Congenital malformations

Congenital malformations or birth defects represent alterations in the structure and function of the organ systems of the newborn. The malformation occurs in intrauterine life and is identified before, at or later after birth. Congenital malformations account for a significant cause of perinatal mortality and morbidity. Their causes can be categorized into 1) chromosomal abnormalities, 2) separation abnormalities of the zygote, 3) abnormalities encountered in early pregnancy, and 4) unknown etiology. Representative features of congenital malformations are briefly summarized herein.

Ref: Chimah OU, et al. Congenital malformations: prevalence and characteristics of newborns admitted into Federal Medical Center, Asaba. Health Sci Rep 2022; 5(3): e599. doi: 10.1002/hsr2.599

Congenital malformations

- **Chromosomal abnormalities**
- **Separation abnormalities of the zygote**

  Conjoined twins (Siamese twins)

  Epignathus (mature teratoma of the oropharynx)
- **Abnormalities encountered in early pregnancy**

  Rubella virus infection (congenital rubella syndrome)

  TORCH syndrome (Toxoplasma, Others, Rubella, CMV and HSV)

  Parvovirus B19 infection (hydrops fetalis following erythema infectiosum)

  Irradiation

  Drug use (thalidomide, hormonal medicines, lithium carbonate, anticonvulsants)

  Methylmercury intoxication (congenital Minamata disease)

  Folate deficiency (neural tube defects, anencephaly)
- **Unknown etiology**

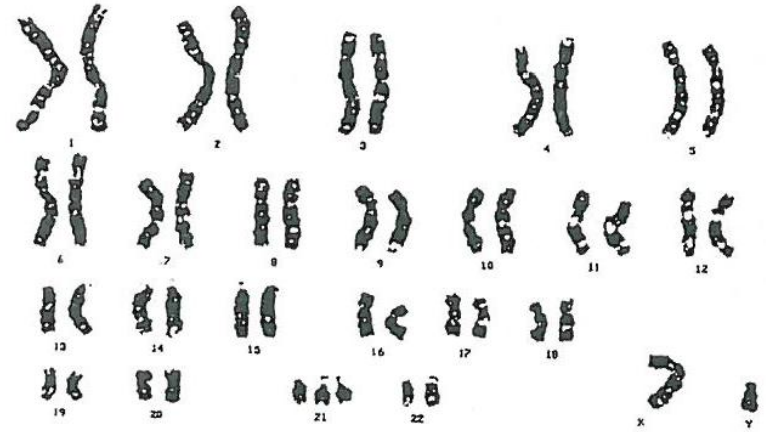
  Cardiac anomaly, urogenital malformation, digestive tract malformation, etc.

  (The etiology of most congenital malformations remains unknown)

  Residues of fetal structures: Meckel's diverticulum, urachal remnant, thyroglossal duct remnant, etc.

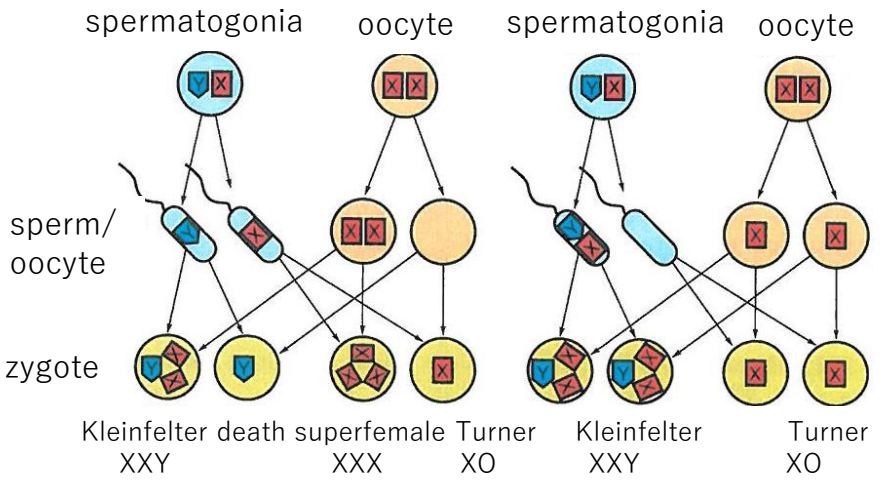
Chromosomal abnormalities

- **Autosomal abnormality**
  1) Down syndrome　(21 trisomy)
  2) Edwards syndrome (18 trisomy)
  3) Patau syndrome (13=D1 trisomy)
  4) crying cat syndrome (5p deletion)

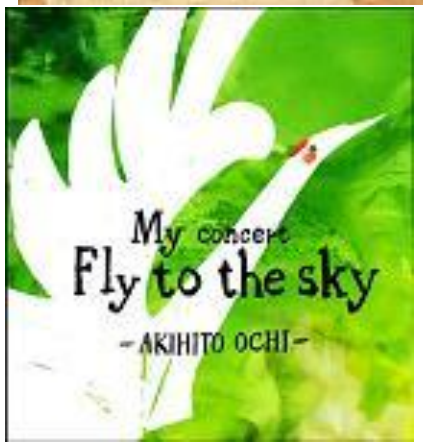


Karyotype of Down syndrome

- **Sex chromosome abnormality**
  1) Kleinfelter syndrome (XXY)
  2) Turner syndrome (XO)
  3) XYY syndrome
  4) XXX syndrome (superfemale)



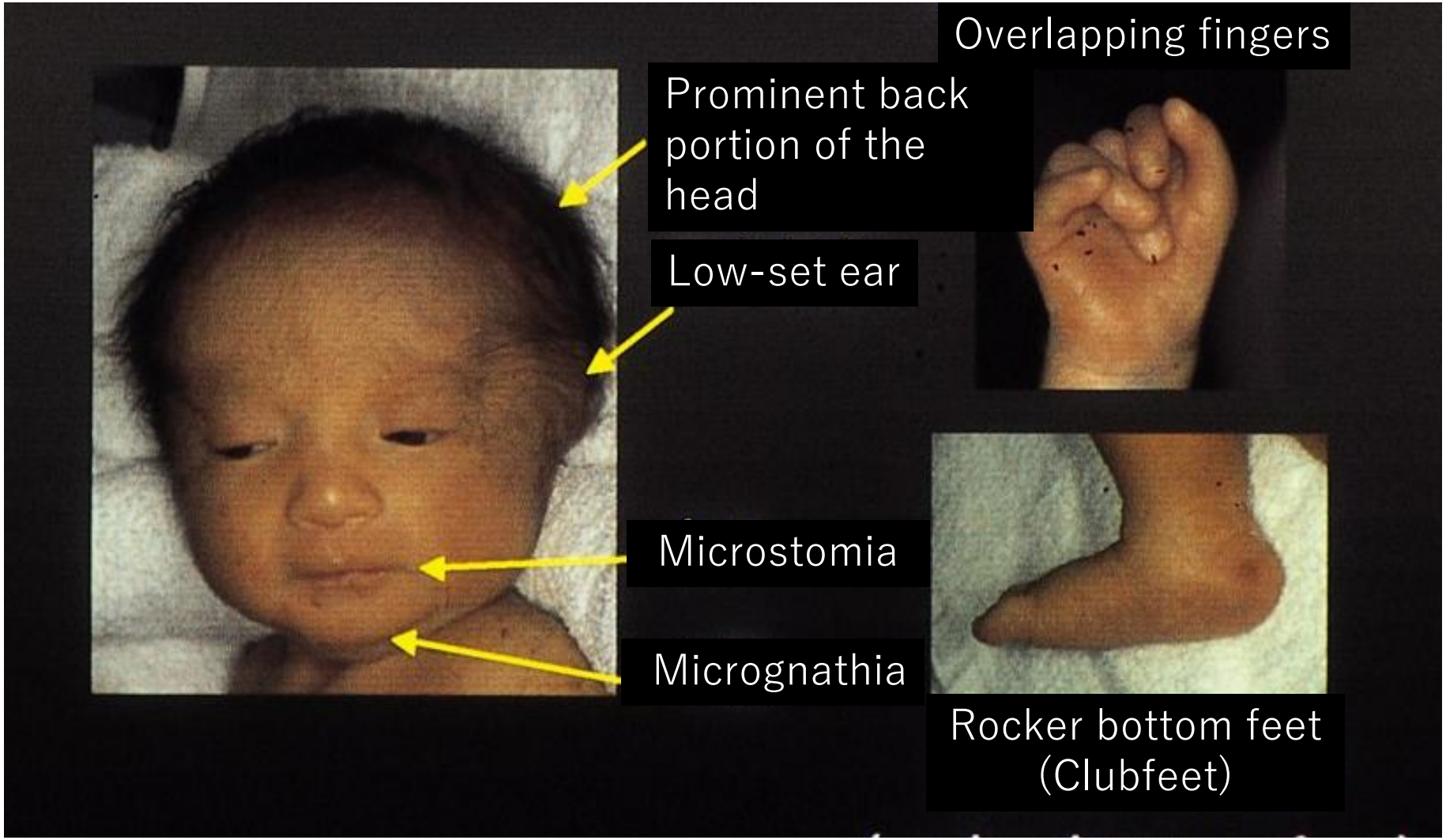
Nondisjunction of sex chromosomes



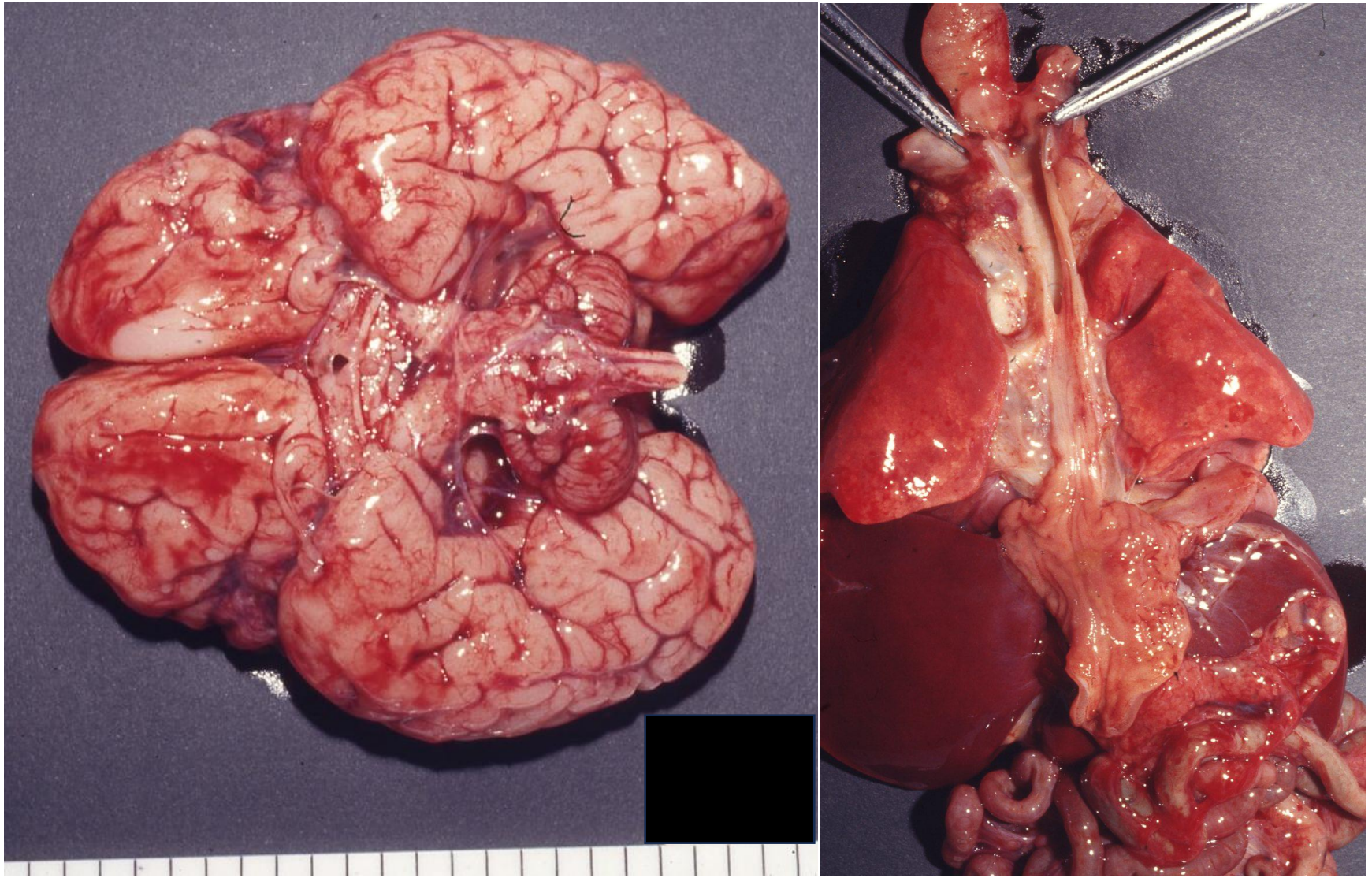
Down syndrome pianist Mr. Akihito Ochi (越智章仁)
～a heartful pianist releasing 4 CDs～

Hematopoietic disorders in Down syndrome

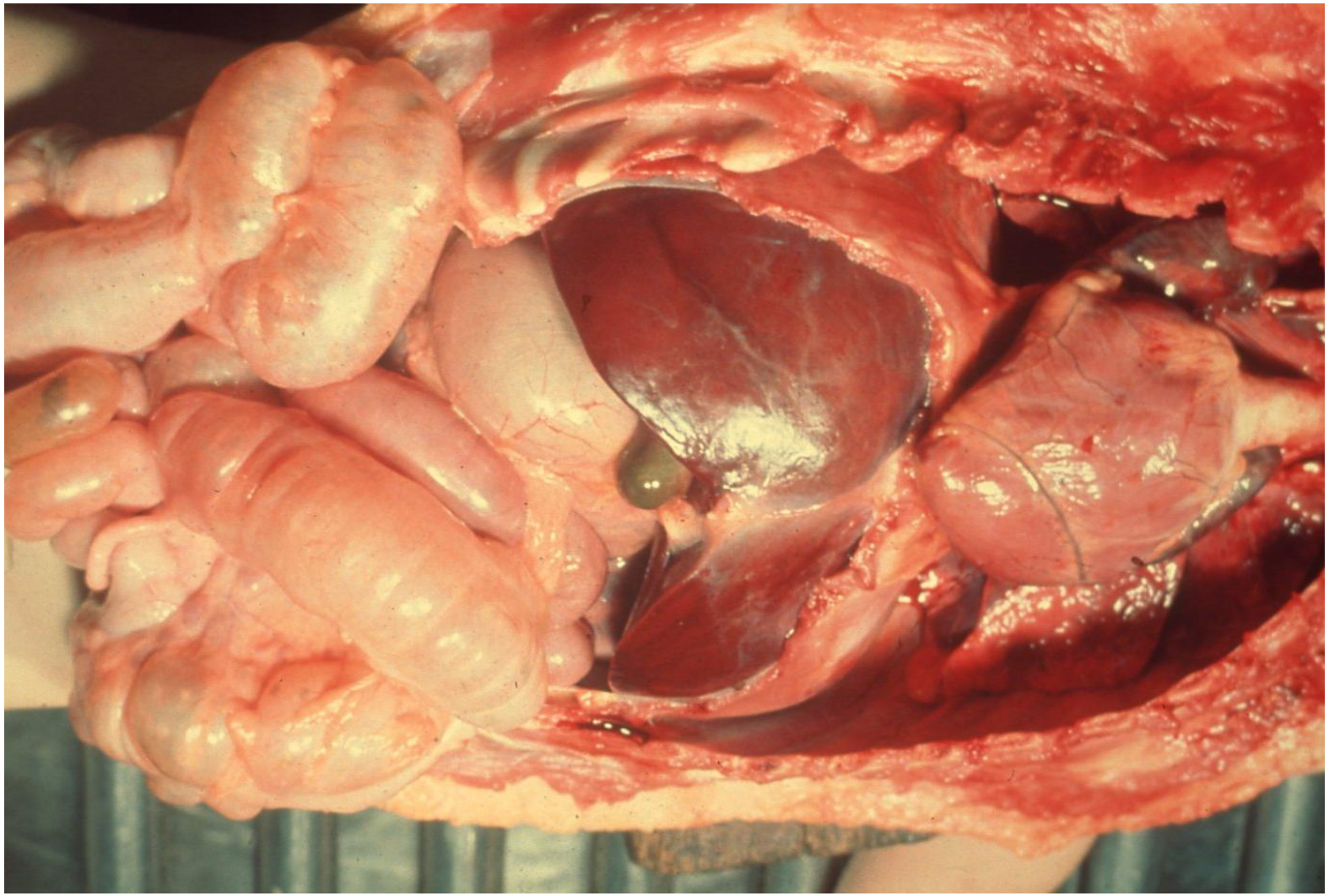
Transient abnormal myelopoiesis (TAM)
Acute megakaryoblastic leukemia with hepatic fibrosis



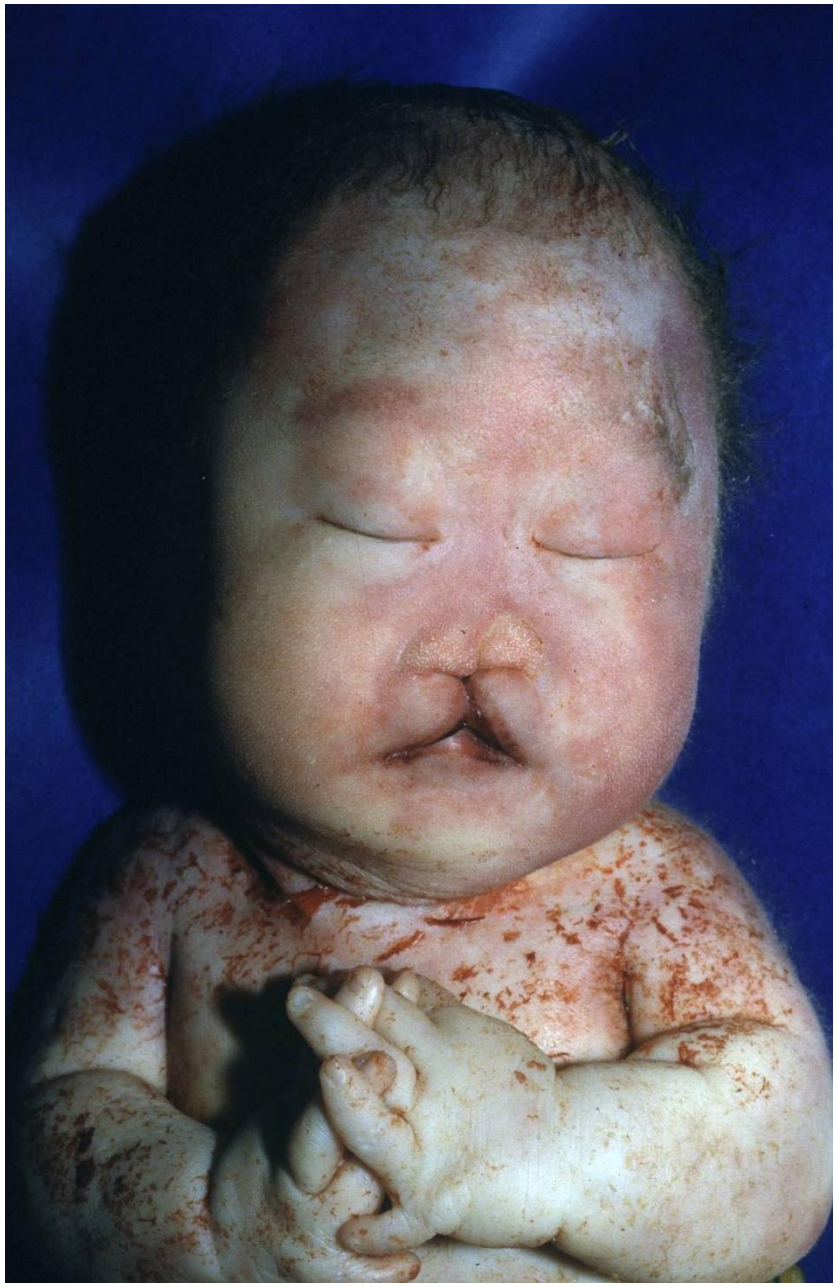
18 trisomy (Edwards syndrome)

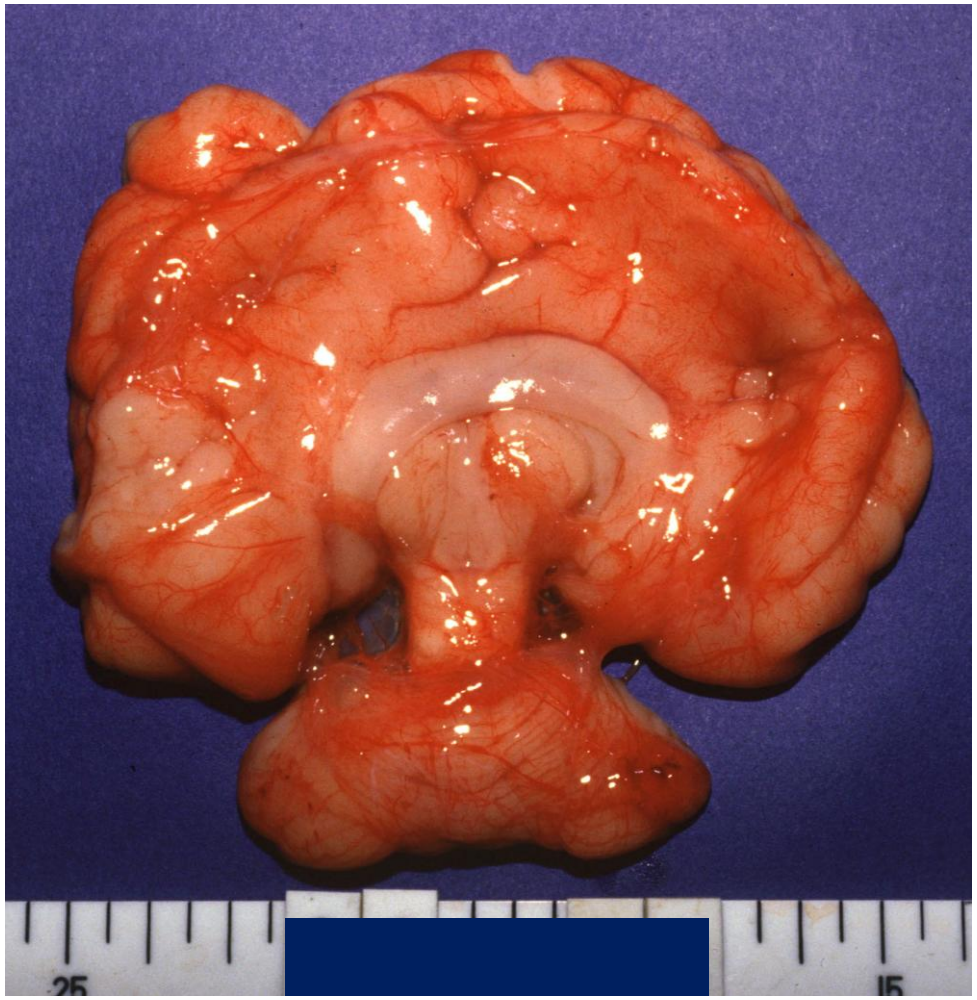


18 trisomy (Edwards syndrome) accompanying cerebellar hypoplasia (left) and esophageal atresia with connection to the trachea (right).



18 trisomy (Edwards syndrome) accompanying **asplenia syndrome** with situs ambiguous (right-isomerism). Note the symmetrical liver with centrally located gallbladder, malrotation of the intestine and truncus arteriosus (a single large blood vessel emerging from the heart).

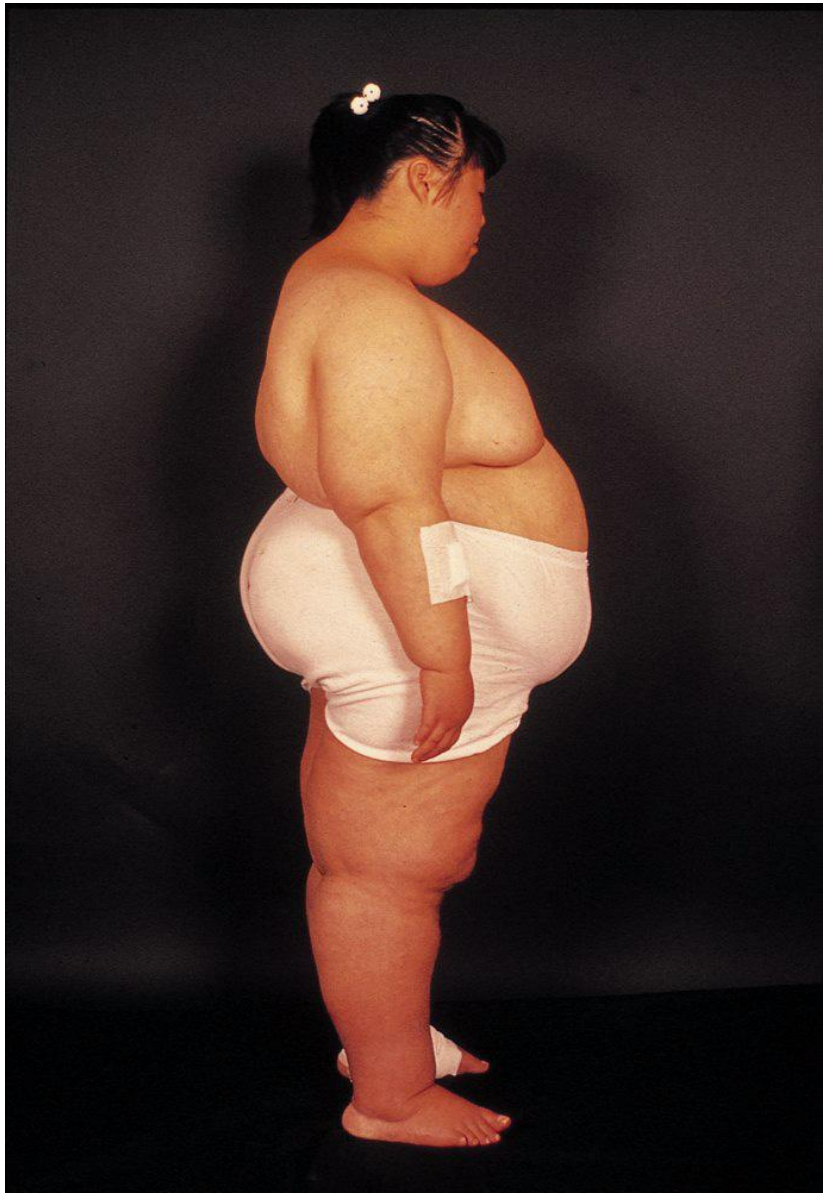




13（D1） trisomy

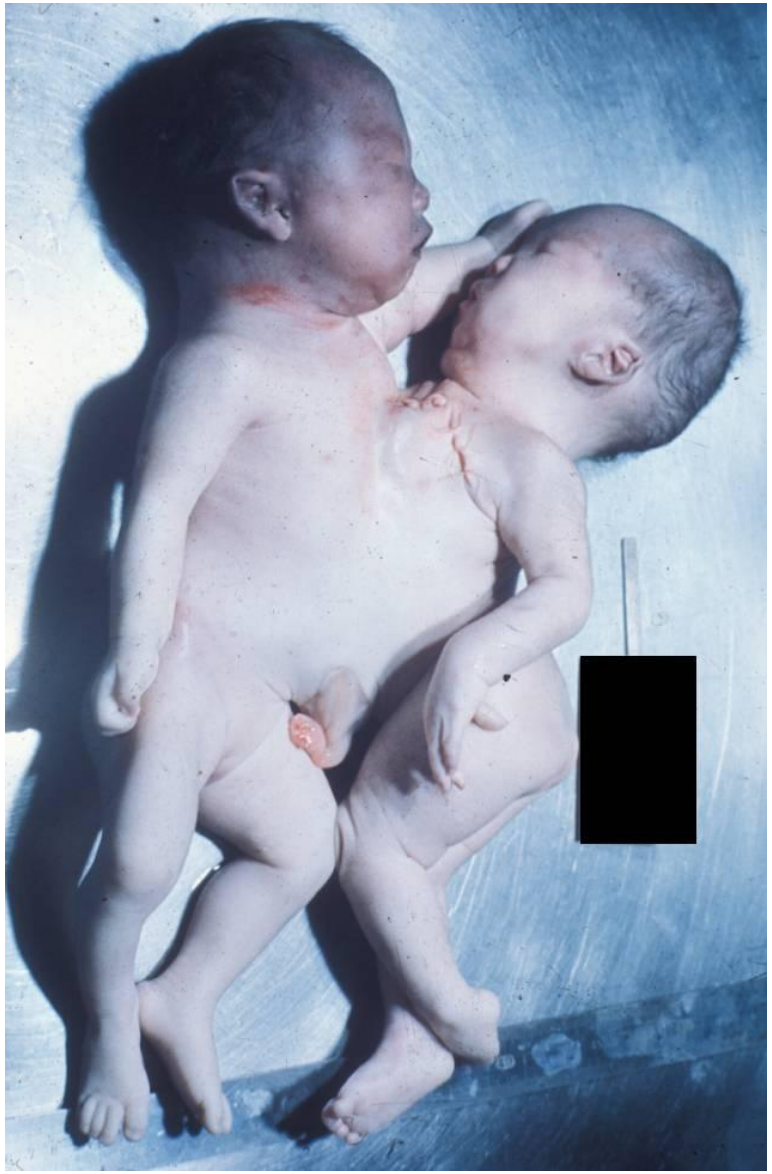
left: cleft lip and palate

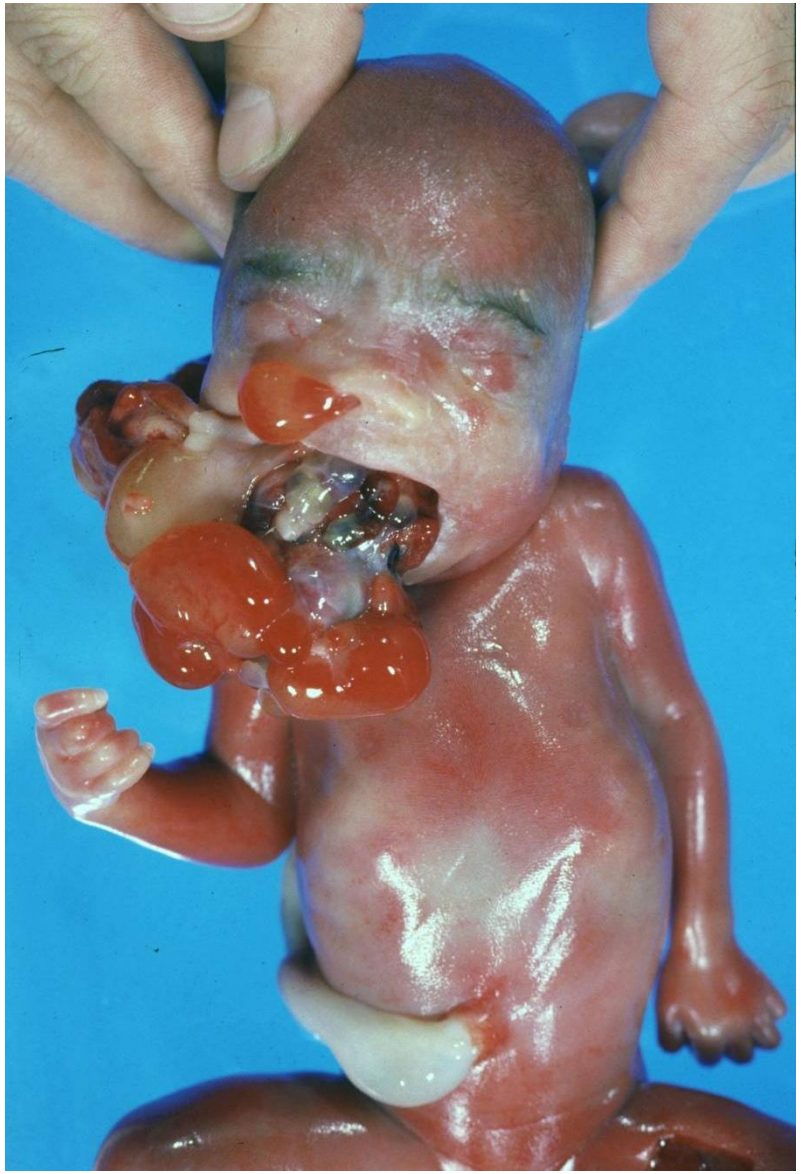
right: holoprosencephaly



Pradder-Willi syndrome (PWS) occurs when part of the father's chromosome 15 is deleted. Another mechanism is that the patient has two copies of the maternal chromosome 15 and lacks the paternal copy. Parts of the chromosome from the mother are turned off through imprinting, they end up with no working copies of certain genes. PWS is related to an epigenetic phenomenon known as imprinting. Due to imprinting, the maternally inherited copies of PW genes (SNRPN and NDN genes) are virtually silent, and the individual relies on the expression of the paternal copies of the genes. In PWS with deletion of the paternal copies of PW genes, functioning PW genes are lacking.

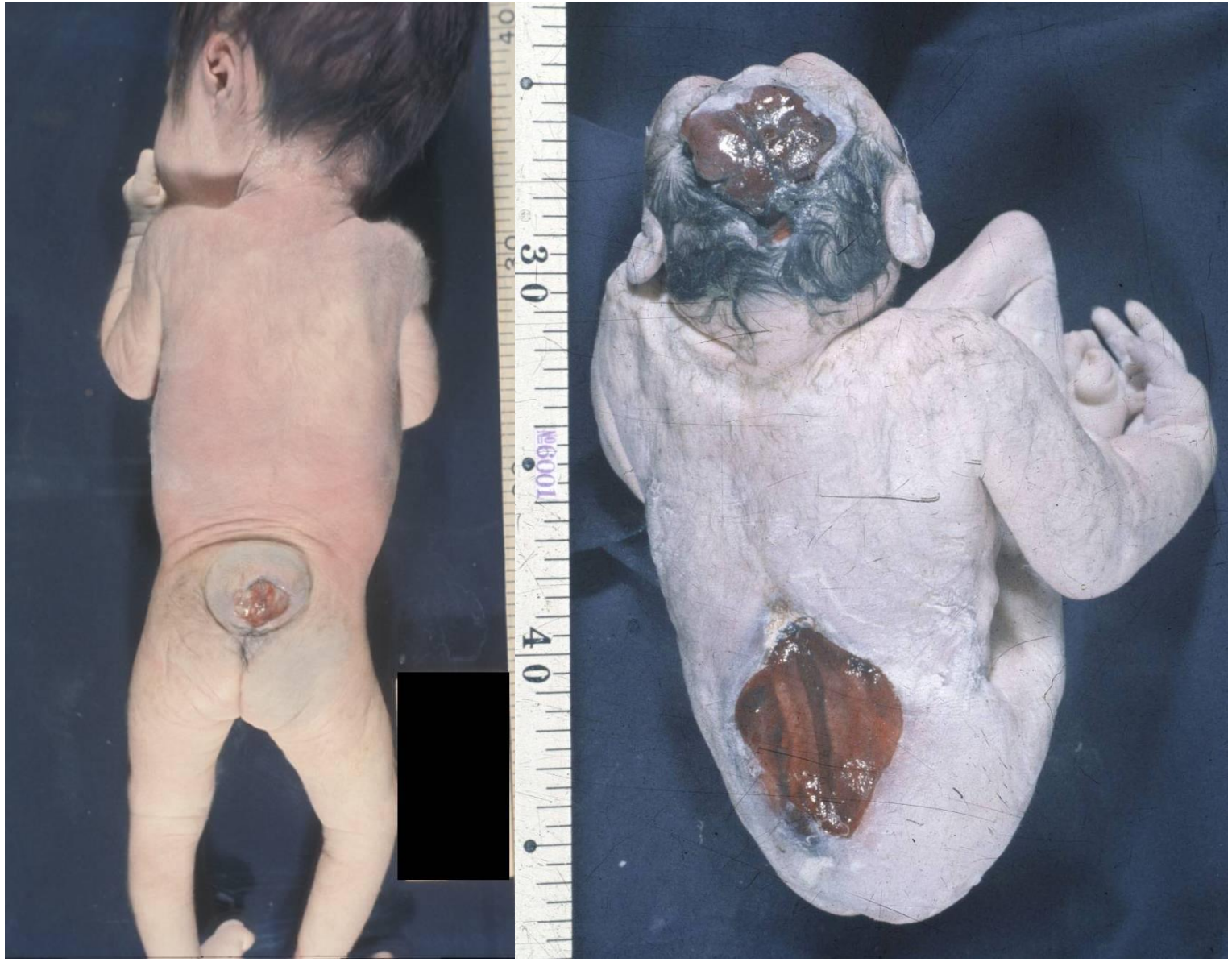
Prader-Willi syndrome caused by partial deletion of chromosome 15. Manifestations include muscular hypotonia, hypogonadism, hypomentia (intellectual impairment) and severe obesity (HHHO syndrome). The disease is not generally inherited.



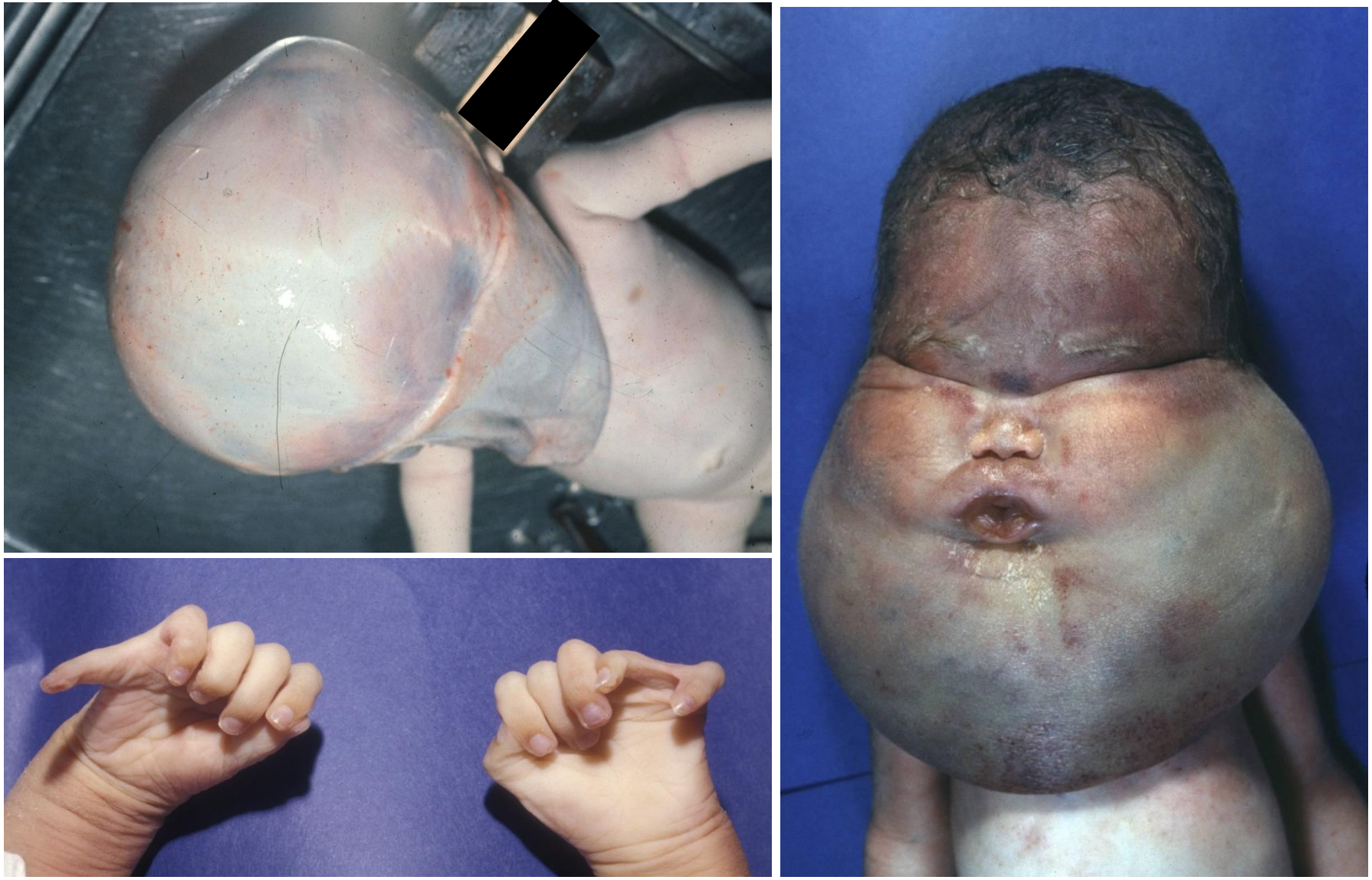


Separation abnormalities of the zygote

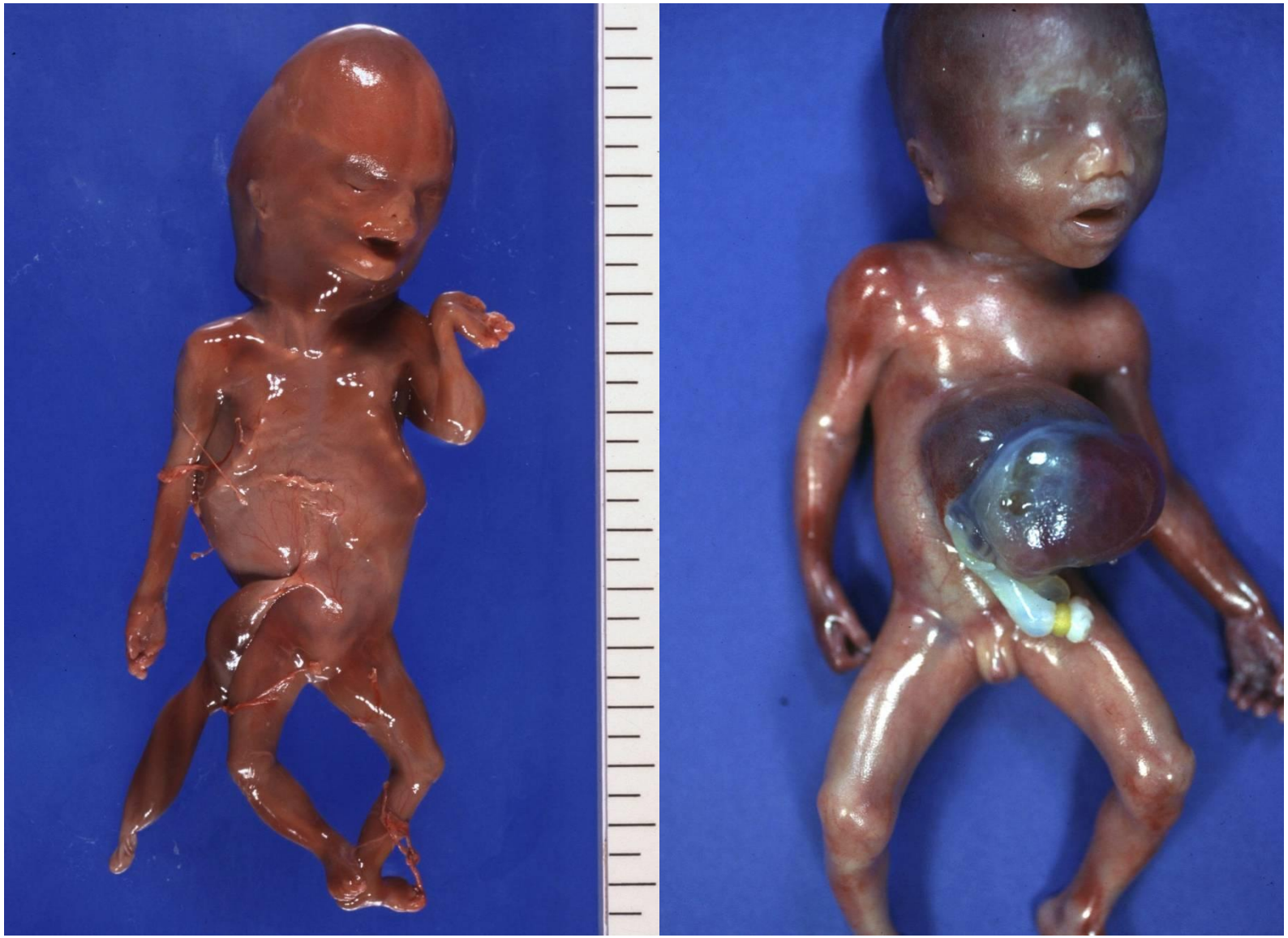
Left: conjoined twins (thoracopagus), right: epignathus



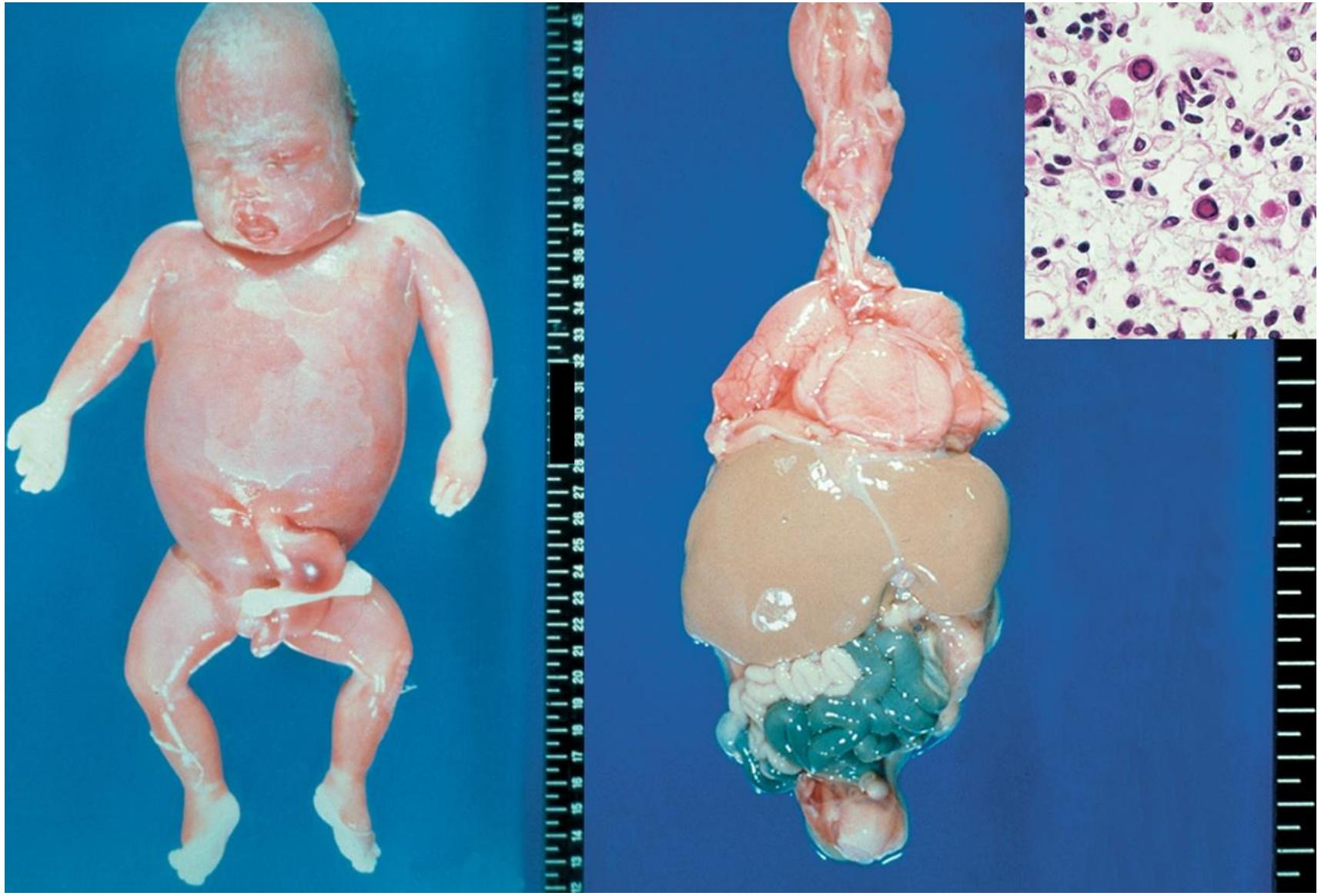
Congenital anomaly (neural tube defects caused by folate deficiency)
Left: spina bifida (meningocele), right: anencephaly plus spina bifida



Congenital anomalies. Left top: congenital hydrocephalus, left bottom: polydactyly, right: cystic hygroma (congenital lymphangioma)



Congenital anomalies. Left: umbilical stenosis, right: umbilical hernia



Hydrops fetalis caused by parvovirus B19 infection (at the 25th gestational week, weighing 1,010 g). The mother contracted erythema infectiosum at the 10th week of gestation. left: hydrops fetalis in a macerated fetus, right: gross appearance of internal organs: Note the anemic color of the liver. Inset: eosinophilic nuclear inclusions in the nucleated red blood cells in the fetal lung (H&E). Severe anemia has caused systemic edema.

Congenital anomalies in the digestive tract

Cleft lip and palate

Bochdalek-type diaphragmatic hernia

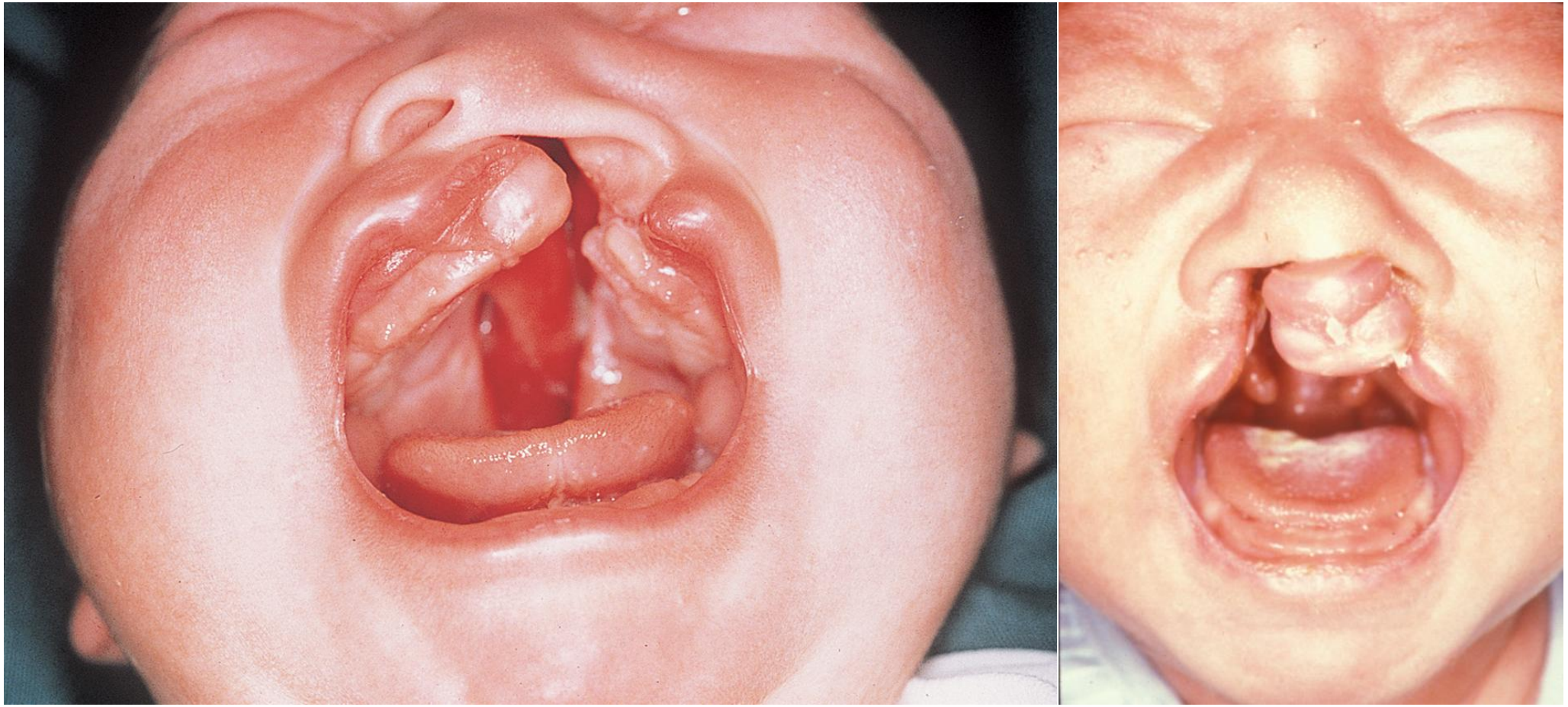
Congenital atresia of the digestive tract
(esophageal atresia, duodenal atresia)

Meckel's diverticulum

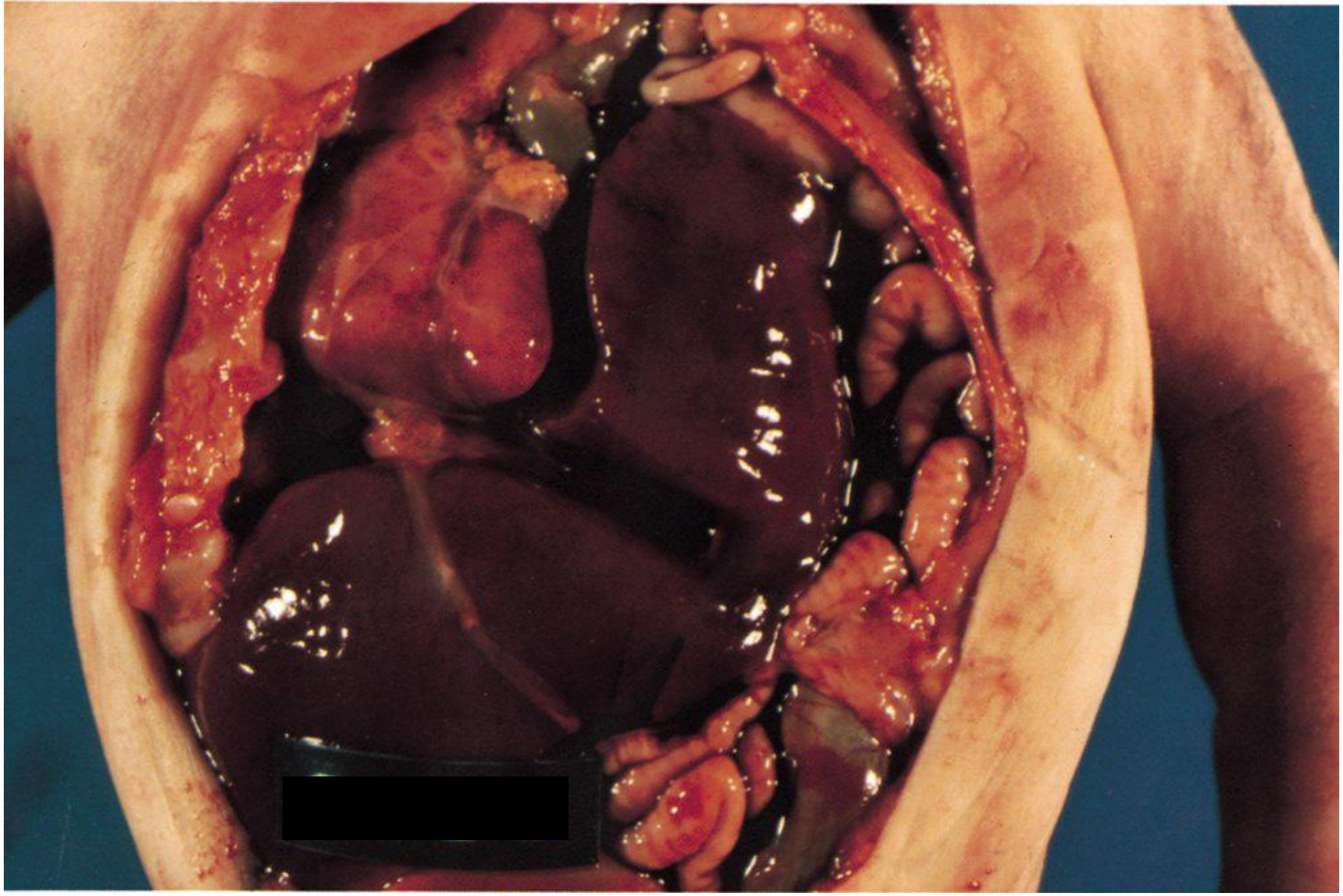
Hirschsprung disease

Anal atresia (imperforate anus)

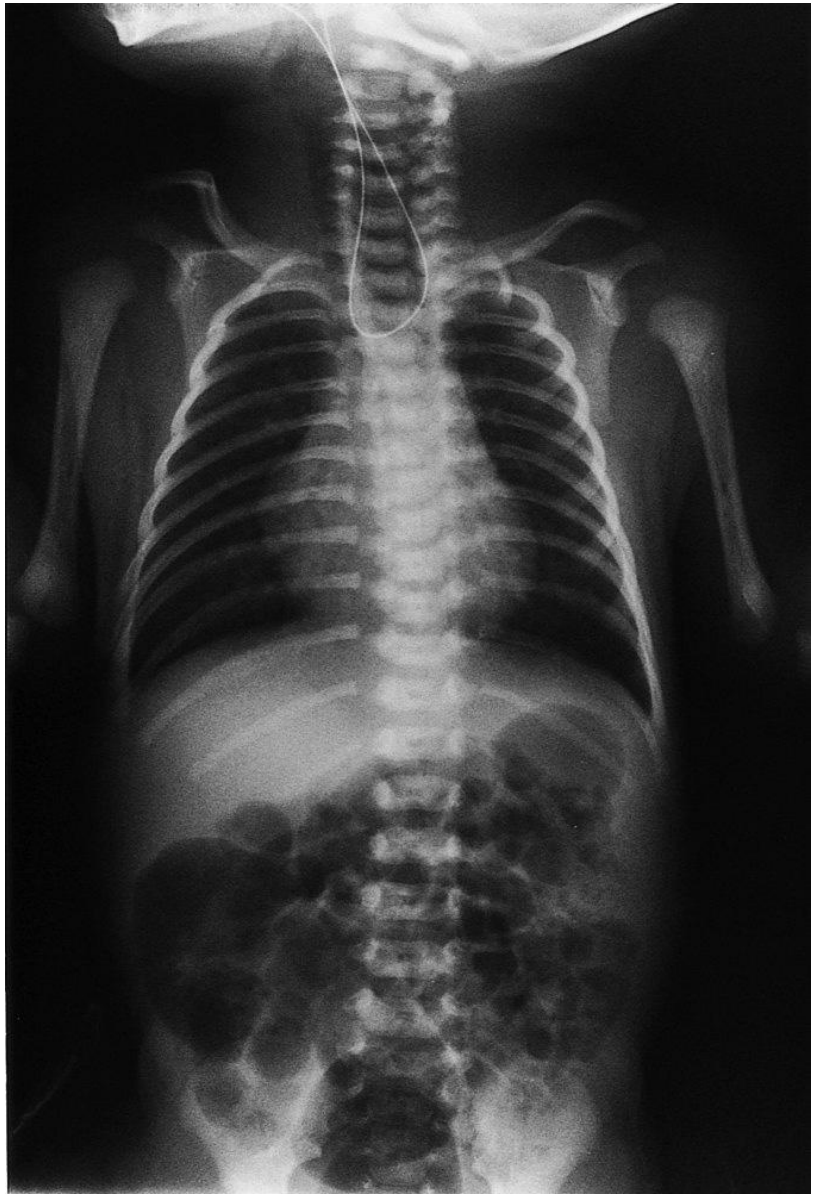
Biliary atresia (postnatal inflammation causes atresia of the extrahepatic bile ducts)



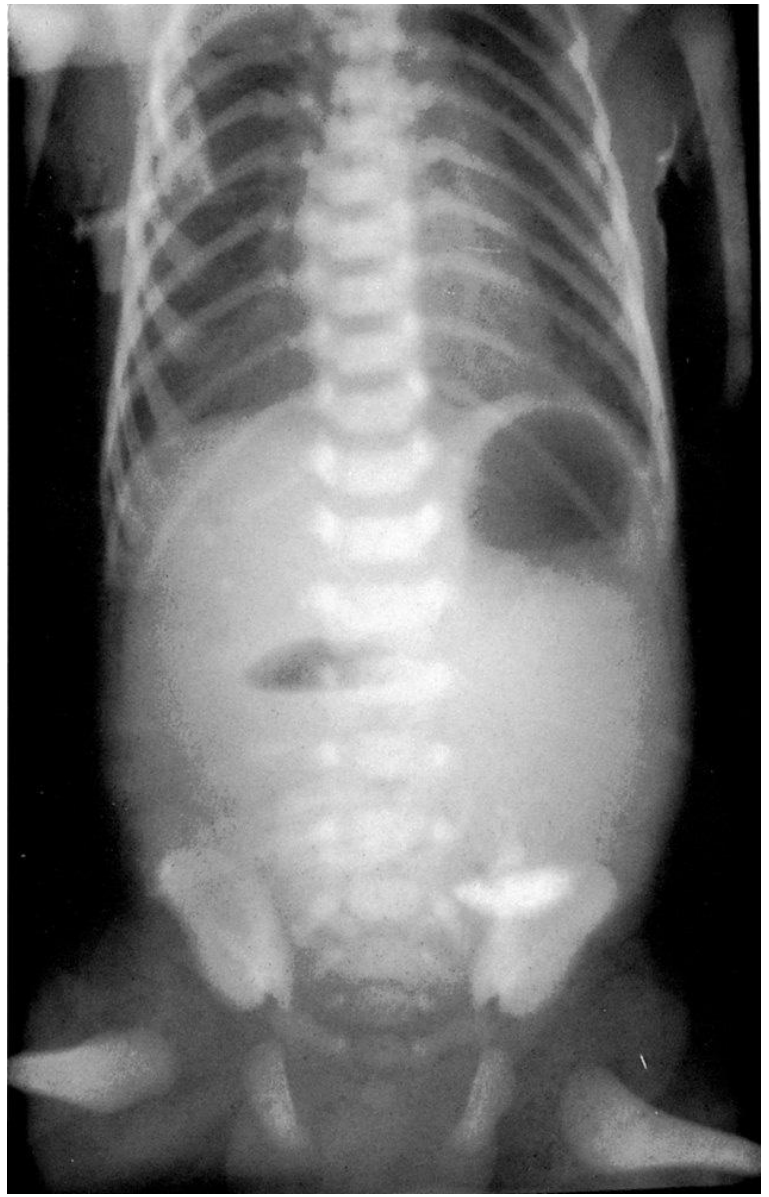
Cleft lip and palate (**orofacial cleft**) of a newborn. Many clefts run in families, and genes involved in cleft formation have been reported, including cleft lip and palate transmembrane protein-1, GAD1 and HYAL2.



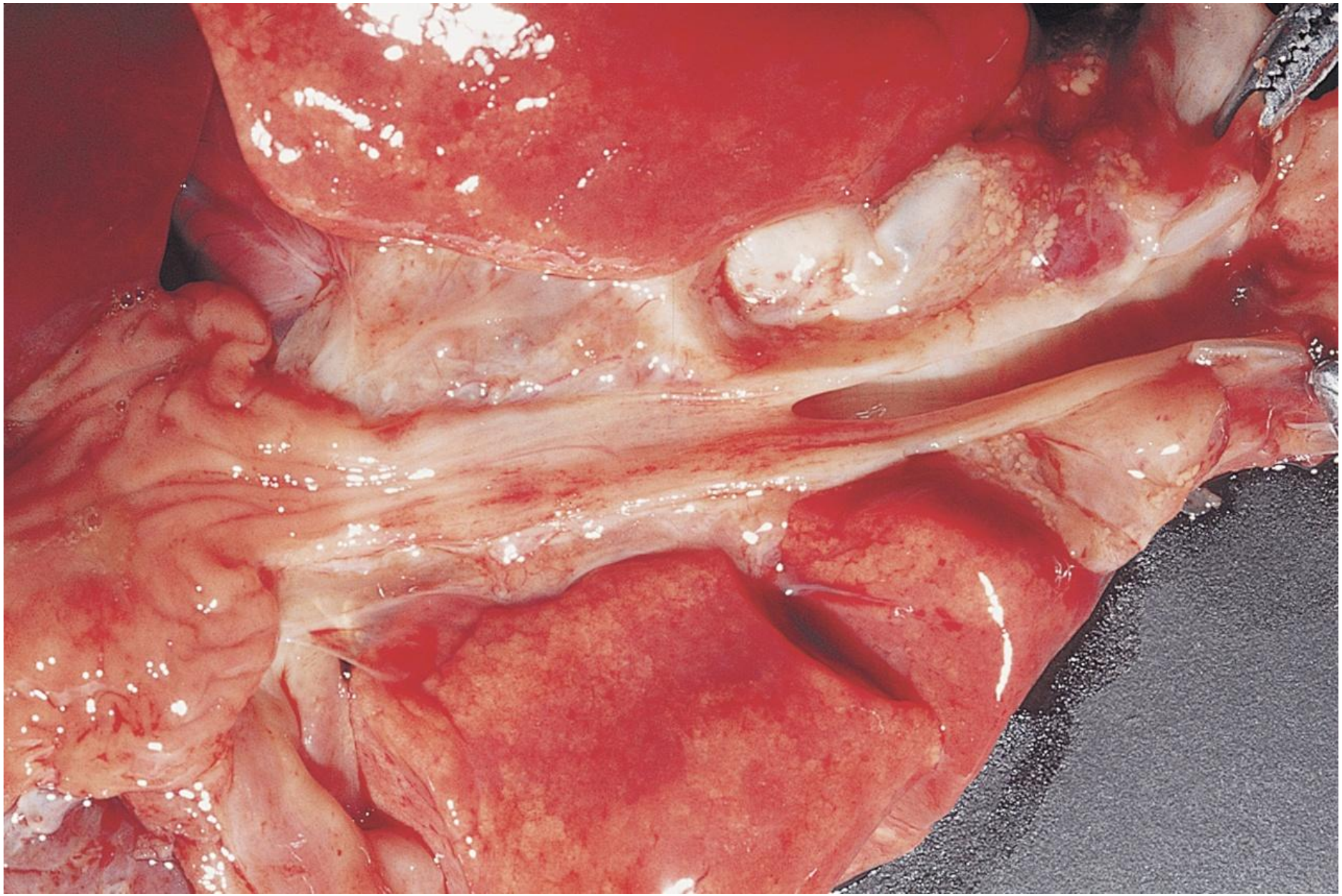
Bochdalek-type diaphragmatic hernia. At autopsy, the left lobe of the liver and intestine are herniated into the left pleural cavity.



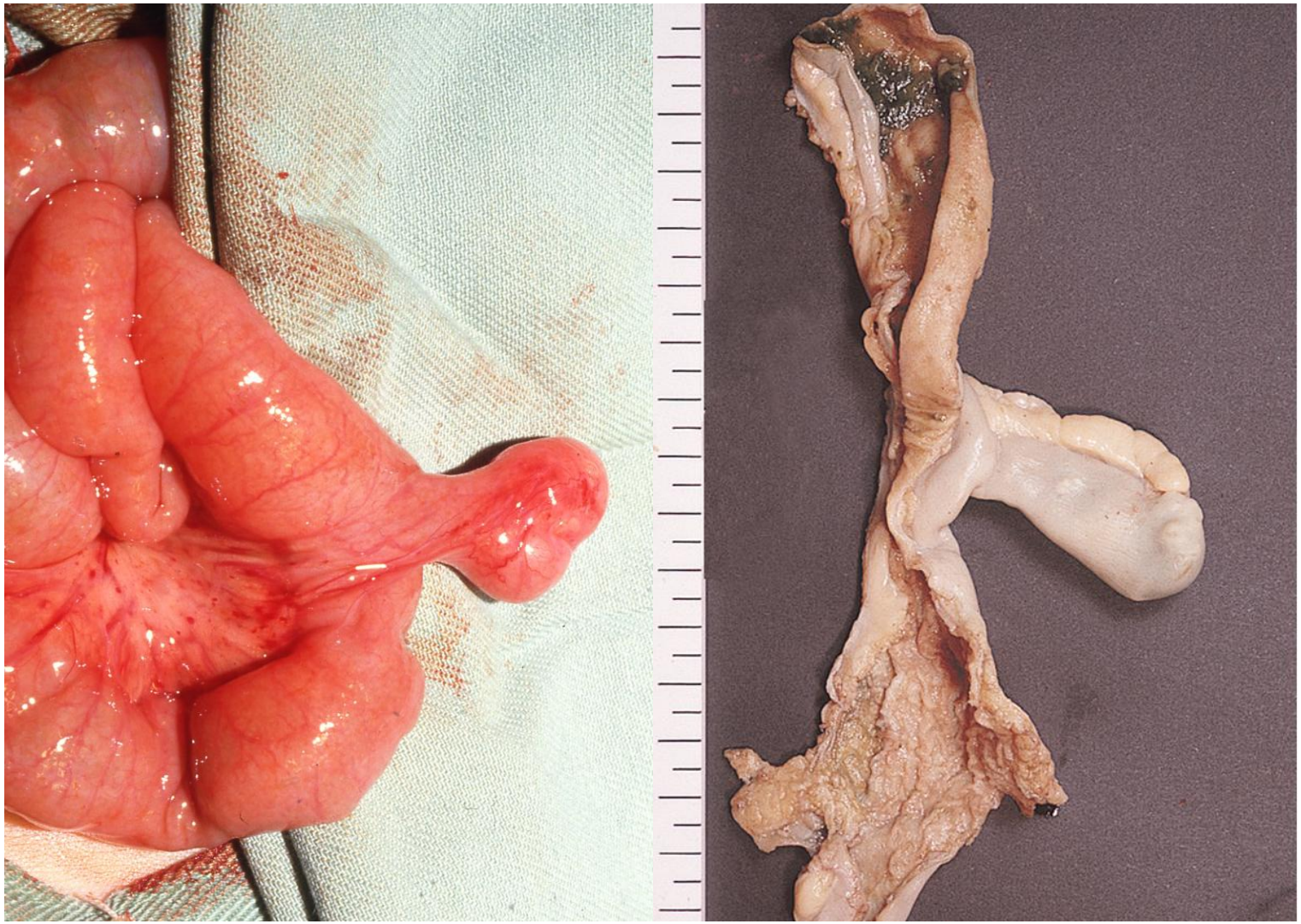
Esophageal atresia, type C, with tracheoesophageal fistula (X-ray appearance)



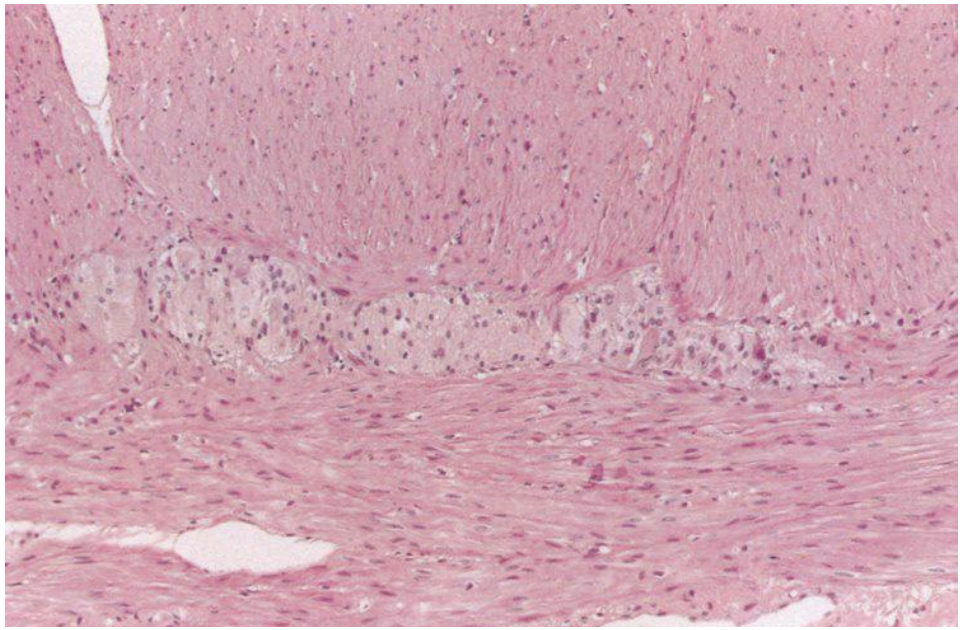
Duodenal atresia with double bubble sign (X-ray appearance)



Esophageal atresia, type C, with tracheoesophageal fistula



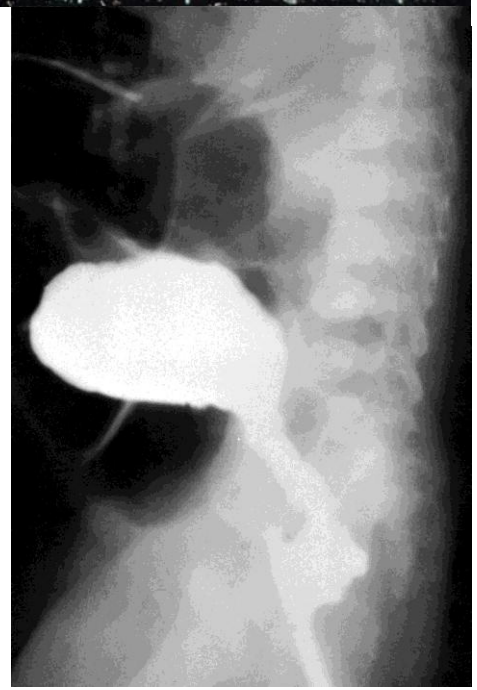
Meckel's diverticulum of the ileum. Gross appearance. Left: pediatric case (1 year and 5 months-old female baby) found at surgery, right: adult case (73-year-old male patient) found at autopsy

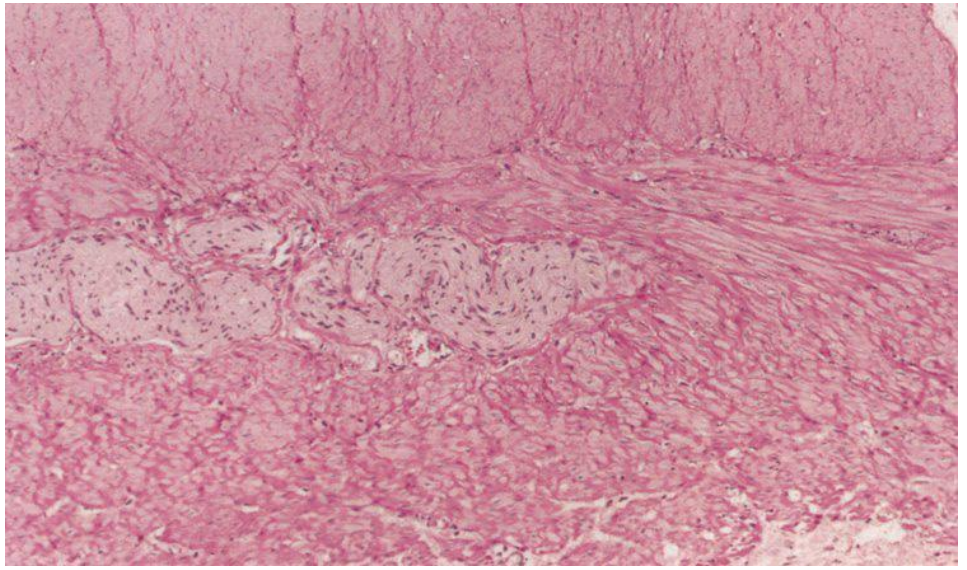


Normal Auerbach’s nerve plexus (H&E)

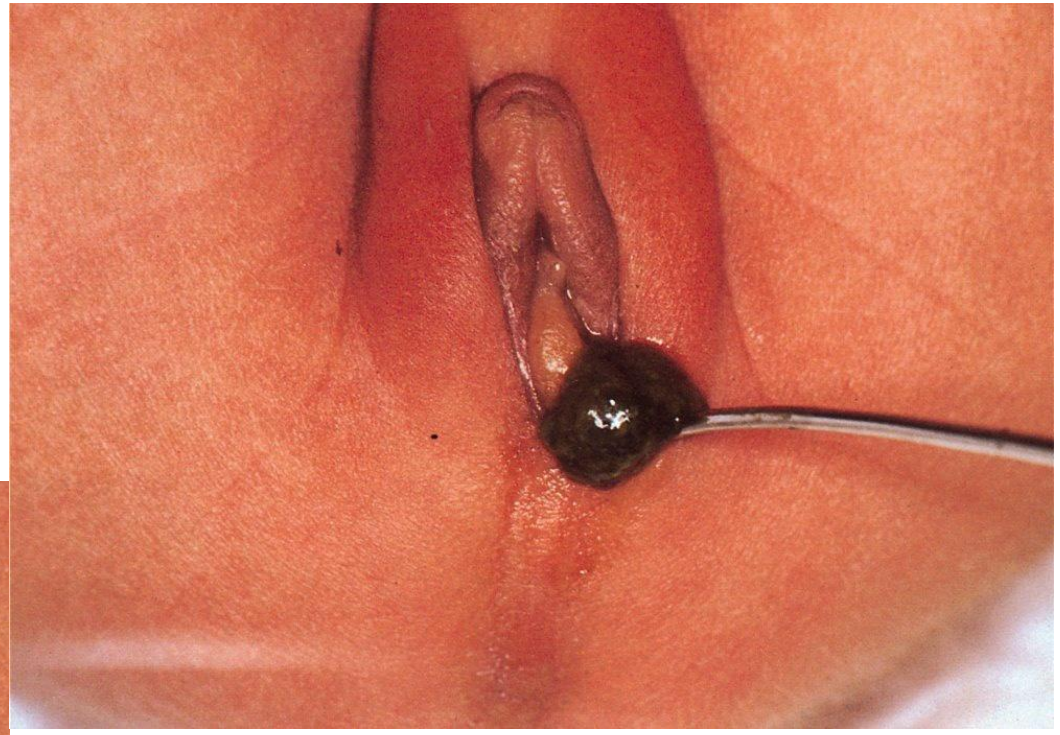
Hirschsprung disease (congenital megacolon)

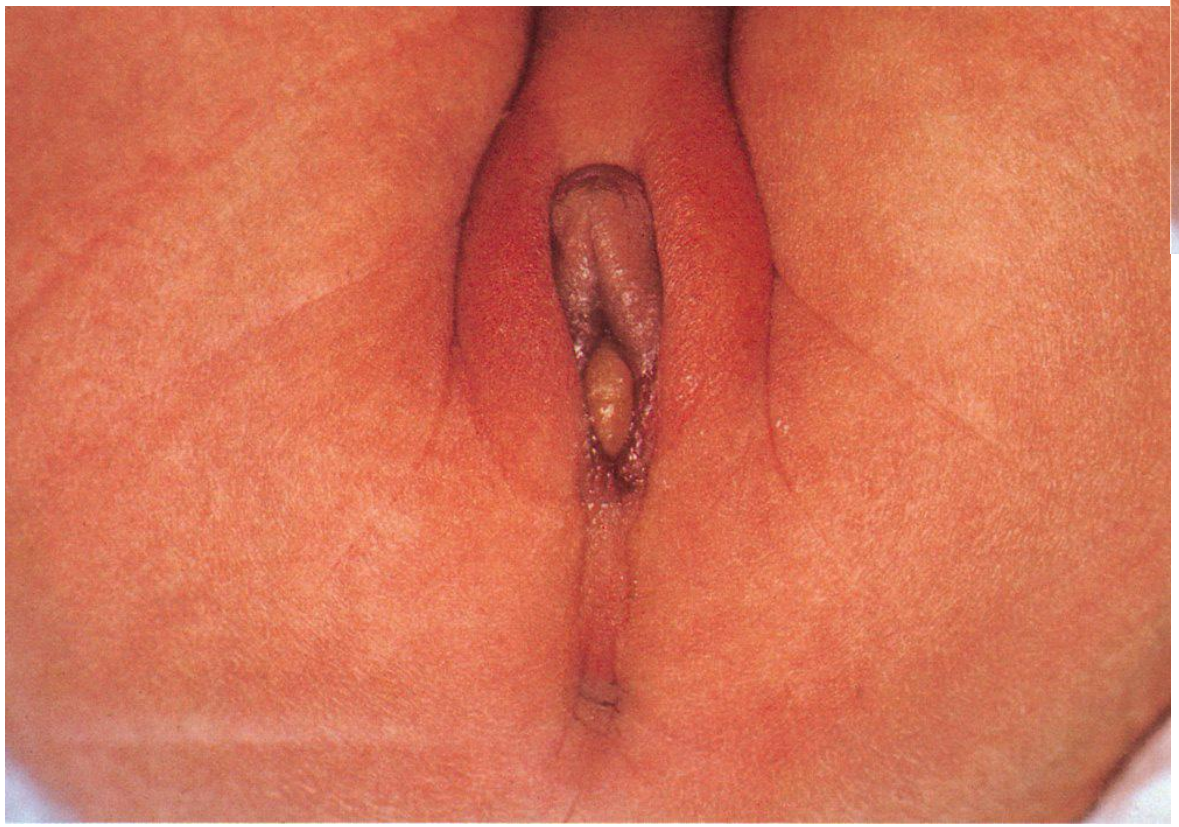
Left top: surgical specimen after formalin fixation
Left bottom: barium enema showing “caliber change”





Aganglionosis in Hirschsprung disease (H&E)





Imperforate anus, low lesion in a female baby, with vestibular fistula. The anus is not formed in the regular position.

Cardiovascular anomaly

Ventral septal defect

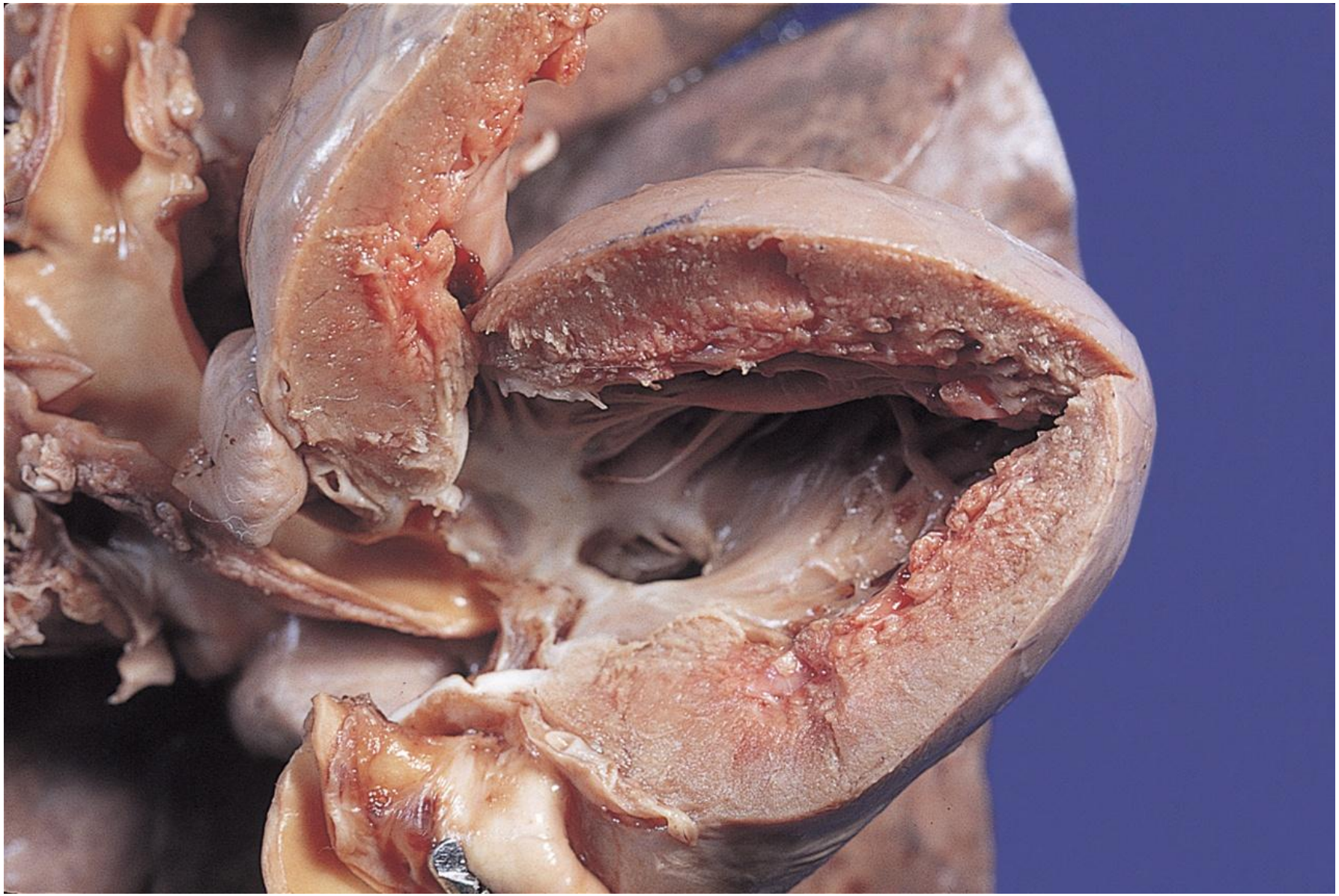
Tetralogy of Fallot

Coarctation of aorta

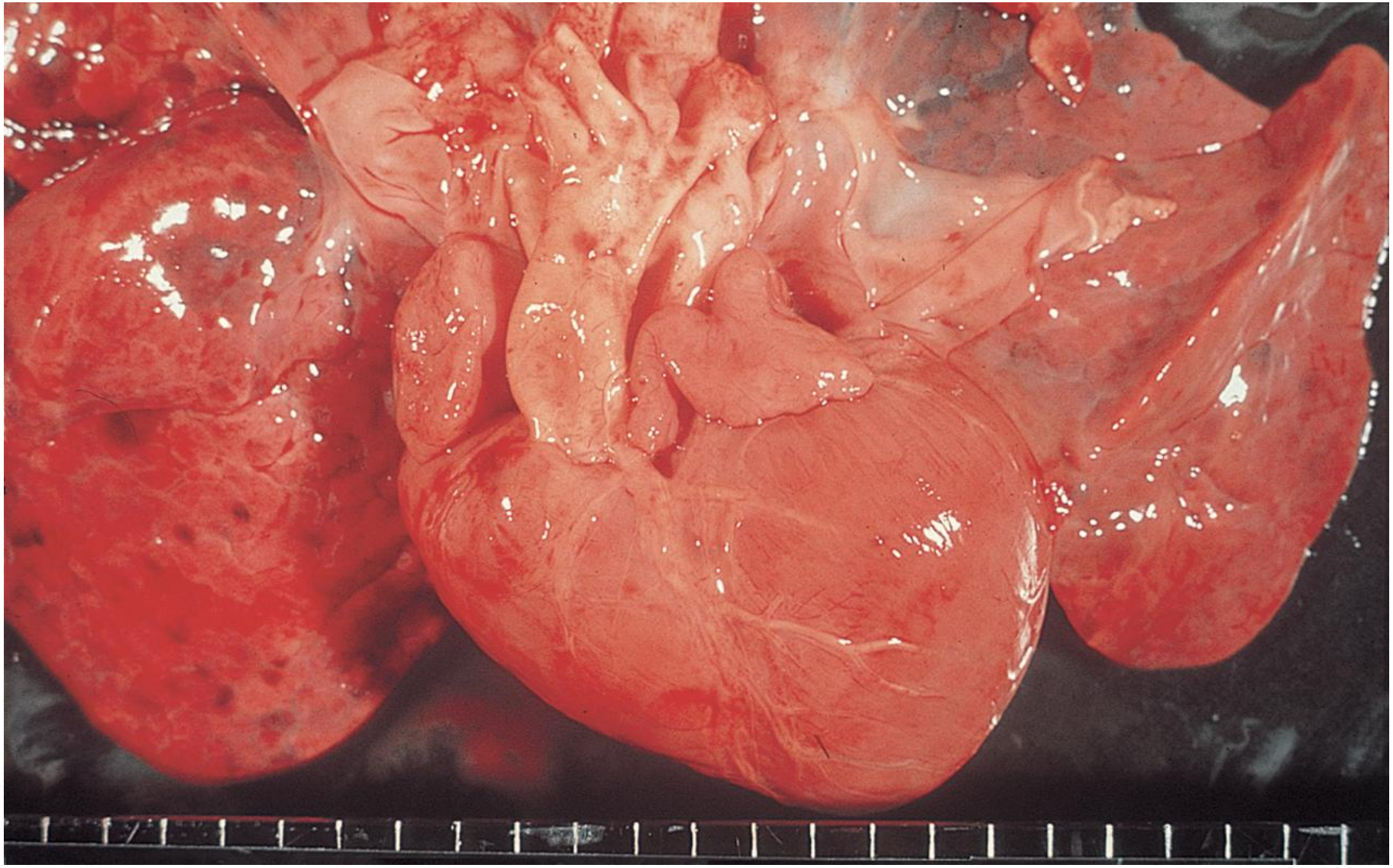
Asplenic syndrome

Kartagener syndrome

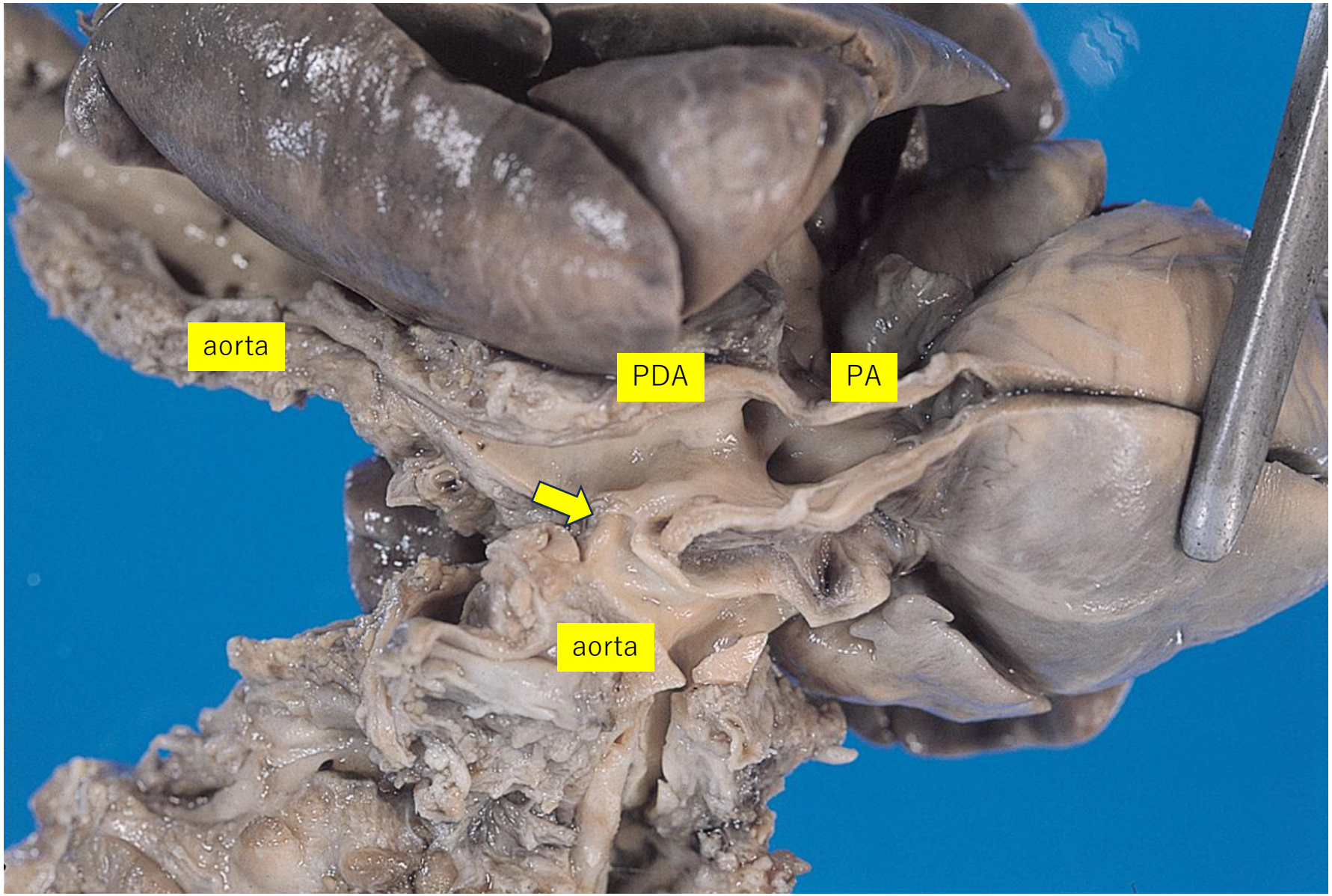
Single umbilical artery



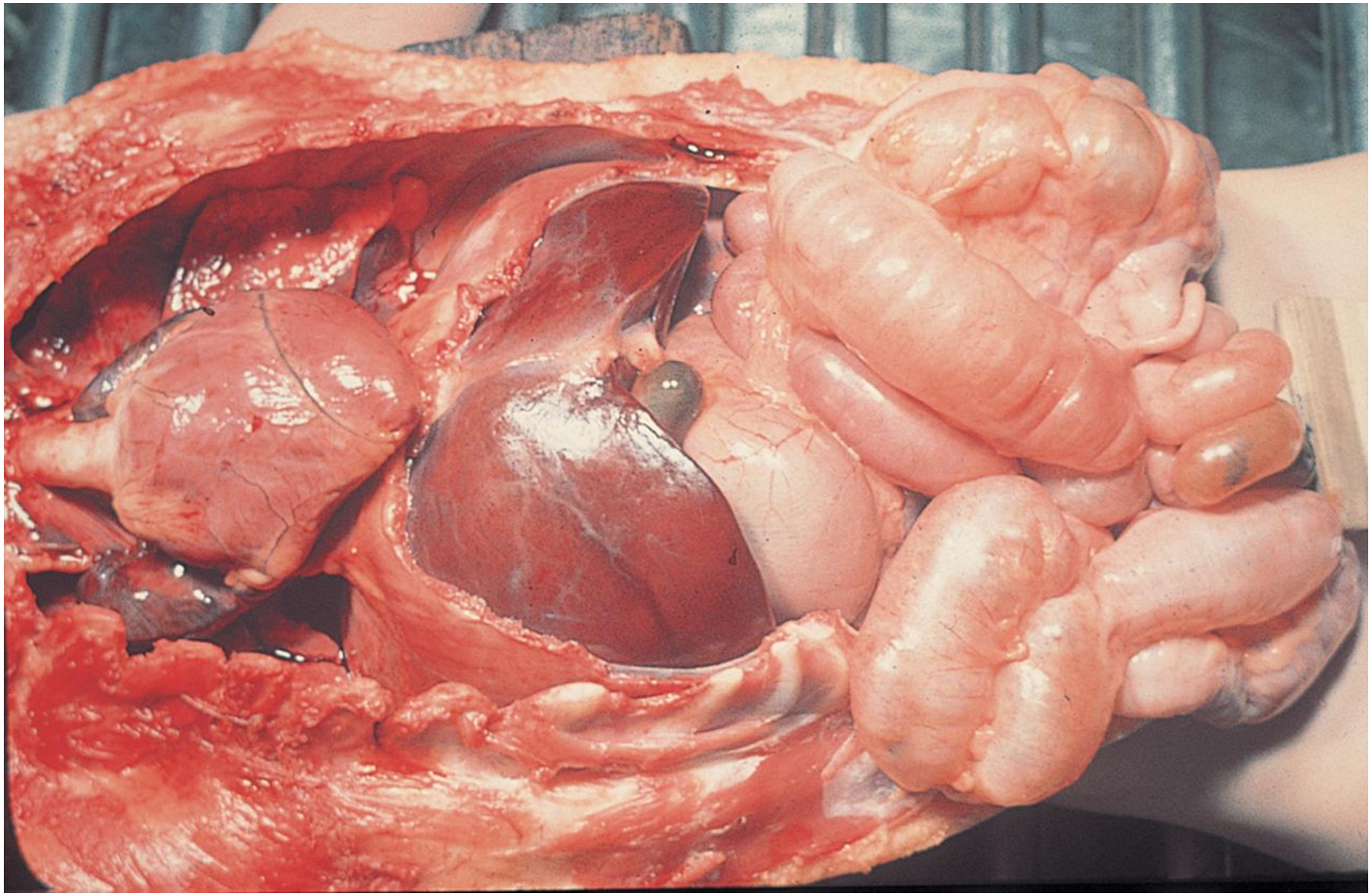
Ventricular septal defect (after formalin fixation)



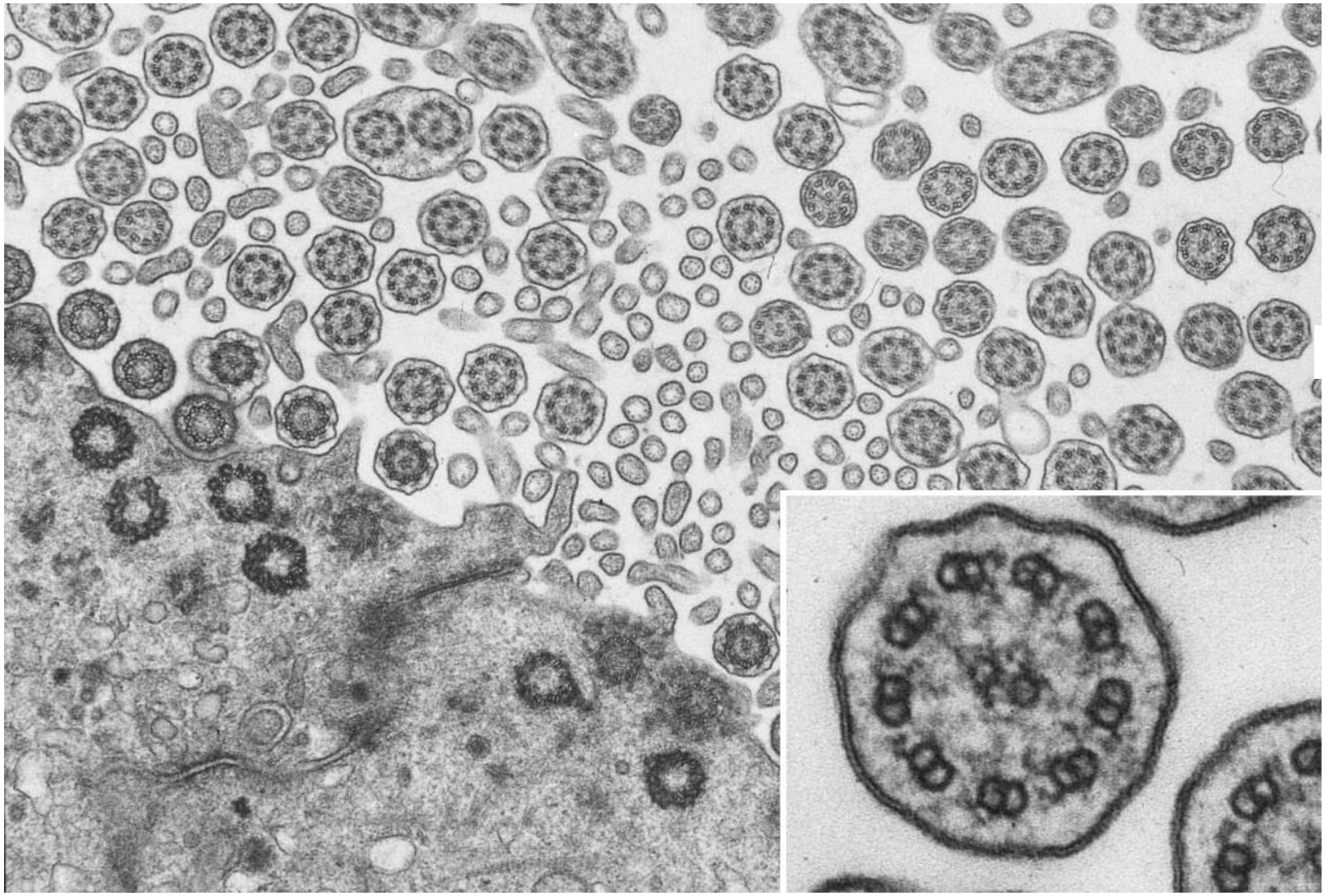
Tetralogy of Fallot: overriding of the aorta and right ventricular hypertrophy



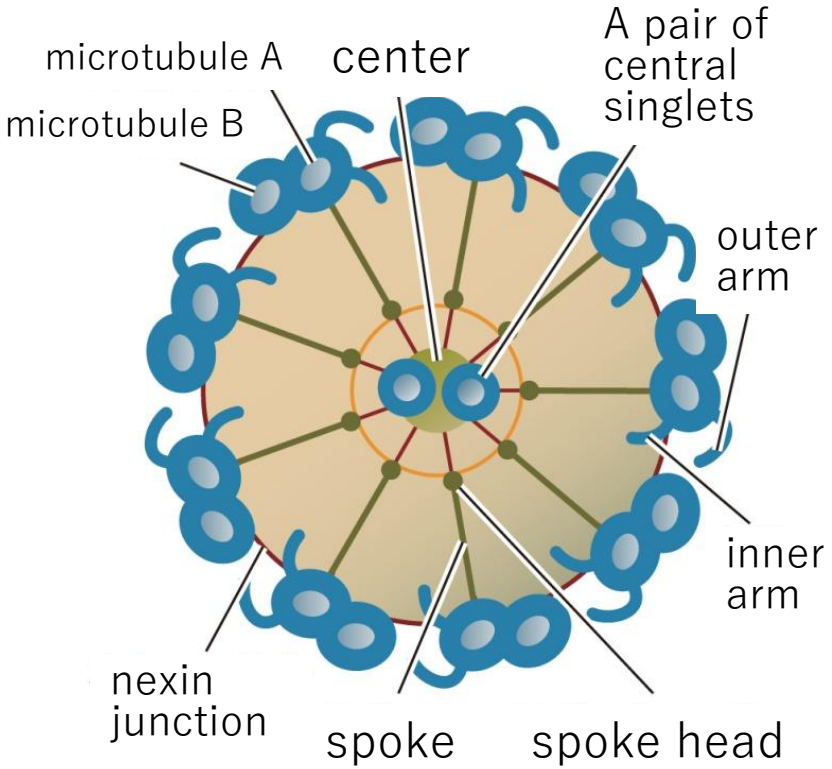
Coarctation of aorta, pre-ductal type (after formalin fixation). Arrow indicates stenosis of the aorta, PA: pulmonary artery, PDA: patent ductus arteriosus



Asplenia in a case of 18 trisomy. Severe cardiac anomaly and symmetry of the internal organs are grossly observed.

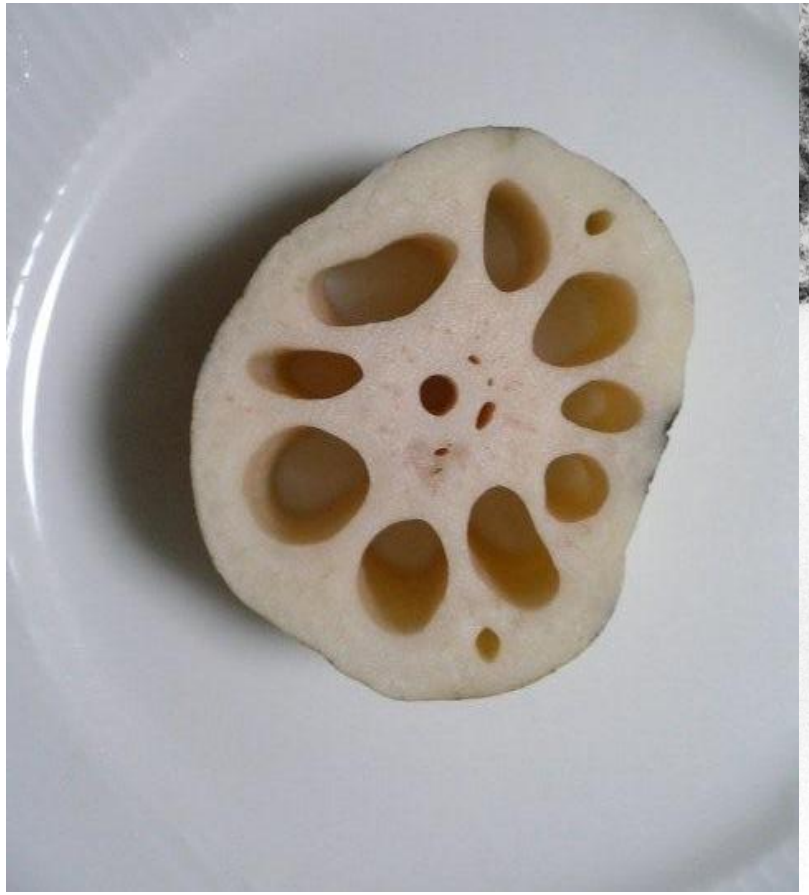


Primary ciliary dyskinesia (**immotile cilia syndrome**) in Kartagener syndrome with dextrocardia. The inner dynein arms are lacking ultrastructurally.

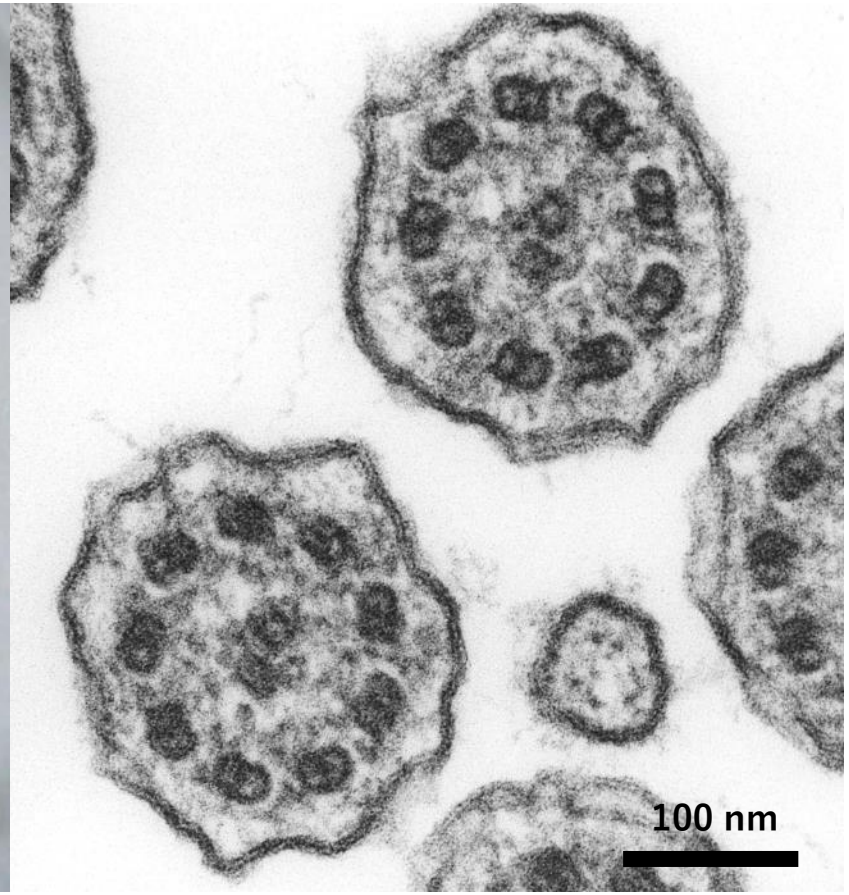


A scheme of the cut surface of the cilium. Nine pairs of peripheral doublets and a pair of central singlets are noted.

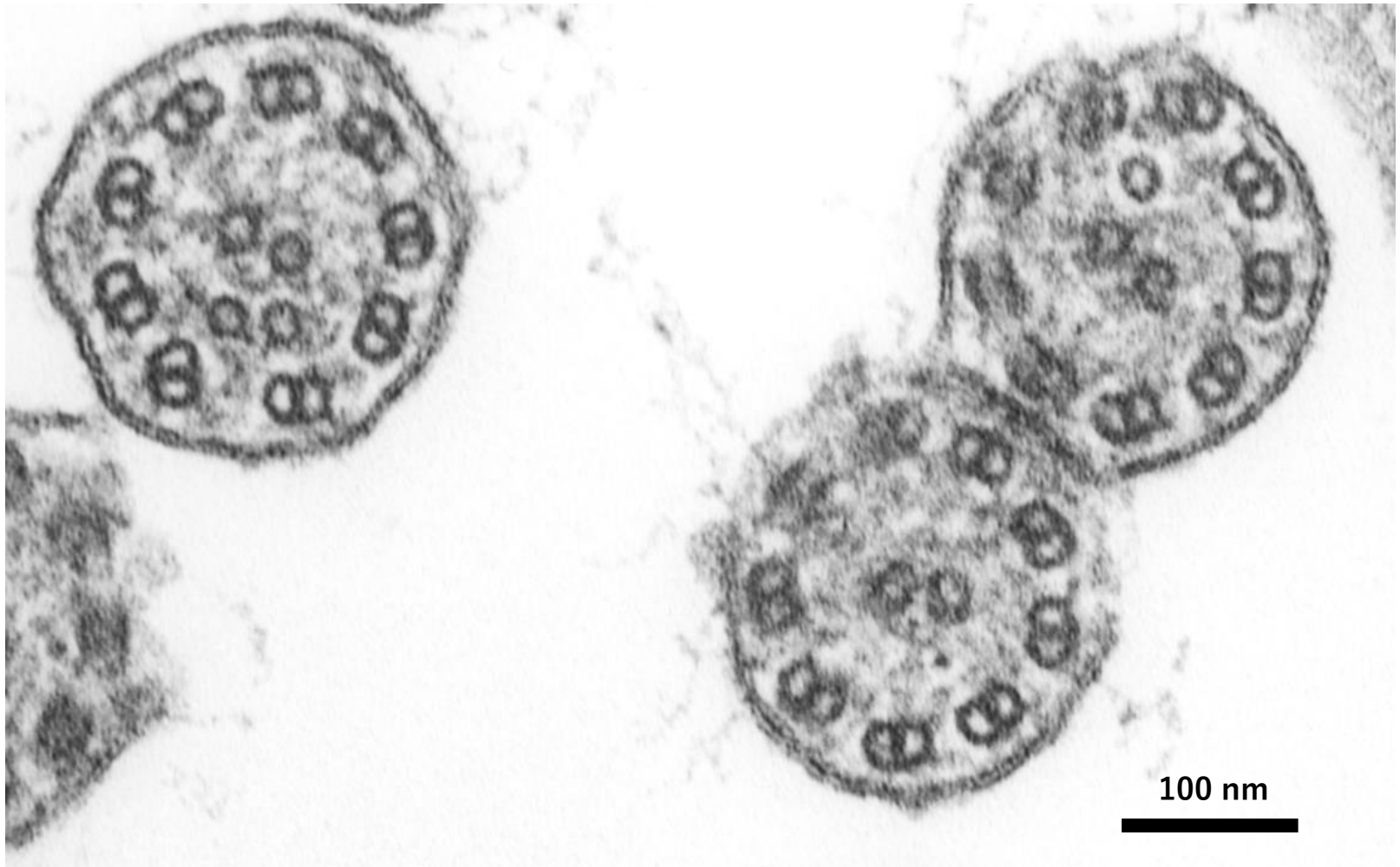
Cut surfaces of the lotus root and normal cilia



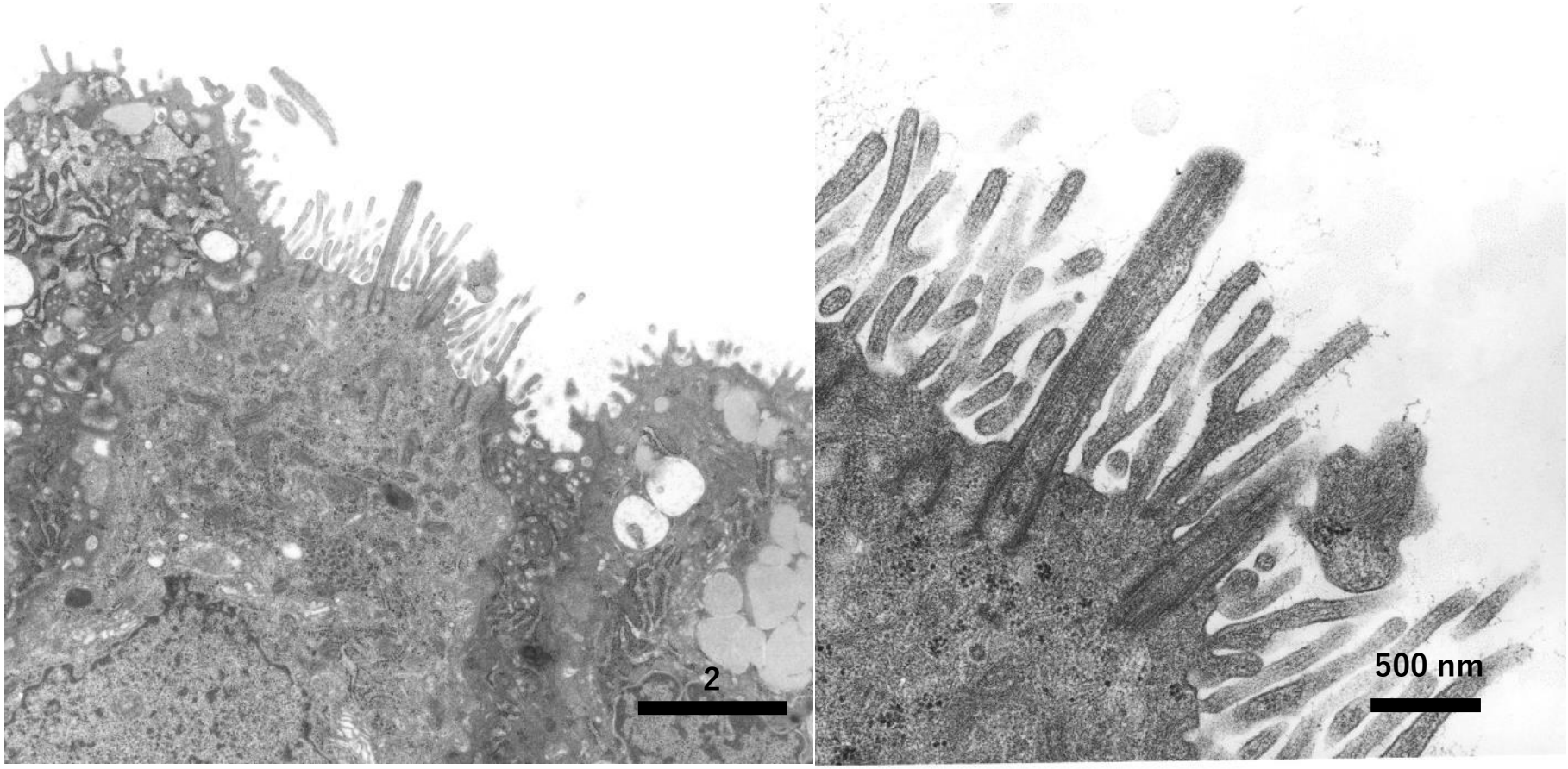
The **lotus root** contains nine pairs of the peripheral canals and a pair of central canals, resembling the normal cilia.



Ultrastructure of normal cilia on the bronchial mucosa of an adult man



Another case of **immotile cilia syndrome in Kartagener syndrome**, the nasal mucosa of 1-year-old boy. Ultrastructurally, both dynein arms are lacking, and additional ectopic occurrence of the central singlets is also noted.



A severe form of **immotile cilia syndrome**. Ultrastructurally, the cilia are poorly formed on the apical surface of the epithelial cells (the nasal mucosa of a newborn girl).

Single umbilical artery seen in the cut surfaces of the umbilical cord

Congenital anomalies in the urogenital tract

Horseshoe kidney, double ureter

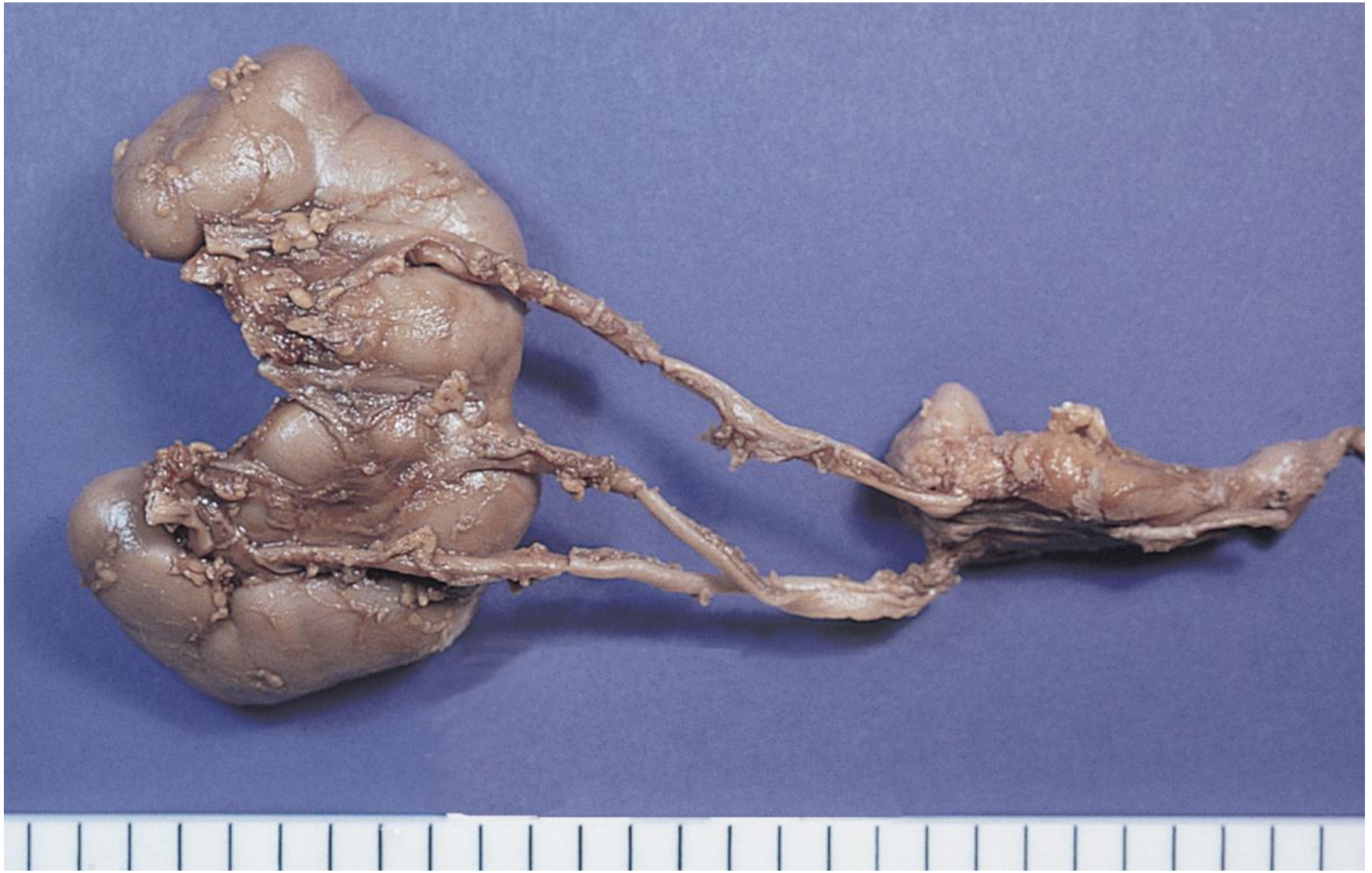
Vesicoureteral reflux

Hypospadias

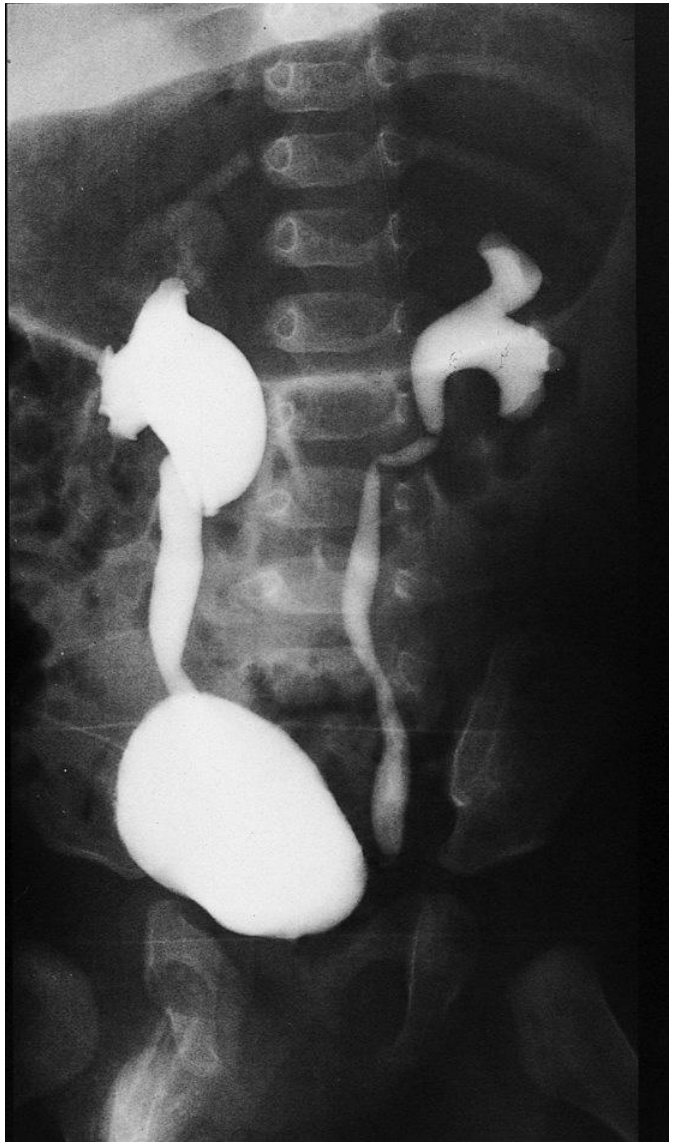
Patent urachus

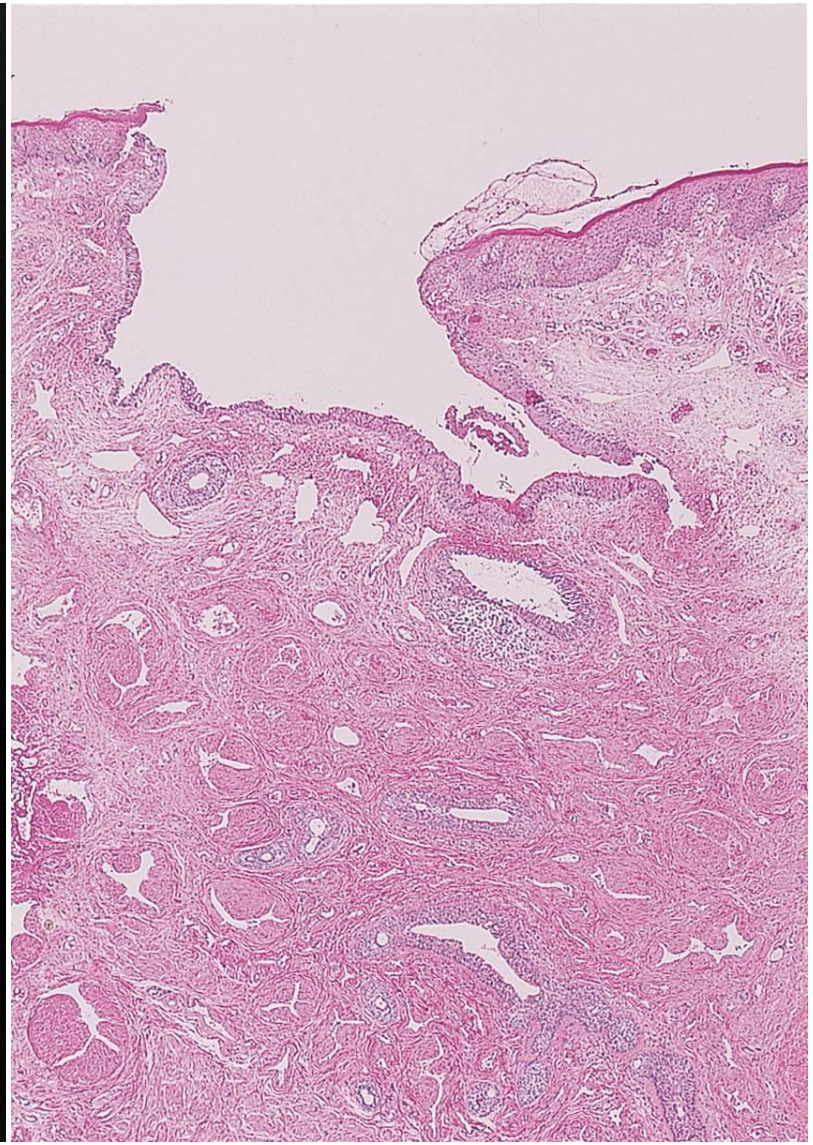
Ovotestis (hermaphroditism)

Cryptorchism (undescended testis)

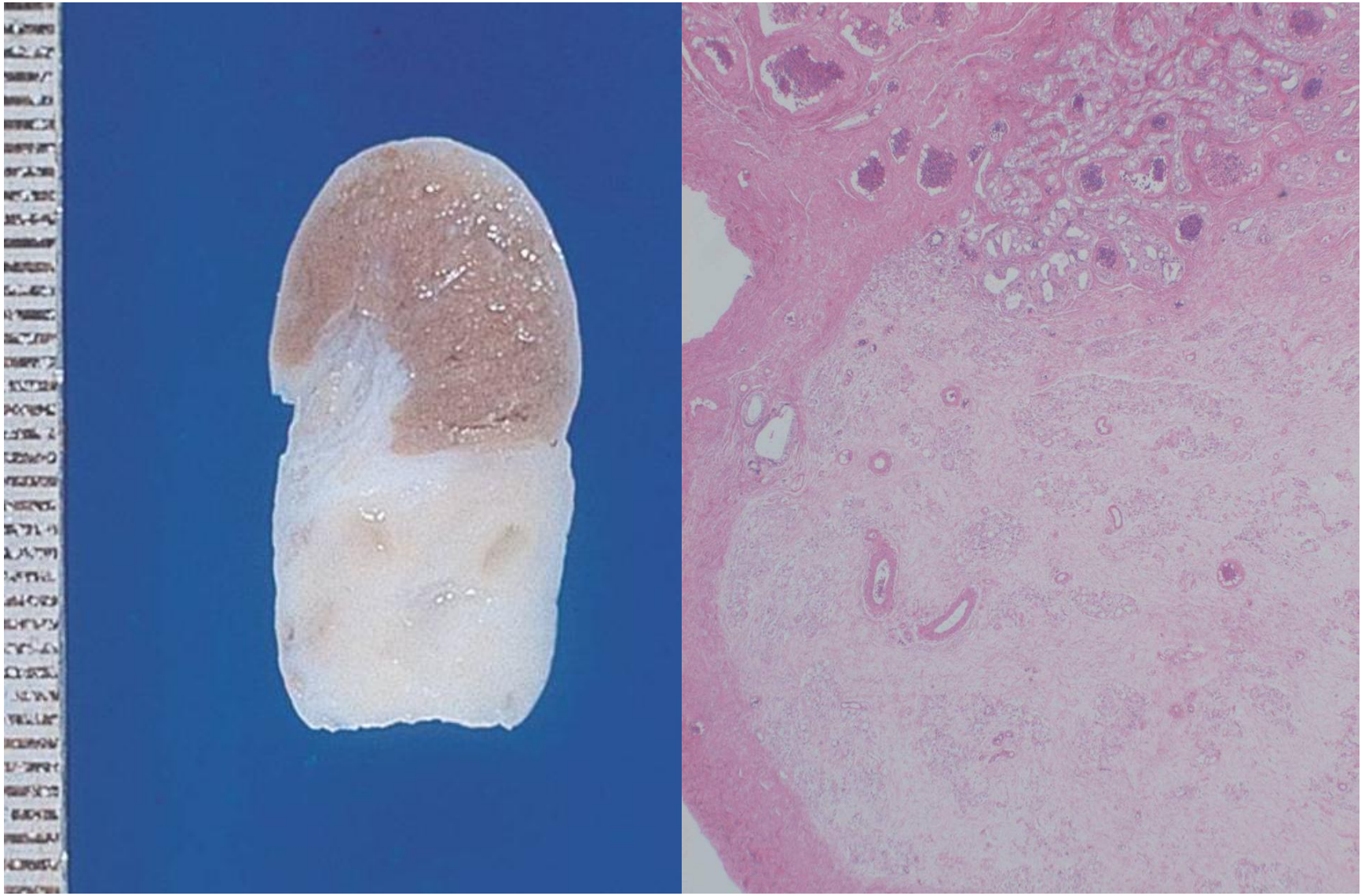


Horseshoe kidney and unilateral **double ureter**
(gross appearance after formalin fixation)





Vesicoureteral reflux (left: vesicography) and **hypospadias** (H&E). The vesicoureteral reflux has provoked hydroureter and hydronephrosis. In hypospadias, the ureter is exposed onto the skin.



Gross appearance of ovotestis (left) and microscopic appearance of cryptorchism (right: H&E). The light brown colored testicular tissue is seen adjacent to the white-colored ovarian tissue. Cryptorchism microscopically reveals marked atrophy of the testicular tubules.

Congenital anomalies of the skeleton

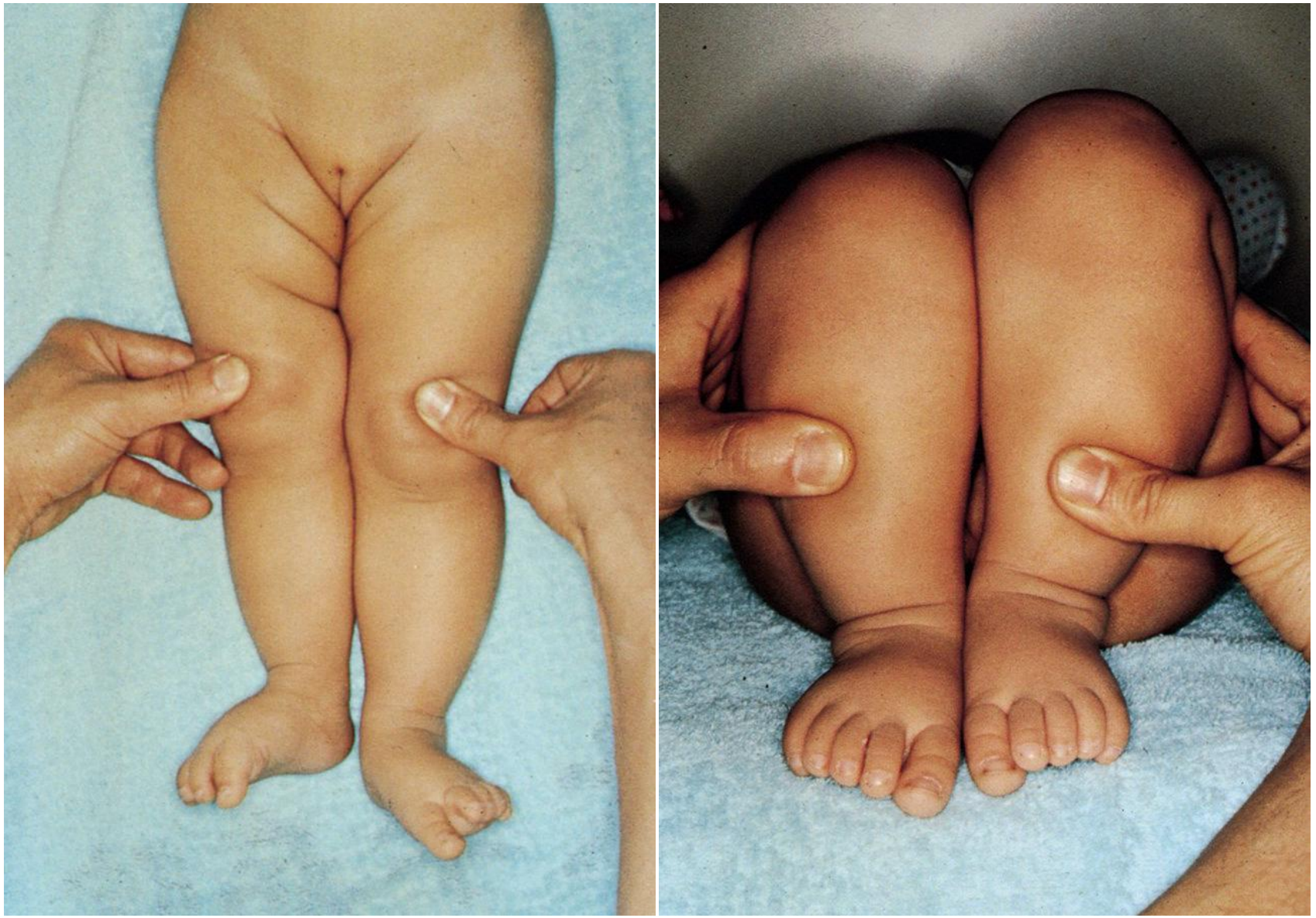
Congenital dislocation of the hip (luxatio coxae congenita)

Torticollis

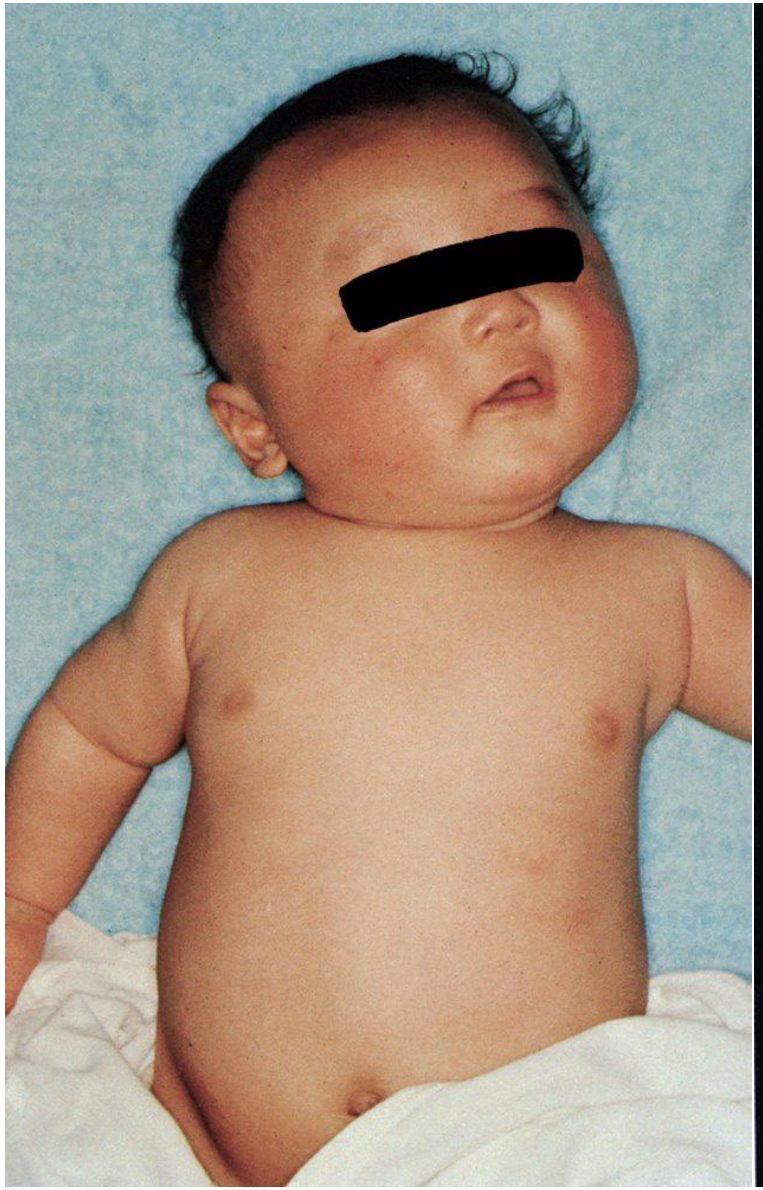
Club foot (talipes equinovarus)

Hereditary disorders often associate skeletal abnormalities.

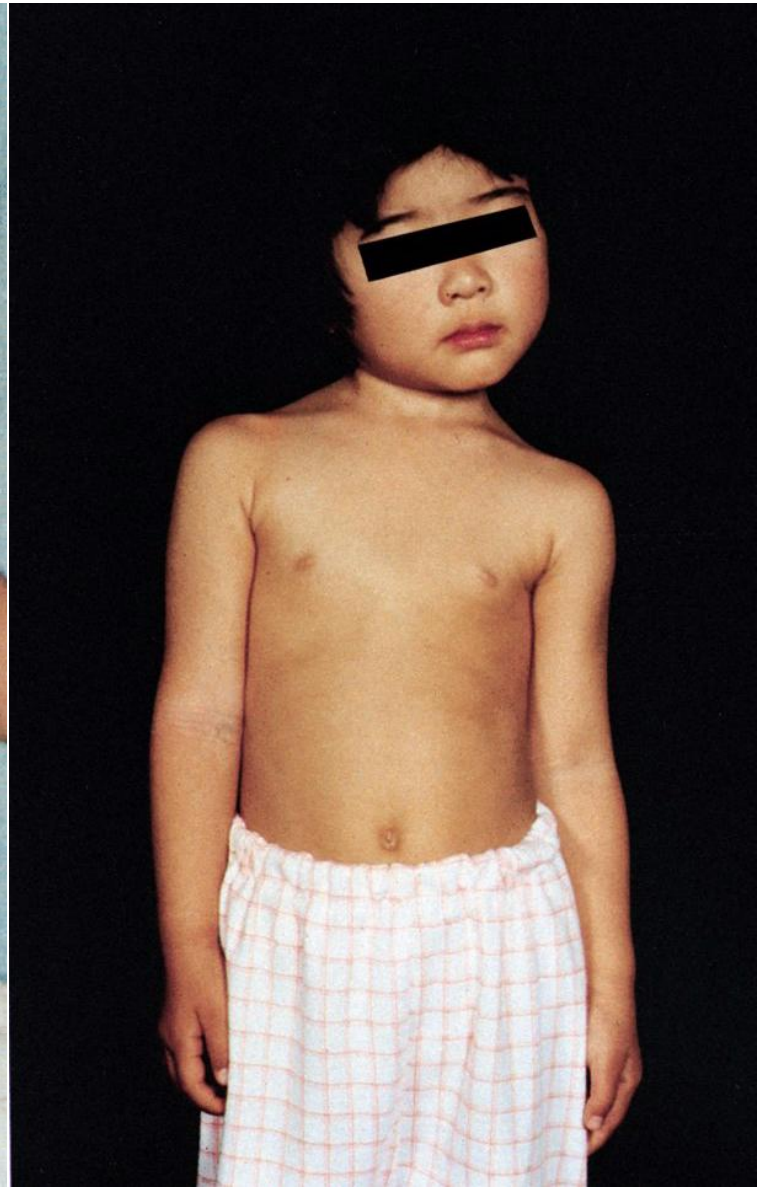
- Hurler/Hunter syndrome (mucopolysaccharidosis)
- Osteogenesis imperfecta
- Achondroplasia
- Marfan syndrome



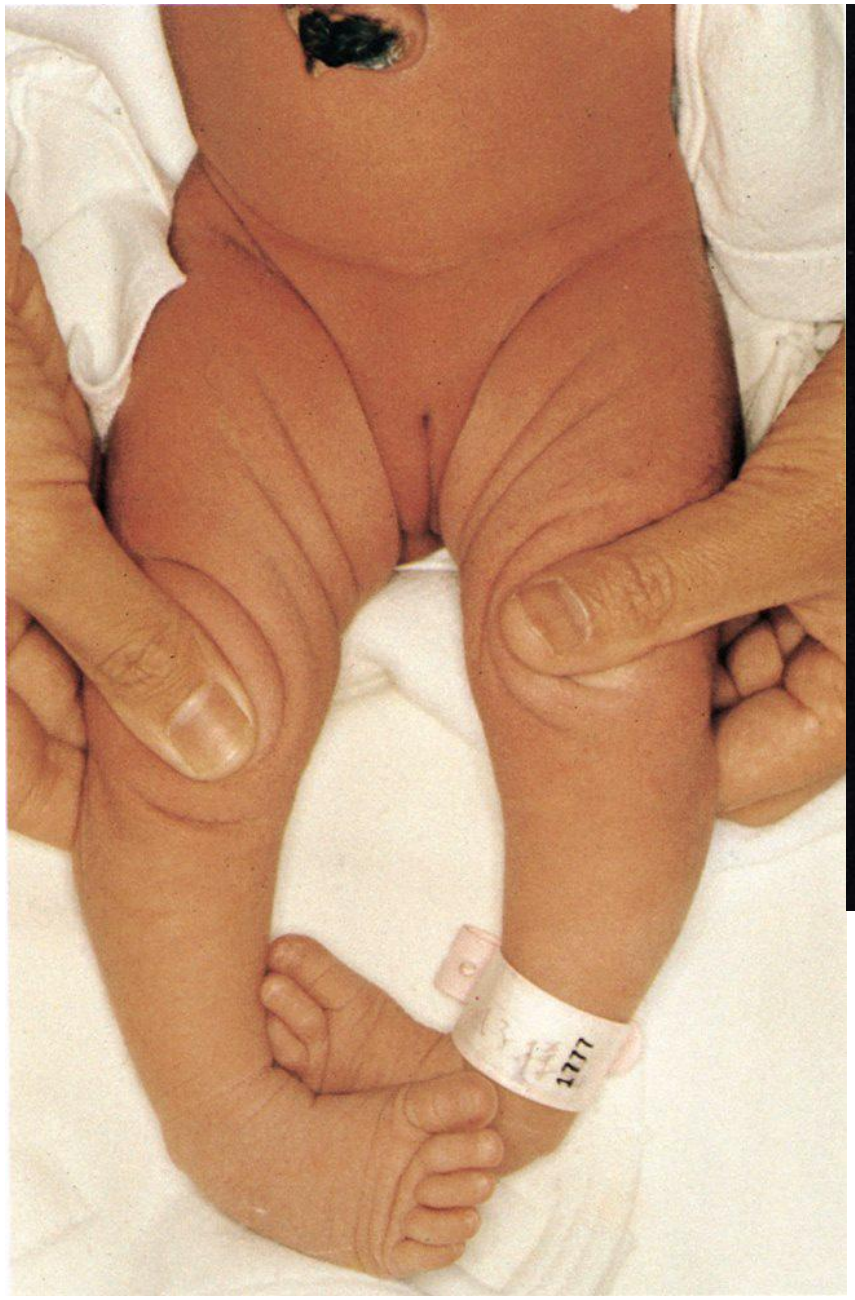
Congenital dislocation of the hip (**luxatio coxae congenita: LCC**).
Left: the length of the legs is different, right: Allis sign showing the shortening of the thigh. LCC is often seen in female infants.

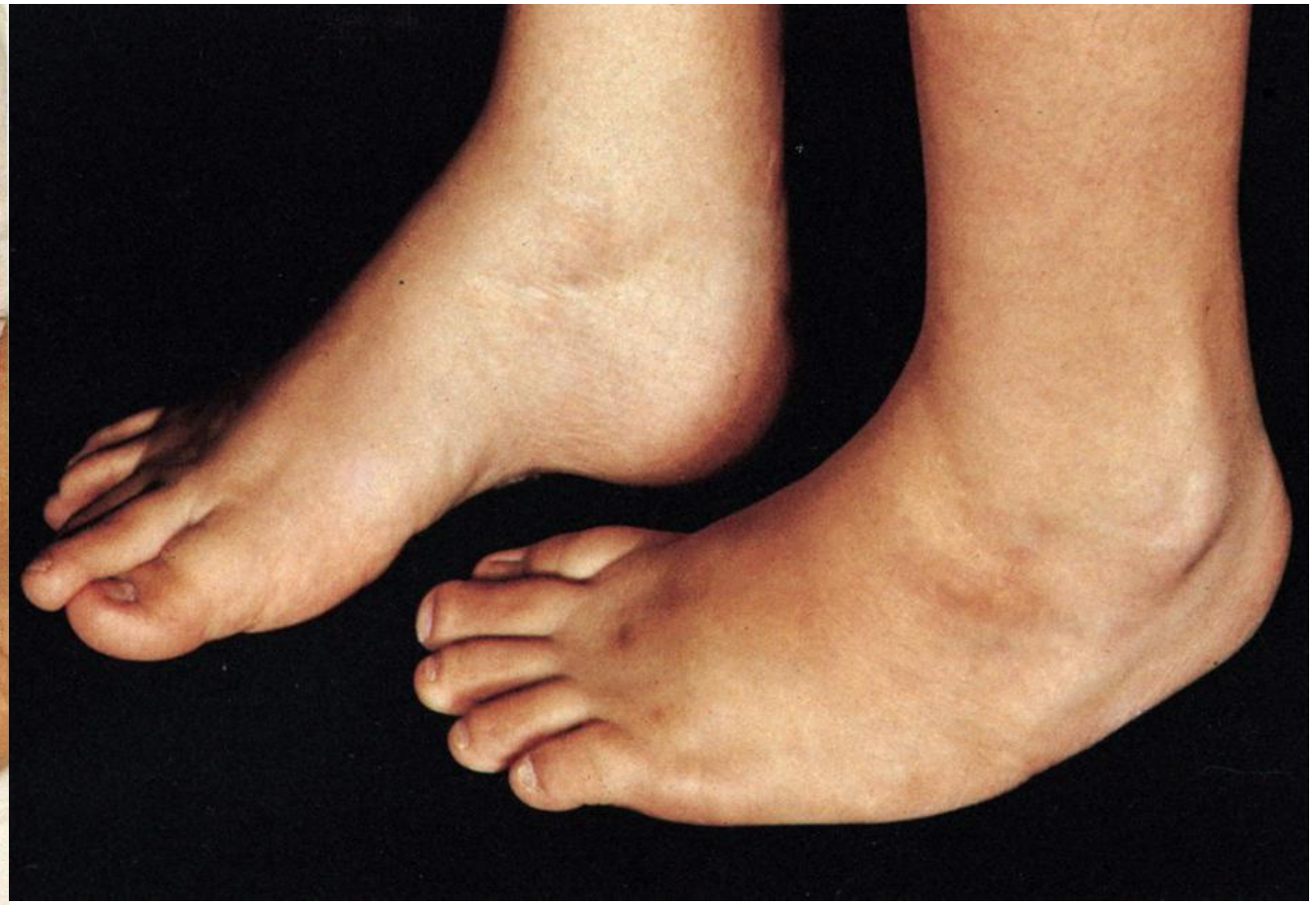


Torticollis in a newborn period is caused by scar formation in the right sternocleidomastoid muscle



Torticollis in a school age caused by cervical scoliosis protruding to the right





Congenital club foot (talipes equinovarus).
Left: bilateral club feet in a newborn,
Right: unilateral club foot in an adult
The exact cause is usually not identified. Both genetic and environmental factors may be involved.