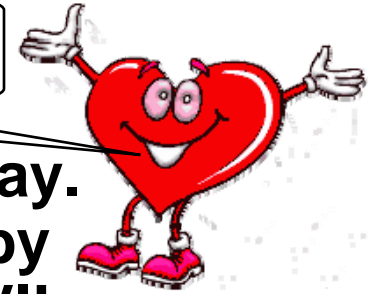


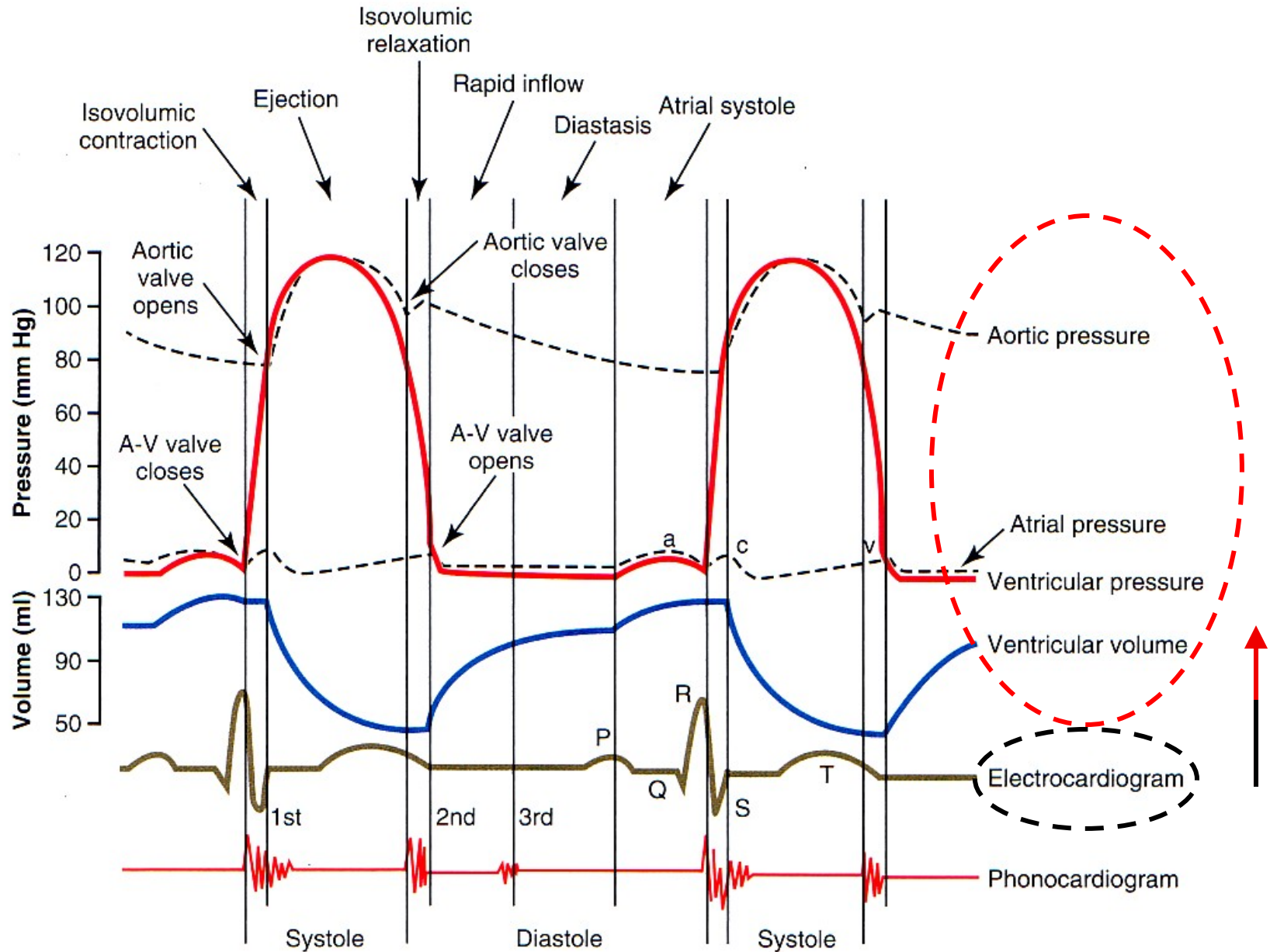
## BI 358 Lecture 10

Next Tuesday Presentations, next  
Thursday Dr. Padgett, OHVI, Hooray!!

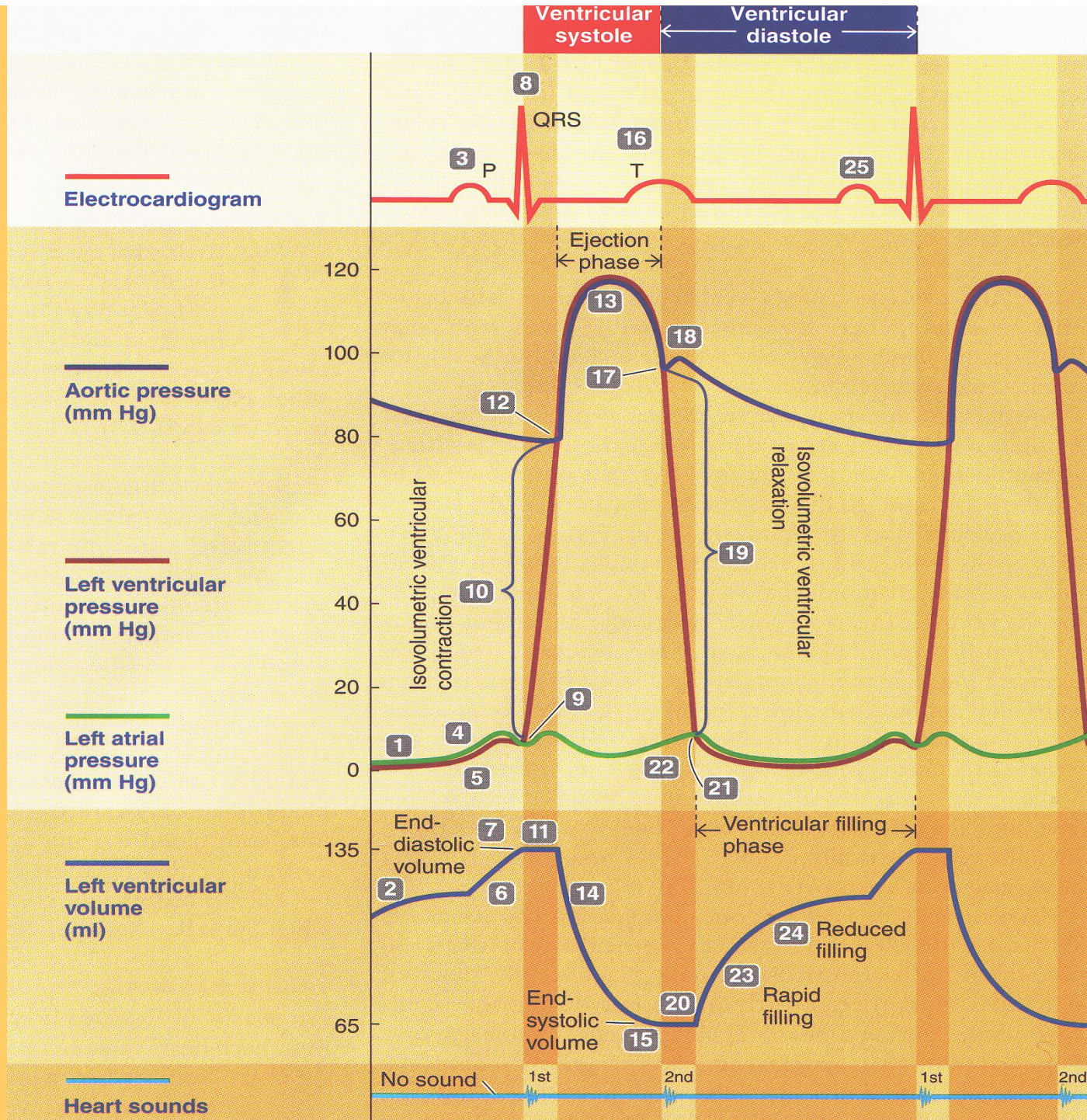


- I. **Announcements** CV Physiol + Atherosclerosis today.  
Next Tuesday Endocrinology, then Presentations by Group I! Next Thursday, Richard Padgett, MD, OHVI!  
Remember, tomorrow is AHA's **GO RED FOR WOMEN**  
<https://www.goredforwomen.org/get-involved/national-wear-red-day/what-it-means-to-go-red-for-women/>
- II. **Cardiovascular Connections** G&H fig 9-6, 10-1, 10-2, 9-12 + LS
  - A. Composite events of cardiac cycle
  - B. Autorhythmic cells & the ♥'s electrical highway
- III. **Lymphatic System** D Chiras, Torstar Books, LS +...
- IV. **CVDs** Definitions, US ♥ Disease Statistics: CDC 2012 + AHA
- V. **Atherosclerosis + Mechanisms** Torstar Books, G&H, +...
  - A. Linking proposed historical mechanisms  
Endothelial Injury Hypothesis (Ross & Glomset)  
Lipid Infiltration Hypothesis (Steinberg & Witzum) + new!
  - B. Cholesterol metabolism: Dr. Kottke's bathtub analogy
  - C. 1° modifiable risks: cigarette smoking, hypertension, hypercholesterolemia/hyperlipidemia, lack of exercise
  - D. Treatment triad, *PTCA*, *CABG*, prevention, practical tips!

# Electrical Events Precede **Mechanical Events!**



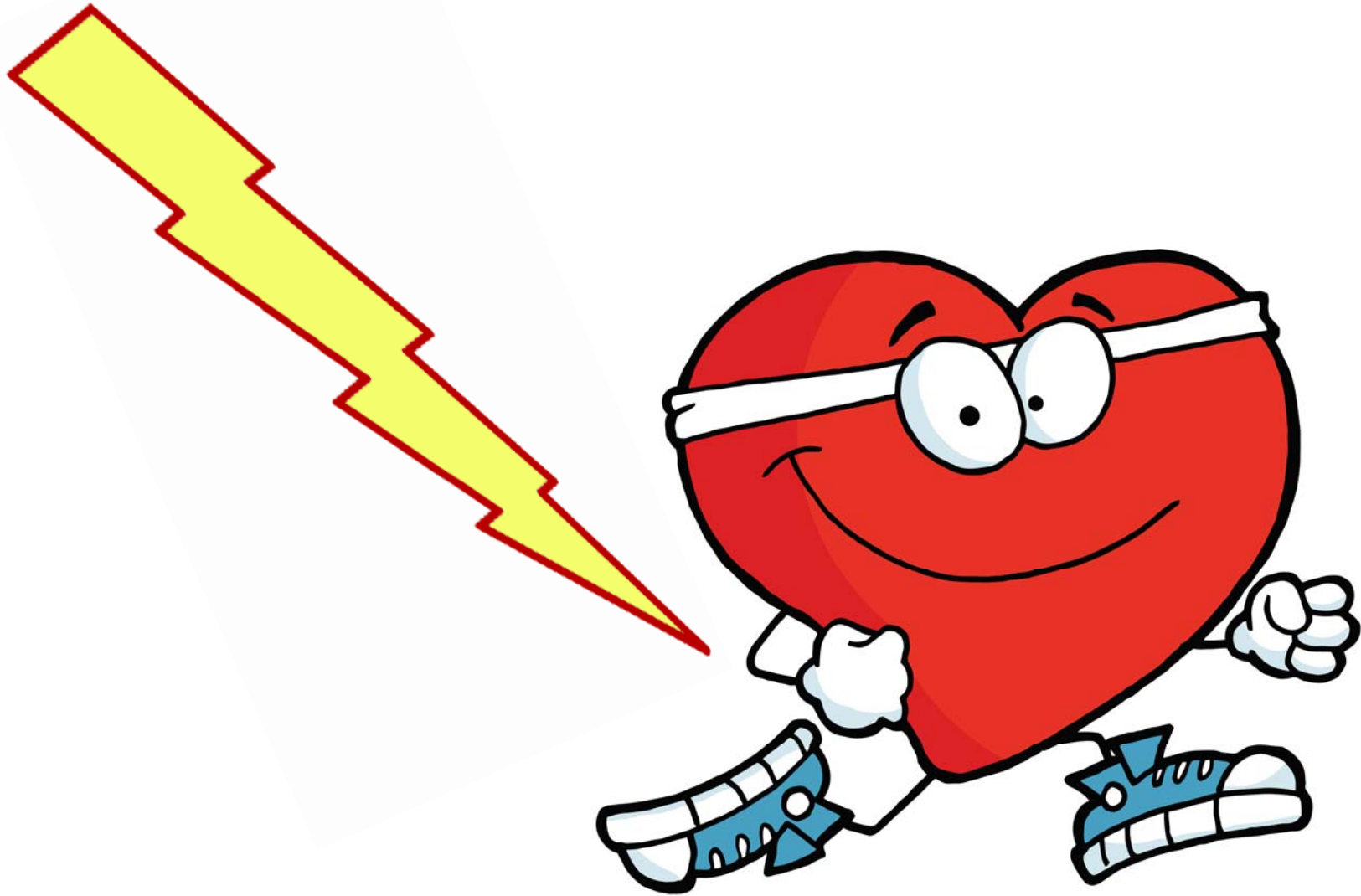




L Sherwood  
2012 fig 9-15

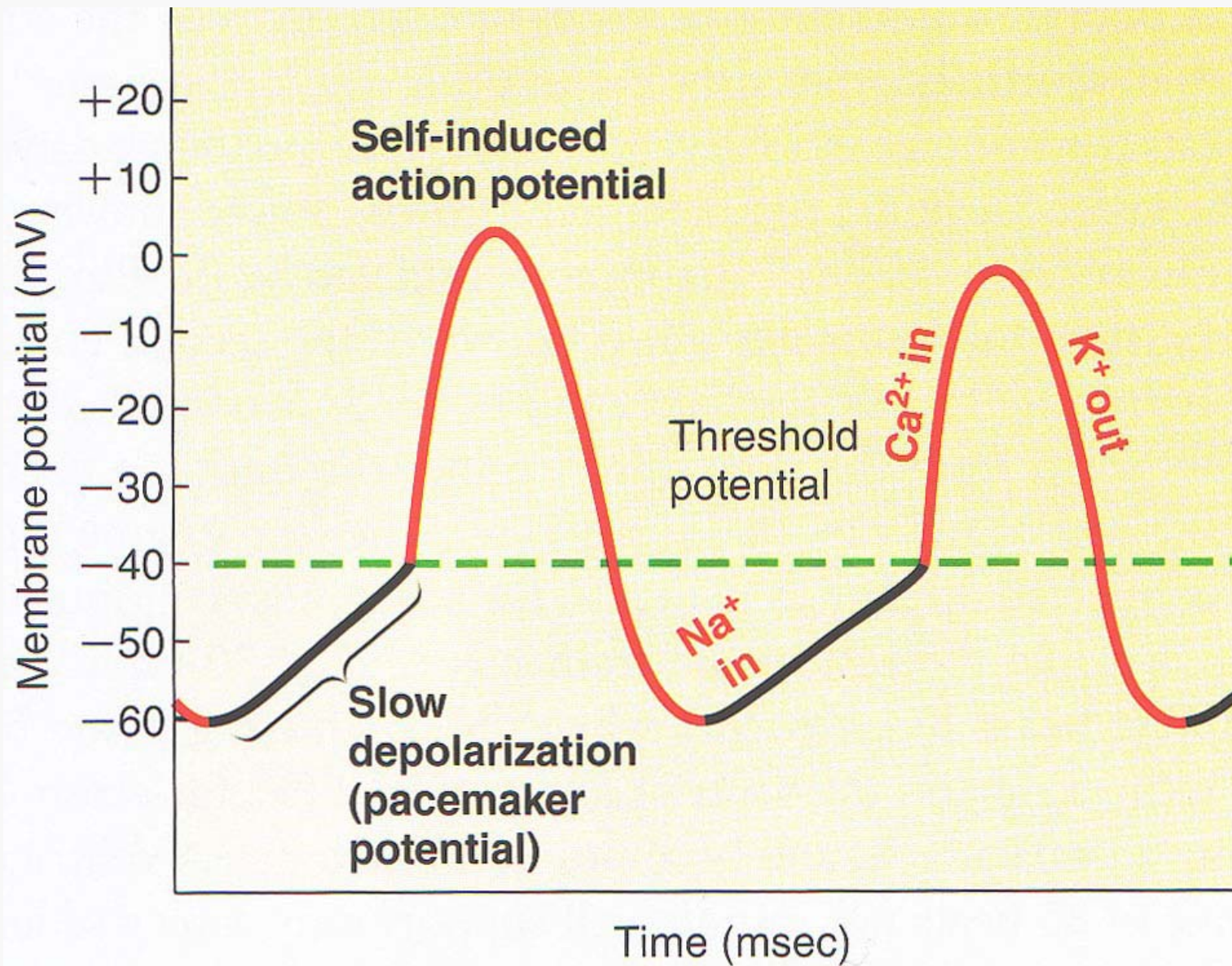


***(Automatically) Shock the Heart then it Contracts!***



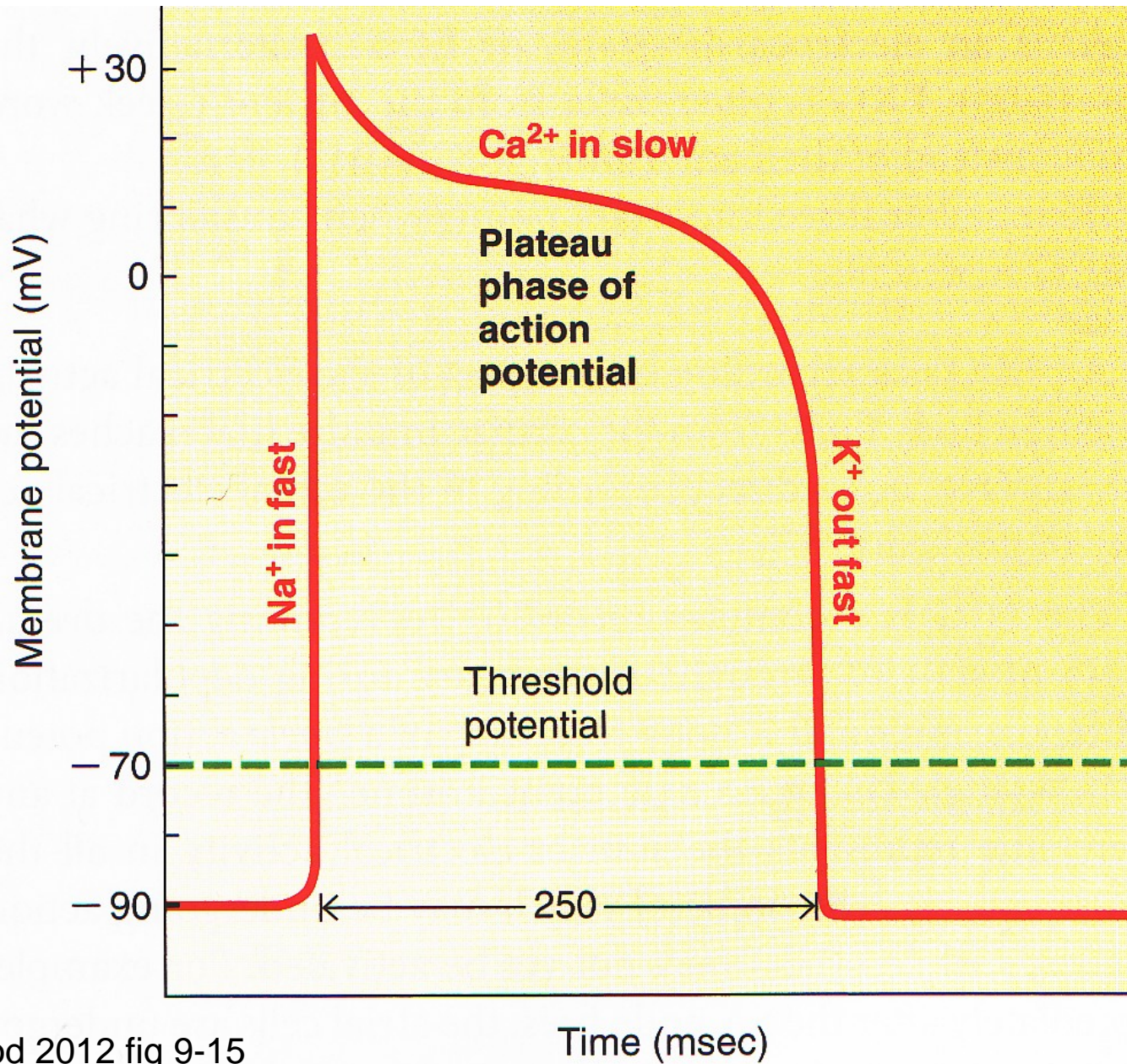


# Pacemaker Potentials in Sinoatrial Node



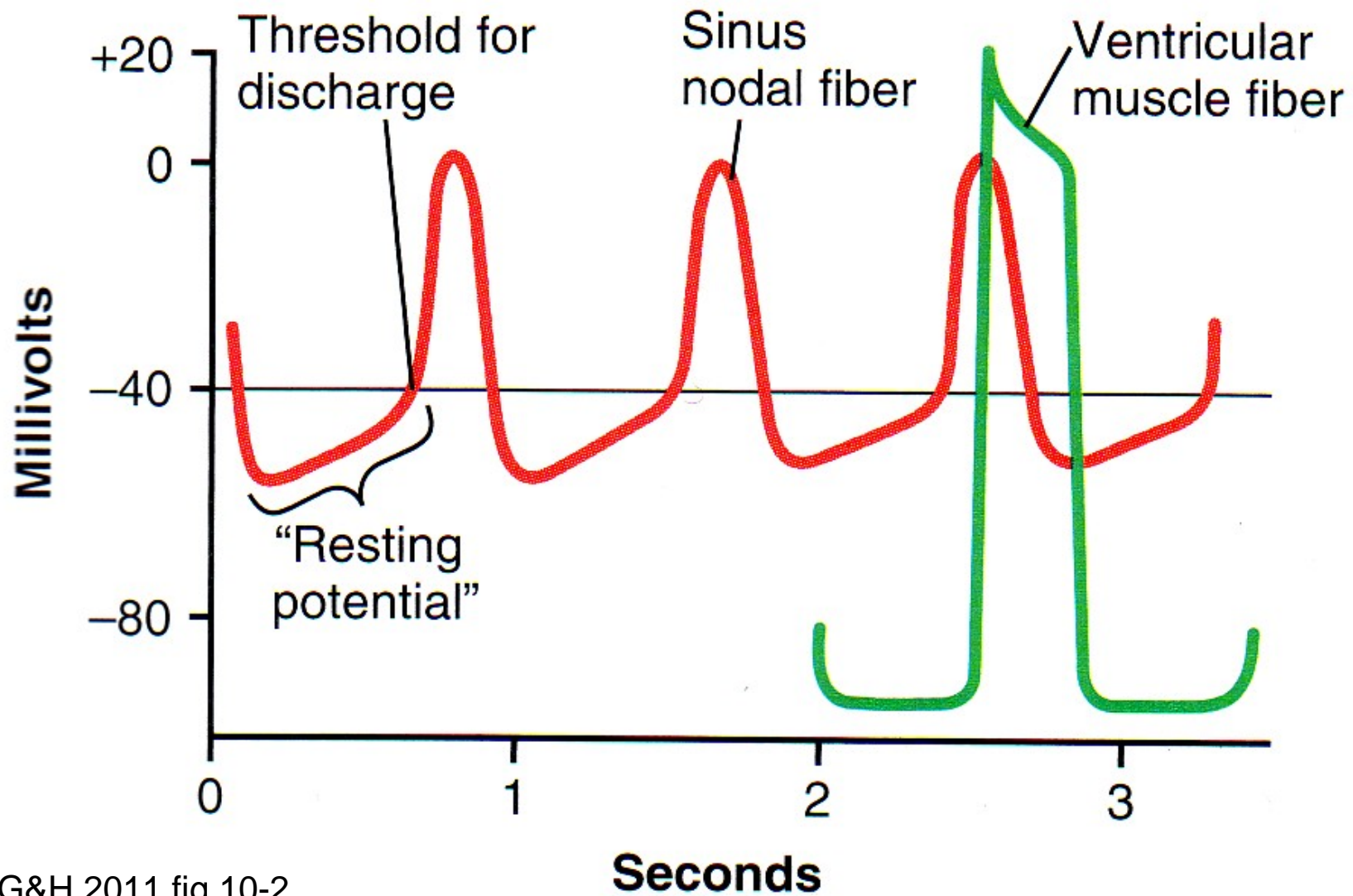


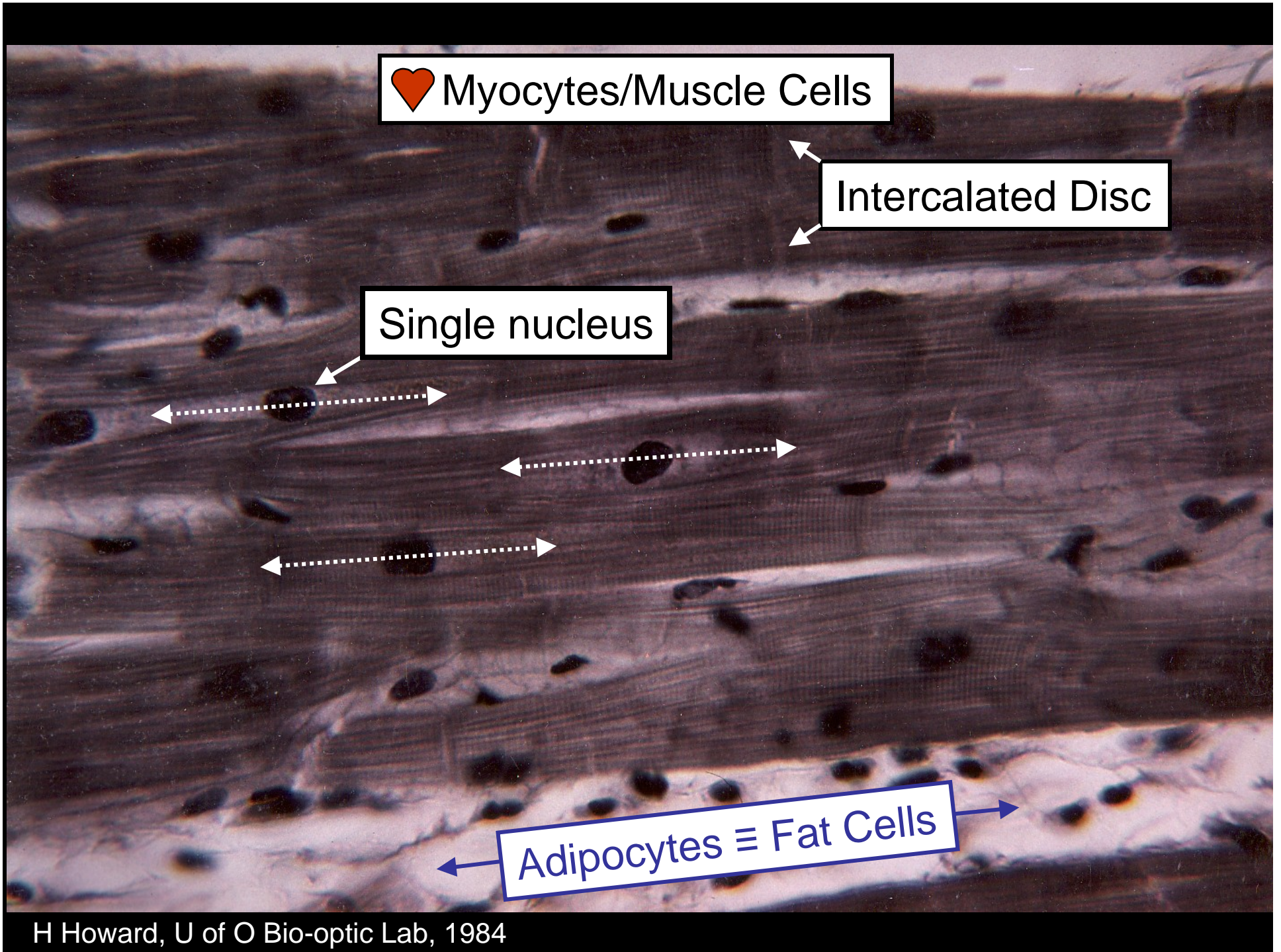
# Action Potential in Ventricular Myocytes





## Comparing Potentials in SA Node vs. Ventricular Myocytes





♥ Myocytes/Muscle Cells

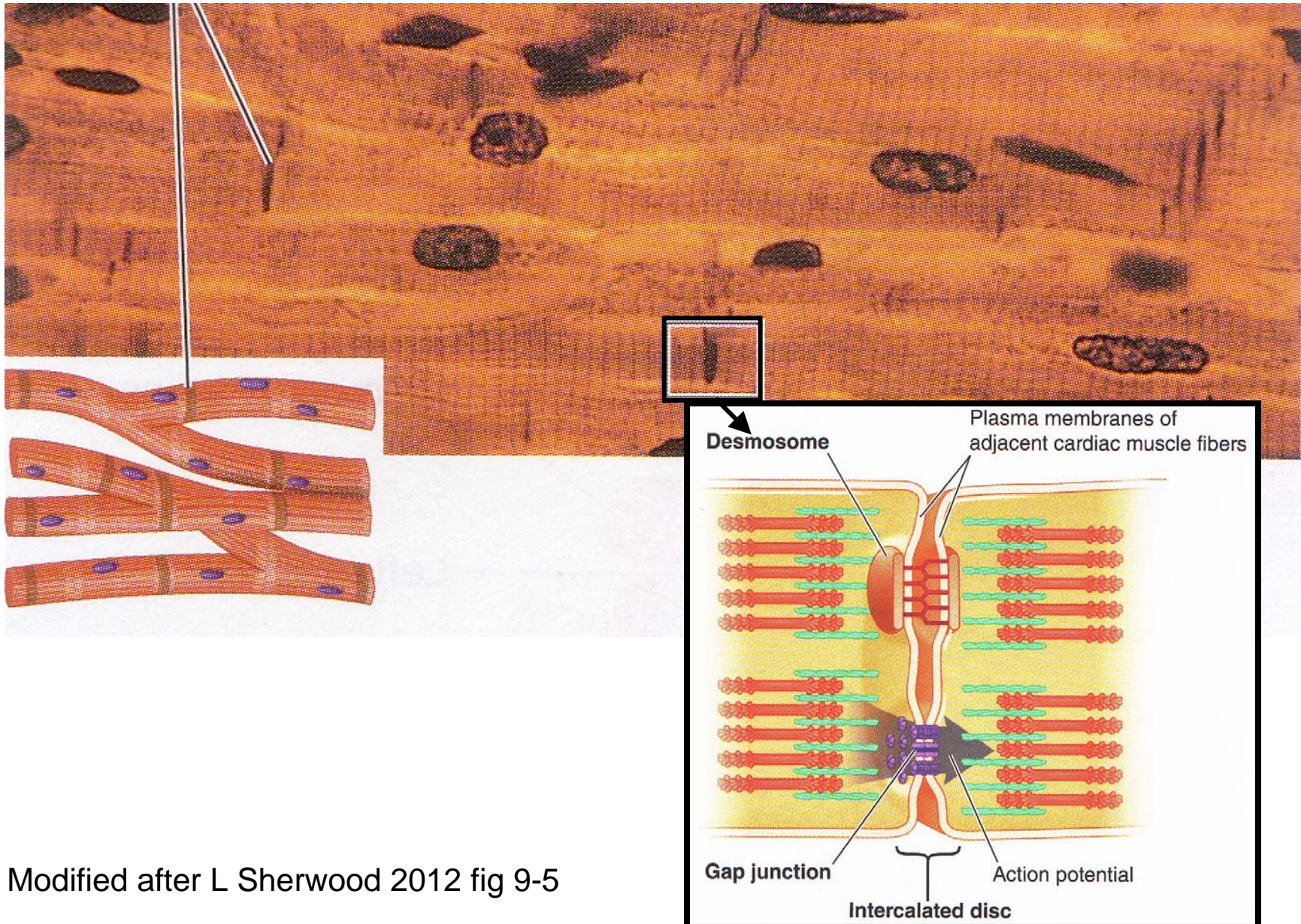
Intercalated Disc

Single nucleus

Adipocytes ≡ Fat Cells



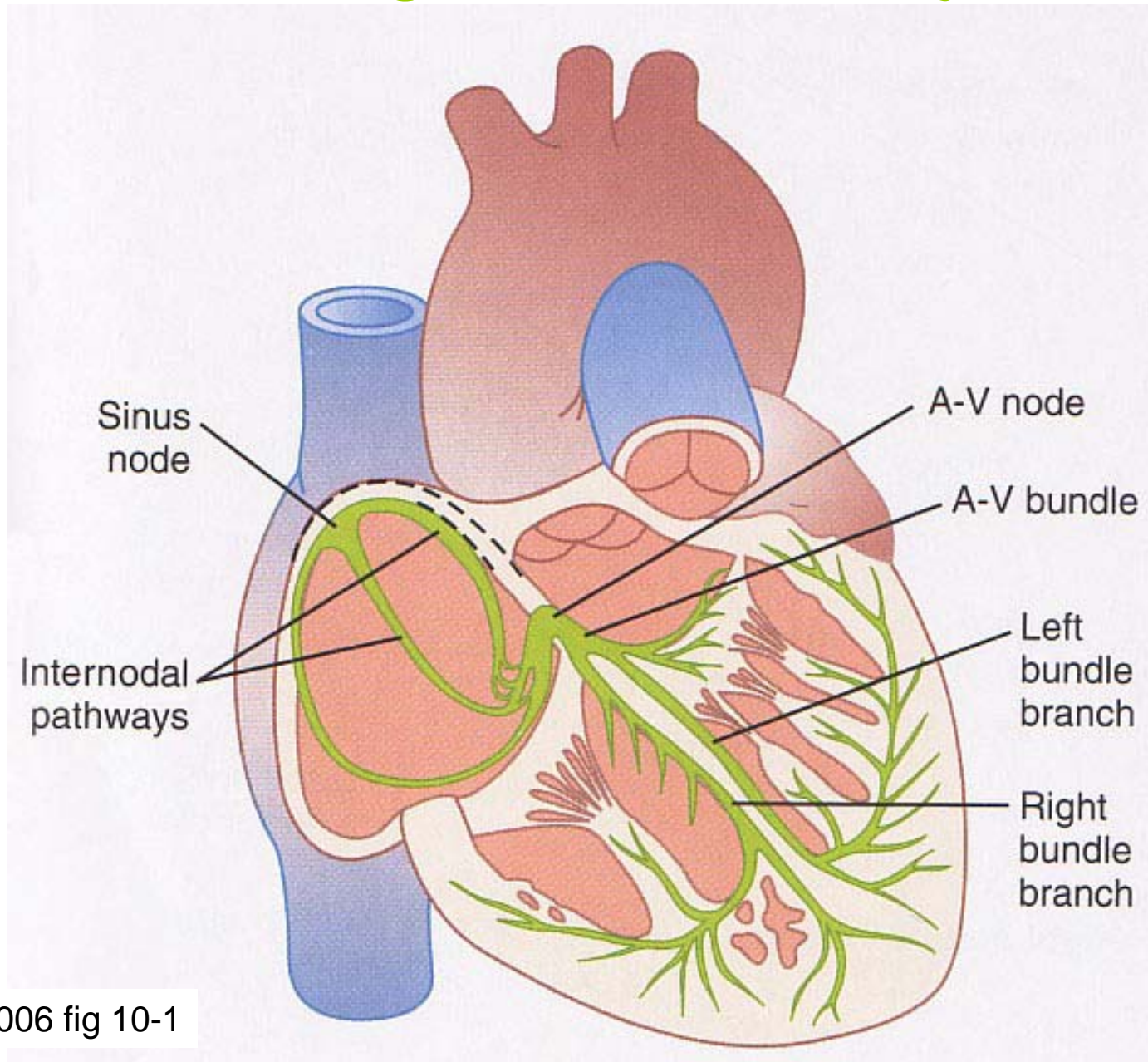
# Cardiac myocytes are mechanically linked & electrically connected!



Modified after L Sherwood 2012 fig 9-5

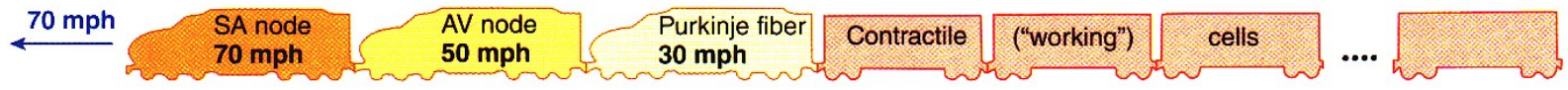


# *Intrinsic Regulation: Autorhythmic*

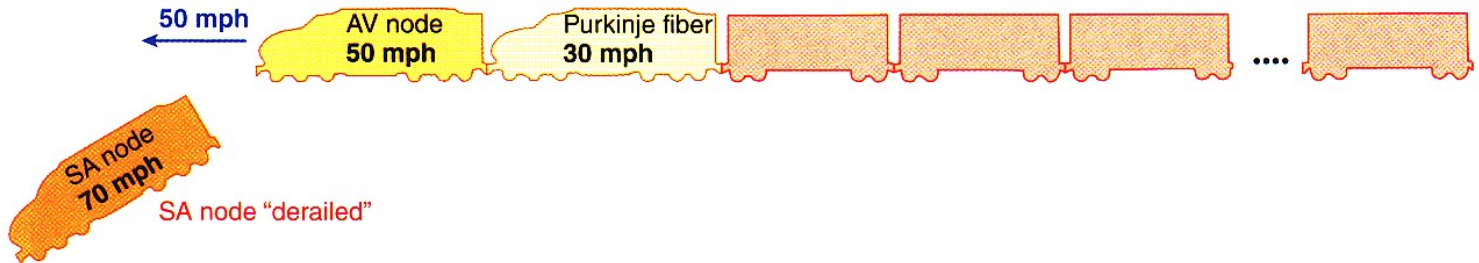


G&H 2006 fig 10-1

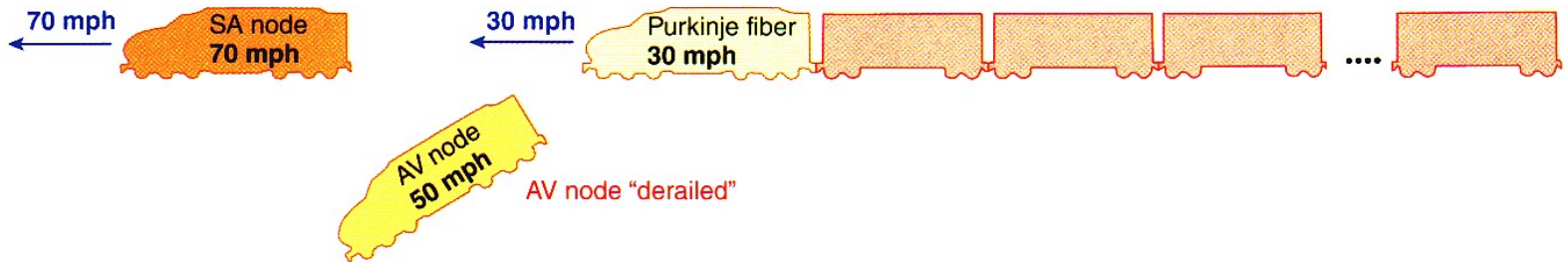




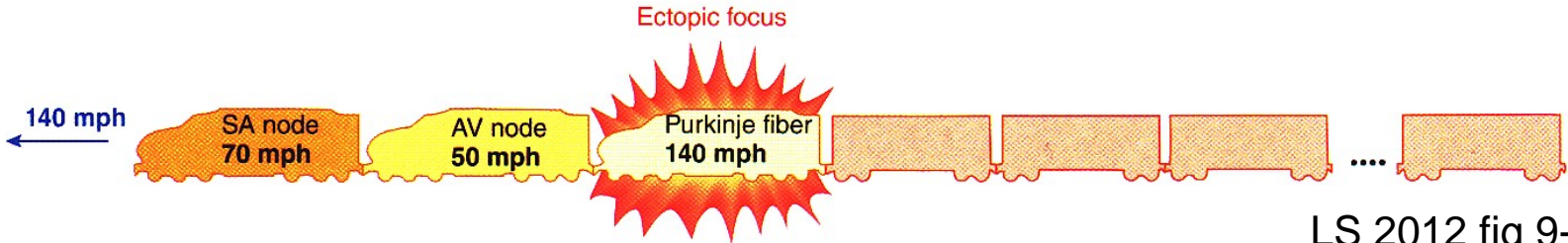
(a) Normal pacemaker activity: Whole train will go **70 mph** (heart rate set by SA node, the fastest autorhythmic tissue).



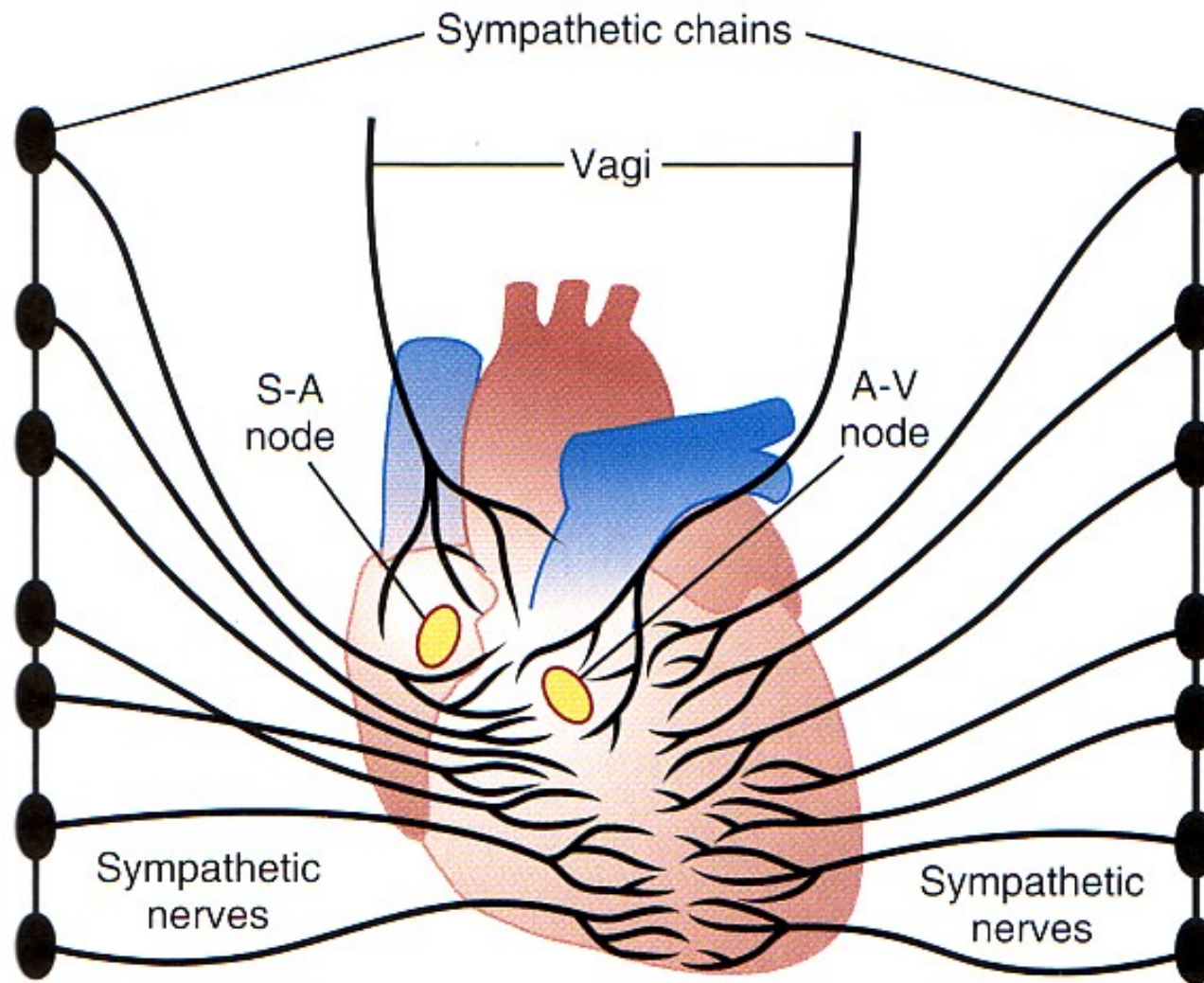
(b) Takeover of pacemaker activity by AV node when the SA node is nonfunctional: Train will go **50 mph** (the next fastest autorhythmic tissue, the AV node, will set the heart rate).



(c) Takeover of ventricular rate by the slower ventricular autorhythmic tissue in complete heart block: First part of train will go **70 mph**; last part will go **30 mph** (atria will be driven by SA node; ventricles will assume own, much slower rhythm).

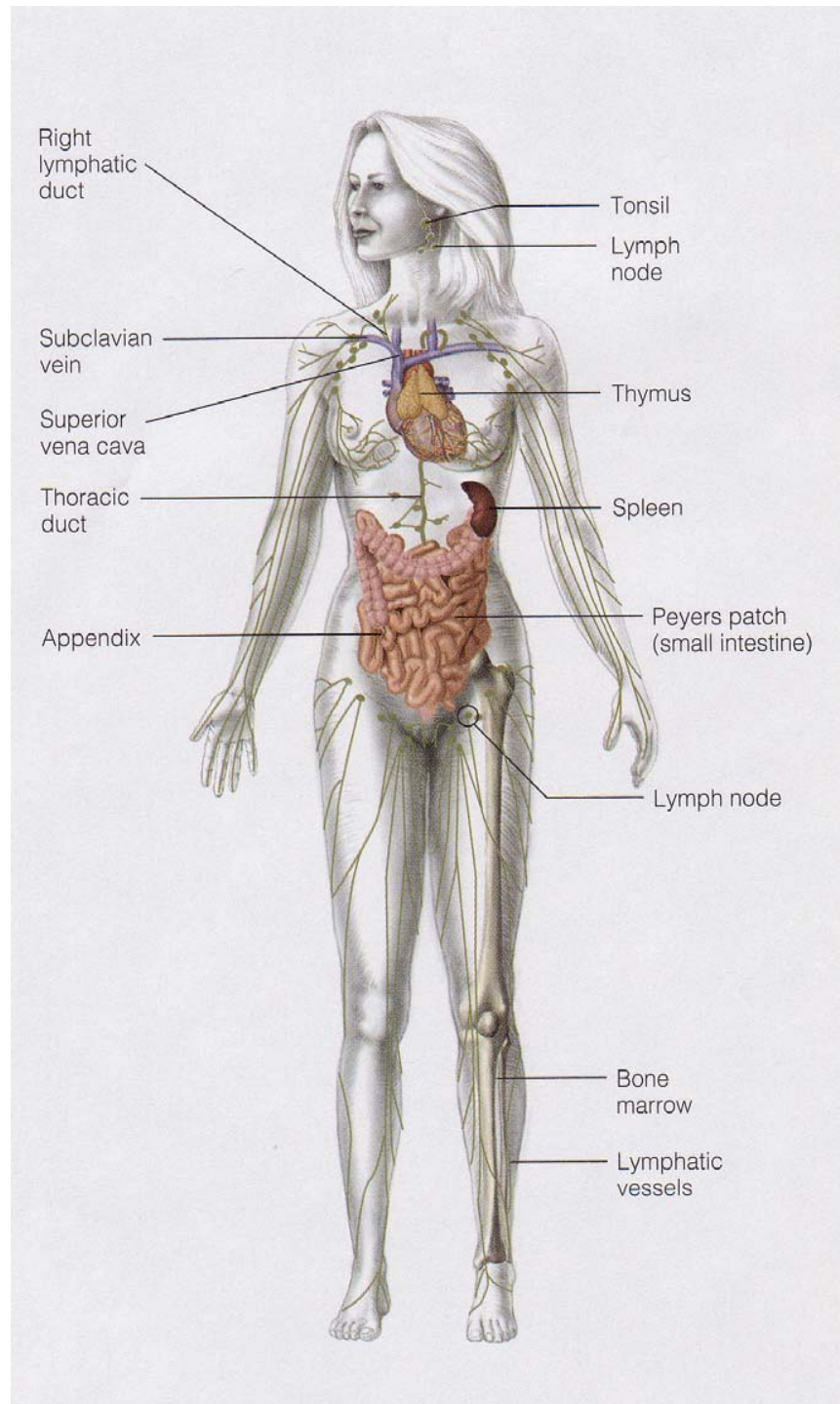


# ***Extrinsic Regulation: Nervous***



**NB: + Extrinsic Hormonal  
e.g. Adrenal Epi + NE**



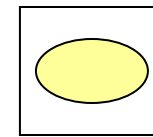


# ***Lymphatic System***

## **1. Lymph Nodes**

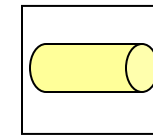
## **2. Vessels**

## **3. Lymph**

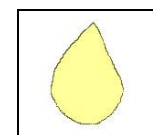


**No pump!**

**+**



**+**

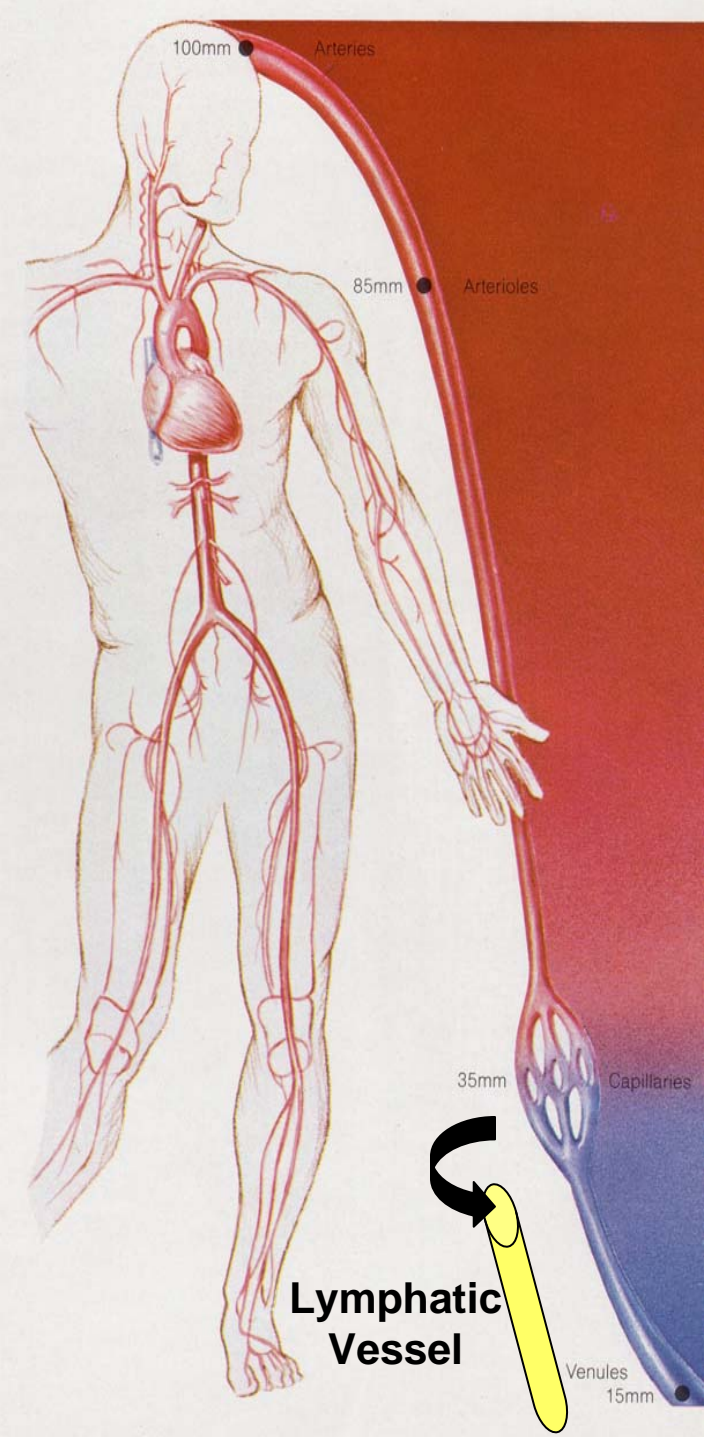


# *Lymphatic System*

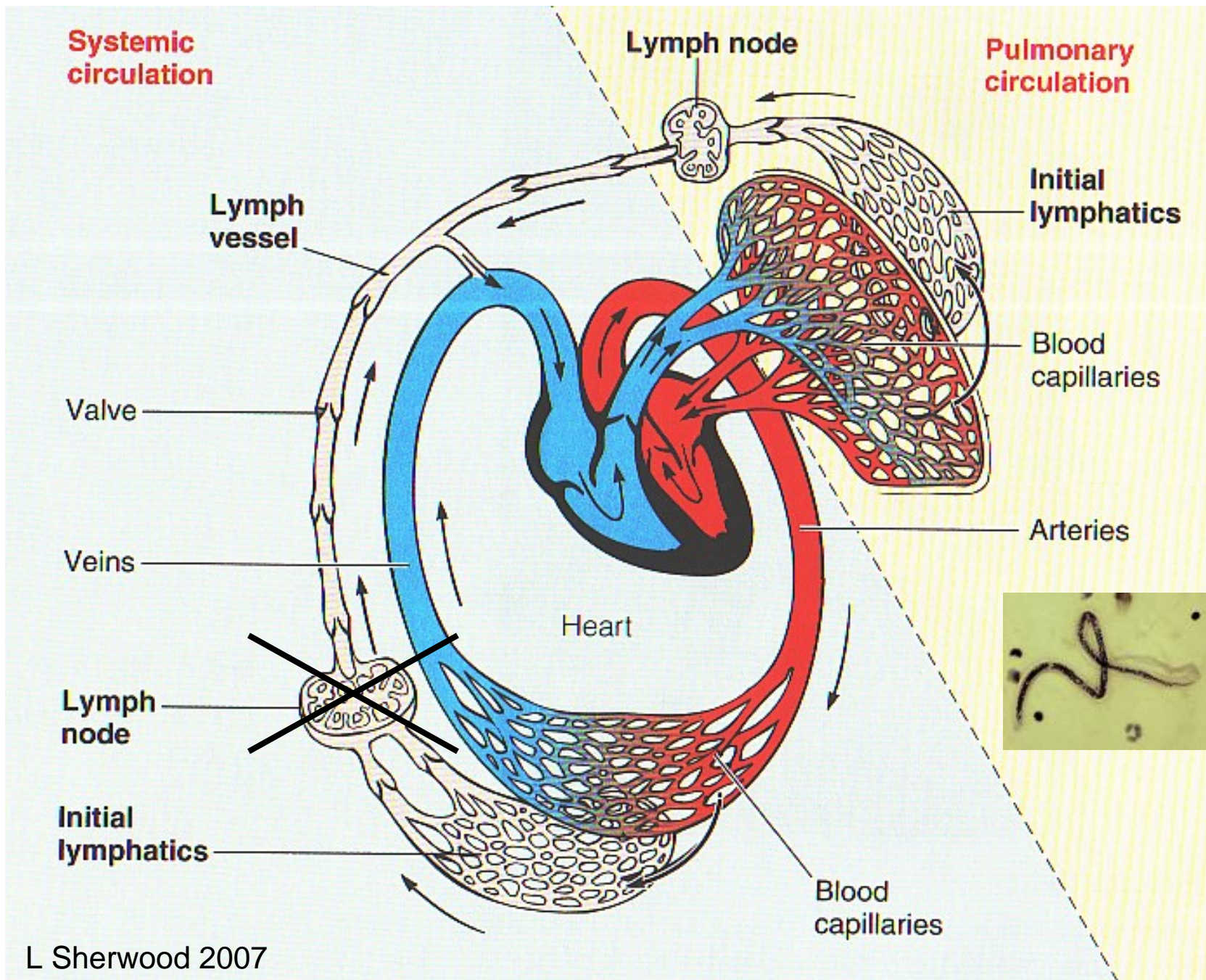
**Alternative System of  
Circulation  
or  
Drainage System**

*Lymph Vessels || Veins*





Torstar Books 1984



L Sherwood 2007



# Elephantiasis: Lymphatic Blockage Due to Mosquito-Borne Parasitic Worm





# Break for questions!





# Did you know?

- **Every year ~785,000 Americans have a first heart attack. Another 470,000 who've had  $\geq 1$  have another attack.**
- **In 2008, > 616,000 people died of heart disease. Heart disease caused almost 25% of deaths in the US.**
- **In 2010, coronary heart disease US costs ~\$108.9 billion including health care, medications & lost productivity.**

*SOURCE:* Heart Disease Facts, Centers for Disease Control, 2012

# CVDs

**AMI**

**CVA**



**TIA**

**HTN**

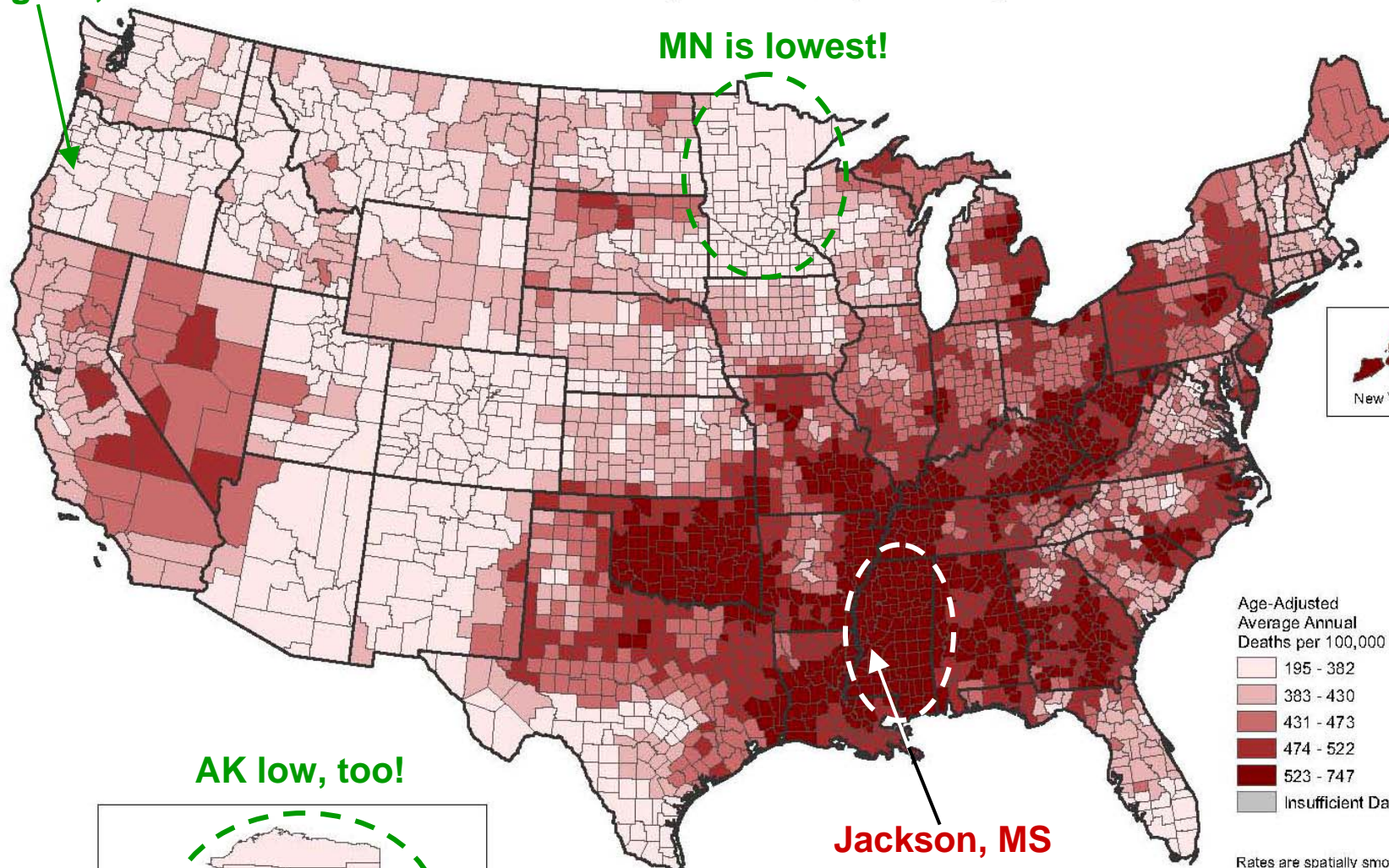
**PAD/PVD**



# Heart Disease Death Rates, 2000-2006 Adults Ages 35+, by County

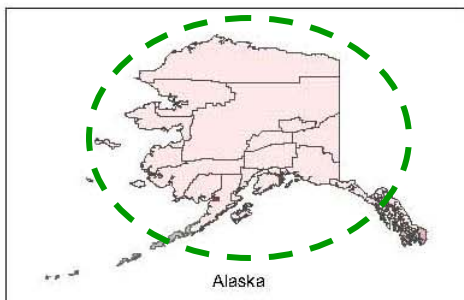
Eugene, OR

MN is lowest!



Age-Adjusted Average Annual Deaths per 100,000	Number of Counties
195 - 382	632
383 - 430	648
431 - 473	629
474 - 522	624
523 - 747	606
Insufficient Data	2

AK low, too!



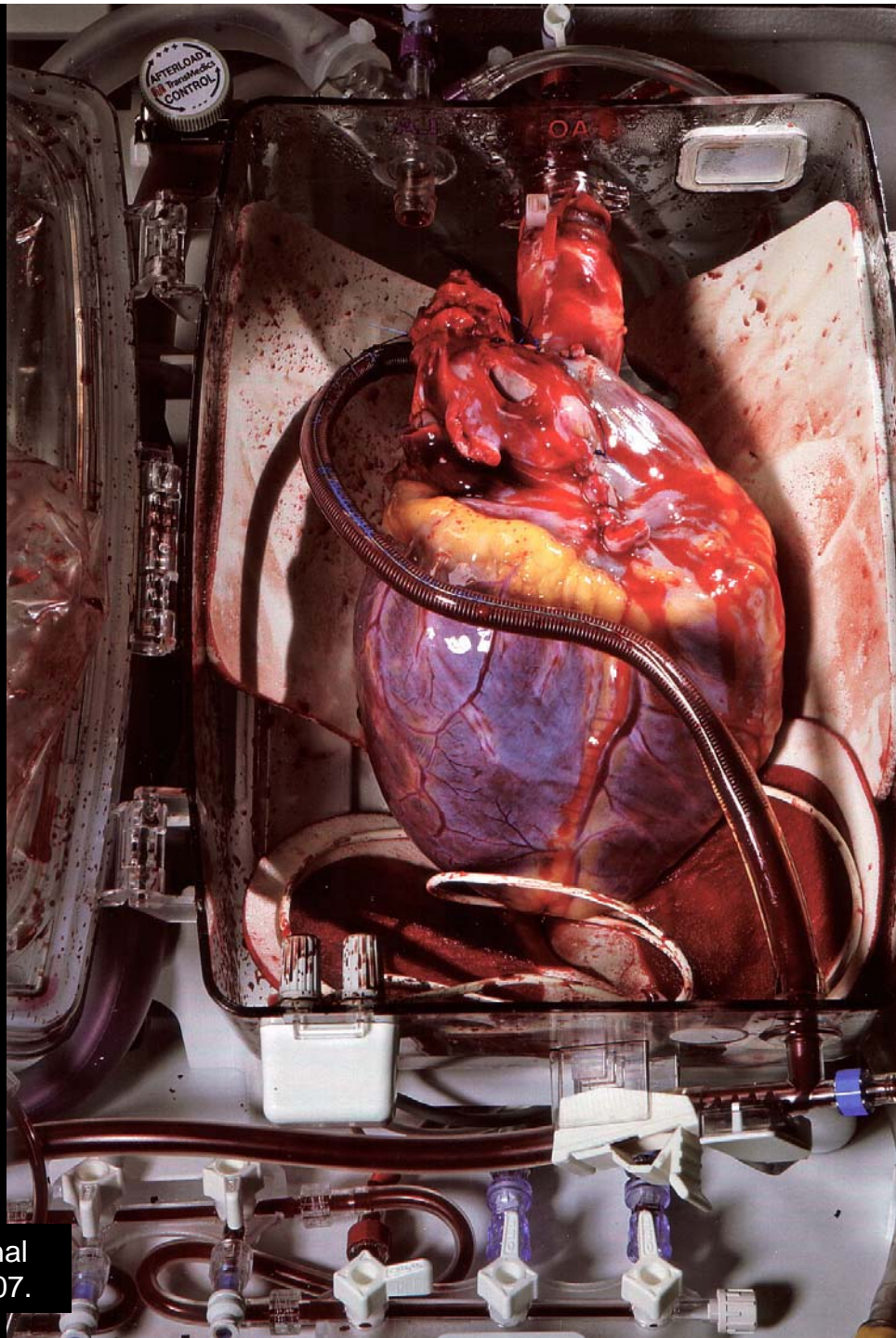
Jackson, MS

Rates are spatially smoothed to enhance the stability of rates in counties with small populations.

ICD-10 codes for heart disease: I00-I09, I11, I13, I20-I51

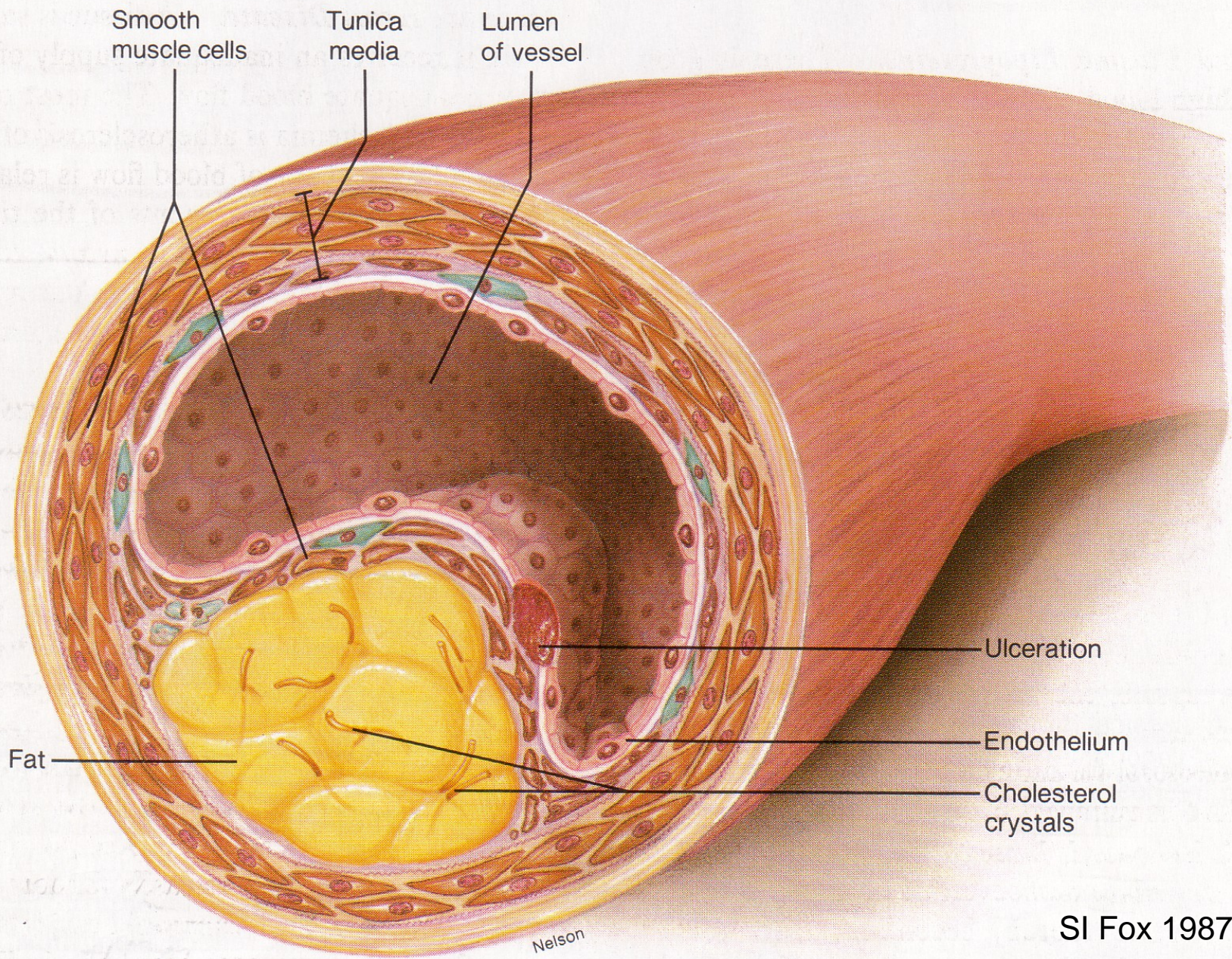
Data Source: National Vital Statistics System and the U.S. Census Bureau





SOURCE: Kahn & Clark, National Geographic, Feb 2007.



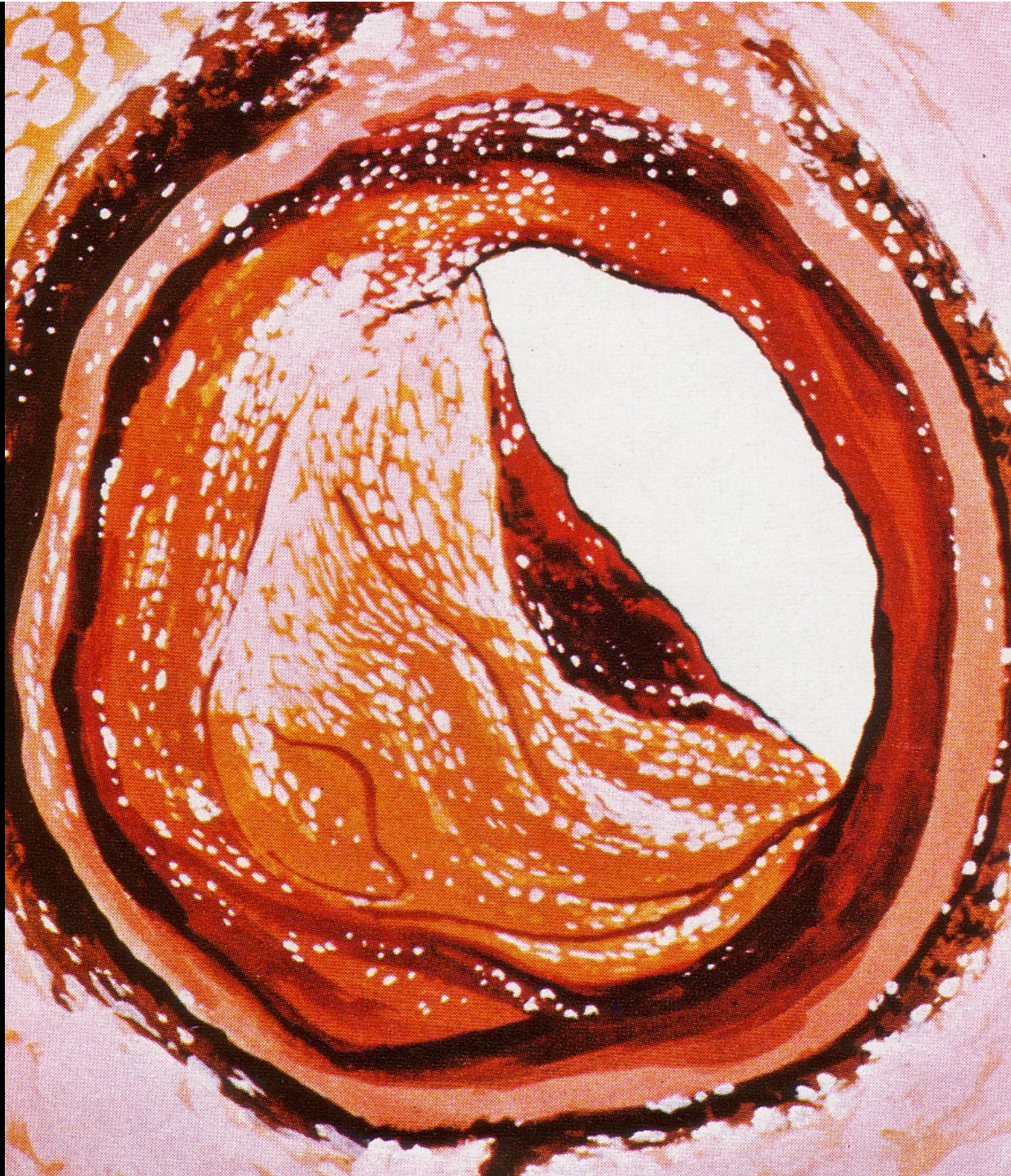




100 yr ♀

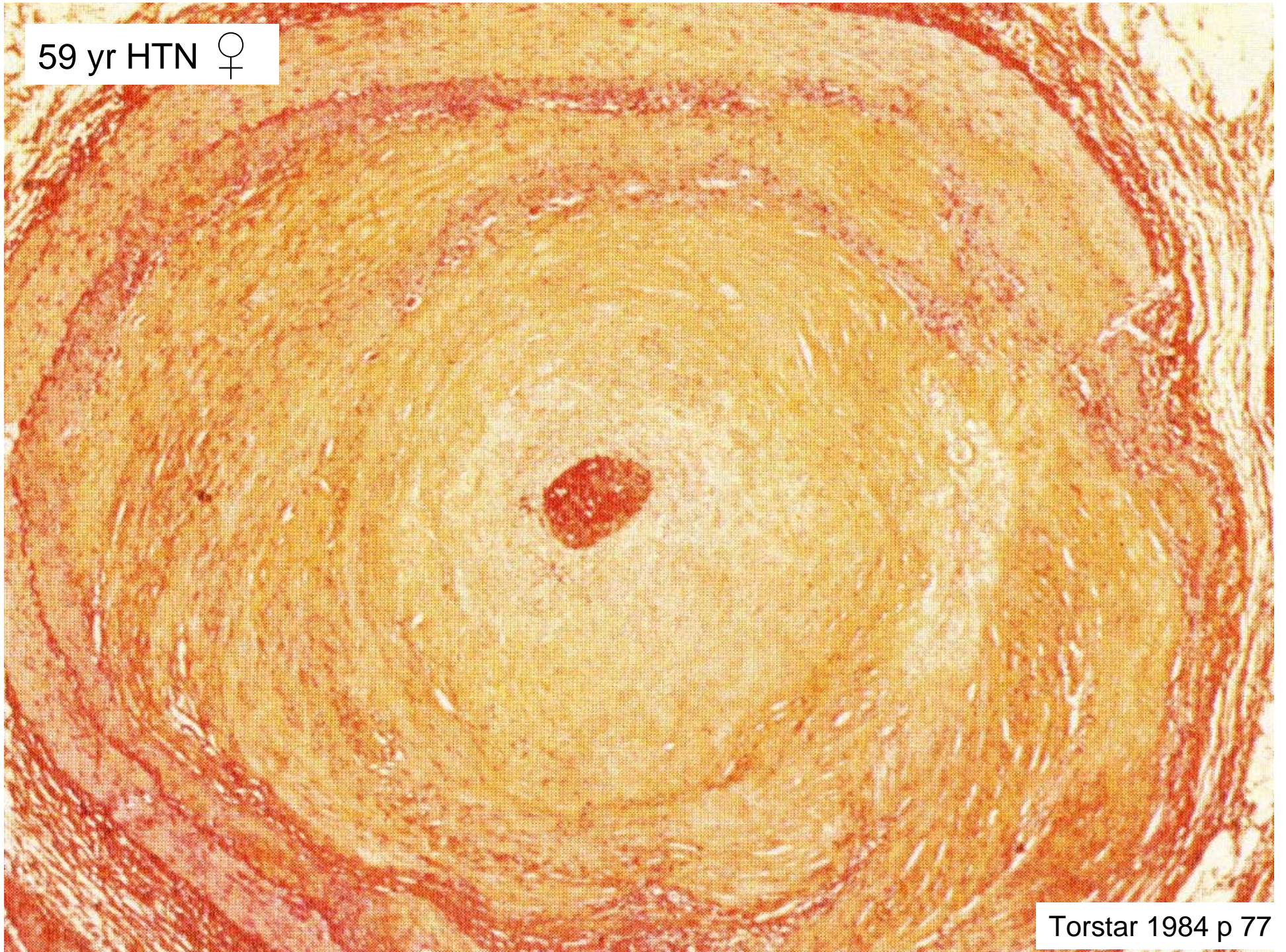








59 yr HTN ♀

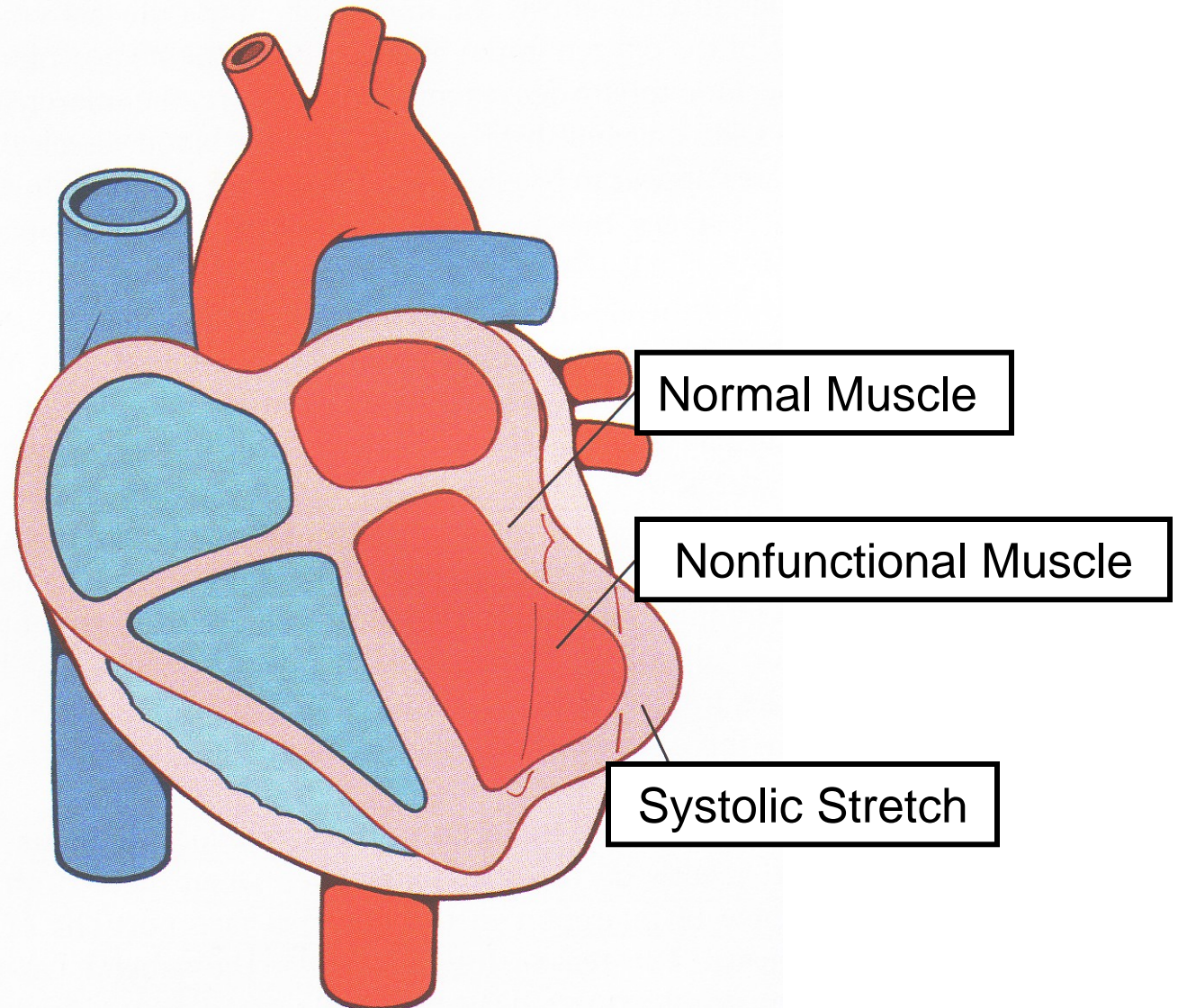




# ***What is the Ultimate Cause of Death?***

1.  $\downarrow \dot{Q}$ , CO or Cardiac Output
2. Pulmonary damming w/edema
3. Cardiac fibrillation
4. Thromboembolism
5. Cardiac rupture

# Systolic Stretch Due to Necrotic Tissue



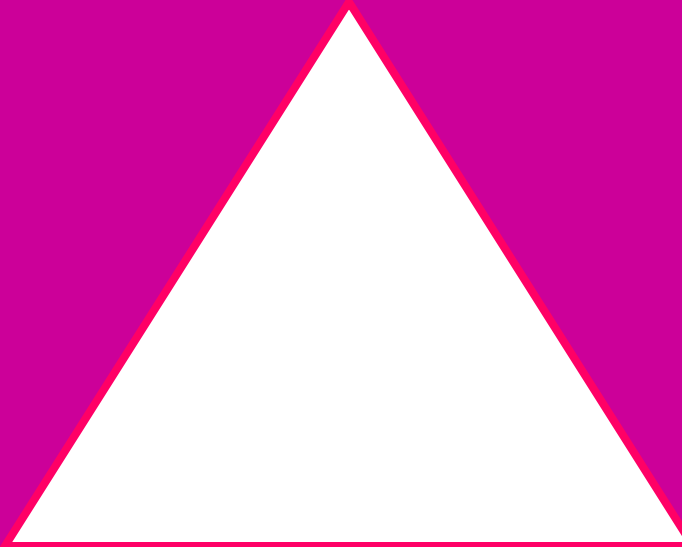


# ***Treatment Triad***

NB: Last blasted resort!!

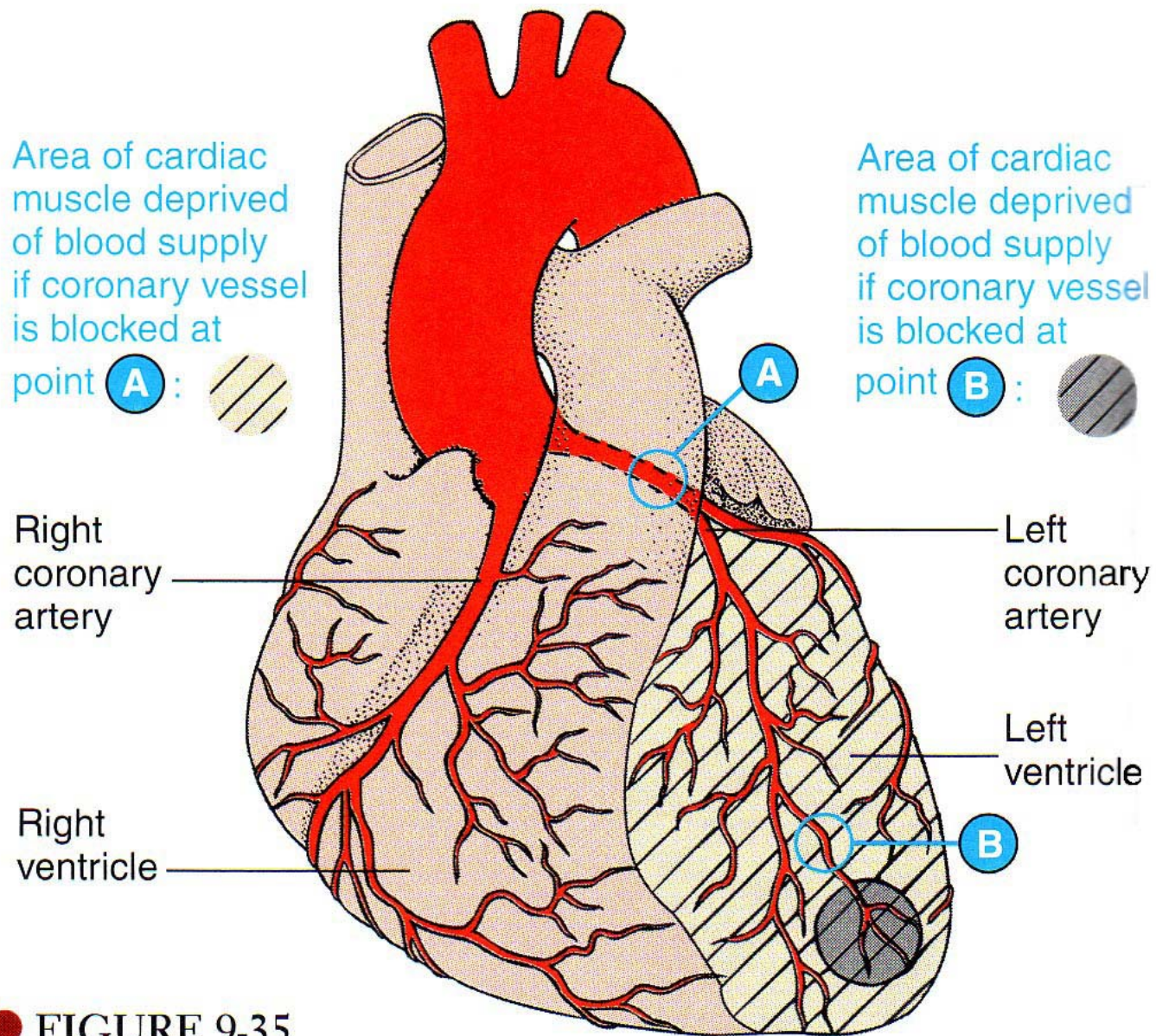


***Drugs/Surgery***



***Exercise***

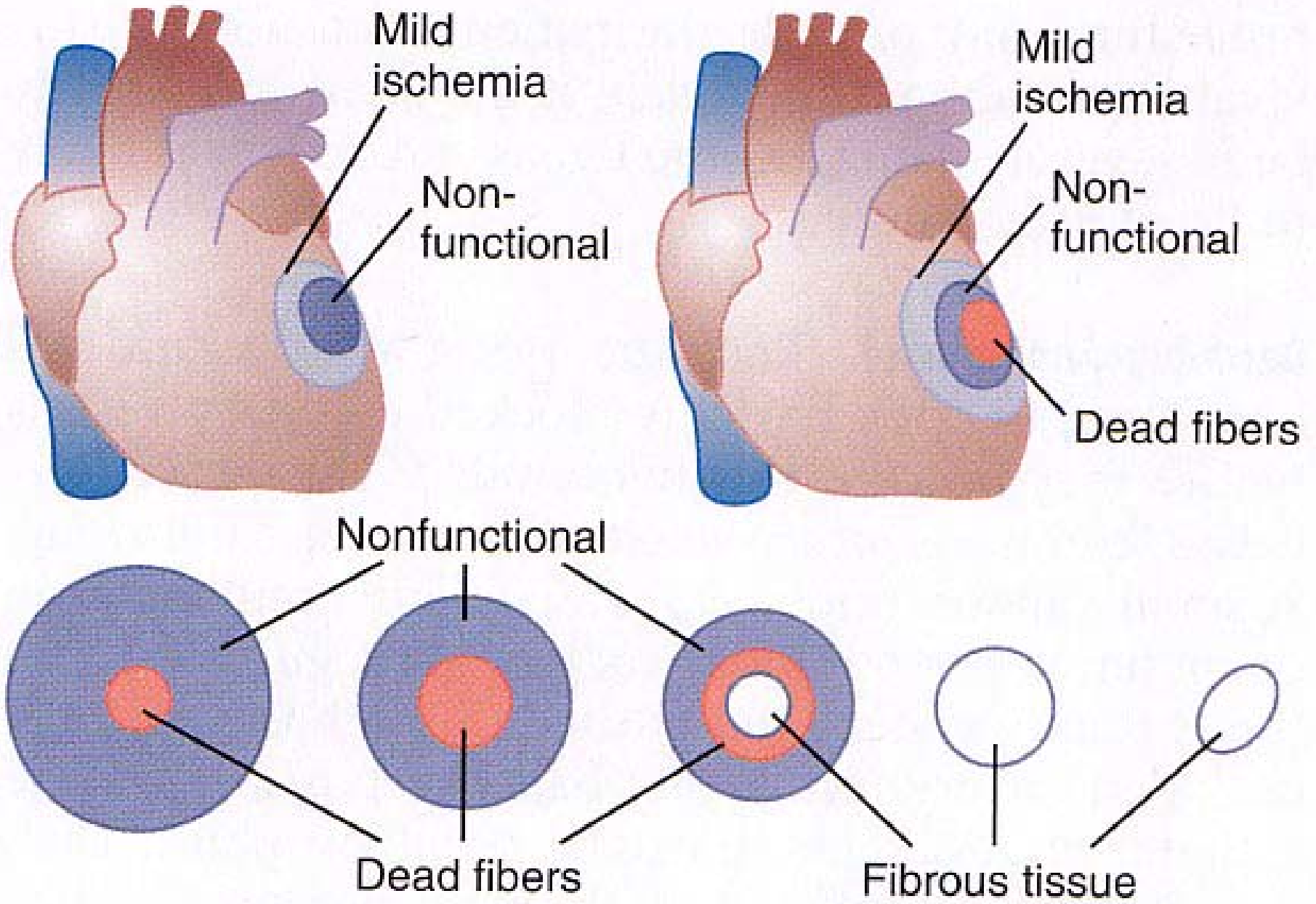
***Dietary  
Modification***



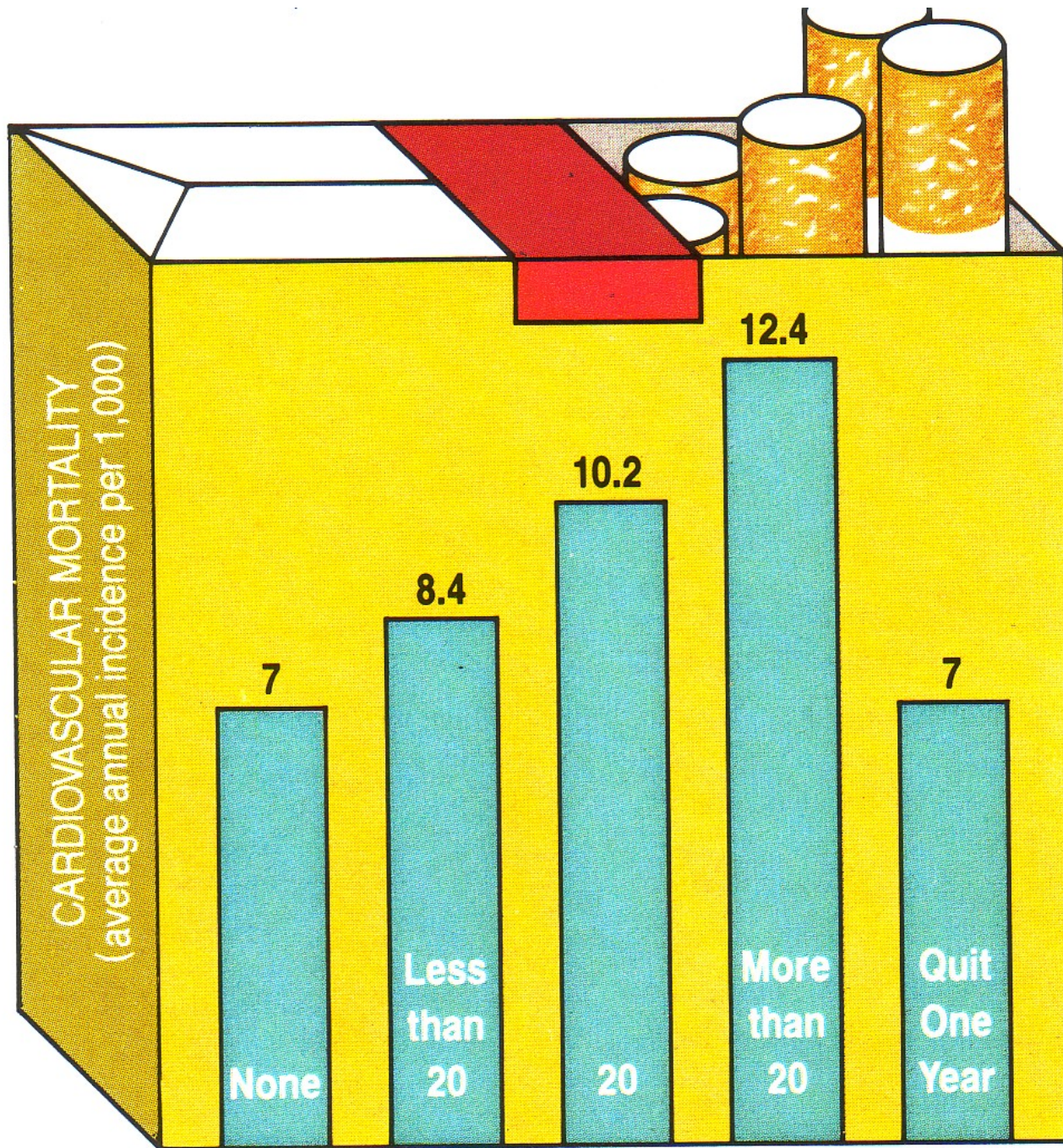
● **FIGURE 9-35**

**Extent of myocardial damage as a function of the size of the occluded vessel**



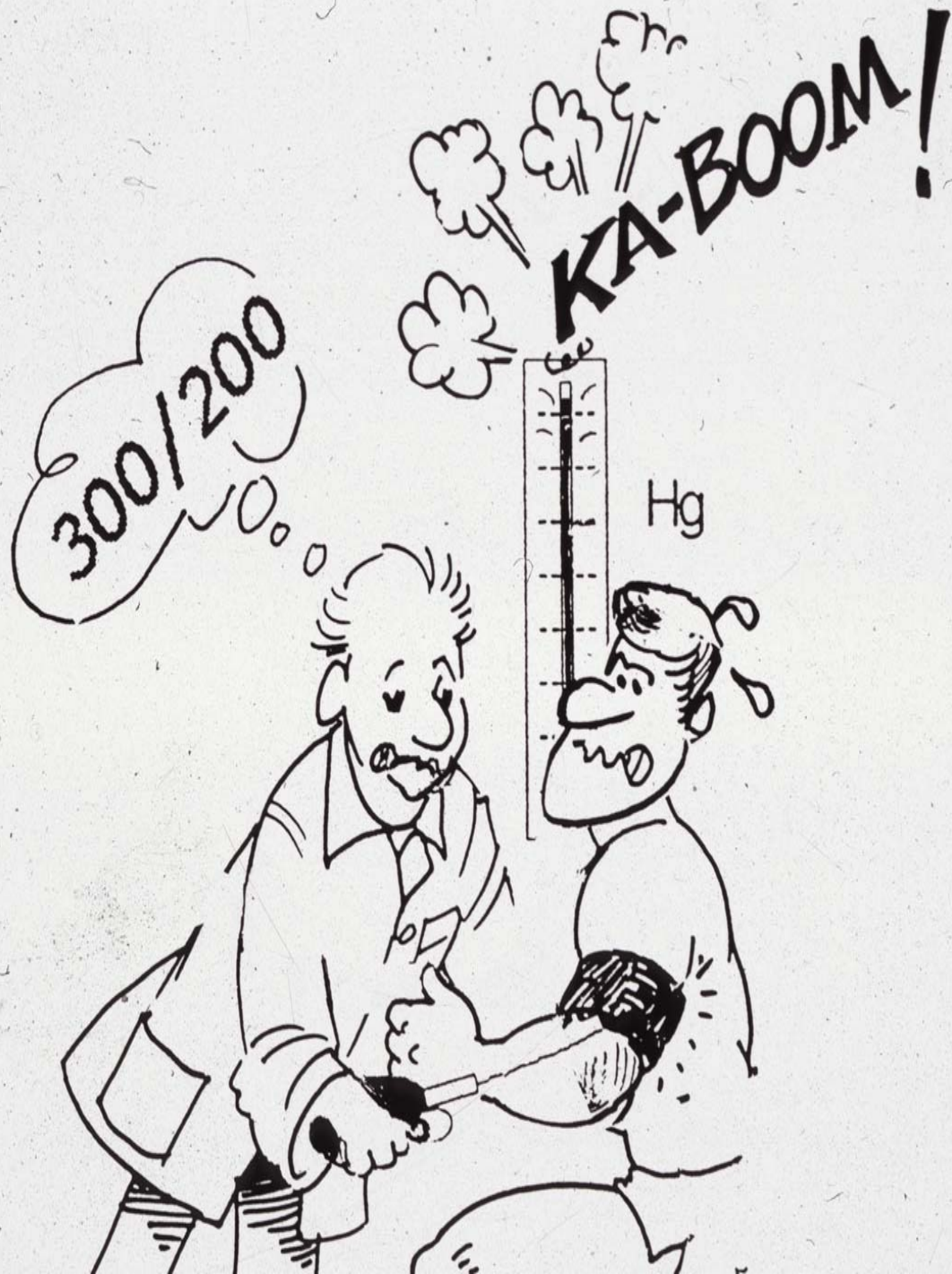


G&H fig 21-8

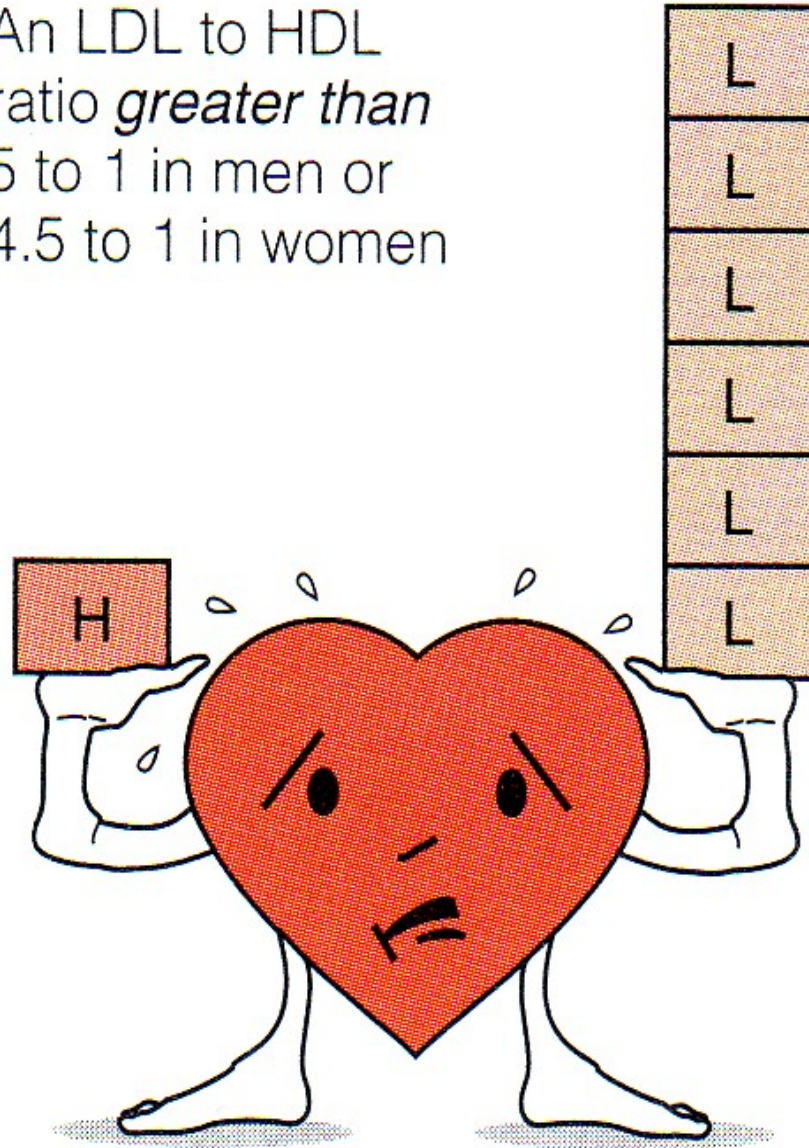


CIGARETTES SMOKED PER DAY



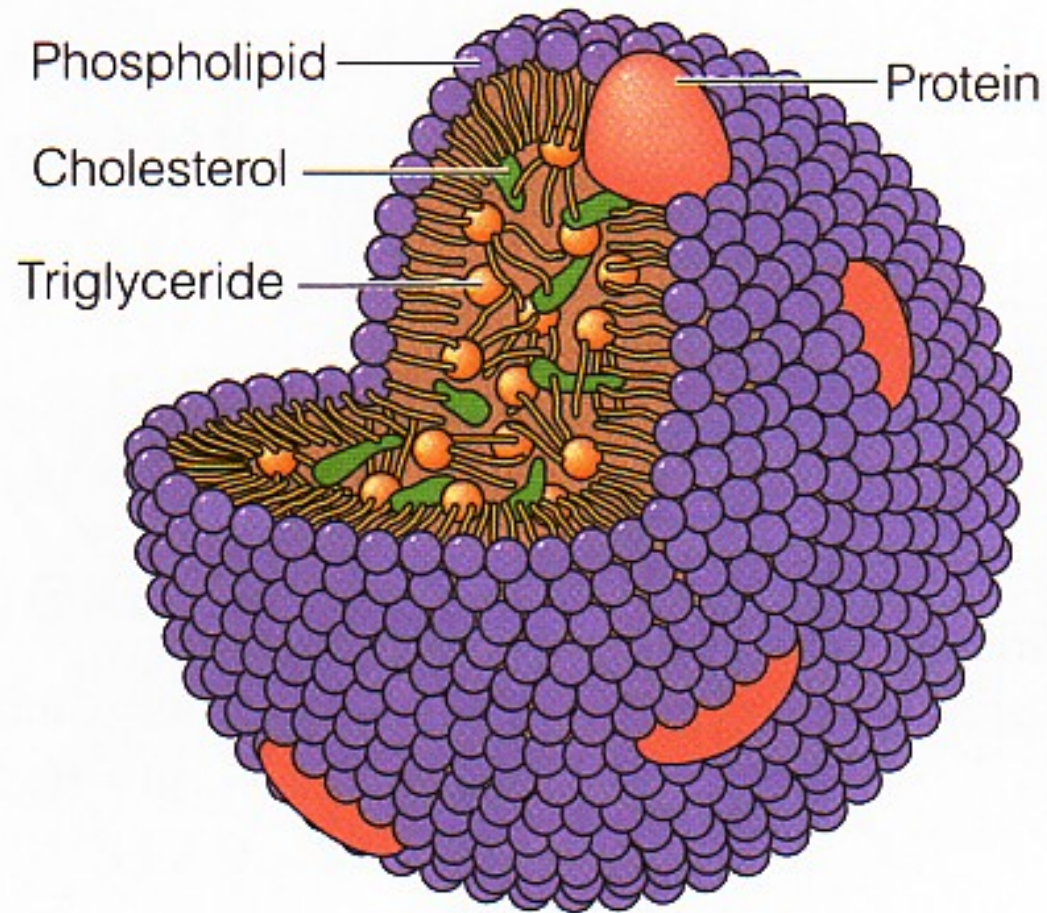


An LDL to HDL  
ratio *greater than*  
5 to 1 in men or  
4.5 to 1 in women

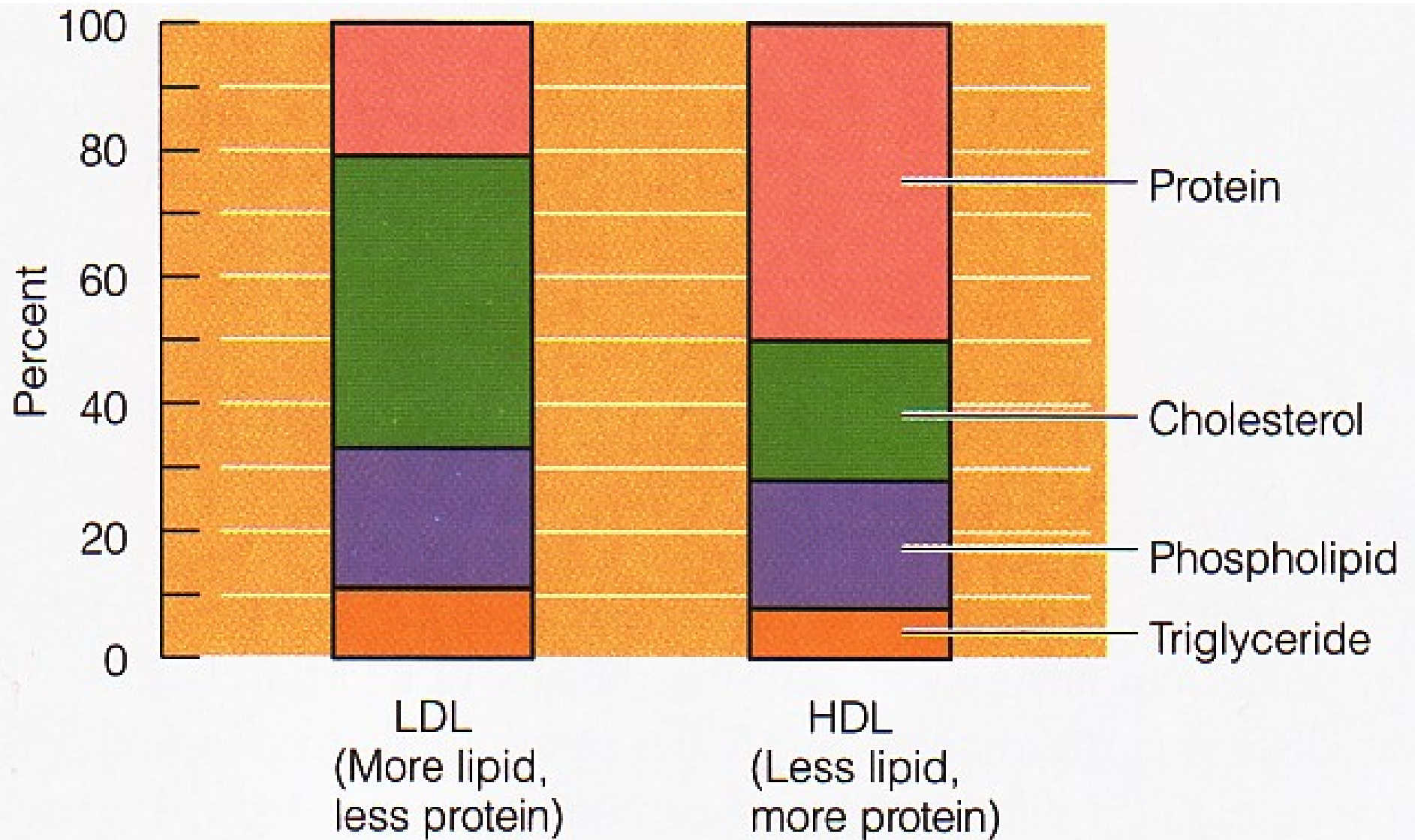


Increased risk of  
heart disease





A typical lipoprotein



Lower density

Higher density



## **? *Selected Atherosclerotic Genetic Determinants – Ultra-short List!* ?**

**Genes for HDL, LDL+ receptors, Apolipoproteins Apo B-100, Apo-E, Apo-M, lipoprotein a/Lp<sub>a</sub>, homocysteine metabolism enzymes N5,N10-methylene-tetrahydrofolate reductase, cystathione beta-synthase, Type I antithrombin, mitochondrial haplogroup A, Protein tyrosine phosphate PTPN22 C/T single nucleotide polymorphism (SNP) @ +1858, HMG COA reductase, SNPs in TNF-alpha, IL-1beta & TGF-beta1, IL-6, IL-10, CD14, TLR-4 receptors, Human Leukocyte Antigens HLA-DRB1\*01, HLA-B\*07 + haplotype LTA+253a-LTA+633g-C4A3-C4B1, HDL-associated paraoxonase (PON1), lysosomal acid lipase (LAL), MEF2A protein affecting artery walls...**

# Bruce Kottke's Bathtub Analogy

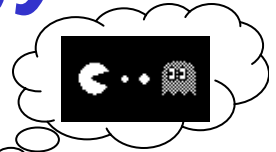


Bruce Kottke

5 forms of cholesterol:

Chylomicrons, VLDL, LDL, IDL, HDL

$\beta$

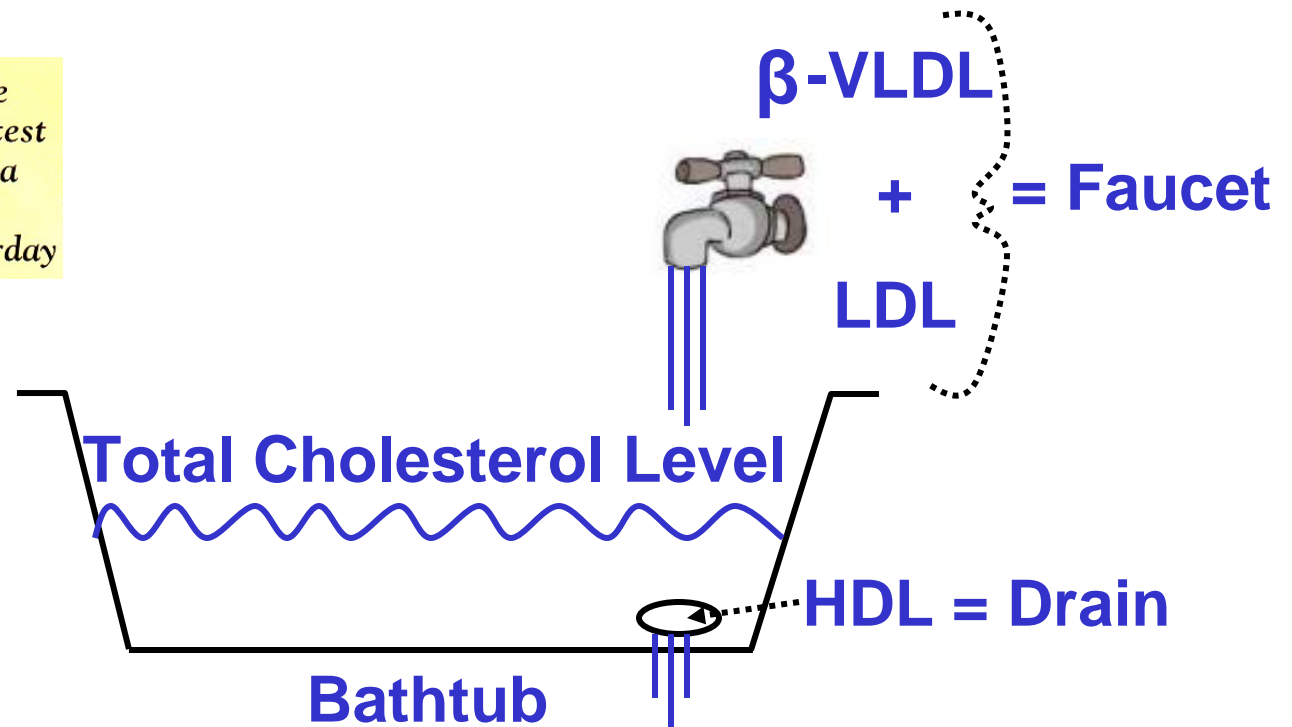


Atherogenic

Anti-Atherogenic

Biological Artifact!?

"I don't think the total cholesterol test by itself is worth a damn."  
—Eliot Corday

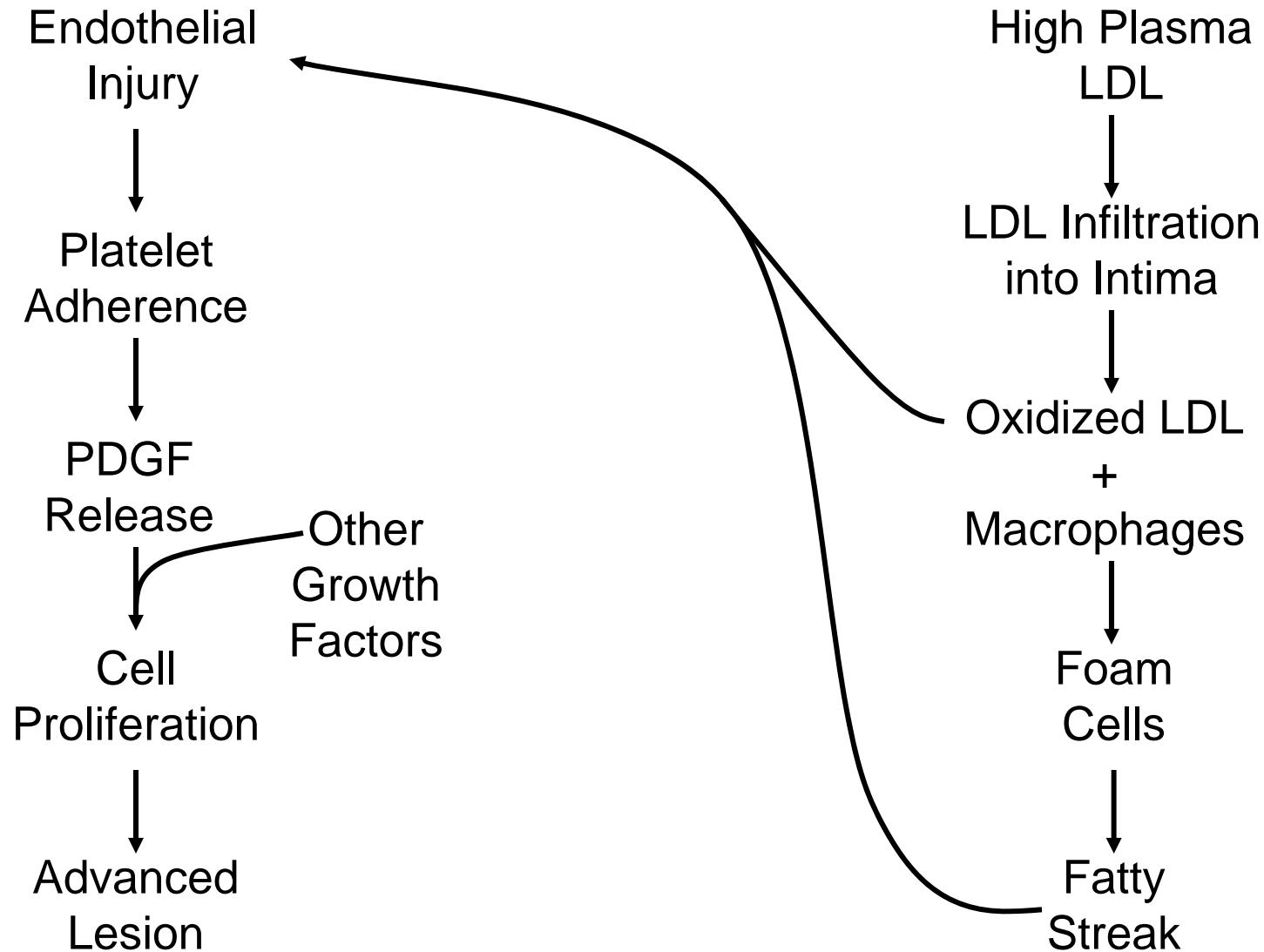




# Historical Hypotheses for Atherosclerosis Development

Ross & Glomset

Steinberg & Witztum



# How Inflammation Attacks the Heart

**1**

Oxidized LDL cholesterol creates the "injury" by burrowing into the artery wall. Cigarette smoking, high blood pressure, and high blood sugar make the injury worse.

**2**

In response to the injury, the immune system sends in a team of inflammatory cells, including white blood cells called monocytes.

**3**

Monocytes migrate into the artery wall, where they turn into macrophages. The macrophages' job: gobble up the LDL cholesterol.

**4**

The macrophages, now stuffed with LDL cholesterol, form a "fatty streak" in the artery wall.

**5**

Over the decades, more cholesterol, connective and elastic tissue, calcium, and cell debris accumulate and turn the fatty streak into plaque. As the artery tries to heal itself, smooth muscle cells migrate in to cover the plaque, forming a fibrous cap around it.

**6**

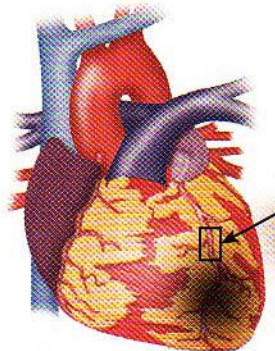
Macrophages kill the smooth muscle cells and release enzymes that break down the fibrous cap.

**7**

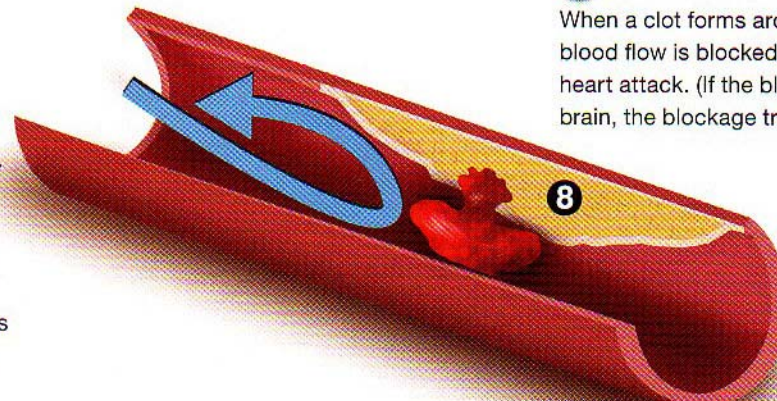
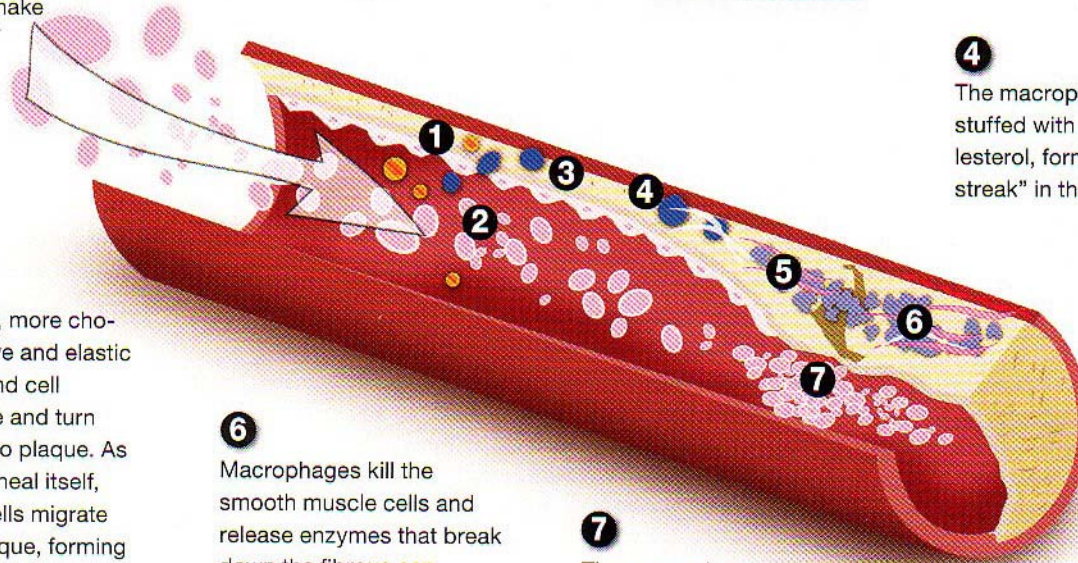
The cap ruptures.

**8**

When a clot forms around the rupture, blood flow is blocked, which triggers a heart attack. (If the blocked artery feeds the brain, the blockage triggers a stroke.)



Coronary artery (supplies blood and oxygen to the heart muscle).







# TROUBLE AHEAD?

## HOW TO KEEP YOUR BRAIN SHARP

So far, no one has found a magic bullet to stop Alzheimer's disease, which gums up the brain with protein clumps and tangles. But it's not just clumps and tangles.

### Brain Basics

Plaques and tangles. Those are the classic hallmarks of Alzheimer's disease.

The plaques are clumps of a protein fragment called beta-amyloid. The tangles are clusters of misshapen "tau" proteins that show up later in the disease.

But plaques and tangles alone don't explain what happens to many aging brains.

"Thirty percent of people over the age of 70 have elevated beta-amyloid and are cognitively normal," says David Knopman, professor of neurology at the Mayo Clinic in Minnesota.

Scientists aren't sure why.

"The most prevalent idea is that amyloid deposits are only the initiating step

Damage to the brain's blood vessels—often due to high blood pressure, smoking, or diabetes—can also play a role, not just in dementia but in milder memory loss as well.

Here's how to keep a clear head for as long as possible.

often assume that it's just Alzheimer's," notes Reed. "But it's uncommon to find people with dementia who just have a single pathology. Very often, it's mixed pathology."

The most common other problem: damaged blood vessels in the brain.<sup>1,2</sup>

"The arteries become stiffened, narrowed, and sort of tortuous," says Reed. "It's much harder for the blood flow to occur normally."

That can lead to a stroke that's obvious, or to one that's never noticed. "Around

"In fact, some of the symptoms we think of as normal brain aging may be due to injury to the brain's blood vessels," he notes.

Researchers know the major threats. "The big risks for

vascular brain injury are smoking, high blood pressure, and diabetes," says Reed.

The causes of Alzheimer's pathology are more murky. But new evidence suggests that insulin may play a role.

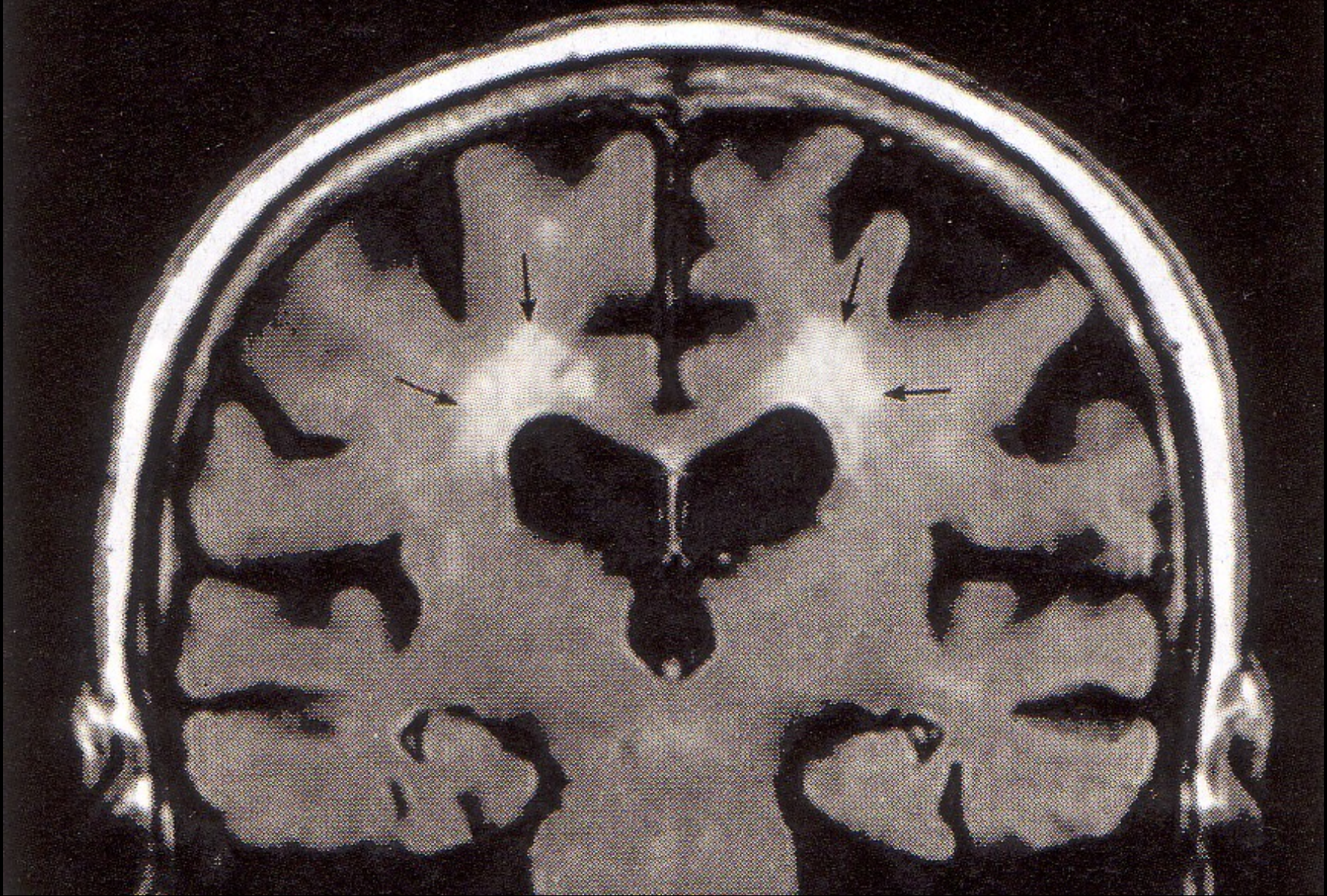
Here's how to keep your brain in good working order.

### 1. Watch your blood pressure

"There's a wealth of evidence that high blood pressure is a risk factor for late-life cognitive impairment," says Knopman.



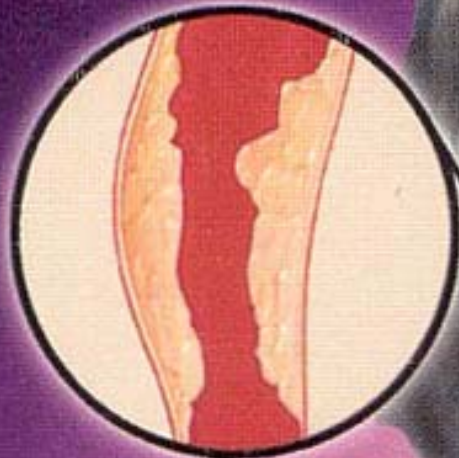
# MRI Hyperintensities, Hypertension & Dementia



NAHL CSPI, Jan-Feb 2014



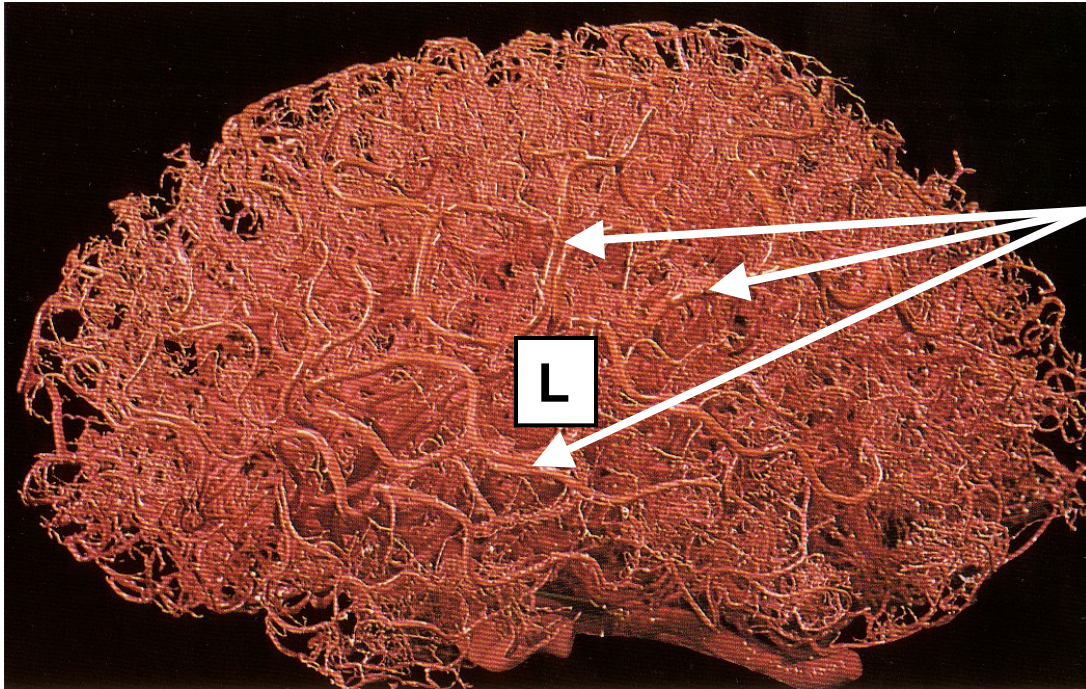
**DISEASED CAROTID ARTERY**



**HEALTHY CAROTID ARTERY**

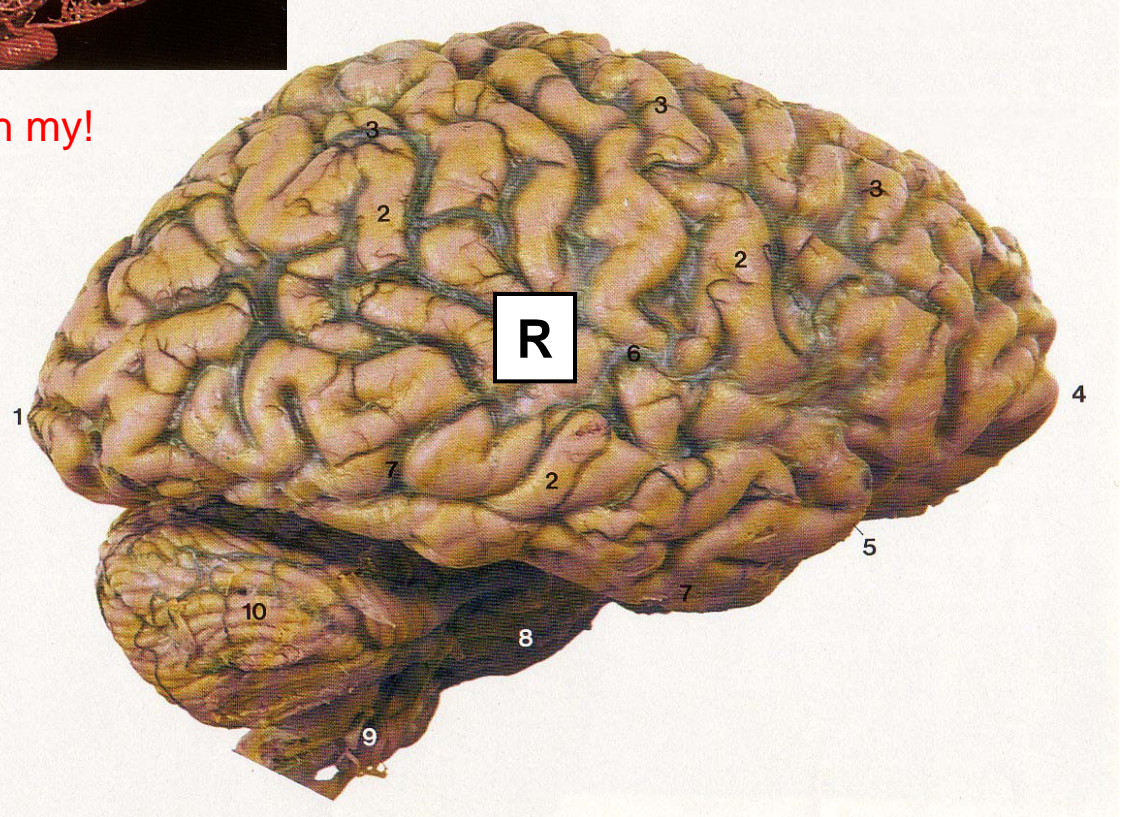
*SOURCE:* Lifeline Screening, 2007





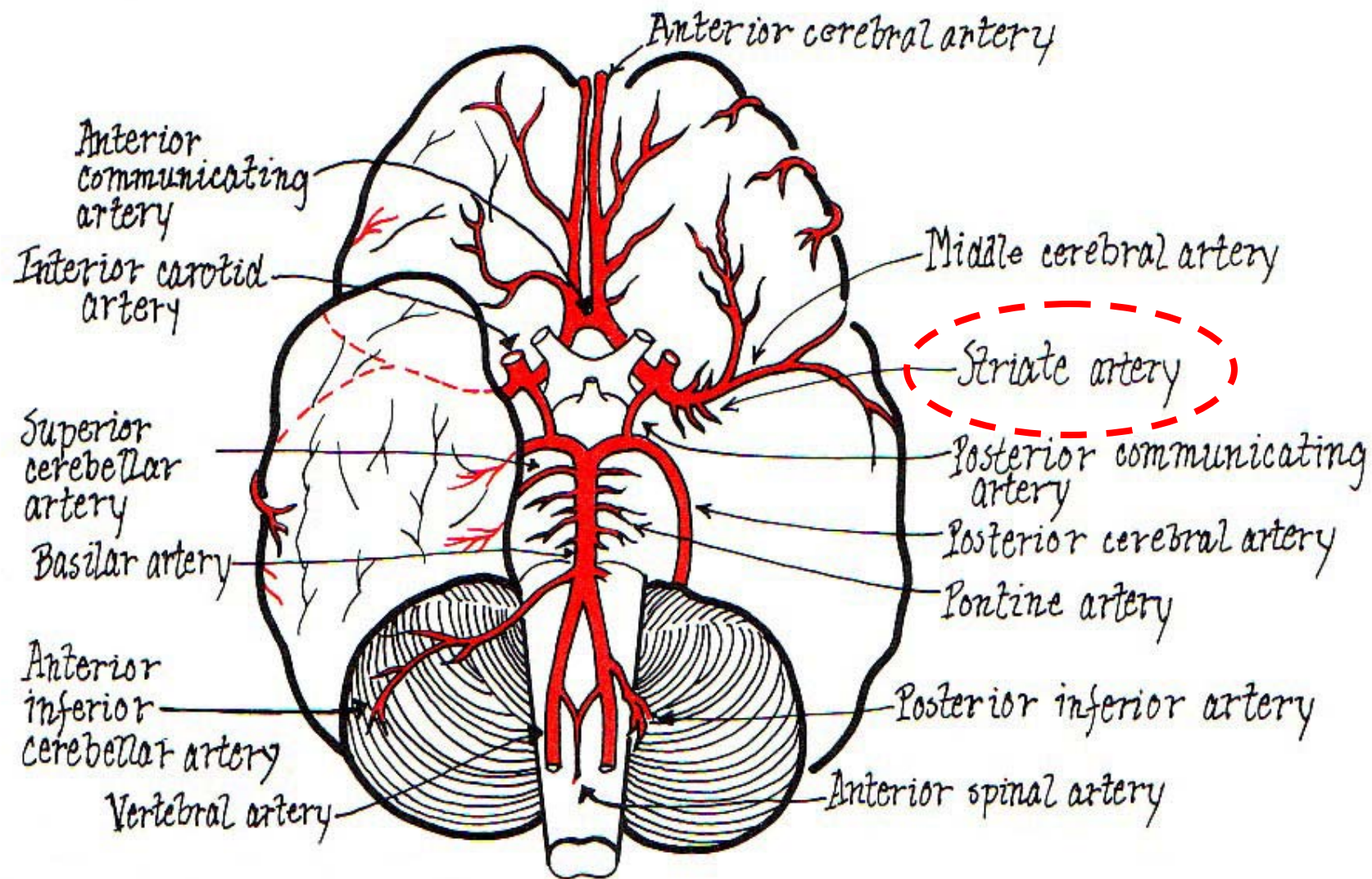
Middle Cerebral Artery Branches

...Cerebral vasculature! Oh my!



SOURCE: McMinn & Hutchins, 1977.

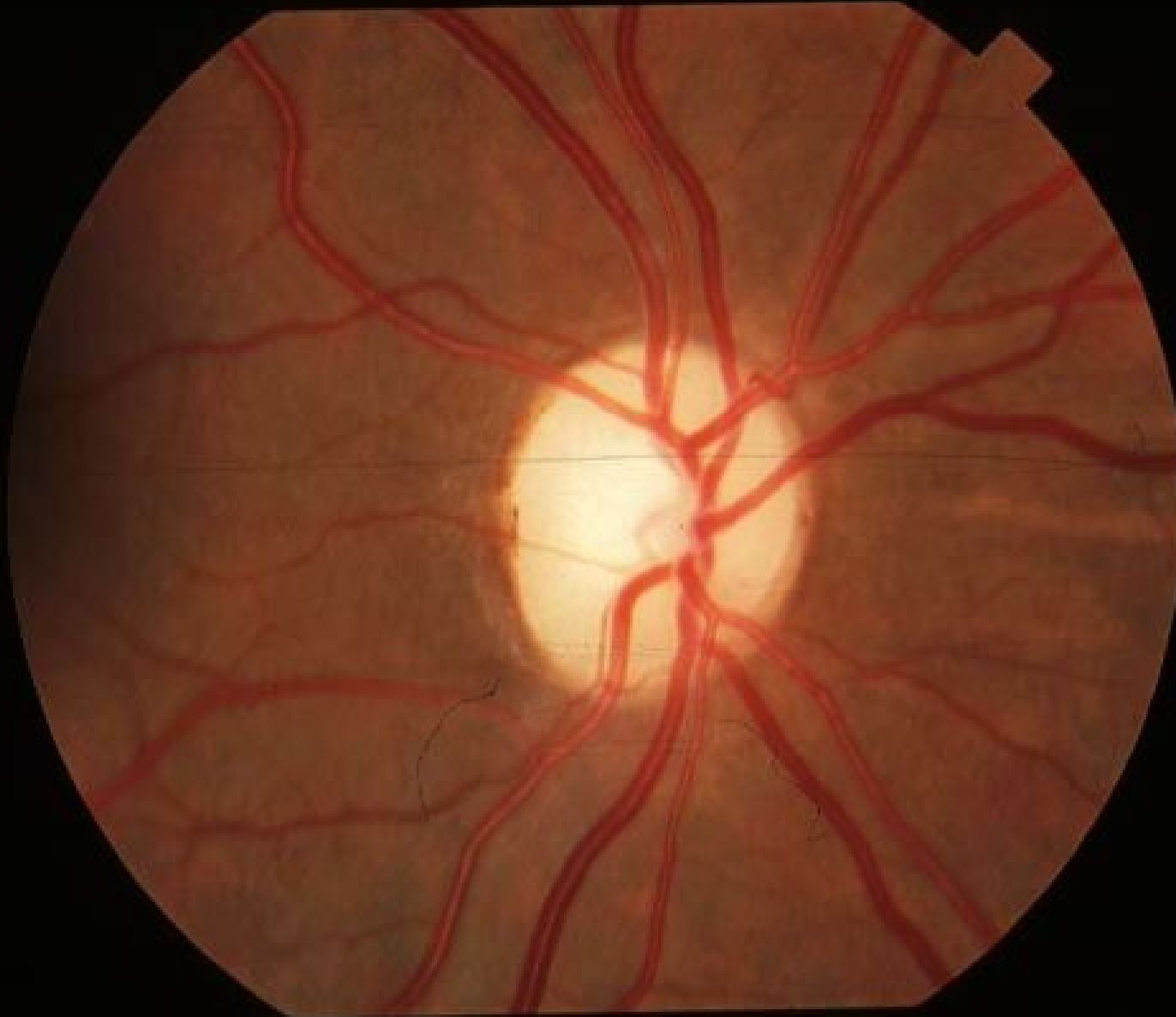




**( ) = Artery of Stroke**

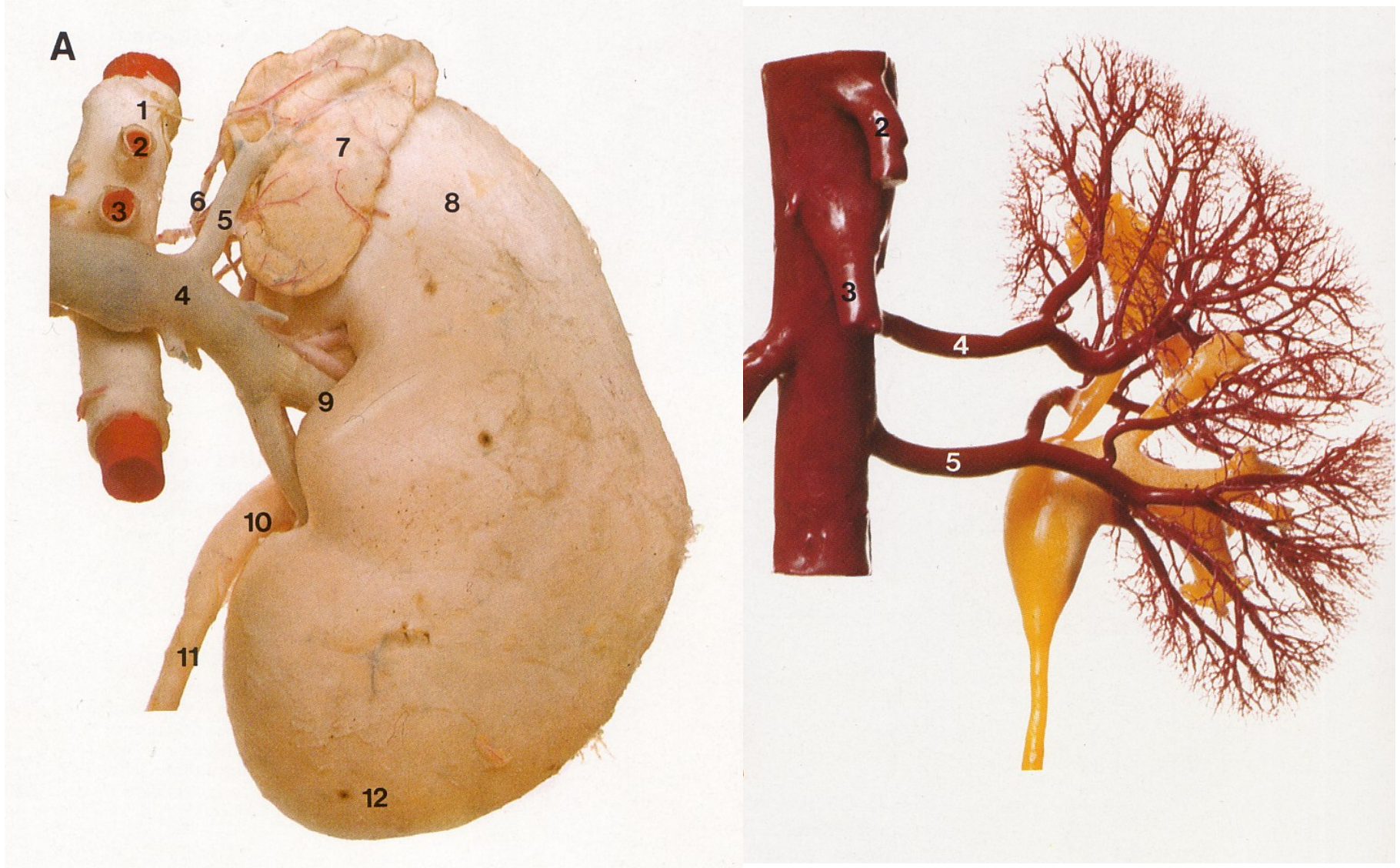
SOURCE: Liebman, 1979.

# ***The Window to the CV System?***



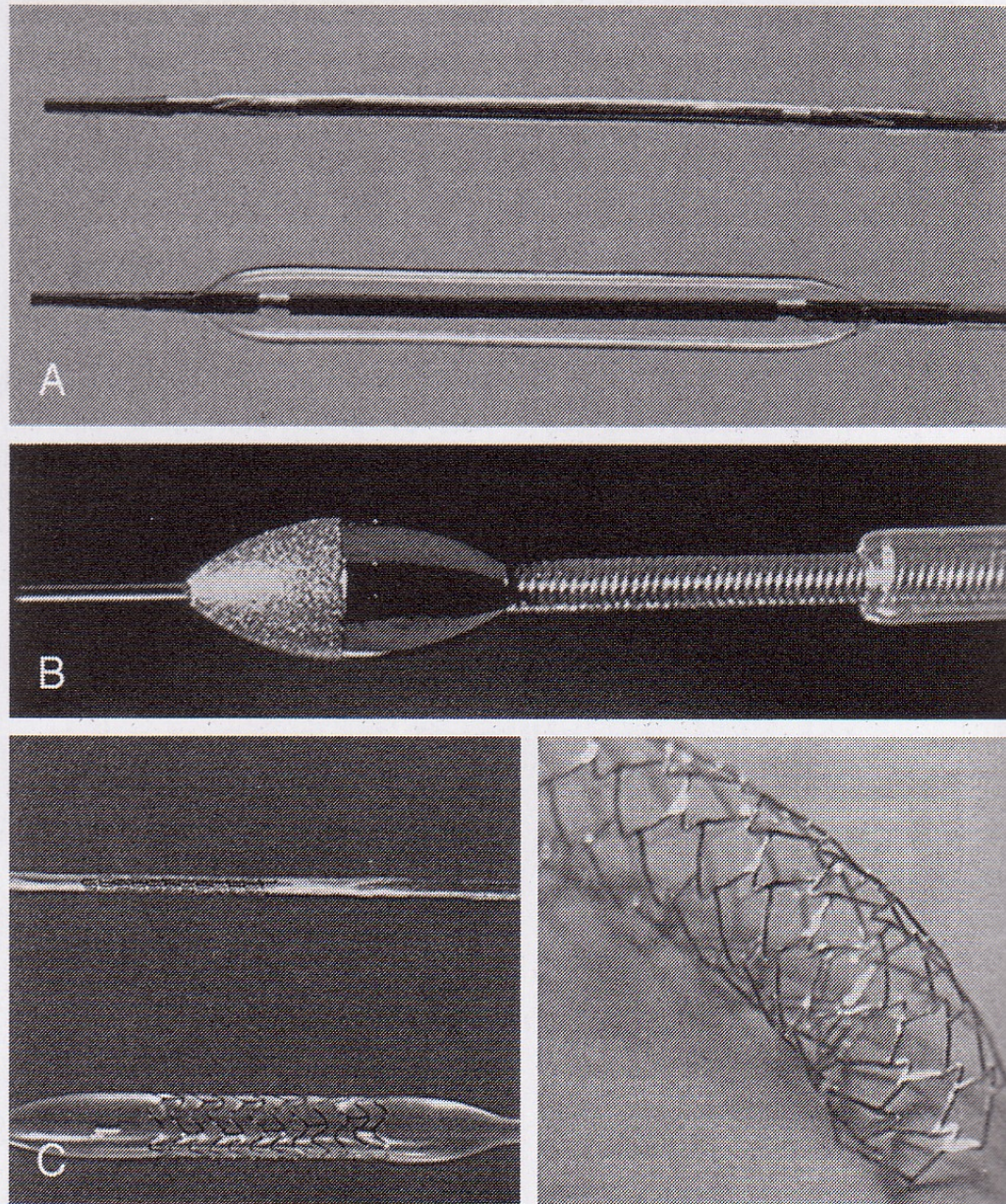


# Renal Vasculature



SOURCE: McMinn & Hutchins, 1977.

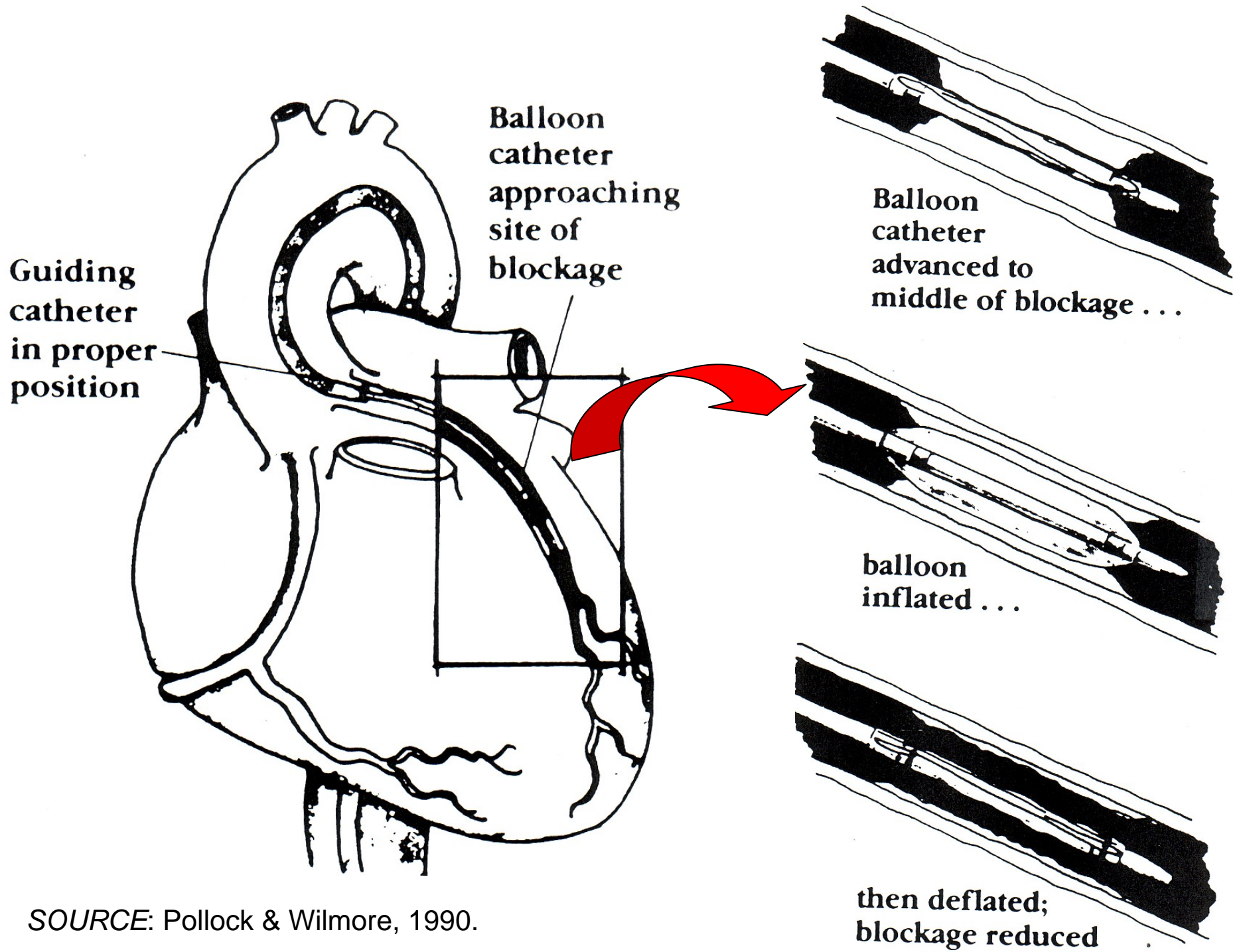




**FIGURE 37-1** Devices for percutaneous transluminal coronary interventions. **A**, Coronary balloon. **B**, Rotational atherectomy burr (Rotablator). **C**, Coronary stent.

SOURCE: Willerson & Cohn, 2000.





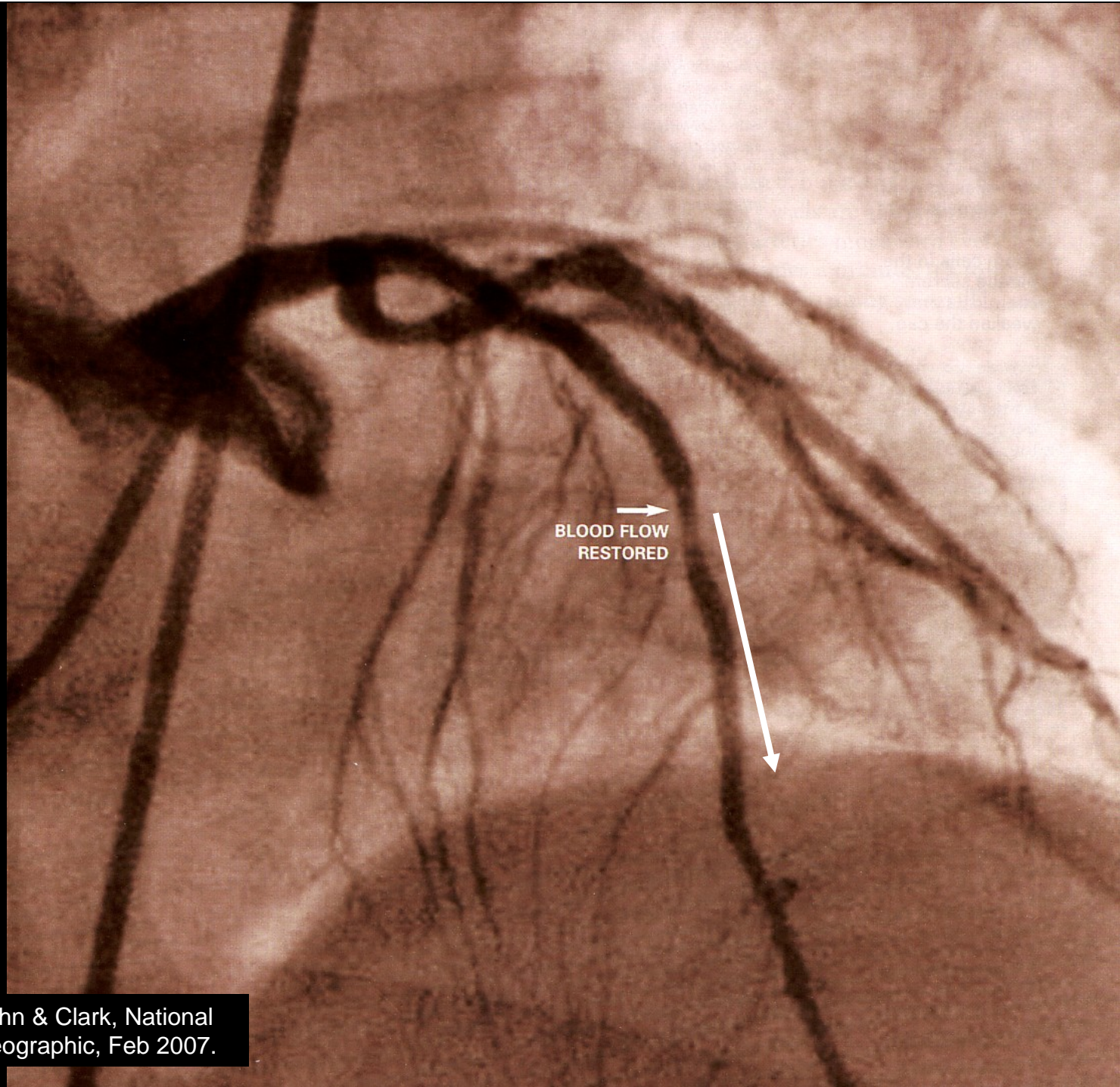




BLOCKED  
ARTERY

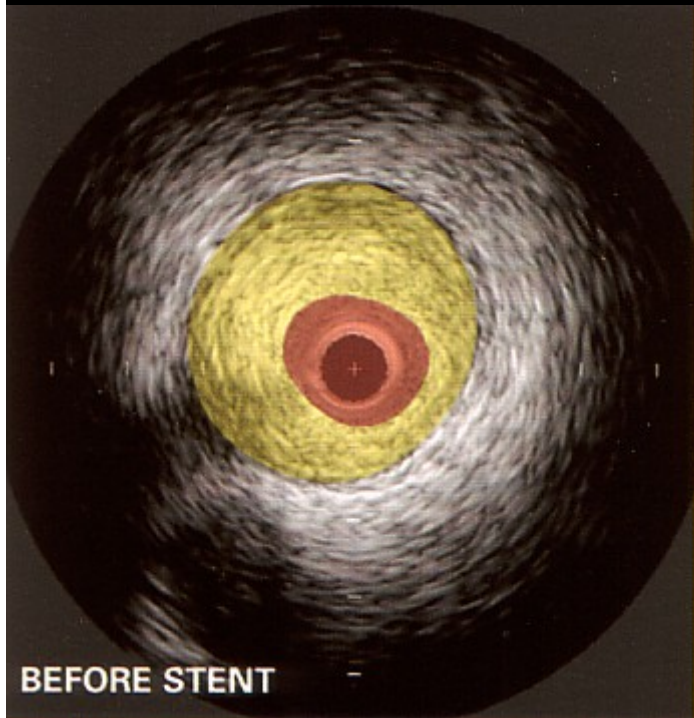
SOURCE: Kahn & Clark, National  
Geographic, Feb 2007.



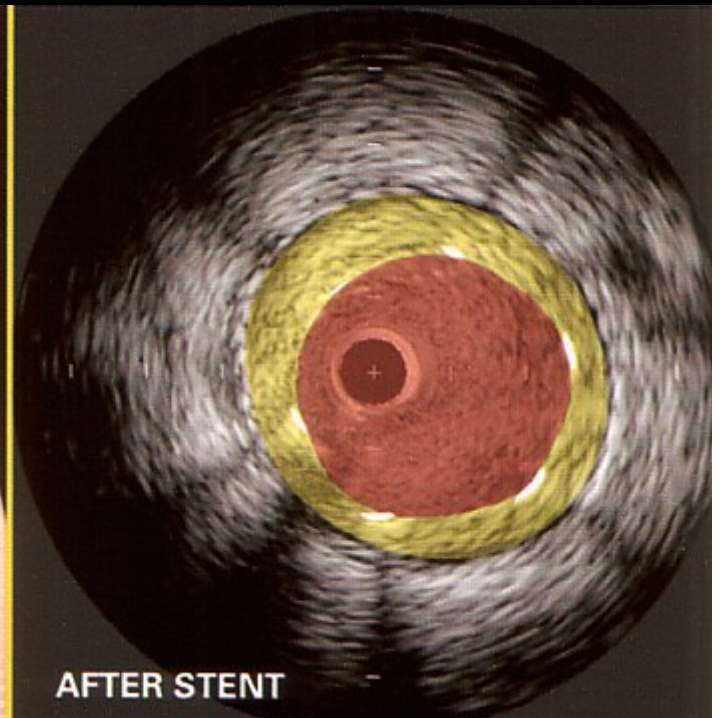


→  
BLOOD FLOW  
RESTORED

SOURCE: Kahn & Clark, National Geographic, Feb 2007.



BEFORE STENT

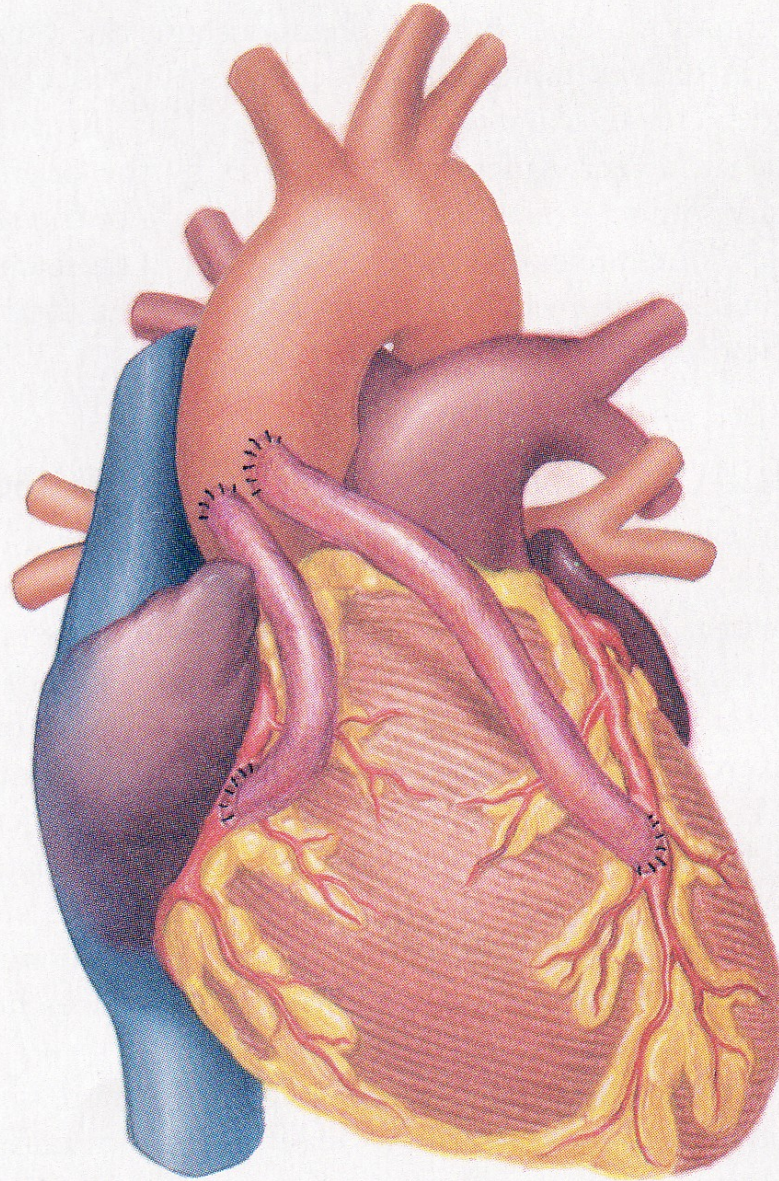


AFTER STENT

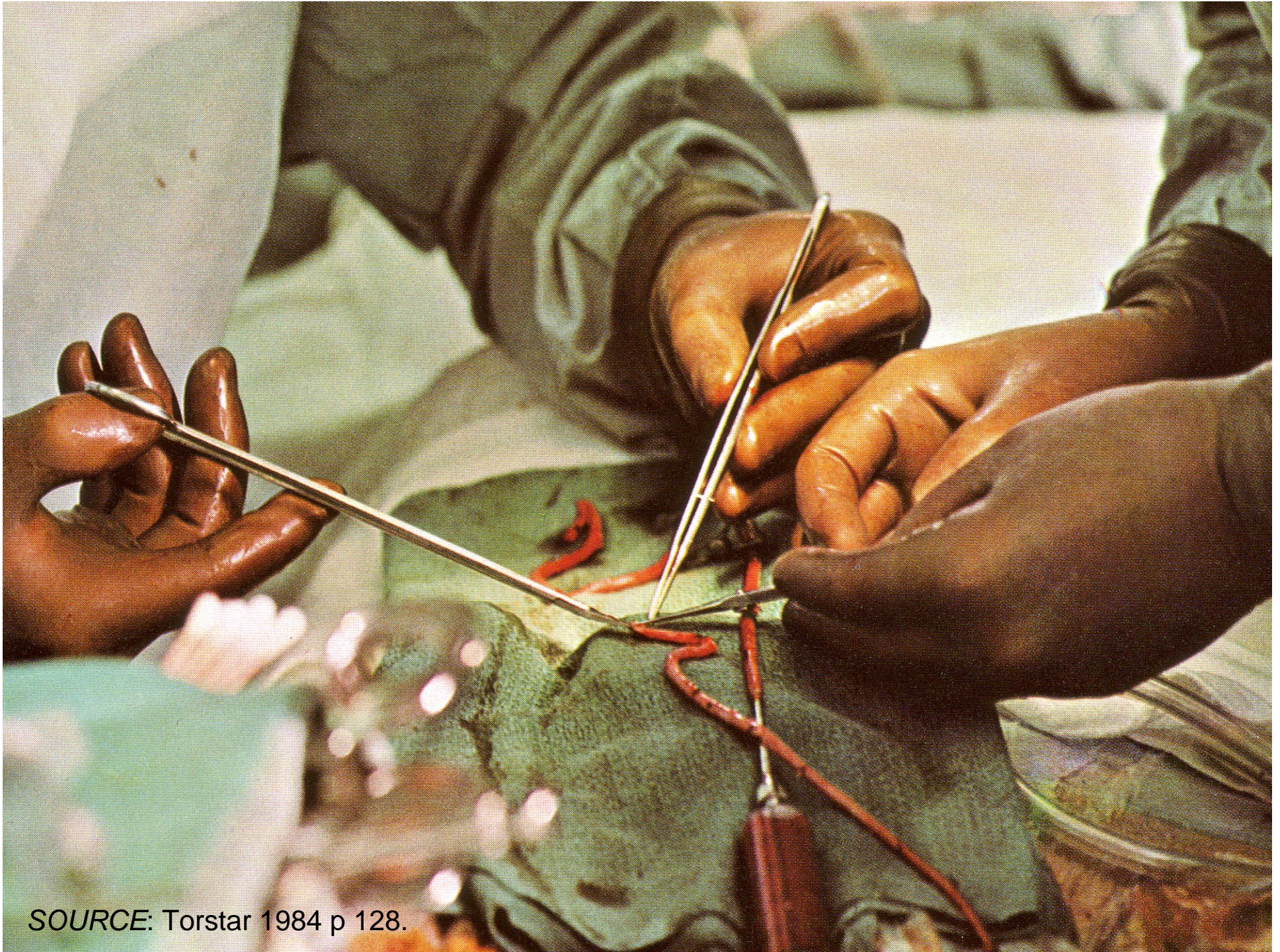
SOURCE: Kahn & Clark, National Geographic, Feb 2007.



***CABG = Coronary Artery Bypass Graft***





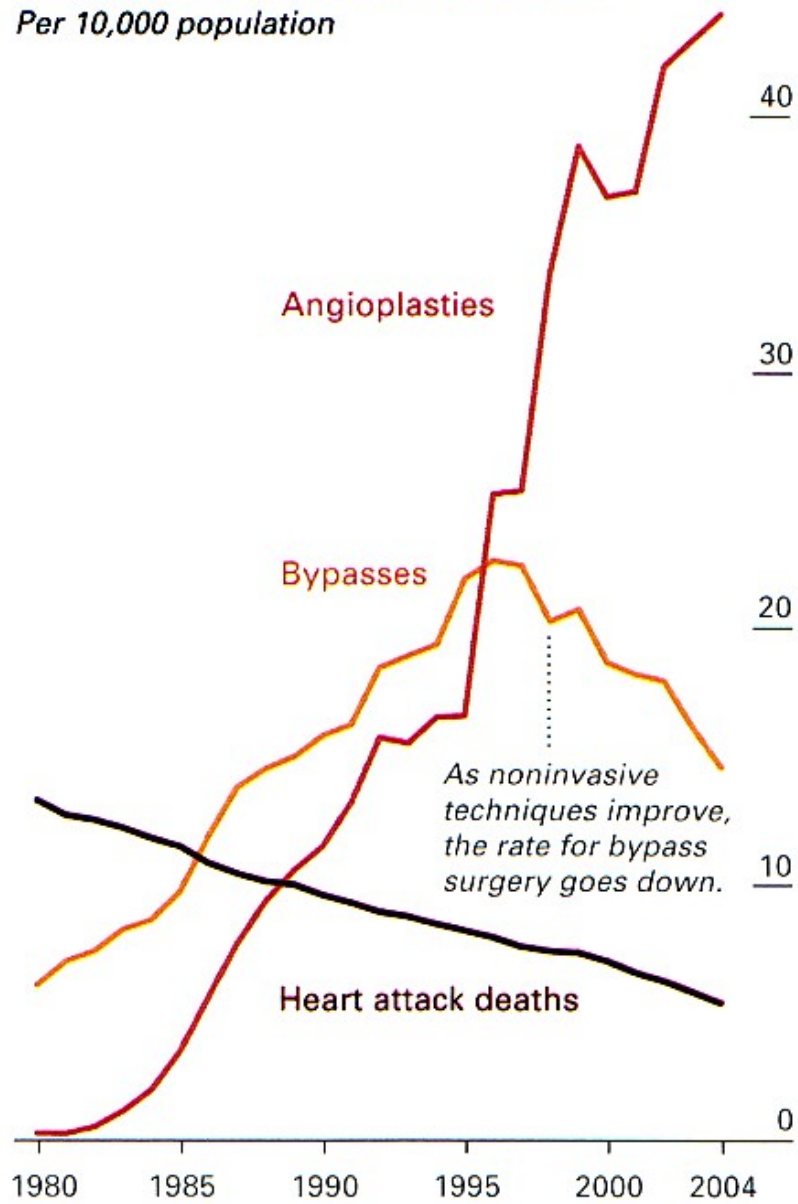


SOURCE: Torstar 1984 p 128.



## Procedures and heart attack deaths

Per 10,000 population



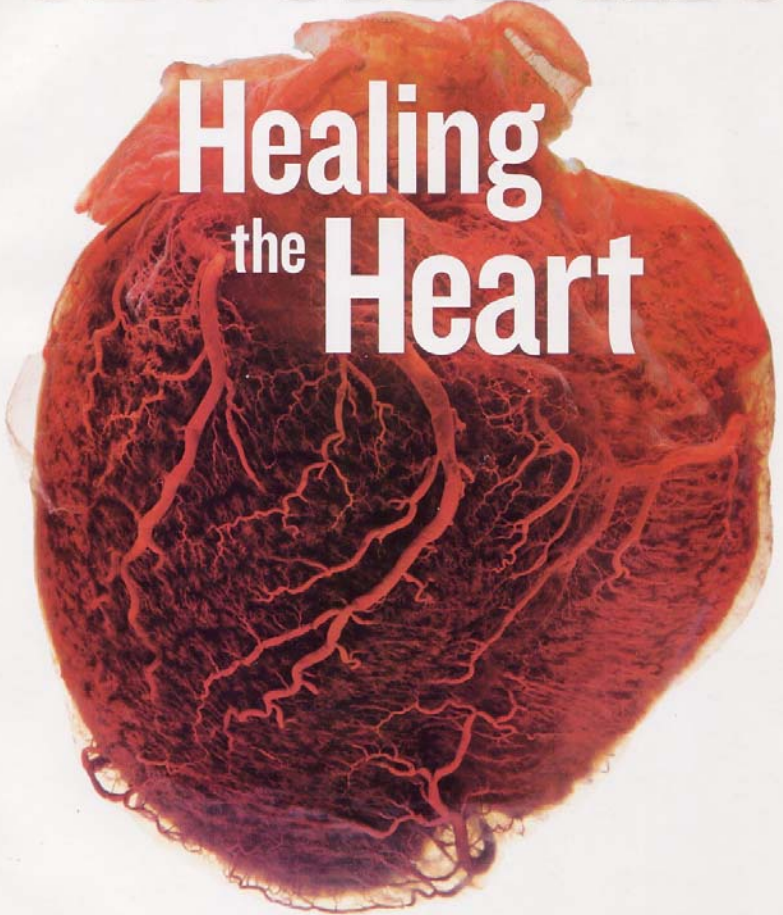
SOURCES: THOMAS THOM, NATIONAL HEART, LUNG, AND BLOOD INSTITUTE; GAUTAM GOWRISANKARAN, WASHINGTON UNIVERSITY IN ST. LOUIS; SALIM YUSUF, McMASTER UNIVERSITY, THE INTERHEART STUDY



NATIONALGEOGRAPHIC.COM/MAGAZINE

FEBRUARY 2007

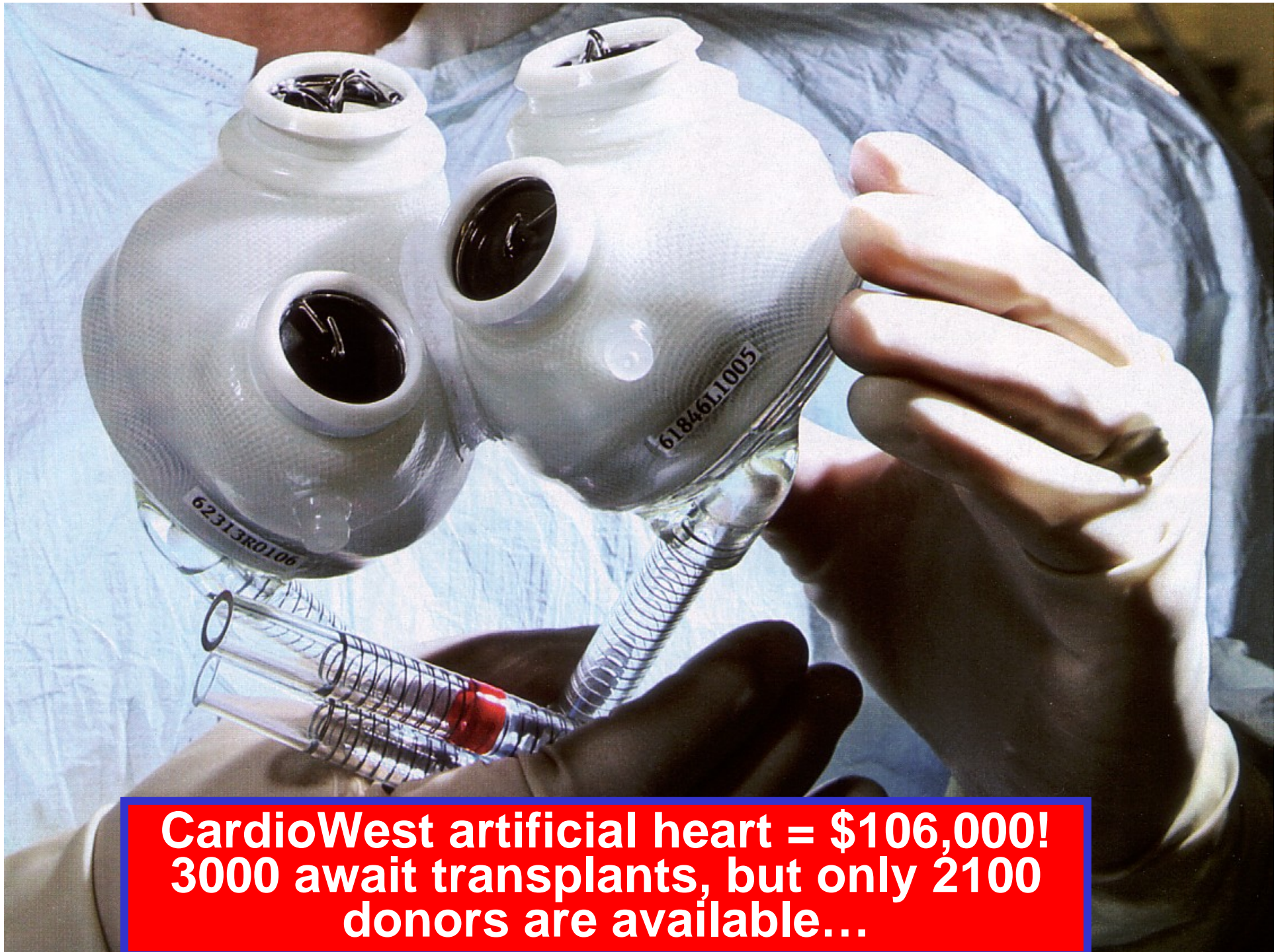
# NATIONAL GEOGRAPHIC



## Healing the Heart

Beauty on the Border 66    Curse of Nigerian Oil 88  
Hawaii's Unearthly Worms 118    Forests of the Tide 132





**CardioWest artificial heart = \$106,000!  
3000 await transplants, but only 2100  
donors are available...**

<http://ngm.nationalgeographic.com/2007/02/hearts/hearts-text.html>



Photograph by Robert Clark