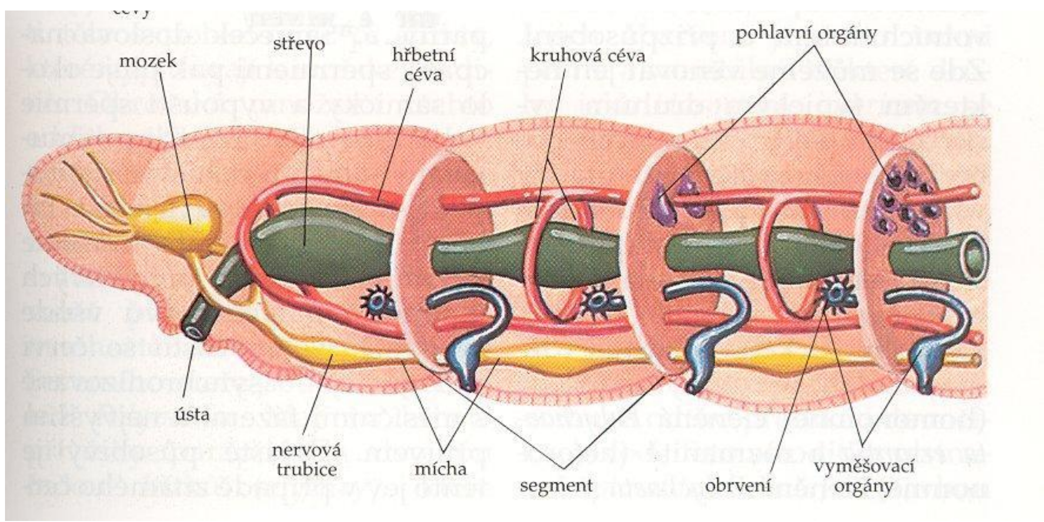
Face development and defects

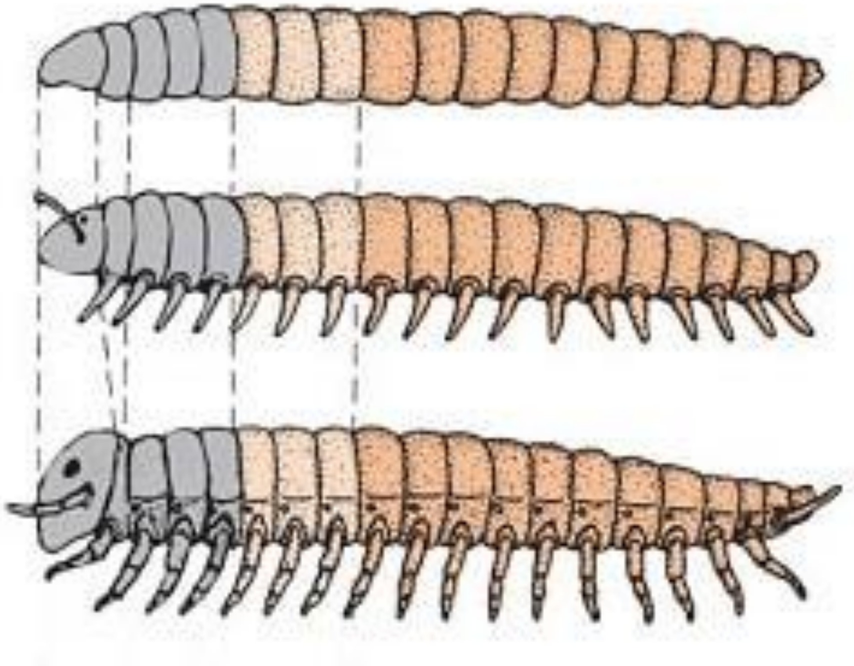
(face, jaws, palates, nose)

17. 4. 2024

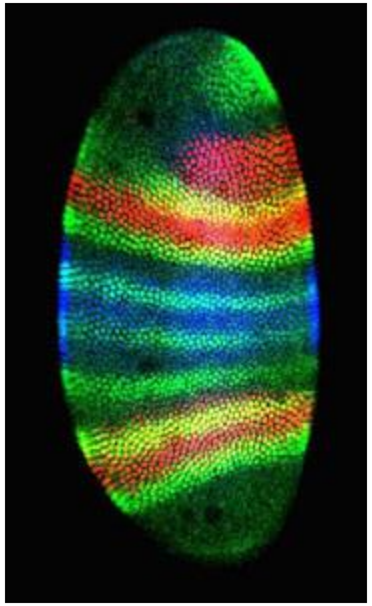
Jan Křivánek

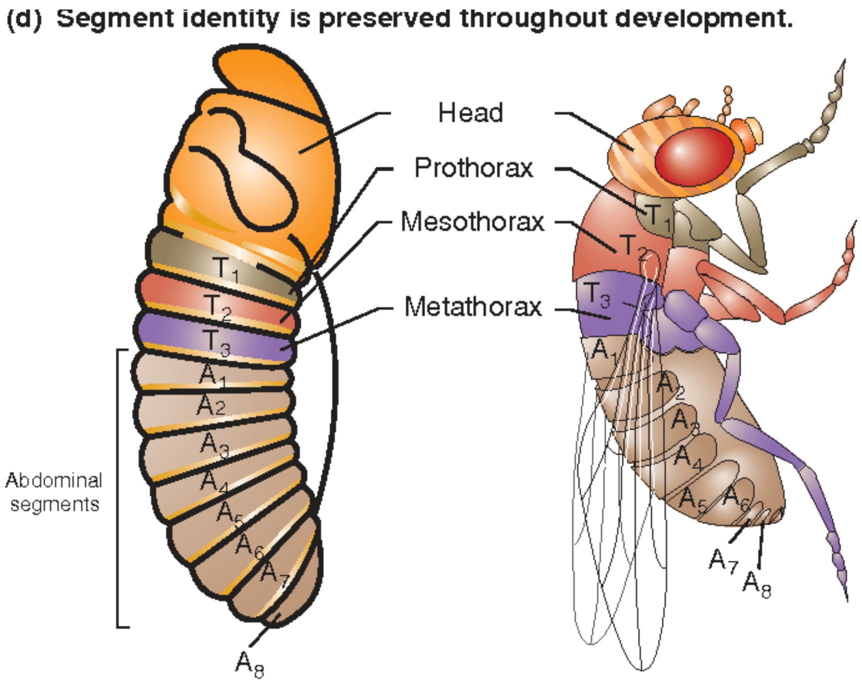
Body segmentation

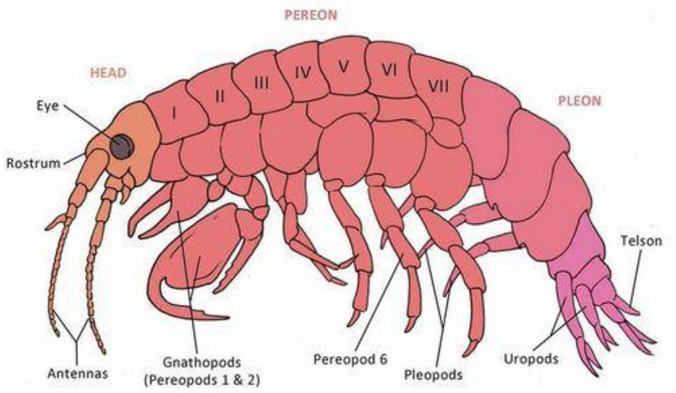


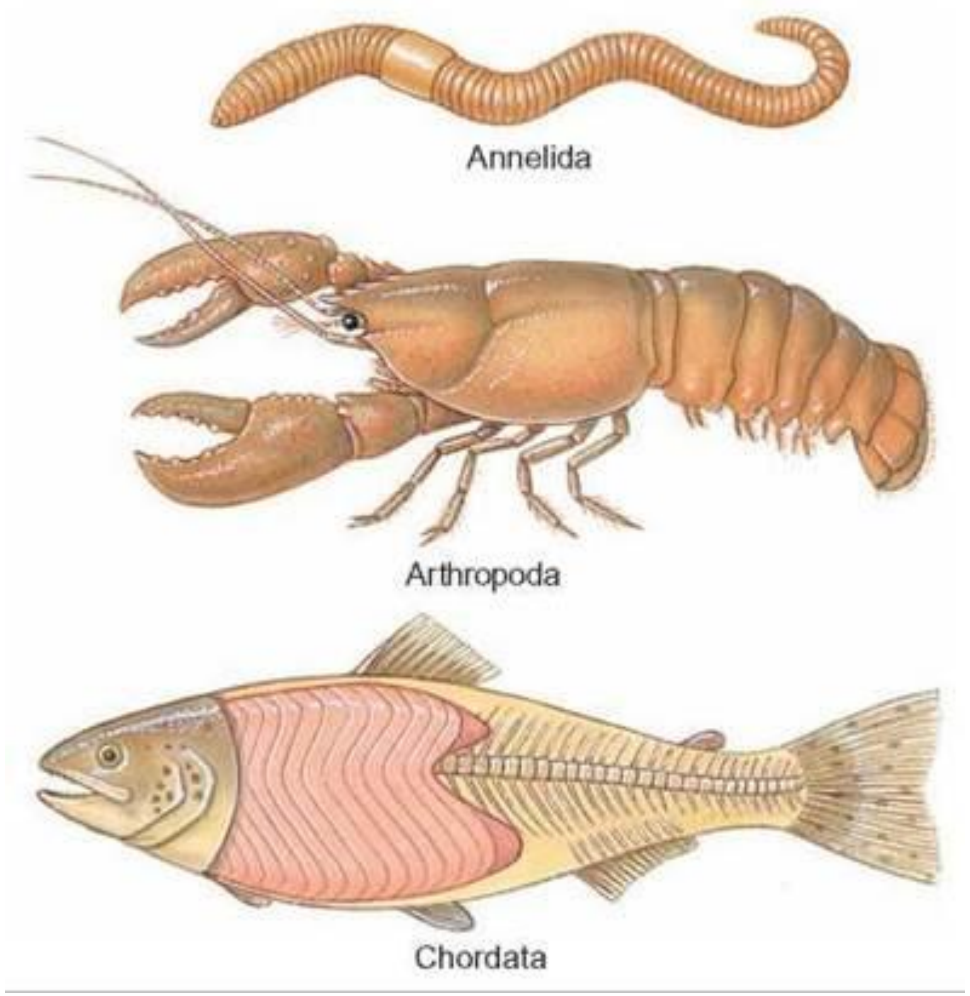


Body segmentation

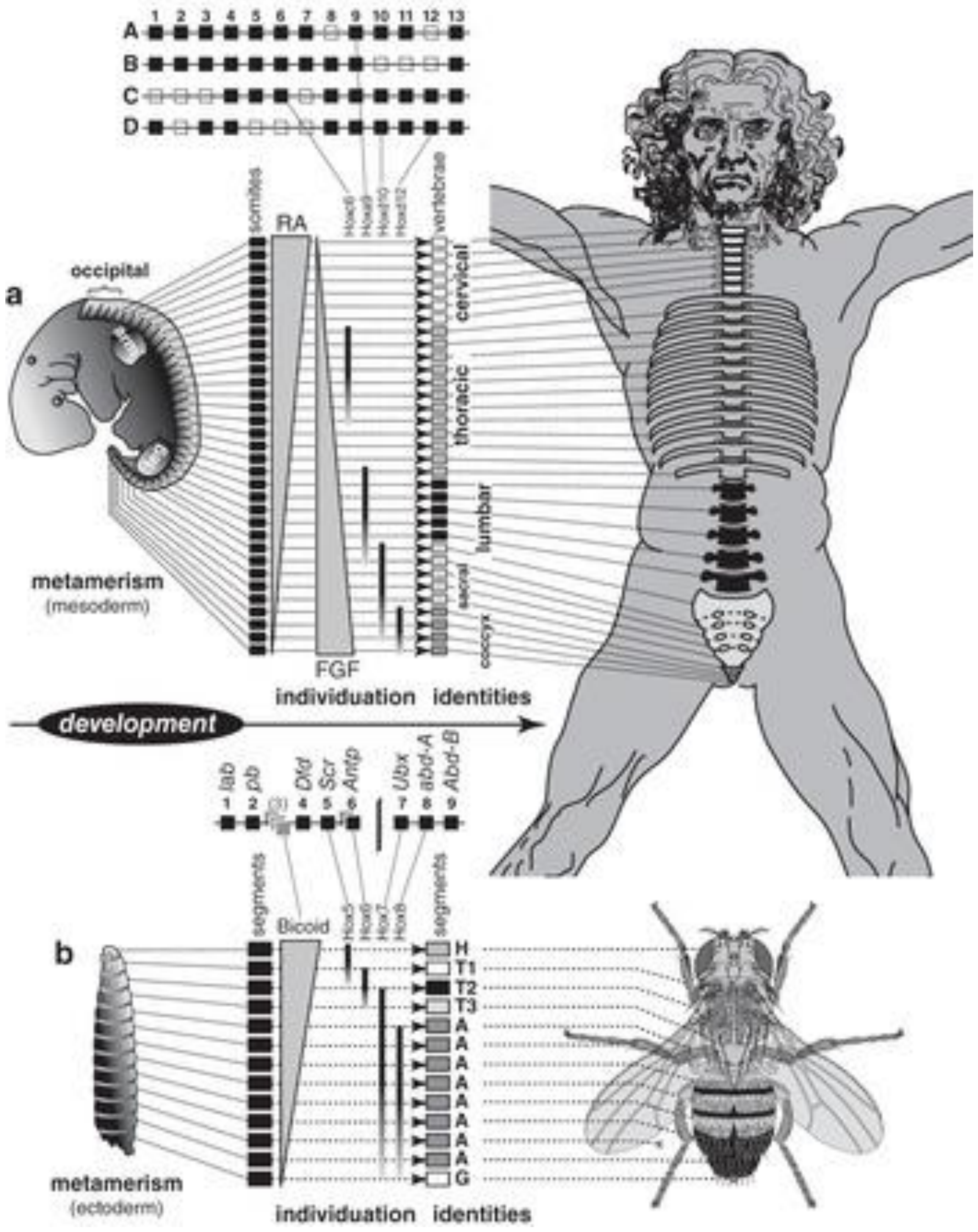








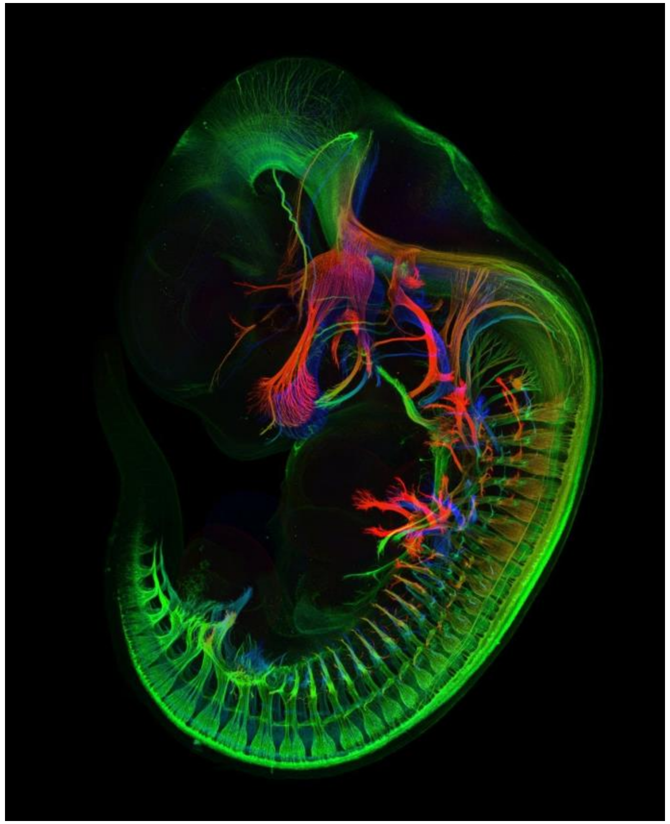
Body segmentation – is a human body segmented?



The same segmentation pattern as in a primitive species

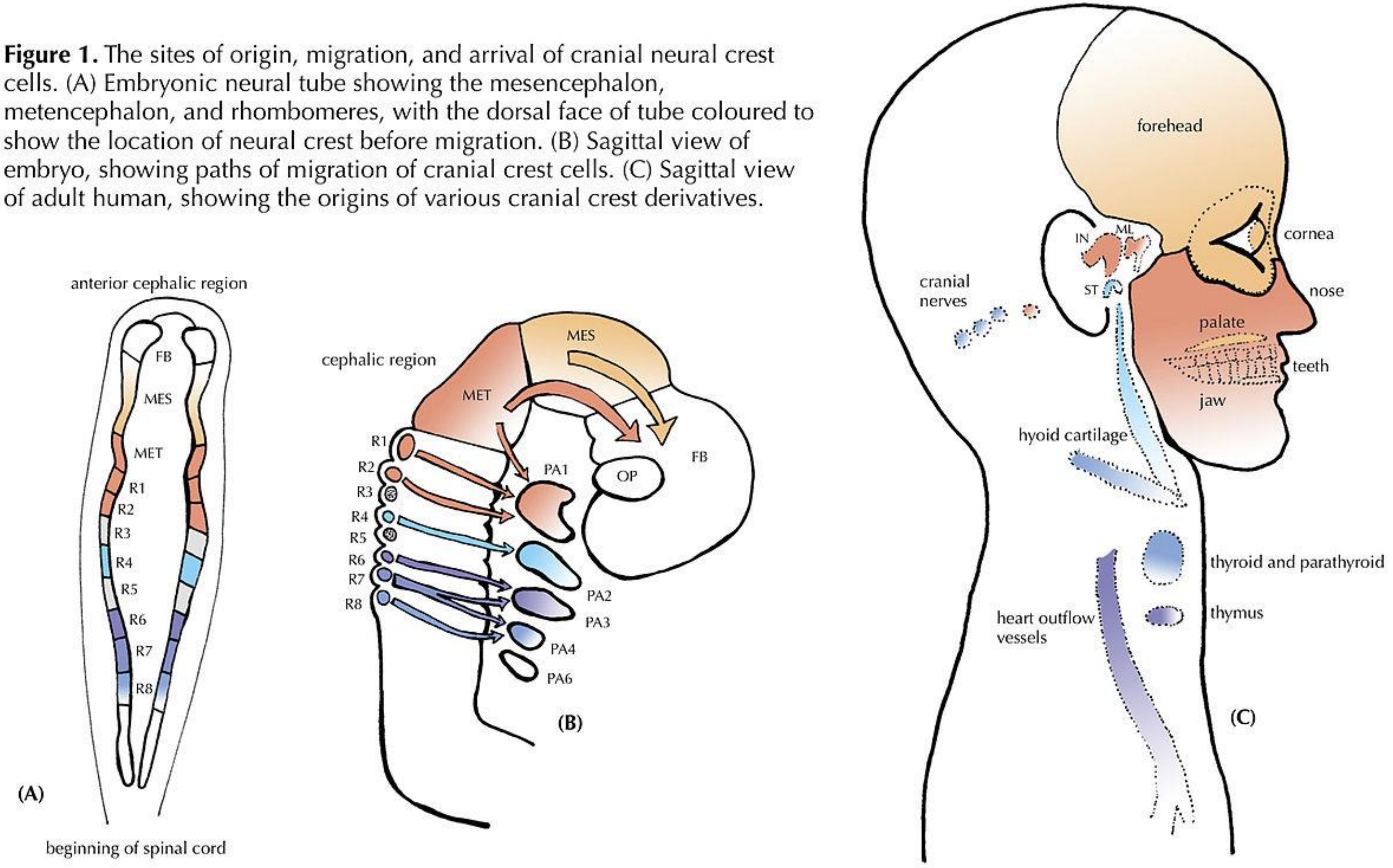
The same signalling pathways

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



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.

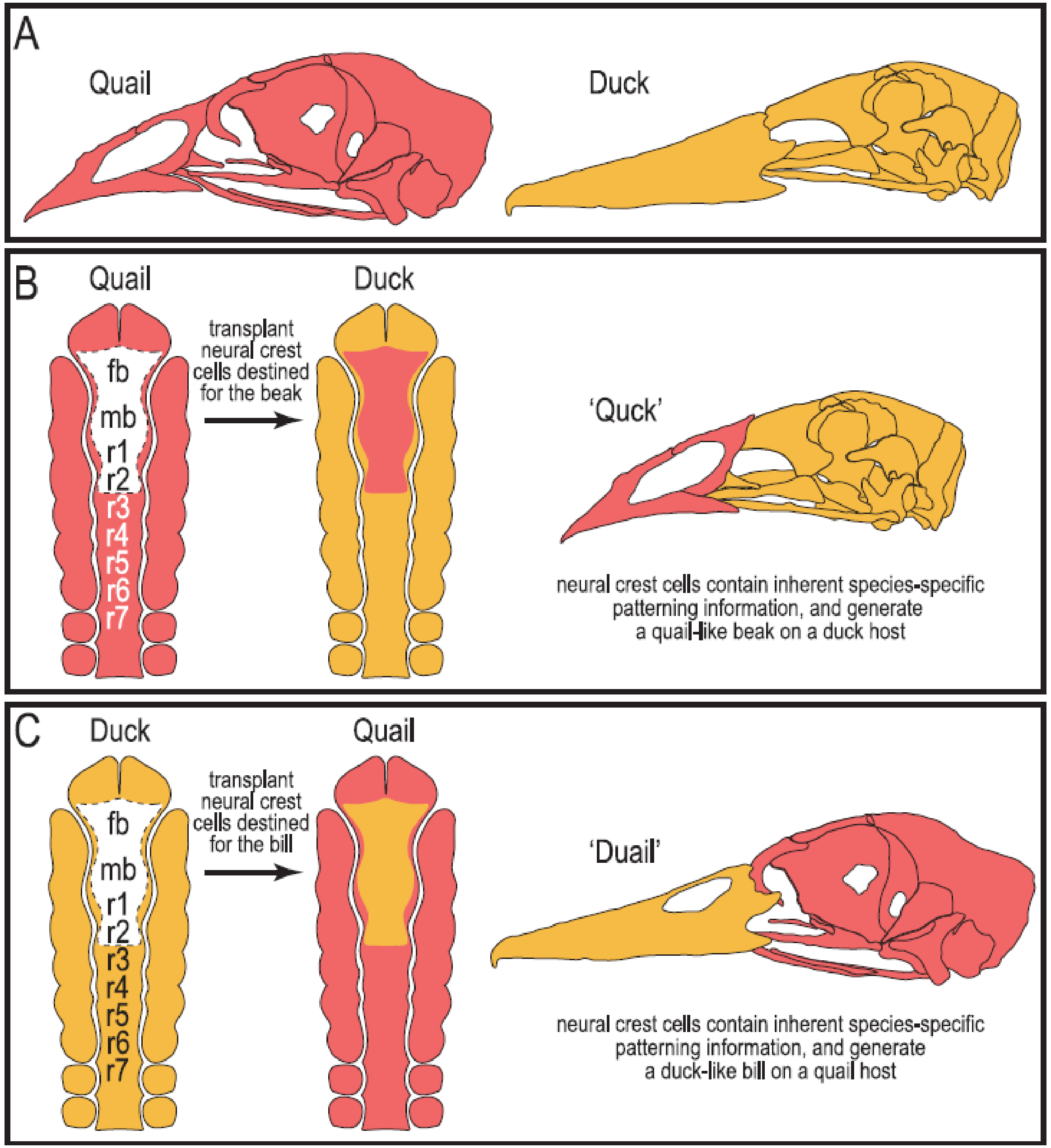


MES mesencephalon
MET metencephalon
FB forebrain
OP optic vesicle
R1 rhombomere 1
R2 rhombomere 2
R3 rhombomere 3
R4 rhombomere 4
R5 rhombomere 5
R6 rhombomere 6
R7 rhombomere 7
R8 rhombomere 8
PA1 first pharyngeal arch
PA2 second pharyngeal arch
PA3 third pharyngeal arch
PA4 fourth pharyngeal arch
PA6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

Face development – Neural crest



Doc. Petr Vaňhara

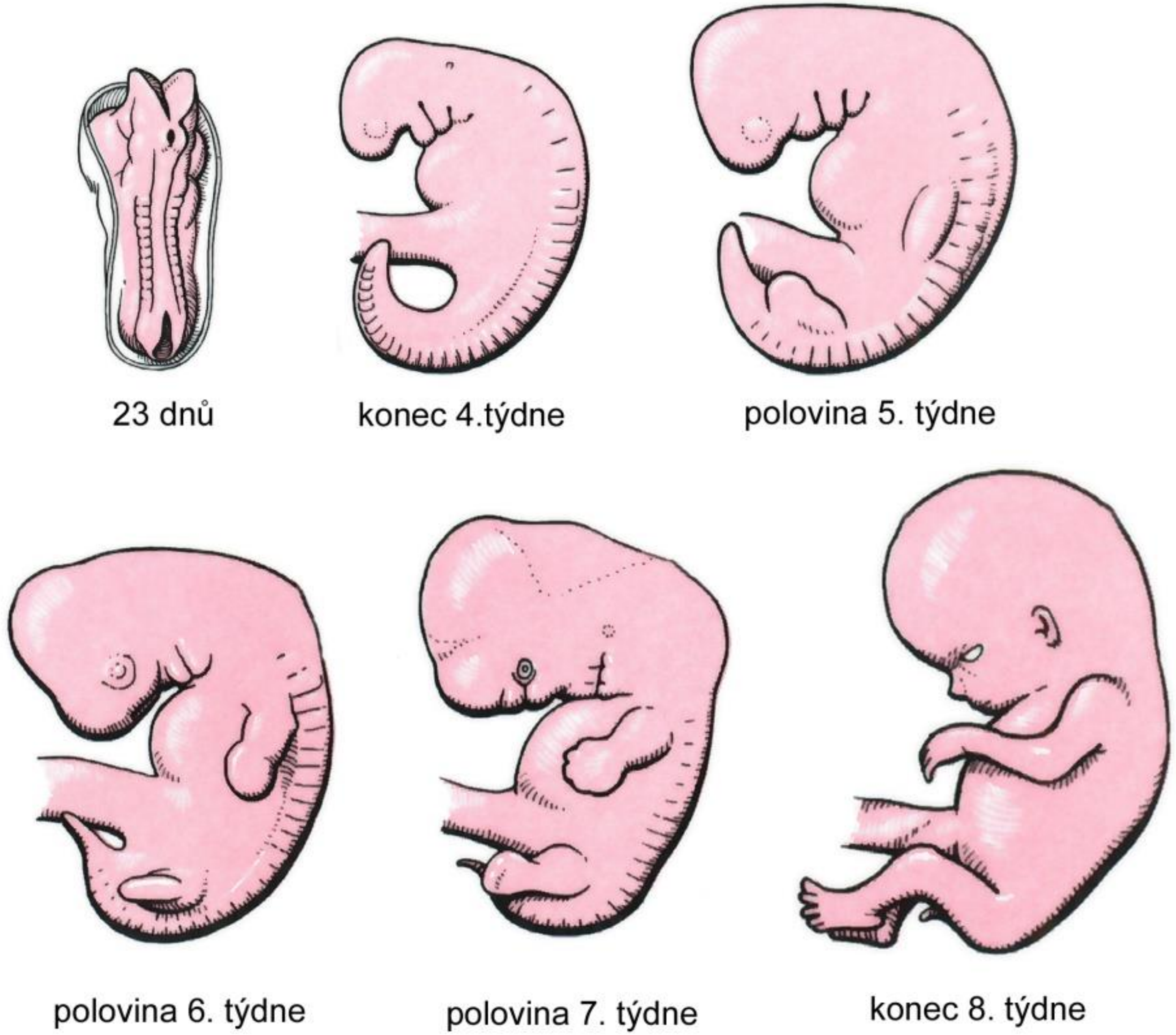
Development from zygote

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

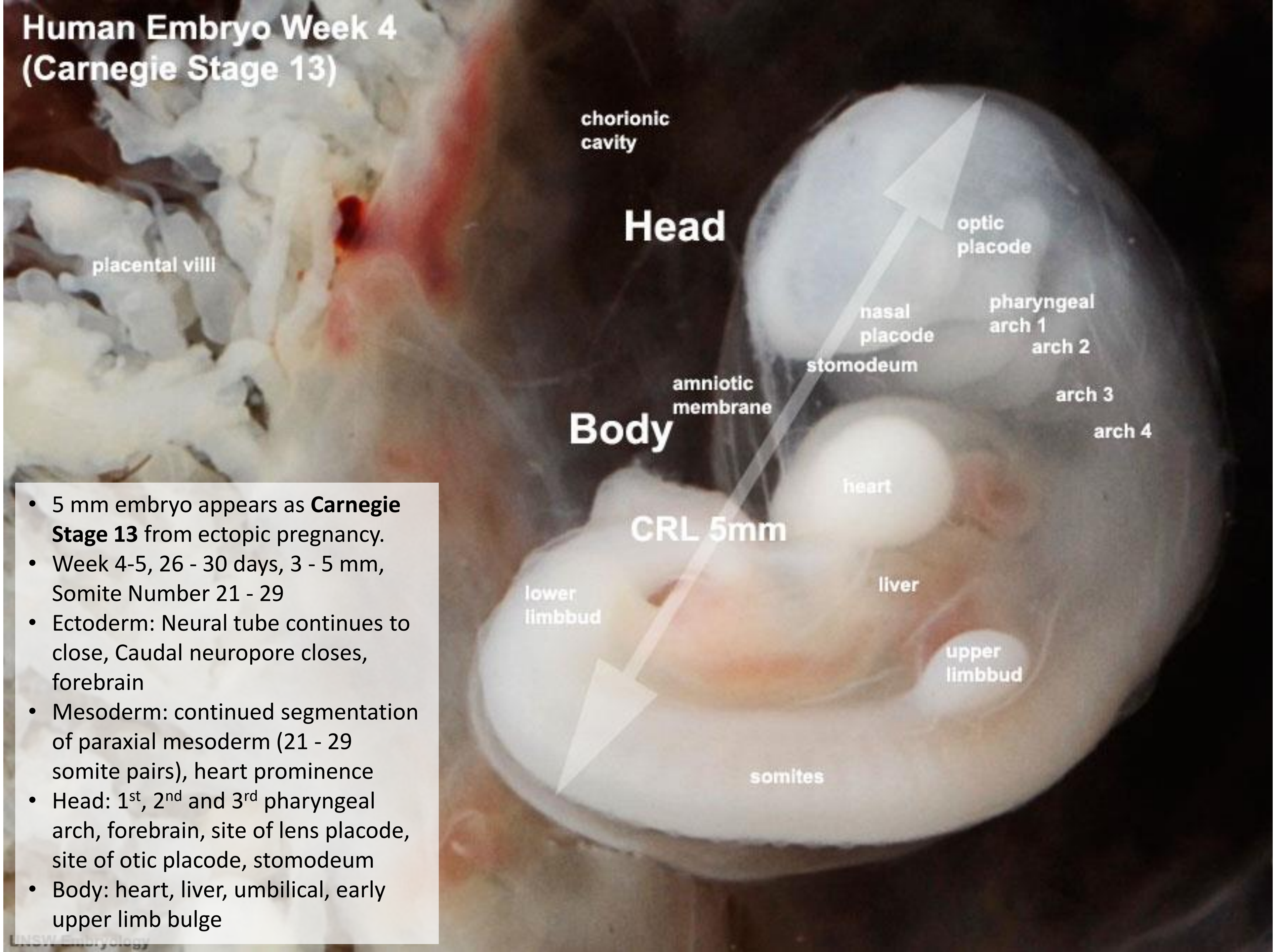
Face development

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

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


23 dnů
konec 4.týdne
polovina 5. týdne
polovina 6. týdne
polovina 7. týdne
konec 8. týdne

Human Embryo Week 4 (Carnegie Stage 13)



- 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: 1^{st}, 2^{nd} and 3^{rd} 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

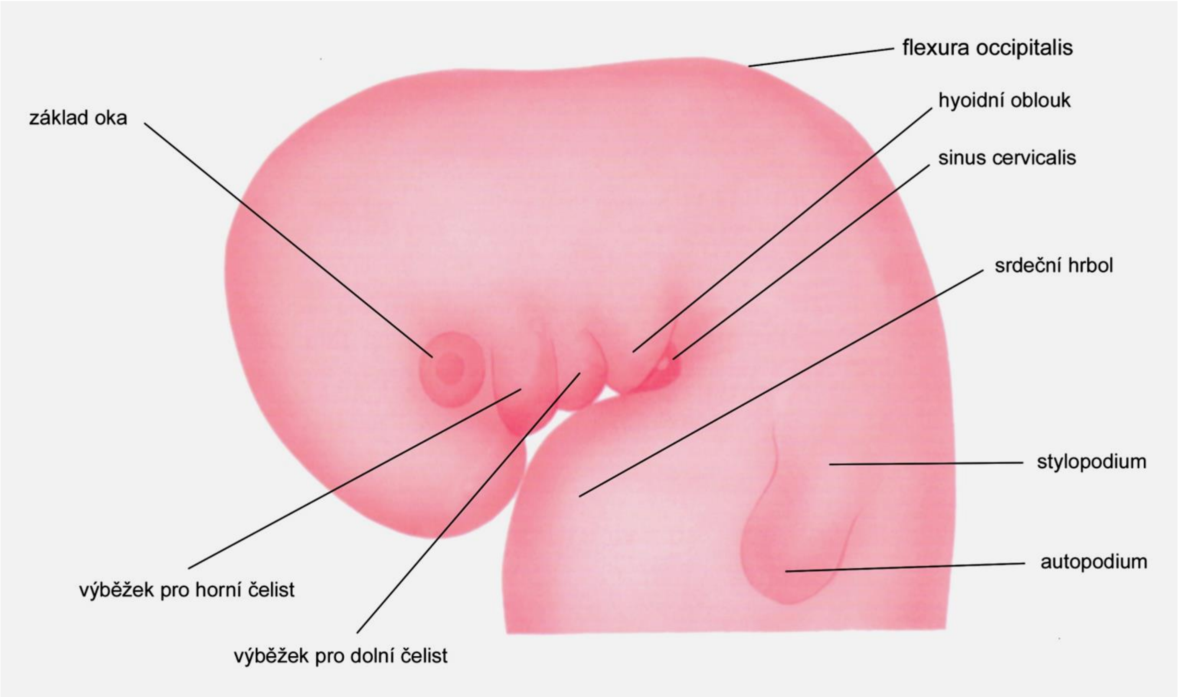
Body parts: head, neck, body and tail

Length of the embryo is 8 -10 mm

Frontal prominence with prosencephalon

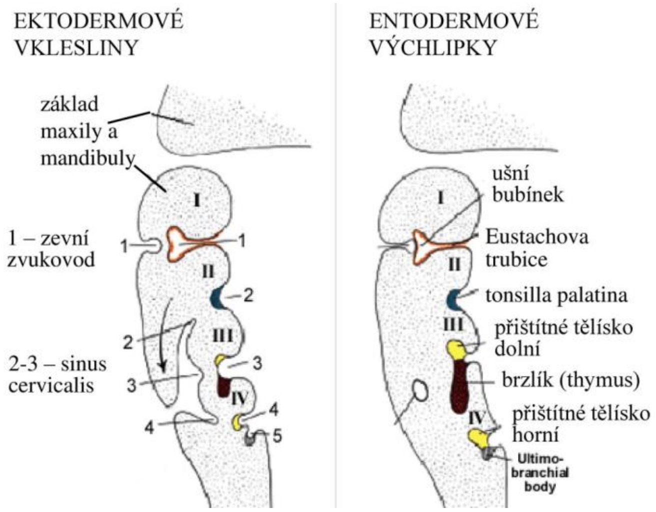
Mesencephalic prominence with mesencephalon - flexura cephalica

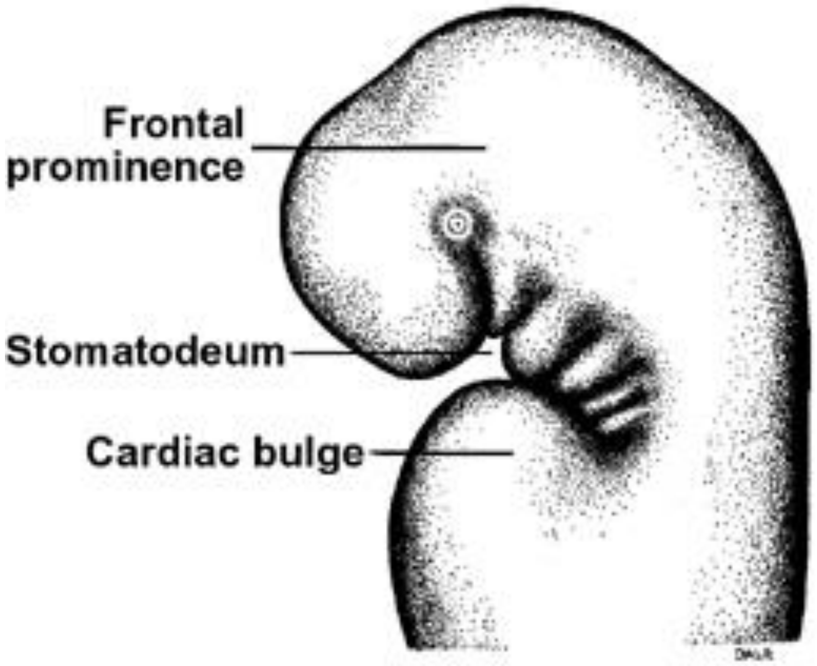
Occipital prominence with rhombencephalon - flexura occipitalis

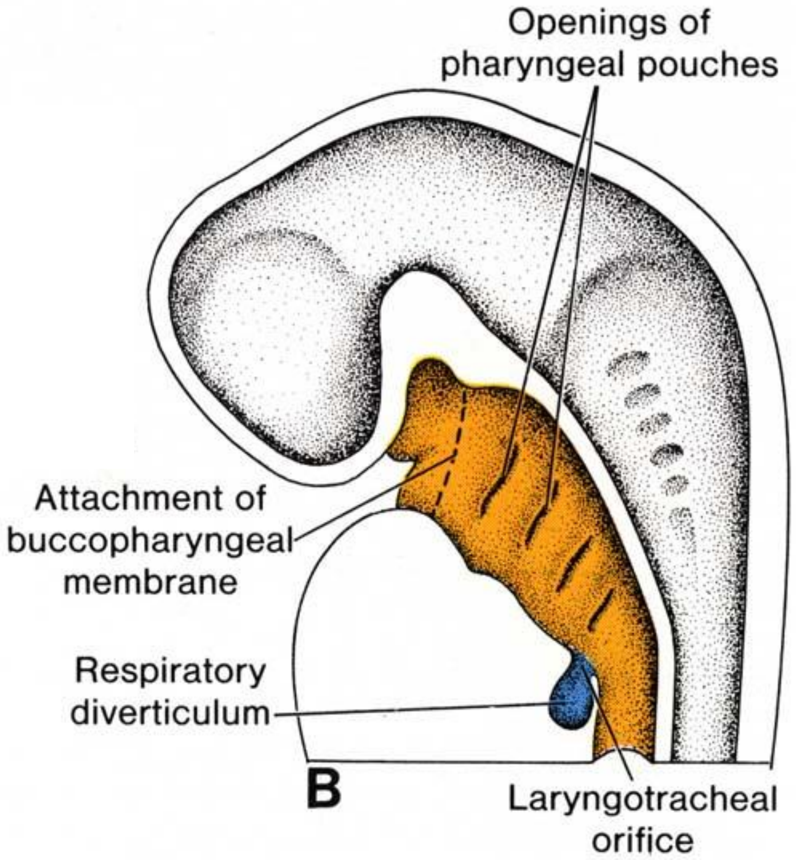


Human fetus at the end of 1st month of development

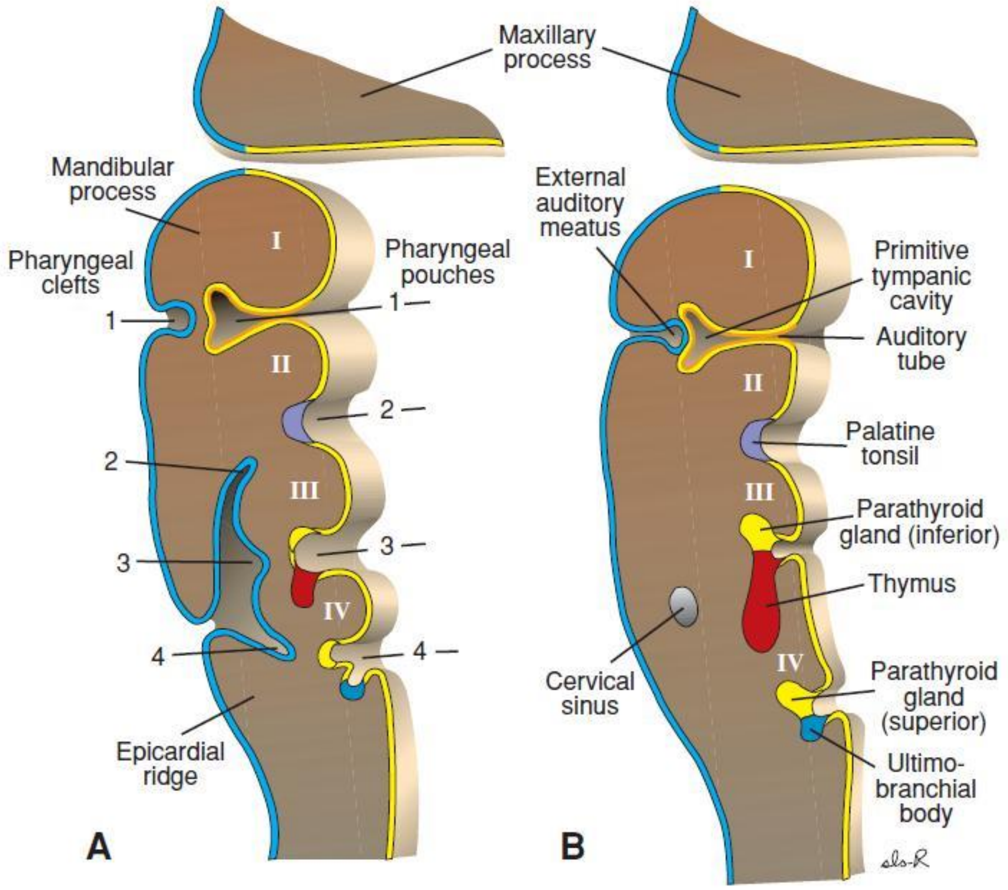
Pharyngeal (branchial) aparatus:
6 Branchial arches
4 Branchial clefts (grooves) (ectodermal)
5 Branchial pouches (entodermal) Separated by **membranae obturantes**

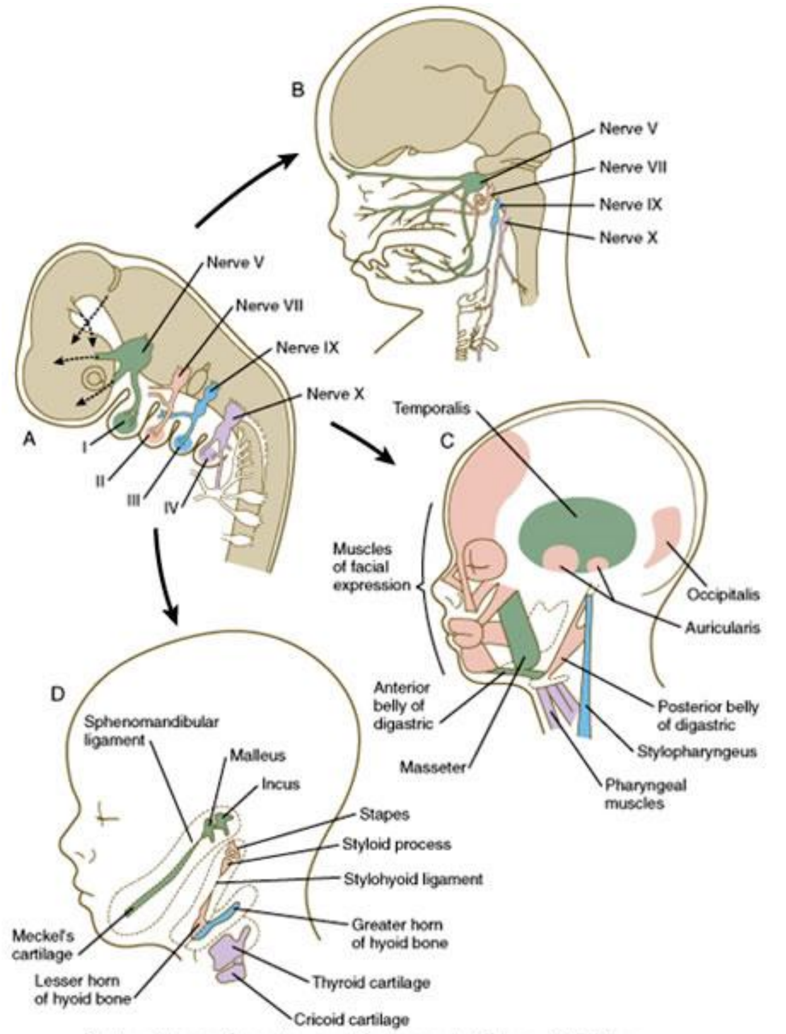






Branchial aparatus

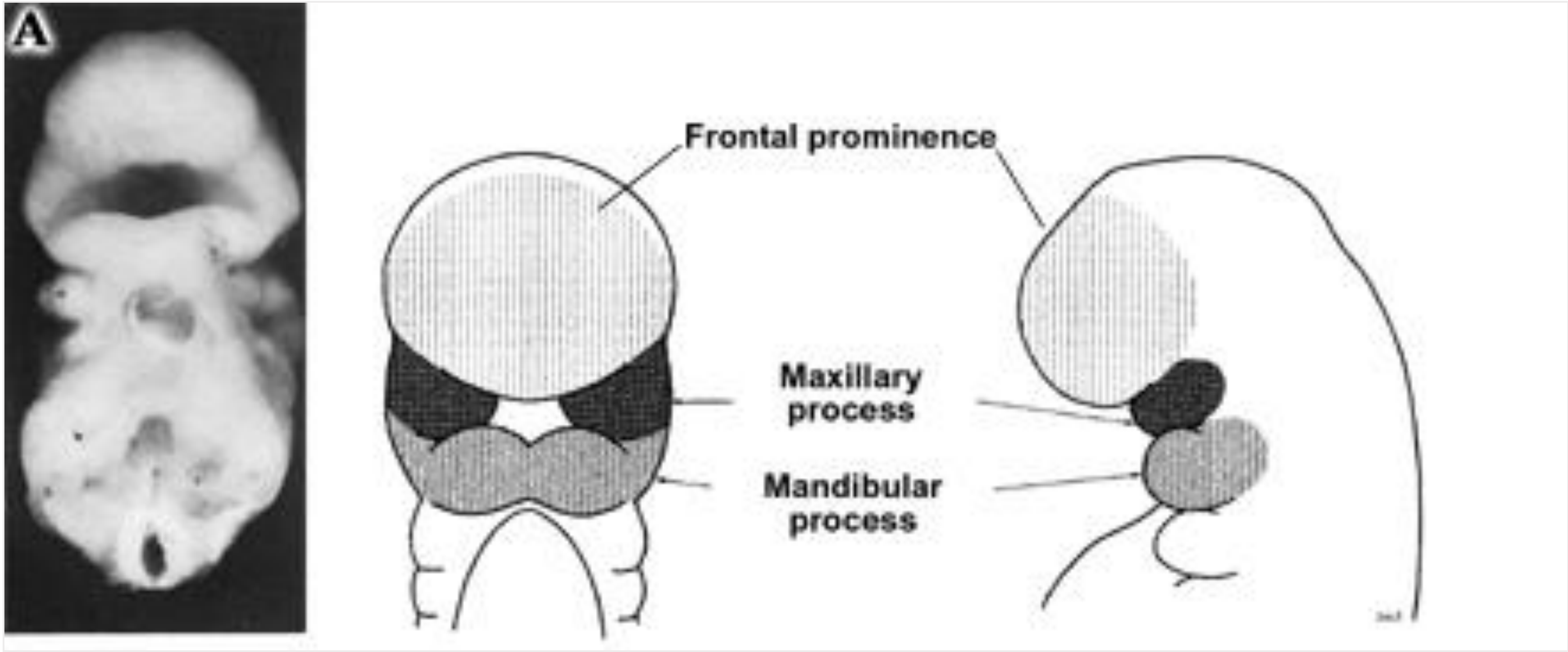




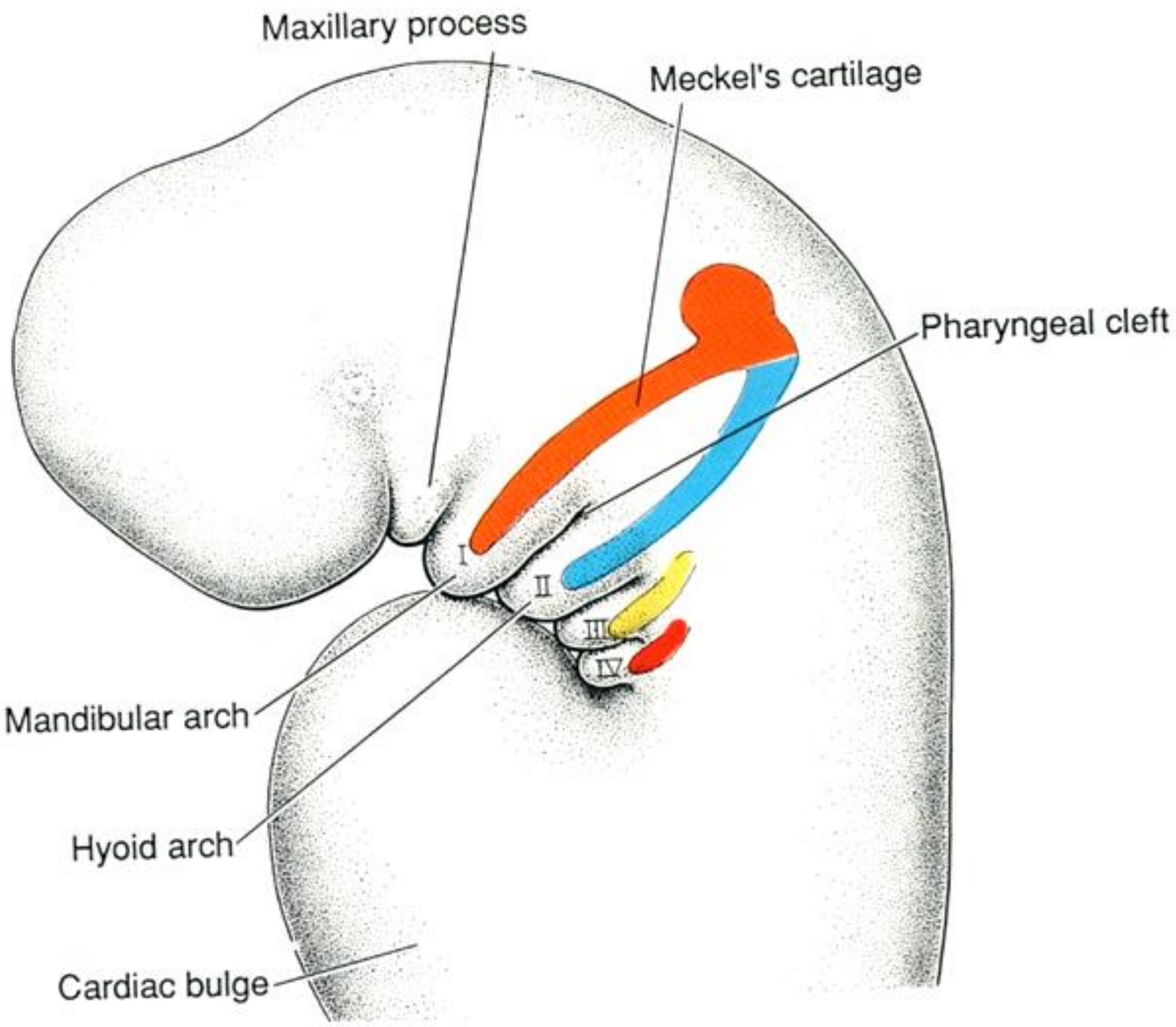
Carlson: Human Embryology and Developmental Biology, 4th Edition.

<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)

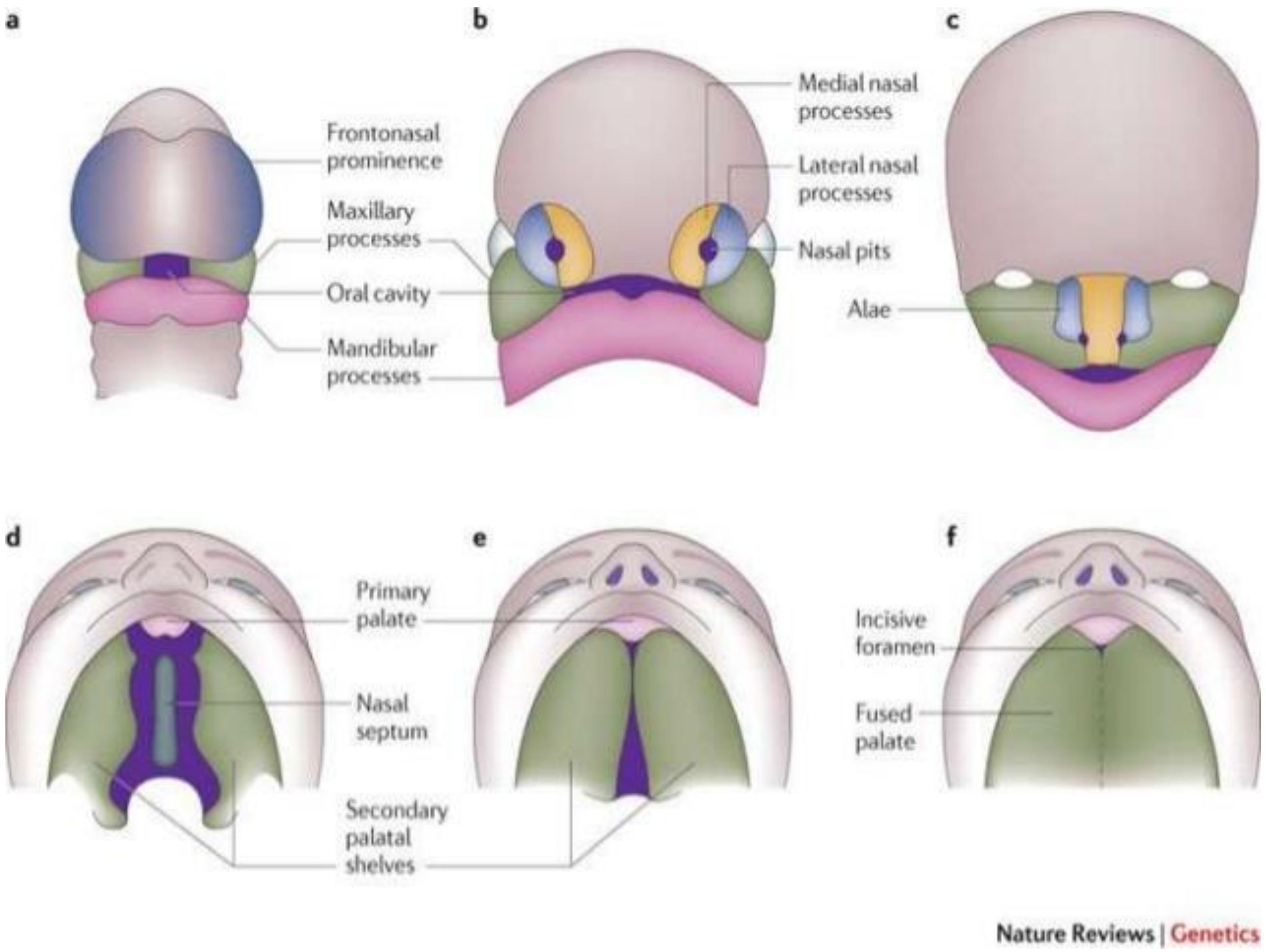
The base of the prominences is formed by an **ectomesenchyme**, which populated them from the lower mesencephalic and upper rhombencephalic section of the neural crest.

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



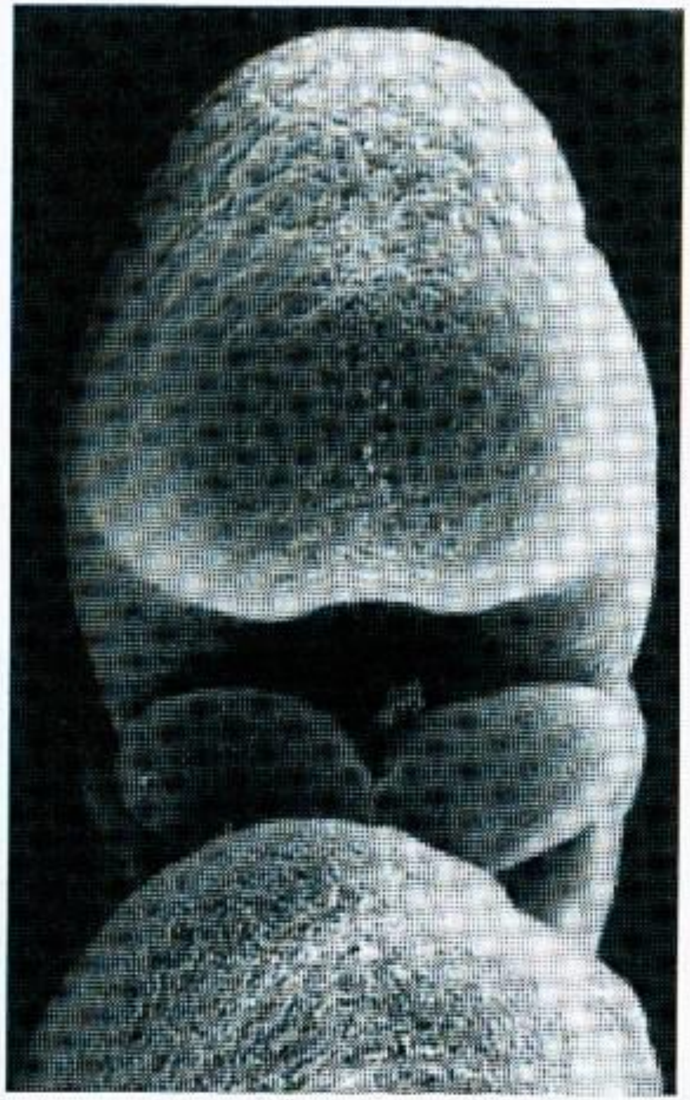
Doc. Petr Vaňhara

Face development

Frontonasal prominence
(processus frontonasalis)

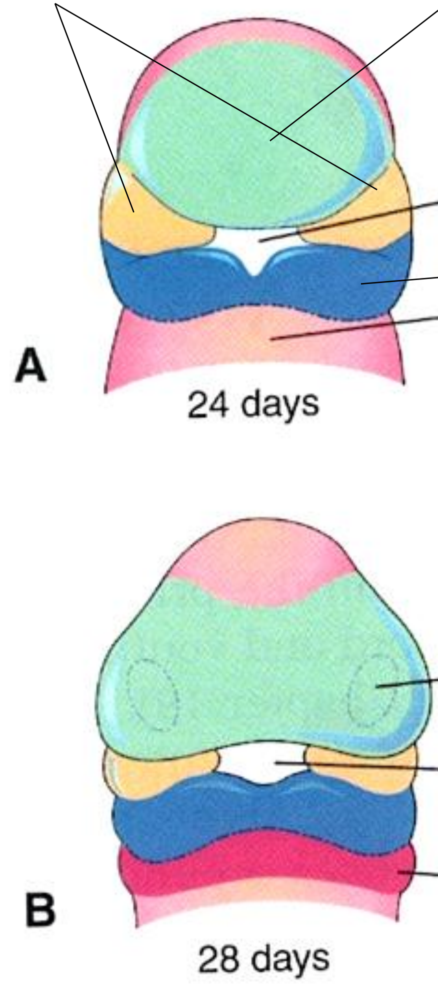
Paired prominences for upper jaw
(processus maxillares)

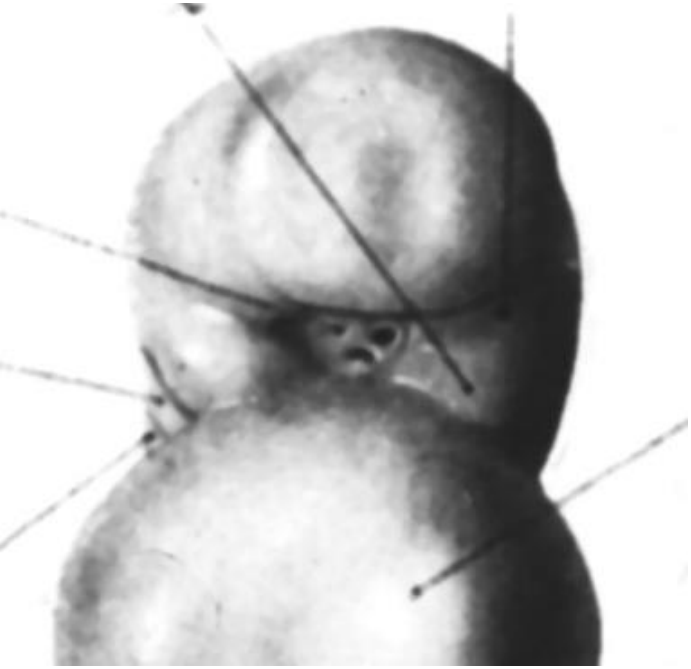
aired prominences for lower jaw
(processus mandibulares)



4th week

Face development





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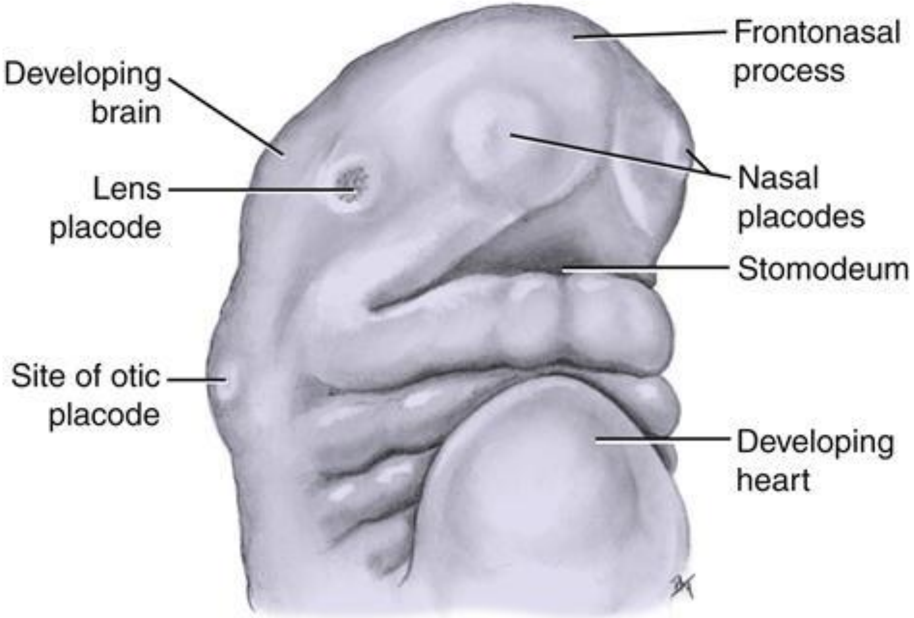
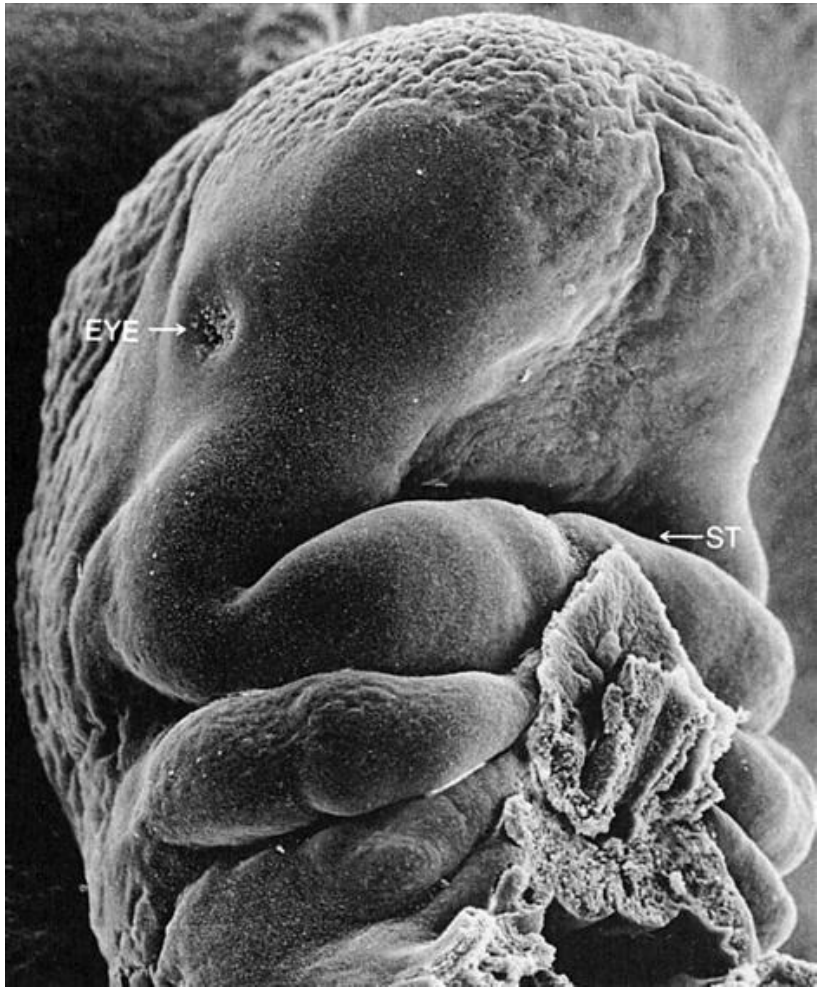
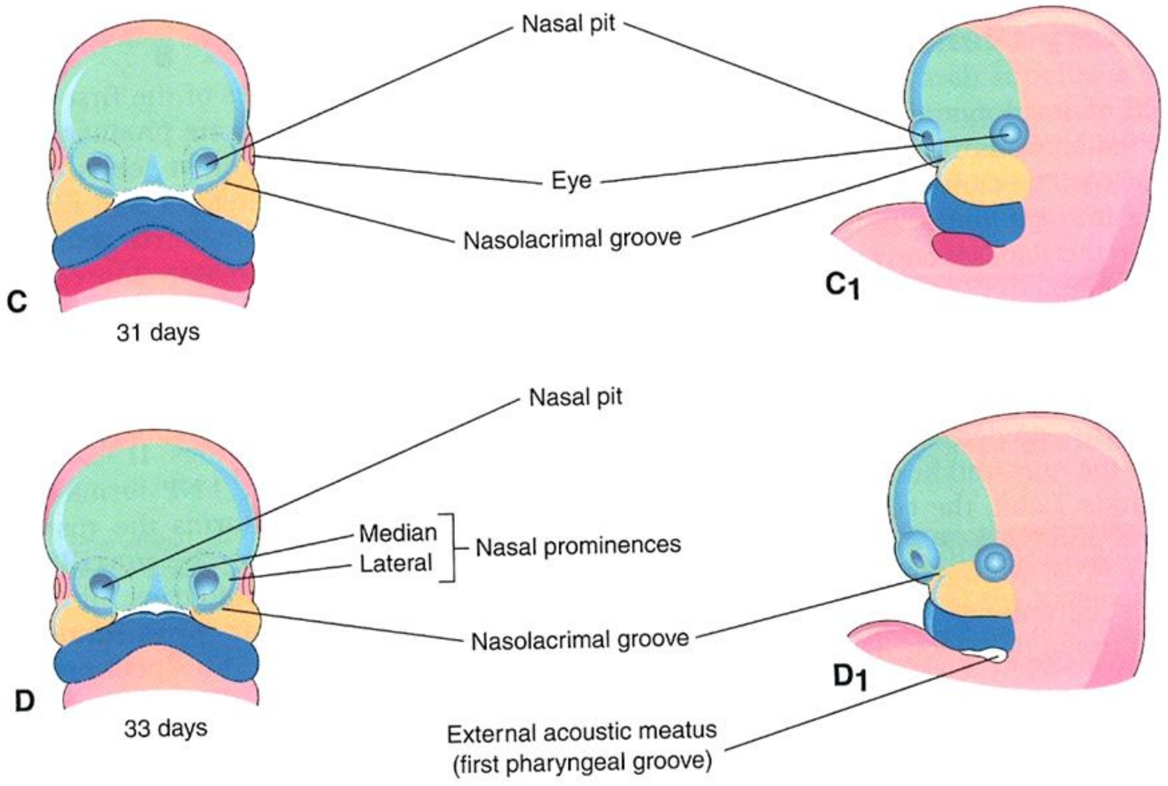
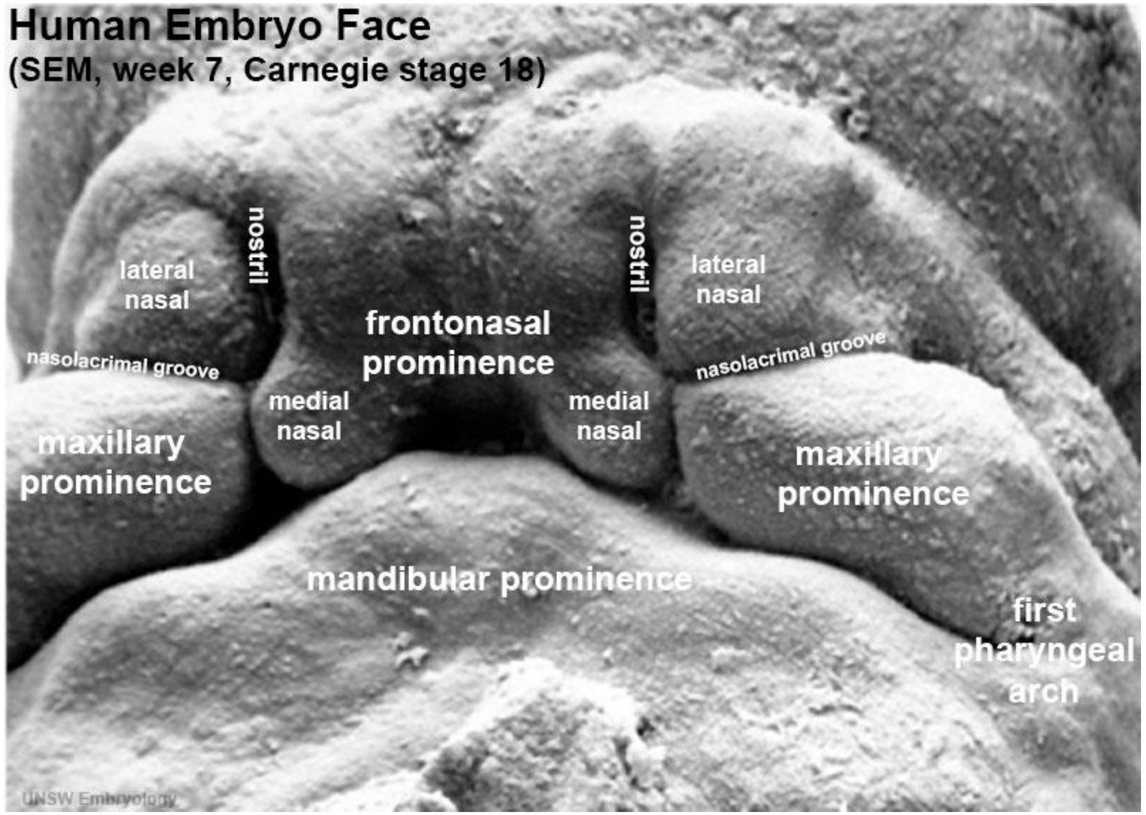
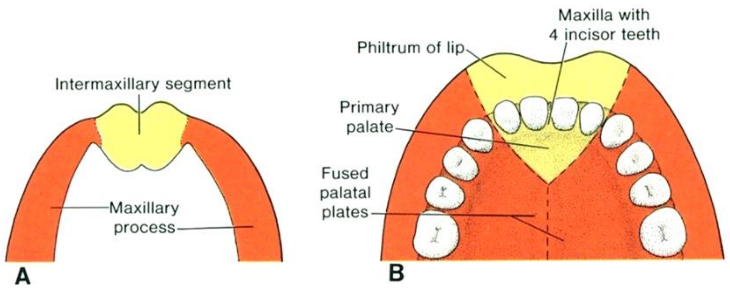

Developing brain
Lens placode
Site of otic placode
Frontonasal process
Nasal placodes
Stomodeum
Developing heart


EYE
ST

Face development





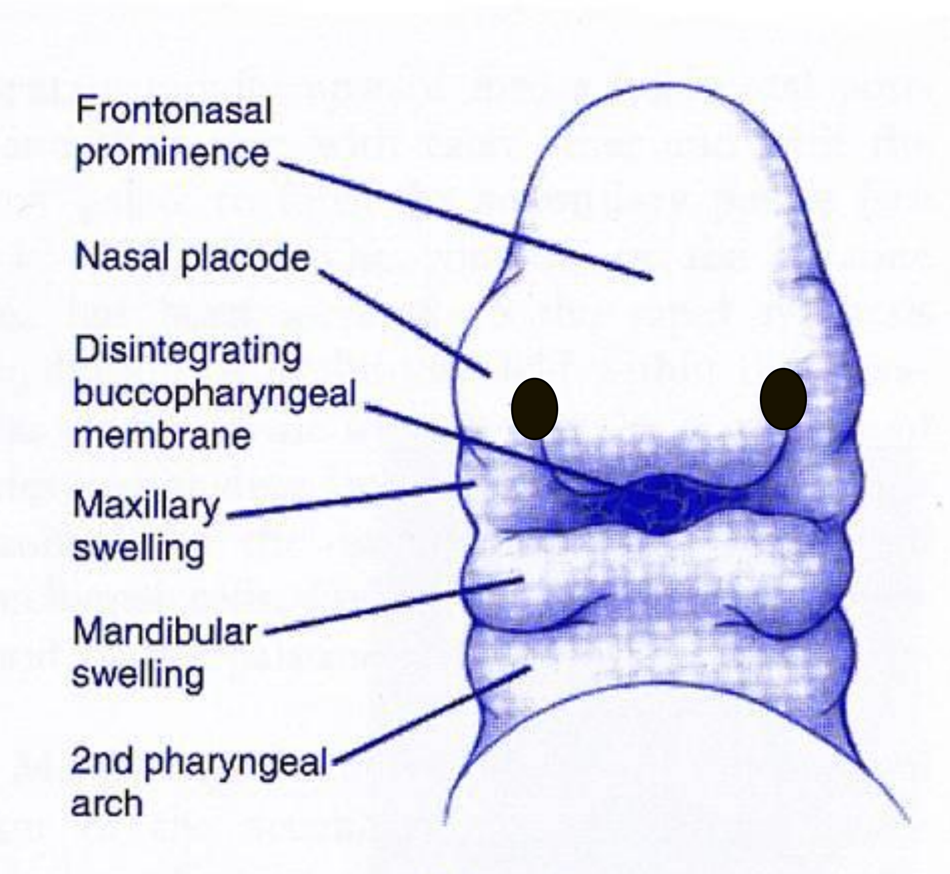


- Nasal pits surrrounded by paired prominences – **medial and lateral nasal prominence**
- **Area triangularis** (nose)
- **Intermaxilary segment** (medial part of upper lip, part of upper jaw, primary palate)

Doc. Petr Vaňhara

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

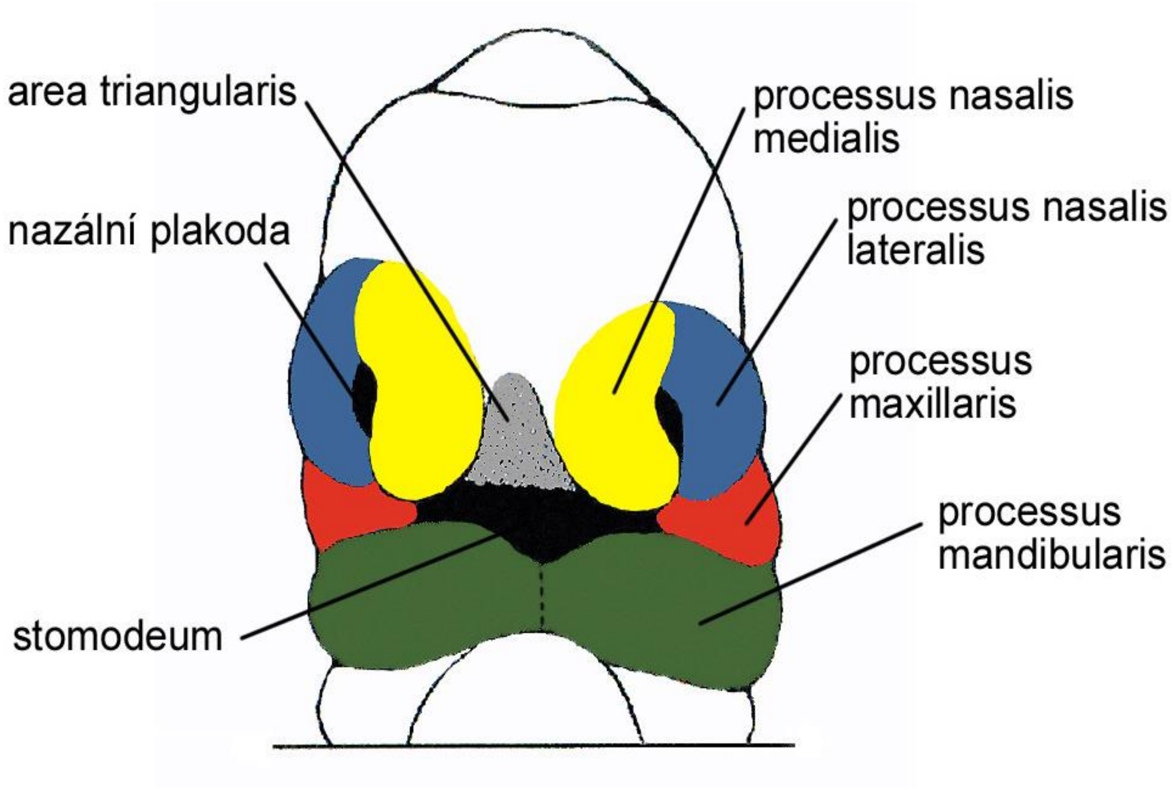
4th week

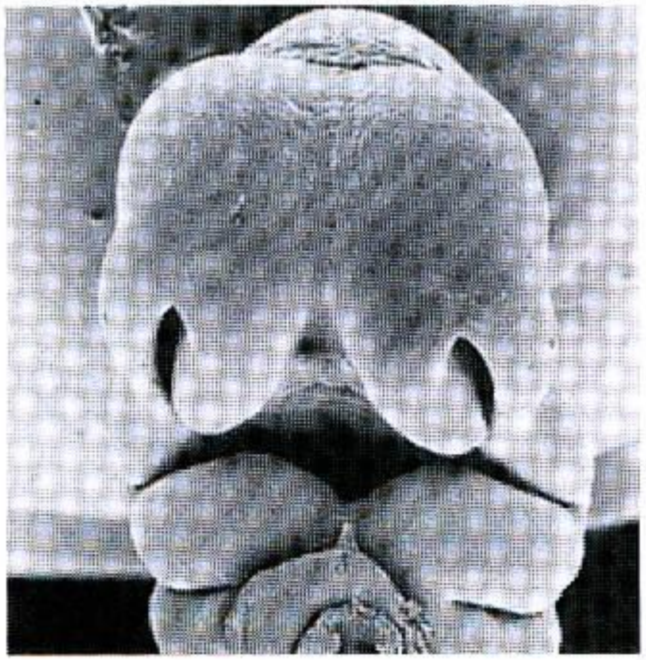


5th week

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***





Early 6th week

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**

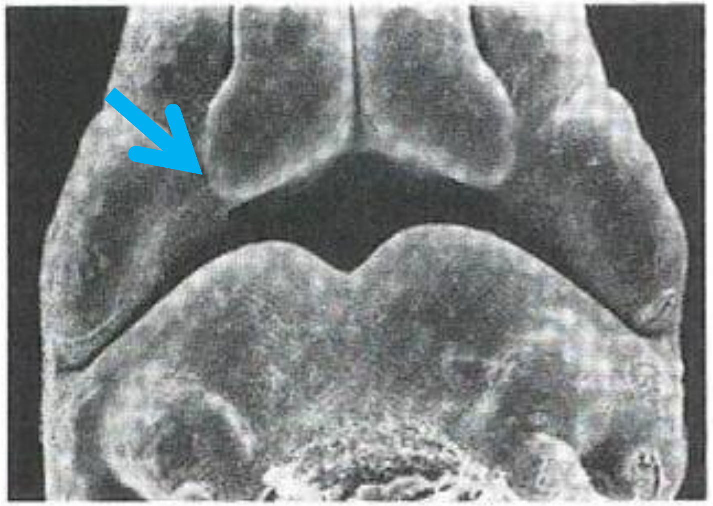
The intermaxillary segment gives rise to:

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

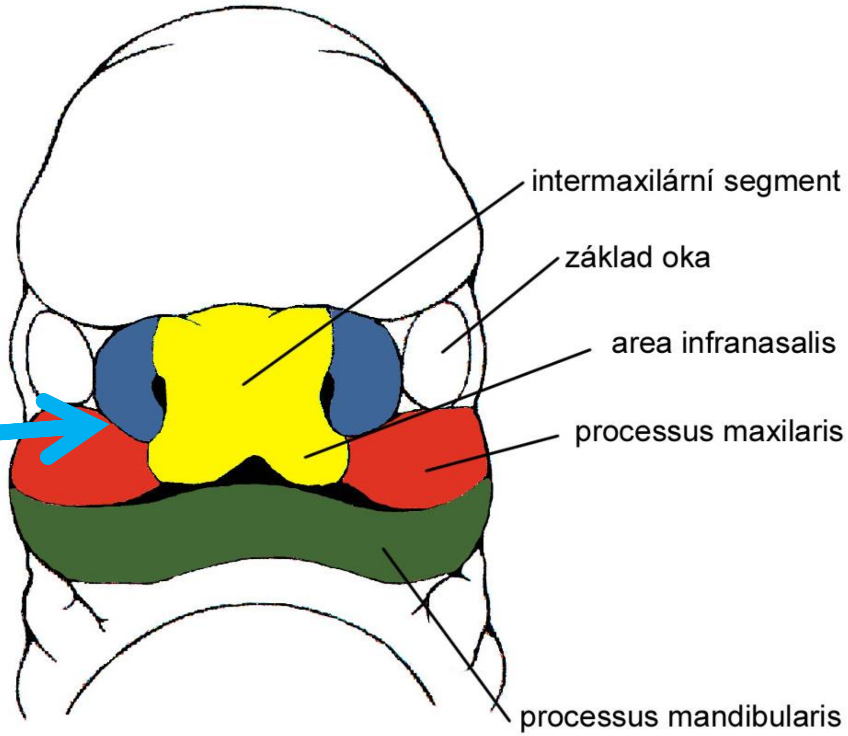
The common upper lip is formed after the intermaxillary segment has fused with the maxillary processes

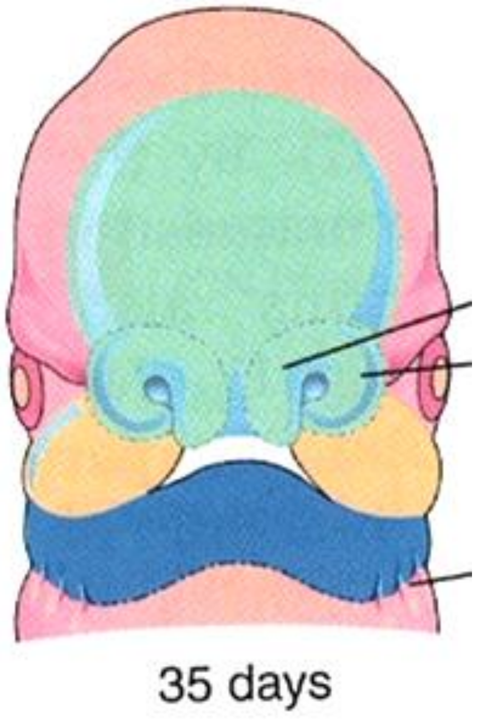
At first, lateral nasal prominences are separated from the maxillary prominences by a furrow, called the **nasolacrimal groove**

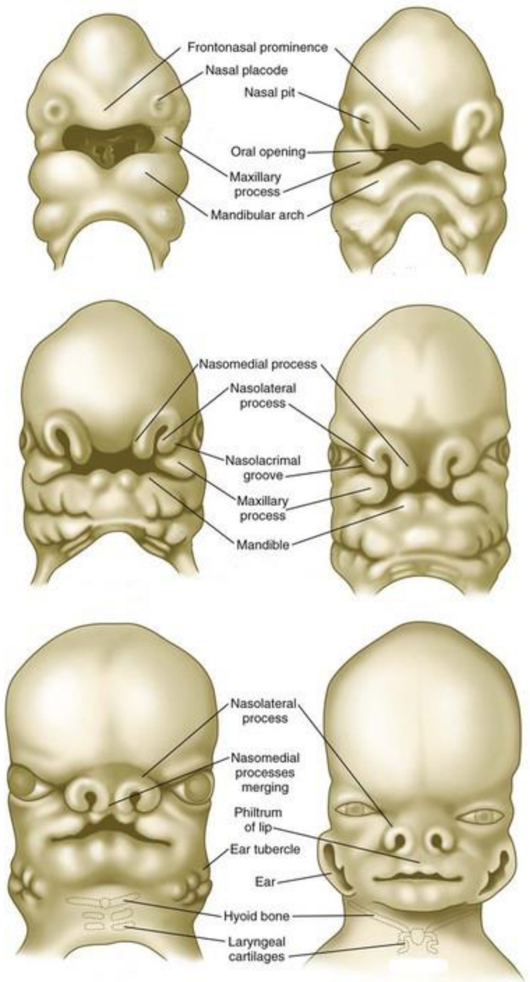
During next days, the maxillary prominences enlarge and fuse with lateral nasal prominences.



Early 7th week







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**

Doc. Petr Vaňhara

Summary of face development timing

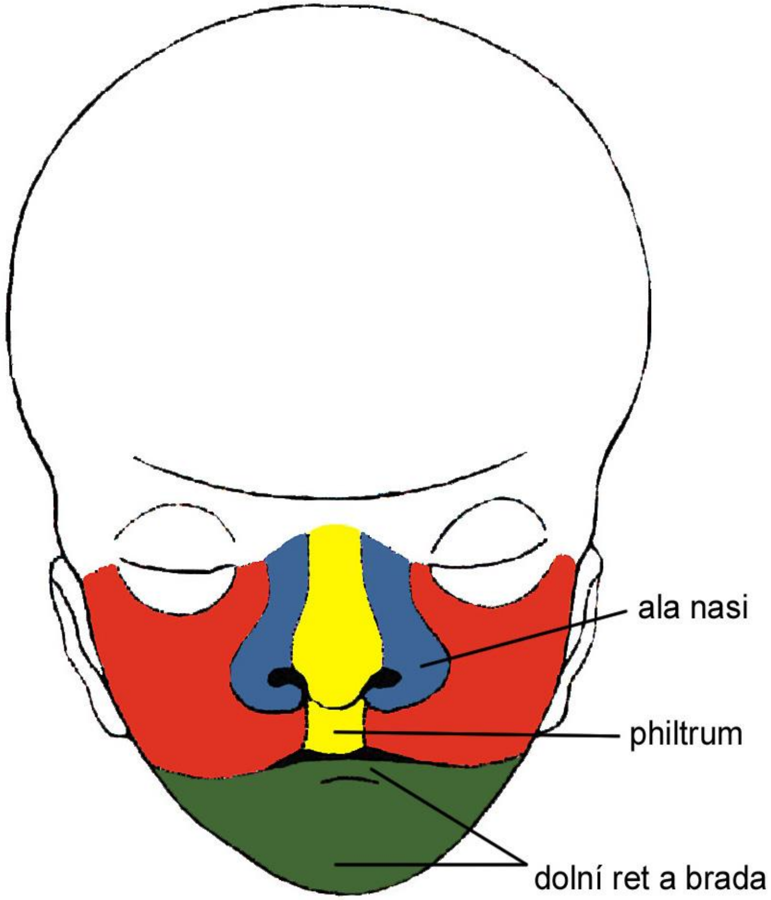
Between **5. - 7. week**

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

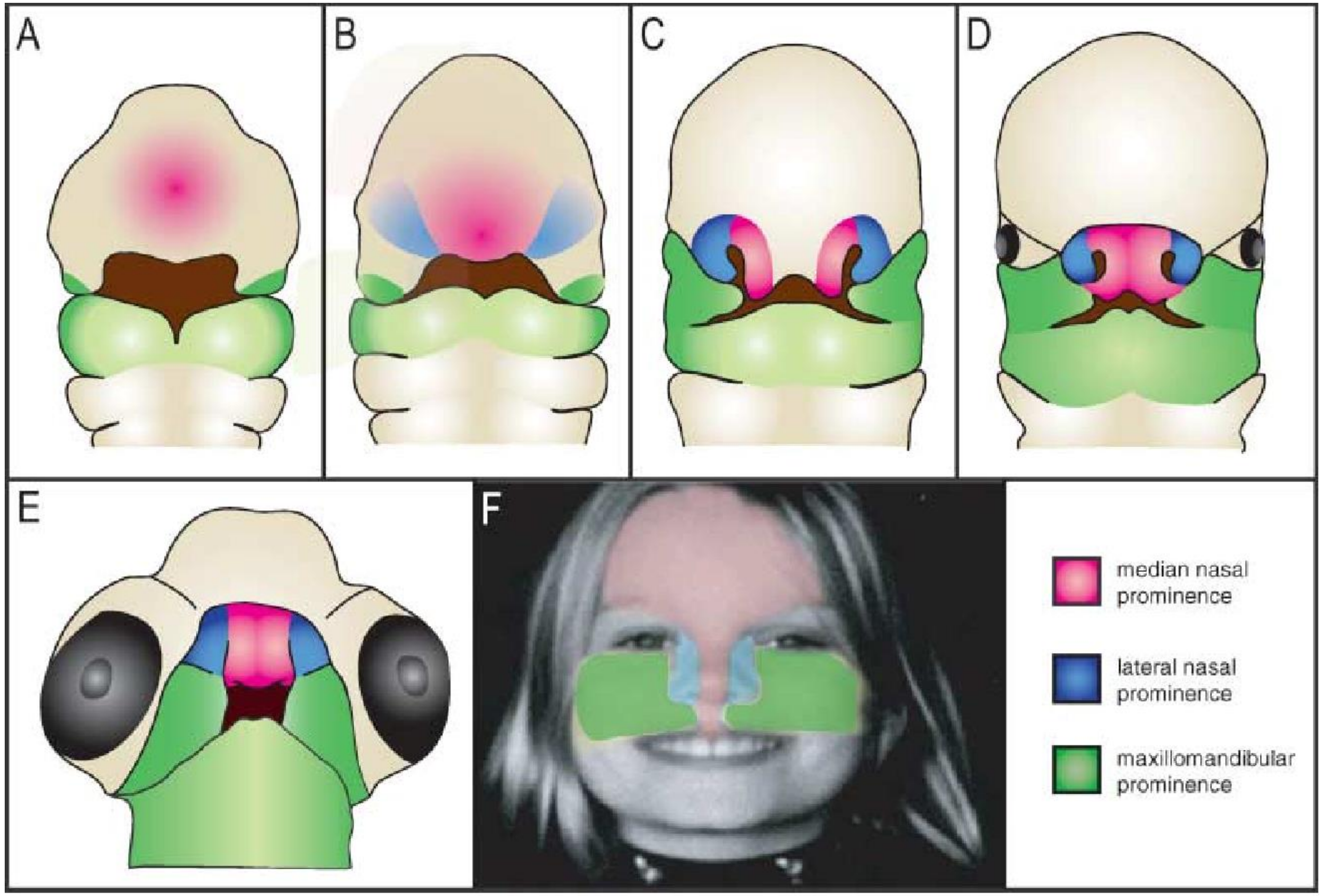
Beginning of 6th week: fusion of medial edges of maxillary prominences with intermaxillary segment: **common upper lip**

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

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

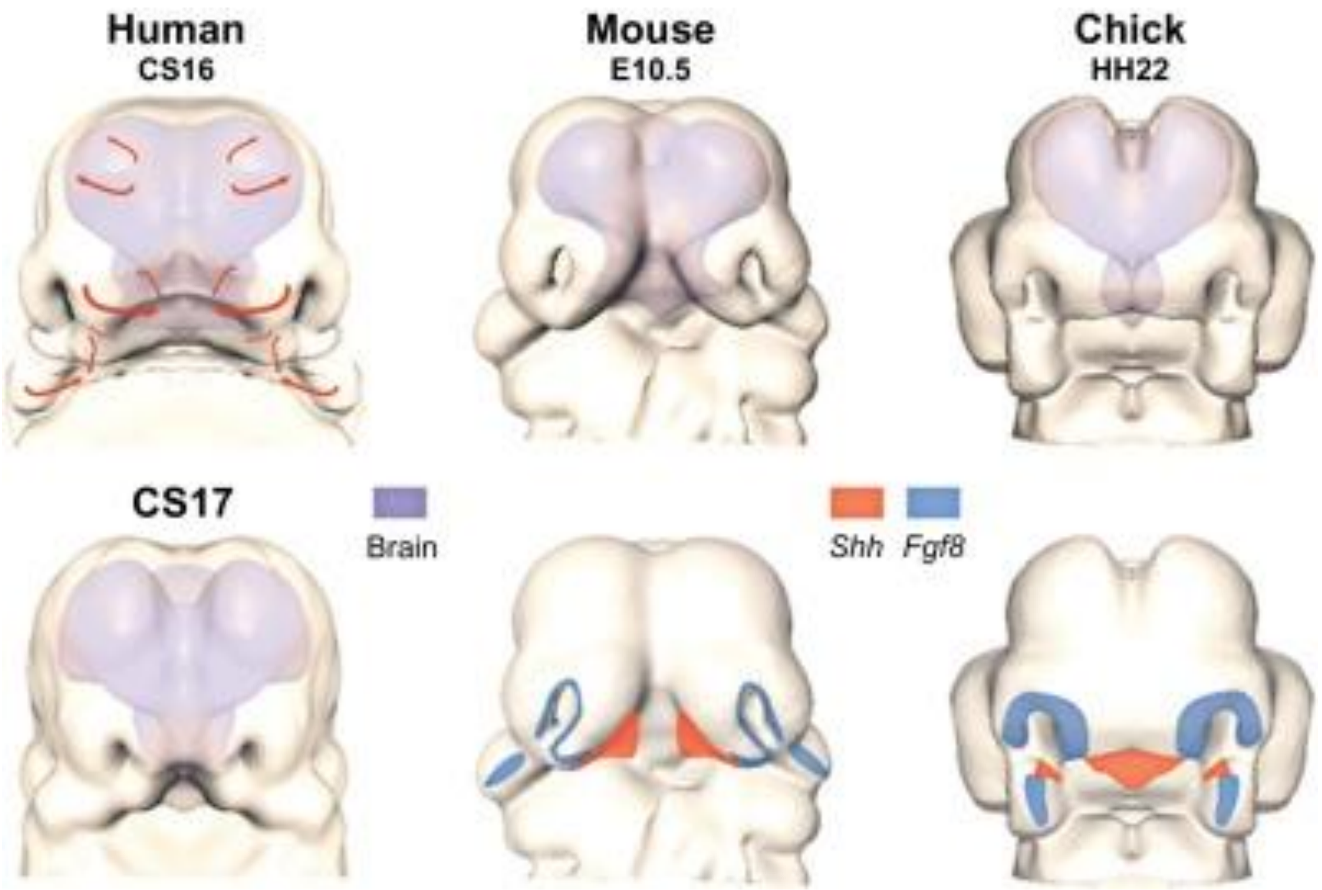


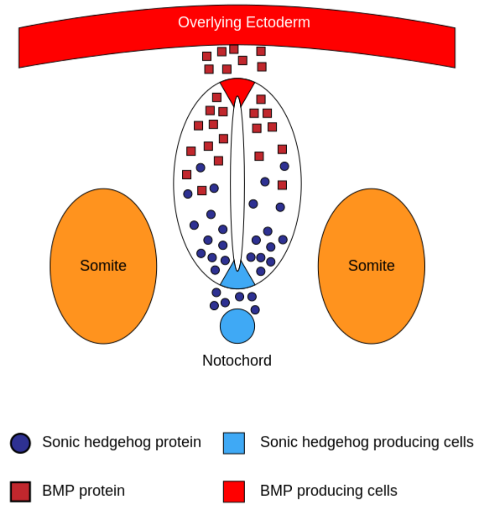
Face development



Shh a FGF

Face development – Shh (Sonic Hedgehog)





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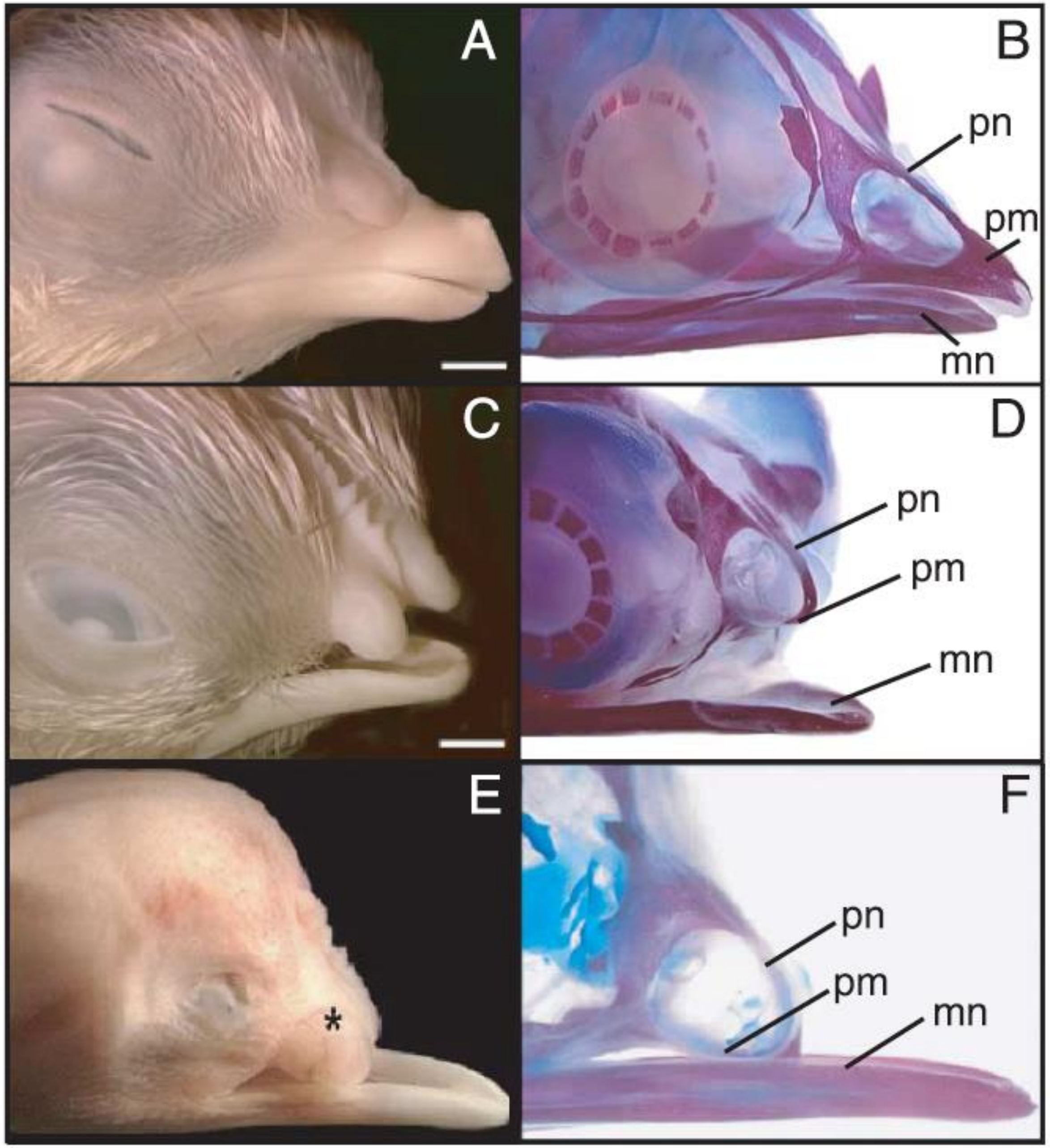
Face development



Normal

Cyclopamine (teratogen)

anti-SHH Ab

Orofacial clefts

When the processes fuse, the basis of the brain, in particular the telencephalon, grows rapidly and so does the neurocranium

The originally laterally oriented eyes shift forward.

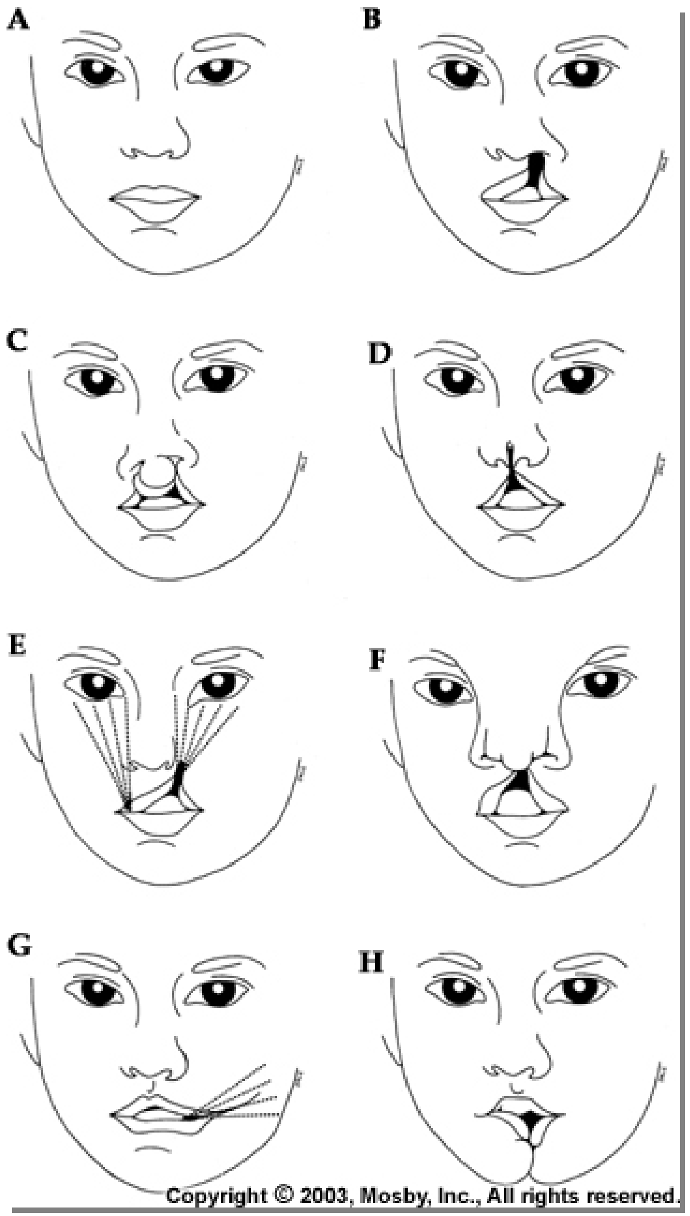
By the end of the second month, the embryo's face already shows characteristic human features

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 developmental 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



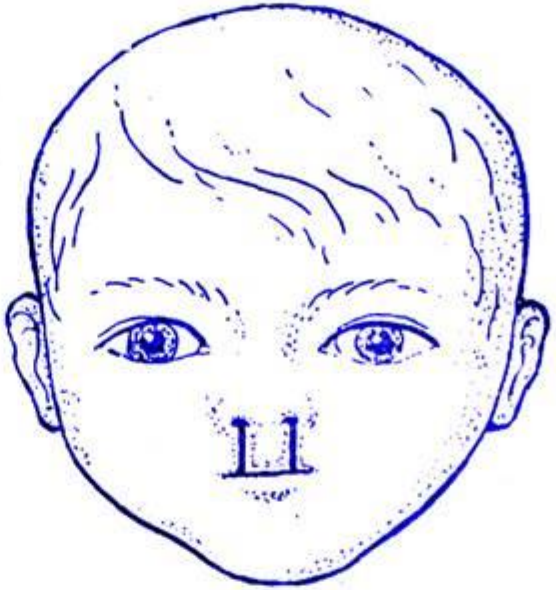
<u>Clefts of the upper lip</u> - cheiloschisis superior

Lateral or medial

<u>Lateral:</u>

- **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

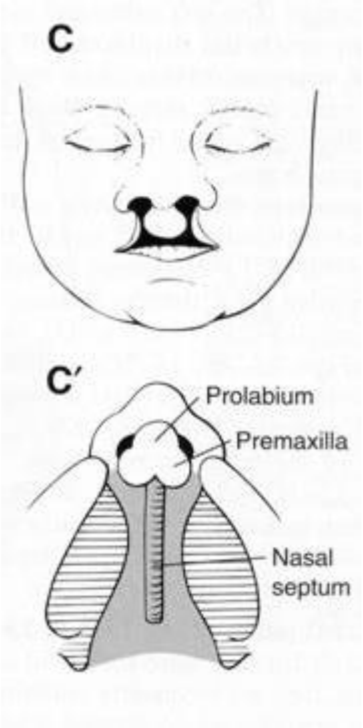


(Bi)lateral clefts of the lip and palate

Bilateral clefts of the lip and maxilla are very hard defect

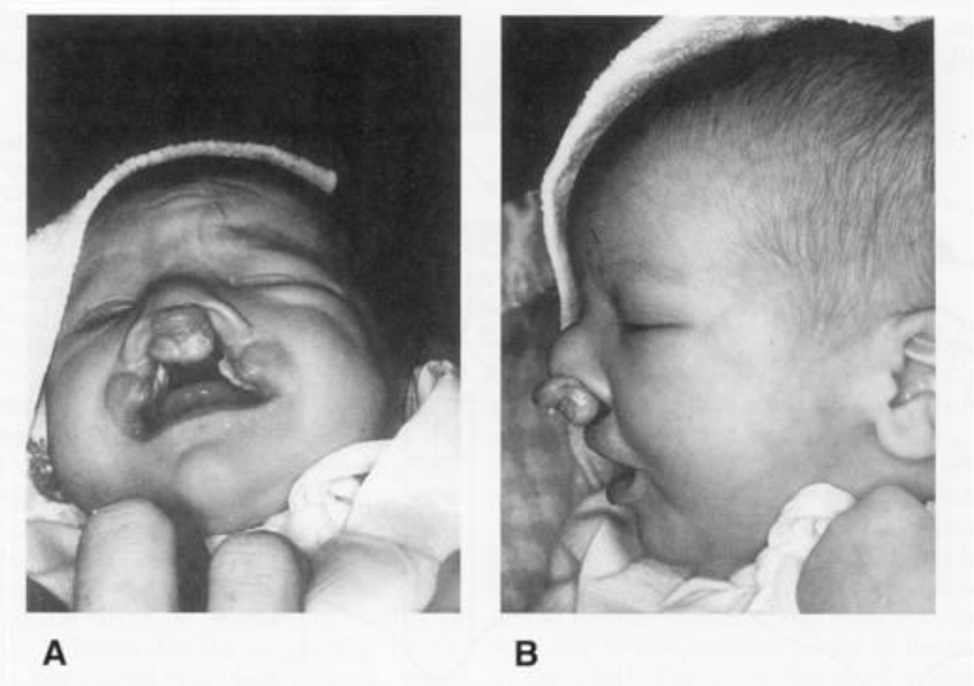
Clefts can be uni and bilateral

The child can not be fed and is in danger of aspiration of food



Unilateral cleft lip.

Bilateral cleft lip.



Median cleft lip – cheiloschisis mediana

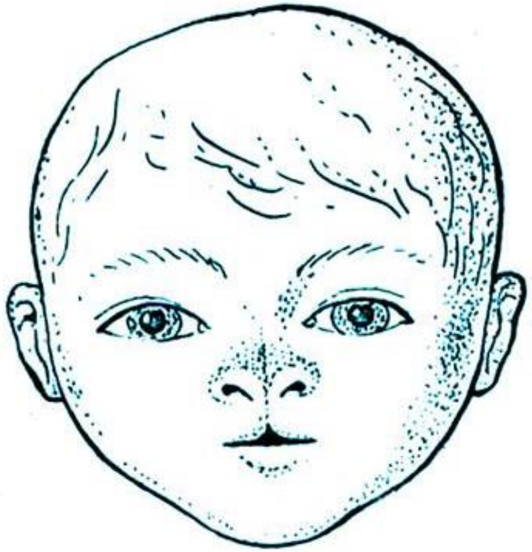
Is caused by delay in development of intermaxillary segment due failure of the medial nasal prominences (processus nasales mediales) to merge

Delay in the development of the intermaxillary segment

Rarely with the cleft of apex nasi
Variable extent
Isolated or in combination with facial skeletal clefts

Critical period: 27. - 35. day

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

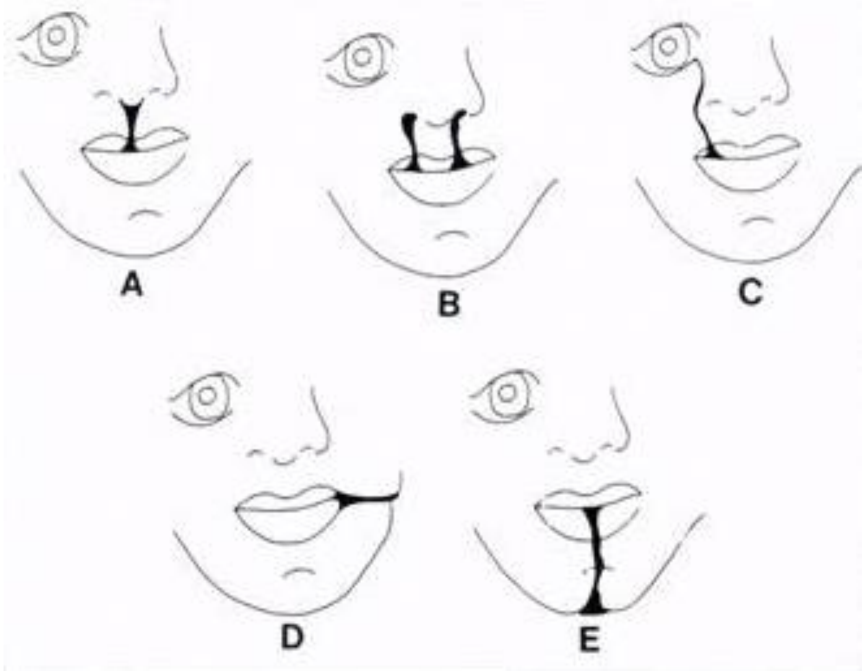


Oblique facial cleft
(coloboma faciale, fissura orbitofacialis)

The processus maxillaris is not fused with the processus nasalis medialis (intermaxillary segment) and the processus nasalis lateralis
Oculonasal groove is preserved

Uni- or bilateral

Rare incidence

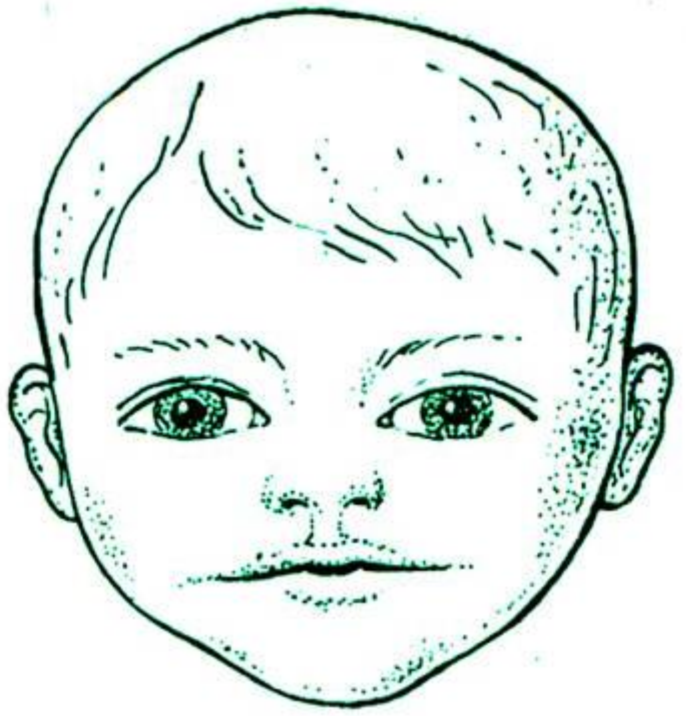


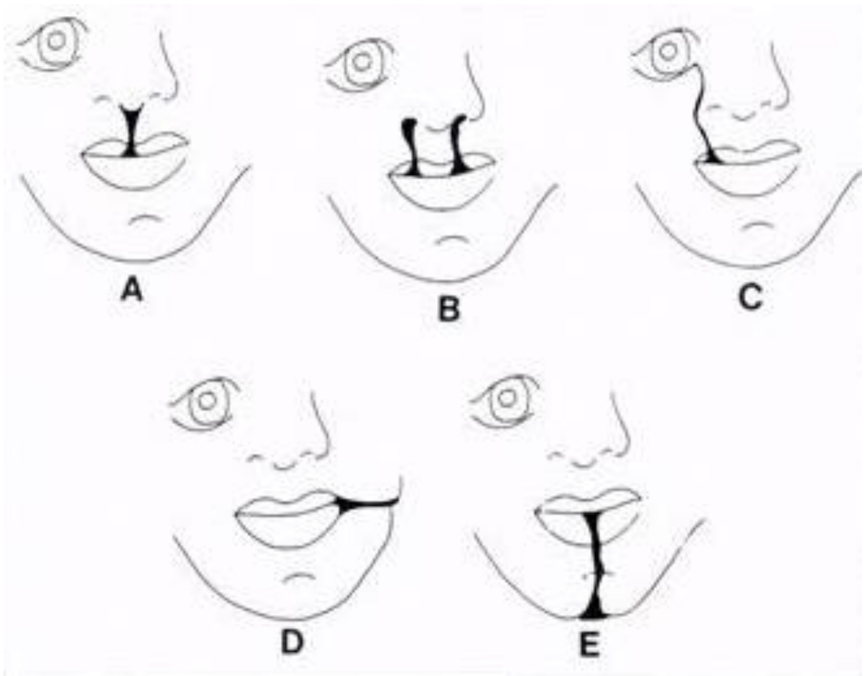
Lateral/transverse facial cleft
fissura transversa faciei, macrostomia

Runs from the mouth toward the ear

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

Rare incidence



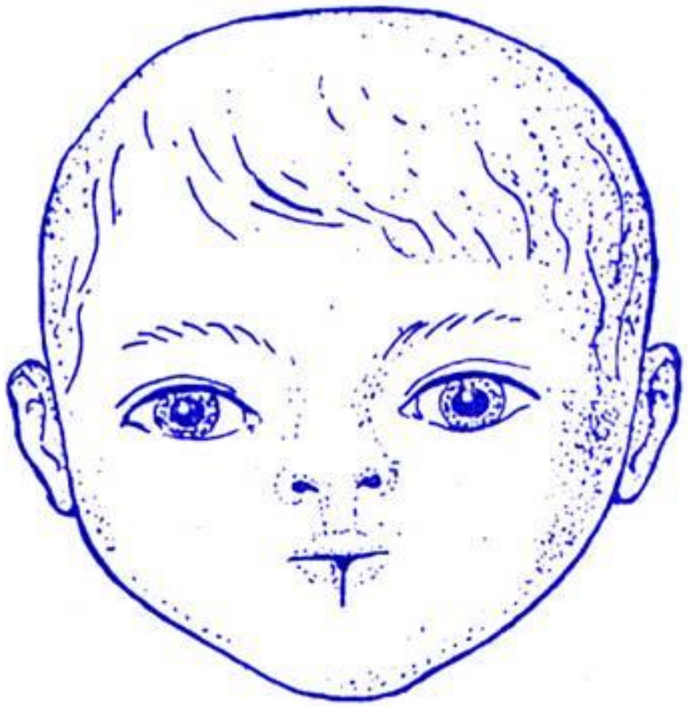


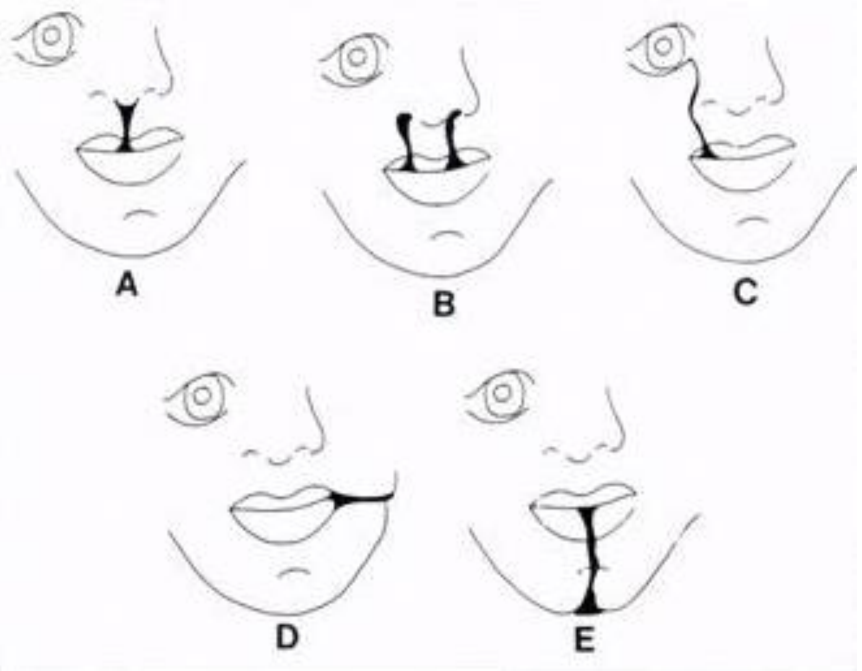
Median cleft of the lower lip and chin (mandible)
cheiloschisis et gnathoschisis inferior

Cleft resulting from failure of the mesenchymal masses of the mandibular prominences to merge completely

Always connected with cleft of the mandible and tongue

Rare incidence



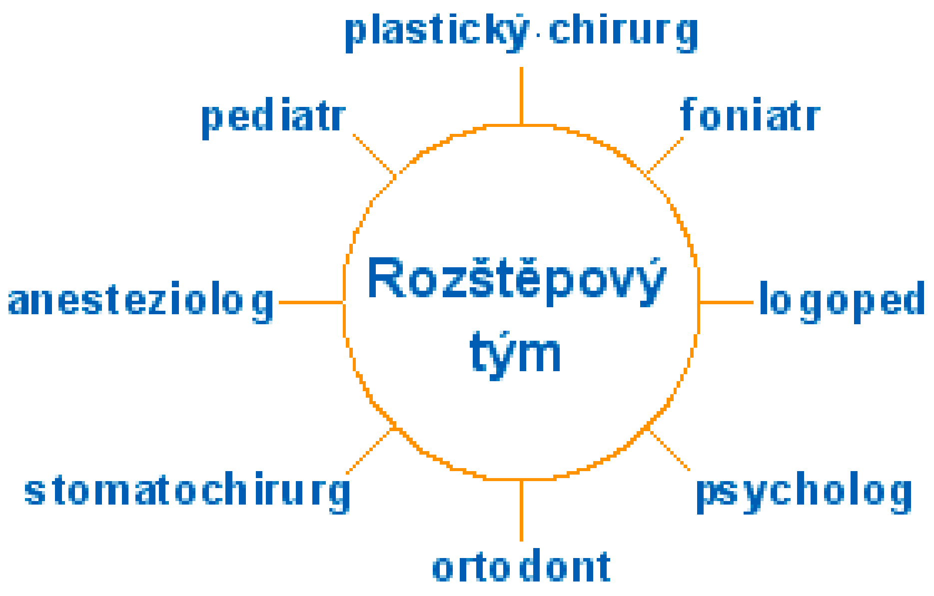


Treatment: a comprehensive approach (cleft teams)

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

Pediatrician's recommendation:

1) plastic surgery examination no later than 2 months after birth
2) for simple cleft lip - cheiloplasty: 2nd - 5th month
3) cleft lip combined with lateral cleft of the jaw and primary palate: treated between 2 and 4 years
4) between 12 - 18 months: phoniatric examination + possibly speech therapist
5) orthodontic care - replacement of missing teeth



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)

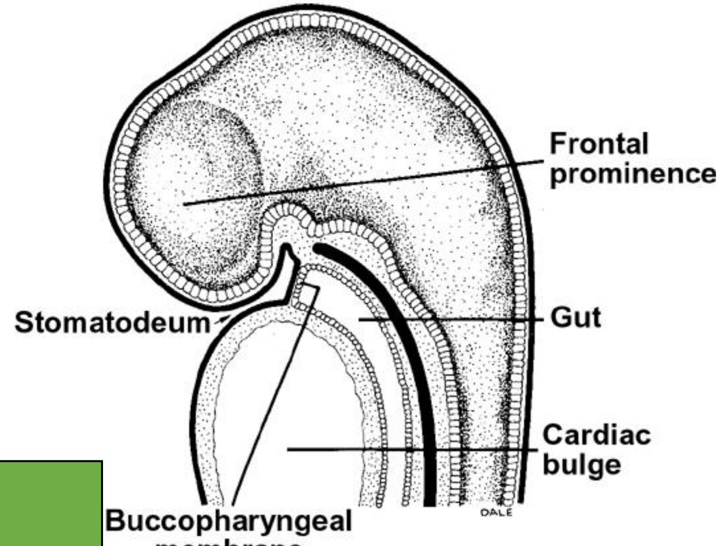
paired mandibular prominences (processus mandibulares) on sides

Stomodeum communicates with the body surface via primitive oral entrance

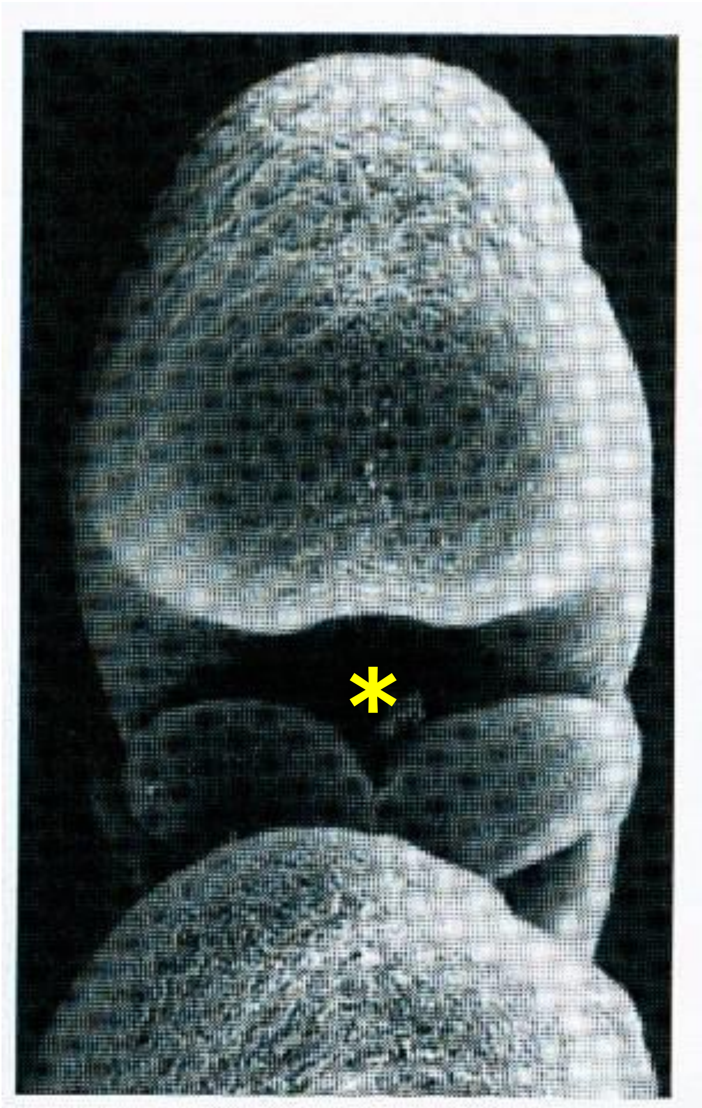
Bottom of the stomodeum - oropharyngeal membrane (membrana oropharyngea)

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

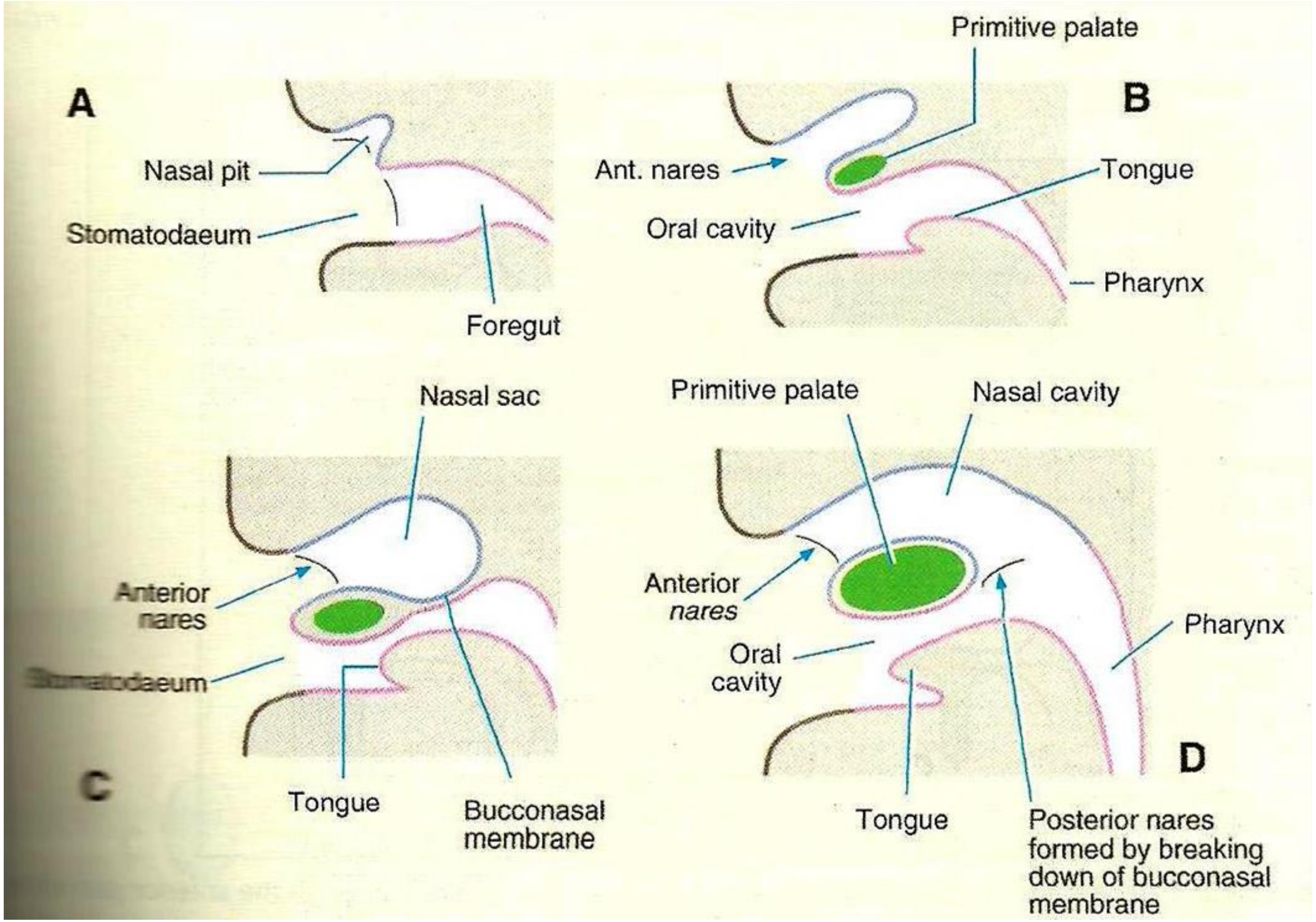
Roof of the stomodeum consists of a mesenchyme and ectoderm of the frontonasal prominence



membrana oropharyngea



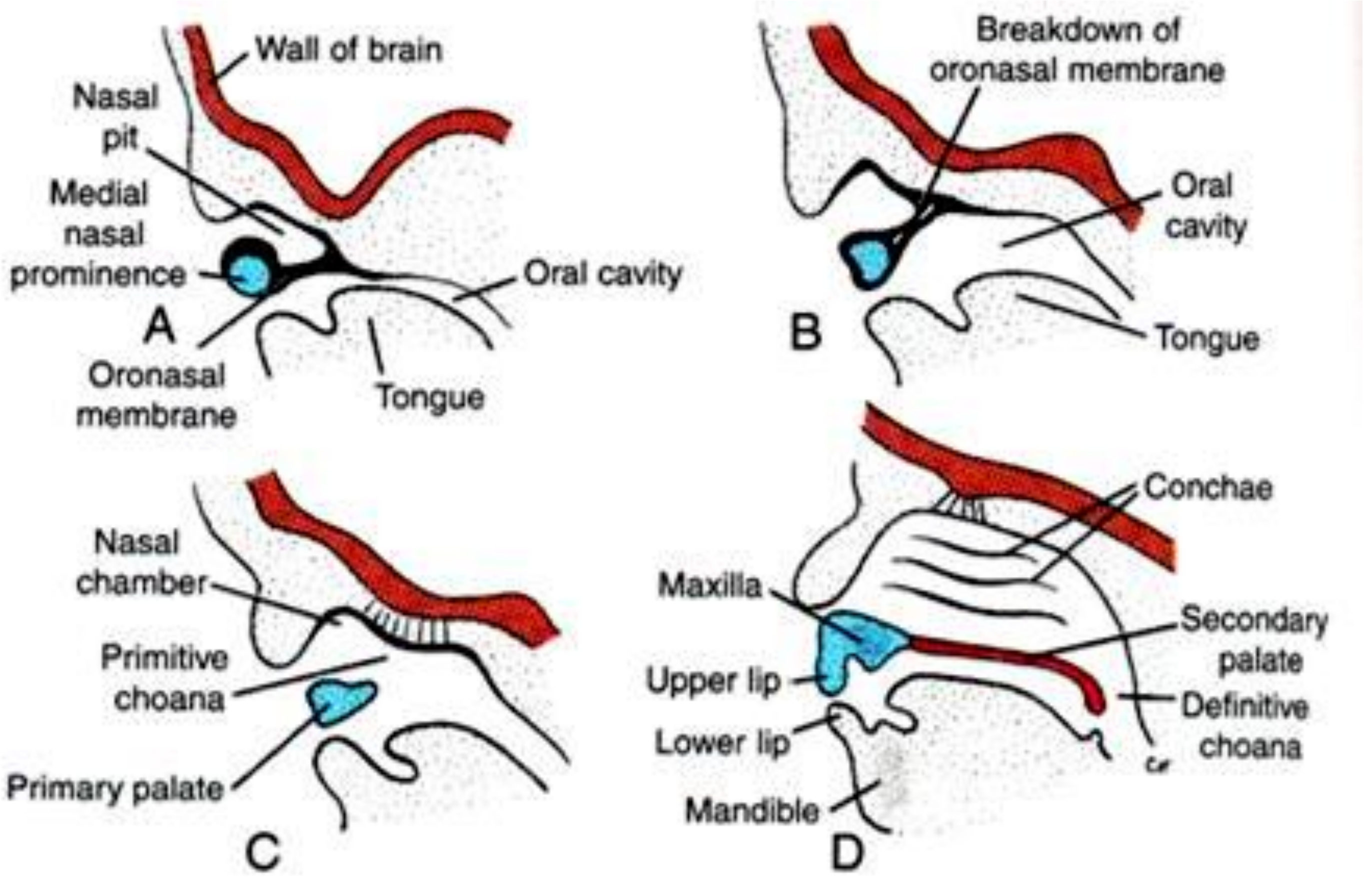
4th week



connection of the nasal passages to the stomodeum

They are separated by a two-layered epithelial septum - the ectoderm of the nasal canal and the ectoderm of the stomodeum **oronasal (bucconasal) membrane**

When the membrane perforates (end of 5 week), the nasal canals open into the stomodeum through an opening - primitive choana



common oral and nasal cavity (oronasal cavity)

approx. 7 days

Palatogenesis

In the middle of the **6th week**, the oronasal cavity begins to split with the horizontal septum into the definitive **nasal cavity and oral cavity**

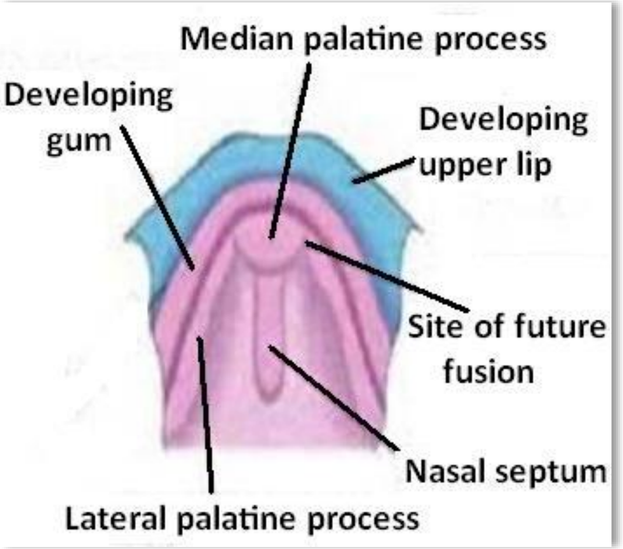
Begins at week 6, ends at about week 12 (the fusion of uvula)

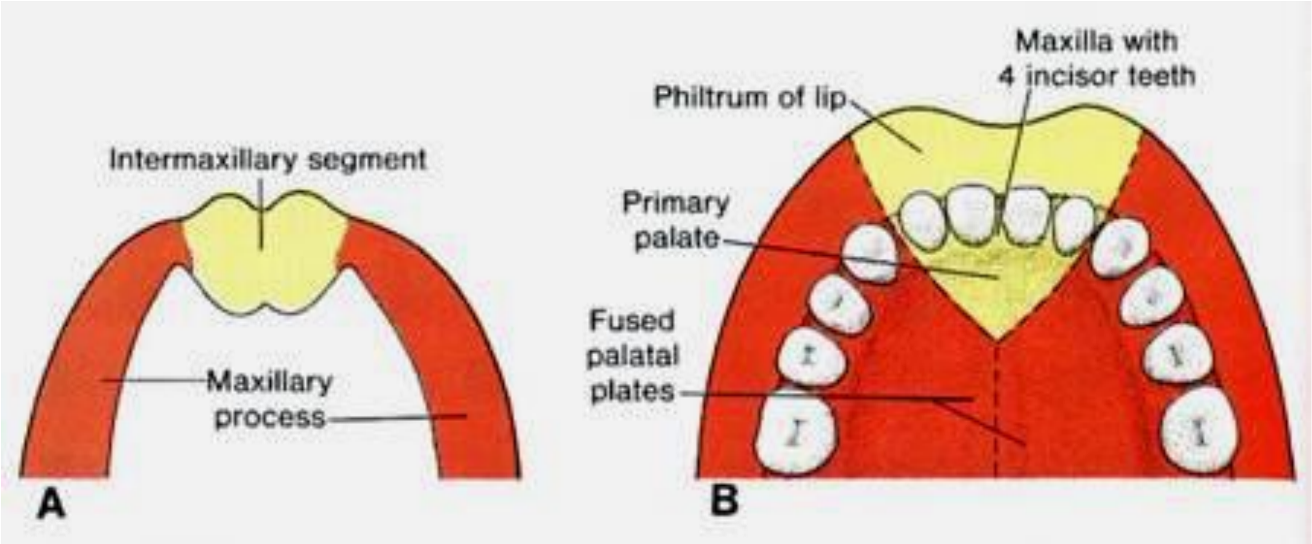
<u>3 primordia:</u>

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

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

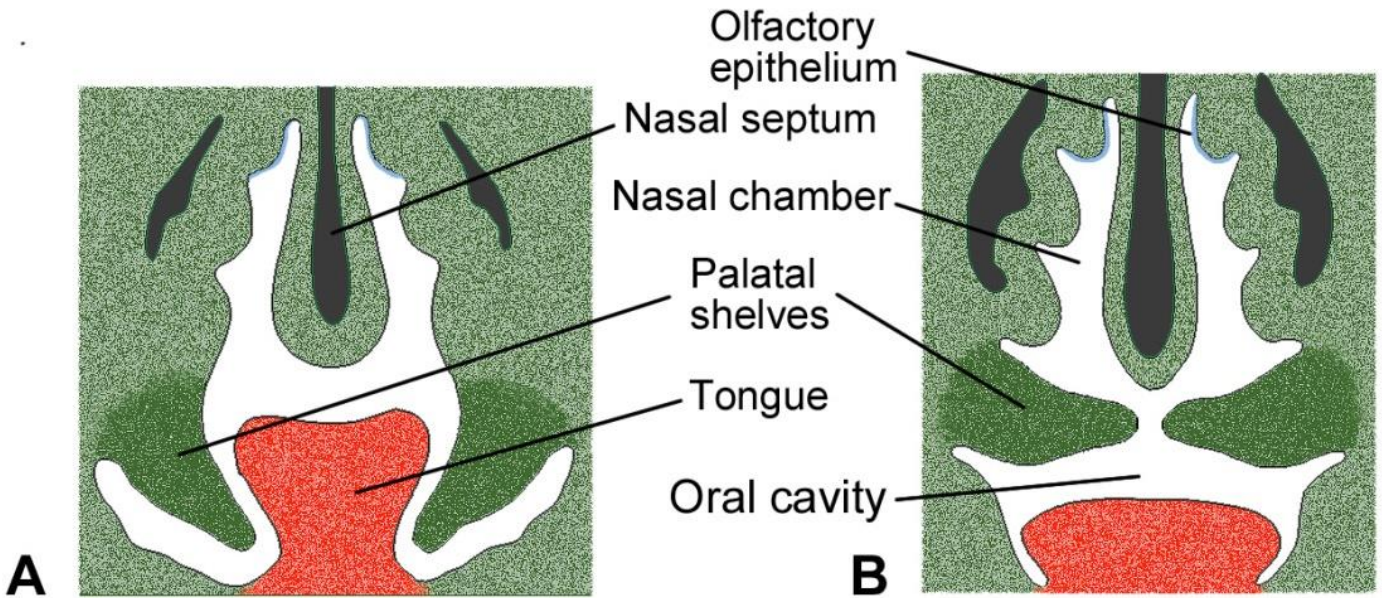
Grows from the dorsal side of the intermaxillary segment at the end of the 5th week and gives rise to primary palate

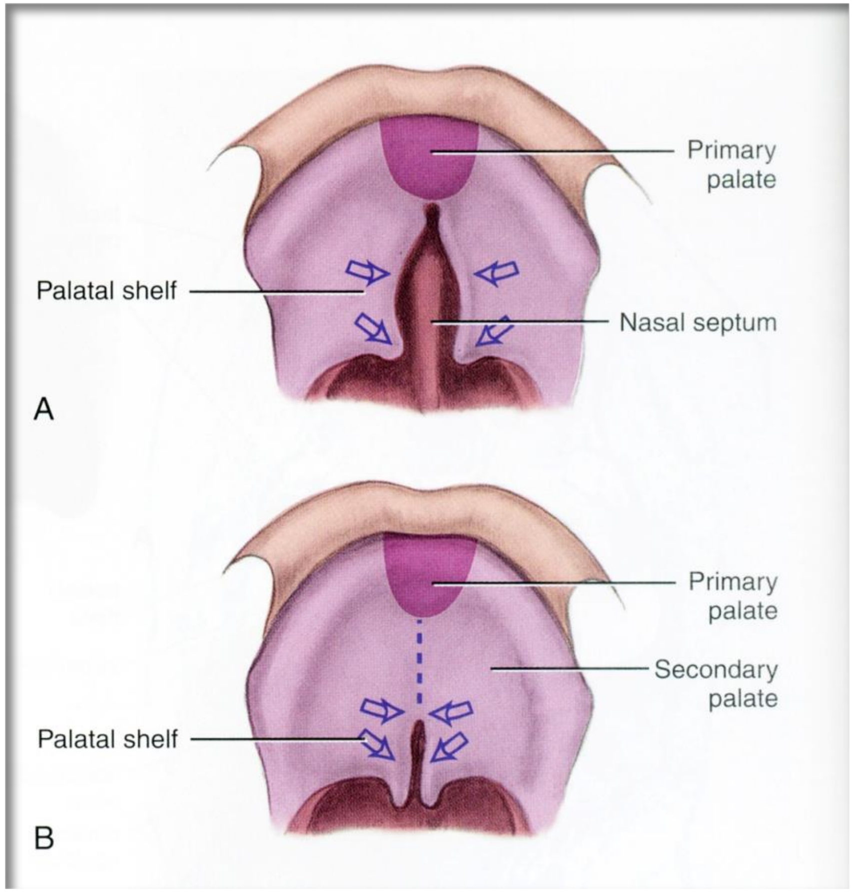




Palatogenesis

b) Lateral palate processes - grow out from medial aspects of the maxillary prominences and give rise to **the secondary palate** (end of 6th week)





The palatal plates initially grow caudally (on the sides of the base of the tongue), at the end of the 7th week they rise to the horizontal position of "horizontalisation of the palatal plates" (caudal descent of the tongue caused by the vertical growth of the mandibular processes), the medial ends of the plates grow opposite each other - **at the beginning of the 8th week they meet anteriorly.**

Palatogenesis

During the 12th week, palatal fusion is completed at the site of the uvula

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

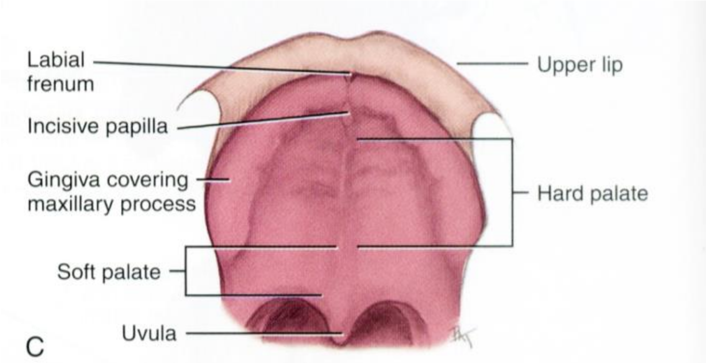
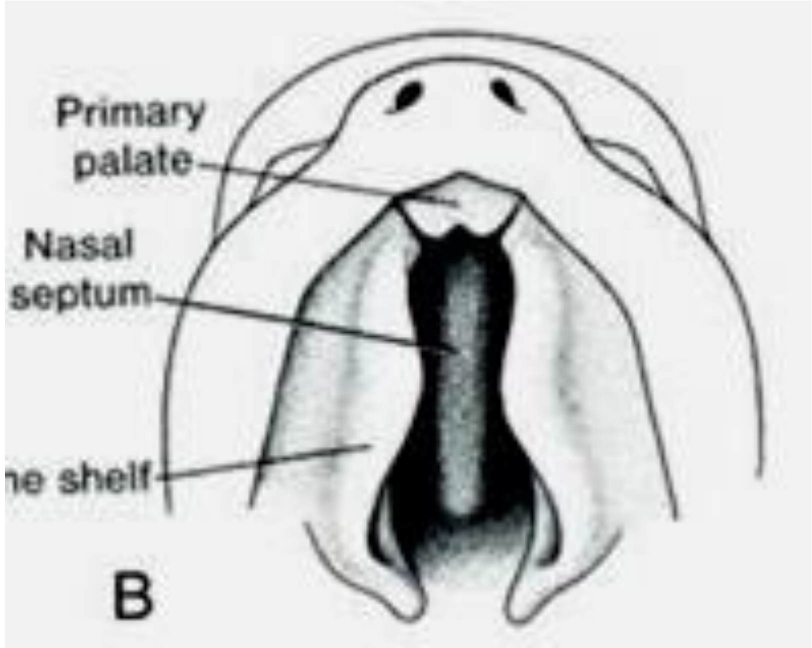
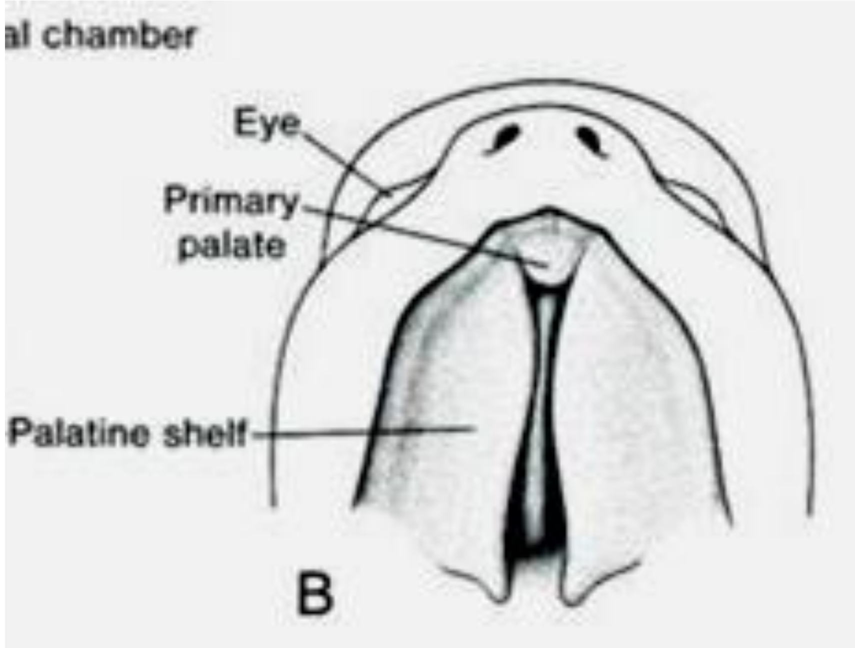
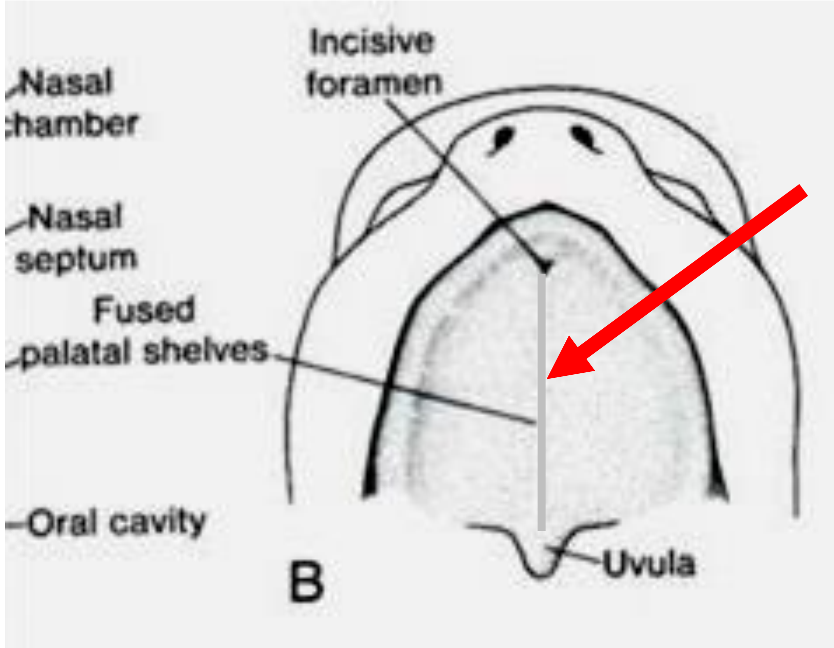


FIGURE 5-10 Later stages of nasal septum development showing its fusion with the final palate (A and B) in order to separate the nasal and oral cavities completely (C).







Palatogenesis

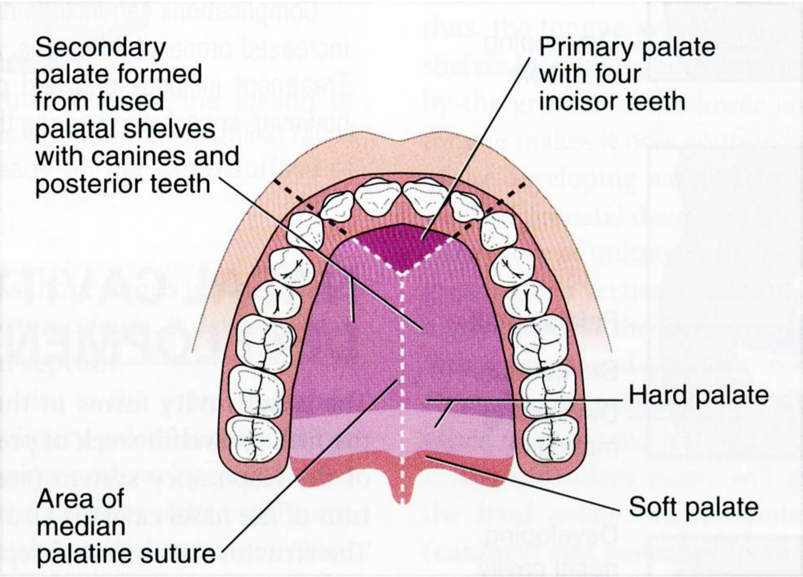
At the same time, the anterior edges of the lateral palatal plates fuse with the unpaired medial plate - single palate

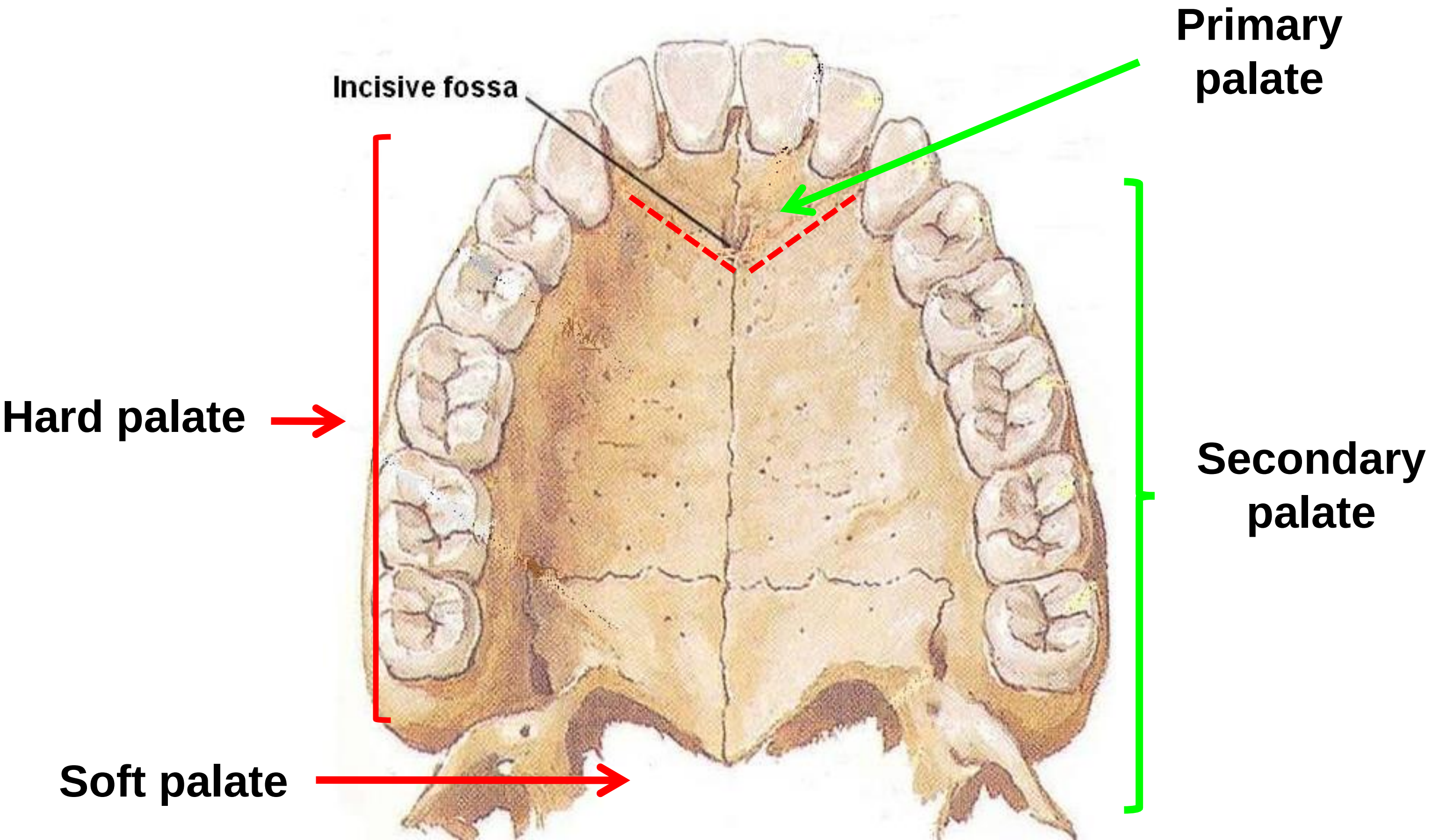
Foramen incisivum opens in the line of growth of all three parts

The mesenchyme of the primary palate and the secondary palate (except for a short dorsal section) then ossify (intramembranous) and the palate is differentiated into:

Hard palate - palatum durum

Soft palate - palatum molle and uvula





Palate clefts

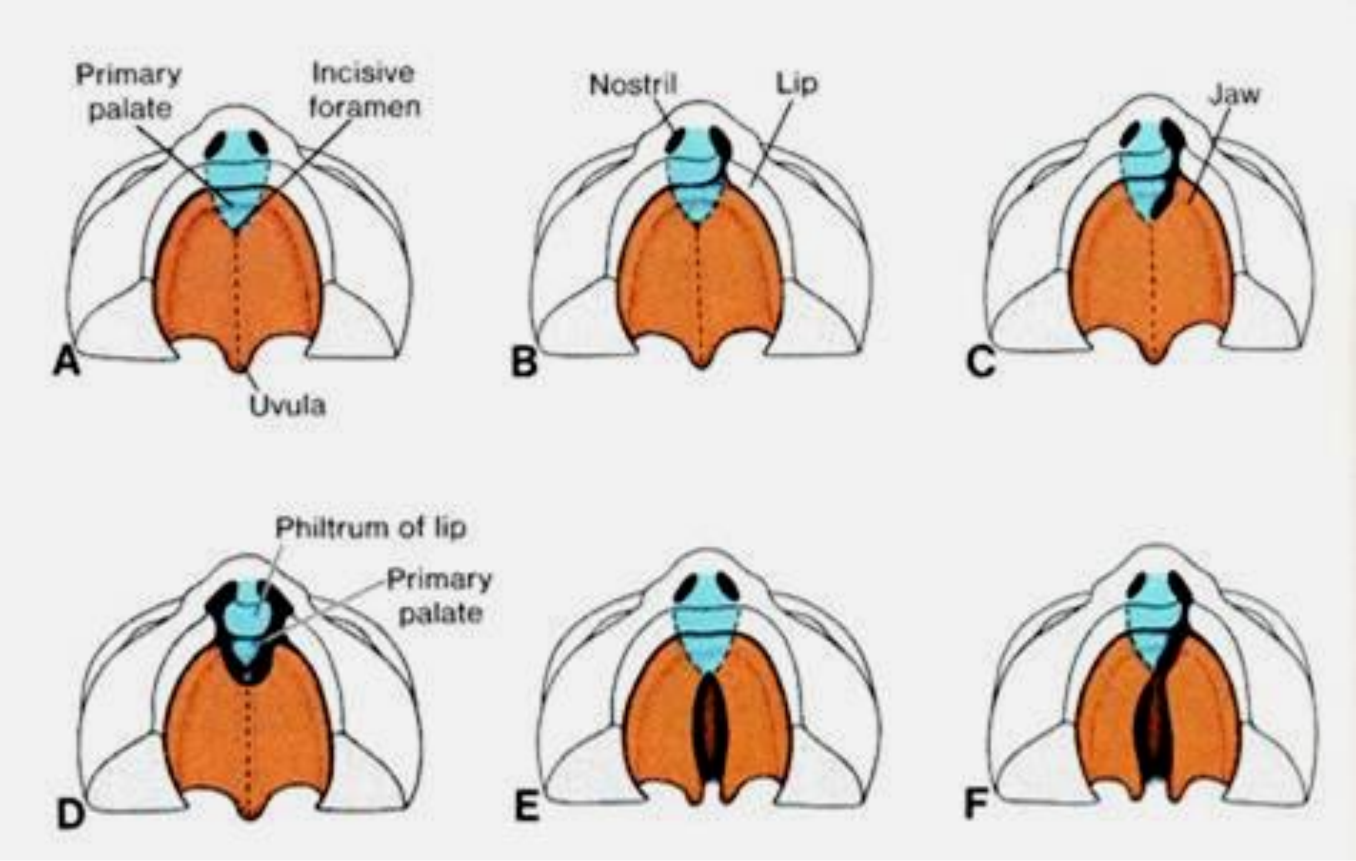
Can be of isolated character or associated with clefts of the and upper lip

Complete or incomplete

unilateral or bilateral

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

1/5 genetic background



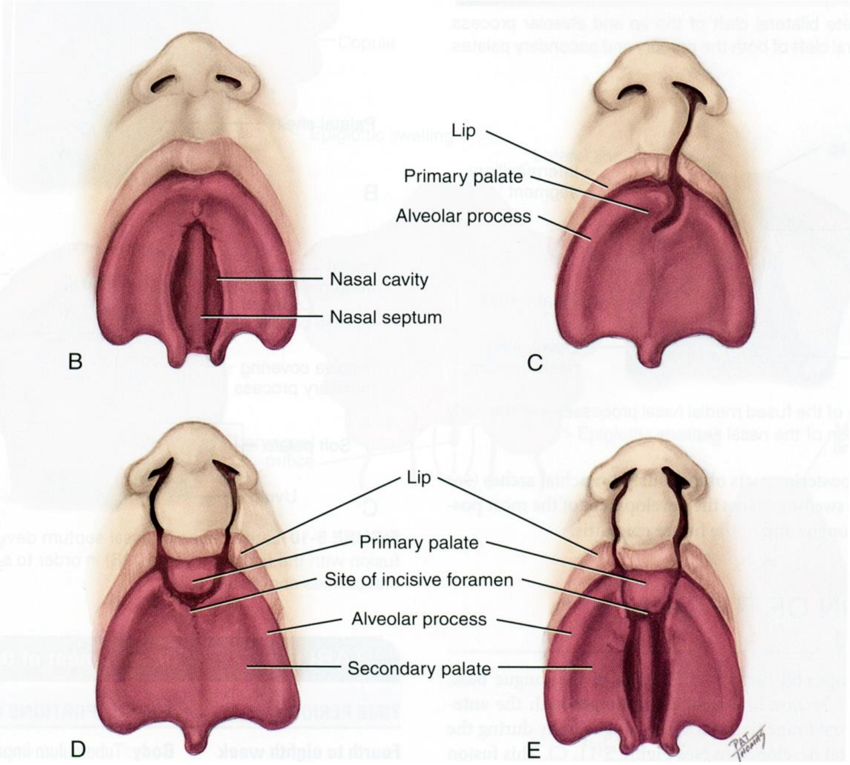
Clefts of primary palate (C, D)

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



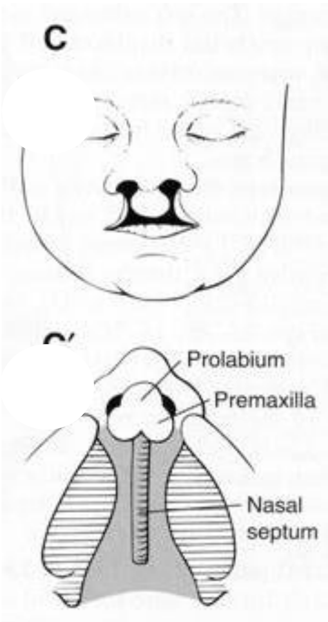
Clefts of both primary and secondary palates (E)

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

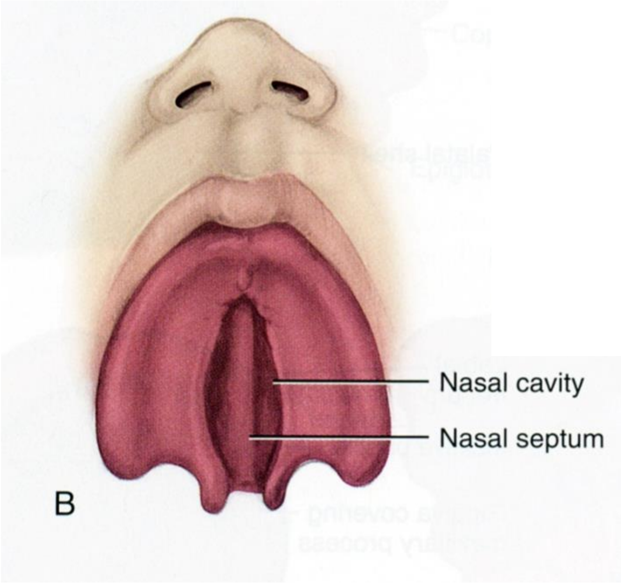
Cause: lateral palatine processes do not fuse

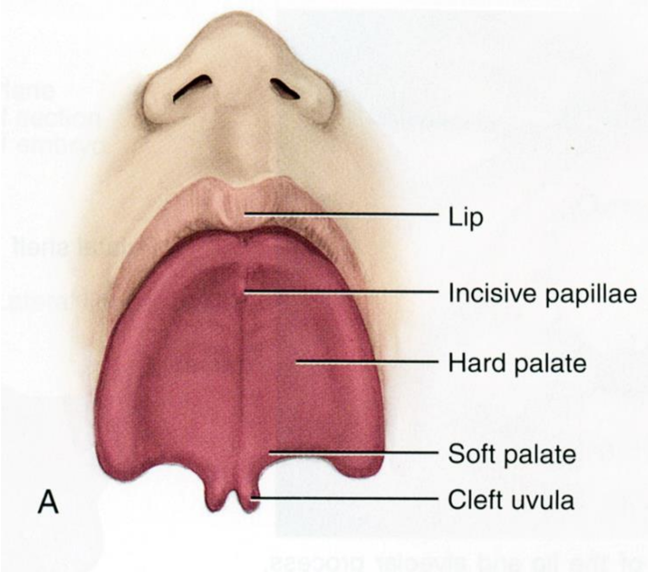
Affect the all sections of palate (hard, soft and uvula - staphyloschisis / uvula bifida)

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)

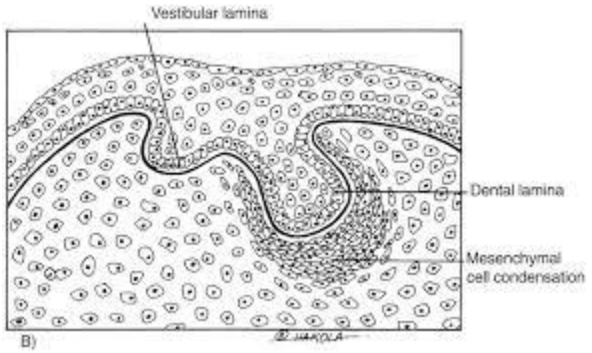
Emerges during the **6th week**

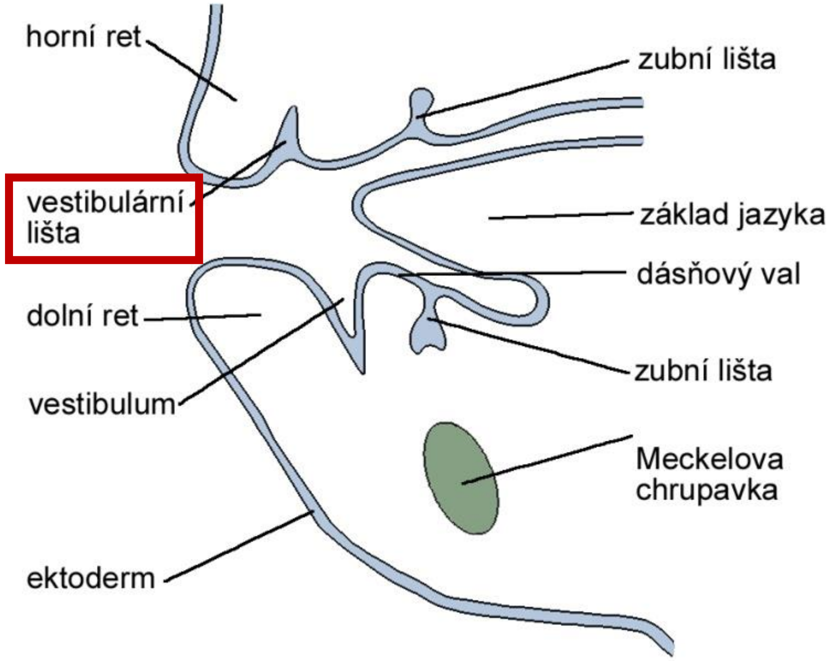
Thickened area of the ectoderm, fast proliferation of ectoderm against mesenchymal core of prominences that delineate the stomodeum

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

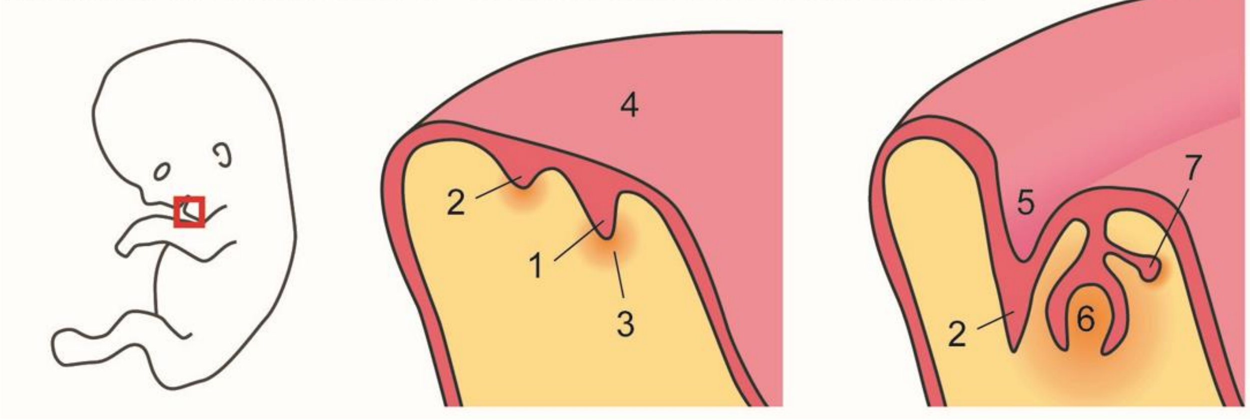
Ventral section - the definitive lip

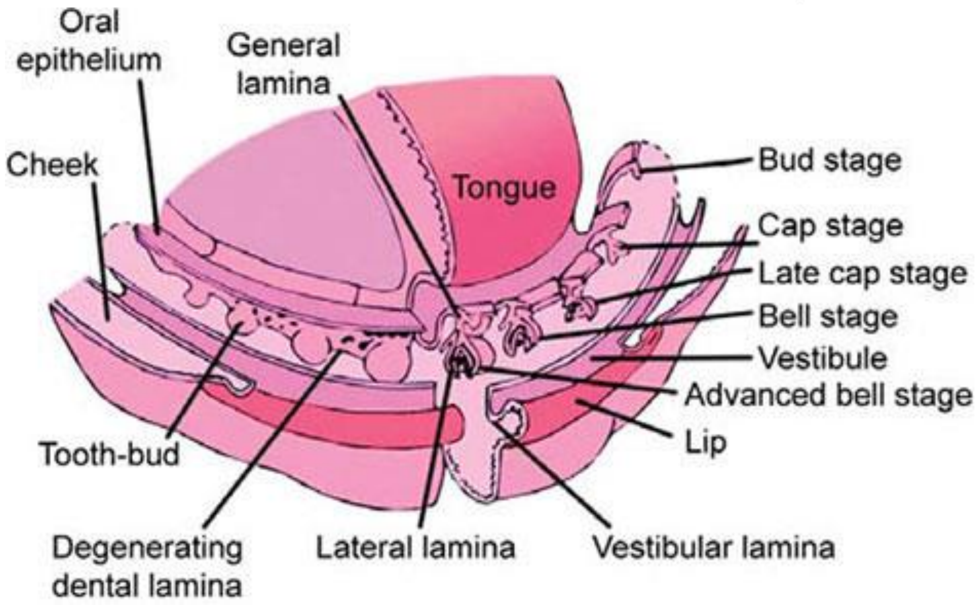
Dorsal section - the gingival ridge (torus)





Vývoj dentální a vestibulární laminy – Dental and vestibular lamina development





Development of maxilla and mandible

Maxilla

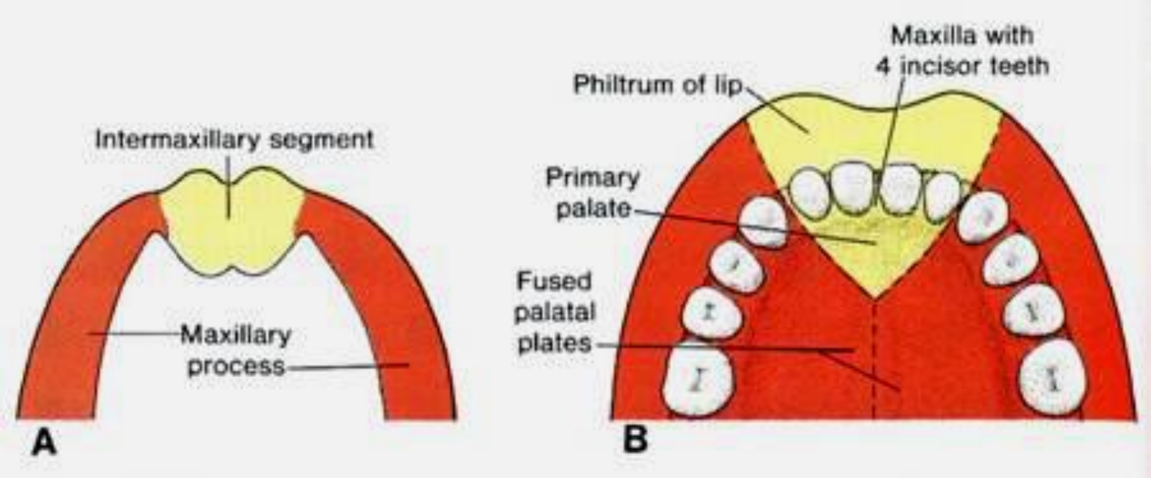
Paired bone, intramembranous ossification

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

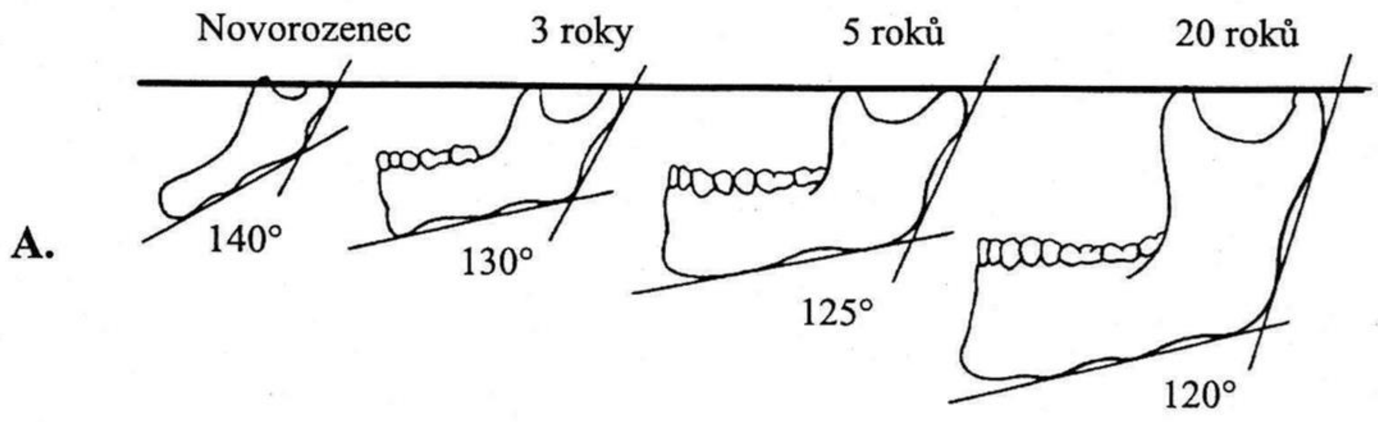
Body of mandible and both ramus of mandible are of intramembranous origin (for ossification is used mesenchyme located anterolateral to the Meckel cartilage that support the mandibular prominences

Ossification begins in the 6th week.

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

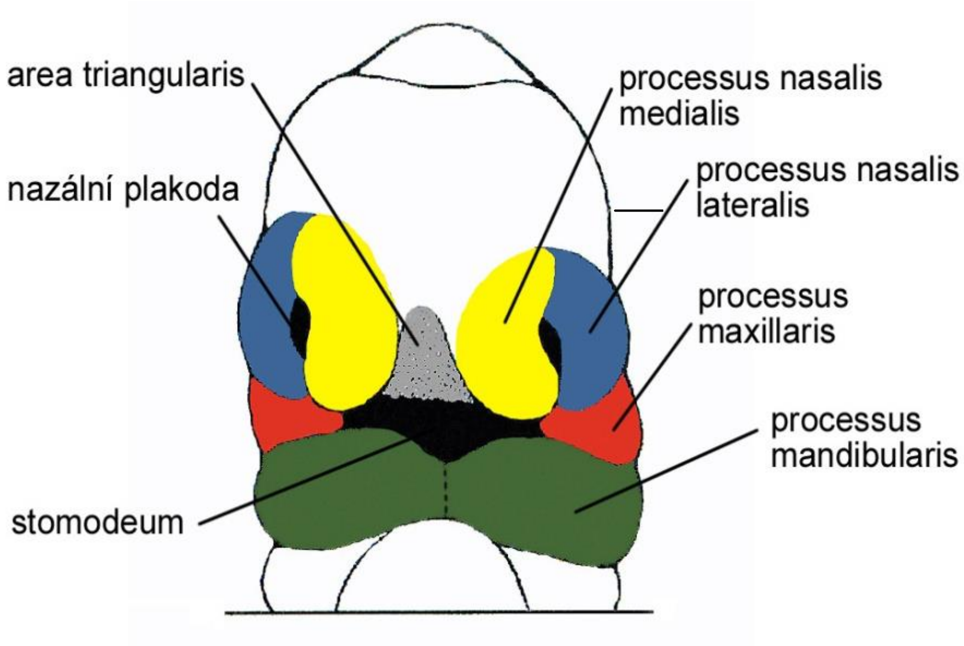
Lower jaw of neonates is low and its development continues in postnatal period

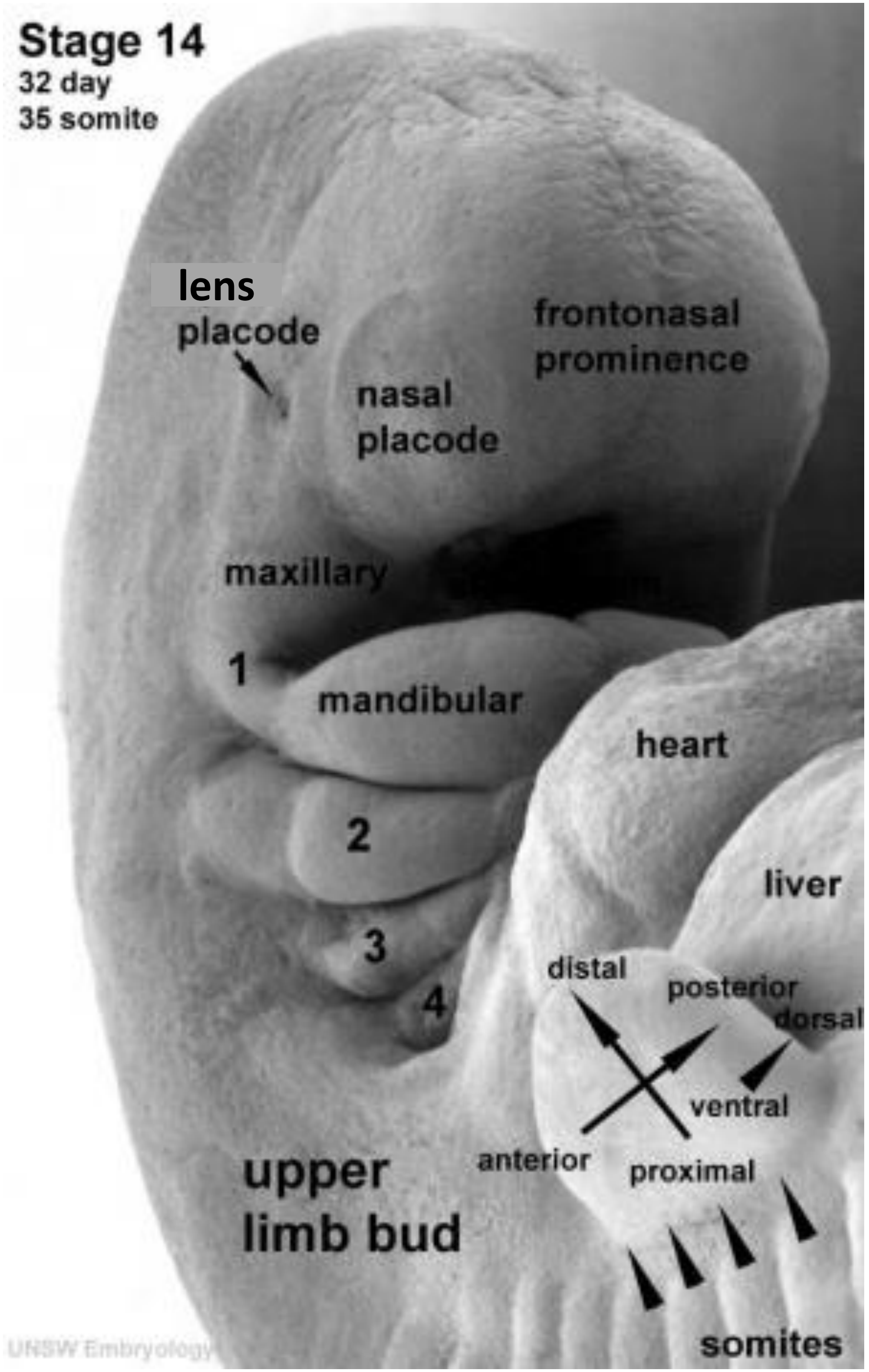
The angle between ramus and body of mandible continual reduces (from 140-150 to 120 for adult)



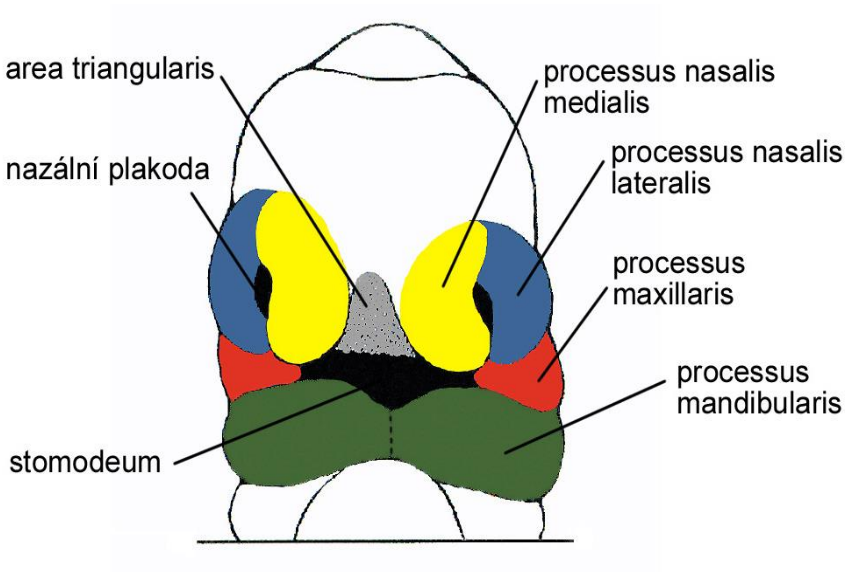
Nasal cavity

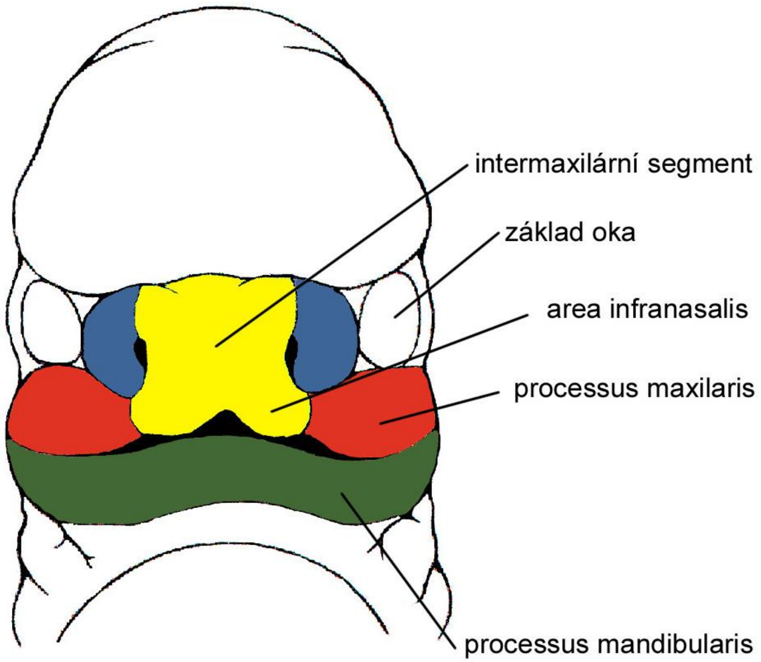
Nosal placodes → Nasal pits → Nasal sacs, grows dorsocaudally to roof of stomodeum, from which are initially separated by the oronasal membrane

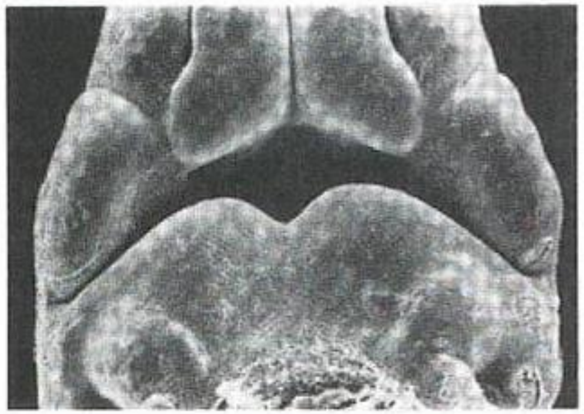




Nose development







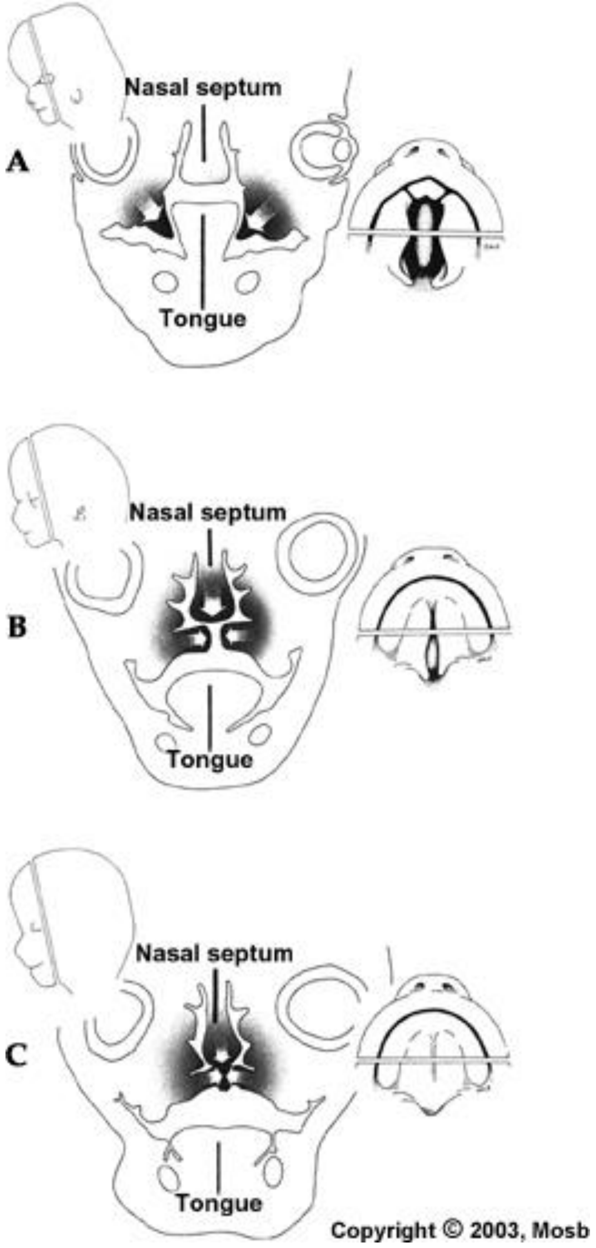
Early 7th week

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**

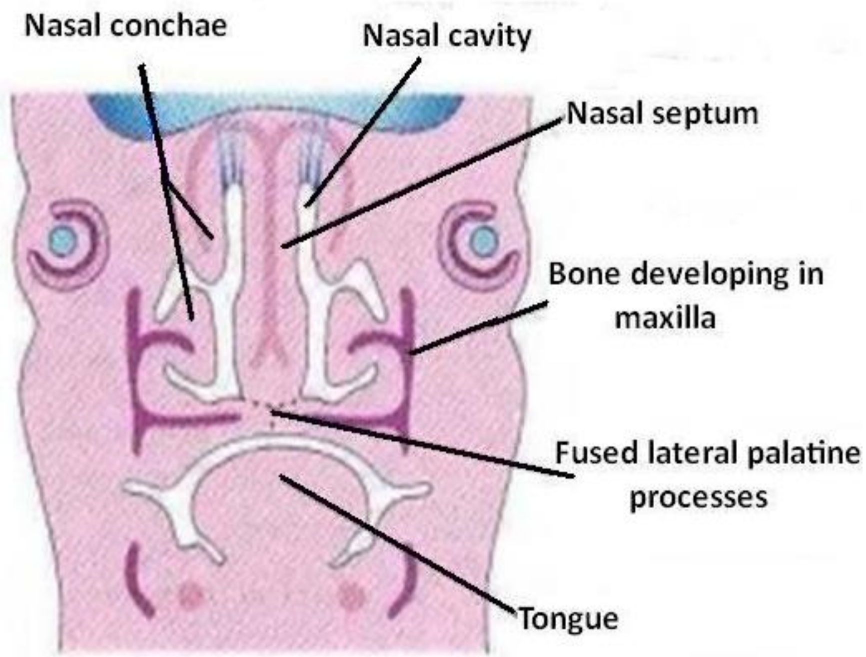
Vývoj nosu a nosních dutin



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

The ventrocranial and dorsocaudal section of the septum intramembraneusly ossifies - giving rise to the lamina mediana ossis ethmoidis and vomer, the remaining part forms the cartilaginous part of the septum.

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



Vývoj nosu a nosních dutin

After the 13th week, the ectoderm of nasal cavity differentiates into olfactory epithelium

Between 13 and 15 weeks, the nostrils are closed by epithelial plugs

Opening (recanalization) occurs in the 6th month

Paranasal sinuses (sinus paranasales) are the last to form (at the end of the fetal period) - they are the protuberances of the definitive wall of the nasal cavity:
- sinus maxilaris - already present at birth
- sinus ethmoidalis - around the 2nd year
- sinus frontalis and sphenoidalis - between 4 and 6 years

The epithelium of the nasal cavity and sinus epithelium is of ectodermal origin

Developmental defects of the nose

Defects are of rare occurrence

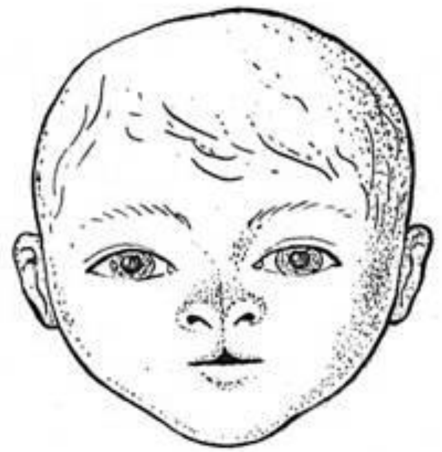
Occur separated or in association with anomalies of the upper lip and jaw or whole face

***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**

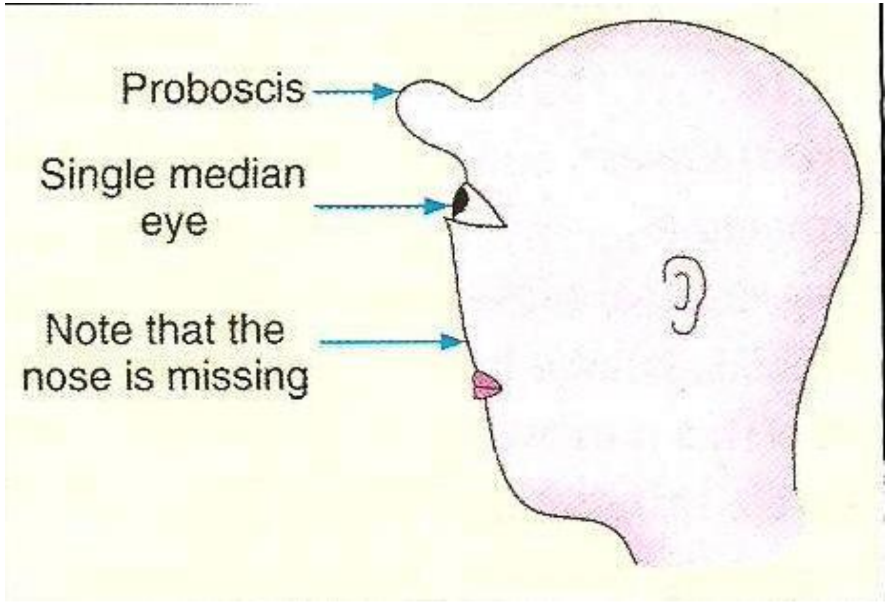


Figura 3. Foto del recién nacido. Se observa ojo único central, con probóscide, confirmando la etmocefalia.

Veratrum californicum

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