# Heart I.

Monika Pávková Goldbergová

## What is the purpose of the cardiovascular system?

- Supply oxygen and nutrients to the tissues and organs, and to remove waste products
- To defend the supply of nutrients to organs by
  - maintaining cardiac output
    - sympathetic, RAAS, endothelin, nitric oxide, fluid retention
    - maintaining organ perfusion pressure


1. **Function of a cardiomyocyte**
2. **Systolic myocardial function**
3. **Diastolic myocardial function**
4. **Etiopathogenesis of systolic and diastolic dysfunction of the left ventricle and of cardiac failure**


## 1. Function of a cardiomyocyte

Cardiomyocytes consist of three linked systems:

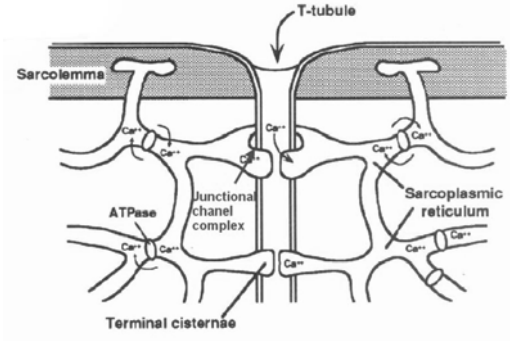
- excitation system: participates in spread of the action potential into adjacent cells and initiates further intracellular events

- excitation-contraction coupling system: converts the electrical signal to a chemical signal

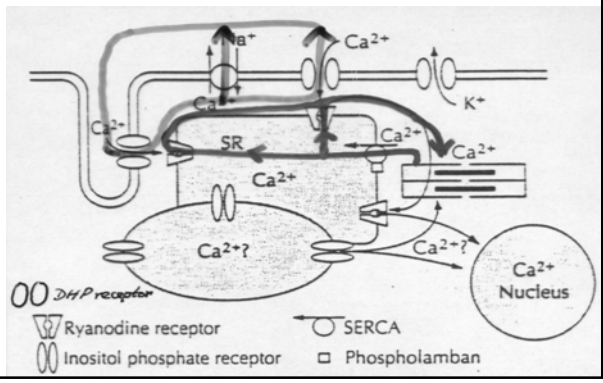
- contractile system: a molecular motor driven by ATP

### Excitation-contraction coupling system

System of intracellular membranes (sarcotubular system) provides for electrochemical coupling between the sarcolemma and the intracellular organelles

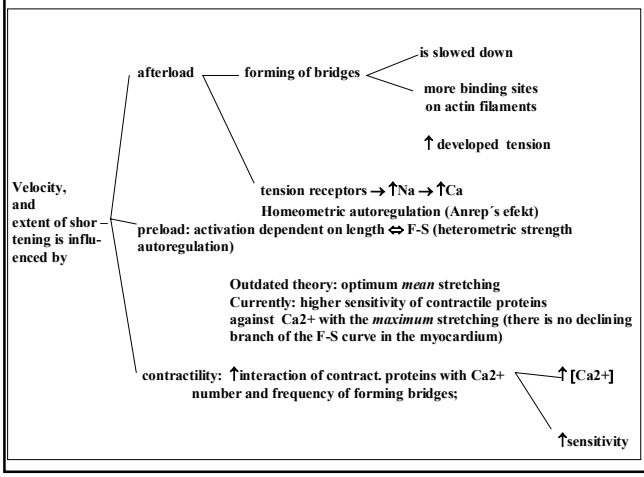



Coupling of excitation and contraction is realized by a cascade of two circuits of calcium ions, by the activity of which the calcium spike is created in the cytosol, inducing contraction of the myofibrilles

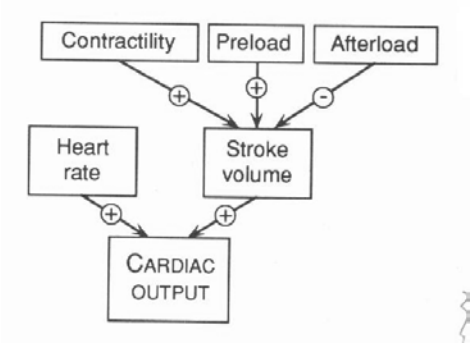


Depolarization and/or a β-adrenergic influence
→ opening of dihydropyridin receptors (DHP)
→ Ca2+ from the T-tubules
→ opening of the ryanodin receptors
→ outflow of Ca2+ from the SR into the myoplasm
→ triggering of the contraction

Na/Ca antiport extrudes the excessive Ca2+ by the end of a diastole – important role in relaxation

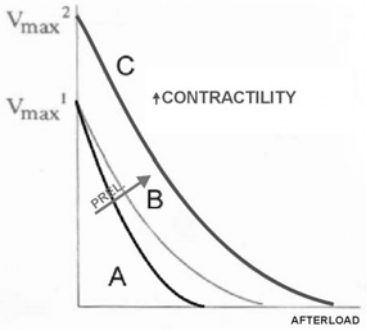



Contractility can be separated from the preceding two terms only with difficulty, the separation has only clinical application

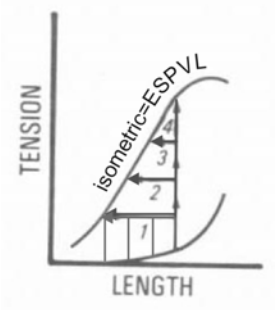



## 2. Systolic myocardial function

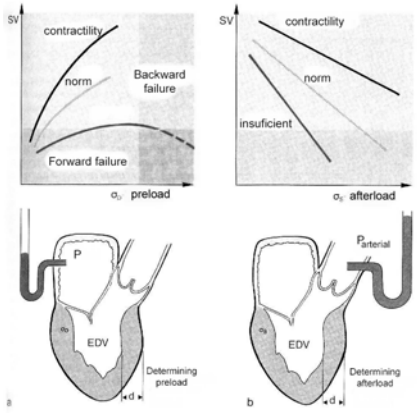
Magnitude of the afterload determines the developed active tension and influences the velocity and extent of shortening




Isometric = isovolumic maxima curve represents a limit (envelope) at the same time on which both isotonic contraction curves and afterloaded contraction curves end. The definitive length of a muscle at the end of the contraction is proportionally dependent on the afterload, but it is independent on the length of a muscle before the contraction, i.e, on a preload




The preload of a ventricle could be defined as an end-diastolic tension in a wall and the afterload as its maximum systolic tension

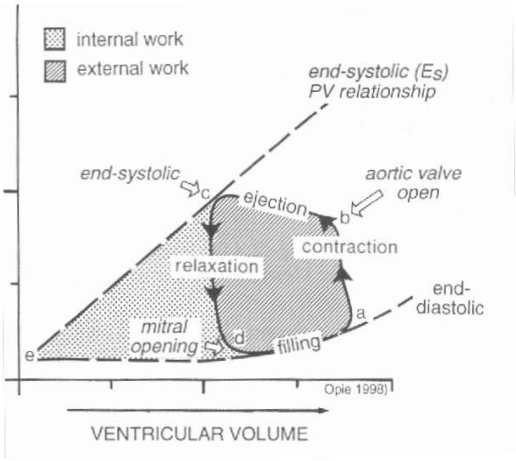


Laplace´s law for a sphere:

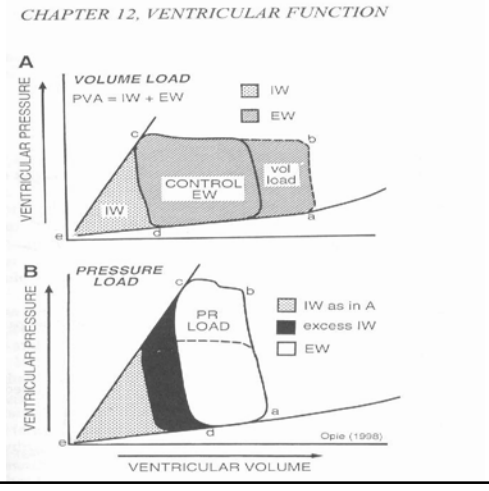
$$\sigma = \frac{P*r}{2h}$$

The preload of a myocardium is defined as its end-diastolic tension in its wall and theafterload as its maximum systolic tension

Working diagramm of the myocardium is situated between the myocardium compliance curve and the end-systolic-pressure-volume-curve (ESPVL, approaching considerably the isovolumic maxima curve)




Sum of the external and internal work represents the total mechanical work of contraction and this is directly proportional to oxygen consumption of the myocardium. Pressure work of the heart consumes more oxygen than volume work, so that the effectivity of the former is lower than that of the latter.



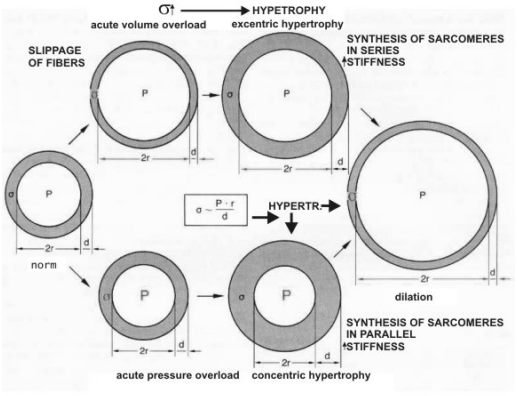

## Compensatory mechanisms for decreased cardiac output

- Increased SNS activity
  Increase HR and SVR which increases BP
- Frank-Starling mechanism:
  ↑ LVEDP = ↑ SV
- Activation of Renin-angiotensinaldosterone
- system (RAAS)
- Myocardial Remodeling
  - Concentric hypertrophy
  - Eccentric hypertrophy

**Table 1** Summary of characteristics for the hypertrophy patterns (concentric and eccentric) and haemodynamic mechanisms influencing pathological and physiological left ventricular hypertrophy (LVH)

| | Pathological LVH | | Physiological LVH | |
|---|---|---|---|---|
| | Concentric | Eccentric | Concentric | Eccentric |
| Stimulating haemodynamic mechanism | Increased pressure (afterload) | Increased volume (preload) | Increased pressure (afterload) | Increased volume (preload) |
| Potential aetiology of stimulus | Hypertension, aortic stenosis | Valvular disease | Strength training | Long-term endurance exercise |
| Ventricle morphology | Parallel addition of new myofibrils (wall thickening), frequently with myocyte necrosis and increased fibrosis | Series addition of sarcomeres (wall dilation and thinning) frequently with myocyte necrosis | Parallel addition of new myofibrils (wall thickening) with increased capillary density | Series addition of new sarcomeres (chamber volume enlargement) |
| Ventricular mechanics | Diastolic dysfunction with stiffness and decreased contractility | Decreased contractility often associated with side-to-side slippage of myocytes | Normal or enhanced contractility and myocardial efficiency | Normal or enhanced contractility and myocardial efficiency |
| Ventricular function | Abnormal | Abnormal | Normal | Normal or supranormal |
| Potential to regress | No | No | Yes | Yes |

## Pathological hypertrophy of the myocardium

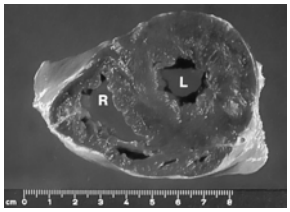



Volume overload → excentric hypertrophy
- Prolongation of myocytes by serial apposition of sarcomeres → ↑velocity and extent of shortening with an unchanged tension
- Less internal work expended than in pressure overload

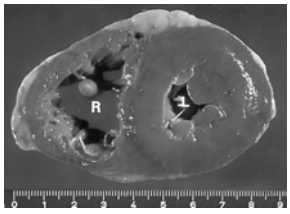
Pressure overload → concentric hypertrophy
- Thickening of myocytes by parallel apposition of sarcomeres → ↑tension with an unchanged extent of shortening

Hypertrophy generally:
↓ratio capillaries/cardiomyocytes → ischemization →
→ ↓ contractility→ temporary maintaining od CO →
later cardiac failure
→ fibrotization → ↓compliance
→ ↓ active relaxation
thickening → ↓compliance = diastolic dysfunction

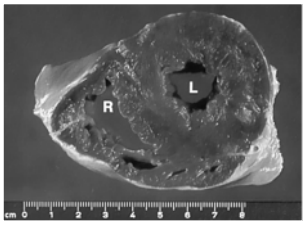
Normal heart (cross section)

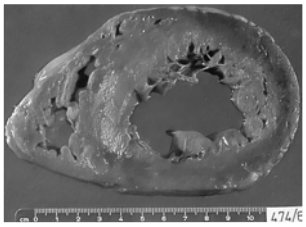



Concentric hypertrophy of the left ventricle; there is myocardial thickening without dilatation of the ventricular lumen. There is increased ratio of wall thickness to cavity radius. This change is associated with pressure overload as in HTN, and aortic stenosis.



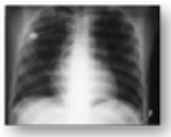

Normal heart (cross section)

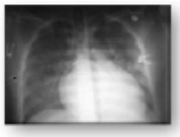


Eccentric hypertrophy (hypertrophy and dilatation) of the left ventricle. This may be seen in HTN heart disease. Don't confuse eccentric hypertrophy, with the asymmetric hypertrophy you see in IHSS

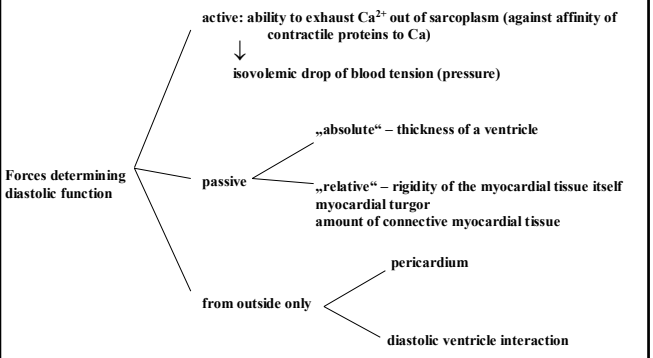
## Left Ventricular Hypertrophy





- Normal chest x-ray (left)
- Patient with heart failure (right)

## 3. Diastolic myocardial function




## Normal Cardiac Function

- Cardiac Output = Heart rate x Stroke volume
- Heart rate – controled by SNS and PNS
- Stroke – dependent on preload, afterload and contractility
- Preload = LVEDP and is measured as PCWP
- Afterload = SVR
- Contractility: ability of contractile elements to interact and shorten against a load

  (+ inotropy  - inotropy)

## Cardiac Innervation

- **Parasympathetic System**
  - Slow heart rate
  - Reduce cardiac output
- **Sympathetic System**
  - Increase heart rate
  - Increase force of contraction
  - Increase cardiac output

## Heart Failure

- A condition that exist when the heart is unable to pump sufficient blood to meet the metabolic needs of the body

## Forms of Heart Failure

- **Systolic & Diastolic**
- **High Output Failure**
  - Pregnancy, anemia, thyrotoxisis, A/V fistula, Beriberi, Pagets disease
- **Low Output Failure**
- **Acute**
  - large MI, aortic valve dysfunction---
- **Chronic**

## Left vs. Right Heart Failure

***Left Heart Failure***

- pulmonary congestion

***Right Heart Failure***

- peripheral edema
- sacral edema
- elevated JVP
- ascites
- hepatomegaly
- splenomegaly
- pleural effusion

# Systolic dysfunction

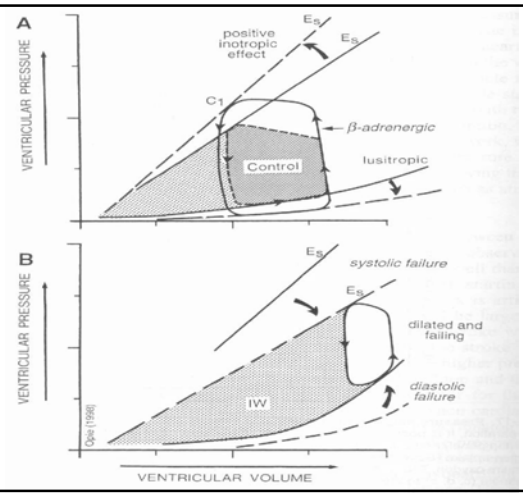
- Impairment of the contraction of the left ventricle such that stroke volume (SV) is reduced for any given end-diastolic volum (EDV)
- Ejection fraction (EF) is reduced (below 40-45%)
- EF=SV/EDV

# Diastolic Dysfunction

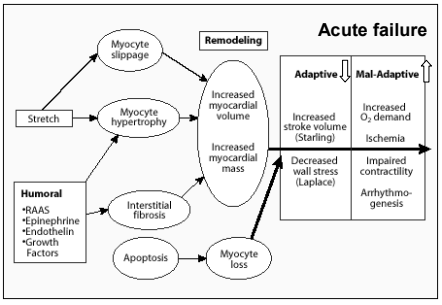
- Ventricular filling rate and the extent of filling are reduced or a normal extent of filling is associated with an inappropriate rise in ventricular diastolic preassure. Normal EF is maintained.

# Systolic vs. Diastolic Dysfunction

| | | |
|---|---|---|
| Presentation | • Pulmonary edema | • Pulmonary edema |
| Mechanism | • PCWP<br>• LVEDV | • PCWP<br>• LV stiffness |
| Diagnosis | • EF<br>• Dilated LV | • Normal EF<br>• Small LV diameter<br>• LVH (hypertension) |



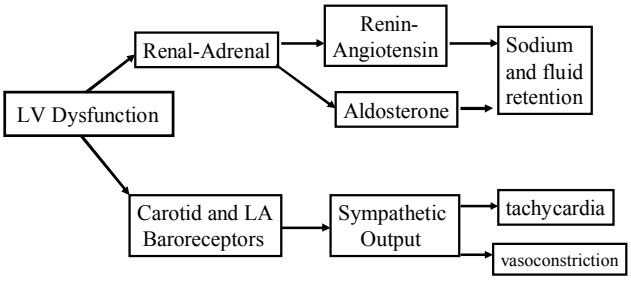

Pathophysiology of Acute Congestive Heart Failure




## Compensatory Mechanisms in Heart Failure

- increased preload
- increased sympathetic tone
- increased circulating catecholamines
- increased Renin-angiotensin-aldosterone
- increased vasopressin
- increased atrial natriuretic factor

## Physiologic Response to Heart Failure

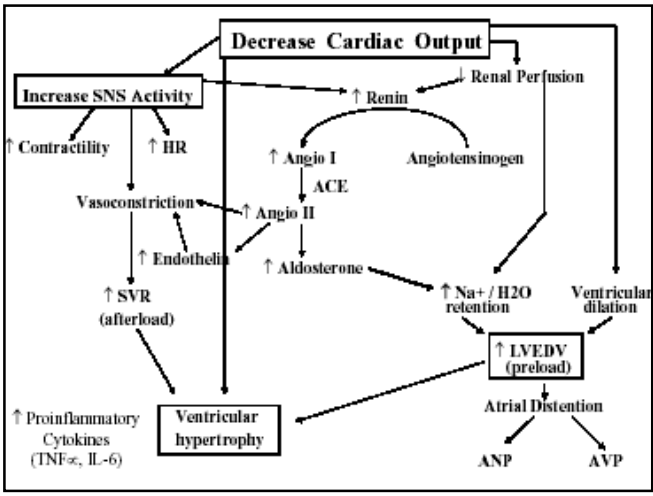



## Neurohumoral mechanismus of CHF

- Direct toxic effects of Norepinephrine (NE) and AngiotensinII (AII)
  (Arrhythmias, Apoptosis)
- Impaired diastolic filling
- Increased myocardial energy demand
- Increased pre- and after-load
- Platelet aggregation
- Desenzitization to catecholamines

## *Neurohormonal Mechanism of CHF*

- **Components**
- Endothelin
- Vasopressin (ADH)
- Natriuretic Peptides
- Endothelium-Derived Relaxing Factor
- RAAS
- SNS
- Cytokines




## NYHA Functional Classification

- **Class I**: *patients with cardiac disease but no limitation of physical activity*
- **Class II**: *ordinary activity causes fatigue, palpitations, dyspnea or anginal pain*
- **Class III**: *less than ordinary activity causes fatigue, palpitations, dyspnea or angina*
- **Class IV**: *symptoms even at rest*

## Stages of Heart Failure

- Stage A
  - High risk for development of heart failure
- Stage B
  - Structural heart disease
  - No symptoms of heart failure
- Stage C
  - Symptomatic heart failure
- Stage D
  - End-stage heart failure

## Precipitating Causes of Heart Failure

1. ischemia
2. change in diet, drugs or both
3. increased emotional or physical stress
4. cardiac arrhythmias (eg. atrial fib)
5. infection
6. concurrent illness
7. uncontrolled hypertension
8. New high output state (anemia, thyroid)
9. pulmonary embolism
10. Mechanical disruption (sudden MR, VSD, AR)

## Heart Failure

*Clinical Manifestations*

**Symptoms**

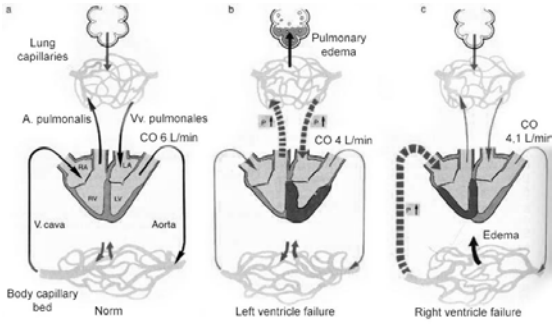
- dyspnea
- fatigue
- exertional limitation
- weight gain
- poor appetite
- cough

**Signs**

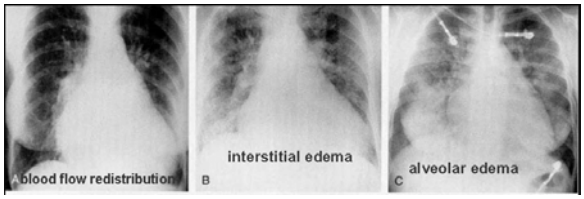
- tachycardia, tachypnea
- edema
- jugular venous distension
- pulmonary rales
- pleural effusion
- hepato/splenomegaly
- ascites
- cardiomegaly
- S3 gallop

## Organismic consequencies of the heart failure

„Forward“ and „backward“ failure




## Cardiogenic Pulmonary Edema




## Cardiomyopathies Classification

- Dilated (congestive)
- Hypertrophic
- Restrictive

## Systolic Dysfunction

- **Dilated Cardiomyopathy**

- Ischemic disease
  - myocardial ischemia
  - myocardial infarction

- Non-ischemic disease
  - Primary myocardium muscle dysfunction
  - valvular abnormalities
  - hypertension
  - alcohol and drug-induced
  - idiopathic

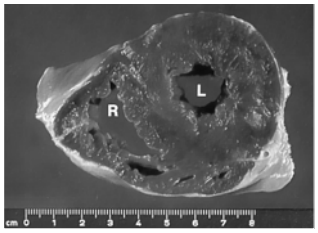
# Cardiomyopathies
# Dilated (congestive)

Ejection fraction-- <40%

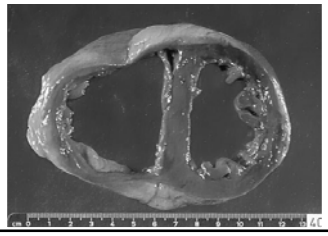
- Mechanism of failure--
  - Impairment of contractility (systolic dysfunction)
- Caues--
  - Idiopathic, alcohol, peripartum, genetic, myocarditis, hemochromatosis, chronic anemia, doxorubicin, sarcoidosis
- Indirect causes (not considered cardiomyopathies)--
  - Ischemic heart disease, valvular disease, HTN, congenital heart disease

Cross section of a normal heart, with right and left ventricles (R &L) having normal myocardial thickness and chamber size.

*normal thickness LV 1.3-1.5 cm; RV 0.3-0.5 cm*




Dilated cardiomyopathy (cross section), with both right and left ventricular chambers showing dilatation. The myocardium appears to be normal or slightly thin in this case.



# Diastolic Dysfunction

- **Hypertrophic Cardiomyopathy**
- Hypertension
- Myocardial ischemia and infarction

- **Restrictive Cardiomyopathy**
- Amyloidosis
- Sarcoidosis

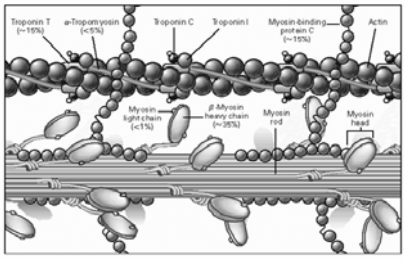
# Cardiomyopathies
# Hypertrophic

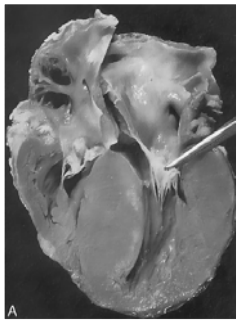
- Ejection fraction-- 50-80%
- Mechanism of failure-- impairment of compliance (diastolic dysfunction)
- Causes-- Idiopathic, genetic, Friedreich ataxia, storage dz, DM mother
- Indirect causes-- HTN heart dz, aortic stenosis

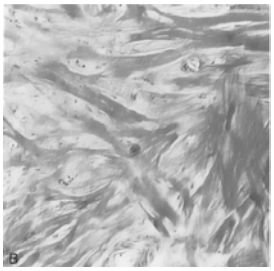
# Etiology

Familial in ~ 55% of cases with autosomal dominant transmission
Mutations in one of 4 genes encoding proteins of cardiac sarcomere account for majority of familial cases
Remainder are spontaneous mutations

β-MHC
cardiac troponin T
myosin binding protein C
α-tropomyosin




A gross example of IHSS (left) with prominent asymmetric hypertrophy with a prominent septum. The anterior leaflet of the mitral valve is held in the clamp; you can imagine how the high pressure flow through the outflow tract might pull this leaflet down (Venturi effect) further compromising the LV outflow. The micro photo on the right shows the myocyte disarray and large amounts of interstitial collagenous fibrosis (blue material) typical of IHSS (trichrome stain).

# Cardiomyopathies Restrictive

- Ejection fraction-- 45-90%
- Mechanisms of failure-- Impairment of compliance (diastolic dysfuntion)
- Causes-- Idiopathic, amyloidosis, radiation-induced fibrosis
- Indirect causes-- pericardial constriction

# Restrictive (infiltrative) Cardiomyopathy Etiology

- Infiltration of the myocardium with something other than muscle
- Stiff heart that cannot fill or pump well
  (Filling appears to be the main problem)

# Etiologies

**TABLE 4.** CAUSES OF RESTRICTIVE CARDIOMYOPATHY.

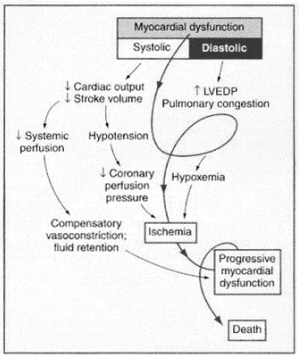
**Myocardial**
Noninfiltrative disorders
- Idiopathic disease
- Familial disease
- Hypertrophy
- Scleroderma
- Diabetes mellitus
- Pseudoxanthoma elasticum

Infiltrative disorders
- Amyloidosis
- Sarcoidosis
- Gaucher's disease
- Hurler's syndrome
- Fatty infiltration

Storage disorders
- Hemochromatosis
- Fabry's disease
- Glycogen storage disease

**Endomyocardial**
Endomyocardial fibrosis
Hypereosinophilic (Löffler's) syndrome
Carcinoid syndrome
Metastatic cancer
Exposure to radiation
Toxins
Anthracycline (doxorubicin or daunorubicin)
Serotonin
Methysergide
Ergotamine
Mercurial agents
Busulfan

# The vicious circle in cardiogenic shock




*Ann Intern Med 131:47–59, 1999*