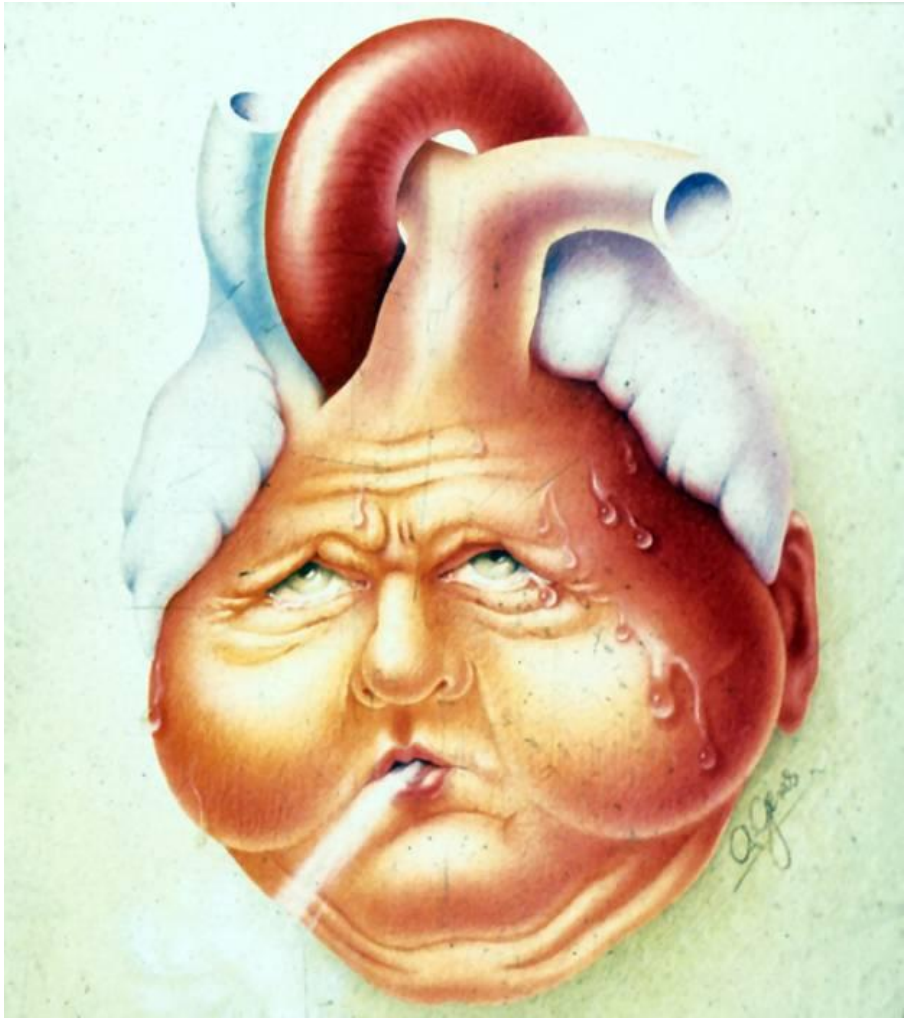
The Clinical Syndrome of Heart Failure



Brian Jensen MD
UNC Mini Medical School
February 3, 2020

Case Presentation

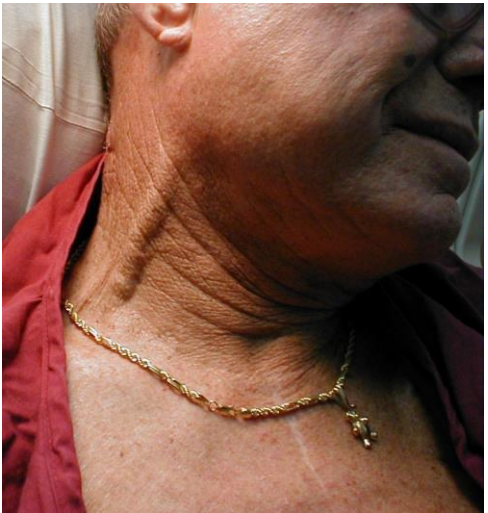
HPI: 57 year-old man with a history of myocardial infarction in 2016 presents with worsening shortness of breath for the past two weeks. He was able to walk around WalMart three times prior to Thanksgiving, but now becomes short of breath walking around his house. He also reports leg swelling to his knees, abdominal bloating, and a 20 lb weight gain. He has had difficulty sleeping as he becomes short of breath when he lies down. As a result he has been sleeping on 3 pillows and occasionally has to sit up on the edge of the bed to catch his breath. These are all new symptoms for him.

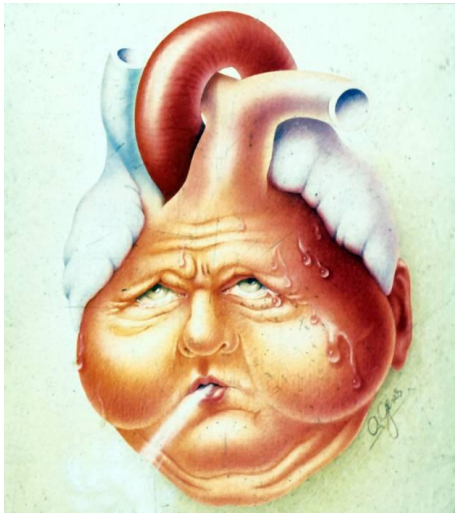
Physical Exam: mildly tachypneic with prolonged conversation
HR 105 bpm BP 98/74 mmHg O2 88% on RA, 95% on 2L N
JVP 14-16 cm H2O
Bibasilar rales
Tachycardic S1S2 +S3 and 2/6 holosystolic murmur at the apex
Distended, non-tender, liver edge 3cm below costal margin
LE slightly cool to touch, 2+ pitting edema to mid thigh

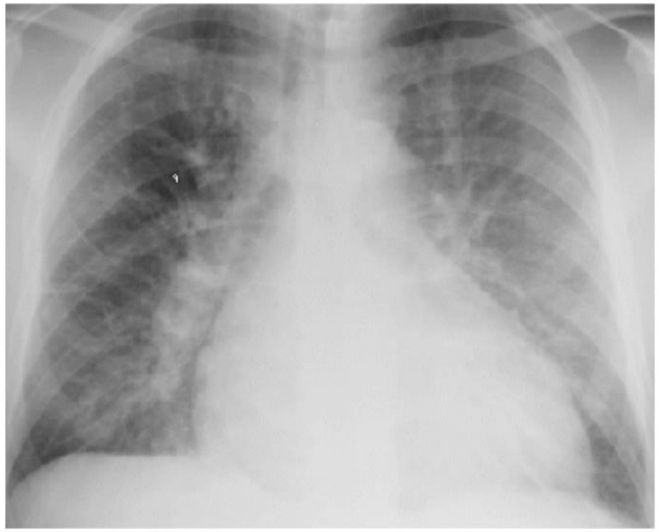
Definition (Practical)

Heart Failure

A complex *clinical syndrome* that results from maladaptive neurohormonal responses to decreased cardiac performance and is most commonly characterized by fluid retention and effort intolerance





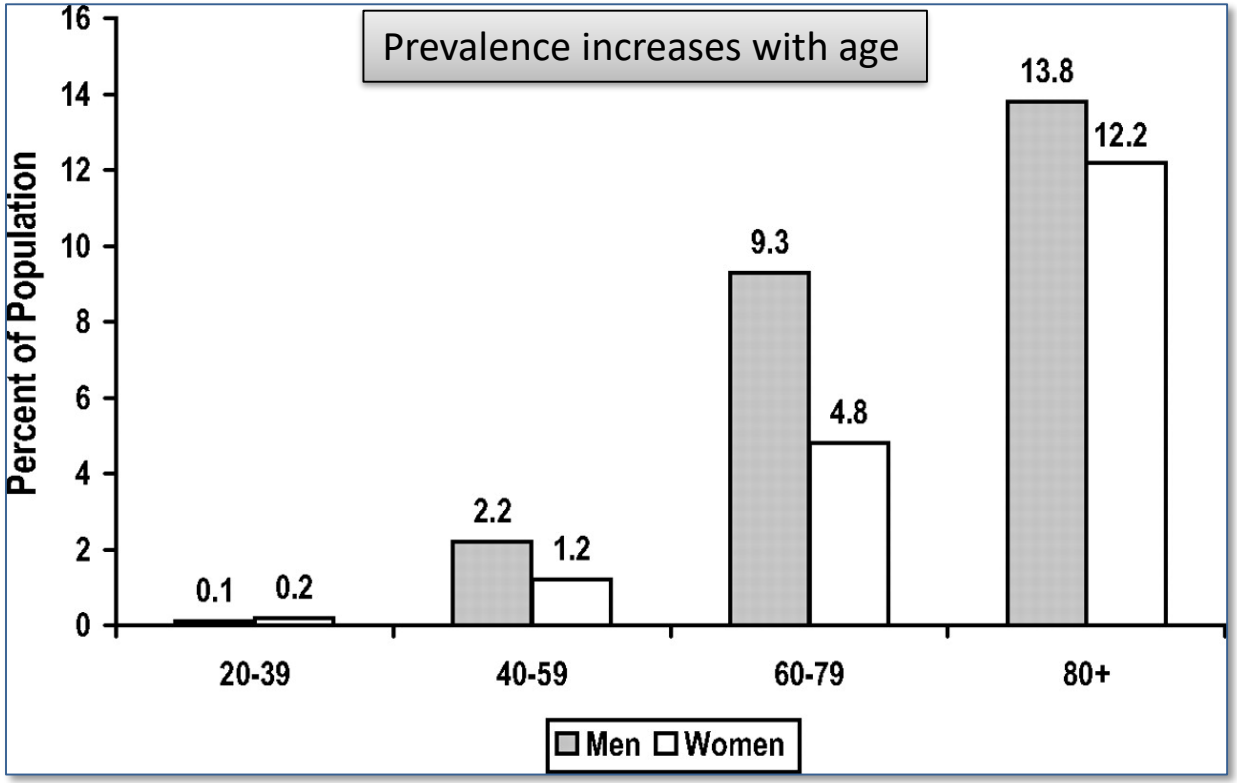


Heart Failure Statistics

The obligatory burden of disease slide…

6 million people have HF

~700,000 new cases annually



~300,000 annual deaths due to HF

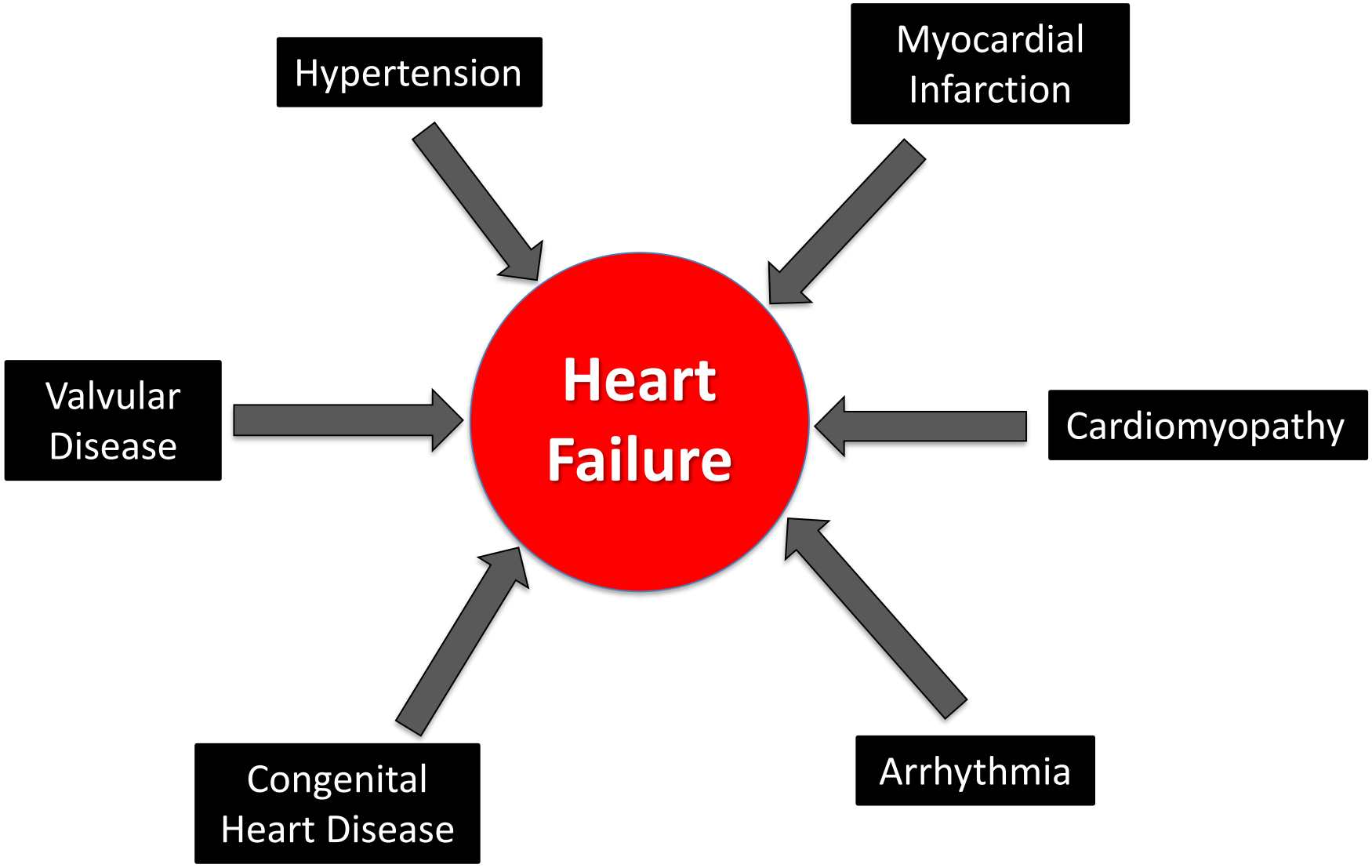
1.1 million hospitalizations per year

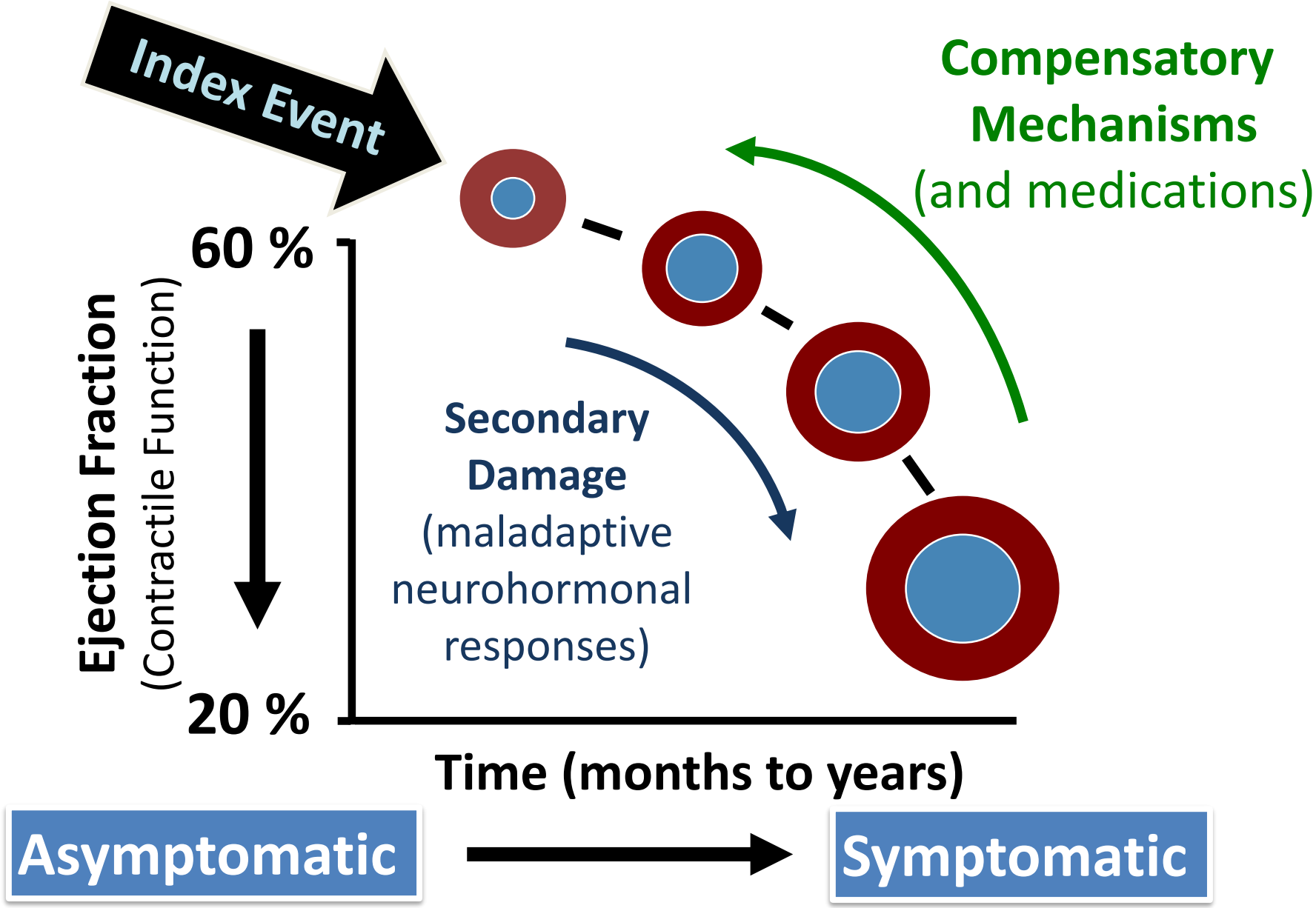
Largest Medicare expenditure…$35-40 billion yearly

AHA Statistical Update

Causes of Heart Failure

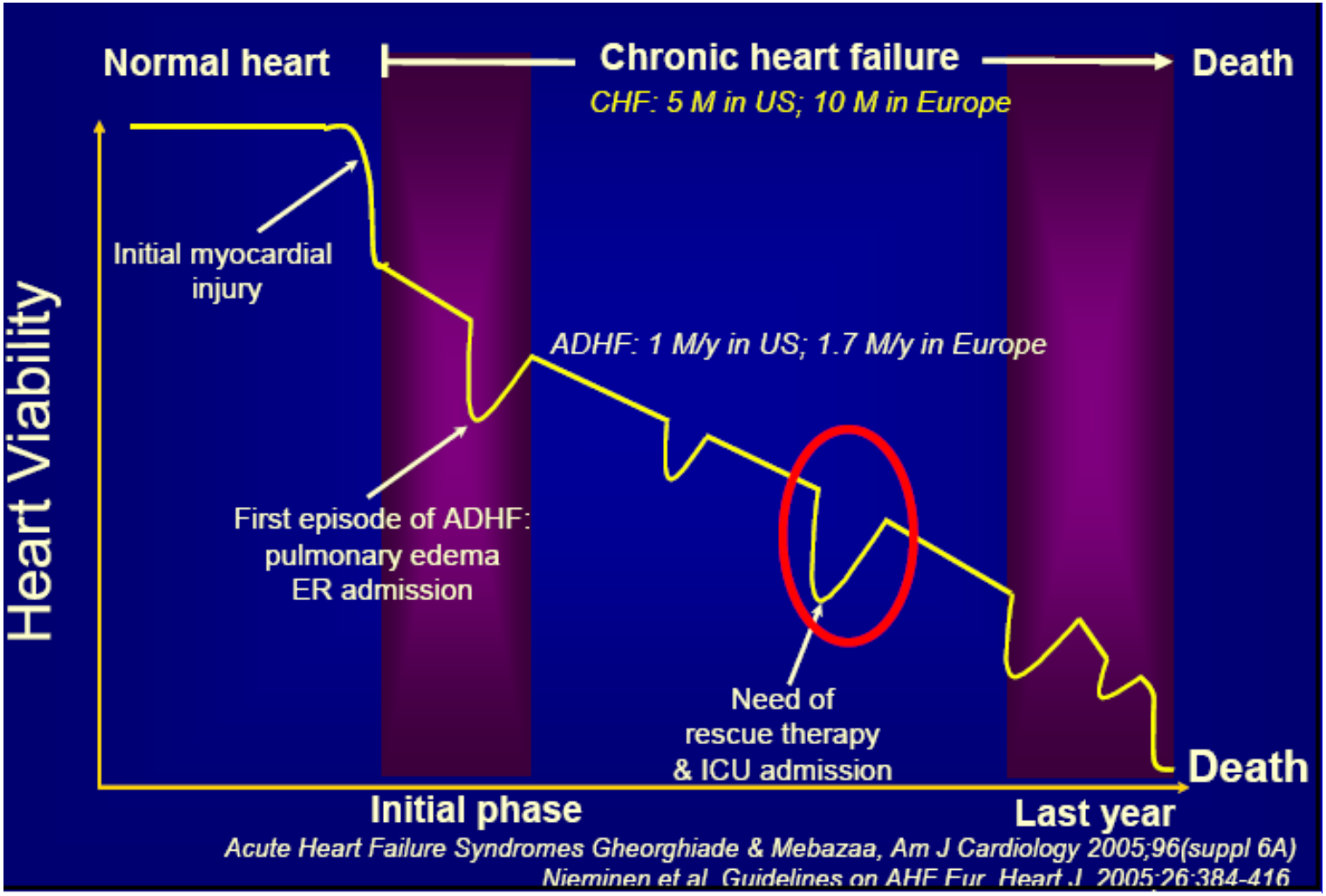
Heart Failure as a final common pathway





Mann, Circulation 1999; 100: 999-1008

Heart failure is progressive and has a poor prognosis

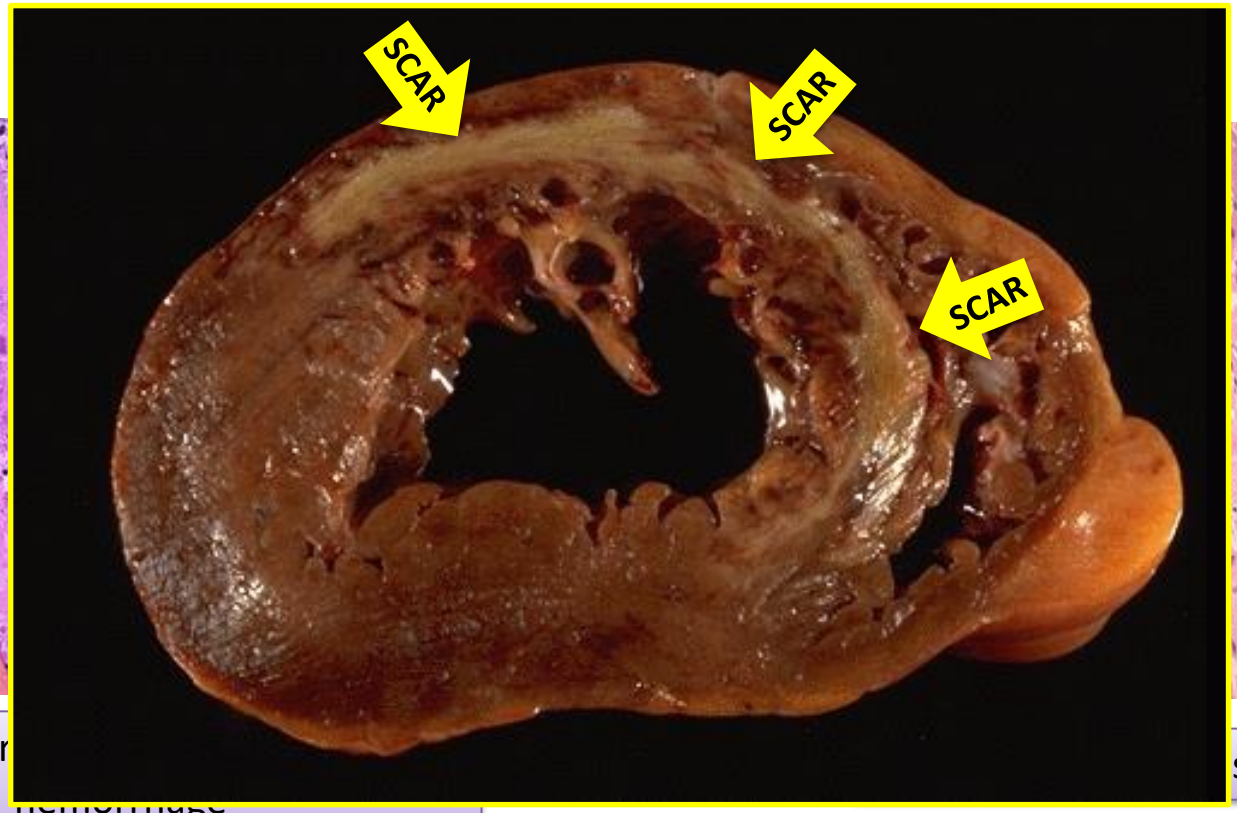


Mean survival after diagnosis of heart failure is 5 years

Mean survival after first hospitalization for acute decompensated HF (ADHF) = 2.4 years

Causes of Heart Failure

Ischemic "Cardiomyopathy"



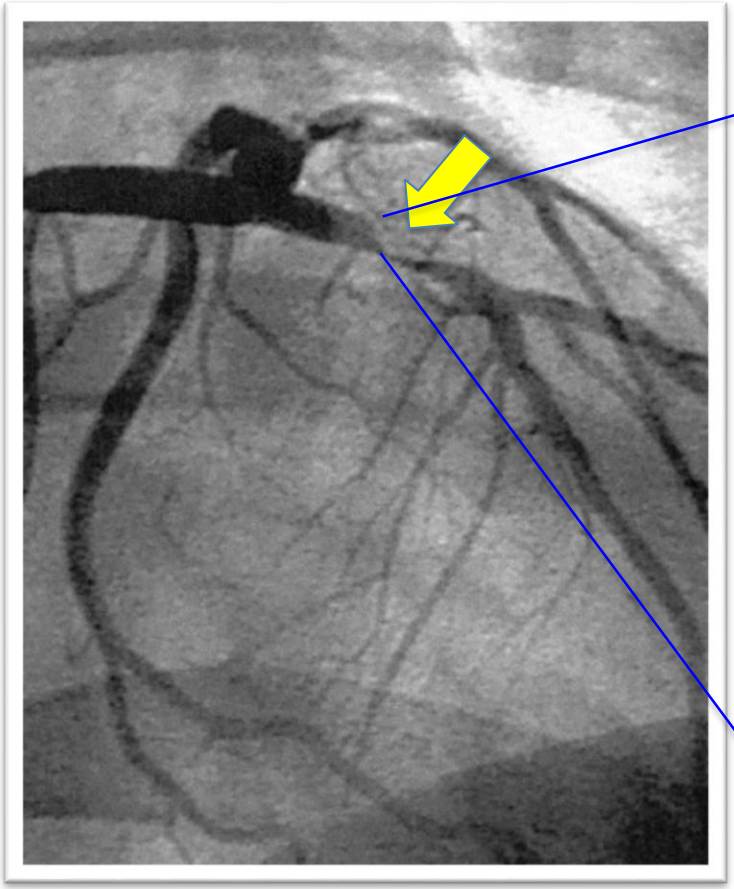
EARLY: Neutr

sis

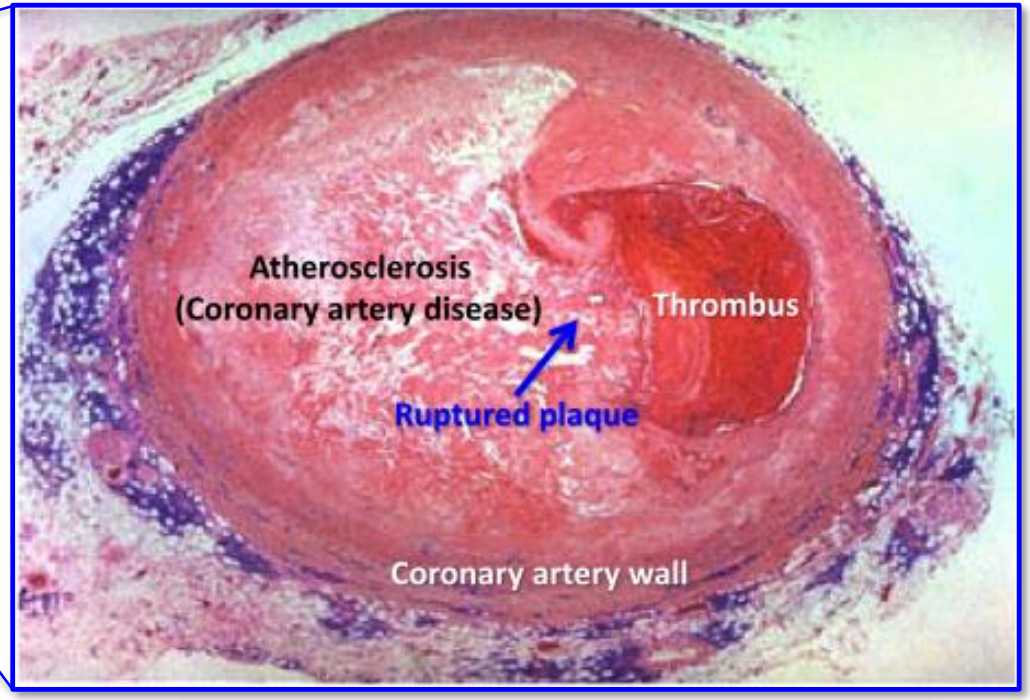
Myocardial infarction ("ischemic cardiomyopathy") is the most common cause of HF. The problem with the muscle is secondary to a problem in the coronary arteries

Causes of Heart Failure

Myocardial Infarction: Dead Meat Don't Beat



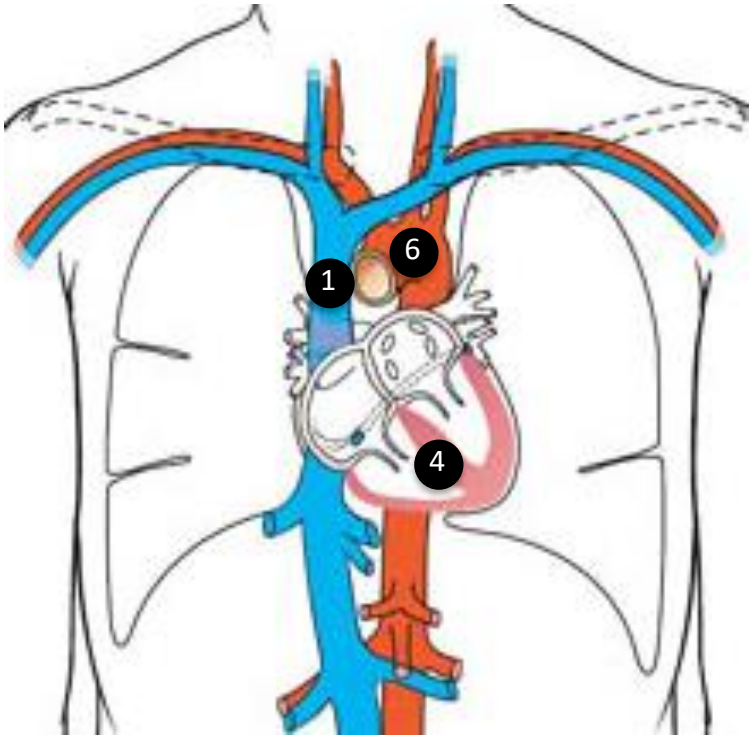
Coronary Angiogram



Coronary artery with plaque rupture

Yeah, but what *is* heart failure?

The Hemodynamic or "Mechanical" Paradigm



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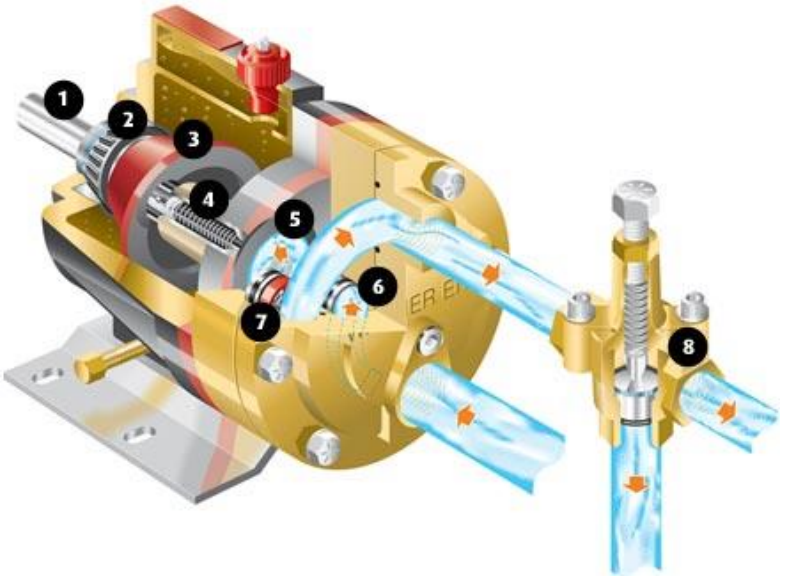
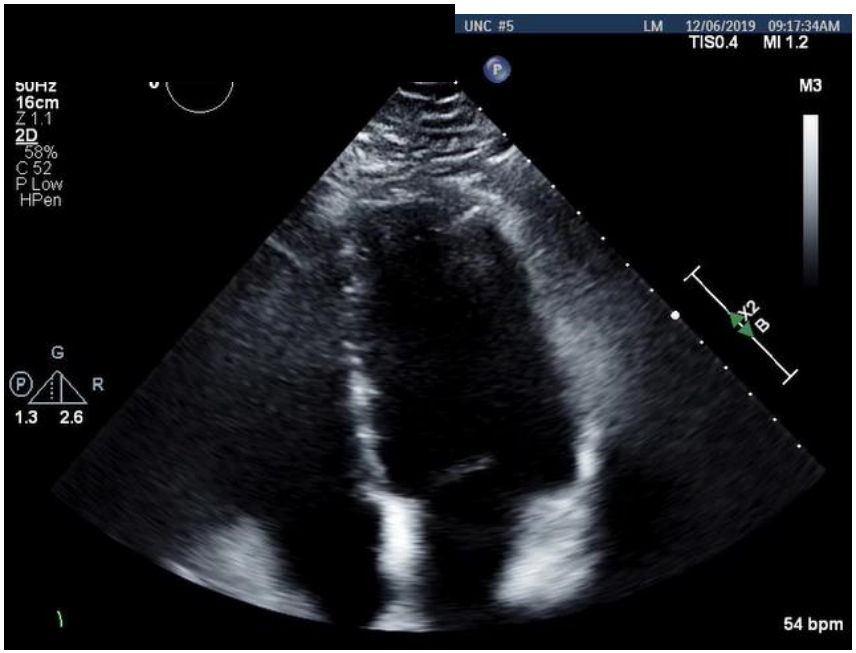


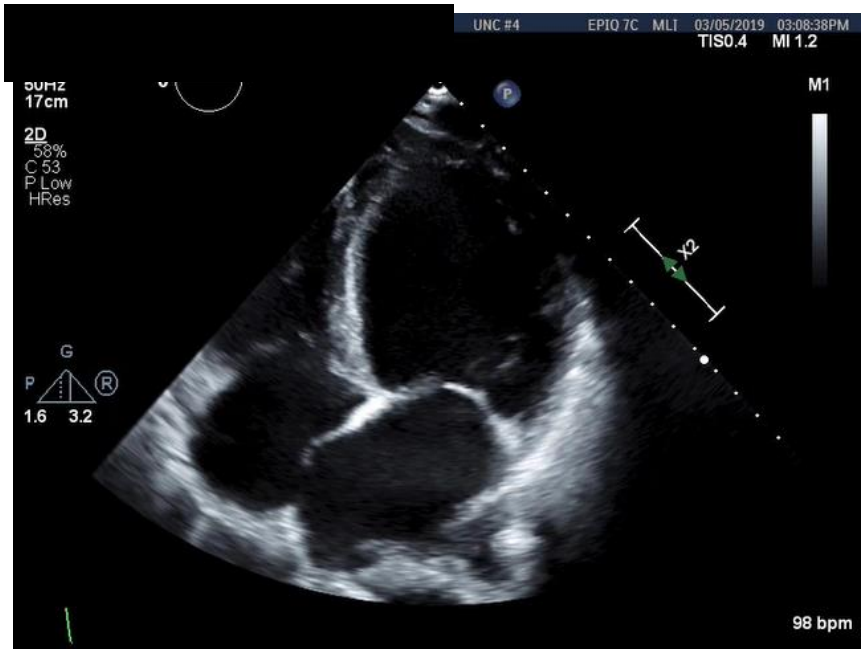
The heart is a pump.
The blood vessels are pipes that enter and leave the pump.
Heart failure is pump failure…

https://www.clevelandclinic.org/heartcenter/images/guide/heartworks/heart_bloodvessels.jpg

Diagnosis of heart failure

Echocardiogram (cardiac ultrasound)





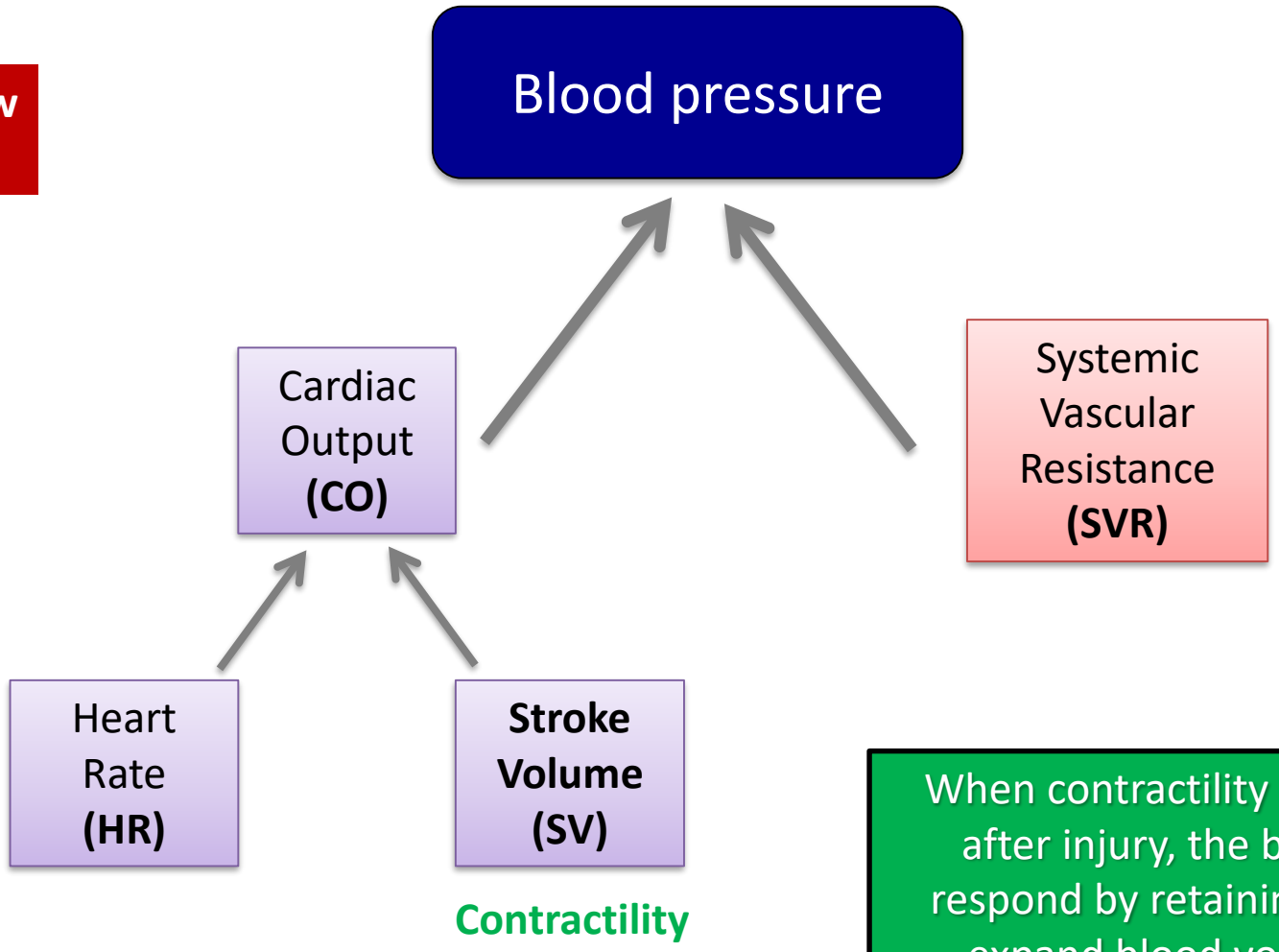
Normal

Heart Failure

Systole = contraction
Diastole = relaxation

Regulation of blood pressure is the central function of the cardiovascular system

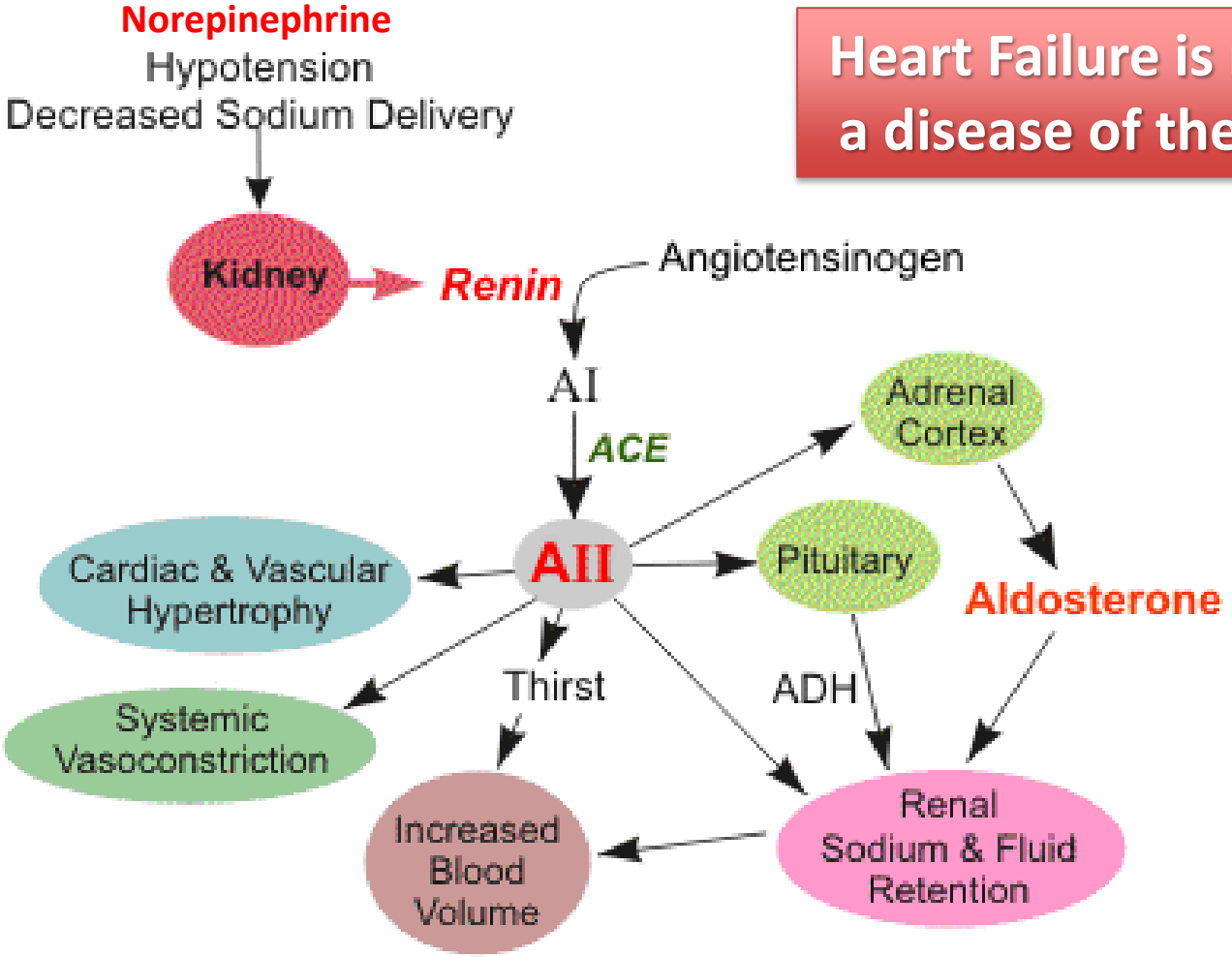
Ohm's Law
V = IR



When contractility decreases after injury, the body will respond by retaining fluid to expand blood volume to increase stroke volume.

Neurohormonal Paradigm

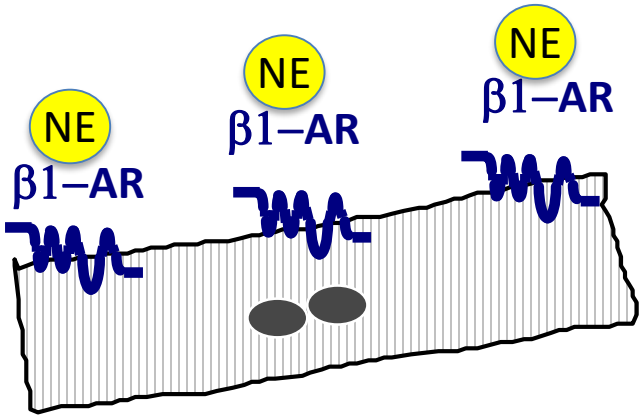
A series of Maladaptive Responses



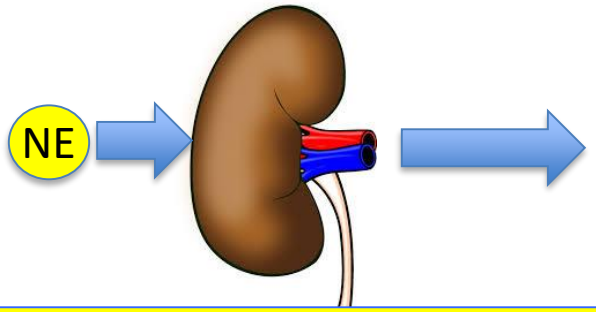
http://www.cvphysiology.com/Blood%20Pressure/BP015.htm

Sympathetic nervous system activation

"Fight or flight" with epinephrine and norepinephrine



β1-AR stimulation by norepinephrine increases heart rate (chronotropy) and contractility (inotropy)



Increased renin release
Increase fluid retention (preload)

Acutely, these changes are adaptive and can improve cardiac output in a heart with impaired contractility

Maladaptive chronic sympathetic surge

All this fighting or fleeing is tough on the heart

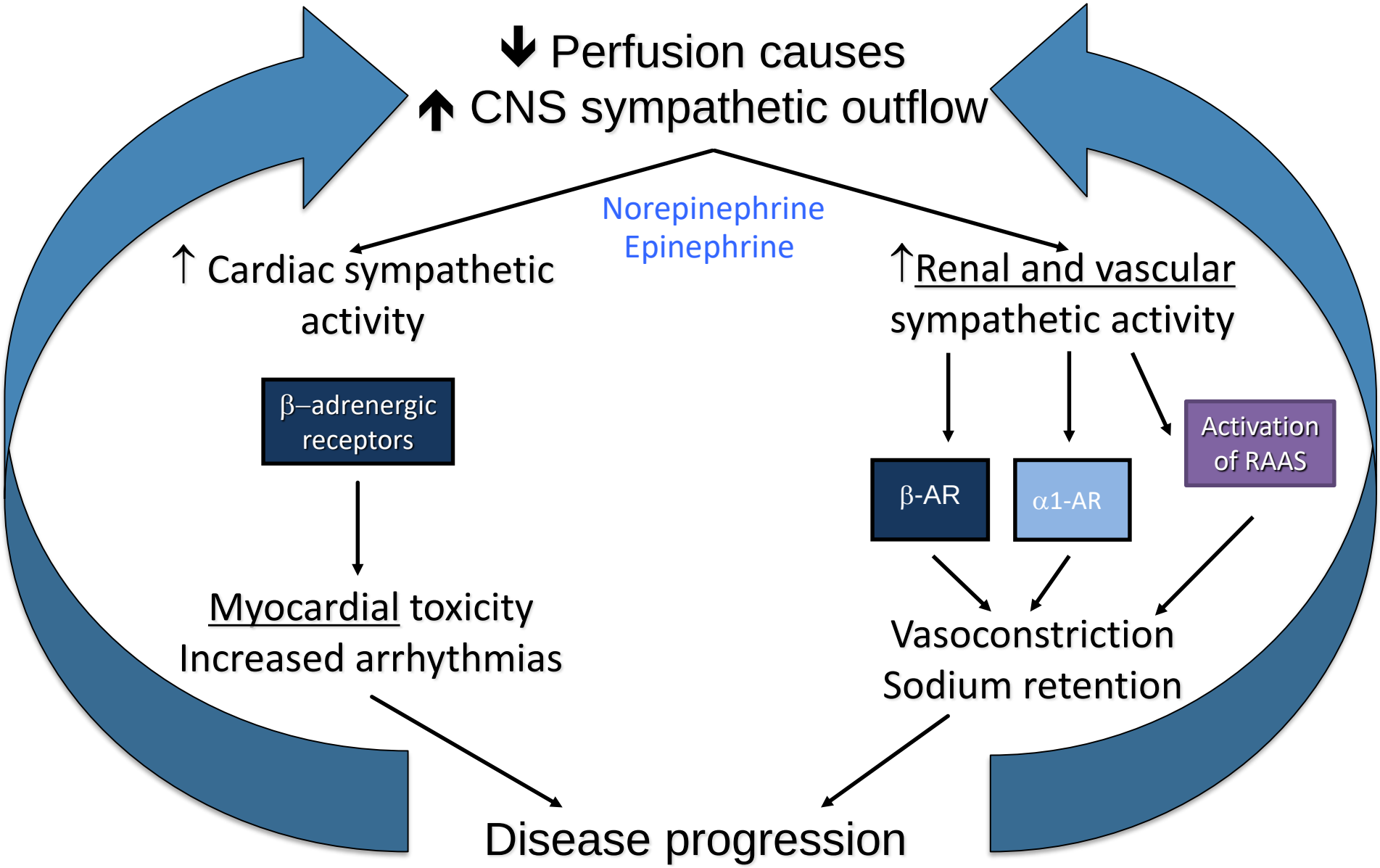
Cardiovascular response to chronic β-AR stimulation

- ✧ Downregulation of β1-ARs
- ✧ Unfavorable changes in β1-AR signaling
- ✧ Energy starvation
- ✧ Cardiomyocyte death
- ✧ Ventricular arrhythmias
- ✧ Fibrosis

Norepinephrine and Epinephrine
Great for acute responses, but toxic with sustained exposure

Sympathetic Activation in Heart Failure

Catecholamines are elevated in HF and contribute to its progression



Adapted from Packer M. Progr Cardiovasc Dis. 1998;39(Supp I):39-52

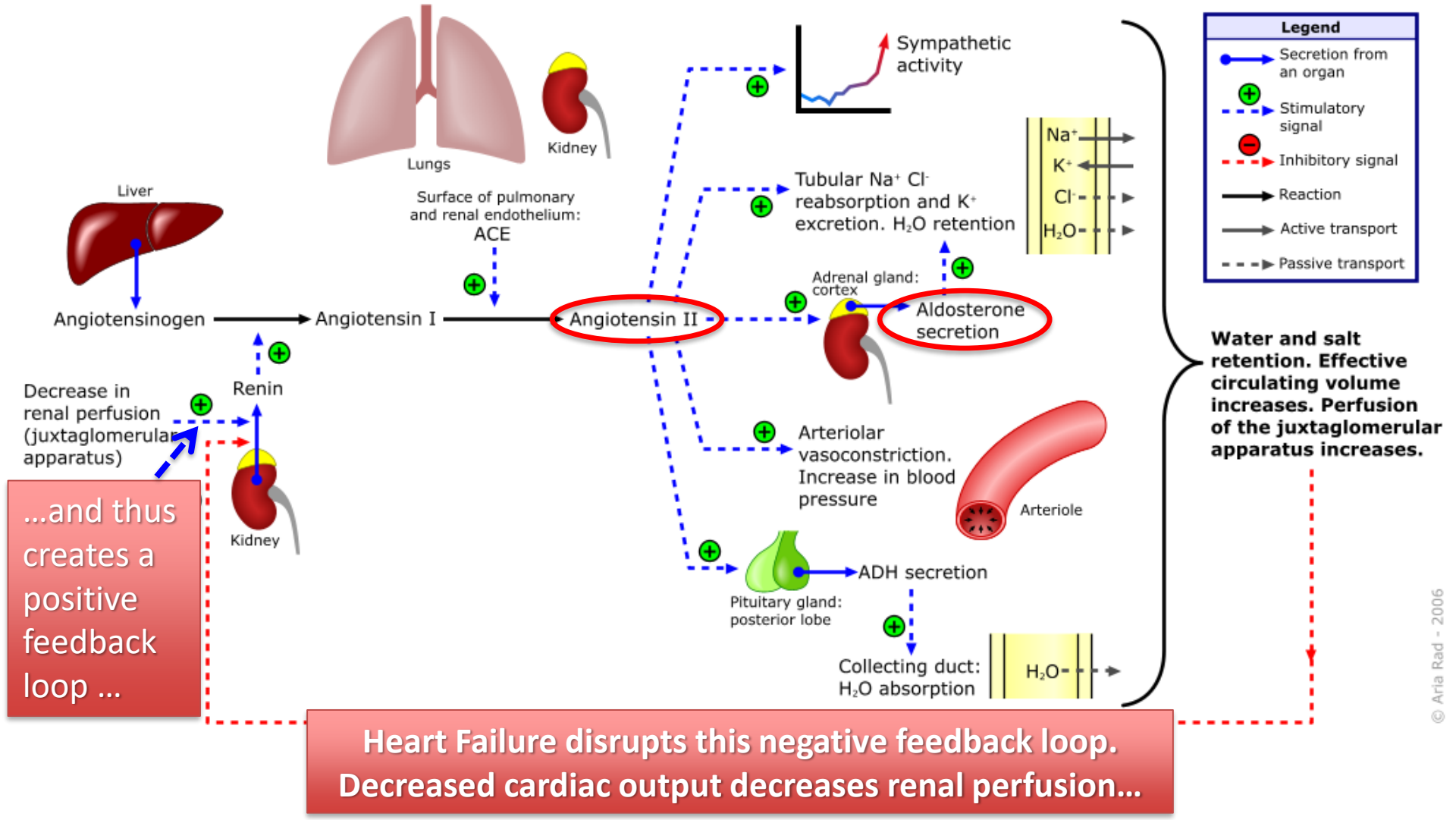
Renin-Angiotensin-Aldosterone System (RAAS)

The response to decreased stroke volume

The kidneys sense decreased effective arterial blood volume and increase renin release from the juxtaglomerular apparatus, leading to increased angiotensin II and aldosterone levels -> increased blood volume and vasoconstriction.

Renin-Angiotensin System

Promotes retention of sodium/water and vasoconstriction

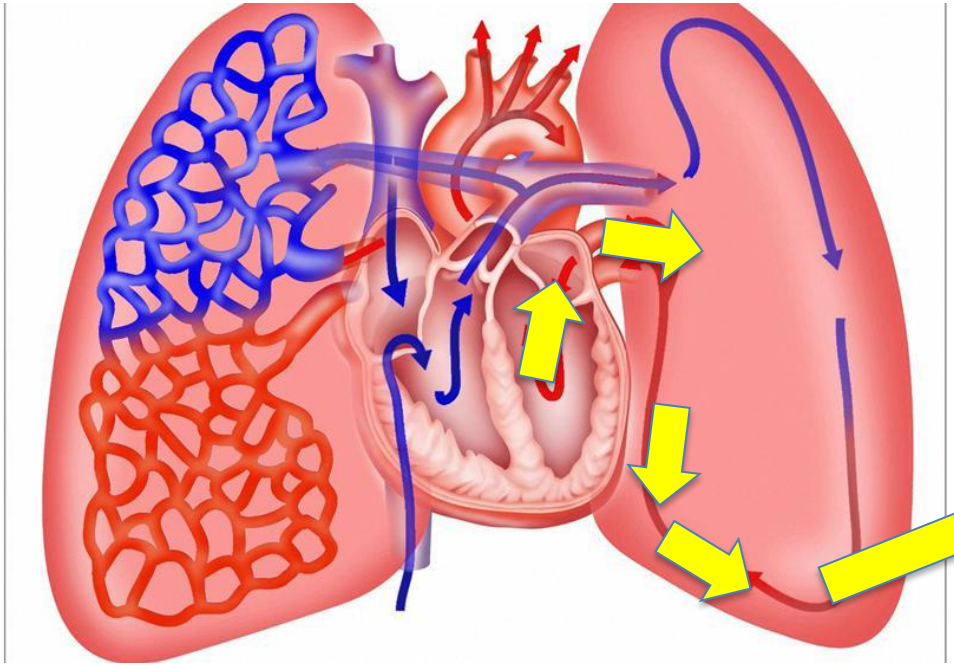


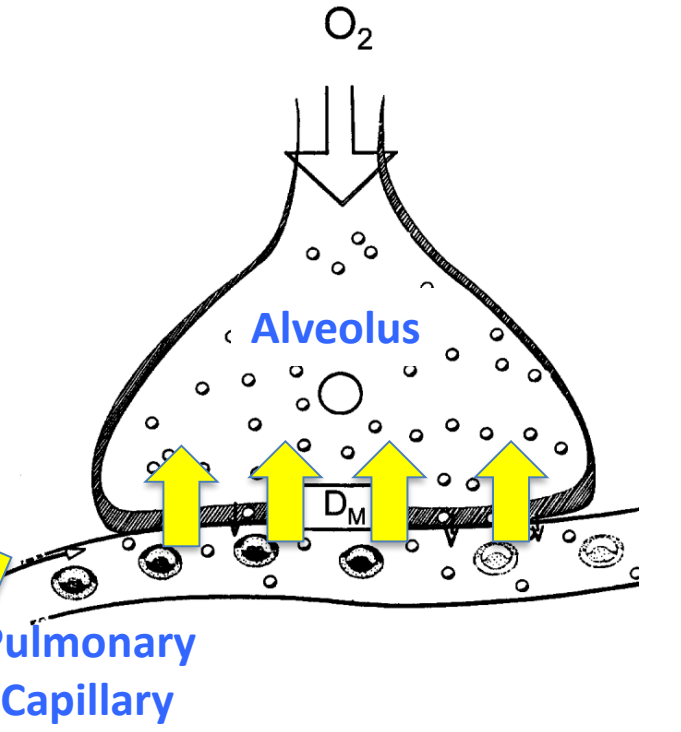
…and thus creates a positive feedback loop …

Heart Failure disrupts this negative feedback loop. Decreased cardiac output decreases renal perfusion…

http://en.wikipedia.org/wiki/File:Renin-angiotensin-aldosterone_system.png

Fluid retention increases pressure in the heart, which causes edema





High LVEDP = high left atrial pressure

↓

High pulmonary vein pressure

↓

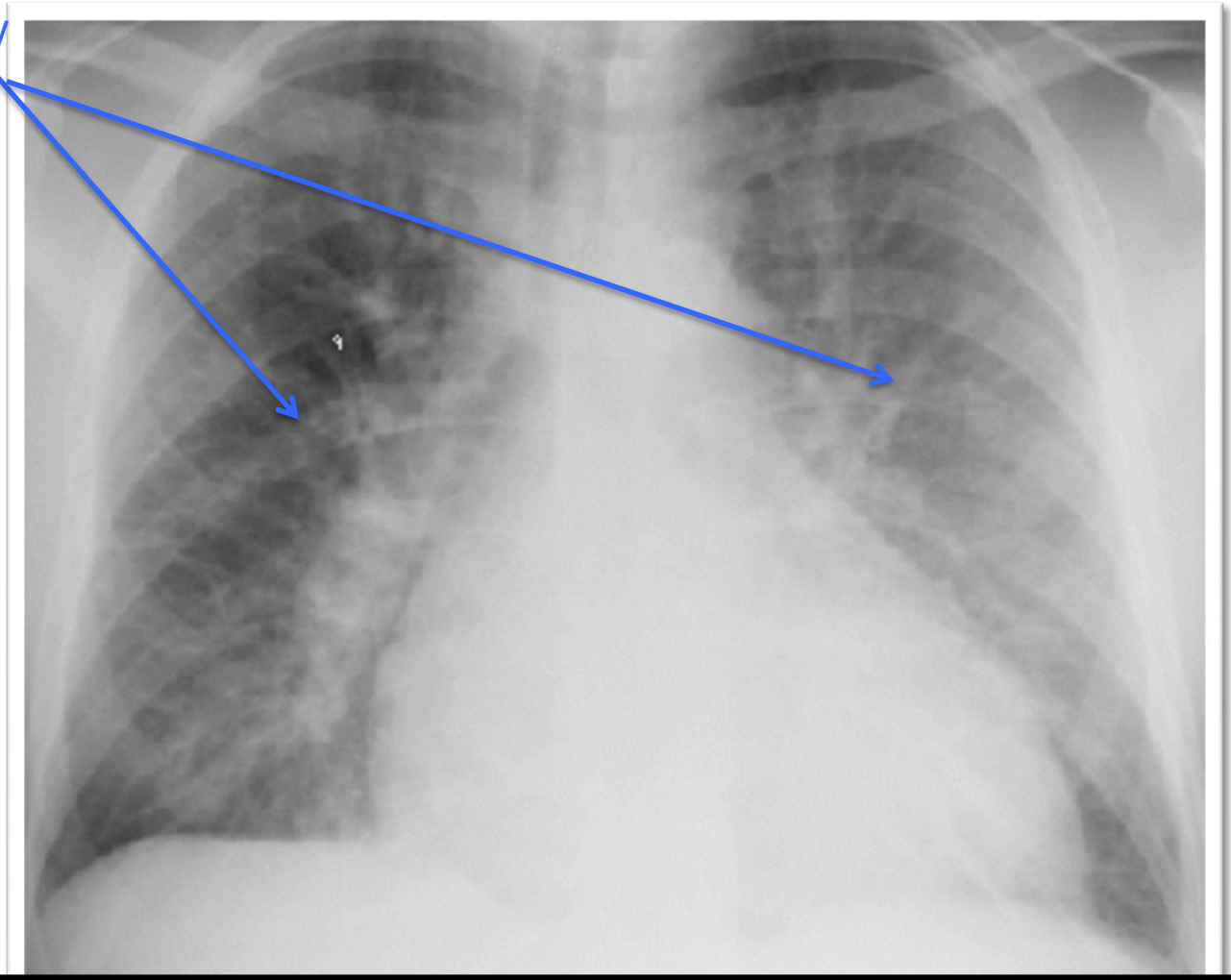
High pulmonary capillary pressure

Many of the symptoms of heart failure, regardless of cause, result from increased left atrial pressure

https://www.clevelandclinic.org/heartcenter/images/guide/heartworks/heart_bloodvessels.jpg

Left Heart Failure

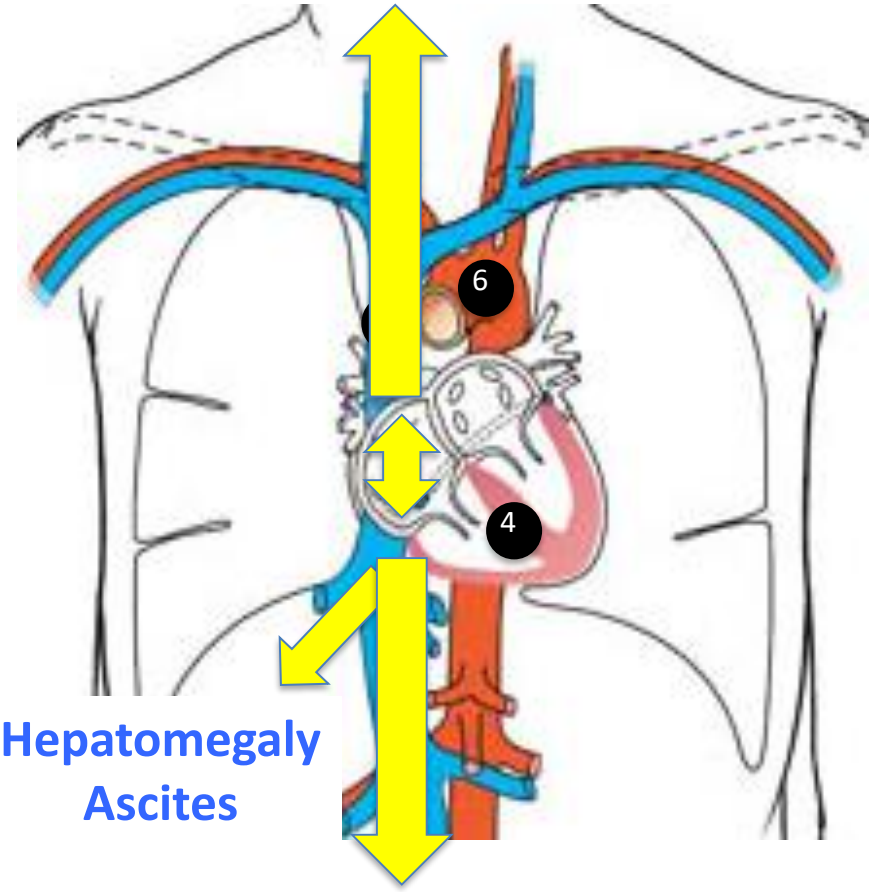
Pulmonary Edema

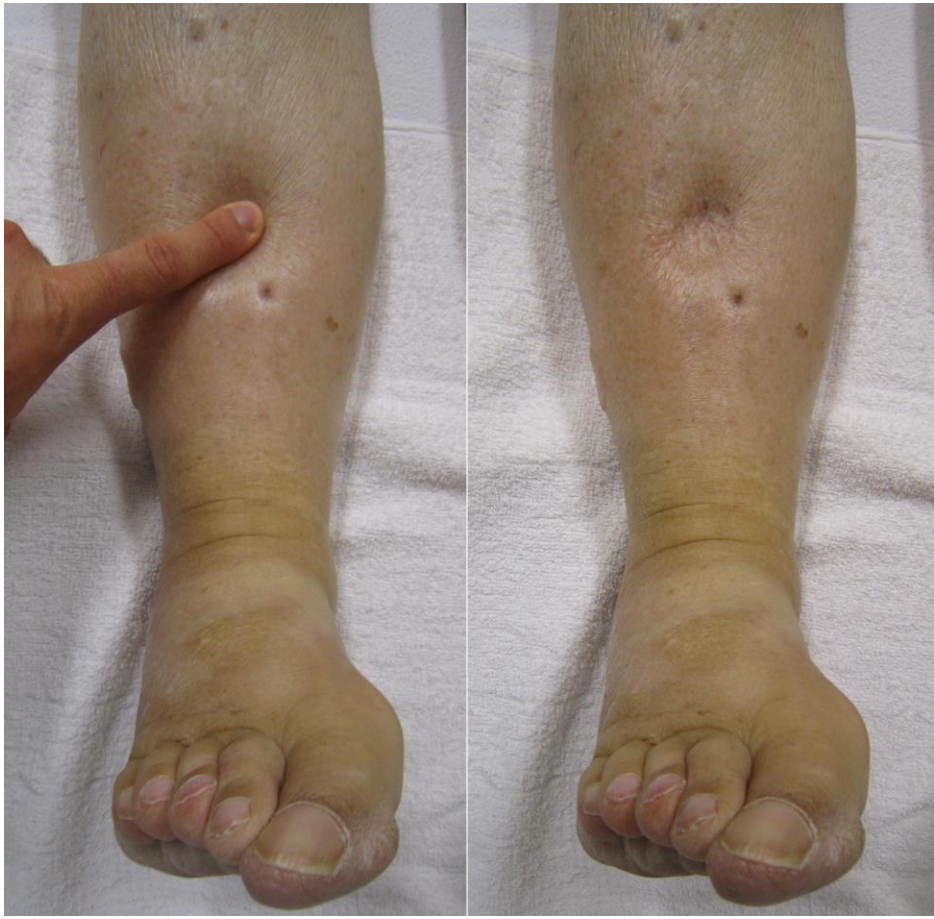


Markedly elevated preload can cause pulmonary edema
(fluid in the lungs), contributing to dyspnea (most common symptom of HF)

Right Heart Failure = increased RA pressure

Increased right ventricular preload communicated to systemic veins

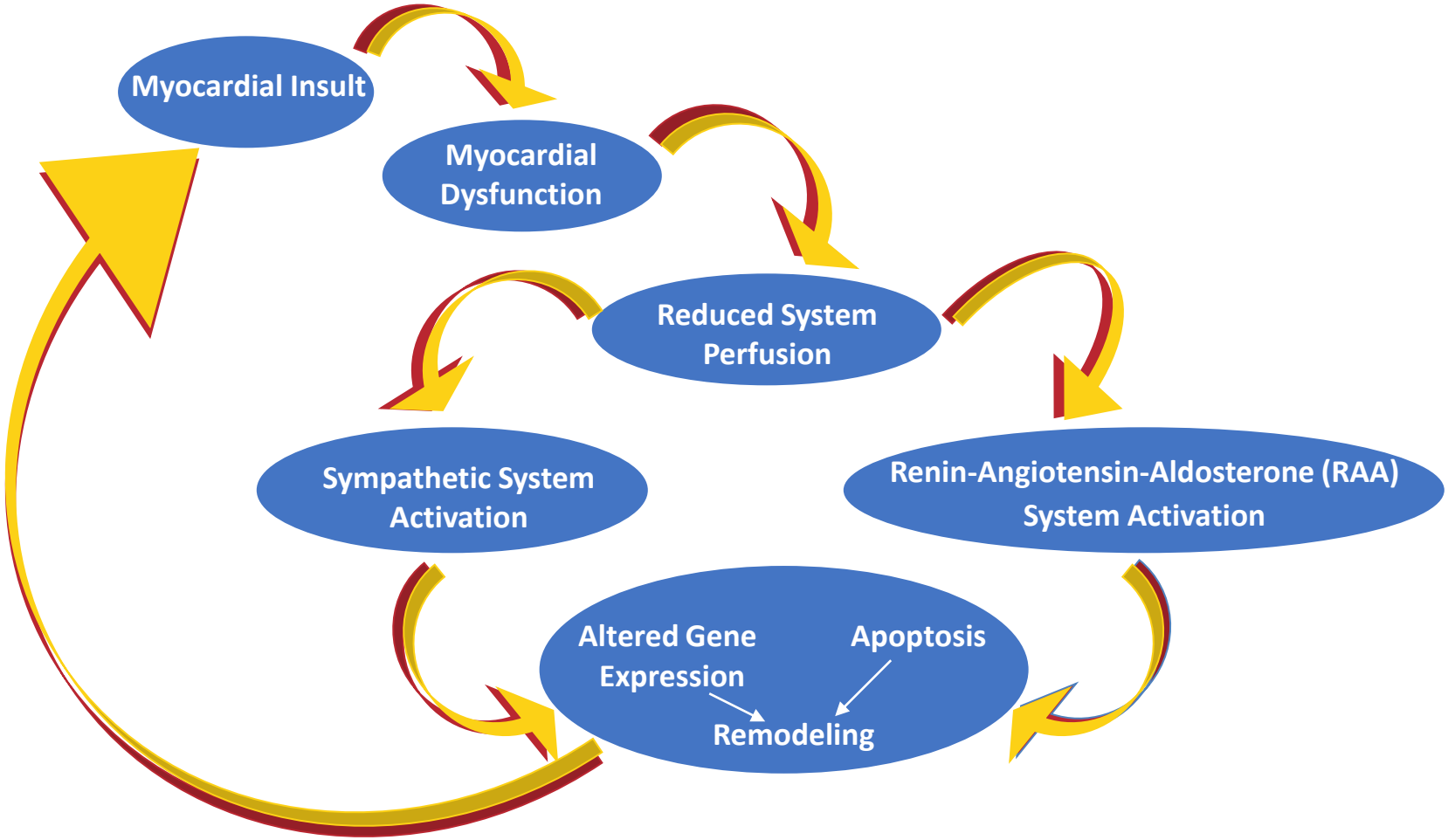




https://www.clevelandclinic.org/heartcenter/images/guide/heartworks/heart_bloodvessels.jpg

Neurohormonal responses underlie heart failure

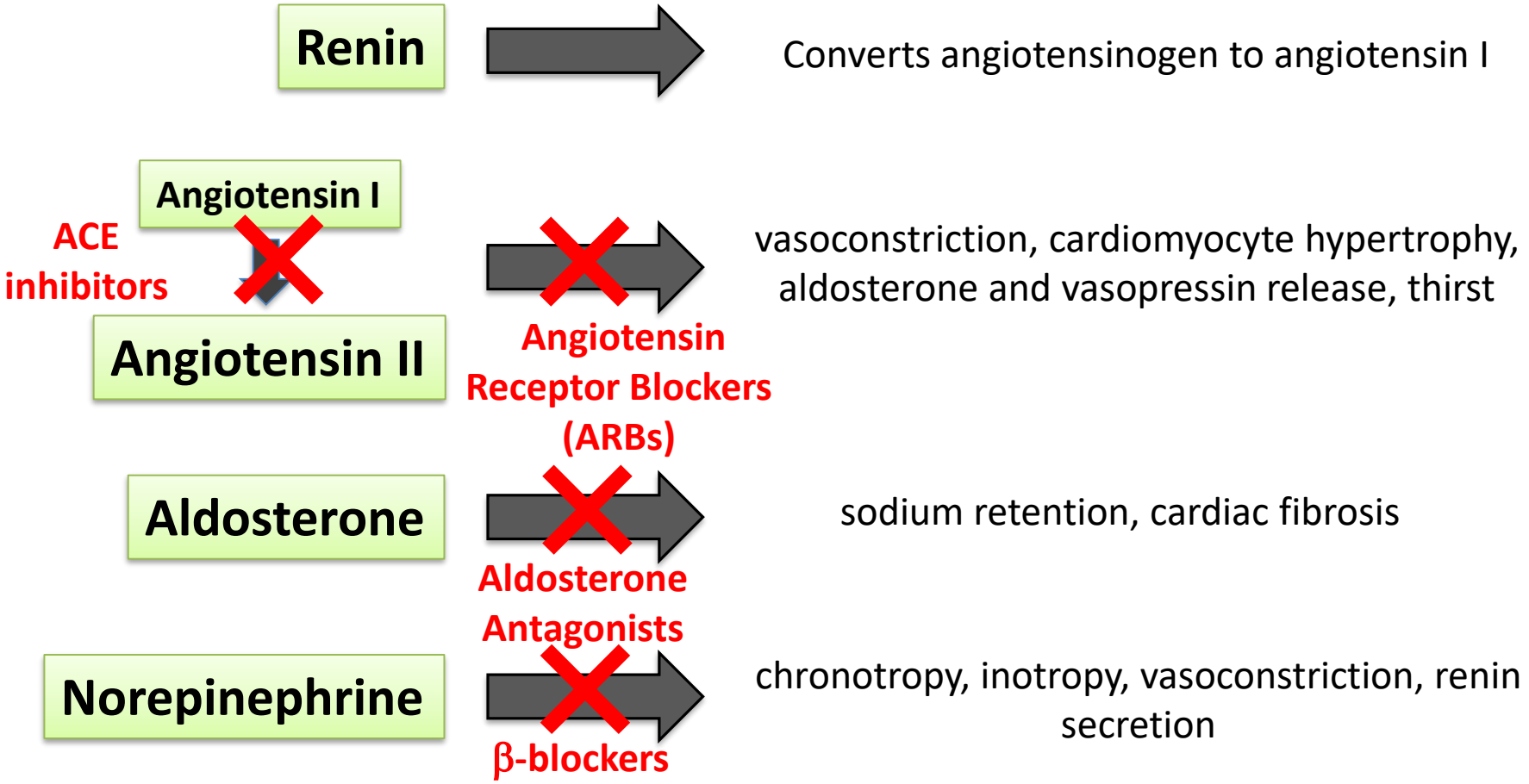
Heart failure results from maladaptive feedback loops



These processes drive the transition from injury to heart failure

Neurohormonal Paradigm Revisited

Targets for Evidence-Based Therapy

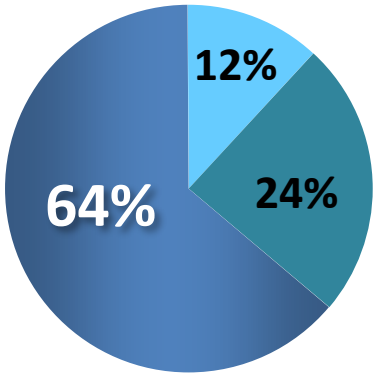


Other players: Endothelin, Vasopressin, ANP, BNP, etc

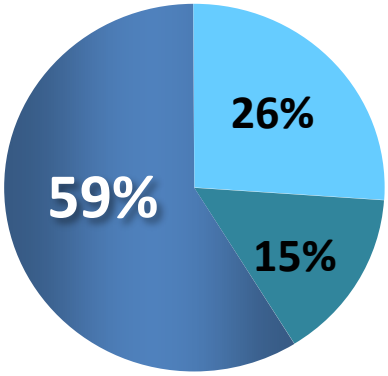
What Kills Heart Failure Patients?

Sudden Cardiac Death (SCD)/Arrhythmia

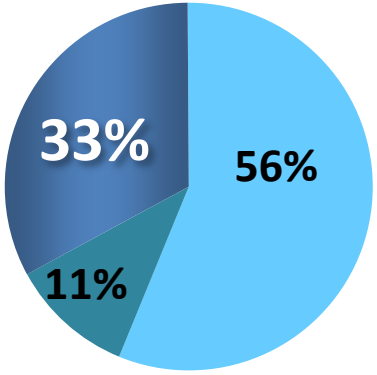
NYHA Class II

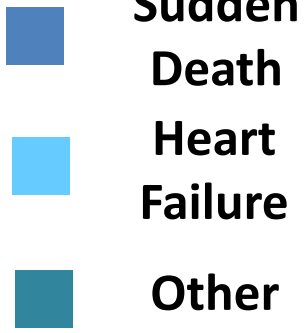


NYHA Class III



NYHA Class IV





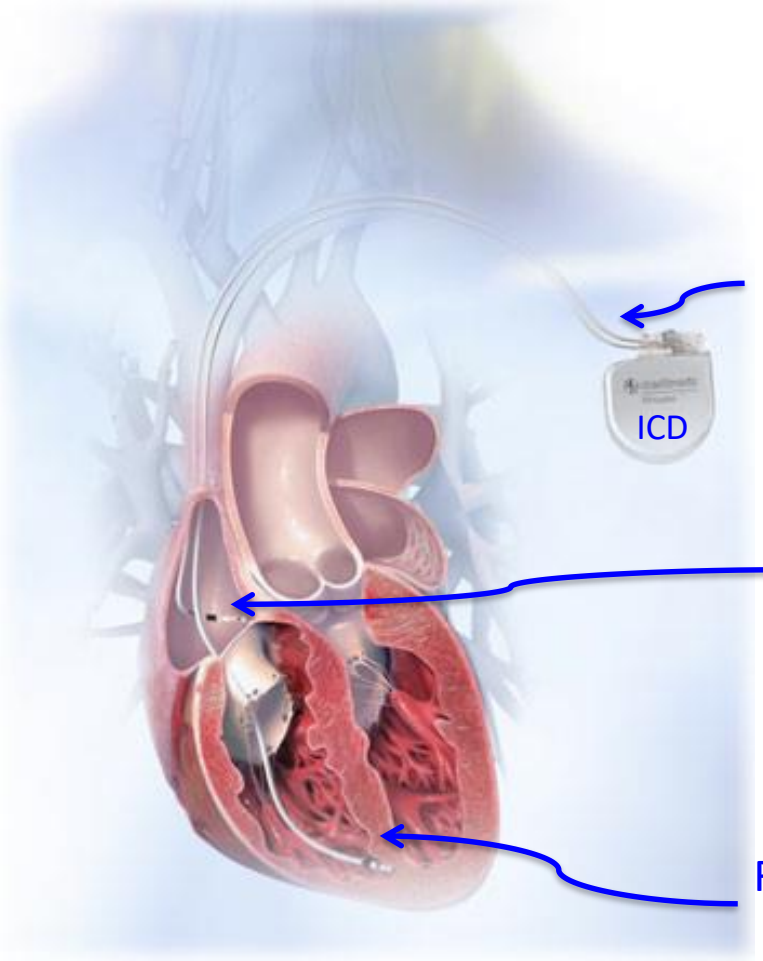
5-year mortality following HF diagnosis = 45-60%

MERIT-HF Study Group. *LANCET.* 1999;353:2001-2007.

Implantable Cardioverter Defibrillators

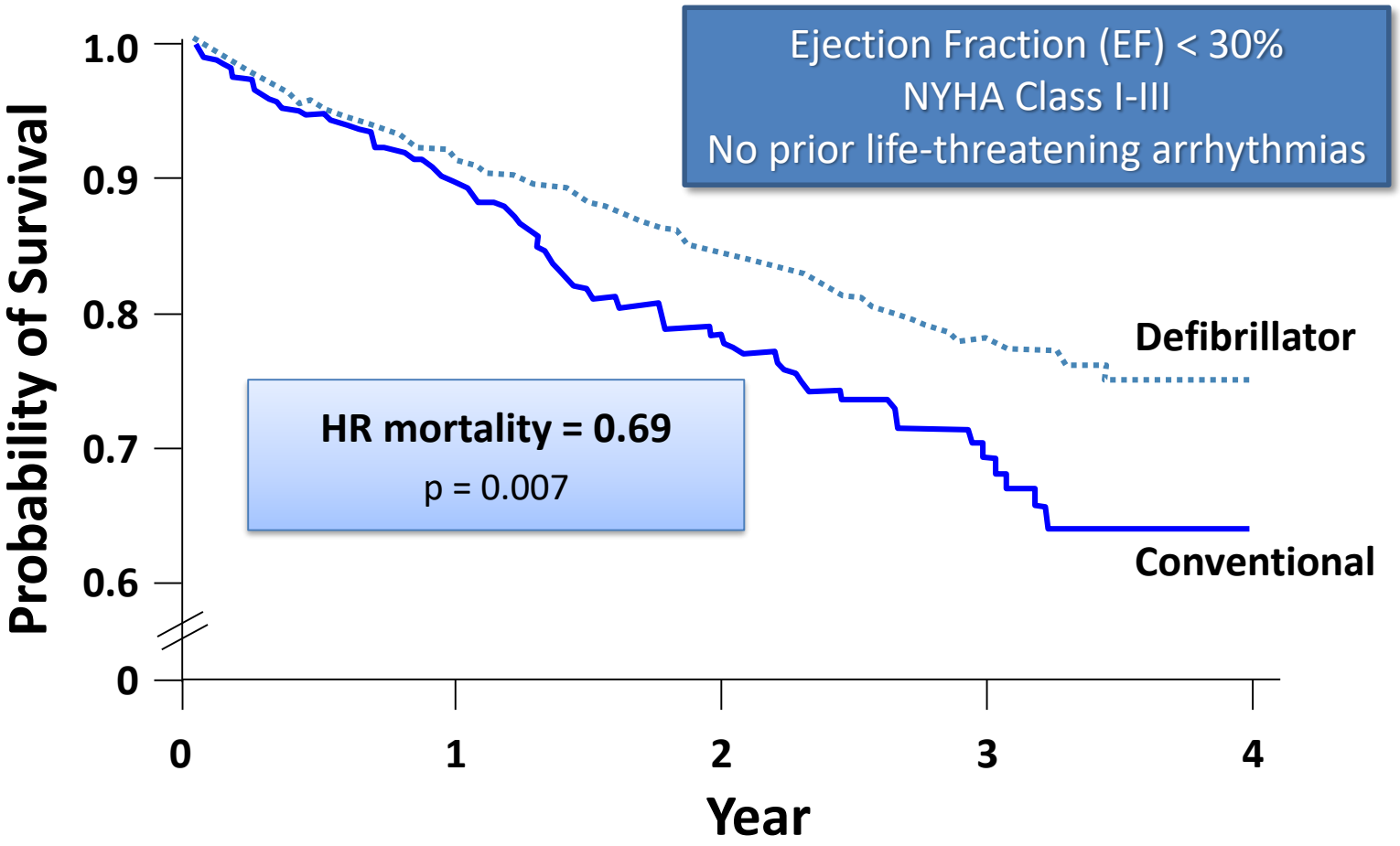
ICDs

- Senses life-threatening rhythms and electrically terminates them
- Serves as a pacemaker for slow rhythms
- All abnormal rhythms are recorded
- 2006-2009 ICD Registry:
  - 486,000 implants in US
  - 141,000 implants in 2009



ICDs prevent SCD in Heart Failure

MADIT-II (**primary** prevention)

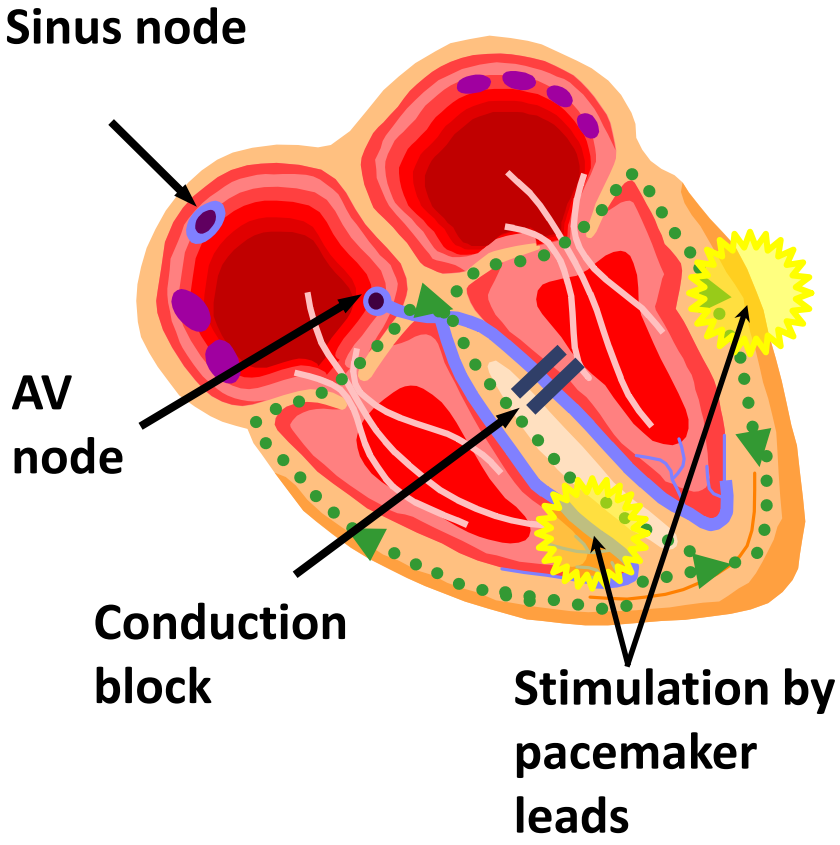


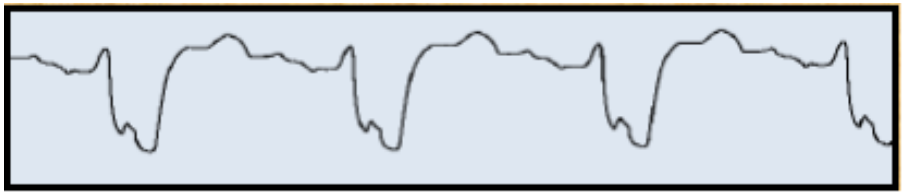
N.B. Normal Ejection Fraction (EF) ≥ 55%

Moss AJ. *N Engl J Med*. 2002;346:877-83.

Cardiac Resynchronization Therapy (CRT)

Implantation of a Biventricular Pacemaker



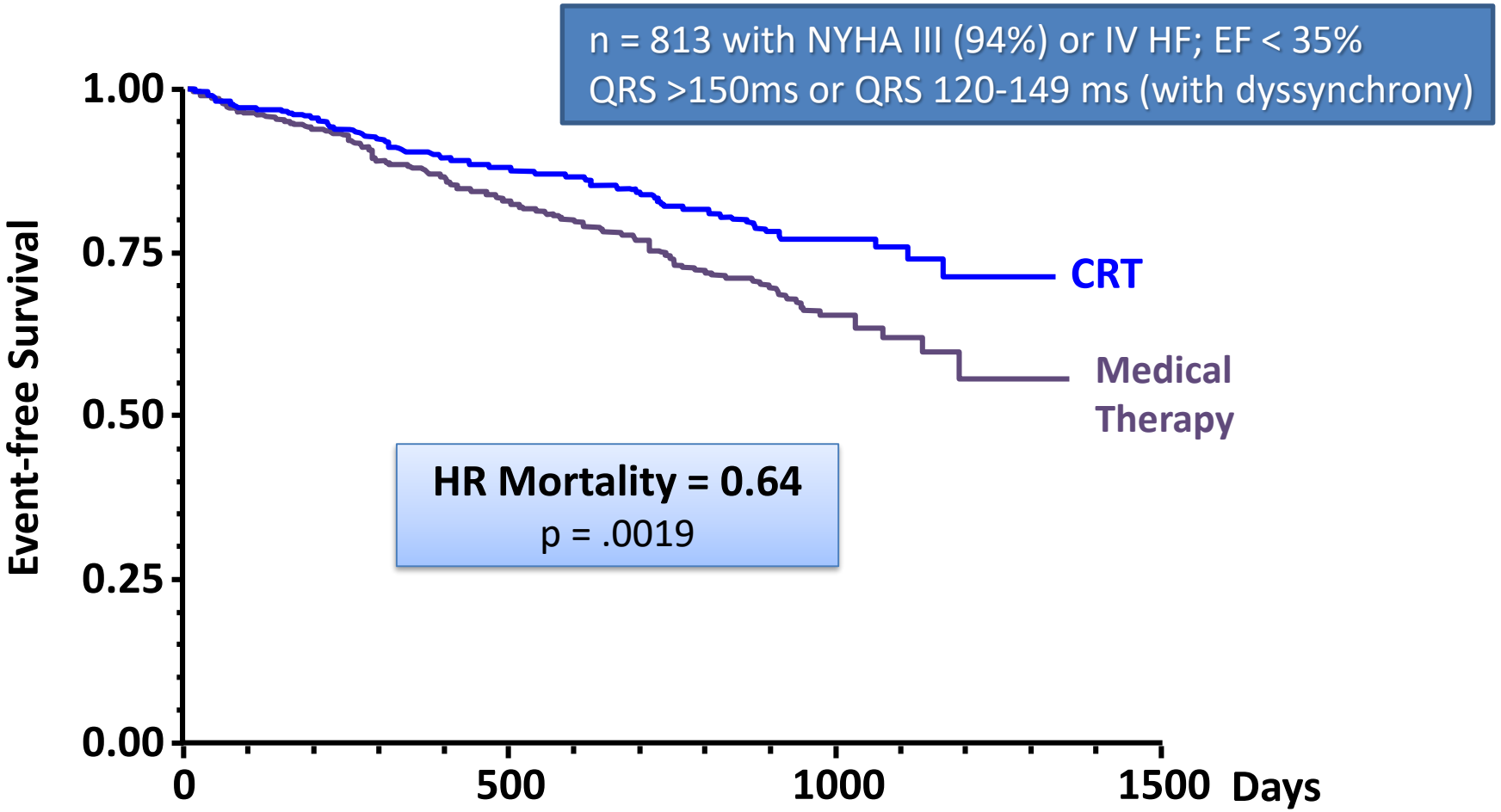


Wide QRS

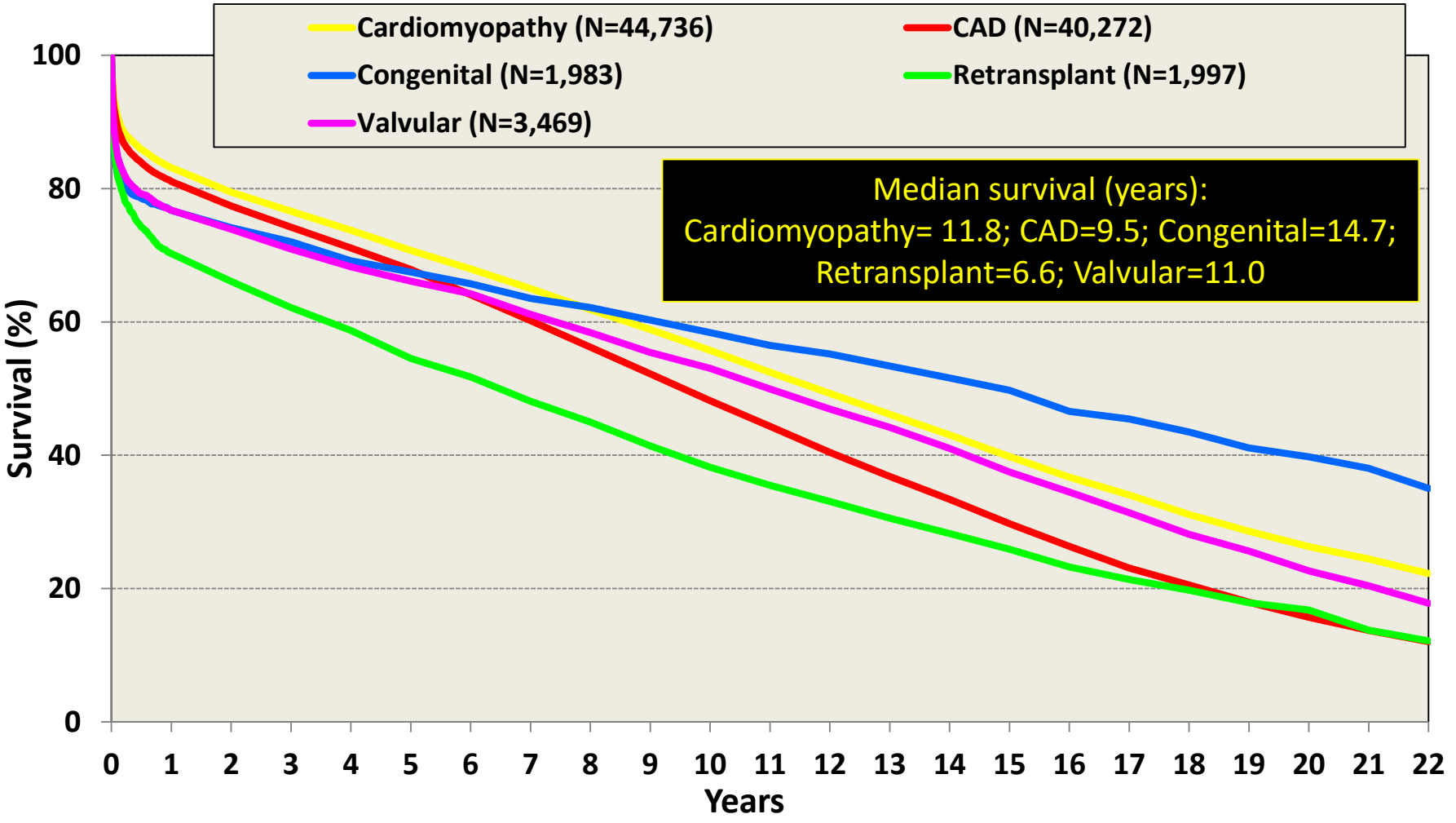
- Long ventricular conduction time causes dyssynchrony and inefficient contraction
- QRS > 120 msec required to derive benefit
- Pacing the interventricular septum ("RV lead") and LV free wall resynchronizes contraction
- Improved pumping efficiency results from resynchronization

CRT decreases all-cause mortality

CARE-HF Trial



Heart transplant is the only cure for heart failure



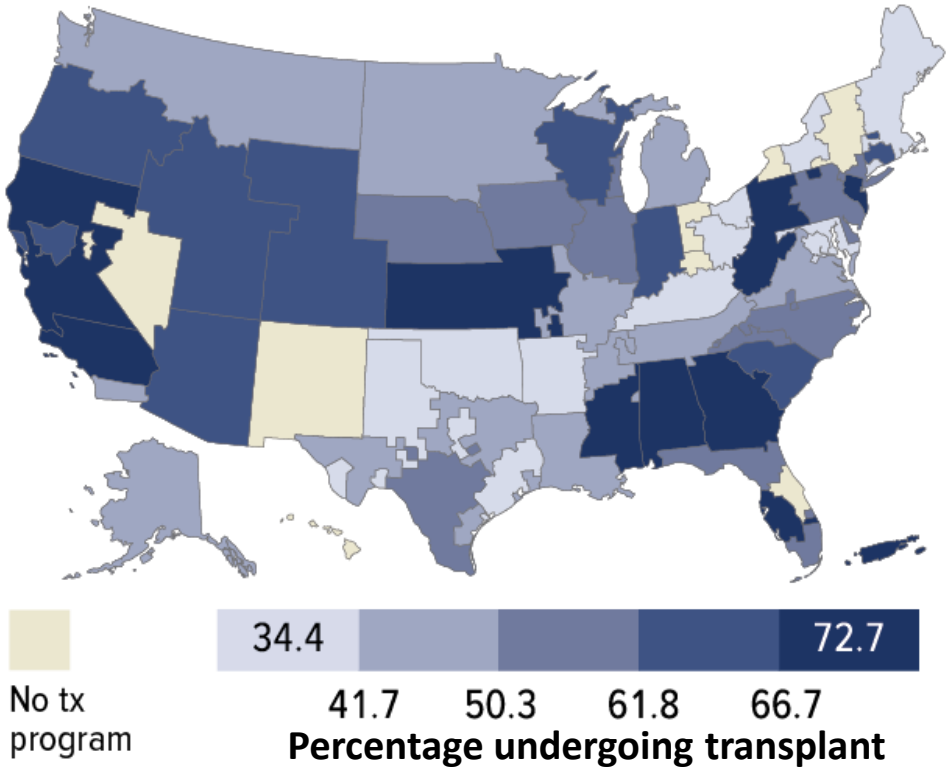
ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

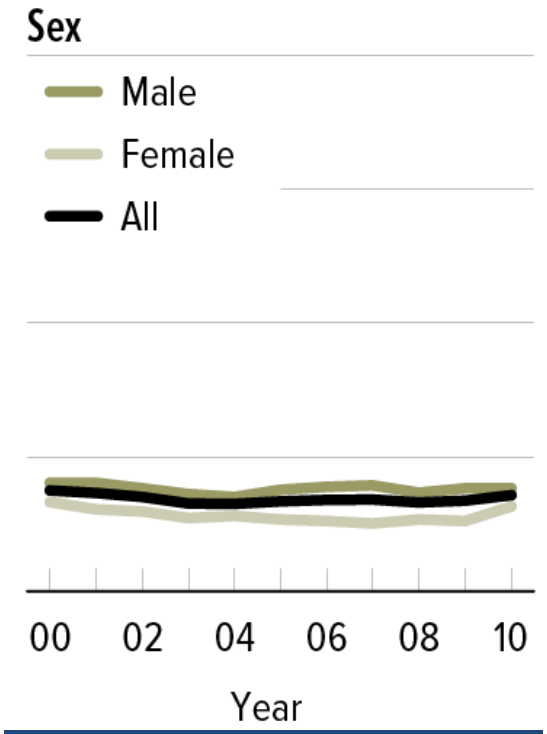
2014

JHLT. 2014 Oct; 33(10): 996-1008

Organ (donor) shortage

Roughly 50% of wait-listed patients are transplanted yearly



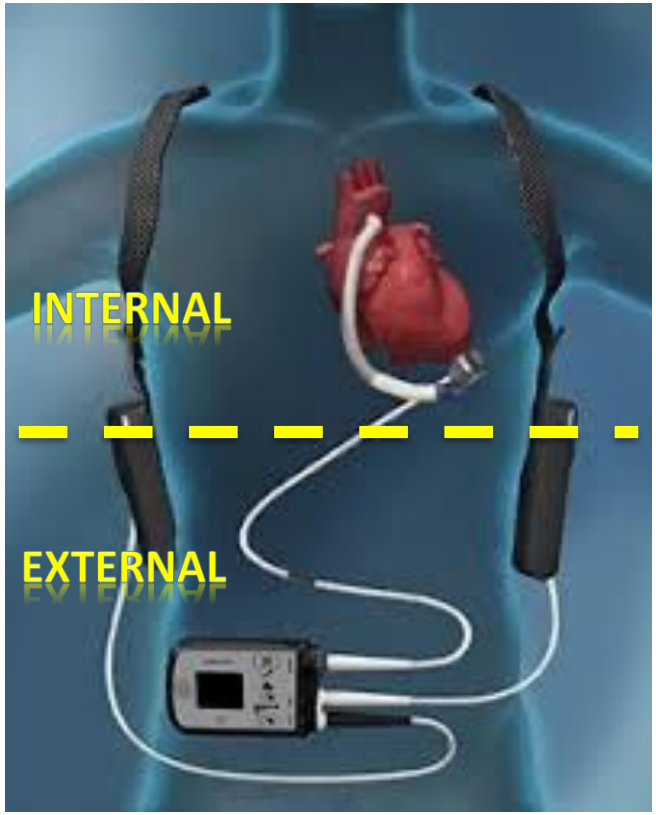


Donation rates are stable at roughly 4 per 1000 deaths

US Dept of HHS Scientific Registry of Transplant Recipients
srtr.transplant.hrsa.gov

Left Ventricular Assist Devices

Bridge to Transplant (or “Destination Therapy”)



Flow is directed from the apex of the left ventricle to the ascending aorta

THANK YOU