Congenital Heart Disease: Classification Systems

- Anatomic
- Physiologic
- Surgical Procedures
- Genetic or causal -

  The developmental stage determines the extent of the defect: Cardiac looping occurs early in development so heterotaxias are associated with mulitple, varied defects; VSDs may occur early or late and are, therefore, the most common defects.

Congenital Heart Disease: Prevalence

- 1.5-2.5/1000 live births.
- Bicuspid aortic valve in 1-2% live births.
- Estimated: 20,000 open heart procedures yearly for CHD.
- Post-op secundum ASD, pulmonary stenosis, patent ductus have normal life expectancy.
- Estimated > 500,000 adults in US with CHD.

Congenital Heart Disease: Etiologies

- 70-80% Multifactorial
- 6-12% Gross Chromosomal Anomaly
- 10-15% Single gene defect
- 1% Maternal Disease
- 1% Teratogen Exposure

Congenital Heart Disease: Etiologies

Most cases (70-80%) are "multifactorial"

The Recurrence Risk with:

- 1 sib with CHD: 2-4%
- 2 sibs with CHD: 6-12%
- Mother with CHD: 6-12%
- Father with CHD: 2-4%

In 1/2 of these families the same defect recurs.

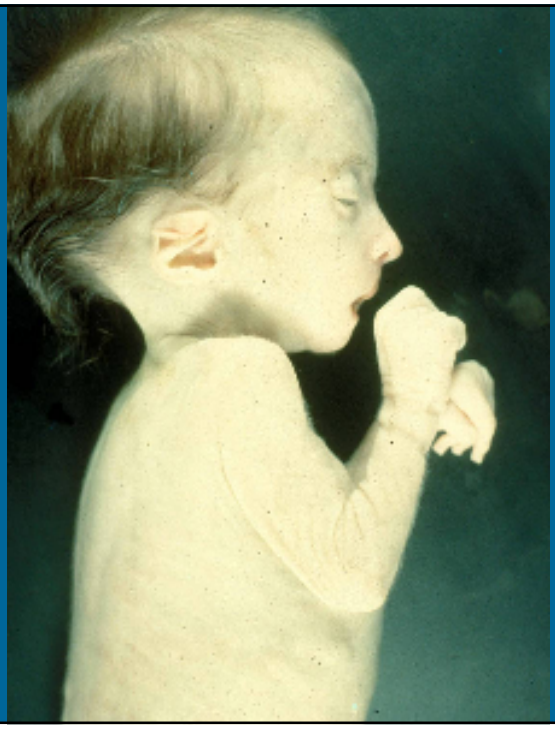
Congenital Heart Disease: Etiologies

6-12% have gross chromosomal anomalies

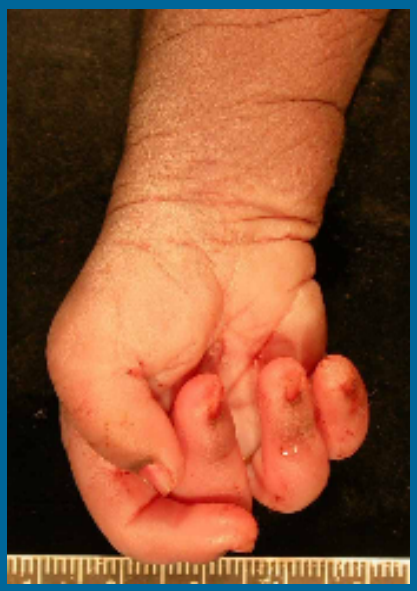
- Trisomy 21 (40% have CHD): AV canal
- Trisomy 18 (100% have CHD): VSD, PS
- Trisomy 13-15: VSD, ASD, TGV
- XO (Turner): Coarc, AS, VSD
- XXY (Klinefelter): Ebstein, Tetralogy

Trisomy 18

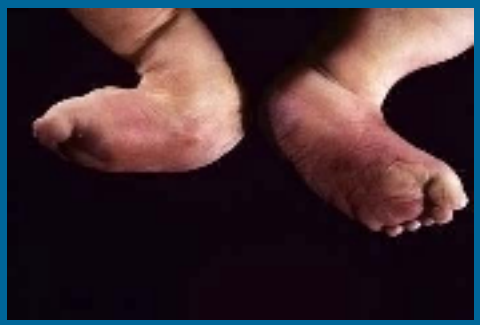
100% have congenital heart disease



Trisomy 18

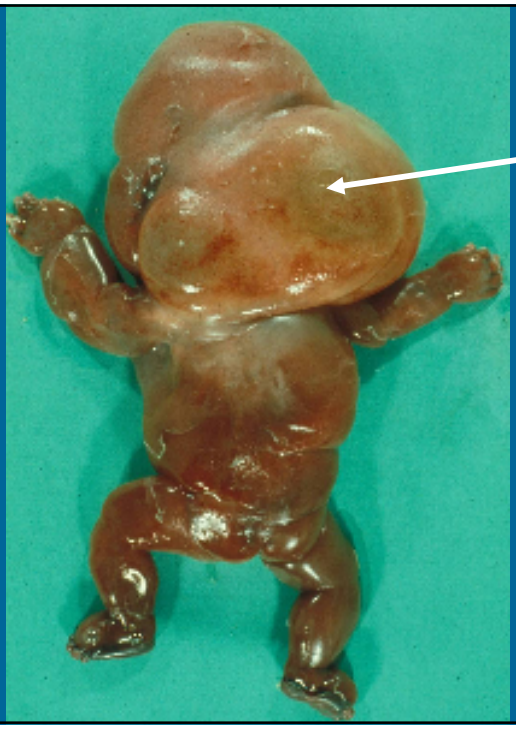


Trisomy 13



Turner Syndrome

XO



Cystic hygroma (lymphatic malformation)

Congenital Heart Disease: Etiologies

10-15% Single gene defects

- Williams/elastin (del7q11.23): AS, PS
- Cri-du-chat (del5p15): VSD, AS, PDA
- Connexin 43: PS, heterotaxia
- Holt-Oram/*TBX5* (12q24.1): ASD + limb
- *NKX2.5* (5q35): ASD + heart block
- DiGeorge/velo-cardio-facial syndrome
  22q11.2 hemizygous microdeletion

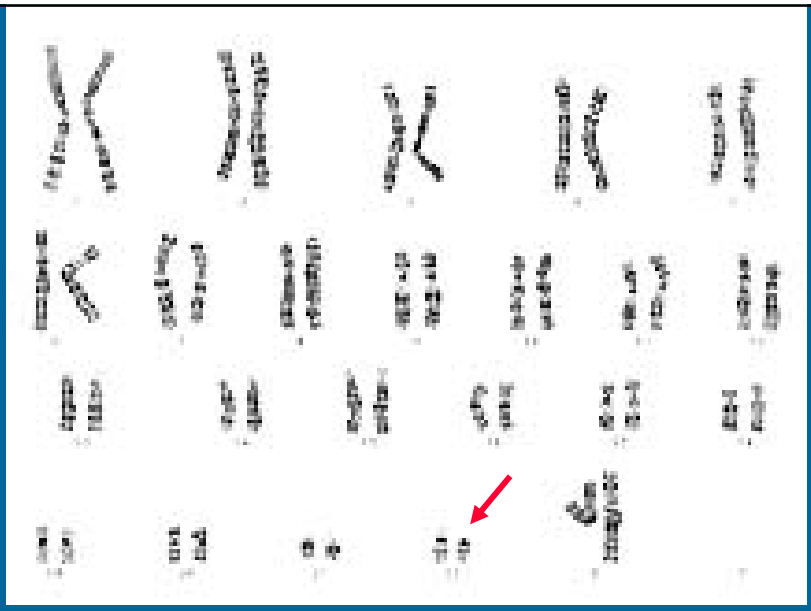
DiGeorge / velocardiofacial syndrome

Cardiac
Abnormal facies
Thymic hypoplasia
Cleft palate
Hypocalcemia
22nd chromosome

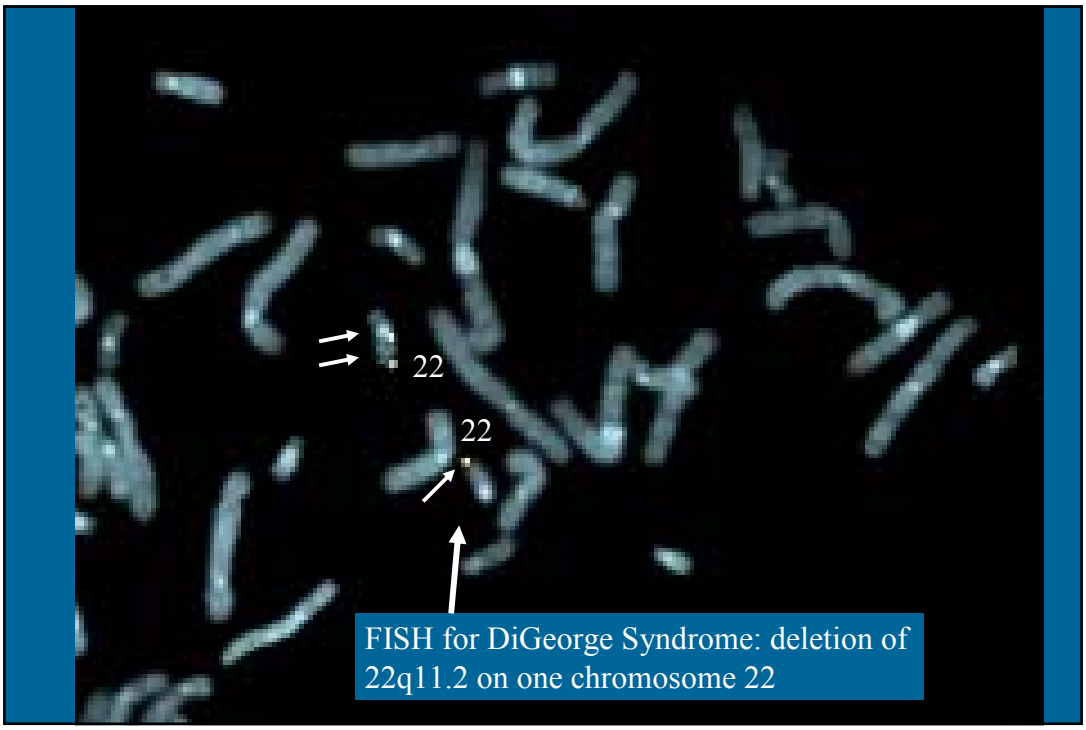
22q11.2 microdeletions are also found in isolated congenital heart diseases: interrupted aortic arch, truncus arteriosus, Tetralogy of Fallot, transposition, VSD, aortic coarctation, and double outlet RV.

DiGeorge / velocardiofacial syndrome (1 in 6,000; 5% of CHD)

- **C**ardiac anomalies - 80%
- **A**bnormal facies - 41%
- **T**hymic hypoplasia – rare (but 75% have some immunodeficiency)
- **C**left palate – 11% (70% have some palatal anomaly)
- **H**ypocalcemia - 50%



DiGeorge syndrome; deletion of material from long arm of chromosome 22.



FISH for DiGeorge Syndrome: deletion of 22q11.2 on one chromosome 22

22q11.2 deletion syndrome

- Autosomal dominant
- 93% of probands have a *de novo* deletion
- 7% inherited from parent
- ***Tbx1*** (but patients with *Tbx1* mutations do not have CNS manifestations – retardation, cerebellar atrophy, polymicrogyria, neural tube defects, seizures seen in 22q11.2 deletion syndrome)
- 90% of DiGeorge syndrome: other patients have del 10p13, del 18q21.33, del 4q21.3-q25

22q11.2 deletion syndrome: congenital heart defects in 80%

- Tetralogy of Fallot – 22%
- Interrupted aortic arch – 15%
- Ventricular septal defect – 13%
- Truncus arteriosus – 7%
- Vascular ring – 5%
- Aortic arch anomaly – 3%

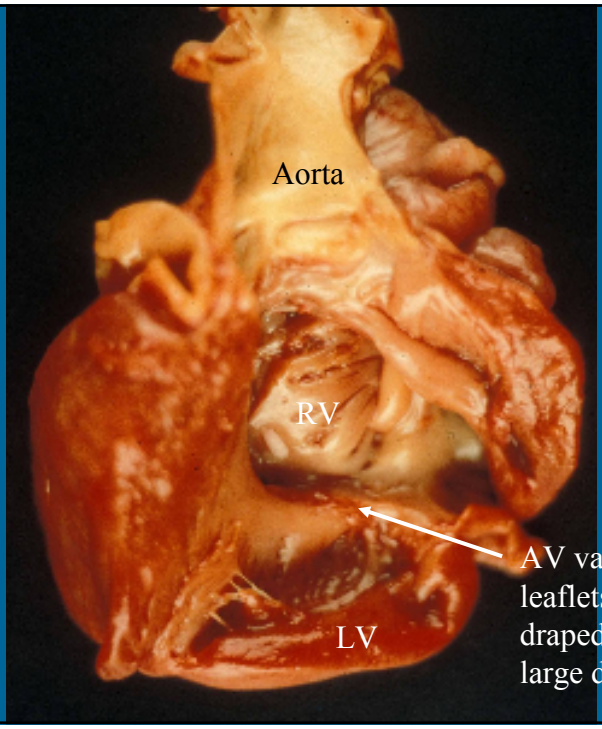
McDonald-McGinn, et al., Genet Couns 10:11-24, 1999

Congenital Heart Disease: Etiologies

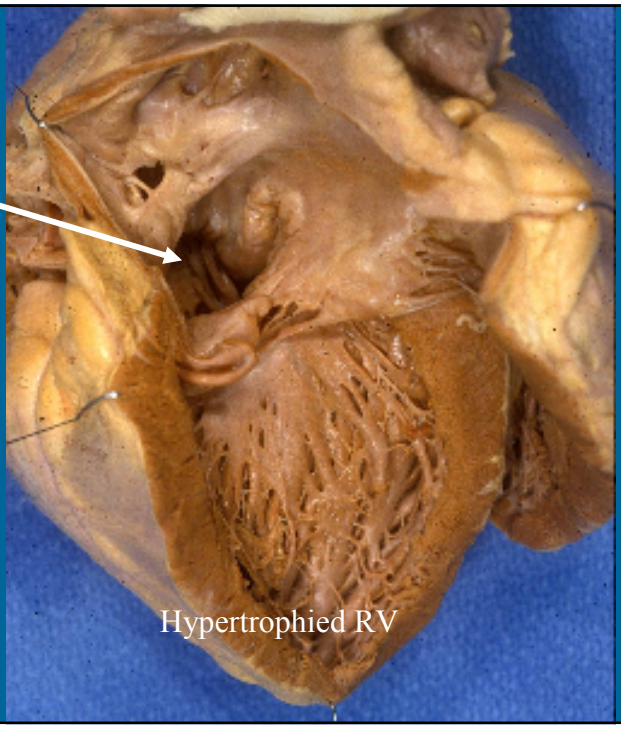
- 1% Maternal Disease
- Type I diabetes mellitus (2% affected)
- Phenylketonuria (if not controlled)
- Systemic lupus erythematosus (heart block & structural)

- 1% Teratogen Exposure
- Alcohol (30% have some defect)
- Anticonvulsants (2-3x increased risk)
- Lithium
- Retinoic acid
- Rubella

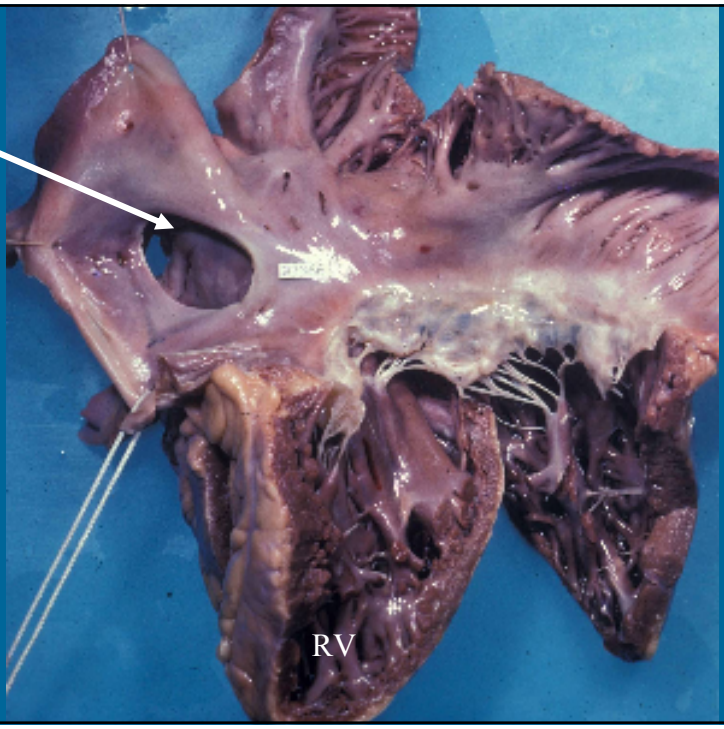
AV Canal or Endocardial Cushion Defect



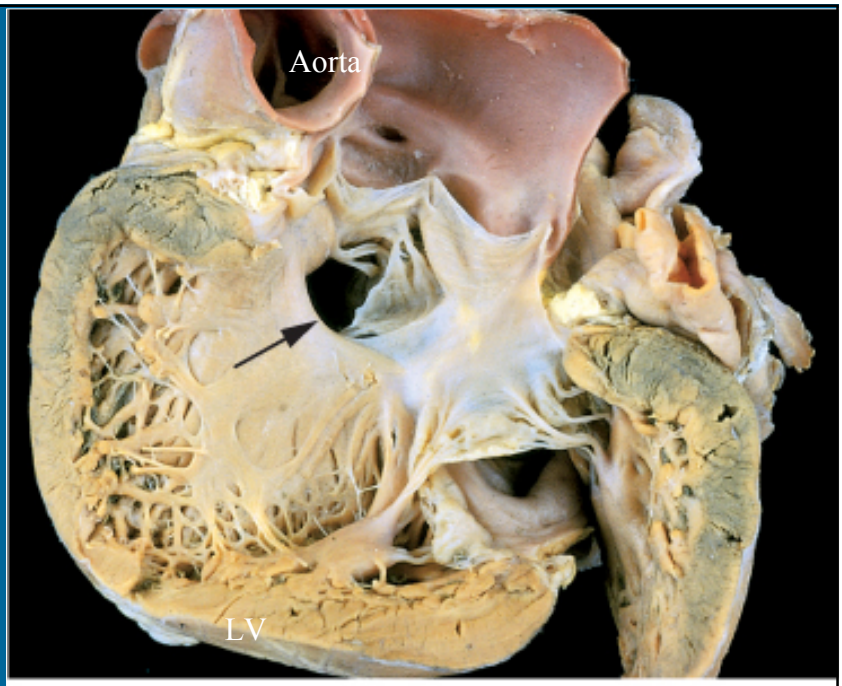
Atrial septal defect - Primum

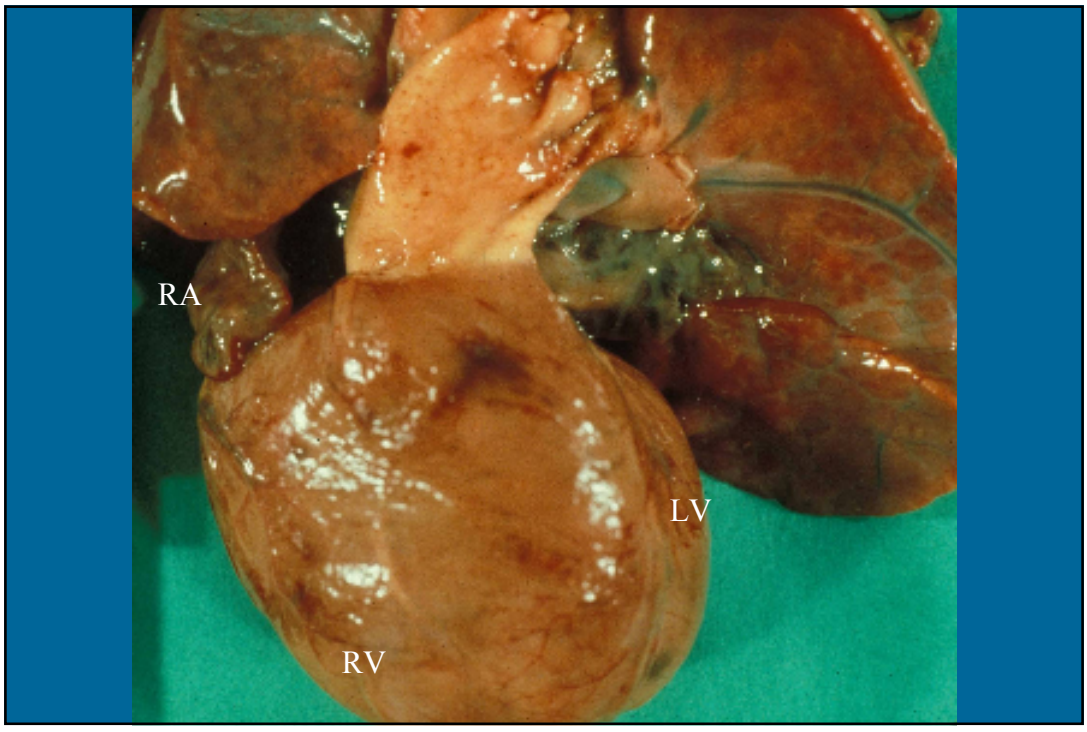


ASD – Secundum type



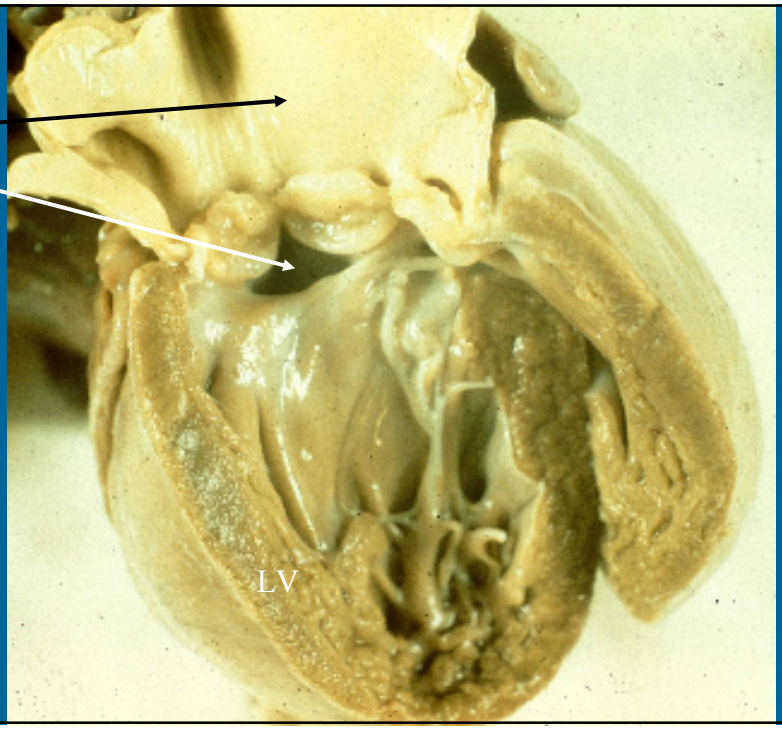
VSD- membranous type



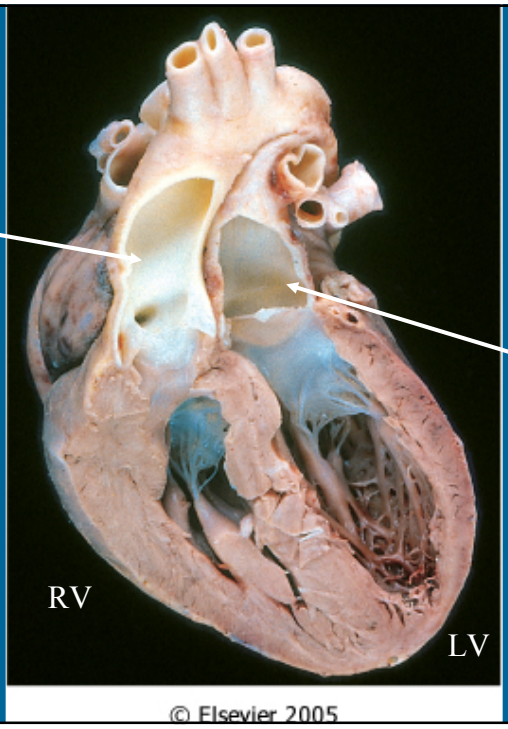

RA
LV
RV

Truncus arteriosus

with VSD



Aorta

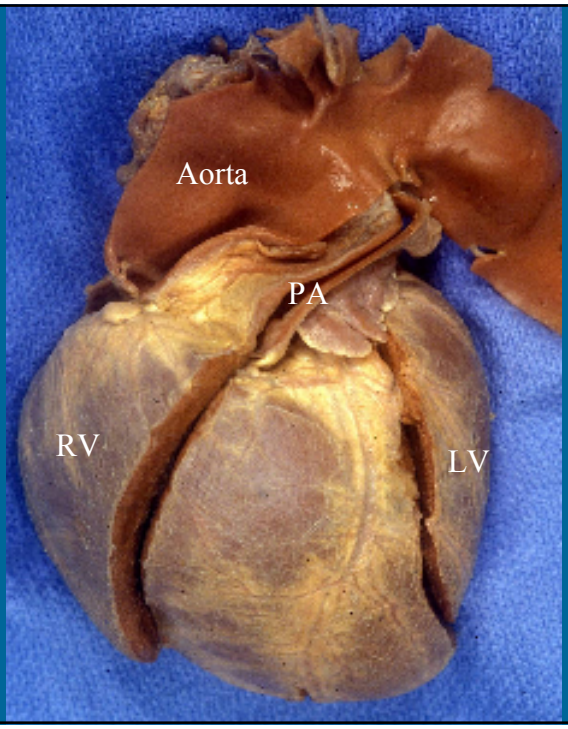


Transposition of the Great Arteries

Pulmonary artery

Double outlet

right venticle



Double outlet right ventricle