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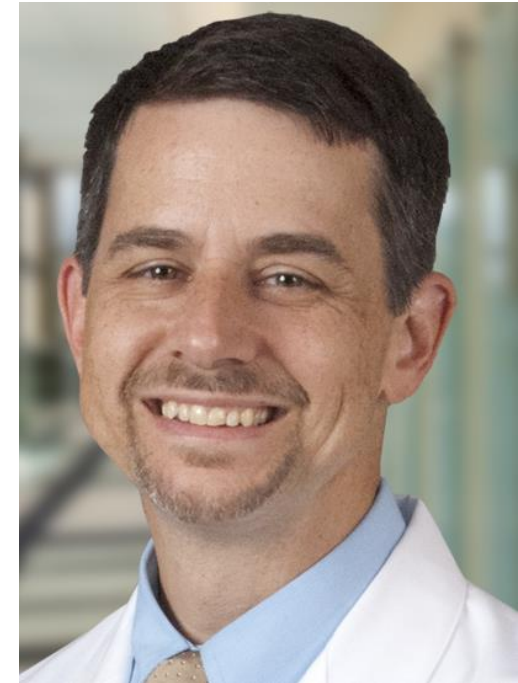
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# Are Troponins, BNP's, d-dimers bankrupting Healthcare?

## Order Wisely!

Martin R. Siegfried, MD/PhD

CARDIOVASCULAR GROUP



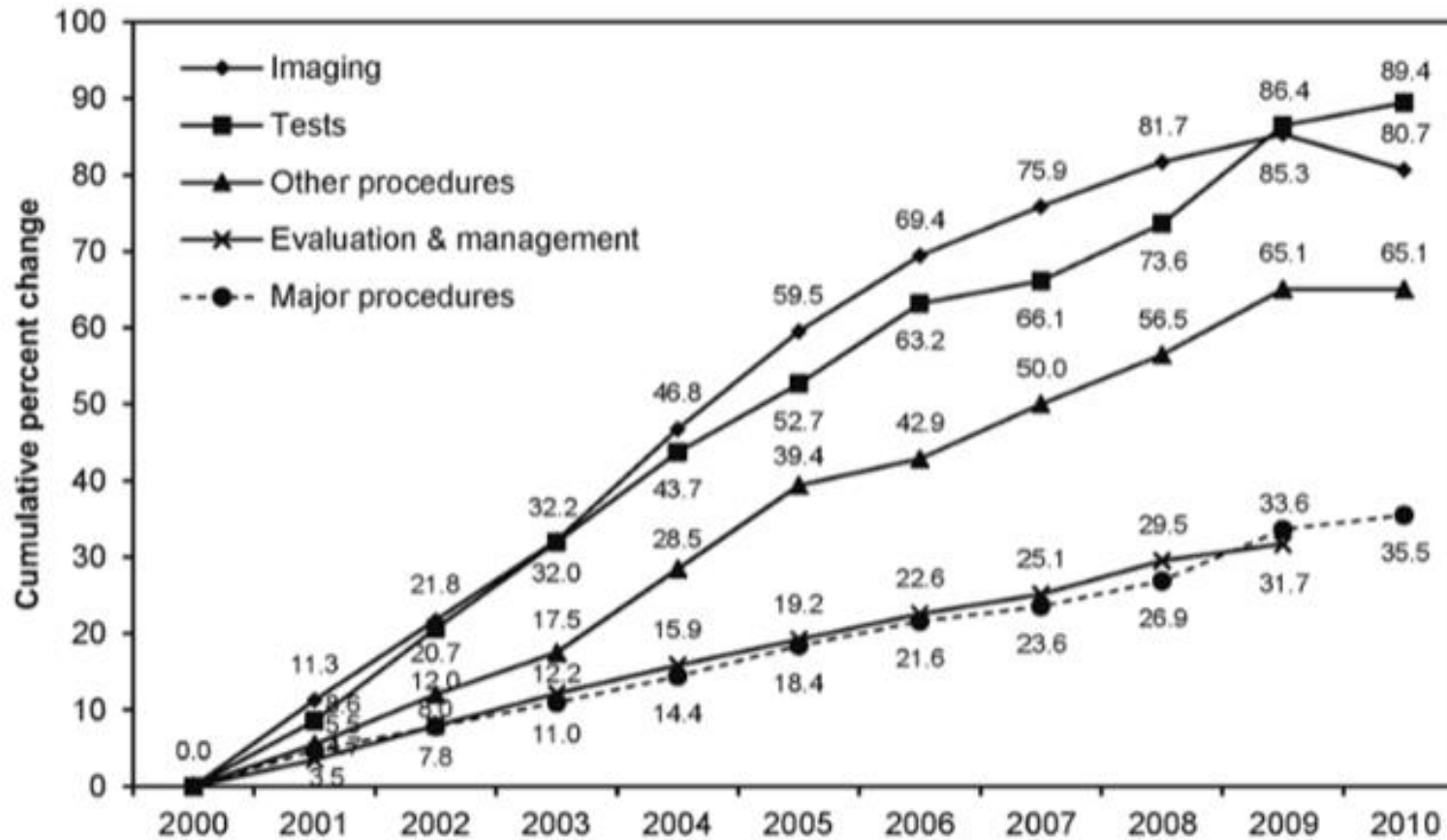


# Laboratory Testing

CARDIOVASCULAR GROUP



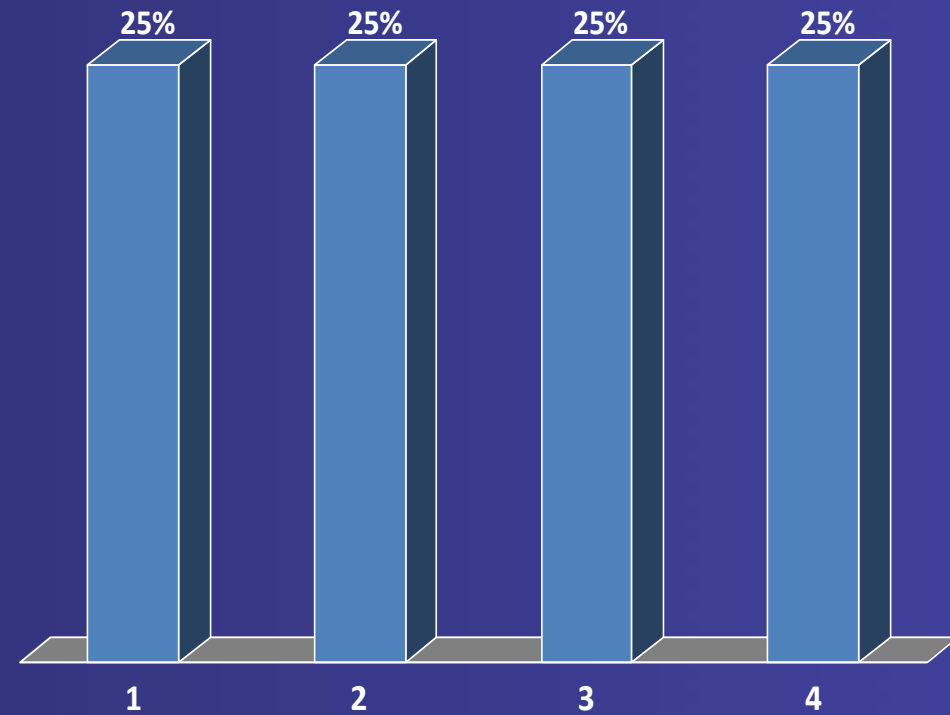
# Lab Testing



← Tests  
← Imaging

# How much was spent on lab tests in 2016 in the US ?

1. \$20 billion
2. \$80 billion
3. \$100 billion
4. \$3 trillion



# Lab Testing

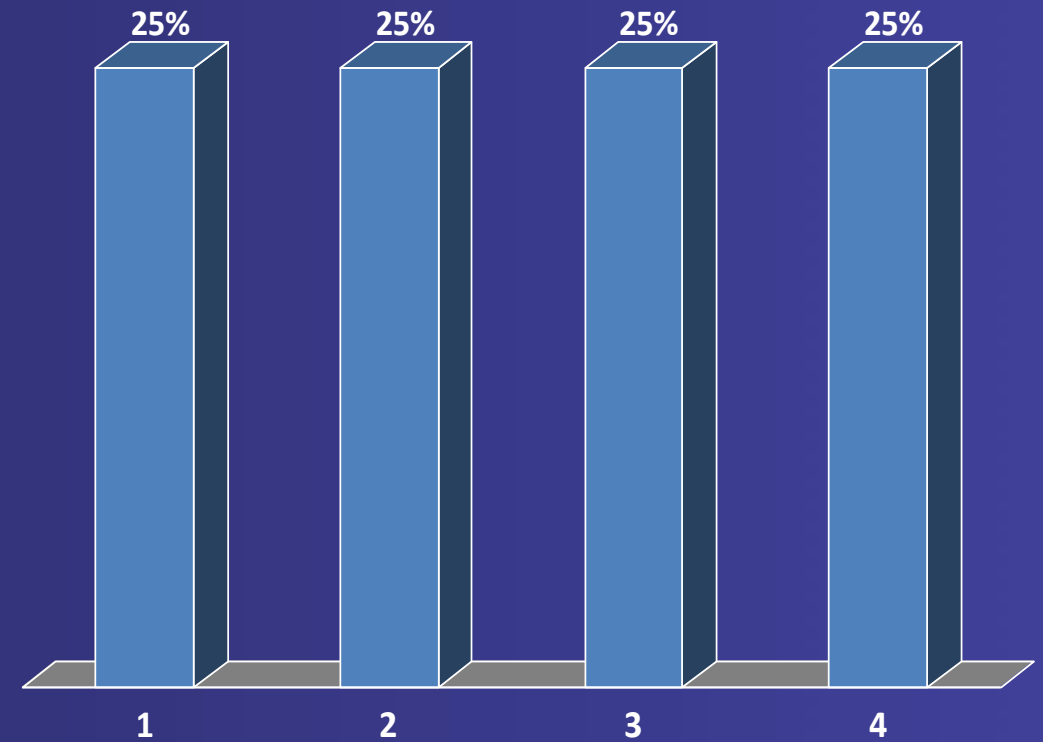
For 2016 (last year that costs have been officially calculated)

\$3.3 trillion

\$200 billion in UNNECESSARY tests

# What is the approximate cost to check a single troponin T?

1. \$20
2. \$50
3. \$200
4. \$400



special thanks: Vicki T. Winkles,  
Laboratory Supervisor Clinical Laboratory GMC



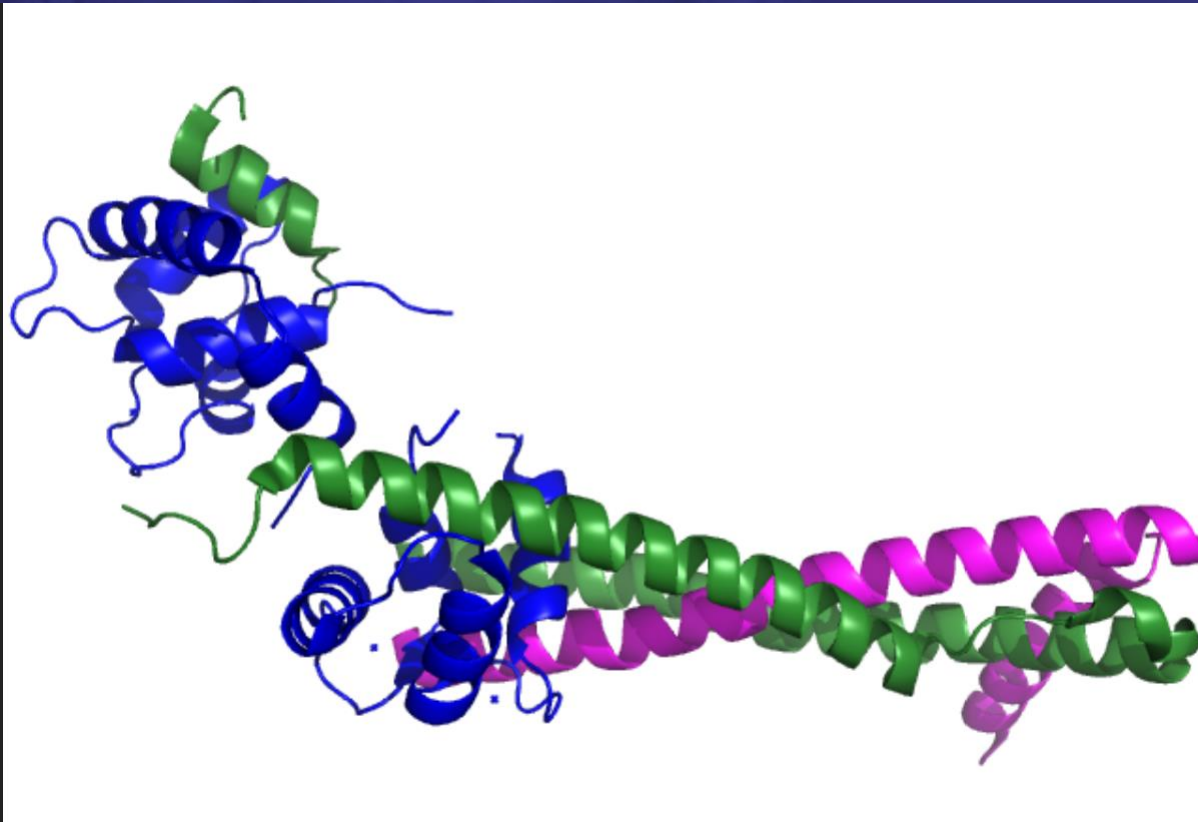
# Lab Testing

## At GMC

Troponin T	\$228
Troponin iStat	\$228
BNP	\$103
d-dimer	\$248



# Troponin Elevation



# Troponin

## Diagnosis of MI requires:

Troponin  $>99^{\text{th}}$  % of the upper reference limit (URL) for the normal range of the assay being used.

A rise and/or fall of the troponin value should be observed.

Cardiac troponin concentrations usually begin to rise two to three hours after the onset of acute MI.

# Troponin in type I vs Type II injury

- Type I: Classic atheroma obstructing coronary artery
- Type II: Intact coronary blood flow with overwhelming myocardial oxygen demand
  - Tachycardia
  - Anemia
  - Hypoxia
  - Extreme hypertension
  - Hypotension

# Non-ACS Troponin Elevation

- Myocarditis
- Takotsubo Cardiomyopathy
- Pulmonary embolus
- Analytical problems (eg, heterophile antibodies)
- Chronic kidney disease.

Look for a dynamic rise or fall in concentration

Look at the absolute concentration

Assess the clinical presentation

# Potential Causes of Elevated Troponin

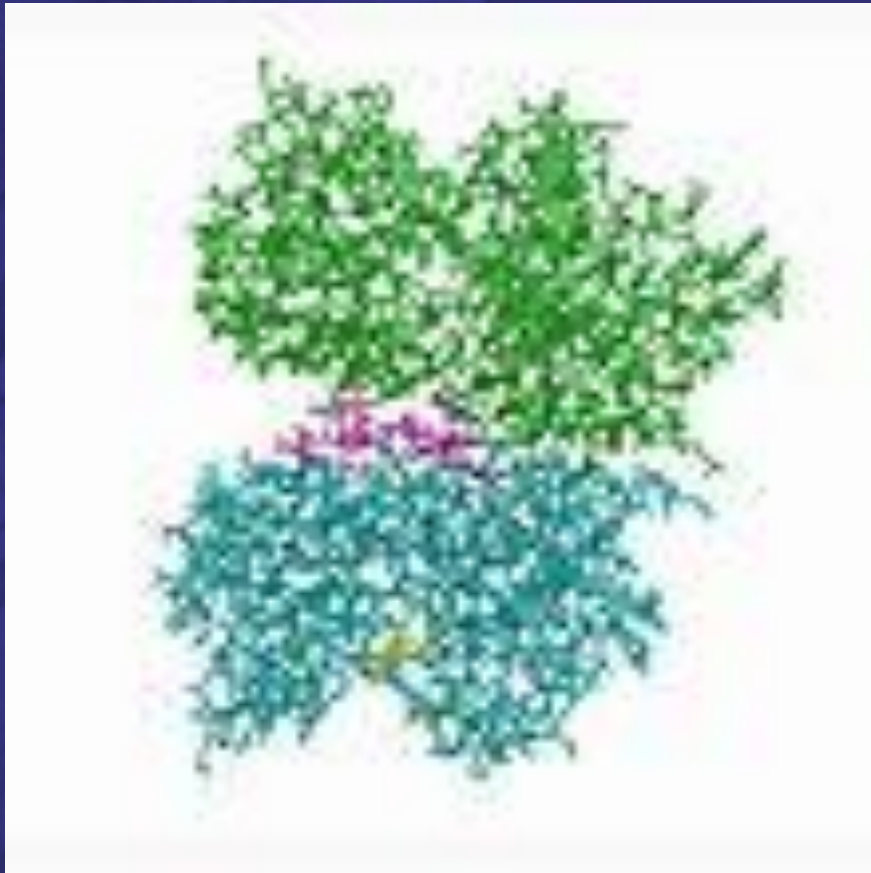
- Acute coronary syndrome
- Demand ischemia
- LVH
- CHF
- Tachycardia
- Atrial Fibrillation
- Critical Illness
- Burns
- Direct Cardiac Trauma
- Acute Stroke
- Amyloidosis
- High dose chemotherapy
- Defibrillation
- Pericarditis/Myocarditis
- Pulmonary Embolus
- Pulmonary Hypertension

# Troponin: Conclusions

- Much better tool to exclude than to diagnose ACS
- More suggestive of ACS if ischemic ECG changes, chest pain, wall-motion abnormalities on echo, and/or the presence of atherosclerotic risk factors.
- Generally speaking, if low probability of CAD in a patient with elevated troponin, better look for underlying cause of troponin elevation than to treat for CAD
- Elevation in non-ACS situations do predict worse short- and long-term survival.



# BNP and CHF





# BNP

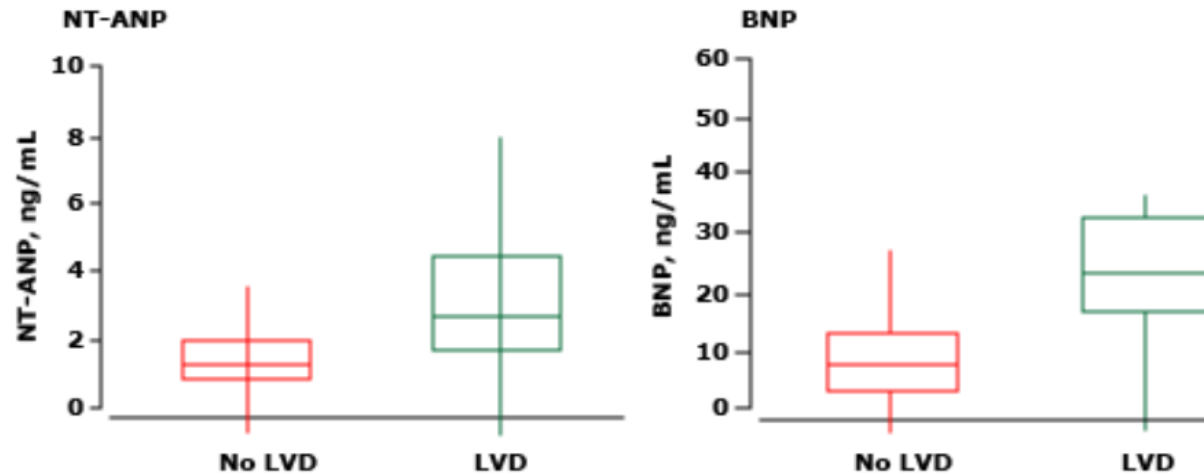
- A peptide synthesized and released in response to ventricular stretch
- very little is stored
- a lag often occurs between the appearance of the natriuretic peptides and the onset of clinical deterioration.
- Genetic factors may account for 40% of the variation in plasma BNP levels in normal subjects

# BNP

- Diuretic
- Natriuretic
- Vasodilator
- Inhibits the renin-angiotensin system
- Inhibits endothelin secretion
- Inhibits systemic and renal sympathetic activity
- Inhibits cardiac fibrosis

# BNP

## Serum ANP and BNP correlate with LV dysfunction



Among 1252 subjects from the general population, median serum concentrations of N-terminal atrial natriuretic peptide (NT-ANP) and brain natriuretic peptide were significantly higher in those with left ventricular systolic dysfunction (LVD) as assessed with echocardiography. Among the patients with LVD, 77 percent were asymptomatic. Boxes are median concentrations and vertical lines are the ranges.

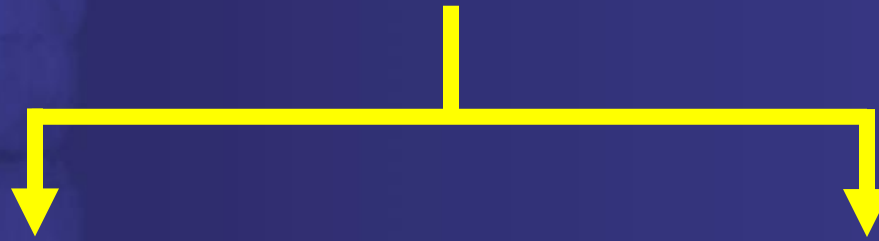
*Data from McDonagh TA, Robb SD, Murdoch DR, et al. Lancet 1998; 351:9.*

# BNP

Pre-pro BNP



Pro BNP (108 amino acids)



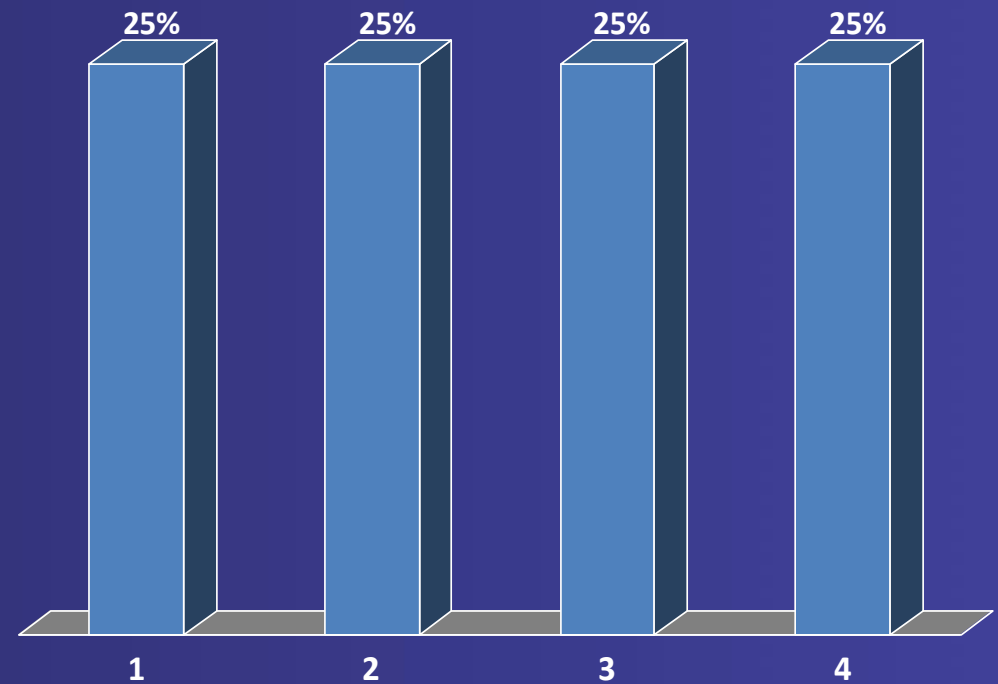
BNP (32 amino acids)  
active

NT pro-BNP (76 amino acids)  
inactive

# BNP

Which medicine is associated with elevated BNP levels?

1. Natricor
2. Aldactone
3. Entresto
4. Coreg



# Triggers which Elevate BNP

- Pulmonary Diseases
  - Acute pulmonary embolism
- Cardiac
  - Pulmonary Hypertension
  - CHF (systolic or diastolic, R, L or bi-V)
  - Sleep apnea
  - Valve disease
  - Pneumonia
  - Myocardial disease (LVH or myocarditis)
- Neurologic Disorders
  - Ischemic or hemorrhagic CVA
  - Myocardial Trauma (surgery, contusion, cardioversion)
- Other
  - Arrhythmia
  - Acute or chronic renal insufficiency
  - Pericardial disease
  - Sepsis
  - Chemotherapy
  - Anemia
  - Cirrhosis
  - Hypertension

# BNP

## Which of the following is the “sickest” patient?

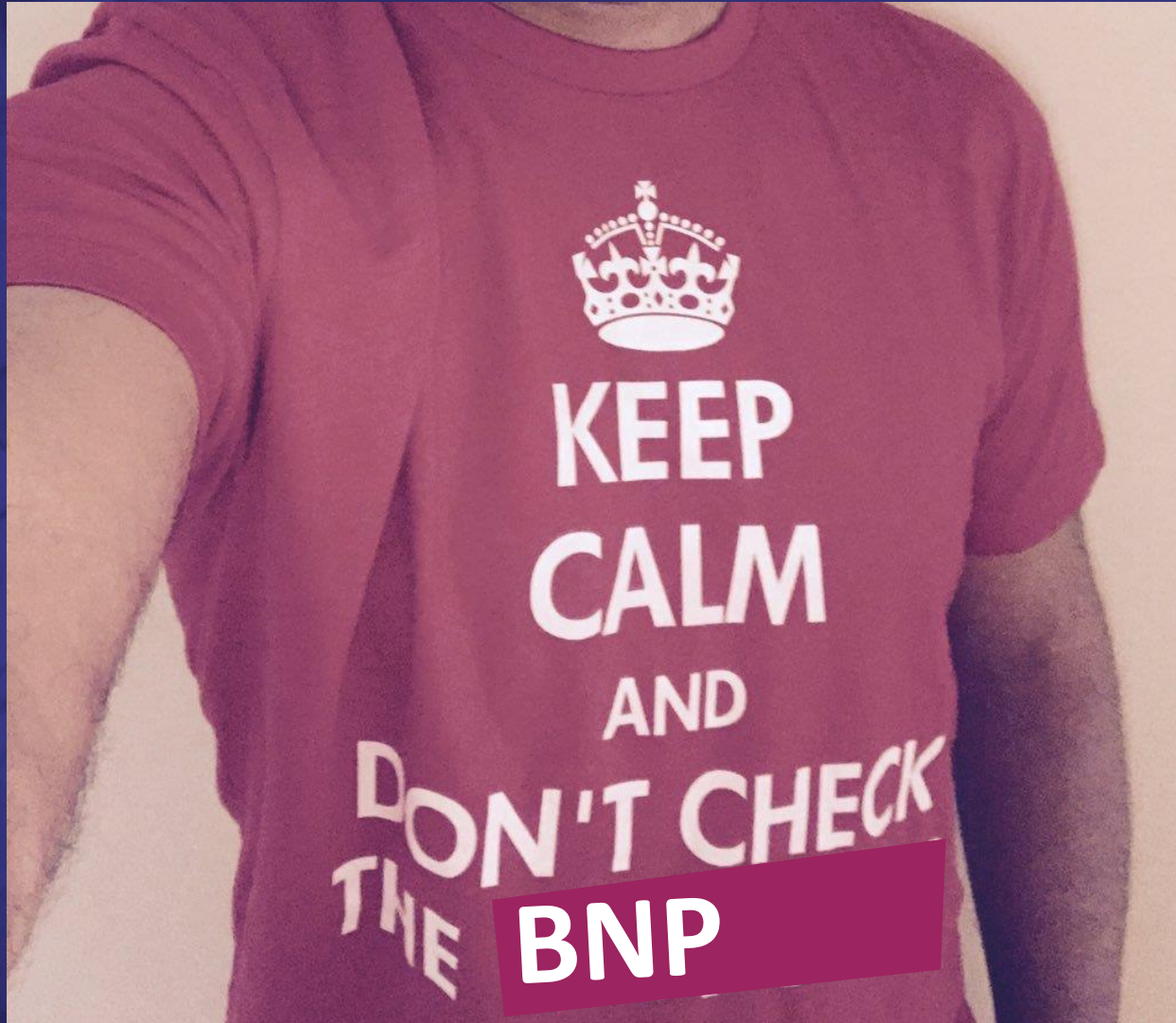
1. An ER patient with a history of an EF of 25% and a BNP level of 2030, HR 80, BP 135/87, RA Sats 85%, “ran out of meds” a month ago
2. A stable 49YO with a known EF 10%, a BNP of 30,000, compliantly taking coreg, Entresto, Lasix/potassium, Aldactone, who presented to the hospital for initiation of hemodialysis
3. A 65YO with an unknown EF, moderately anemic from known leukemia, currently on chemotherapy, BNP 25,000



# BNP, future directions

- to assess adequacy of CHF therapy in heart failure patients. (conflicting results)
- prognostic value in CHF, as higher levels are predictive of increased morbidity and mortality.
- Valvular diseases higher levels associated with worsening valvular lesions and poorer outcomes

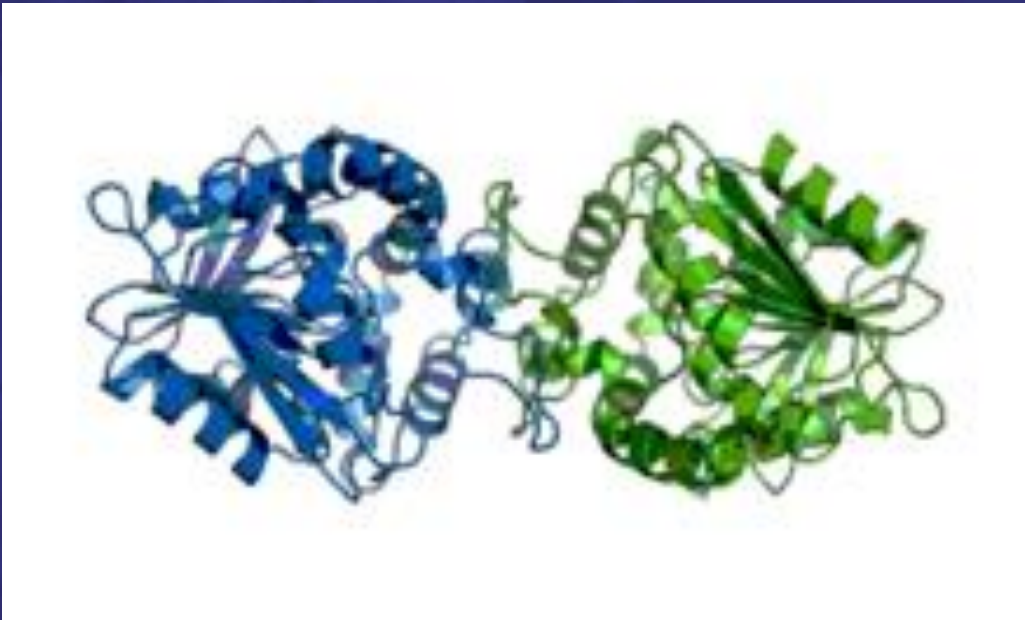
# BNP



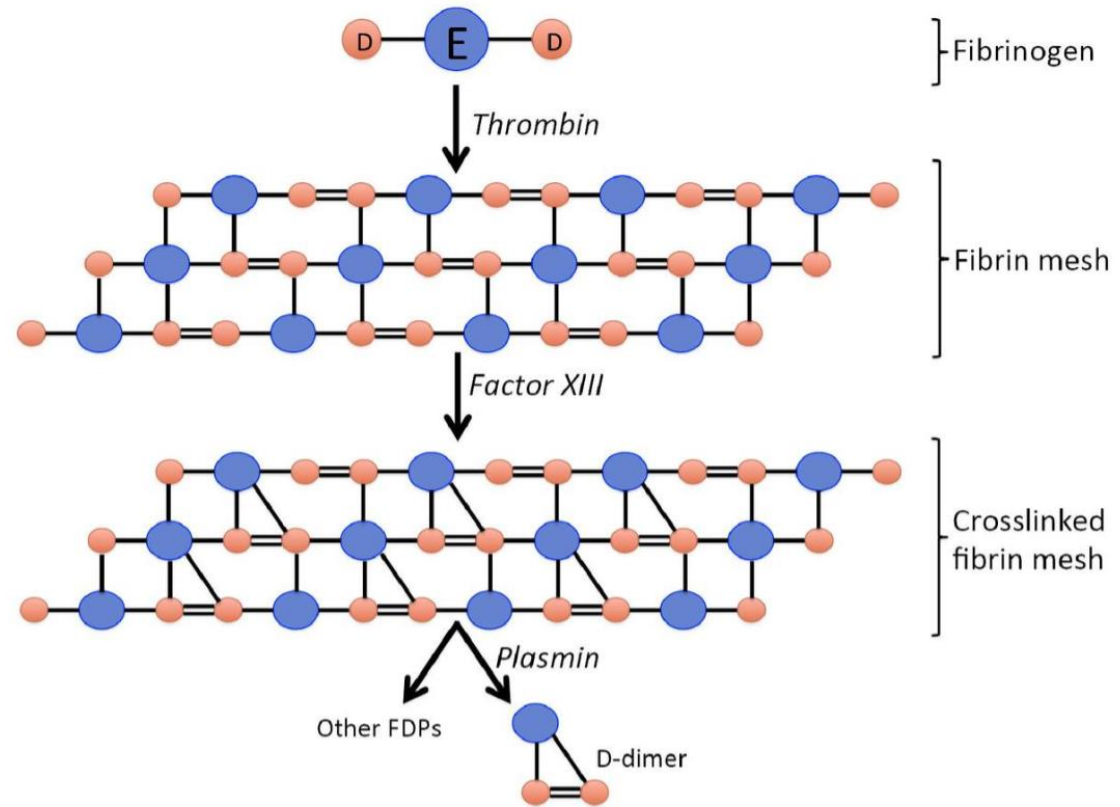
# BNP conclusion

- If the BNP is negative your patient **PROBABLY** doesn't have decompensated heart failure.
- If the BNP is elevated decompensated CHF is one of more than 20 possible disease states that could be present

# D-Dimer



# d-dimer





# d-dimer

- Sensitivity: 90-96%
- Specificity: 40-60%

## Disorders associated with increased plasma levels of fibrin D-dimer

Arterial thromboembolic disease
Myocardial infarction
Stroke
Acute limb ischemia
Atrial fibrillation
Intracardiac thrombus
Venous thromboembolic disease
Deep vein thrombosis
Pulmonary embolism
Disseminated intravascular coagulation
Preeclampsia and eclampsia
Abnormal fibrinolysis; use of thrombolytic agents
Cardiovascular disease, congestive failure
Severe infection/sepsis/inflammation
Surgery/trauma (eg, tissue ischemia, necrosis)
Systemic inflammatory response syndrome
Vaso-occlusive episode of sickle cell disease
Severe liver disease (decreased clearance)
Malignancy
Renal disease
Nephrotic syndrome (eg, renal vein thrombosis)
Acute renal failure
Chronic renal failure and underlying cardiovascular disease
Normal pregnancy
Venous malformations



# d-dimer

## Wells criteria and modified Wells criteria: clinical assessment for pulmonary embolism

Clinical symptoms of DVT (leg swelling, pain with palpation)	3.0
Other diagnosis less likely than pulmonary embolism	3.0
Heart rate >100	1.5
Immobilization (≥3 days) or surgery in the previous four weeks	1.5
Previous DVT/PE	1.5
Hemoptysis	1.0
Malignancy	1.0
<b>Probability</b>	<b>Score</b>
<b>Traditional clinical probability assessment (Wells criteria)</b>	
High	>6.0
Moderate	2.0 to 6.0
Low	<2.0
<b>Simplified clinical probability assessment (Modified Wells criteria)</b>	
PE likely	>4.0
PE unlikely	≤4.0

DVT: deep vein thrombosis; PE: pulmonary embolism.

Data from van Belle A, Buller HR, Huisman MV, et al. Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. JAMA 2006; 295:172.

# d-dimer

Age > 65	No 0	Yes +1	
Previous DVT or PE	No 0	Yes +3	
Surgery (under general anesthesia) or lower limb fracture in past month	No 0	Yes +2	
Active malignant condition Solid or hematologic malignant condition, currently active or considered cured < 1 year	No 0	Yes +2	
Unilateral lower limb pain	No 0	Yes +3	
Hemoptysis	No 0	Yes +2	
Heart rate	< 75 0	75-94 +3	≥ 95 +5
Pain on limb palpation	No 0	Yes +4	

Low Risk: 0-3\*  
 Intermed Risk: 4-10  
 High Risk: ≥11

\*<10% risk PE

# Conclusions

- \$200 billion is wasted each year on unnecessary laboratory testing
- In most cases, “shotgunning” lab tests does neither you nor you patient any favors
- Elevation in either BNP, d-Dimer, or troponin alone is insufficient to make a diagnosis
- The first step in any patient interaction should be to take a proper history and conduct a physical, not to batch a bunch of labs

# Conclusions

- Take some time to get a history (10 minutes)
- Perform a 5 min physical exam
- ECG and CXR are almost always a good idea, no recent available
- Order appropriate labs to the situation