Genetics of Cardiovascular Disease

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Cardiovascular Genetics

- Environmental causes- trauma, malnutrition, drug abuse-defined by body response- phenotype
- Genotype-how patient suffers or recovers
- Therefore, genetics plays a role in both cause and process; etiology and pathogenesis

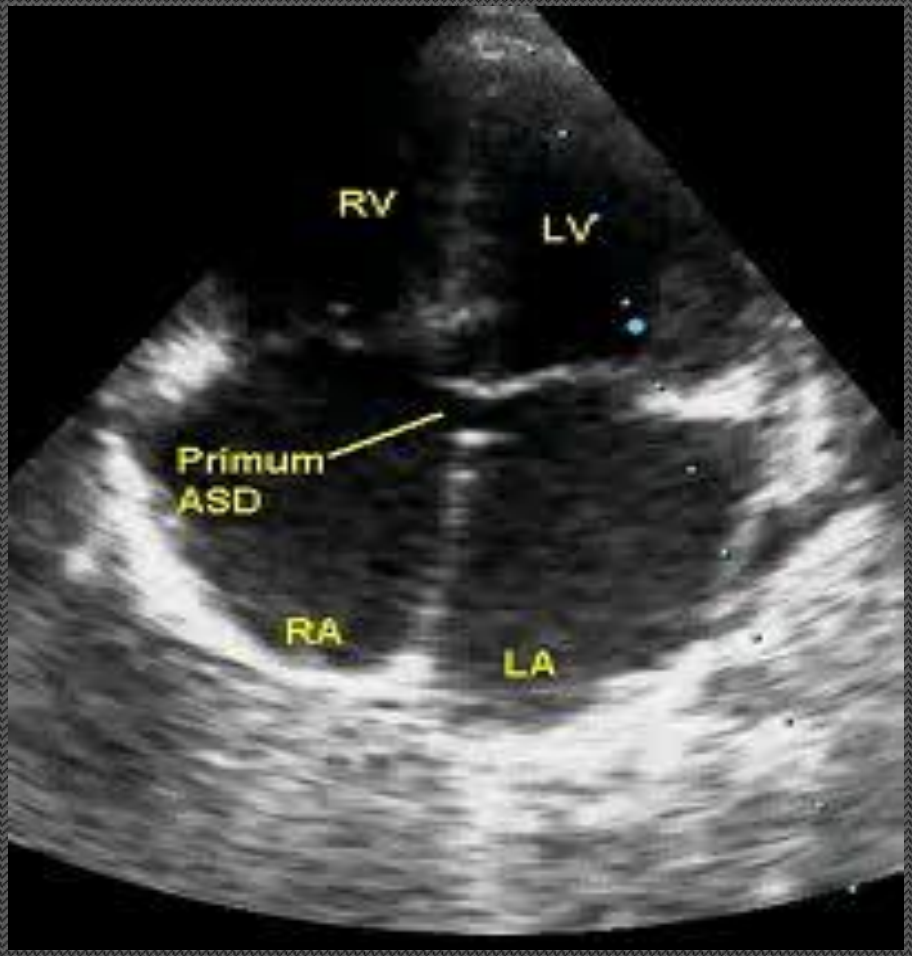
Cardiovascular Genetics

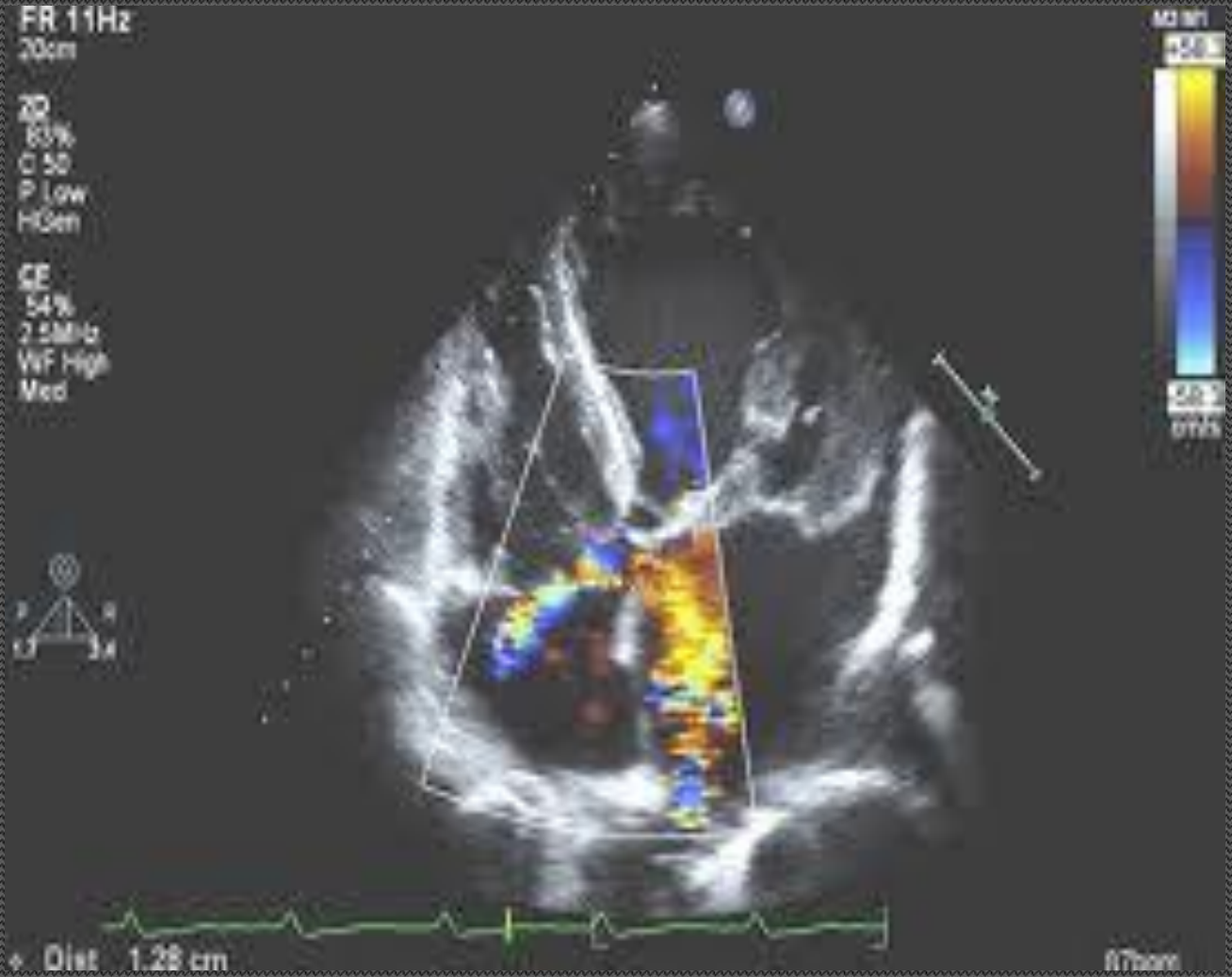
- Genotype-detrimental in two distinct ways-
  - Mutant genes upset embryology or physiology
  - Known as genetic diseases

  - Facilitate the action of an extrinsic cause in producing a disease-coronary artery disease
  - Inherited susceptibilities

Cardiovascular Disorders Associated with Chromosome Aberrations

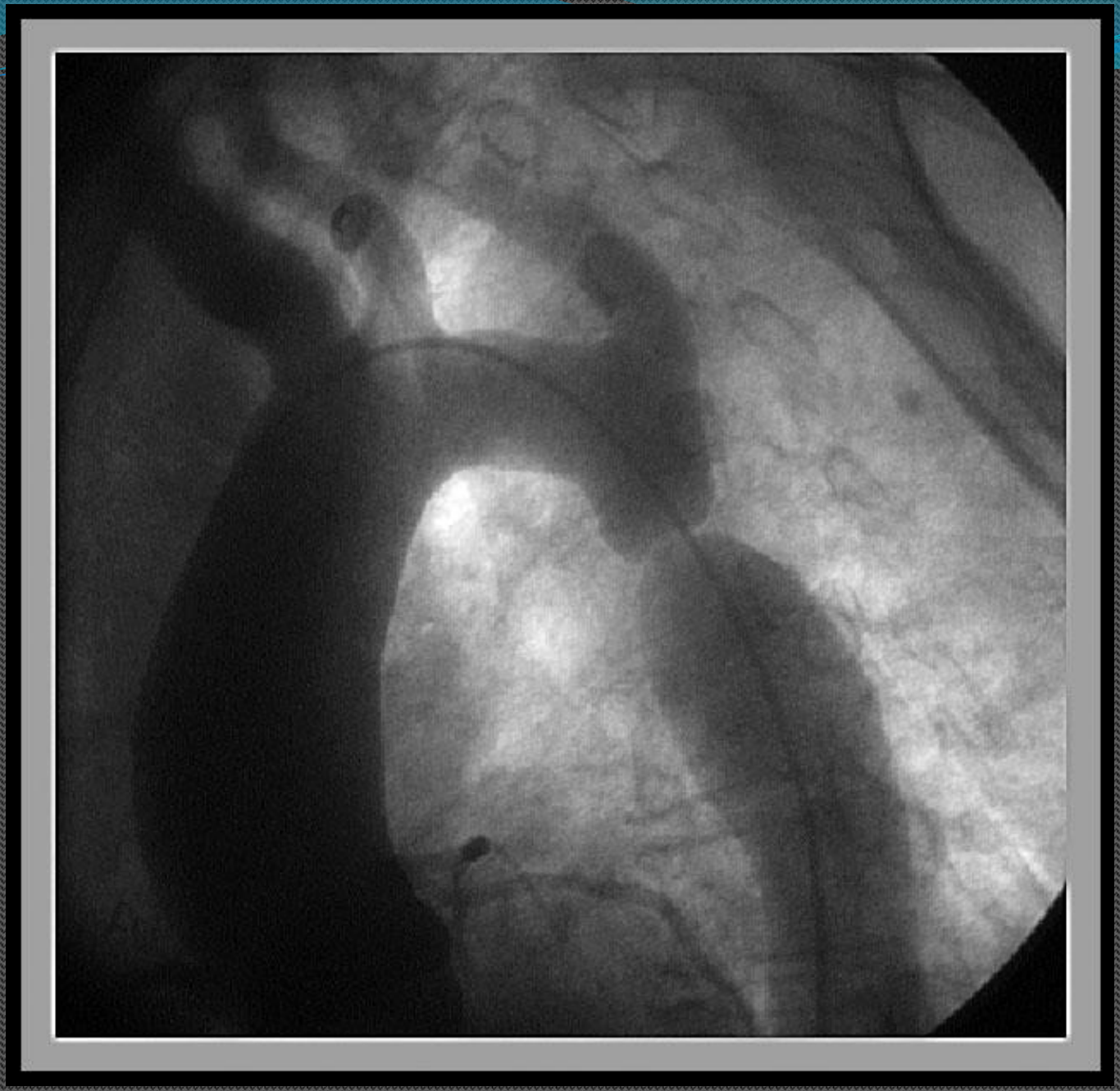
- Trisomy 21- Downs Syndrome
  - Most common phenotype
  - 1/600 births
  - Maternal age; >35 years and greatest >45(4%)
  - CHD present in 40-50%
  - Endocardial cushion defect
  - Atrial septal defect with cleft mitral valve
  - Pulmonary Hypertention


RV
LV
Primum
ASD
RA
LA


FR 11Hz
20cm
2D
83%
C 50
P Low
HiGen
CE
54%
WF High
Med
Dist 1.28 cm

Cardiovascular Disorders Associated with Chromosome Aberrations

- Turner syndrome- 45,X karyotype
  - 1/2500 females lacks an X chromosome
  - Short stature or amenorrhea is evaluated
  - 20-50% report cardiovascular abnormalities
  - Aortic coarctation
  - Bicuspid aortic valve
  - Dilated aortic root



Congenital Heart Disease

- Incidence- 3.1-3.5/1000
- Two mechanisms- multifactorial and mutations of single genes

Multifactorial Processes

- Familial Atrial Septal Defect-primum/secundum
- Holt-Oram Syndrome-autosomal dominant
  - Dysplasia of upper limbs and ASD
    "Digitalization of the thumb"
    Secundum ASD

- Supravalvular Aortic Stenosis
  - Asymptomatic
  - Williams Syndrome-sporadic,,haighly variable autosomal dominant
  - Elfin facies
  - Pulmonic stenosis
  - Supravalvular aortic stenosis
  - Mitral valve prolapse

- Mitral Valve Prolapse
  - Heterogeneous
  - Most common abnormality of human heart valve
  - Autosomal dominant-minimal form
  - Autosomal dominant-variable
    - Marfan syndrome

Teratogenic Effects

- Ethanol- 50% CHD: VSD, ASD
  - Most common teratogen to which fetal embryo and fetus are exposed-first trimester
  - Warfarin- 10% CHD: PDA, PS, intracranial hemorrhage
  - Fetal Rubella- 50% of fetuses become infected with rubella virus when mother is infected during first trimester. PDA and ASD, PS

Hypertrophic Cardiomyopathy

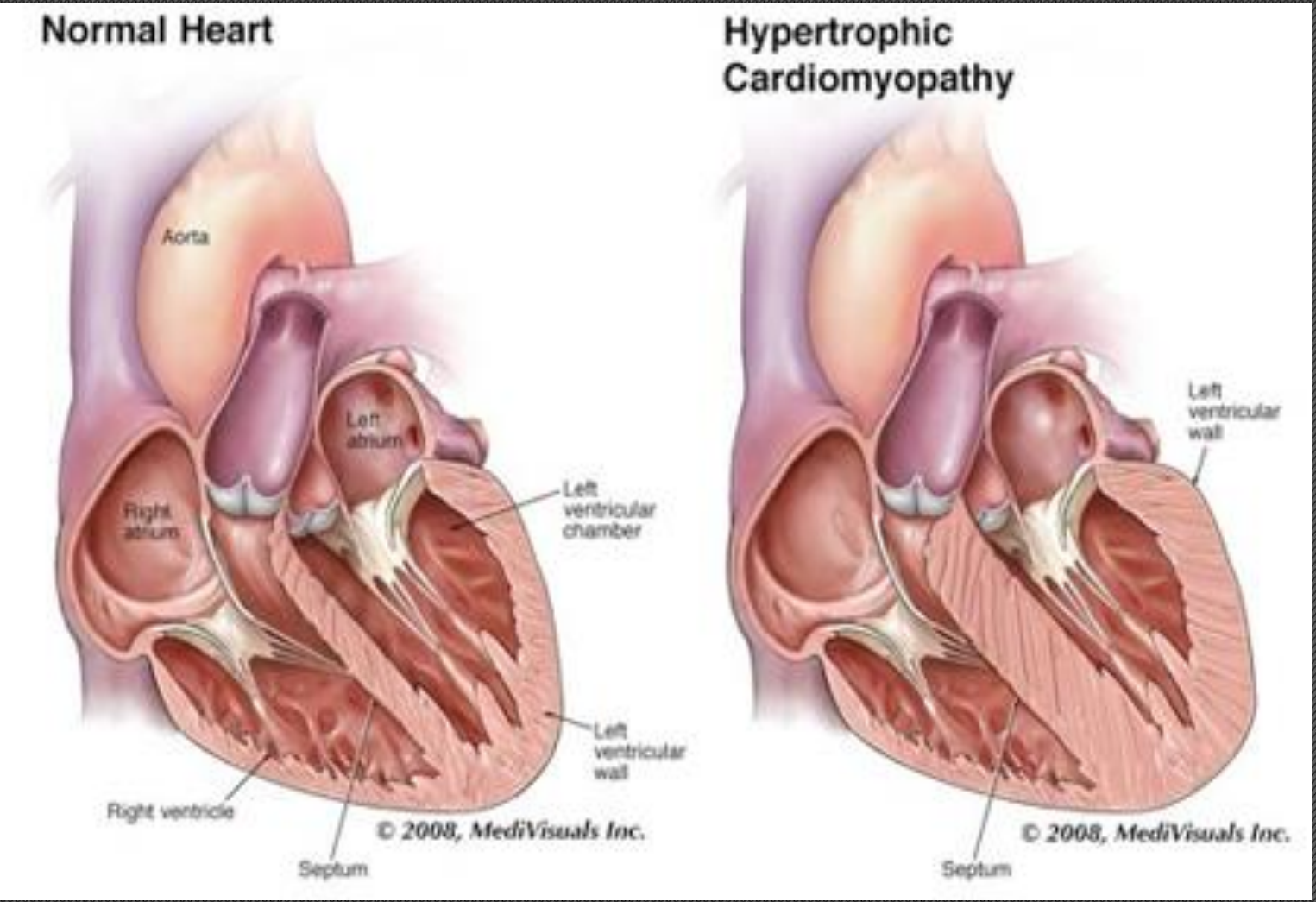
- Phenotype is anatomic and histologic
- Myocardial hypertrophy without secondary cause; cellular and myofiber disarray, fibrosis and cad.
- No pathognomonic findings
- Affects first degree relatives and in families the phenotype is inherited and an autosomal dominant, familial hypertrophic cardiomyopathy

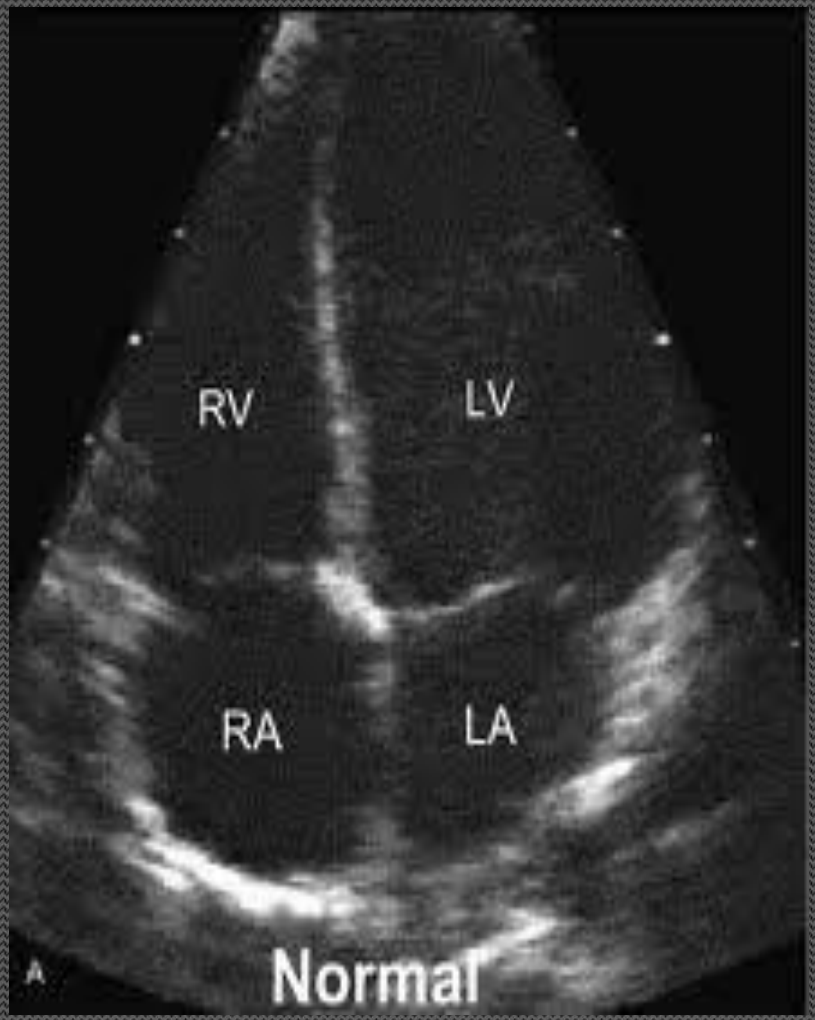
Hypertrophic Cardiomyopathy

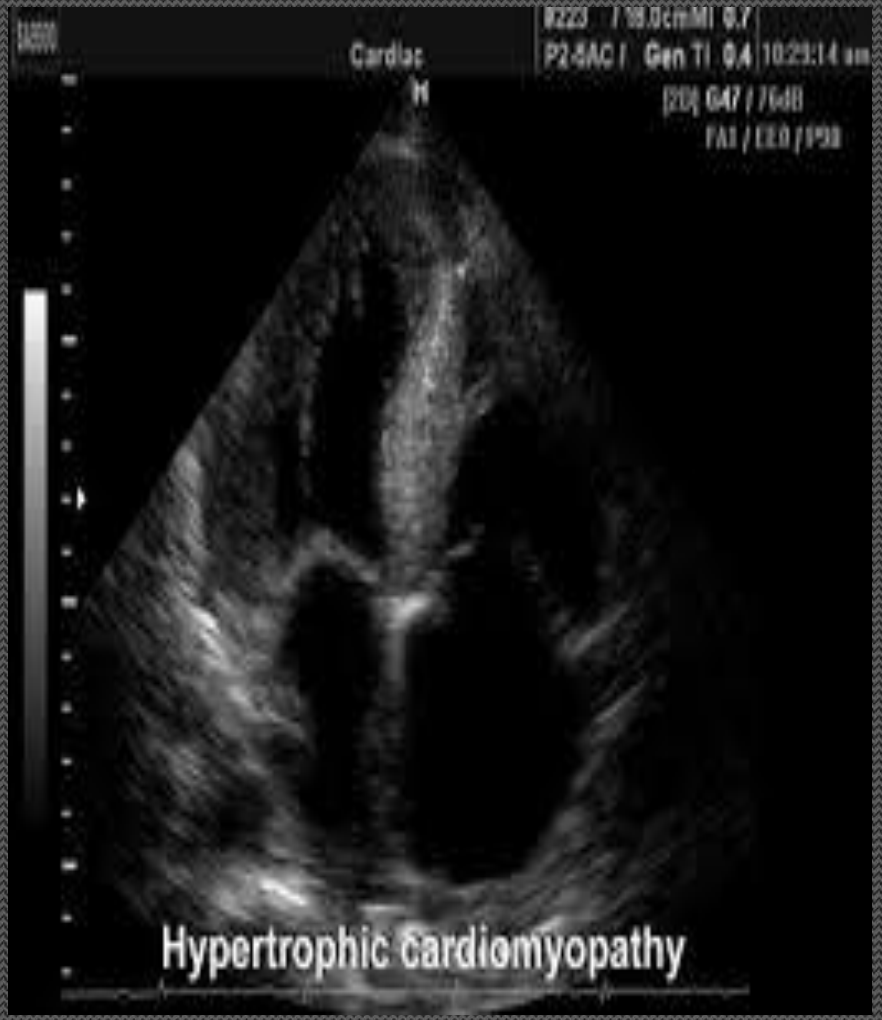
- Wide range of expression due to age
  - Older age has less expression
  - Therefore, pedigree screening by phenotype for clinical, counseling purposes isn't complete without the following:
    - Echocardiogram-segmental hypertrophy
    - LVH without any other explanation

Hypertrophic Cardiomyopathy

- FHC-disease of the sarcomere
- Classic mutations of at least six loci
  - The first is 14q1 and the cardiac B-myosin heavy chain gene
  - 50% of all FHC occur here


Normal Heart
Aorta
Left atrium
Right atrium
Left ventricular chamber
Left ventricular wall
Right ventricle
Septum
© 2008, MediVisuals Inc.
Hypertrophic Cardiomyopathy
Left ventricular wall
Septum
© 2008, MediVisuals Inc.


RV
LV
RA
LA
Normal


Cardiac
M
Hypertrophic cardiomyopathy