Vznik obličejových rozštěpů a jejich klasifikace

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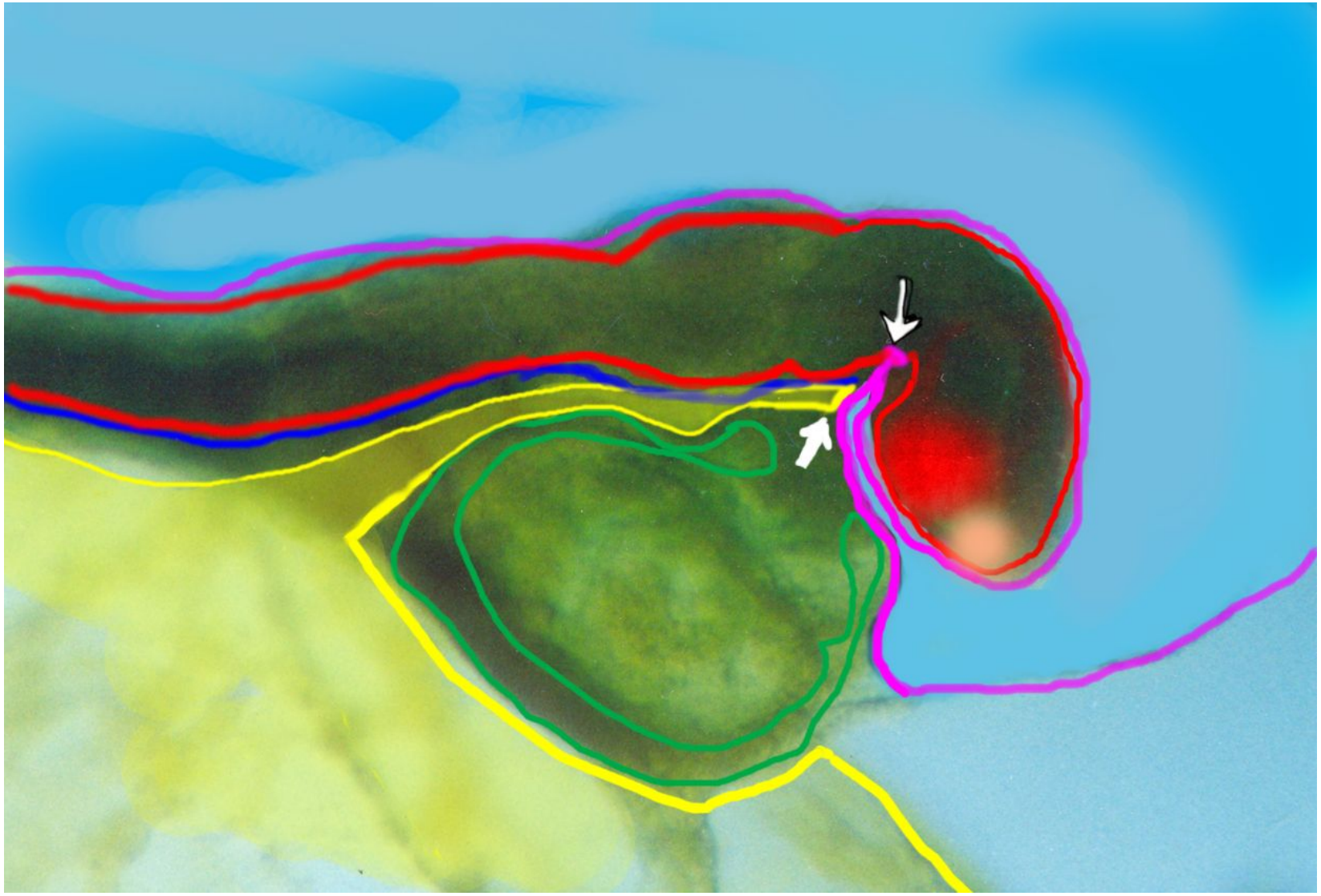
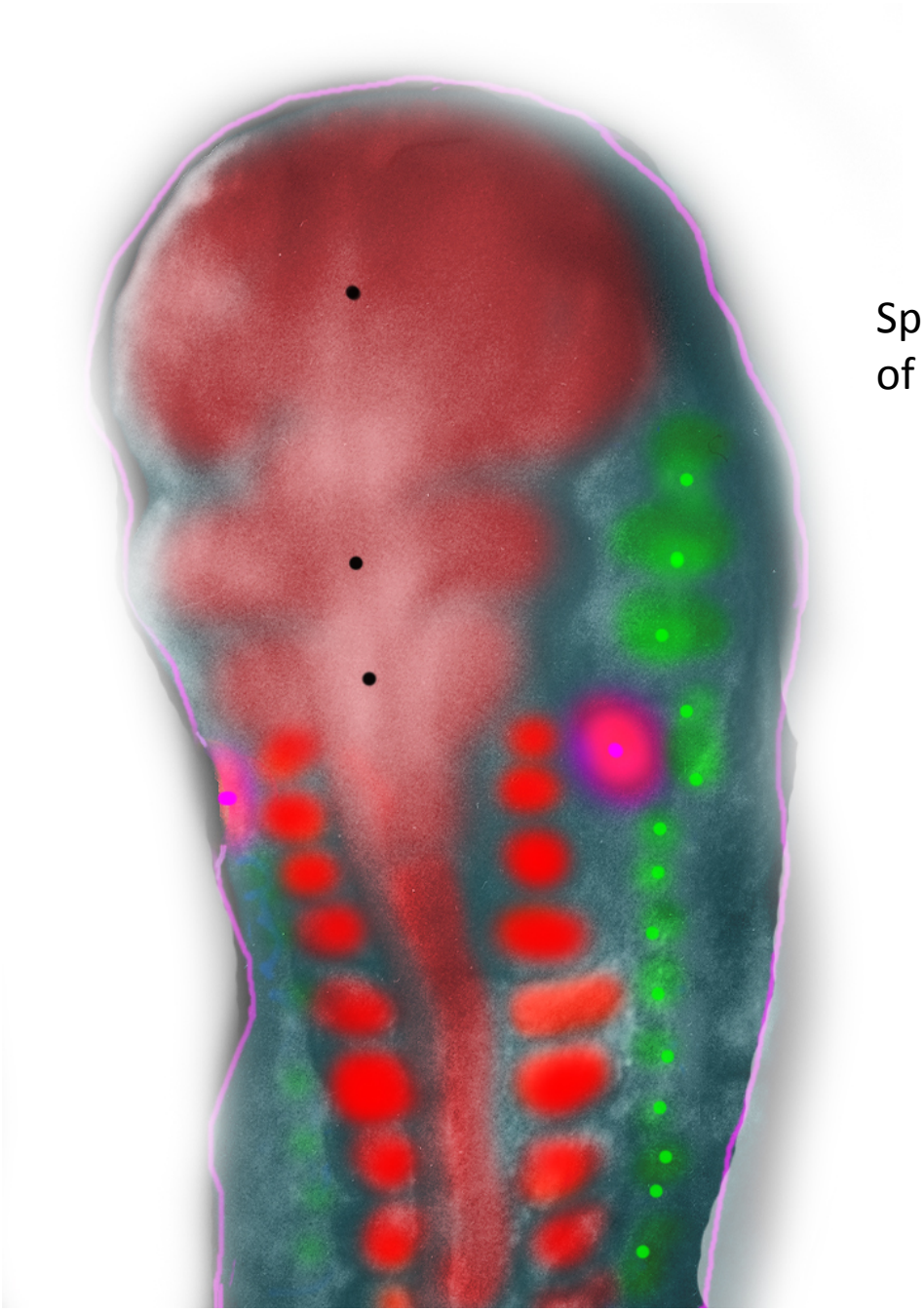
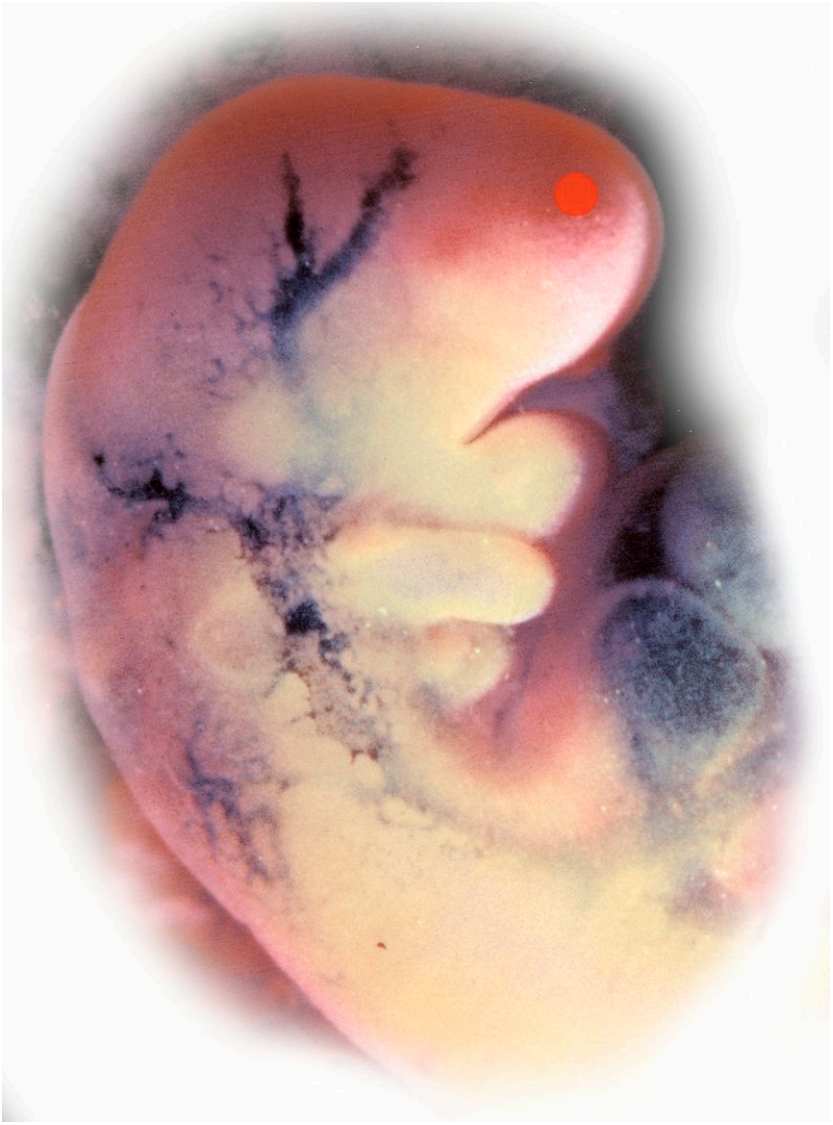
Ústav pro péči o matku a dítě, Praha - Podolí

Morfogenesis

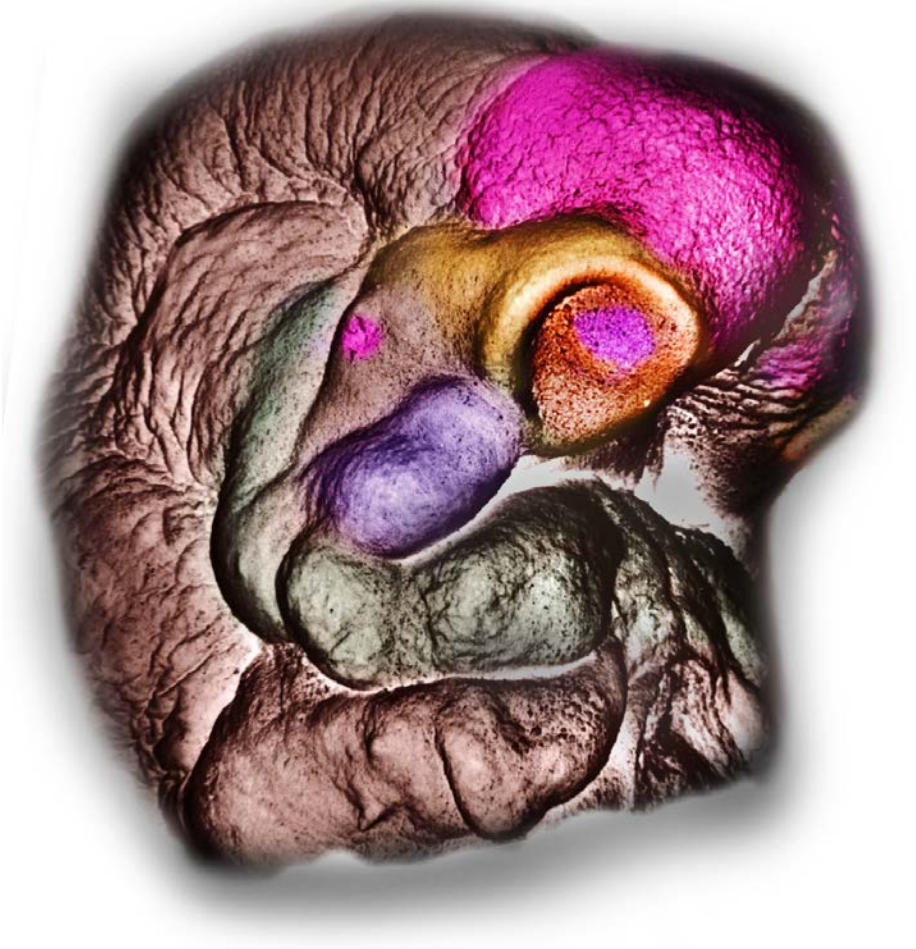




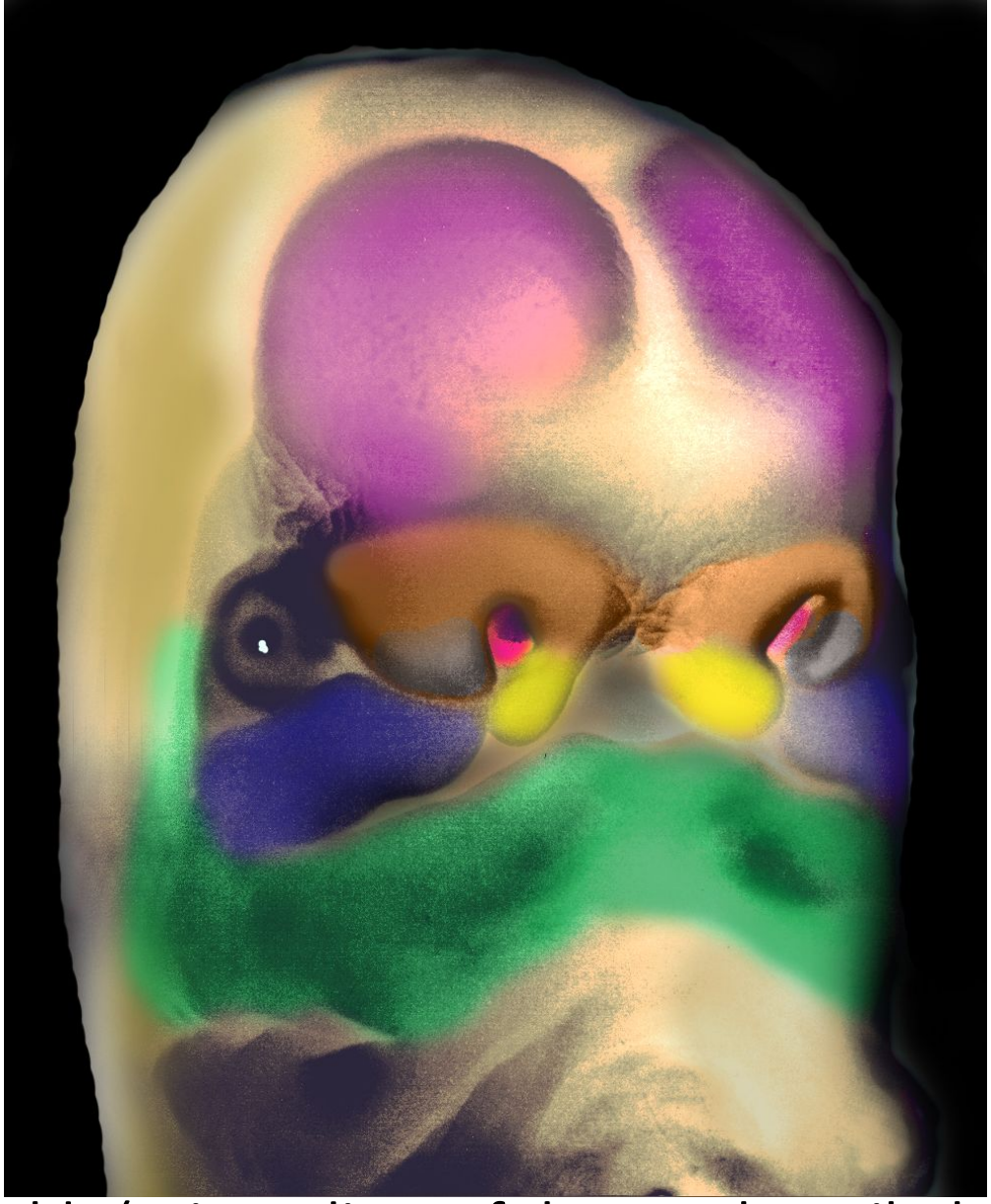
Spinal ganglia and somites of the head



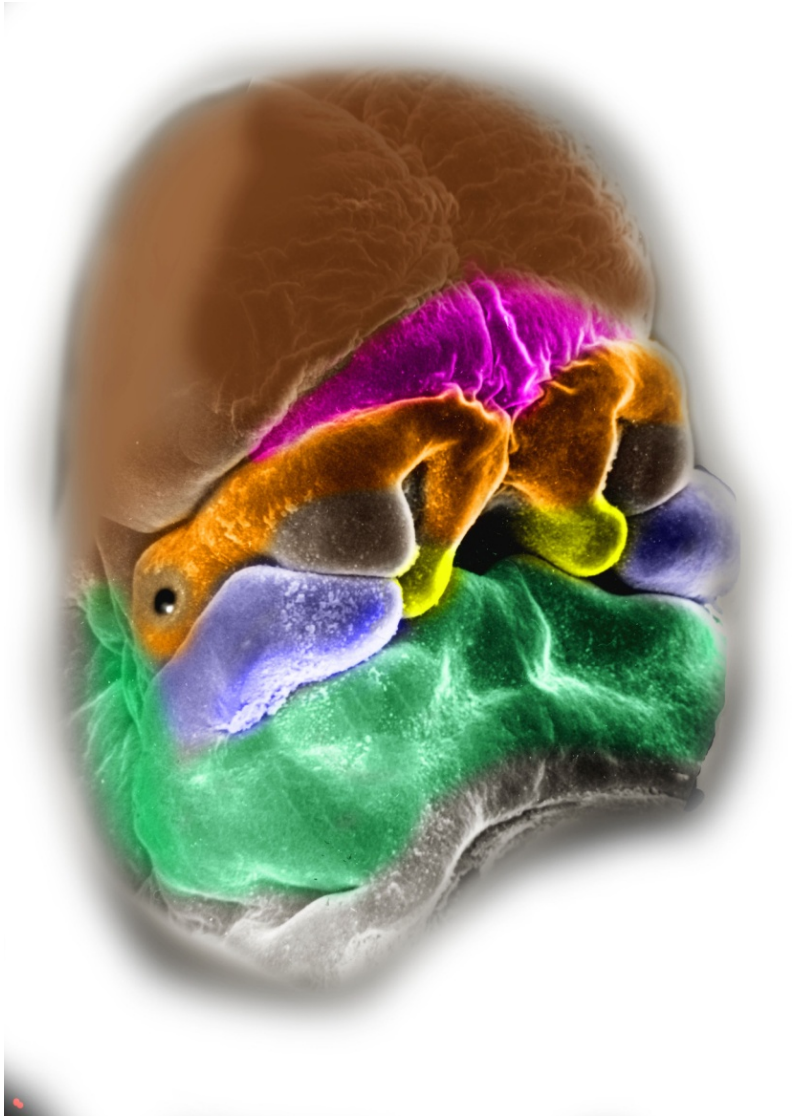
Migration of the olphactory neuromesenchym and induction of the brain hemisphere



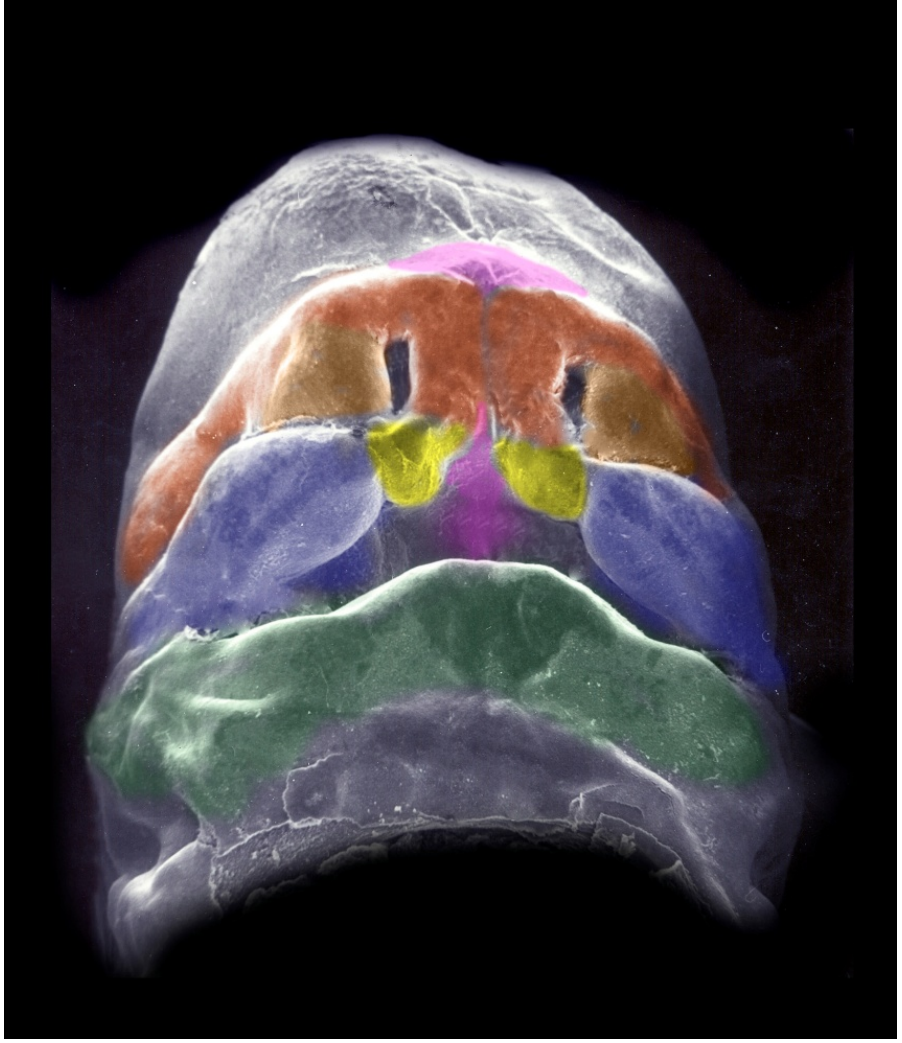
The olphactory placode attached to the maxillary primordium of the first pharyngeal arch. The placode is delineated by the nasal fold.



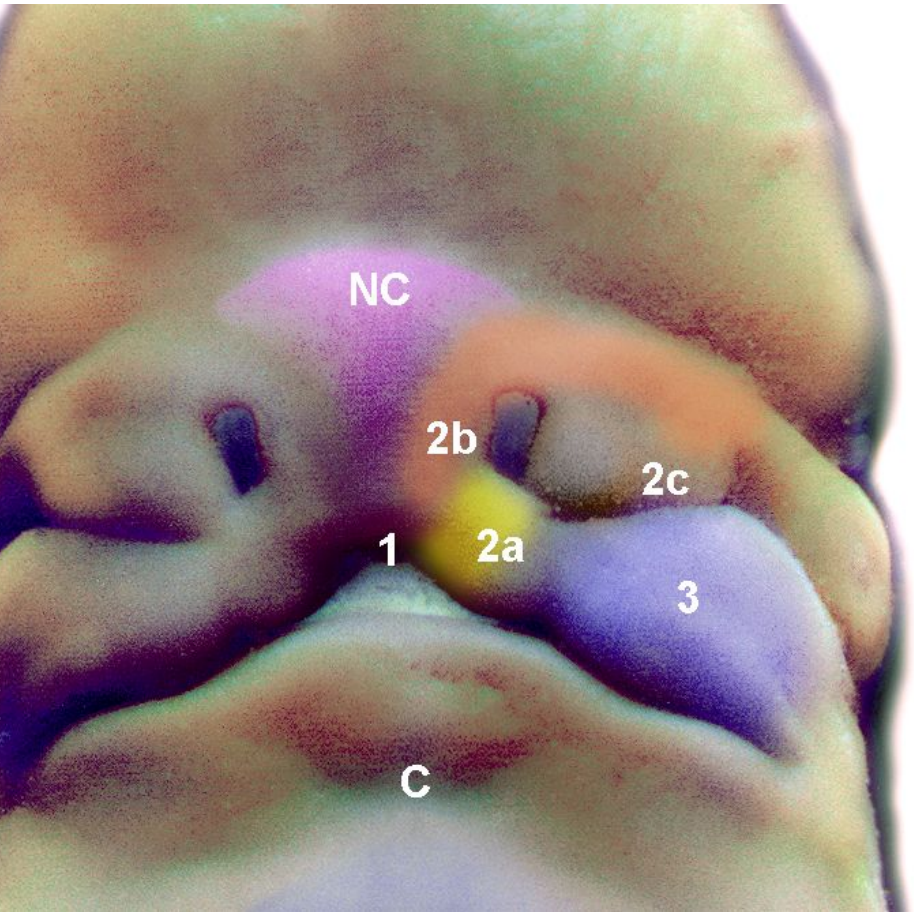
The nasal folds (primordium of the nasal vestibule) have three components: a premaxillary (yellow), a medionasal (orange) and a lateral (brown).



The nasal capsule (purple; primordium of the nasal dorsum and apex) appears in the area between the front and the nasal vestibule.



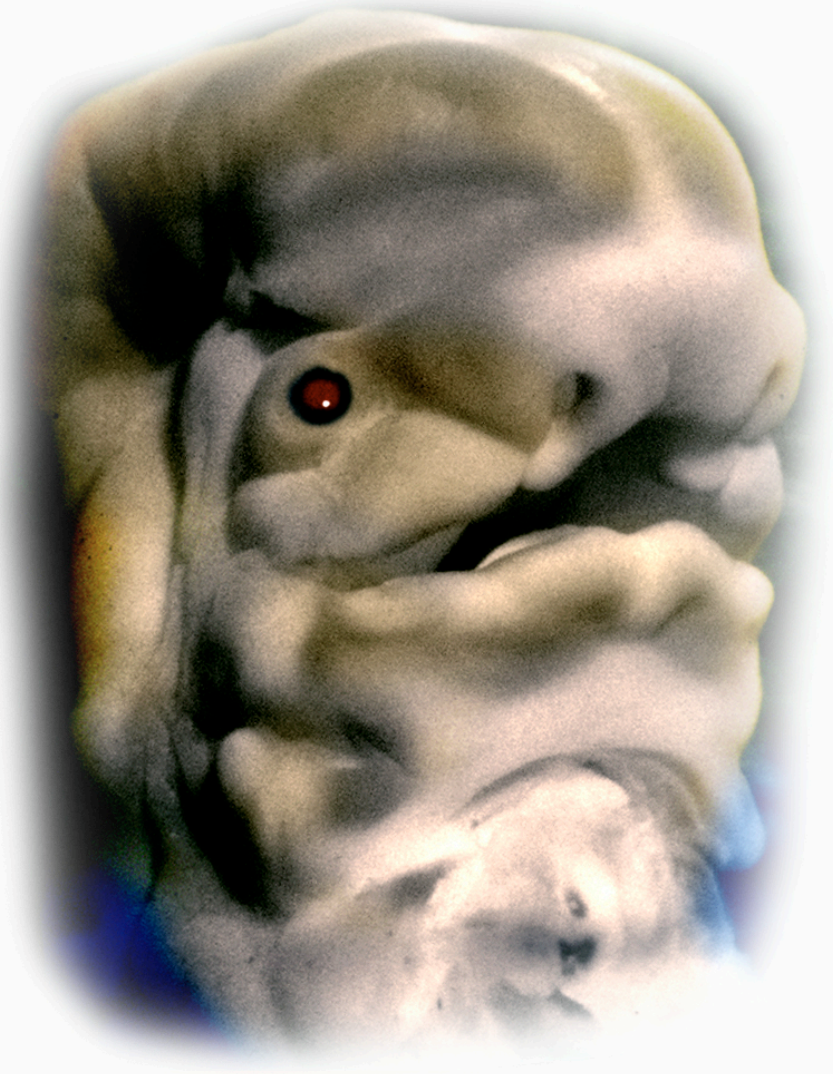
The primordium of premaxilla and philtrum of the upper yaw (yellow) is interposed between the maxillar primordia. The nares are delineated medially by the middle portion of the nasal folds (orange). The lateral portion of nasal folds changes into the nasal wings and delineates the nares lateral.

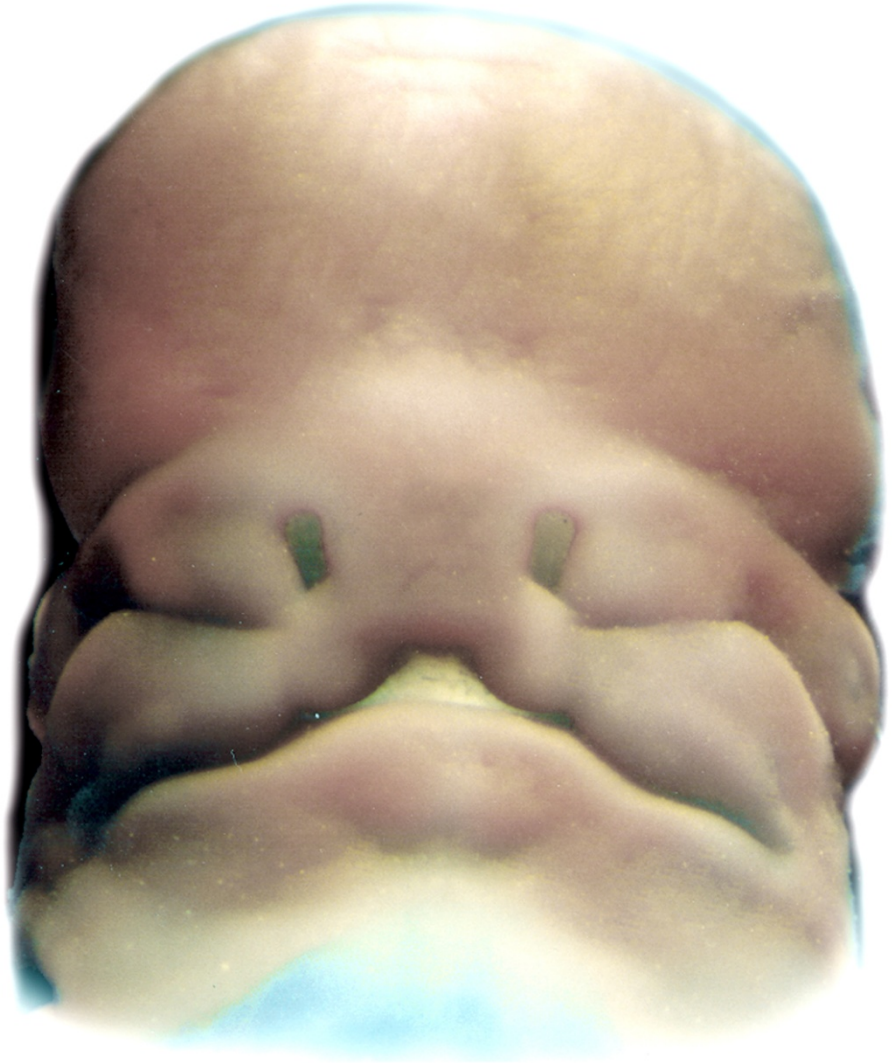


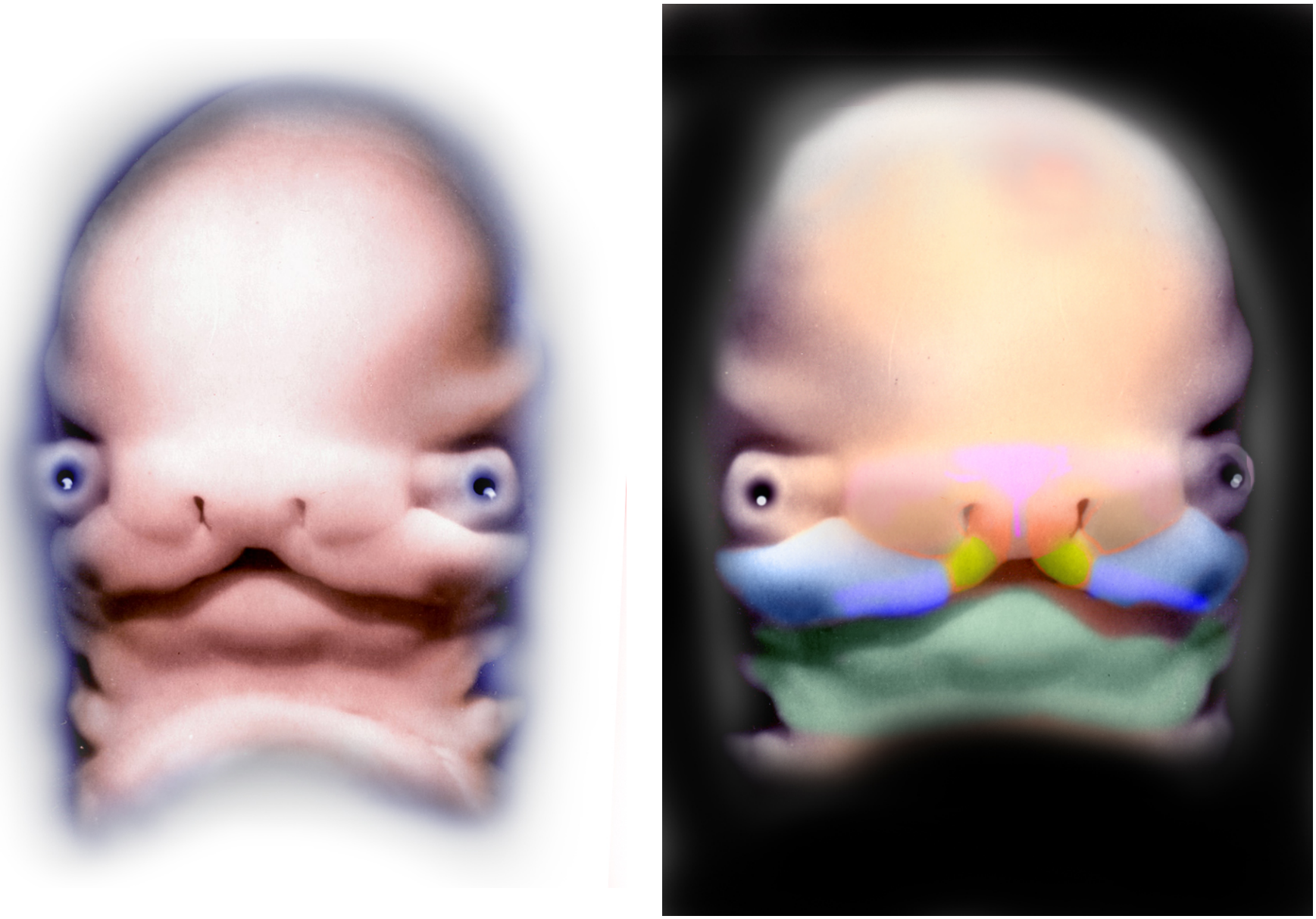
The closure of the primary pallate

NC – midline elevation related to nasal capsule, 1 - midline incisure of the upper yaw, 2 – delineation of the nasal pit: 2a – premaxillar portion, 2b –medial portion, 2c – lateral portion of the nasal folds, 3 – maxillary primordium. The primordium of the nasal vestibule is not delineated from the eyeball.

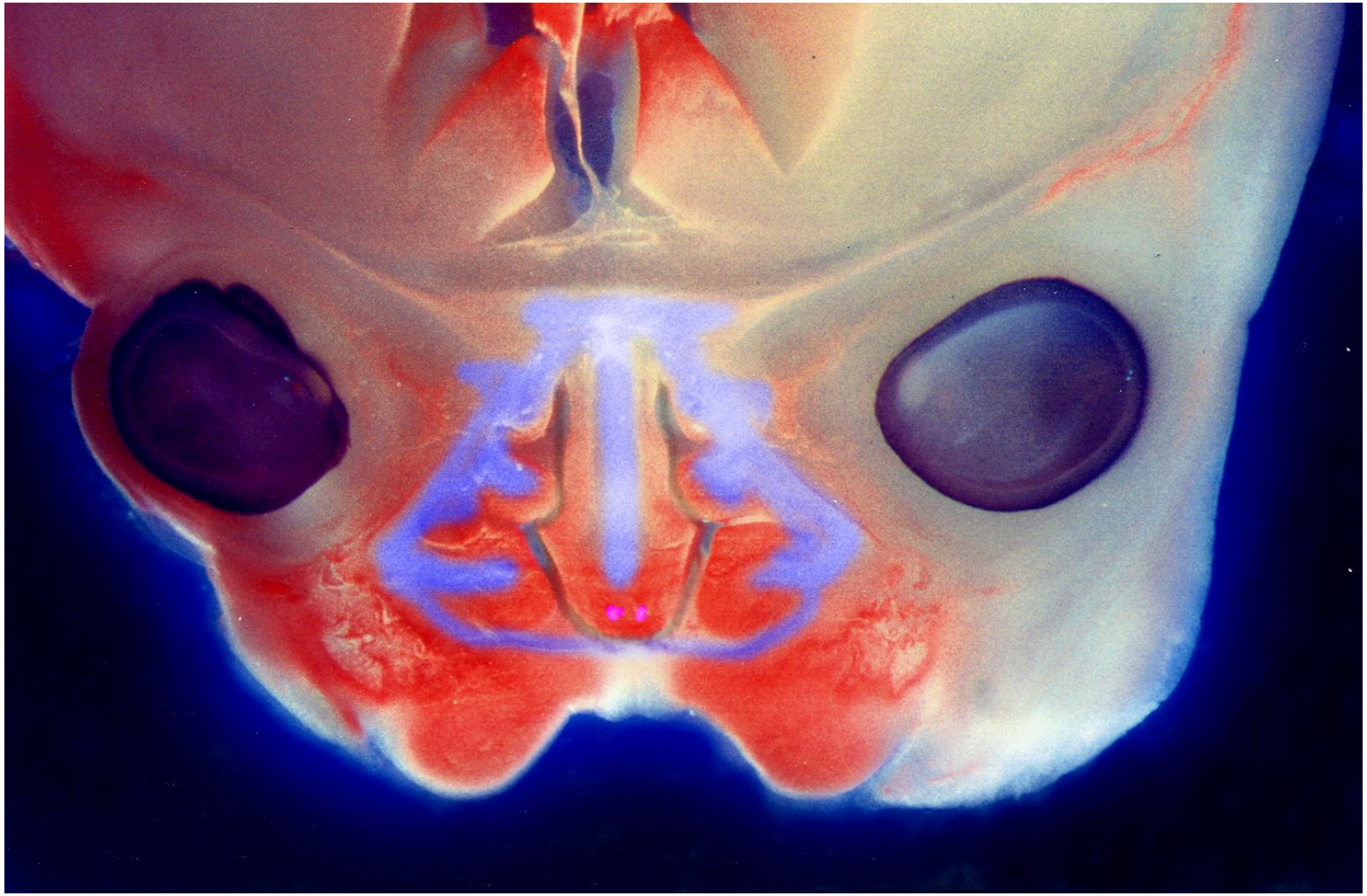
The lines of clefting are the premaxillar-maxillar junction and the naso-lacrimal canal located between the nasal fold and the maxilla.



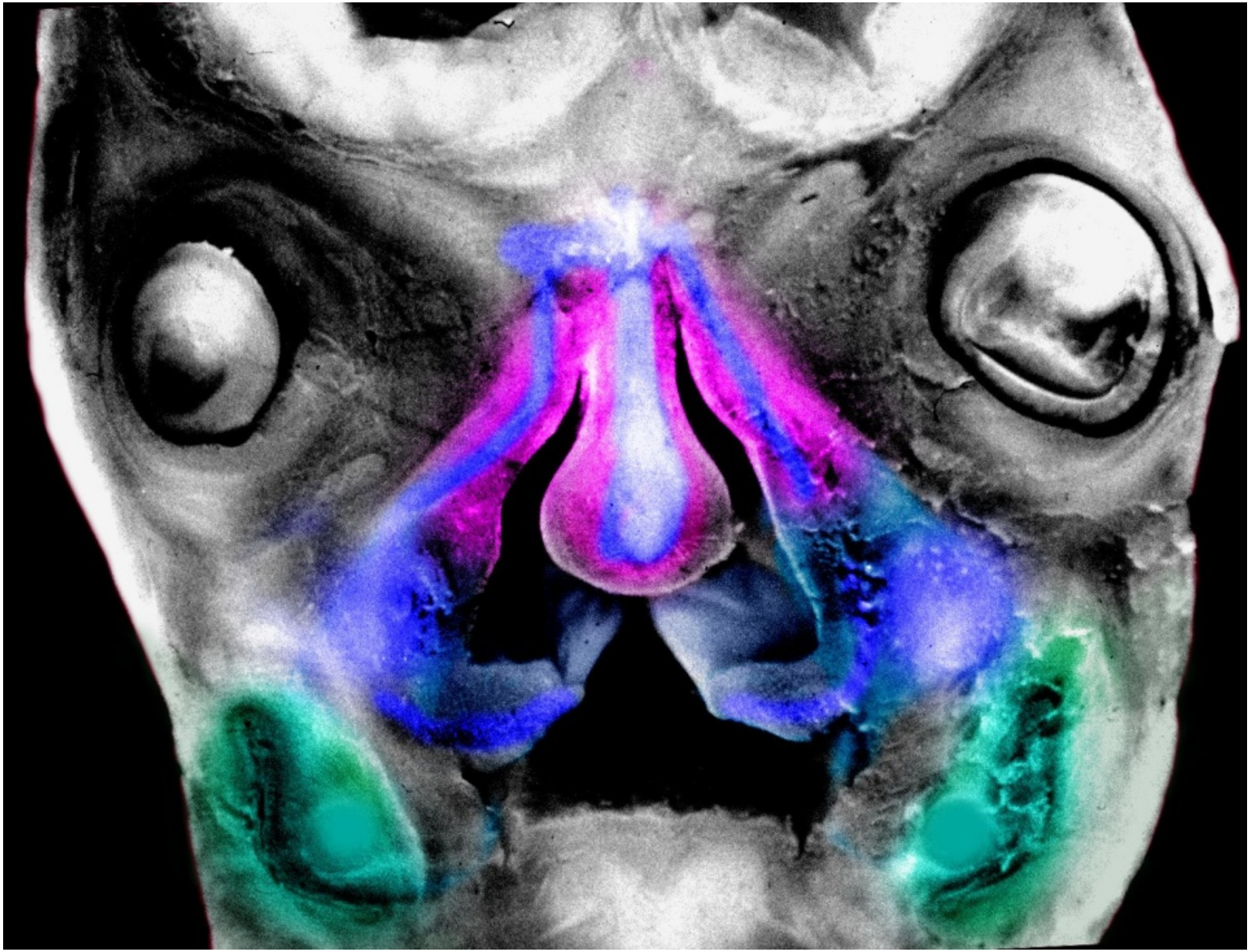




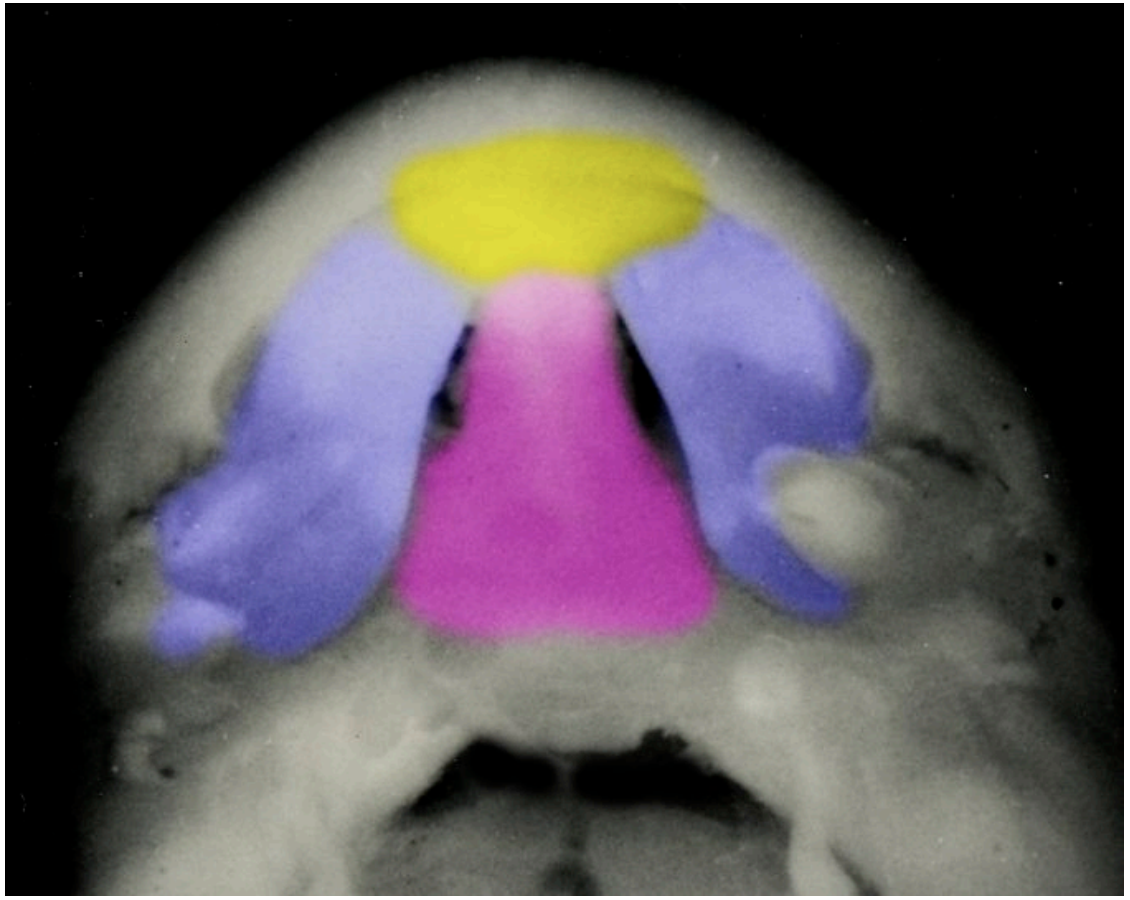
Closure of the primary palate: days 48 – 49 +- 2

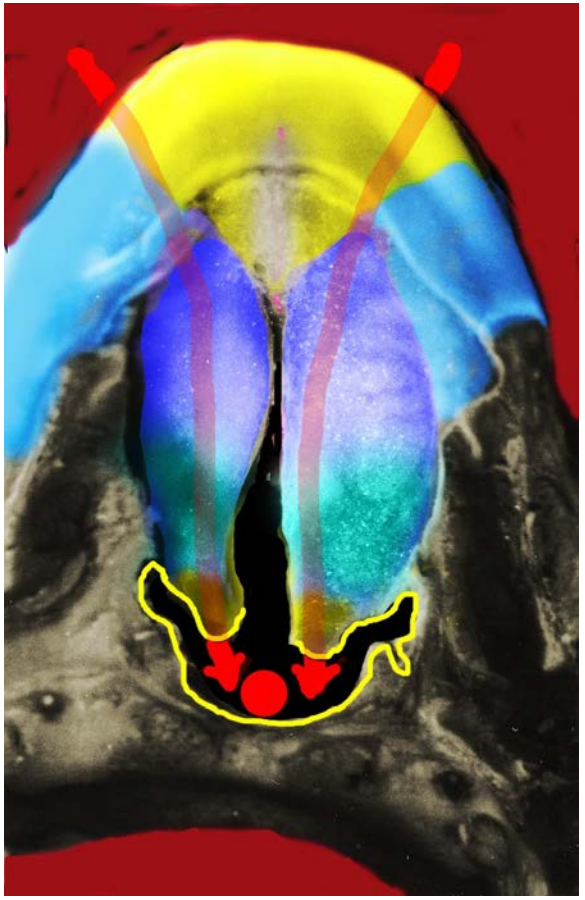


The nasal capsule is formed by cartilages located anterior to hypophyseal sella and are primordium of the olphactory bone, conchae, vomer and cartilagineous nasal septum. Nasal cavities are located between the nasal septum and conchae.

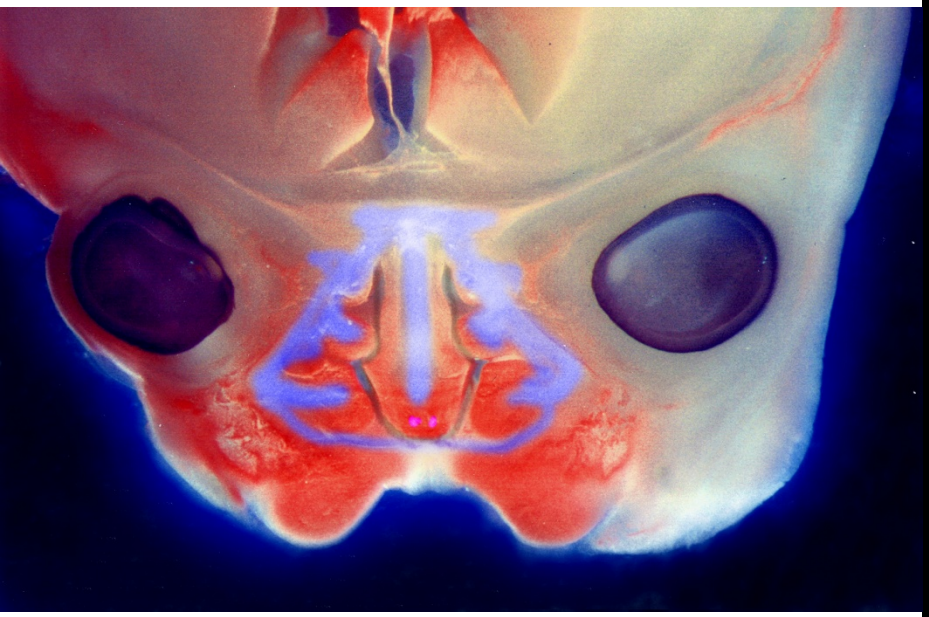


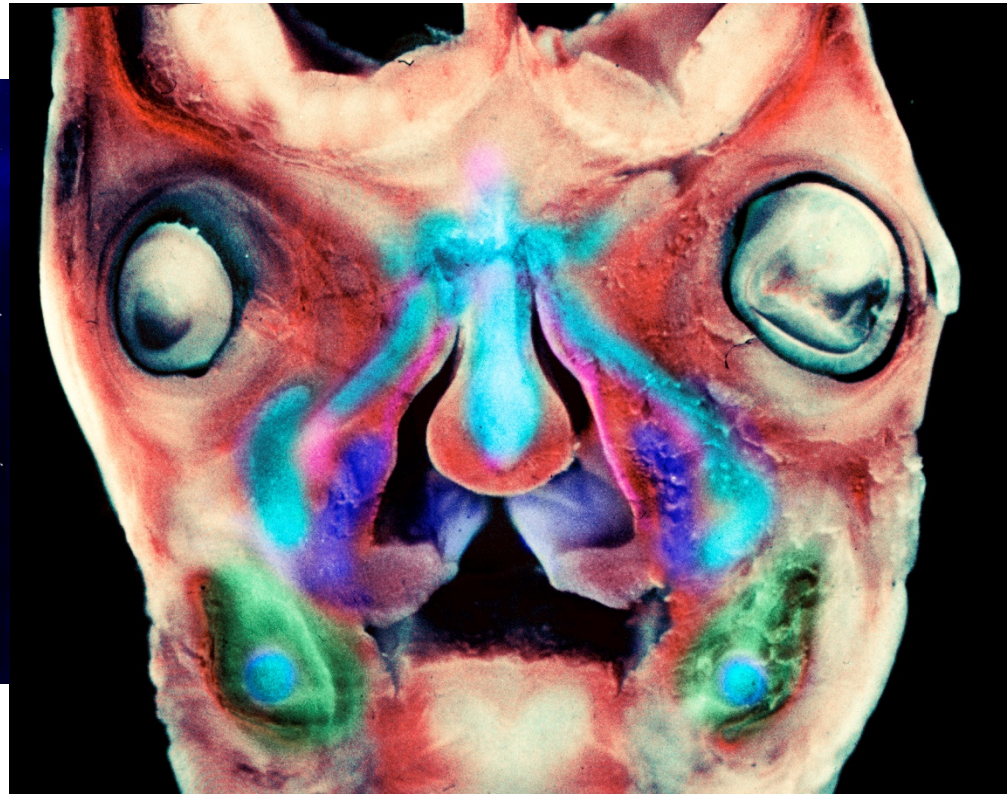
The nasal cavities contributed by the nasal capsule are located between nares and choanae, which open into the oropharynx.



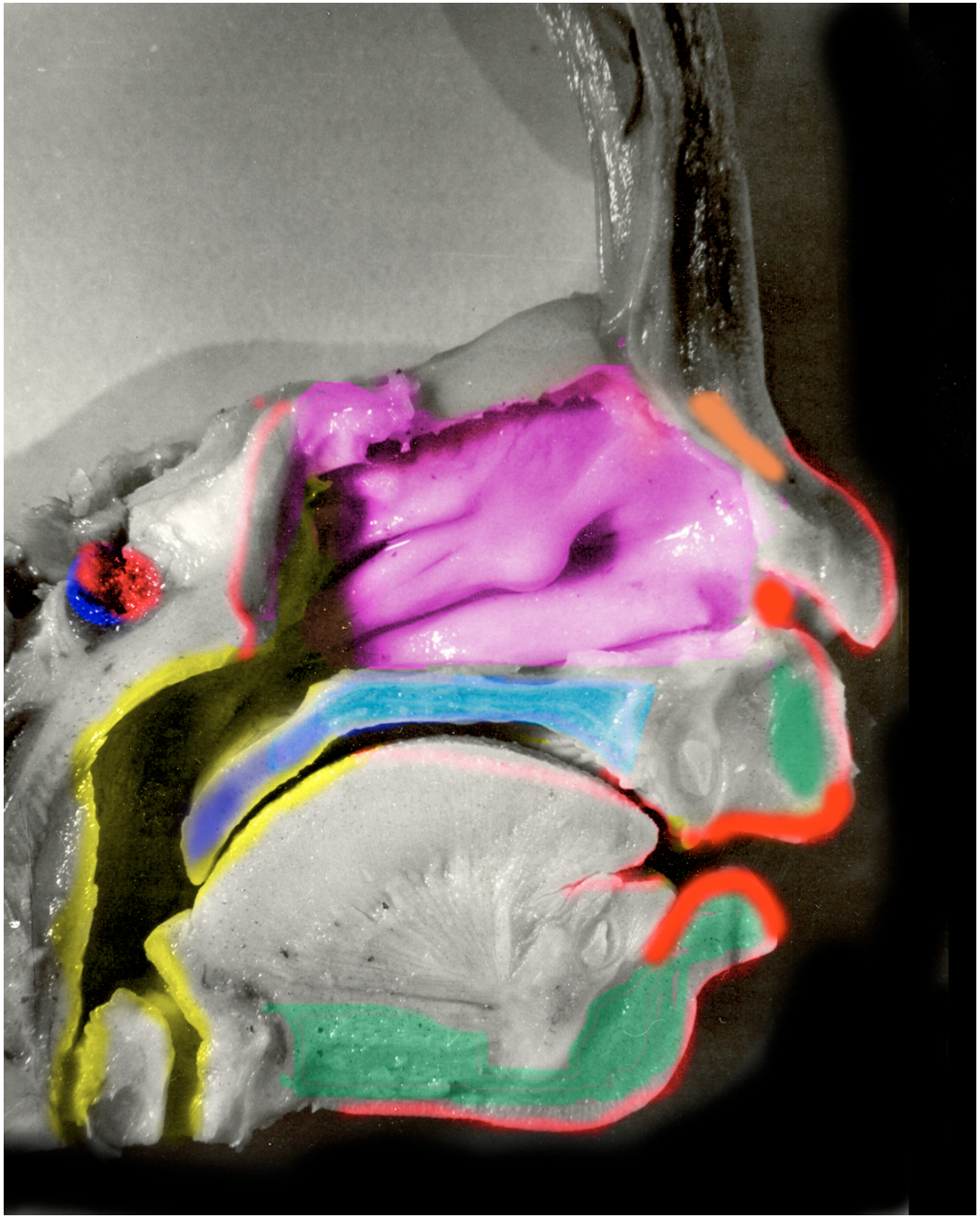


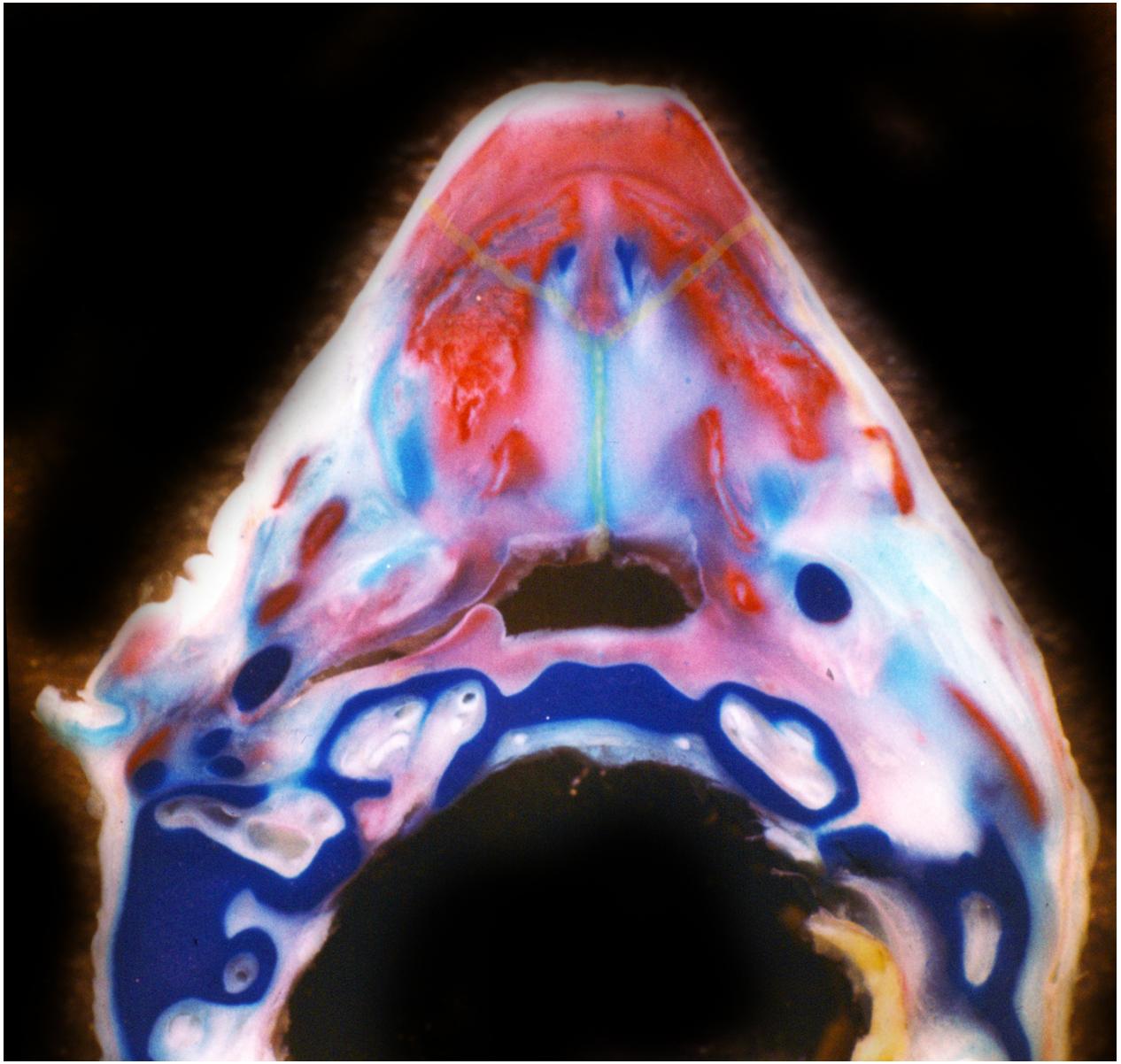
The secondary pallate is formed by two maxillary palatinal shelves growing from the maxillary primordium to the midline. Anterior they join the premaxilla, in the midline they approache each other and join by a midline suture isolating the nasal and oral cavities. The palatinal shelves are primordia of the hard palate, soft palate and uvula.





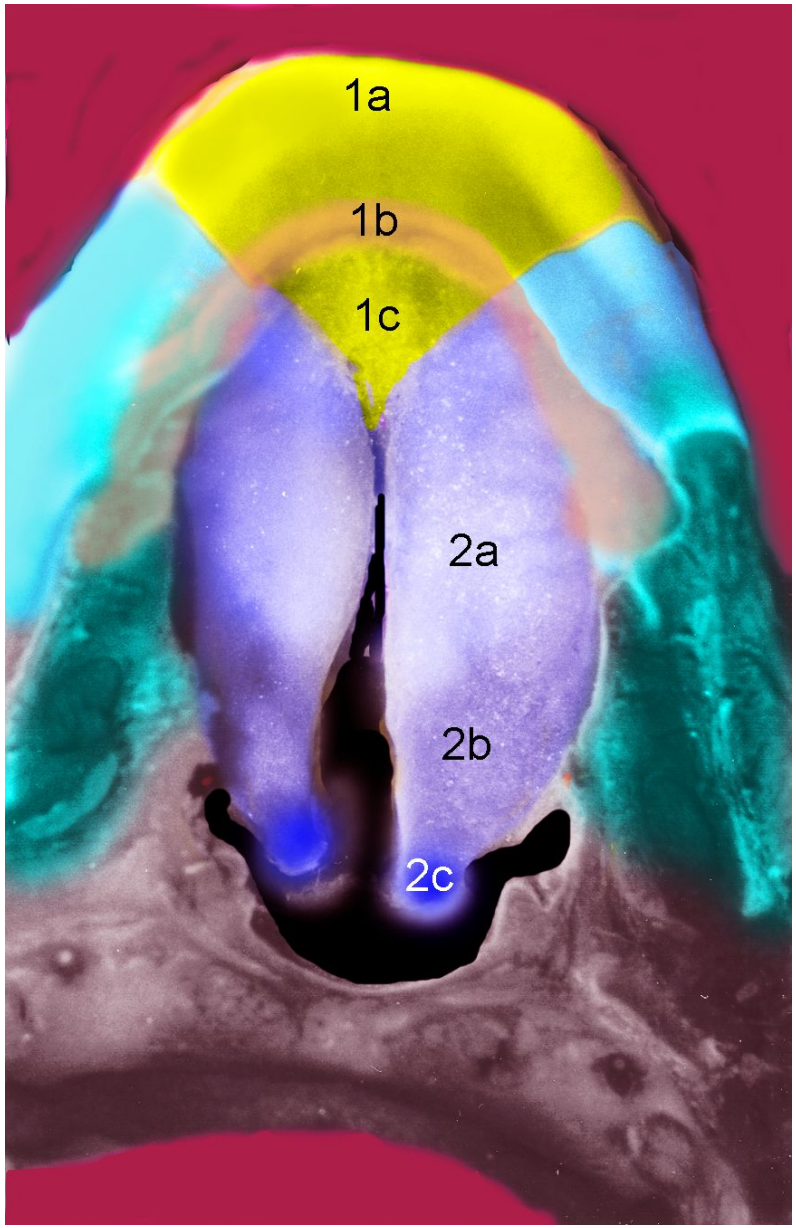
Formation of the nasal capsule and of the secondary palate

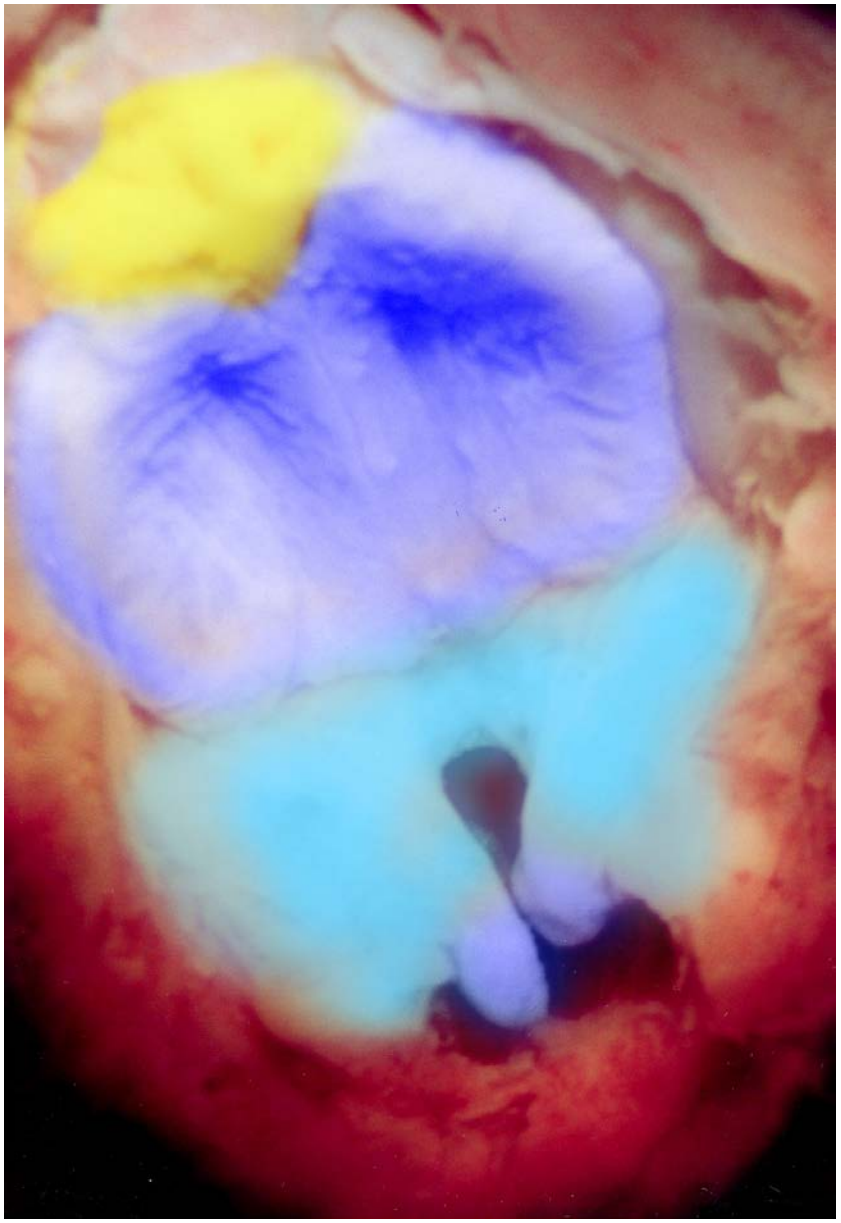




The border of the premaxilla (primary palate) and secondary palate is marked by the incisive foramen.
The oral vestibule results from the apoptosis of the multiple squamose ectodermal epithelium from the labiogingival lamina. The endportion of the labiogingival lamina is the dentogingival lamina which provides primordia of the teeth.

Closure of the secondary palate
(12th gestational week)

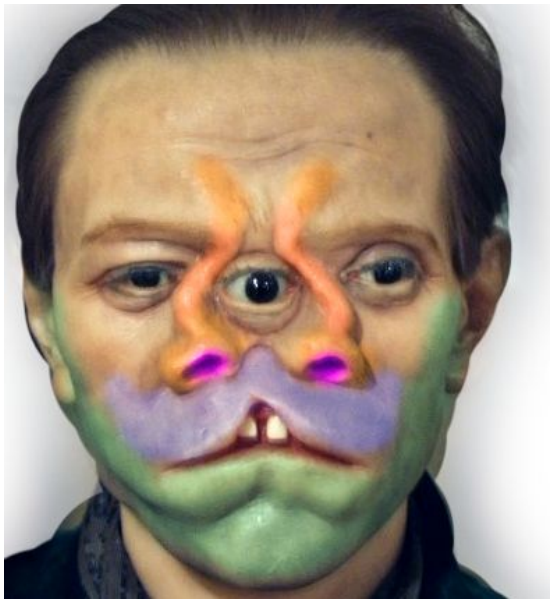




1 – primordium of the premaxilla, 1a – labial portion, 1b – gnathoalveolar portion, 1c- palatinal portion, 2 Palatinal shelves of the maxillar primordium, 2a- primordium of the hard palate, 2b- primordium of the soft palate, 2c – primordium of the uvula

Malformations
Duplications

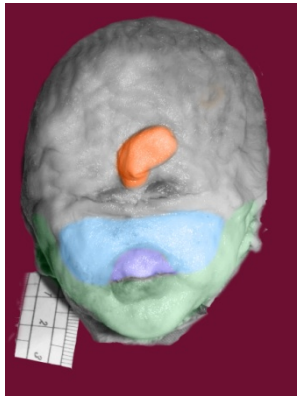
Olphactory Placodes Induce Development of Brain Hemispheres



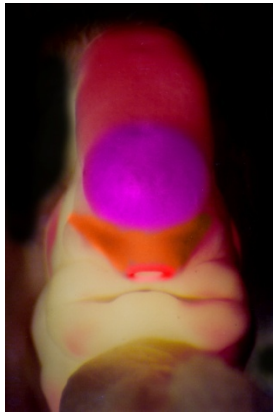
Triphtalmia, midline labioschizis

Malformations

Olphactory placodes, brain development, holoprosencephaly



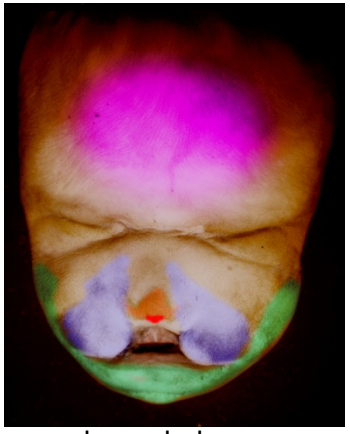
synophtalmia
frontal proboscis



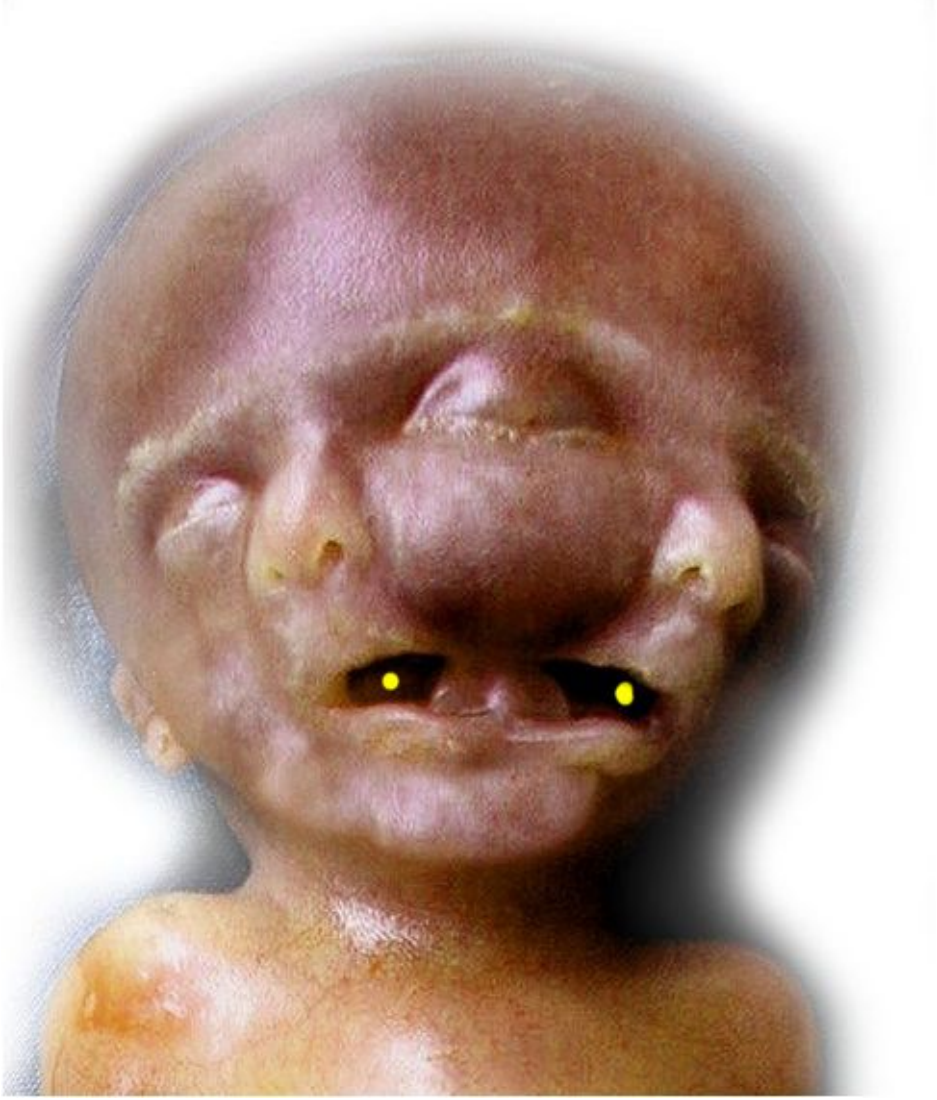
ethmocephaly
holoprosencephaly
8 mm embryo

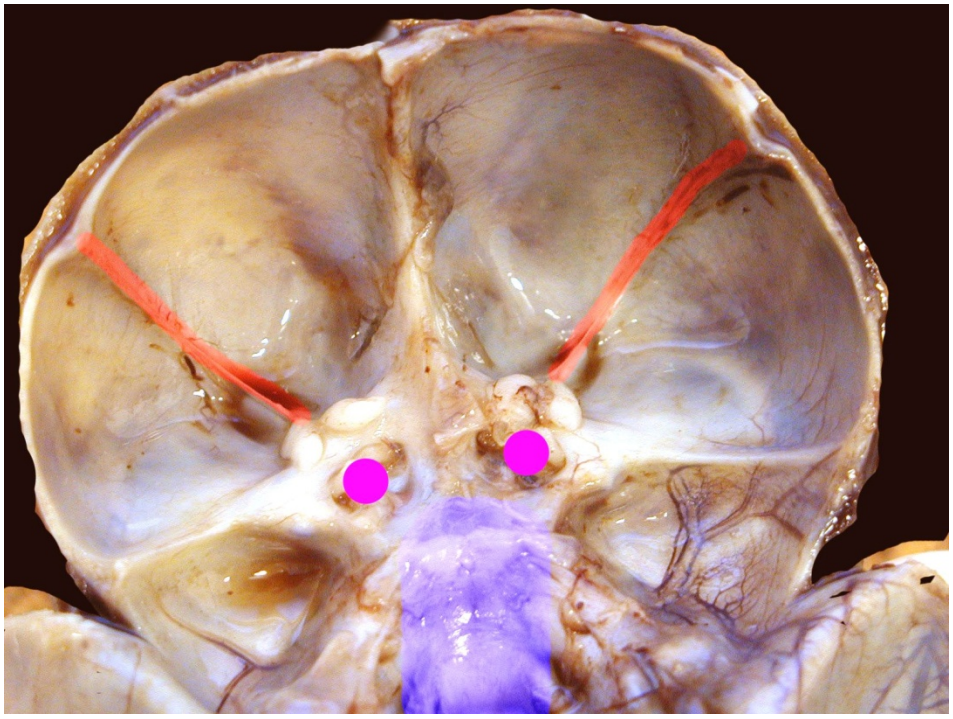
ethmocephaly
holoprosencephaly
22 mm embryo

ethmocephaly
holoprosencephaly
newborn



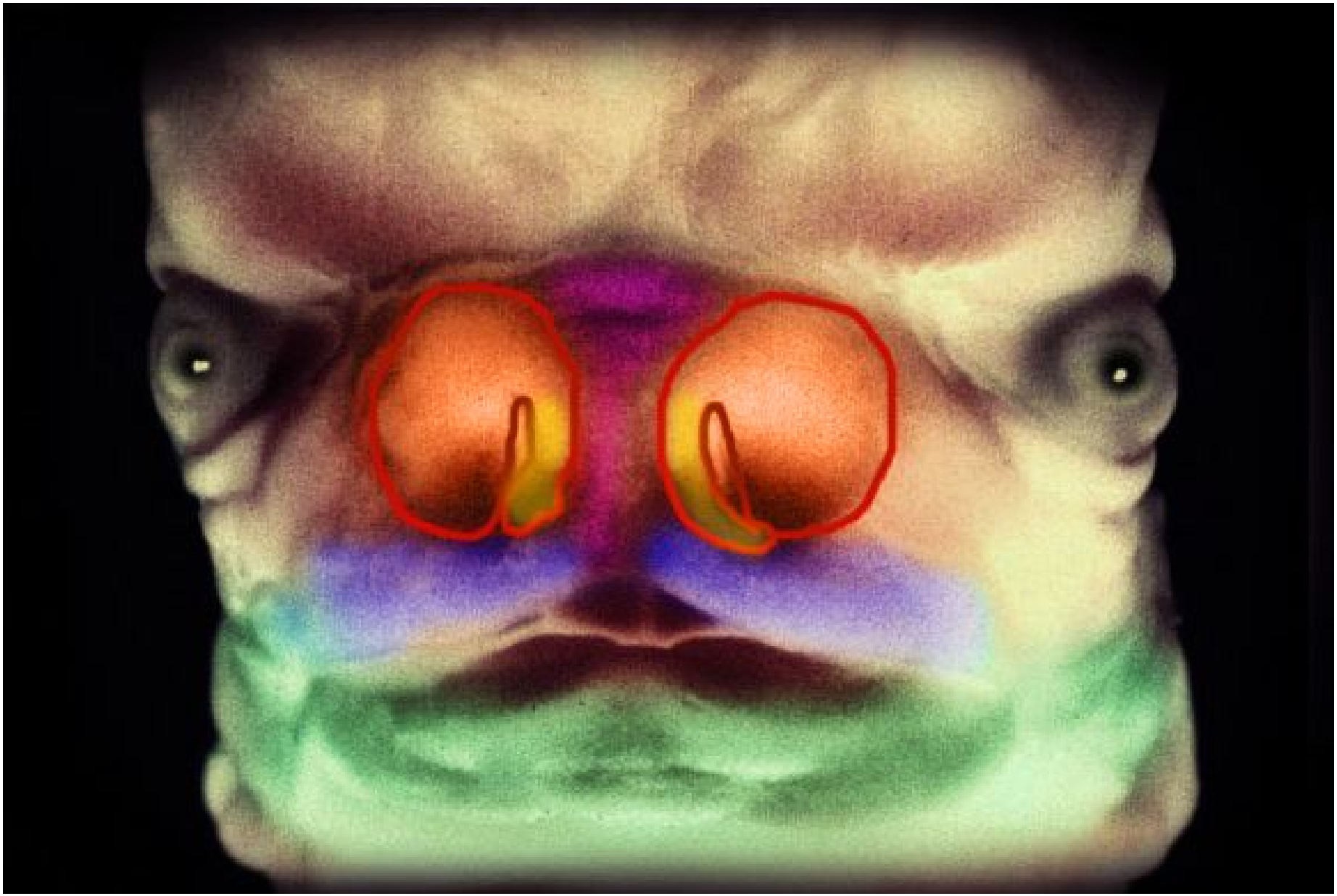
cebocephaly
premaxillar agenesis
holoprosencephaly
newborn



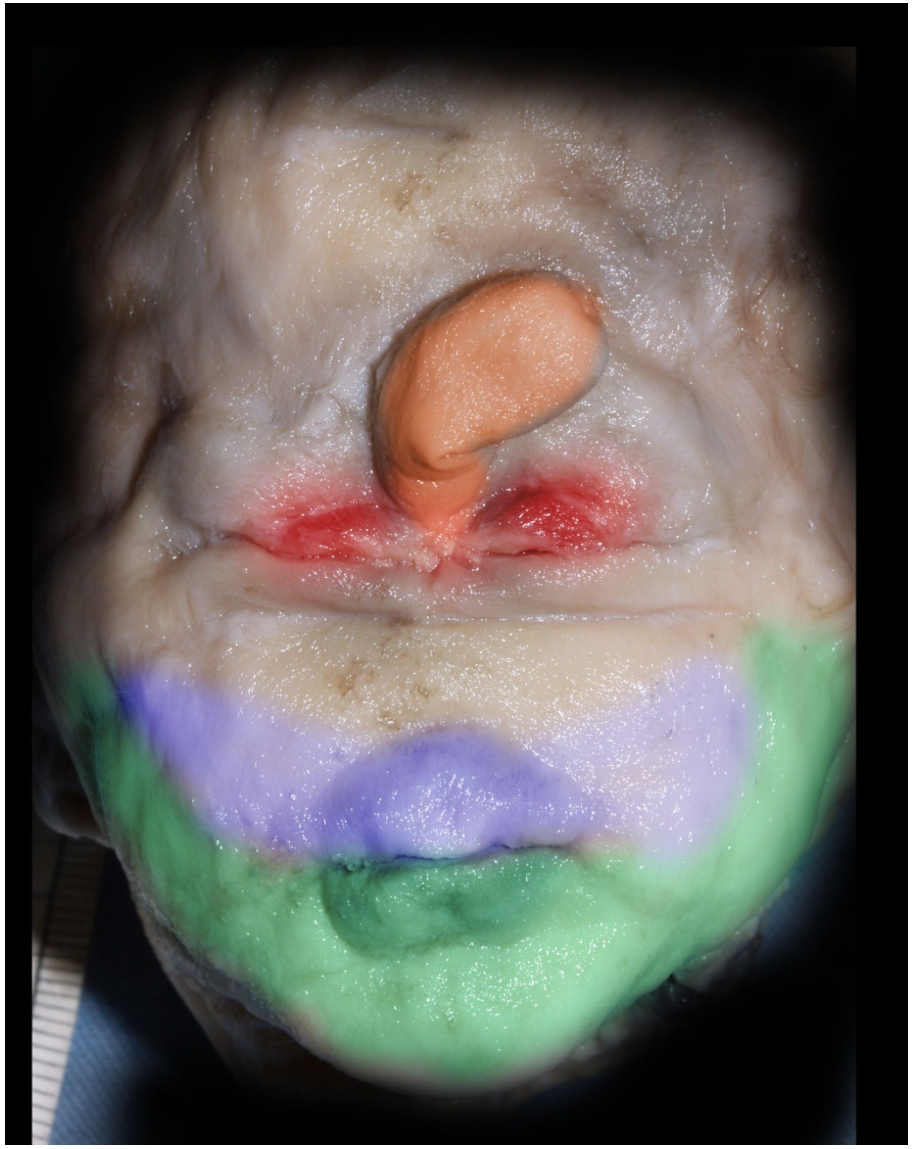


Diprosopus

The malformation results from duplications of neuroectodermal ectoderm adhesion (which is the tip of the Rathke's pouch) and from the endoderm –ectodermal adhesion between the AVE and surface ectoderm of the stomodeum.



Frontofacial dysplasia

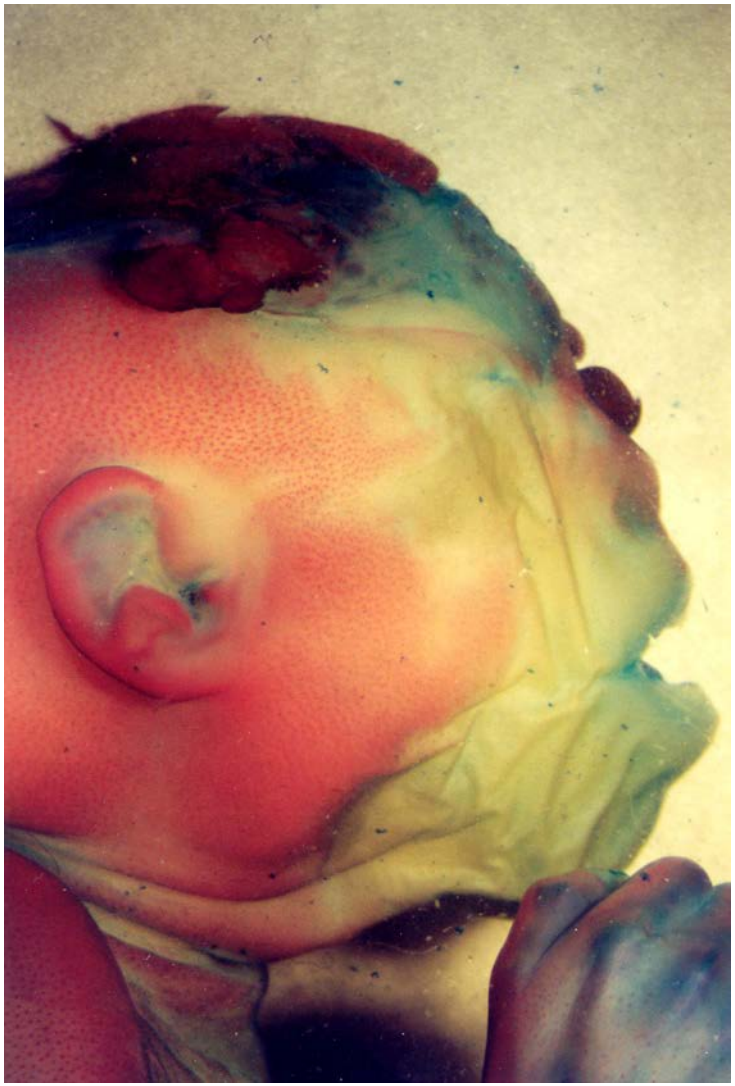


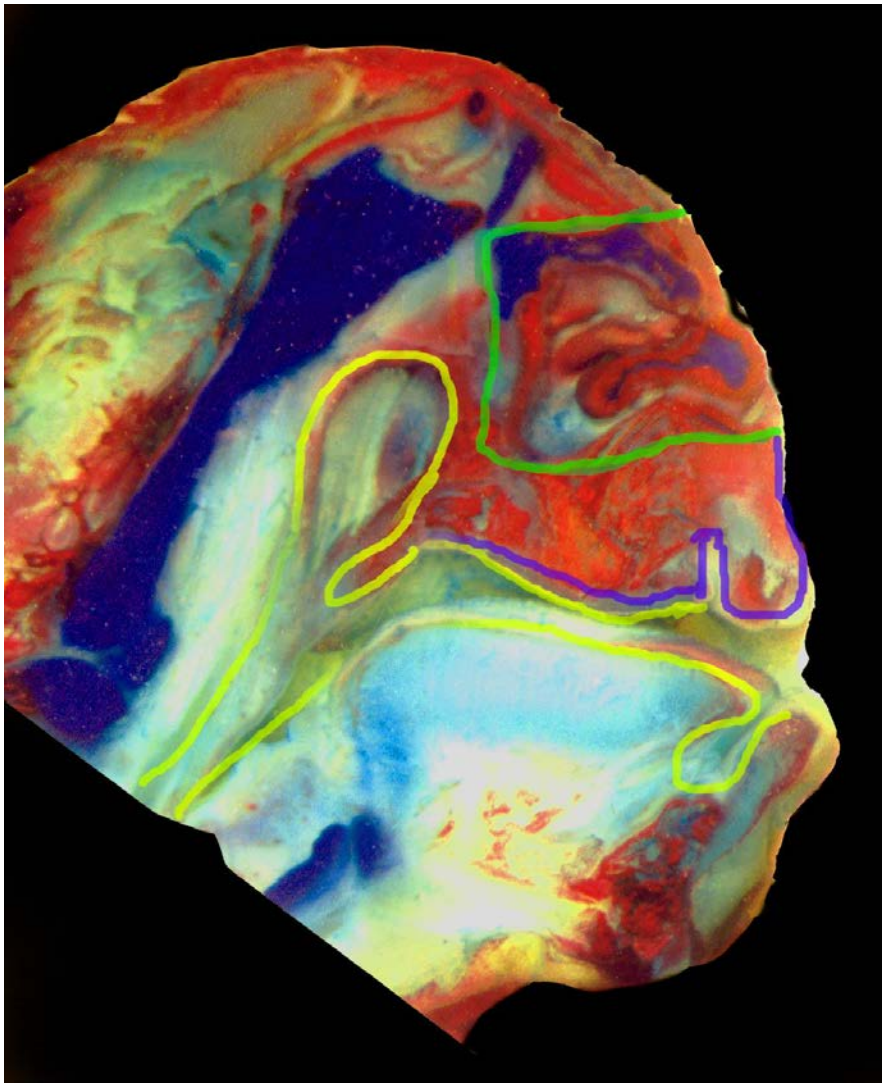
Synophtalmia
frontal proboscis

Ektopic placodes turn into the **proboscis.**

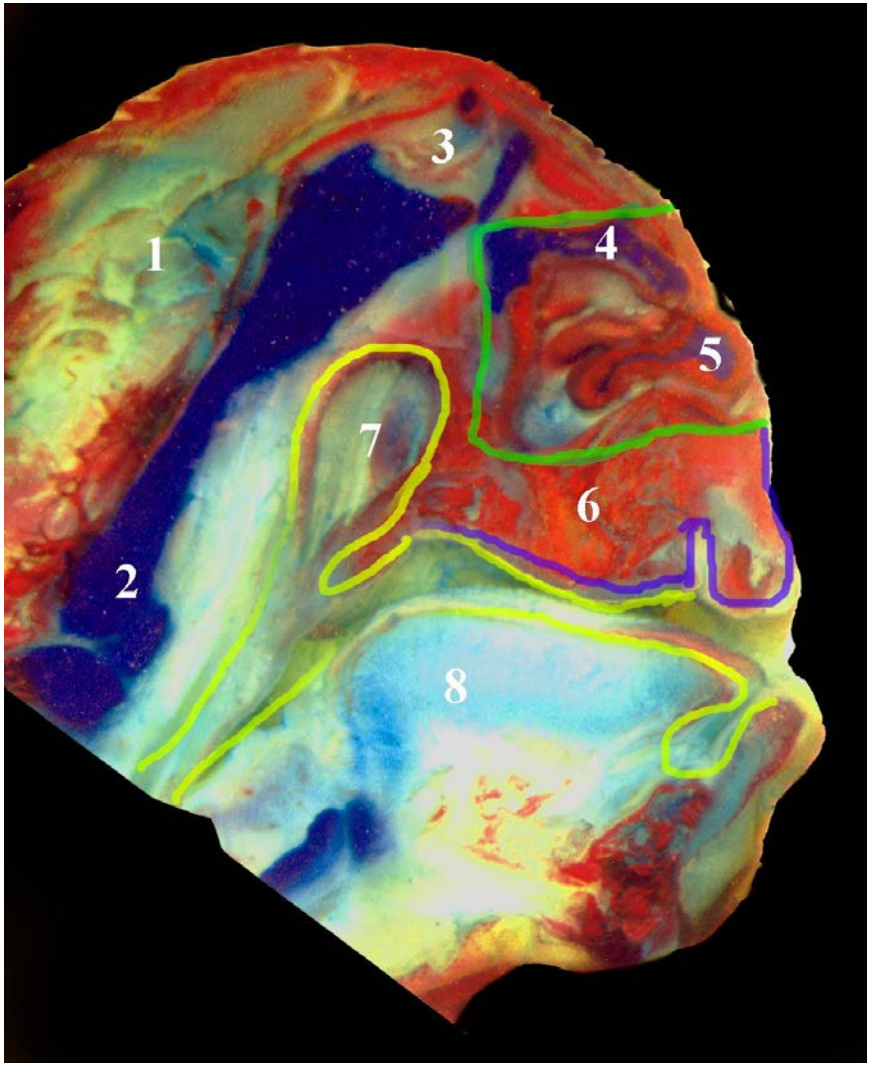
Synophtalmia is related to the insufficient lateralization of paired structures resulting in fusion of olphactory placodes. The single olphactory placode located before the obstacle turns into the proboscis.

The upper jaw closes by maxillary primordia of the first pharyngeal arch. There is the premaxillary agenesis.





The midtrimester fetus affected by anencephaly, cyclopia, nasal aplasia and premaxillary agenesis. (a- lateral view, b - midline dissection)



1- anencephalic brain (area cribrovascularis),
2 - cartilage of the brain plate
3 - sella turcica
4 - cartilage of the olphactory bone – nasal capsule,
5 - optic vesicle (there is no lens primordium)
6 - primordium of the maxilla originating from the first pharyngeal arch.
7 – oropharynx separated from the nasal cavity (there are no choanae),
8 - tongue

The malformation results from nonclosure of the anterior neuroporus and formation of only one optic vesicle, which was surrounded by the olphactory neuroectoderm. The cartilages of the nasal capsule contributing the olphactory bone and conchae formed consequently.

Clefts

primary palate: lip and jaw
secondary palate: hard palate, soft palate and uvula

Clefts – lip, jaw (primary palate) palate (seconadary palate)

Craniofacial clefts of embryos and fetuses

(unilateral or bilateral)

- **Maxillofacial clefts**
  - Midline:
    - premaxillary agenesis or hypoplasia
    - interpremaxillary clefts
  - **Lateral:** **of primary palate (unilateral or bilateral)**

    incomplete - labioschisis

    complete – labiognatoschisis

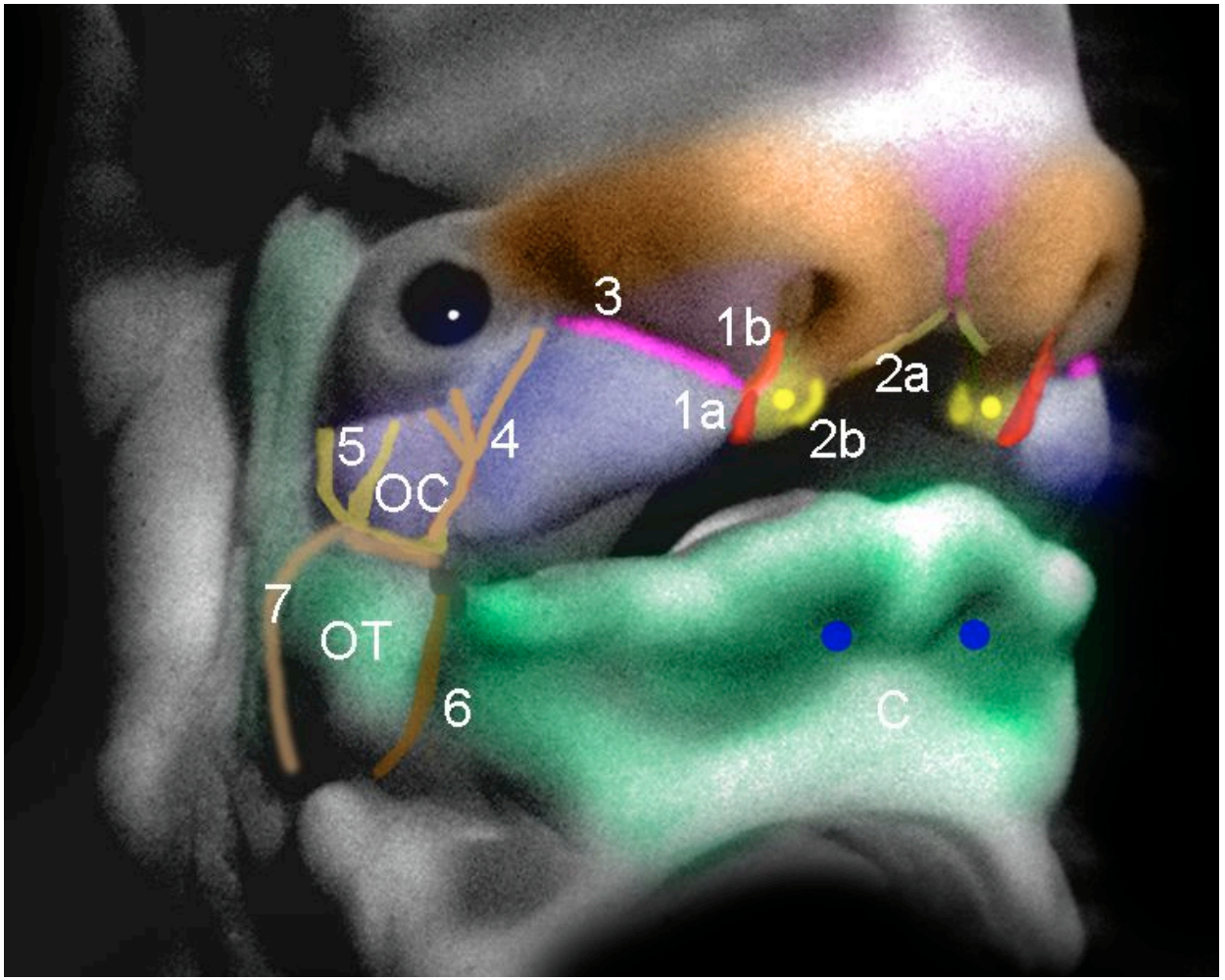
    of secondary palate (palatinal clefts)

    of primary and secondary palate – palatognathoshisis
  - **Oblique: palato - naso - lacrimo – orbital**

- **Mandibular clefts**
  - midline
  - oto-mandibular (otocephaly)
  - oro-otic

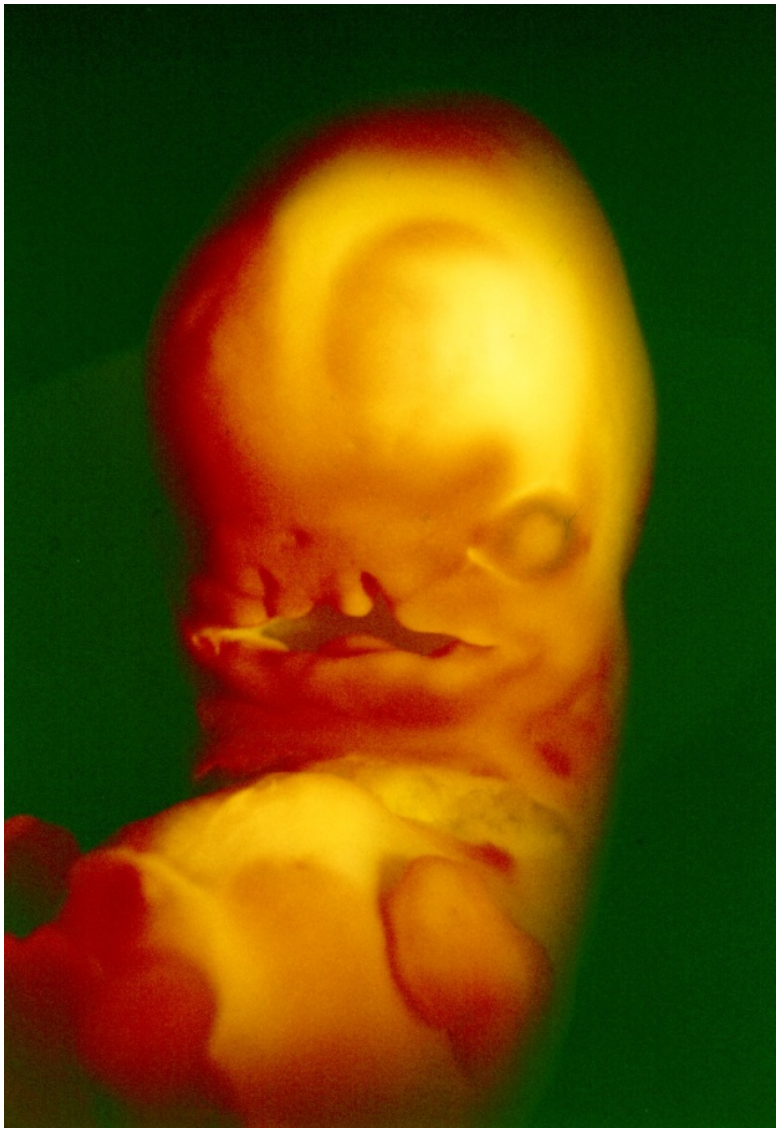
Lines of clefts

(embryonal face, end of the 6th developmental week)

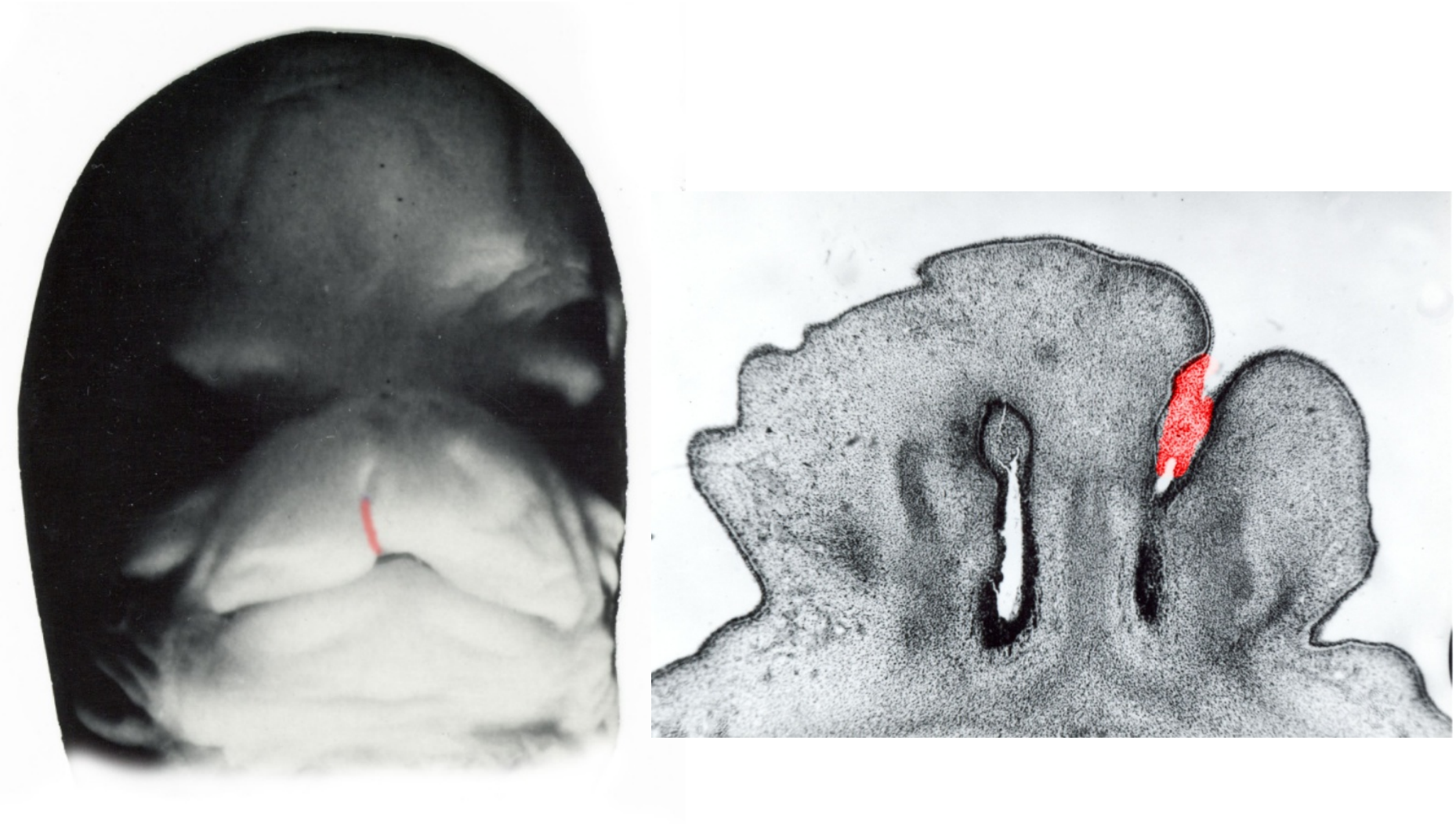


1a – labioschisis, 1b – gnathoschsis, 2a - interpremaxillar agenesis, 2b – medial cleft, 3 – oblique clefts,

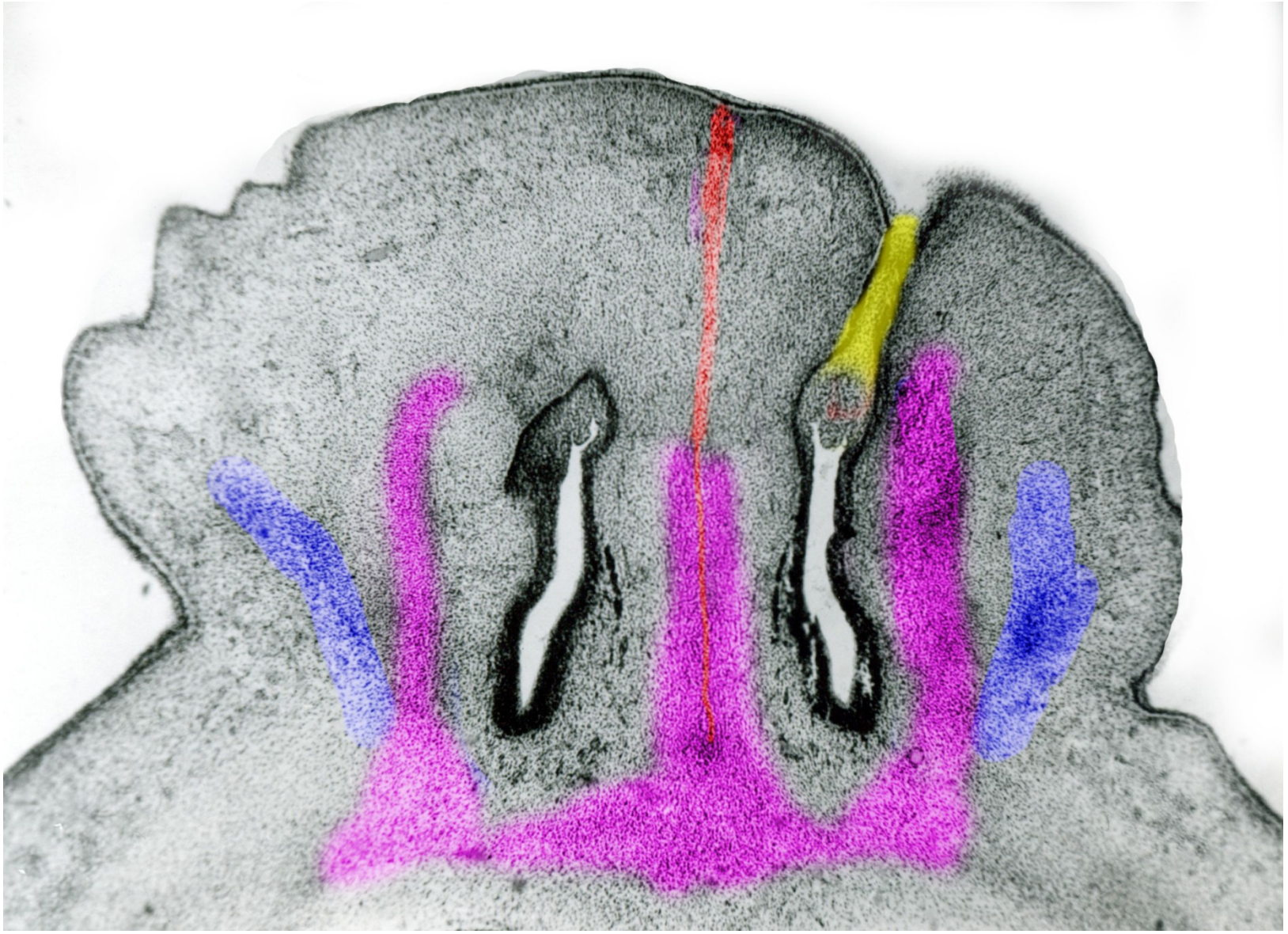
4 – oro-ocular cleft (medial), 5 – oro-ocular cleft (lateral), 6 – oro-otic cleft (anterior), 7- oro-otic cleft (posterior), OC – oro-ocular tubercle, OT – oro-otic tubercle, C – chin, blue dots – lip pits

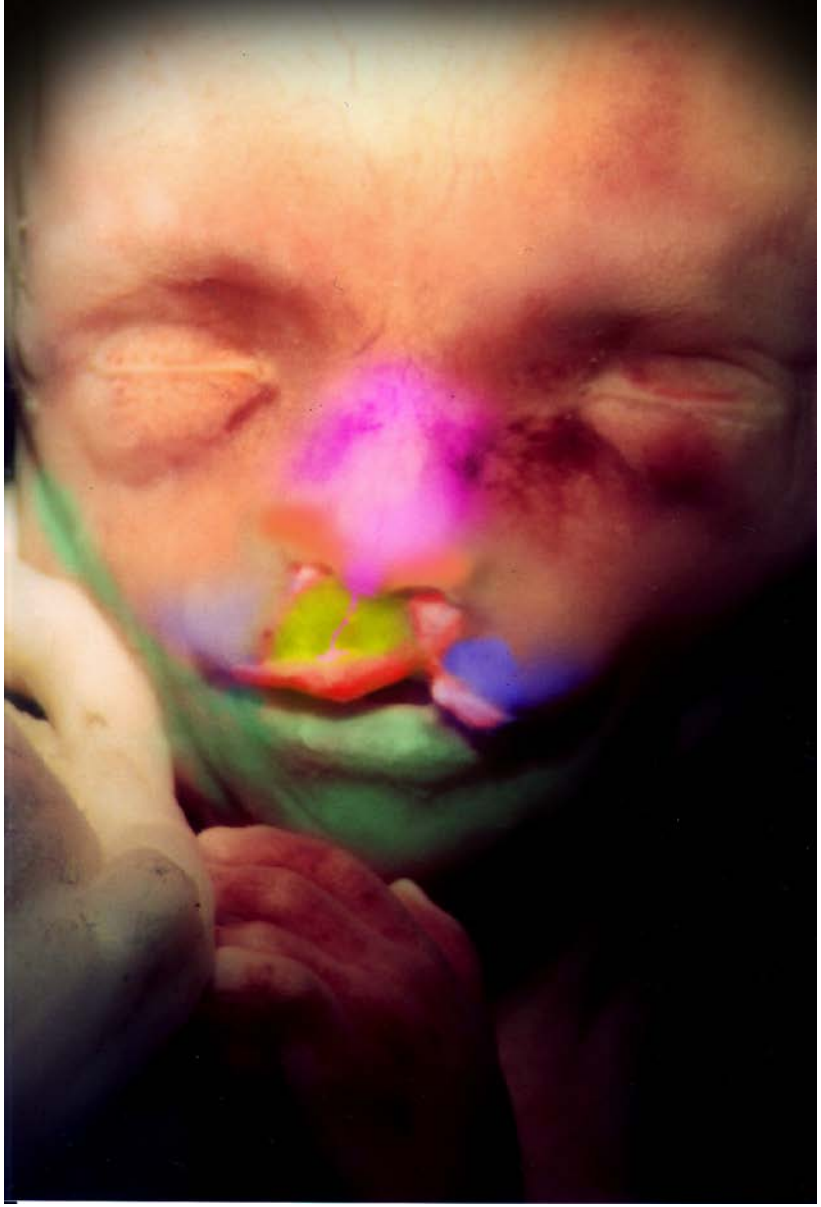


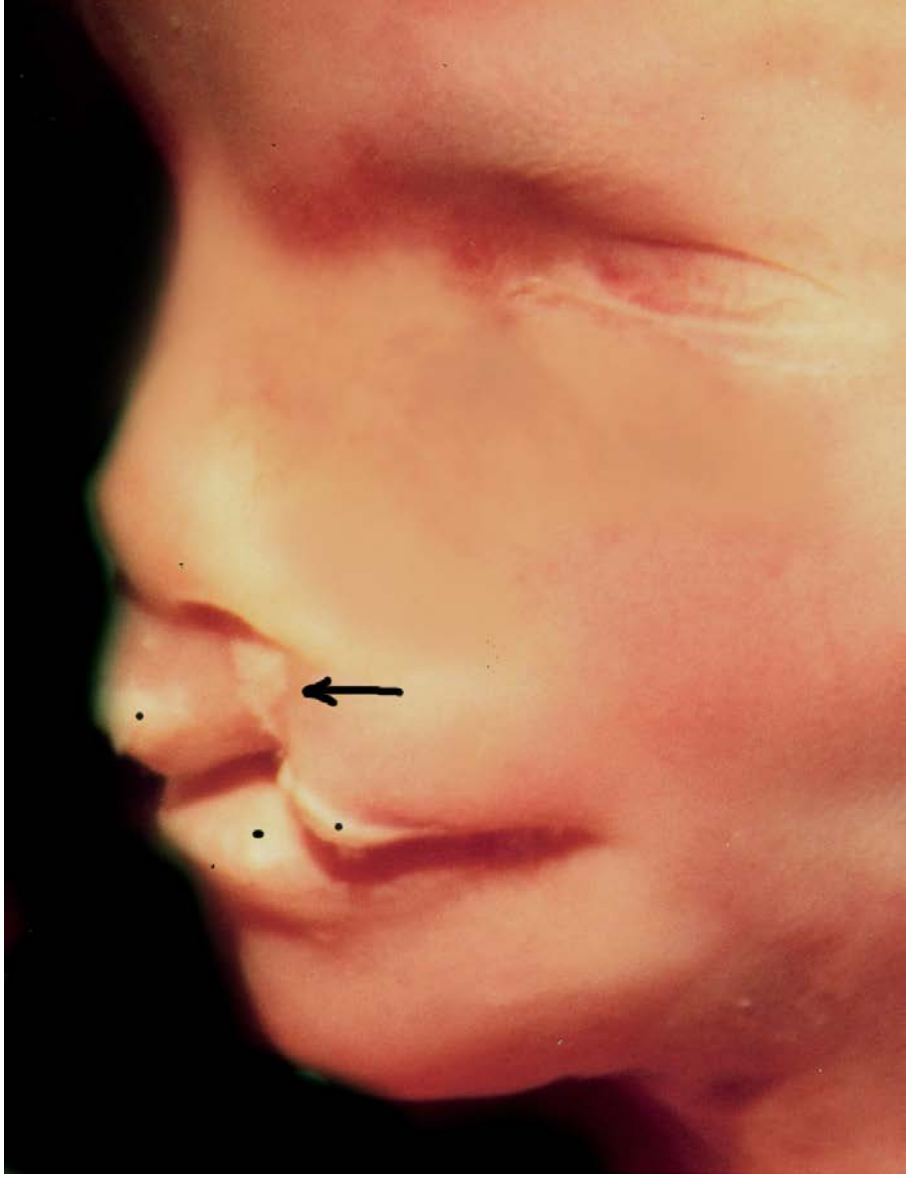
Complete bilateral cleft of both nasal folds in a 7th developmental week. The malformation is accompaned by failure of differentiation of finger rays (orodigital malformation).



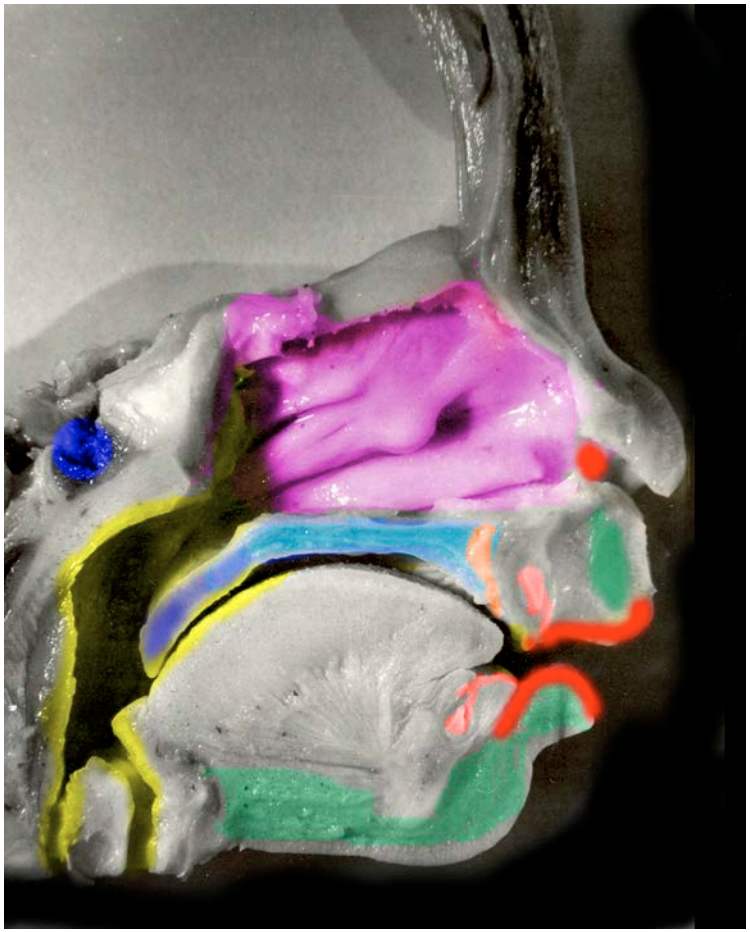
Unilateral cleft in a 22 mm embryo (8th week) related to the persistent plate of squamous multilayered epithelium interposed between the lateral and the medial portion of the nasal fold and between the maxillary primordium and the premaxilar portion of the nasal fold

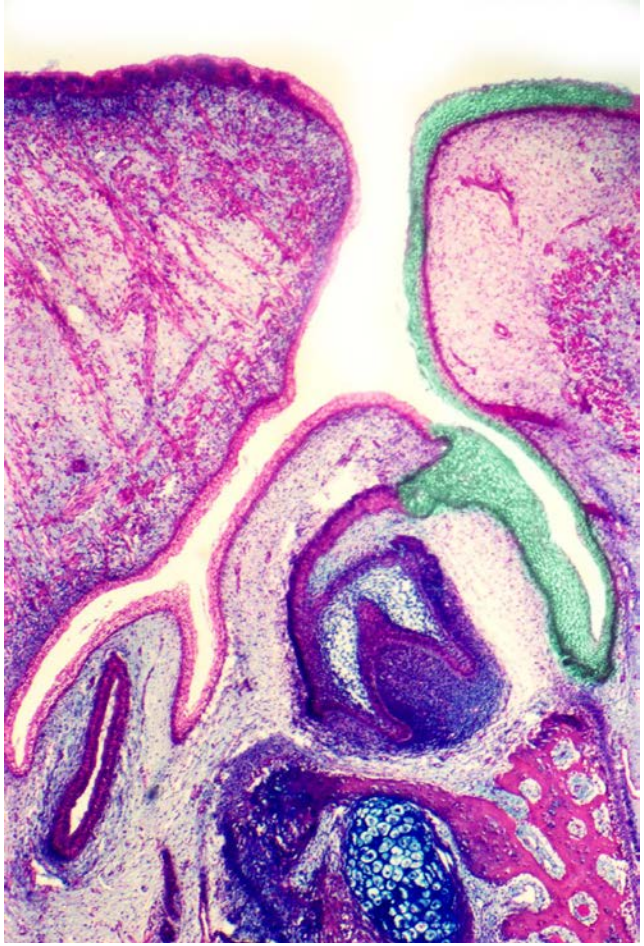




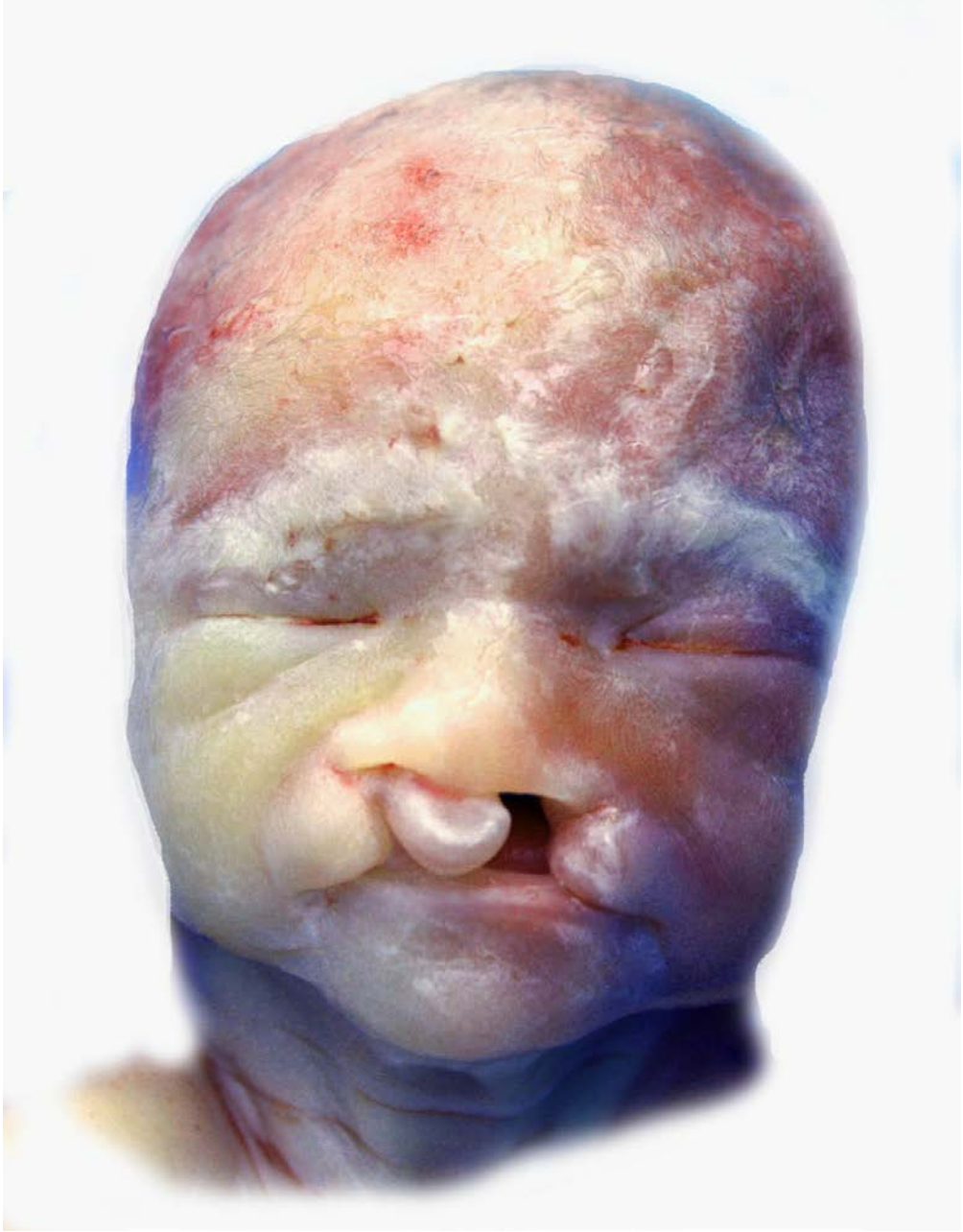


Uncompleted lateral cleft lip in a 18 weeks fetus with persistance of the hypertrophic multilayered squamose epithelium separating the premaxillar portion of the nasal fold and the maxillary primordim.

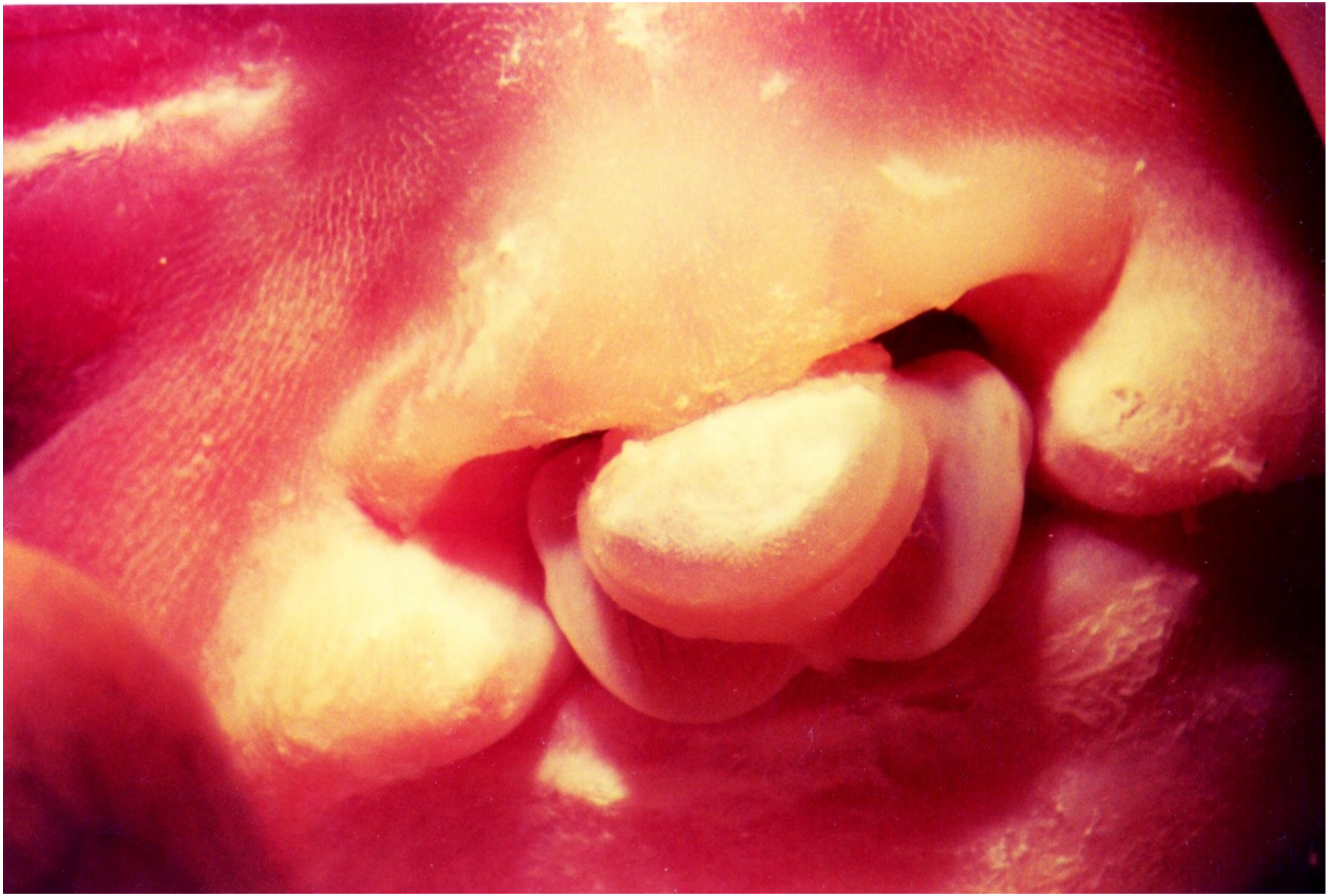




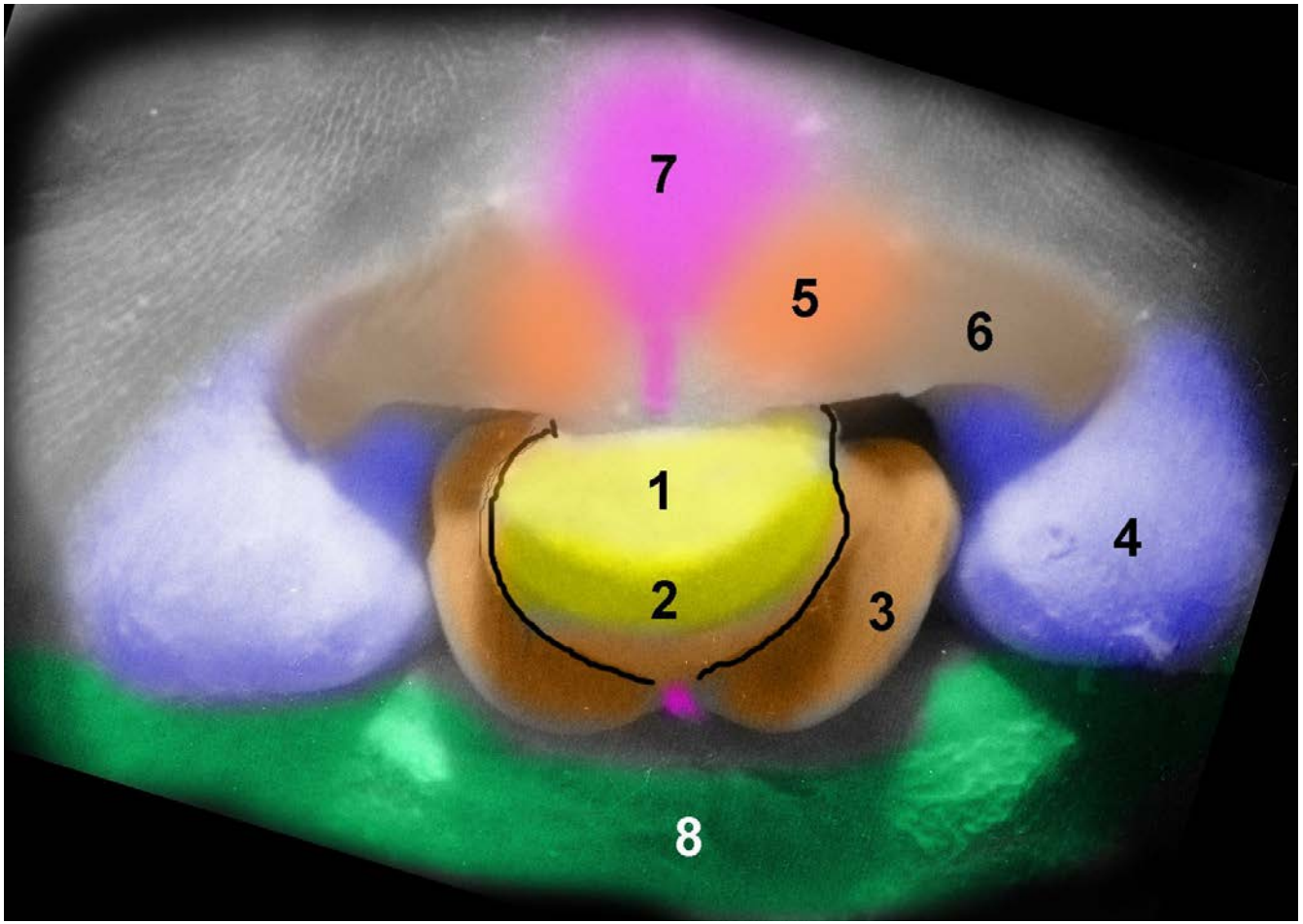
Sagital disection of the oral and nasal cavities of a 16th weeks fetus. The relations between the squamose multilayered epithelium of the skin of the nasal vestibulum and of the red skin of lips and of the mucose membrane of the oral vestibulum (the labiogingival lamela) are difficult to evaluace. The labiogingival lamela ends as the labiodental lamela giving rise to dental vesicles.



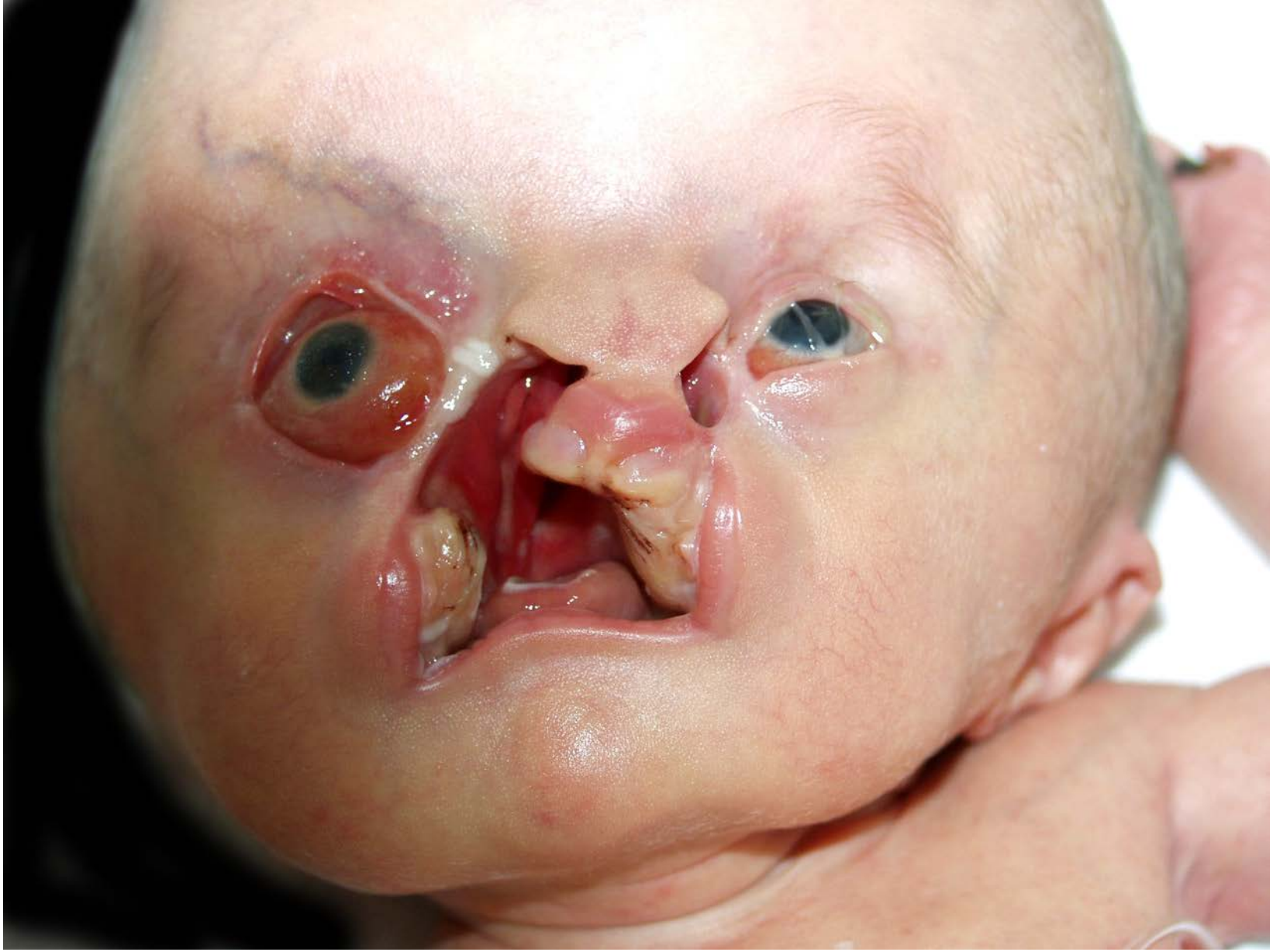
Bilateral cleft of the lip, jaw and palate complete on the left side, incomplete on the right side.



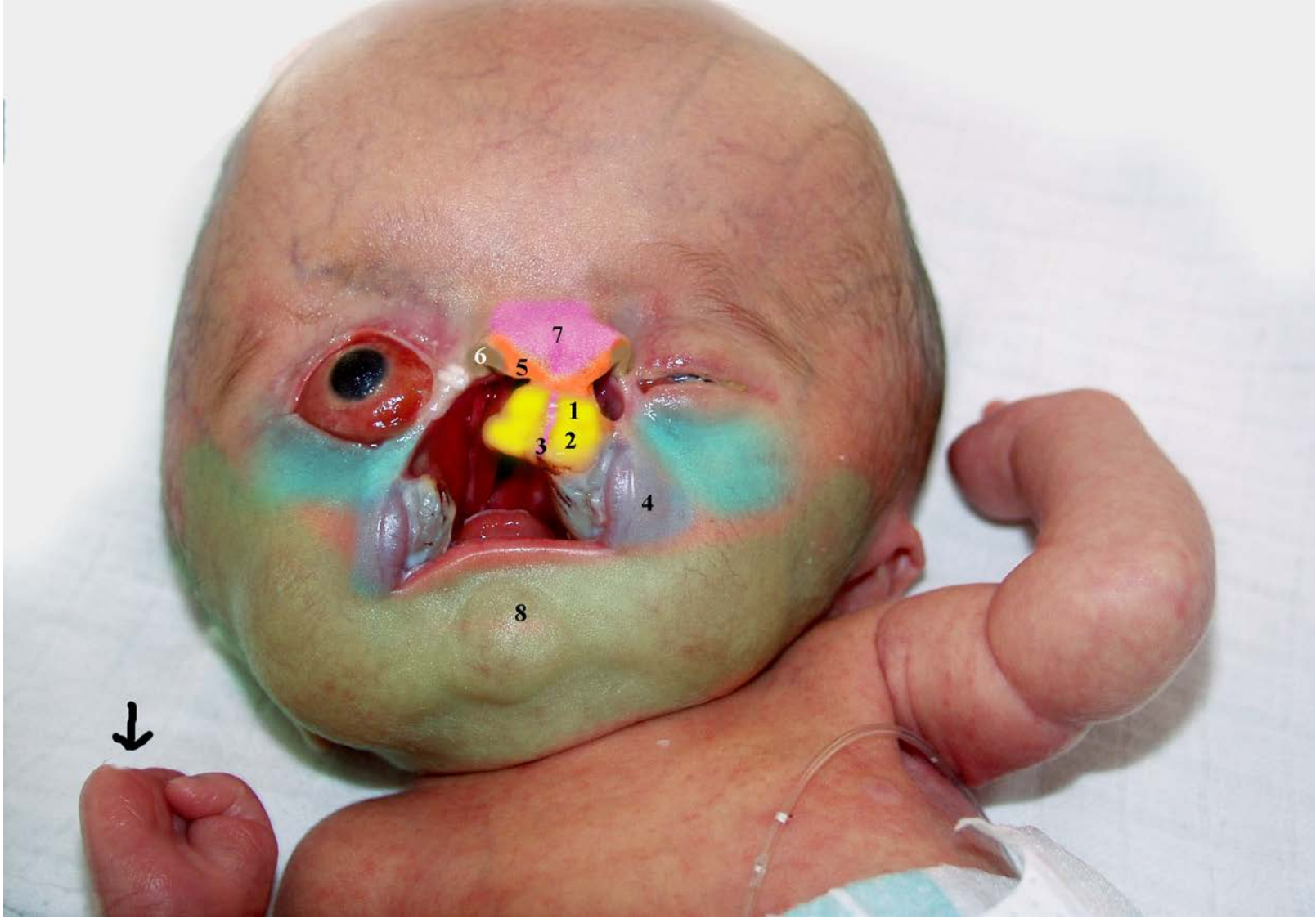
Bilateral complete clefts of the lip, jaw and palate.
The premaxilar portions of jaw and lips is isolated from the maxillar primordium



1 – skin of the philtrum, 2- red zone of the premaxillar portion,
3 – the zone of the premaxillar vestibulum, 4 – maxillar primordium
5 medial portion of the nasal fold, 6 lateral portion of the nasal fold,
7 – nasal tip contributed by nasal capsule, 8 – mandibular arch.
The purple dot is the primordium of the phrenulum of the philtrum.

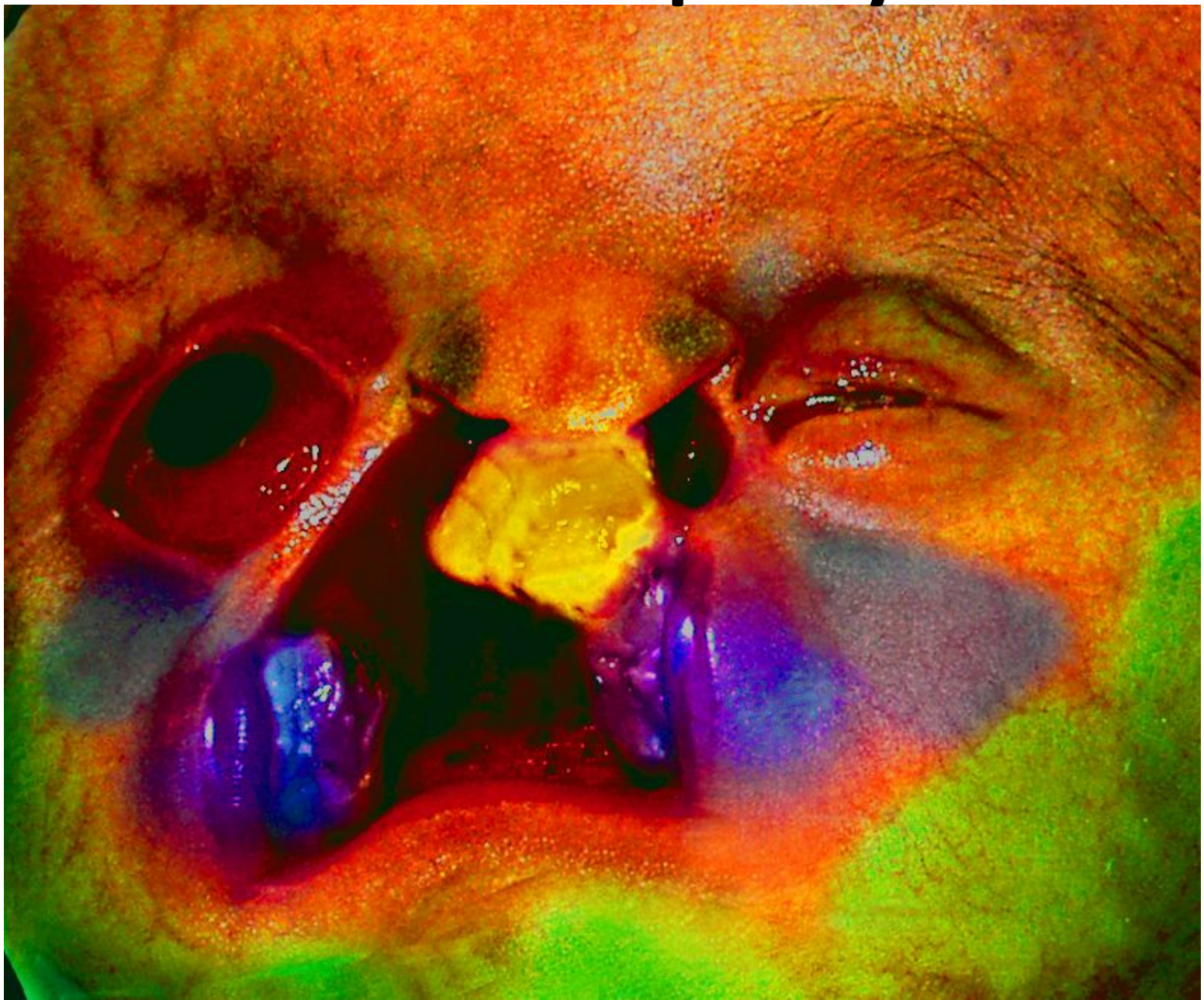


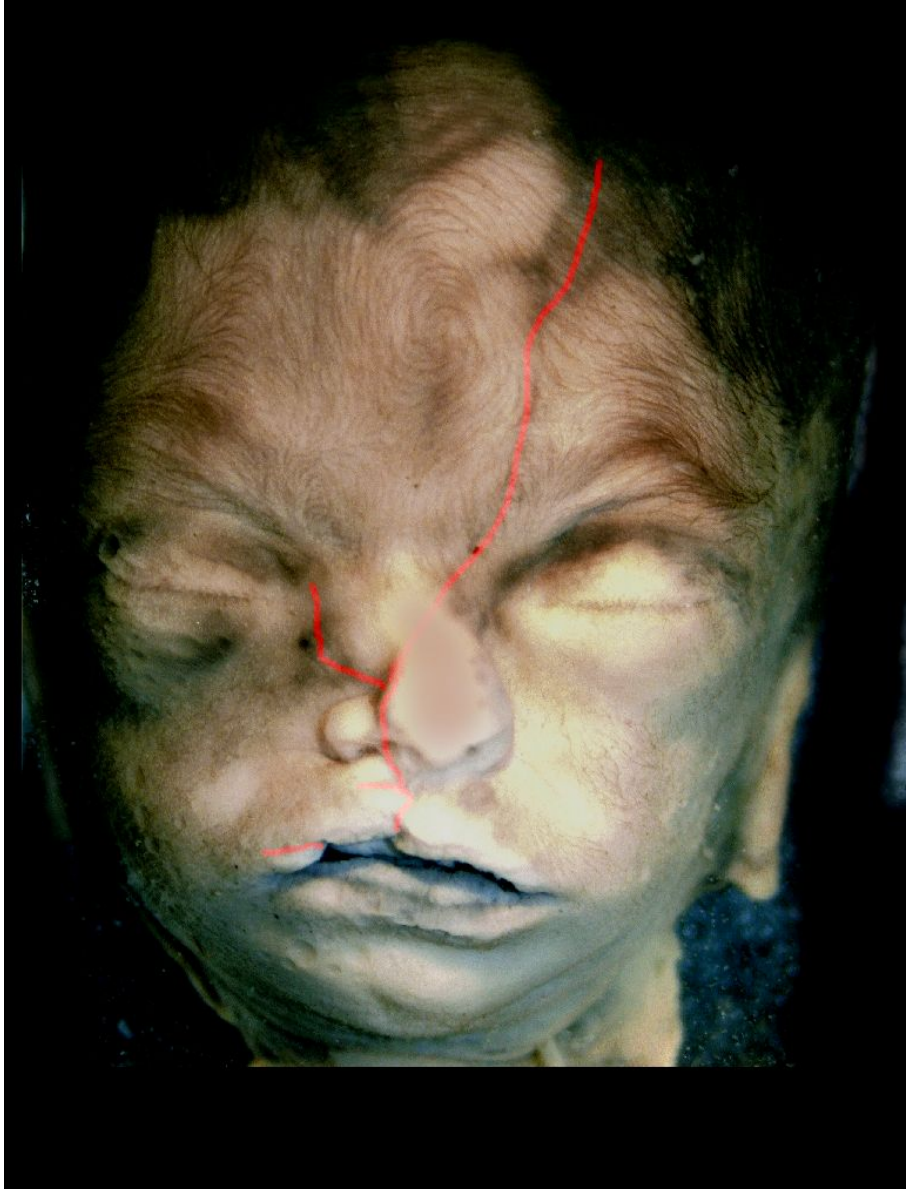
The combination of a bilateral oblique clefts (incomplete on the left side, complete on the right side) with a cleft lip, jaw and palate



1 – skin of the philtrum, 2- red zone of the premaxillar portion, 3 – the zone of the premaxillar vestibulum, 4 – maxillar primordium
5 medial portion of the nasal fold, 6 lateral portion of the nasal fold, 7 – nasal tip contributed by nasal capsule, 8 – mandibular arch.
The arrow turns attention to the absent fingers related to amputation by amnionic bands.

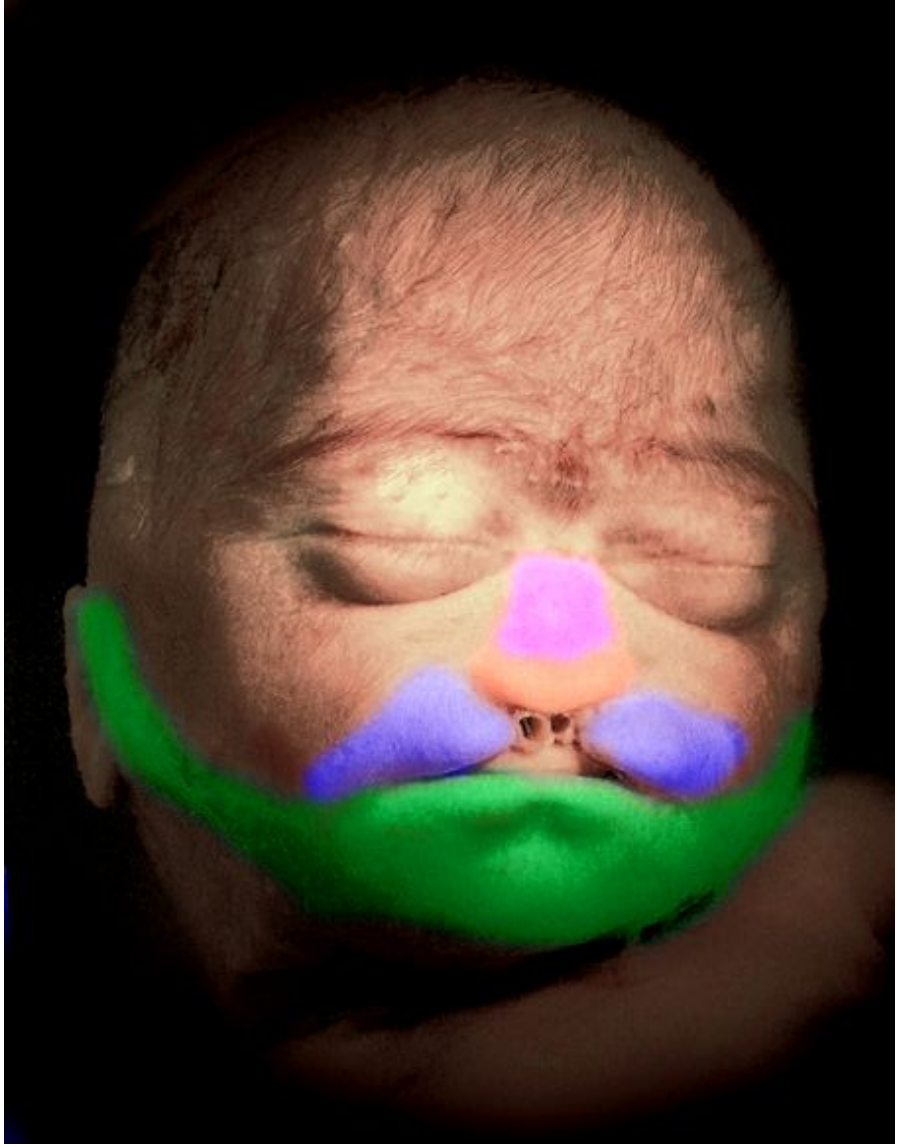
Think about the quality of life !





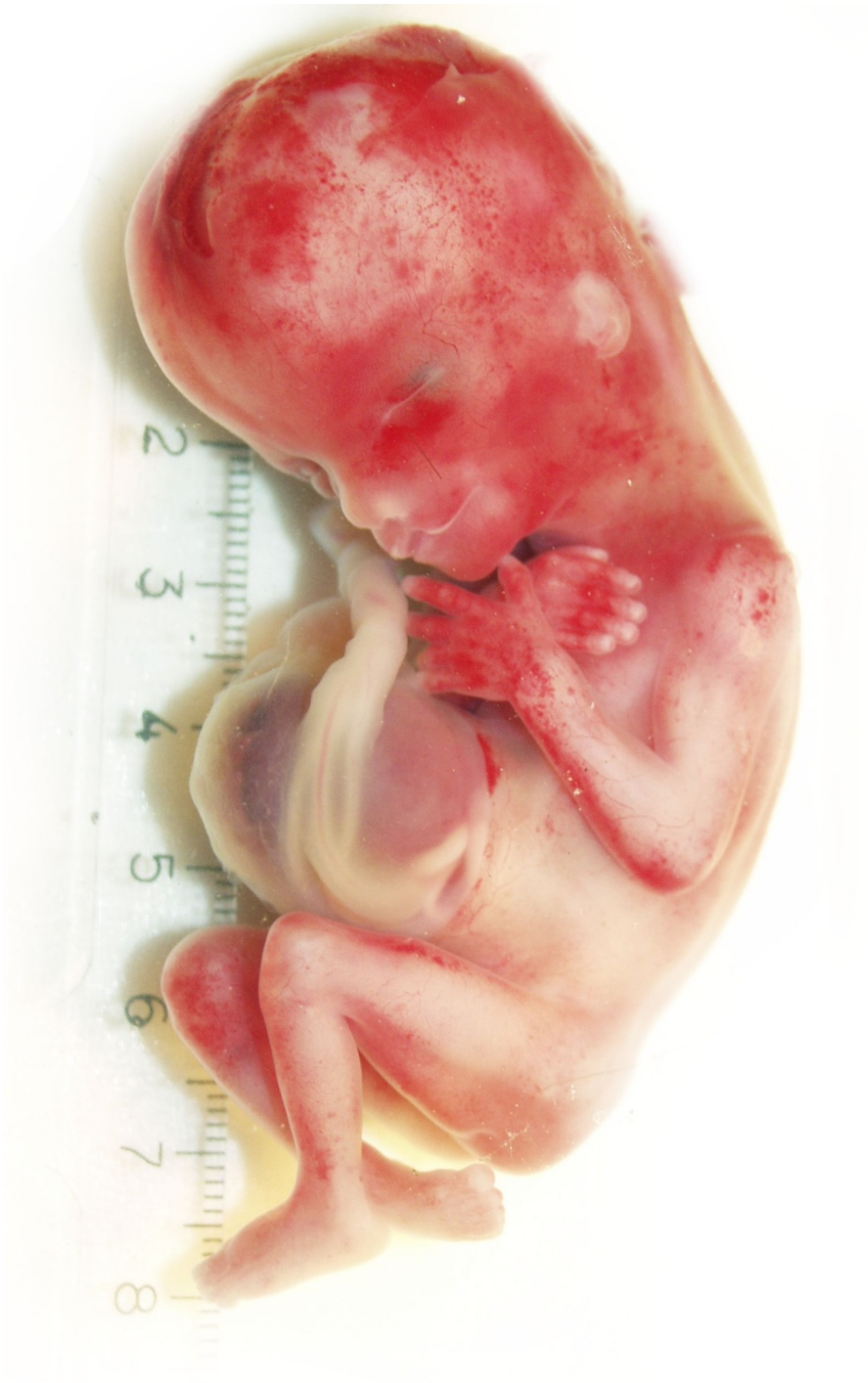
Plagiocephaly

Plagiocephaly is the assymetrical development of the face and scull resulting in most cases from multiple partially healed fractures after car injuries



Triploidy

The face of a triploid fetus from the 16th week. Premaxillar genesis (the widening of the dorsum of the nose is related to a frontal encephalocele and to the hypoplasia of the nasal capsule).



About 50 % of facial clefts are related to different syndromes with a prognosis very difficult to evaluate relating the quality of life.

Syndrom Backwit – Weedeman
cleft lip, omphalocele

Statistic and genes

The involved genes:

- No evidence of any gene crutial for Mendelian inheritance. Some of suspect genes are related to the sonic hadgehog and lateralization of paired structures
- The microdeletion of chromosome 22q11.2(velocardial syndrom, DiGeorge syndrome, OFC 1,2,3 – 6p23-24, 2q13, 19q13.2 and loci on 4q25-4q31.3, 17q21
- Frequency: 60 - 80 % males
- Isolated cleft lip: 21 %
- CL/CP: 46 %
- Isolated cleft palate (CP): 33 %
- Unilateral clefts : left to right = 2 : 1
- Unilateral cleft : bilateral cleft = 9 : 1
- Unilateral cleft and palatinal cleft: 68 %
- Bilateral cleft lip with palate cleft: 86%

Conclusion:

- **Facial clefting may occure in association with every maformation syndrome**

Clefts: isolated – 50%
syndromic
Recurence risks

Nonsyndromic risk for CL,CP

- unaffected parent
  - no affected child – 0.1 % = general risk
  - one affected child – 4%
  - two affected children – 14 %
- one affected parent
  - no affected child – 4 %
  - one affected child – 12%
  - two affected children – 25 %
- two affected parents
  - no affected child – 35 %
  - one affected child – 45 %
  - two affected children – 50 %

Recurence risk for nonsyndromic CP

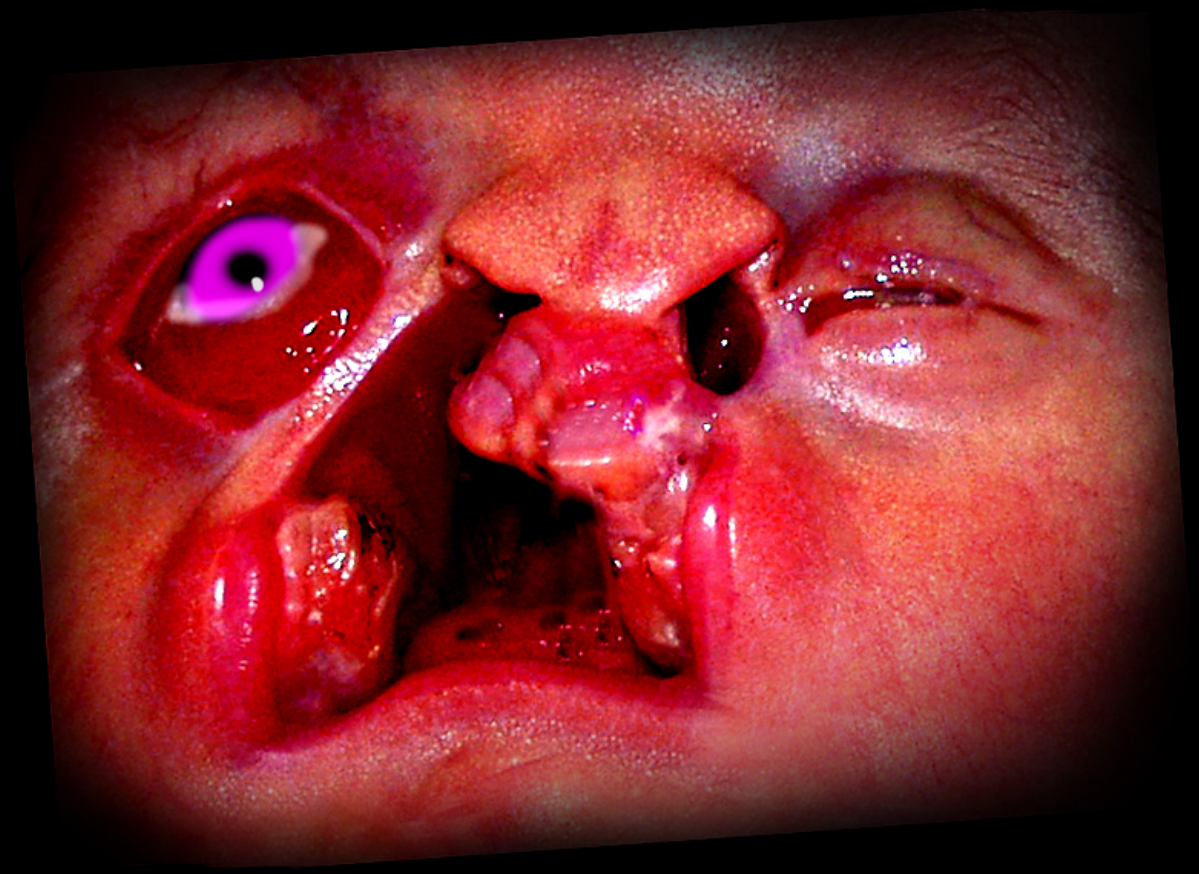
- unaffected parent
  - no affected child – 0.4 % = general risk
  - one affected child – 3.5 %
  - two affected children – 13 %
- one affected parent
  - no affected child – 3.5 %
  - one affected child – 10%
  - two affected children – 24 %
- two affected parents
  - no affected child – 2.5 %
  - one affected child – 40 %
  - two affected children – 45 %

Recurence in syndromes

- a) AD – Apert syndrom
- b) AR – S-L-O syndrome
- c) X-linked – OPD (oto-palato-digital syndrome)
- d) Chromosomal – T13

What is the final solution ?

- Possibility of survival
- Possibilities of therapy versus pregnancy termination
- Quality of life
- Costs related to care and treatment



HELP

WHY

ABORTION?