Heart in Foetopathology

Dr Christian Dugauquier

• ANATOMOPATHOLOGIE
• GÉNÉTIQUE CLINIQUE
• BIOLOGIE MOLÉCULAIRE
ET CELLULAIRE

Congenital Heart Defects (CHD)

- Relative frequency in humans
- Short reminder of cardiogenesis and induction period
- Potential causes of CHD
- Classification
- **Illustration of the most common anomalies**

Frequency of congenital defects

- For 1000 live birth :

cardiac anomaly	**5 to 8 (°/°°)**
anencephaly	2
hypospadias	1,8
hydrocephaly	1,4
spina bifida	1,4
polydactyly	1,1
cleft palate	0,6
diaphragmatic hernia	0,5
cleft lip	0,4
omphalocele	0,4
renal agenesis	0,4
anal imperforation	0,4

Frequency of congenital defects

Prevalence of CHD and Non-Chromosomal CHD

Country	Total* prev CHD per 1,000 births	Total* prev chromosomal CHD per 1,000 births	Total* prev non-chromosomal CHD per 1,000 births
Austria	15.34	1.42	13.91
Belgium	6.66	0.84	5.82
Croatia	5.39	0.62	4.77
Denmark	8.91	0.81	8.09
France	8.38	1.18	7.19
Germany	11.90	1.14	10.76
Ireland	6.60	1.60	5.00
Italy	6.86	0.47	6.40
Malta	15.25	1.99	13.27
Netherlands	6.08	0.77	5.31
Norway	10.27	0.90	9.37
Poland	11.18	0.92	10.26
Spain	5.58	0.91	4.67
Switzerland	13.62	1.47	12.15
Ukraine	7.78	0.81	6.97
UK	6.88	1.03	5.86
Total	8.03	0.98	7.05

Frequency of congenital defects

- CHD = the most frequent group of major congenital anomalies

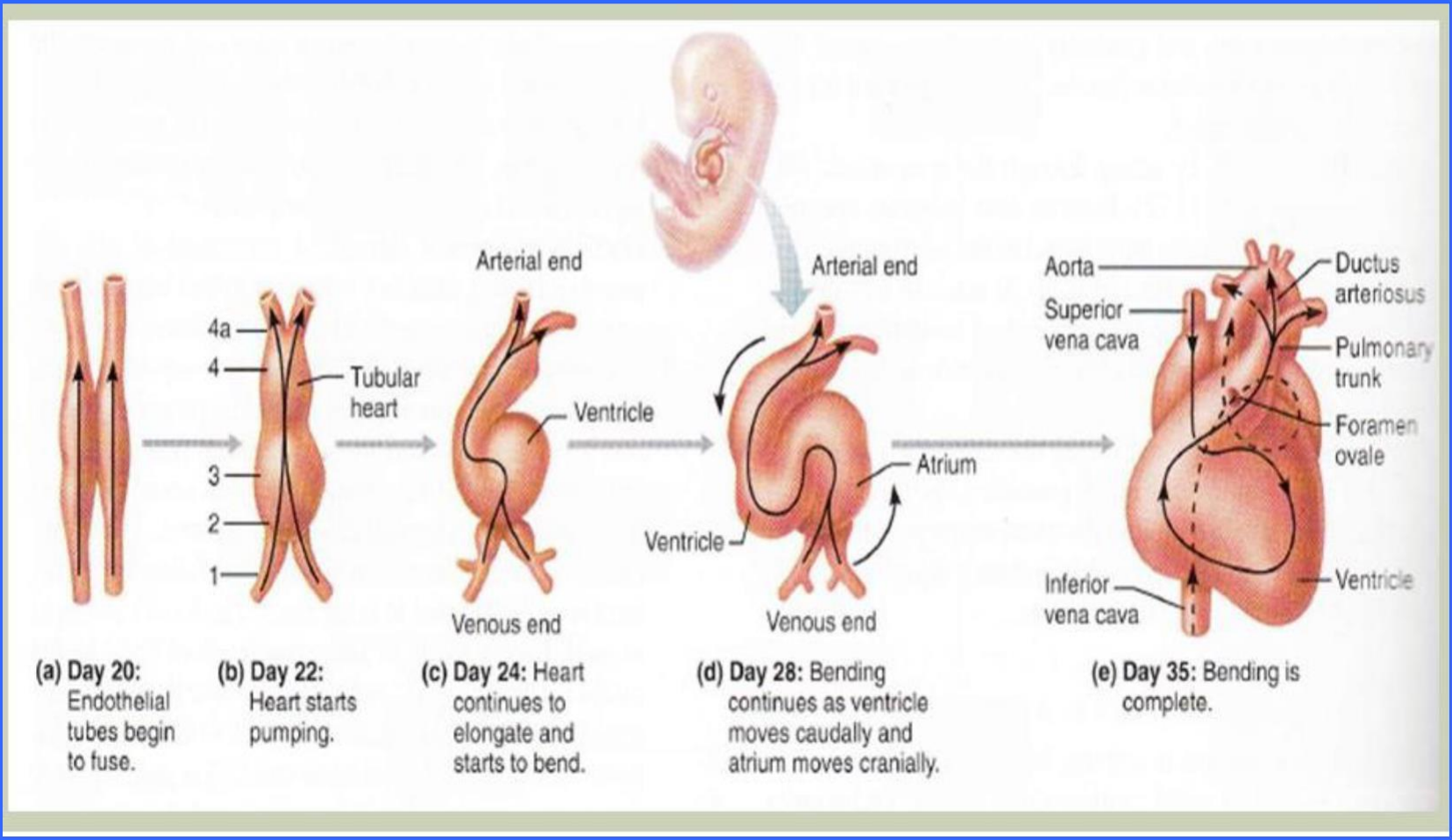
- Total prevalence of 7 – 8 per 1,000 births (*).
- The majority survive the first week of life,
- but one in six require surgery.

- Even so, CHD remain a major cause of fetal and perinatal mortality, with a combined mortality of 0.7 per 1,000 births (**)

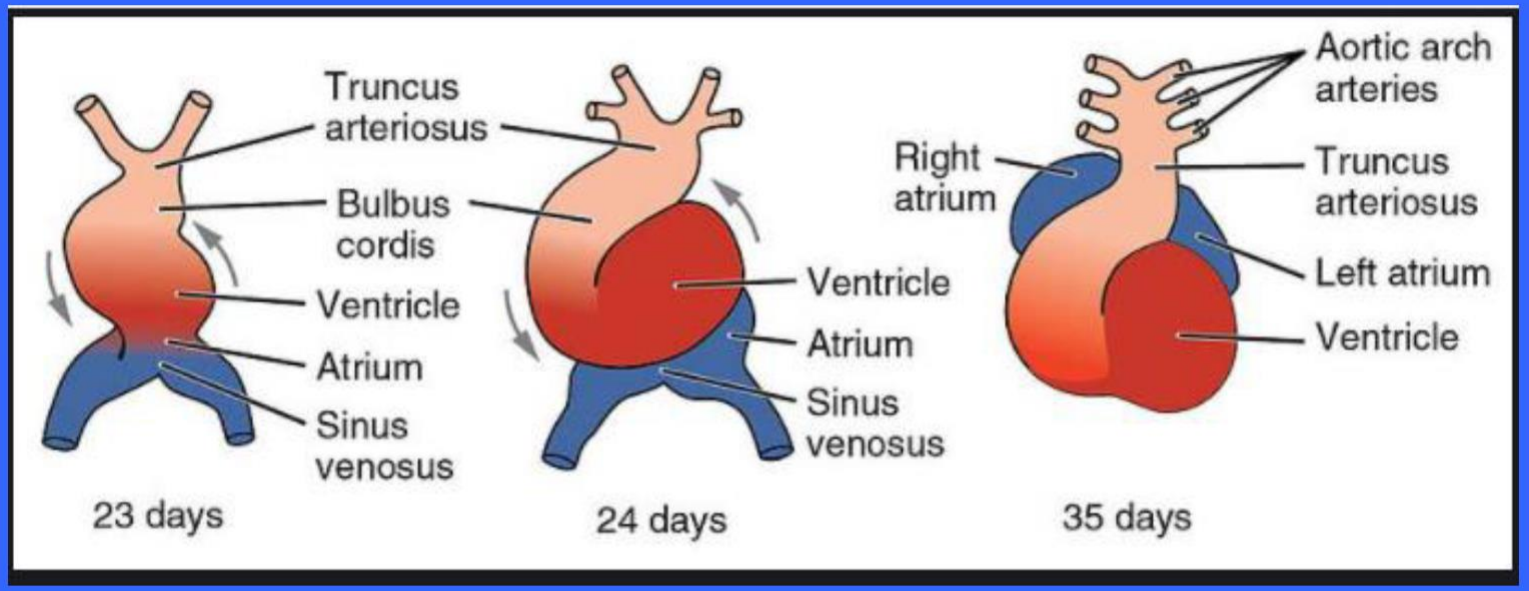
(*) isolated + syndromic

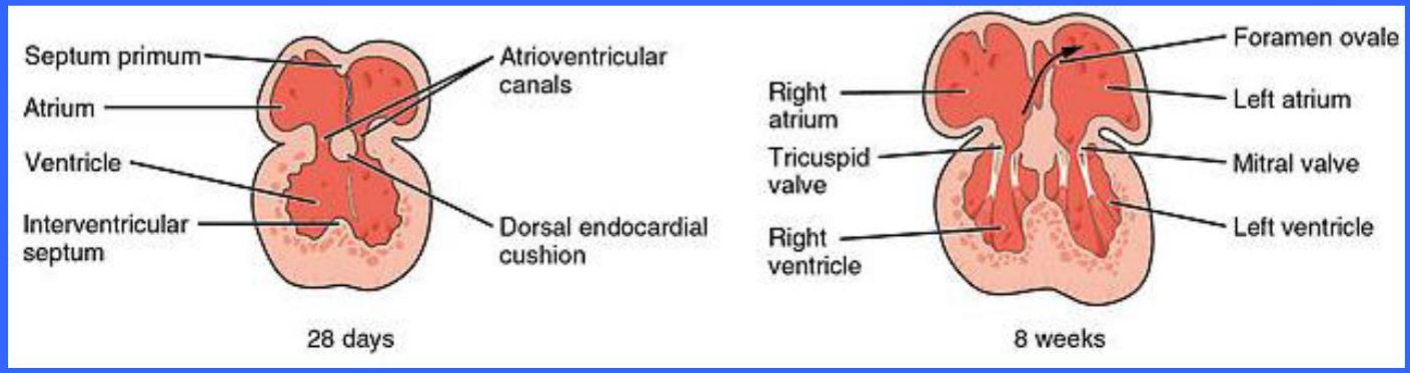
(**) In Europe.

Cardiogenesis

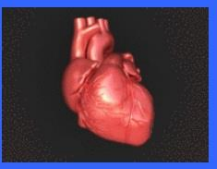


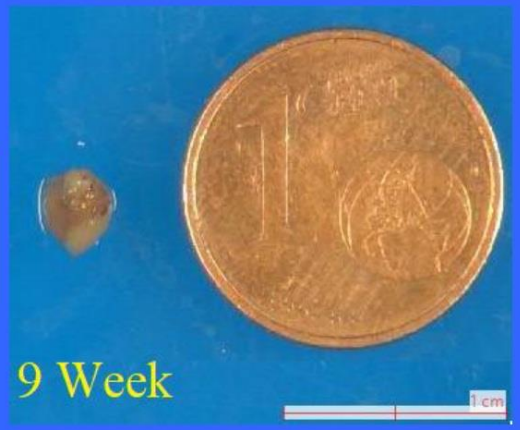
Cardiogenesis

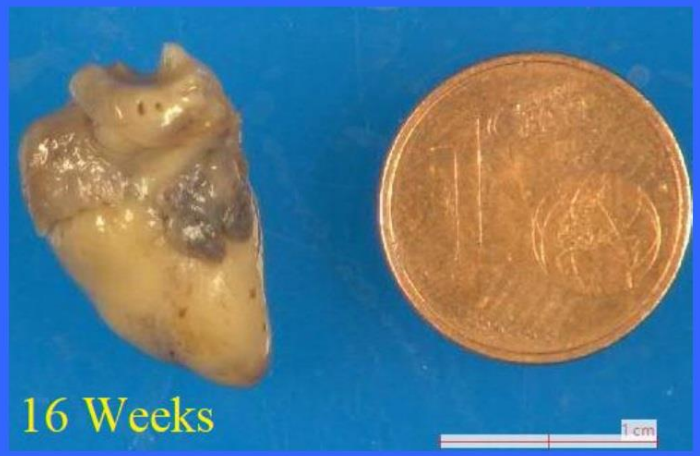


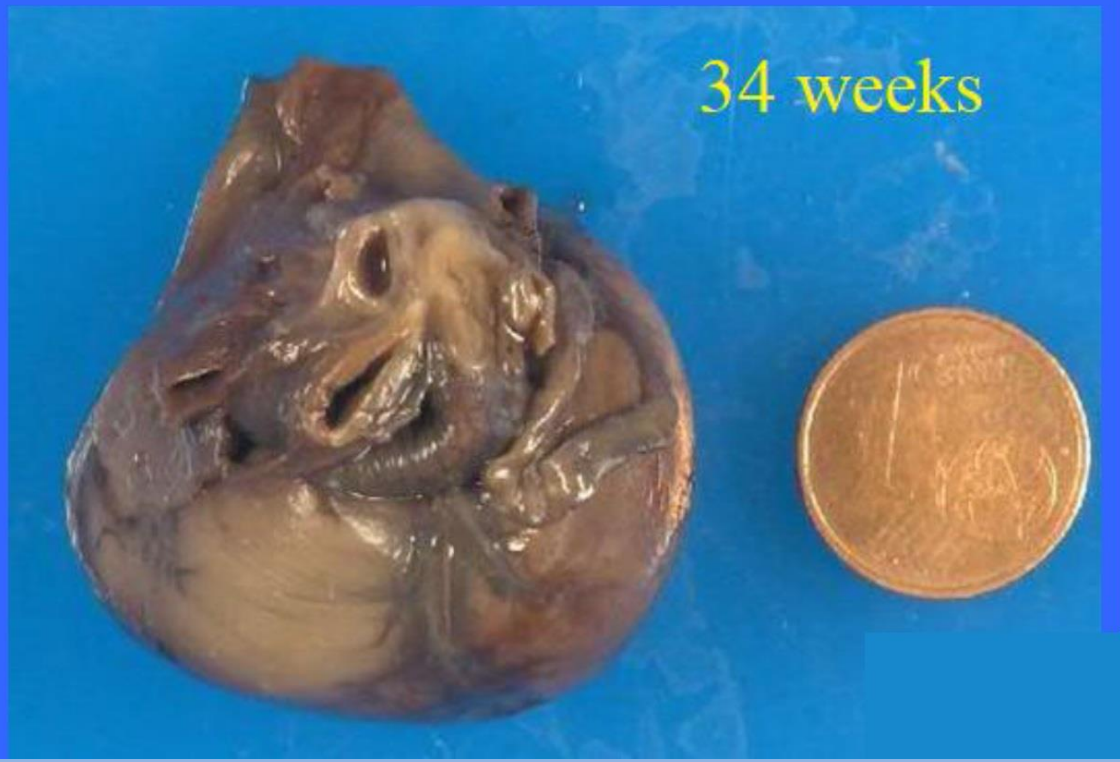


Heart size evolution









Causes of CHD are multiples

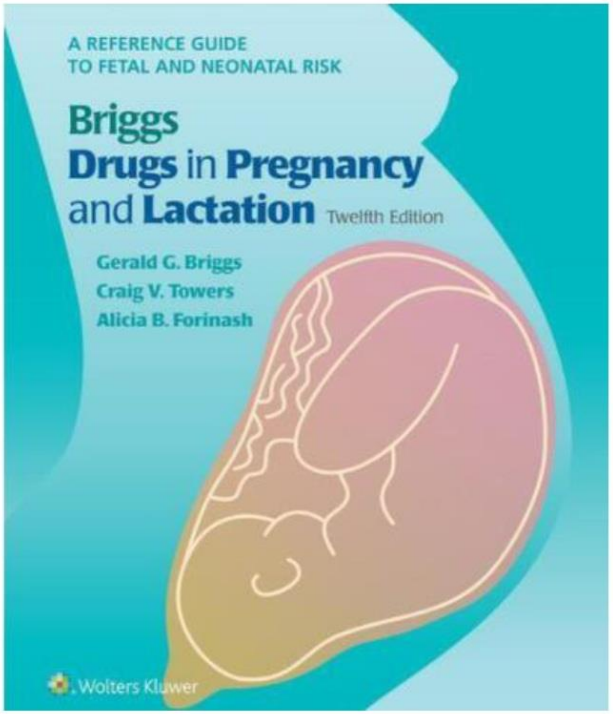
- Mono-/poly- genic 15-25%
- Chromosomal 5 - 15%

- Environmental 10-15%
  - Radiation <1%
  - Infection 3-5%
  - Maternal metabolism 2%-5%
  - Iatrogenic / Toxic 6%

- **Still unknown 40-50 %**

Cardioteratogenic agents

Drug/Exposure	Possible Associated Cardiac Lesion
Paroxetine	ASD, VSD, ventricular outflow tract obstruction
Bupropion	Left outflow tract obstruction
Valproic acid	ASD, VSD, TOF, PA, HPRH
Nitrofurantoin	HPLHS, ASD
Cephalosporins	ASD
Lithium	Ebstein's anomaly, mitral atresia, AO
Ibuprofen	TGV, VSD, bicuspid aortic valve
Indomethacin	Premature closure of the ductus arteriosus
Rubella	PDA, VSD, pulmonary valve abnormalities
Diabetes mellitus (hyperglycemia)	TGV, VSD, AVSD, HPLHS, PDA, CM
Fever (hyperthermia)	Conotruncal and obstructive defects
Phenylketonuria	VSD, PDA, TOF, single ventricle
Vitamin A	PS, outflow tract abnormalities
Organic solvents	Conotruncal defects, TOF, PS, HPLHS, TAPVR, AO, TAPVR



Abbreviations: AO, coarctation of the aorta; ASD, atrial septal defect; AVSD, atrioventricular septal defect; CM, cardiomyopathy; HPLHS, hypoplastic left heart syndrome; HPRH, hypoplastic right heart; PA, pulmonary atresia; PDA, patent ductus arteriosus; PS, pulmonary stenosis; TAPVR, total anomalous pulmonary venous return; TGA, transposition of the great vessels; TOF, tetralogy of Fallot; VSD, ventricular septal defect.

Cardioteratogenic agents

Sometimes it take decades before a product is identified as teratogenic.

Valproic Acid (antiepileptic)

Comercialized in the 60's

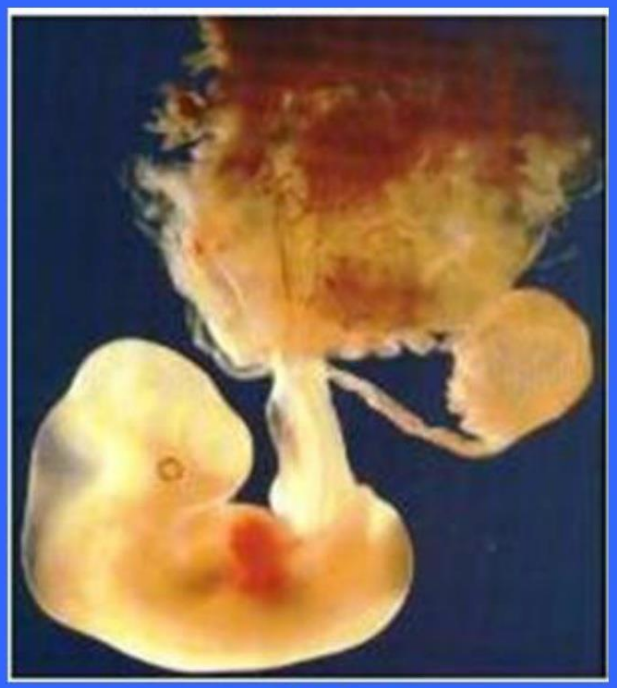
Identified as a human teratogen in the 80's:

Neural tube defects, CHD, autistic and behavioral troubles

Induction period

The cardiovascular system is one of the first body systems to appear within the embryo.

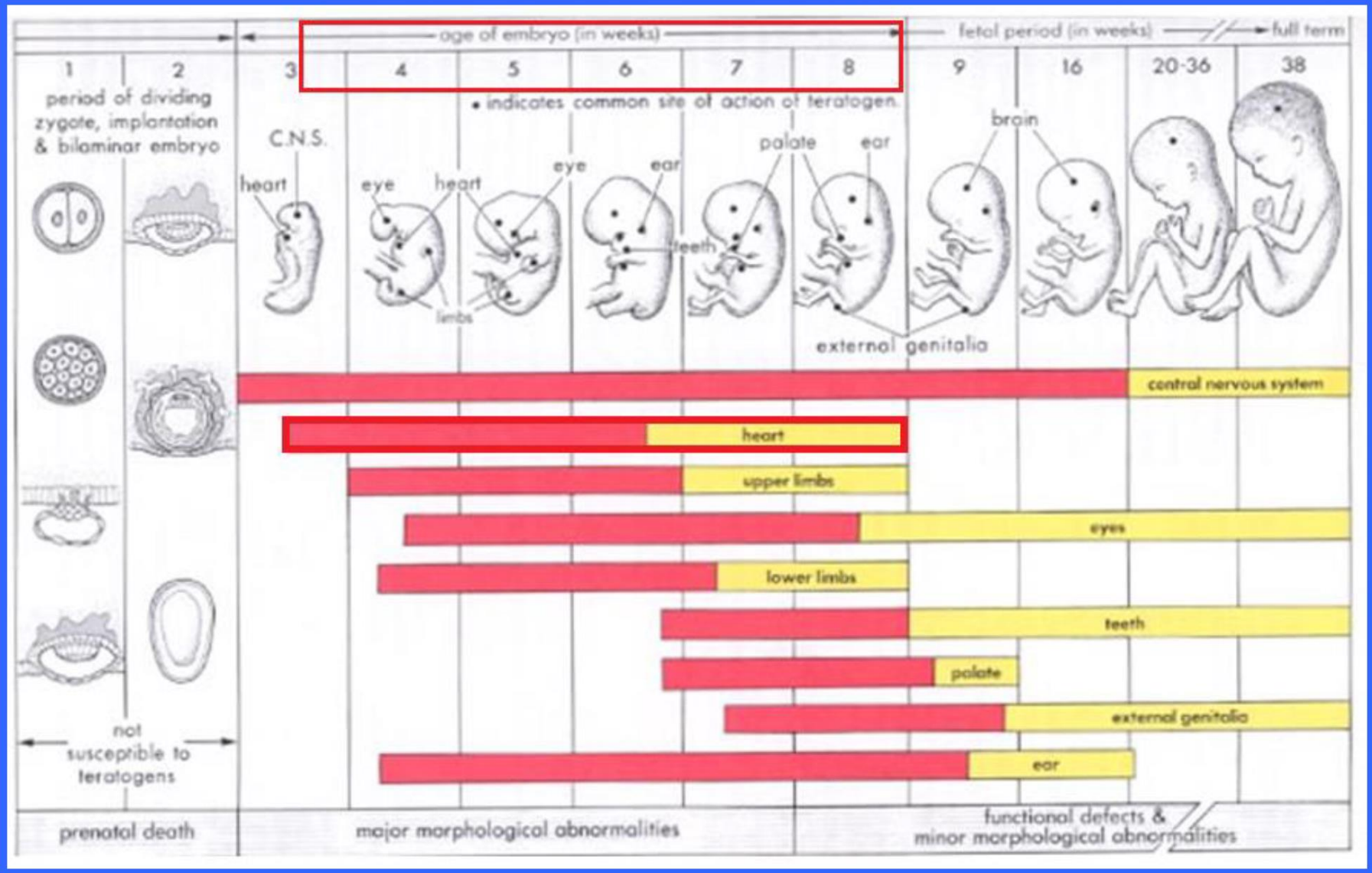
It is active by the beginning of the fourth *week.*



4 Week

All CHD are induced at last before the 8 week of gestation.

Induction period > sensibility to teratogenic agents



Classification

Various classification are used, the « simpliest »

Cyanotic Heart Disease	Acyanotic Heart Disease
• Decreased pulmonary flow: – Tetralogy of Fallot – Tricuspid atresia – Other univentricular heart with pulmonary stenosis. • Increased pulmonary flow: – Transposition of great arteries – Total anomalous pulmonary venous return.	• Left – Right shunt lesions: – Ventricular septal defect – Atrial Septal Defect – Atrio-ventricular Septal Defect – Patent Ductus Arteriosus • Obstructive lesions: – Aortic stenosis – Pulmonary valve stenosis – Coarctation of Aorta

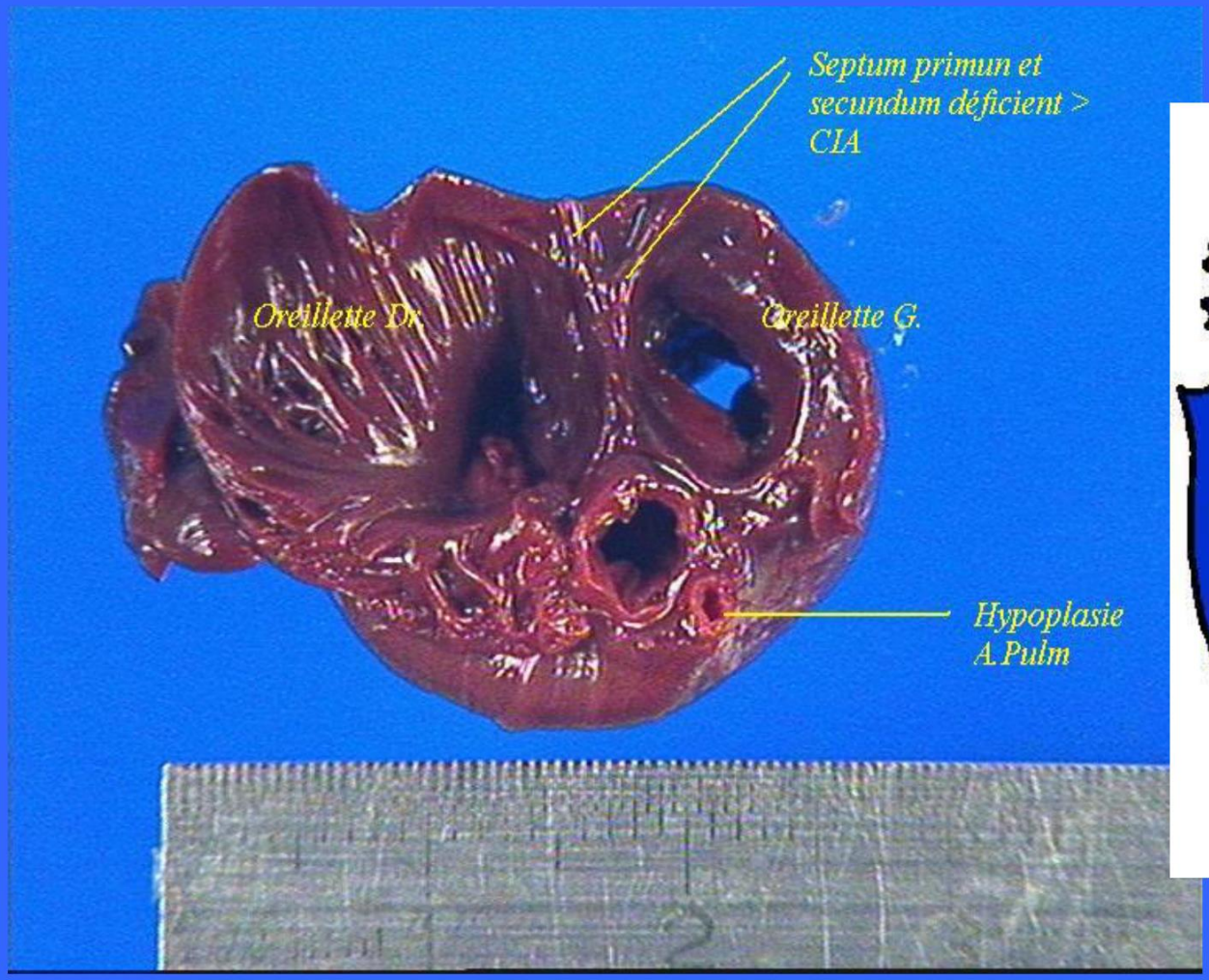
Illustration of the most common anomalies

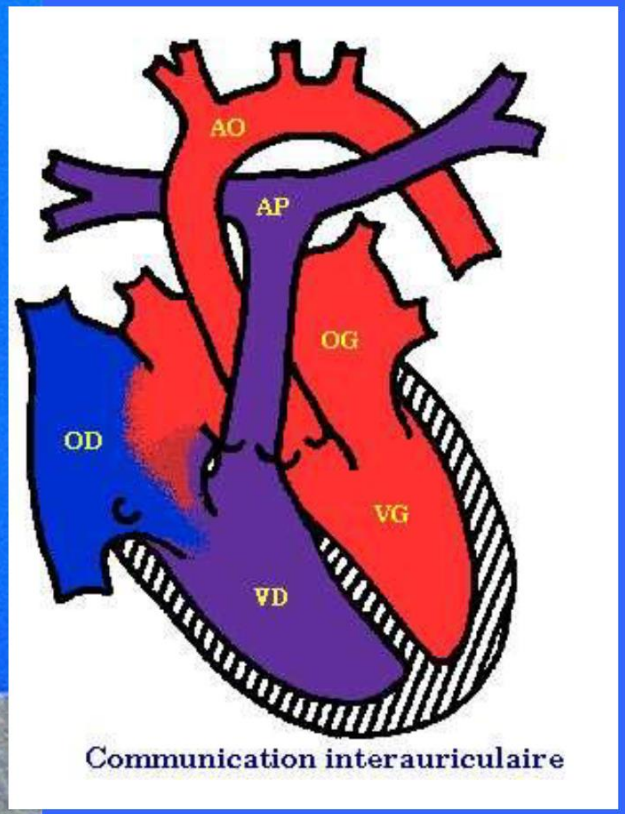
- Illustrations from spontaneous IU deaths and medical abortion for wich an autopsy was performed in our institute.

- % are approximative (Mix of various studies from UK / US and Eurocat).

Atrial Septal Defect

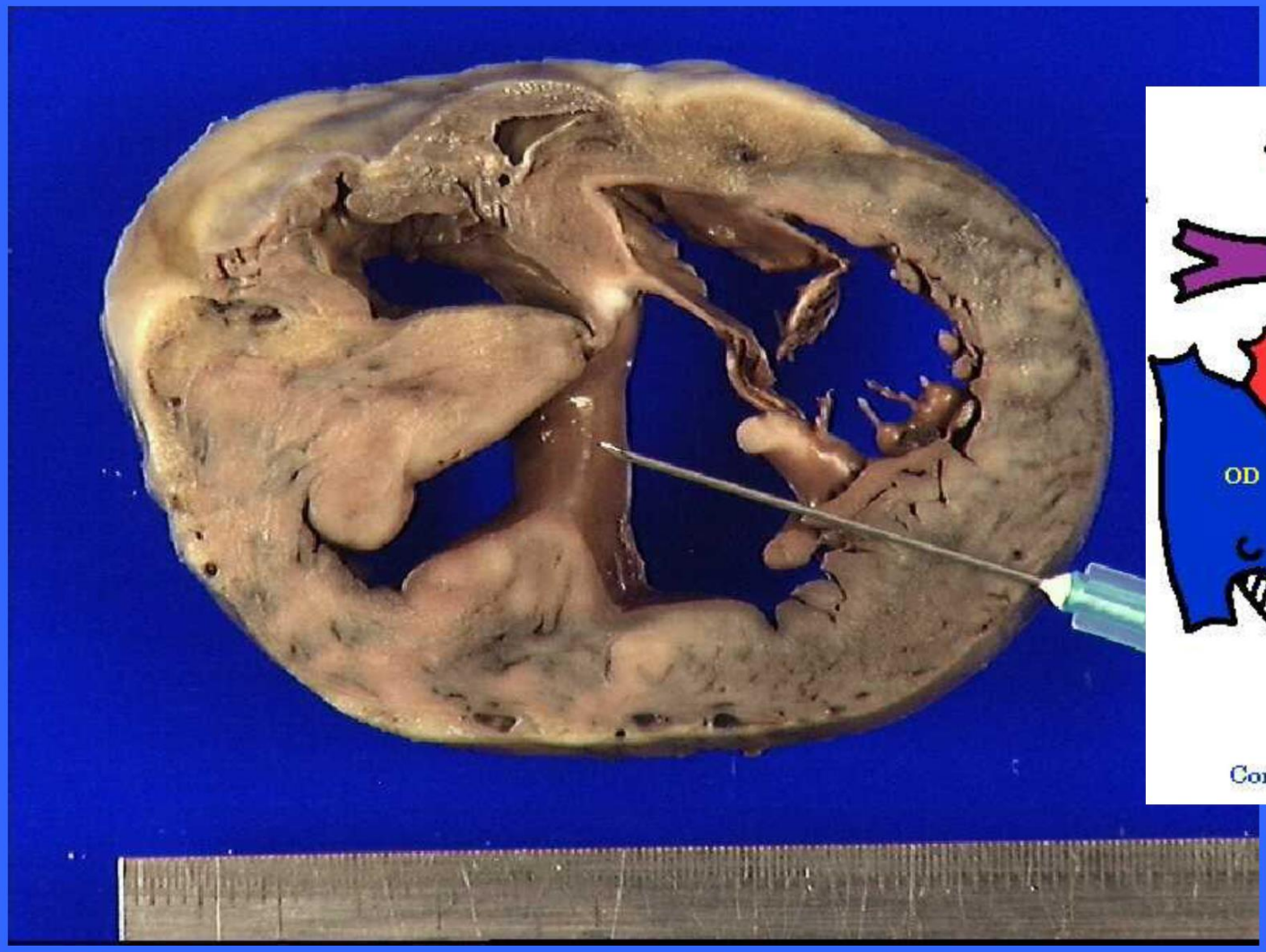
- 10% of CHD

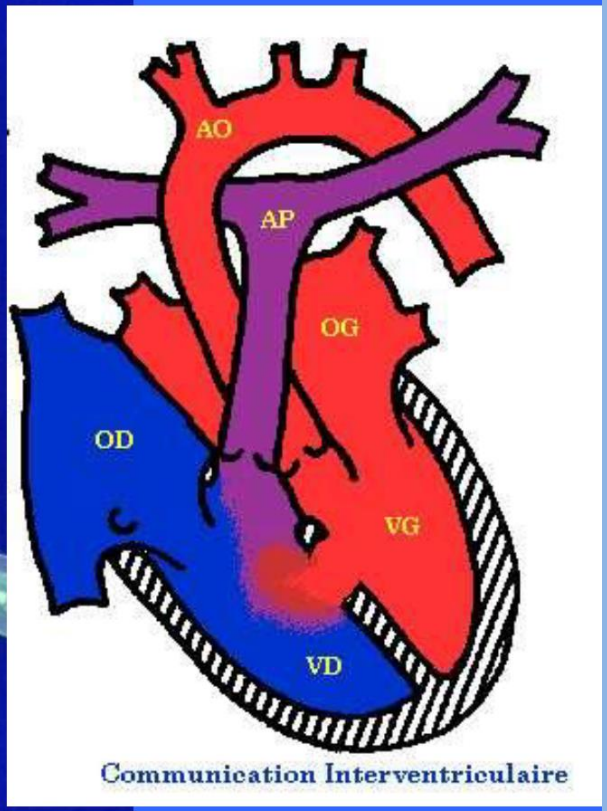




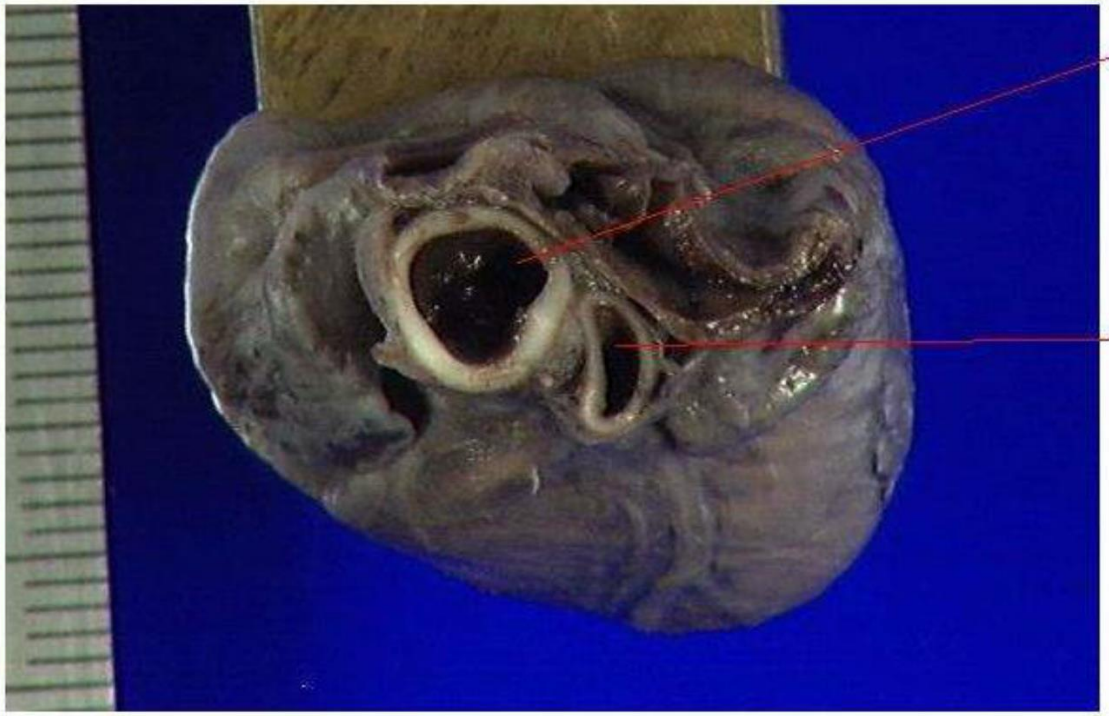
Ventricular septal defect

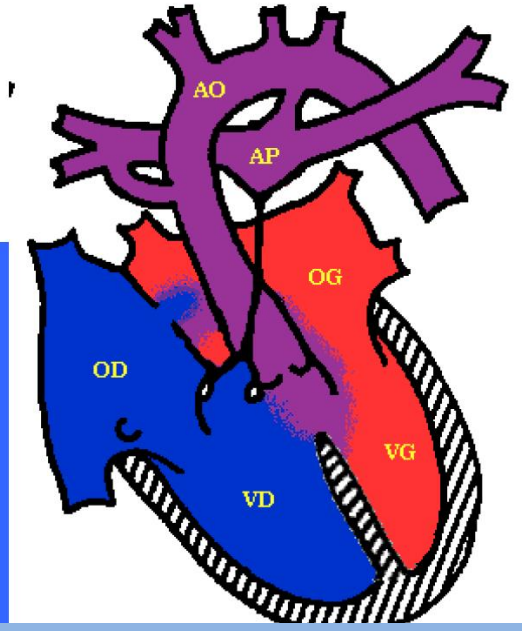
+/- 20-30 % of CHD





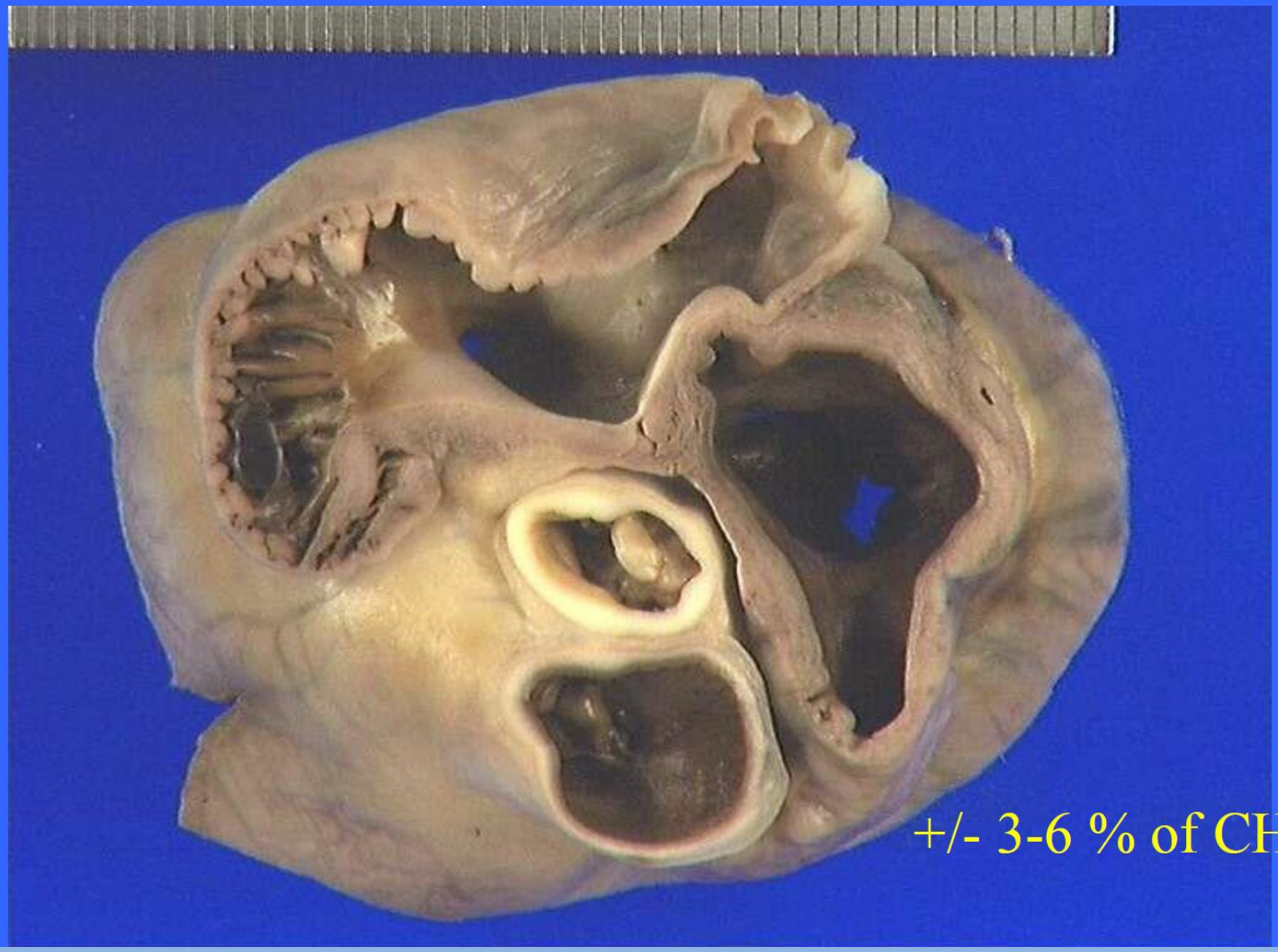
Pulmonary stenosis





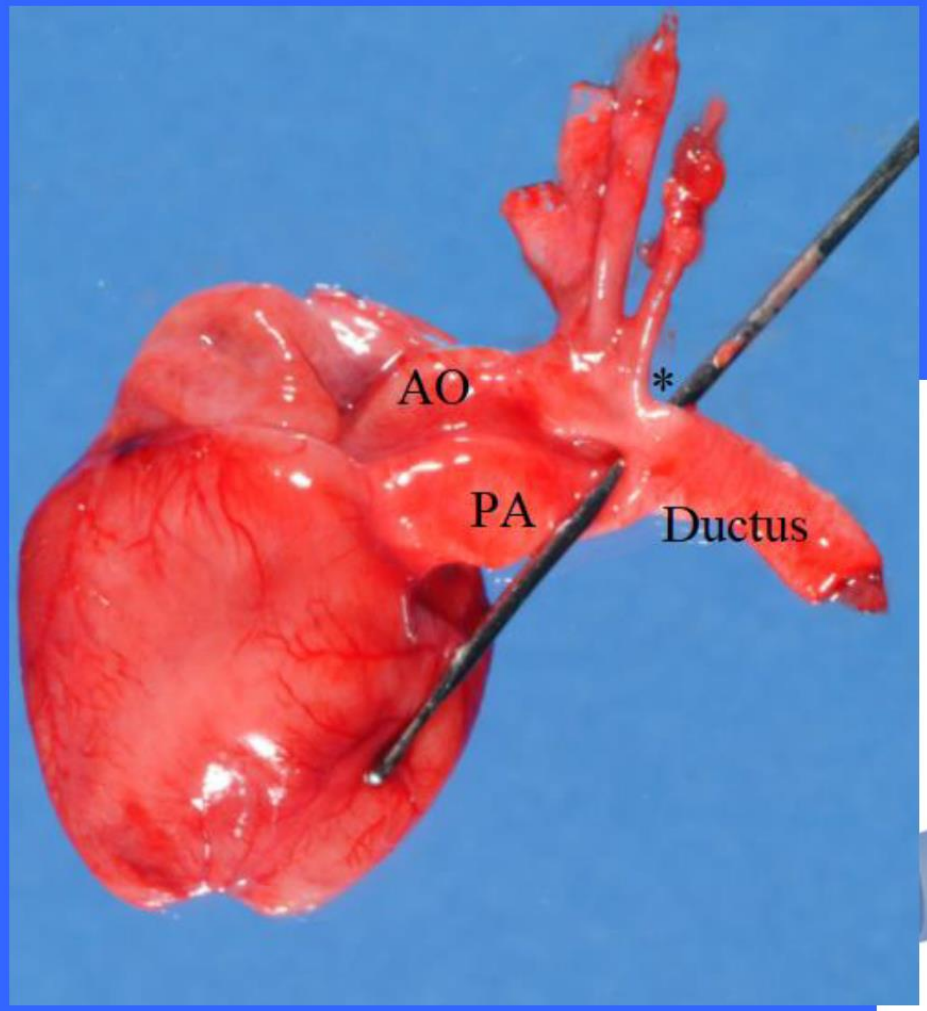
+/- 5-10 % of CHD

Aortic stenosis

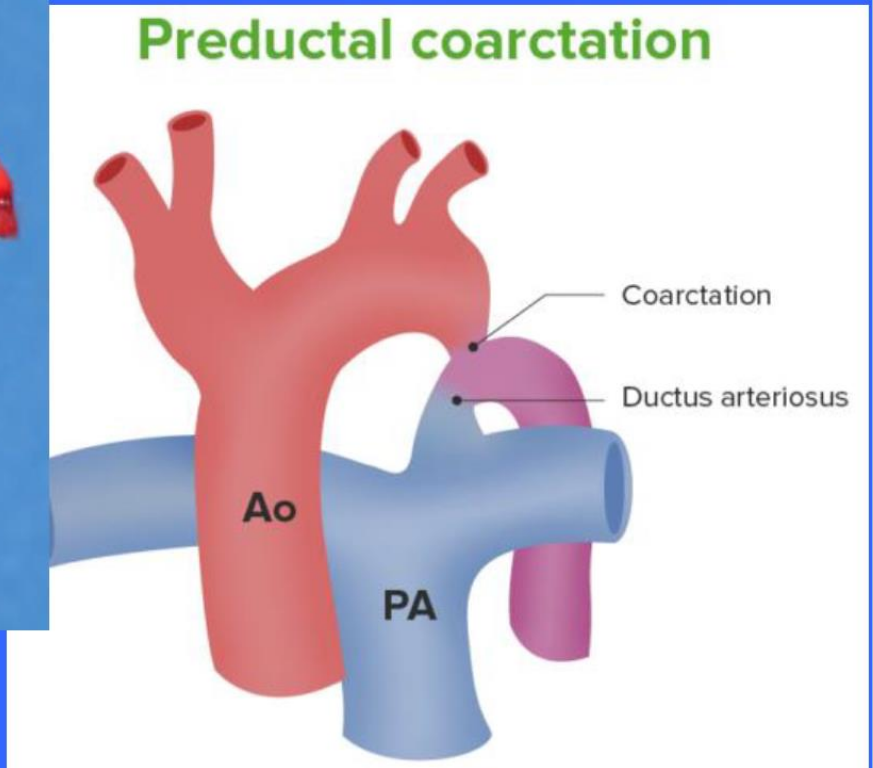


+/- 3-6 % of CHD

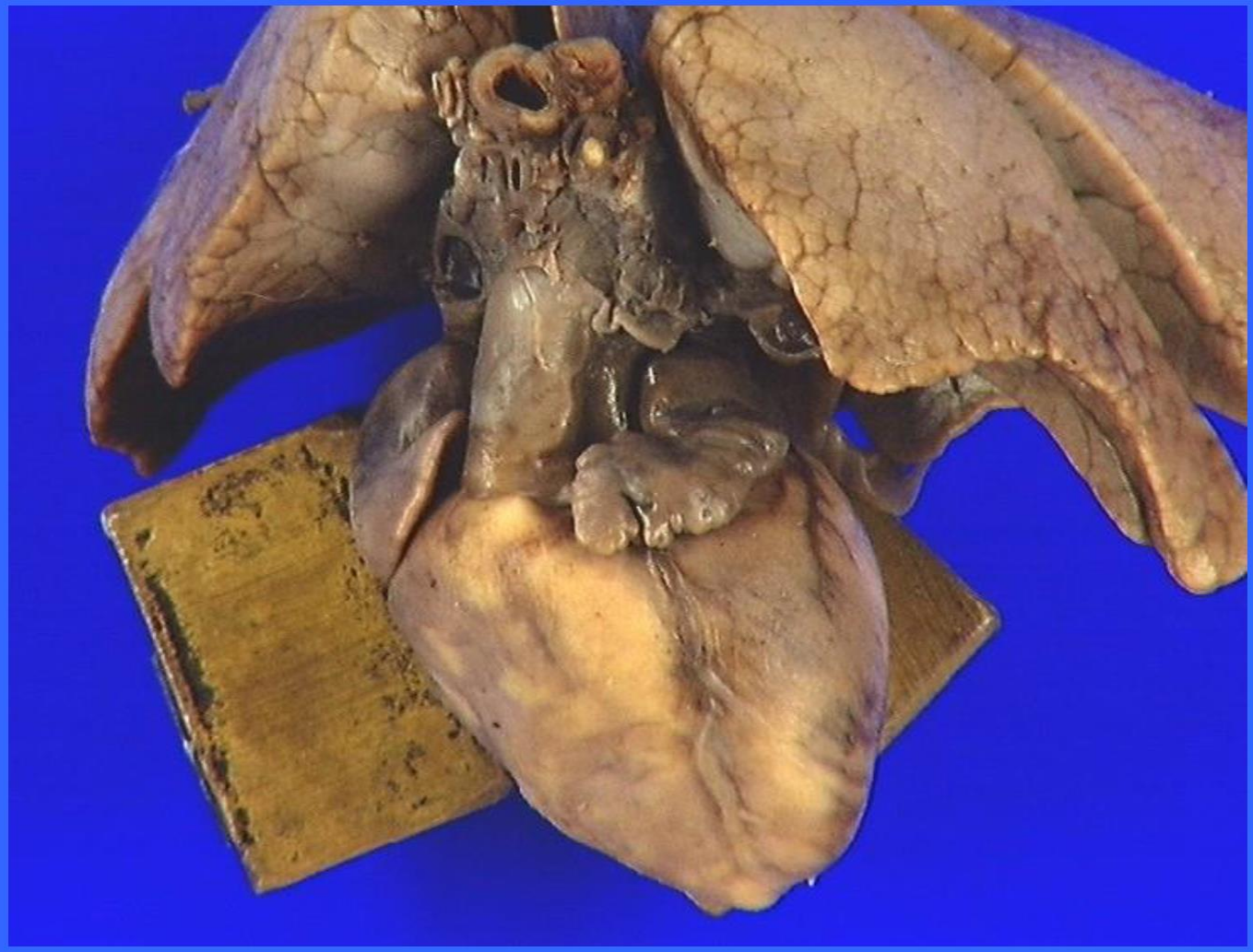
Coarctation of Aorta



+/- 5-10 % of CHD



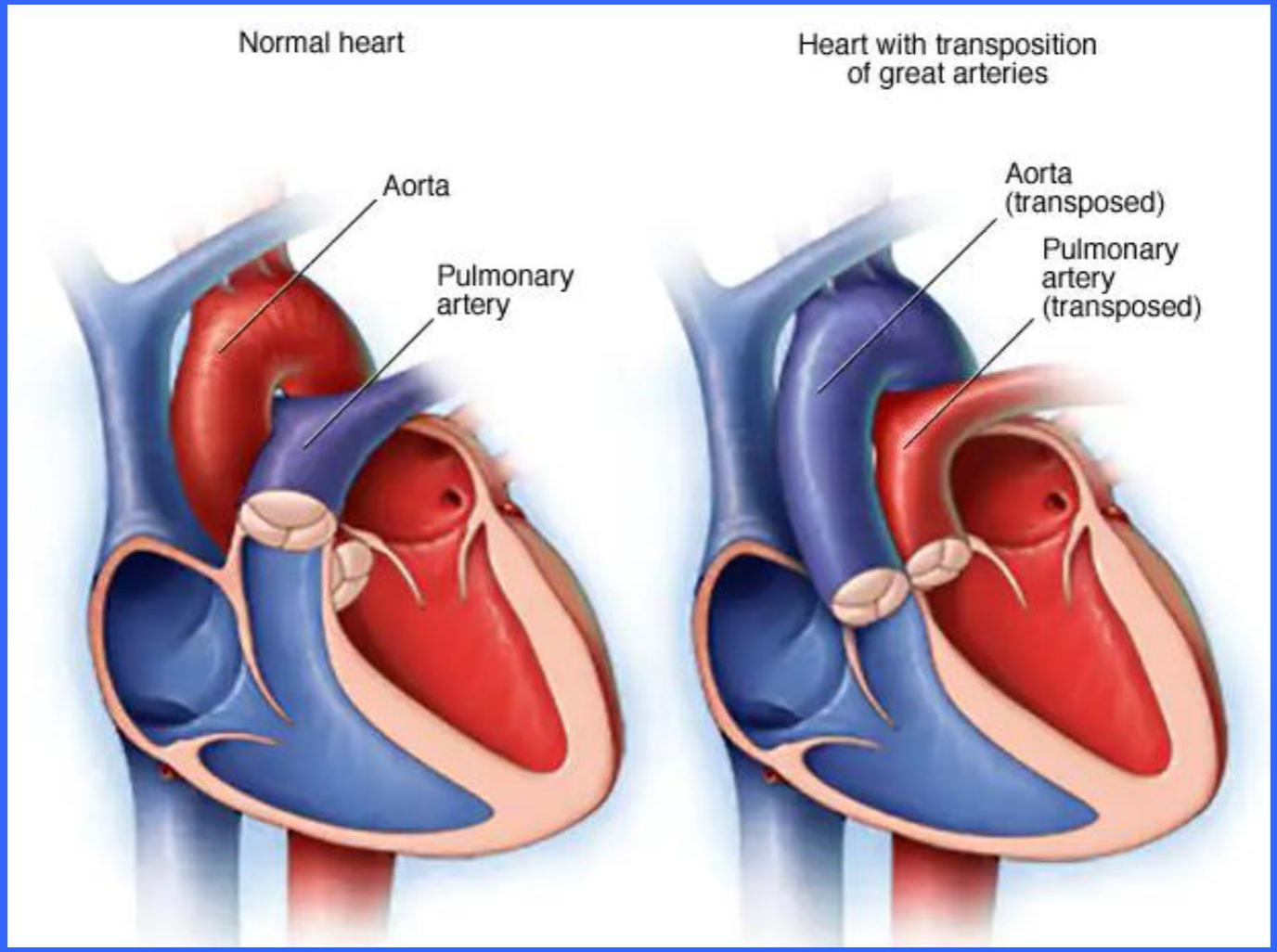
Transposition of great arteries



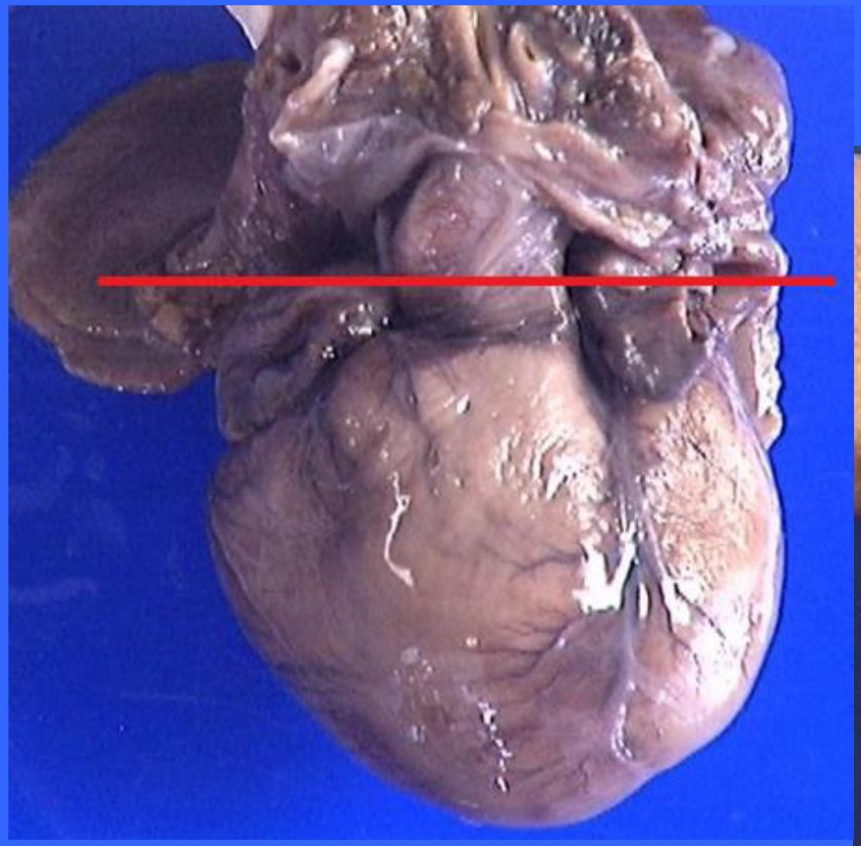
+/- 3 % of CHD

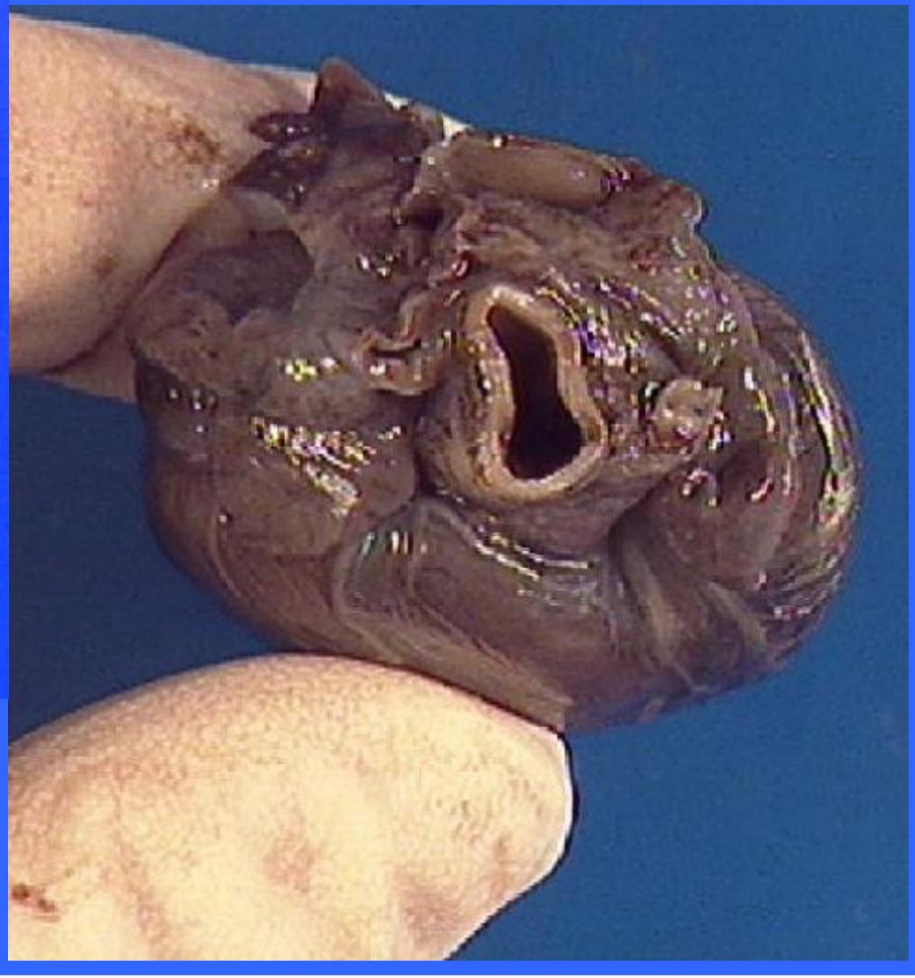
Transposition of great arteries

Transposition of great arteries



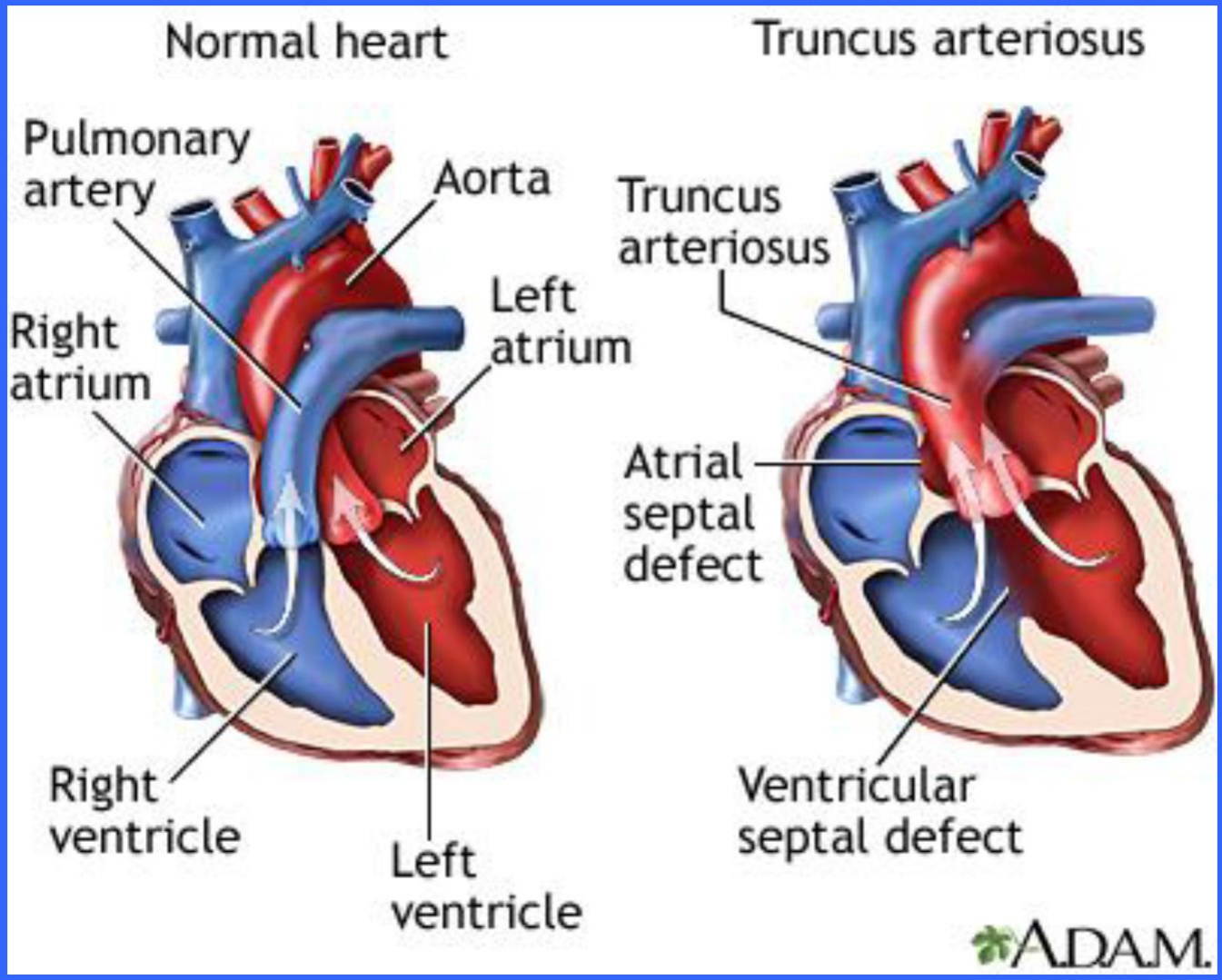
Truncus Arteriosus



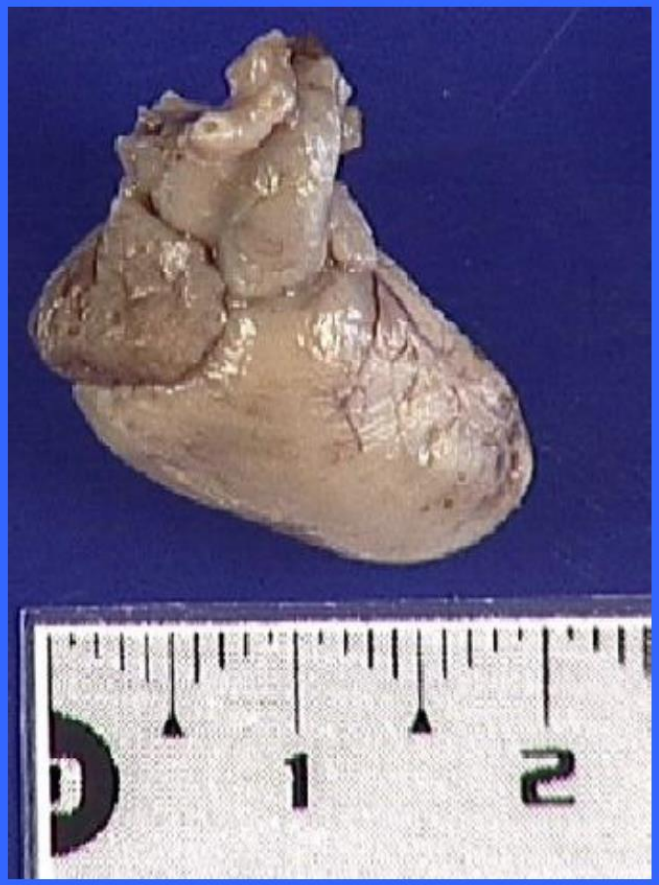


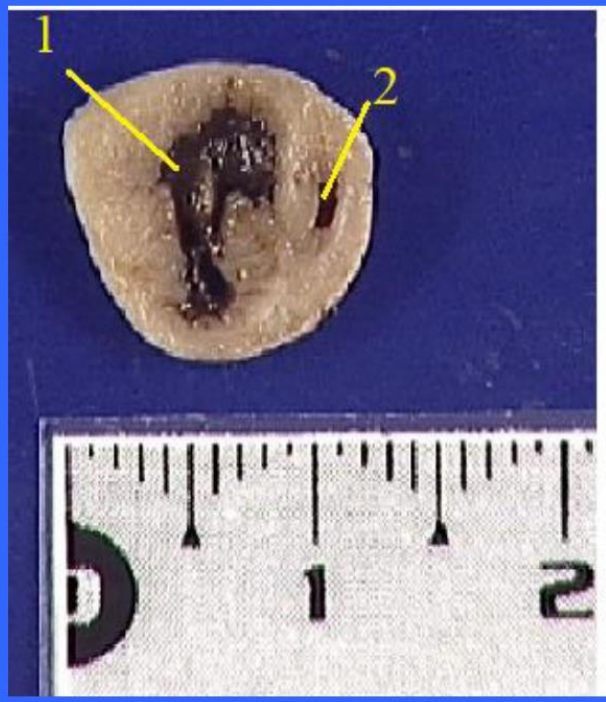
+/- 1 % of CHD

Truncus Arteriosus



Hypoplastic left heart

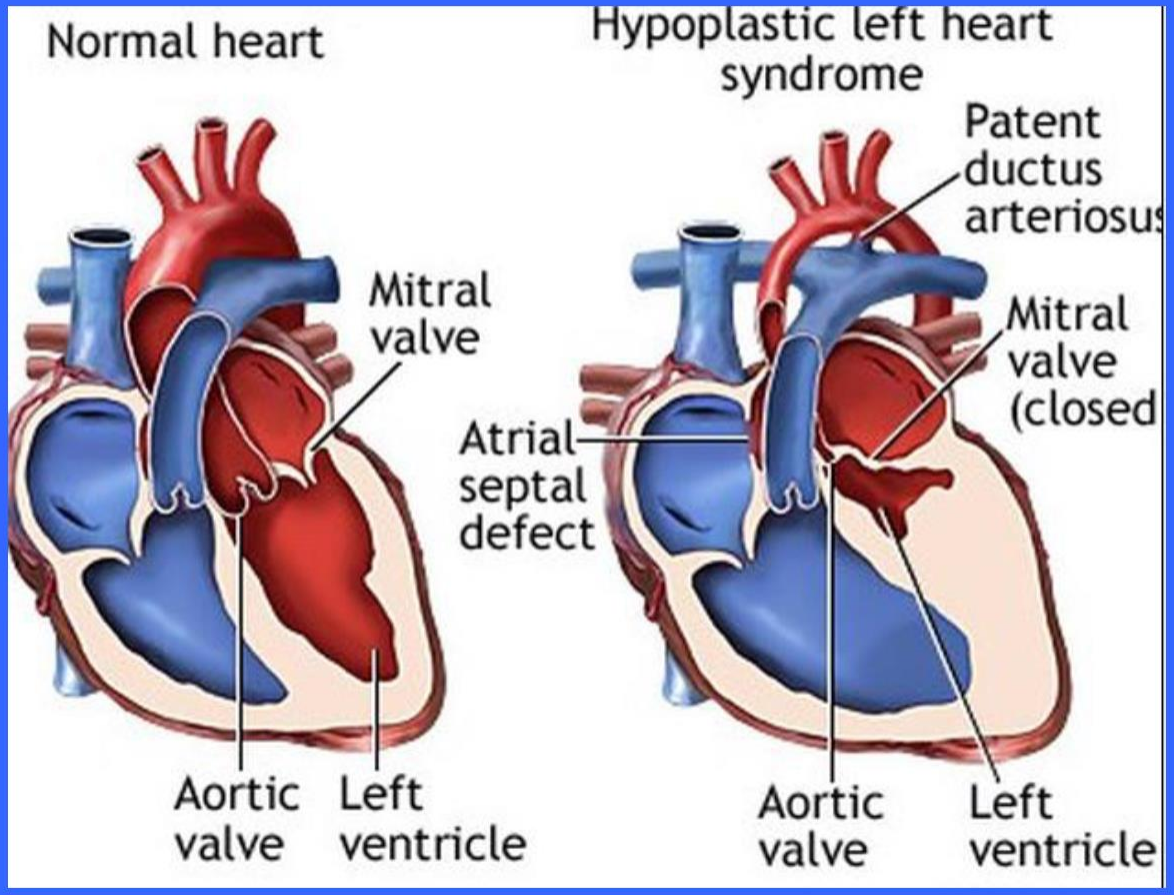




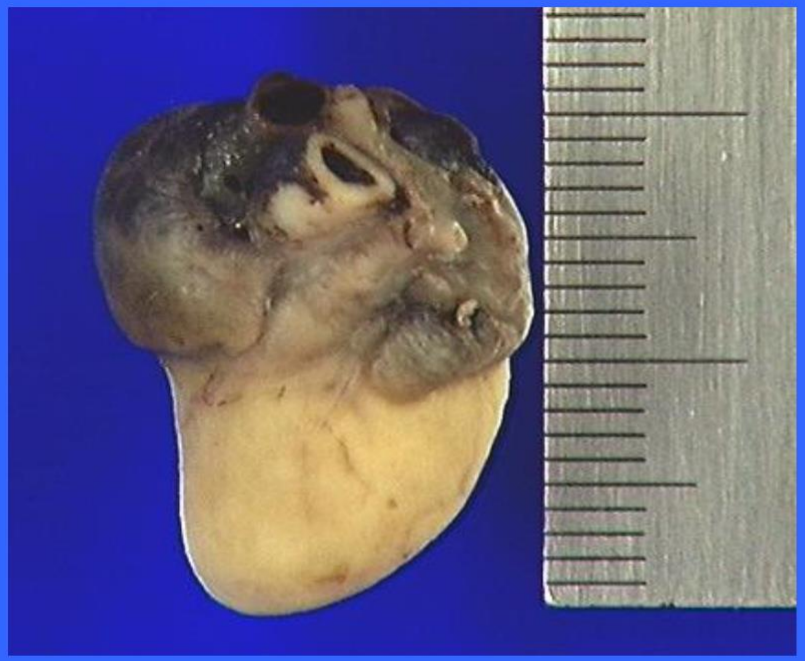
1 Right Ventricule
2 Hypoplastic left ventricule

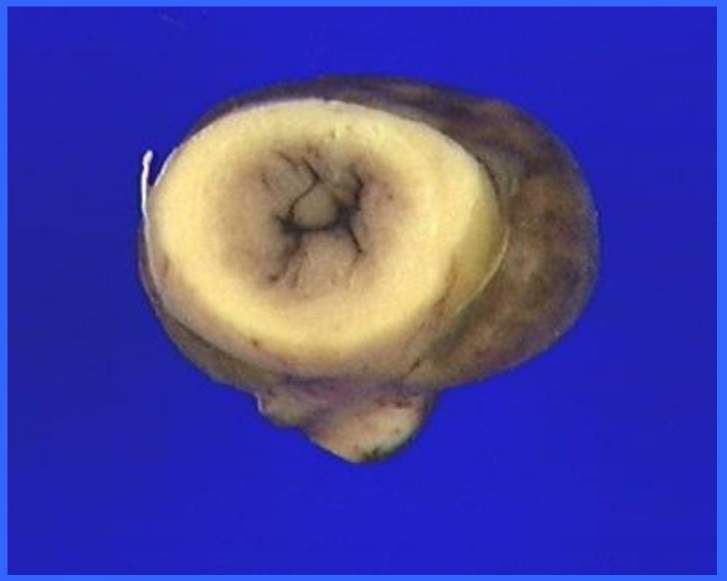
+/- 2 - 9 % of CHD

Hypoplastic left heart



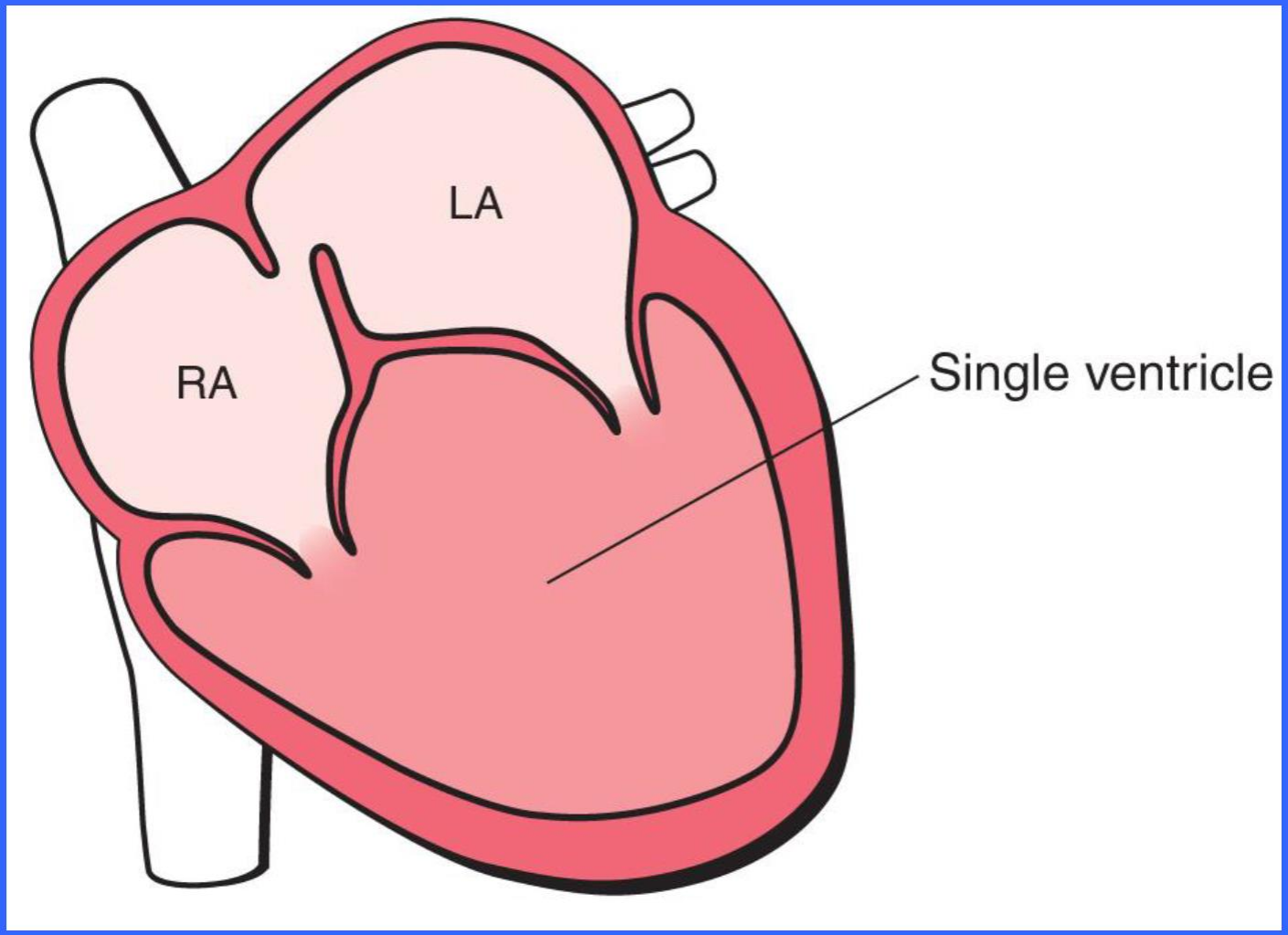
Univentricular Heart



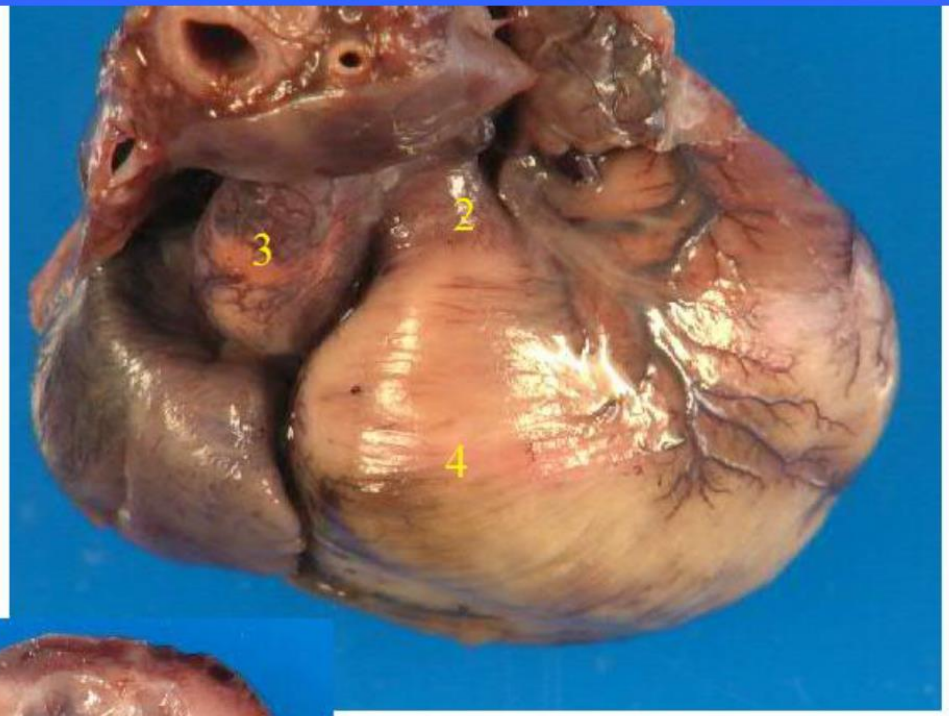


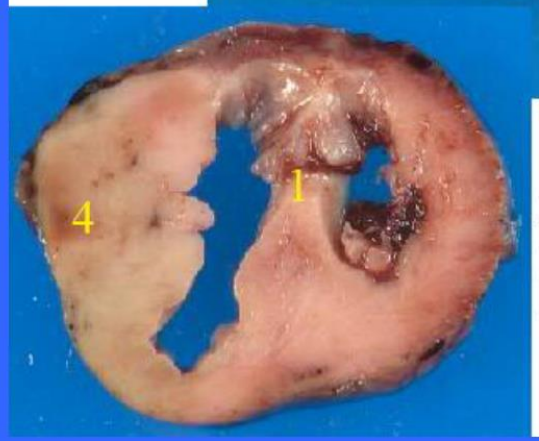
<1 % of CHD

Univentricular Heart

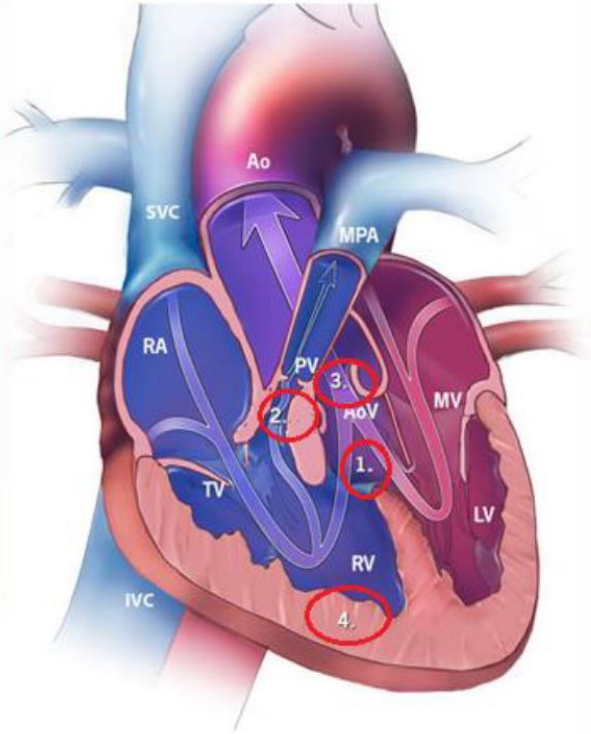


Tetralogy of Fallot



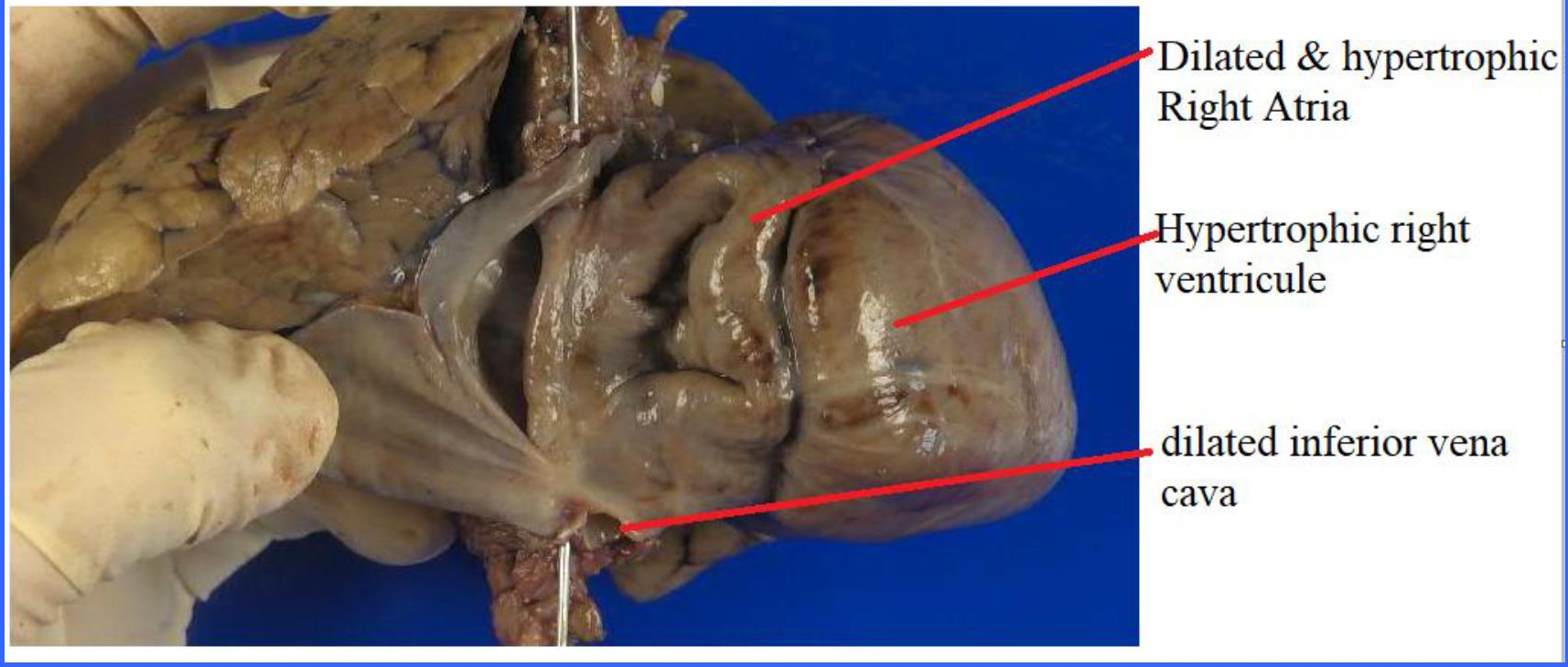


1 = VSD
2 = pulmonary stenosis
3 = dextroposition of aorta
4 = right ventricule hypertrophy

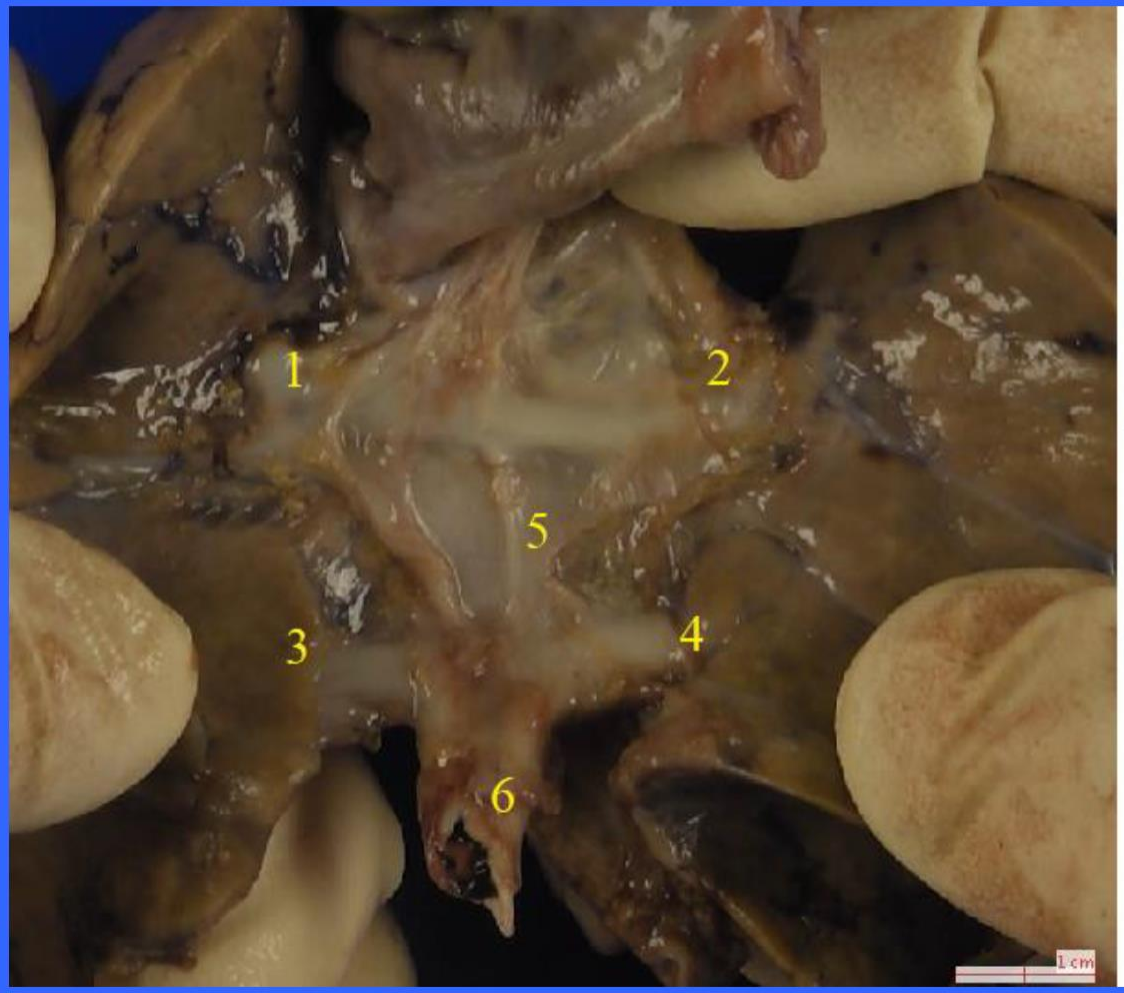


+/- 5-10 % of CHD

Abnormal pulmonary venous return



Abnormal pulmonary venous return



1 = left sup pulm. vein

2 = right sup pulm. vein

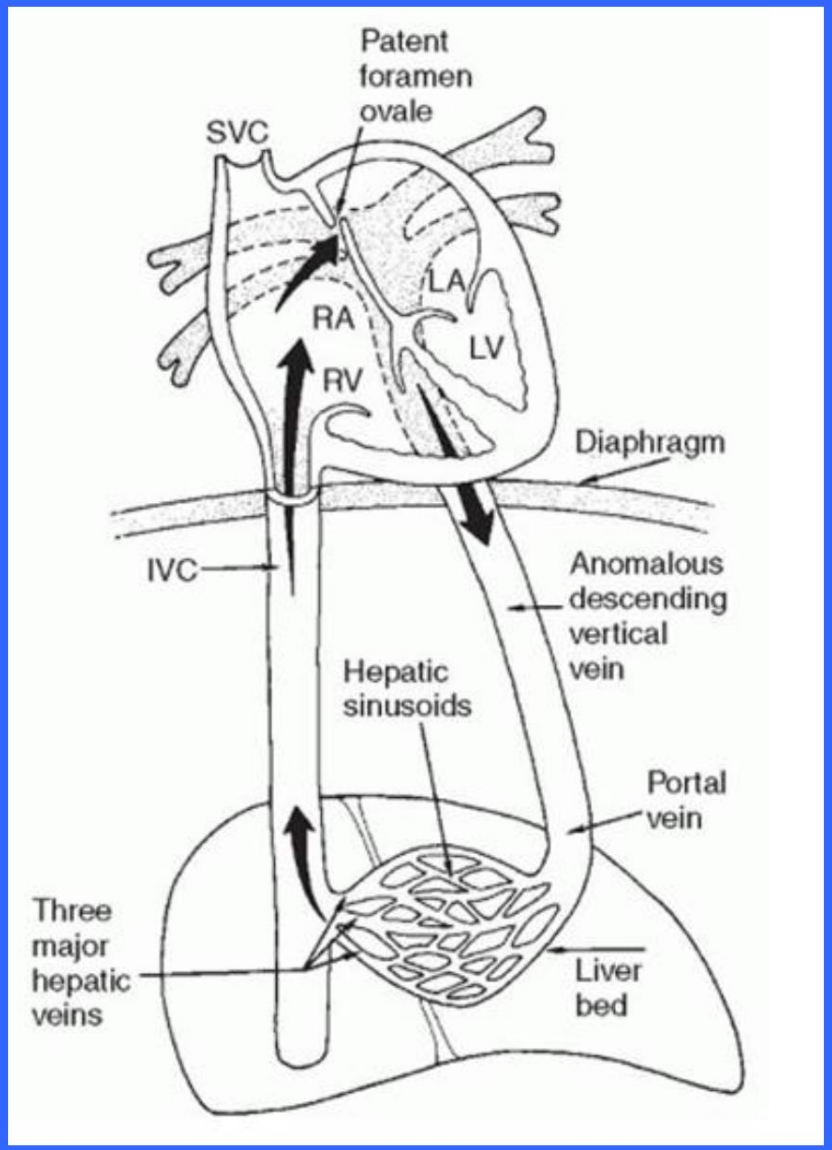
3 = left inferior pulm. vein

4 = right inferior pulm. vein

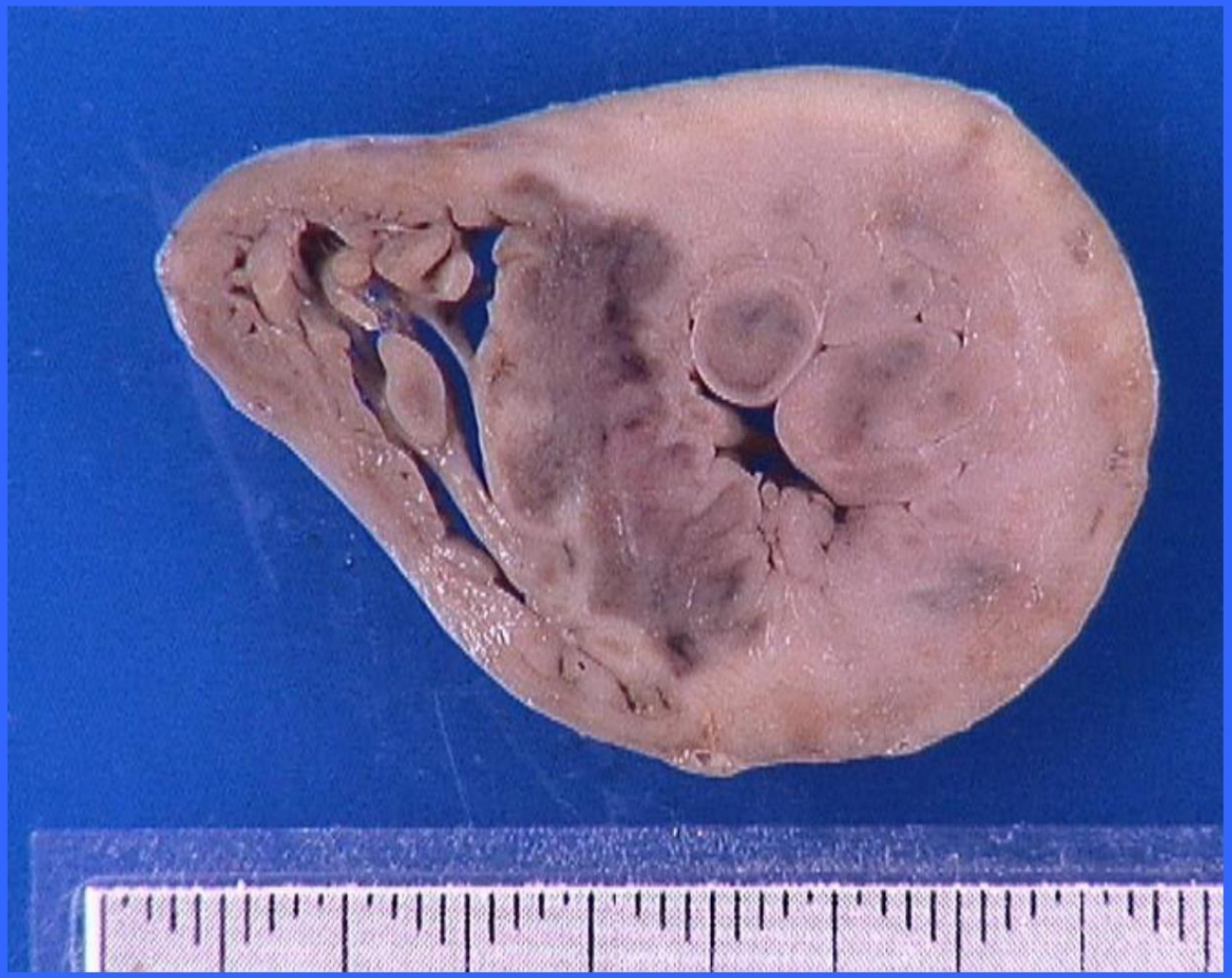
5 = small bridging vein

6 = Abnormal vein to the portal system

Abnormal pulmonary venous return



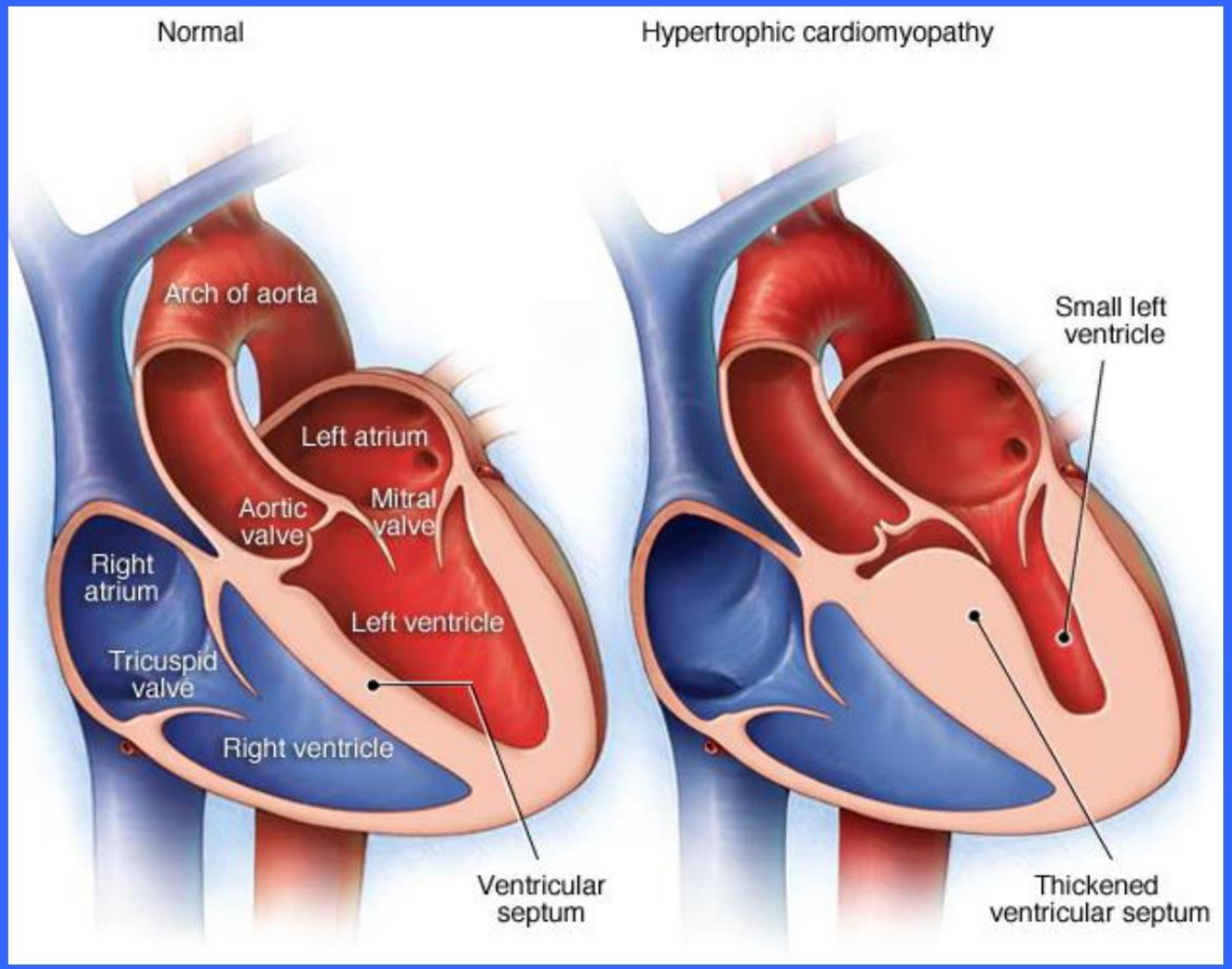
Hypertrophic Cardiomyopathy



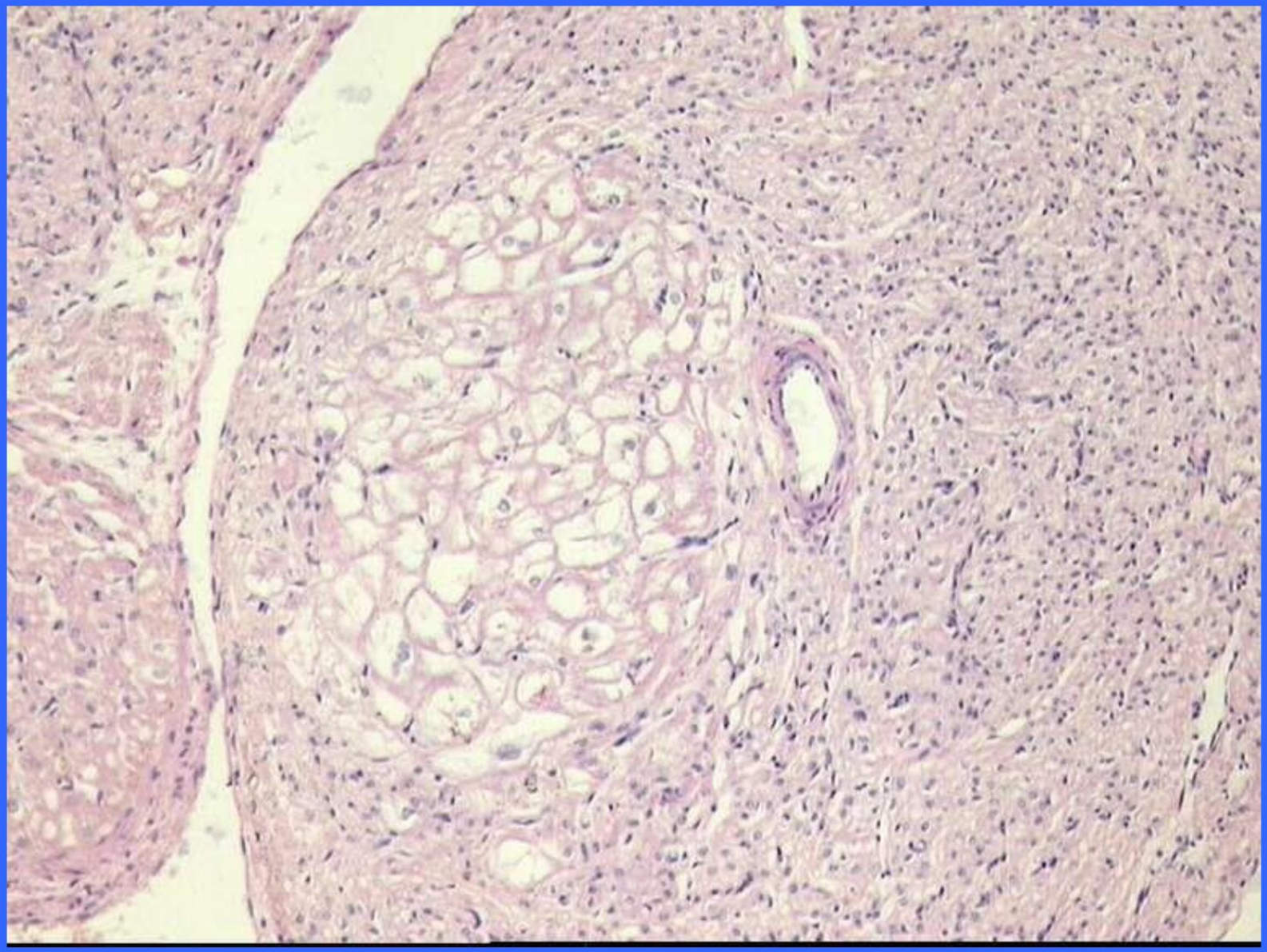
< 1 (‰) of CHD

Hypertrophic Cardiomyopathy

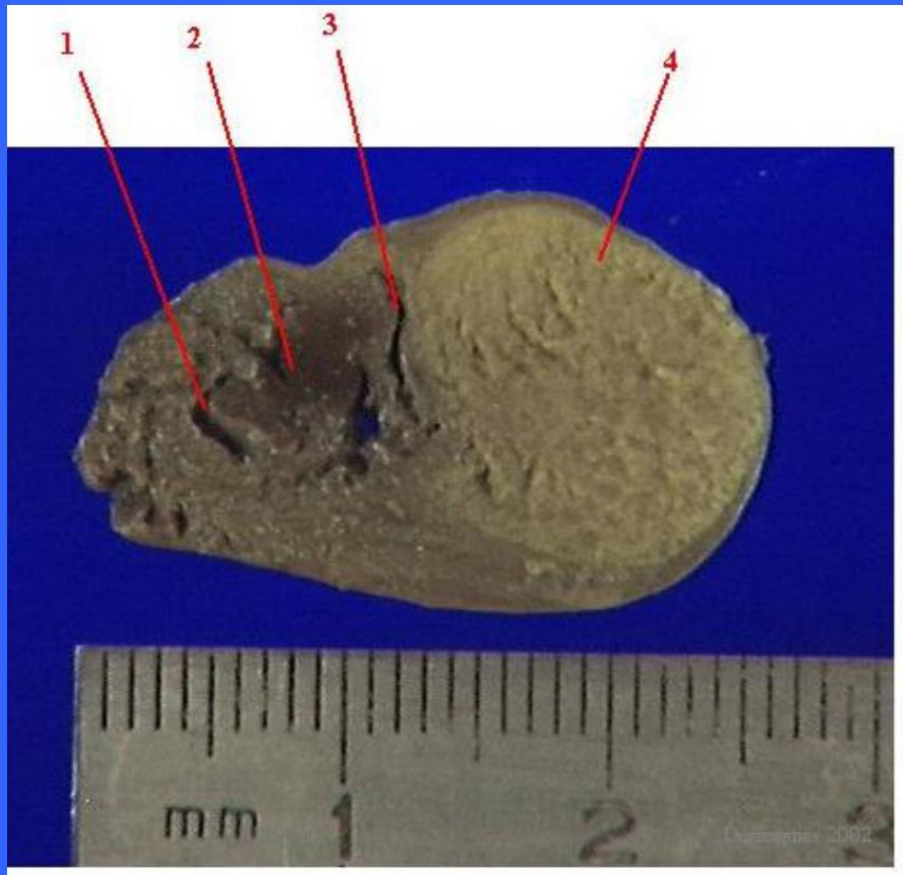
Hypertrophic Cardiomyopathy



Tumors: rhabdomyoma, teratoma, lipoma



Cardiac teratoma > cardiac failure> IU Death



1 Right Ventricule

2 septum

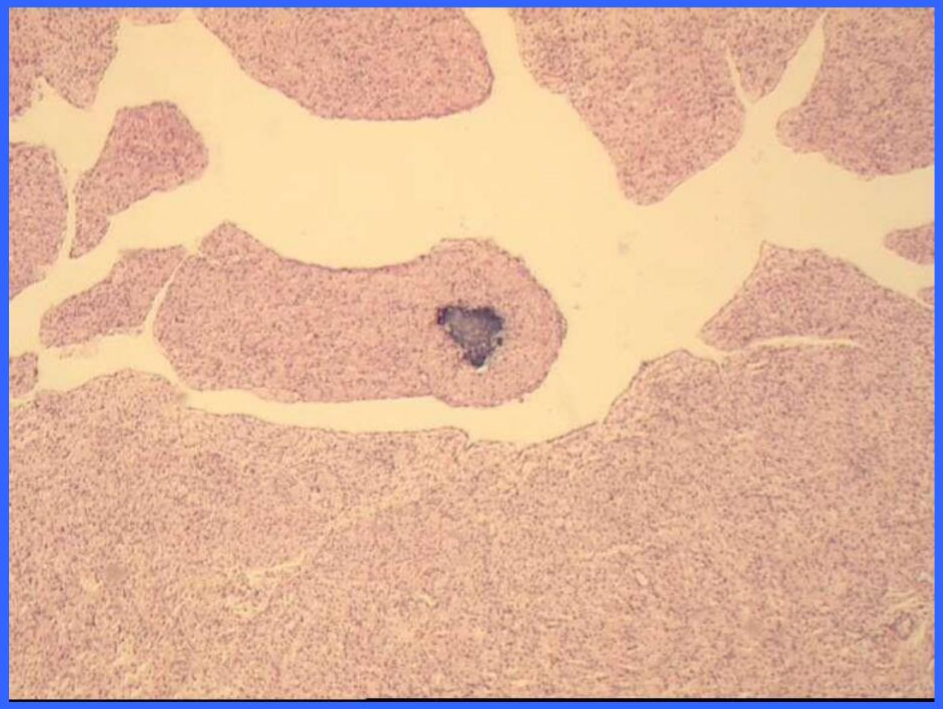
3 Left ventricula

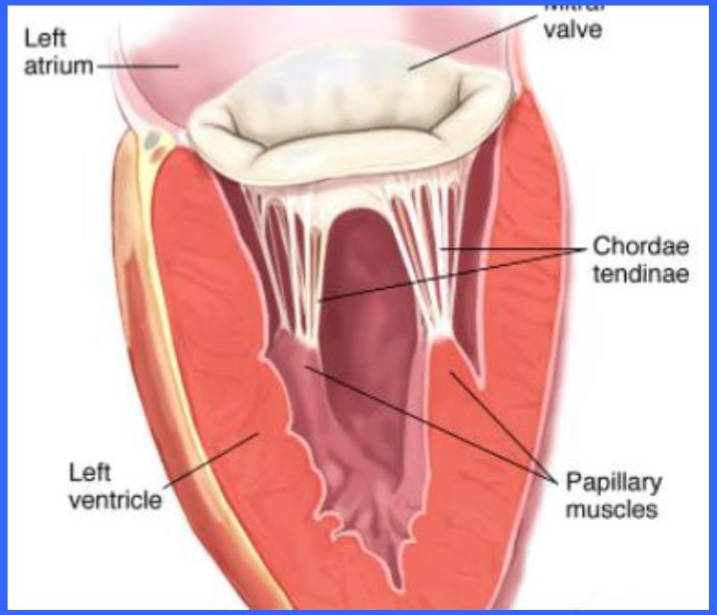
4 Tumor

Heart Calcification

<u>isolated</u> myocardic calcification

- Generally in papillary muscle
- More frequent in Trisomy 21, but also seen in Triploid foetuses and more rarely in other chromosomal anomaly.

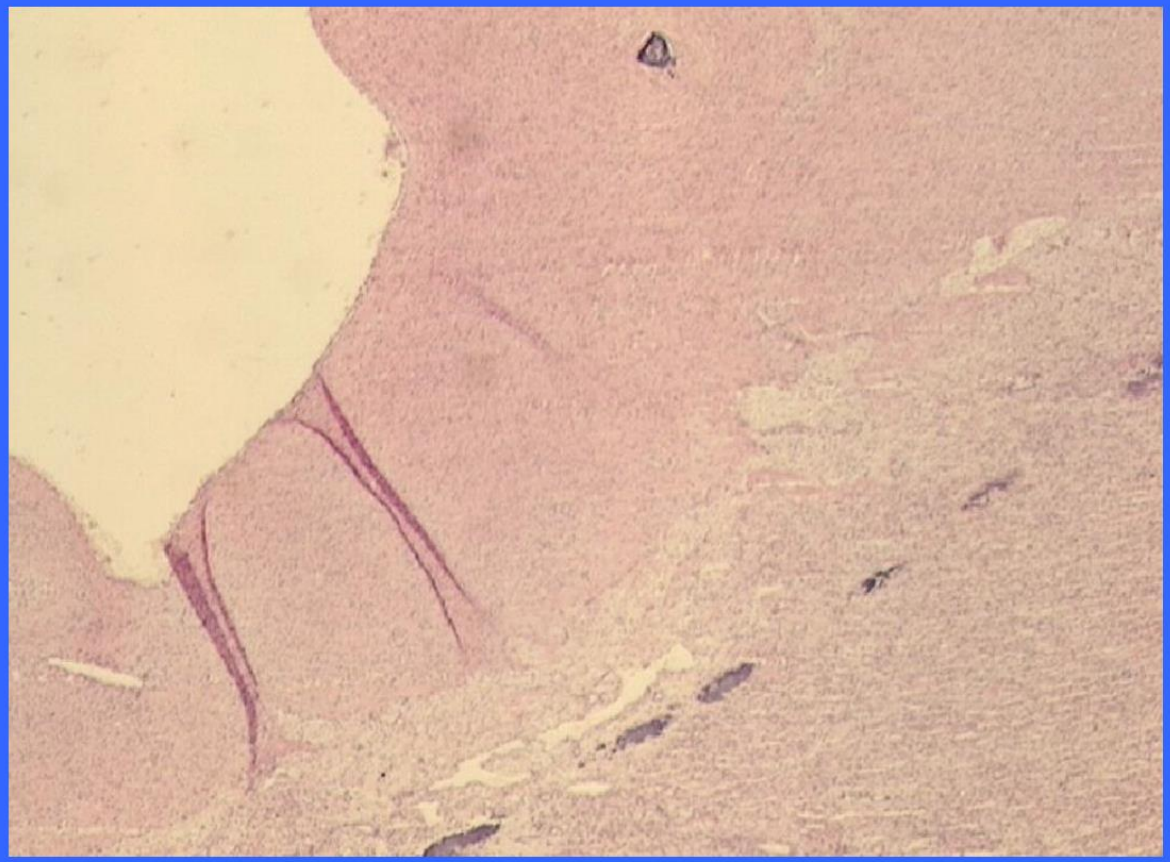




Heart Calcification

<u>Multiple linear</u> myocardic calcification

- In septum or ventricle
- Association with fibroelastosis



Heart Calcification

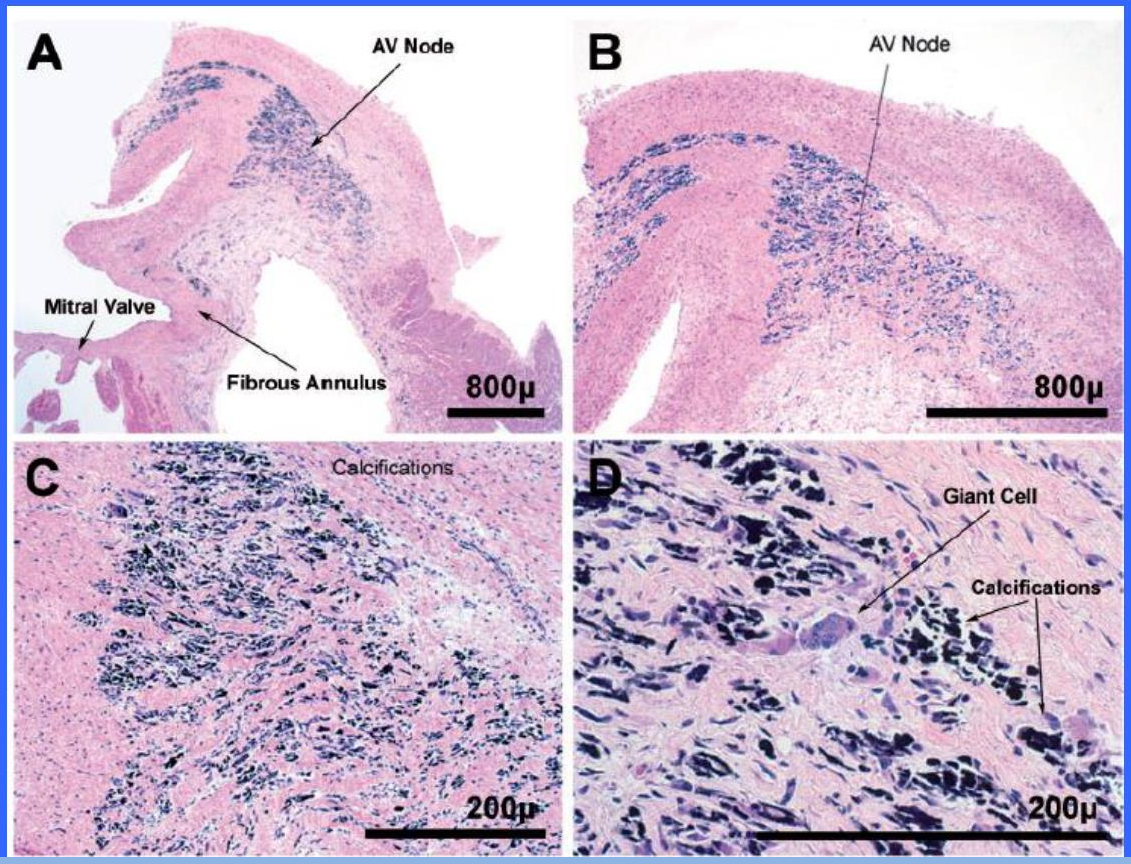
<u>Multiple linear</u> myocardic calcification

- Association with fibroelastosis

Heart Calcification

Multiple of various size around nodes

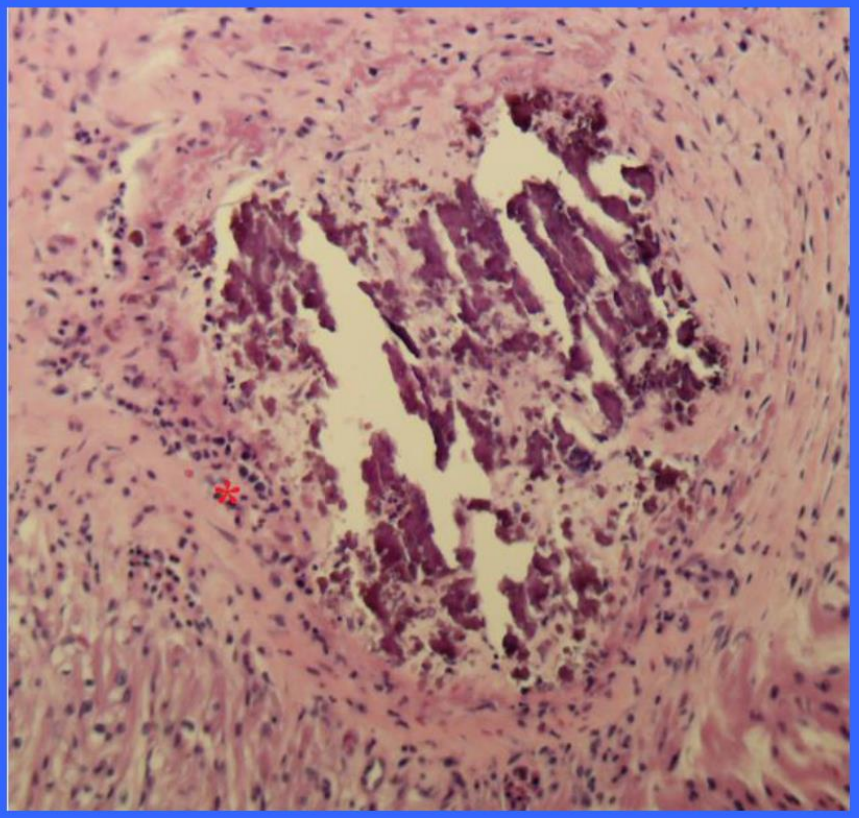
Congenital Lupus



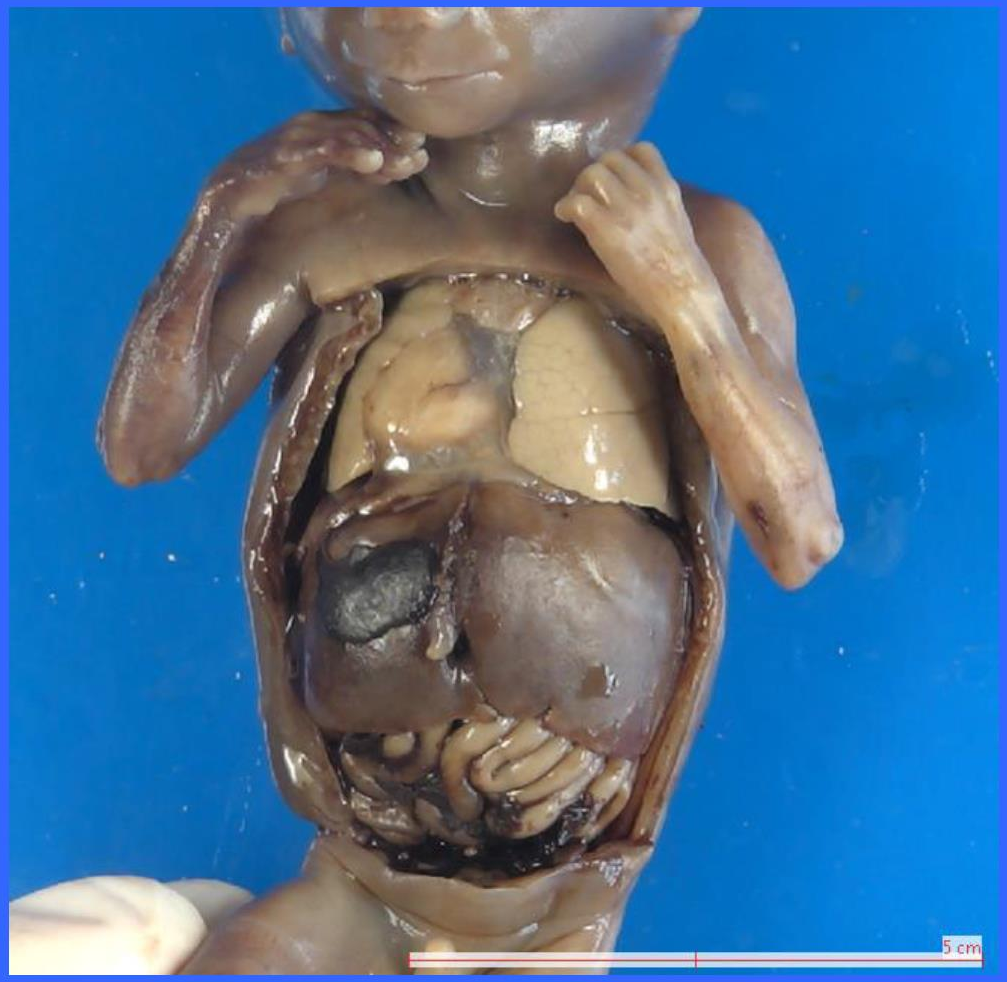
Heart Calcification

Isolated or multiple

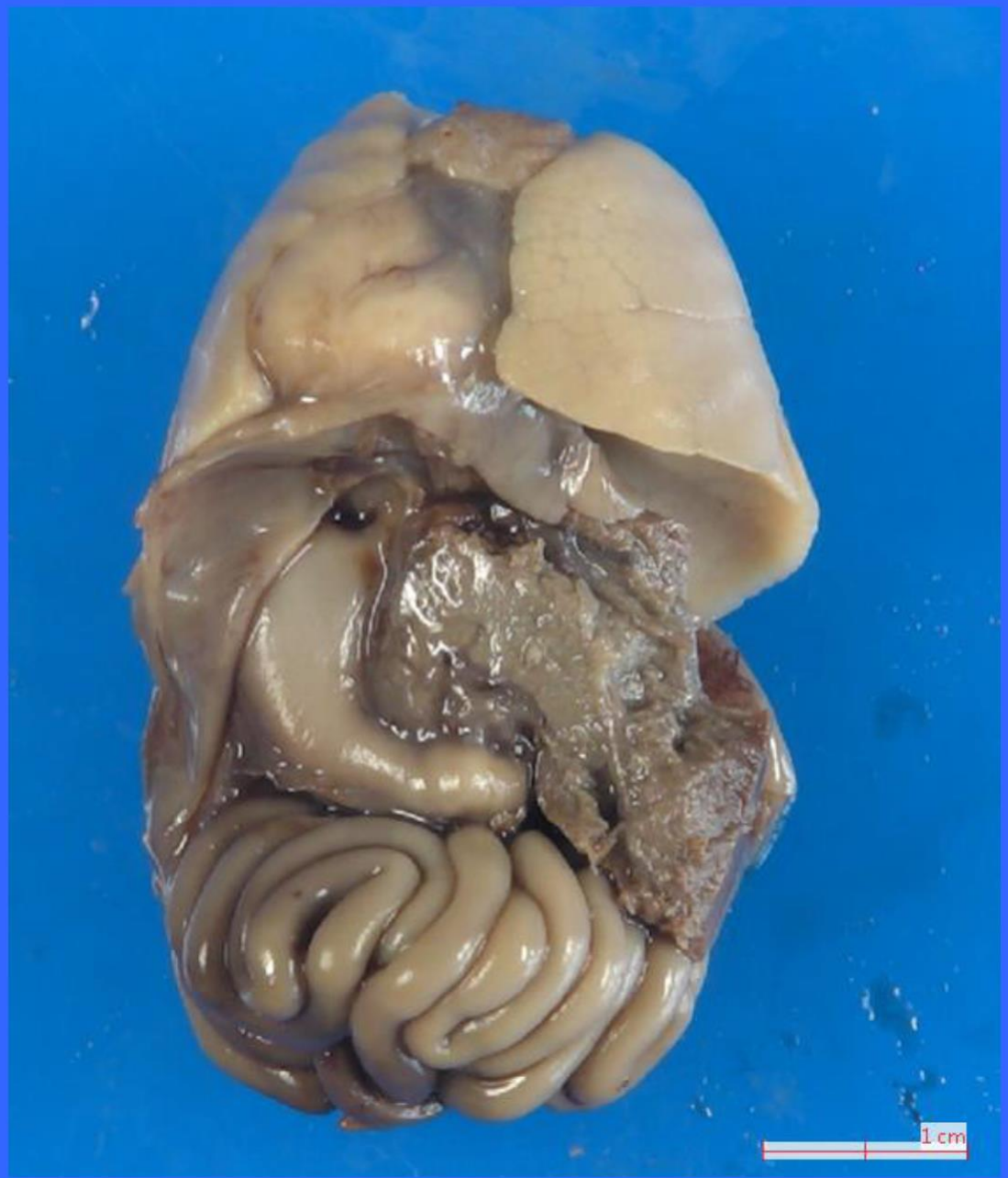
Myocardic necrosis (ischemic or infectious)



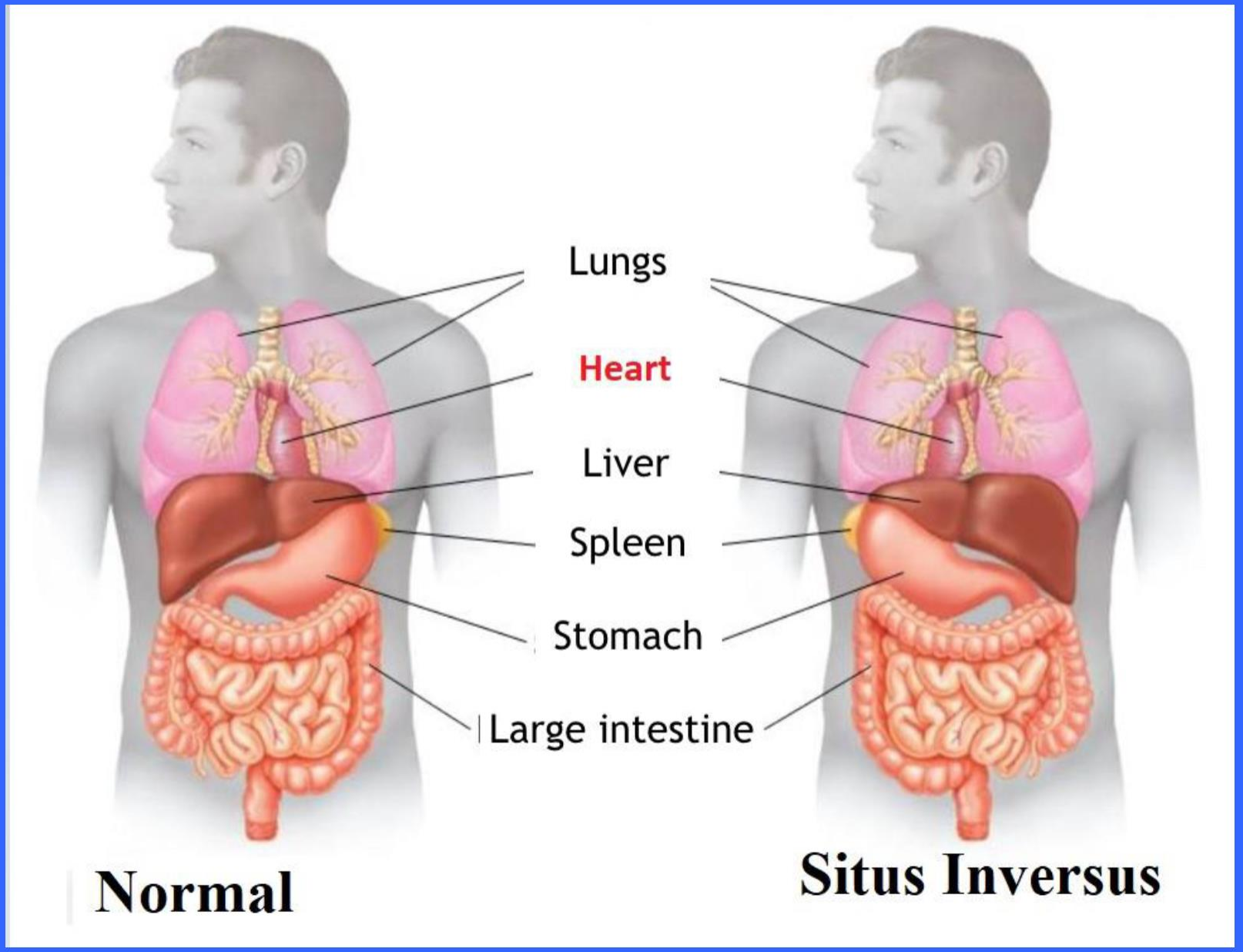
Situs Inversus



Situs Inversus



Situs Inversus



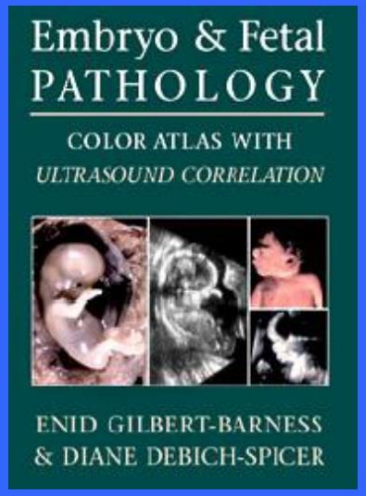
Situs Inversus

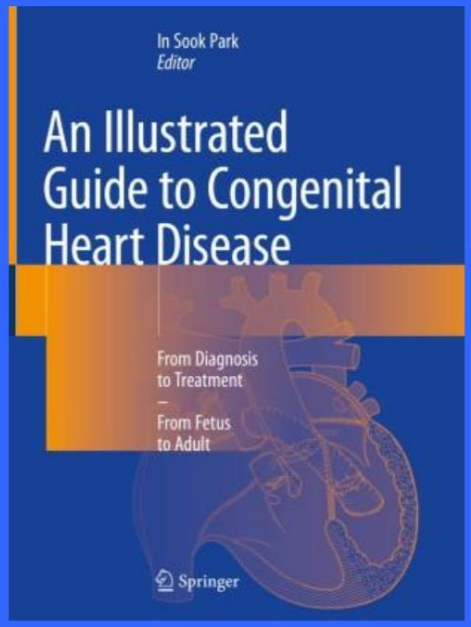
Affected people have no associated health issues when the condition is isolated.

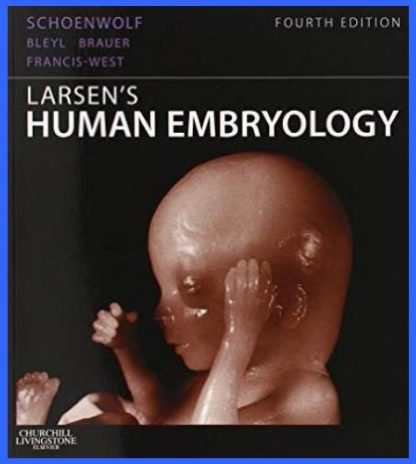
When situs inversus occurs in association with other conditions such as Kartagener syndrome or primary ciliary dyskinesia, additional signs and symptoms relating to these conditions will be present.

The genetics of situs inversus is heterogenous.

Familial cases have been reported as either autosomal recessive (most commonly), autosomal dominant, or X-linked







Dr DUGAUQUIER Christian