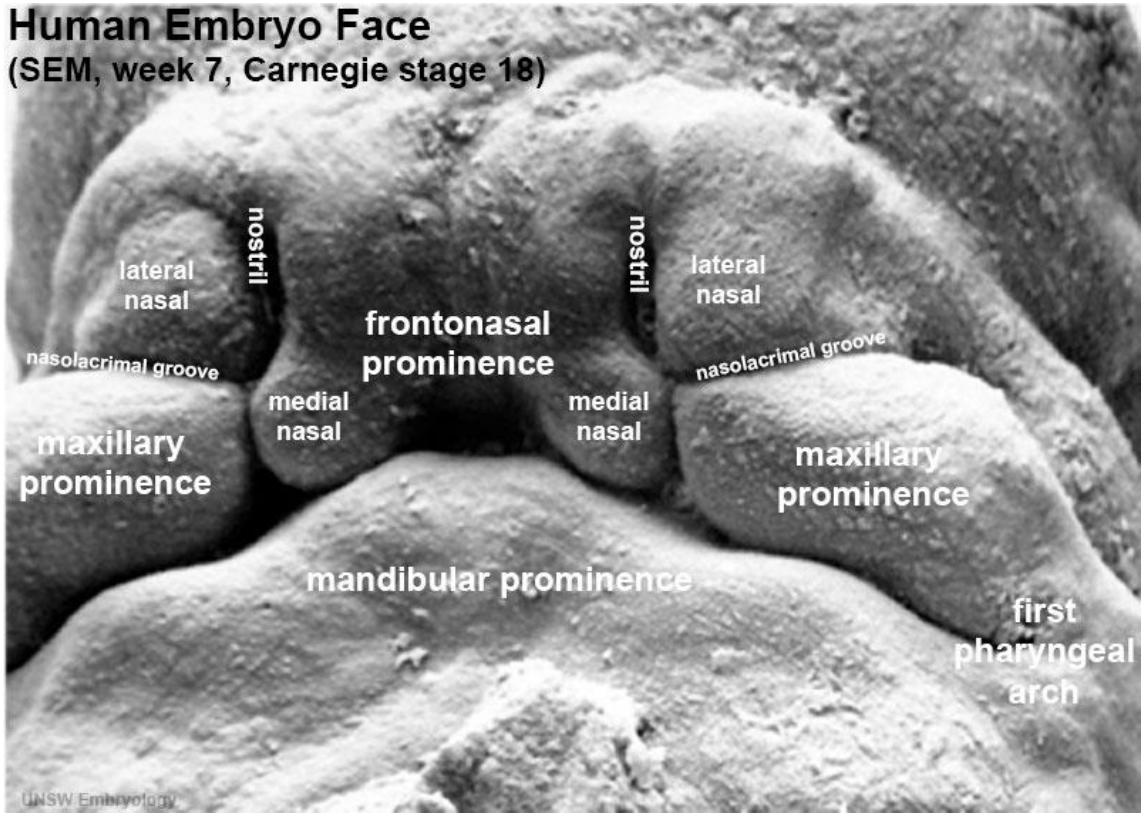
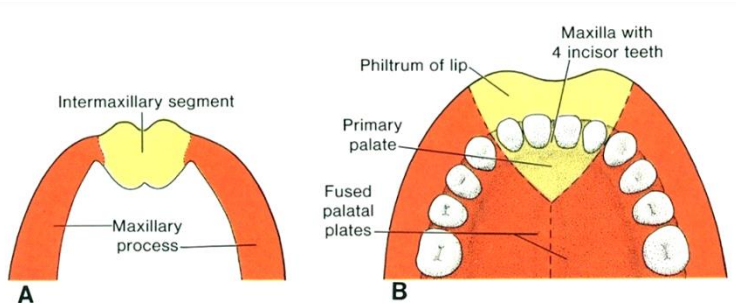
Face development







- Nasal pits surrrounded by paired prominences – **medial and lateral nasal prominence**
- **Area triangularis** (nose)
- **Intermaxilary segment** (medial part of upper lip, part of upper jaw, primary palate)

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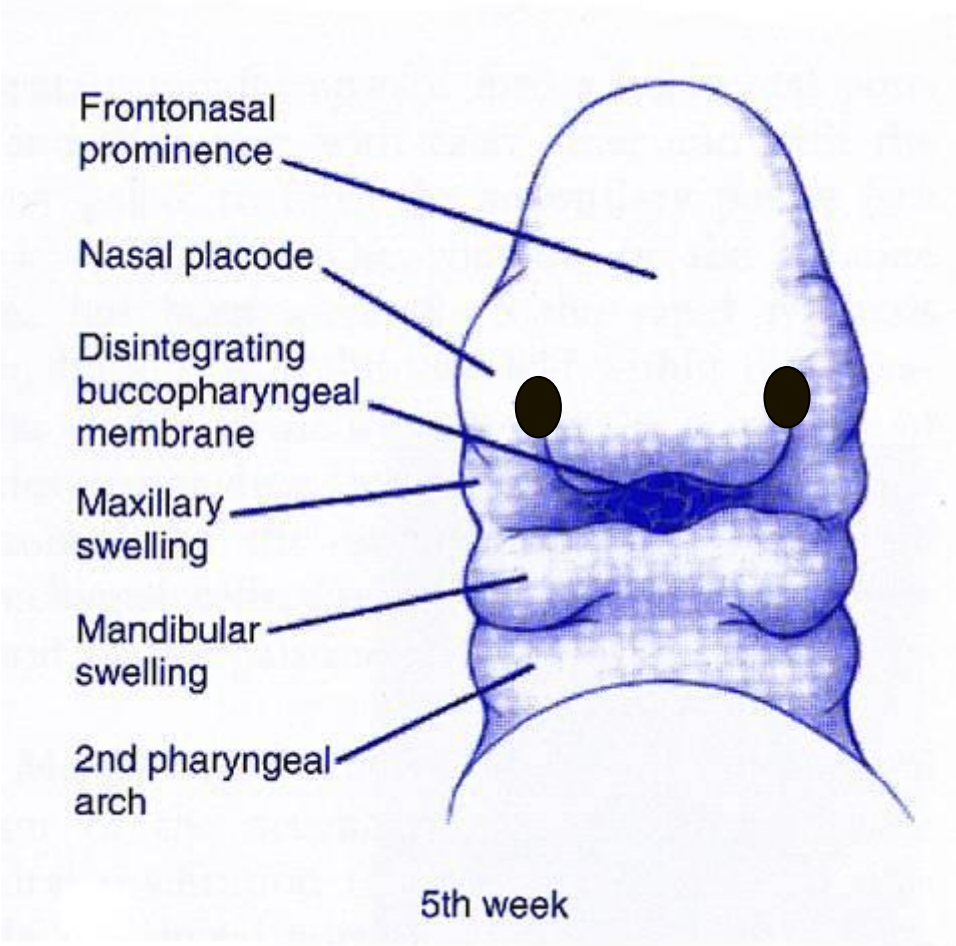
<u>Frontonasal prominence</u> (gives rise to forehead, nose and middle part of upper lip - *philtrum*)

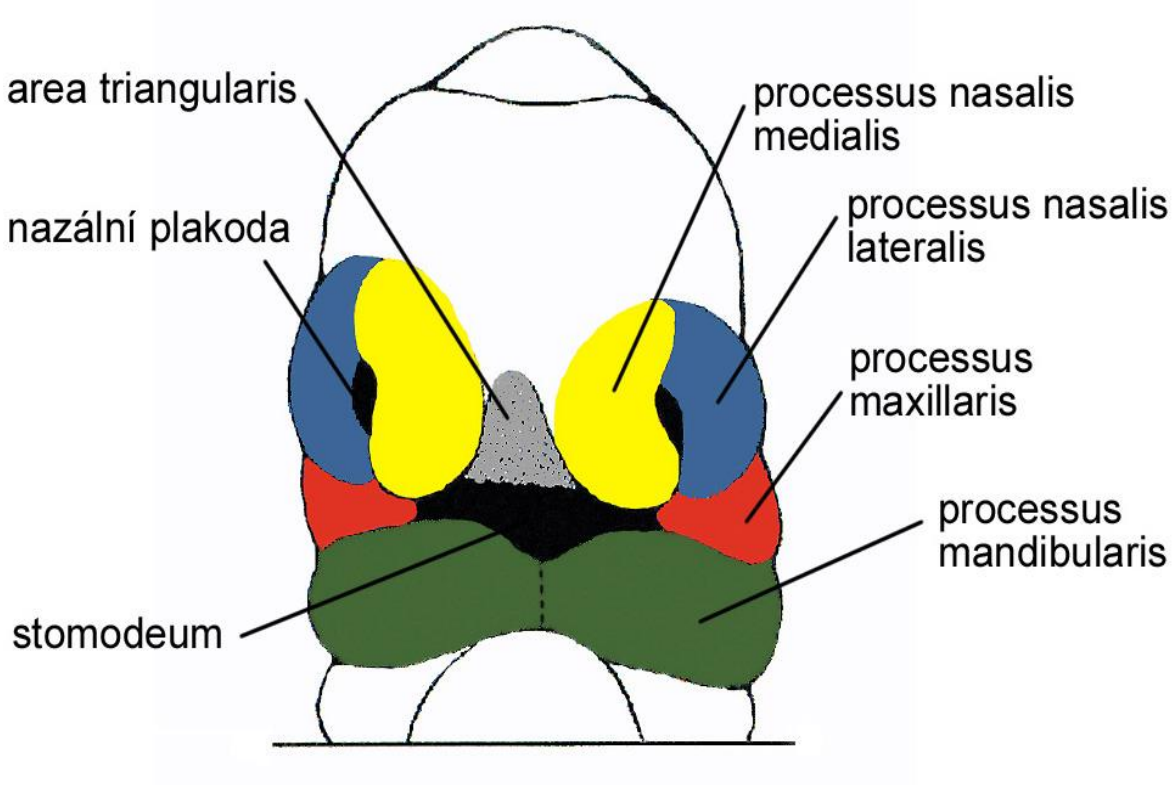
4th week

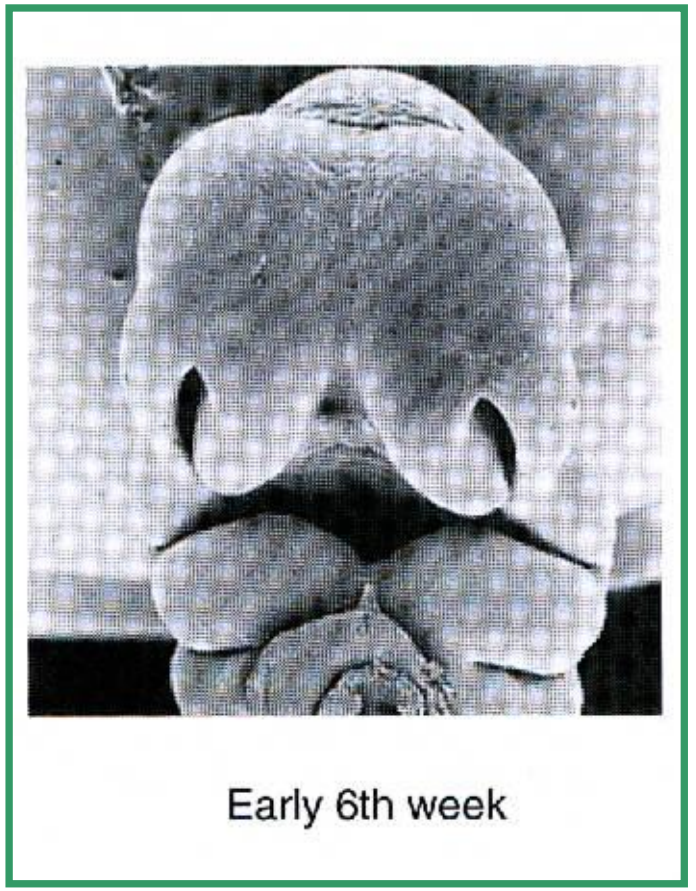


5th week

After the formation of nasal pits the ectomesenchyme is divided into parts:
Processus nasalis medialis
Processus nasalis lateralis

*Triangular area between medial nose processes is called **area triangularis***





Intermaxillary segment

By the end of the **5th week**, the **medial nasal prominences fuse with each other to form the intermaxillary segment**

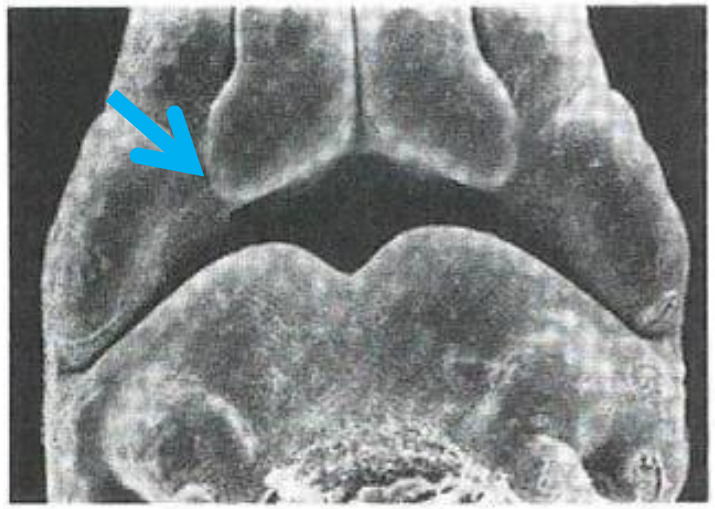
The segment proliferates caudally and inserts between ends of maxillary prominences which merge with it during the **6th week**

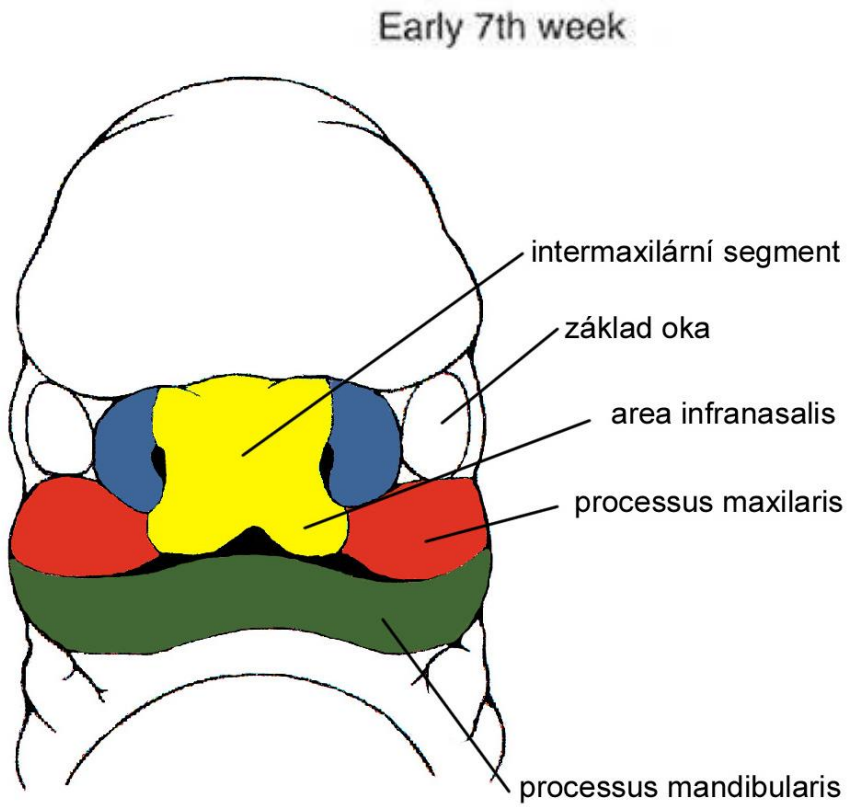
The intermaxillary segment gives rise to:

a) middle portion of the upper lip, or philtrum
b) the premaxillary part of the maxilla
c) the primary palate

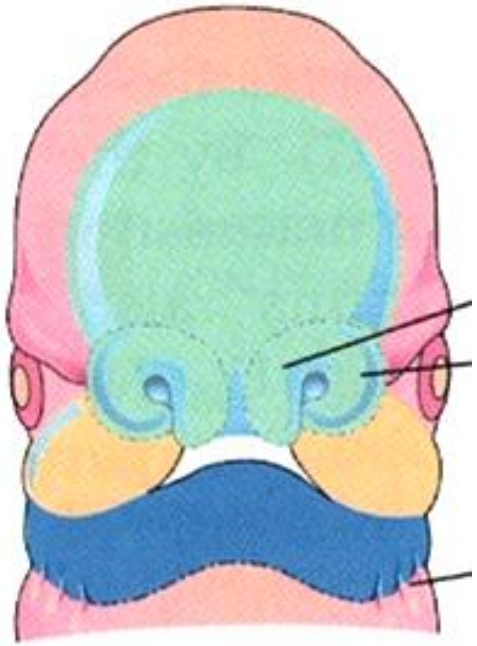
At first, lateral nasal prominences are separated from the maxillary prominences by a furrow, called the **nasolacrimal groove**

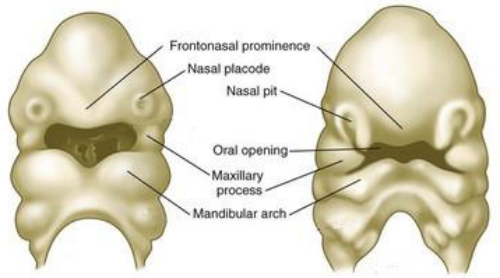
During next days, the maxillary prominences enlarge and fuse with lateral nasal prominences.

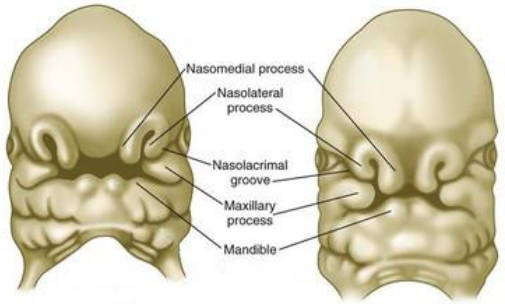


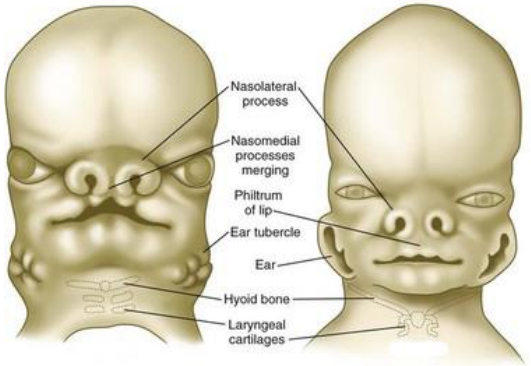


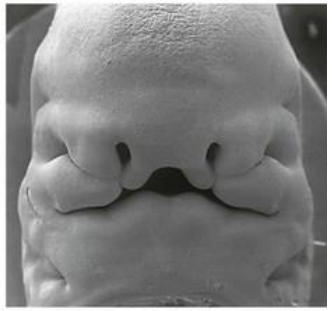
Face development









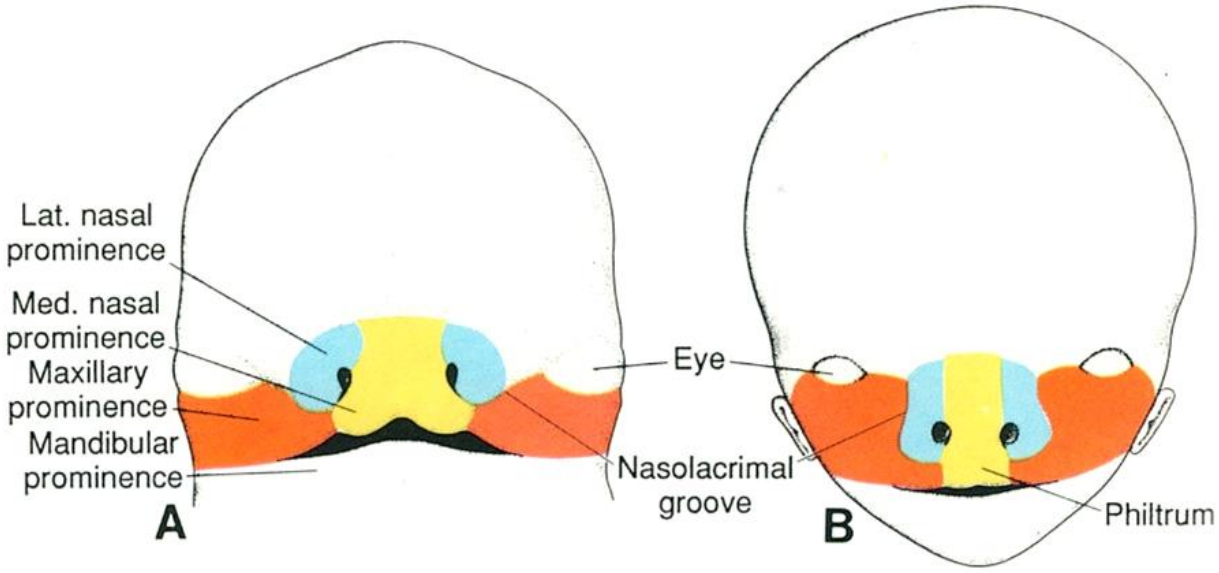


Maxillary prominences fuse with:

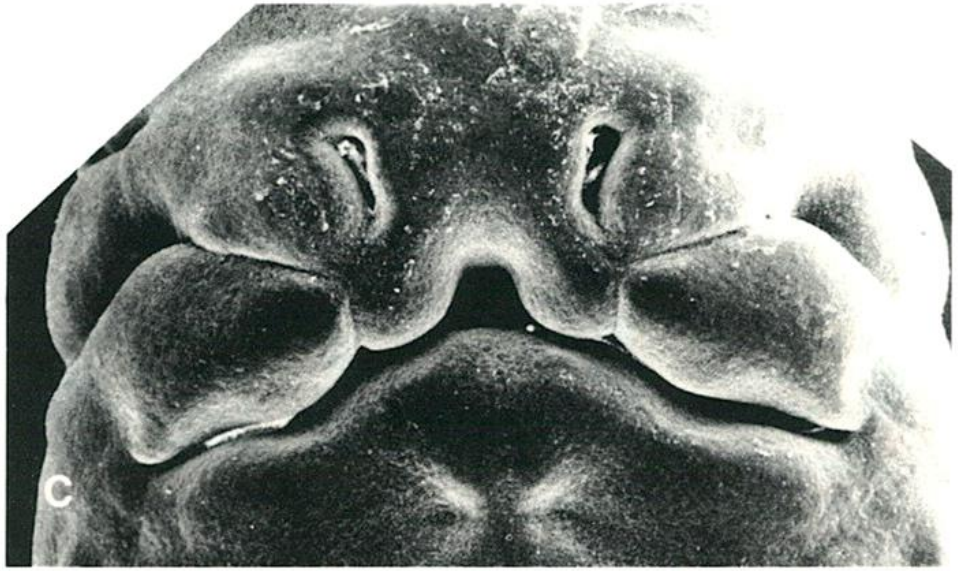
1. **Intermaxillar segment** (formation of upper lip and palate)
2. **Lateral nasal prominences** (the rest of upper lip and part of nose)

Lateral nasal prominences are divided from the maxillary prominences by - **sulcus nasolacrimalis**

Face development



7th week



Summary of face development timing

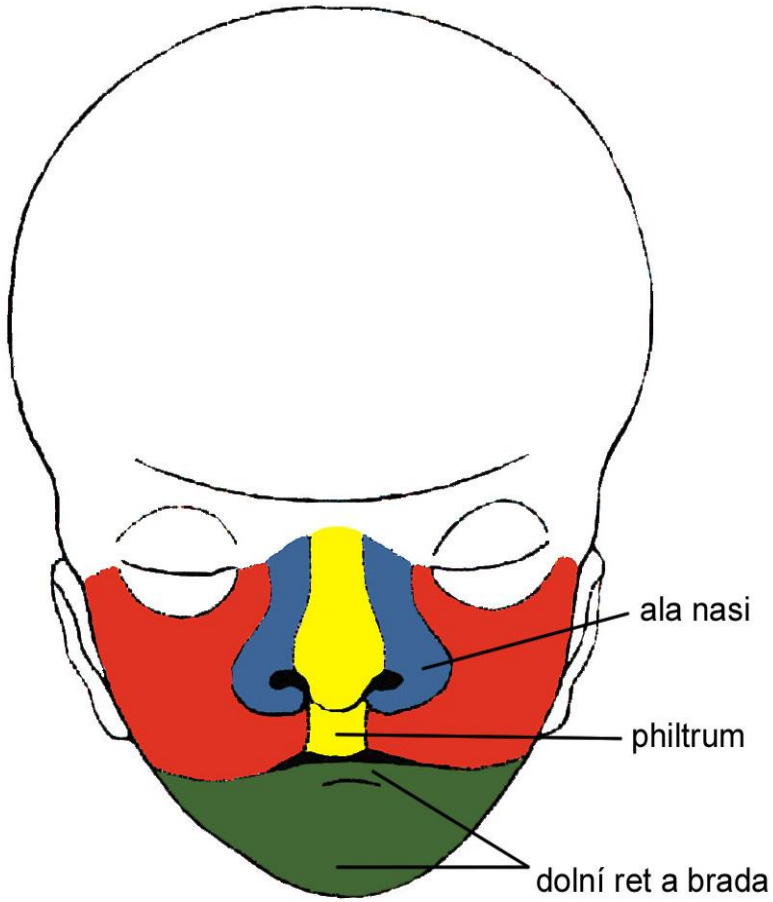
Between **5. - 7. week**

Beginning of 5th week: fusion of medial edges of mandibular prominences: **lower lip and chin**

Beginning of 6th week: fusion of medial edges of maxillary prominences with intermaxillary segment: **upper lip**

In the middle of 7th week: processus nasalis lateralis (at both sides) fuse with the upper part of maxillary prominence

Between 7th-8th week: the fusion of maxillary and mandibular processes: narrowing of **rima oris**



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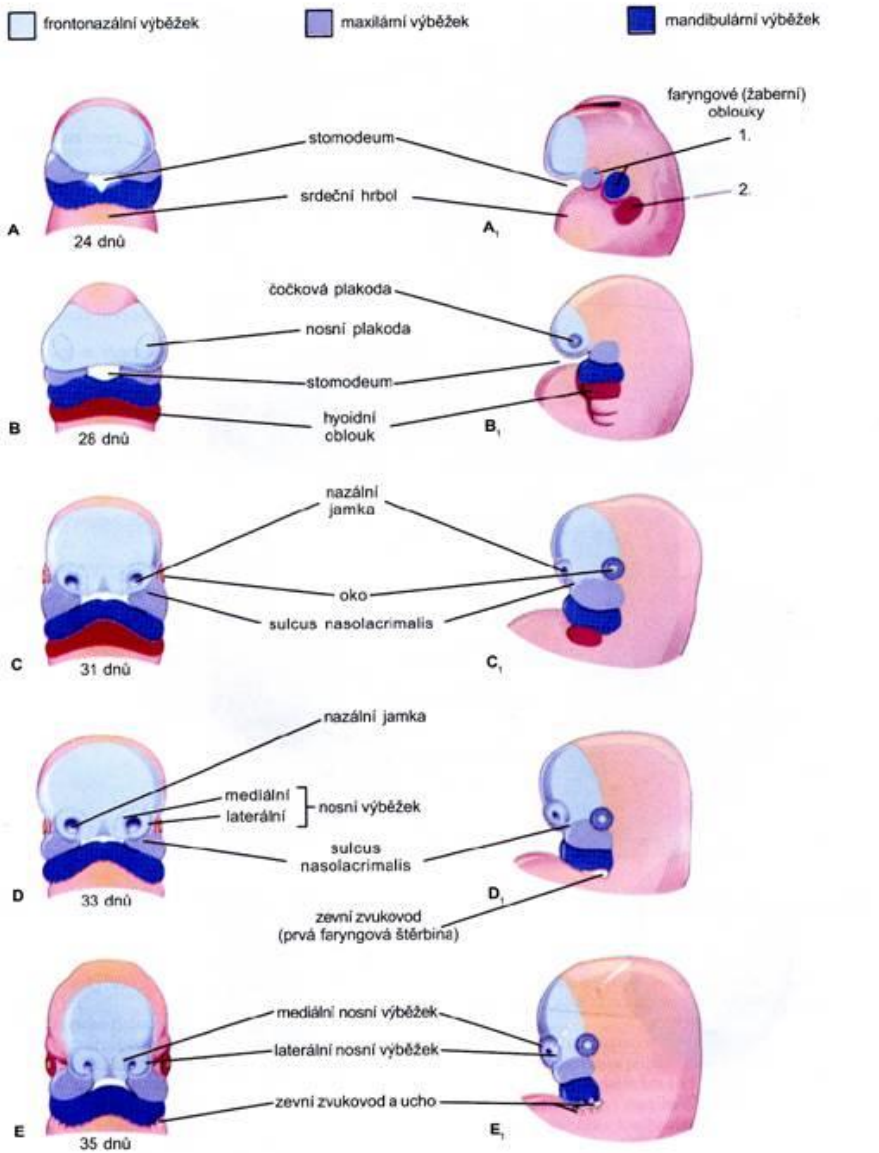
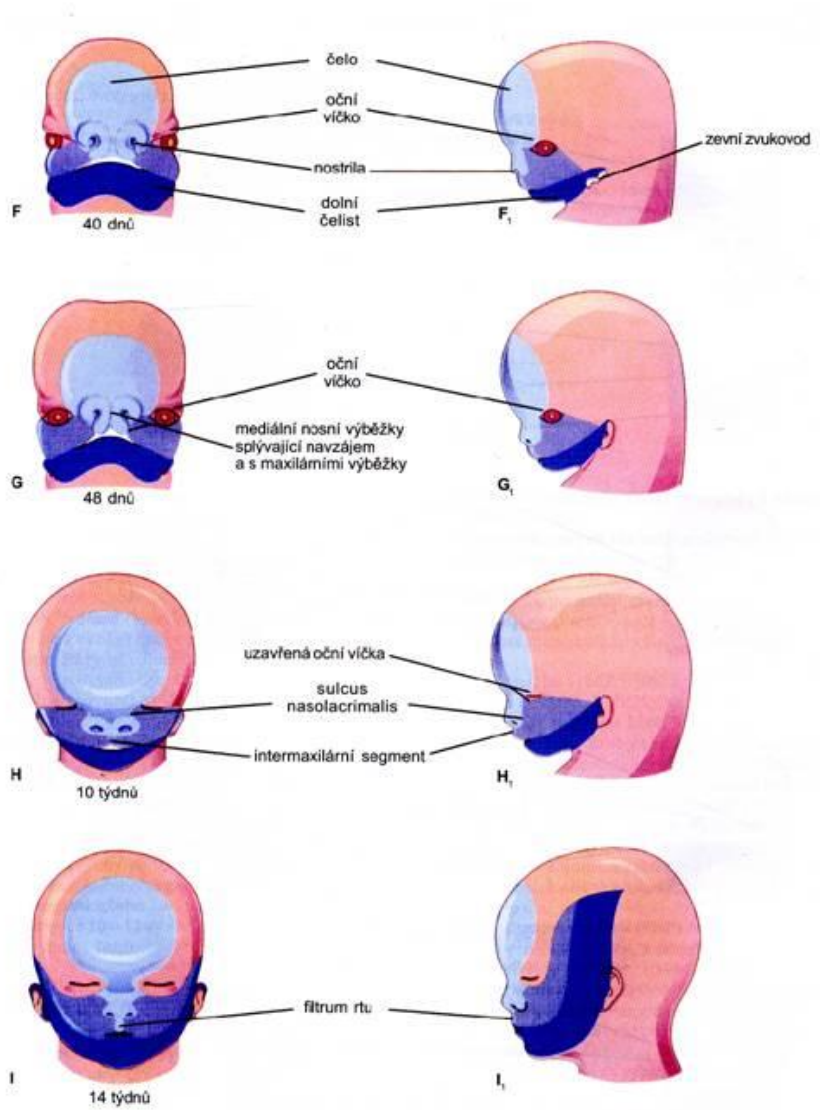
Face development - summary

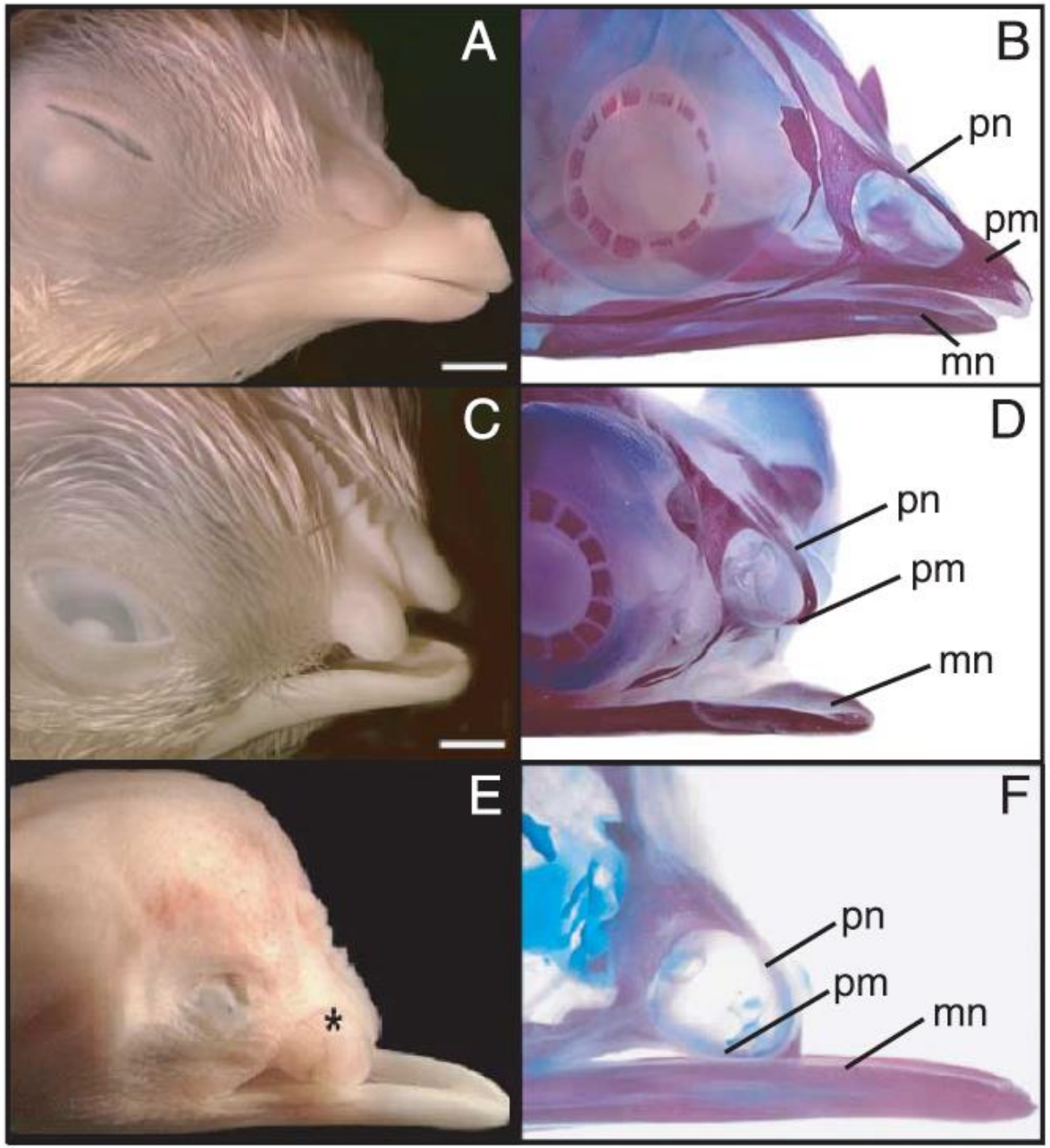


Obr. 10-26. Schémata zobrazující stadia vývoje lidského obličeje.
Ilustrace pokračuje na příští stránce



Obr. 10-26. *Pokračování*

Face development



Normal

Cyclopamine (teratogen)

anti-SHH Ab

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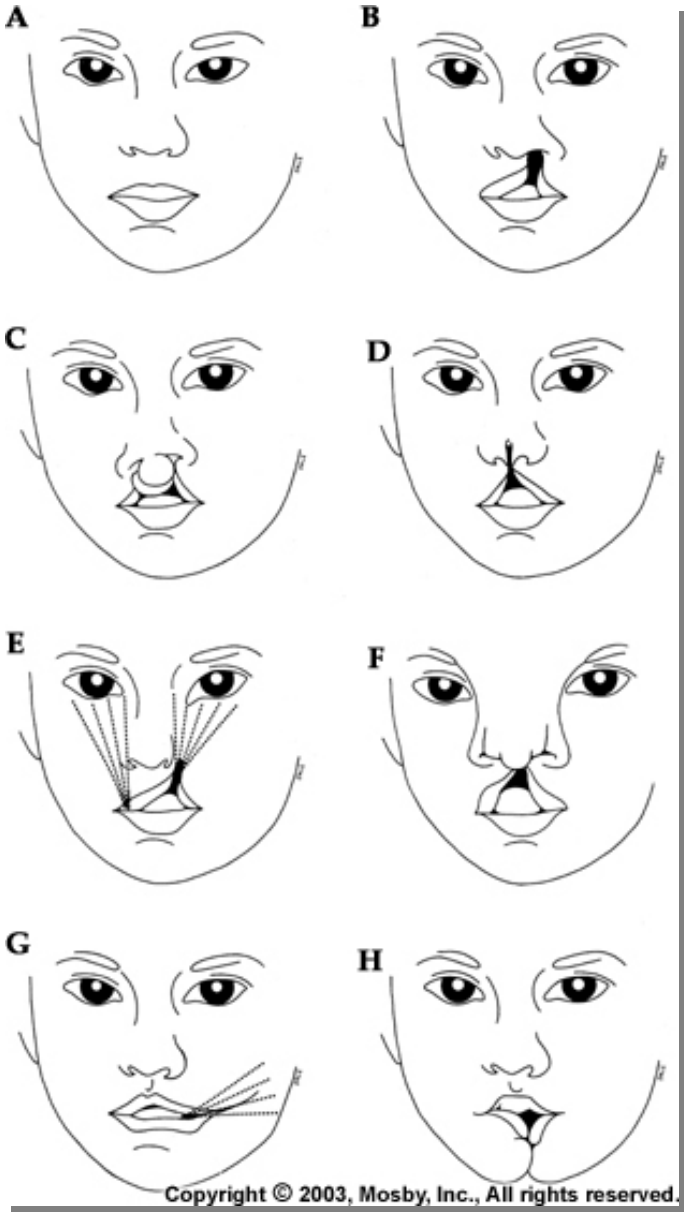
Orofacial clefts

Clefts emerge when the development of prominences was incorrect**: prominences did not fuse, were not established, belated migration or proliferation**

Facial clefts belong to the most common defects

Incidence: 1,7 : 1 000 newborns



Clefts of the upper lip

Median clefts of the lower lip and chin (mandible)

Oblique facial clefts

Lateral, or transverse, facial clefts

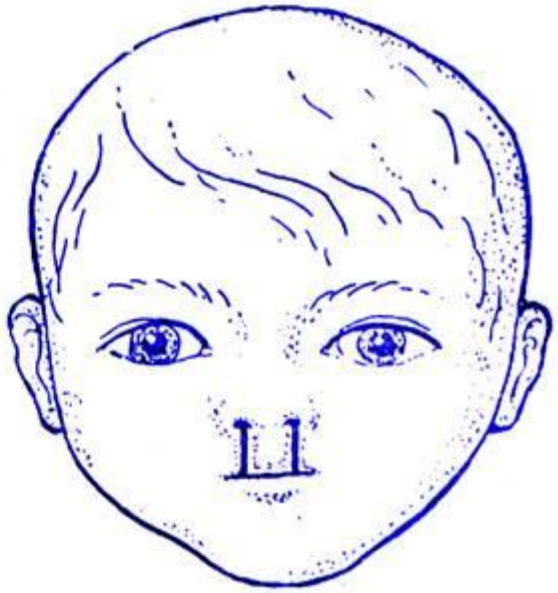
Clefts of the upper lip - cheiloschisis superior

Lateral or medial

Lateral:

- **Unilateral cleft lip** - results from failure of maxillary prominence to merge with the lateral edge of intermaxillary segment on the one side
- **Bilateral cleft lip** - results from failure of mesenchymal masses of both maxillary prominences to merge with lateral edges of intermaxillary segment

cheiloschisis unilateralis / cheiloschisis bilateralis

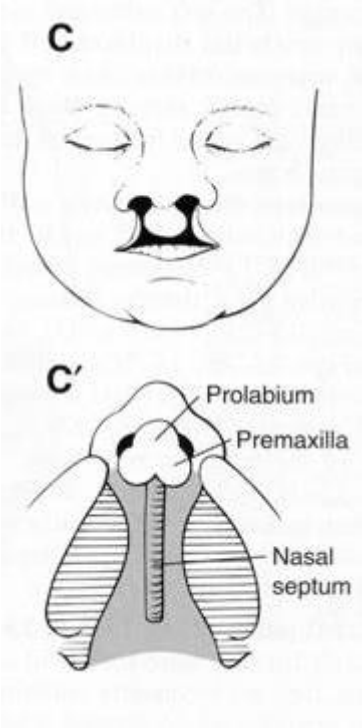


(Bi)lateral clefts of the lip and palate

Bilateral clefts of the lip and maxilla are very hard defect

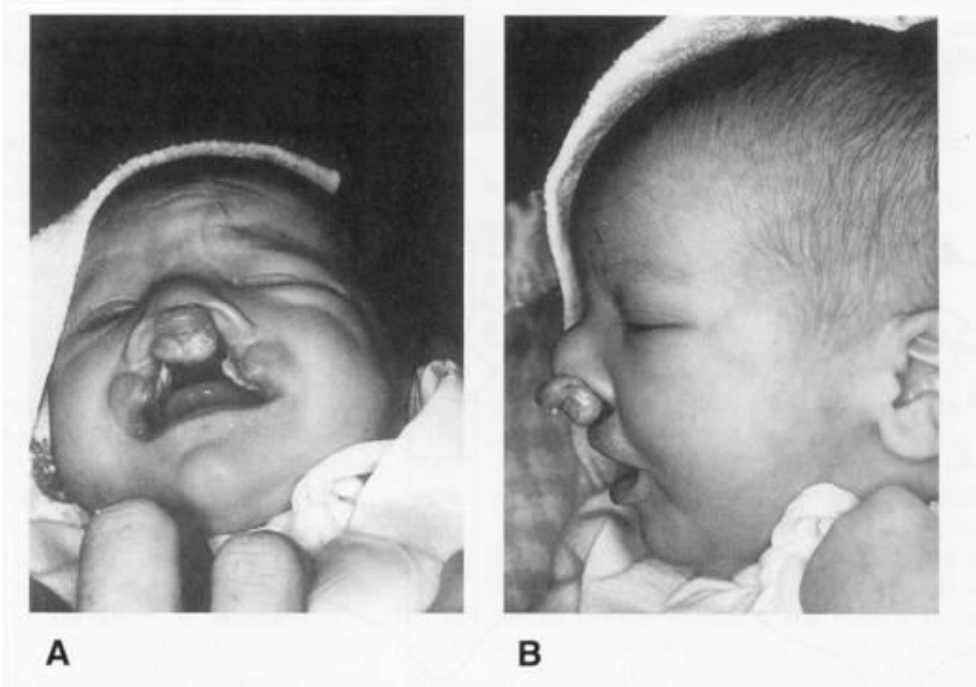
Clefts can be uni and bilateral

The child can not suck and is in danger of aspiration of food

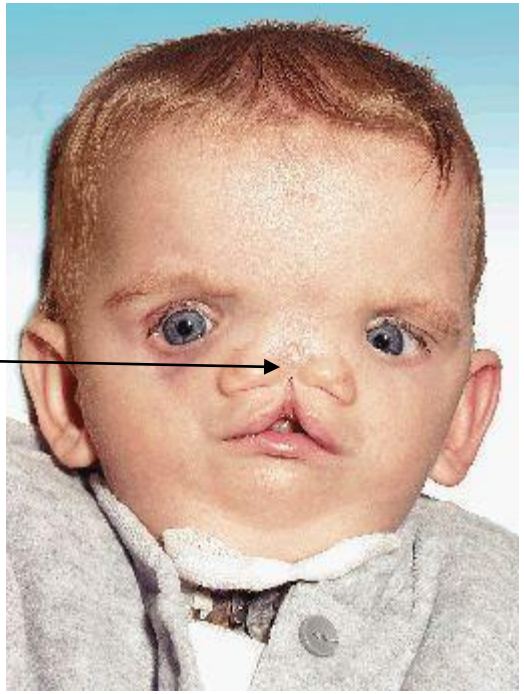


Unilateral cleft lip.

Bilateral cleft lip.



Median cleft lip (labium leporinum) **cheiloschisis mediana**

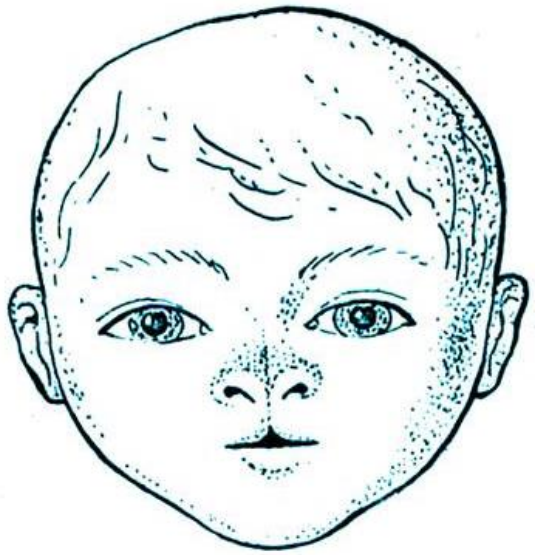


Is caused by delay in development of intermaxillary segment due failure of the medial nasal prominences (processus nasales mediales) to merge

Rarely with the cleft of apex nasi
Variable

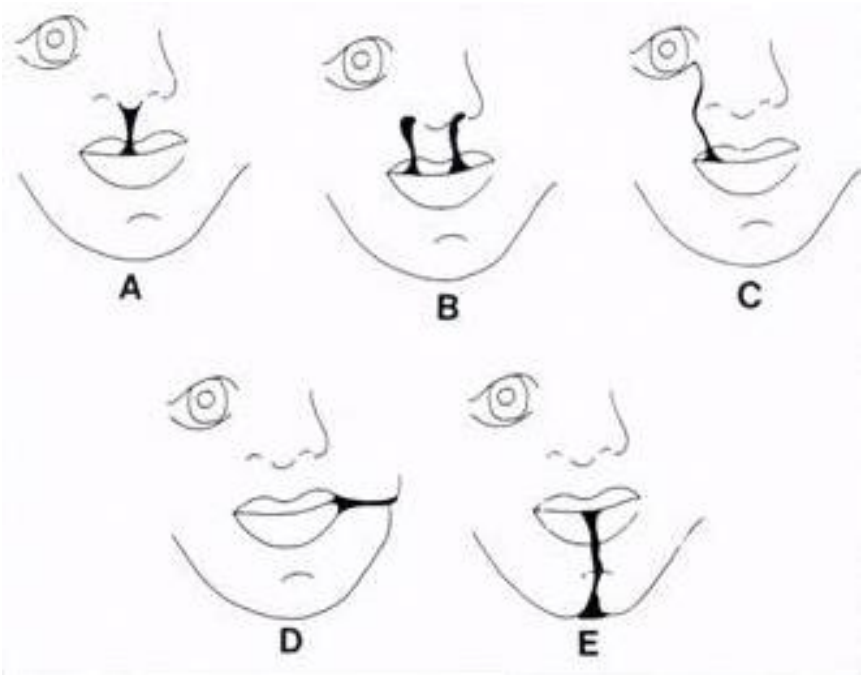
Critical period: 27. - 35. day

The median cleft lip is one of symptoms of the **Mohr syndrome**



Oblique facial cleft
(coloboma faciale, fissura orbitofacialis)

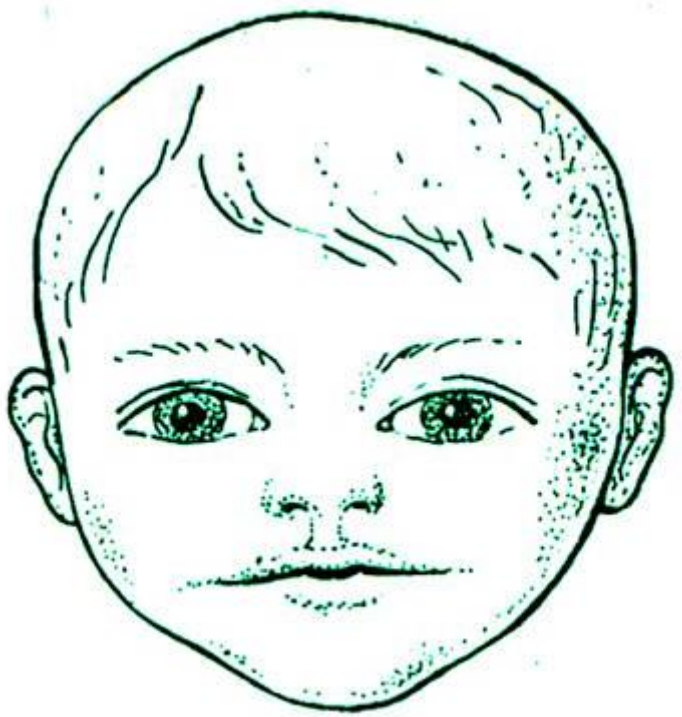
Uni- or bilateral, arises if the nasolacrimal groove us preserved
Combined always with the unilateral lip cleft and extends to the medial margin of the orbit
Results from failure of the mesenchymal masses of the maxillary prominences to merge with lateral and medial nasal prominences
rare

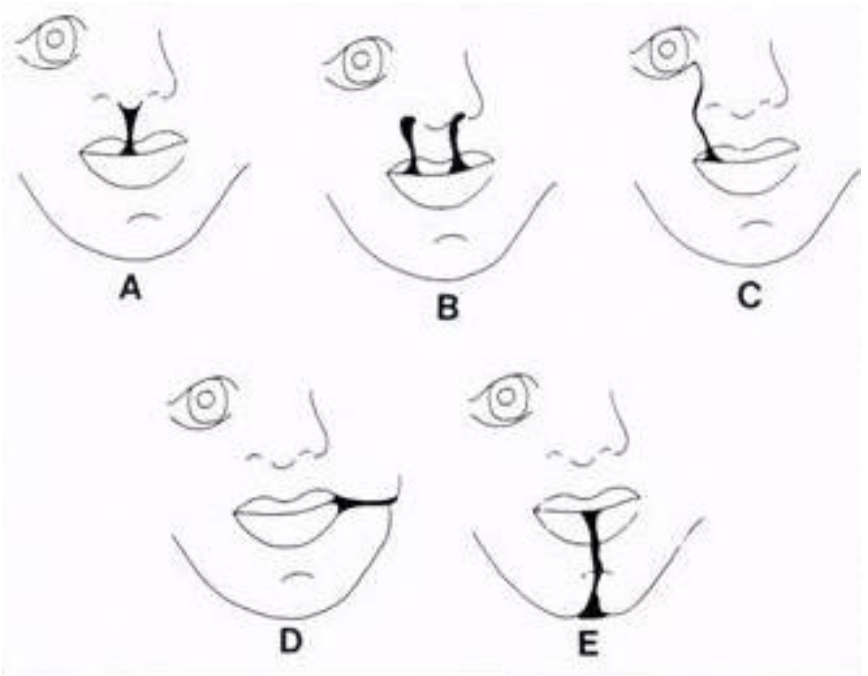


Lateral/transverse facial cleft
fissura transversa faciei, macrostomia

Runs from the mouth toward the ear

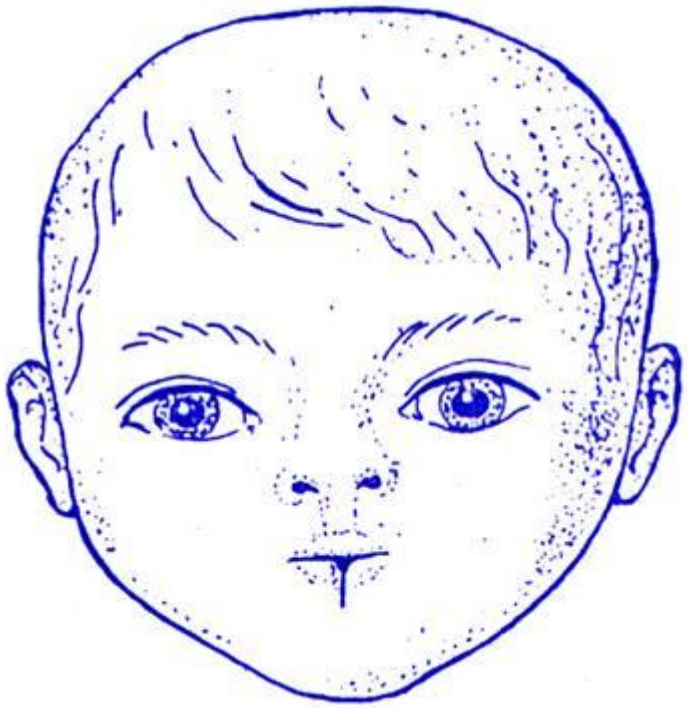
Bilateral clefts results in a very large rima oris (macrostomia or „frog mouth“)
Results from failure of the lateral parts of the maxillary and mandibular prominences to merge
very rare

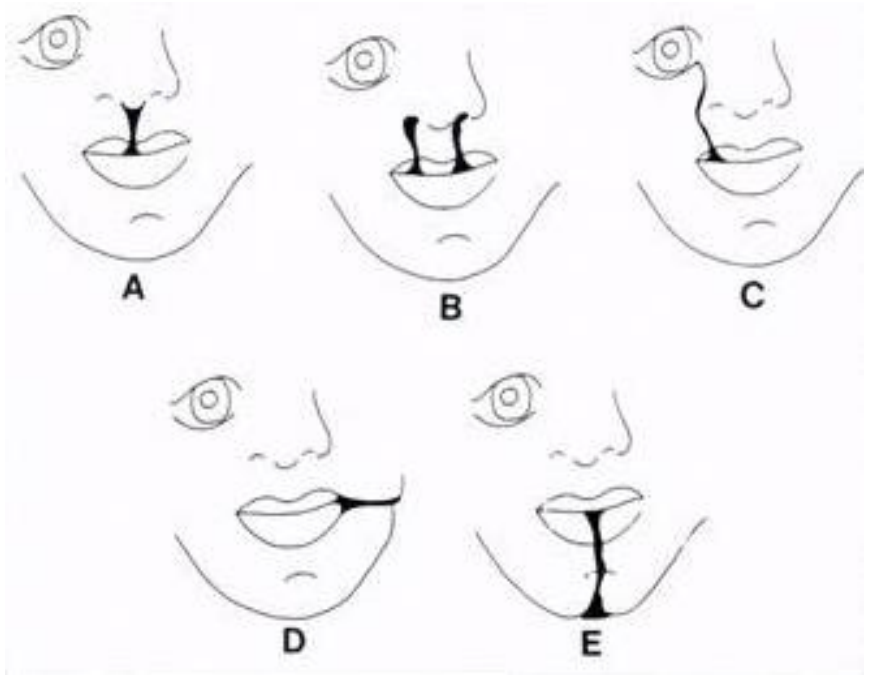




Median cleft of the lower lip and chin (mandible)
cheiloschisis et gnathoschisis inferior

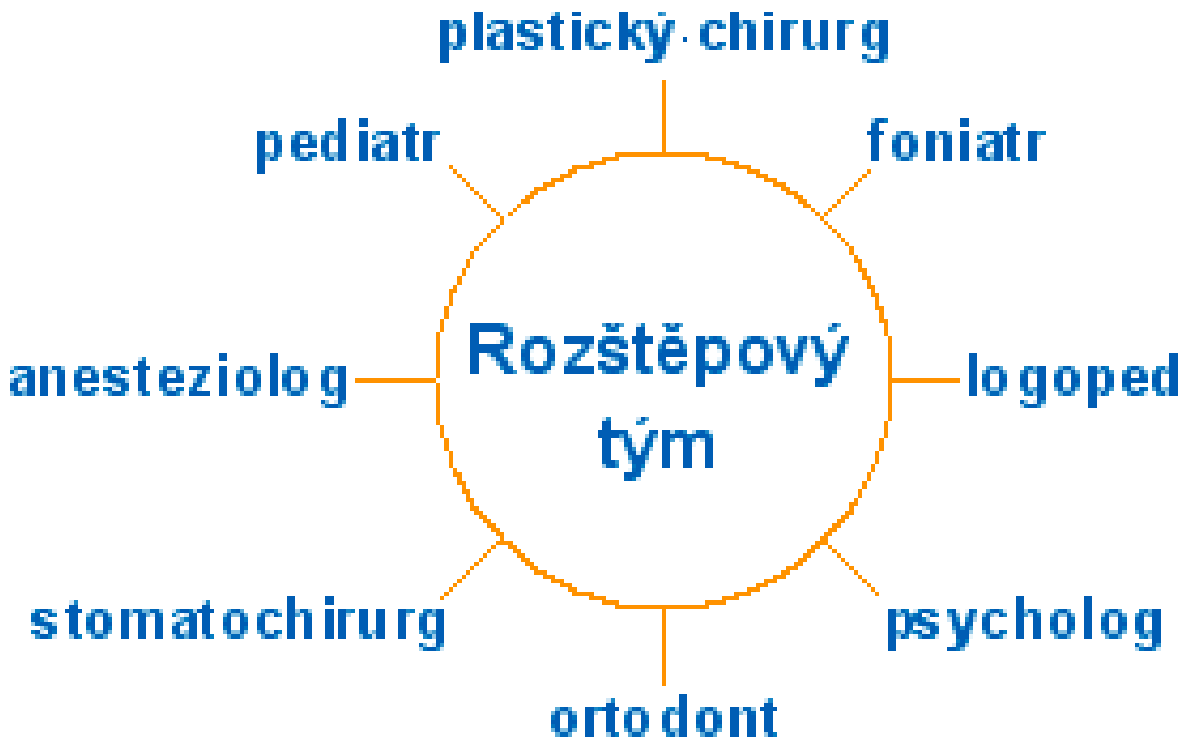
Cleft resulting from failure of the mesenchymal masses of the mandibular prominences to merge completely with each other
Always connected with cleft of the mandible and tongue
rare





Treatment: a comprehensive approach (cleft teams)

plastic surgeon, dentist - orthodontist, phoniatrist / anthropologist, event. psychologist



Development of oral cavity

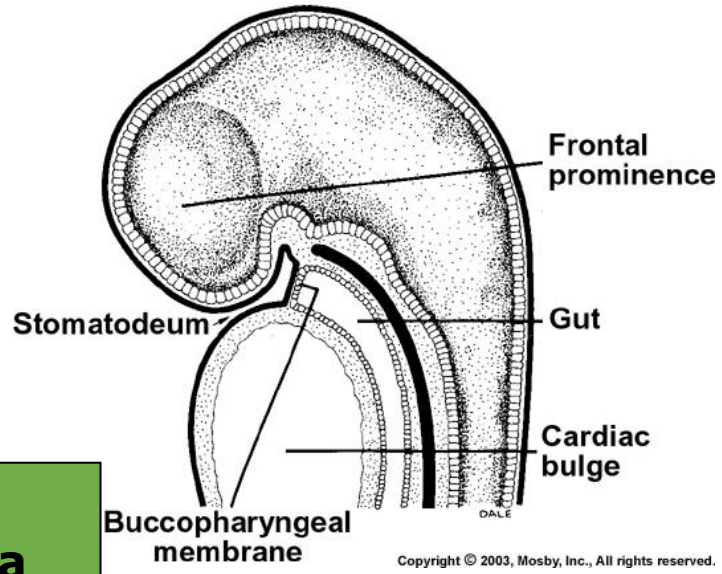
Oral cavity develops from the stomodeum or primitive mouth
5 processes limit the stomodeum:
frontonasal prominence
paired maxillary prominences (processus maxillares)
paired mandibular prominences (processus mandibulares) on sides

Stomodeum communicates with the body surface via primitive oral entrance

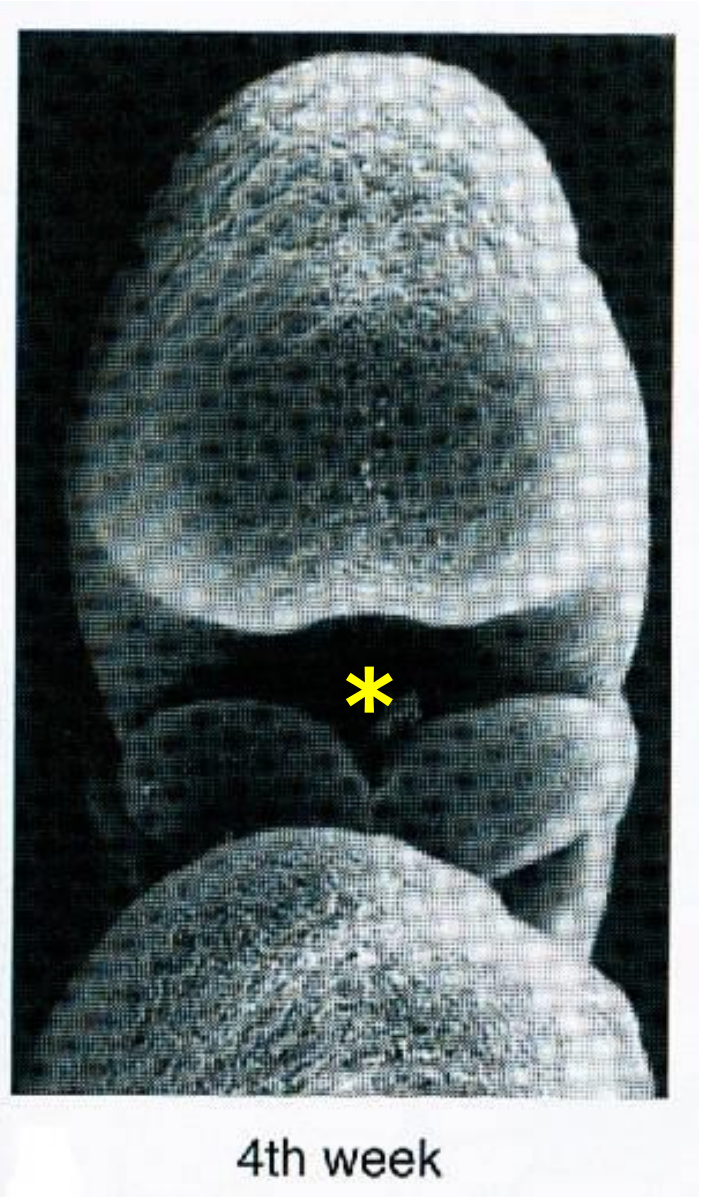
Bottom of the stomodeum - oropharyngeal membrane (membrana oropharyngea)

When the oropharyngeal membrane ruptures, the stomodeum becomes continuous with the foregut

Roof of the stomodeum consists of a mesenchyme and ectoderm of the frontonasal prominence



membrana oropharyngea



Palatogenesis

Begins at the 7th week

Completed by the end of the 12th week

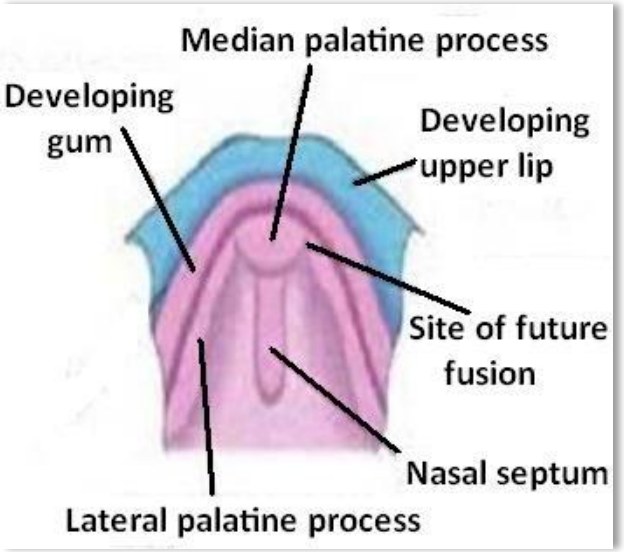
The most critical period for the development of palate is from the beginning of 7th week to the beginning of 9th week

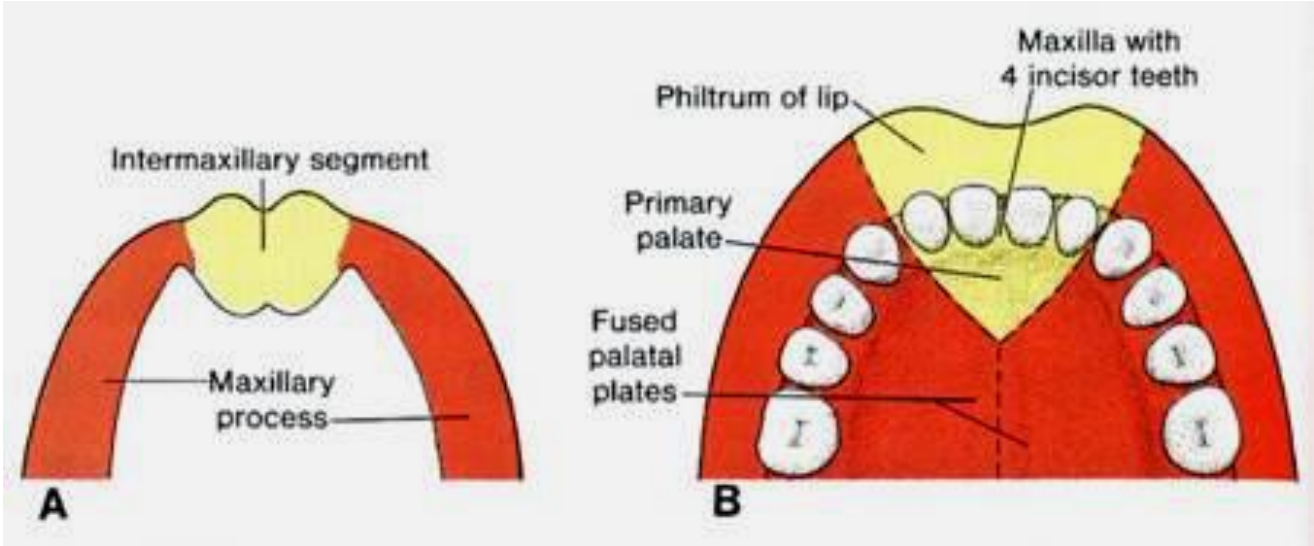
<u>3 primordia:</u>

Unpaired medial palate process and **paired lateral palate processes** (palatal shelves)

a) <u>The medial palate process</u>

Grows from the dorsal side of the intermaxillary segment at the end of the 5th week and gives rise to primary palate

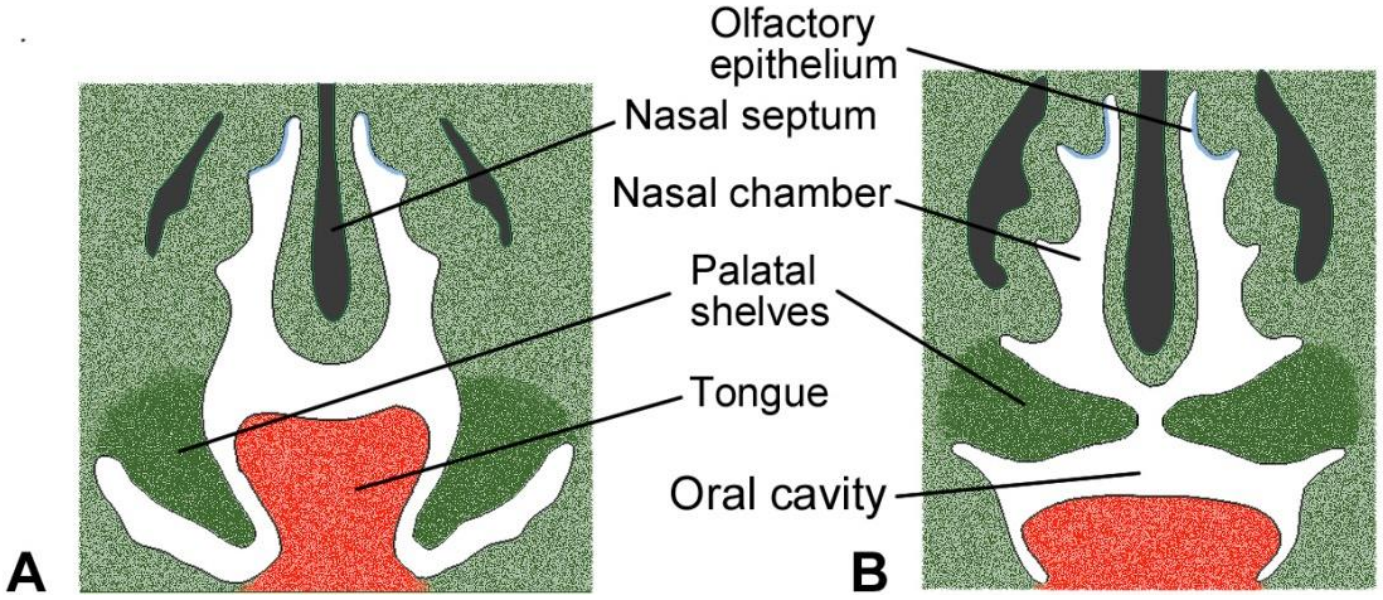


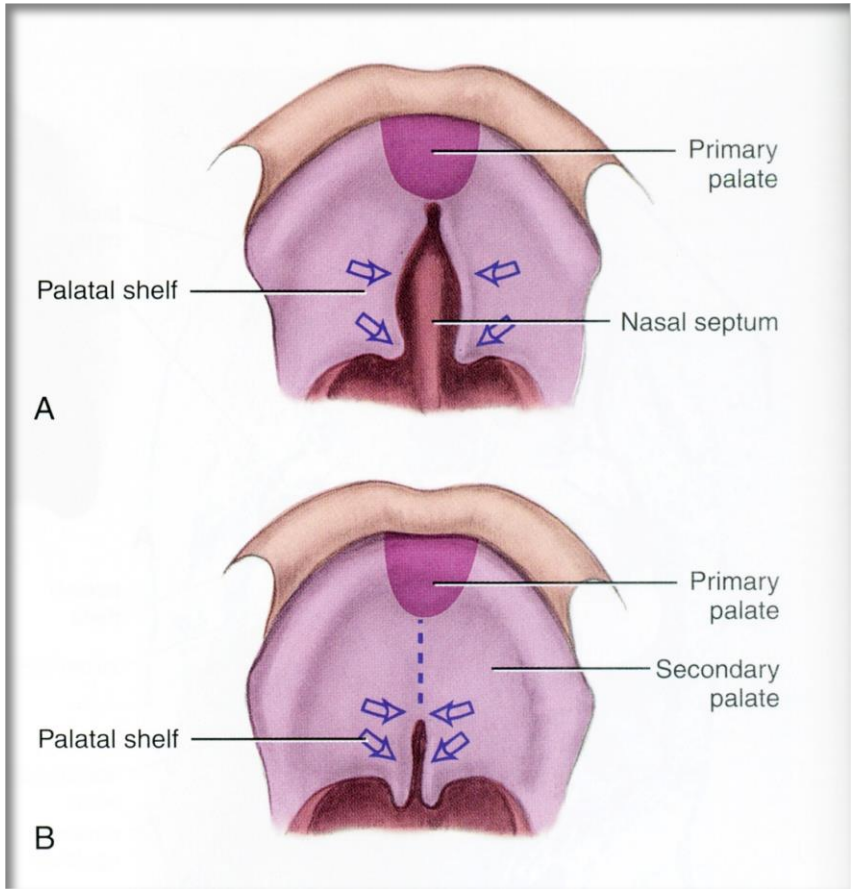


Palatogenesis

b) Lateral palate processes - grow out from medial aspects of the maxillary prominences and give rise to the secondary palate

lateral palate processes are formed by mesenchyme, are covered by ectoderm a have shelf-like form (palatal shelves)





Palatal shelves initially grow in caudal direction and laterally along to primordium of the tongue later, due more rapid vertical growth of mandibular processes the tongue descends caudally

Palatogenesis

During the 10th week shelves meet in the midline to finally fuse

The site of fusion of both lateral palate processes is known as **raphe palati**

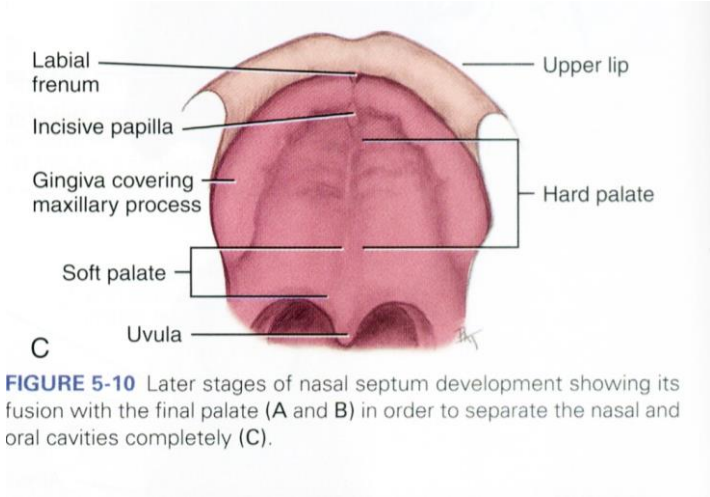
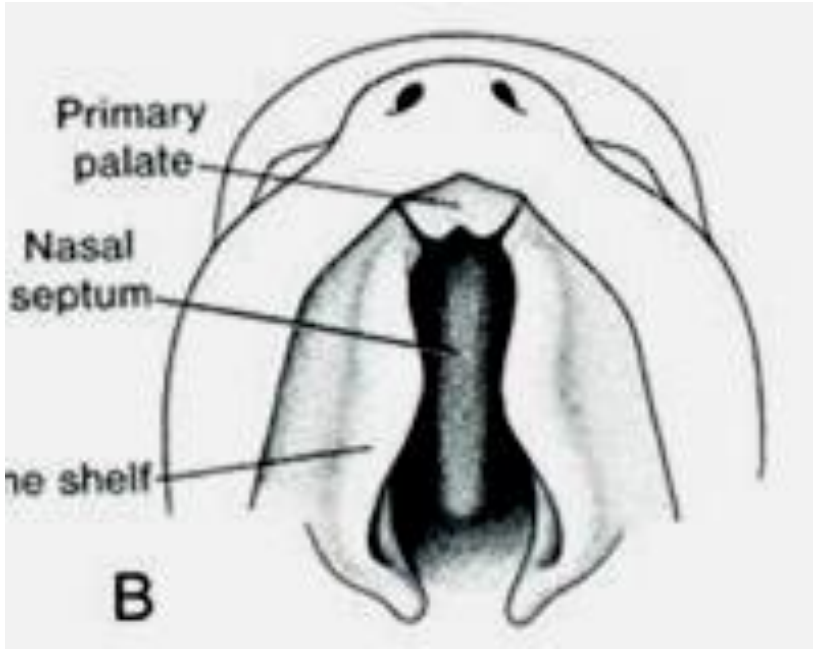
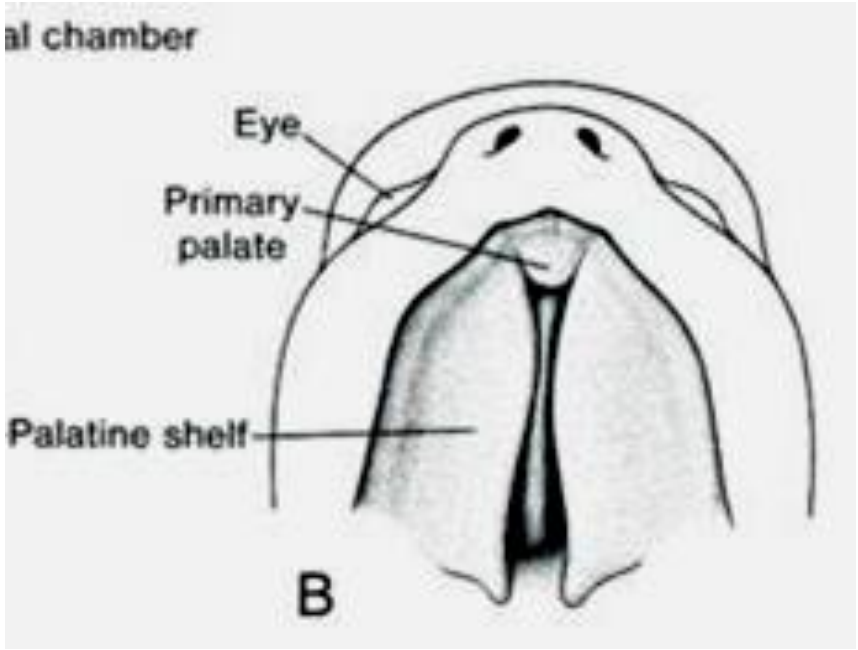
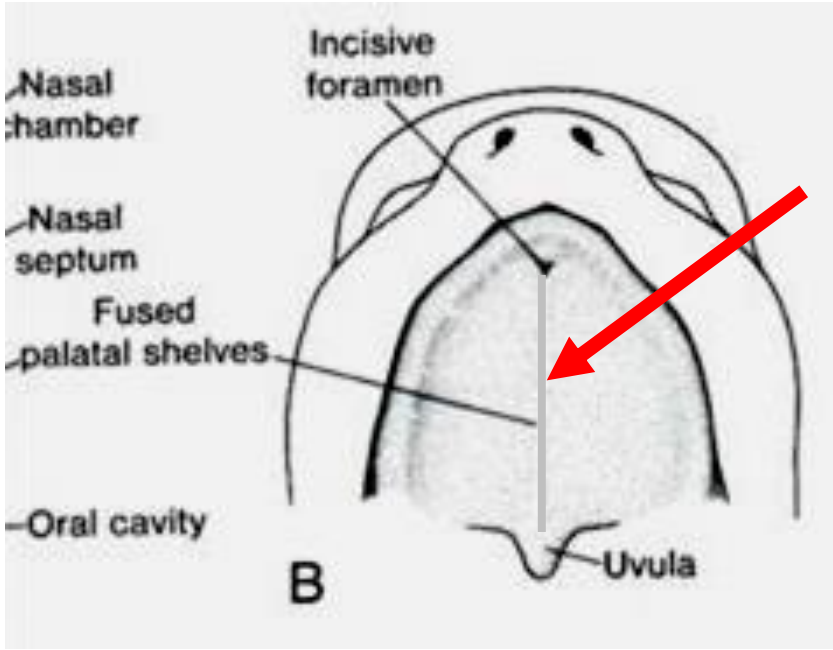


FIGURE 5-10 Later stages of nasal septum development showing its fusion with the final palate (A and B) in order to separate the nasal and oral cavities completely (C).







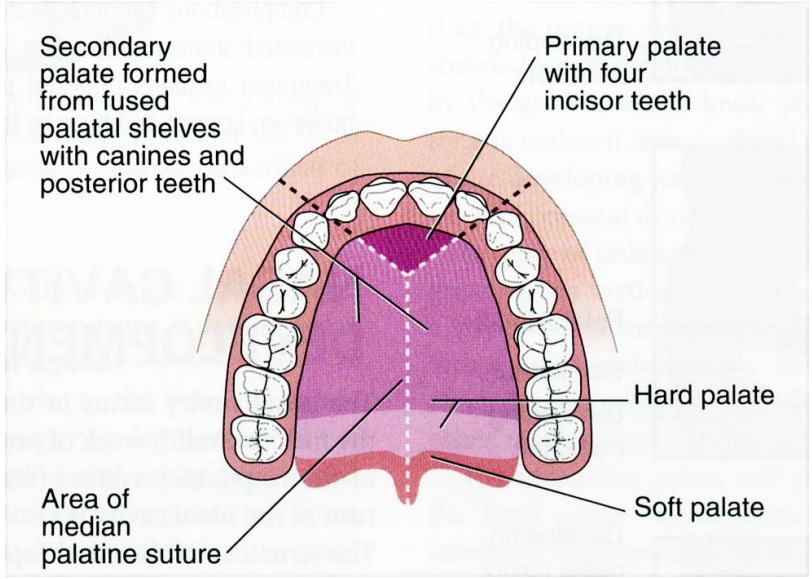
Palatogenesis

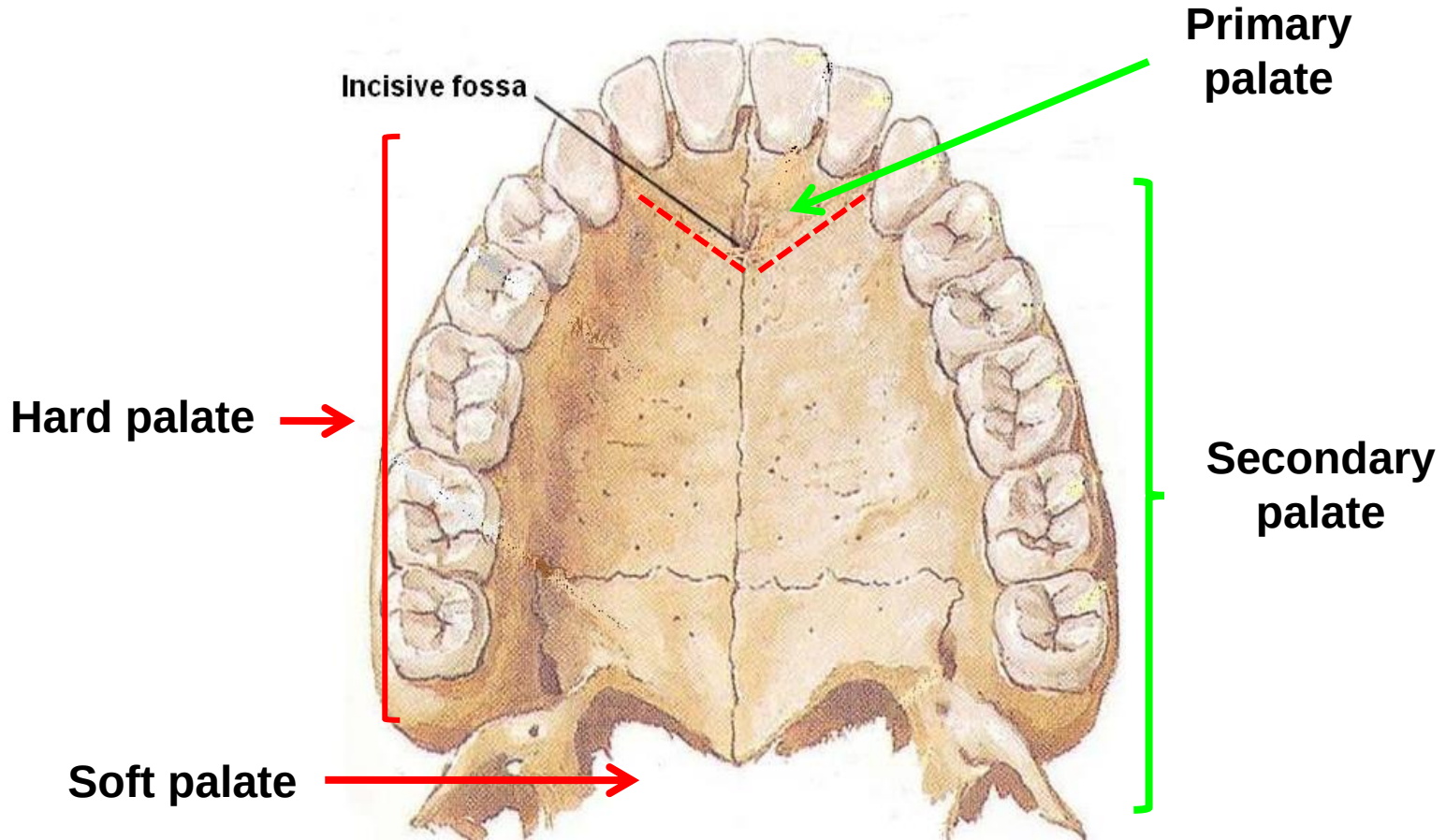
definitive palate originates by fusion of ventral edges of both lateral palatal shelves with the medial palate process

Line of fusion corresponds to the incisive canal (canalis incisivus)

The region of medial palate process (primary palate) and ventral parts of lateral palate processes undergo endesmal ossification

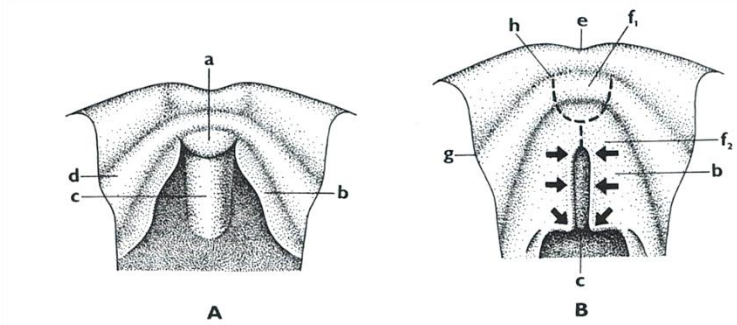
The posterior portions of the lateral palate processes do not undergo ossification and give rise to the soft palate and uvula

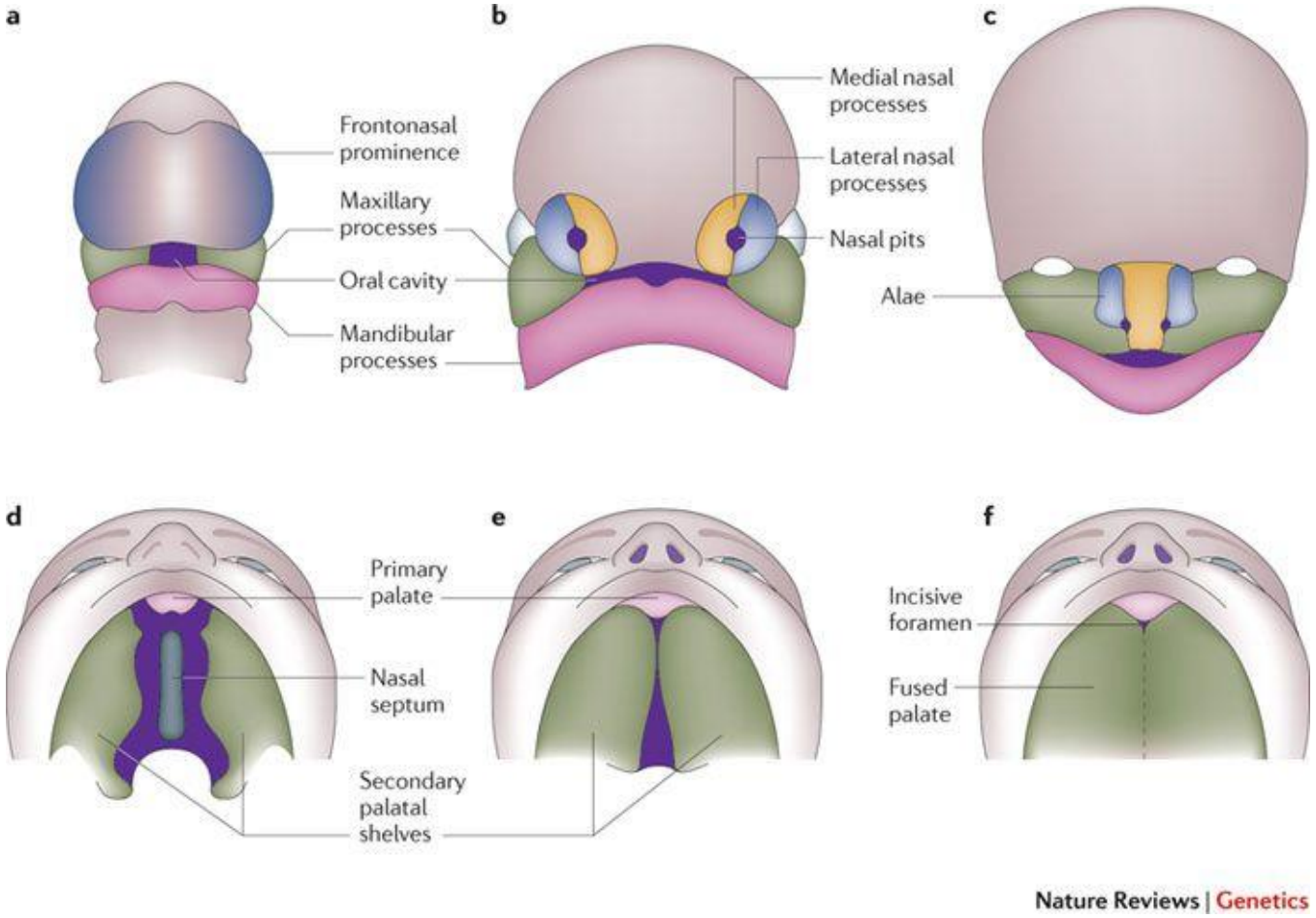




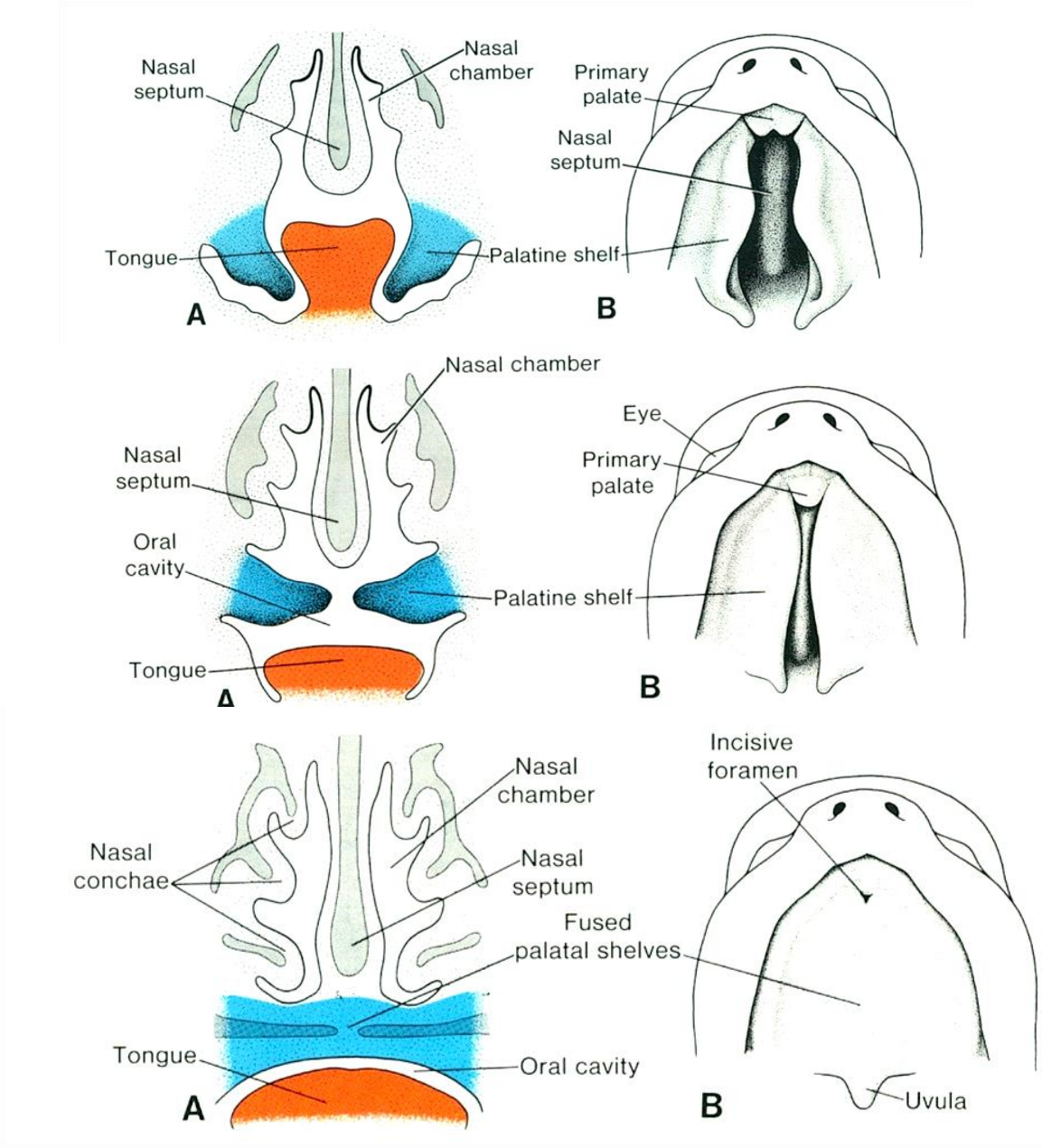
Palatogenesis

- **Primary palate** (intermaxillary segment)
- **Secondary palate** (lateral maxillary plates)





Palatogenesis



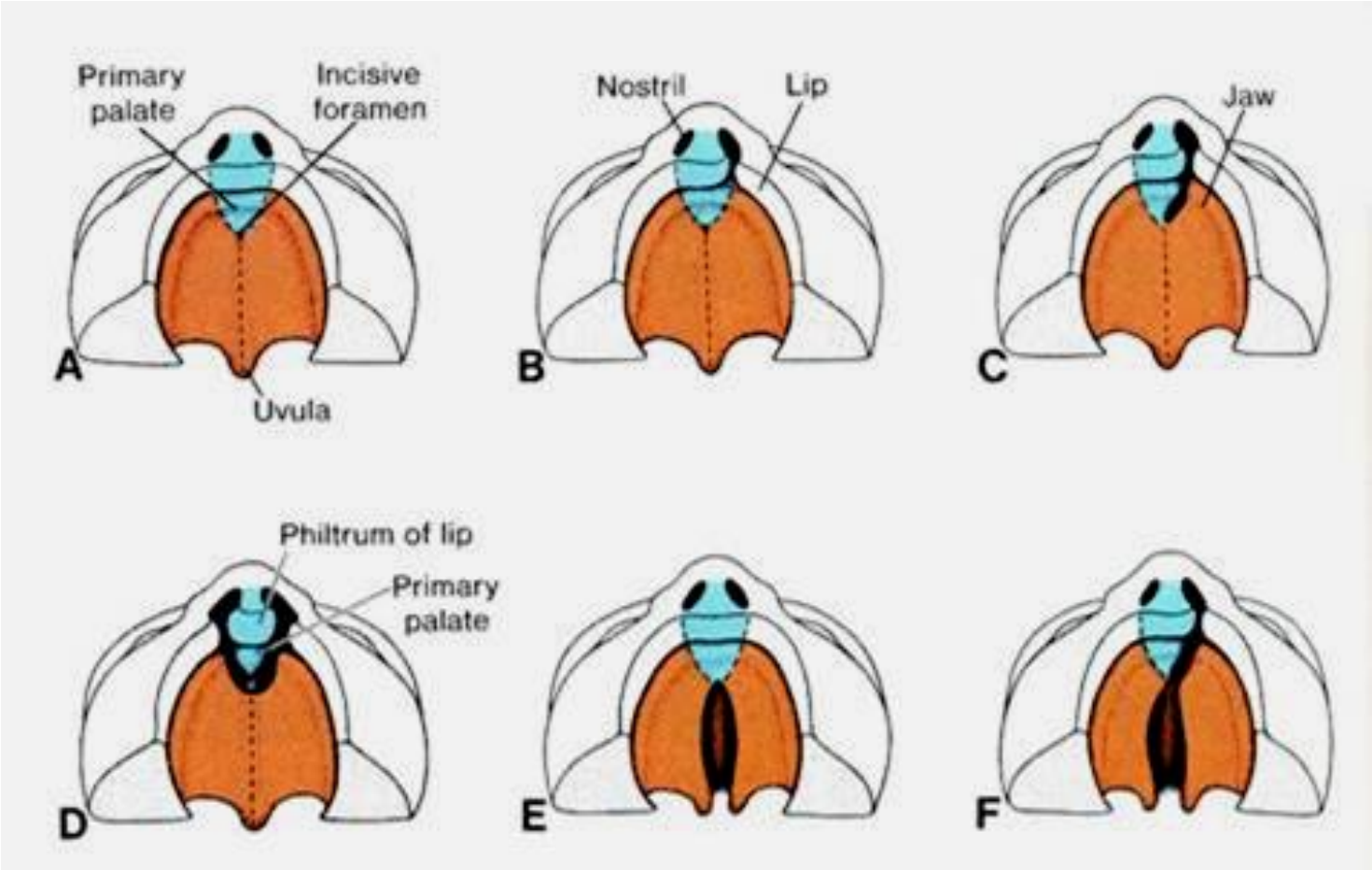
Palate clefts

Can be of isolated character or associated with clefts of the and upper lip

Complete or incomplete

unilateral or bilateral

The **incidence** of palate clefts is **1 : 2500** live births



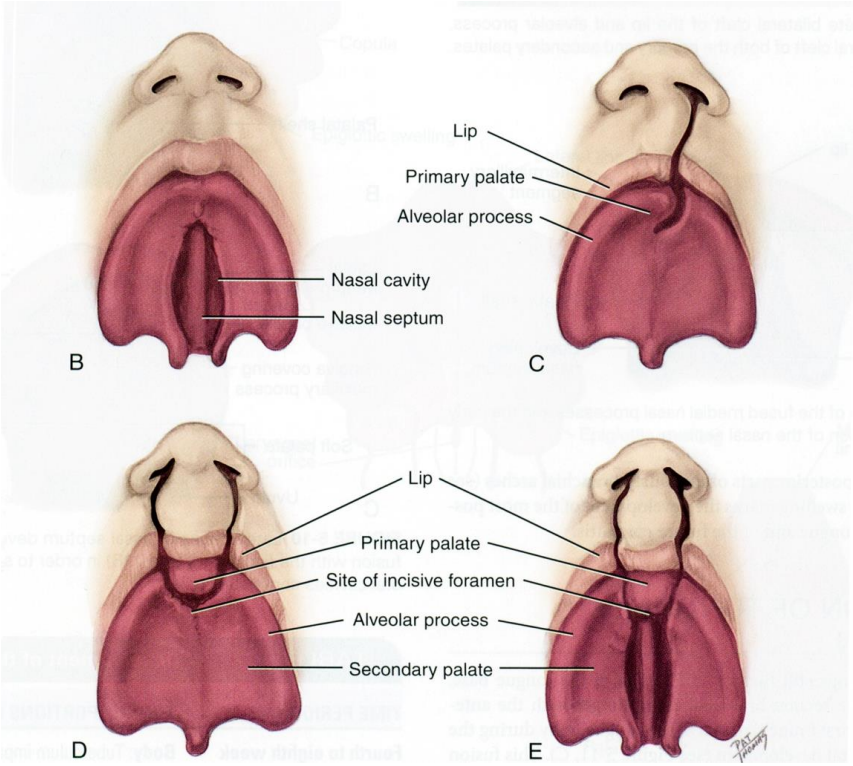
Clefts of primary palate (C, D)

clefts of both primary and secondary palate (E)

clefts of secondary palate (F)

Clefts of primary palate (C,D)

Anteriorly to the incisive foramen
The primary and secondary palates are separated
Results from failure of fusion of lateral palatal shelves with the primary palate
Unilateral/bilateral



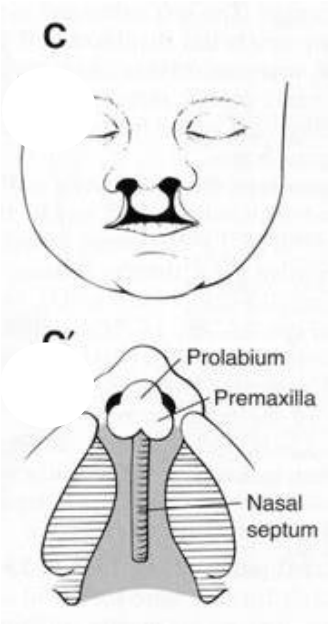
Clefts of both primary and secondary palates (E)

Both anteriorly and posteriorly to the incisive foramen

Lateral palate processes are not fused and separated from the primary palate

The nasal septum is free

Usually associated with lateral cleft of the maxilla and upper lip - **cheilognathopalatoschisis** unilateralis / bilateralis (very serious malformation)



Clefts of secondary palate (palatoschisis)

Posteriorly to the incisive foramen

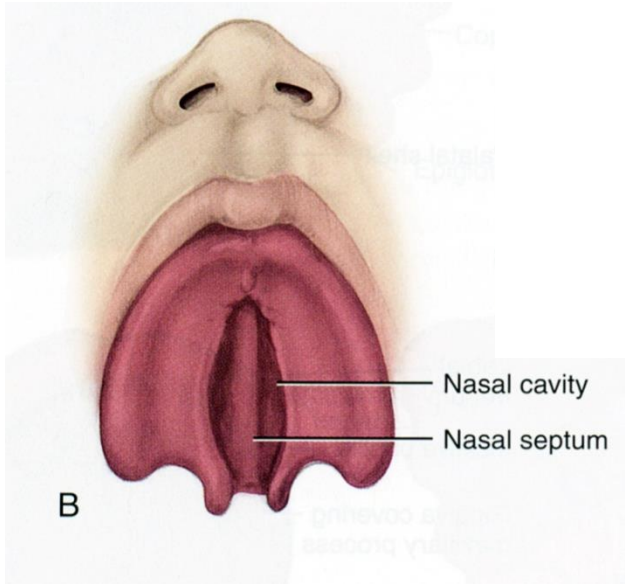
Cause: lateral palatine processes do not fuse

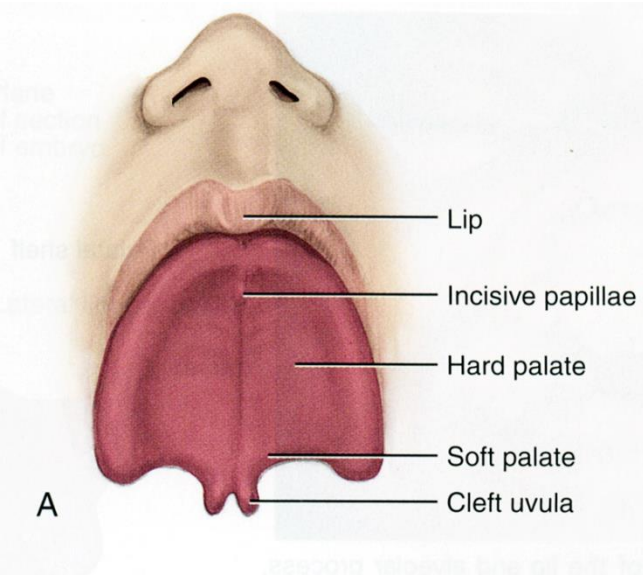
Affect the all sections of palate (hard, soft and uvula - staphyloschisis / uvula bifida)

Clefts of the secondary palate occur more frequently in females than males (3:2)

Pierre-Robin syndrom: cleft of palate, hypoplasia of the lower jaw, glossoptosis and pseudomacroglosia - malformation with recessive inheritance bound to the X chromosom

Staphyloschisis (uvula bifida) – rozštěp uvuly





Critical period in palatogenesis:

37. - 53. day (cleft of primary or both palates)

53. - 57/58. day (cleft of secondary palate)

Prediction of clefts (in general)

Healthy parents having child with cleft:

2% probability of the cleft of the second child

7% probability of the cleft (if both has cleft)

One parent had cleft and child with cleft is born

15% probablity of the cleft of the next child

Oral vestibule development

Oral vestibule develops from the **labiogingival lamina** (vestibular lamina)

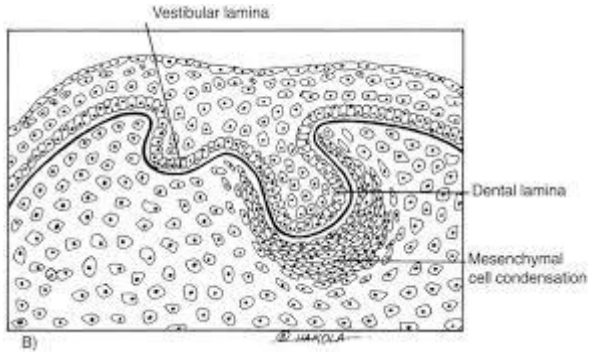
Emerges during the **6th week**

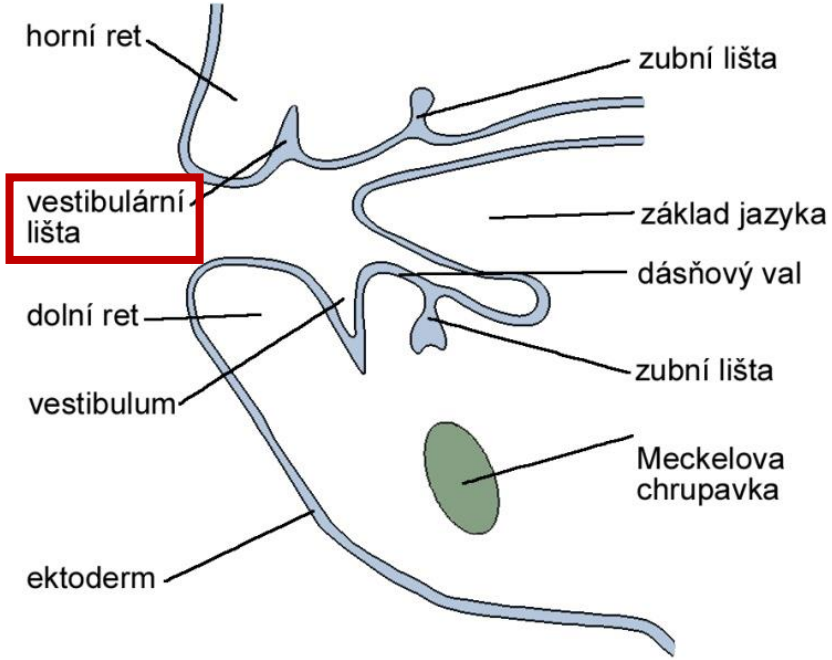
Thickened area of the ectoderm, fast proliferation of ectoderm against mesenchymal core of prominences that delineate the stomodeum

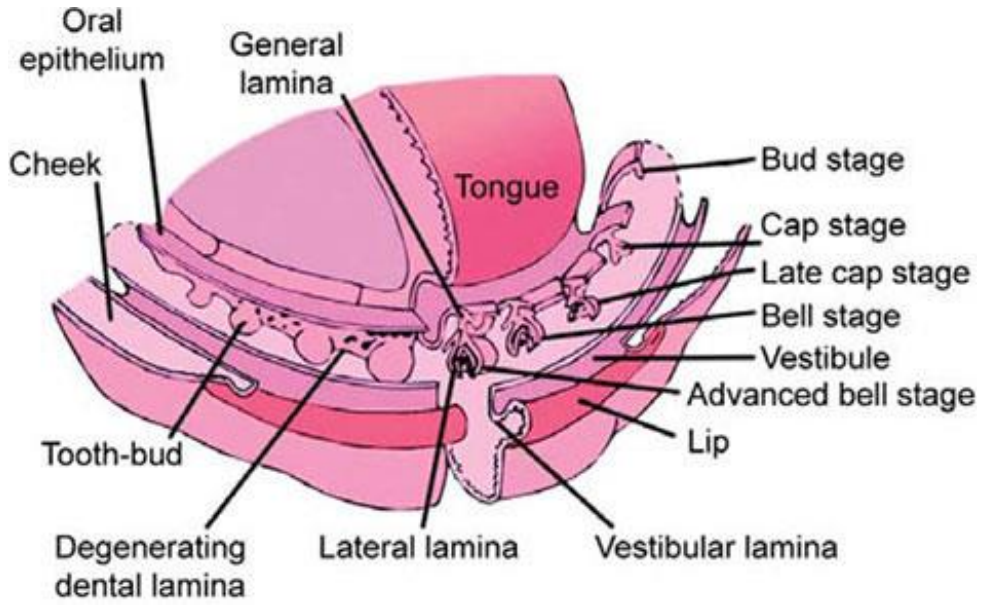
Cells in the center of lamina then undergo apoptosis - **labiogingival groove** is established

Ventral section - the definitive lip

Dorsal section - the gingival ridge (torus)







Development of maxilla and mandible

Maxilla

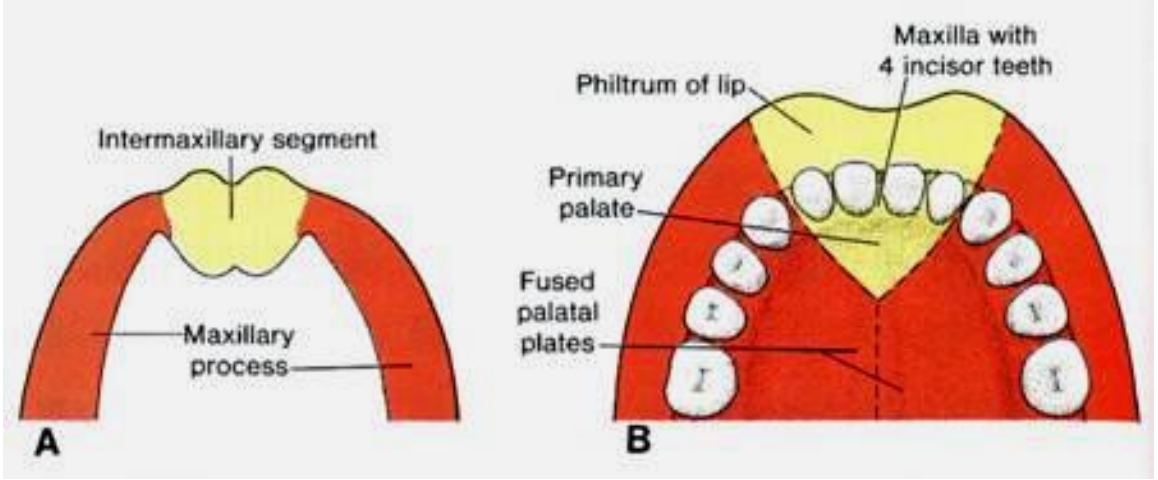
Paired bone, intramembranous ossification

Fusion of 3 parts:

Frontal part of the bone with incisors (intermaxilla) - intermaxillary segment

Lateral parts of the bone - both maxillary prominences (processus maxillares)

Lateral parts fuse to the frontal segment in incisive suture (sutura incisiva) on both sides
Ossification begins between 6 - 8 week



maxilla in newborns is shallow because has not formed alveolar processes yet (developed during the eruption of deciduos dentition)

Development of maxilla and mandible

Mandible

develops partly by intramembranous, partly by intracartilaginous ossification

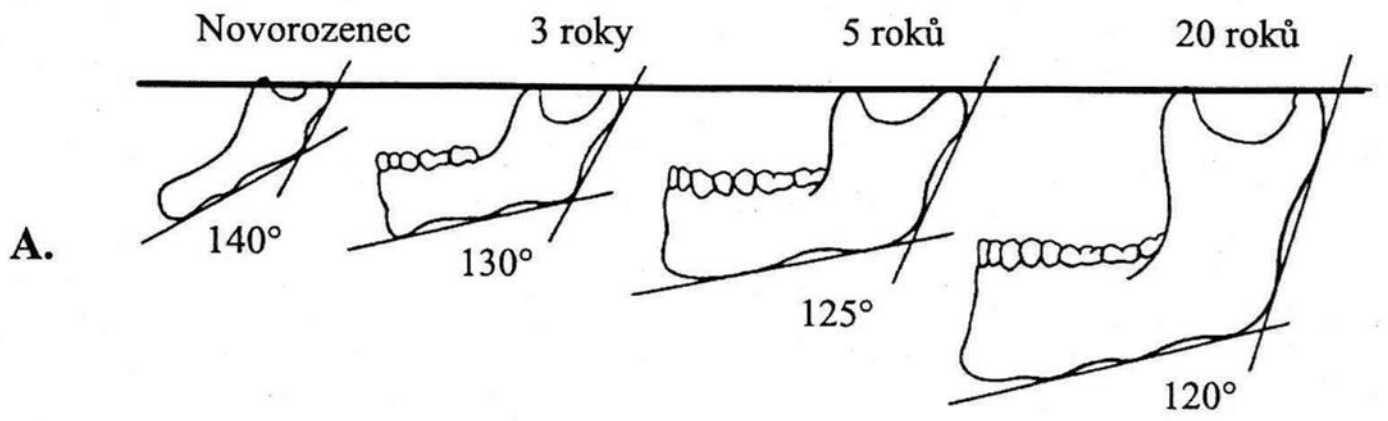
Body of mandible and both ramus of mandible are of intramembranous origin (for ossification is used mesenchyme located anterolateral to the Meckel cartilage that support the mandibular prominences

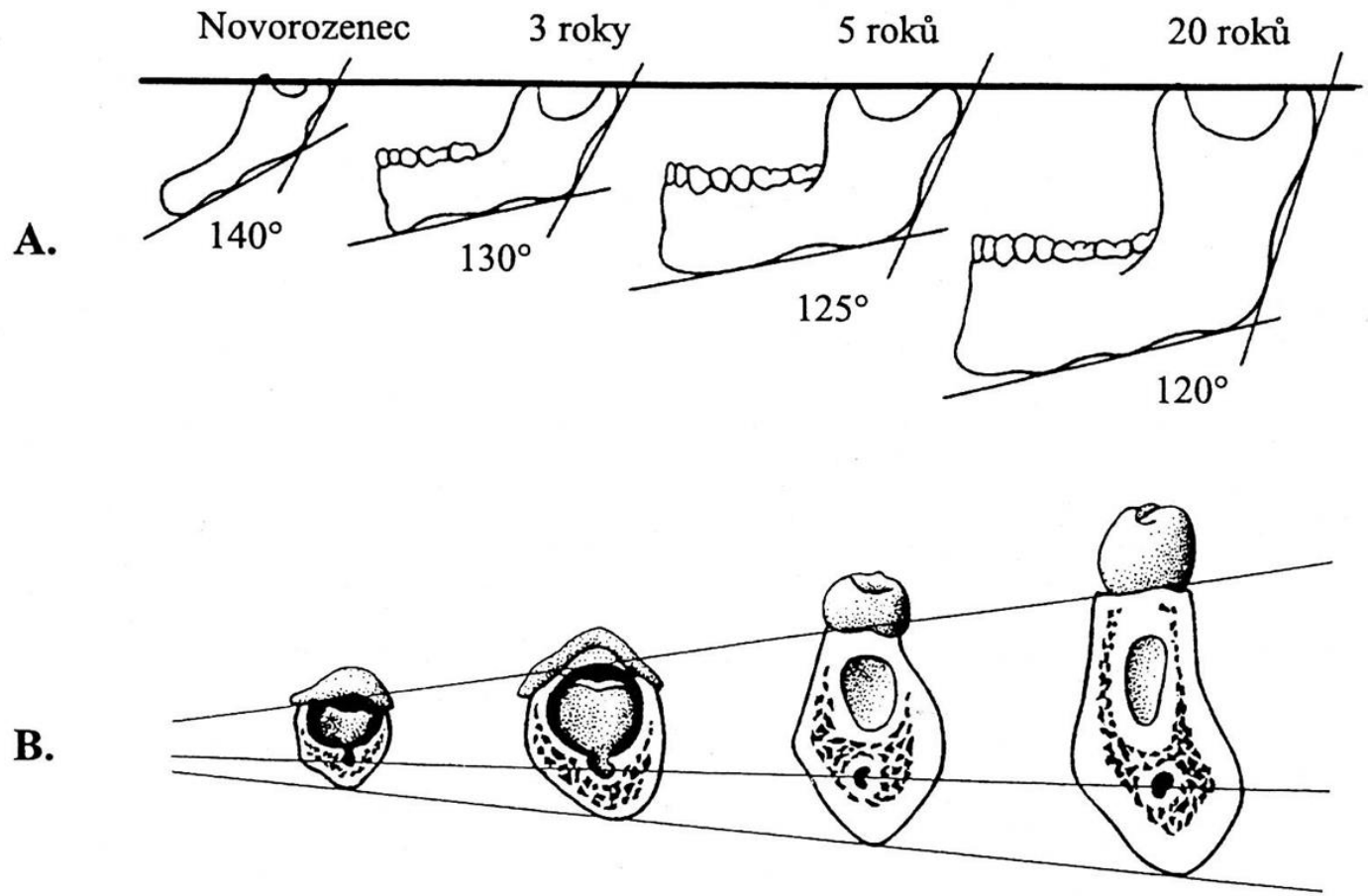
Ossification begins in the 6th week.

Condyle and coronoid process develop by intracartilaginous ossification (condyle between 12 - to 20 weeks, coronoid process yet later)

Lower jaw of neonates is low and its development continues in postnatal period

The angle between ramus and body of mandible continual reduces (from 140-150 to 120 for adult)

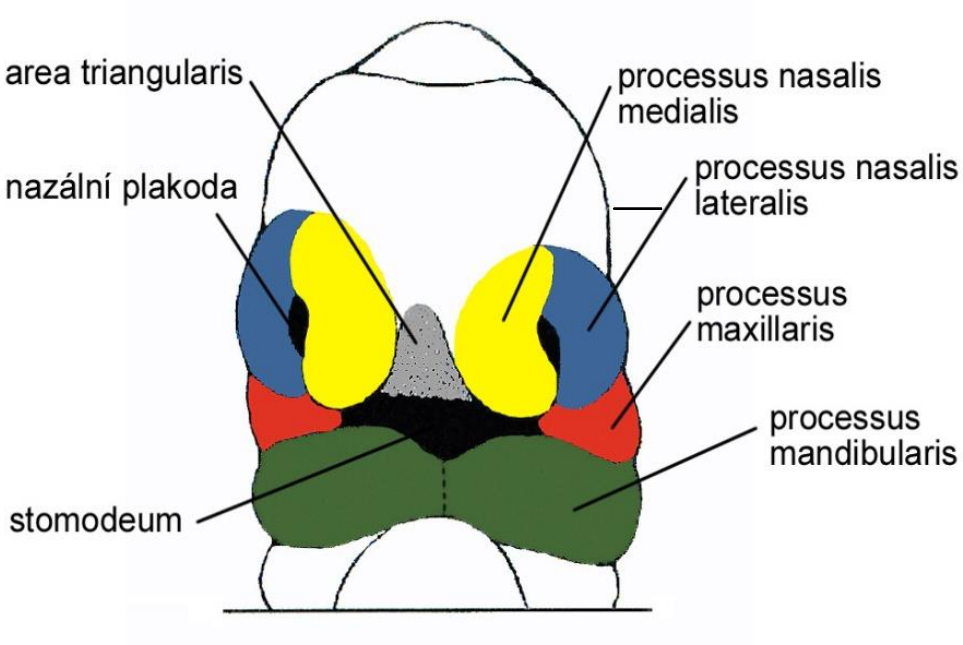


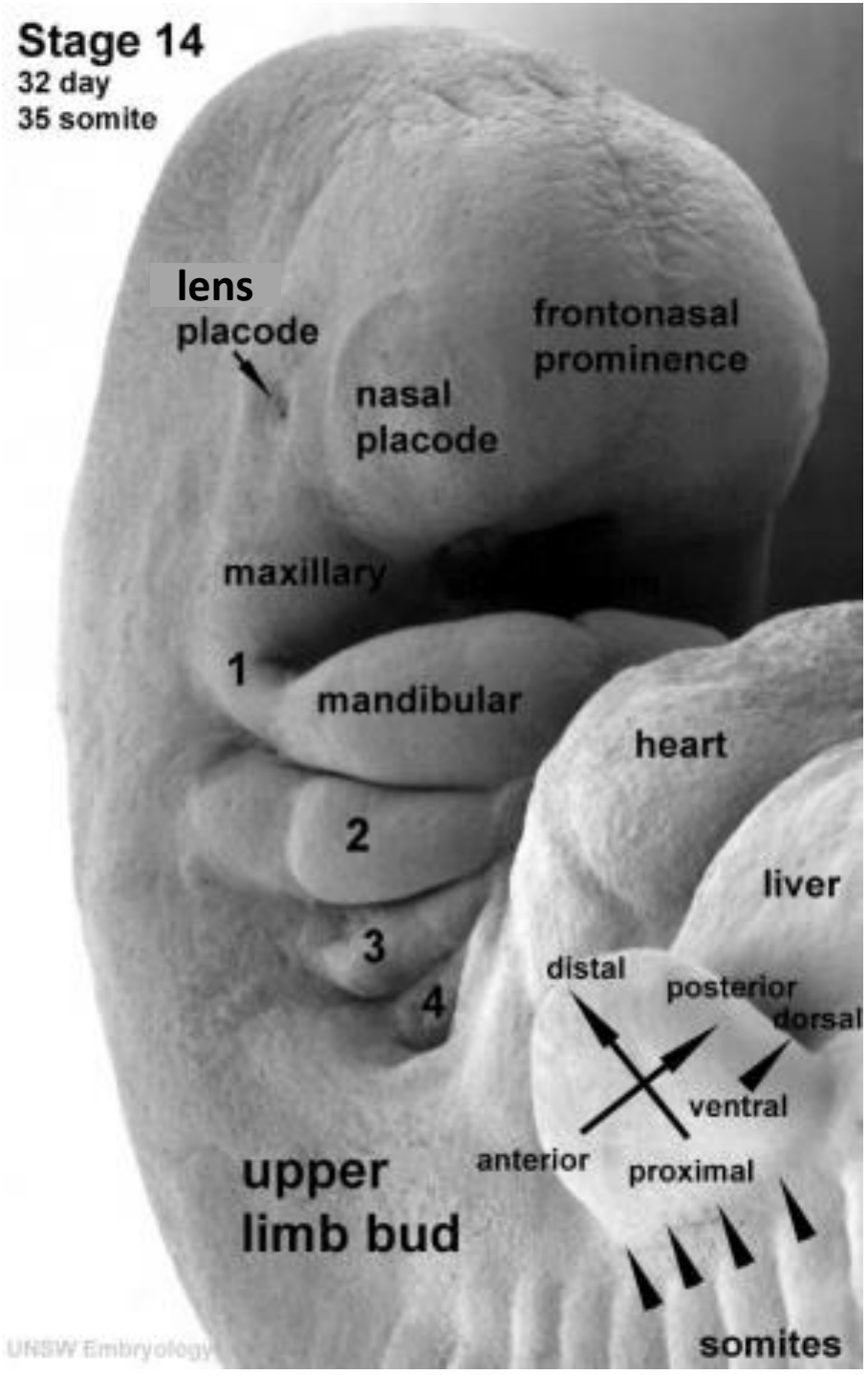


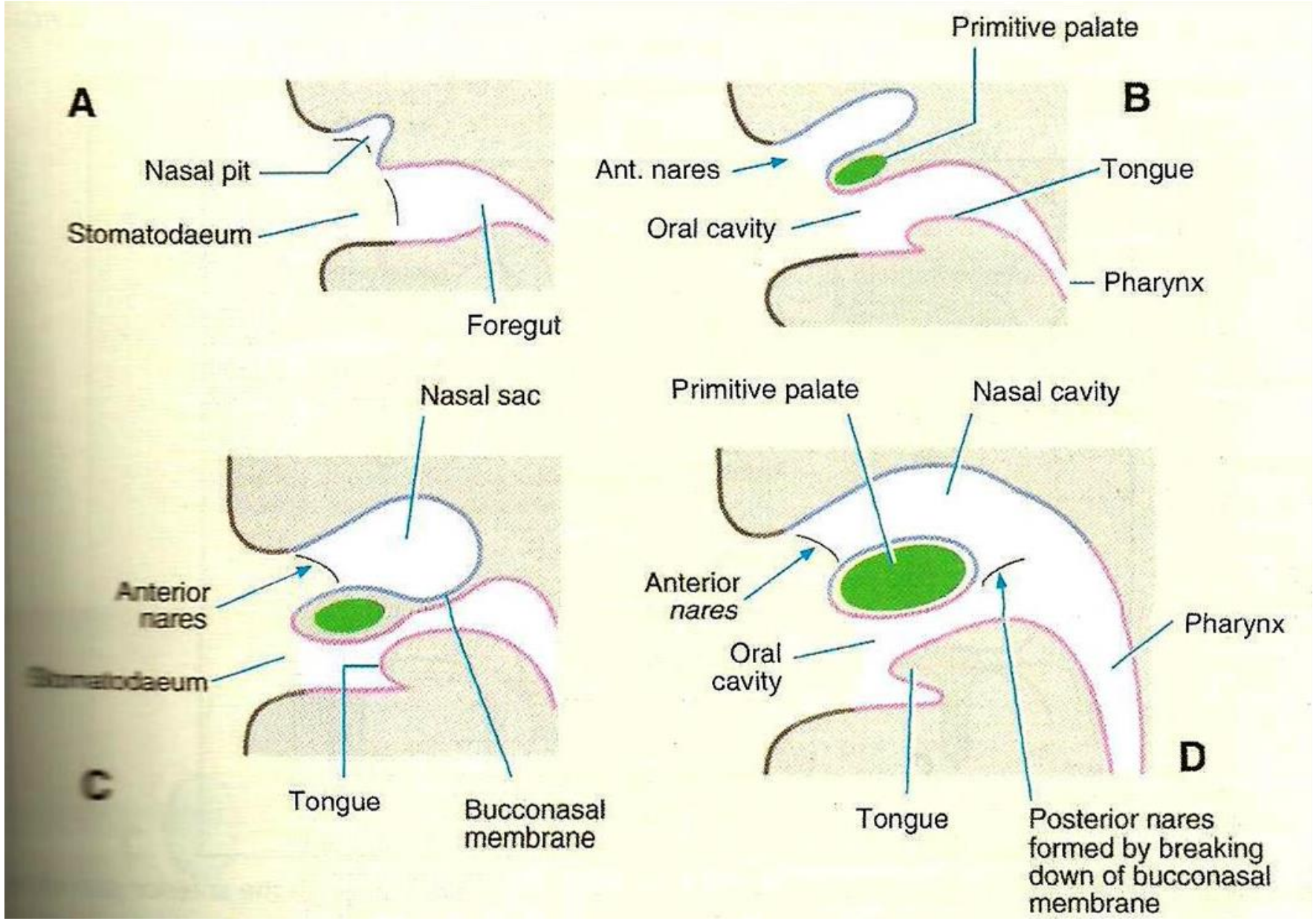
Obr. 16–3. Změny mandibuly v postnatálním vývoji. **A.** Zvětšuje se délka ramus mandibulae a zmenšuje se úhel mandibuly. **B.** Vývoj alveolární části vede k celkovému zvětšení tloušťky. Horizontální linie na obrázku prochází přes canalis mandibulae.

Nasal cavity

Nosal placodes → Nasal pits → Nasal sacs, grows dorsocaudally to roof of stomodeum, from which are initially separated by the oronasal membrane





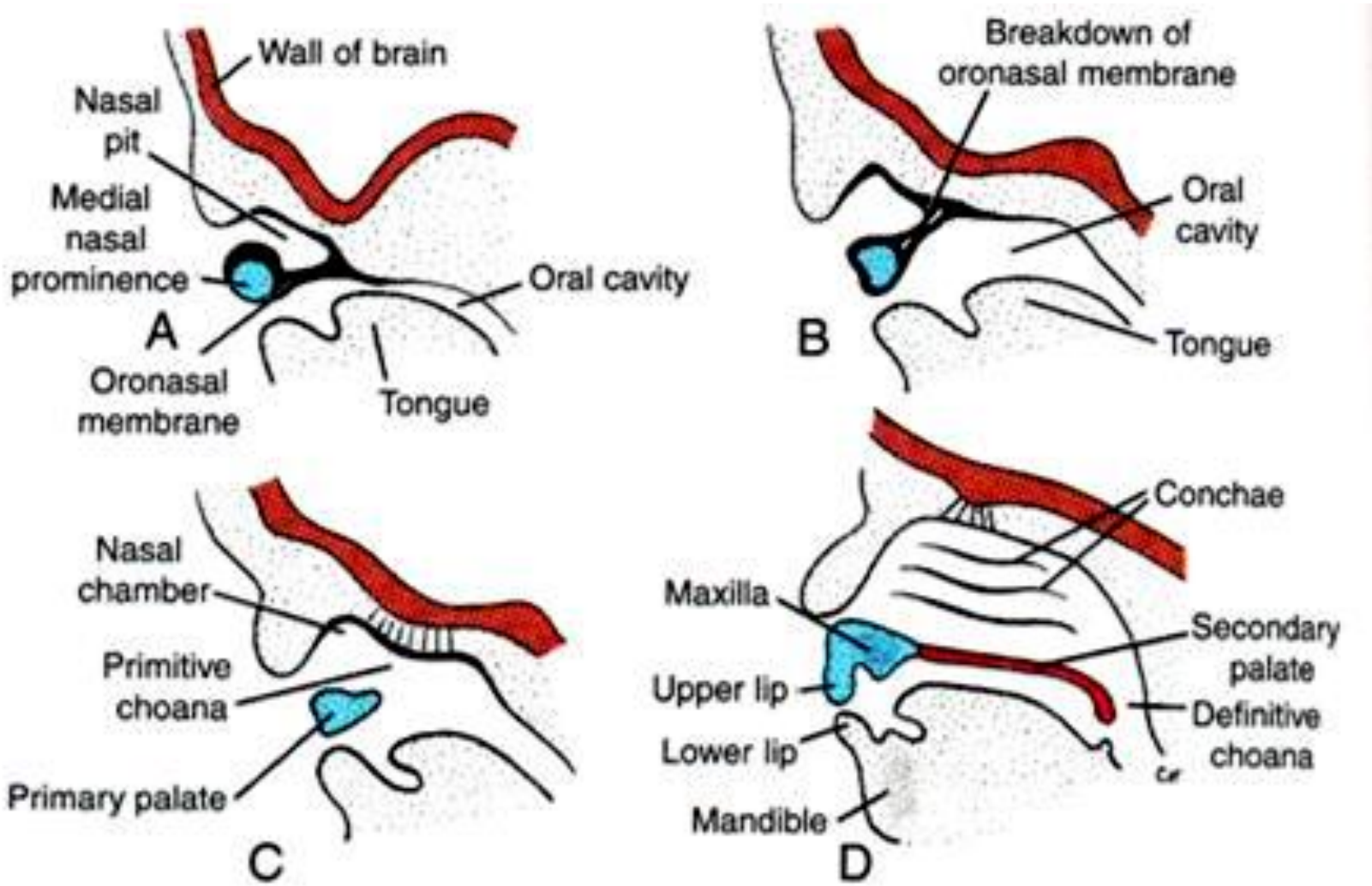


Connection of nasal and oral cavities

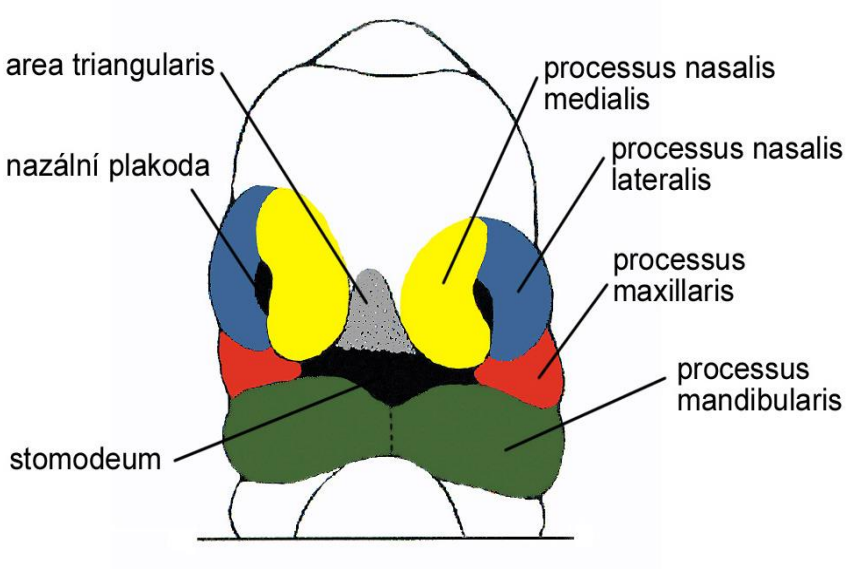
During the 5th week the oronasal membrane perforates via openings - the primitive choanae and both nasal sacs communicate to the stomodeum to form common mouth and nasal cavity (**oronasal cavity, only for +-7 days**) - see C

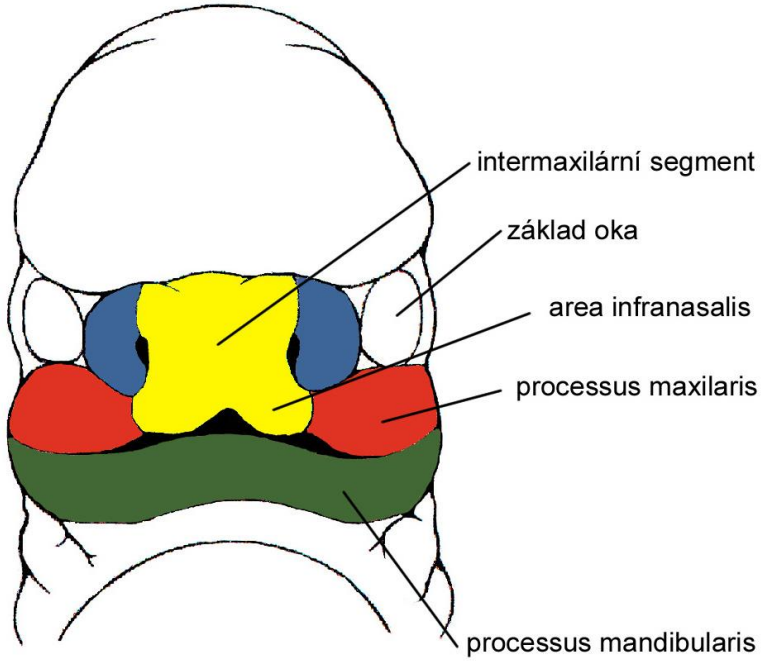
Sagittal sections through nasal pit and stomodeum:

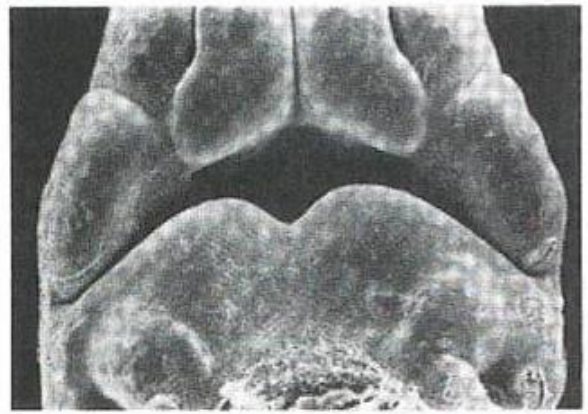
Double-layered **oronasal membrane** (ectoderm of nasal cavity and stomodeum)



Nose development







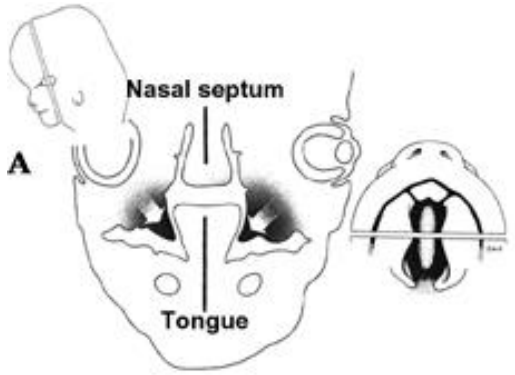
Early 7th week

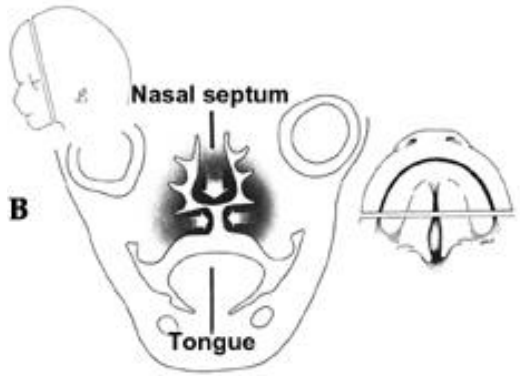
Nose develops from 3 primordia simultaneously with development of face:

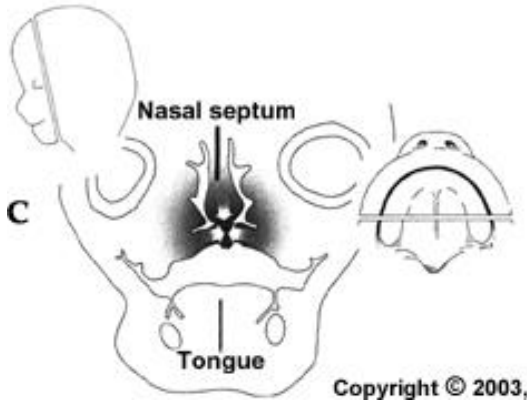
Middle and upper part of the intermaxillary segment - gives rise to the **apex**
Lateral nasal processes give rise to **Dorsum et radix nasi, alae nasi**
All primordia rapidly proliferate ventrally and nose protrudes (firstly flattened structure)

Lower part of intermaxillar segment – **philtrum**

Nose development





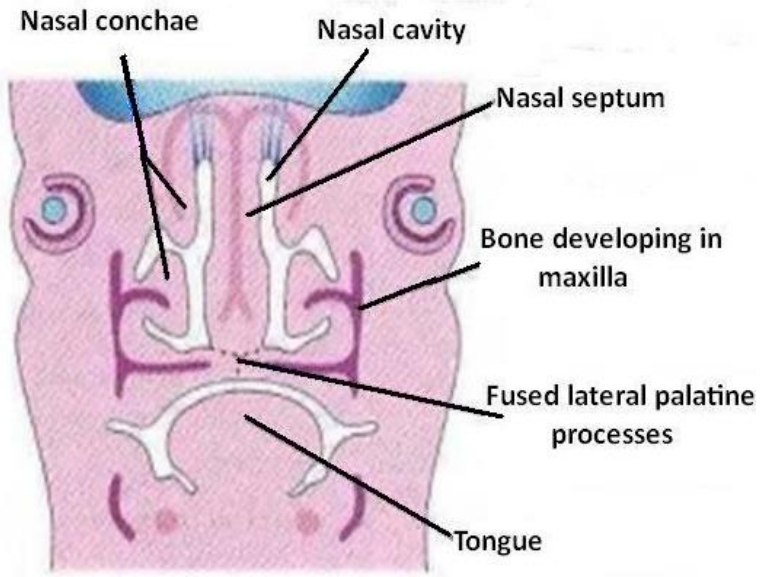


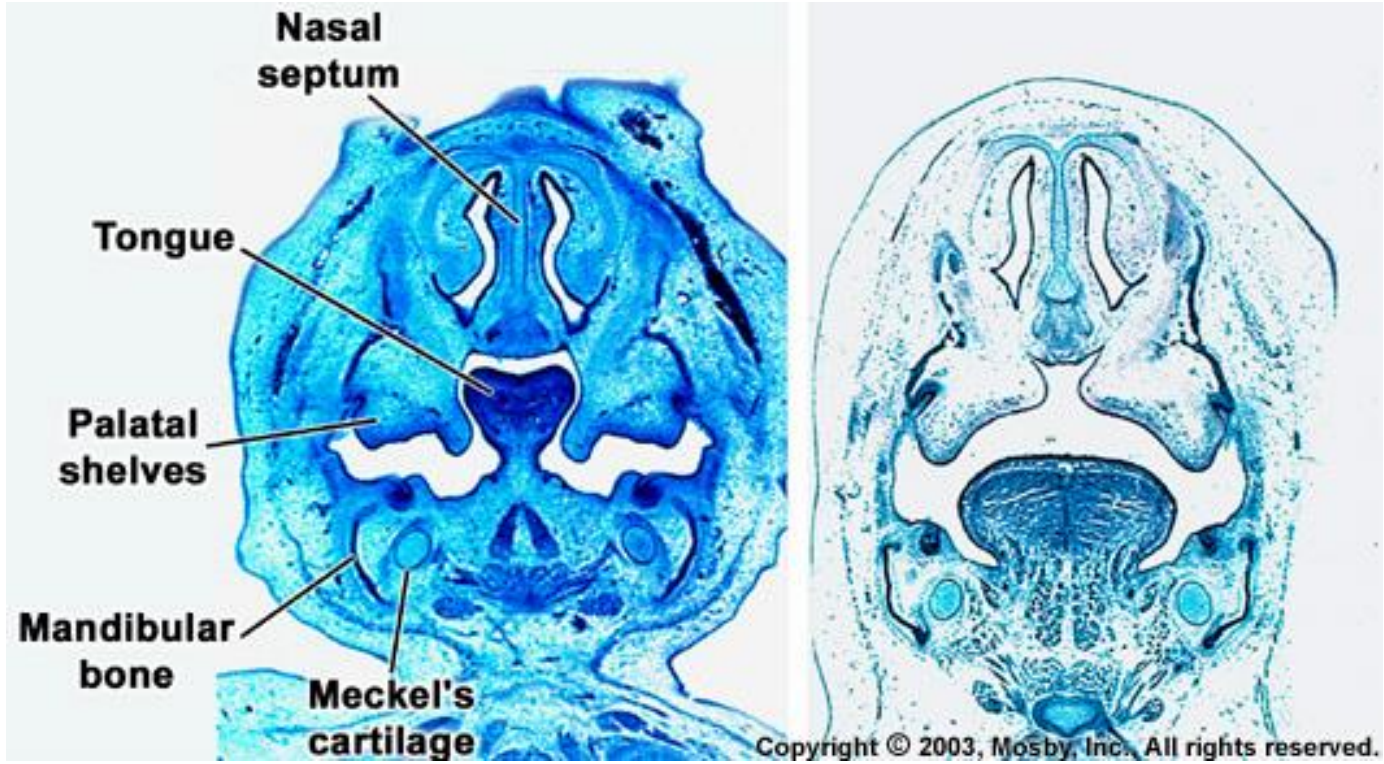
Septum nasi - grows from the intermaxilary segment in form of vertical plate, which fuses with lateral palate processes in the middle line (during 9-10th week)

At the time of development of the septum, bases of conchae develop on the lateral wall of each nasal fossa (lower, middle and upper)

After 13 week, the ectoderm covering roof of both nasal fossae transforms in the olfactory epithelium consisting of olfactory cells (unipolar neurons), whose axons constitute **fila olfactoria**

The epithelium of sinuses is of the ectodermal origin





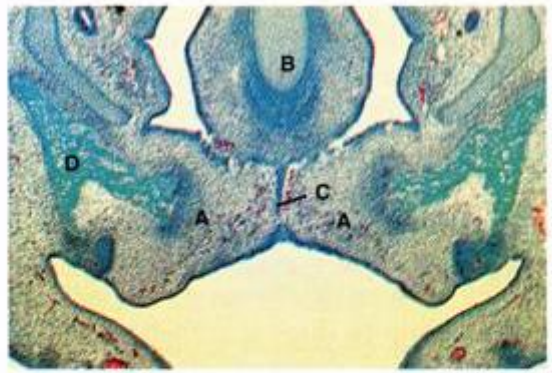
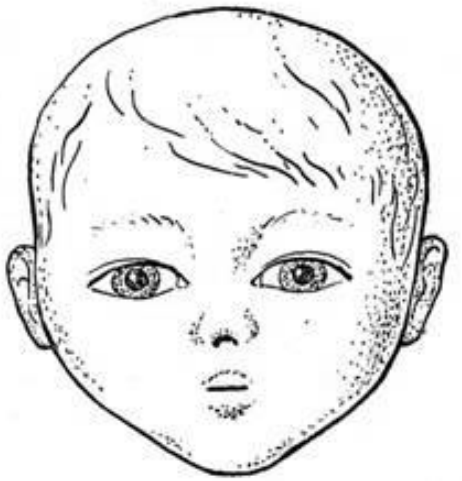


Fig. 18.5 Coronal section through developing oronasal regions following contact of the palatal shelves (A) and secondary nasal septum (B). C = Midline epithelial seam; D = developing bone of maxilla (Masson's trichrome; × 30).

Developmental defects of the nose

Defects are of rare occurrence

Occur separated or in association with anomalies of the upper lip and jaw or whole face

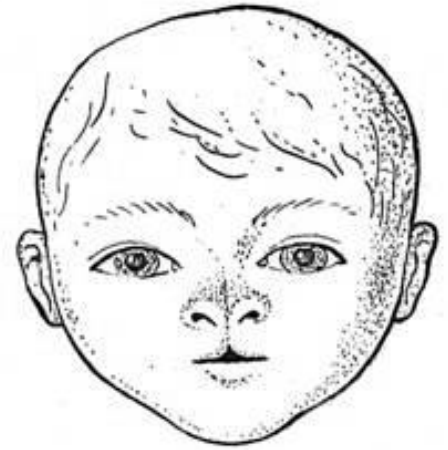


Aplasia (agenesis) of the nose - *caused by lack of nasal placodes*

Hypoplasia of the nose - a small nose with a single cavity

combined with micrognathy

Nasoschisis (nares bifides) - median cleft of the nose - caused by non-fused medial nasal prominences
The extent of cleft is variable - from shallow groove on the nose apex to the complete duplication of the nasal septum



Atresia introitus nasi (vestibuli nasi) - vestibulum nasi is closed by thin funnel shaped membrane (caused of persistence of epithelial plugs, which obturate nostrils of the fetus in the 3rd month)

Atresia choanarum – choana is closed with connective tissue membrane or bone plate

persistence of the oronasal (buconasal) membrane

1: 10 000

autosomal dominant inheritance

Other defects: nasus duplex (rhinodynia), **proboscis**

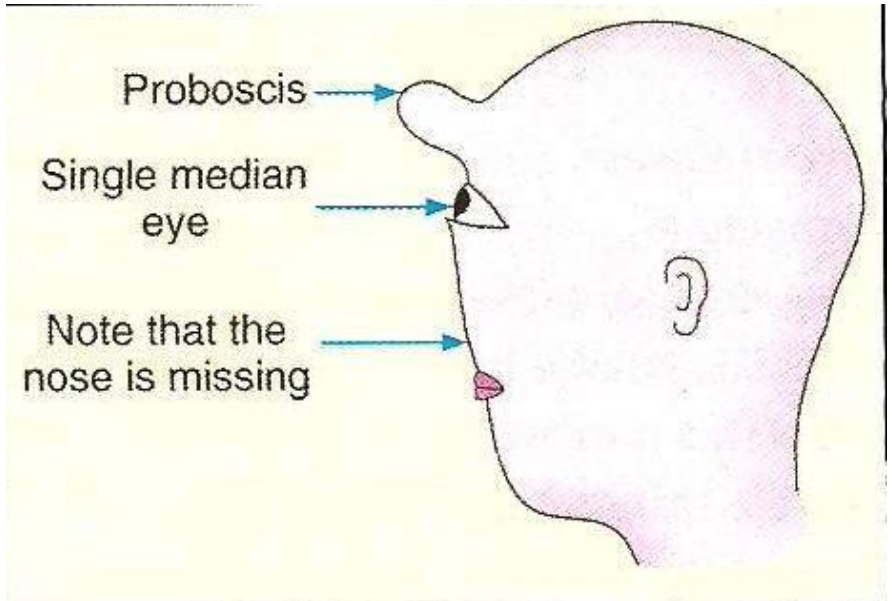


Figura 3. Foto del recién nacido. Se observa ojo único central, con probóscide, confirmando la etmocefalia.

Veratrum californicum

http://www.sci-news.com/othersciences/anthropology/newborn-babies-skills-pick-out-individual-words-06863.html