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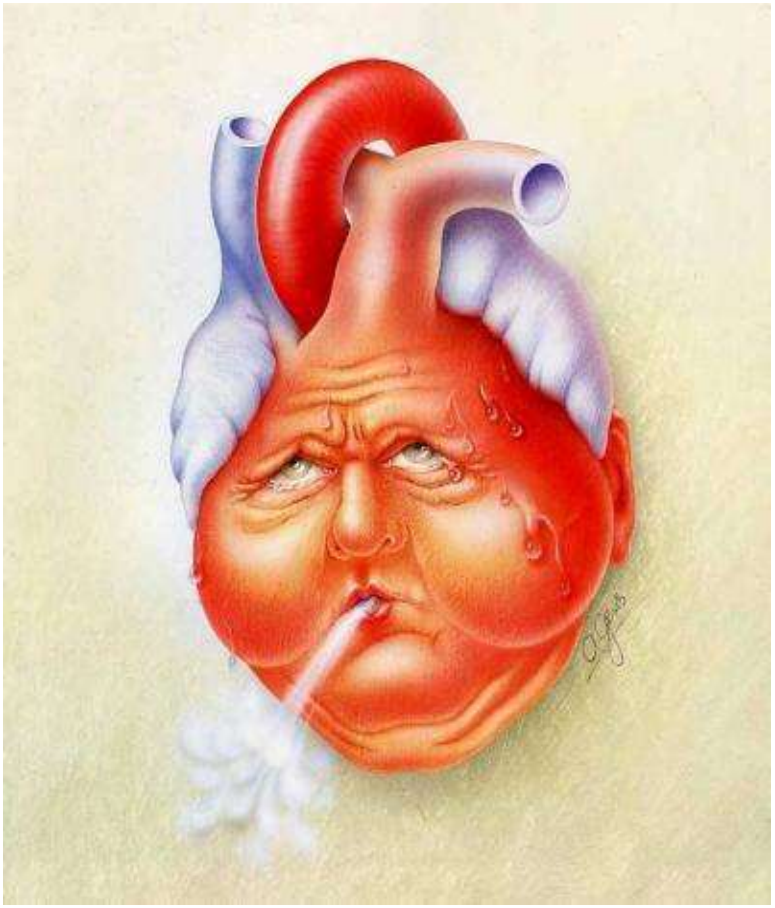
Part 1: Chronic Heart Failure

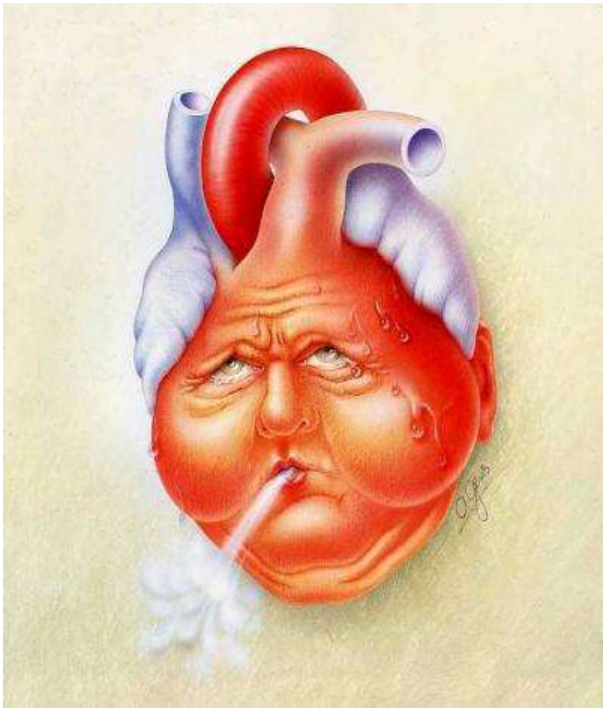


Karen Kopacek, M.S., R.Ph.
Associate Professor (CHS)
Spring 2021

Objectives for Part 1

- Explain the pathophysiology of HF with reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF).
- Define the components that affect cardiac output.
- Describe the main compensatory mechanisms that lead to HF.
- List the symptoms of congestion and hypoperfusion.
- Review the classification and stages of HF.

HF Part 1

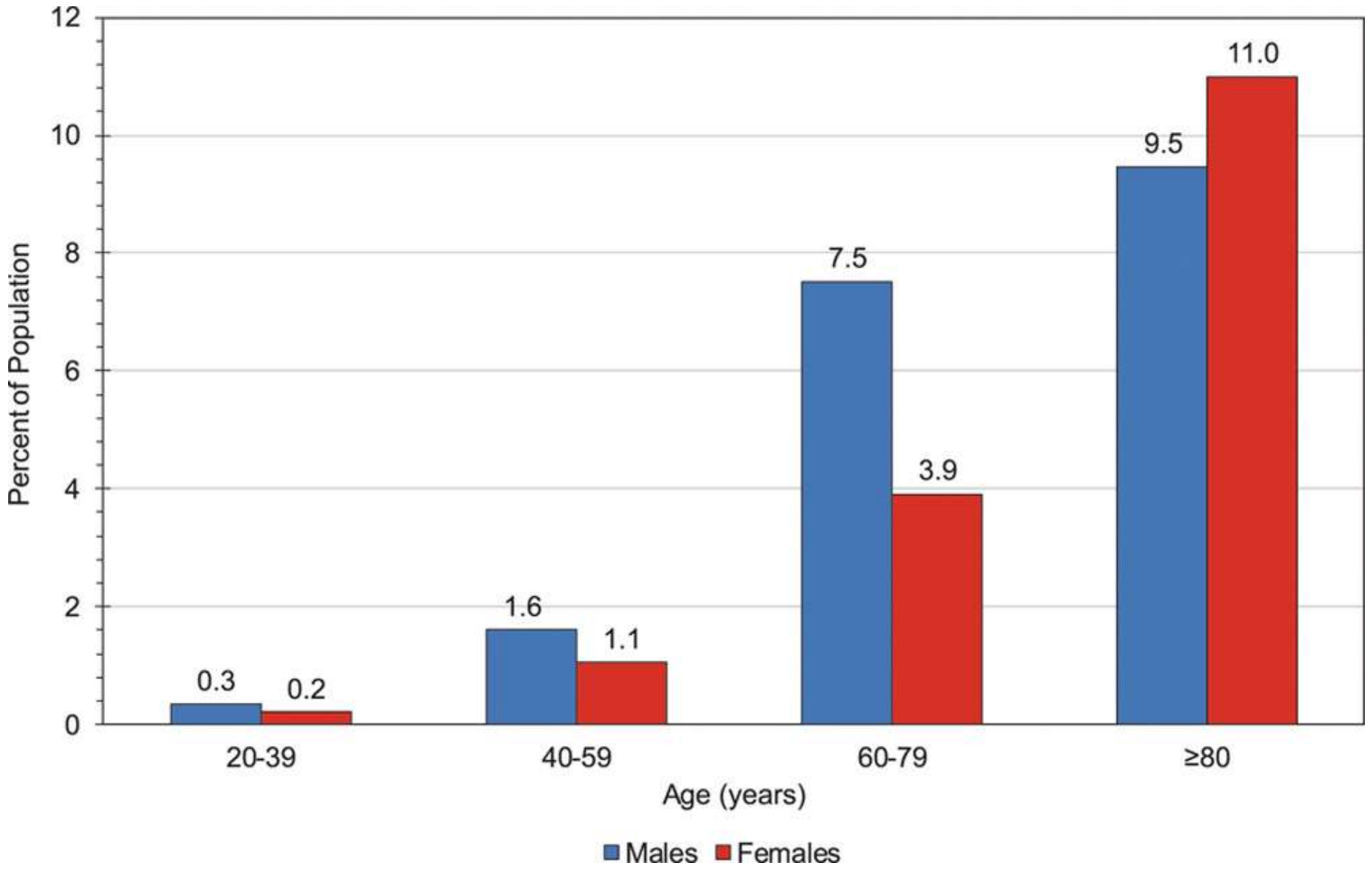


- **Statistics**
- Definitions
- Risk Factors
- Compensatory Mechanisms
- Symptoms of HF
- Classification and Staging
- Patient Case

HF Statistics 2021

- Estimated 6 M Americans ≥ 20 years have HF (~2.5%)
  - By 2030, prevalence will be > 8 M Americans
  - 1 M new cases diagnosed each year
  - AA have highest risk of developing HF, followed by Hispanic, Caucasian, and Chinese Americans
  - Lifetime risk for HF increases with higher BP and BMI at any age
- Common cause of hospitalization and 30-day readmission in the US
  - Incidence: 11.6/1000 people per yr; recurrent 6.6/1000 per yr
- Mortality: 83,616 patients died in 2018 from HF
  - 1-year HF mortality rate 29.6%
  - 5-year HF mortality rate ~ 50%
- Total cost for HF ~ $30.7 B in 2012; by 2030, cost will increase to $69.8 B

Prevalence of HF in Adults
(NHANES: 2015-2018)



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Heart Disease and Stroke Statistics- 2021 Update

Why is HF incidence so high?

- Baby boomer generation is aging
  - By 2040, people >/= 75 years will increase to 77.2M
- HF is a progressive condition amendable to preventive interventions at early stages
  - Better treatment of HTN and CHD
  - Patients surviving CV events
  - Valvular disease is a treatable disorder
- Patients are being identified earlier

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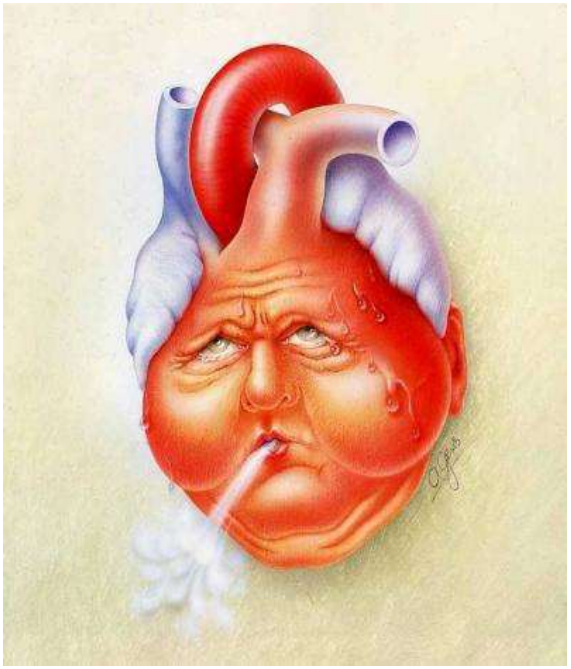
HF Part 1



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Etiology of Cardiomyopathy

CM defined as a group of diseases that negatively affect the heart muscle

1. Ischemic CM
   - CHD is cause in 67% of HF population
   - MI or other event
2. Non-ischemic CM
   - Prolonged HTN (70%), valvular disorders (regurgitation and stenosis), endocrine disorders (thyroid), pregnancy, viral illness, chemotherapy, alcohol or illicit drug use
3. Idiopathic CM
   - Unknown

Regardless of the initial cause, the resulting pathophysiology is the SAME.

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ACC/AHA Guideline Update for the Evaluation and Management of Chronic Heart Failure in the Adult. 2013.

Working Definition of HF

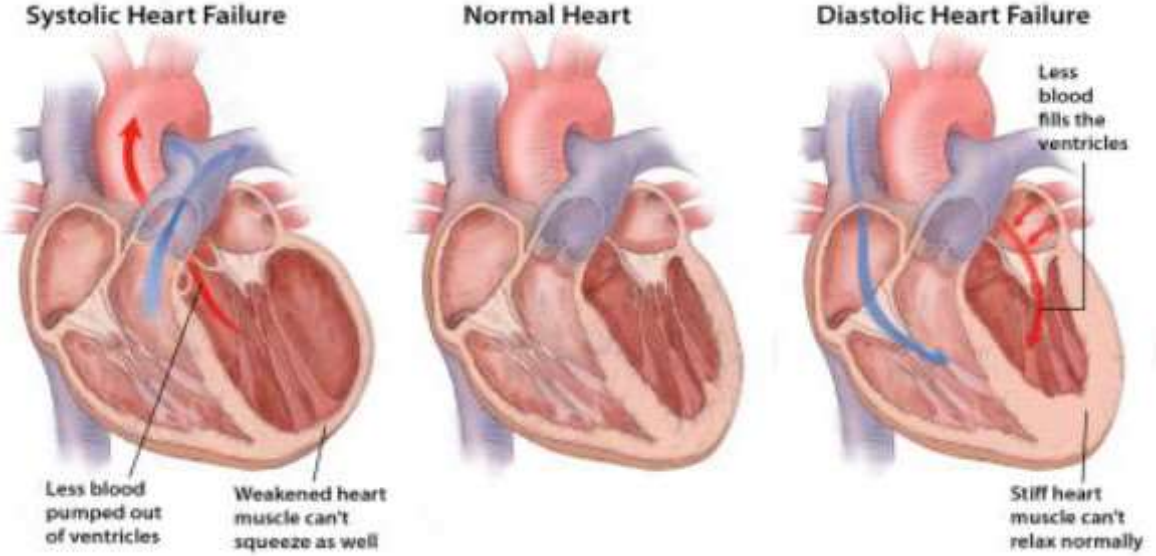
- HF: complex and progressive clinical syndrome characterized by a constellation of symptoms and signs caused by a structural or functional cardiac disorder that impairs the ability of the heart to generate a cardiac output sufficient to meet the body's demand.
  - Disorders of pericardium, myocardium, endocardium, or great vessels; most due to left ventricular dysfunction
- Result is impairment in ventricular filling (diastolic failure) or loss of pumping capacity to eject blood (systolic failure)

HF Definition Continued

- **HF*r*EF: EF < 40% (systolic dysfunction)**
- **HF*p*EF: EF > 50% (diastolic dysfunction)**

Inability to pump

Inability to fill



Both phenotypes have decreased SV and CO that leads to failure!

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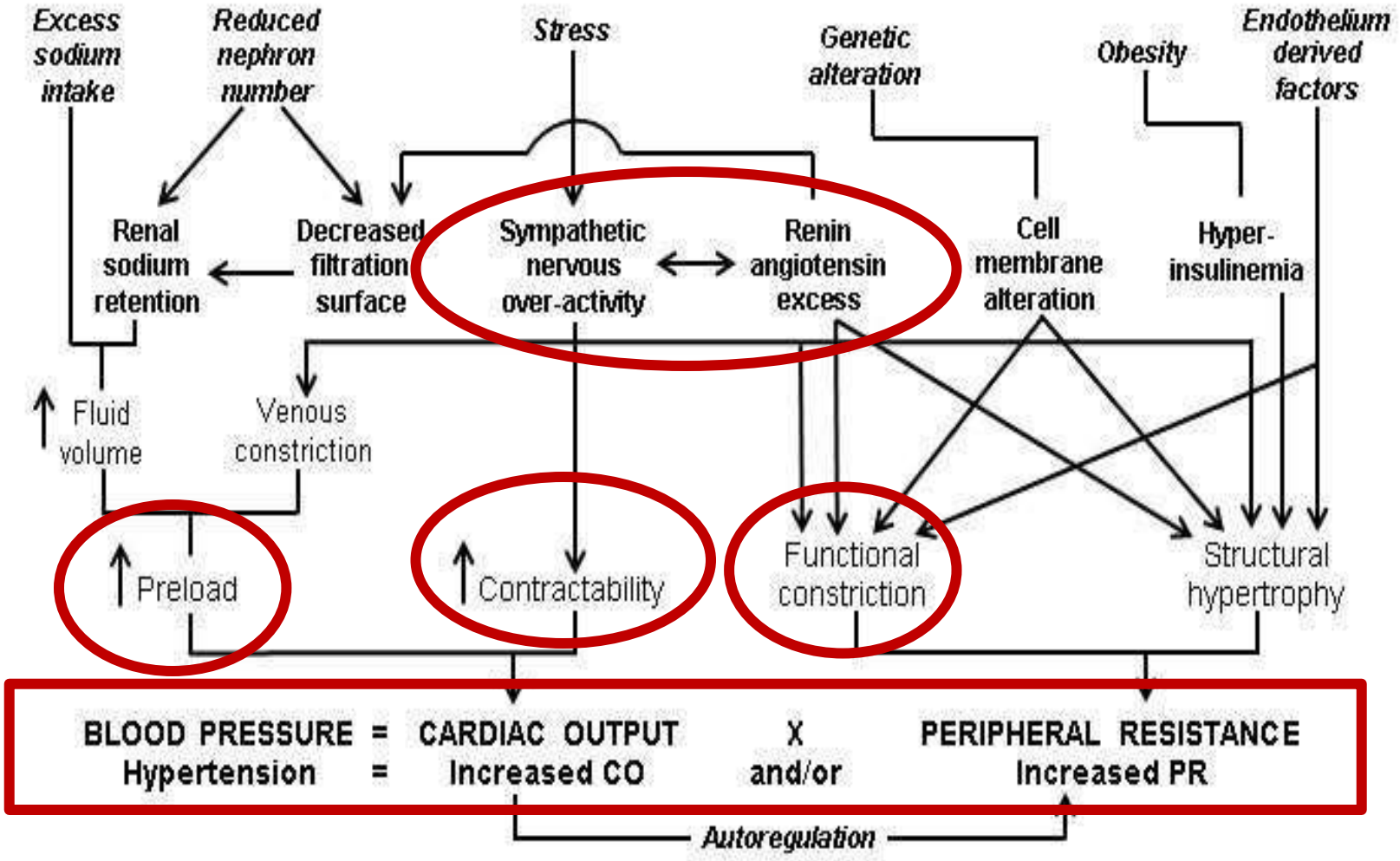
BP Pathophysiology

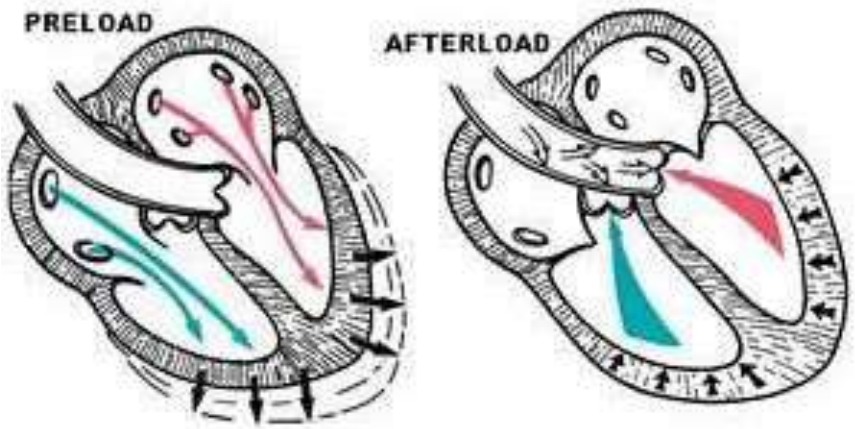
Adapted from Clinical Hypertension 6th Edition, Figure 3.1



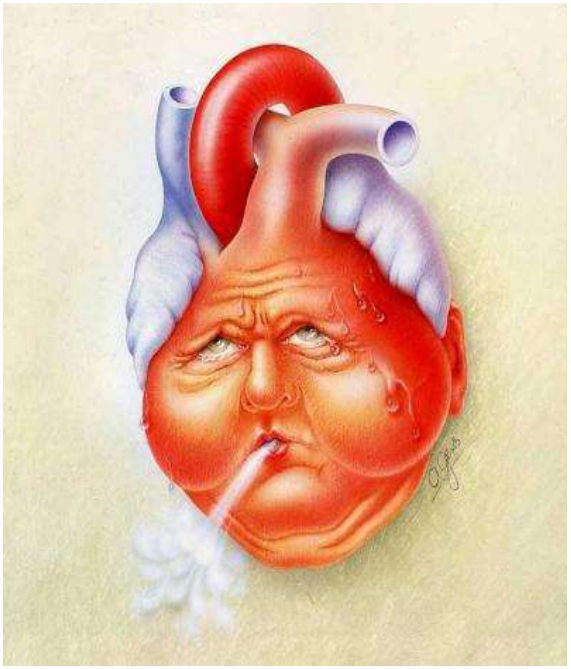
CO = HR x SV (SV determined by preload, afterload, contractility)

HF Definitions Continued

- Preload: measure of ventricular filling pressure, or volume of blood in left ventricle (LVEDP)
  - Determined by venous return and atrial contraction
- Afterload: resistance to ventricular ejection
  - Determined by ejection impedence, wall tension, regional wall geometry



HF Part 1



- Statistics
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- **Risk Factors**
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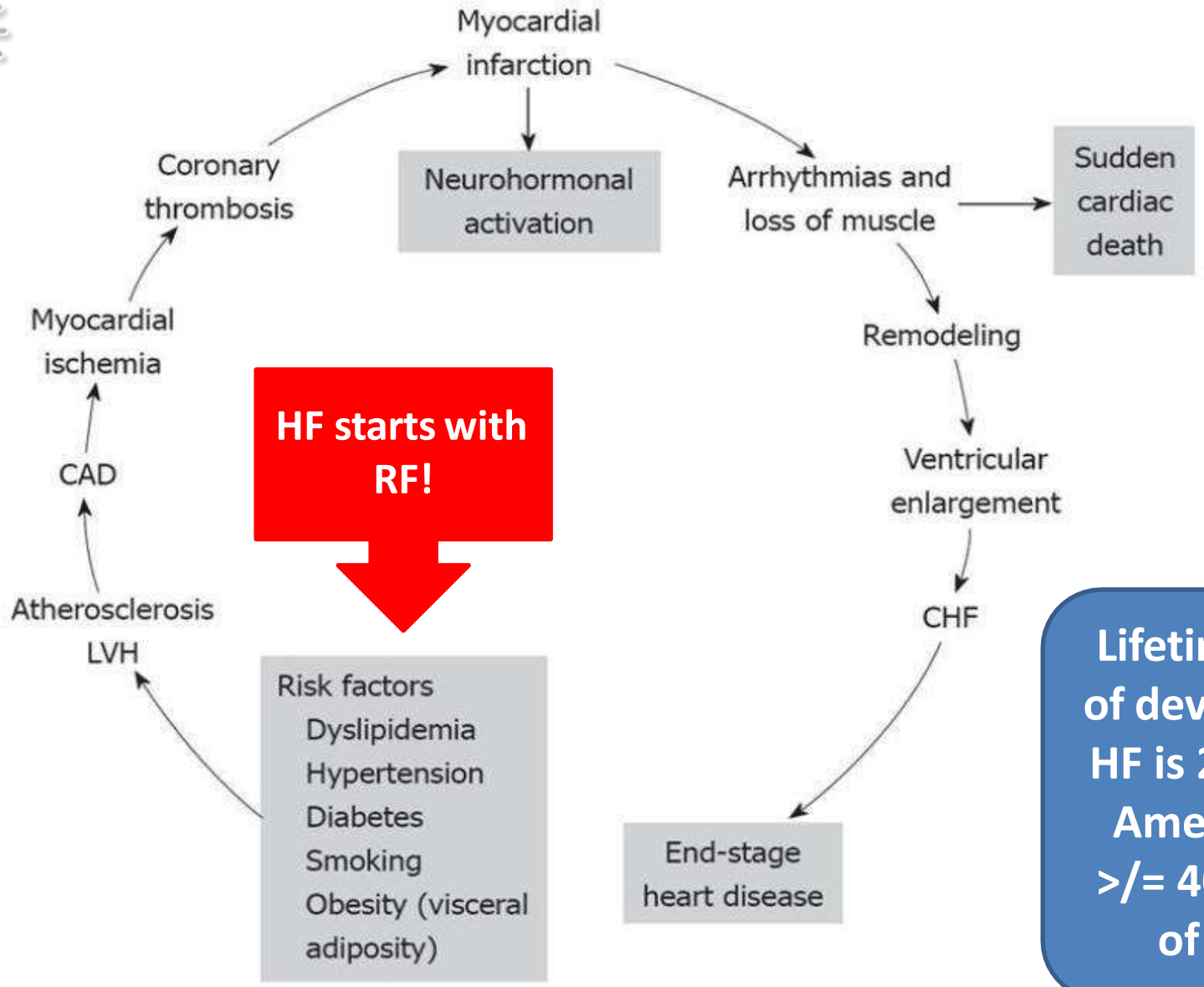
Risk Factors for HF in the CV Continuum



Dzau et a. Am Heart J 1991;121:1244

Lifetime risk of developing HF is 20% for Americans >/= 40 years of age

Differences in HF

HFrEF

- ~ 50% of all pts with HF
- Decreasing prevalence
- Improving survival rate
- RF: CHD, HTN, valvular heart disease (aortic or pulmonic), toxins (alcohol, chemotherapy, cocaine), viral infections (HIV), peripartum, pulmonary hypertension

HFpEF

- ~50% of all pts with HF
- Increasing prevalence due to increasing age and rate of obesity
- Highest risk: elderly, women
- Other RF: HTN, DM, A fib, CHD, renal insufficiency, valvular heart disease (mitral or tricuspid)
- No improvement in survival rate
- Have more co-morbidities; non-cardiac causes of death more common

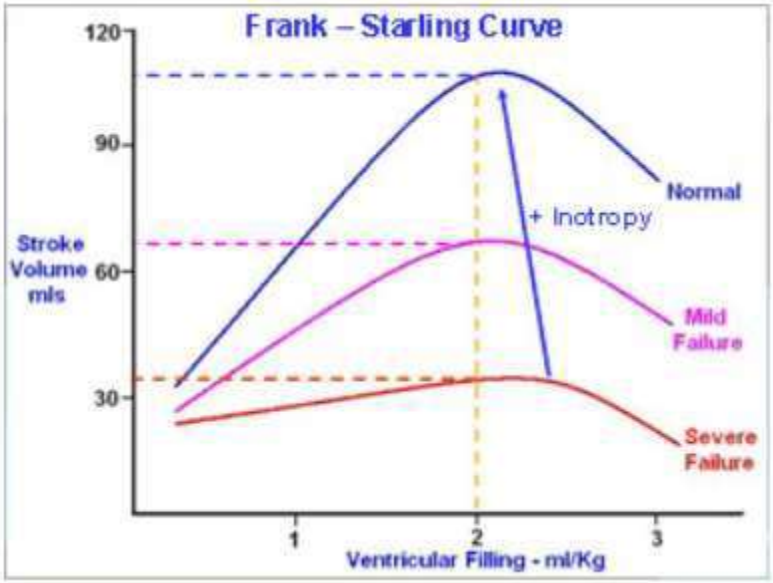
HF Part 1

- Statistics
- Definitions
- Risk Factors
- **Compensatory Mechanisms**
  1. Preload and Frank-Starling Mechanism
  2. Tachycardia and increased afterload
  3. Cardiac hypertrophy and remodeling
  4. Natriuretic peptides
- Symptoms of HF
- Classification and Staging
- Patient Case

Compensatory Mechanism #1
Preload & Frank-Starling Mechanism

- Body responds to decreased contractility and CO by decreasing blood flow to periphery to maintain perfusion for the heart and brain
- Drop in blood flow leads to decreased renal perfusion, kidneys responds by activating the renin-angiotensin-aldosterone system (RAAS)
- Aldosterone causes sodium and water retention to increase preload
- This increase in preload **in normal hearts** leads to stretch of sarcomeres, increase in cross-bridges formed between actin & myosin for increased force of contraction (inotropy)
- **Diseased hearts** are unable to adapt to the increase in preload, leading to further decrease in CO

Frank-Starling Law

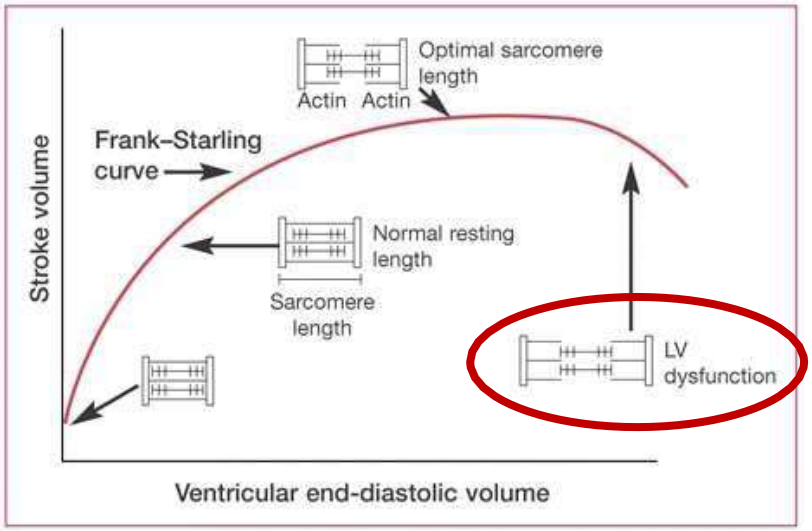


1.The more forcefully cardiac muscle is stretched within physiologic limits, the more forcefully it will contract (inotropy).

2.Increased blood volume in the ventricles increases the stretch and thus the force generated by ventricular wall contraction.

3. Greater stretch means more blood volume is pumped out, up to its physical limits.

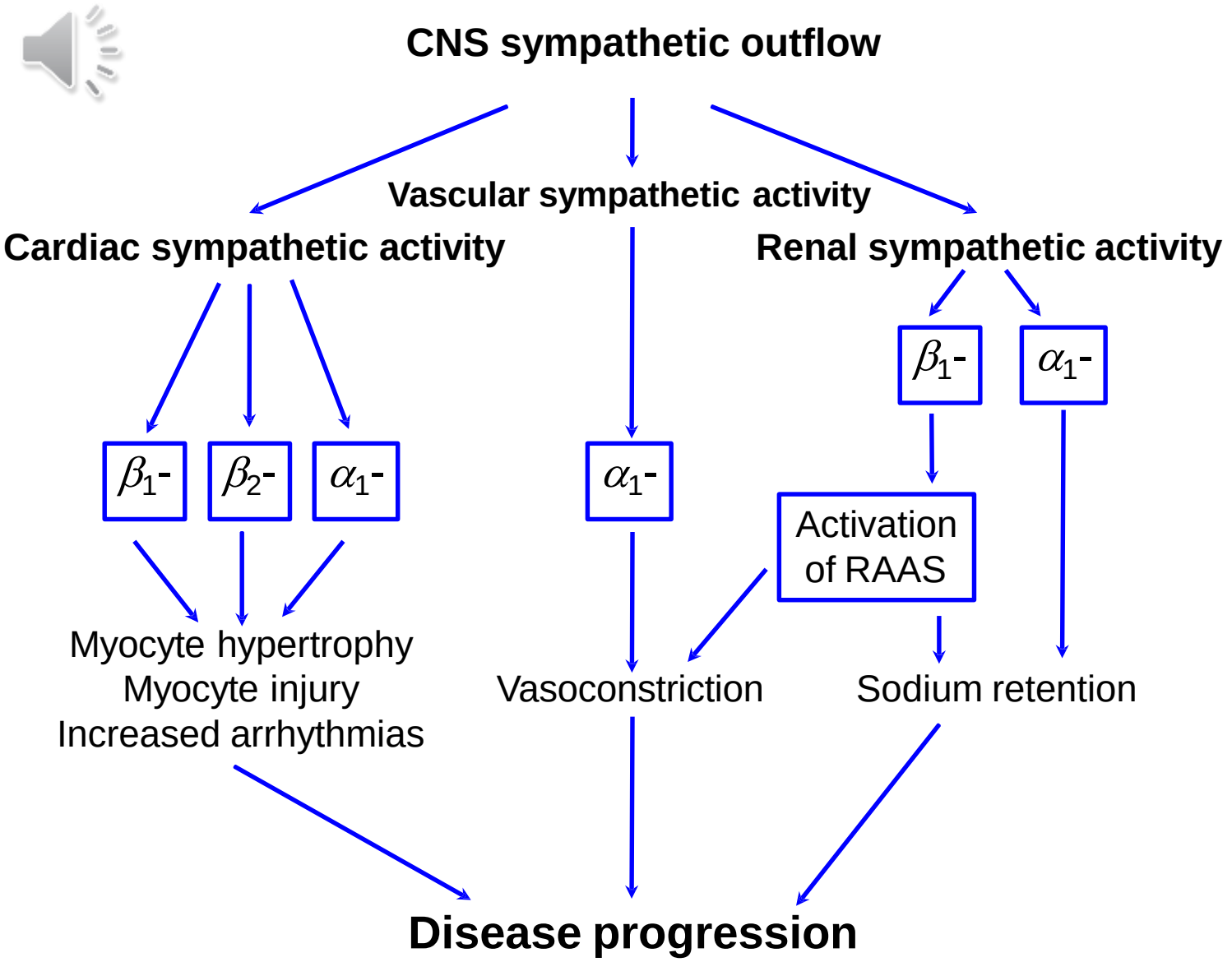
3. However, failing hearts reach a point where further stretching does not lead to increased force of contraction with increased blood volume. Thus force of contraction declines, as does CO.



Compensatory Mechanism #2 Tachycardia and Increased Afterload

- Decreased contractility and CO also results in activation of sympathetic nervous system (SNS) to increase HR through β receptors
- Increased HR leads to increased myocardial oxygen demand and worsening ischemia
- Both RAAS and SNS cause vasoconstriction which increases afterload and impairs forward blood ejection from ventricles

Adrenergic Pathway in HF Progression



Compensatory Mechanism #3 Cardiac Hypertrophy and Remodeling

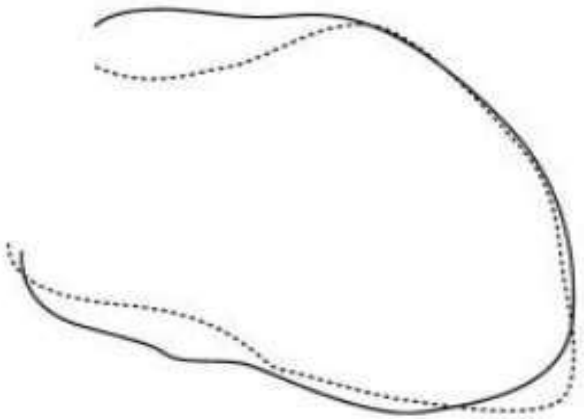
- Angiotensin II leads to myocyte growth in response to volume and pressure overload
  - Helps reduce cardiac wall stress short term, increases oxygen demand and accelerates cell death
- Remodeling (caused by neurohormones) leads to changes in myocardial and extracellular matrix composition and function
  - Results in structural and functional alterations to the heart

Relation of Neurohumoral Activation to Development and Reversal of Remodeling

Relatively normal chamber size and geometry[1]

Myocyte dysfunction
Structural alteration

Cardiac adrenergic
RAAS signaling



Remodeled Ventricle[1]

Improved function
Reverse remodeling

ACE I, Ald antagonists, and β-blocker therapy[2]

2. Burnett JC Jr. *J Hypertens.* 1999;17(suppl 1):S37–S43

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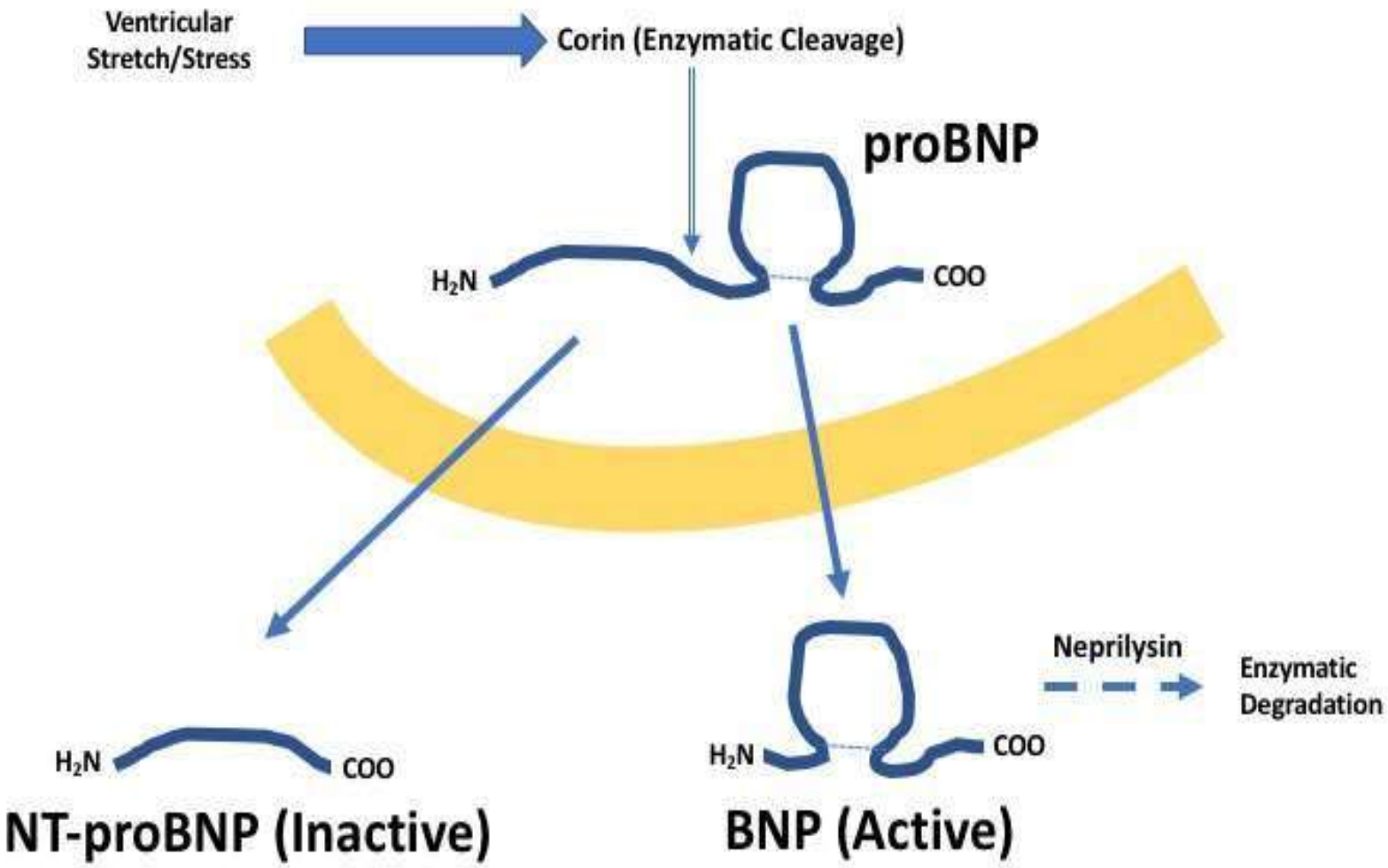
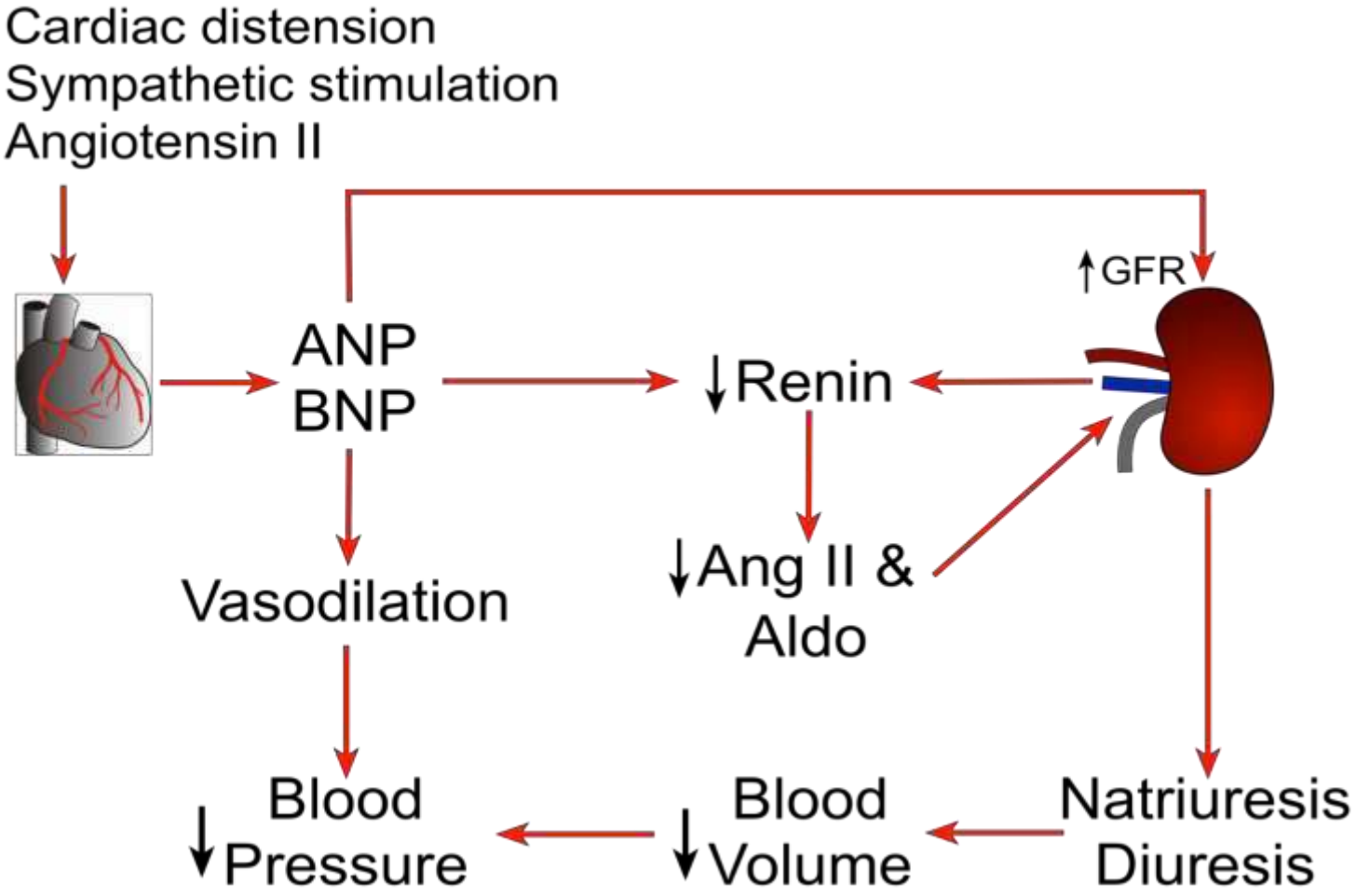
1. Cohn JN et al. *J Am Coll Cardiol.* 2000;35:569–582.

Compensatory Mechanism #4
Natriuretic Peptides



Natriuretic Peptides Continued



Summary: Effects of Compensatory Mechanisms in HF

Compensatory Response	Beneficial Effects of Compensation	Detrimental Effects of Compensation
Increased Preload (sodium and water retention)	Optimize SV via Frank-Starling mechanism	• Pulmonary and systemic congestion and edema • Increased myocardial oxygen demand
Vasoconstriction	• Maintain BP in face of reduced CO • Shunt blood from non-essential organs to brain and heart	• Increased myocardial oxygen demand • Increased afterload decreases SV and further activates the compensatory responses

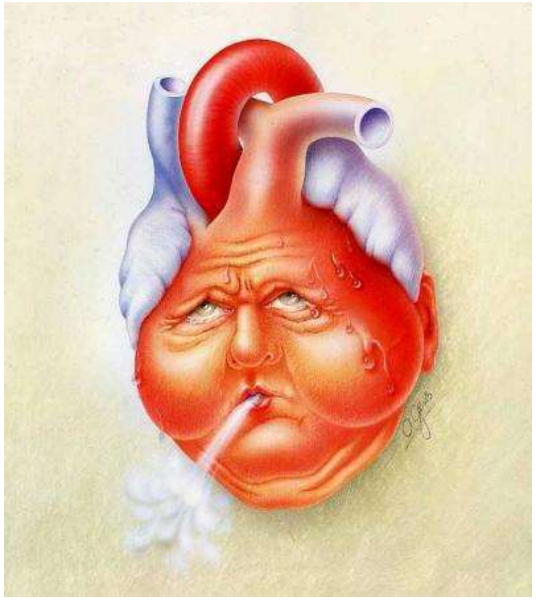
Summary: Effects of Compensatory Mechanisms in HF

Compensatory Response	Beneficial Effects of Compensation	Detrimental Effects of Compensation
Tachycardia and increased contractility (due to SNS activation)	Helps maintain CO	• Increased myocardial oxygen demand • Shortens diastolic filling time • Beta receptor downregulation, decreased receptor sensitivity • Precipitation of ventricular arrhythmias • Increased risk of myocardial cell death

Summary: Effects of Compensatory Mechanisms in HF

Compensatory Response	Beneficial Effects of Compensation	Detrimental Effects of Compensation
Ventricular hypertrophy and remodeling	• Helps maintain CO • Reduces myocardial wall stress • Decreases myocardial oxygen demand	• Diastolic dysfunction • Systolic dysfunction • Increased risk of myocardial cell death • Increased risk of myocardial ischemia • Increased risk of arrhythmias • Fibrosis

HF Part 1



- Statistics
- Definitions
- Risk Factors
- Compensatory Mechanisms
- **Symptoms of HF**
  - **Pulmonary**
  - **Periphery**
  - **Kidneys**
- Classification and Staging
- Patient Case

Clinical Symptoms- Pulmonary

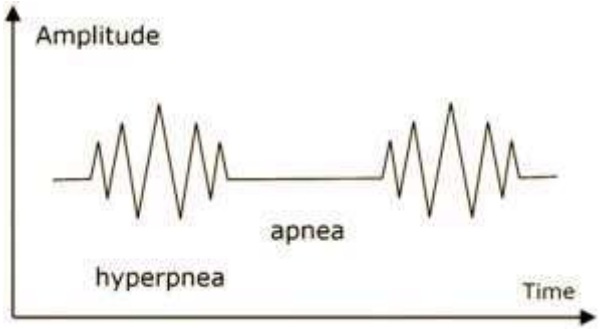
- **Dyspnea (SOB)**
  - SOB with exertion, or uncomfortable awareness of breathing with exertion
  - Lower level of activity causes breathlessness
  - Activities: climbing stairs, carrying groceries, walking a particular distance
  - Severity of HF inversely proportional to amount of activity required to produce SOB
- **Orthopnea**
  - Pulmonary congestion and dyspnea in supine position
  - Measured by # of pillows/angle required for comfortable rest (or elevating head of the bed)

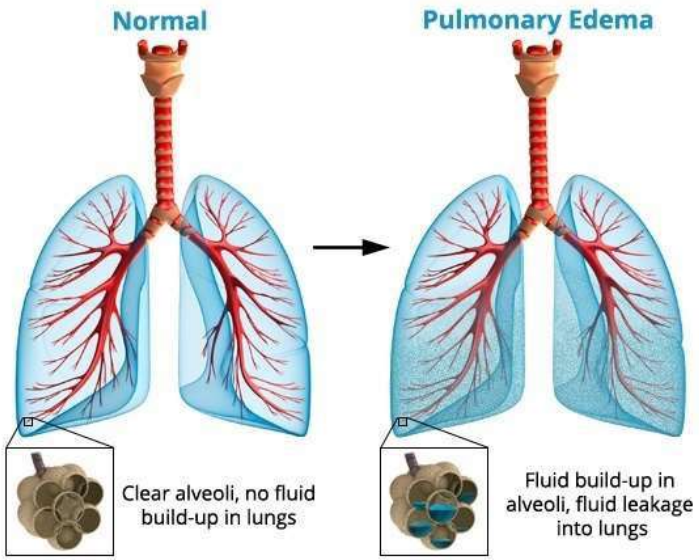
Clinical Symptoms- Pulmonary Continued

- **Paroxysmal Nocturnal Dyspnea (PND)**
  - Sudden awakening from sleep due to cough/ wheezing ("cardiac asthma")
  - Occurs within 1-4 hours of sleep
  - May persist after moving to upright position (unlike orthopnea)
- **Cough**
  - Usually non-productive, occurs at night or with exertion, caused by pulmonary congestion

Clinical Symptoms- Pulmonary Continued

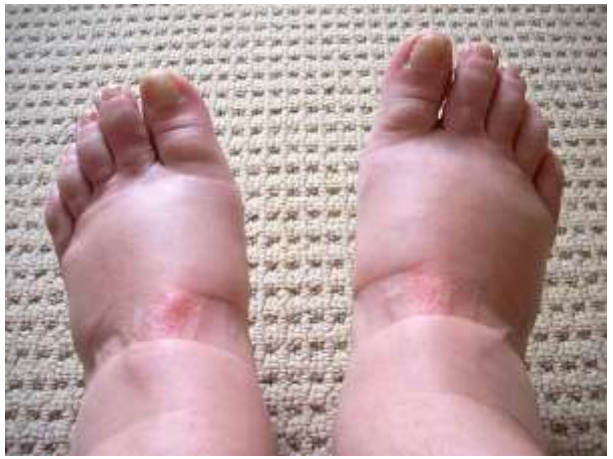
- **Cheyne-Stokes respiration**
  - Rapid breathing followed by apnea, common in advanced HF
- **Pulmonary edema**
  - From pulmonary congestion
  - May produce pink, frothy sputum
  - Feel extremely breathless

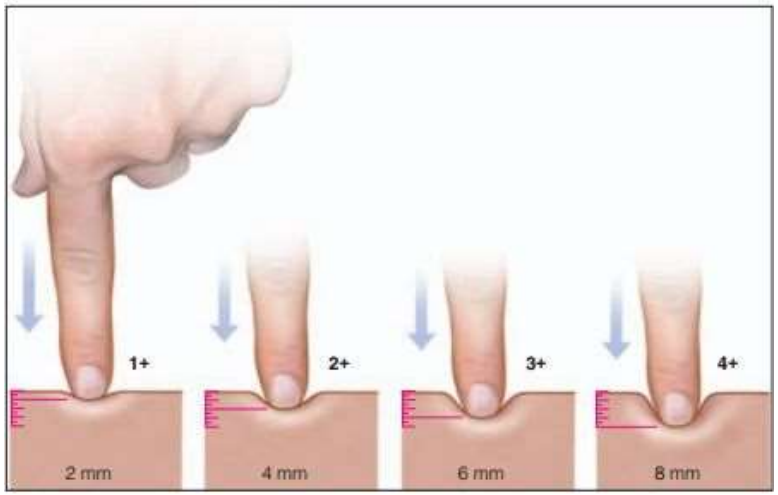




Clinical Symptoms- Periphery

- **Peripheral edema**
  - Tight shoes or clothing
  - Pitting edema scale
- **Gut edema**
  - Secondary to congested liver/portal venous system; edema of gut wall
  - Includes abdominal fullness, nausea, bloating, early satiety, reduced appetite, ascites





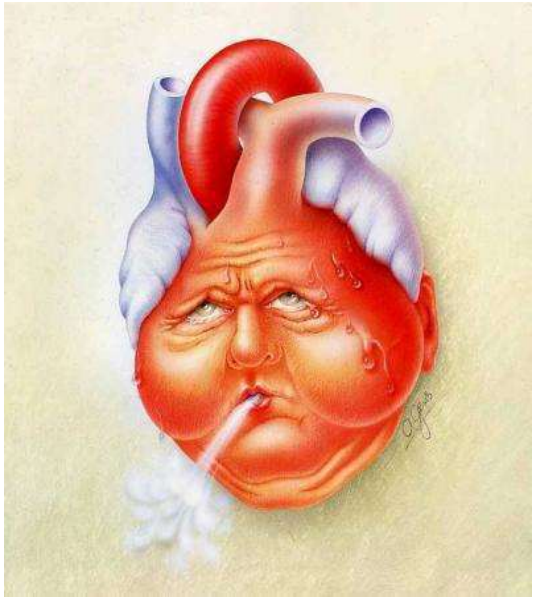
Clinical Symptoms- Peripheral Hypoperfusion

- **Decreased perfusion to CNS leads to:**
  - Confusion, hallucinations, insomnia, lethargy
- **Decreased perfusion to periphery leads to:**
  - Cool extremities
- **Decreased perfusion to skeletal muscle leads to:**
  - Fatigue
- **Decreased perfusion to kidneys leads to:**
  - Drop in GFR, increase SCr

Clinical Symptoms- Kidneys

- **Polyuria (frequent urination)**
  - Increase release of natriuretic peptides due to volume overload
- **Nocturia (nighttime urination)**
  - Increased renal perfusion due to reduced SNS activity at night

HF Part 1



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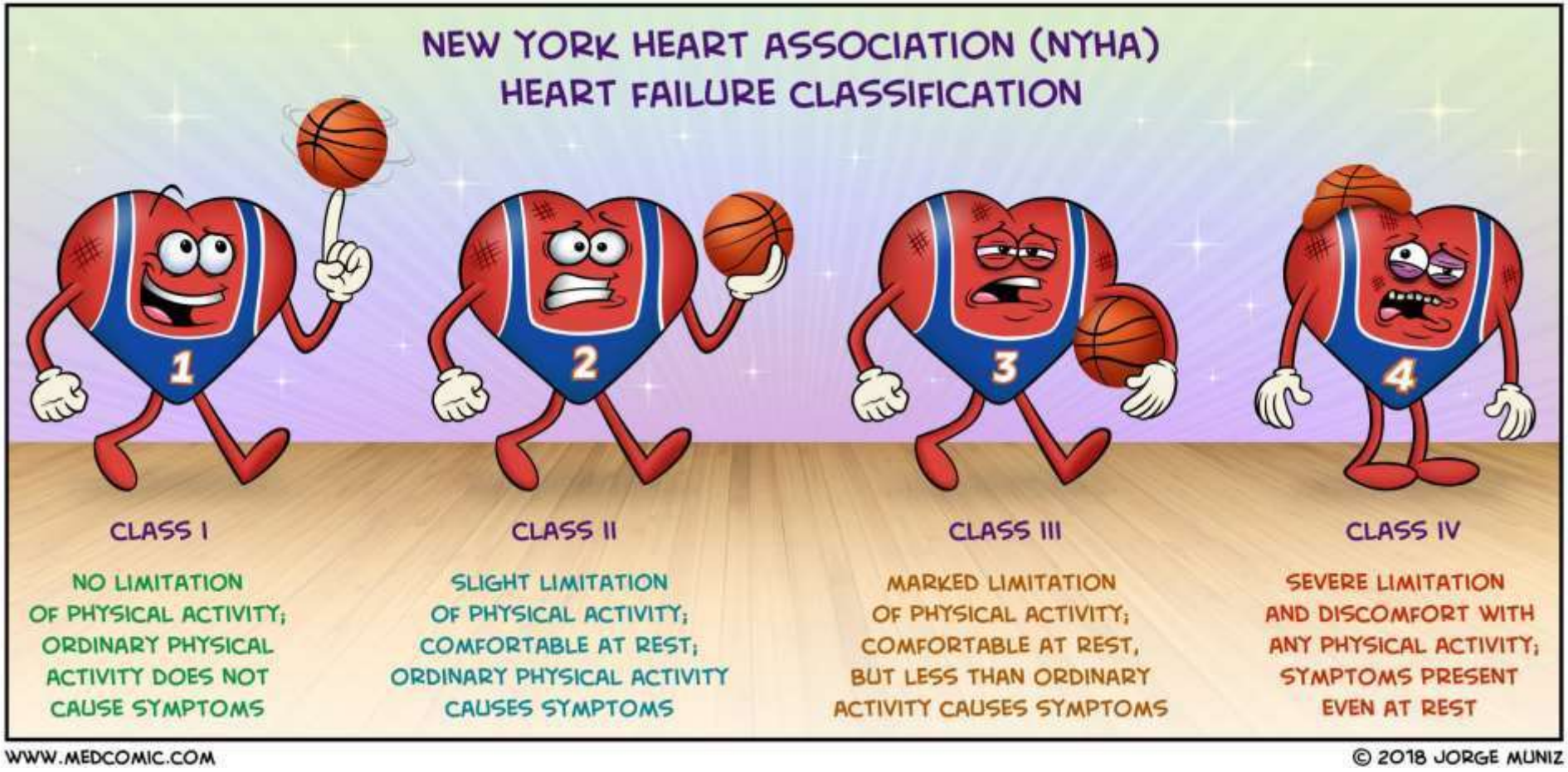
- **Classification and Staging**
  - **NYHA Functional Classification**
  - **ACC/AHA Staging of HF**
- Patient Case

New York Heart Association Functional Classification

Functional Class	Patient Limitations
Class I	• **No limitation** • Ordinary physical activity does not cause excess fatigue, SOB, palpitations
Class II	• **Slight limitation of physical activity** • Patient comfortable at rest • Ordinary physical activity results in fatigue, SOB, palpitations, or angina

New York Heart Association Functional Classification

Functional Class	Patient Limitations
Class III	• **Marked limitation of physical activity** • Patient is comfortable at rest • Ordinary activities of daily living will lead to symptoms
Class IV	• **Severe limitation; symptomatic at rest** • Inability to carry on any physical activity without discomfort • Increased discomfort is experienced with any physical activity


NEW YORK HEART ASSOCIATION (NYHA)
HEART FAILURE CLASSIFICATION
1
2
3
4
CLASS I
NO LIMITATION OF PHYSICAL ACTIVITY; ORDINARY PHYSICAL ACTIVITY DOES NOT CAUSE SYMPTOMS
CLASS II
SLIGHT LIMITATION OF PHYSICAL ACTIVITY; COMFORTABLE AT REST; ORDINARY PHYSICAL ACTIVITY CAUSES SYMPTOMS
CLASS III
MARKED LIMITATION OF PHYSICAL ACTIVITY; COMFORTABLE AT REST, BUT LESS THAN ORDINARY ACTIVITY CAUSES SYMPTOMS
CLASS IV
SEVERE LIMITATION AND DISCOMFORT WITH ANY PHYSICAL ACTIVITY; SYMPTOMS PRESENT EVEN AT REST
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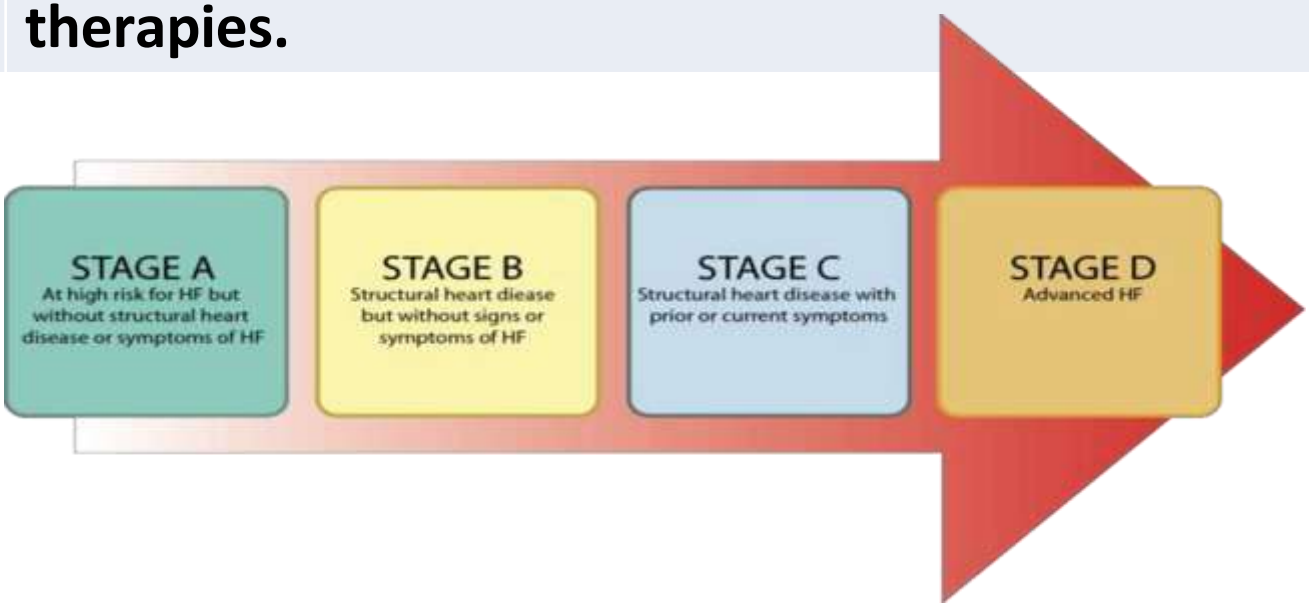
ACC/AHA Stages of HF

Stages	Description
Stage A (At risk for HF)	**Patient at high risk for HF but without current or prior s/sx of HF and without structural or biomarkers evidence of heart disease.** • Includes patients with HTN, CAD, obesity, DM, H/O drug or alcohol abuse, H/O rheumatic fever, FH of cardiomyopathy, and treatment with cardiotoxins.
Stage B (Pre-HF) Bozkurt B et al. J Cardiac Failure 2021; 27:387-413	**Patient without current or prior s/sx of HF, but with evidence of structural heart disease or abnormal cardiac function, or elevated BNP levels.** • Includes patients with previous MI, LV remodeling including LVH and low EF, and asymptomatic valvular disease.

ACC/AHA Stages of HF

Stages	Description
Stage C (HF)	**Patients with current or prior symptoms and/or signs HF caused by a structural and/or functional cardiac abnormality.**
Stage D (Advanced HF)	**Patients with severe s/sx HF at rest, recurrent hospitalizations despite GDMT, refractory or intolerant to GDMT, requiring advanced therapies.**



Bozkurt B et al. J Cardiac Failure 2021; 27:387-413

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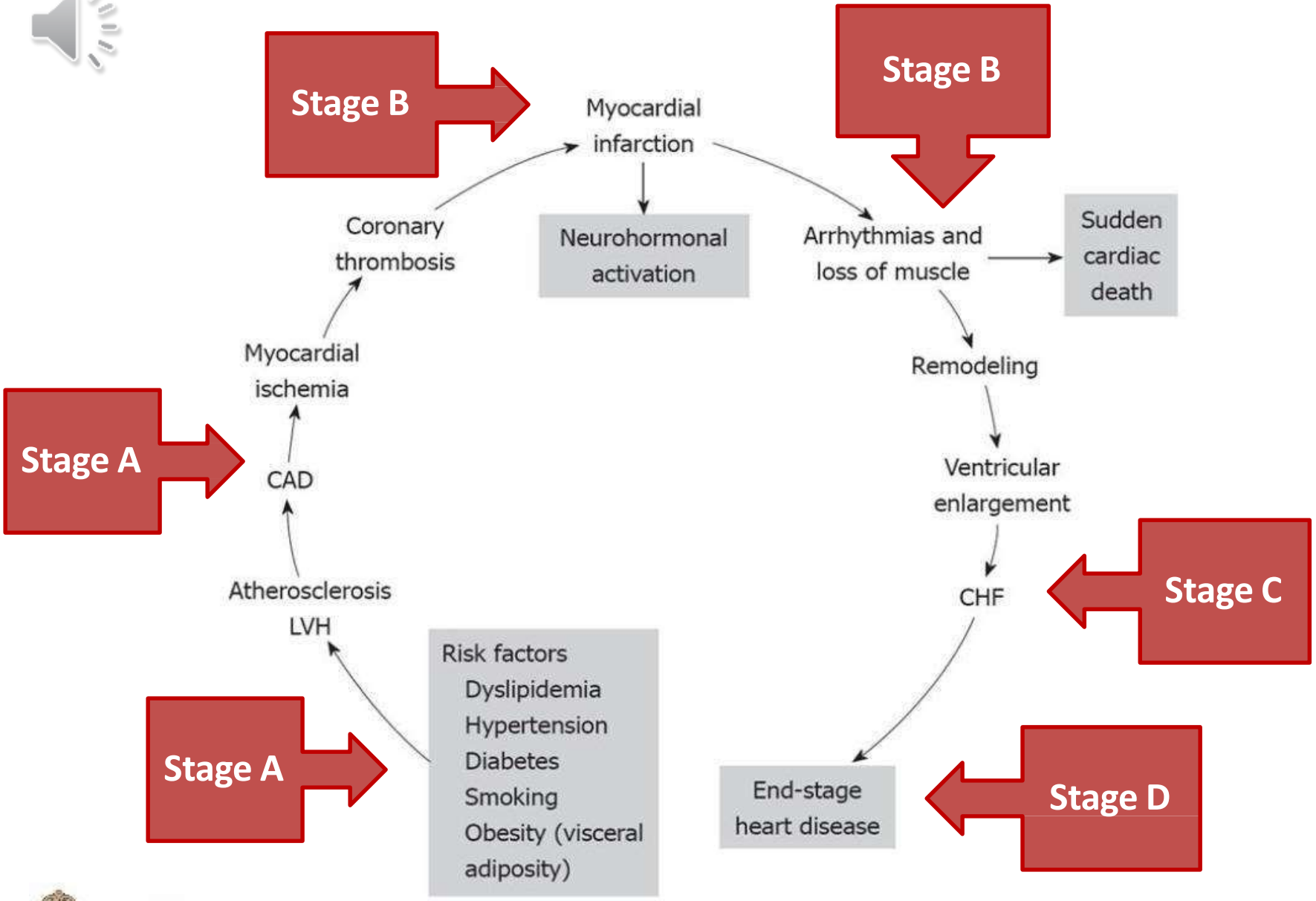
FYI

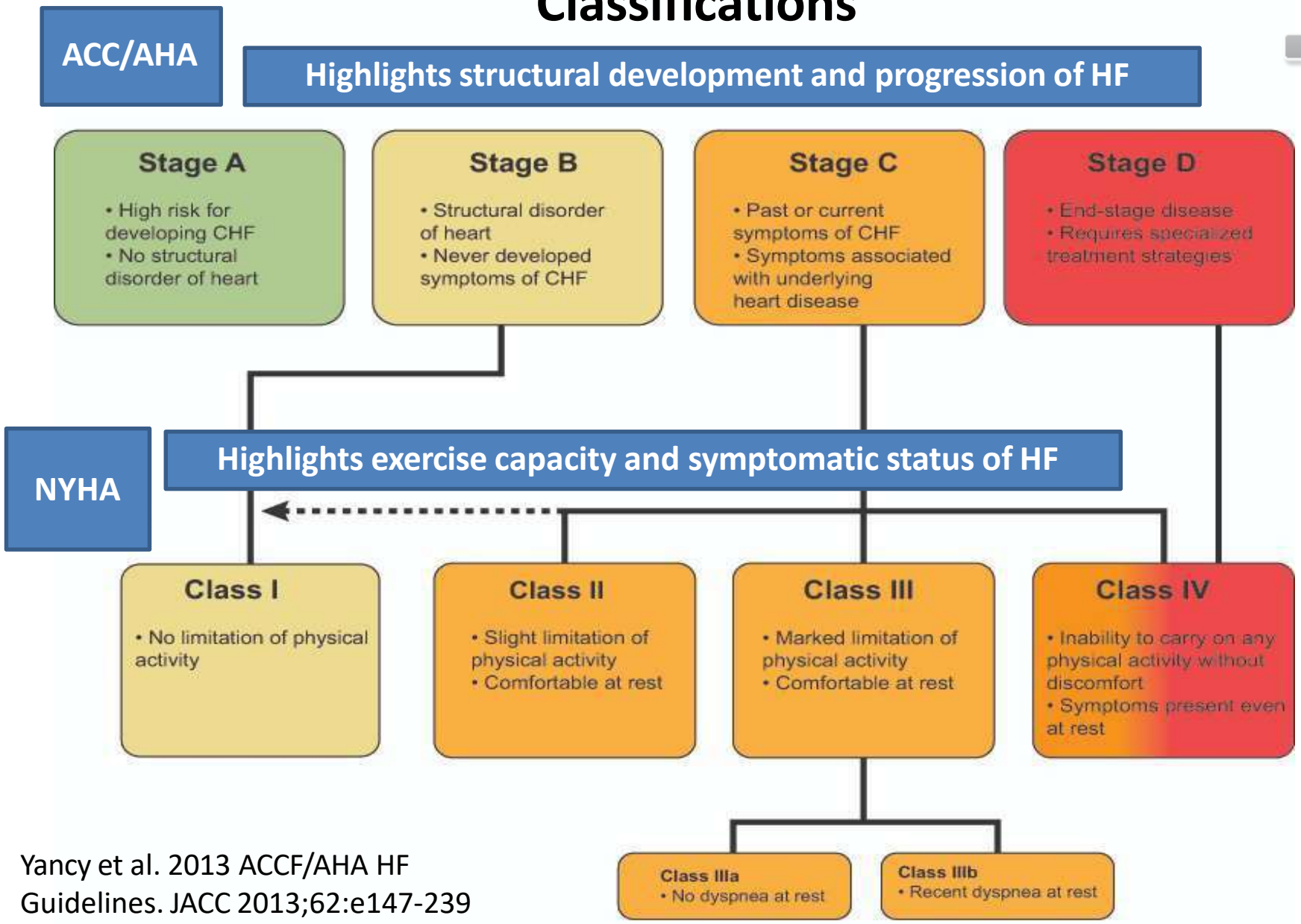
Stage D: Advanced HF

- Findings used to ID patients with advanced HF:
  - Repeated (>/=2) hospitalizations or ED visits for HF in the past year
  - Progressive deterioration in renal fxn (rise in BUN and SCr)
  - Weight loss without other cause (e.g. cardiac cachexia)
  - Intolerance to ACE inhibitors due to hypotension and/or worsening renal fxn
  - Intolerance to BB due to worsening HF or hypotension
  - Frequent SBP < 90 mmHg
  - Persistent dyspnea with dressing or bathing requiring rest
  - Inability to walk 1 block on level ground due to dyspnea or fatigue
  - Recent need to escalate diuretics to maintain fluid status, reaching daily furosemide dose > 160 mg/day and/or use of supplemental metolazone therapy
  - Progressive decline in serum sodium, usually to < 133 mEq/L
  - Frequent ICD shocks

CV Continuum

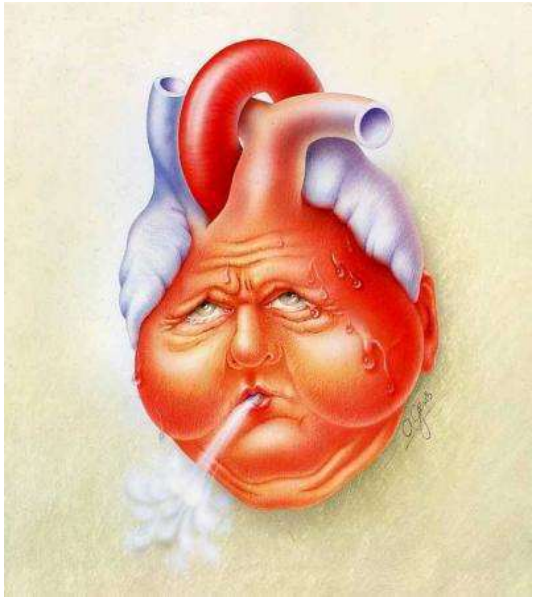


Comparison of Stages of HF and NYHA Functional Classifications



Yancy et al. 2013 ACCF/AHA HF Guidelines. JACC 2013;62:e147-239

HF Part 1



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- **Patient Case**

HF Case: Part I

- SB is a 64 yo female who presents to clinic complaining of SOB with getting dressed and difficulty sleeping at night due to coughing.
- She notices her ankles are swollen and her socks leave a pronounced mark on her legs.
- She feels nauseous and gets full after eating only half of her meals.
- She can't exercise lately due to fatigue and weakness.

Questions

1. What symptoms of HF does SB have?

2. What Stage of HF does SB have?

3. What NYHA Functional Class does SB have?

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End of Part 1

Thank you!