
Pathophysiology: Heart Failure

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Objectives

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

1. Define heart failure as a clinical syndrome
2. Define and employ the terms preload, afterload, contractility, remodeling, diastolic dysfunction, compliance, stiffness and capacitance.
3. Describe the classic pathophysiologic steps in the development of heart failure.
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

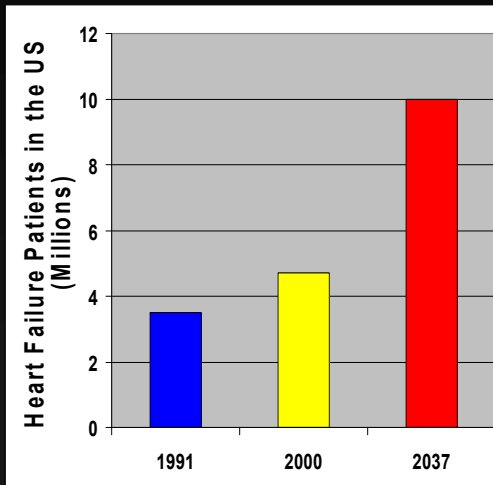
Heart Failure

- 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: Definitions

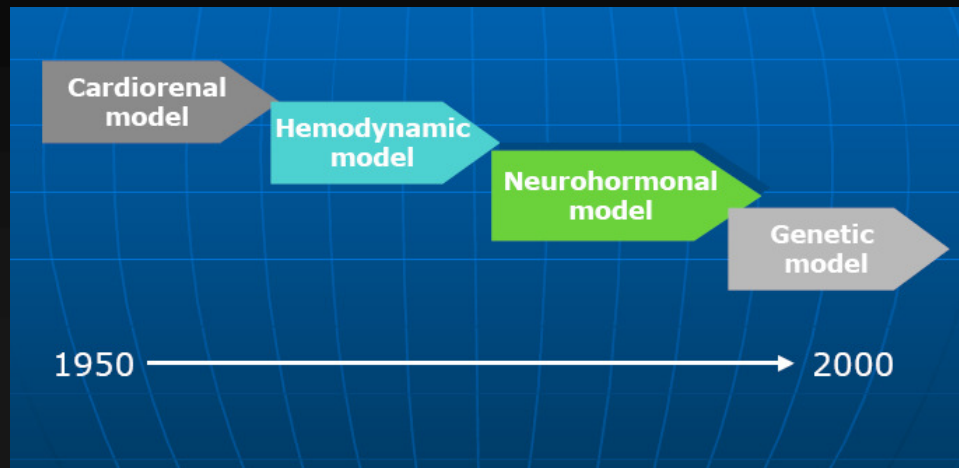
- An inability of the heart to pump blood at a sufficient rate to meet the metabolic demands of the body (e.g. oxygen and cell nutrients) at rest and during effort or to do so only if the cardiac filling pressures are abnormally high.
- A complex clinical syndrome characterized by abnormalities in cardiac 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.

Epidemiology Heart Failure: The Problem

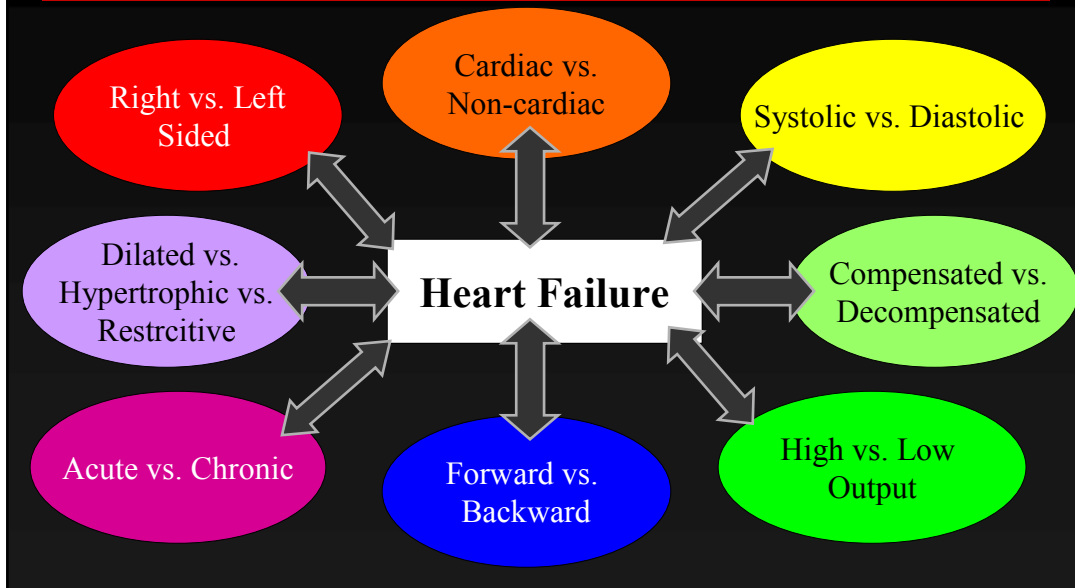


- 3.5 million in 1991, 4.7 million in 2000, estimated 10 million in 2037
- Incidence: 550,000 new cases/year
- Prevalence: 1% ages 50--59, >10% over age 80
- More deaths from HF than from all forms of cancer combined
- Most common cause for hospitalization in age >65

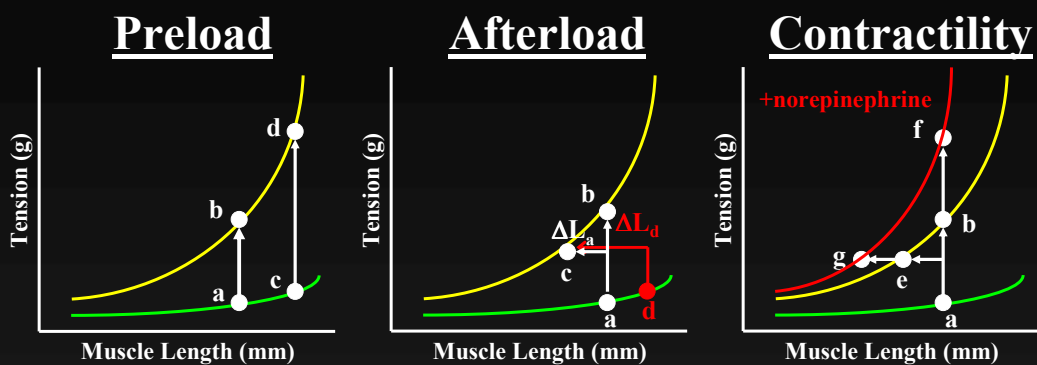
Heart Failure Paradigms



Heart Failure: Classifications



Cardiac Muscle Function

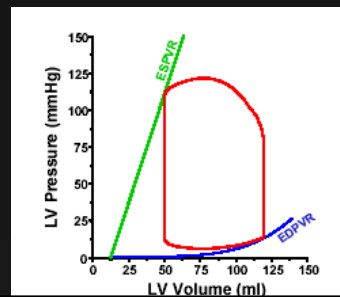
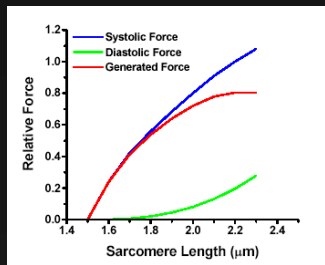
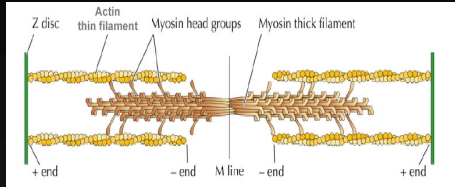


- The length of a cardiac muscle fiber prior to the onset of contraction.
- Frank Starling

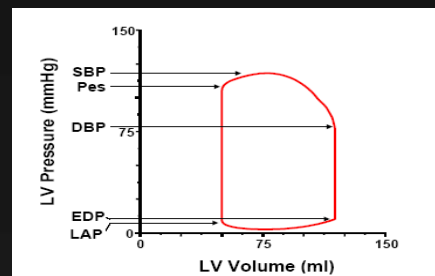
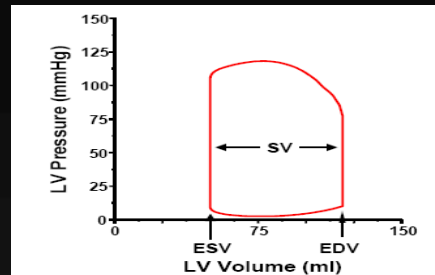
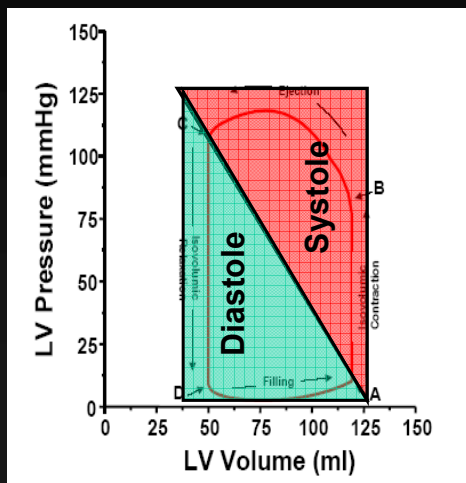
- The force against which a cardiac muscle fiber must shorten.
- Isotonic Contraction

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

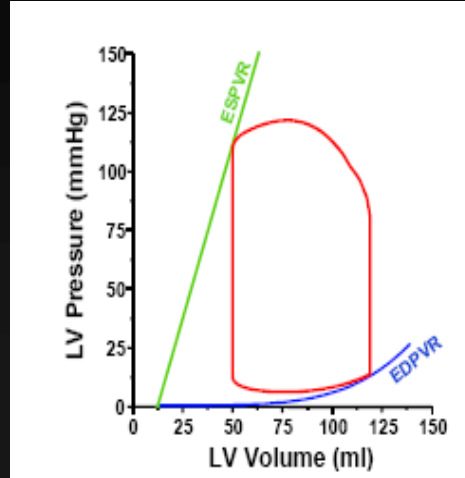
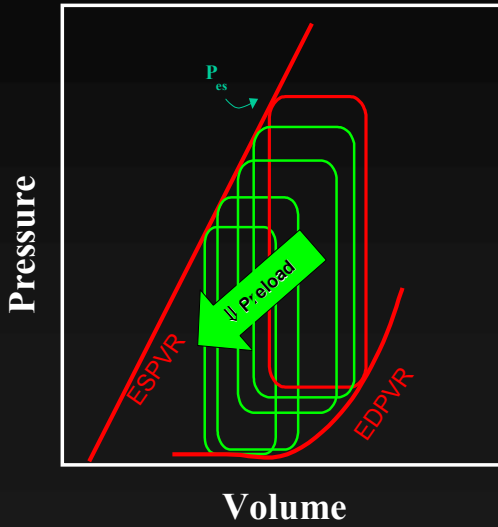
From Muscle to Chamber



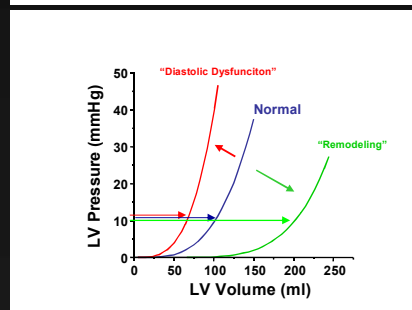
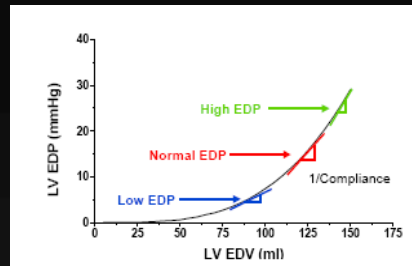
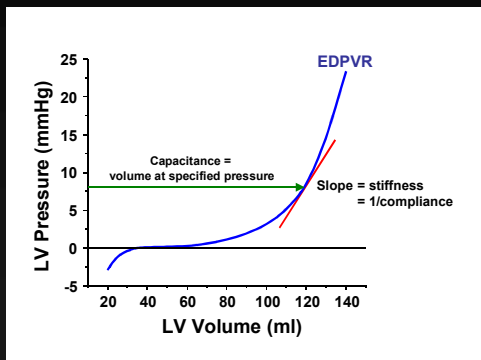
The Pressure Volume Loop



The Pressure Volume Loop



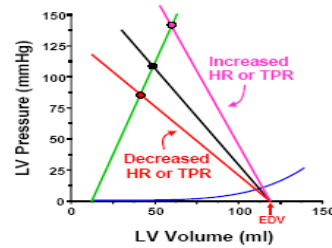
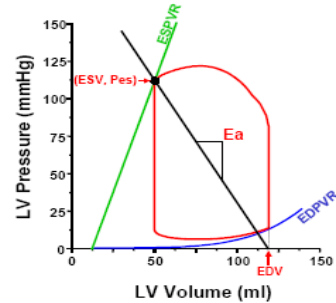
Compliance/Stiffness vs Capacitance



Afterload (Arterial Properties)

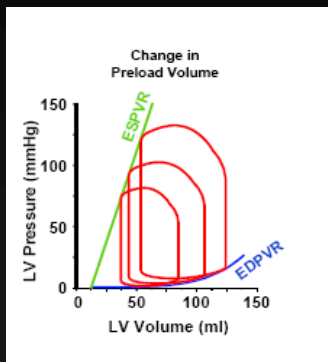
Ea (Arterial Elastance)

- If
 - $TPR = [MAP - CVP] / CO$, and
 - $CO = SV * HR$
- Substituting the second equation into the first we obtain:
 - $TPR = [MAP - CVP] / (SV * HR)$
- Making two simplifying assumptions.
 1. CVP is negligible compared to MAP.
 2. MAP is approximately equal to the end-systolic pressure in the ventricle (P_{es}).
- Then,
 - $TPR = P_{es} / (SV * HR)$
- Which can be rearranged to:
 - $P_{es} / SV \cong TPR * HR$.



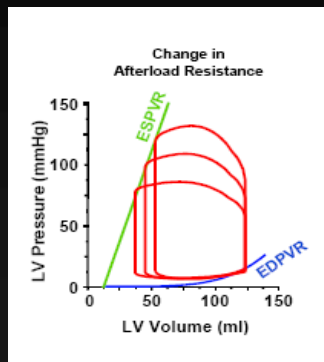
Cardiac Chamber Function

Preload



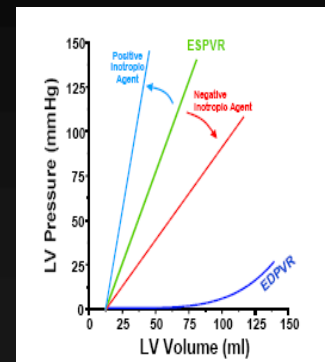
- EDV
- EDP
- Wall stress at end diastole

Afterload



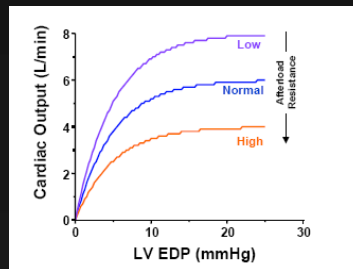
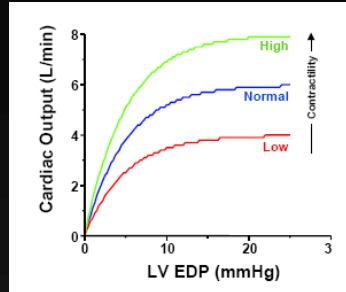
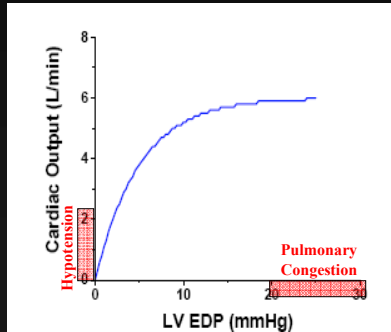
- Aortic Pressure
- Total peripheral resistance
- Arterial impedance
- Wall stress at end systole

Contractility

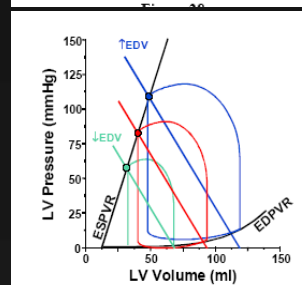
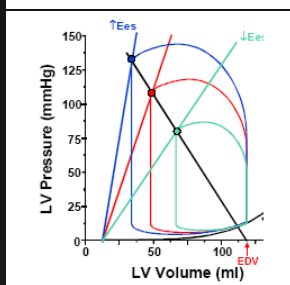
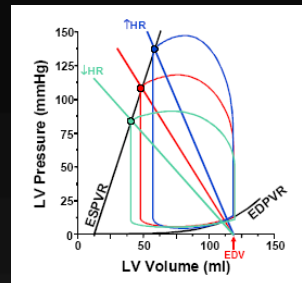
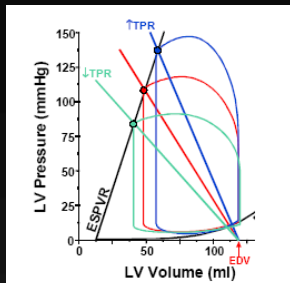


- Pressure generated at given volume.
- Inotropic State

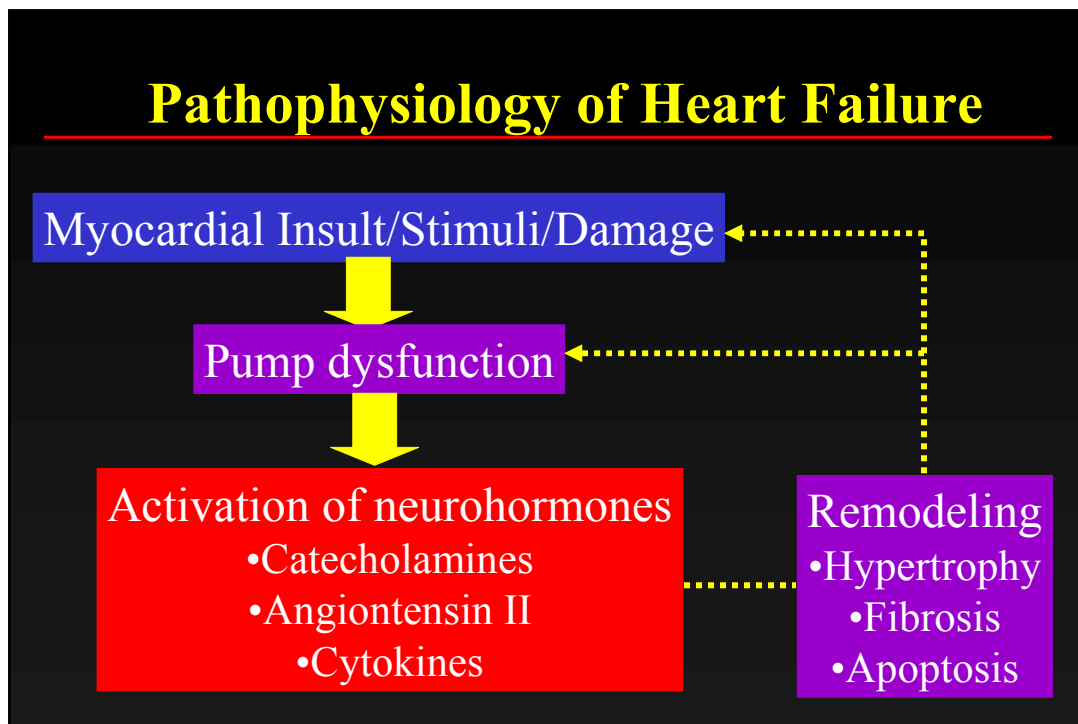
Frank Starling Curves



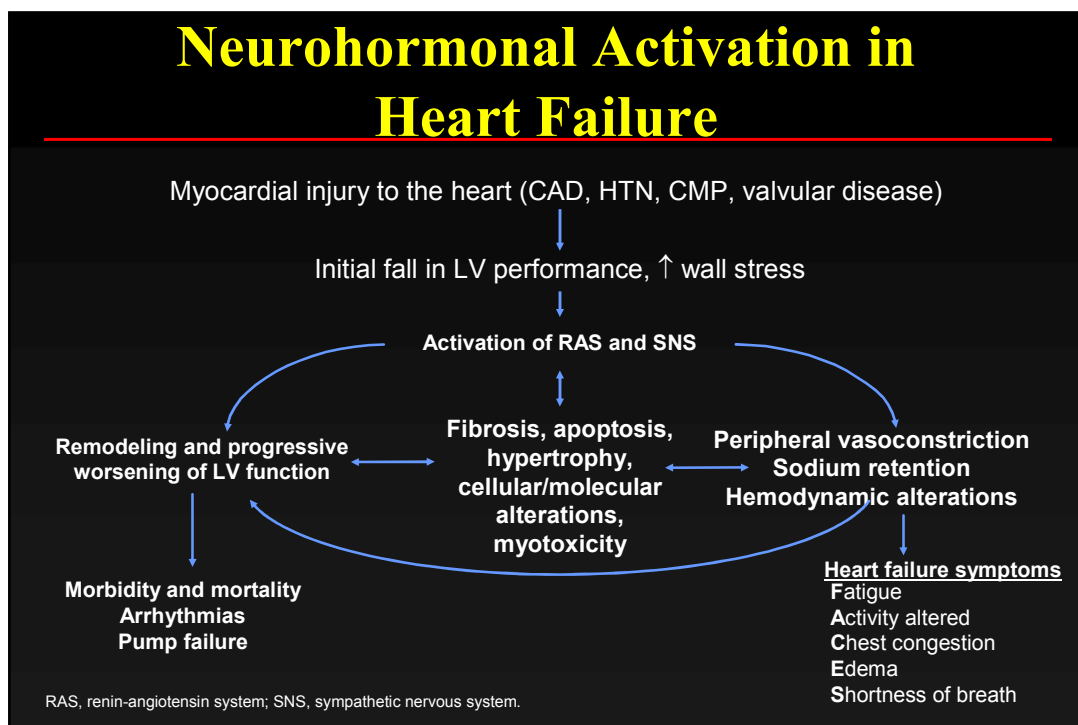
Pathophysiology - PV Loop



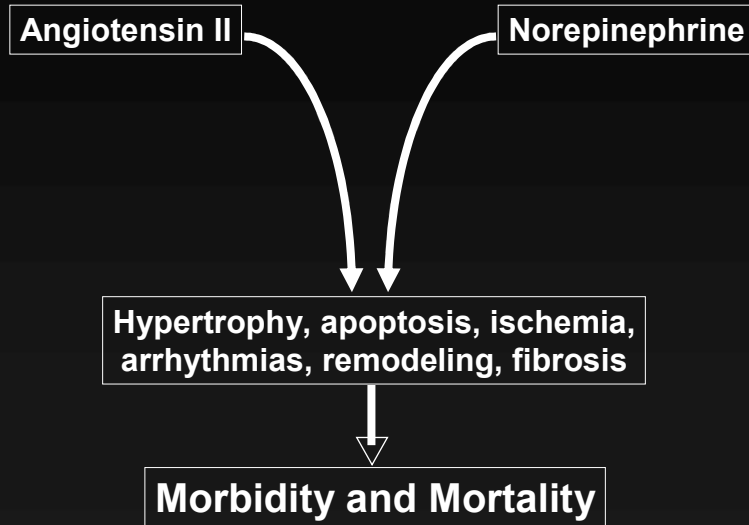
Pathophysiology of Heart Failure



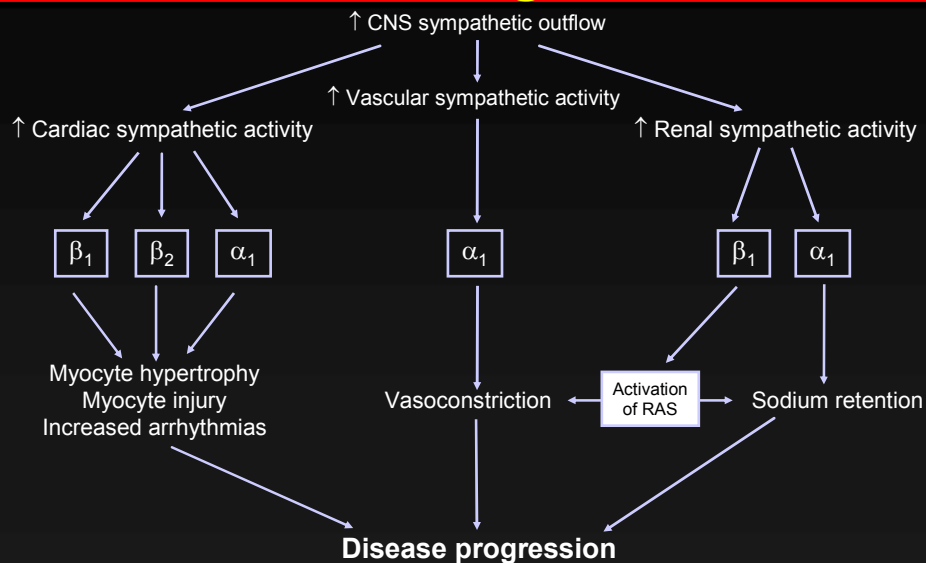
Neurohormonal Activation in Heart Failure



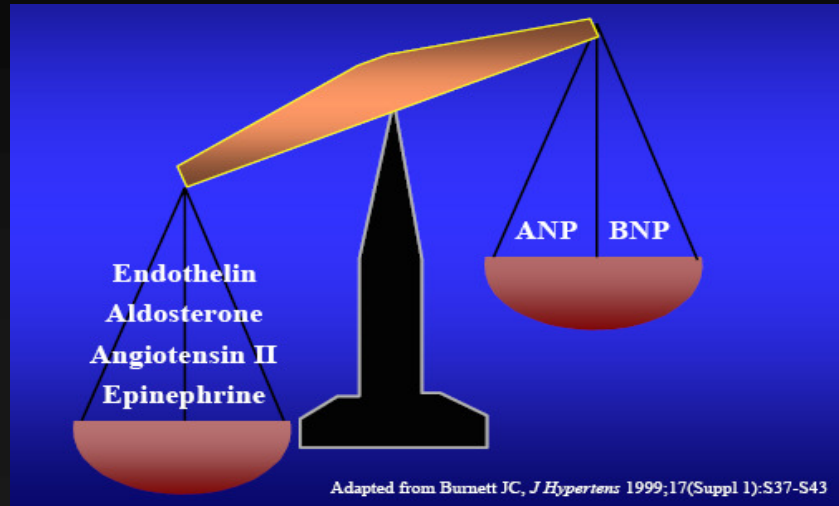
Neurohormonal Activation in Heart Failure



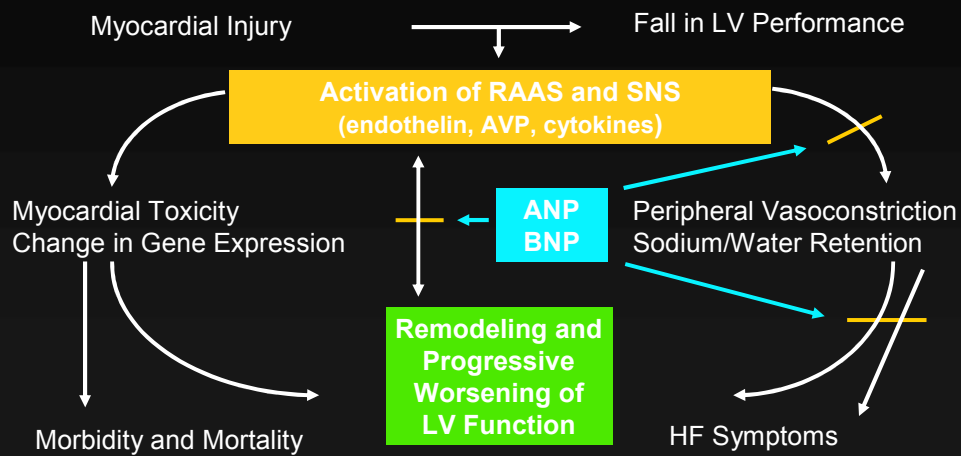
Adrenergic Pathway in Heart Failure Progression



Neurohormonal Balance in Heart Failure

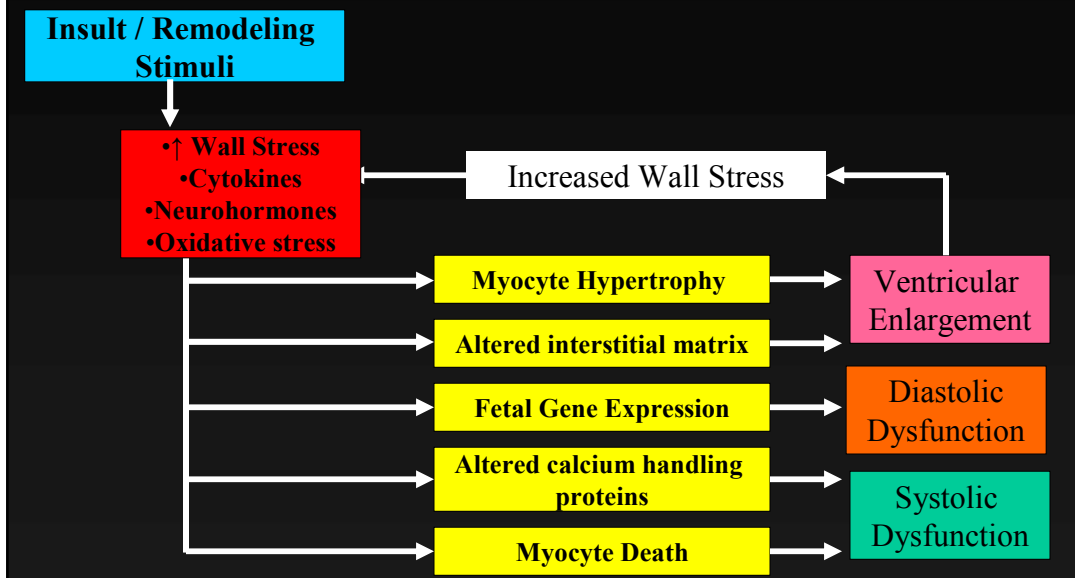


Neurohormones in Heart Failure



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

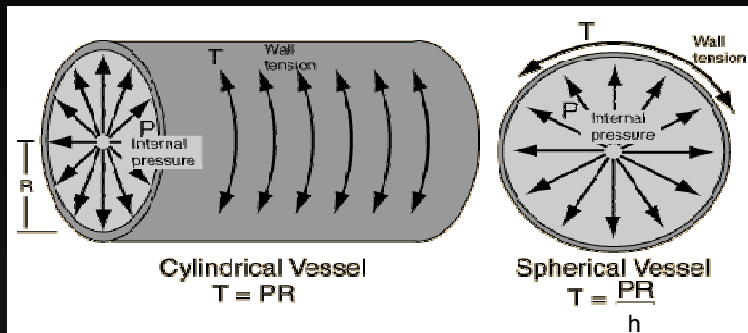
Pathophysiology of myocardial remodeling:



Acute and Chronic Responses – Benefits and Harm

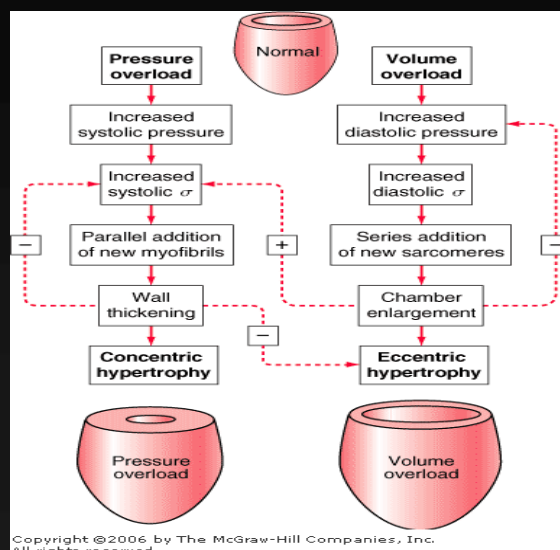
Response	Short-term Effects (mainly adaptive; hemorrhage, acute heart failure)	Long-term Effects (mainly deleterious; chronic heart failure)
Salt and water retention	Augments preload	Pulmonary congestion, anasarca
Vasoconstriction	Maintains pressure for perfusion of vital organs (brain, heart)	Exacerbates 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

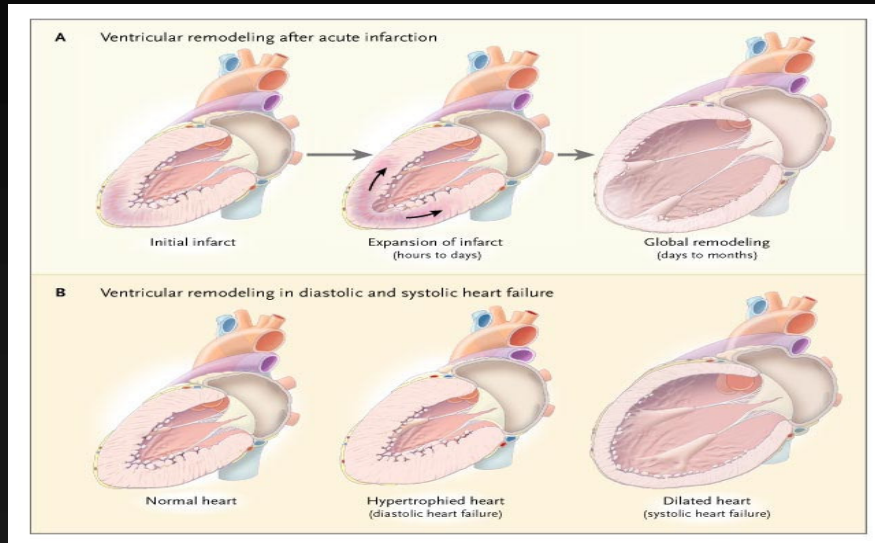


Where P = ventricular pressure, r = ventricular chamber radius and h = ventricular wall thickness

Remodeling – Concentric vs. Eccentric



Ventricular Remodeling

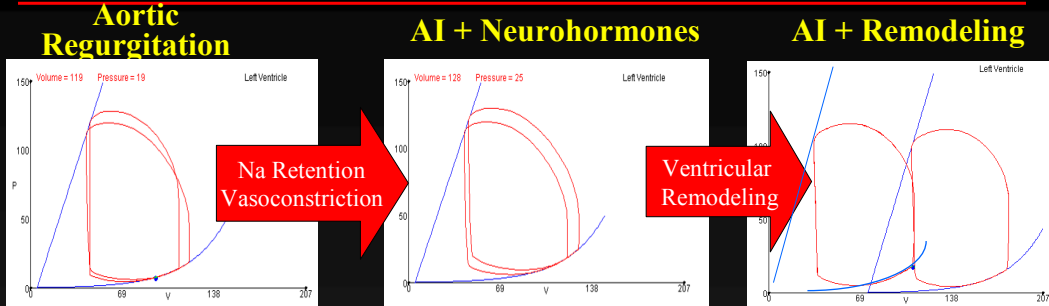


Pathophysiology of Heart Failure

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

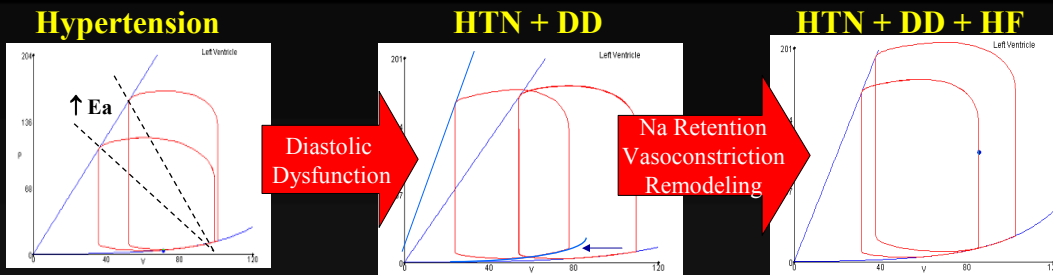


Etiologies

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

Parameter	Normal	AI	AI+Neuro-Hormones	AI + Remodeling
BP (mm Hg)	140/75	128/50	130/50	104/45
SV (ml)	64	80	82	63
Cardiac Output (L/min)	3.8	3.0	4.3	2.6
PCWP (mm Hg)	10	15	25	20

Increased Afterload

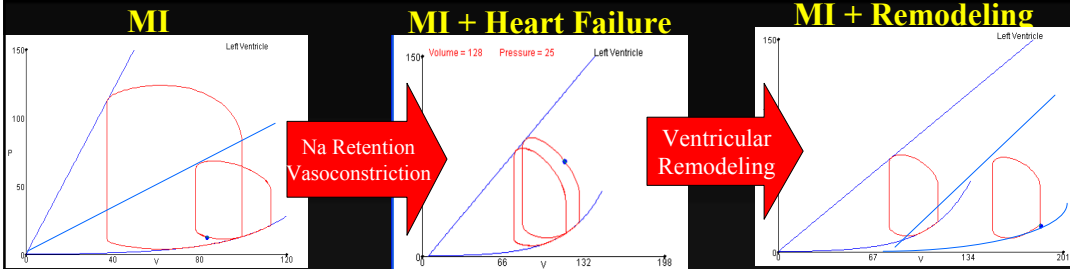


Etiologies

- Aortic Stenosis
- Aortic Coarctation
- Hypertension

Parameter	Normal	HTN	HTN + DD	HTN + Heart failure
BP (mm Hg)	131/76	150/100	140/92	161/105
SV (ml)	57	52	49	57
Cardiac Output (L/min)	4.0	3.6	3.4	4.0
PCWP (mm Hg)	10	10	13	23

Decreased Contractility

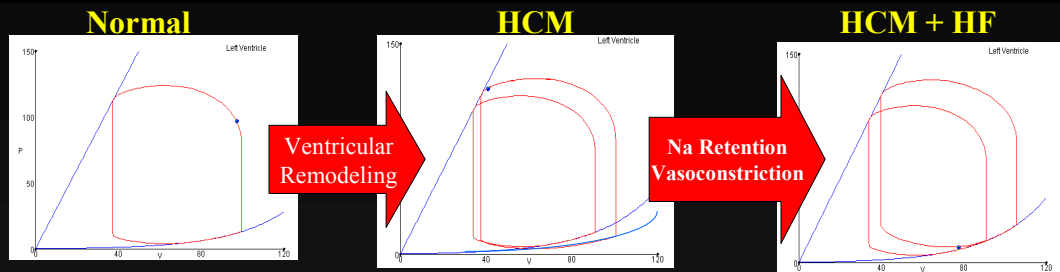


Etiologies

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

Parameter	Normal	MI	MI + Neurohormones	MI + Remodeling
BP (mm Hg)	124/81	80/40	90/54	87/44
SV (ml)	60	42	46	46
Cardiac Output (L/min)	4.2	3.0	3.2	3.2
PCWP (mm Hg)	12	17	25	23

Decreased Filling



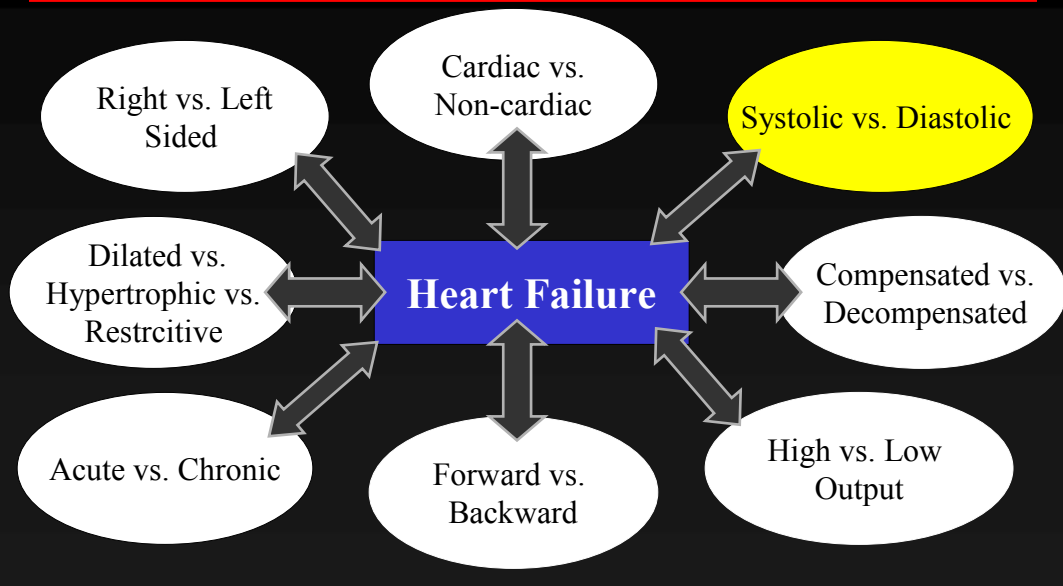
Etiologies

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


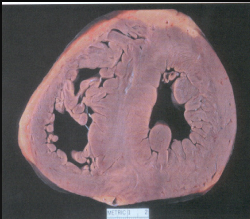
Parameter	Normal	HCM	HCM + HF
BP (mm Hg)	124/81	95/47	105/53
SV (ml)	63	50	55
Cardiac Output (L/min)	4.4	3.5	3.8
PCWP (mm Hg)	10	17	26

Part II

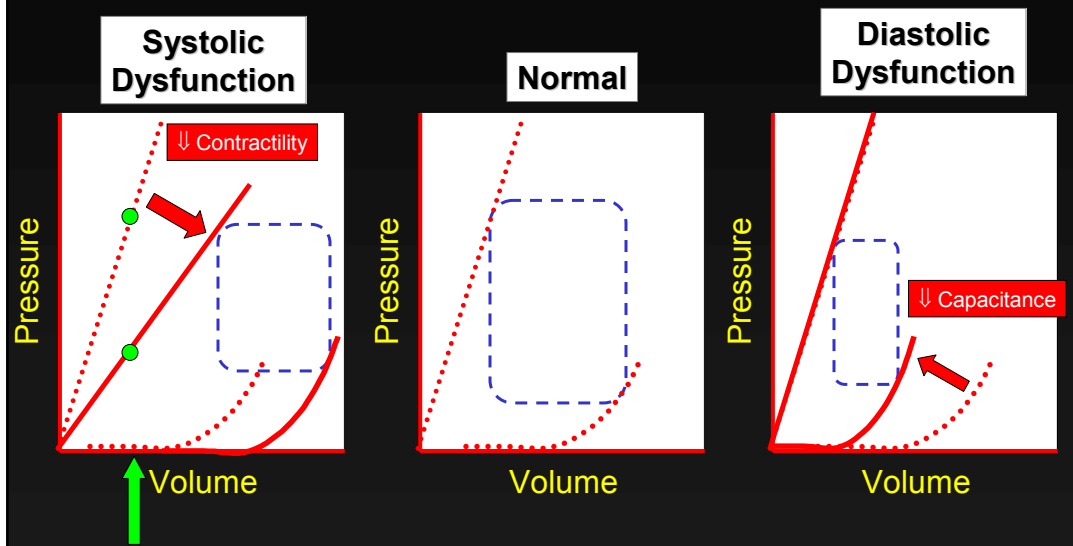
Heart Failure: Classifications



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



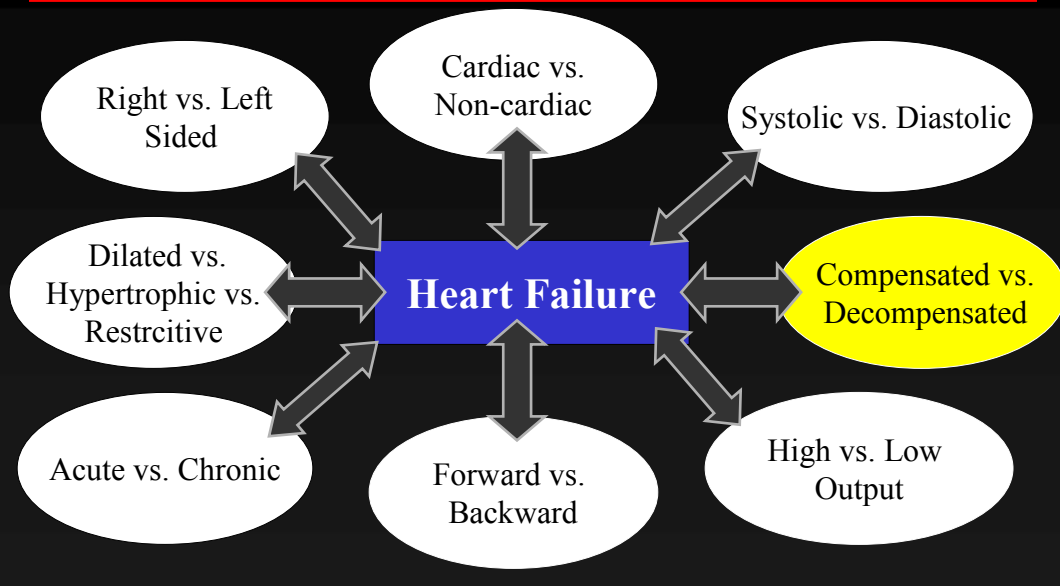
Systolic Versus Diastolic Failure

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



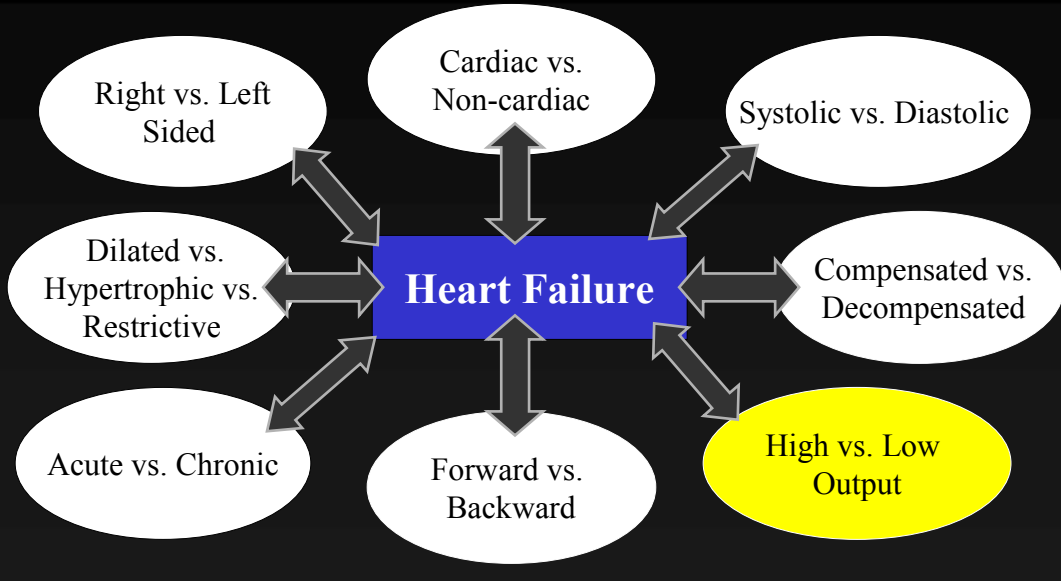
Decompensated Heart Failure

		Congestion at Rest?	
		No	Yes
Low Perfusion at Rest?	No	Warm and Dry A	Warm and Wet B
	Yes	Cold and Dry L	Cold and Wet C

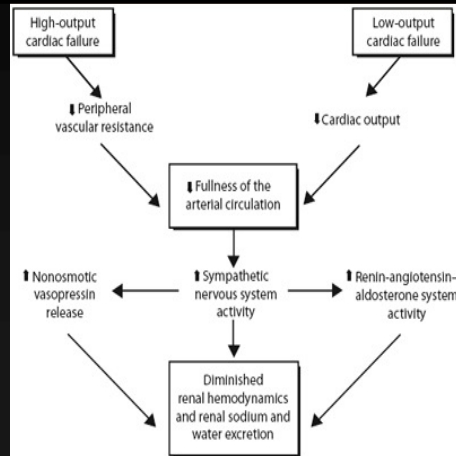
Evidence for Low Perfusion
 Narrow Pulse Pressure
 Pulsus Alterations
 Cool Forearms and Legs
 May Be Sleepy, Obtunded
 ACE Inhibitor-Related
 Symptomatic Hypotension
 Declining Serum Sodium Level
 Worsening Renal Function

Evidence for Congestion (Elevated Filling Pressure)
 Orthopnea
 High Jugular Venous Pressure
 Increasing S₃
 Loud P₂
 Edema
 Ascites
 Rales (Uncommon)
 Abdominojugular Reflux
 Valsalva Square Wave

Heart Failure: Classifications



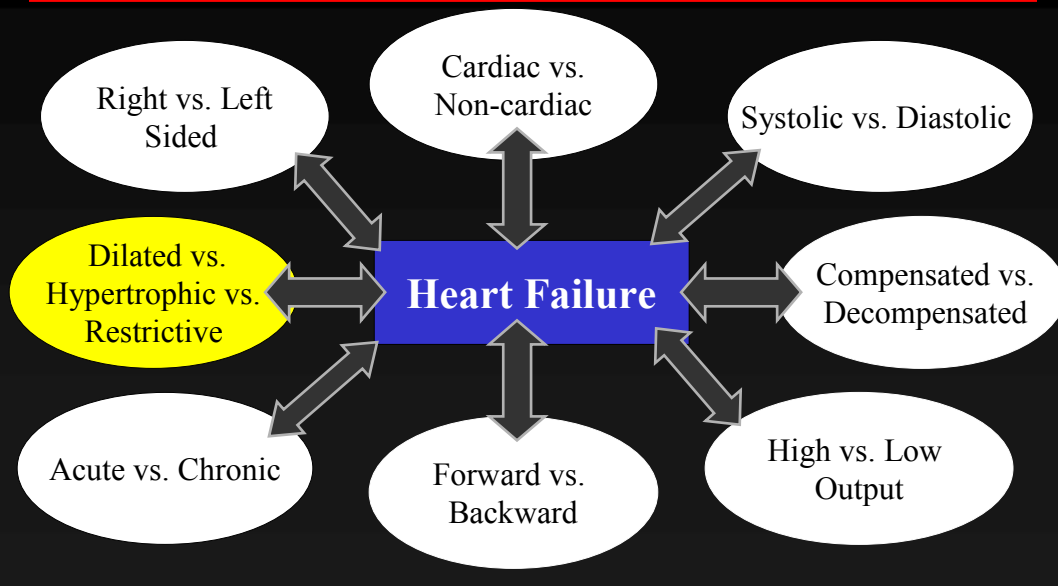
High vs. Low Output Failure



• 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

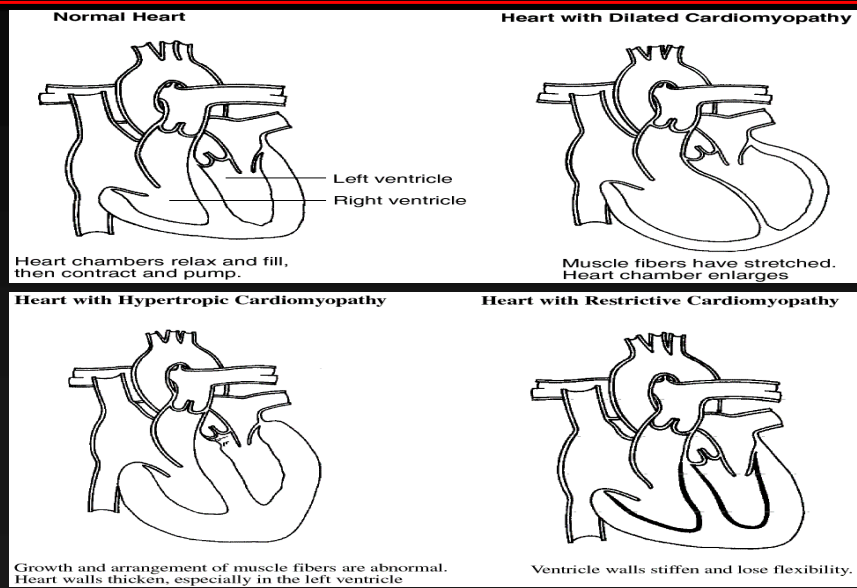
Heart Failure: Classifications



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

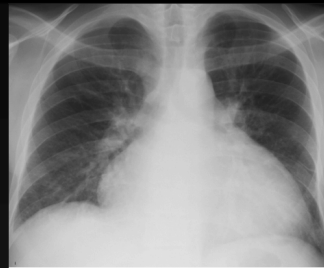
Symptoms

- 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	<ul style="list-style-type: none"> • No limitation of physical activity • No undue fatigue, palpitation or dyspnea
II	Mild	<ul style="list-style-type: none"> • Slight limitation of physical activity • Comfortable at rest • Less than ordinary activity results in fatigue, palpitation, or dyspnea
III	Moderate	<ul style="list-style-type: none"> • Marked limitation of physical activity • Comfortable at rest • Less than ordinary activity results in fatigue, palpitation, or dyspnea
IV	Severe	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none">• Hypertension• Coronary artery disease• Diabetes mellitus• Family history of cardiomyopathy
B	Asymptomatic heart failure	<ul style="list-style-type: none">• Previous myocardial infarction• Left ventricular systolic dysfunction• Asymptomatic valvular disease
C	Symptomatic heart failure	<ul style="list-style-type: none">• Known structural heart disease• Shortness of breath and fatigue• Reduced exercise tolerance
D	Refractory end-stage heart failure	<ul style="list-style-type: none">• 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.

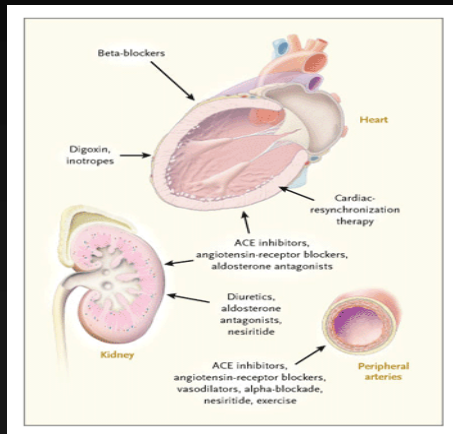
Etiologies

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

Precipitants /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



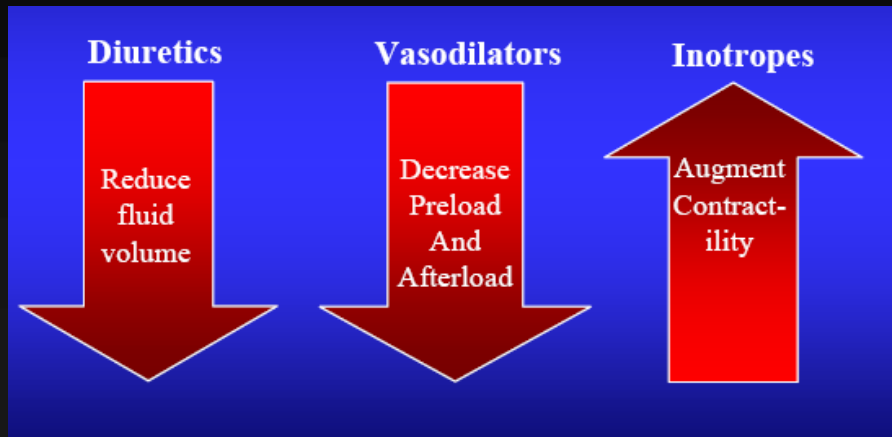
Standard Pharmacological Therapy

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

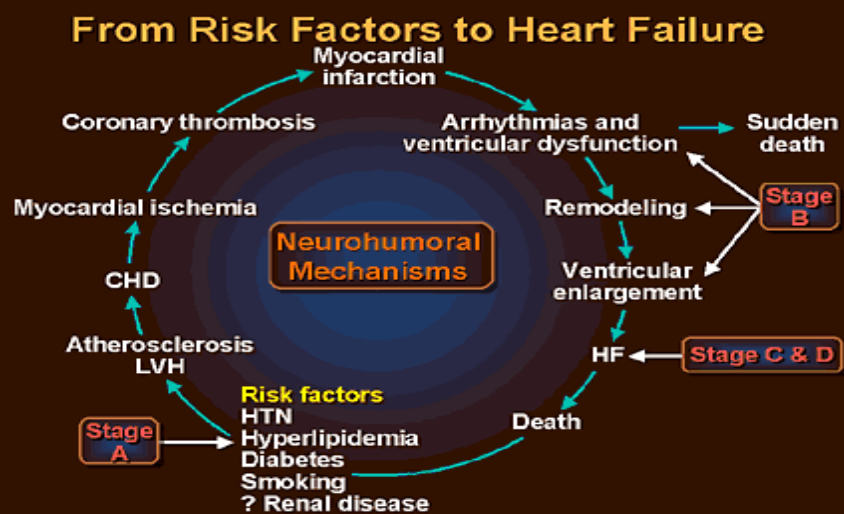
Treatment

	Stage	Patient Treatment
A	High risk for developing heart failure	<ul style="list-style-type: none"> • Optimal pharmacologic therapy (OPT) • Aspirin, ACE inhibitors, statins, b-blockers, a-b-blockers (carvedilol) diabetic therapy
B	Asymptomatic heart failure	<ul style="list-style-type: none"> • OPT • ICD if left ventricular (LV) dysfunction (systolic) present
C	Symptomatic heart failure	<ul style="list-style-type: none"> • OPT • ICD if LV dysfunction (systolic) present • CRT (if QRS wide, LVEF≤35%)
D	Refractory end-stage heart failure	<ul style="list-style-type: none"> • OPT • Intermittent IV inotropes • ICD as a bridge to transplantation • CRT • 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/>