Pathophysiology: Heart Failure

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Outline

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

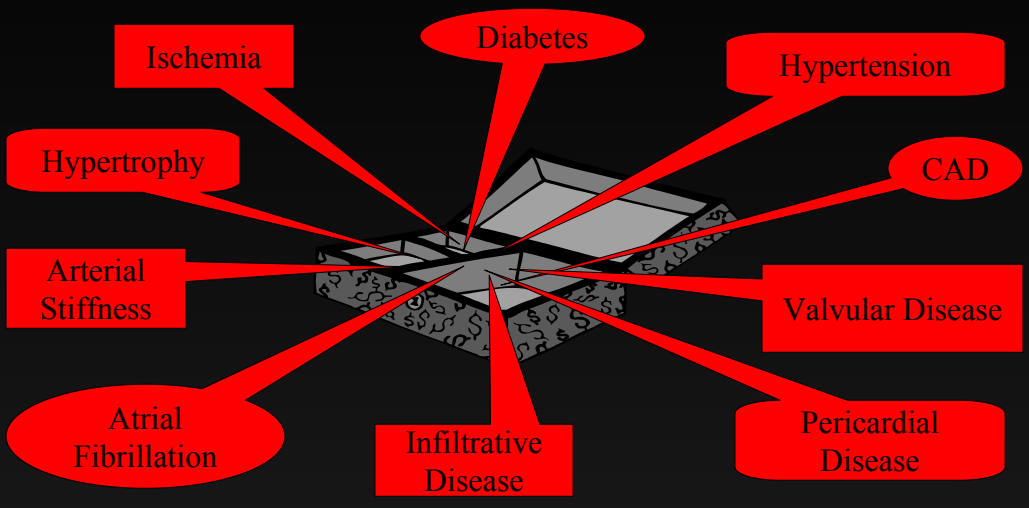
Heart Failure: Definitions

- 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

Etiologies

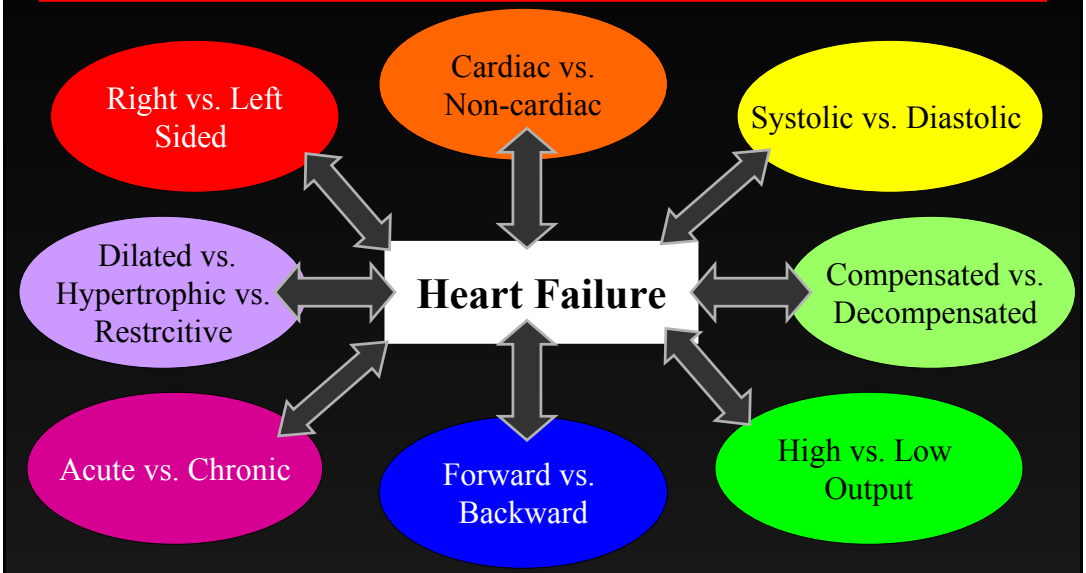


Etiologies

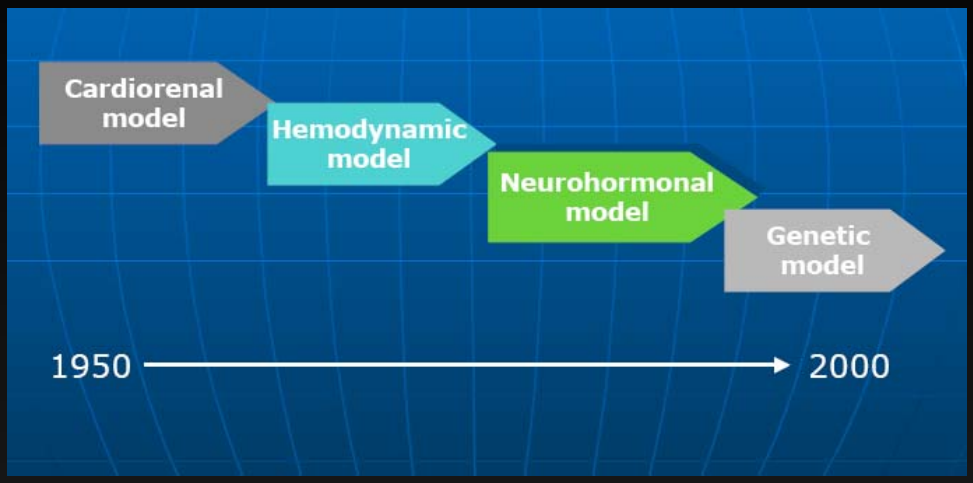
- **Ischemic cardiomyopathy**
- **Valvular cardiomyopathy**
- **Hypertensive cardiomyopathy.**
- **Inflammatory cardiomyopathy**
- **Metabolic cardiomyopathy**
- **General system disease**
- **Muscular dystrophies.**
- **Neuromuscular disorders.**
- **Sensitivity and toxic reactions.**
- **Peripartal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

Circulation. 1996;93:841-842

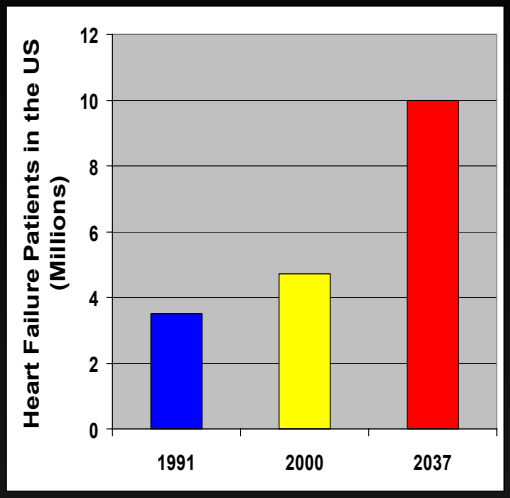
Heart Failure: Classifications



Heart Failure Paradigms



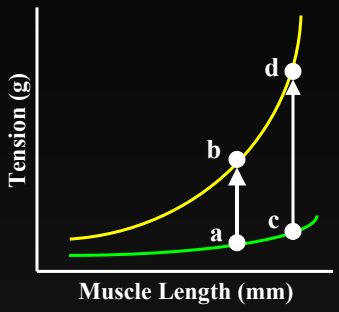
Epidemiology Heart Failure: The Problem



- 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

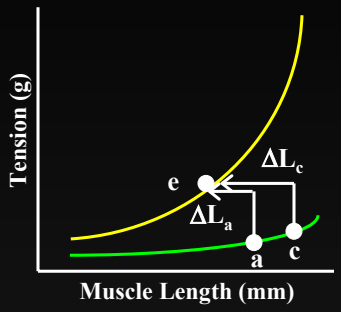
Cardiac Muscle Function

Preload



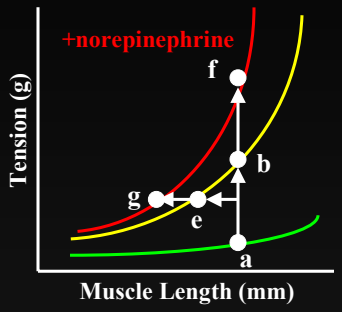
•The length of a cardiac muscle fiber prior to the onset of contraction.
•Frank Starling

Afterload



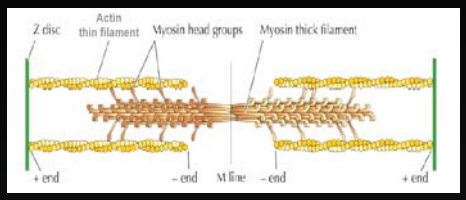
•The against which a cardiac muscle fiber must shorten.
•Isotonic Contraction

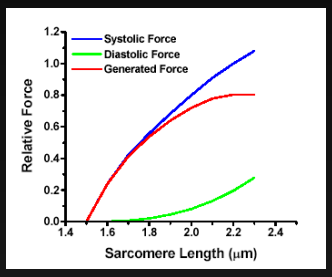
Contractility

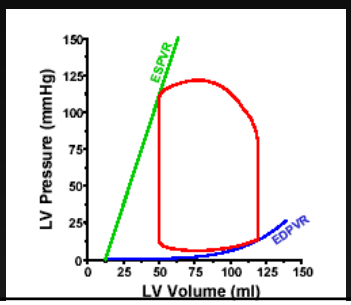


•The force of contraction independent of preload and afterload.
•Inotropic State

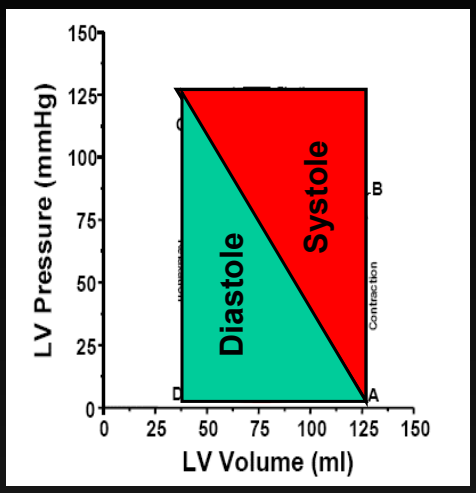
From Muscle to Chamber

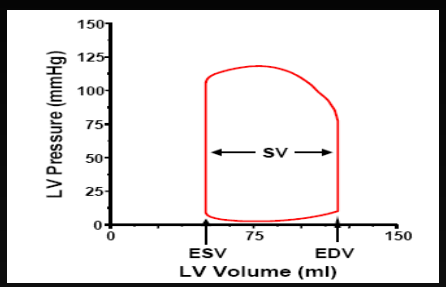


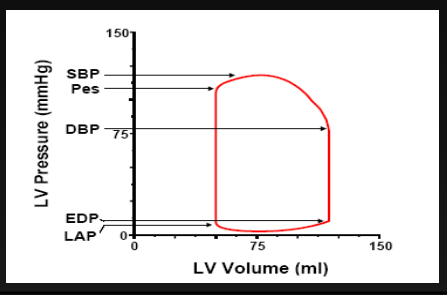




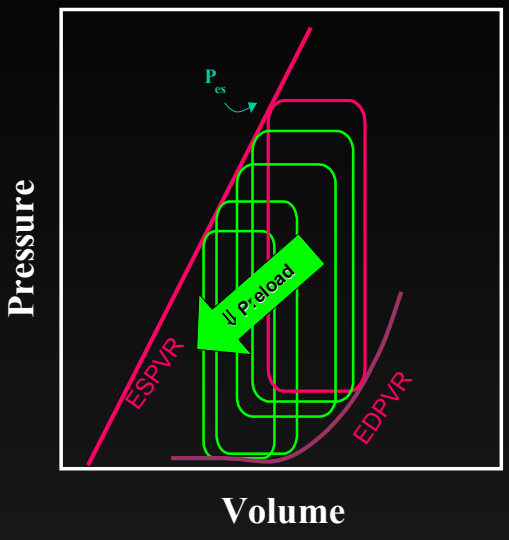
The Pressure Volume Loop

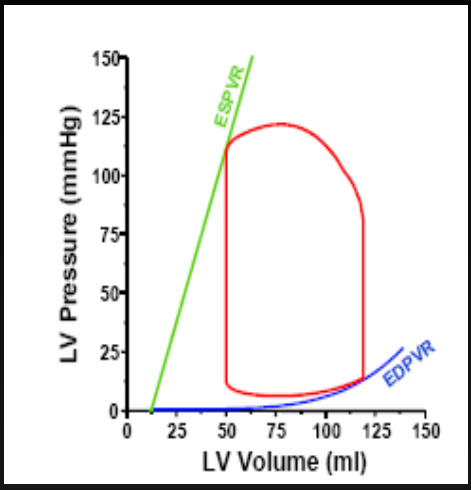




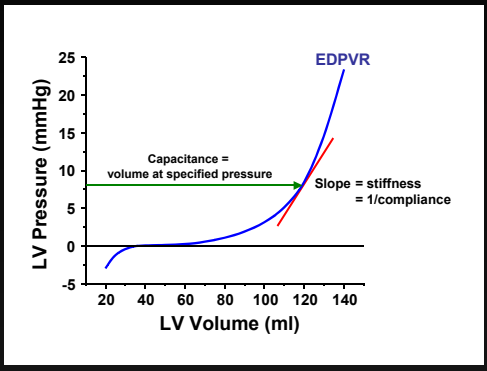


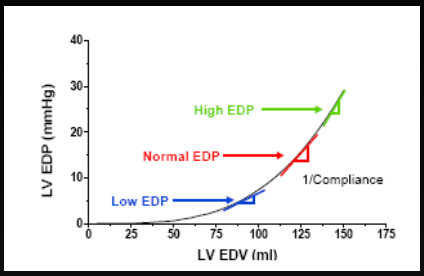
The Pressure Volume Loop

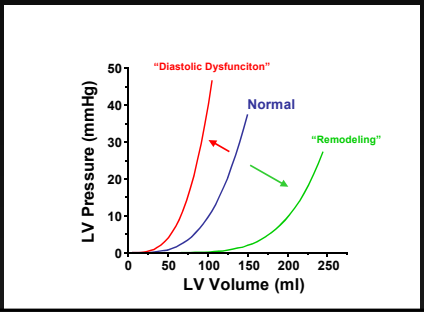




Compliance/Stiffness vs Capacitance

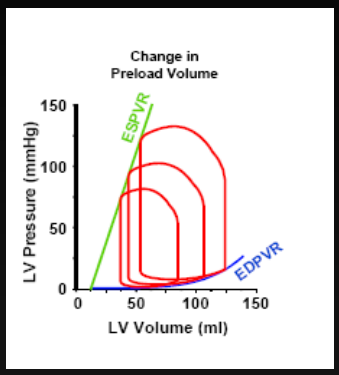






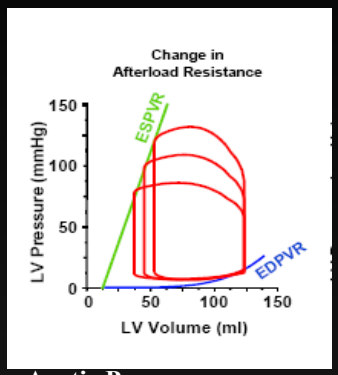
Cardiac Chamber Function

Preload



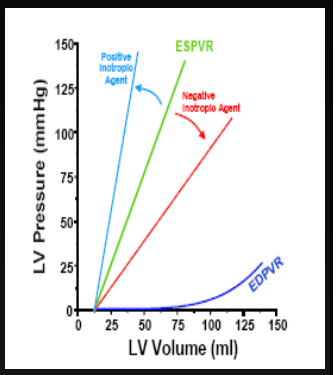
- EDV
- EDP
- Wall stress at end diastole

Afterload



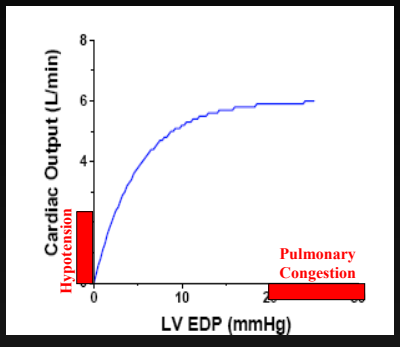
- **Aortic Pressure**
- **Total peripheral resistance**
- **Arterial impedance**
- **Wall stress**

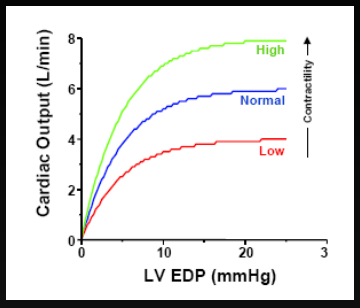
Contractility

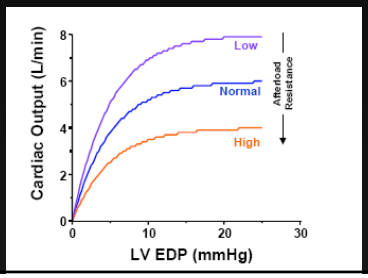


- Pressure generated at given volume.
- Inotropic State

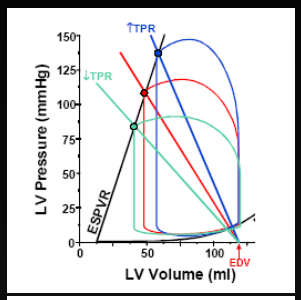
Frank Starling Curves

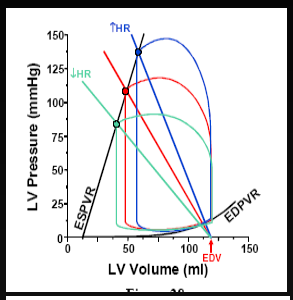


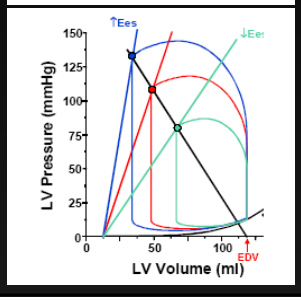


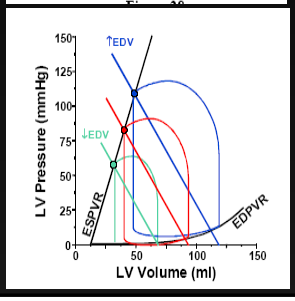


Pathophysiology - PV Loop



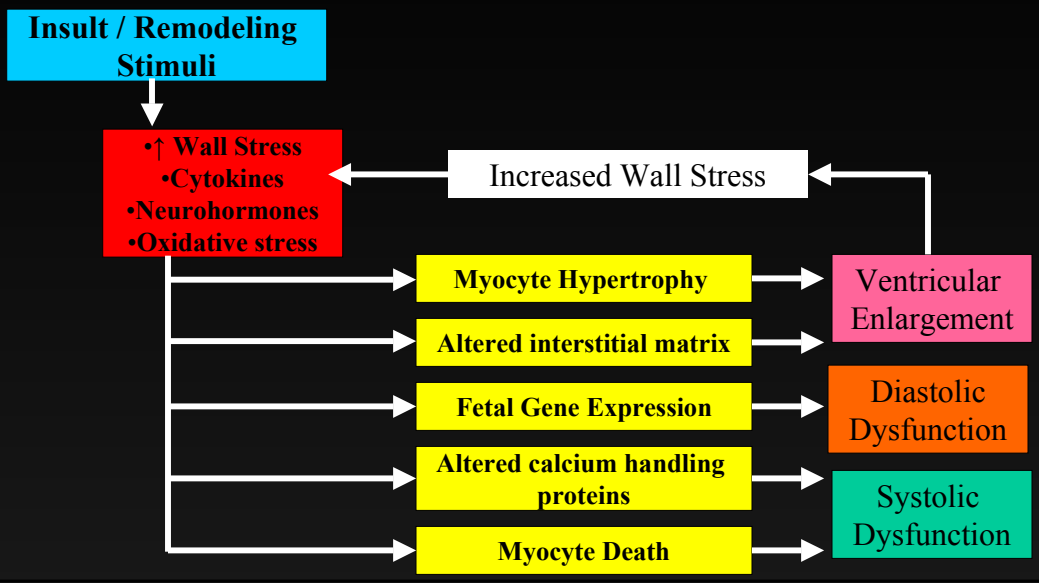




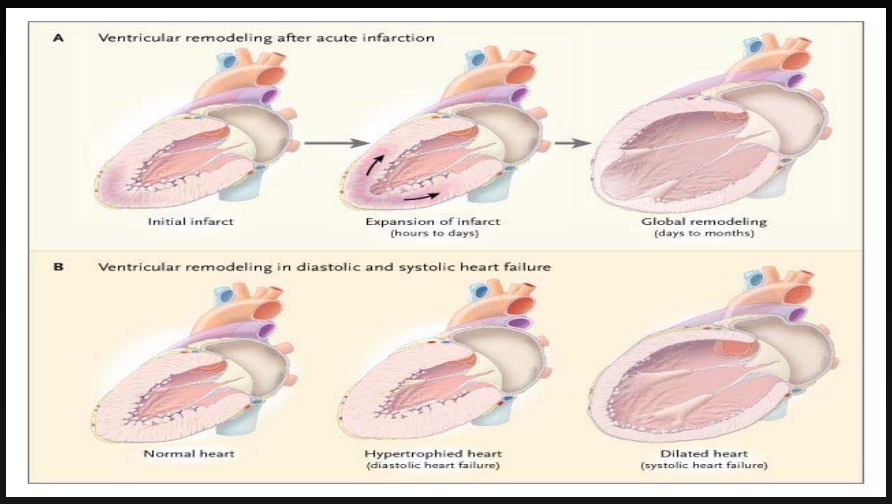


Pathophyisiology of myocardial remodeling:

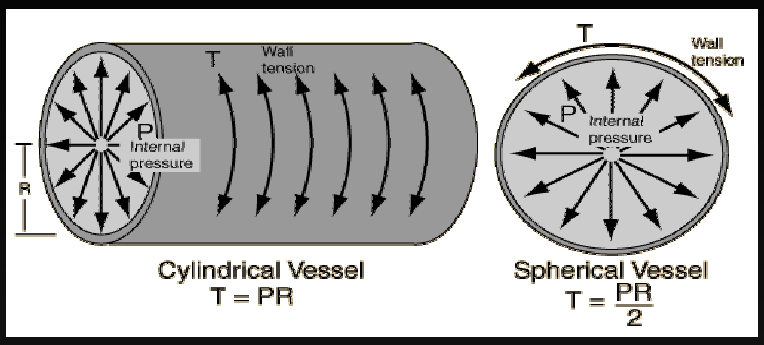
Transition from compensated hypertrophy to heart failure



Ventricular Remodeling

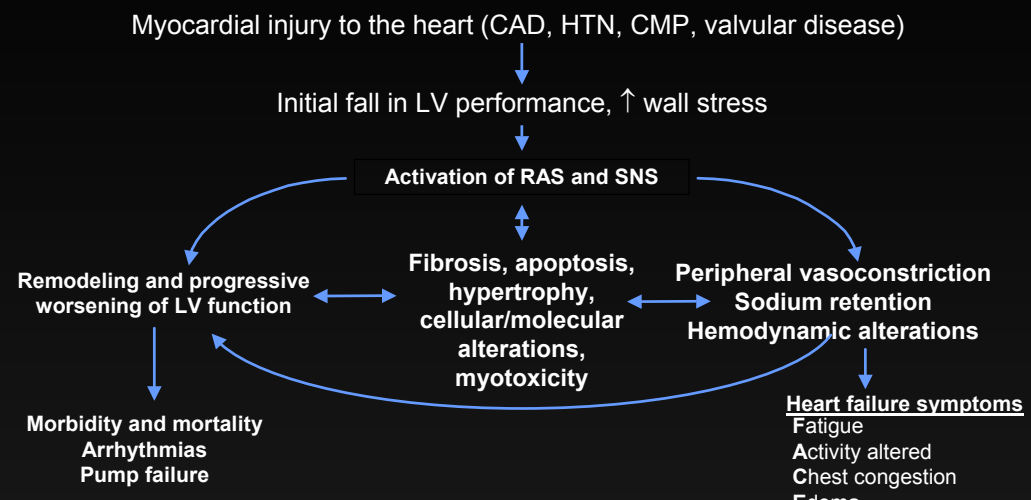


Laplace's Law



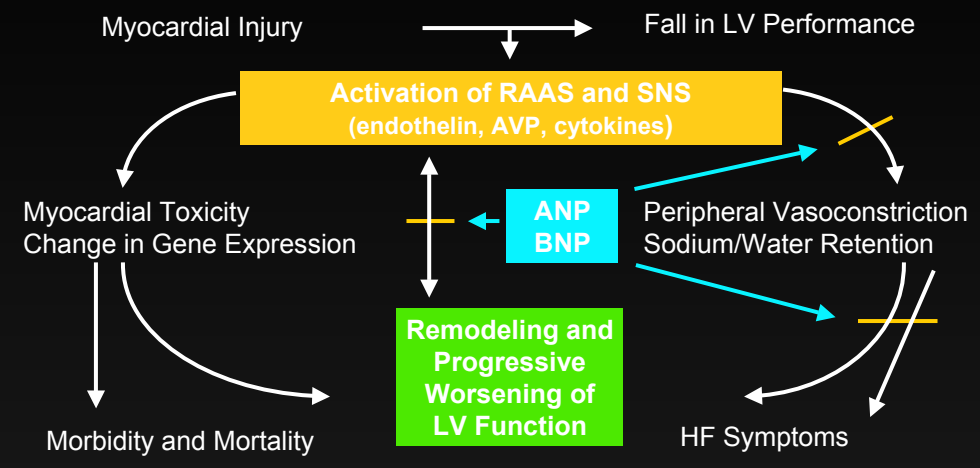
Where P = ventricular pressure, r = ventricular chamber radius and h = ventricular wall thickness

Neurohormonal Activation in Heart Failure



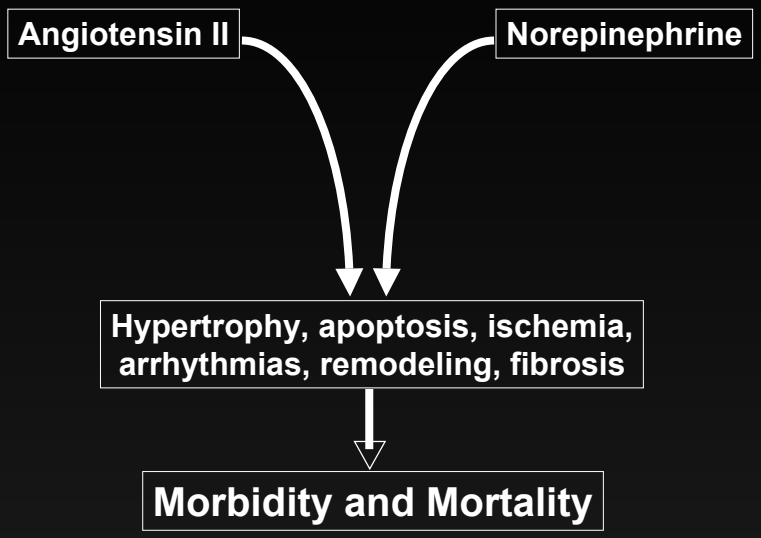
RAS, renin-angiotensin system; SNS, sympathetic nervous system.

Neurohormones in Heart Failure

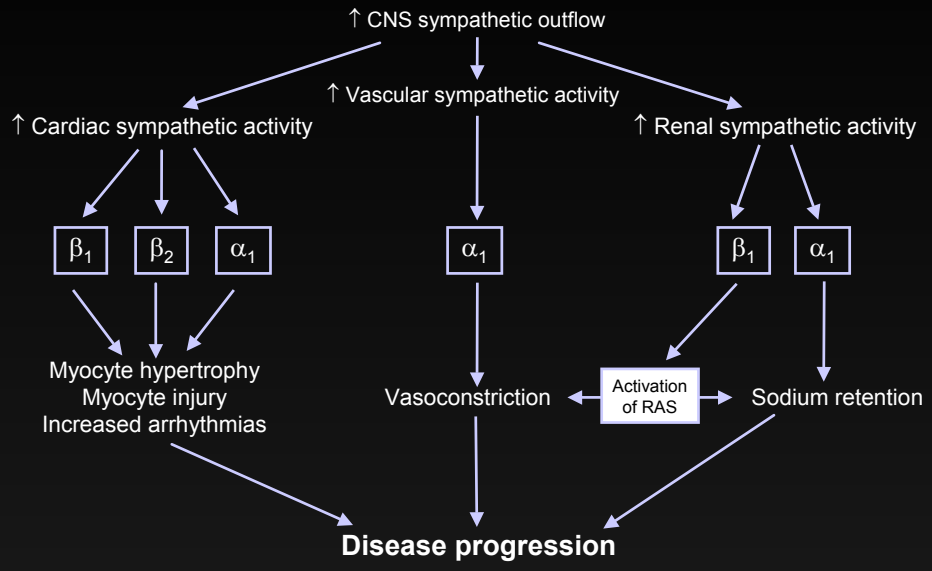


Shah M et al. *Rev Cardiovasc Med.* 2001;2(suppl 2):S2

Neurohormonal Activation in Heart Failure



Adrenergic Pathway in Heart Failure Progression



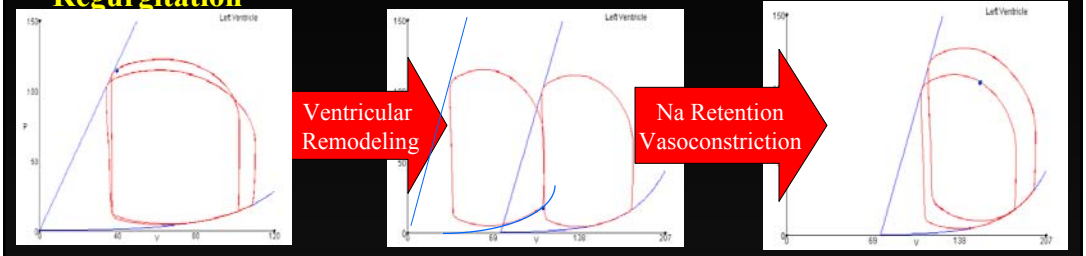
Pathophysiology of Heart Failure

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**



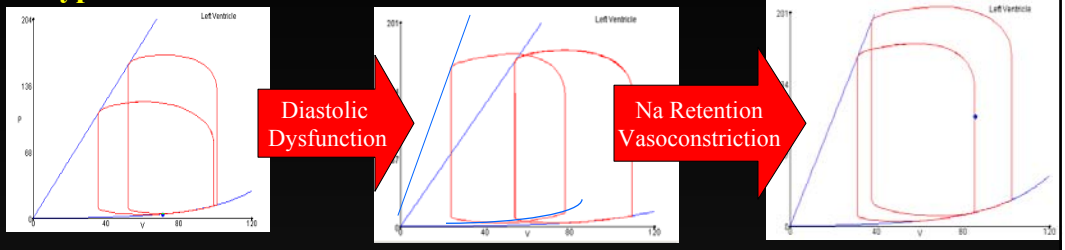
Etiologies

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

Parameter	Normal	AI	AI + Remodeling	AI + Heart failure
BP (mm Hg)	140/75/99	128/5078	85/35/54	104/45/68
SV (ml)	64	80	54	63
Cardiac Output (L/min)	3.8	3.0	2.1	2.6
PCWP (mm Hg)	10	10	10	20

Increased Afterload

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



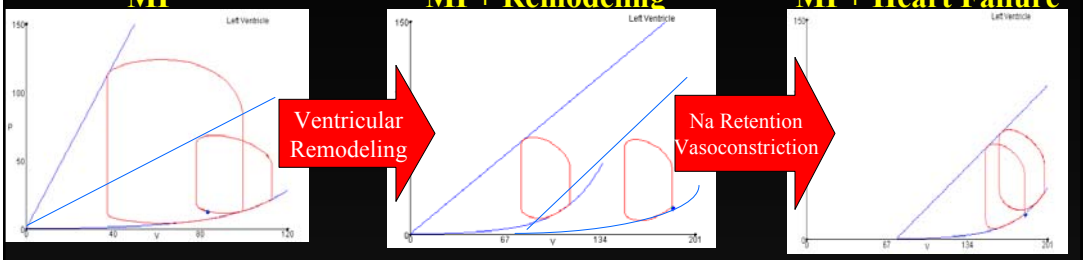
Etiologies

- 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**



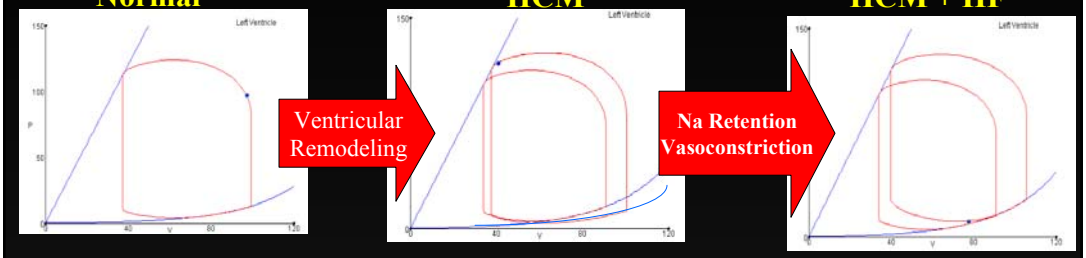
Etiologies

- 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 | **HCM** | **HCM + HF**

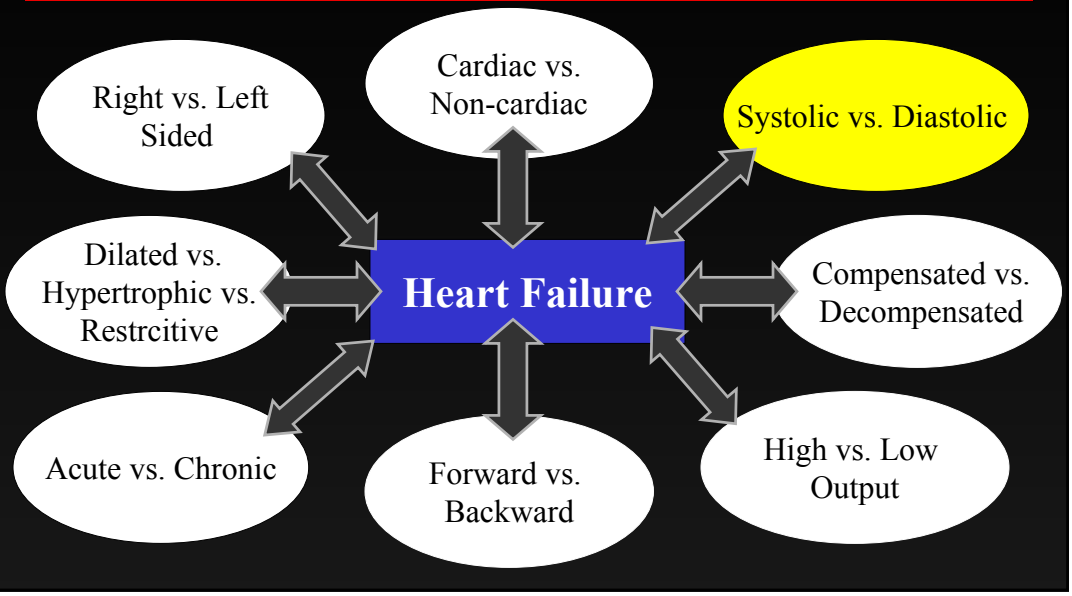


Etiologies

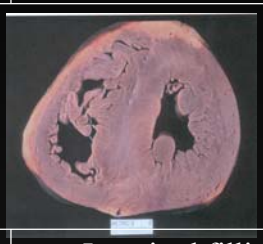
- Mitral Stenosis
- Constriction
- Restrictive Cardiomypoathy
- Cardiac Tamponade
- Hypertrophic Cardiomyopathy
- Infiltrative Cardiomyopathy

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	10	27

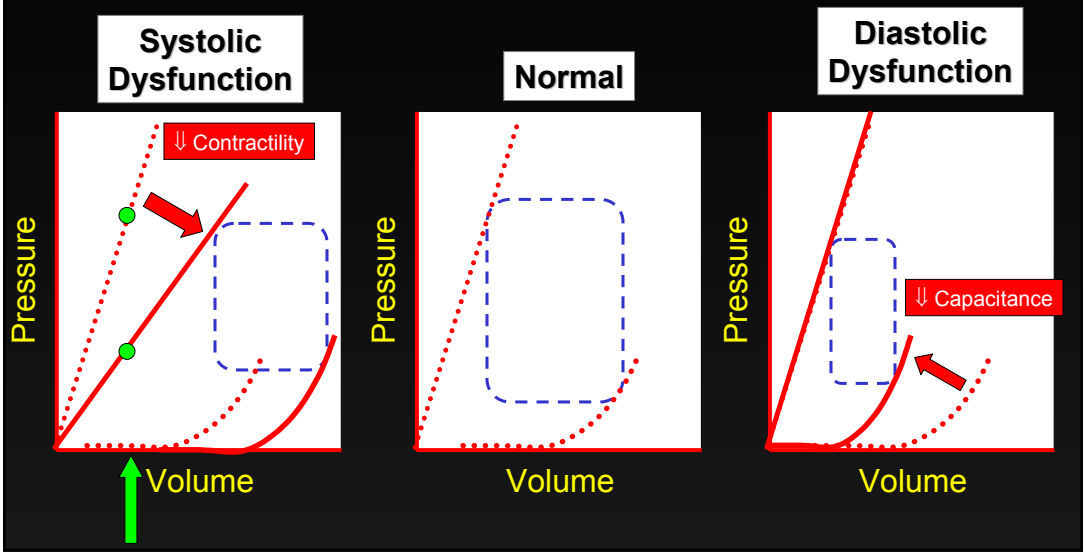
Heart Failure: Classifications



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



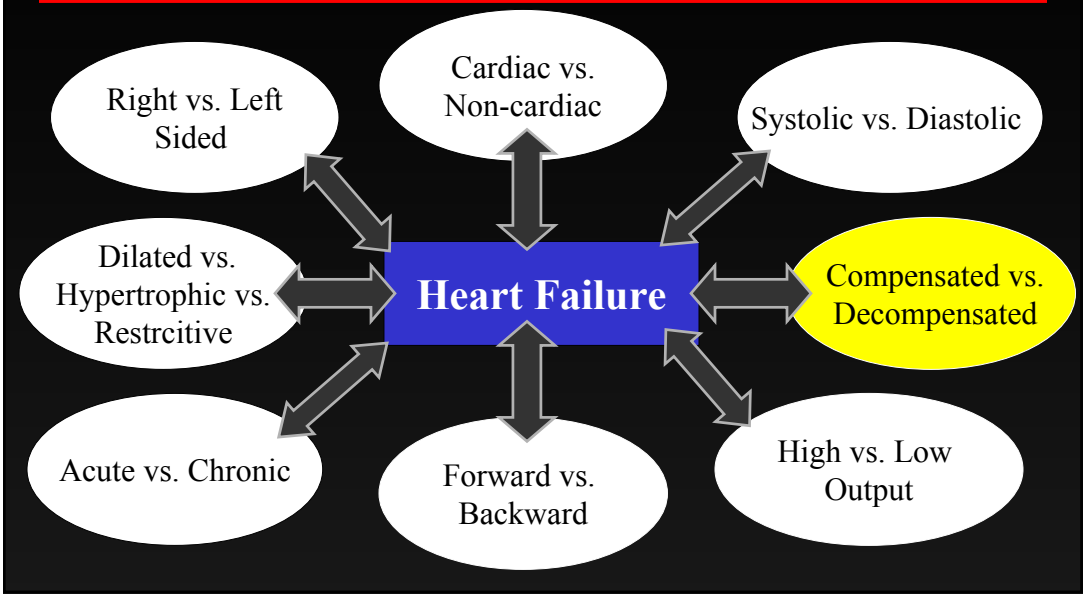
Systolic Versus Diastolic Failure

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

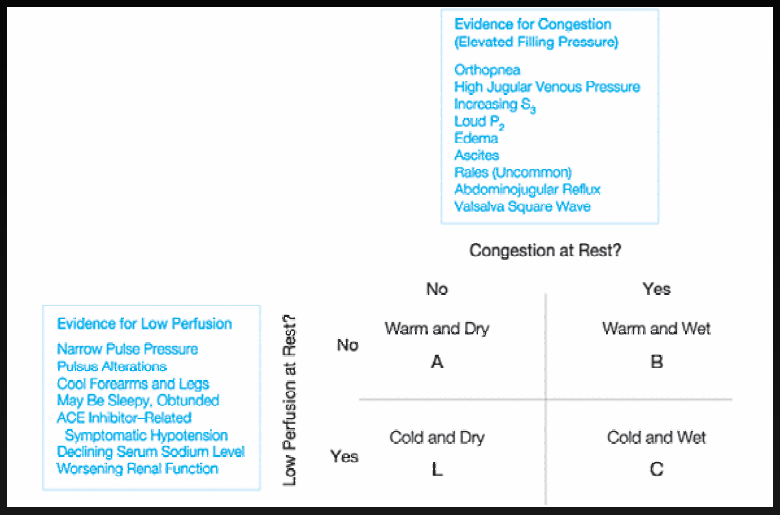
Characteristic	Diastolic Heart Failure	Systolic Heart Failure
Age	Frequently elderly	All ages, typically 50–70 yr
Sex	Frequently female	More often male
Left ventricular ejection fraction	Preserved or normal, approximately 40% or higher	Depressed, approximately 40% or lower
Left ventricular cavity size	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."

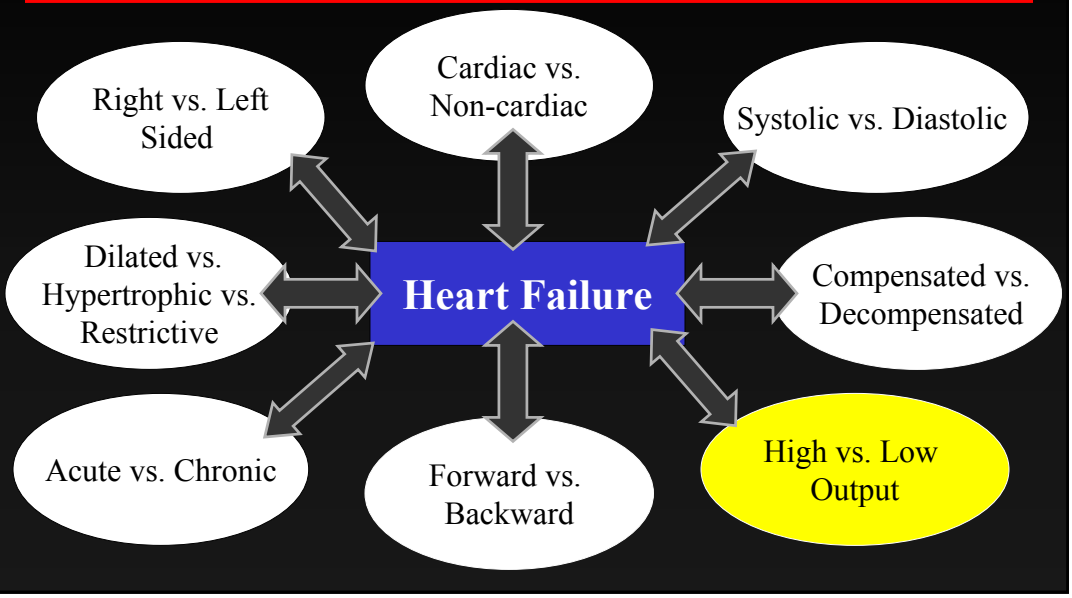
Heart Failure: Classifications



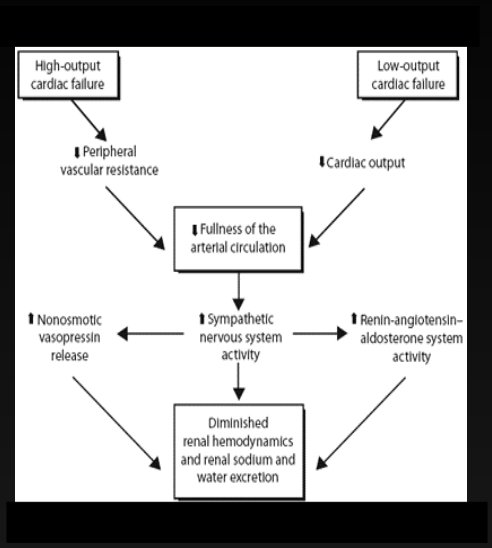
Decompensated Heart Failure



Heart Failure: Classifications

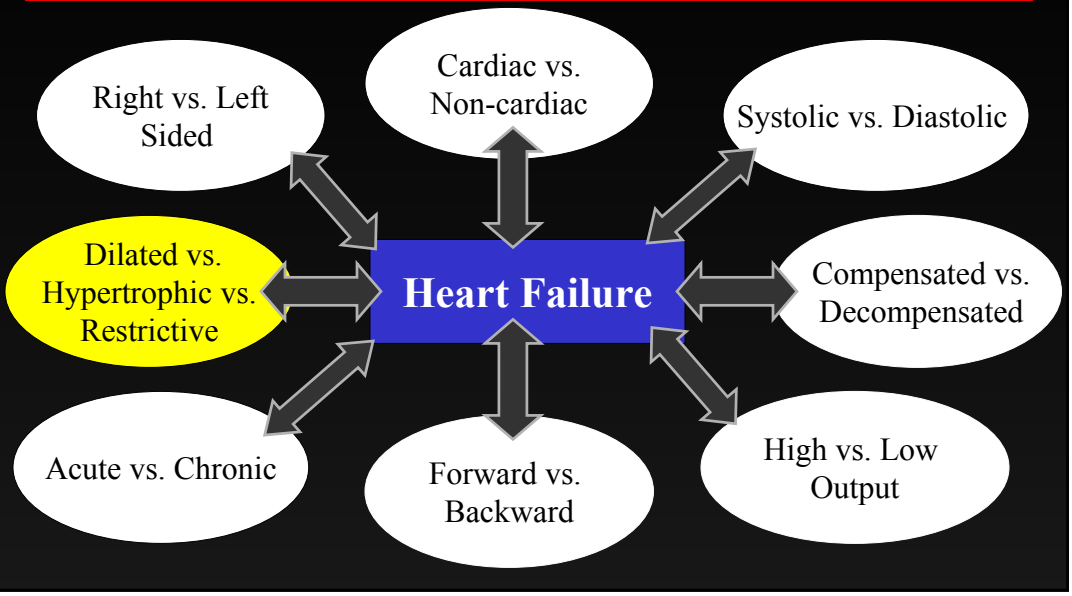


High vs. Low Output Failure



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

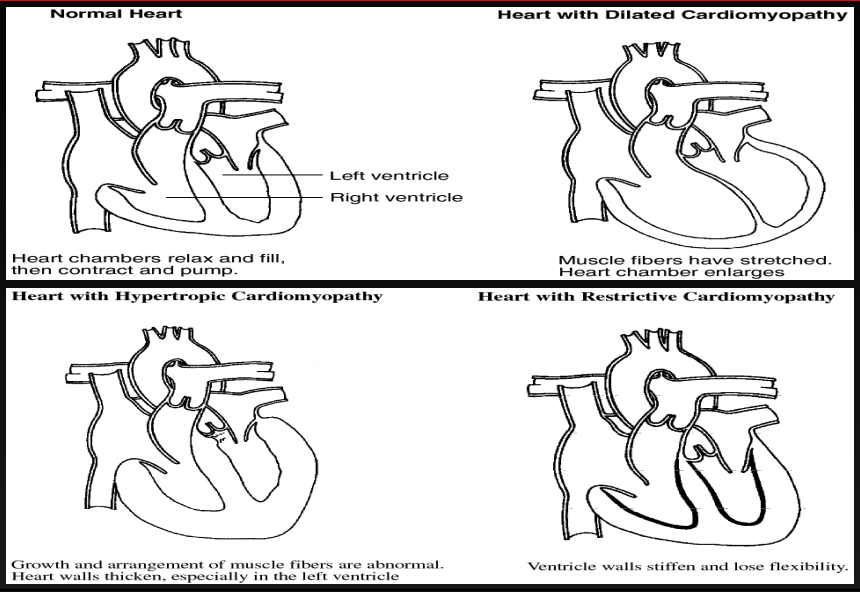
Heart Failure: Classifications



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



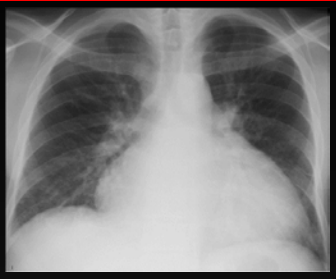
Clinical Manifestations

Symptoms

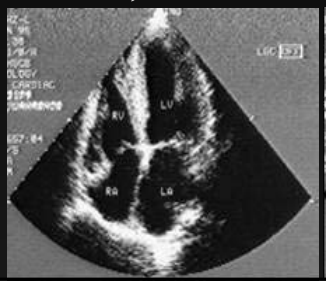
- Reduced exercise tolerance
- Shortness of breath
- Congestion
- Fluid retention
- Difficulty in sleeping
- Weight loss

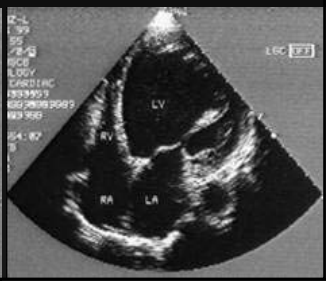
Variable	Sensitivity	Specificity	Accuracy
Hx of HF	62	94	80
Dyspnea	56	53	54
Orthopnea	47	88	72
Rales	56	80	70
S3	20	99	66
JVD	39	94	72
Edema	67	68	68

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 • No undue fatigue, palpitation or dyspnea
II	Mild	• Slight limitation of physical activity • Comfortable at rest • Less than ordinary activity results in fatigue, palpitation, or dyspnea
III	Moderate	• Marked limitation of physical activity • Comfortable at rest • Less than ordinary activity results in fatigue, palpitation, or dyspnea
IV	Severe	• Unable to carry out any physical activity without discomfort • Symptoms of cardiac insufficiency at rest • 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 • Coronary artery disease • Diabetes mellitus • Family history of cardiomyopathy
B	Asymptomatic heart failure	• Previous myocardial infarction • Left ventricular systolic dysfunction • Asymptomatic valvular disease
C	Symptomatic heart failure	• Known structural heart disease • Shortness of breath and fatigue • 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)

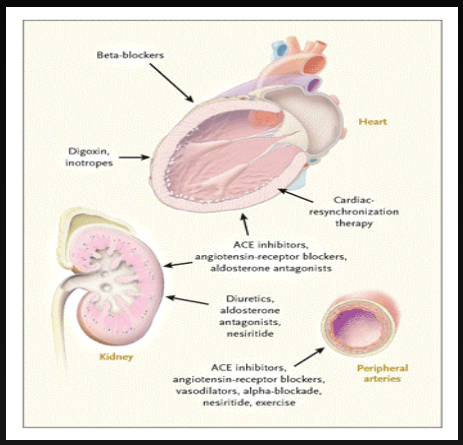
Goals of Treatment

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.

Treatment

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

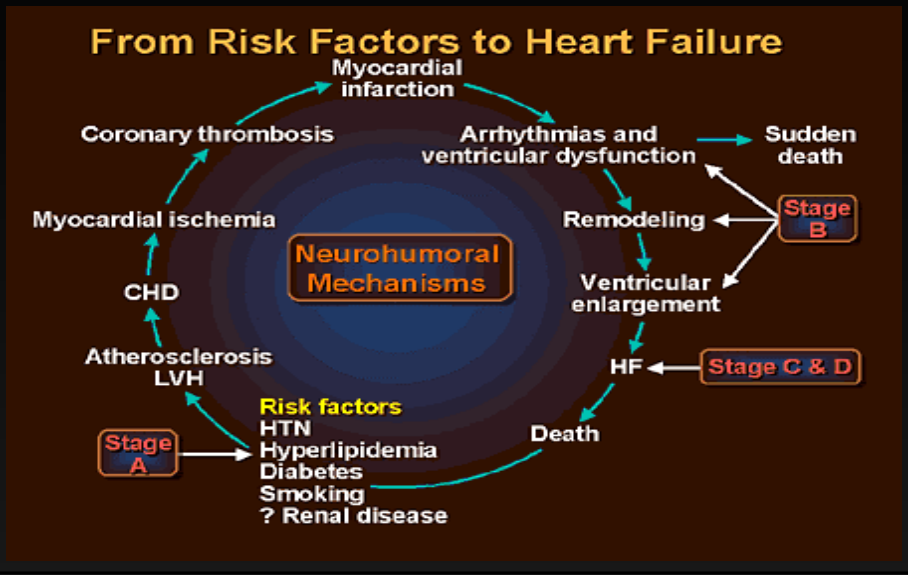
Targets of Treatment



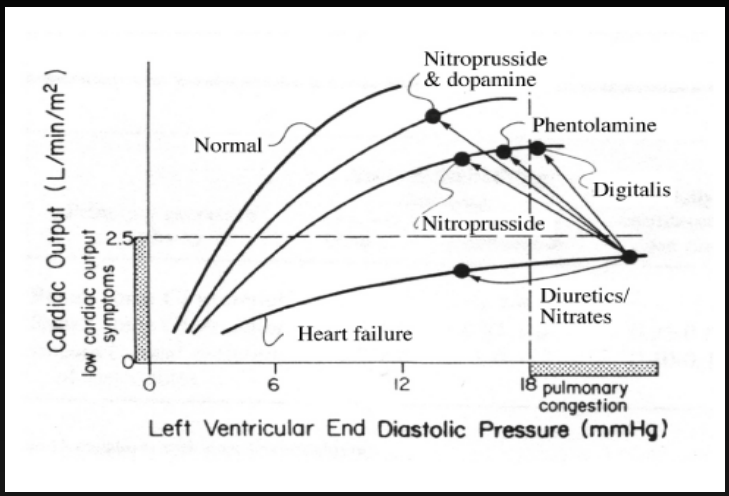
Standard Pharmacological Therapy

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

ACC/AHA Staging System



Treatment



Summary

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

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