# Pathophysiology: Heart Failure

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## Objectives

At the conclusion of this seminar, learner will be able to:

1. Define heart failure as a clinical syndrome
2. Define and employ the terms preload, afterload, contractilty, remodeling, diastolic dysfunction, compliance, stiffness and capacitance.
3. Describe the classic pathophysiologic steps in the development of heart failure: insult/injury/remodeling stimuli ⇒ neurohormonal activation (RAAS and ANS) ⇒ cellular/molecular alterations, hemodynamic alterations (Na retention, volume overload) ⇒ Remodeling ⇒ Morbidity and mortality
4. Delineate four basic mechanisms underlying the development of heart failure
5. Interpret pressure volume loops / Starling curves and identify contributing mechanisms for heart failure state.
6. Understand the common methods employed for classifying patients with heart failure.
7. Employ the classes and stages of heart failure in describing a clinical scenario

## Outline

- Definitions and Classifications
- Muscle and Chamber Function
- Pathophysiology
- Epidemiology
- Clinical Management

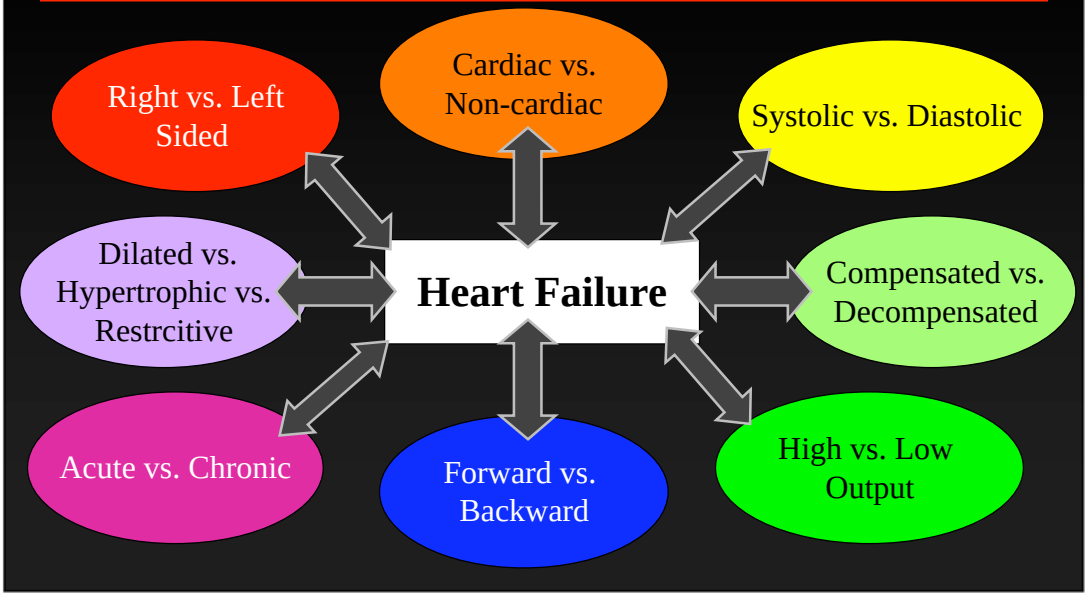
## Heart Failure: Definitions

- An inability of the heart to pump blood at a sufficient rate to meet the metabolic demands of the body (e.g. oxygen and cell nutrients) at rest and during effort or to do so only if the cardiac filling pressures are abnormally high.
- A complex clinical syndrome characterized by abnormalities in cardiac function and neurohormonal regulation, which are accompanied by effort intolerance, fluid retention and a reduced longevity
- A complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood.

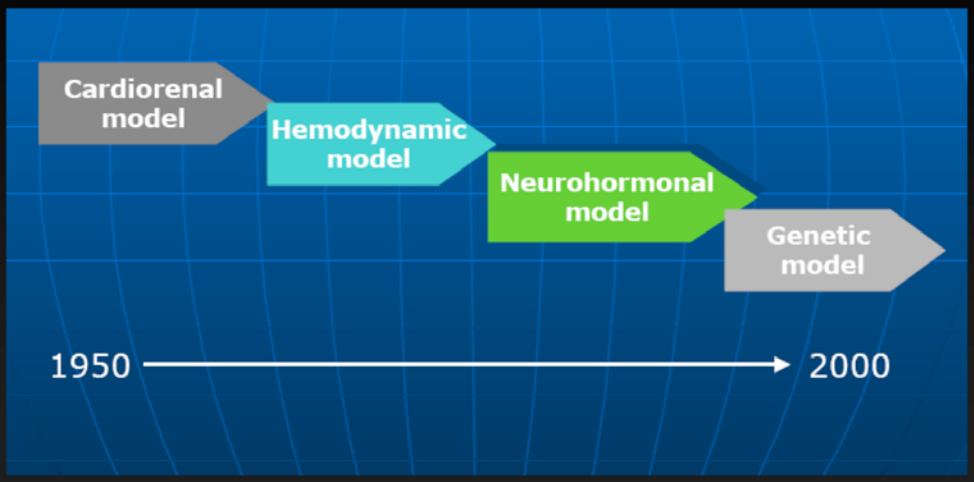
# Heart Failure

- Not a disease
- A syndrome
  - From "syn“ meaning "together“ and "dromos" meaning "a running“.
  - A group of signs and symptoms that occur together and characterize a particular abnormality.
- Diverse etiologies
- Several mechanisms

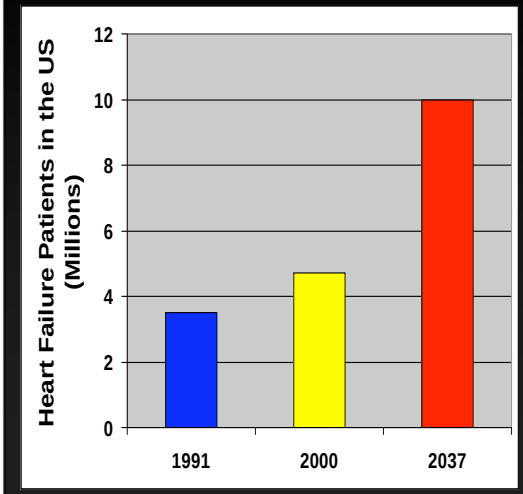
# Heart Failure: Classifications



# Heart Failure Paradigms



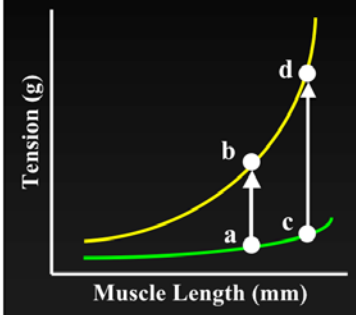

# Epidemiology Heart Failure: The Problem




- 3.5 million in 1991, 4.7 million in 2000, estimated 10 million in 2037
- Incidence: 550,000 new cases/year
- Prevalence: 1% ages 50--59, >10% over age 80
- More deaths from HF than from all forms of cancer combined
- Most common cause for hospitalization in age >65

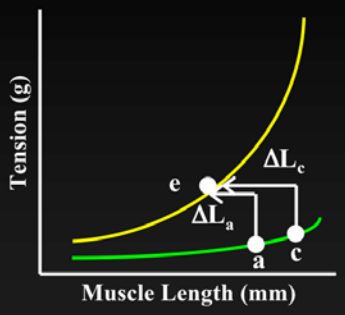
# Cardiac Muscle Function

## Preload



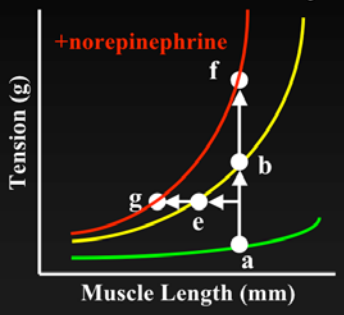

•The length of a cardiac muscle fiber prior to the onset of contraction.
•Frank Starling

## Afterload



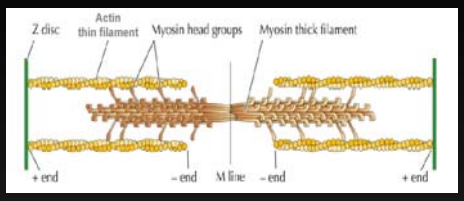

•The force against which a cardiac muscle fiber must shorten.
•Isotonic Contraction

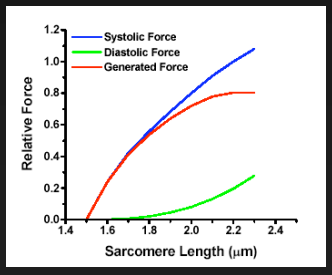
## Contractility

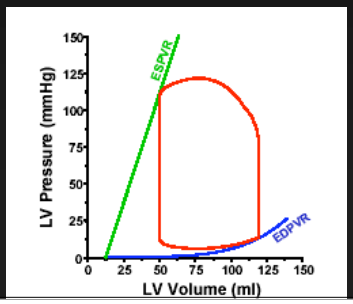



•The force of contraction independent of preload and afterload.
•Inotropic State

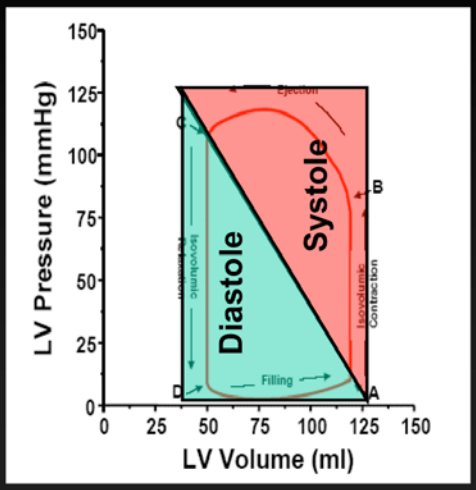
# From Muscle to Chamber

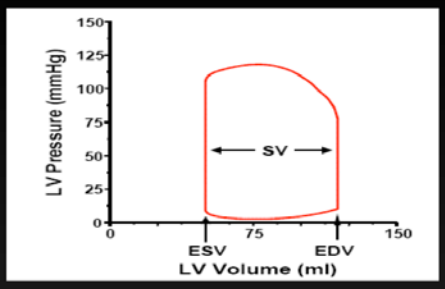


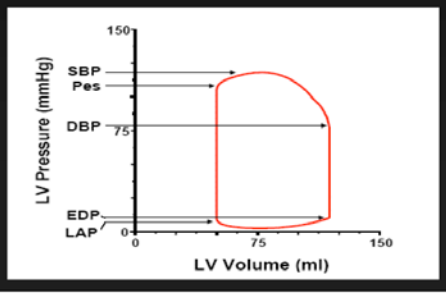



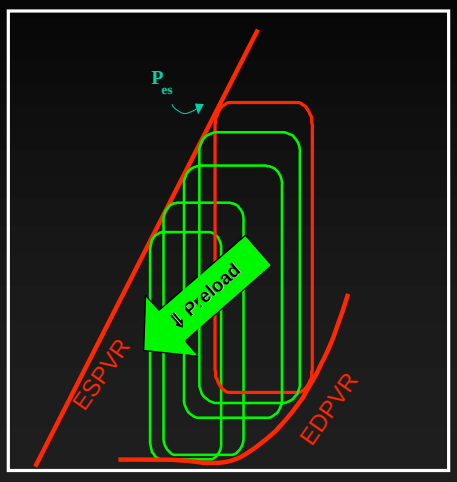
# The Pressure Volume Loop

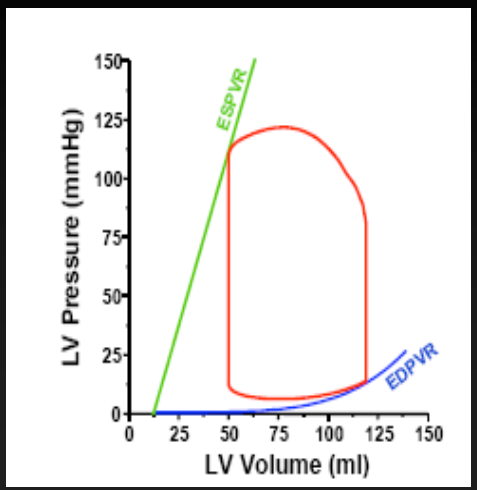


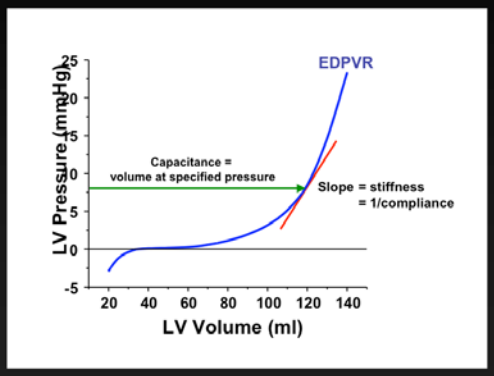



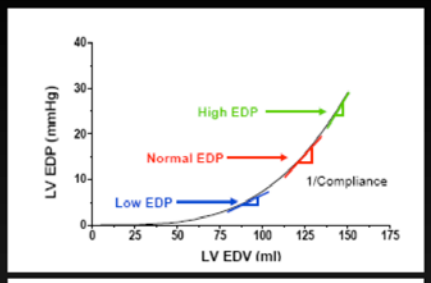

# The Pressure Volume Loop

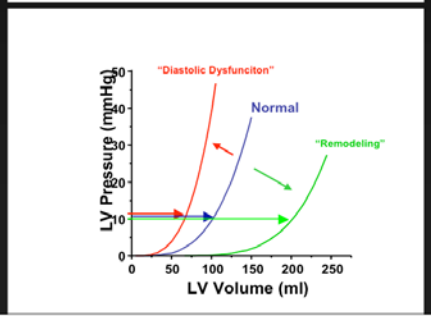


# Compliance/Stiffness vs Capacitance

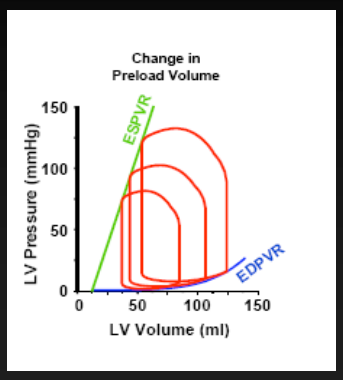


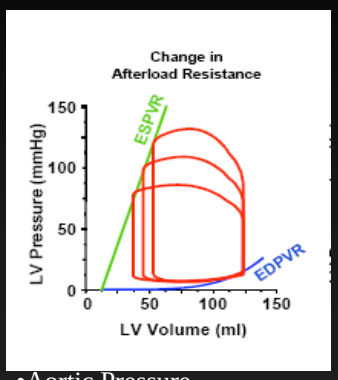

# Cardiac Chamber Function

## Preload



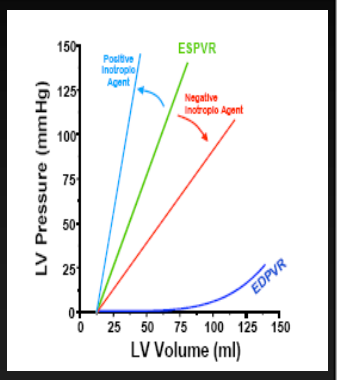

- EDV
- EDP
- Wall stress at end diastole

## Afterload



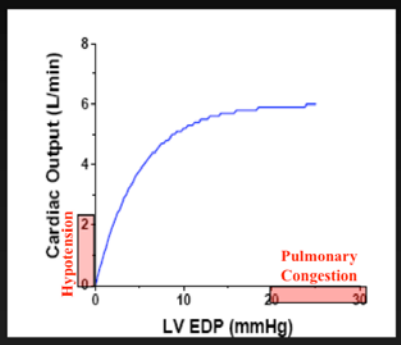

- Aortic Pressure
- Total peripheral resistance
- Arterial impedance
- Wall stress at end systole

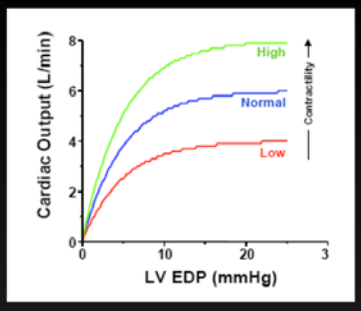
## Contractility

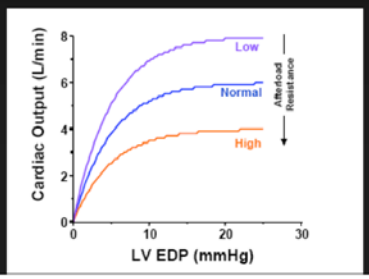



- Pressure generated at given volume.
- Inotropic State

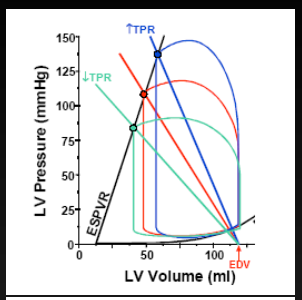
# Frank Starling Curves

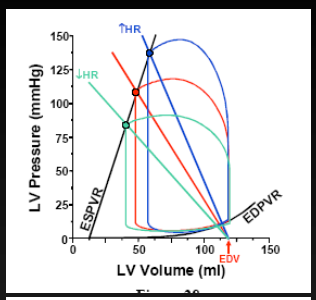


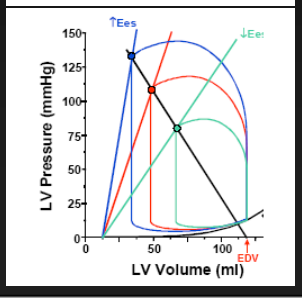



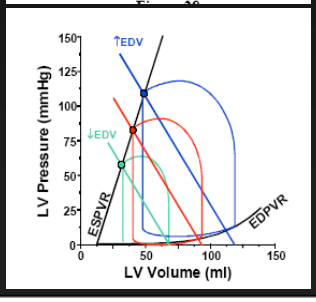



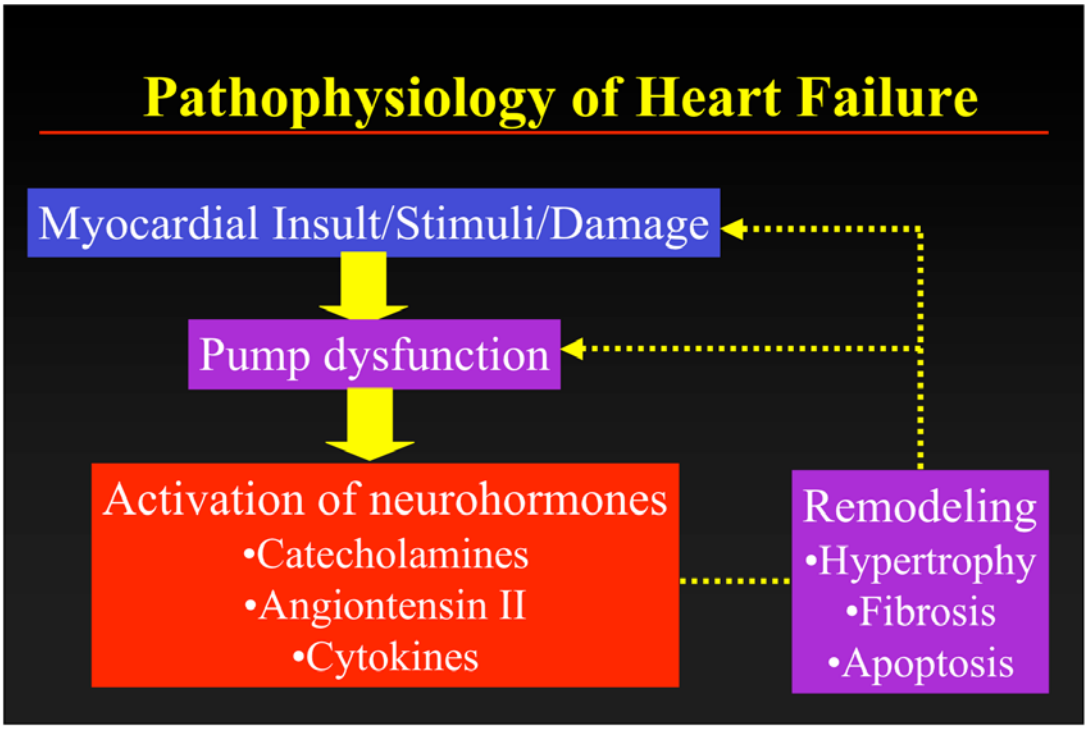

# Pathophysiology - PV Loop

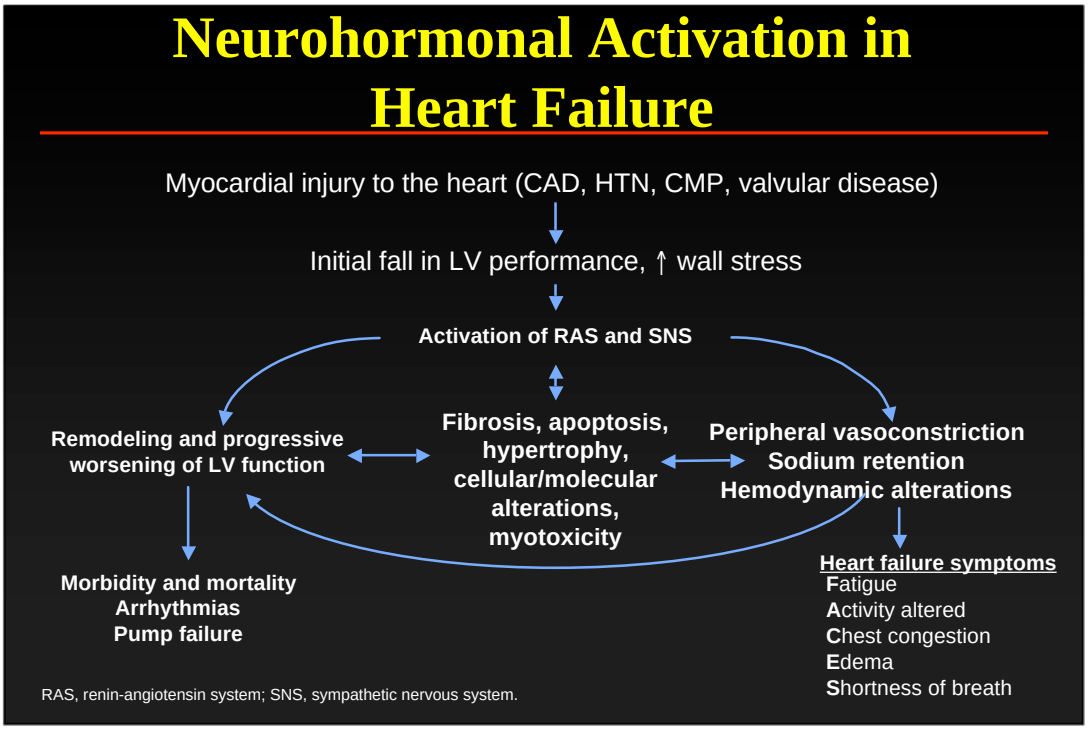


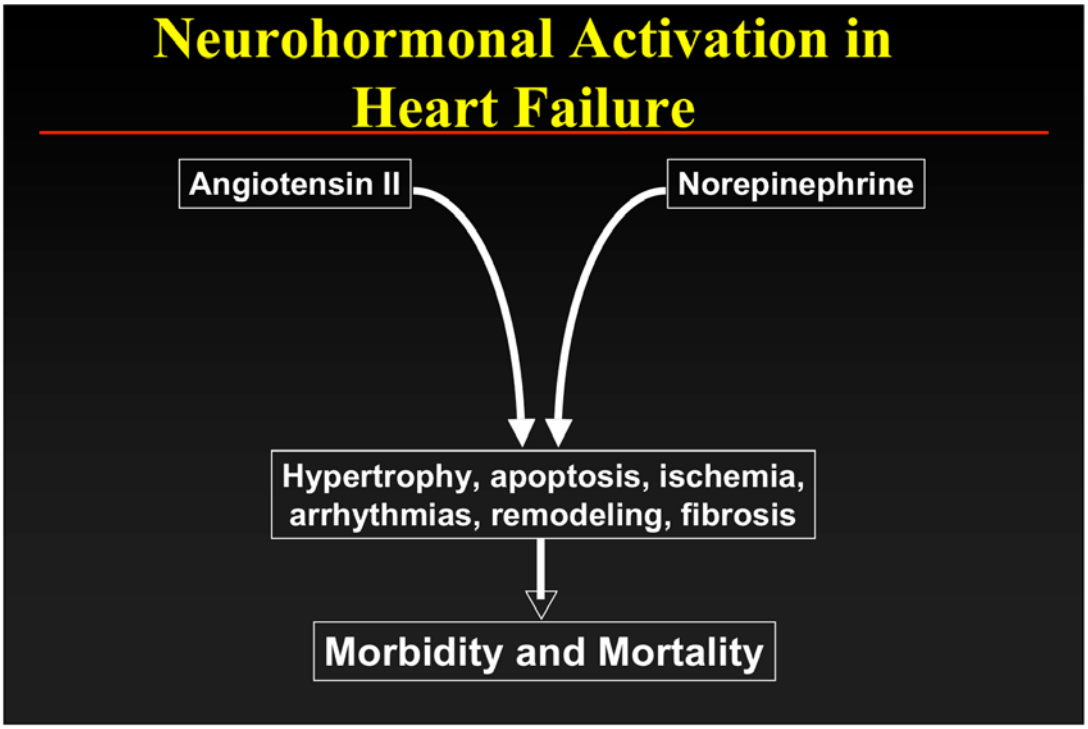



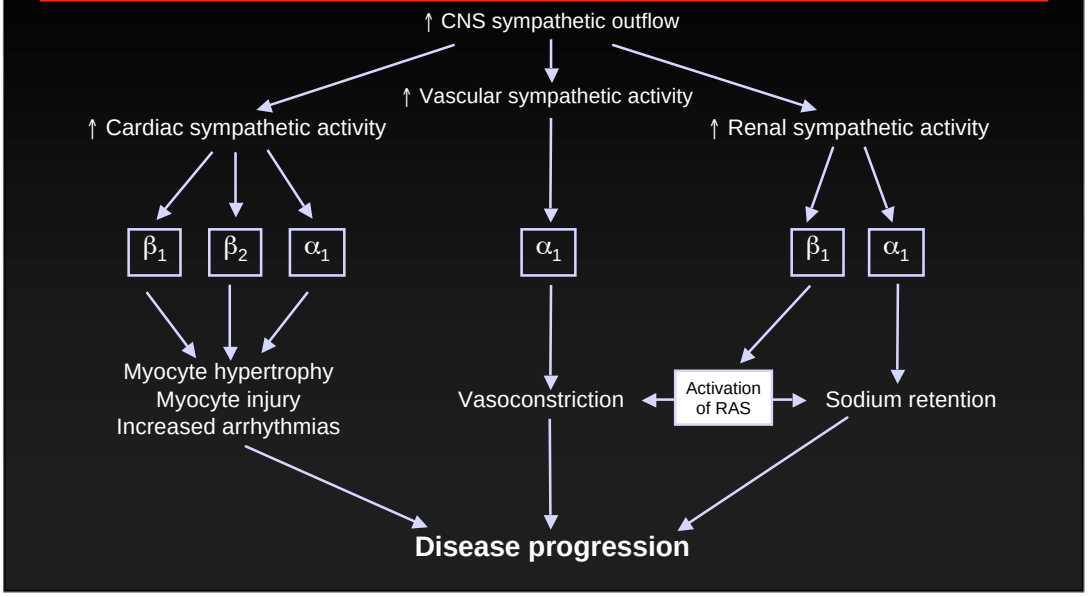

Pathophysiology of Heart Failure
Myocardial Insult/Stimuli/Damage
Pump dysfunction
Activation of neurohormones
•Catecholamines
•Angiontensin II
•Cytokines
Remodeling
•Hypertrophy
•Fibrosis
•Apoptosis


Neurohormonal Activation in Heart Failure
Myocardial injury to the heart (CAD, HTN, CMP, valvular disease)
Initial fall in LV performance, ↑ wall stress
Activation of RAS and SNS
Remodeling and progressive worsening of LV function
Fibrosis, apoptosis, hypertrophy, cellular/molecular alterations, myotoxicity
Peripheral vasoconstriction
Sodium retention
Hemodynamic alterations
Morbidity and mortality
Arrhythmias
Pump failure
Heart failure symptoms
Fatigue
Activity altered
Chest congestion
Edema
Shortness of breath
RAS, renin-angiotensin system; SNS, sympathetic nervous system.

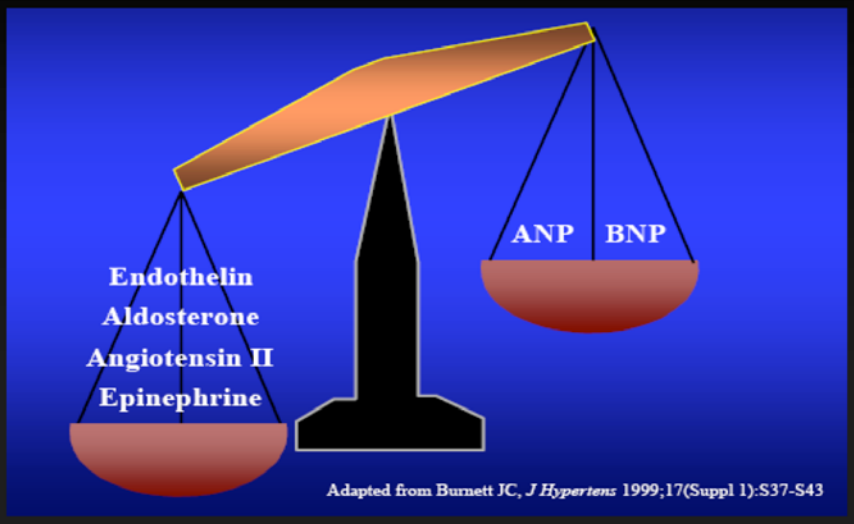
# Neurohormonal Activation in Heart Failure



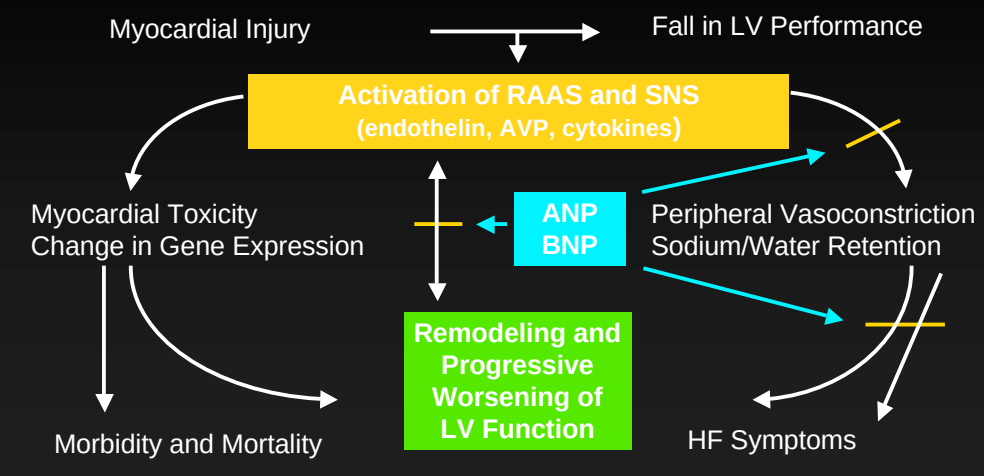

# Adrenergic Pathway in Heart Failure Progression



# Neurohormonal Balance in Heart Failure

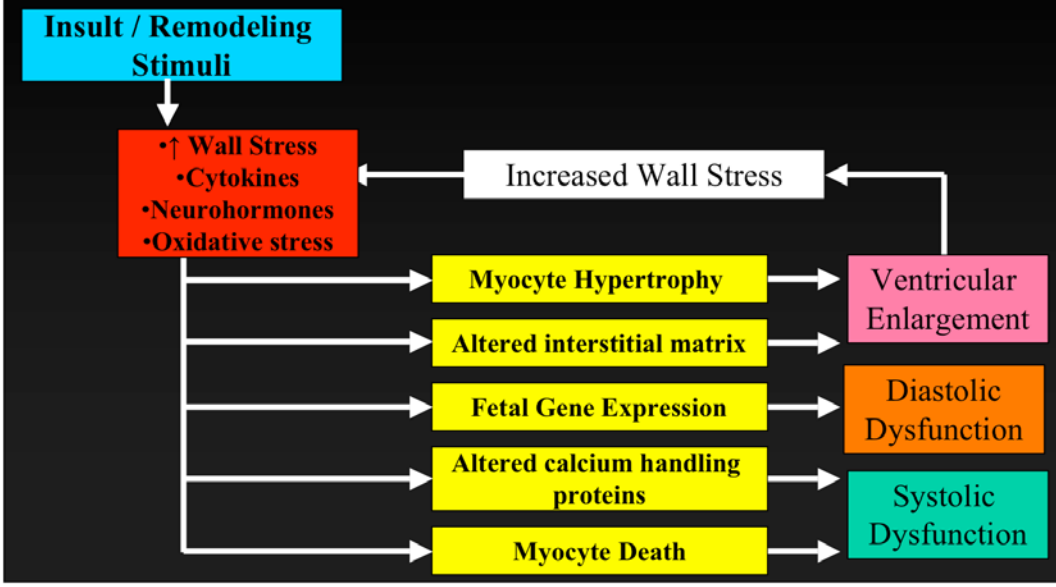



# Neurohormones in Heart Failure




Shah M et al. *Rev Cardiovasc Med.* 2001;2(suppl 2):S2

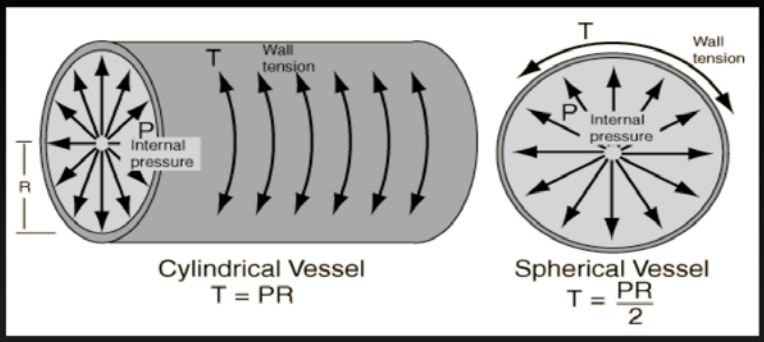
# Pathophyisiology of myocardial remodeling:




# Acute and Chronic Responses – Benefits and Harm

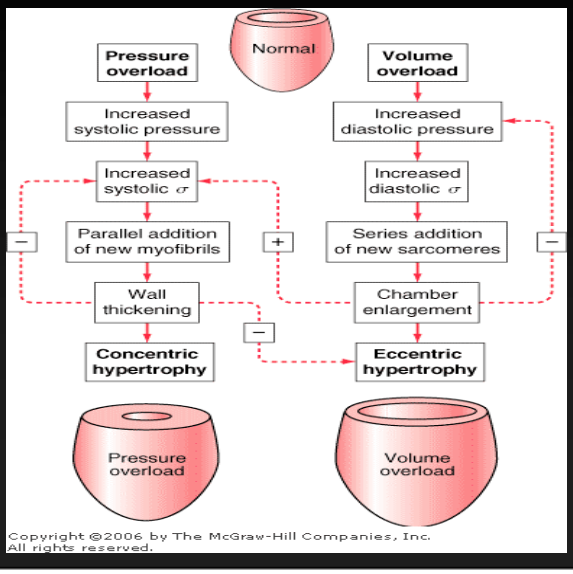
| Response | Short-term Effects (mainly adaptive; hemorrhage, acute heart failure) | Long-term Effects (mainly deleterious; chronic heart failure) |
|---|---|---|
| Salt and water retention | Augments preload | Pulmonary congestion, anasarca |
| Vasoconstriction | Maintains pressure for perfusion of vital organs (brain, heart) | Exacerbates pump dysfunction, increases cardiac energy expenditure |
| Sympathetic stimulation | Increases heart rate and ejection | Increases energy expenditure |
| Cytokine activation | Vasodilatation | Skeletal muscle catabolism, deterioration of endothelial function, impaired contraction, LV remodeling. |
| Hypertrophy | Unloads individual muscle fibers | Deterioration and death of cardiac cells: cardiomyopathy of overload |
| Increased collagen | May reduce dilatation | Impairs relaxation |

# Laplace's Law

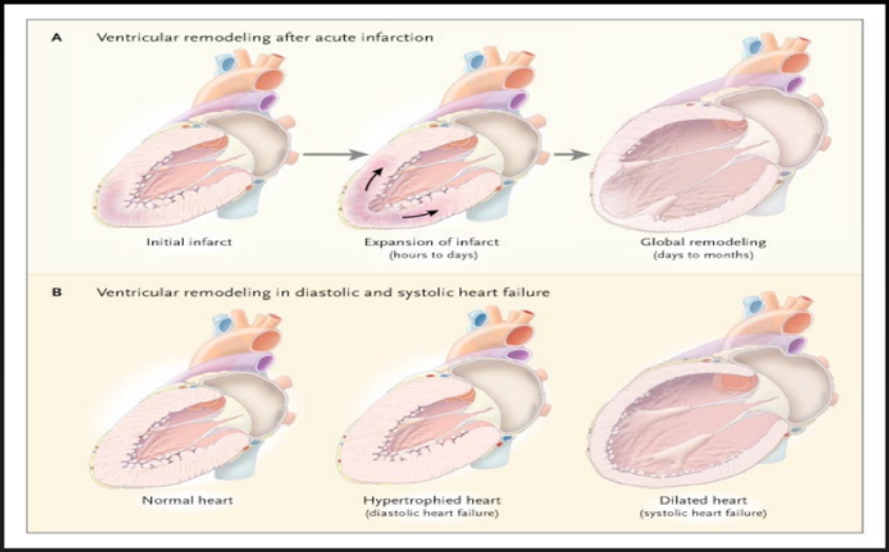



Where P = ventricular pressure, r = ventricular chamber radius and h = ventricular wall thickness

# Remodeling – Concentric vs. Eccentric



# Ventricular Remodeling



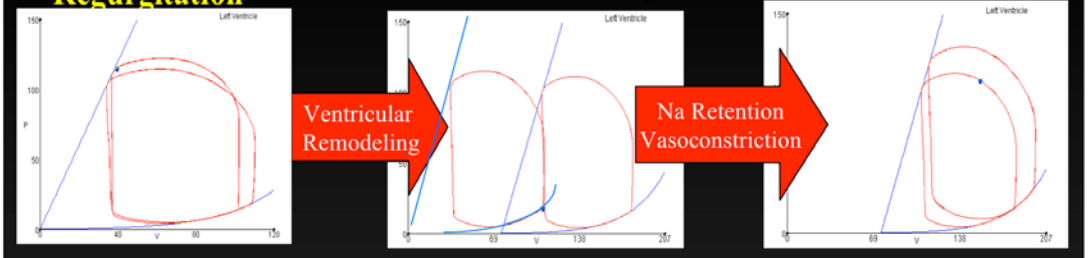

# Pathophysiology of Heart Failure

Four Basic Mechanisms

1. Increased Blood Volume (Excessive Preload)
2. Increased Resistant to Blood Flow (Excessive Afterload)
3. Decreased contractility
4. Decreased Filling

# Increased Blood Volume

**Aortic Regurgitation** → Ventricular Remodeling → **AI + Remodeling** → Na Retention Vasoconstriction → **AI + HF**



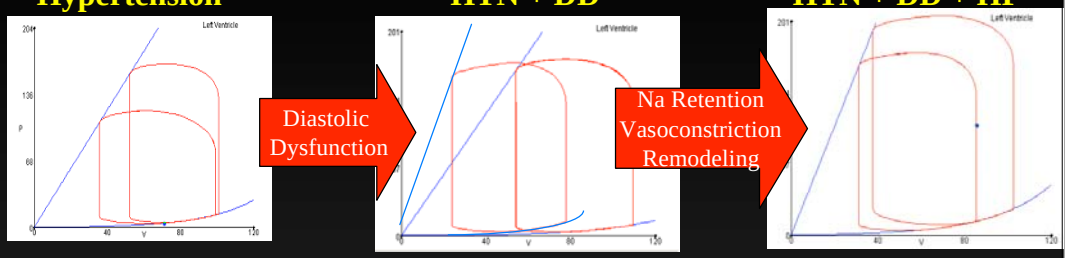
**Etiologies**

- Mitral Regurgitation
- Aortic Regurgitation
- Volume Overload
- Left to Right Shunts
- Chronic Kidney Disease

| Parameter | Normal | AI | AI + Remodeling | AI + Heart failure |
|---|---|---|---|---|
| BP (mm Hg) | 140/75 | 128/50 | 85/35 | 104/45 |
| SV (ml) | 64 | 80 | 54 | 63 |
| Cardiac Output (L/min) | 3.8 | 3.0 | 2.1 | 2.6 |
| PCWP (mm Hg) | 10 | 13 | 13 | 20 |

# Increased Afterload

**Hypertension** → Diastolic Dysfunction → **HTN + DD** → Na Retention Vasoconstriction Remodeling → **HTN + DD + HF**



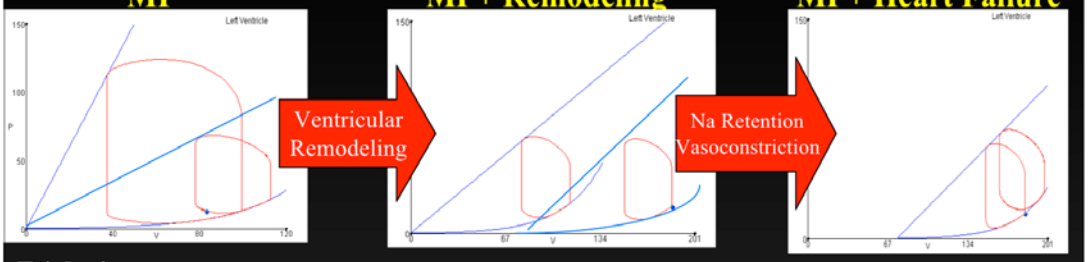
**Etiologies**

- Aortic Stenosis
- Aortic Coarctation
- Hypertension

| Parameter | Normal | HTN | HTN + DD | HTN + Heart failure |
|---|---|---|---|---|
| BP (mm Hg) | 124/81 | 159/122 | 170/129 | 206/159 |
| SV (ml) | 61 | 51 | 54 | 65 |
| Cardiac Output (L/min) | 3.7 | 3.1 | 3.2 | 3.9 |
| PCWP (mm Hg) | 10 | 10 | 12 | 21 |

# Decreased Contractility

**MI** → Ventricular Remodeling → **MI + Remodeling** → Na Retention Vasoconstriction → **MI + Heart Failure**



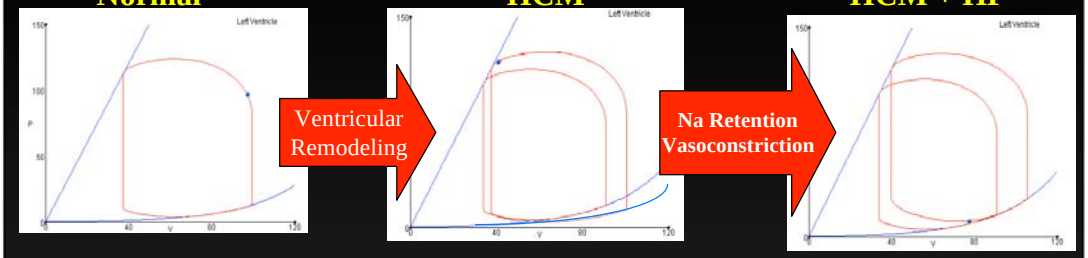
**Etiologies**

- Ischemic Cardiomyopathy
  - Myocardial Infarction
  - Myocardial Ischemia
- Myocarditis
- Toxins
  - Anthracycline
  - Alcohol
  - Cocaine

| Parameter | Normal | MI | MI + Remodeling | MI + HF |
|---|---|---|---|---|
| BP (mm Hg) | 124/81 | 68/46 | 68/45 | 80/50 |
| SV (ml) | 61 | 35 | 34 | 38 |
| Cardiac Output (L/min) | 3.7 | 2.1 | 2.0 | 2.3 |
| PCWP (mm Hg) | 10 | 16 | 18 | 33 |

# Decreased Filling

**Normal** → Ventricular Remodeling → **HCM** → **Na Retention Vasoconstriction** → **HCM + HF**

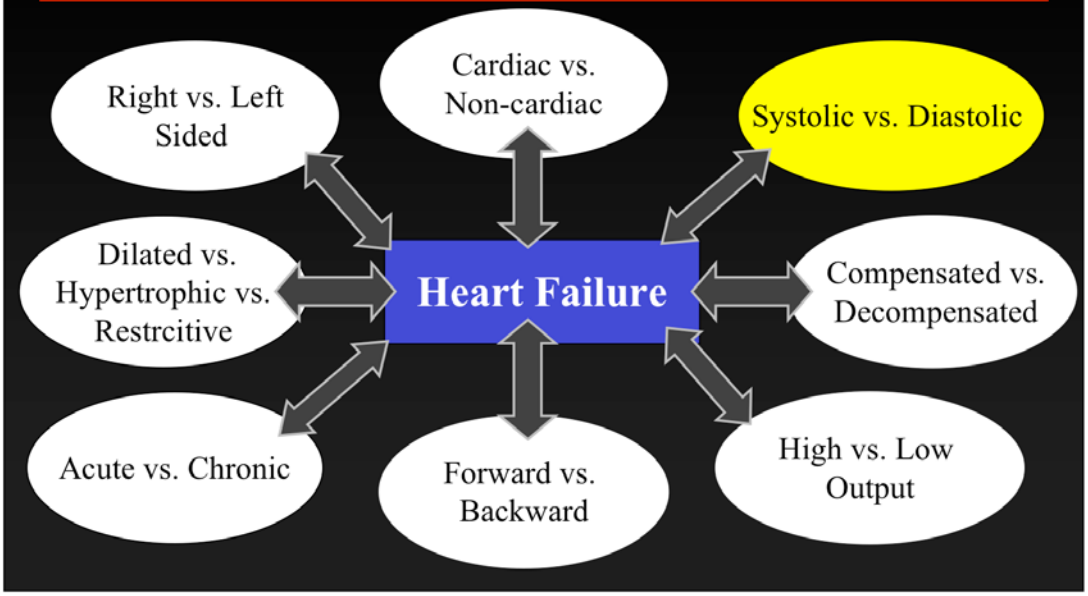


**Etiologies**

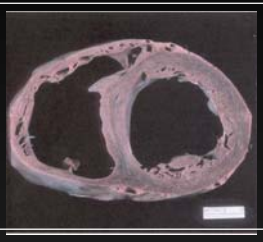
- Mitral Stenosis
- Constriction
- Restrictive Cardiomypoathy
- Cardiac Tamponade
- Hypertrophic Cardiomyopathy
- Infiltrative Cardiomyopathy

| Parameter | Normal | HCM | HCM + HF |
|---|---|---|---|
| BP (mm Hg) | 124/81 | 112/74 | 131/87 |
| SV (ml) | 61 | 57 | 66 |
| Cardiac Output (L/min) | 3.7 | 3.4 | 4.0 |
| PCWP (mm Hg) | 10 | 12 | 27 |

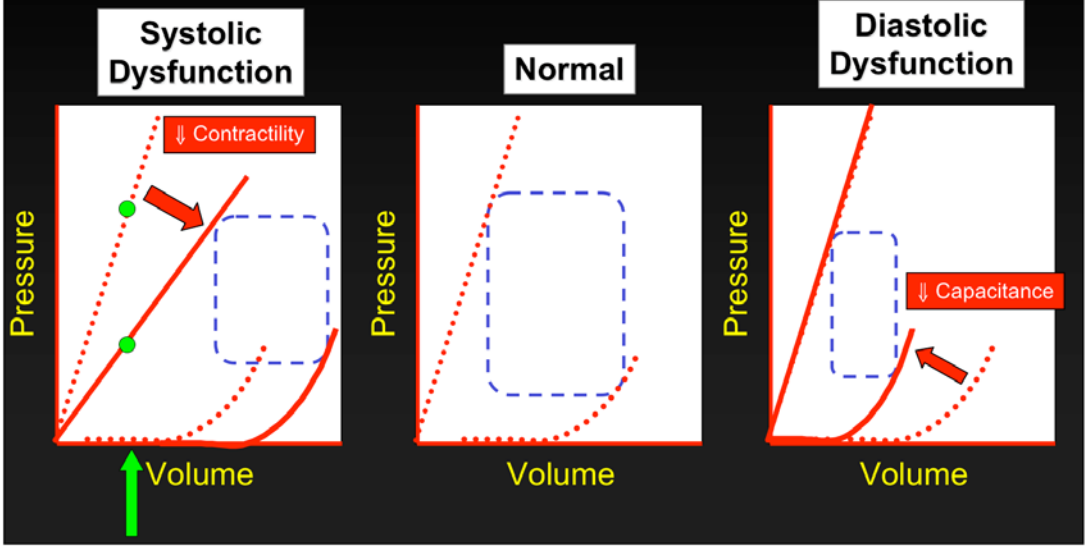
# Heart Failure: Classifications




# Types of Heart Failure

| | SHF | Diastolic |
|---|---|---|
| |  |  |
| Pathophysiology | Impaired Contraction | Impaired filling |
| Demographics | All ages | > 60 years |
| 1° Cause | Coronary Artery Disease | Hypertension |

# Systolic Versus Diastolic Failure



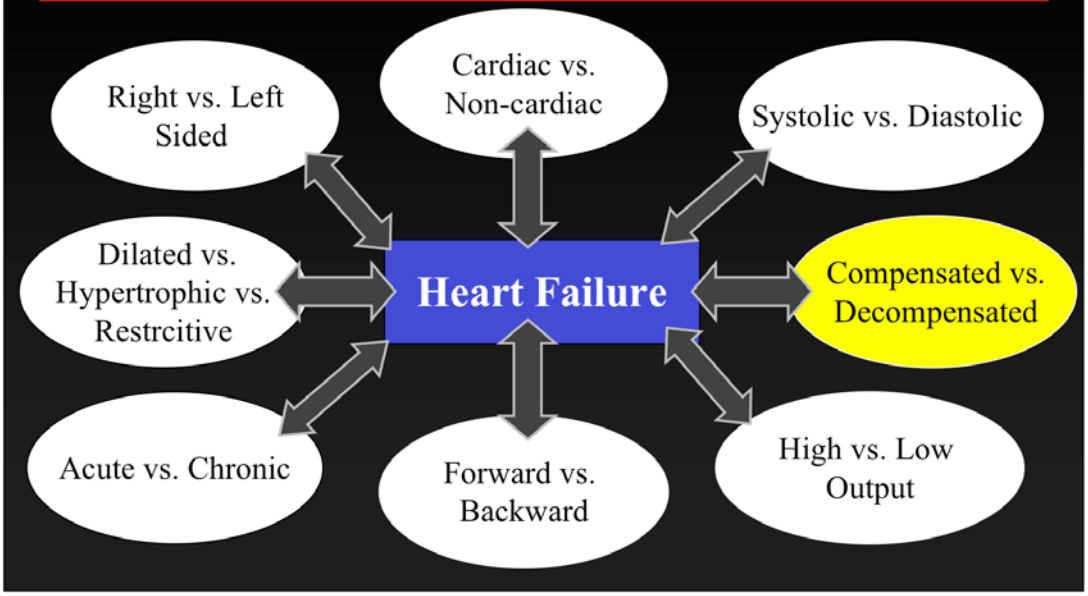

# Systolic Versus Diastolic Failure

**Table 2. Characteristics of Patients with Diastolic Heart Failure and Patients with Systolic Heart Failure.***

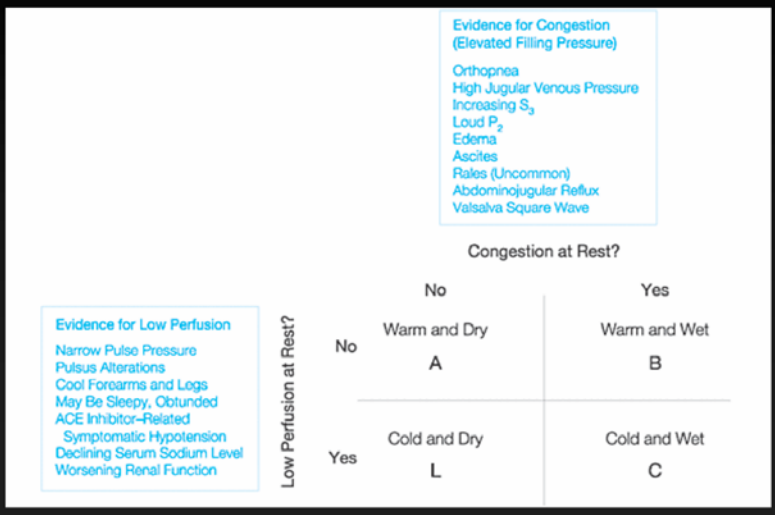
| Characteristic | Diastolic Heart Failure | Systolic Heart Failure |
|---|---|---|
| Age | Frequently elderly | All ages, typically 50–70 yr |
| Sex | Frequently female | More often male |
| Left ventricular ejection fraction | Preserved or normal, approximately 40% or higher | Depressed, approximately 40% or lower |
| Left ventricular cavity size | Usually normal, often with concentric left ventricular hypertrophy | Usually dilated |
| Left ventricular hypertrophy on electrocardiography | Usually present | Sometimes present |
| Chest radiography | Congestion with or without cardiomegaly | Congestion and cardiomegaly |
| Gallop rhythm present | Fourth heart sound | Third heart sound |
| Coexisting conditions | | |
| Hypertension | +++ | ++ |
| Diabetes mellitus | +++ | ++ |
| Previous myocardial infarction | + | +++ |
| Obesity | +++ | + |
| Chronic lung disease | ++ | 0 |
| Sleep apnea | ++ | ++ |
| Long-term dialysis | ++ | 0 |
| Atrial fibrillation | + (usually paroxysmal) | + (usually persistent) |

* A single plus sign denotes "occasionally associated with," two plus signs "often associated with," three plus signs "usually associated with," and a zero "not associated with."

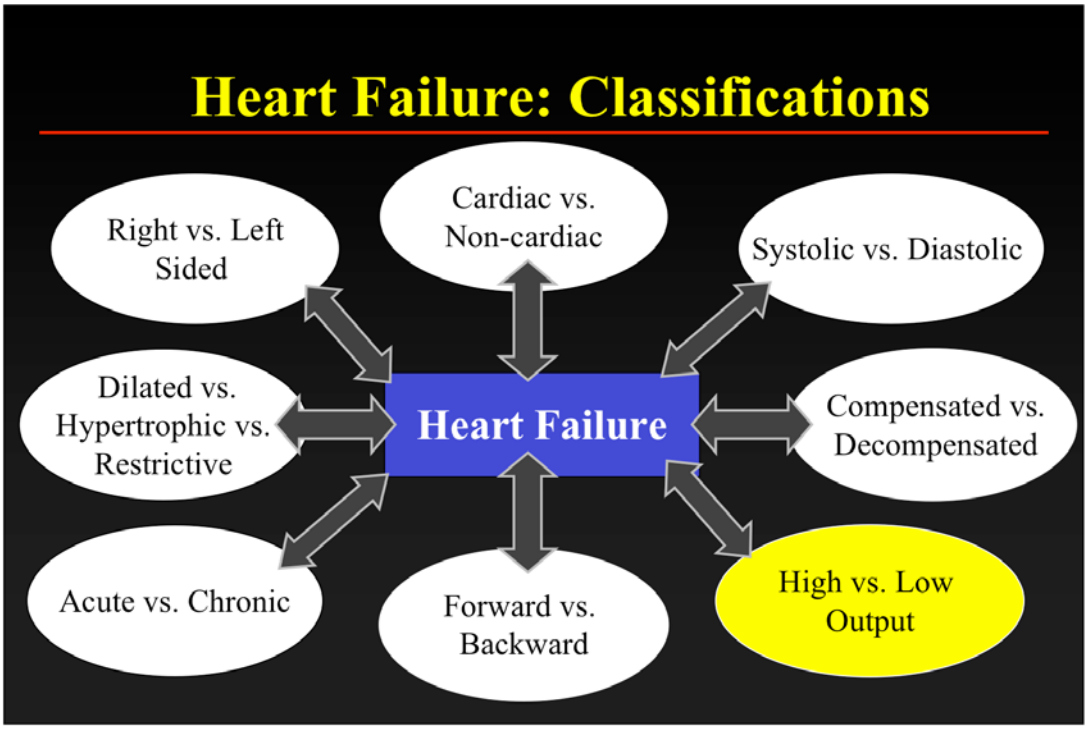
# Heart Failure: Classifications



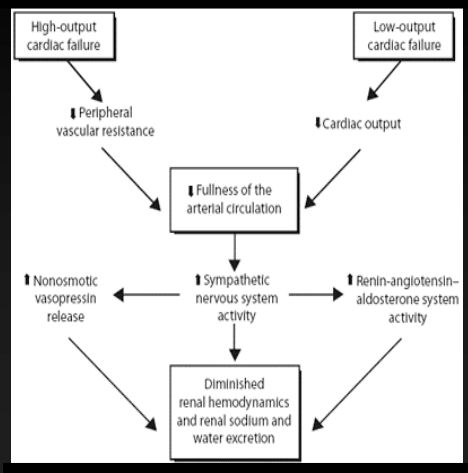

# Decompensated Heart Failure



# Heart Failure: Classifications

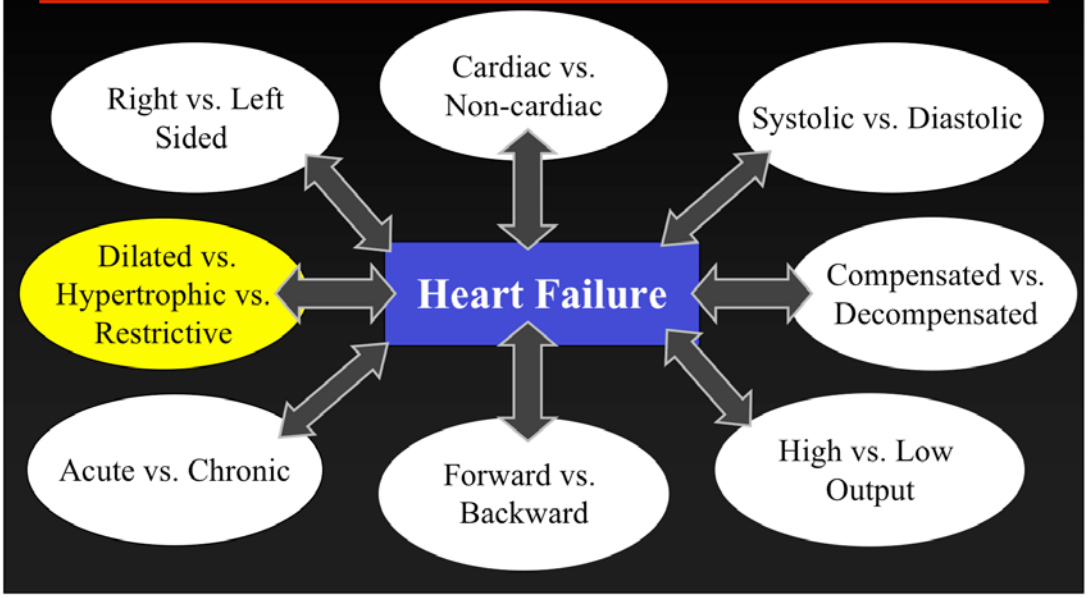



# High vs. Low Output Failure




- Causes:
  - Anemia
  - Systemic arteriovenous fistulas
  - Hyperthyroidism
  - Beriberi heart disease
  - Paget disease of bone
  - Glomerulonephritis
  - Polycythemia vera
  - Carcinoid syndrome
  - Obesity
  - Anemia
  - Multiple myeloma
  - Pregnancy
  - Cor pulmonale
  - Polycythemia vera

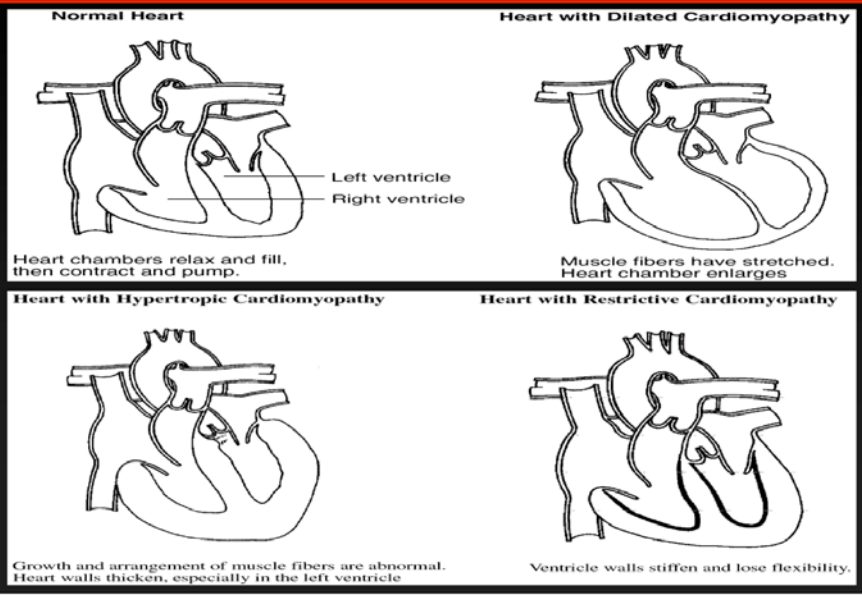
# Heart Failure: Classifications




# Dilated vs. Hypertrophic vs. Restrictive

| Type | Definition | Sample Etiologies |
|---|---|---|
| Dilated | Dilated left/both ventricle(s) with impaired contraction | Ischemic, idiopathic, familial, viral, alcoholic, toxic, valvular |
| Hypertrophic | Left and/or right ventricular hypertrophy | Familial with autosomal dominant inheritance |
| Restrictive | Restrictive filling and reduced diastolic filling of one/both ventricles, Normal/near normal systolic function | Idiopathic, amyloidosis, endomyocardial fibrosis |

# Dilated vs. Hypertrophic vs. Restrictive




# Clinical Manifestations

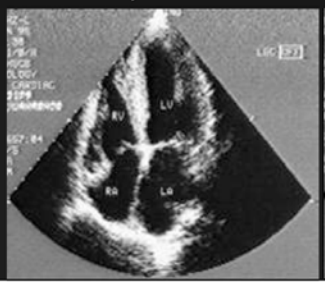
## Symptoms

- Reduced exercise tolerance
- Shortness of breath
- Congestion
- Fluid retention
- Difficulty in sleeping
- Weight loss

| Variable | Sensitivity | Specificity |
|---|---|---|
| Hx of HF | 62 | 94 |
| Dyspnea | 56 | 53 |
| Orthopnea | 47 | 88 |
| Rales | 56 | 80 |
| S3 | 20 | 99 |
| JVD | 39 | 94 |
| Edema | 67 | 68 |

# Diagnosis of heart failure

- Physical examination
- Chest X ray
- EKG
- Echocardiogram
- Blood tests: Na, BUN, Creatinine, BNP
- Exercise test
- MRI
- Cardiac catheterization



# NYHA Classification

| Class | | Patient Symptoms |
|---|---|---|
| I | Mild | • No limitation of physical activity<br>• No undue fatigue, palpitation or dyspnea |
| II | Mild | • Slight limitation of physical activity<br>• Comfortable at rest<br>• Less than ordinary activity results in fatigue, palpitation, or dyspnea |
| III | Moderate | • Marked limitation of physical activity<br>• Comfortable at rest<br>• Less than ordinary activity results in fatigue, palpitation, or dyspnea |
| IV | Severe | • Unable to carry out any physical activity without discomfort<br>• Symptoms of cardiac insufficiency at rest<br>• Physical activity causes increased discomfort |

# ACC/AHA Staging System

**STAGE A** High risk for developing HF

**STAGE B** Asymptomatic LV dysfunction

**STAGE C** Past or current symptoms of HF

**STAGE D** End-stage HF

Hunt, et al. *J Am Coll Cardiol*. 2001; 38:2101-2113.

# ACC/AHA Staging System

| | Stage | Patient Description |
|---|---|---|
| A | High risk for developing heart failure | • Hypertension<br>• Coronary artery disease<br>• Diabetes mellitus<br>• Family history of cardiomyopathy |
| B | Asymptomatic heart failure | • Previous myocardial infarction<br>• Left ventricular systolic dysfunction<br>• Asymptomatic valvular disease |
| C | Symptomatic heart failure | • Known structural heart disease<br>• Shortness of breath and fatigue<br>• Reduced exercise tolerance |
| D | Refractory end-stage heart failure | • Marked symptoms at rest despite maximal medical therapy (e.g., those who are recurrently hospitalized or cannot be safely discharged from the hospital without specialized interventions) |

## Goals of Treatment

1. Identification and correction of underlying condition causing heart failure.
2. Elimination of acute precipitating cause of symptoms.
3. Modulation of neurohormonal response to prevent progression of disease.
4. Improve long term survival.

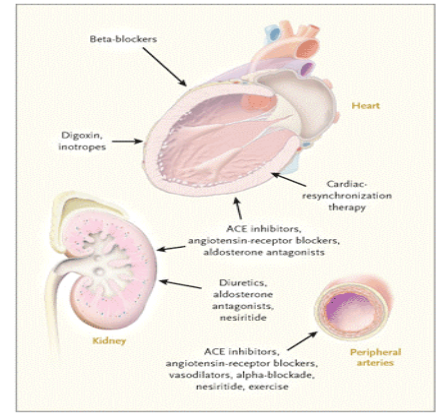
## Etiologies

- Ischemic cardiomyopathy
- Valvular cardiomyopathy
- Hypertensive cardiomyopathy.
- Inflammatory cardiomyopathy
- Metabolic cardiomyopathy
- General system disease
- Muscular dystrophies.
- Neuromuscular disorders.
- Sensitivity and toxic reactions.
- Peripartal cardiomyopathy

# Percipients /Associated Factors

- Inappropriate reduction in the intensity of treatment, including
  - Dietary sodium restriction,
  - Physical activity reduction,
  - Drug regimen reduction, or,
  - most commonly, a combination of these measures.
- Ischemia
- Hypertension
- Anemia
- Volume Overload
- Increased Metabolic Demand
  - Infection
  - Thyroid Disease
- Arrhythmia
- Asthma/COPD

# Targets of Treatment



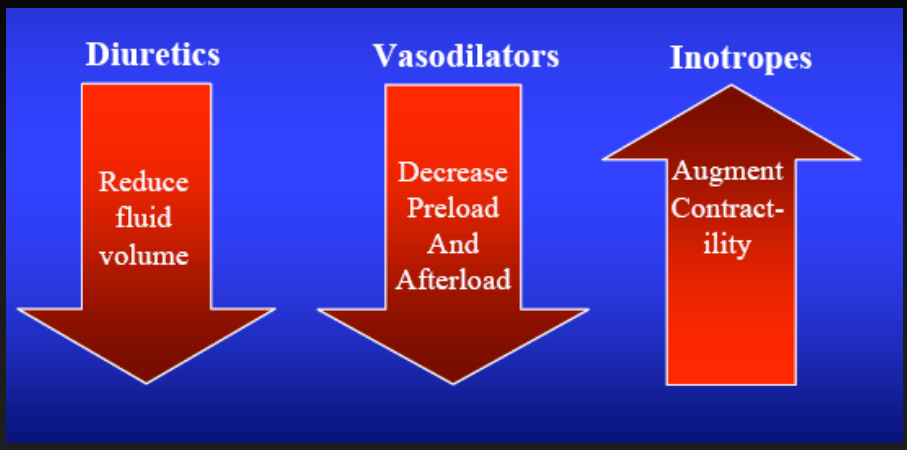

## Standard Pharmacological Therapy

- ACE inhibitors
- Angiotensin Receptor Blockers
- Beta Blcokers
- Diuretics
- Aldosterone Antagonists
- Statins
- Vasodilators
- Inotropes

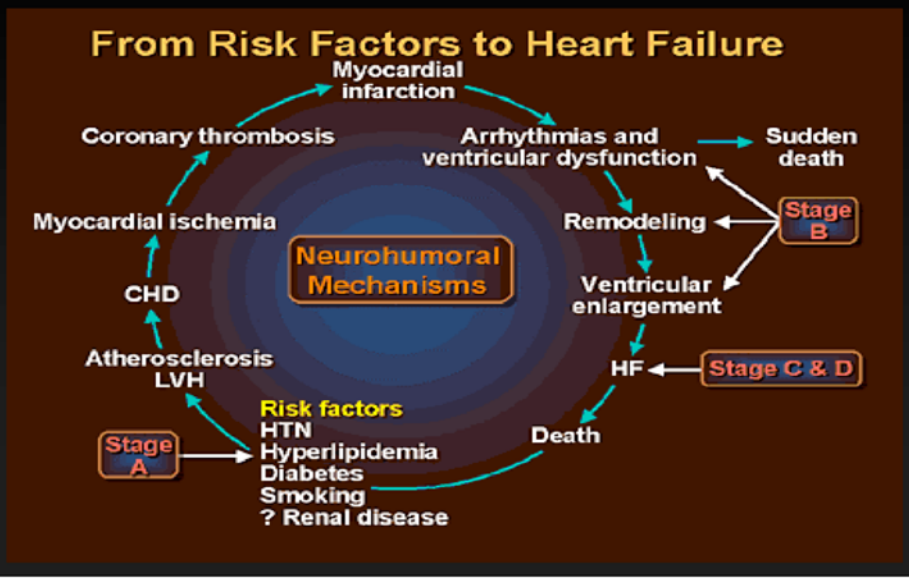
# Treatment

| | Stage | Patient Treatment |
|---|---|---|
| A | High risk for developing heart failure | • Optimal pharmacologic therapy (OPT)<br>• Aspirin, ACE inhibitors, statins, b-blockers, a-b-blockers (carvedilol) diabetic therapy |
| B | Asymptomatic heart failure | • OPT<br>• ICD if left ventricular (LV) dysfunction (systolic) present |
| C | Symptomatic heart failure | • OPT<br>• ICD if LV dysfunction (systolic) present<br>• CRT (if QRS wide, LVEF≤35%) |
| D | Refractory end-stage heart failure | • OPT<br>• Intermittent IV inotropes<br>• ICD as a bridge to transplantation<br>• CRT<br>• Other devices (LVAD, pericardial restraint) |

# Treatment of Acute Heart Failure



# ACC/AHA Staging System




# Summary

- Complex Clinical Syndrome
- Multiple Etiologies and Classification Systems
- Physiologic Understanding Essential

http://www.columbia.edu/itc/hs/medical/heartsim/