

# Heart Failure: Pathophysiology, Diagnosis, and Hemodynamic Targets

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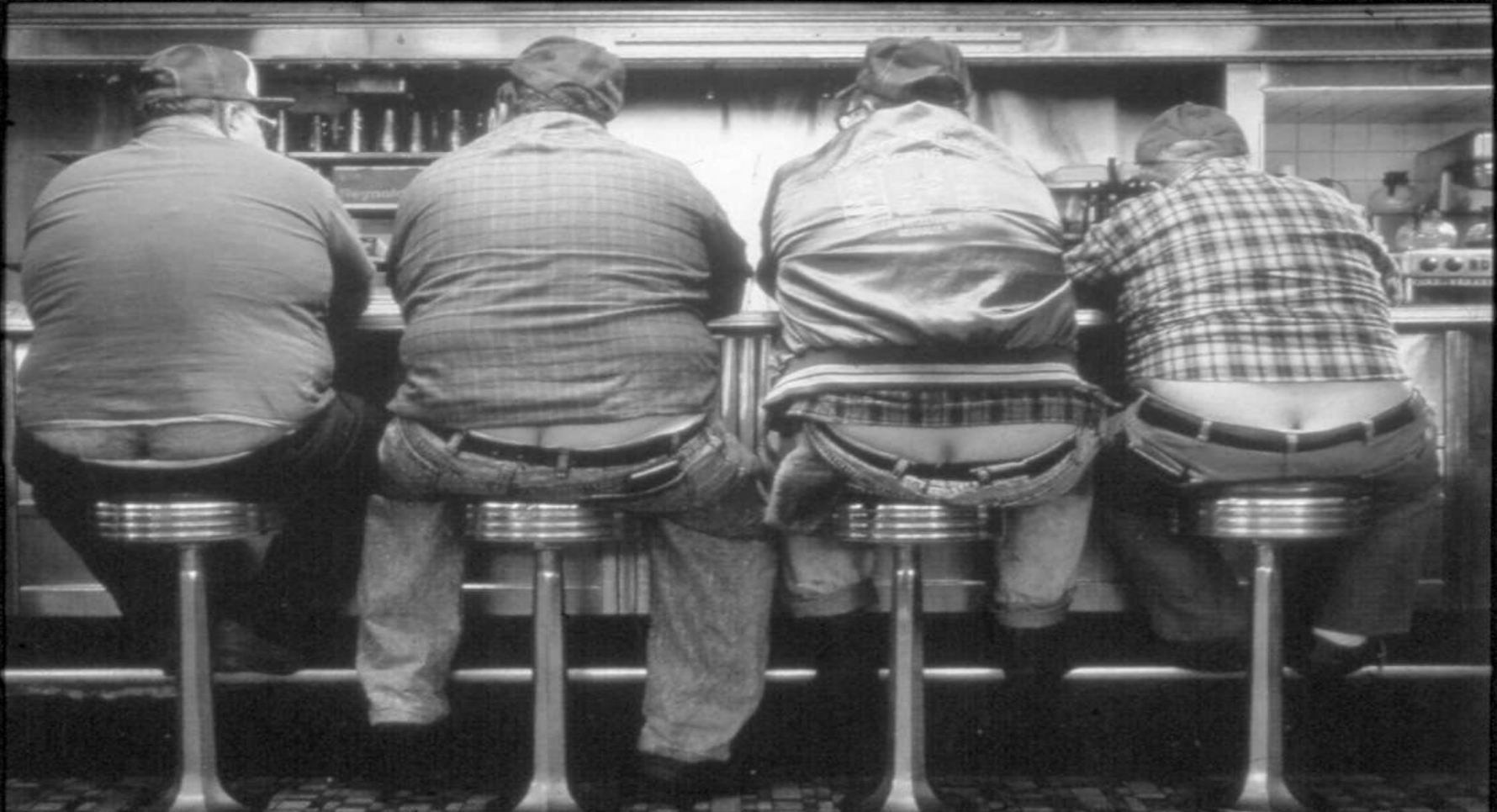


Director Coronary  
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# Heart Failure Rages Through American Cities



# The Boys Go Out For A 'Heart Healthy' Lunch...





# And Then Walk the Dog For Exercise



# Acute Heart Failure

## Magnitude of the Problem

- 1 million admissions annually in the U.S. (*↑50% over the past 10 years*)
- Most common admitting diagnosis for patients  $\geq$  65 years
- Hospitalization costs are considerable (*>60% of amount spent on heart failure*)

# Acute Heart Failure

## Have We Made Progress?

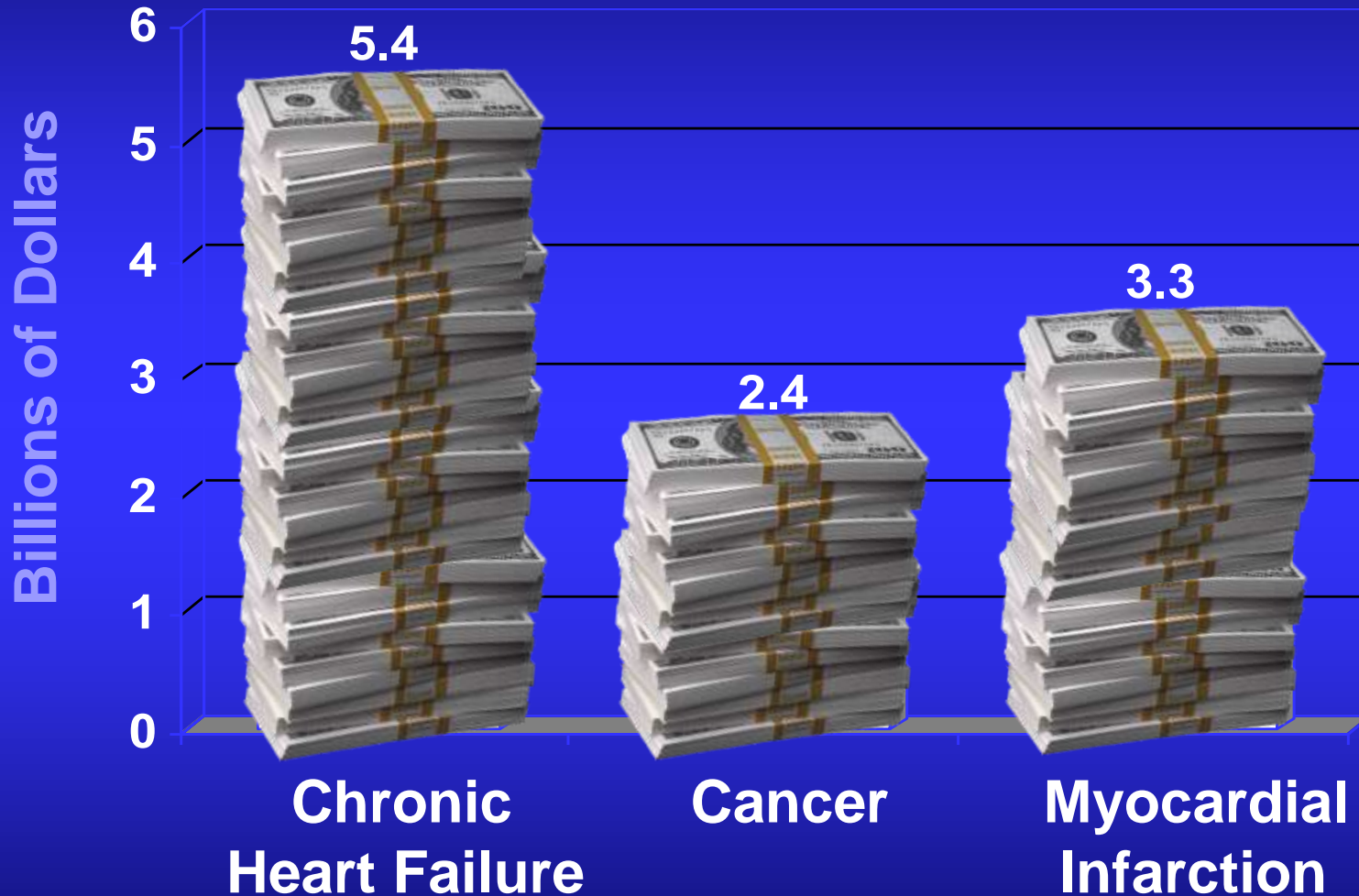
- The good news:

- In-hospital mortality 5% (*↓ 40% in 10 years*)
- Mean length of stay 5-6 days (*↓ 30% in 10 years*)

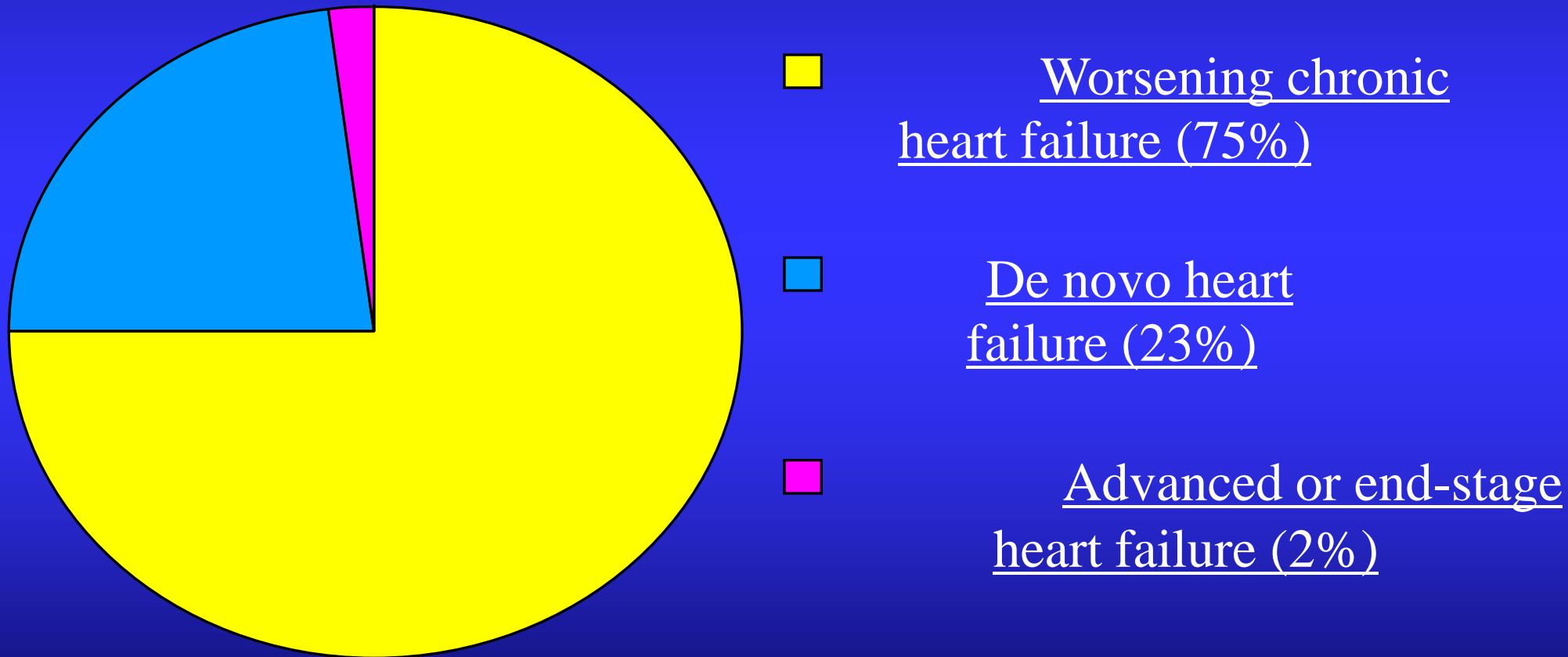
- The bad news:

- Readmission rates remain high
  - 25% within 30 days
  - 50% within 6-12 months
- High mortality rates persist
  - 5-10% at 30 days
  - 20-40% at 6-12 months

# HCFA Hospitalization Costs



# Worsening Chronic Heart Failure Is the Major Reason for Heart Failure Hospitalizations

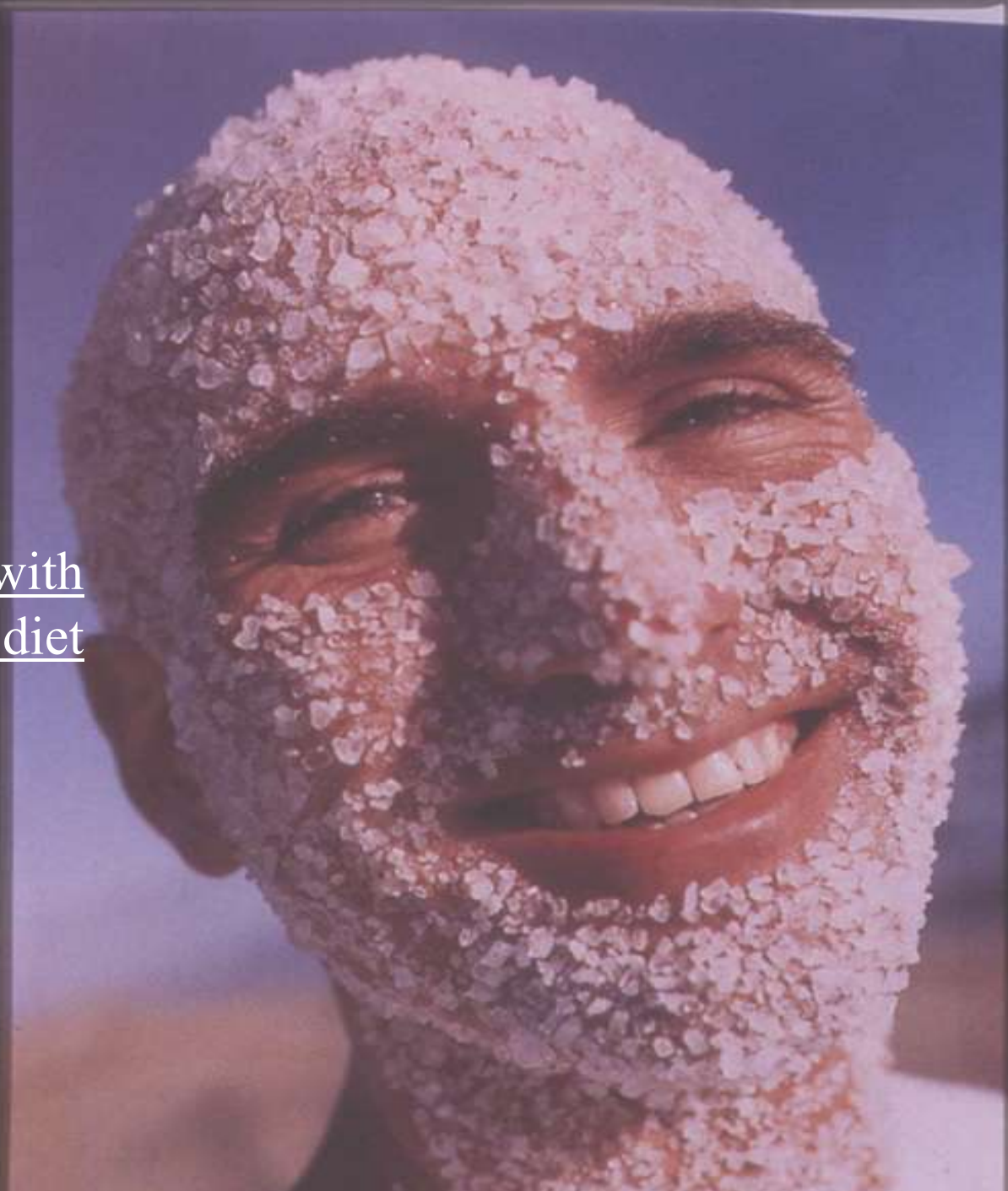




# Compliance with medications



Compliance with  
a low-salt diet



# Acute Decompensated Heart Failure: Patient Characteristics

	ADHERE	OPTIMIZE-HF	Euro-HF
	N = 105,388	N = 48,612	N = 11,327
Mean age (yrs)	72.4	73	71
> 75 years (%)	50	ND	30 men 51 women
Male (%)	48	48	53
Caucasian (%)	72	ND	ND
Prior HF history (%)	75	87	65
Systolic dysfunction (%)	54	46	45

# Heart Failure as a Symptomatic Disorder Functional Class

## ■ NYHA

- Class I: normal exercise tolerance
- Class II: symptoms with ordinary exertion
- Class III: symptoms with only mild exertion
- Class IV: symptoms at rest

Problem: the underlying disease progresses,  
even in the absence of symptoms!!



# Rationale for a New Way of Classifying Patients With HF in 2009

- HF represents a continuum beginning with risk factors and culminating in end-stage or refractory disease
- There are known risk factors and structural prerequisites leading to the development of LV systolic and/or diastolic dysfunction and the clinical syndrome of HF
- HF is a preventable disorder

# Revised Staging System for HF



**At high risk of HF but without  
structural heart disease or HF symptoms**

**Stage A**

# Revised Staging System for HF



**Structural heart disease but  
without signs or symptoms of HF**

**Stage B**

**At high risk of HF but without  
structural heart disease or HF symptoms**

**Stage A**

# Revised Staging System for HF



**Structural heart disease  
with prior or current  
HF symptoms**

**Stage C**

**Structural heart disease but  
without signs or symptoms of HF**

**Stage B**

**At high risk of HF but without  
structural heart disease or HF symptoms**

**Stage A**



# Revised Staging System for HF



Refractory HF  
requiring  
specialized  
interventions

**Stage D**

Structural heart disease  
with prior or current  
HF symptoms

**Stage C**

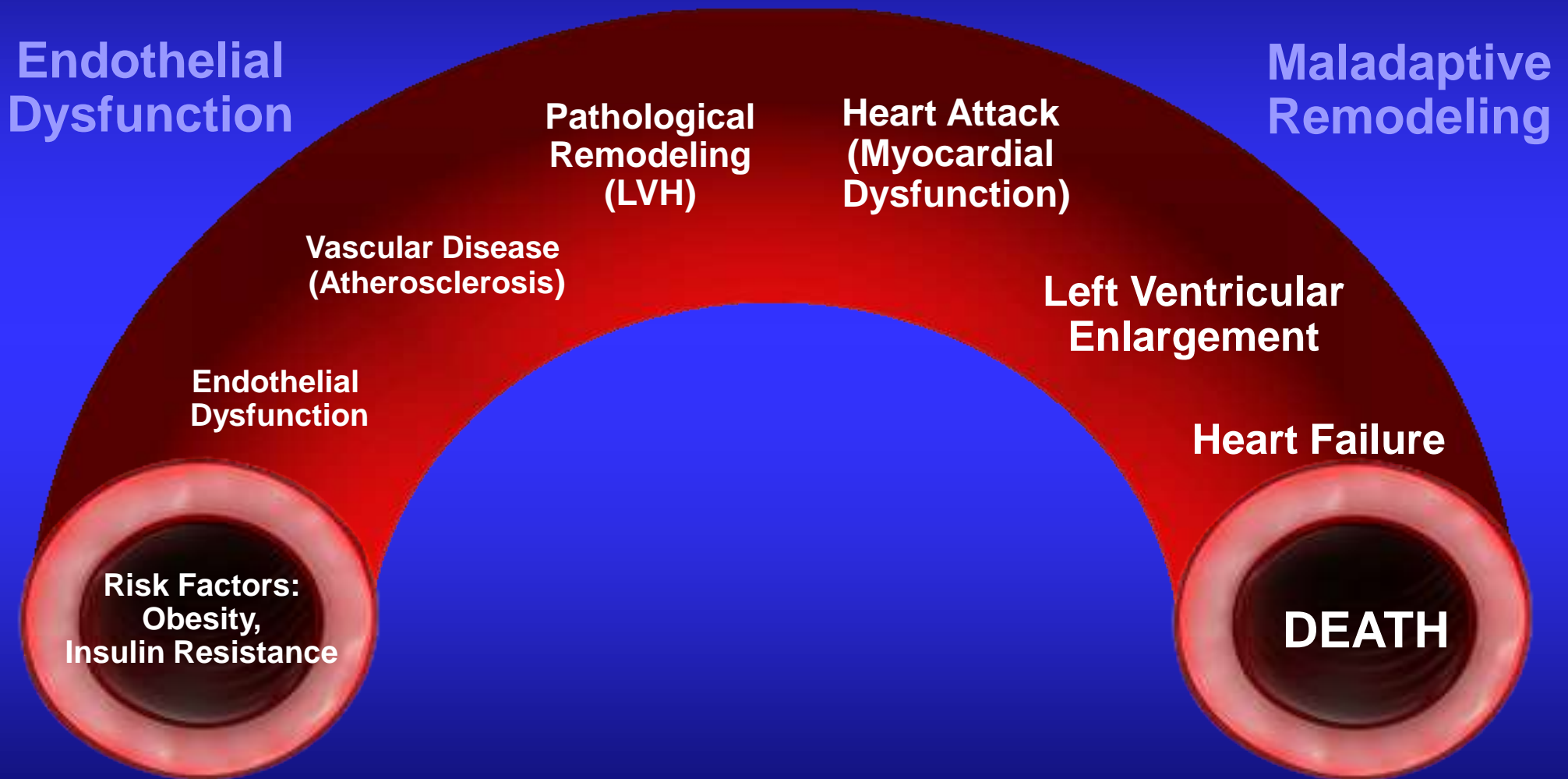
Structural heart disease but  
without signs or symptoms of HF

**Stage B**

At high risk of HF but without  
structural heart disease or HF symptoms

**Stage A**

# The Cardiovascular Disease Continuum



# Heart Failure: A Changing Paradigm

---

1950's - 1980's

## Hemodynamic Model

- Reduced contractility, pump dysfunction
- Treatment:
  - Positive inotropic drugs to stimulate contractility
  - Vasodilators to “unload” the heart
  - Conventional drugs
    - Diuretics
    - Digitalis



1980's - 2004

## Neurohormonal Model

- Progressive remodeling with impaired myocardial performance
- Treatment:
  - Prevention of progression with neurohormonal blockers:
    - ACE inhibitors, aldo blockers
    - $\beta$ -adrenergic blockers, ARBs
  - Conventional drugs
    - Diuretics
    - Digitalis
  - Emerging therapies
    - Bi-Ventricular Pacing
    - Bi-V Pacing + ICD
    - LV Reconstruction surgery (Dor)
    - Acorn, Myosplint

# Structural Remodeling Post-MI

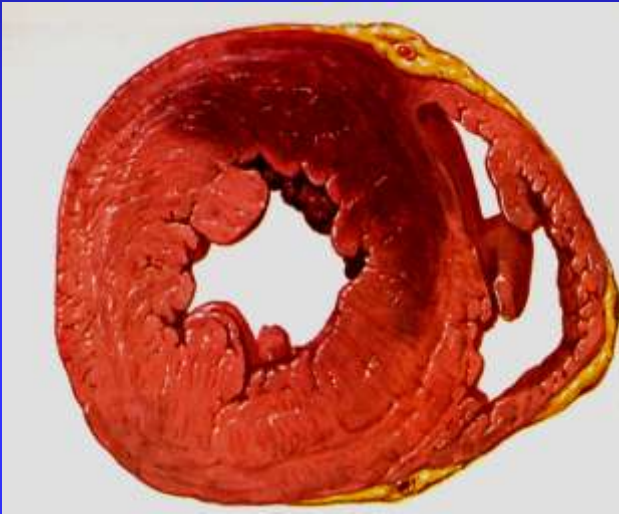
Days



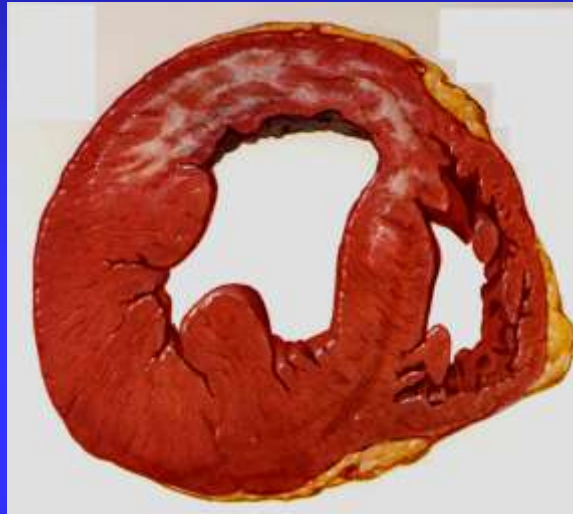
Weeks



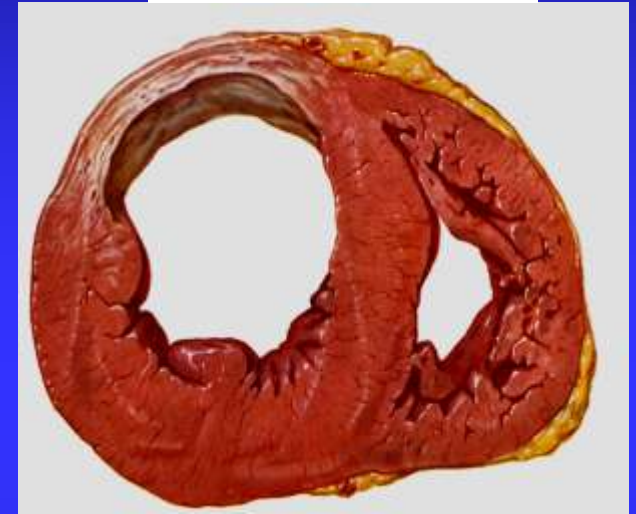
Months - Years



MI due to  
coronary  
occlusion



Scarring and reshaping  
of the heart  
(remodeling)



Heart enlarges and  
leads to congestive  
heart failure



# Remodeling Is The Major Cause of Progressive Cardiac Dysfunction

6 months post-MI



14 months post-MI



# Revised Staging System for HF



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# Revised Staging System for HF



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# Revised Staging System for HF



Refractory HF  
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**Stage D**

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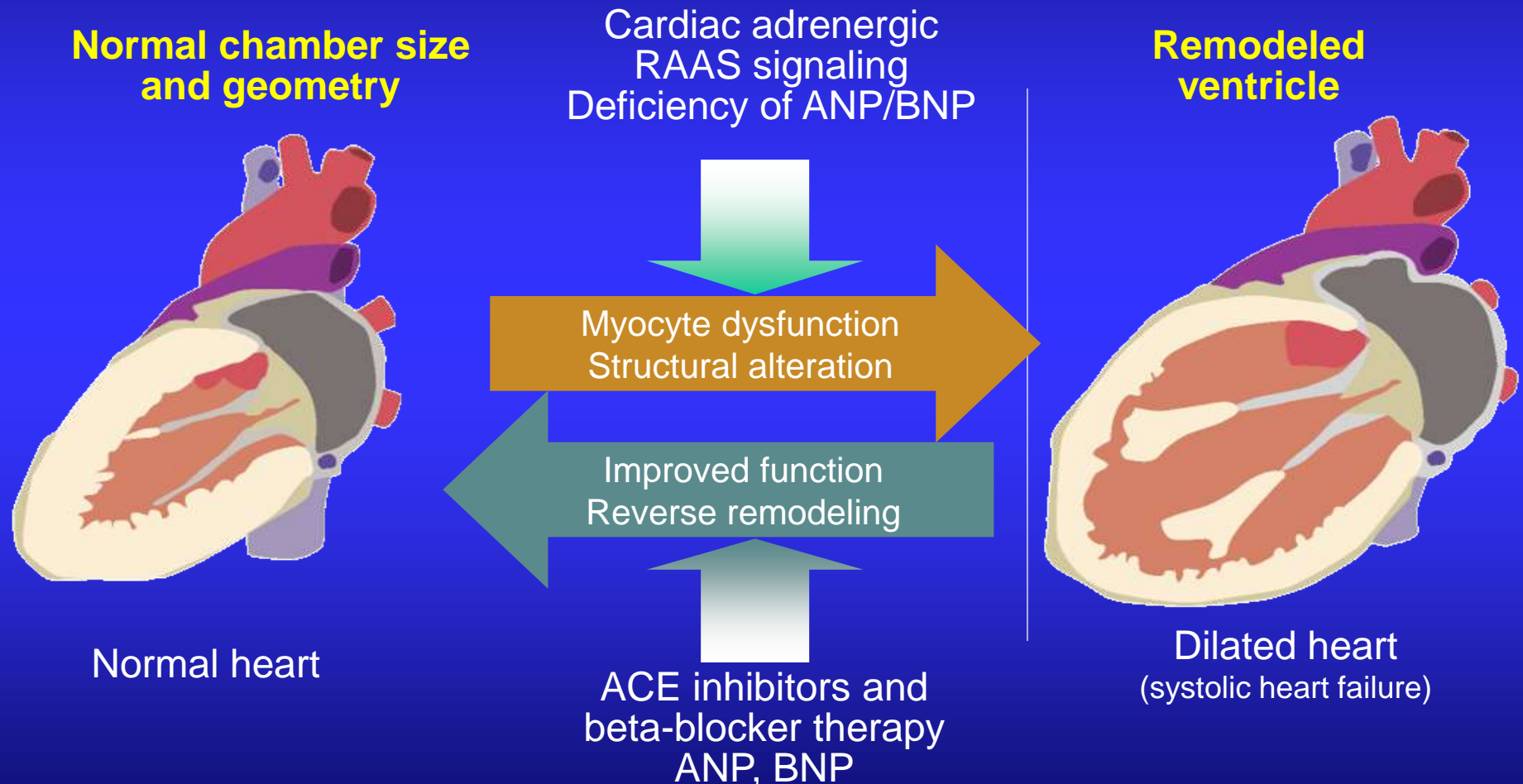
**Stage B**

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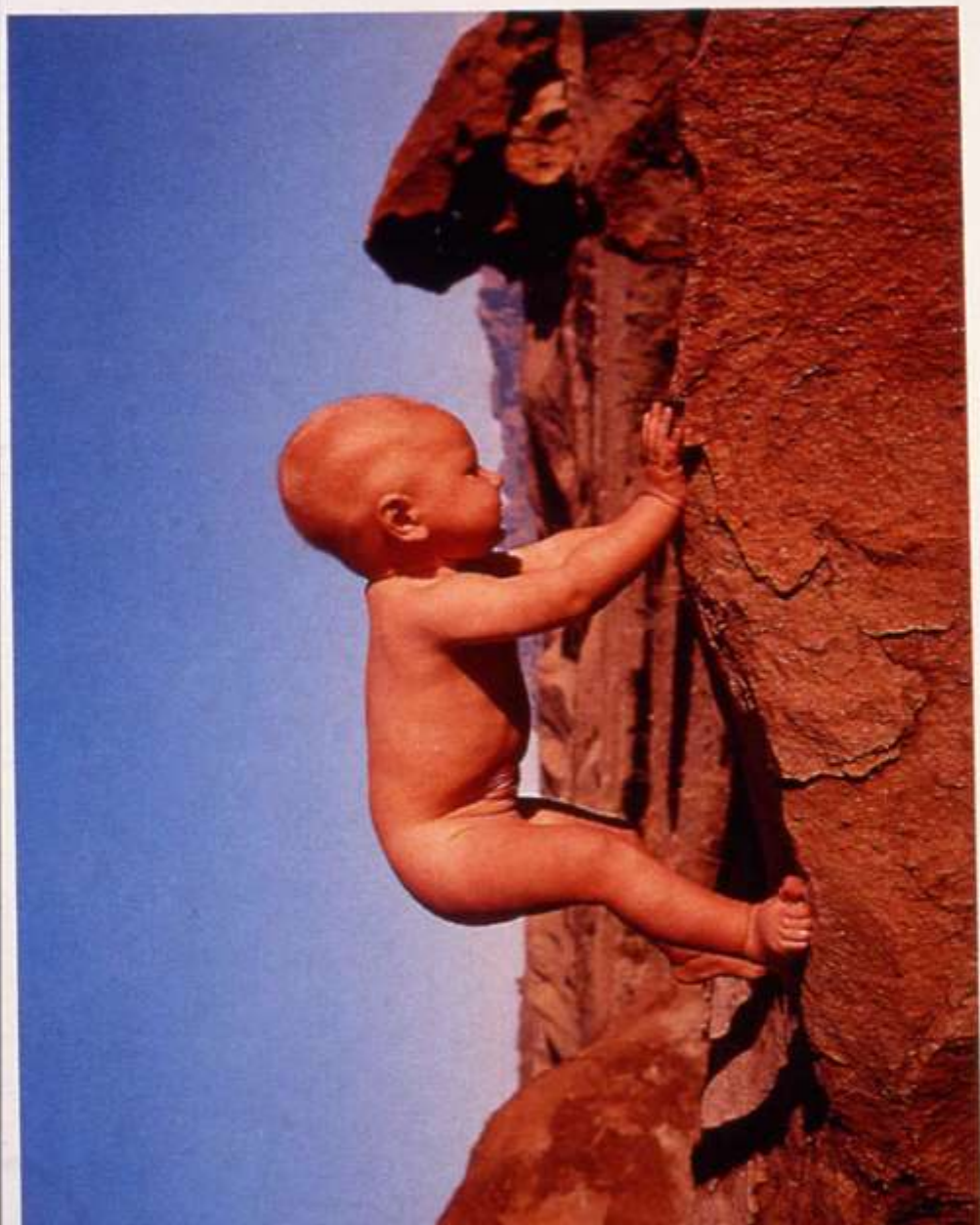


# Role of Neurohormonal Activation in Remodeling

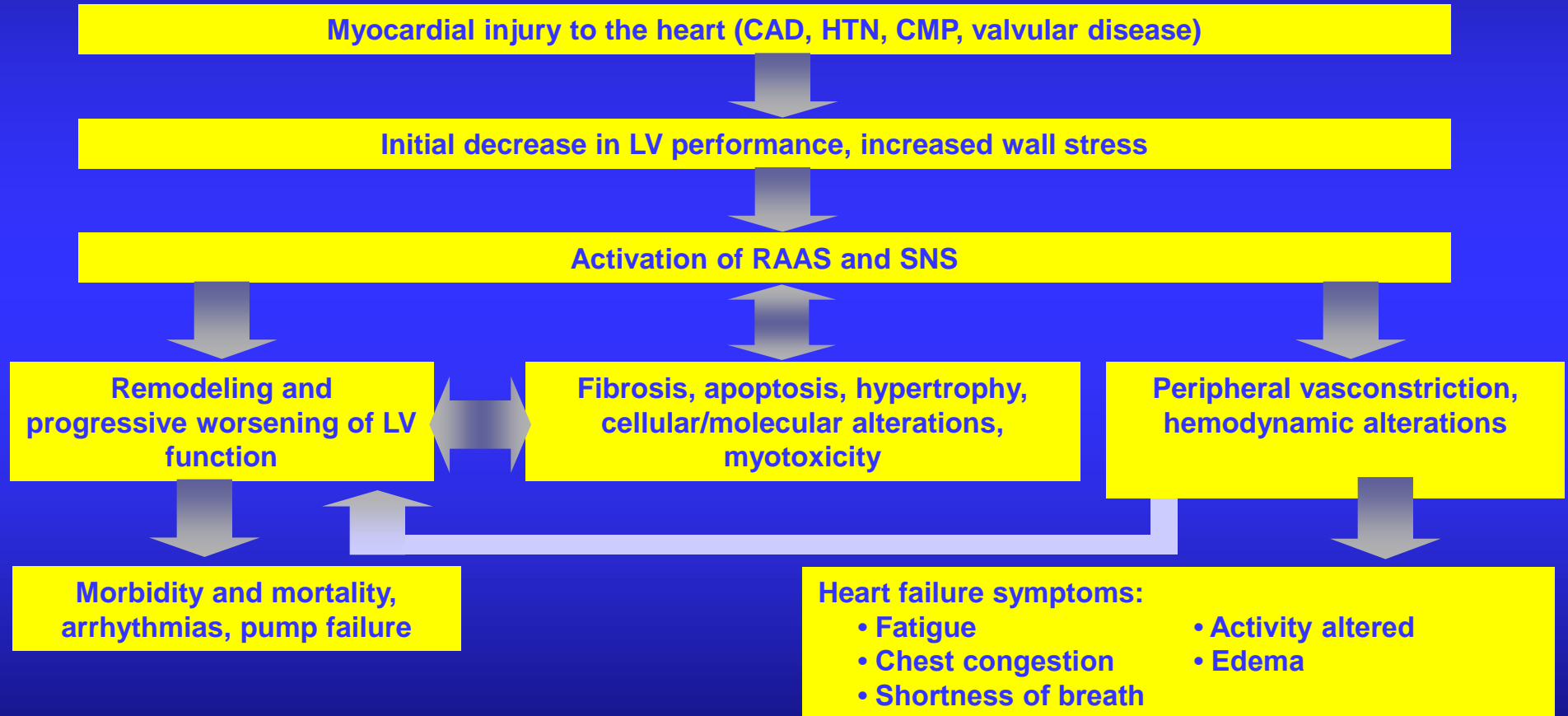


ACE = angiotensin-converting enzyme; ANP = atrial natriuretic peptide; BNP = B-type natriuretic peptide; RAAS = renin-angiotensin-aldosterone system

Cohn JN, et al. *J Am Coll Cardiol.* 2000;35(3):569–582.



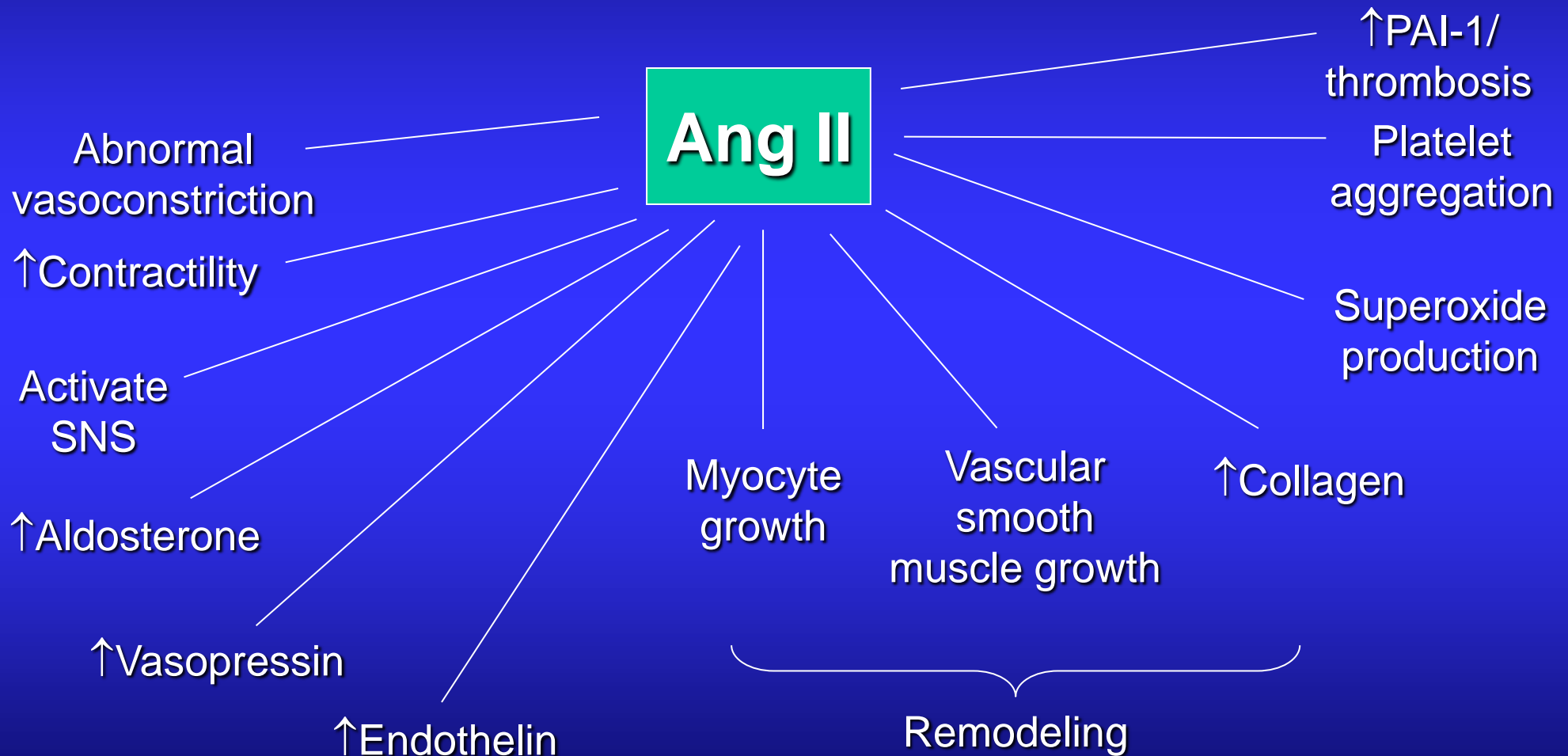
# Progression of Heart Failure



CAD = coronary artery disease; CMP = cardiomyopathy; HTN = hypertension; LV = left ventricular; RAAS = renin-angiotensin-aldosterone system; SNS = sympathetic nervous system

Greenberg BH. *Hosp Physician*. 2002;38(1):43-49.

# Pathophysiologic Effects of Angiotensin II



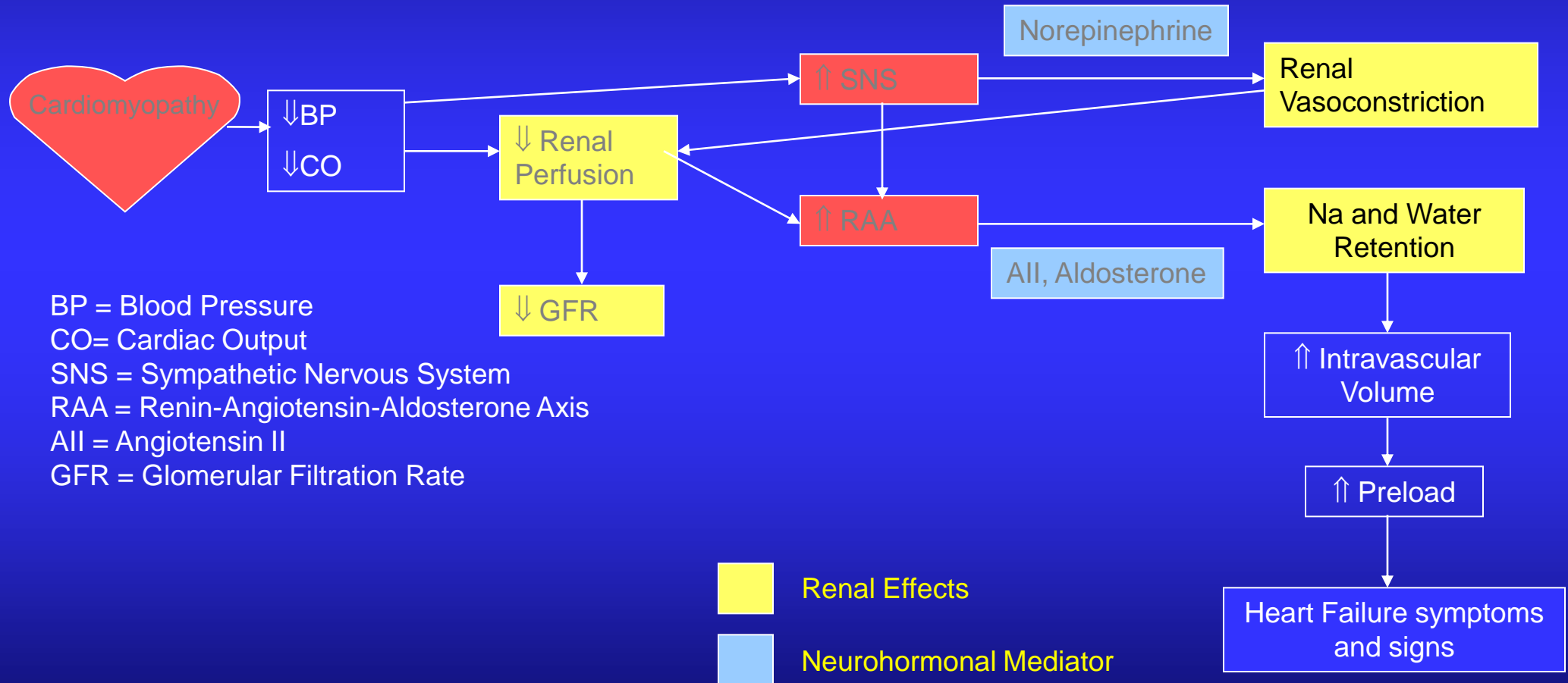
# Effects of CHF on Renal Function

Primary Pathophysiology

Direct Renal Effects

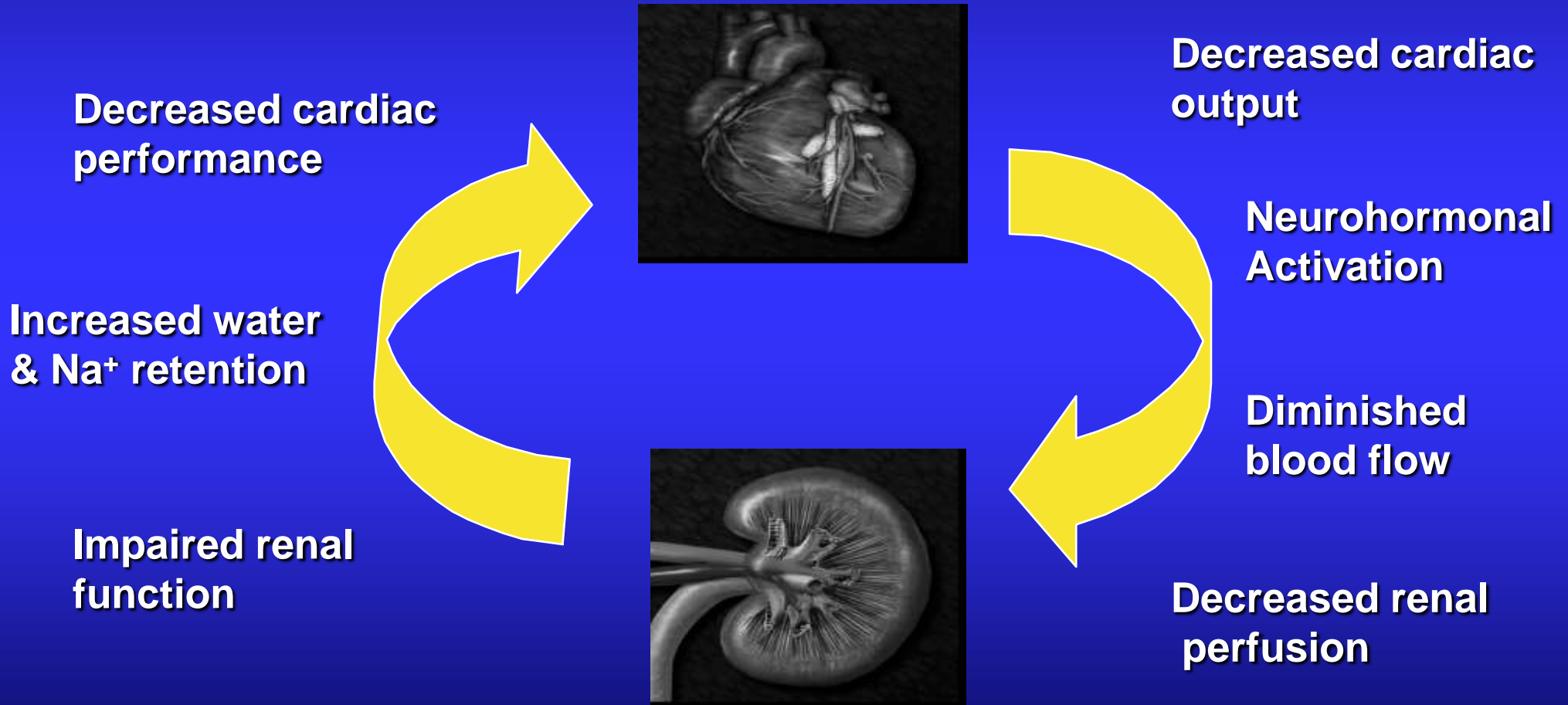
Neurohormonal Activation

Secondary Pathophysiology





# The Cardio-Renal Syndrome of Heart Failure



# Diagnosis of Heart Failure

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# Case- MA- 1

- **HPI:** 65 year old male was visiting relatives in San Diego when over the course of 24 hours he developed progressively worsening dyspnea, occurring first with minimal exertion and culminating with shortness of breath at rest. He denied any chest pain or nausea but said he felt his heart skipping some beats.
- **PMH:** Hypertension, COPD, remote myocardial infarction. He was told he had a normal “ejection fraction” one year ago.

# MA-2

- **Meds:** Two inhalers, clonidine, simvastatin
- **PE:** vitals: 170/100-100-26; JVP-14 cm, rhonchi and wheezing throughout all lung fields. No gallops or edema.
- **ECG:** sinus tachycardia, multifocal pacs, LVH, LAE and old Q waves inferiorly.
- **CXR:** ( poor quality) no cardiomegally. Possible cephalization.
- **Bedside echo** (fellow): mild inferior wall hypokinesis (old). Overall systolic function was normal.

# MA- Questions-a

- What is the diagnosis?
- How can you differentiate between COPD and CHF?
- If this is CHF, what has precipitated it?
- What other tests would you order?



# MA-3

- **Labs:**

TnI <0.4

CBC normal

Electrolytes: normal

BNP: not done

## MA-4

- The diagnosis was COPD exacerbation.
- He was given oxygen, nebulization treatments, and a steroid bolus.
- He felt slightly better and was discharged home two hours later at 8pm.

# Goals in Diagnosis



- For your mother
  - Rapid
  - Highly accurate
  - Non-invasive, if at all possible
  - Spare no expense

# Goals in Diagnosis

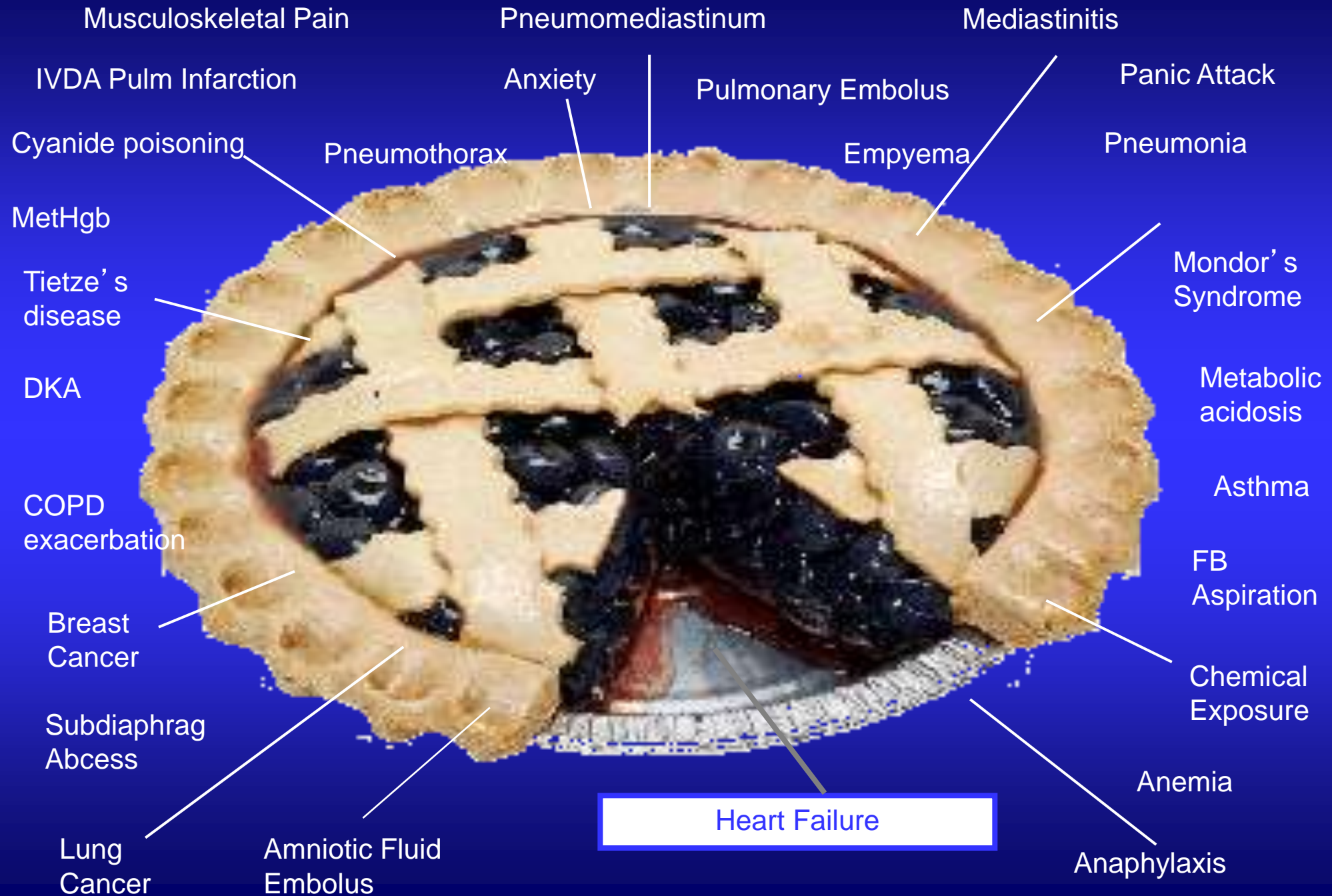


- For your mother-in-law
  - No rush
  - Mistakes happen
  - Invasive studies, got no problem with that
  - She is cheap, don't go wasting money

# The Short of Breath Pie







We need to make rapid, accurate  
diagnoses and triage patients  
accordingly





# The Hall and the physical exam



# The Challenge of Diagnosing Heart Failure: Physical Examination

## JVP on Physical Exam

Great if well seen

In OPTIMIZE and ADHERE, in the majority of hospitalized HF patients, initial exam missed it

Obesity epidemic: good luck

## S3 on Physical Exam

Great if heard

Missed 4/5 times

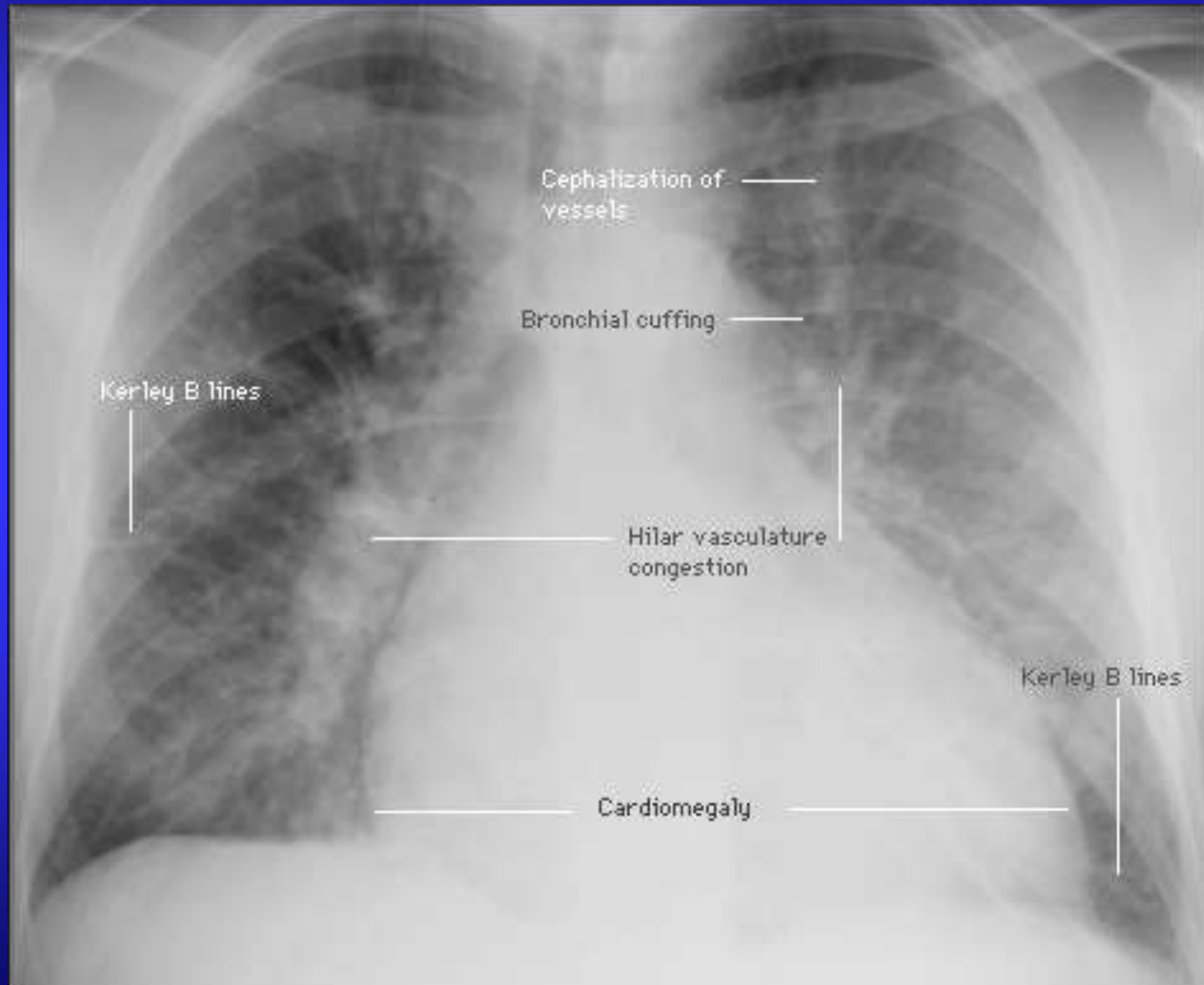


# How Good Is the History and Physical in AHF?

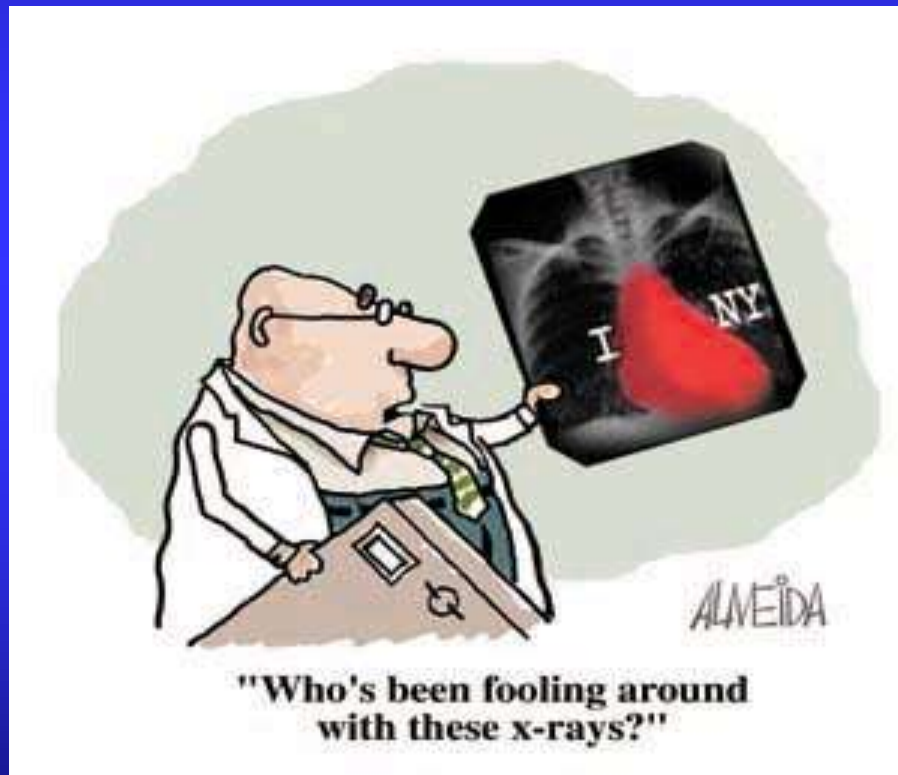
Variable	Sensitivity (%)	Specificity (%)	Accuracy (%)
<b>Hx of HF</b>	62	94	80
<b>Dyspnea</b>	56	53	54
<b>Orthopnea</b>	47	88	72
<b>Rales</b>	56	80	70
<b>S3</b>	20	99	66
<b>JVD</b>	39	94	72
<b>Edema</b>	67	68	68



# Chest X-Ray in Heart Failure

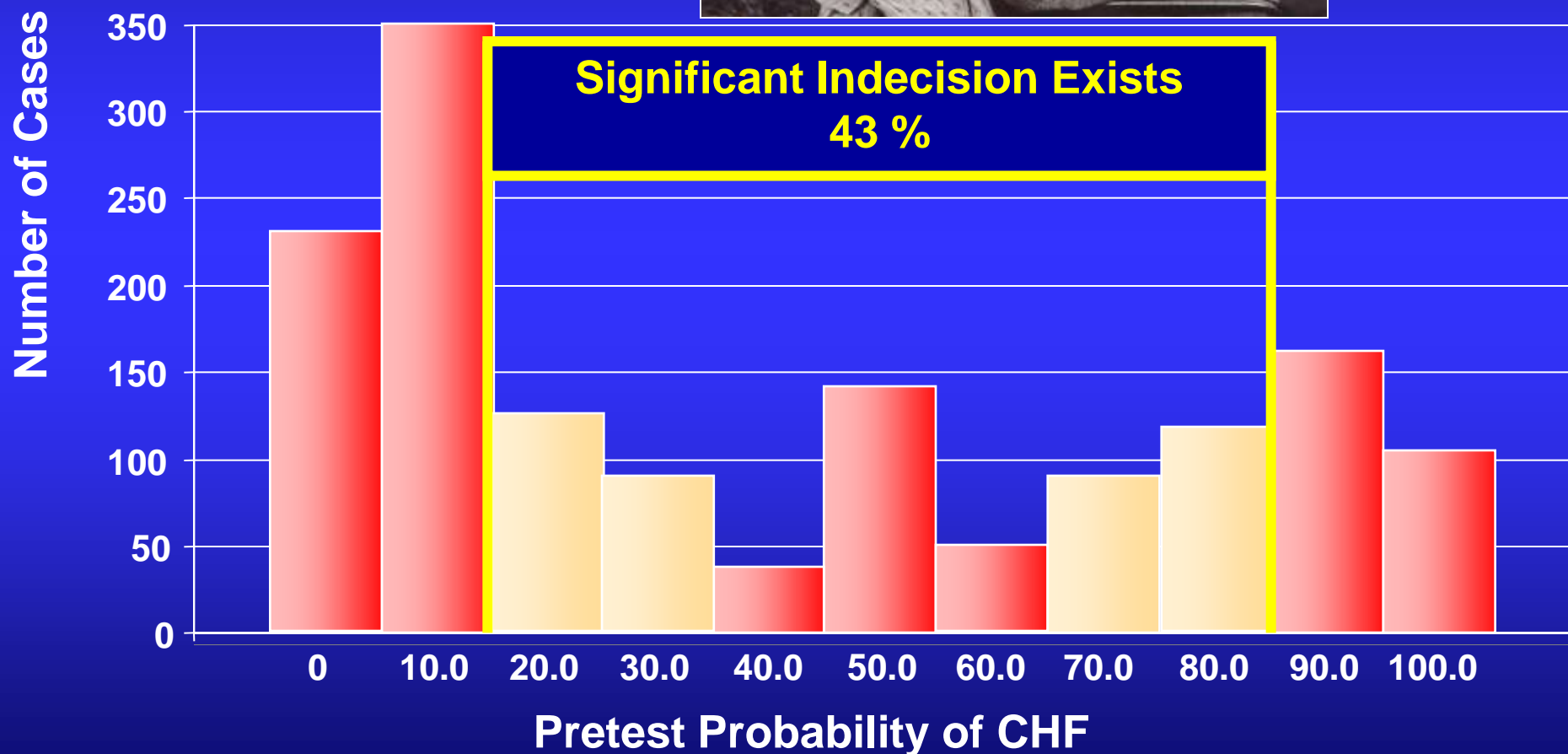


# The CXR is not all it's cracked up to be



- ❑ Misses 20% of echo proven cardiomegaly
- ❑ Detection of pleural effusion if supine
  - 67% sensitivity
  - 70% specificity
- ❑ Even worse if done portable

## How sure are we about the diagnosis of CHF?



# The Challenge of Diagnosing Heart Failure

## ❖ Primary care diagnosis

Correct diagnosis on initial presentation

18% of females

36% of males

## Emergency department diagnosis

12% entirely wrong diagnosis

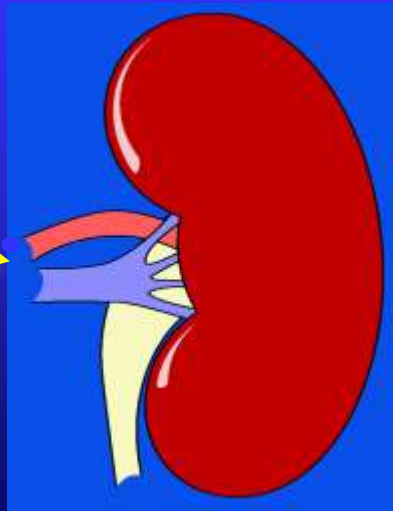
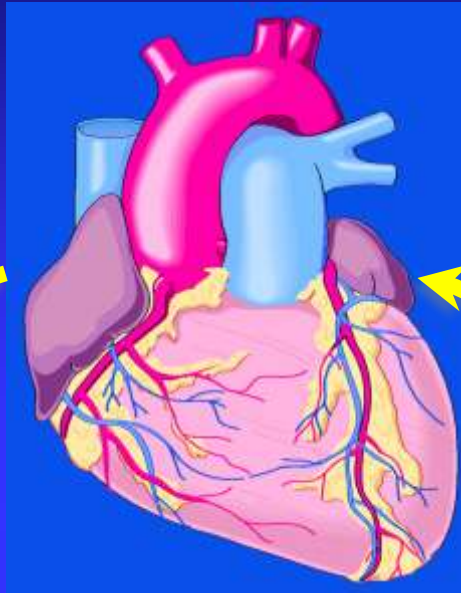
6% over diagnosed

6% under diagnosed

# Cardiorenal Axis

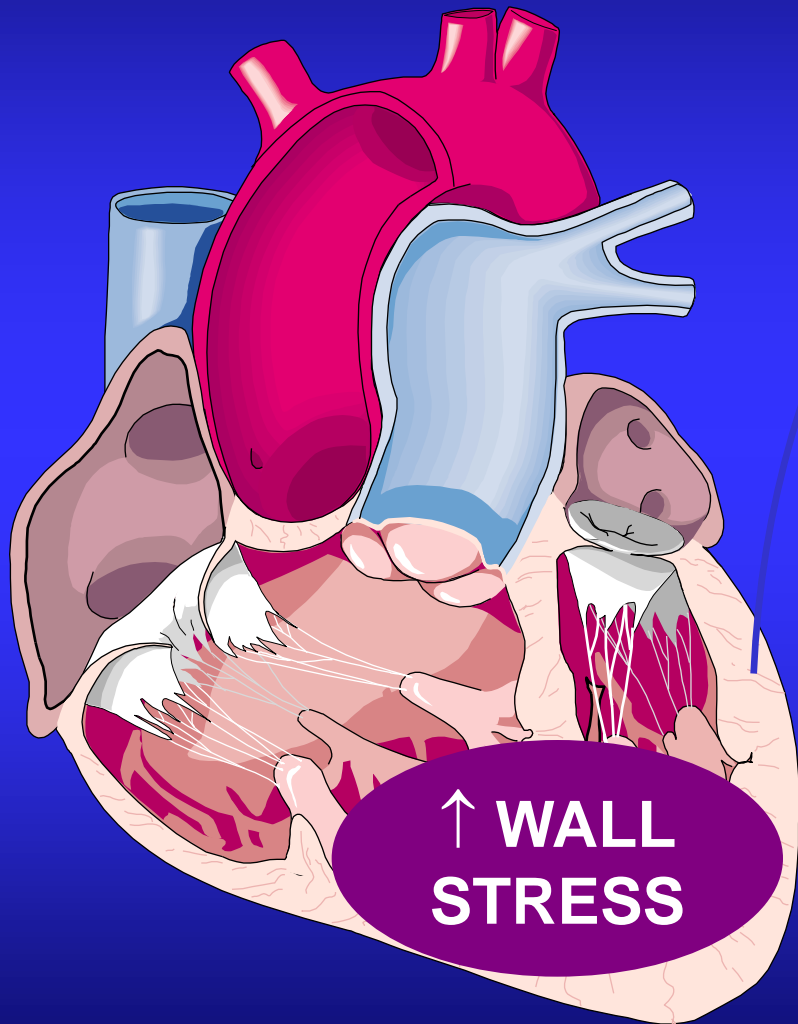
## ANP, BNP, and CNP

- Natriuretic
- Diuretic
- Vasodilating
- Renin and aldosterone inhibiting
- Anti-fibrotic



## Renin-angiotensin-aldosterone system

- Sodium retaining
- Antidiuretic
- Vasoconstricting
- Fibrosis



Pre-Pro-BNP<sub>1-134</sub>

26-aa signal  
sequence

Pro-BNP<sub>1-108</sub>

N-terminal  
Pro-BNP<sub>1-76</sub>

BNP<sub>77-108</sub>

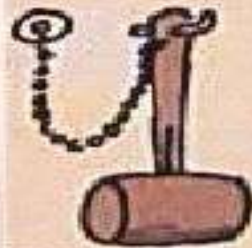
$t_{1/2} = 18 \text{ min}$

Natriuresis  
↑ lusitropy

Vasodilatation  
↓ RAAS



# EMERGENCY PHYSICIAN



BREAK  
GLASS



History

Physical exam

CXR

**NP levels**



# BNP & NT ProBNP: They Look Similar But May Be “Different Animals”



# BNP and NT-proBNP Summary

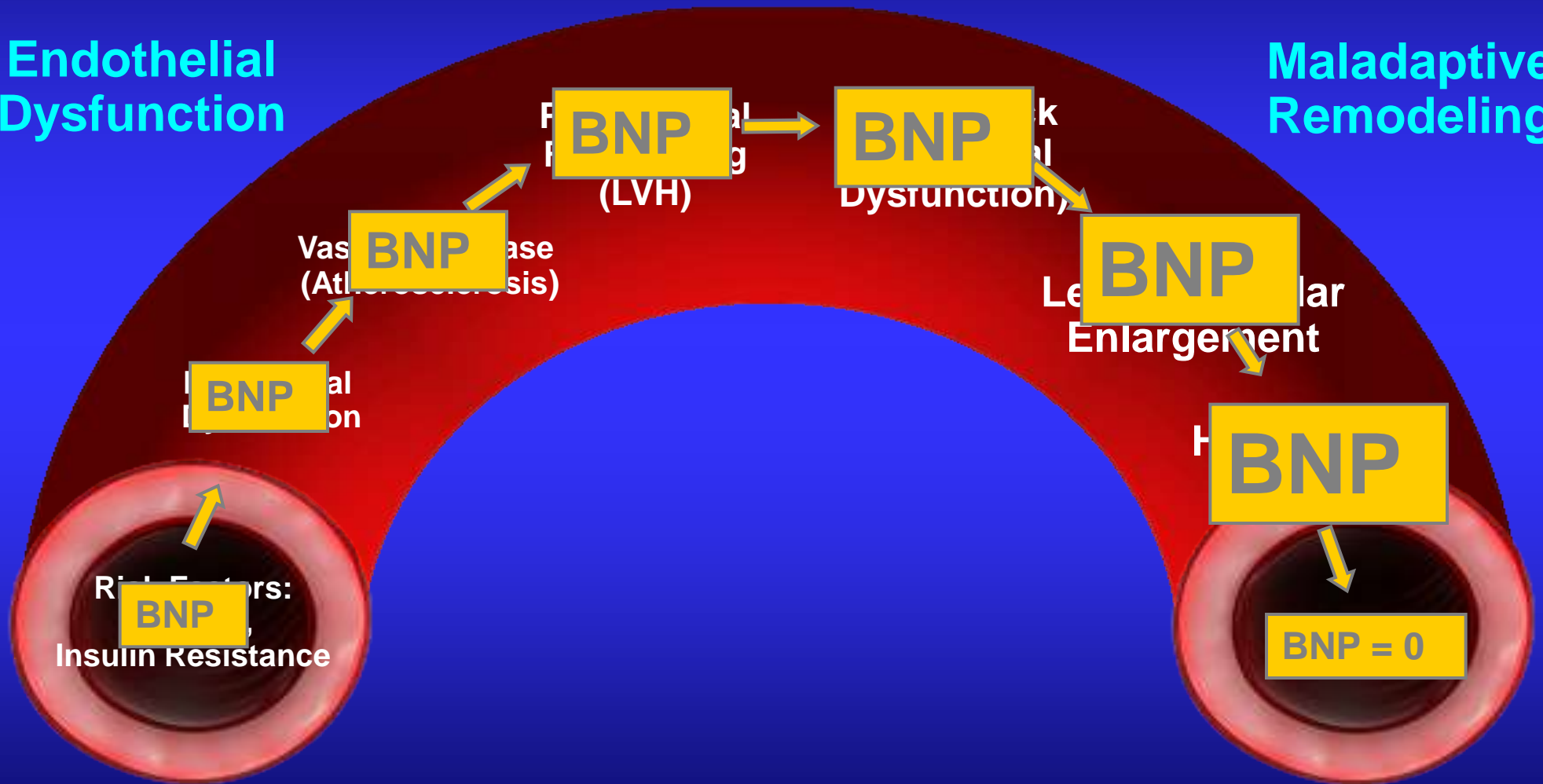
- BNP is a more widely used marker
- Values of the two molecules are NOT interchangeable
- Both are good diagnostic markers in heart failure
- Diagnostic algorithms and cut-offs are more complex for NT-proBNP than for BNP
- Both can be used to screen for LV dysfunction
- Both are good prognostic markers in heart failure
- NT-proBNP values appear to be more effected by renal function
- BNP is a more dynamic marker due to differences in half-lives



# The Cardiovascular Disease Continuum

Endothelial  
Dysfunction

Maladaptive  
Remodeling



# Breathing Not Properly STUDY

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### RAPID MEASUREMENT OF B-TYPE NATRIURETIC PEPTIDE IN THE EMERGENCY DIAGNOSIS OF HEART FAILURE

ALAN S. MAISEL, M.D., PADMA KRISHNASWAMY, M.D., RICHARD M. NOWAK, M.D., MBA, JAMES MCCORD, MD;  
JUDD E. HOLLANDER, M.D., PHILIPPE DUC, M.D., TORBJØRN OMLAND, MD, PhD, MPH;  
WILLIAM T. ABRAHAM, M.D., ALAN H.B. WU, PH.D., CATHRINE WOLD KNUDSEN, MD;  
ARNE WESTHEIM, M.D., PH.D., M.P.H., ALBERTO PEREZ, MD; PAUL CLOPTON, MS;  
PADMA KRISHNASWAMY, MD; RADMILA KAZANEGRA, MD; HOWARD C. HERRMANN, MD;  
for the BREATHING NOT PROPERLY MULTINATIONAL STUDY INVESTIGATORS

## Clinical Investigation and Reports

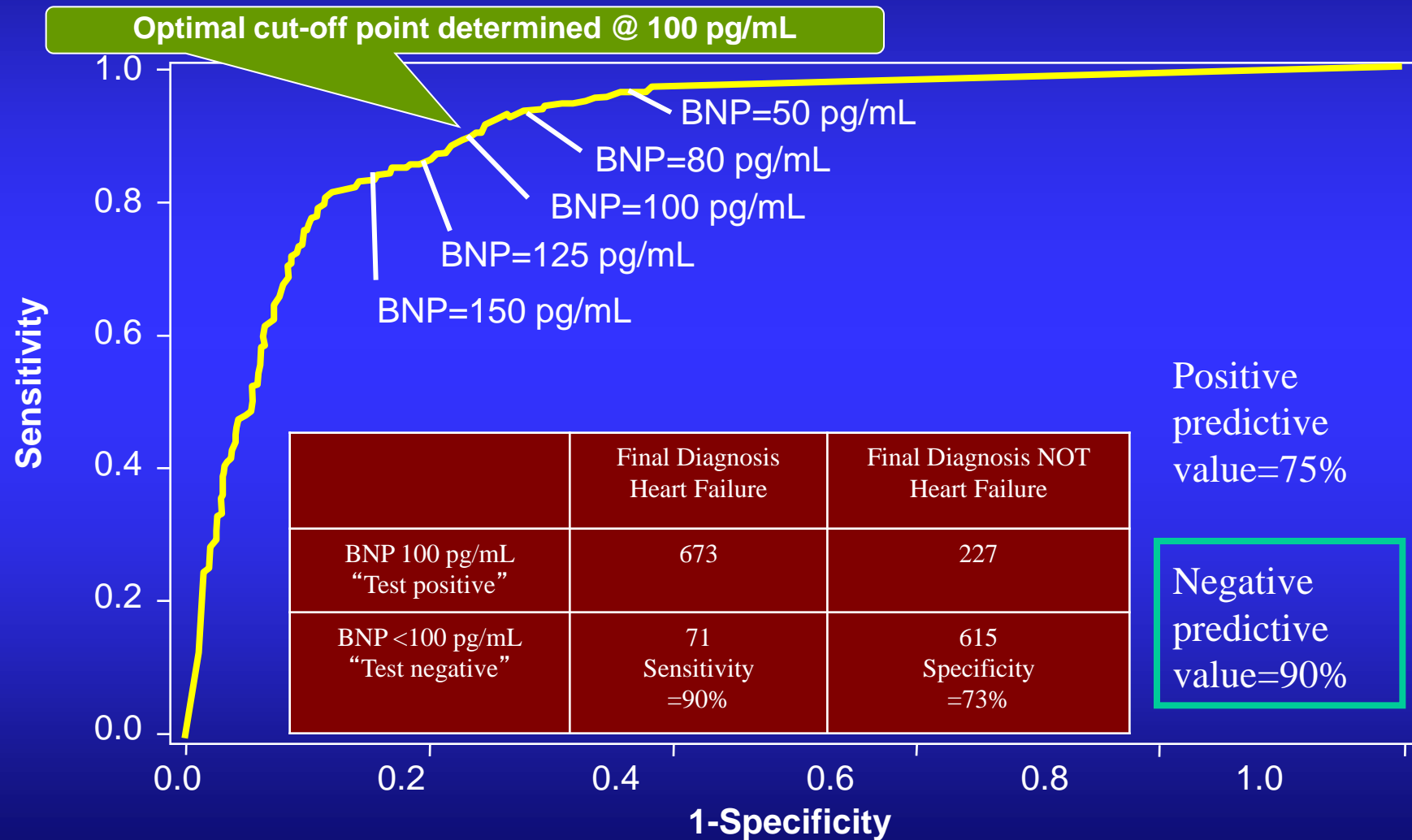
### B-Type Natriuretic Peptide and Clinical Judgment in Emergency Diagnosis of Heart Failure Analysis From Breathing Not Properly (BNP) Multinational Study

Peter A. McCullough, MD, MPH; Richard M. Nowak, MD, MBA; James McCord, MD;  
Judd E. Hollander, MD; Howard C. Herrmann, MD; Philippe G. Steg, MD; Philippe Duc, MD;  
Arne Westheim, MD, PhD; Torbjørn Omland, MD, PhD, MPH; Cathrine Wold Knudsen, MD;  
Alan B. Storrow, MD; William T. Abraham, MD; Sumant Lamba, MD; Alan H.B. Wu, PhD;  
Alberto Perez, MD; Paul Clopton, MS; Padma Krishnaswamy, MD; Radmila Kazanegra, MD;  
Alan S. Maisel, MD; for the BNP Multinational Study Investigators

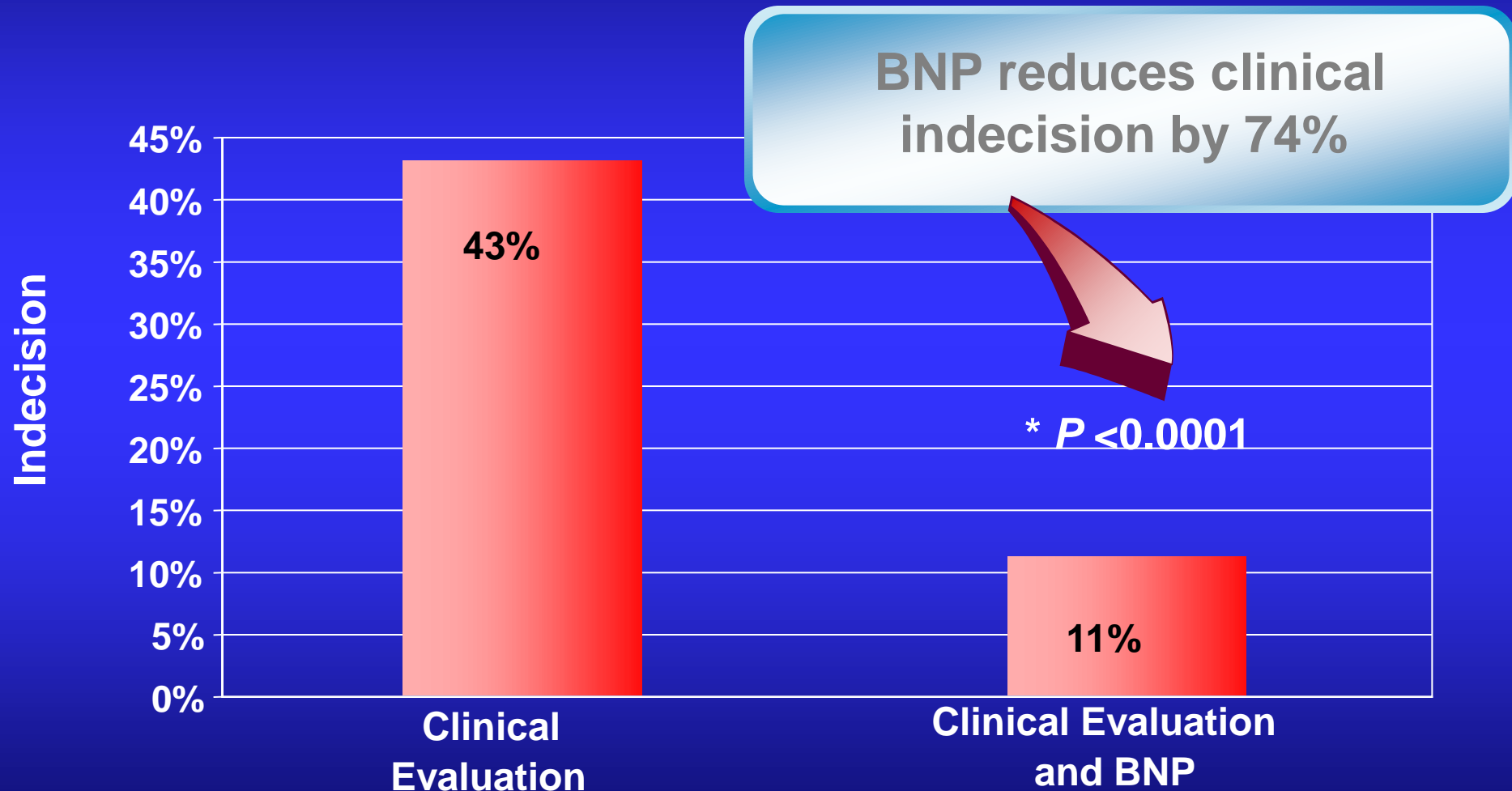




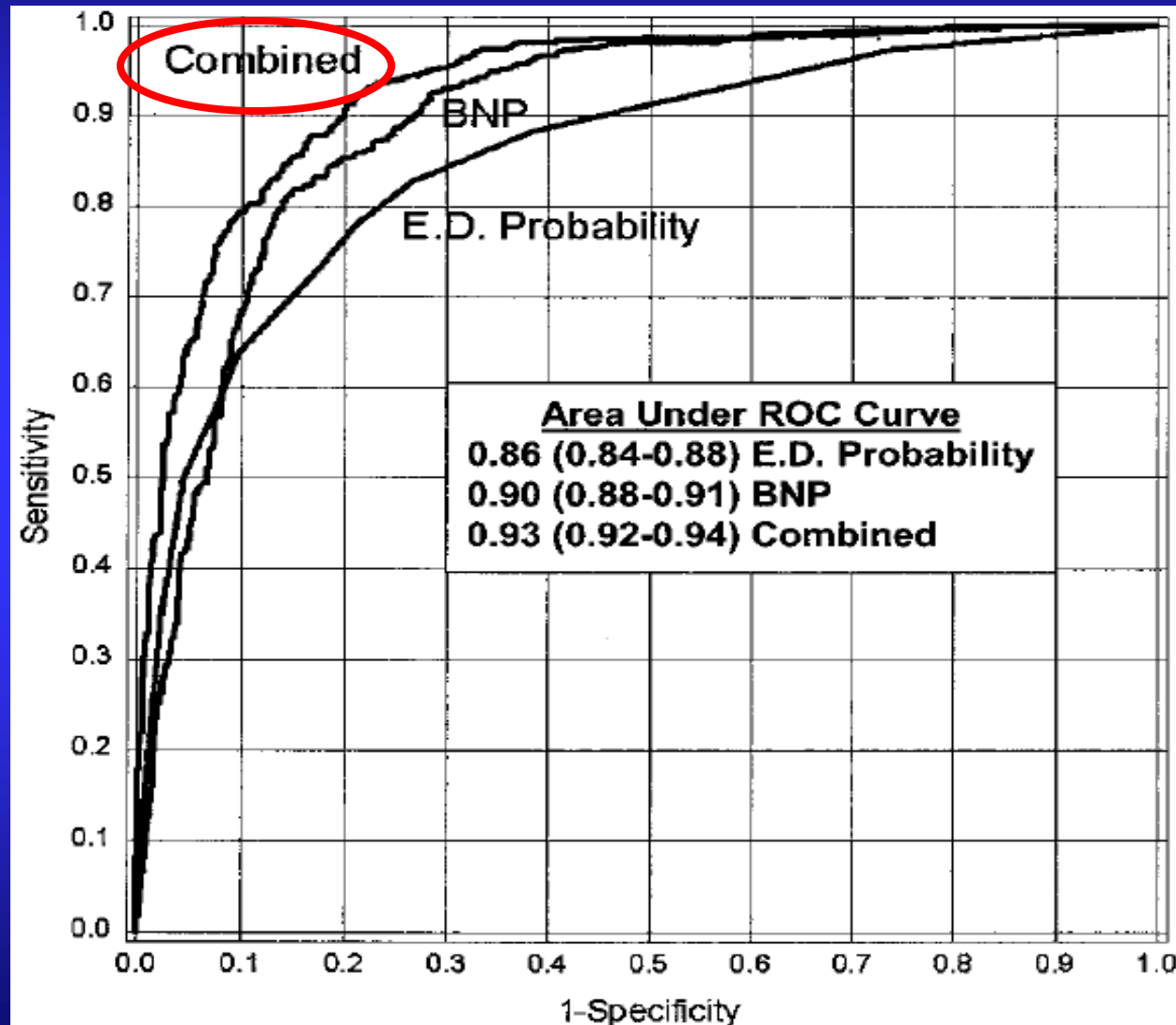
# Specificity, Sensitivity, and Accuracy of BNP Cutoff Value



# Clarification of Diagnosis & BNP



# Acute Dyspnea: BNP ROC Curve



# Results of the BNP for Acute Shortness of Breath Evaluation (BASEL) Study

End Point	Routine Assessment (n=227)	Routine Assessment + BNP (n=225)	<i>P</i> Value
Time to treatment (minutes, median, interquartile range)	90 (20-205)	63 (16-153)	0.03
Time to discharge (days, median, interquartile range)	11.0 (5.0-18.0)	8.0 (1.0-16.0)	0.001
Hospitalization (%)	85	75	0.008
Intensive-care unit admission (%)	24	15	0.01
Total treatment cost (S. median, 95% confidence intervals)	7264 (6301-8227)	5410 (4516-6304)	0.006
In-hospital mortality (%)	9	6	0.21
30-d mortality (%)	12	10	0.45

# Caveats to NP testing

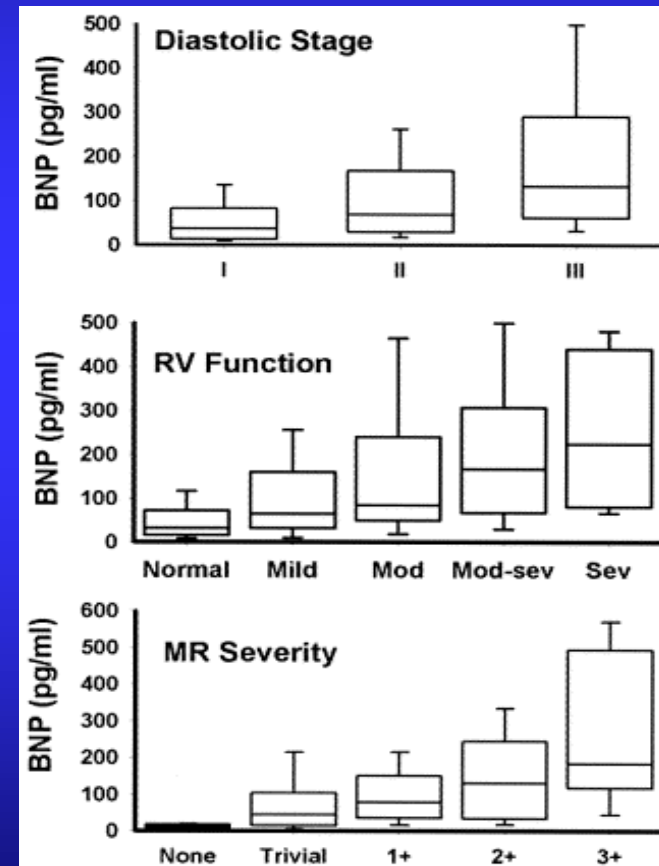


- Gray Zone
- Renal dysfunction
- Obesity
- Heart Failure with normal levels

# “Grey Zone” BNP

## Usually from Right Ventricle

- **Pulmonary disease**
  - COPD with cor pulmonale
  - pulmonary hypertension
- **Right ventricular failure**
  - from long-standing left ventricular failure
  - right ventricular infarction
- **Pulmonary embolism**
- **Knowledge of baseline BNP levels are important**





# Renal dysfunction



- NP are retained in patients with renal dysfunction
- Level much higher in HF with same amt of renal dysfunction
- Need to know baseline values
- Even in dialysis patients- NP above baseline might represent volume overload

<http://go.to/funpic>



# Obesity



- There appears to be a linear inverse relationship between BMI and NP levels
- Patients who are obese ( $\text{BMI} > 30 \text{ kg/m}^2$ ) should have their NP doubled to use the standard cut-points.

# Refractory Edema

---

- 63 year old non-obese man with history of coronary artery disease and bypass surgery 6 years ago
- Complains that he has had leg swelling for several years and is now developing abdominal pain
- Physical exam with elevated JVP, hepatomegaly and ascites with a third heart sound
- Echo reveals normal right and left ventricular function
- BNP 84 pg/ml

# Why is the BNP level low?

- This is a falsely negative BNP. This patient has heart failure.
- The right ventricle makes BNP when overloaded, so this is a false negative reading.
- The patient has neither left nor right heart failure. Another test is in order.



# Constrictive pericarditis







The presence of pericardial calcification on chest x-ray strongly suggests pericardial constriction in patients with symptoms of heart failure.

# Normal levels of BNP

- Heart failure
  - Flash pulmonary edema
  - Acute atrial fibrillation
  - Acute papillary muscle rupture
  - Mitral stenosis
- Looks like HF but not!
  - Tamponade
  - Pericarditis

**IN ACS--Time  
Is Myocardium!**

**So we strive to  
shorten door to  
balloon time**



**So in Acute  
Decompensated  
Heart Failure,  
why don't we strive  
to improve door to  
Diuretic time!!**



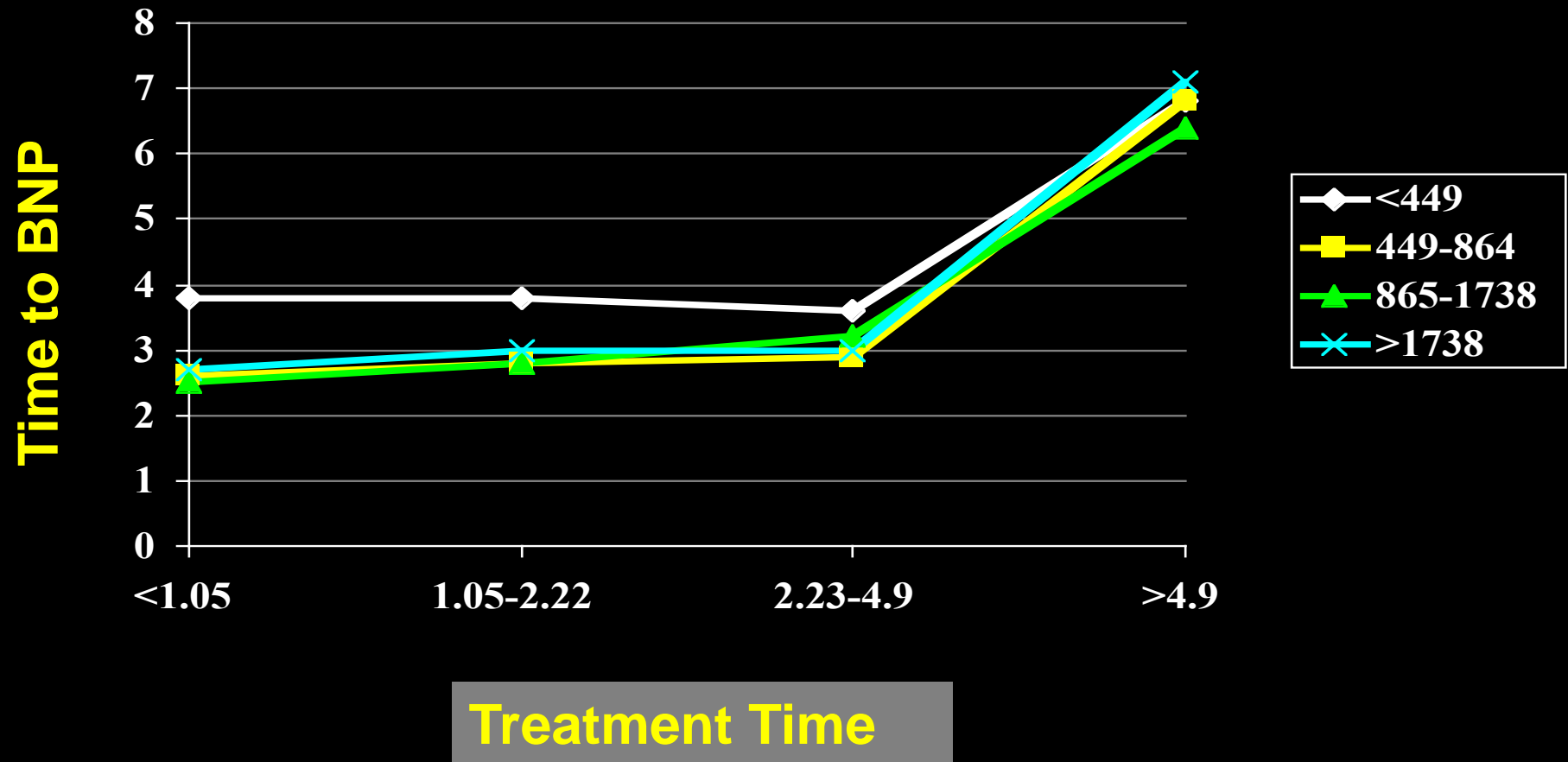


# Sunday in the ER

Is speed important?

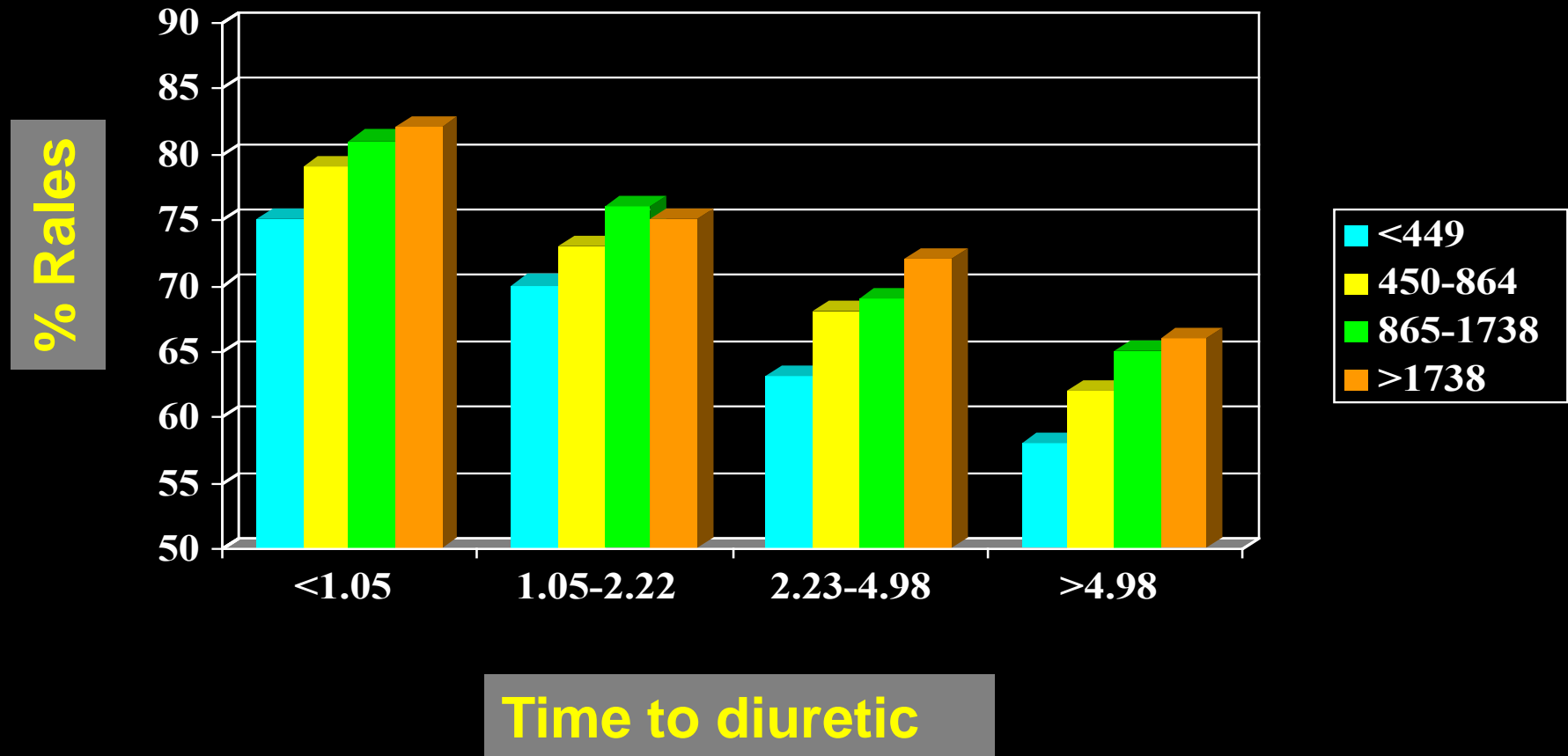


# Delayed BNP Equals Delayed Treatment

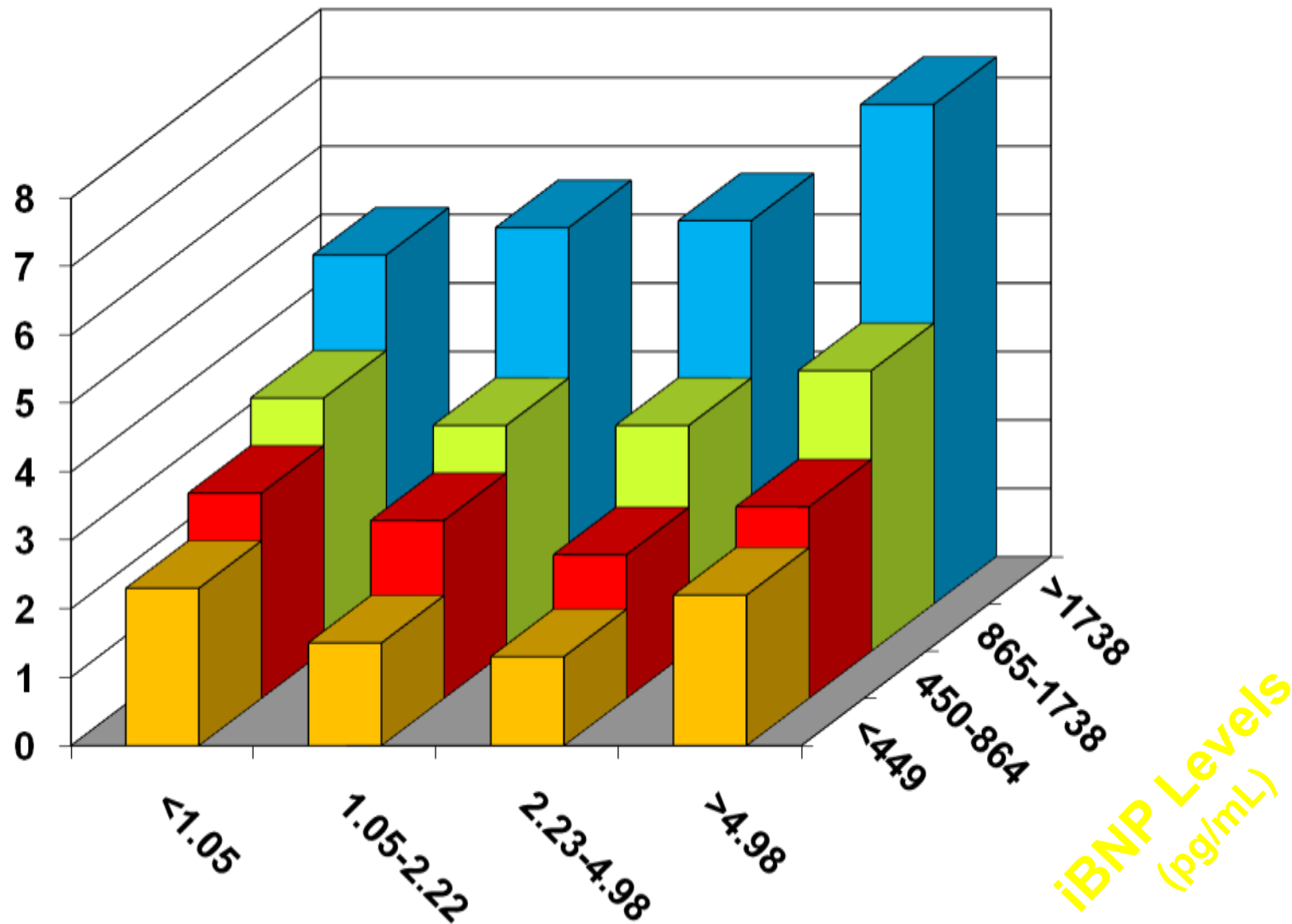




# % Rates vs. Quartiles of Diuretic Time & BNP Level



**Mortality (%)**



**Time to IV Diuretic (hours)**

Lets talk about things that lead to a  
bad pronosis



There is no cardiac biomarker that  
is as good as a NP level for prognosis

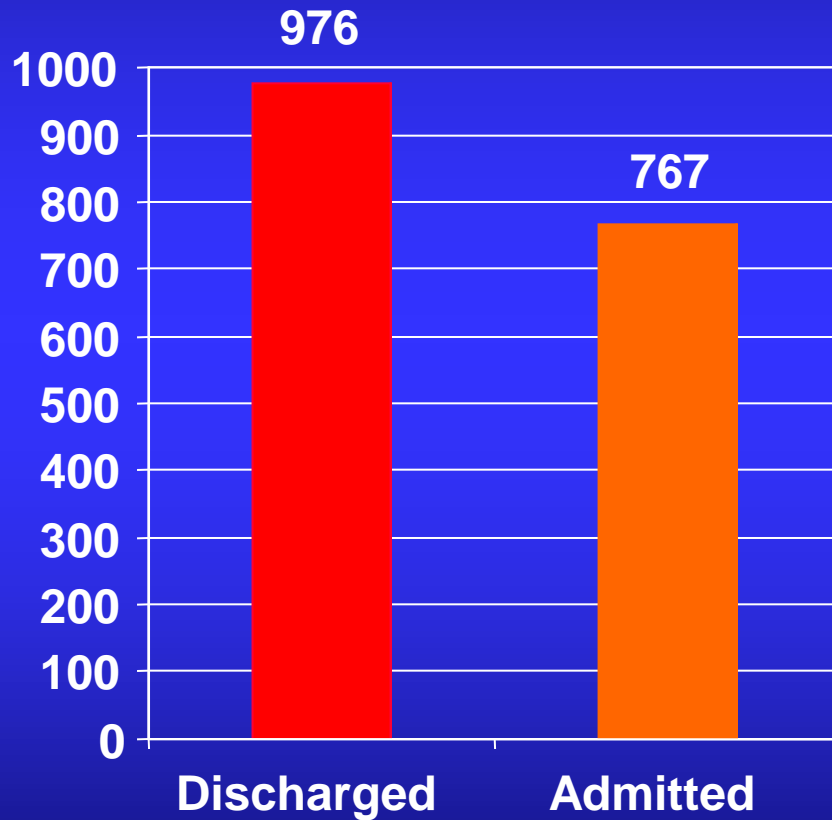




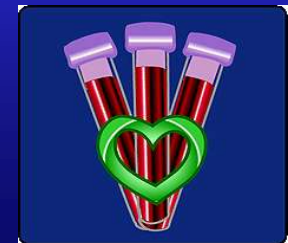


- Multicenter blinded BNP study
  - N= 464, 90% admitted
- If admitted: 11% with BNP < 200
- 90 day events (CHF visit, admit, death)
  - 9% if BNP < 200
  - 29% if BNP > 200
- Disconnect between perceived severity and BNP

# REDHOT BNP Values & Patient Disposition



- Previous data link high BNP to morbidity & mortality
- Actual BNP values blinded to ED physician
- BNP median values  
~22% higher in patients discharged home from ED





## MA-5

- At 11 pm that same night, he awoke with severe shortness of breath. His wife called 911 and he was brought back to the same emergency room (different physician).
- PE: 160/110- pulse-140 (irregular)-26. O<sub>2</sub> sat = 88% . Lungs: Poor air movement. The monitor showed atrial fibrillation.

# MA-questions b

- What is going on?    COPD  
Pulmonary embolism  
CHF  
If CHF- what kind and why?
- What test(s) might be helpful at this point?
  - Cardiac markers
  - D-dimer
  - Lower extremity dopplers
  - BNP

# MA-questions c

The BNP level was 900 pg/ml

- What is going on and why?
- How would you treat this patient?

# MA-6

- He was brought to the ICU where he was given lasix 40 mg ivp, diltiazem 10 mg/hour iv ( heart rate control) and Natreacor 2mcg/kg bolus followed by .01 mcg/kg/min infusion.
- Twenty four hours later he felt much better. His heart rate was back in NSR. His lungs were clear. He had diuresed 3 liters of fluid. Four hours after the discontinuation of Natreacor his BNP level was 150 pg/ml.

# MA-7

- Full doppler echocardiographic exam revealed diastolic dysfunction with  $E/A < .7$  and Deceleration time 320 ms (impaired relaxation).
- He was placed on an ACE inhibitor and beta blocker and discharged 2 days later.

# MA-8- final points

- Patient had COPD with underlying diastolic dysfunction.
- Atrial fibrillation led to severe CHF.
- A BNP level was able to help separate CHF from COPD exacerbation
- Diastolic function is common in the emergency room.
- BNP is elevated in diastolic dysfunction



## **Assessment of Patient with Dyspnea**

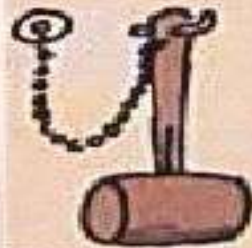
### ***For Your Mother***

- History, physical exam by top gun attending
- Pulse oximetry
- ECG within 5 minutes
- CBC, chem panel
- BNP or NT-pro BNP
- Troponin
- D-dimer, if indicated
- CXR PA and Lateral
- Other testing and imaging as indicated

### ***Mother-in-law***

- Wait in a side room for a few hours
- History, physical exam by 1<sup>st</sup> year med student
- ABG
- CBC, chem panel
- Portable CXR

# EMERGENCY PHYSICIAN



BREAK  
GLASS



History

Physical exam

CXR

**NP levels**