

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

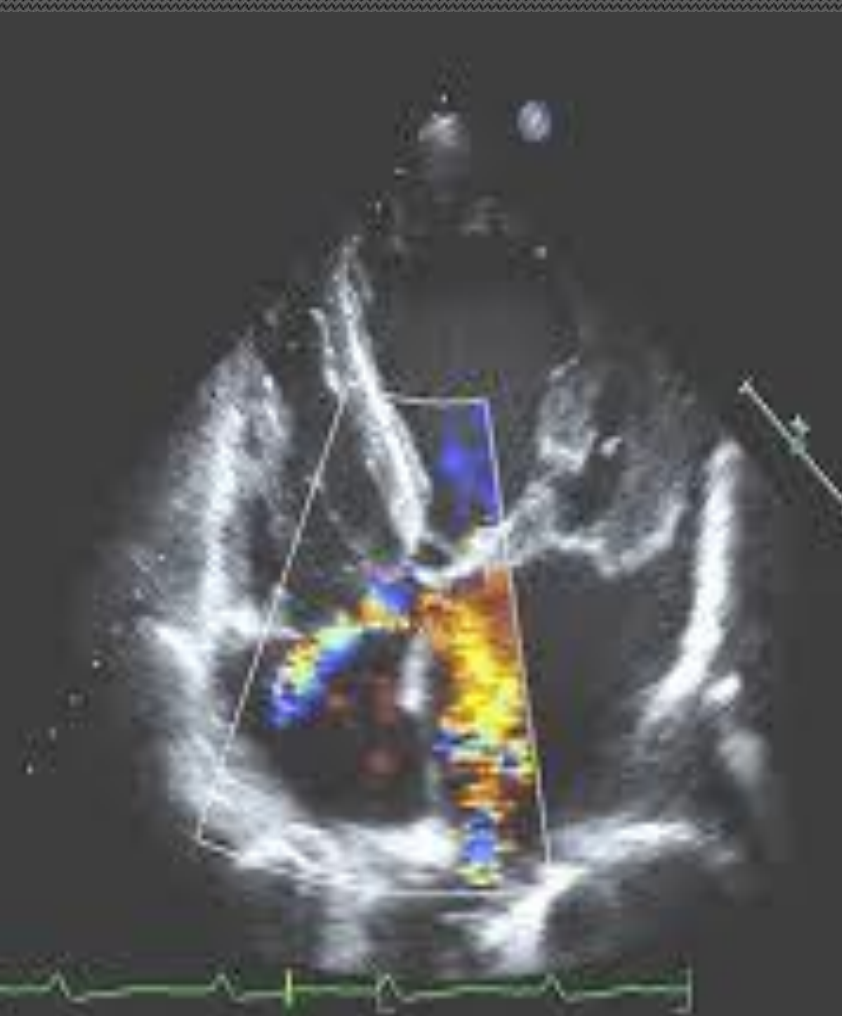
- Trisomy 21- Down's Syndrome
 - Most common phenotype
 - 1/600 births
 - Maternal age; >35 years and greatest >45(4%)
 - CHD present in 40-50%
 - Endocardial cushion defect
 - Atrial septal defect with cleft mitral valve
 - Pulmonary Hypertention



FR 11Hz
20cm

ZD
83%
C 50
P Low
HGen

CE
54%
2.5MHz
WF High
Med

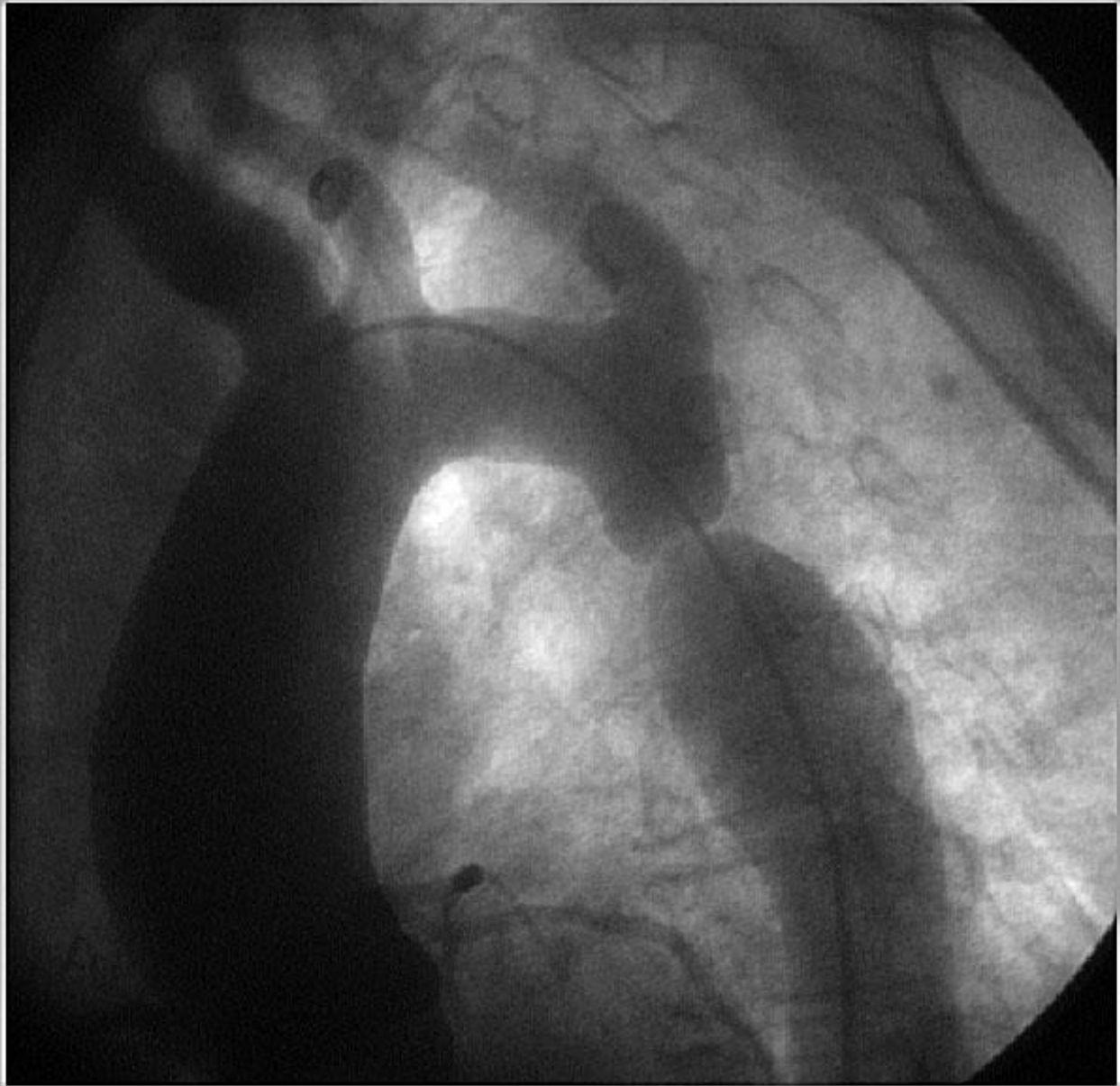


Dist 1.28 cm

117cm

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

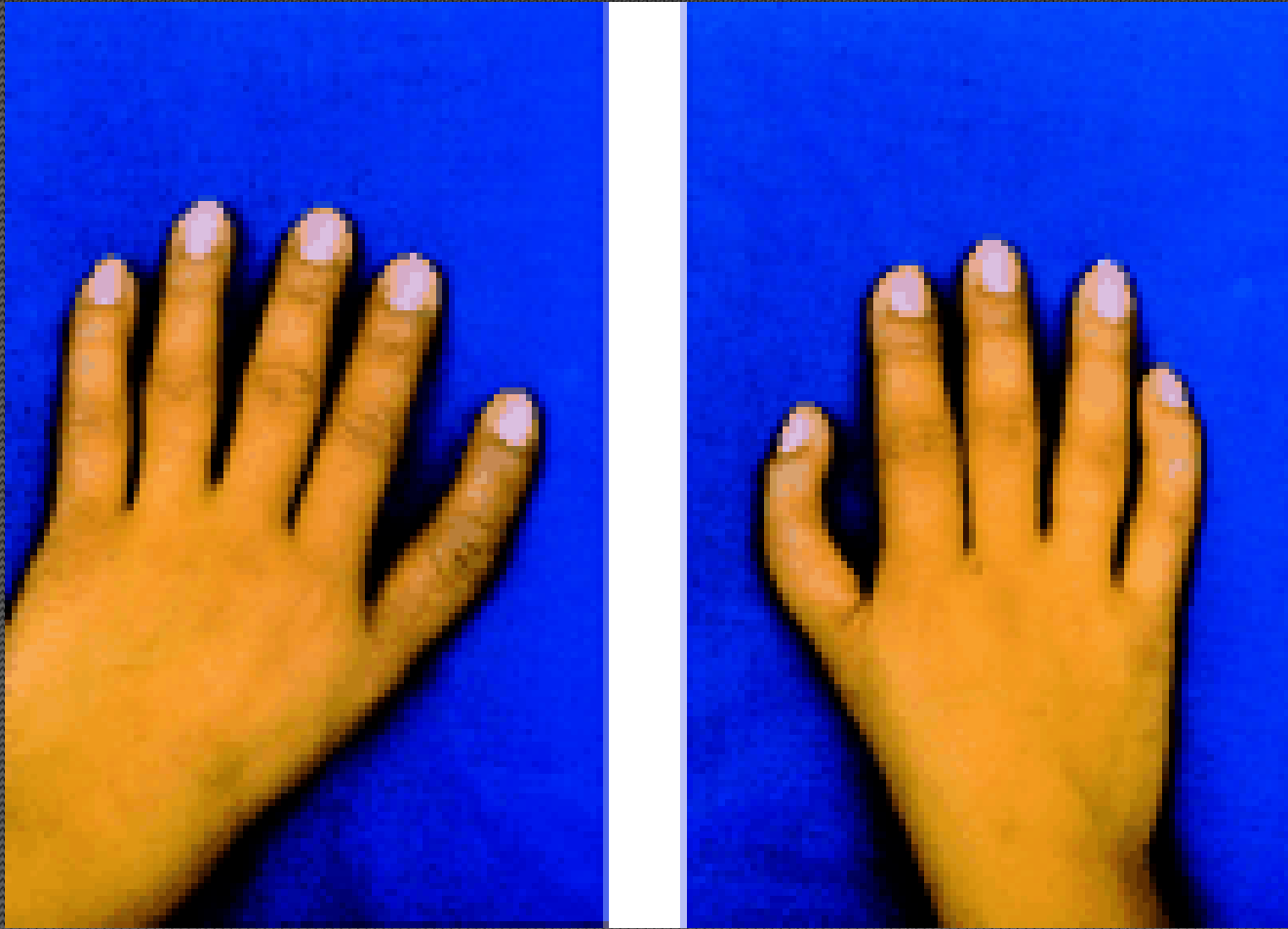


Congenital Heart Disease

- 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



Normal mitral valve



**Degenerative MR
caused by mitral
valve prolapse**

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

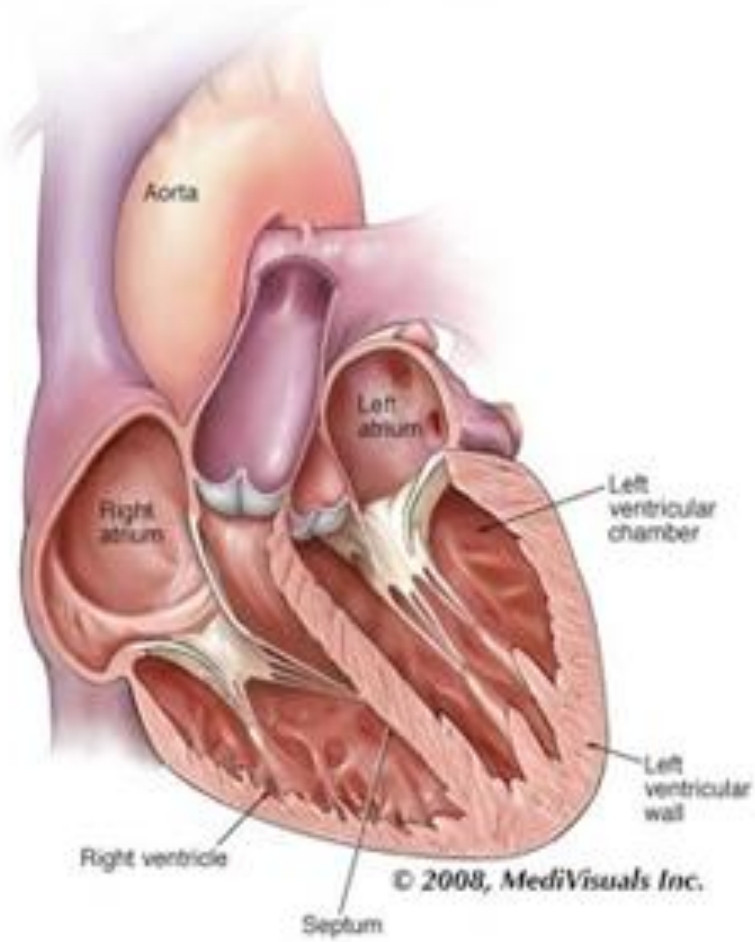
Hypertrophic Cardiomyopathy

- 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



Hypertrophic Cardiomyopathy

