Childhood cardiomyopathies

Damien Bonnet

Unité médico-chirurgicale de Cardiologie Congénitale et Pédiatrique
Hôpital Universitaire Necker Enfants malades – APHP, Université Paris Descartes, Sorbonne Paris Cité
IcarP Cardiology, Institut Hospitalo-Universitaire IMAGINE

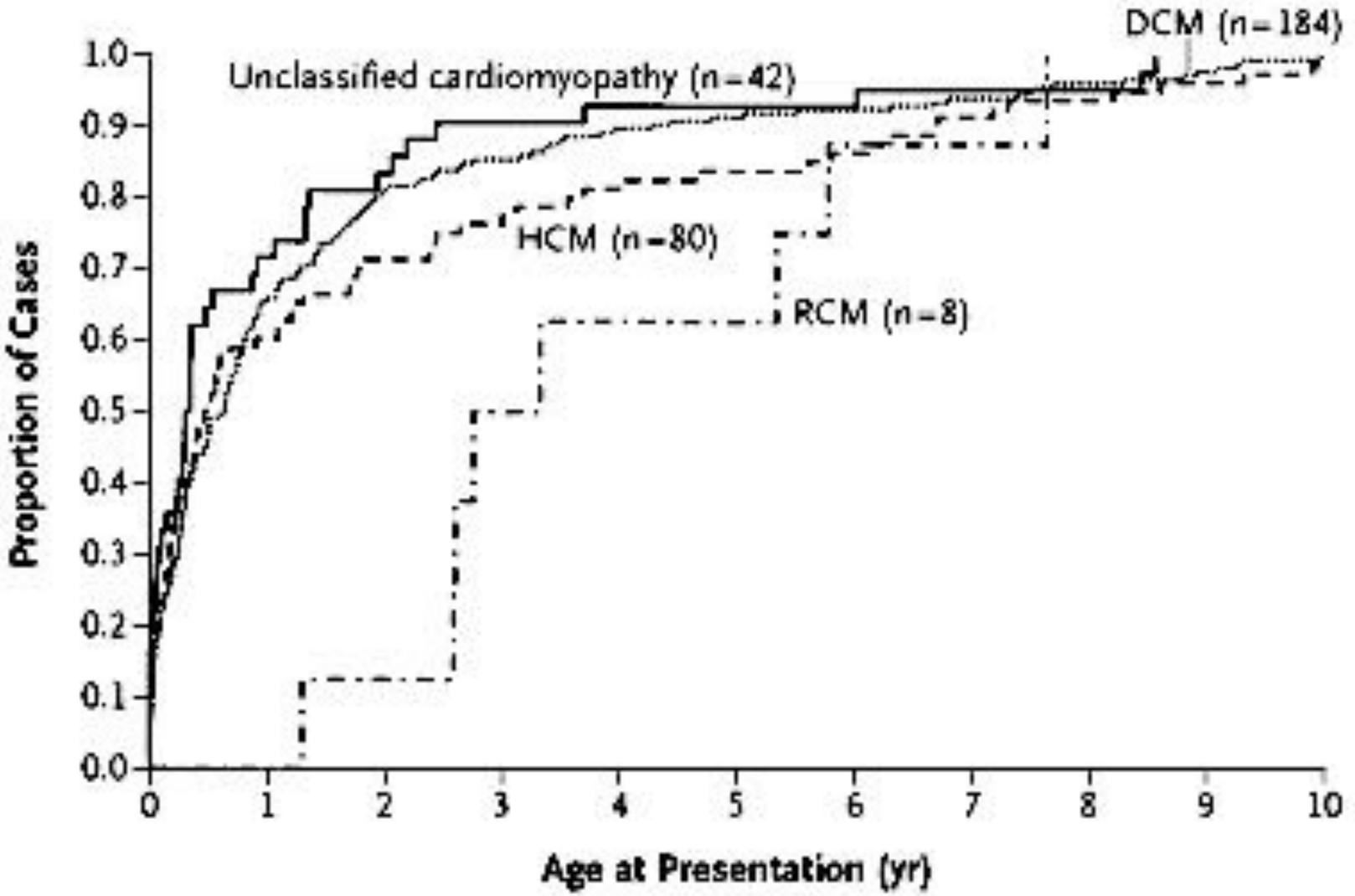
Centre de Référence Maladies Rares
Malformations Cardiaques Congénitales Complexes-M3C
Centre de Référence Maladies Rares
Maladies Cardiaques Héréditaires- CARDIOGEN

Epidemiology

- Annual incidence of childhood cardiomyopathies : 1.13 per 100,000
- Incidence higher among children <1 year : 8.34 vs. 0.70 per 100,000
- Categorized according to type :
  - Hypertrophic 42 %
  - Dilated 51%
  - Restrictive 2.5%
  - Non compaction 9.2%
- Sudden death as presenting symptom 3.5%

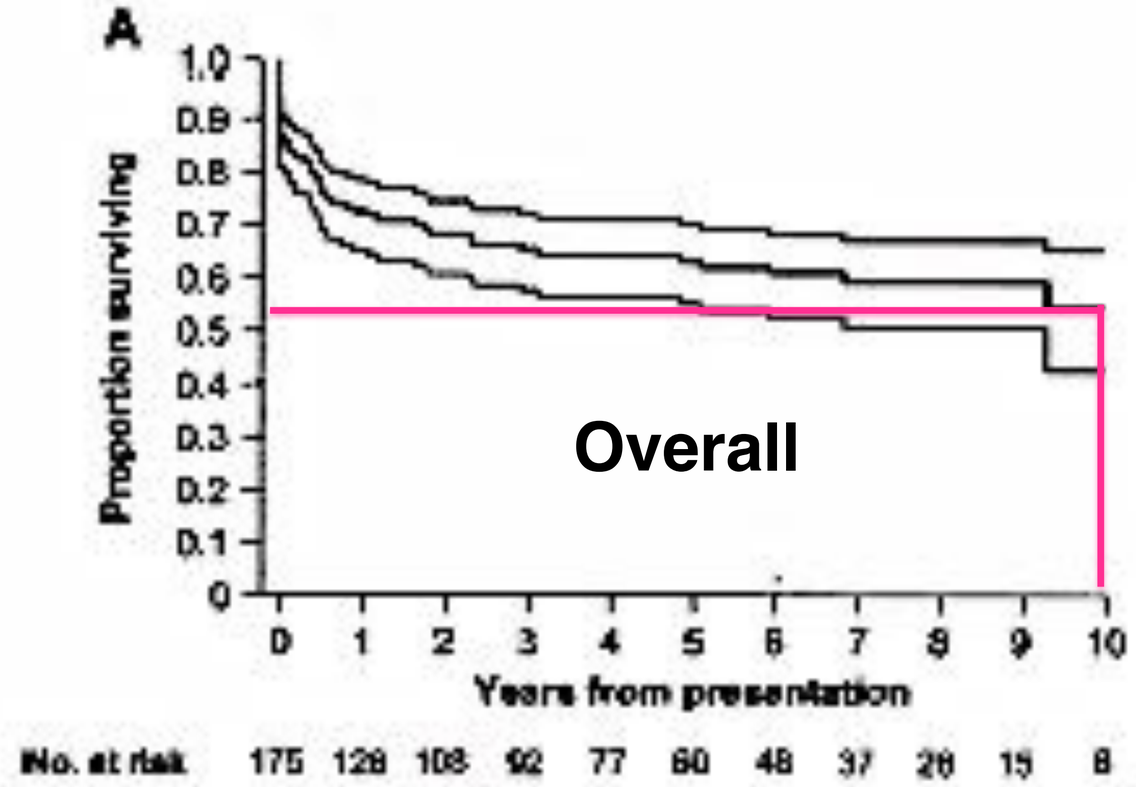
Lipshultz SE et al. NEJM 2003;348:1647-55
Nugent AW et al. NEJM 2003;348:1703-5

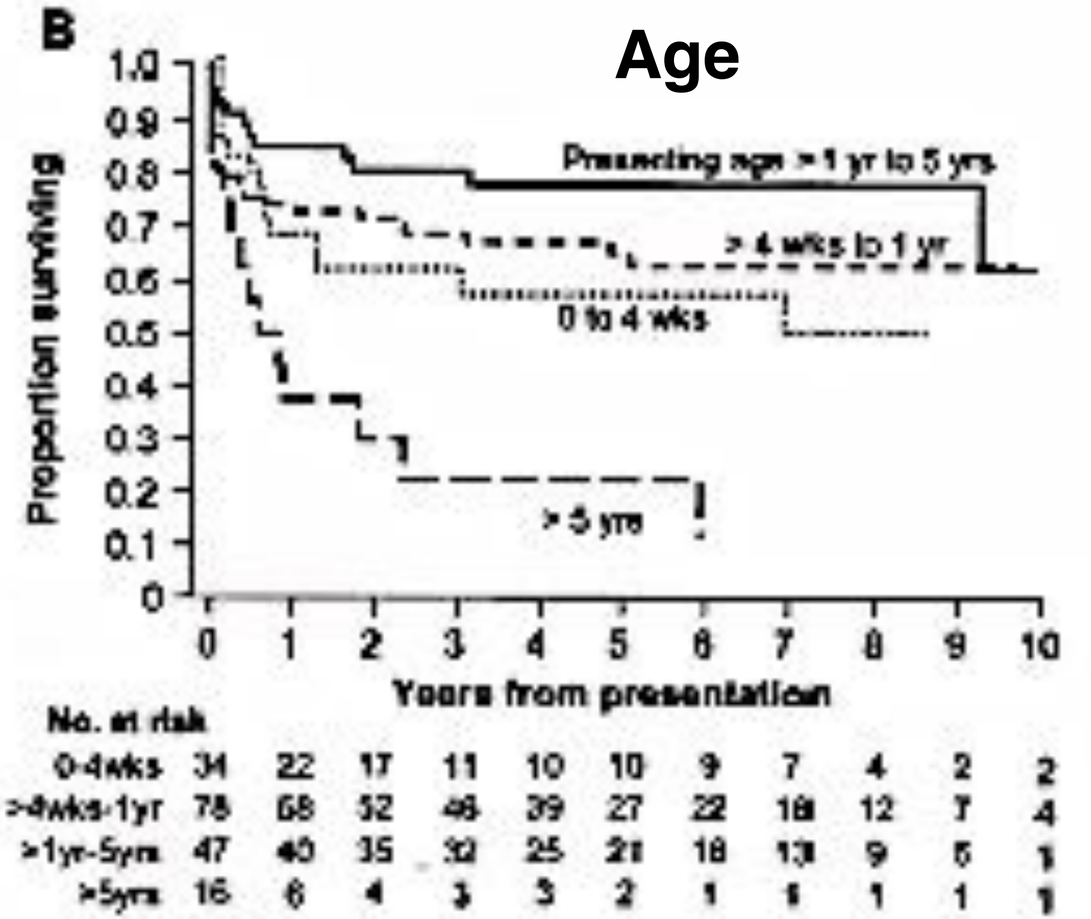
Cumulative frequency distribution of age at presentation



Nugent AW et al. NEJM 2003;348:1703-5

Survival to death or transplantation from time to presentation in pediatric cardiomyopathies

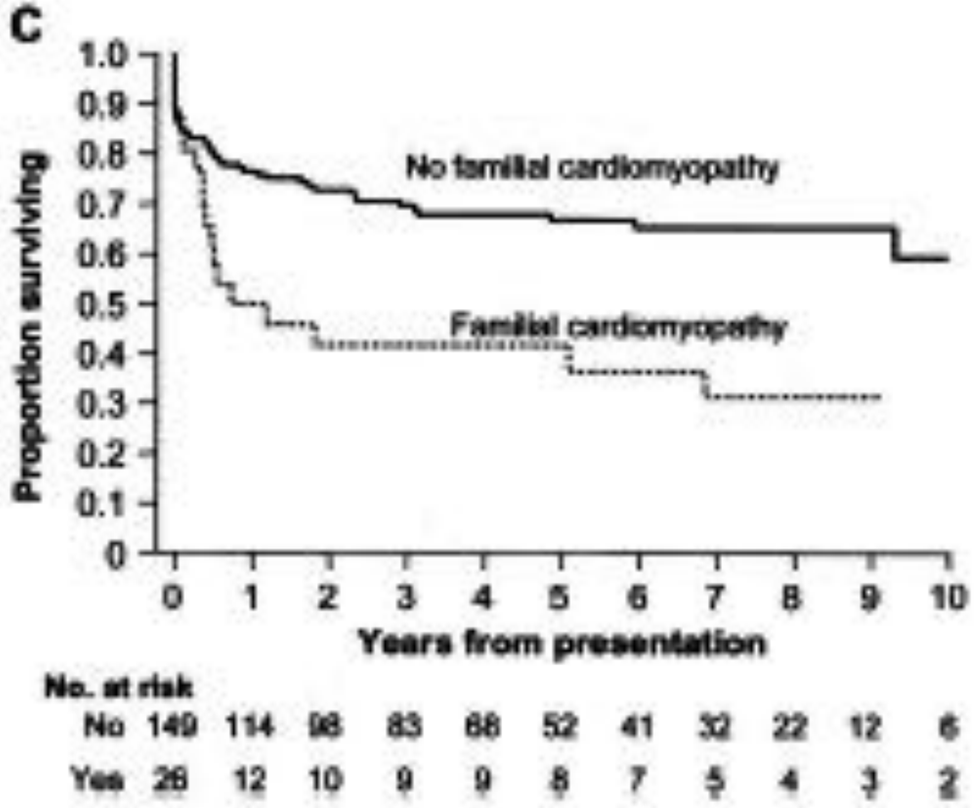


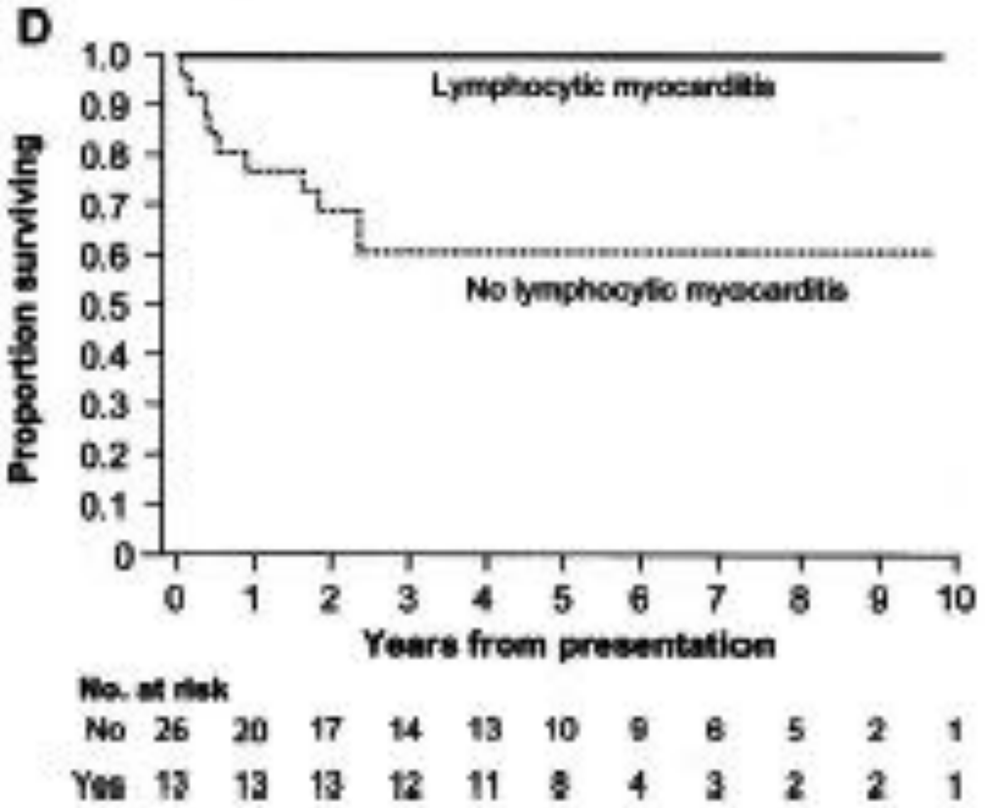


Daubeney PEF et al. Circulation 2006
Alexander PMA et al. Circulation 2013

Wittlieb-Weber CA et al. J Card Failure 2015;21:76-82
Rossano JW et al. J Card Fail 2012;18:459-70.

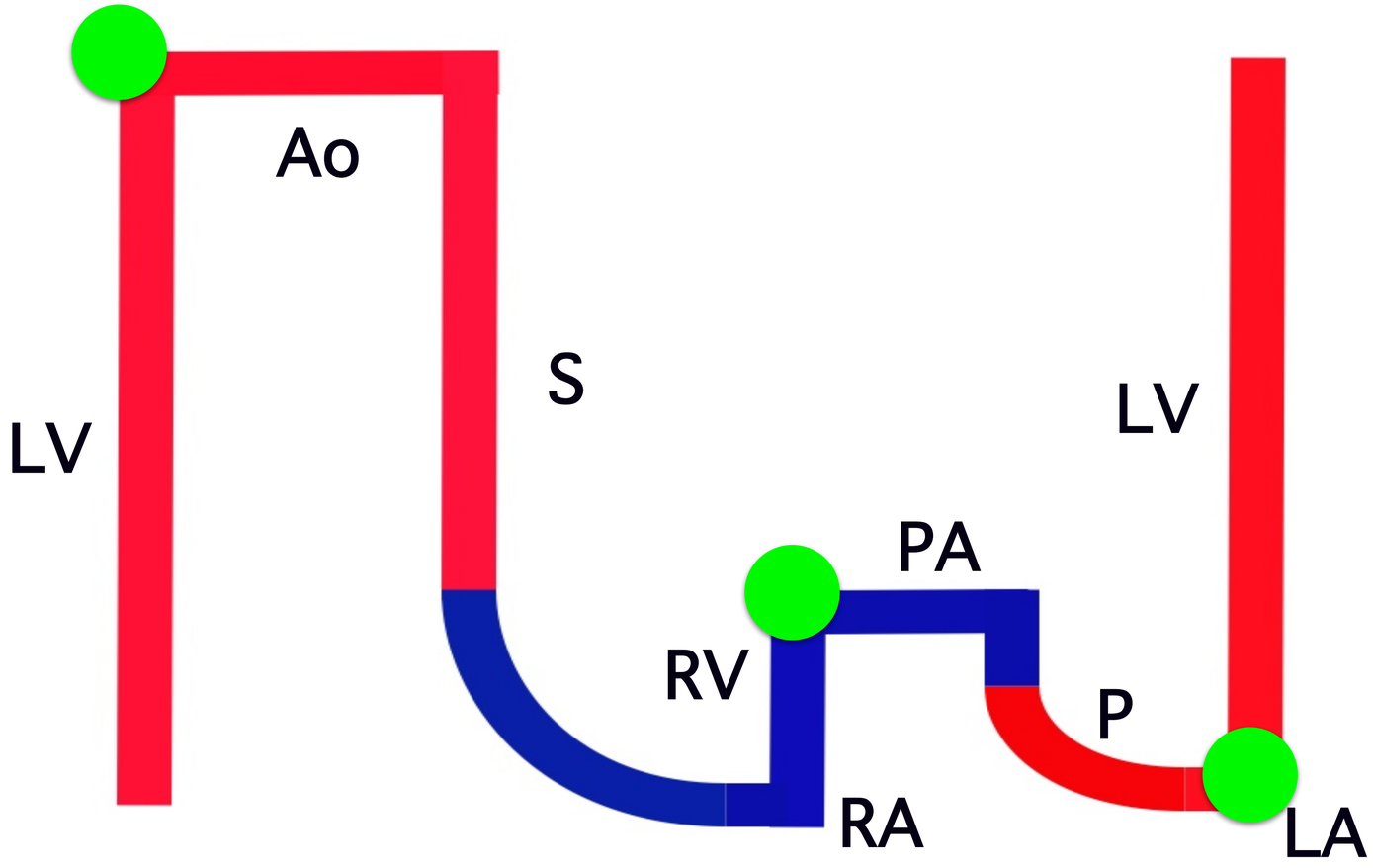
Survival to death or transplantation from time to presentation in pediatric cardiomyopathies

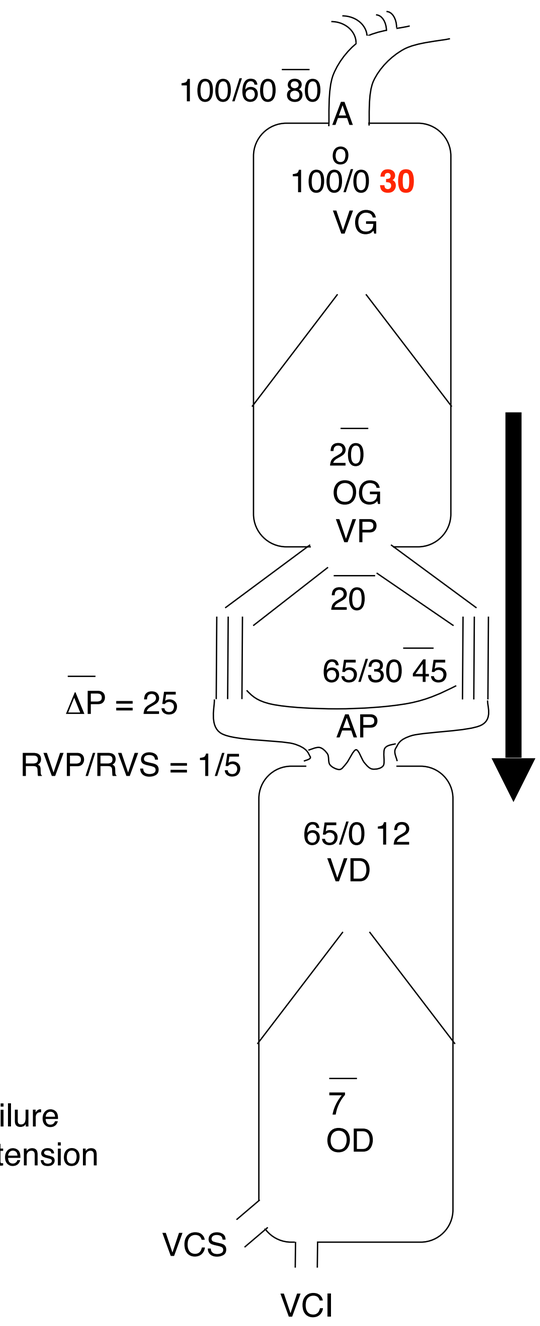




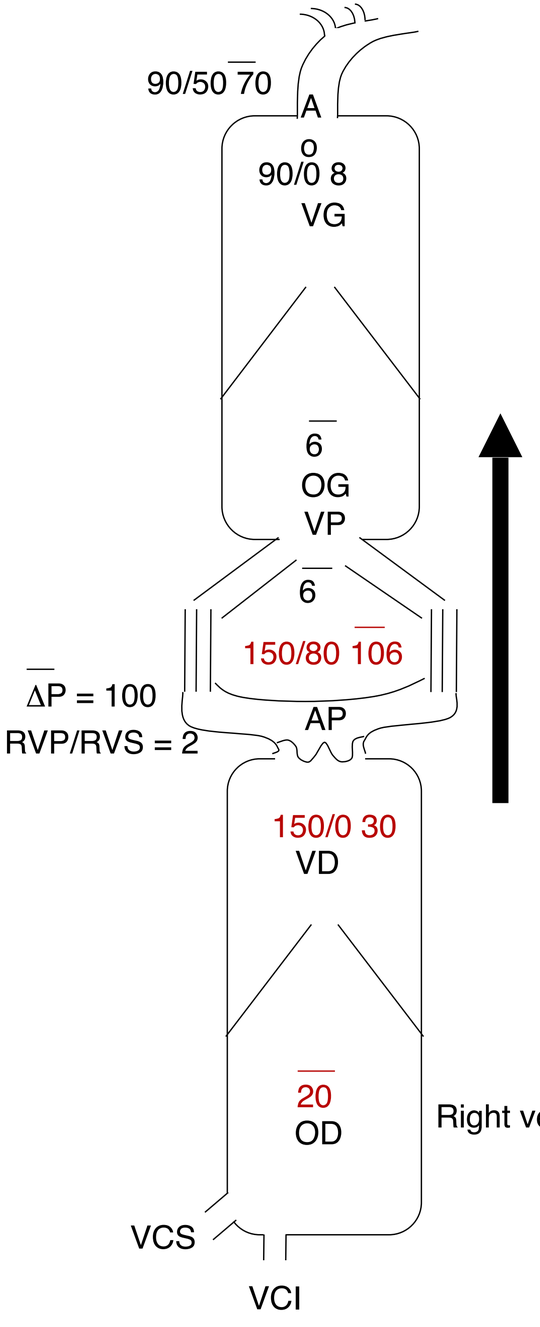
Daubeney PEF et al. Circulation 2006
Alexander PMA et al. Circulation 2013
Wittlieb-Weber CA et al. J Card Failure 2015;21:76-82
Rossano JW et al. J Card Fail 2012;18:459-70.

Hemodynamic in normal heart - Bottlenecks



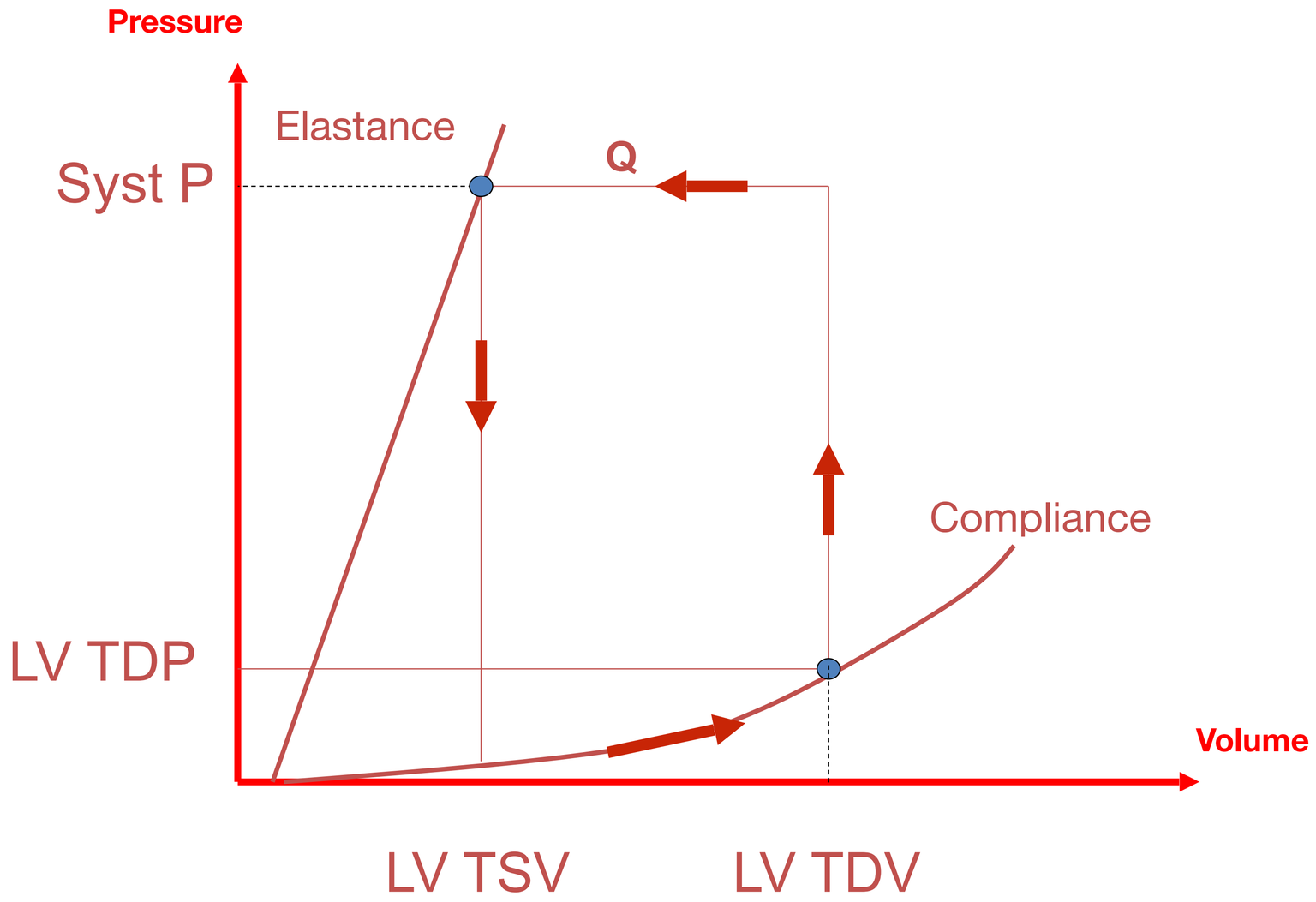


Left ventricular failure
Pulmonary hypertension

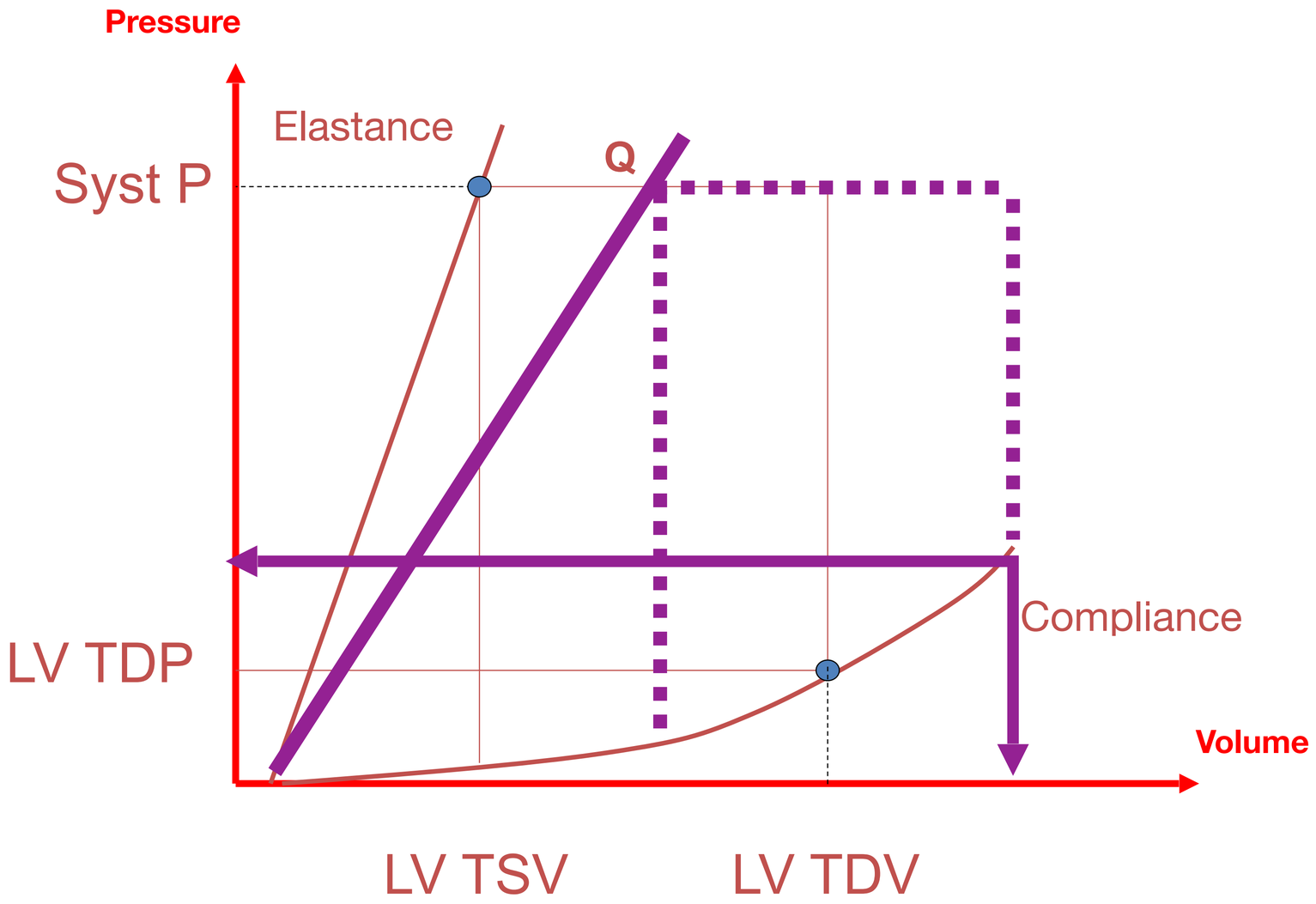


Right ventricular failure - Preload of LV reduced

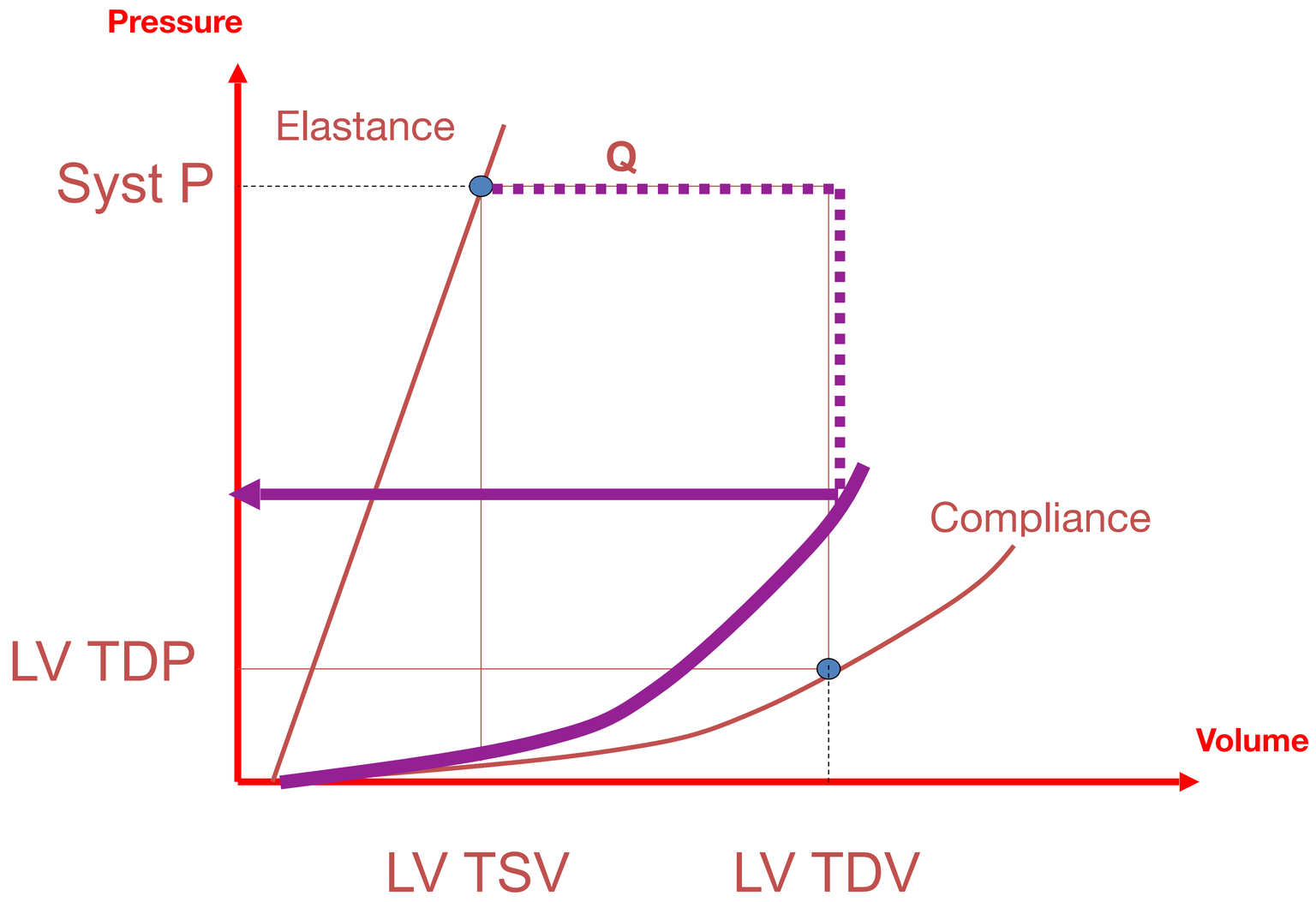
Pressure-Volume loop



Dilated cardiomyopathy with poor contractility

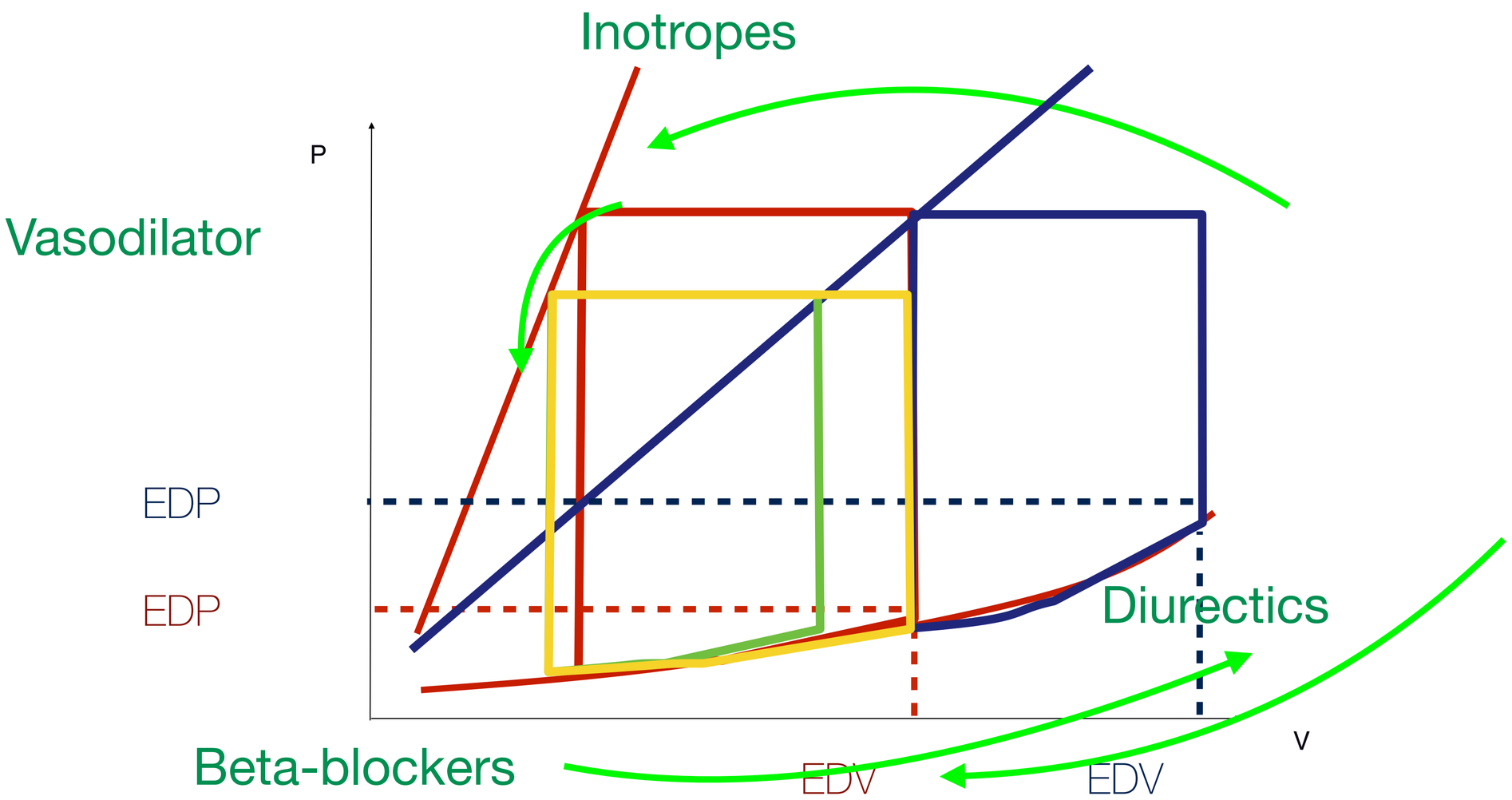


Restrictive cardiomyopathy with poor compliance



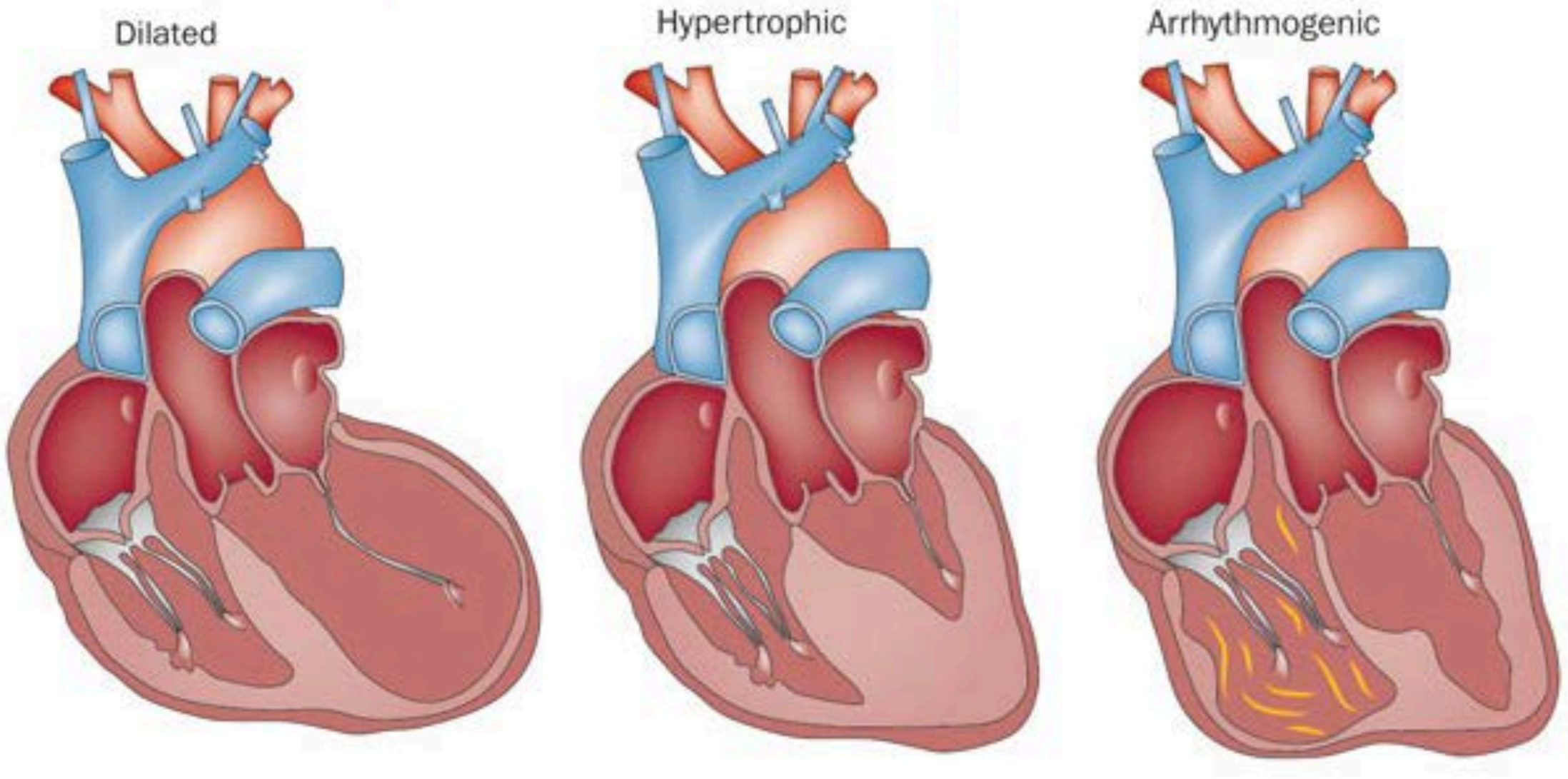
Systolic dysfunction

Low contractility/treatment

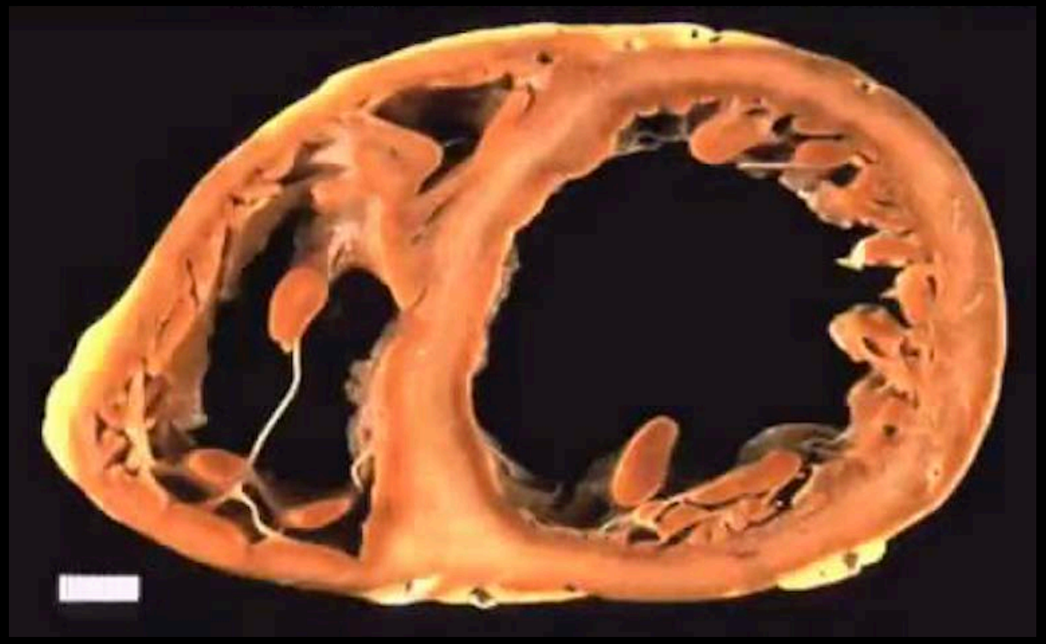


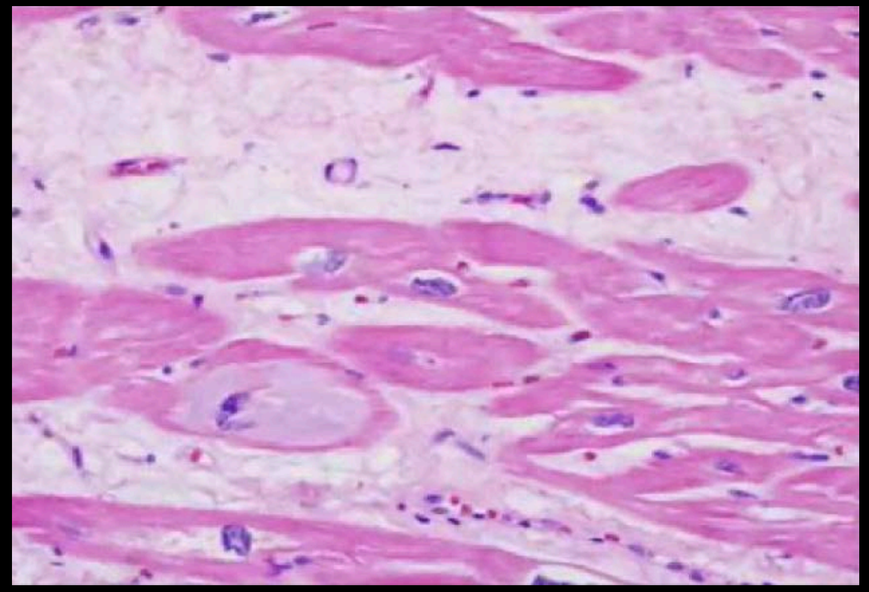
Phenotypes of cardiomyopathies

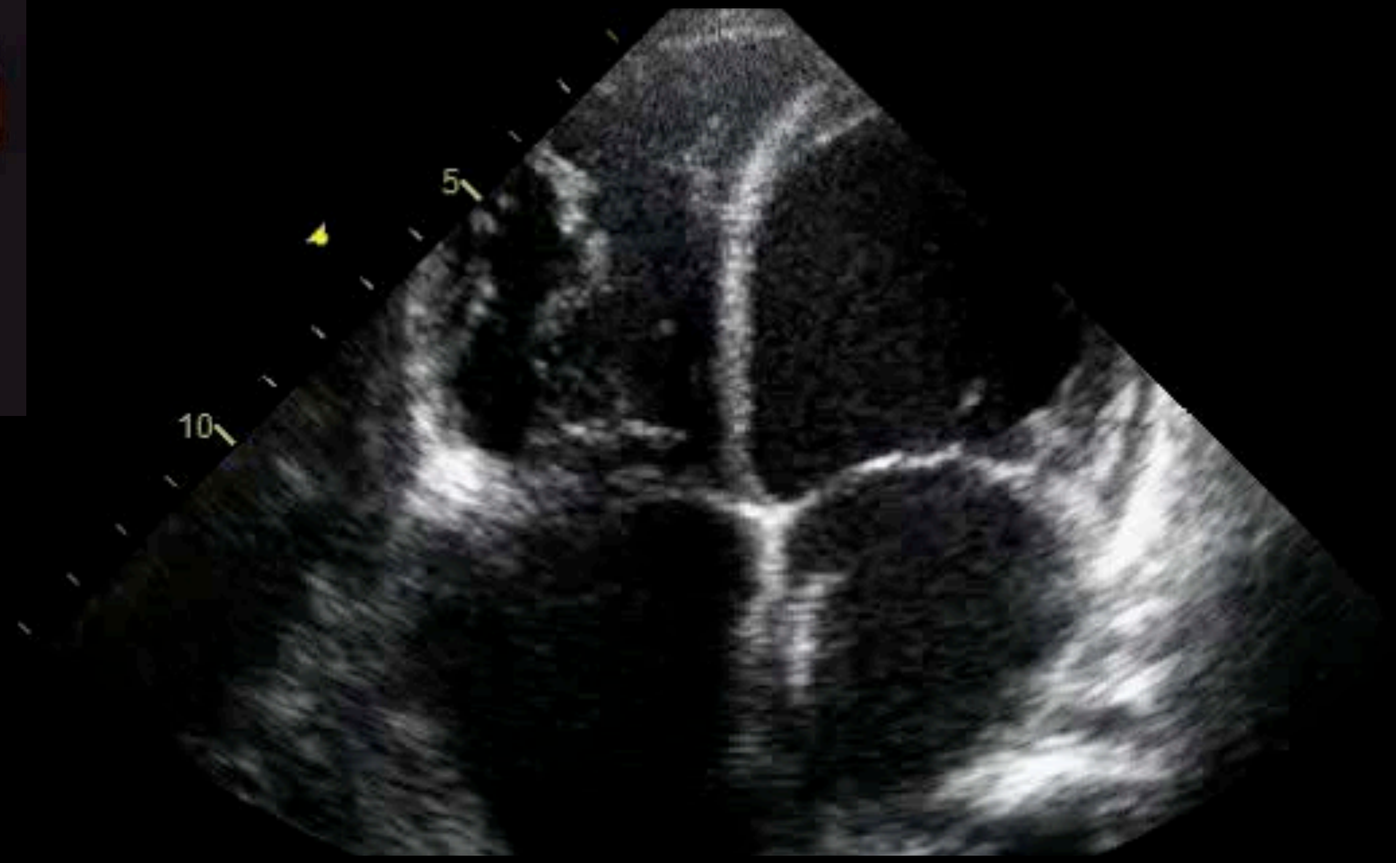
Cardiac phenotypes



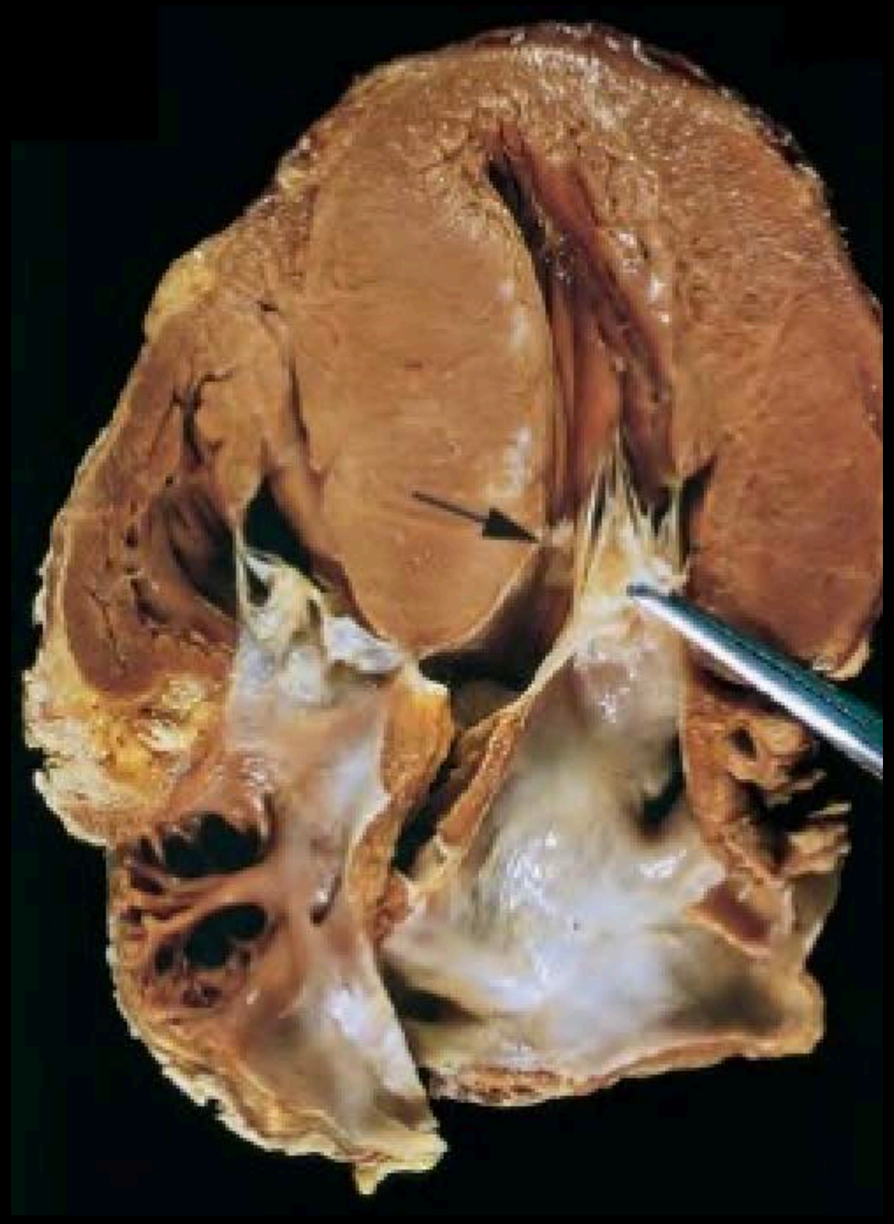
Dilated cardiomyopathy

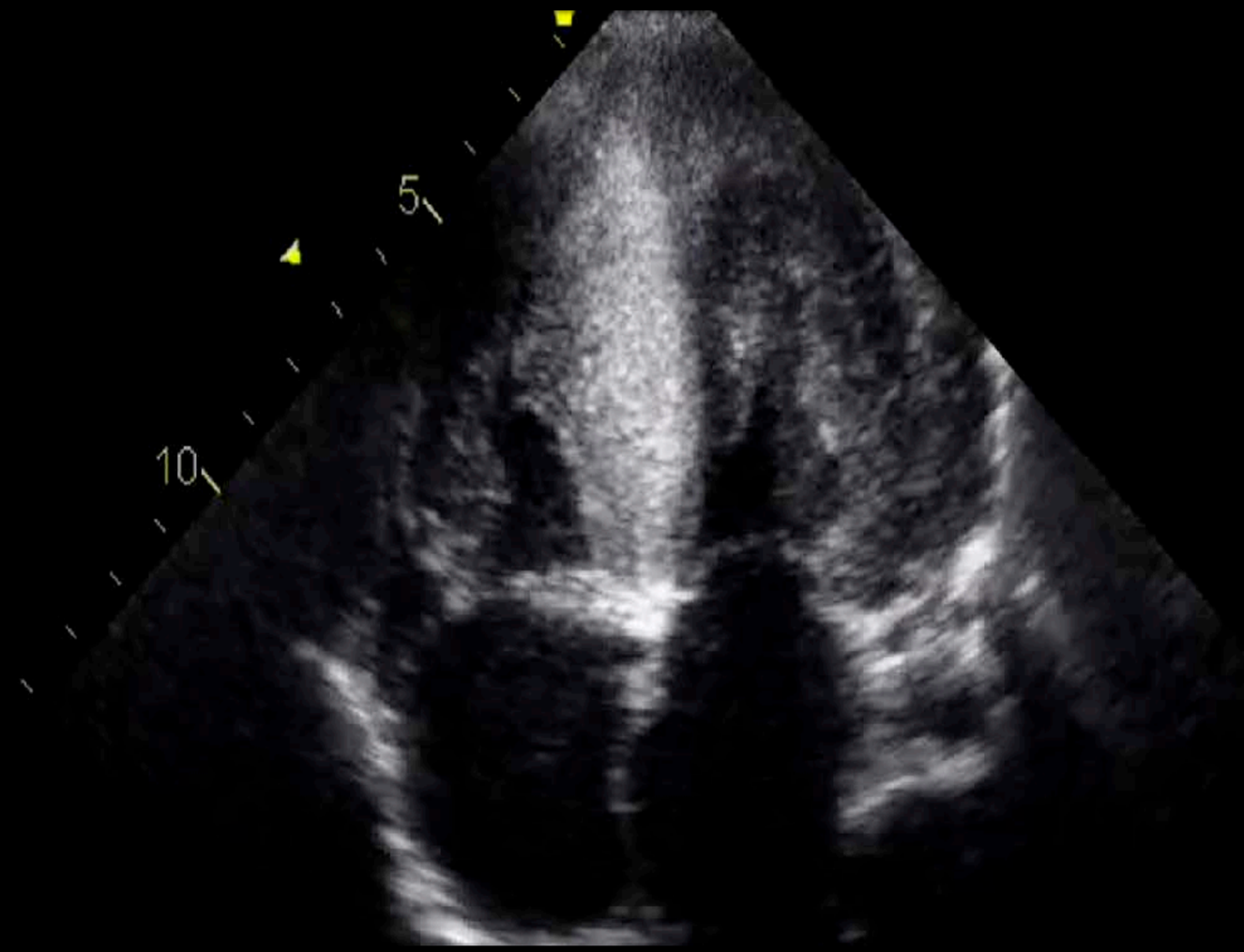




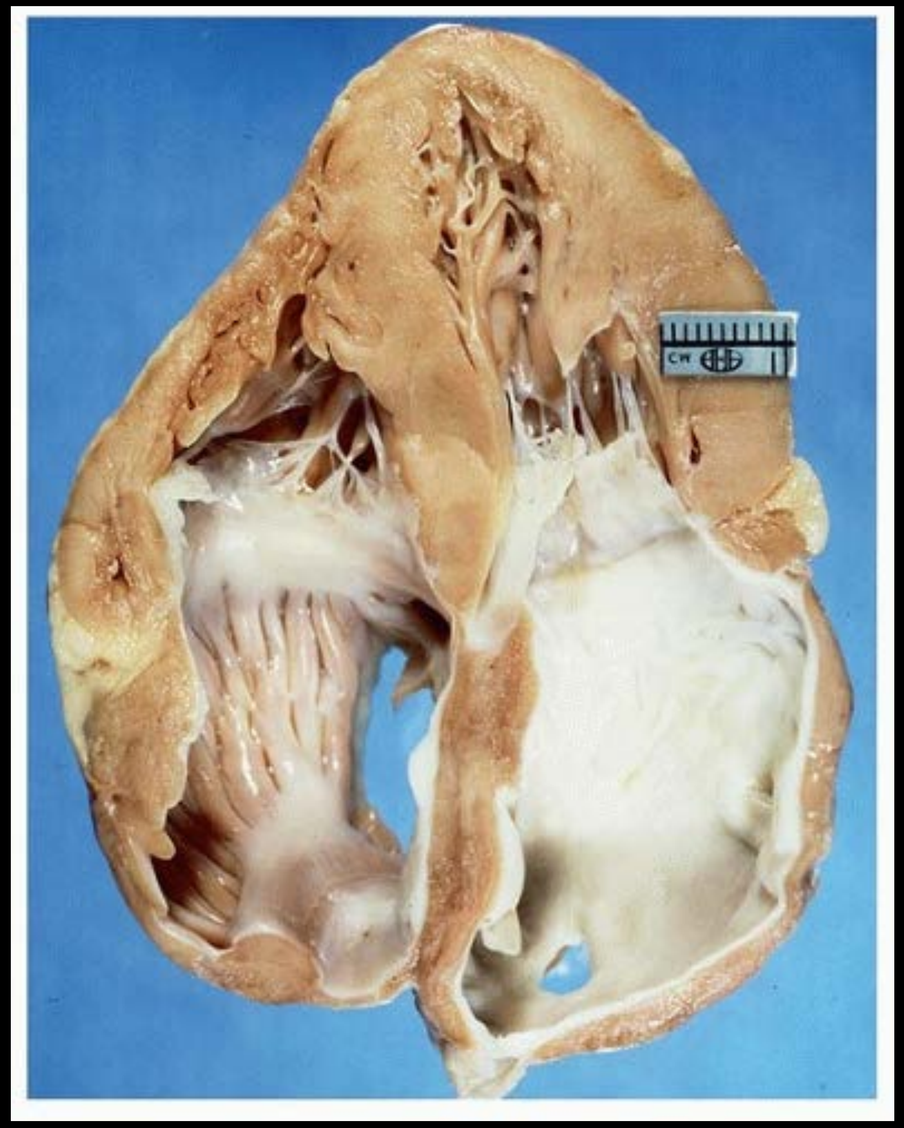


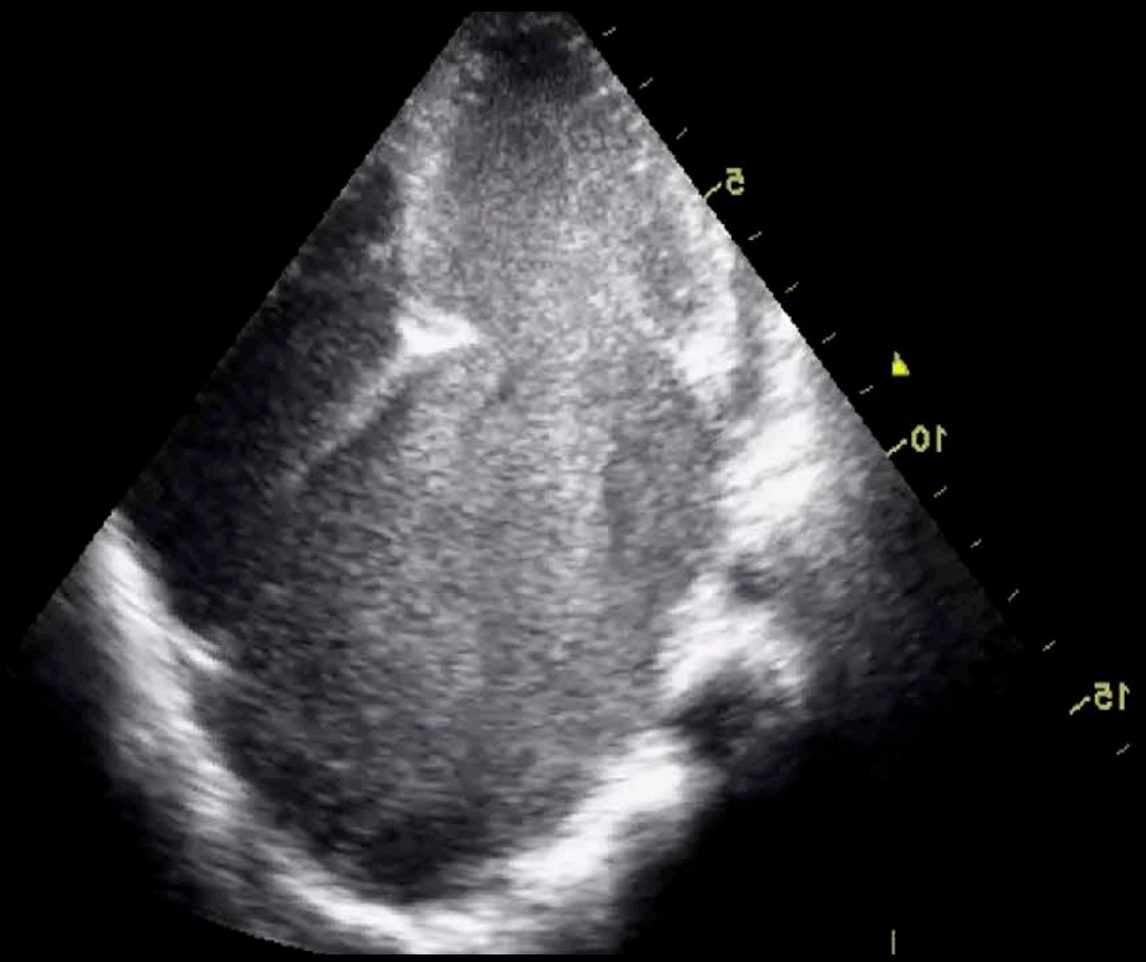
Hypertrophic cardiomyopathy



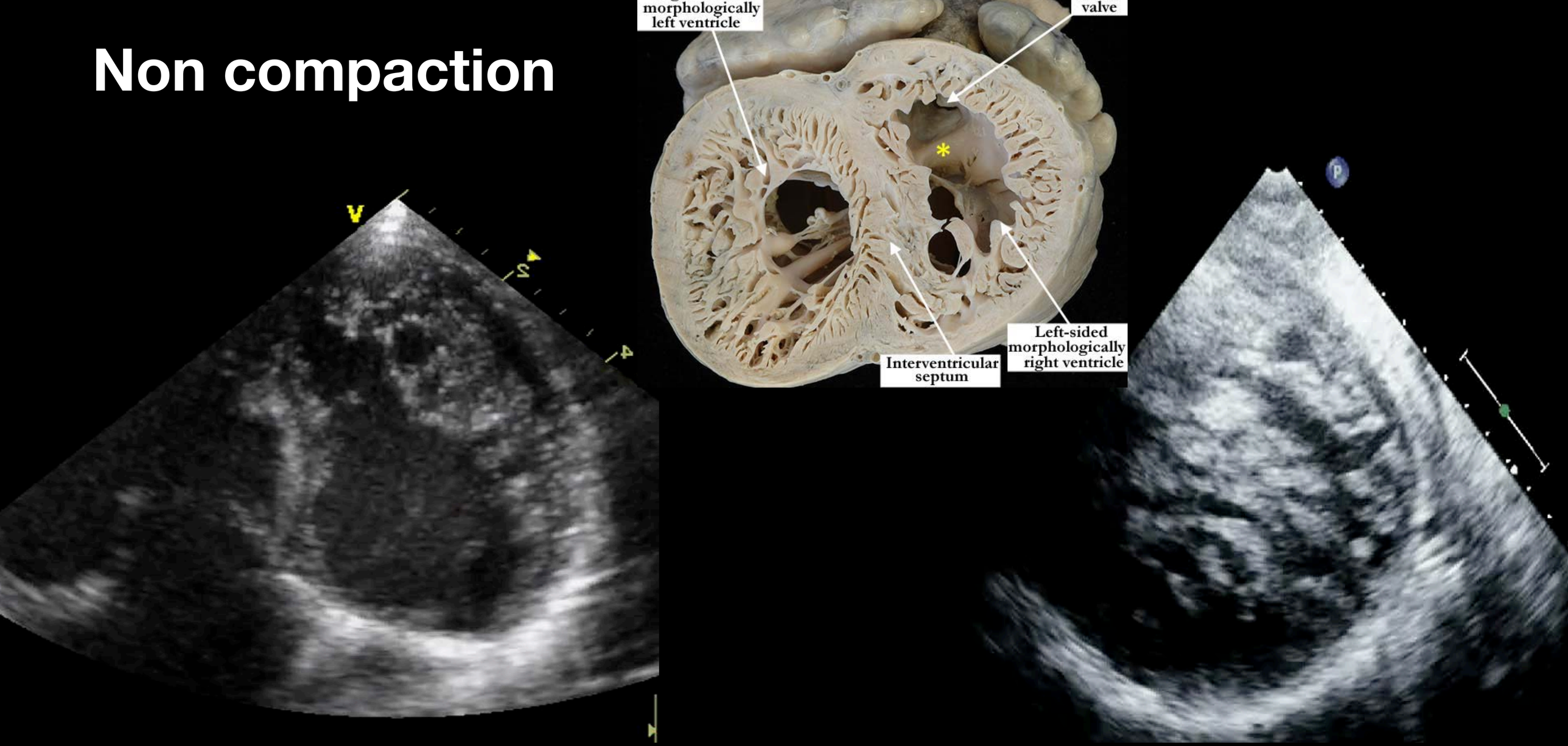


Restrictive cardiomyopathy

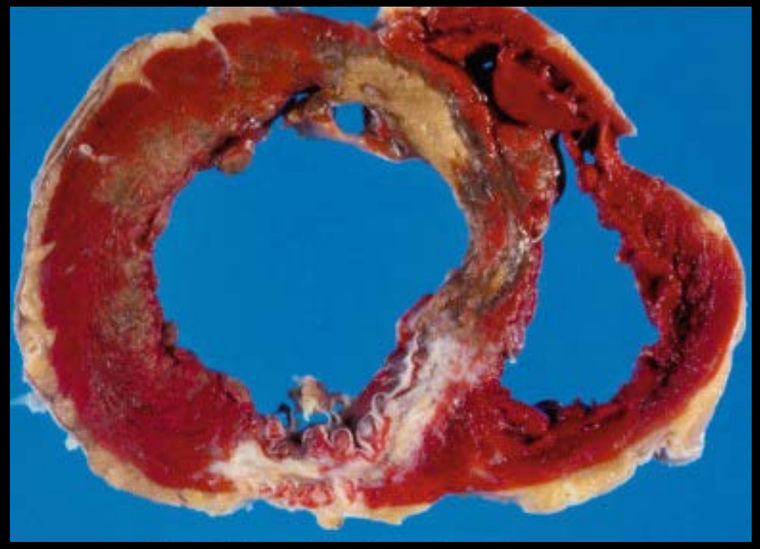


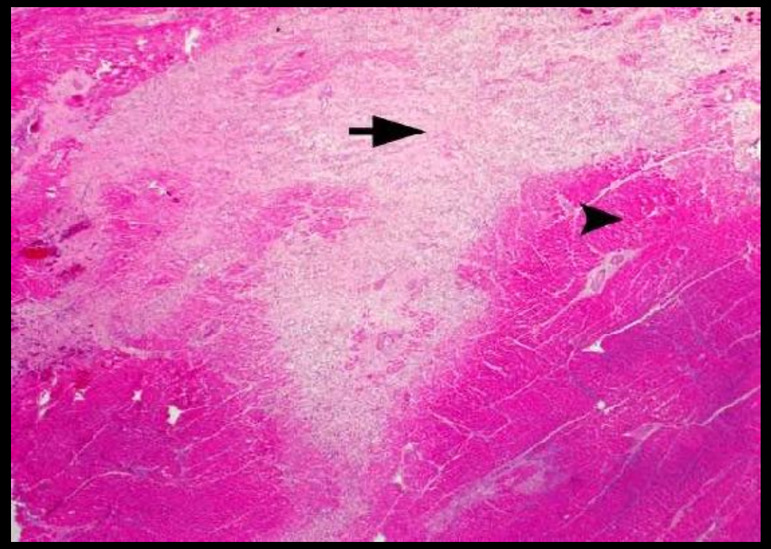


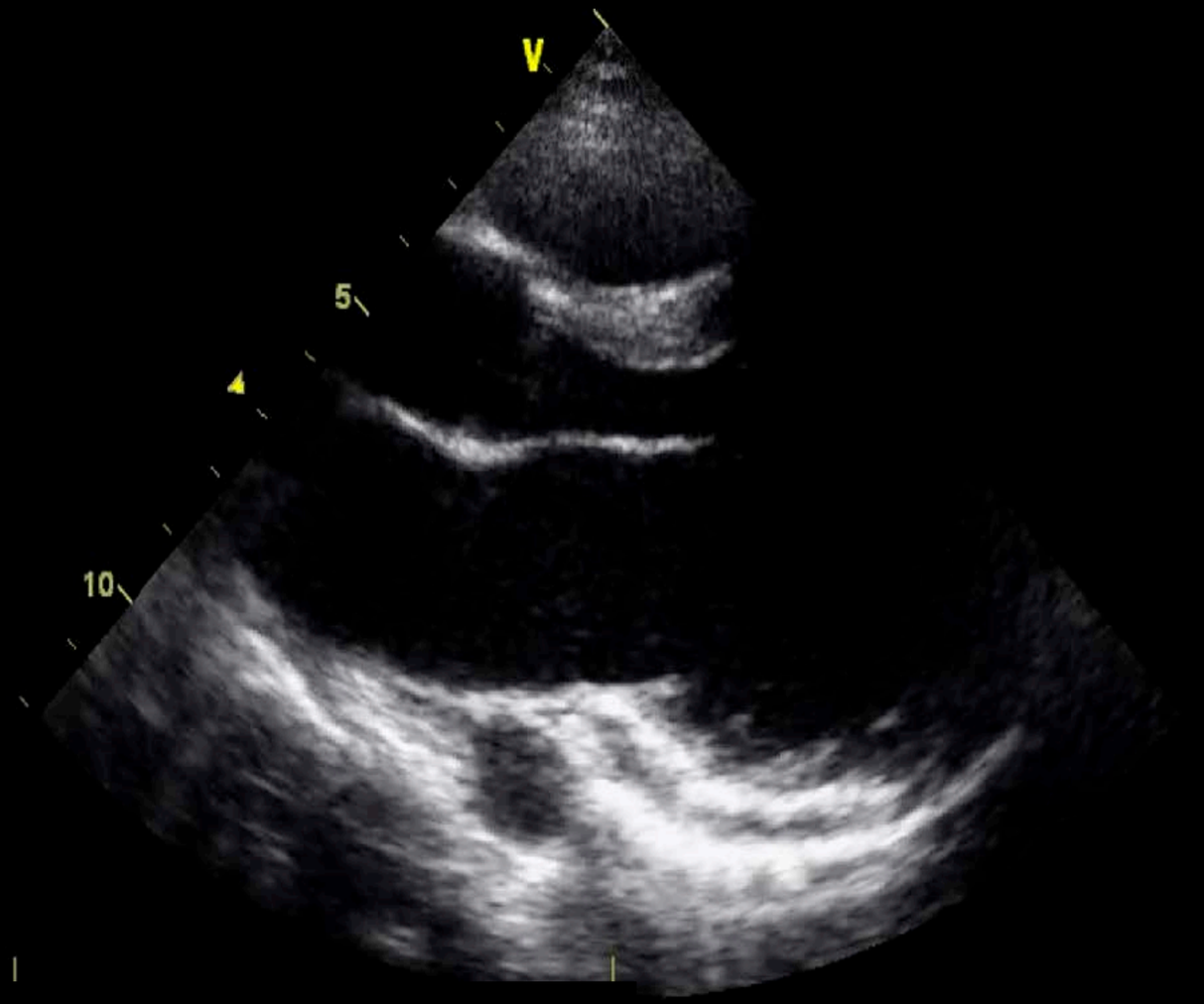
Non compaction



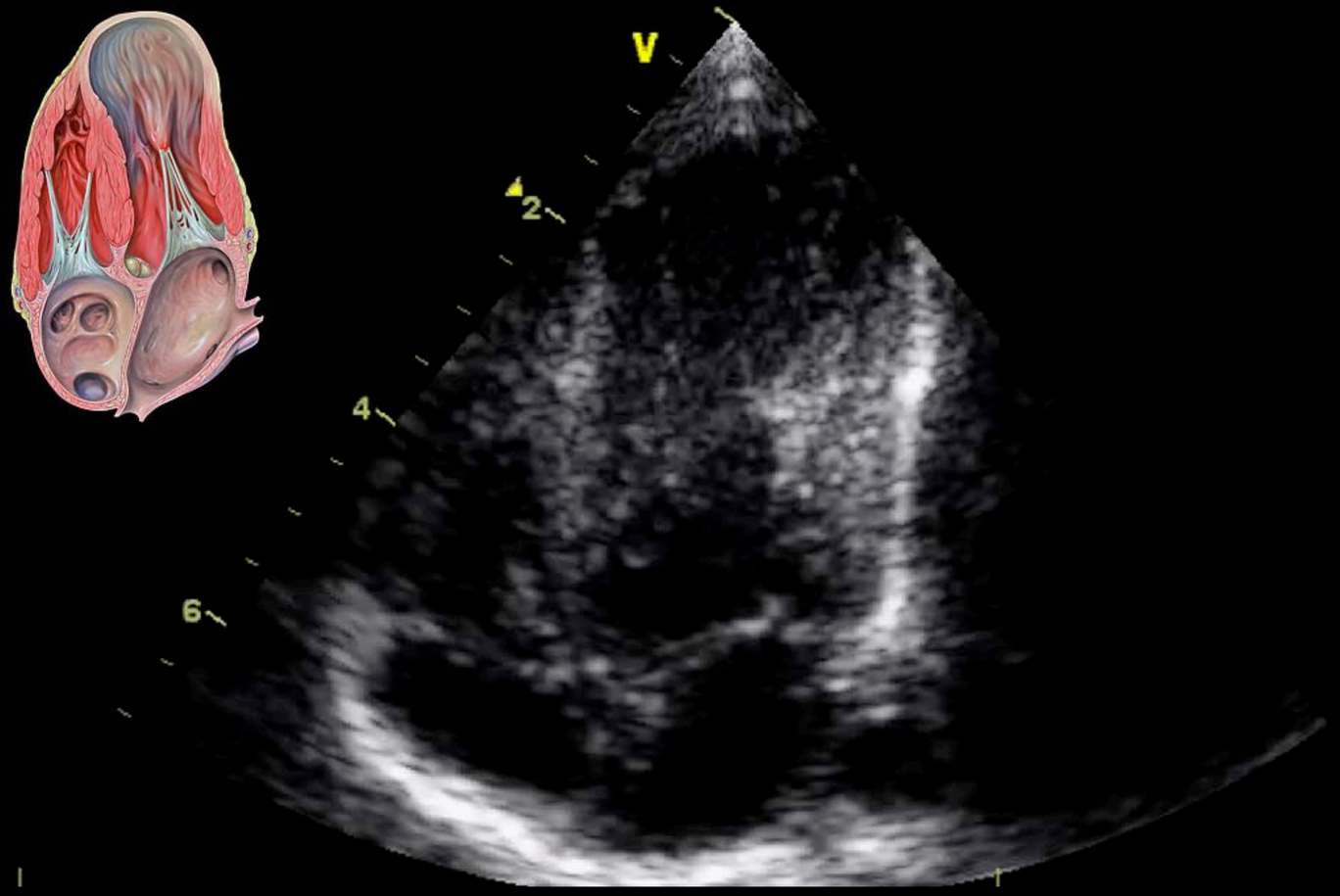
Ischemic cardiomyopathy

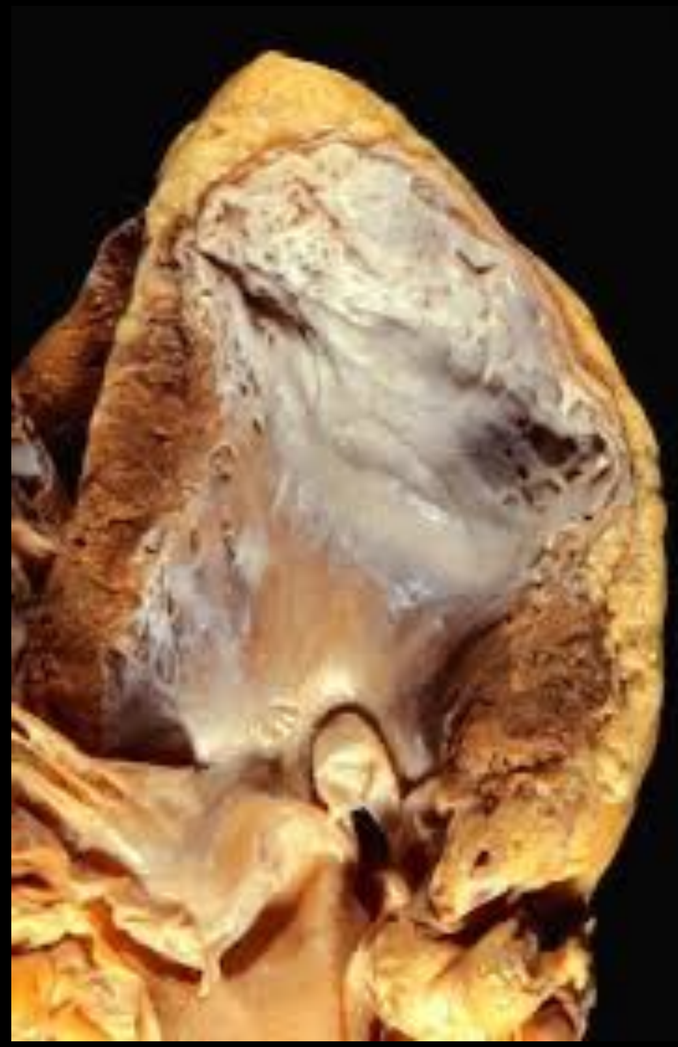




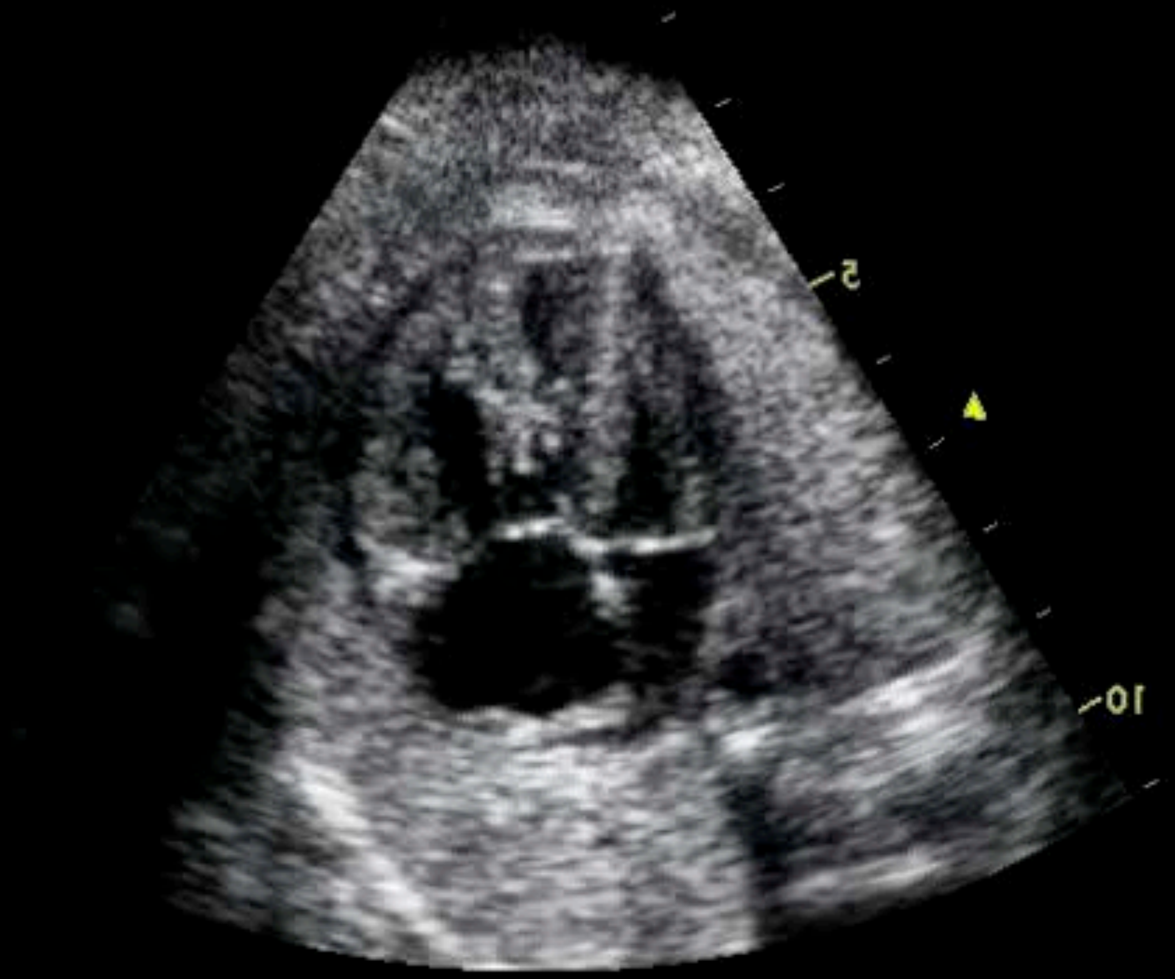


Left ventricular aneurysm

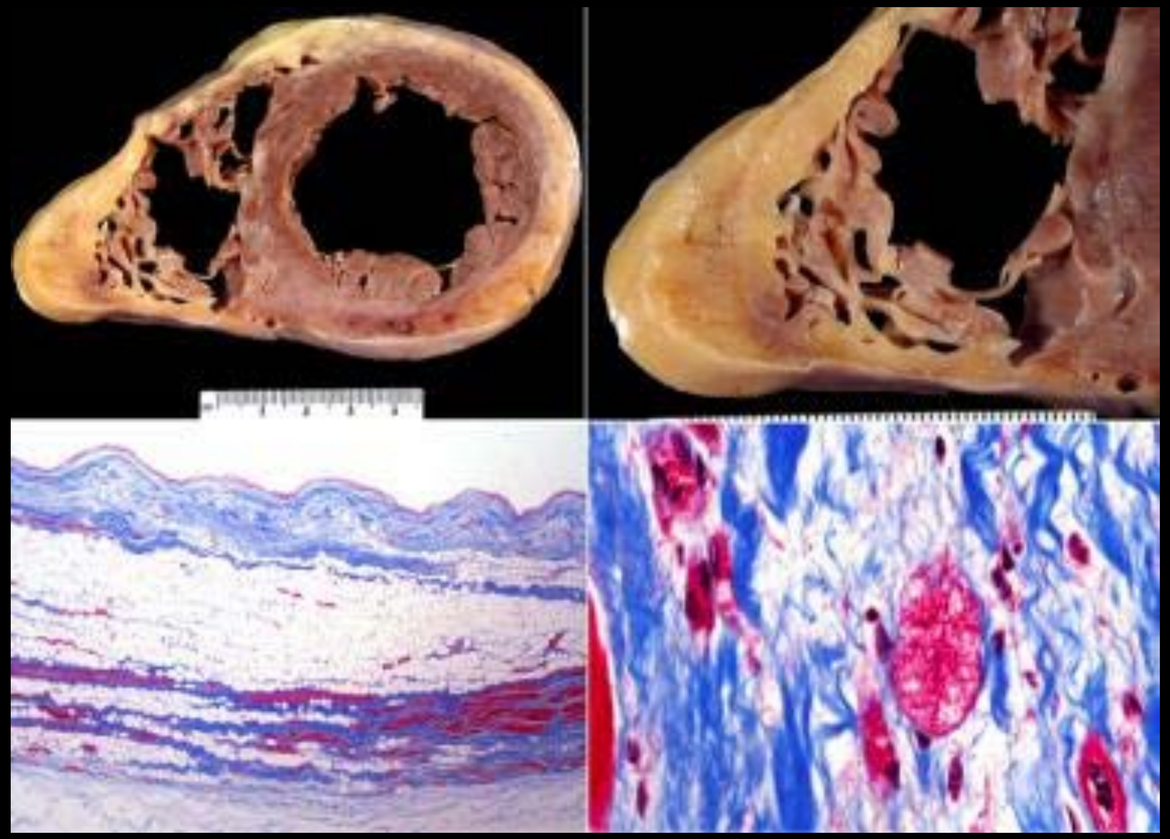


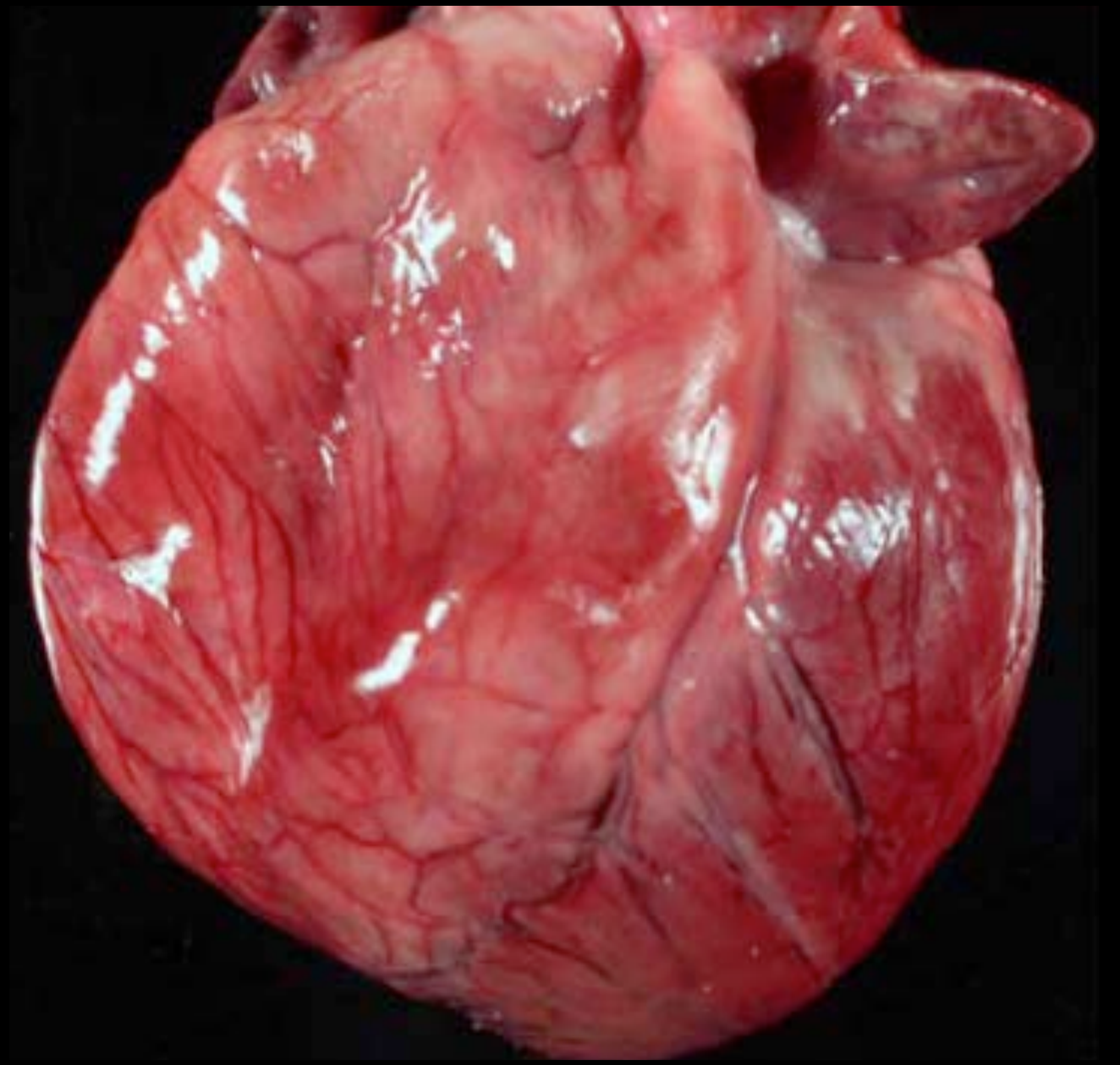


Right ventricular cardiomyopathies



A.R.V.D





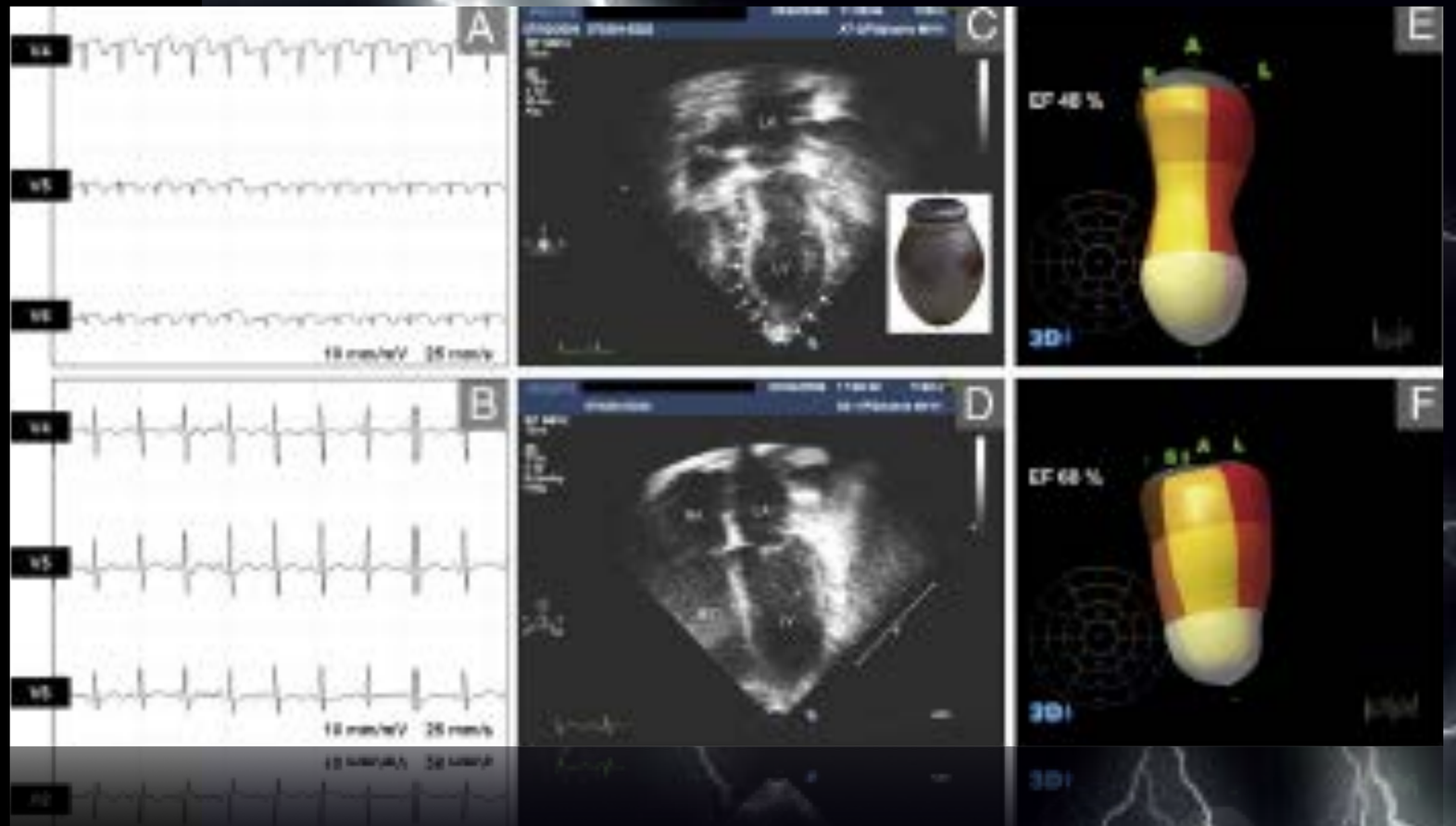
Difficulties in phenotyping

- Unusual phenotypes
  - Dilated with hypertrophic walls and restrictive physiology
- Changing phenotype
  - From hypertrophic to dilated
- Uncertain phenotype
  - Penetrance increasing with age

Cardiomyopathies are rarely familial and a known cause of ventricular dilatation and/or hypertrophy should be extensively searched

- Tako-tsubo
- Volume and pressure overload
- Myocardial ischemia
- Sustained arrhythmias
- Infective myocarditis
- Toxic
- Neuromuscular disorders
- Syndromic cardiomyopathies
- Metabolic diseases

Purely environmental cardiomyopathy ?

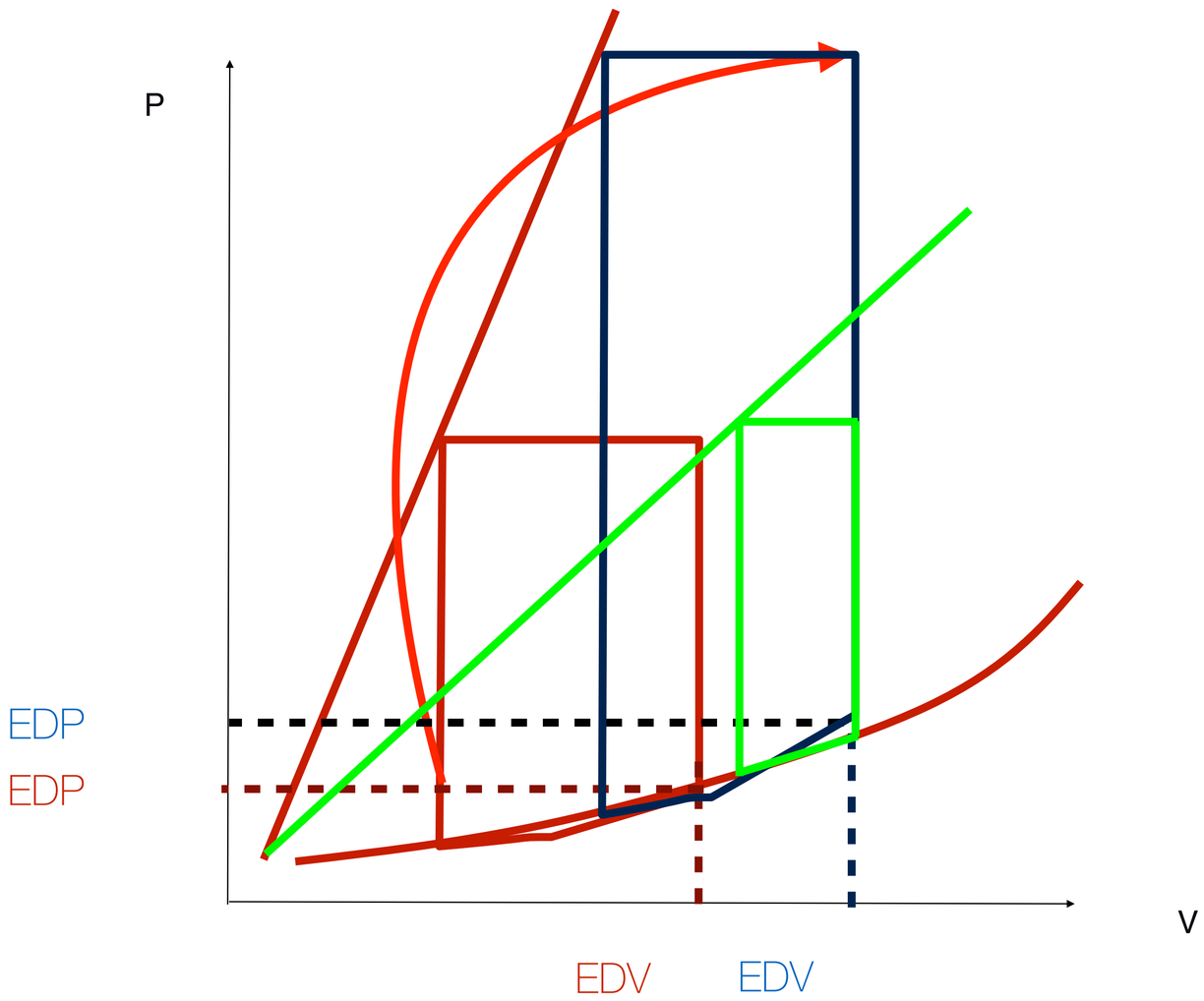


Takotsubo

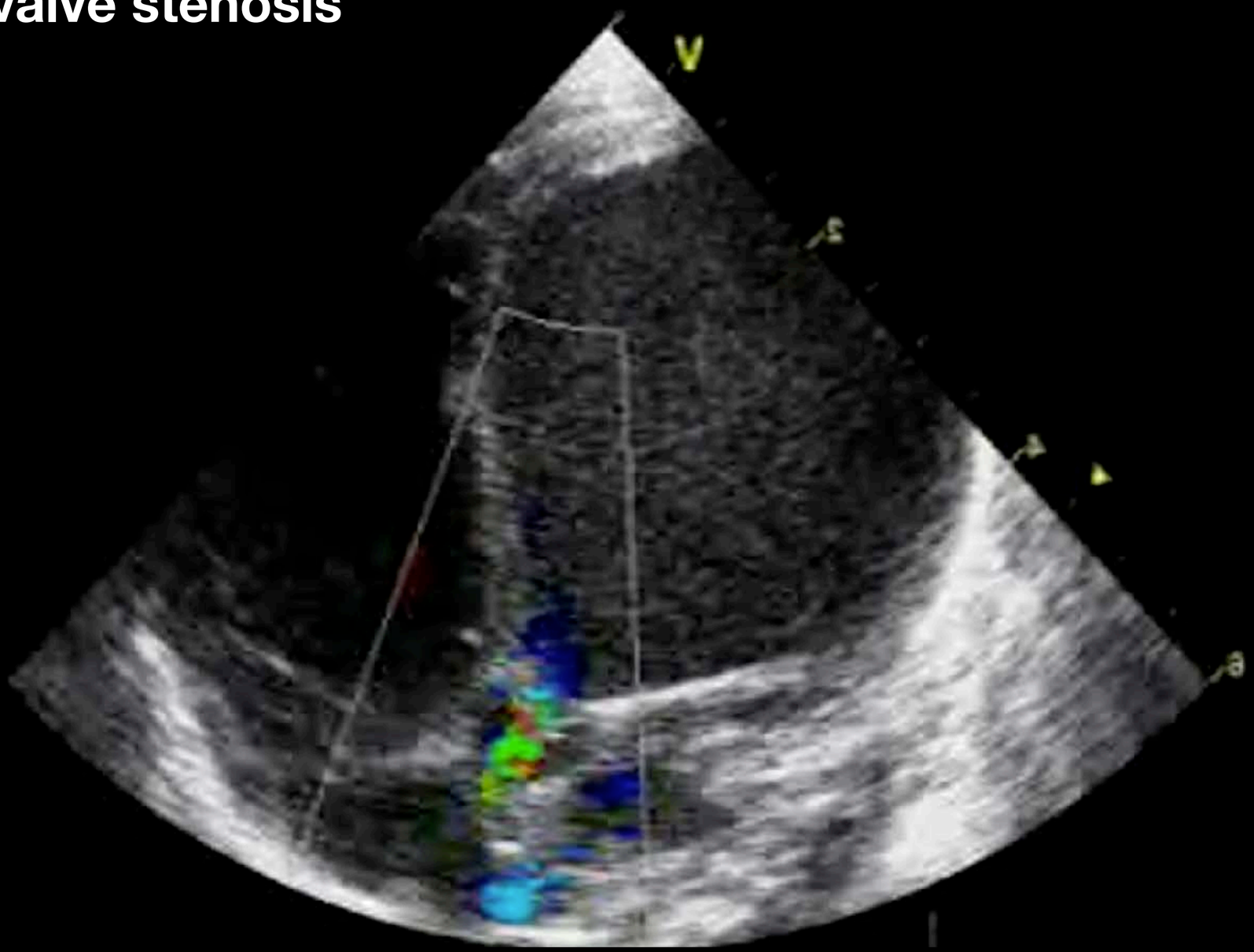
Schoof F et al. J Am Coll Cardiol. 2010 Jan 19;55(3):e5.
Bajolle F et al. Cong Heart Dis 2009;4:387-90

Heart failure due to increased afterload

Normal contractility and compliance

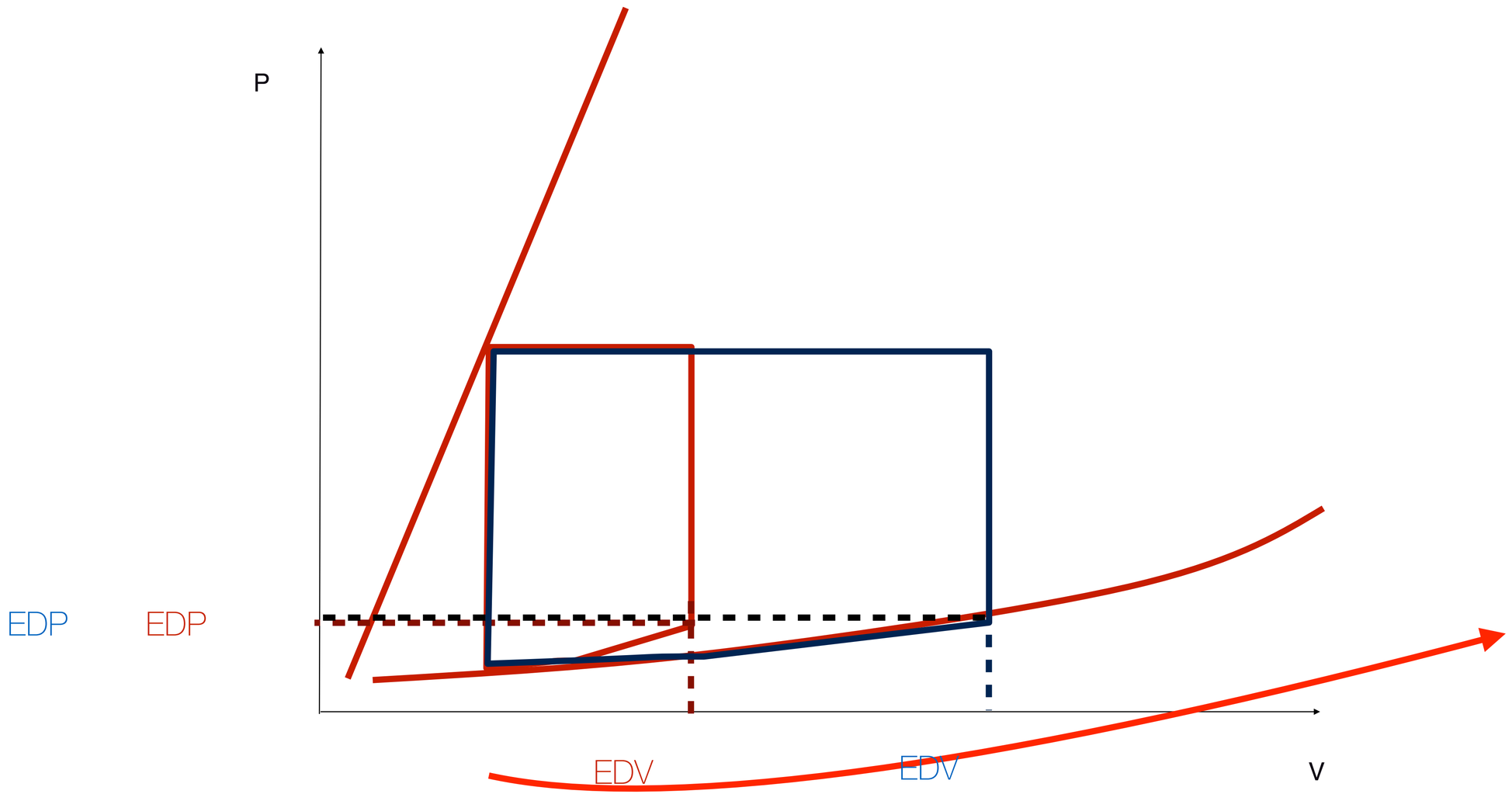


Critical aortic valve stenosis

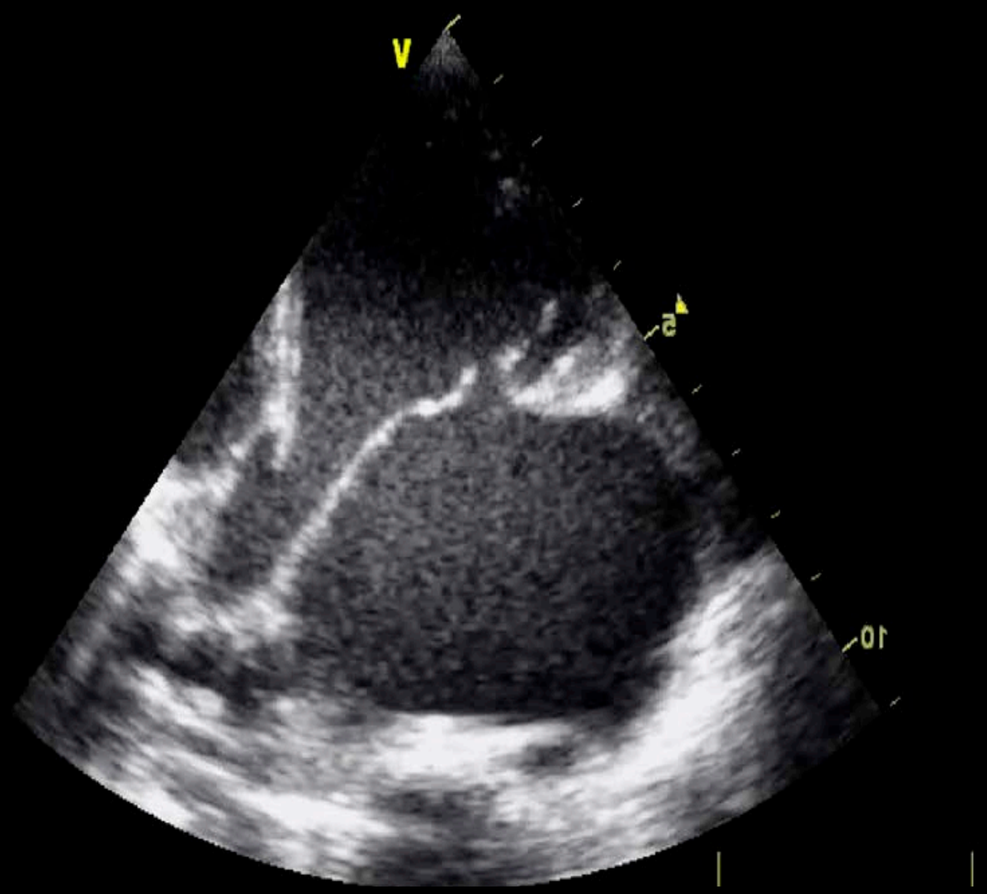


Heart failure due to increased preload

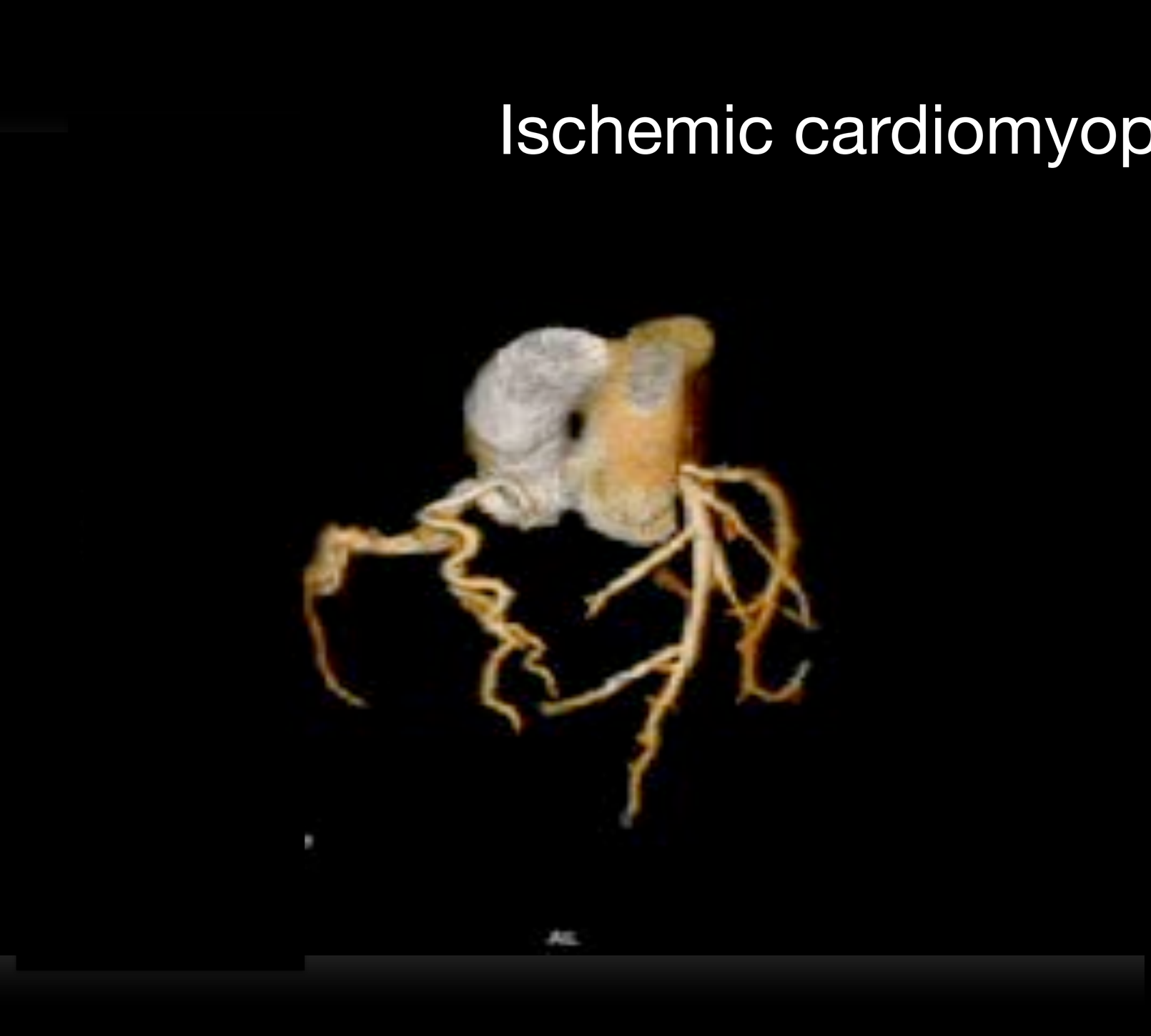
Normal contractility and compliance



Severe mitral valve regurgitation

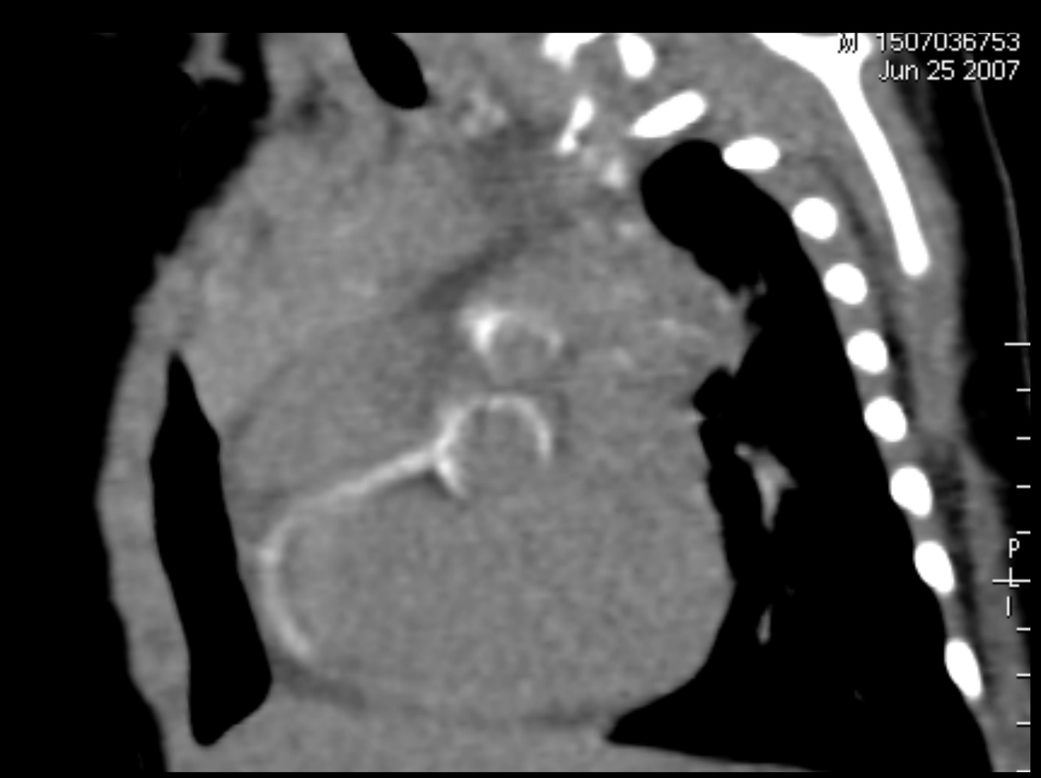


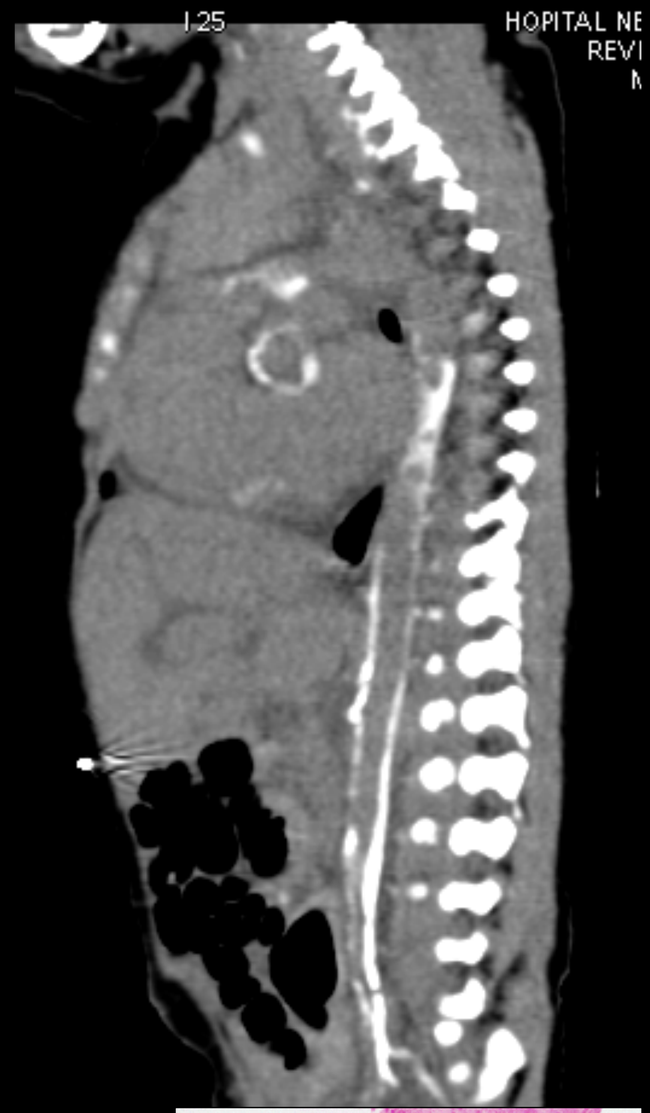
Ischemic cardiomyopathies

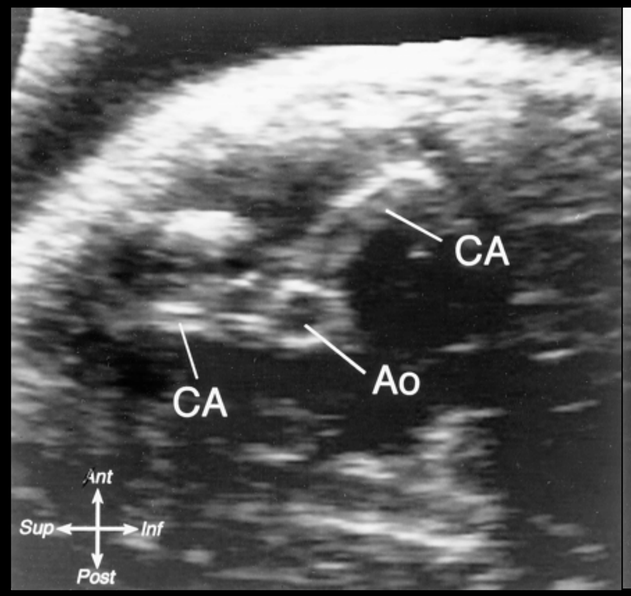


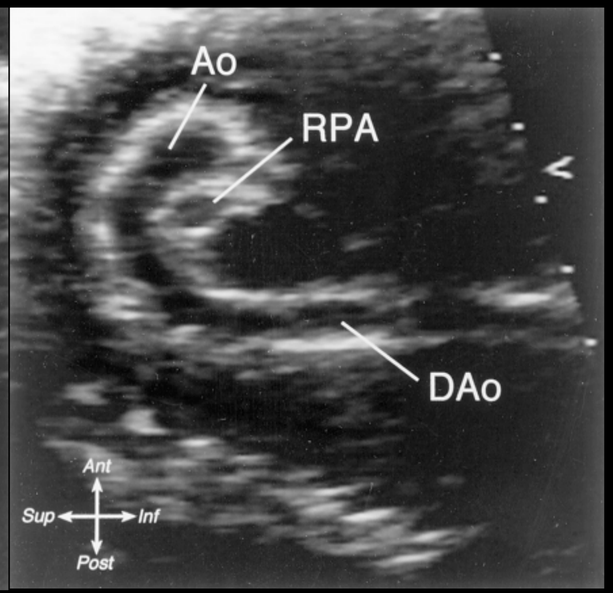
- ALCAPA-Main stem atresia
- Post-operative
  - TGA
- Kawasaki disease
- Hypercholesterolemia
- GACI

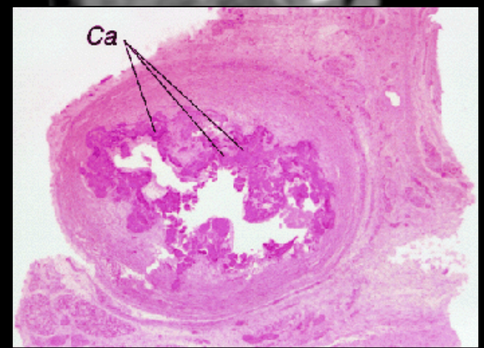
GACI


1507036753
Jun 25 2007


HOPITAL NE
REVI

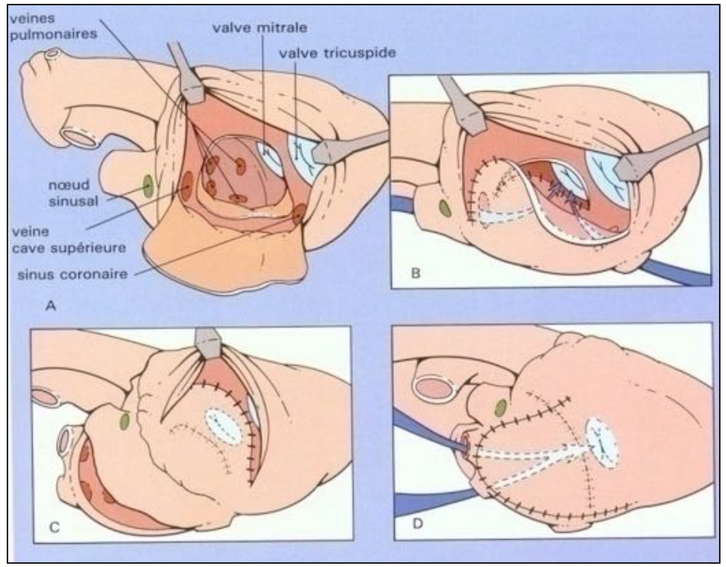

CA
CA
Ao
Ant
Sup
Inf
Post

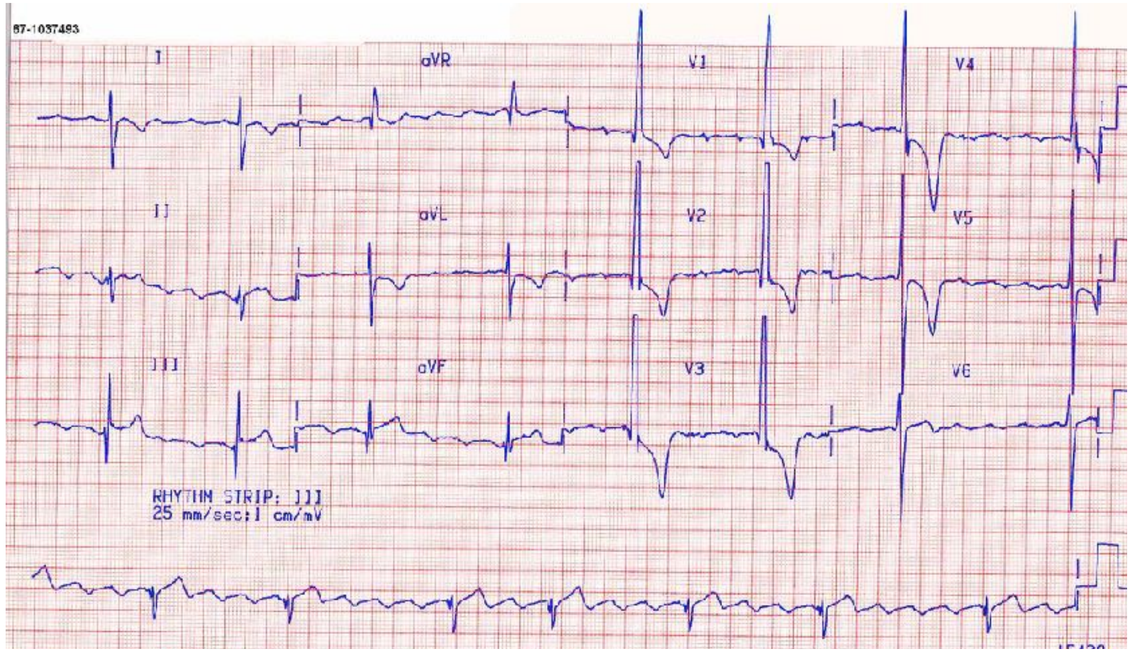

Ao
RPA
DAo
Ant
Sup
Inf
Post


Ca

Arrhythmic cardiomyopathy

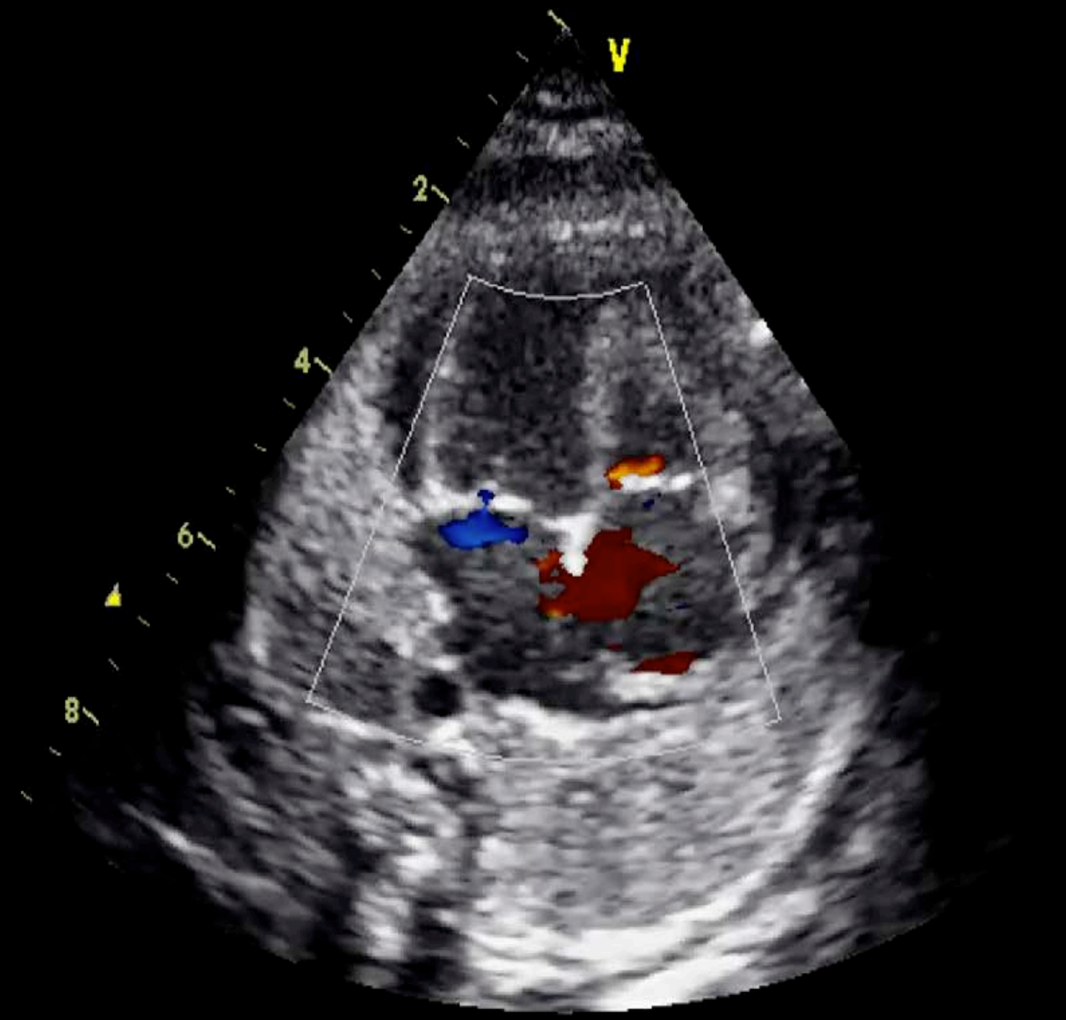
- Supraventricular tachycardia of the newborn
- Booby-traps
  - Atrial arrhythmias after atrial correction of TGA
  - Arrhythmias after TCPC

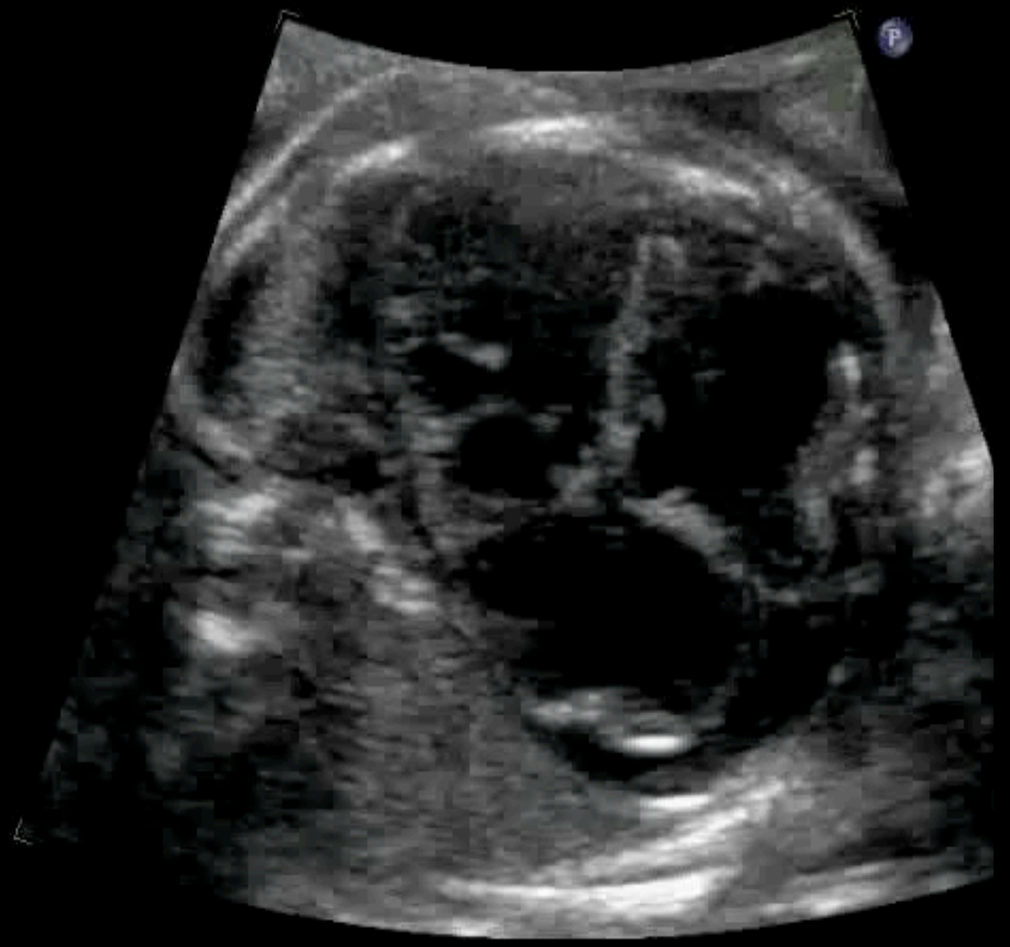




Arrhythmic cardiomyopathy fetal

JT/AVB





Infectious cardiomyopathies

Viral myocarditis

Lyme disease

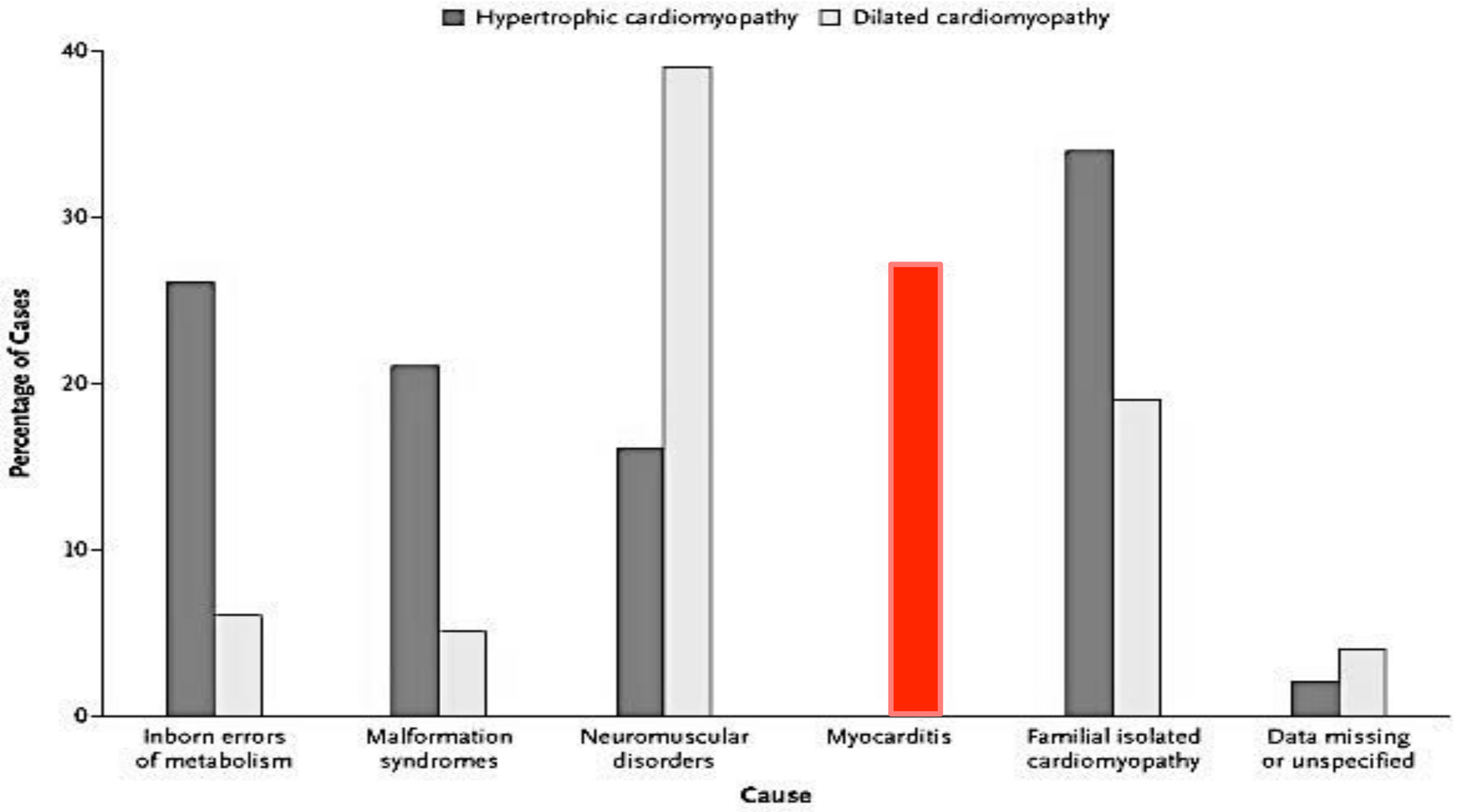
Chagas disease

HIV

Toxoplasmosis

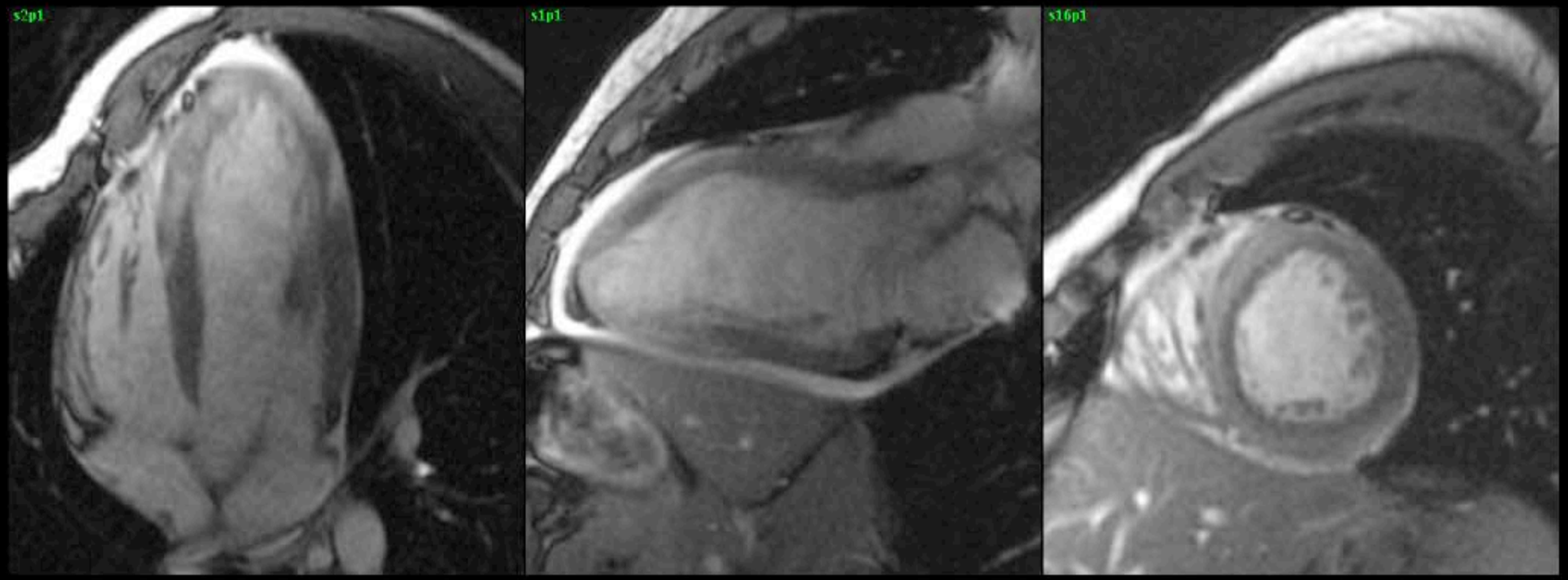
Rheumatic

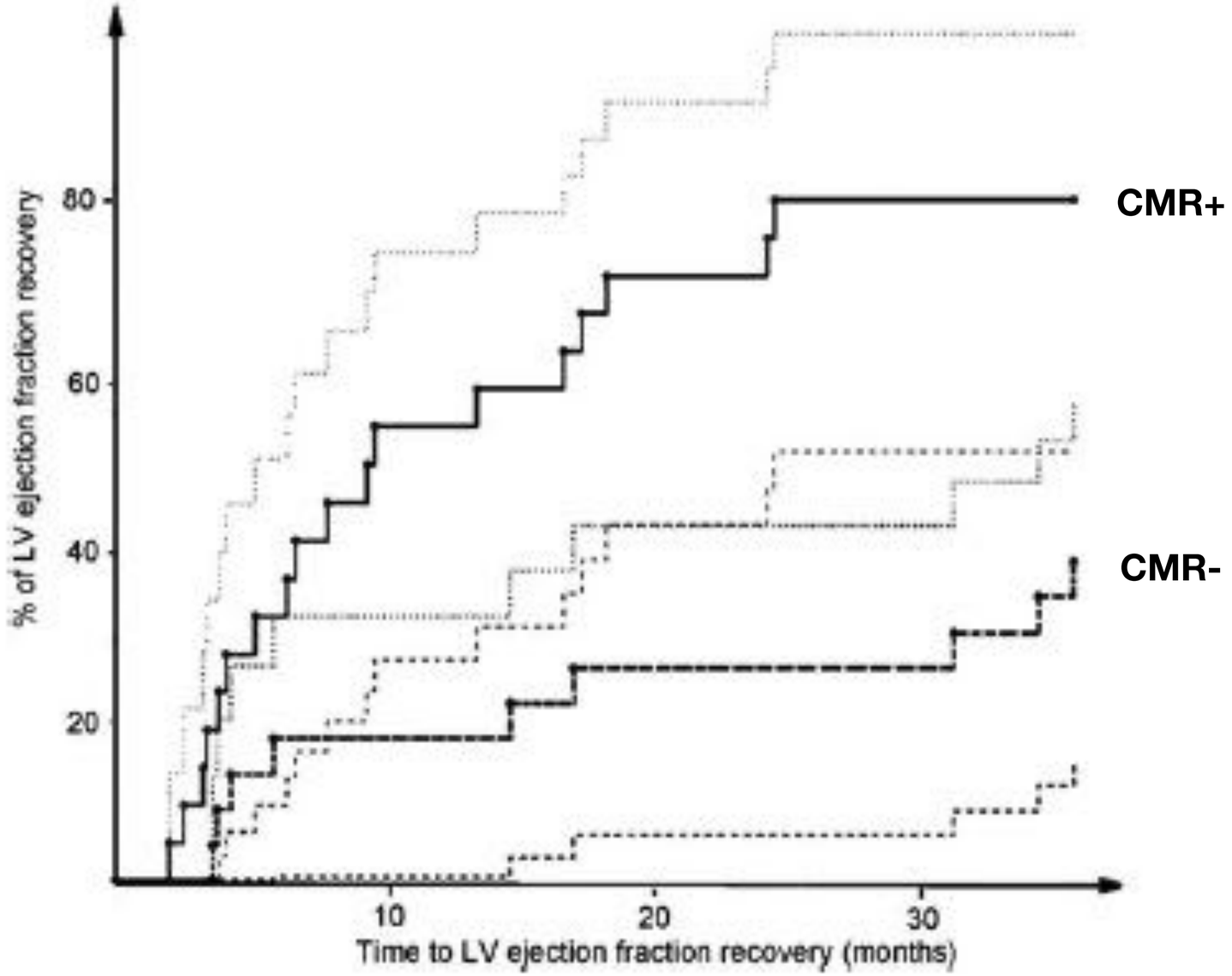
Myocarditis in children



Lipshultz SE et al. NEJM 2003;348:1647-55.

Myocarditis





Time to recovery of left ventricular function in CMR-positive group (full line) and in the CMR-negative group (dotted line) with 95% CI (grey dotted lines).

Raimondi F et al. Eur Heart J Cardiovasc Imaging 2015;16:756-62

Toxic

- Anthracyclines

- Radiations

Neuromuscular disorders

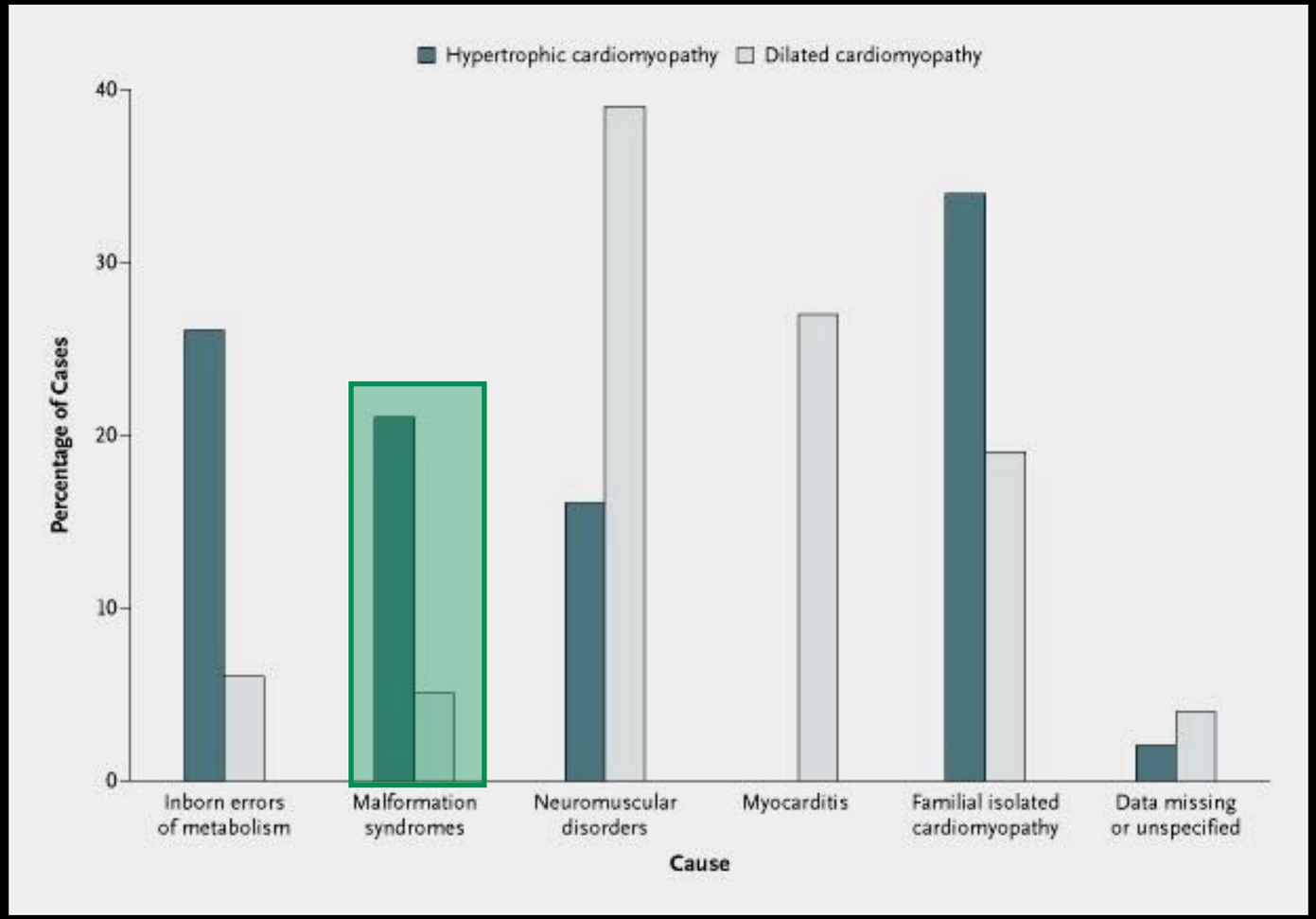
- Dystrophinopathies
  - Duchenne de Boulogne
  - Becker
- Emery-Dreyfus
- Laminopathies
- Steinert
- Friedreich

First stop !

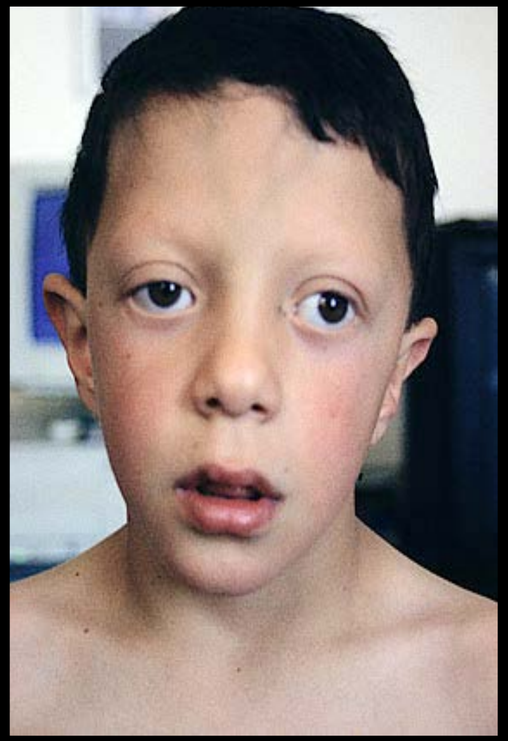
What have you done ?

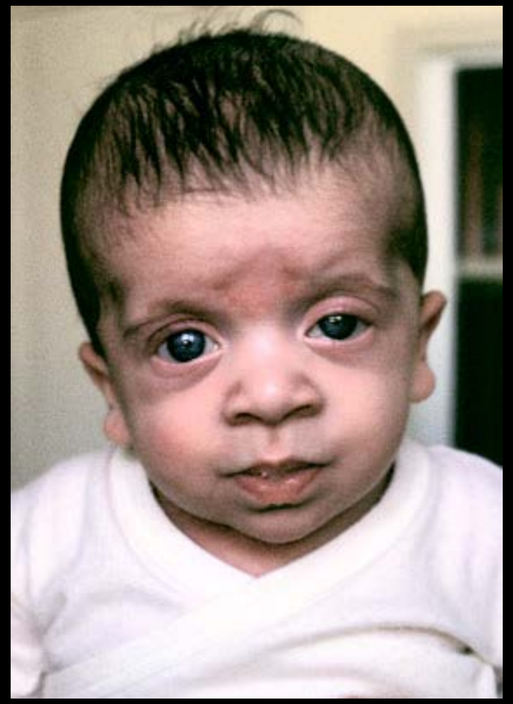
- Clinical examination
- Medical history
- ECG
- Echocardiography
- Troponine
- MRI

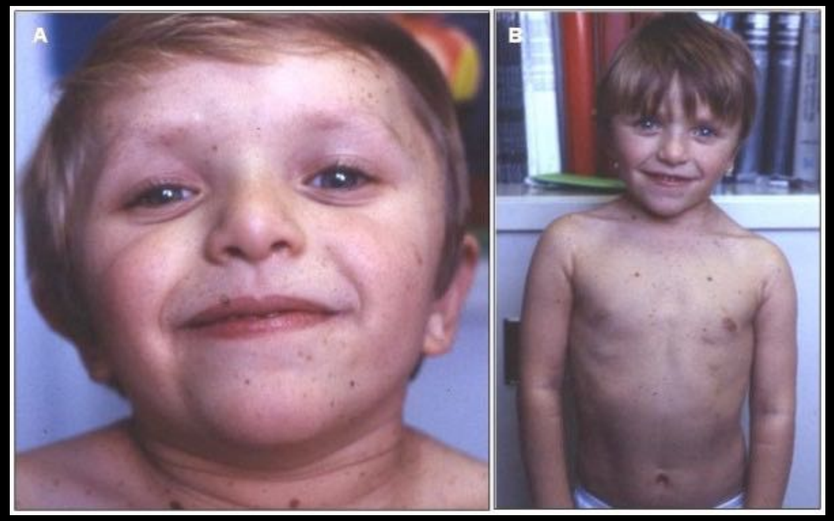
Malformation syndromes and cardiomyopathies

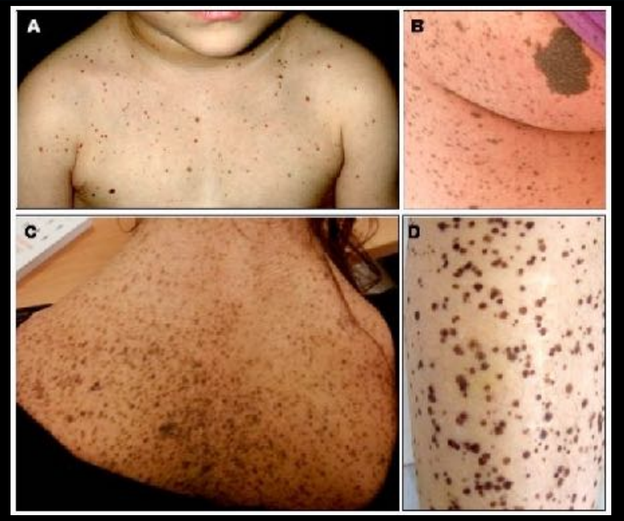


Lipshultz SE et al. NEJM 2003;348:1647-55



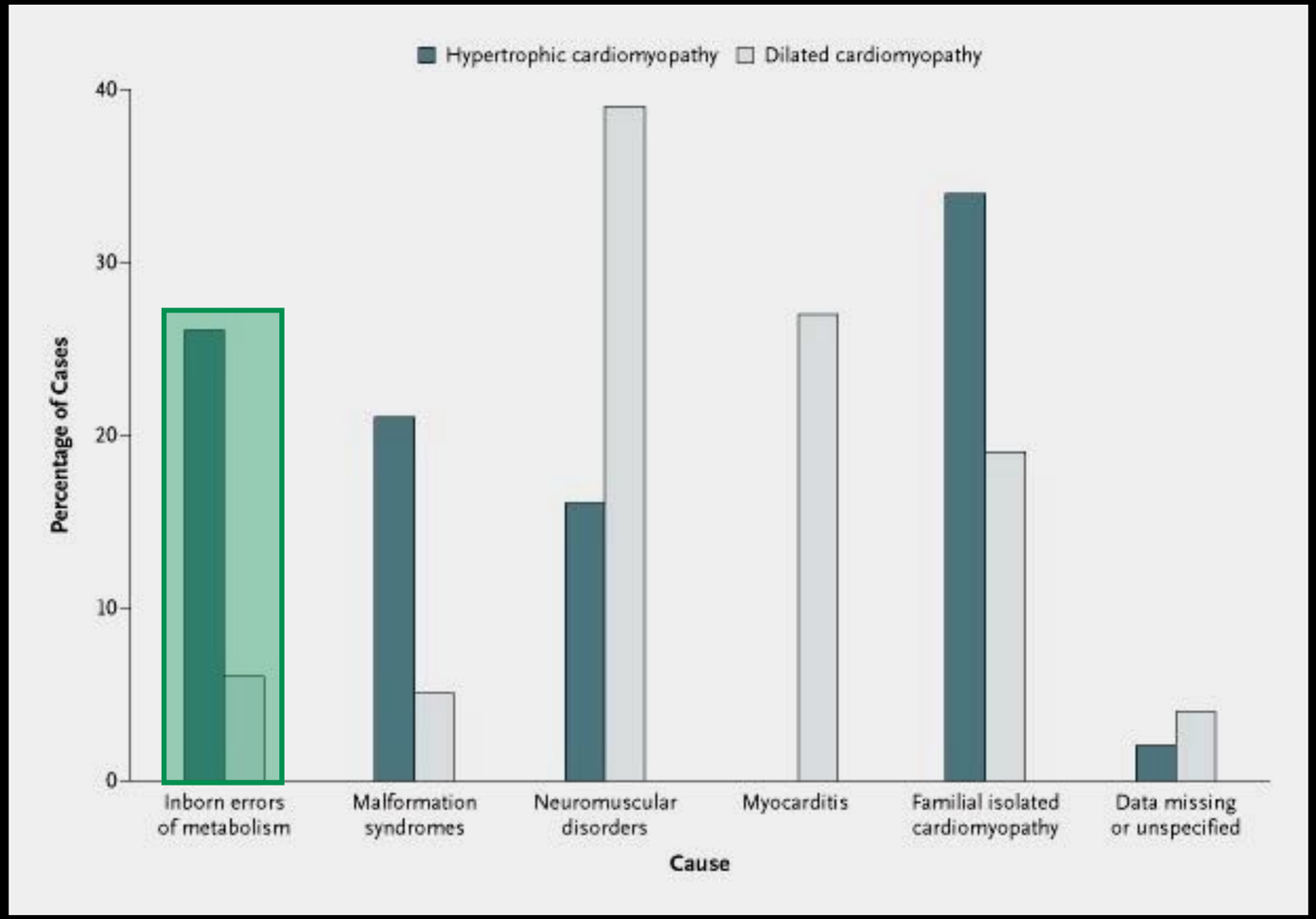






RASopathies

Inborn errors of metabolism and cardiomyopathies



Lipshultz SE et al. NEJM 2003;348:1647-55

Cardiac involvement in IEM

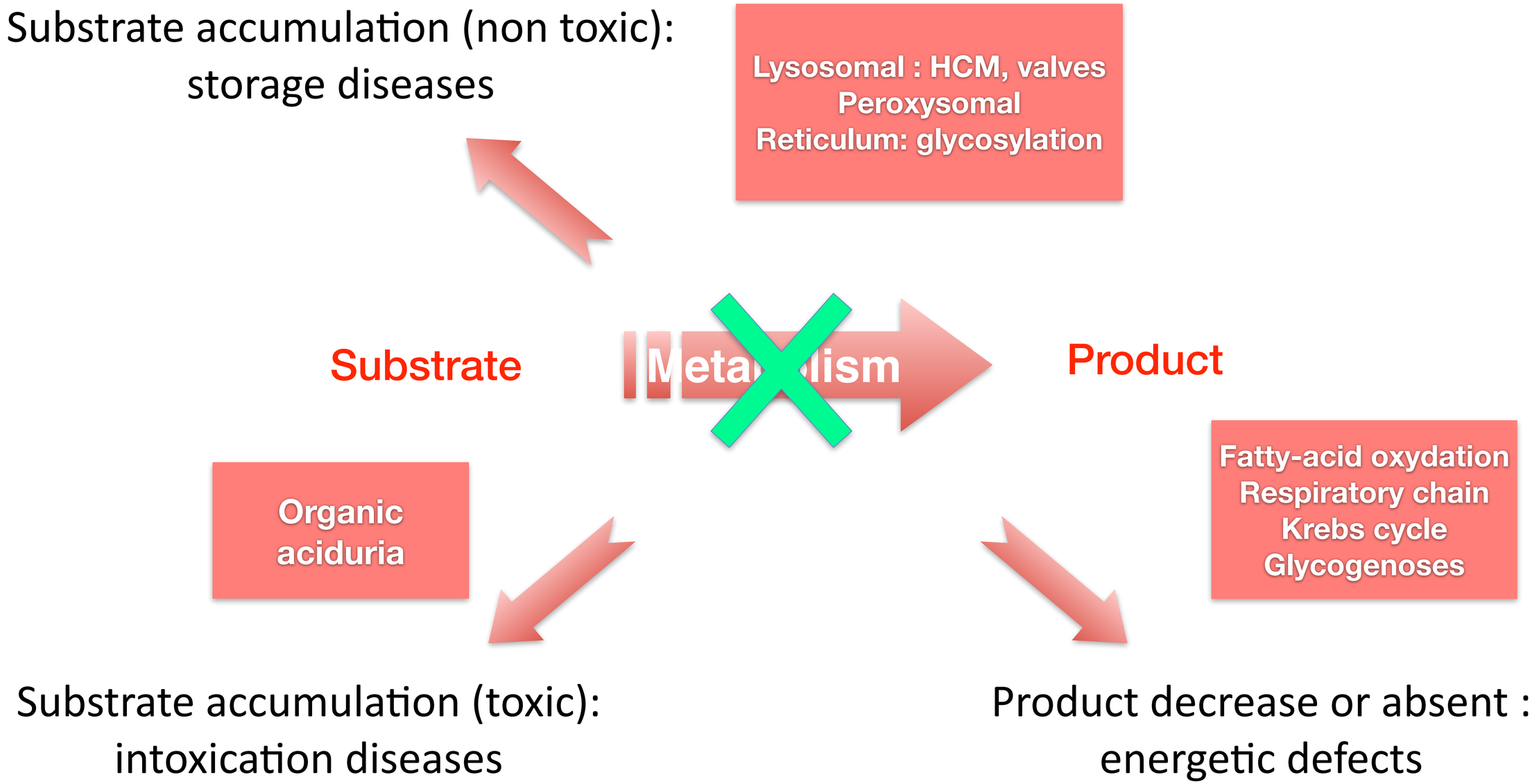
- Cardiomyopathies
  - Storage diseases
  - Systolic dysfunction in energetic defects & intoxications
  - Phenotypic variability and atypical evolution of RC defects
- Arrhythmias
  - Triggered and automatic activities in intoxications
  - Facilitated conduction and accessory pathways in glycogenoses
  - Atypical AV blocks
- Valvular thickening in mucopolysaccharidoses
- Pericardial effusion in glycosylation defects
- Congenital heart defects[1]?

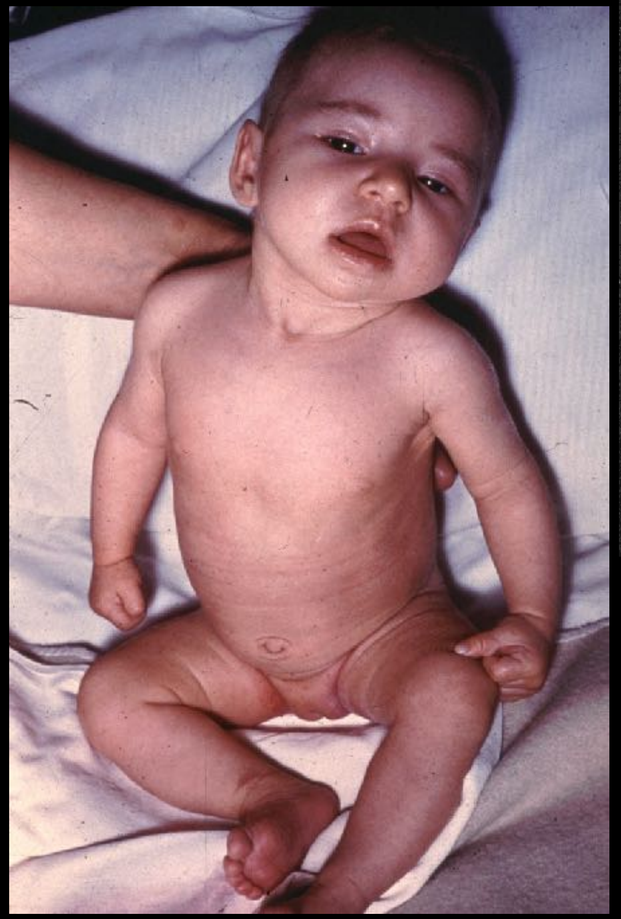
1-Romano S. et al. J Med Genet 2009.
Conotruncal heart defects in three patients with congenital disorder of glycosylation type Ia (CDG Ia)

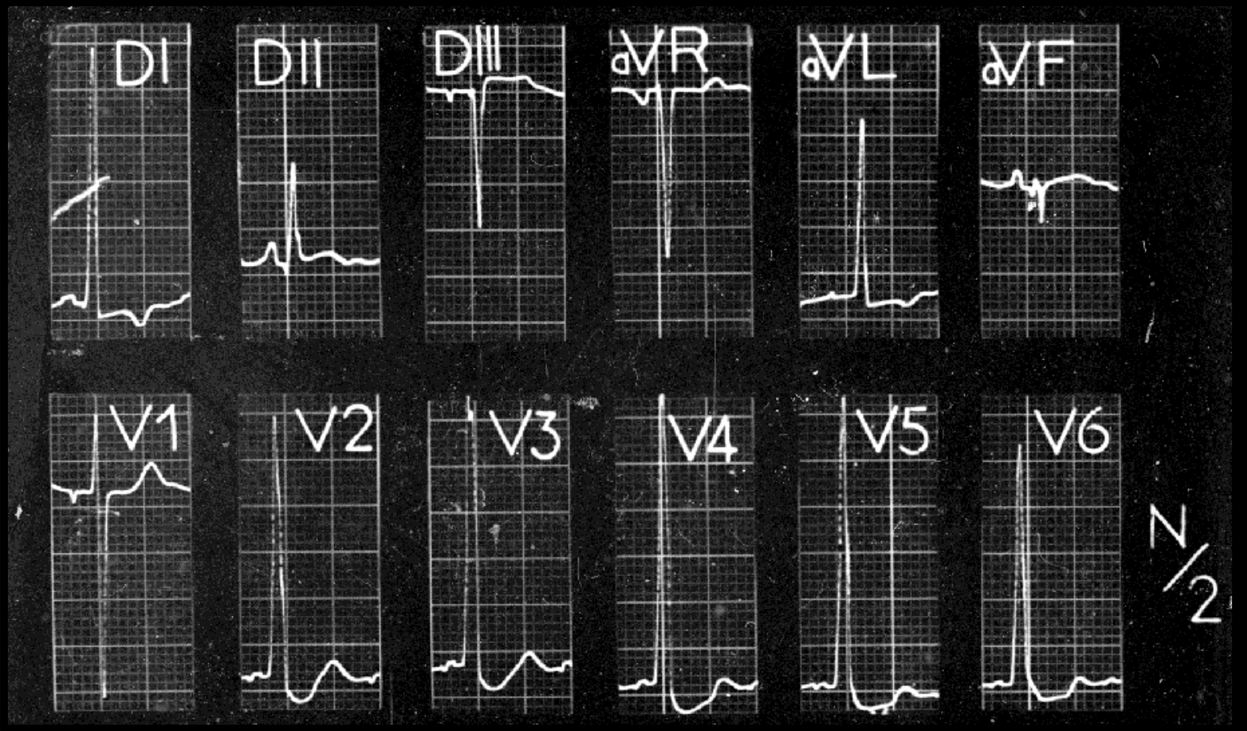
When should you think of metabolic cardiomyopathy ?

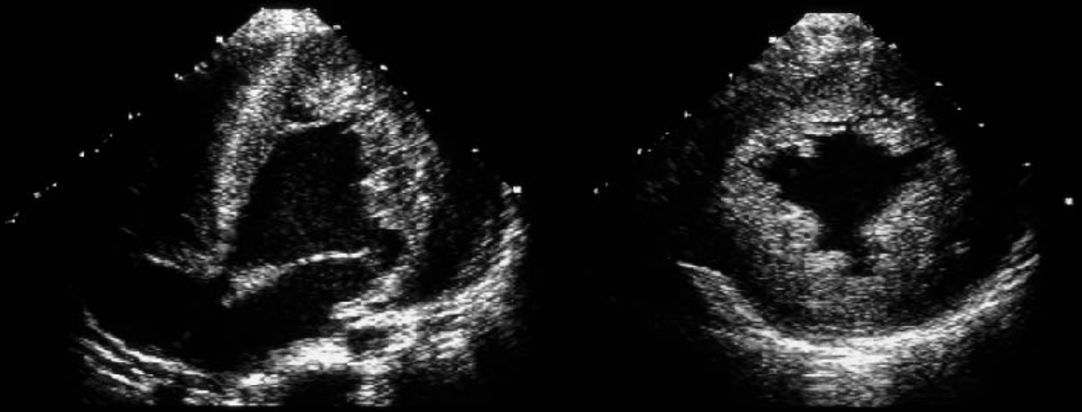
- Family history of sudden death or unexplained death in infancy
- Multisystemic disease
- Changing phenotype
- Severe hemodynamic compromise with mild alteration of LV function
- Atypical anomalies of ECG : left bundle branch bloc, AVB, ventricular tachycardia

Cardiac metabolism for pediatric cardiologists



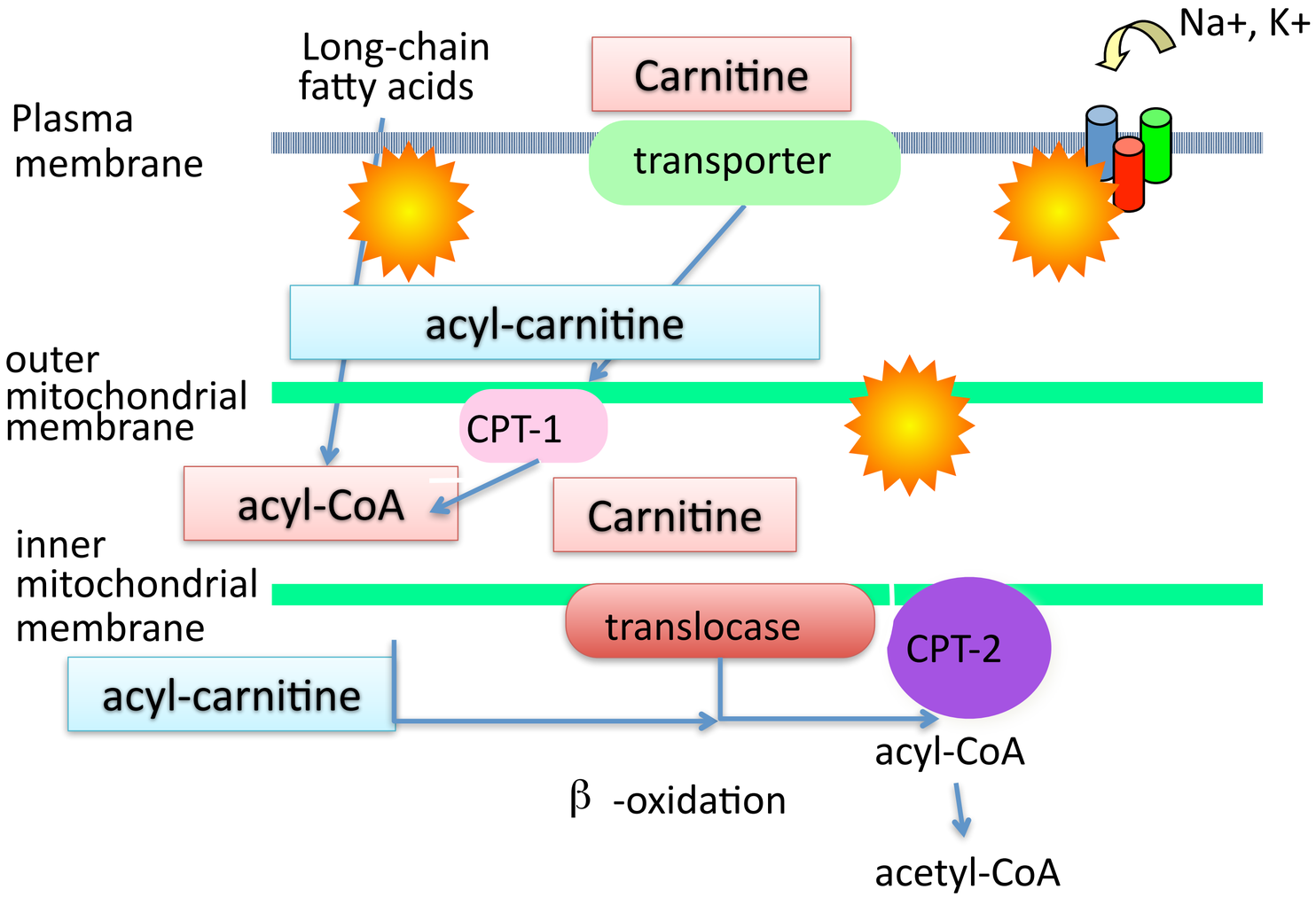






Pompe's disease

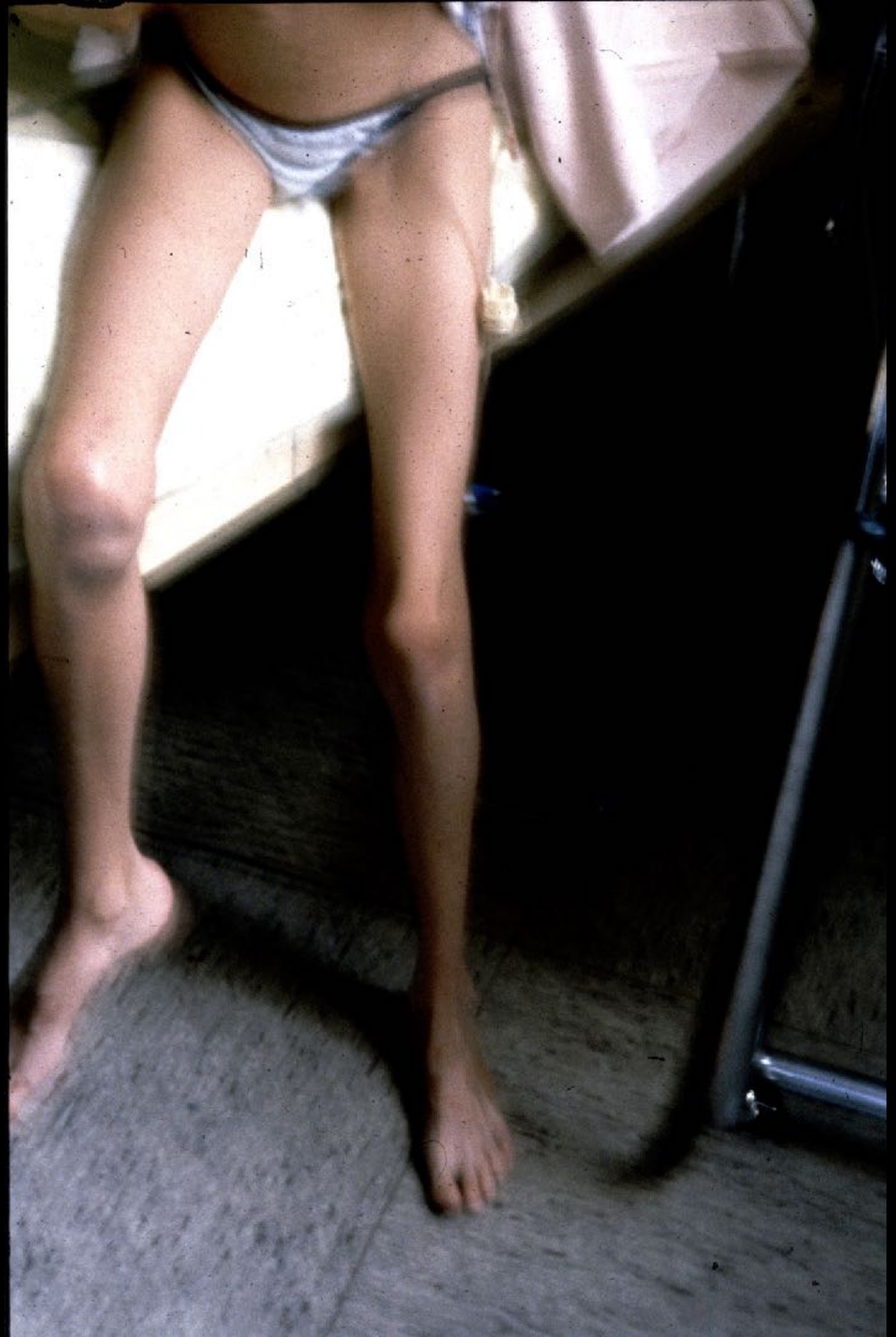
Fatty acid oxidation



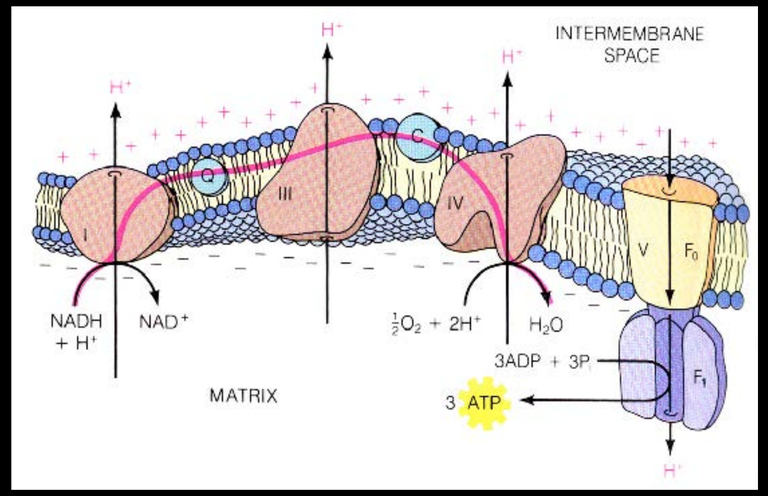
Presenting symptoms of FAO disorders

Neonatal neurological distress	23%
Hypoglycemia Hypoketotic	46%
Reye ’s syndrome	30%
Arrhythmias	**14%**
Cardiomyopathies	**12%**
Sudden death	**7%**
Near-miss	**7%**
Myolysis, myoglobinuria	6%
Muscular weakness	2%
Hepatomegaly	2%
Cholestasis	1%

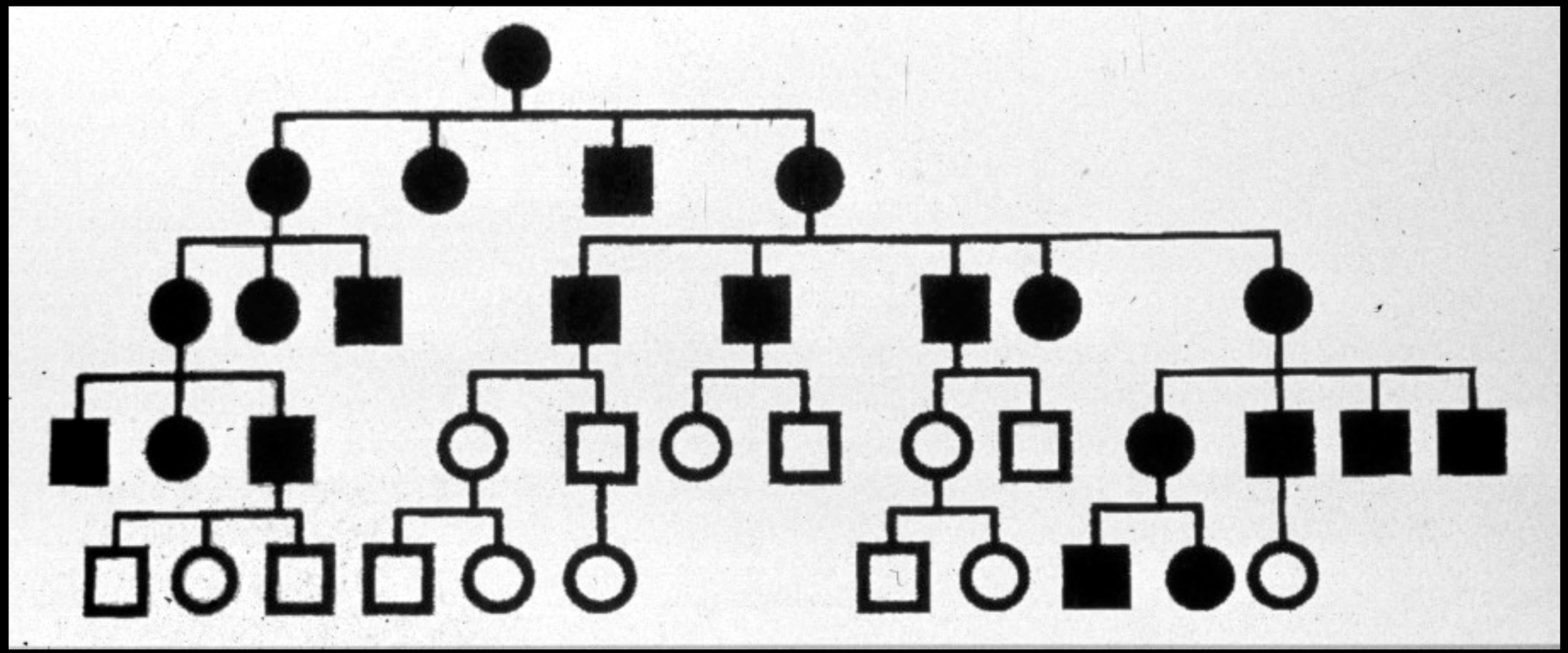
Saudubray J Inher Metab Dis 1999;22:488-502



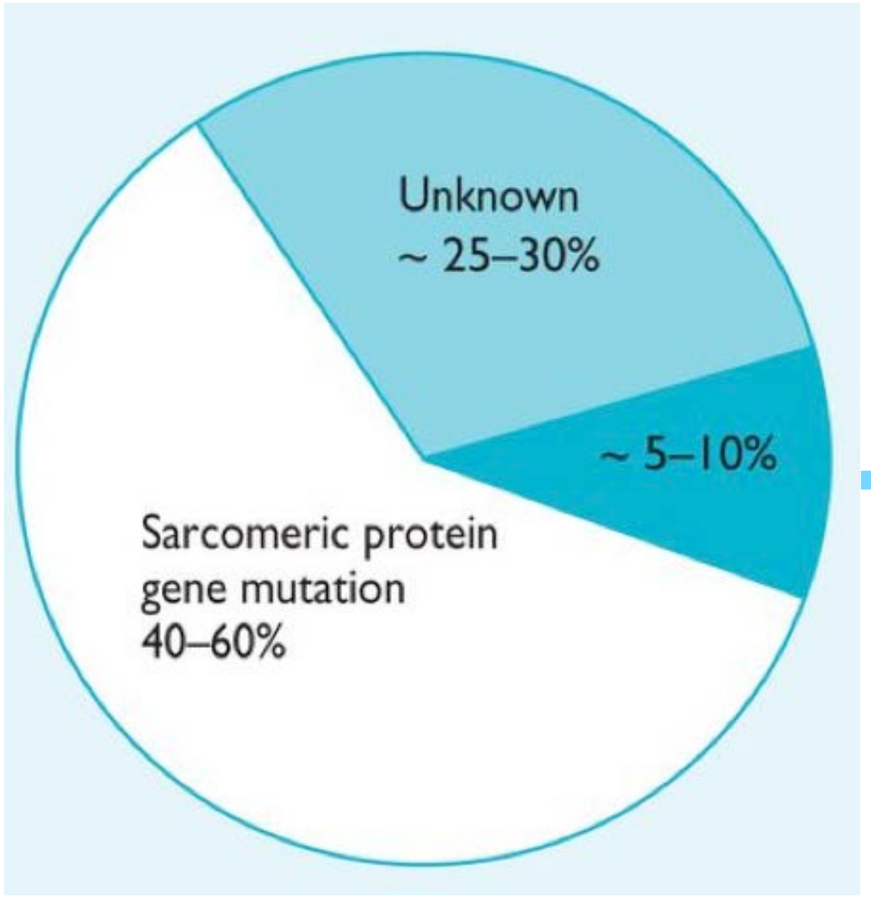
Carnitine deficiency



Mitochondrial disease



Genetic screening for HCM in adults



- **Inborn errors of metabolism**
  Glycogen storage diseases:
  - Pompe
  - Danon
- AMP-Kinase (PRKAG2)
- Carnitine disorders
- Lysosomal storage diseases
  - Anderson-Fabry

- **Neuromuscular diseases**
  - Friedreich's ataxia
  - FHL1

- **Mitochondrial diseases**
  - MELAS
  - MERFF

- **Malformation Syndromes**
  - Noonan
  - LEOPARD
  - Costello
  - CFC

- **Amyloidosis**
  - Familial ATTR
  - Wild type TTR (senile)
  - AL amyloidosis

Familial screening

- First degree relatives
- ECG
- Echocardiography
- Genetic testing according to local practice and legal recommandations for presymptomatic screening

Summary of clinical evaluation and etiology search for cardiomyopathies

- Medical history personal and familial
- Cardiac examination
- ECG + Echocardiography
- MRI + troponin
- Genetic clinic for syndromes
- Metabolic screening
  - Glucose, ketone bodies, lactates,
  - Chromato organic acids, acylcarnitines, carnitine T+F

  - and that’s it!


M3C