Another Super Lecturer, Dr. Richard Padgett, OHVI Medical Director!

BI 358 Lecture 8

I. Announcements **Dr. Padgett next Tuesday! Quiz 3 Q?**

II. Vaccines for Atherosclerosis**…Immune & CVS link!**
https://www.hindawi.com/journals/jdr/2018/1638462/#B9

III. Blood Chemistry Connections **Blood typing & Rhesus factor**

III. Lymphatic System **Alternative circulation Torstar, DC…**

IV. Cardiovascular Physiology **Torstar, G&H, Katz, LS,…**

- **A. ♥ structure & function LS, Torstar, G&H fig 9-8 +… in lab!**
- **B. Blood flow through ♥ & periphery G&H fig 9-1, LS…**
- **C. Coronary circulation & the cardiac cycle G&H, Katz +…**

V. CVDs **Definitions, US Disease Statistics: CDC 2012 + AHA**

VI. 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. 1^0 modifiable risks: cigarette smoking, hypertension, hypercholesterolemia/hyperlipidemia, lack of exercise**
- **D. Treatment triad, *PTCA*, *CABG*, prevention, practical tips!**

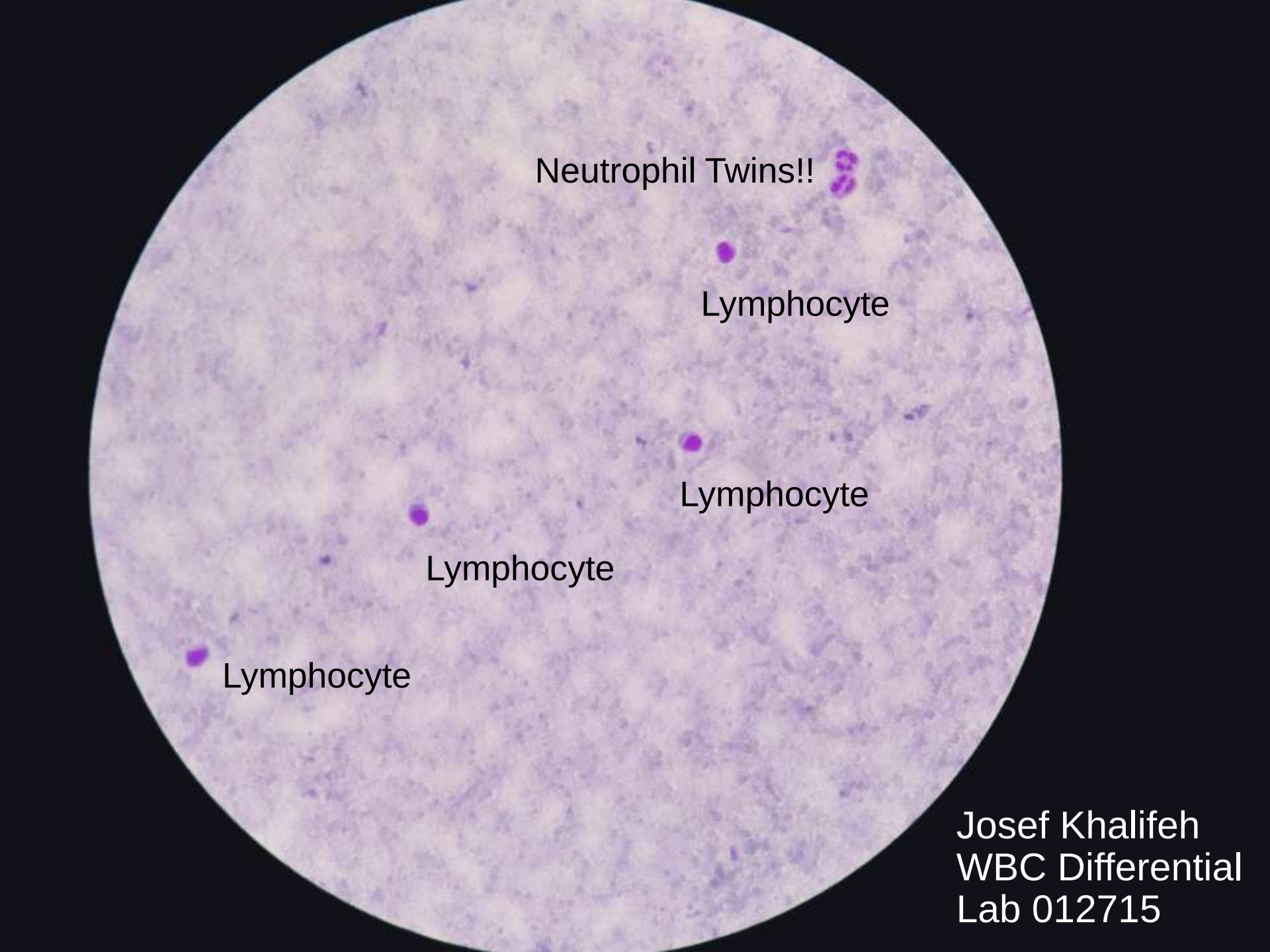
VII. Additional Resources **Development, electrical highway…**

Richard C. Padgett
Medical Director

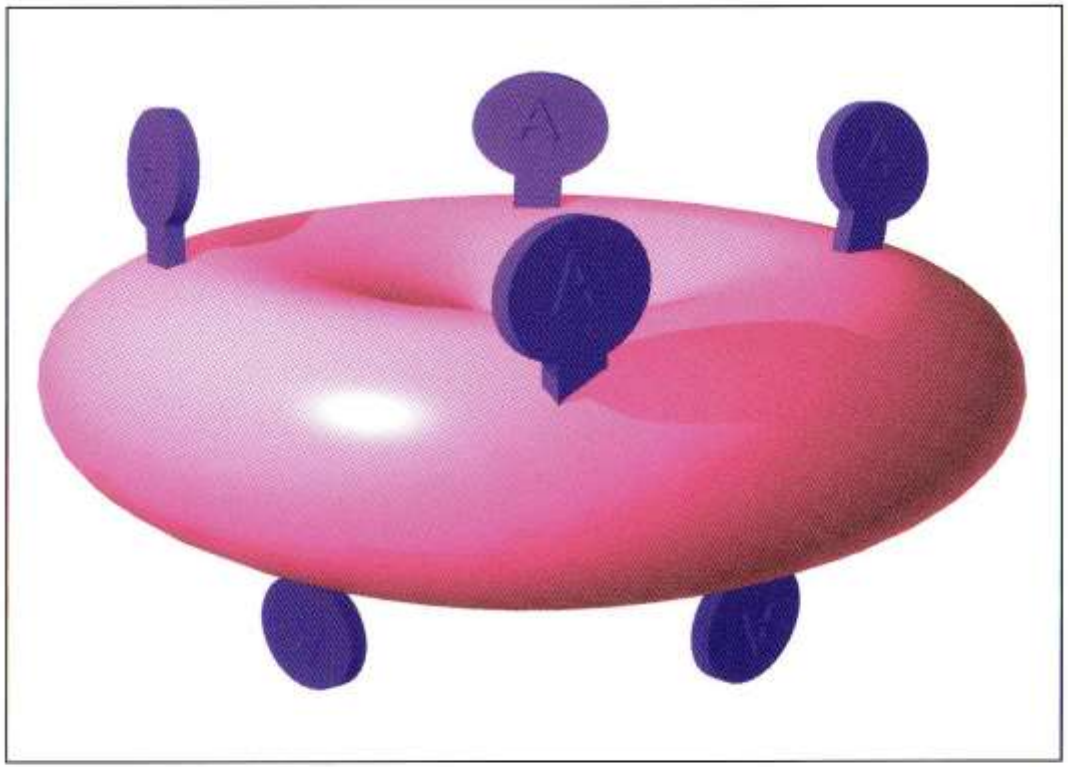
Sacred Heart Medical Center
PeaceHealth

Oregon Heart & Vascular INSTITUTE

https://www.peacehealth.org/ohvi?from=/sacred-heart-ri


Neutrophil Twins!!
Lymphocyte
Lymphocyte
Lymphocyte
Lymphocyte
Josef Khalifeh
WBC Differential
Lab 012715

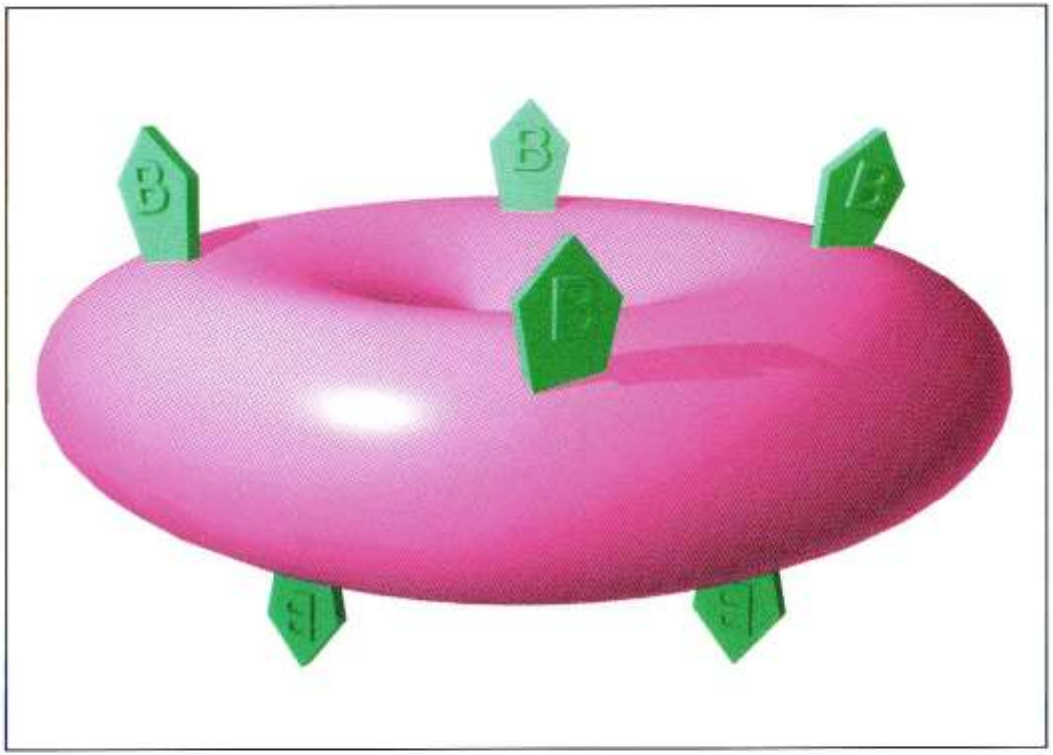
A



A Antigens

(Agglutinogens)

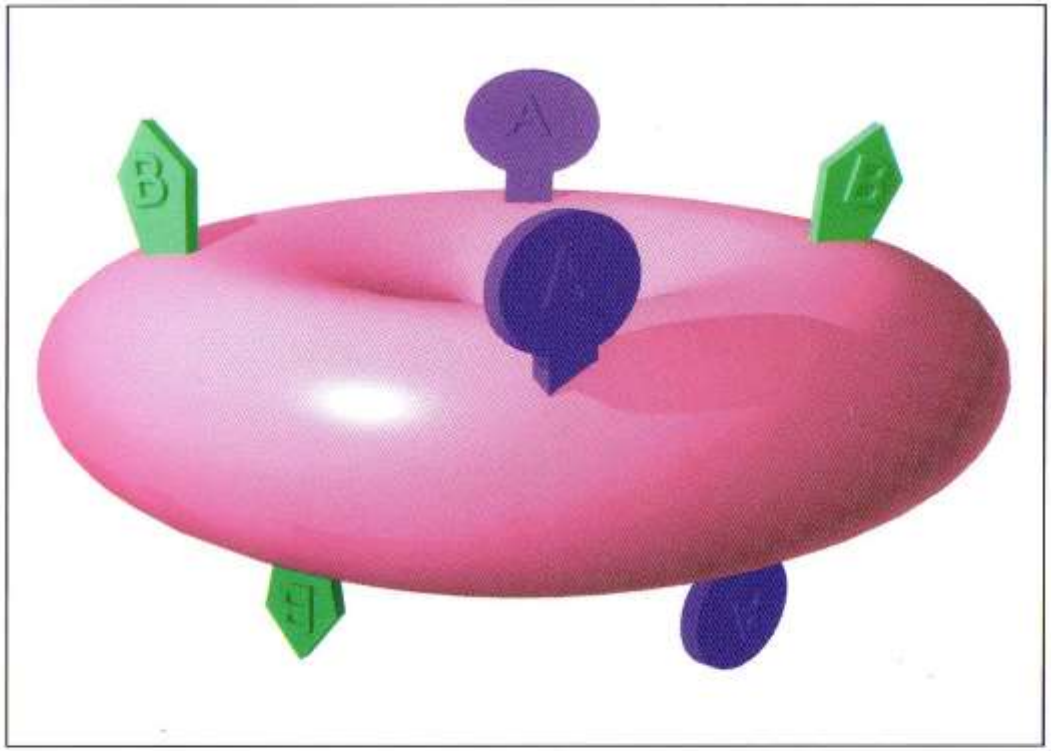
B



B Antigens

(Agglutinogens)

AB



A & B Antigens

(Agglutinogens)

O

No Antigens

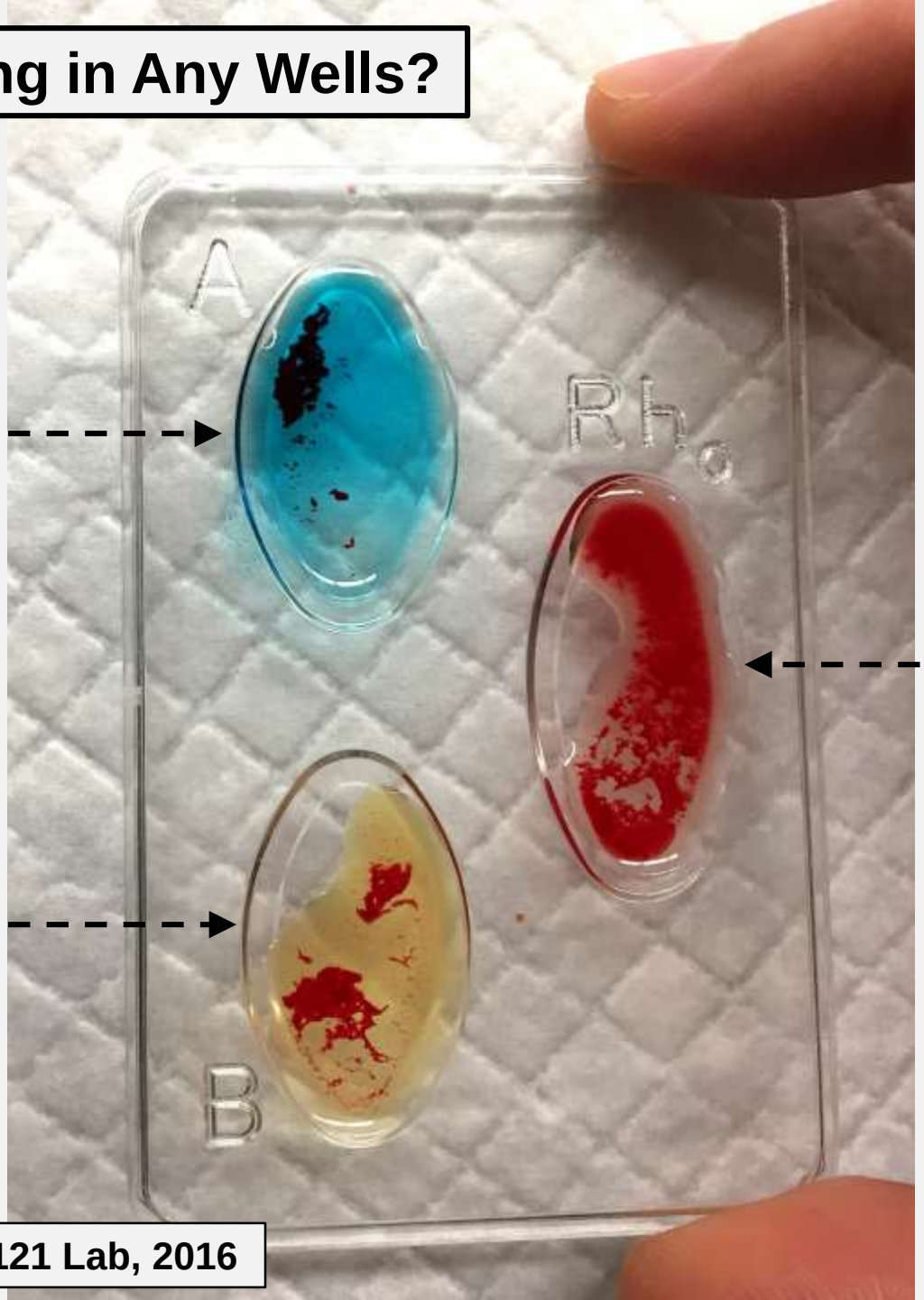
(Agglutinogens)

A Antibodies

(Agglutinins)

1^0 Q? Clumping in Any Wells?

Type AB+



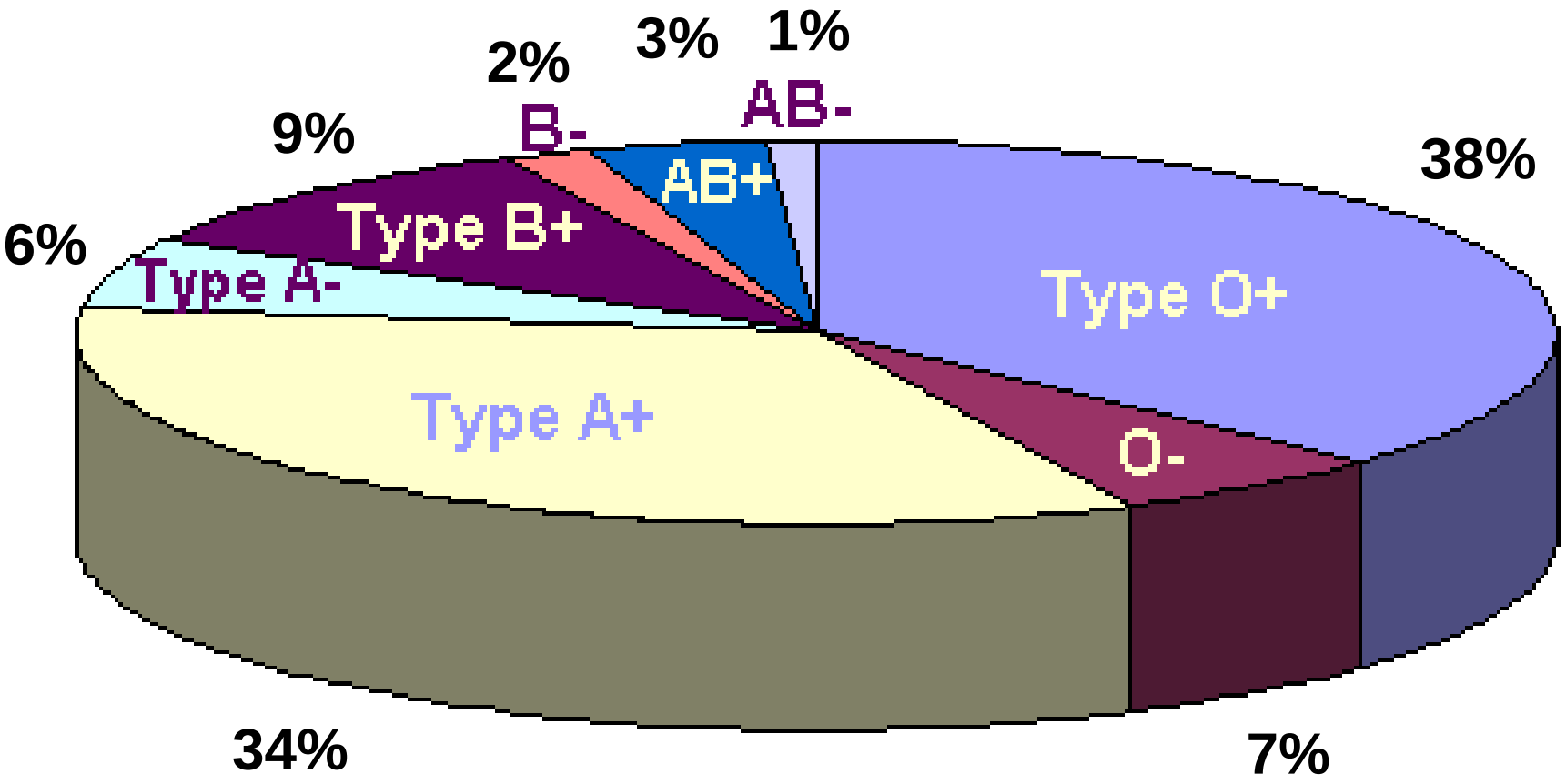
Here?

Here?

Here?

Source: S Wong, BI 121 Lab, 2016

Blood Type Distribution within the United States



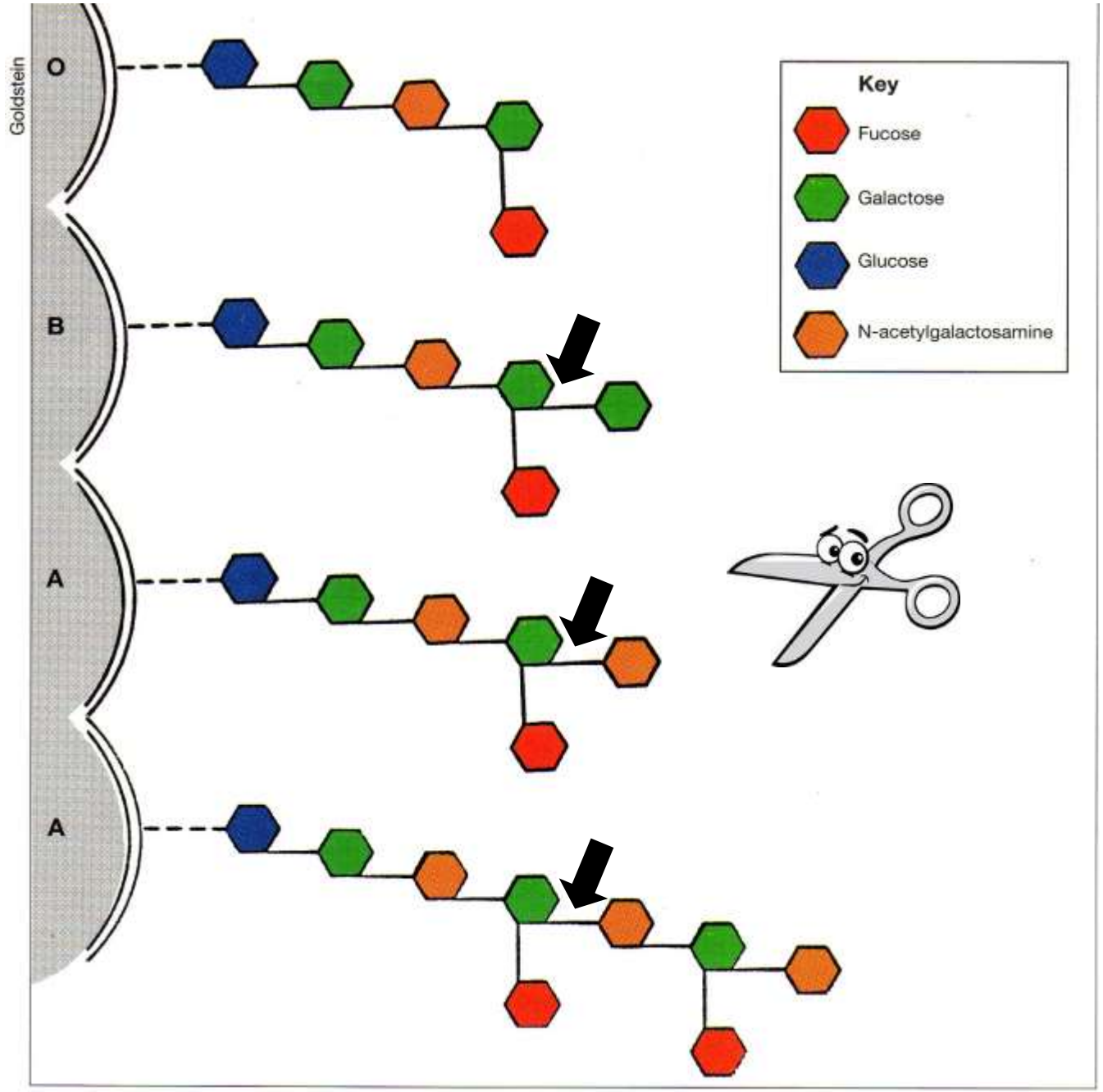
NB: **O+ & A+ make up > 2/3, + > -**

The Weekly Newsmagazine of Science

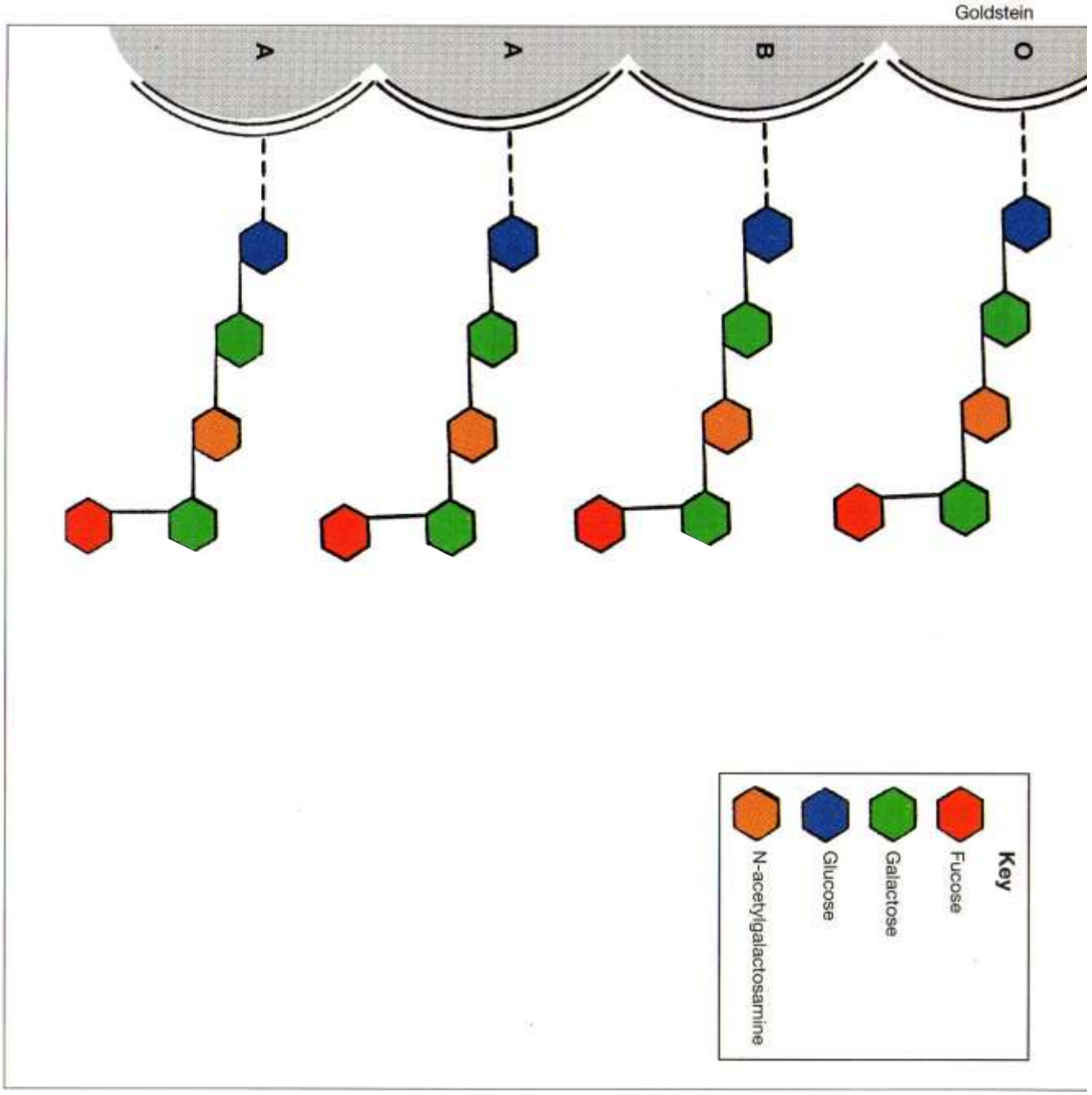
SCIENCE NEWS

January 11, 1997
Vol. 151, No. 2
Pages 17-32

Universal Blood


Goldstein
O
B
A
A
Key
Fucose
Galactose
Glucose
N-acetylgalactosamine

All like Type O!



Erythroblastosis Fetalis?

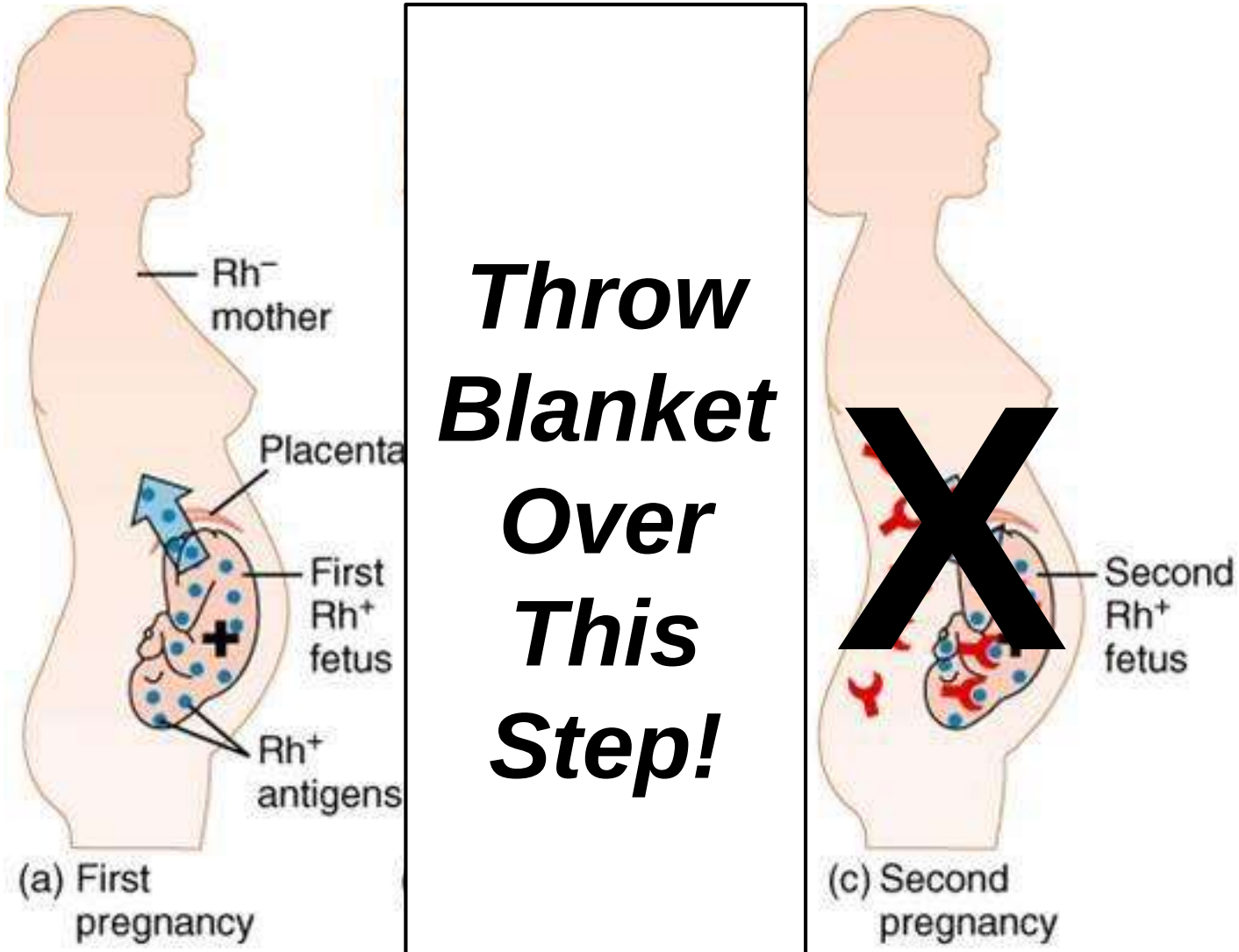
Rh- mom
Rh+ baby

https://www.stanfordchildrens.org/en/topic/default?id=hemolytic-disease-of-the-newborn-90-P02368

https://www.nlm.nih.gov/medlineplus/rhincompatibility.html

http://www.nlm.nih.gov/MEDLINEPLUS/ency/article/001298.htm#Alternative%20Names

Erythroblastosis Fetalis or Hemolytic Disease of the Unborn/Newborn



Inject Mom with RhoGam ≤ 48-72 hr > each Rh+ Pregnancy

The Blanket is RhoGam → Masks the Mom's Immune System!

Wear Red next Friday Feb 7th!)
Help raise awareness about
Women & ♥ disease

http://www.goredforwomen.org/

https://www.goredforwomen.org/en/about-heart-disease-in-women/facts

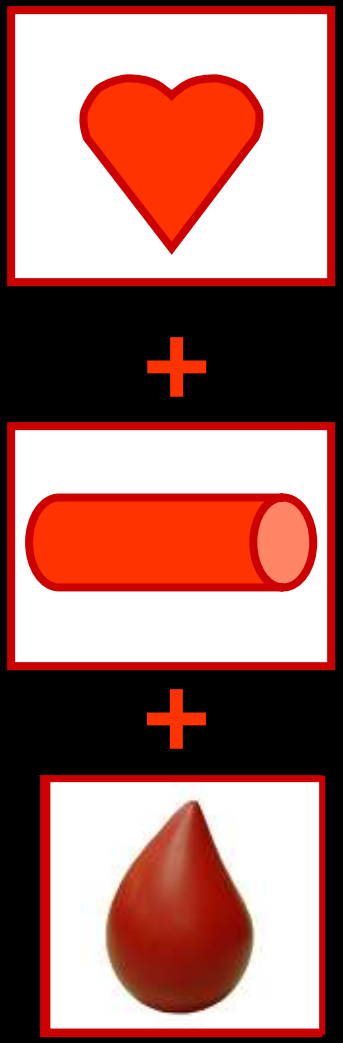
Life's Simple 7 to Improve ♥ Health

- **Manage blood pressure**
- **Control cholesterol**
- **Reduce blood sugar**
- **Get active**
- **Eat a ♥ healthy diet**
- **Lose weight**
- **Stop smoking!**

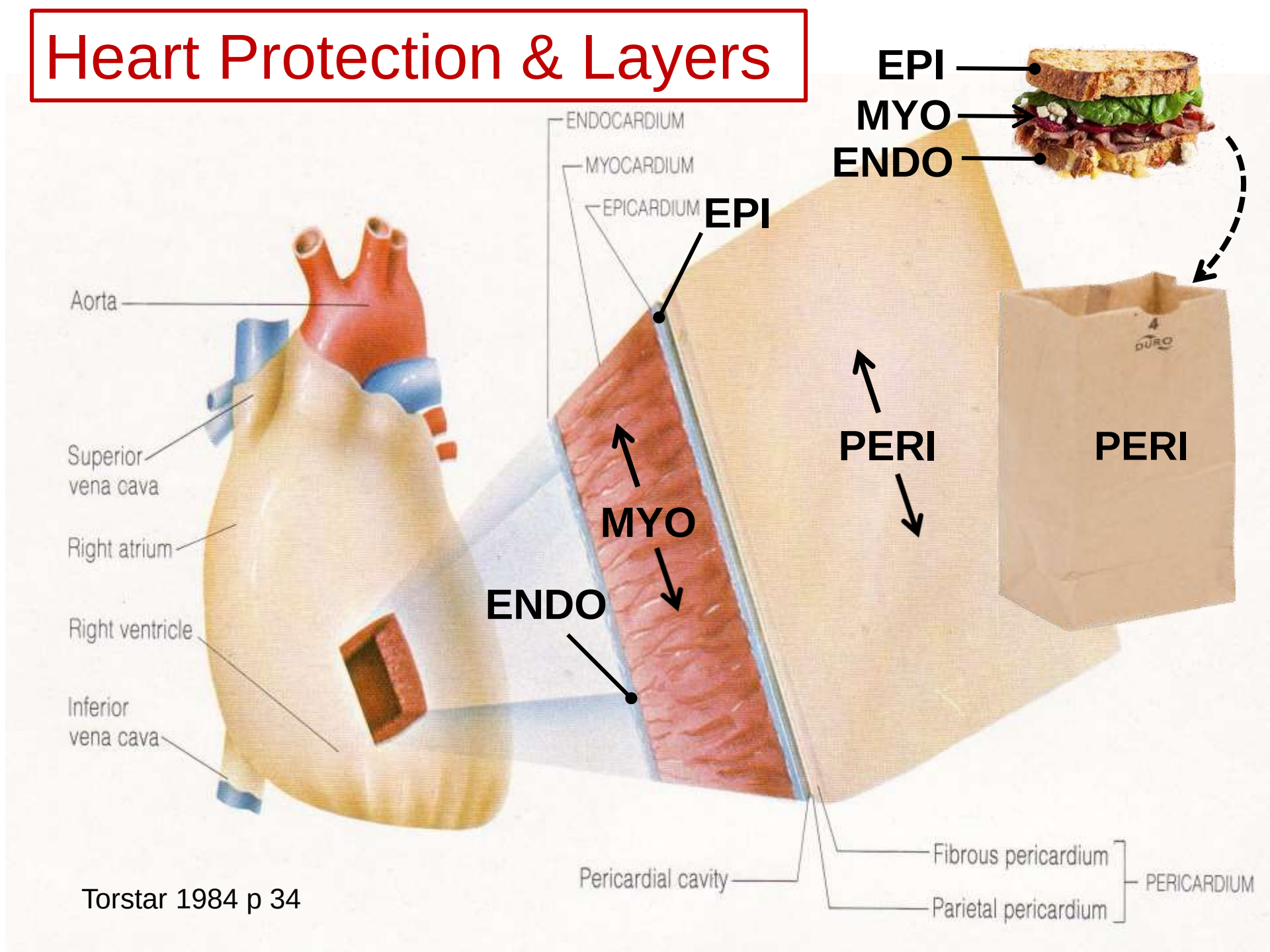
https://www.heart.org/en/healthy-living/healthy-lifestyle/my-life-check--lifes-simple-7

https://www.goredforwomen.org/en/about-heart-disease-in-women/signs-and-symptoms-in-women/just-a-little-heart-attack

Cardiovascular (CV) = Heart + Vessels + Blood!



Heart Protection & Layers



Torstar 1984 p 34

What the heck's a *bruit?*
(brwe, brōōt) [Fr.] sound ≥ 25 subclassifications!

Aneurysmal b. **a blowing sound over an aneurysm.**

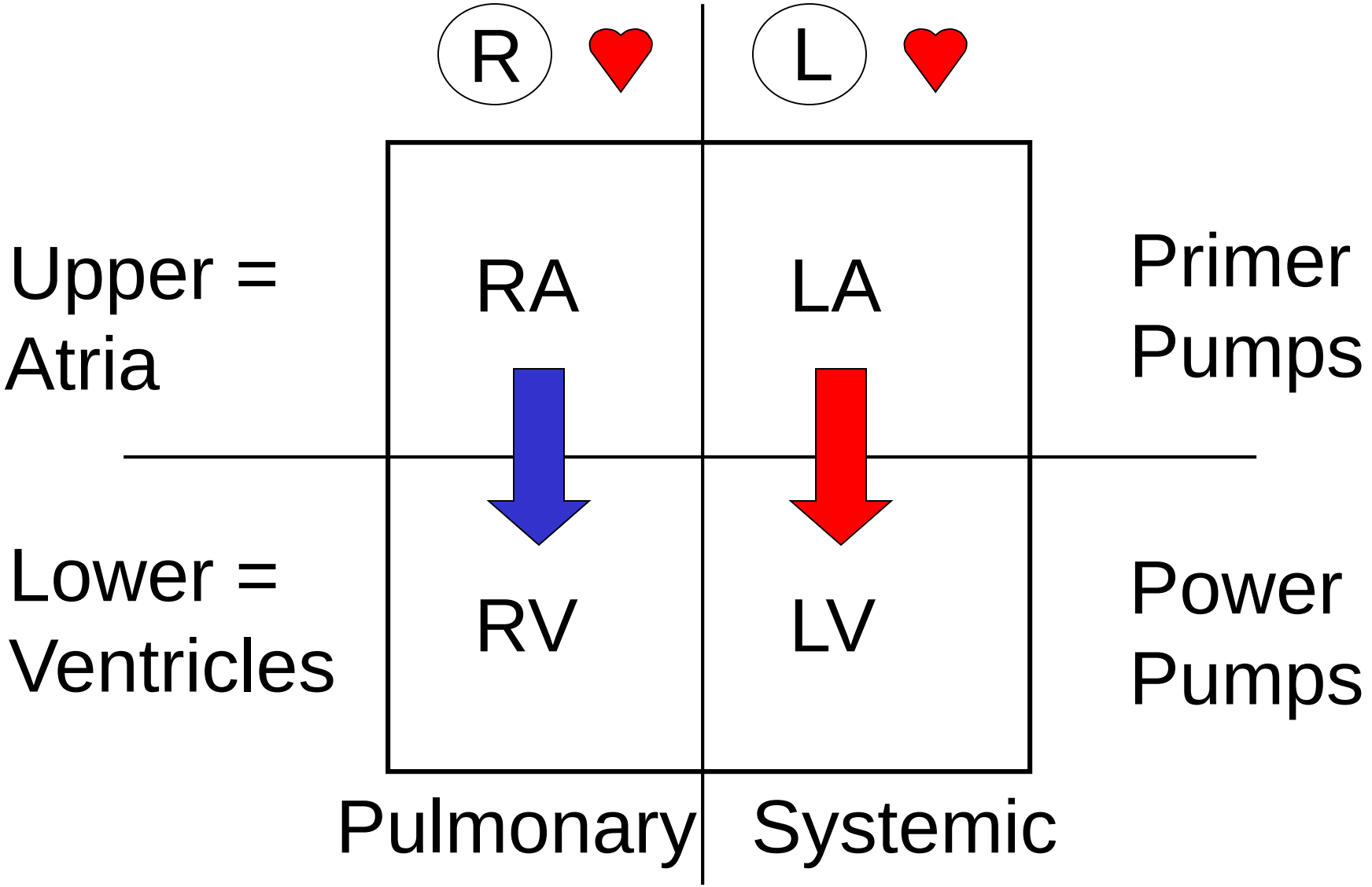
b. de canon **[Fr. sound of cannon] abnormally loud 1st heart sound heard in complete heart block.**

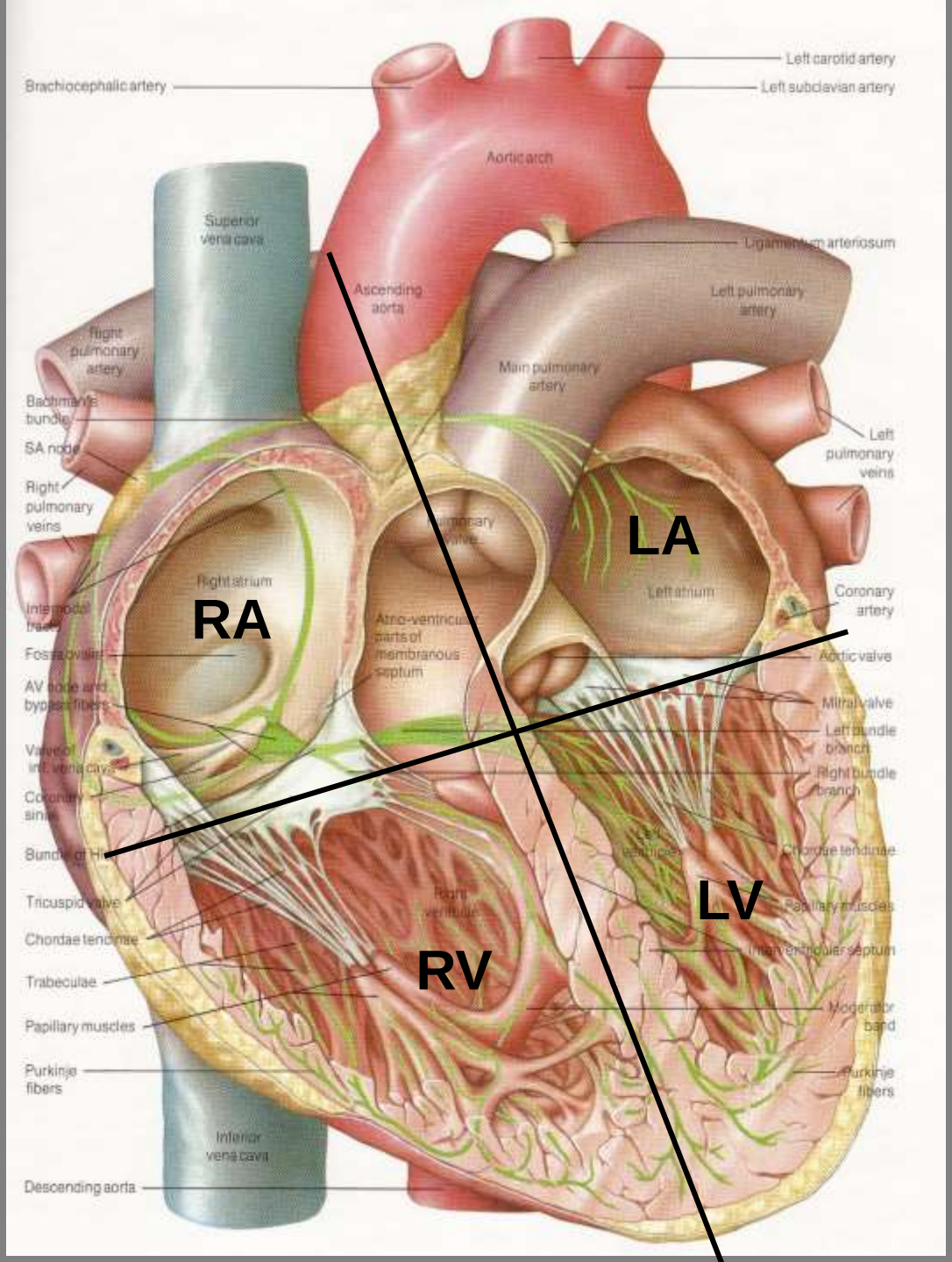
b. de craquement **[Fr. sound of crackling] a crackling pericardial or pleural bruit.**

False b. **artifact caused by pressure of the stethoscope or derived from circulation of the ear.**

b. de lime **[Fr. sound of a file] cardiac sound resembling filing.**

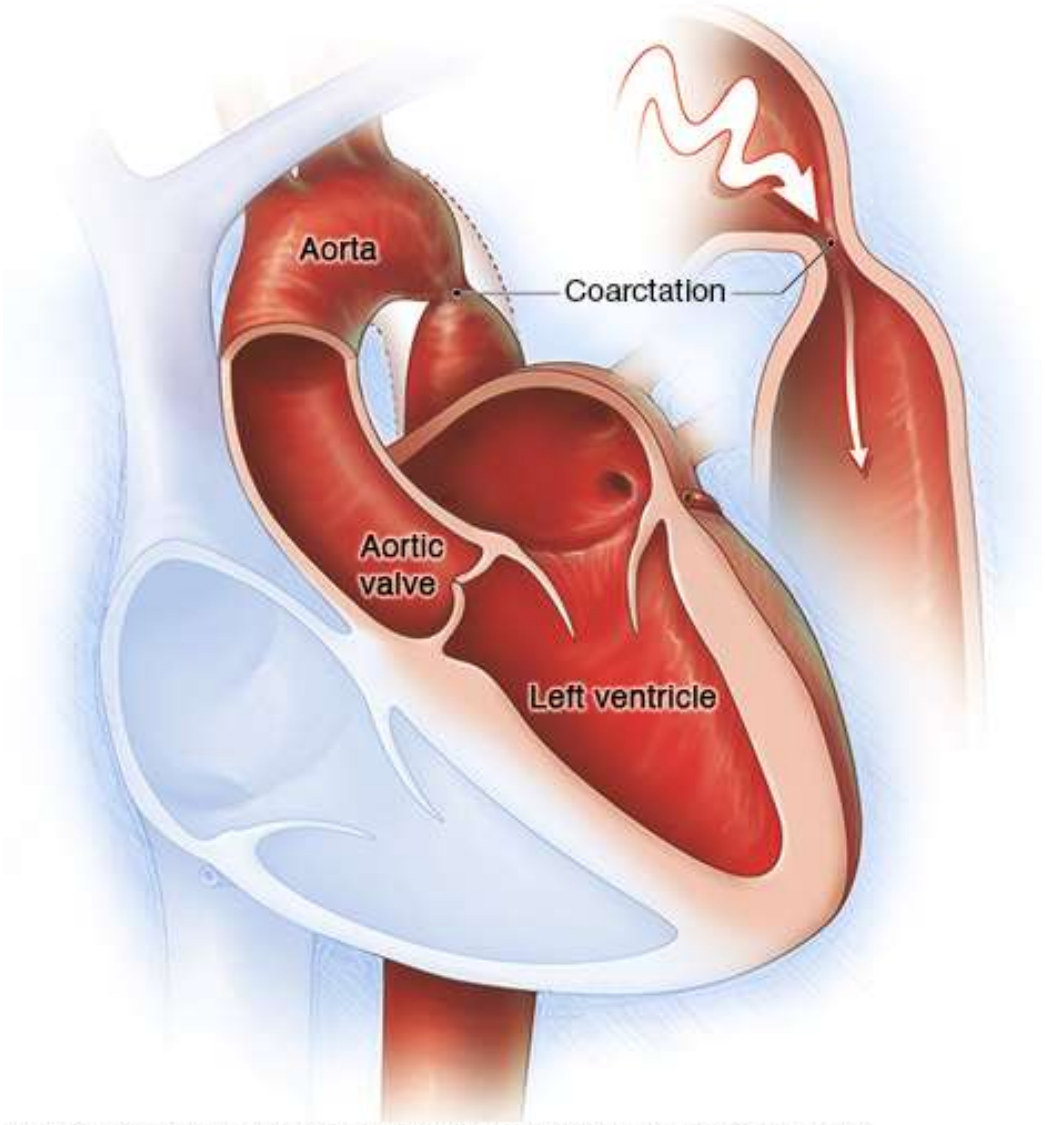
Human ♥ = 4-chambered box?
2 separate pumps?





Torstar 1984 p 53

Coarctation, Crimping or Narrowing of the Aorta



https://www.mayoclinic.org/diseases-conditions/coarctation-of-the-aorta/symptoms-causes/syc-20352529

Human ♥ = 4 unique valves?
2 valve sets?

Semilunar = *Half-moon shaped*

More rigid

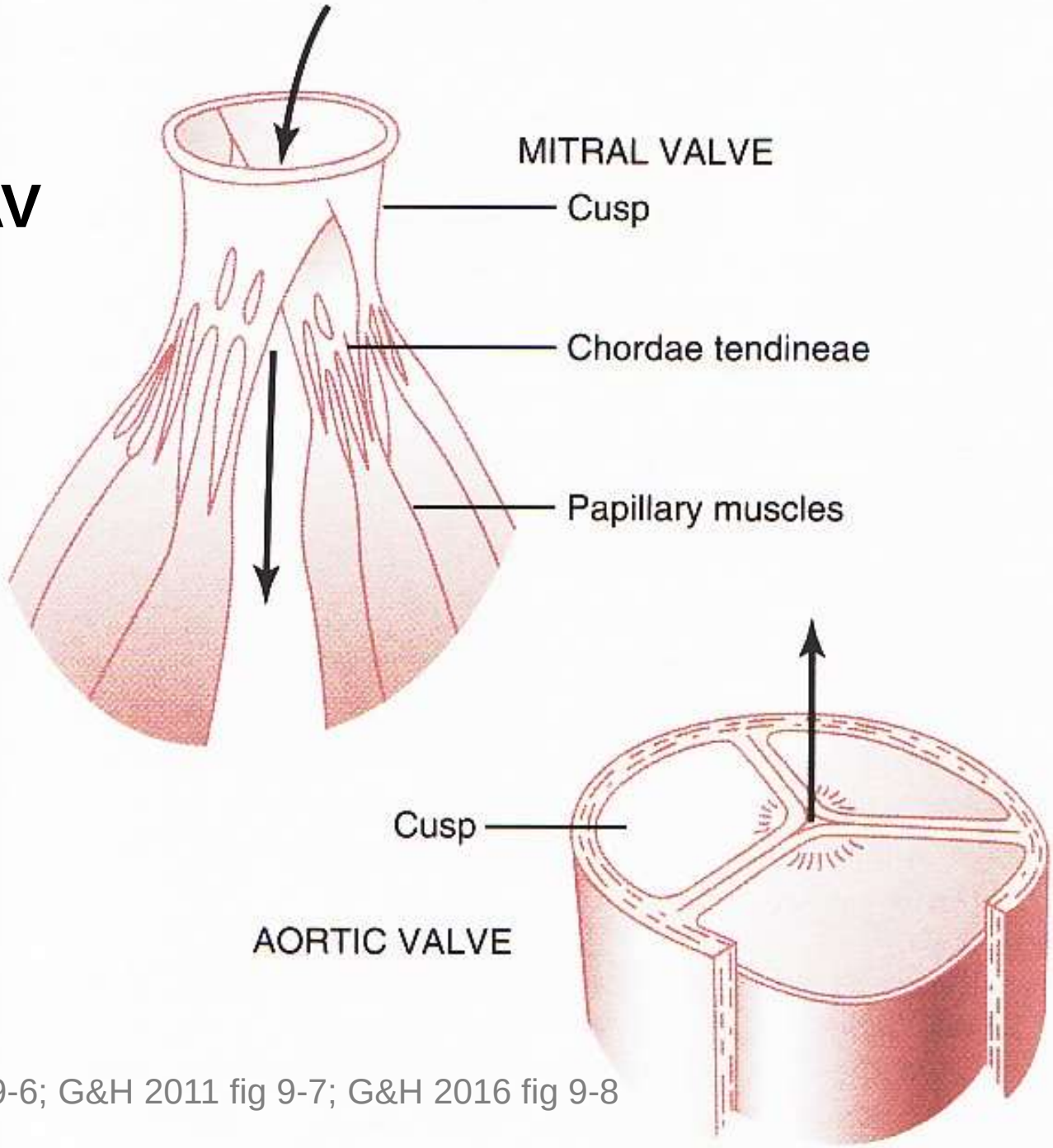
1. Pulmonic/Pulmonary
2. Aortic

AV = *Atrioventricular*

More flimsy

3. (R) AV = Tricuspid
4. (L) AV = Mitral/Bicuspid

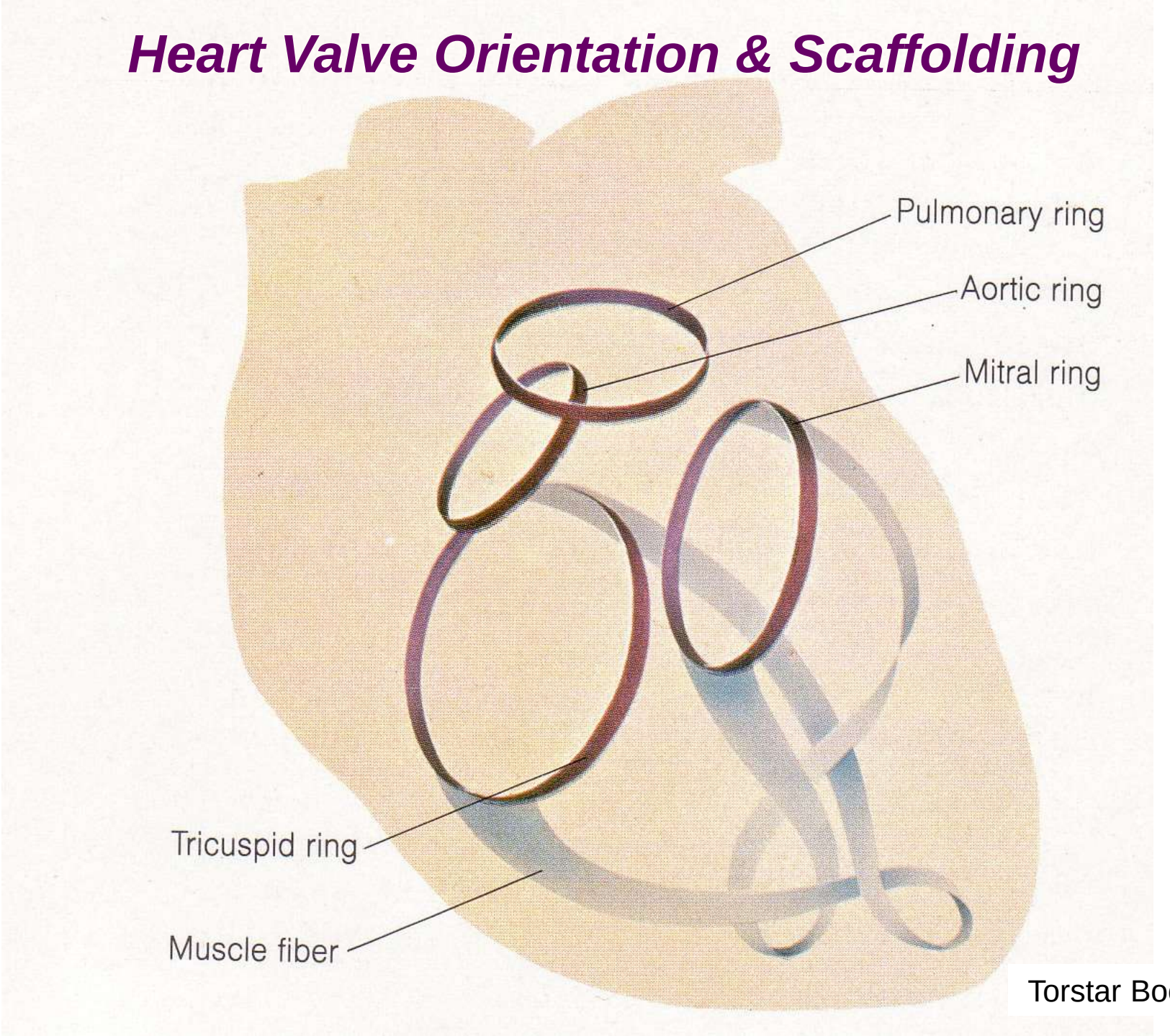
Ⓛ AV



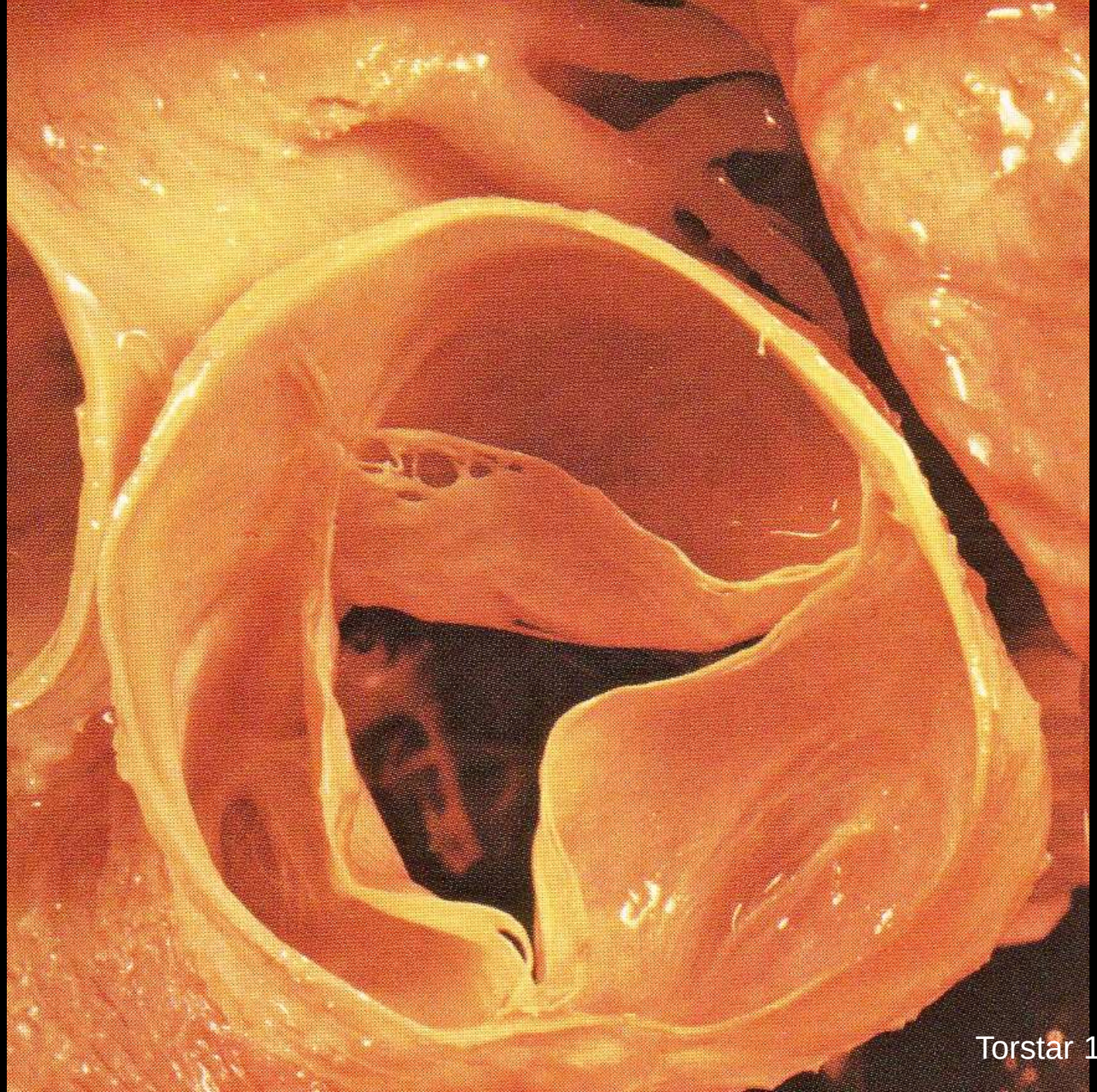
SL

G&H 2006 fig 9-6; G&H 2011 fig 9-7; G&H 2016 fig 9-8

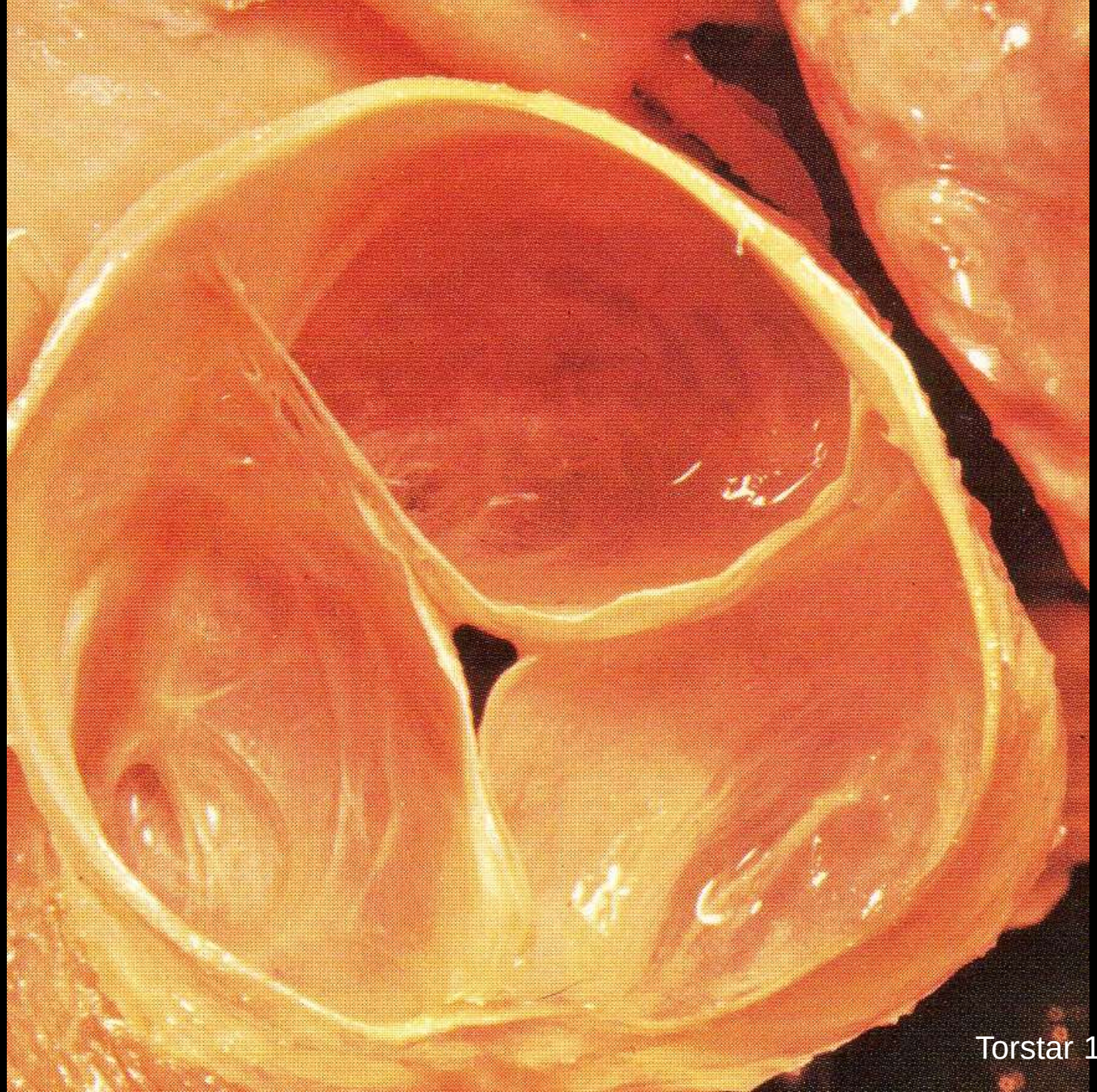
Heart Valve Orientation & Scaffolding



Torstar Books 1984



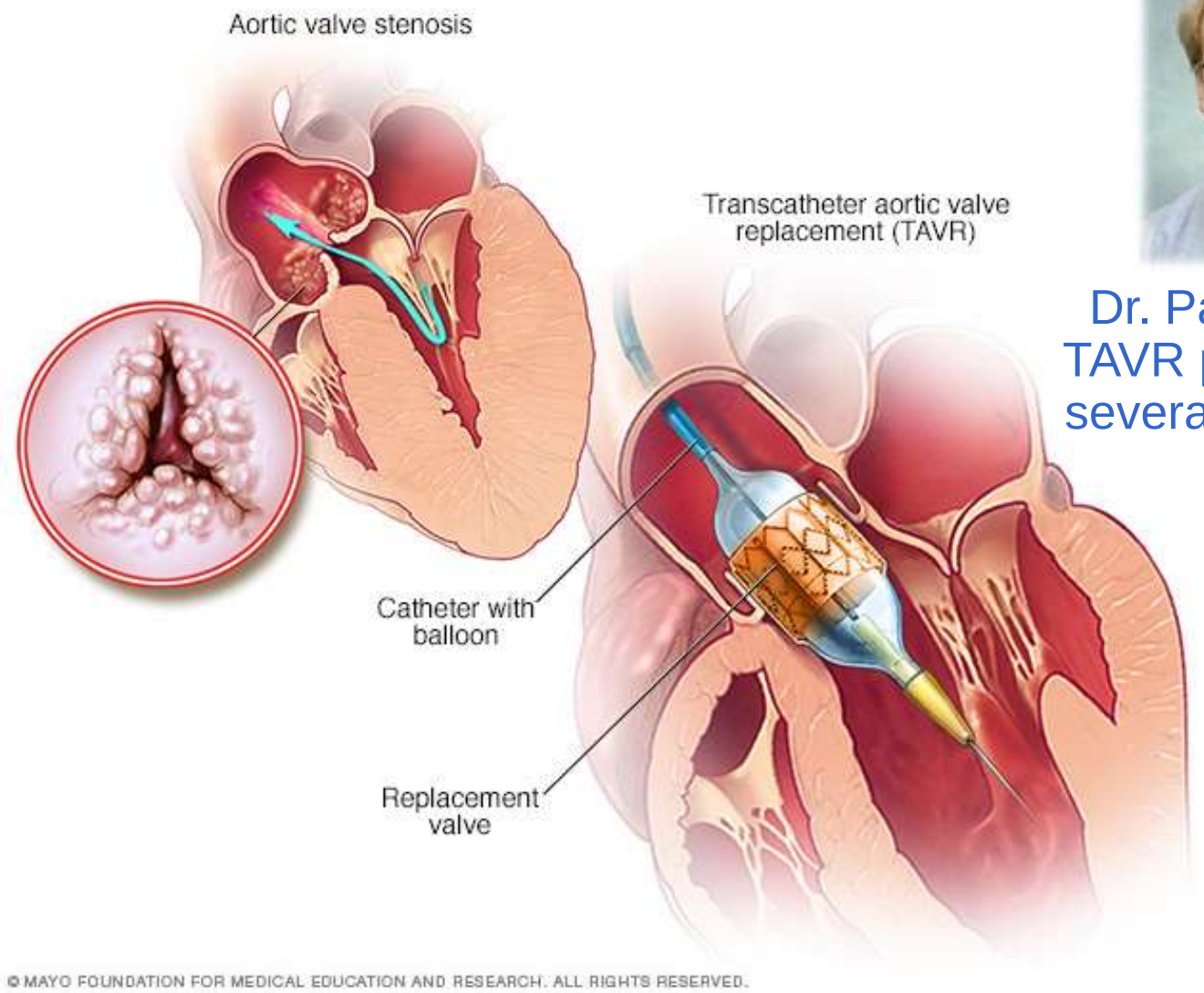
Torstar 1984 p 40



Torstar 1984 p 40

TAVR Transcatheter Aortic Valve Replacement

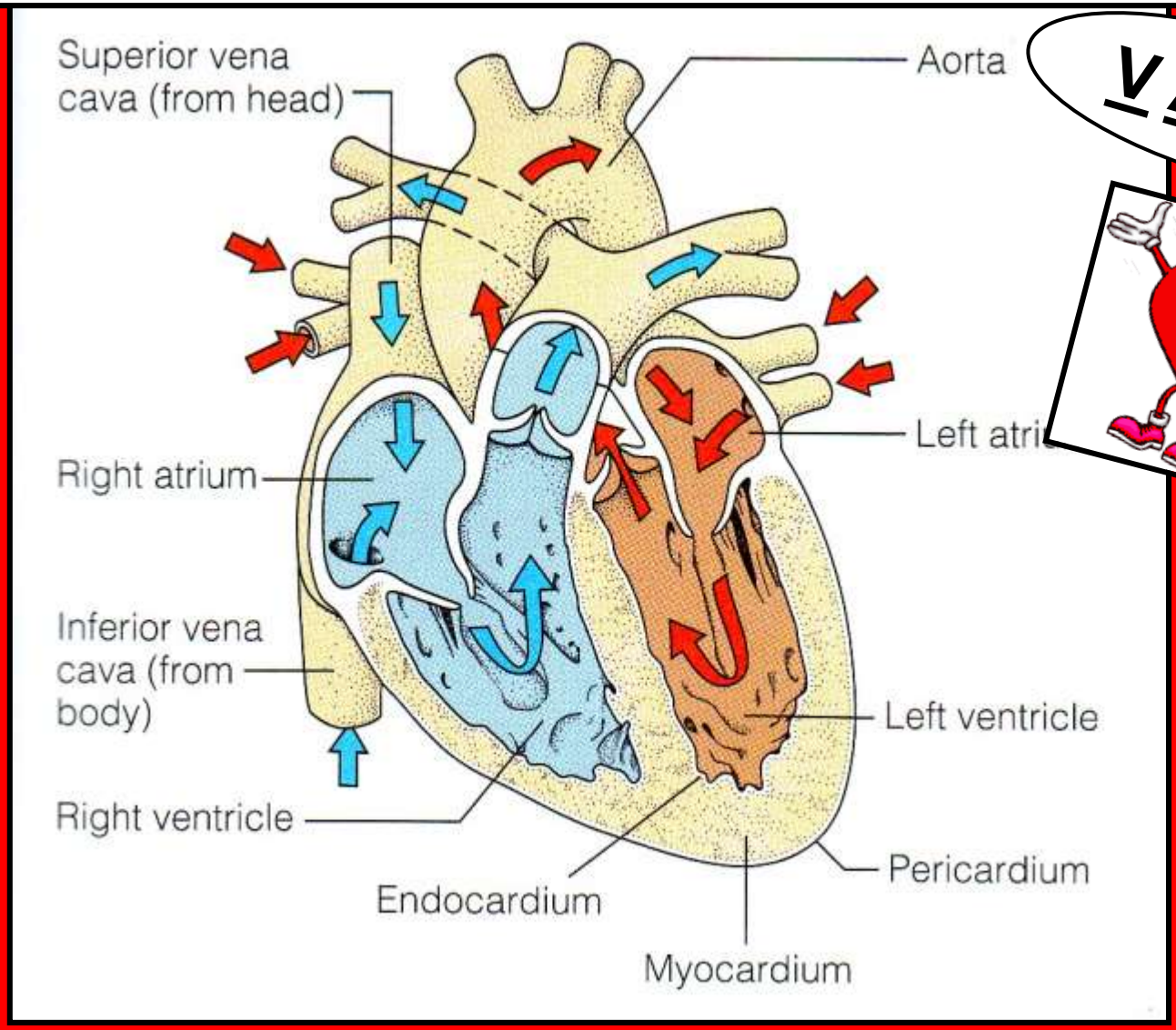
Dr. Padgett is a TAVR pro & doing several right now!

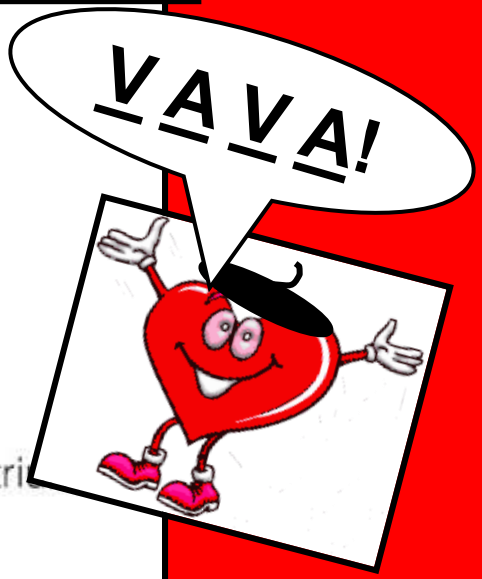


https://www.mayoclinic.org/tests-procedures/transcatheter-aortic-valve-replacement/about/pac-20384698

Torstar 1984 p 41

Veins → Atria → Ventricles → Arteries



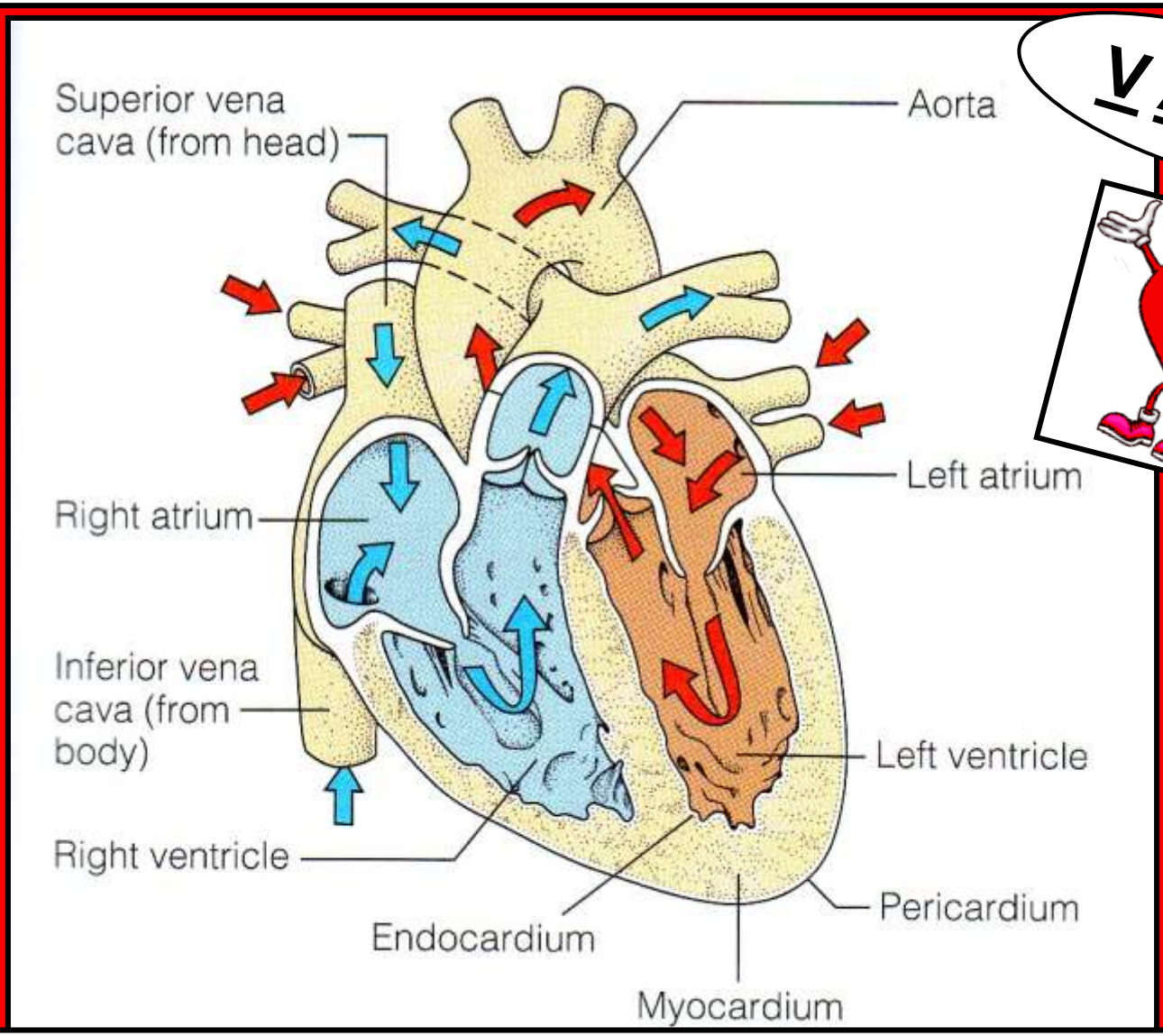


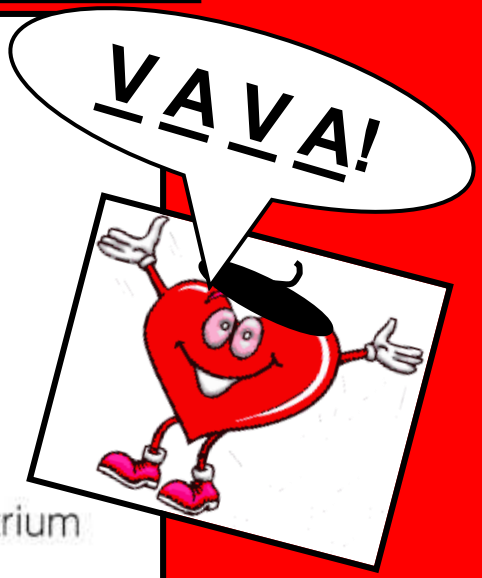
cf: G&H fig 9-1 2011 & 2016 ed

LS2016

https://www.mayoclinic.org/diseases-conditions/heart-disease/multimedia/circulatory-system/vid-20084745

Veins → Atria → Ventricles → Arteries

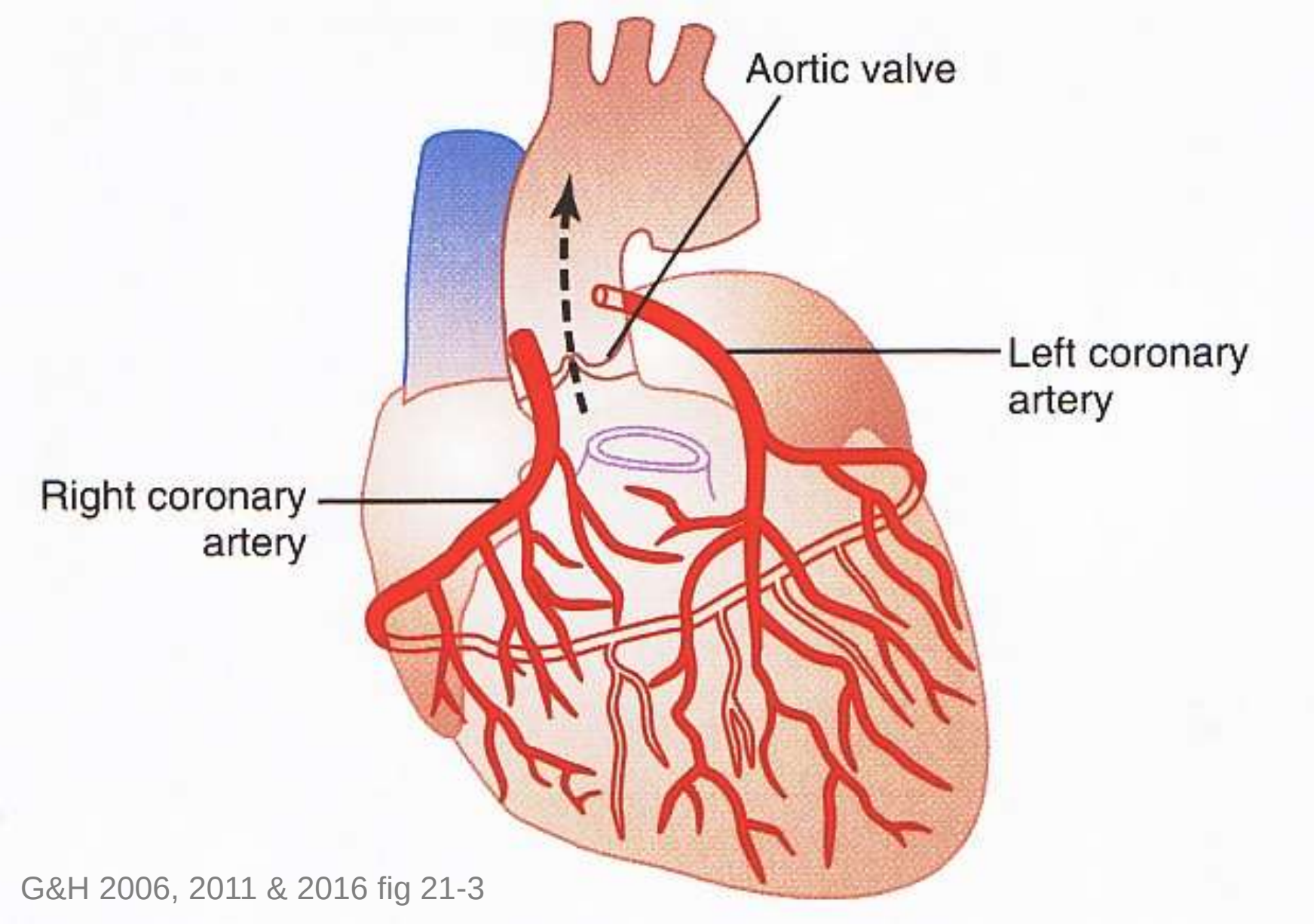




LS2007

https://www.nhlbi.nih.gov/health-topics/how-heart-works
https://www.youtube.com/watch?v=zJXAlh9VDDU

Coronary Circulation ≡ Crowns the Heart!



G&H 2006, 2011 & 2016 fig 21-3

Torstar 1984 p 47

Heart Dominance May Influence Survival?

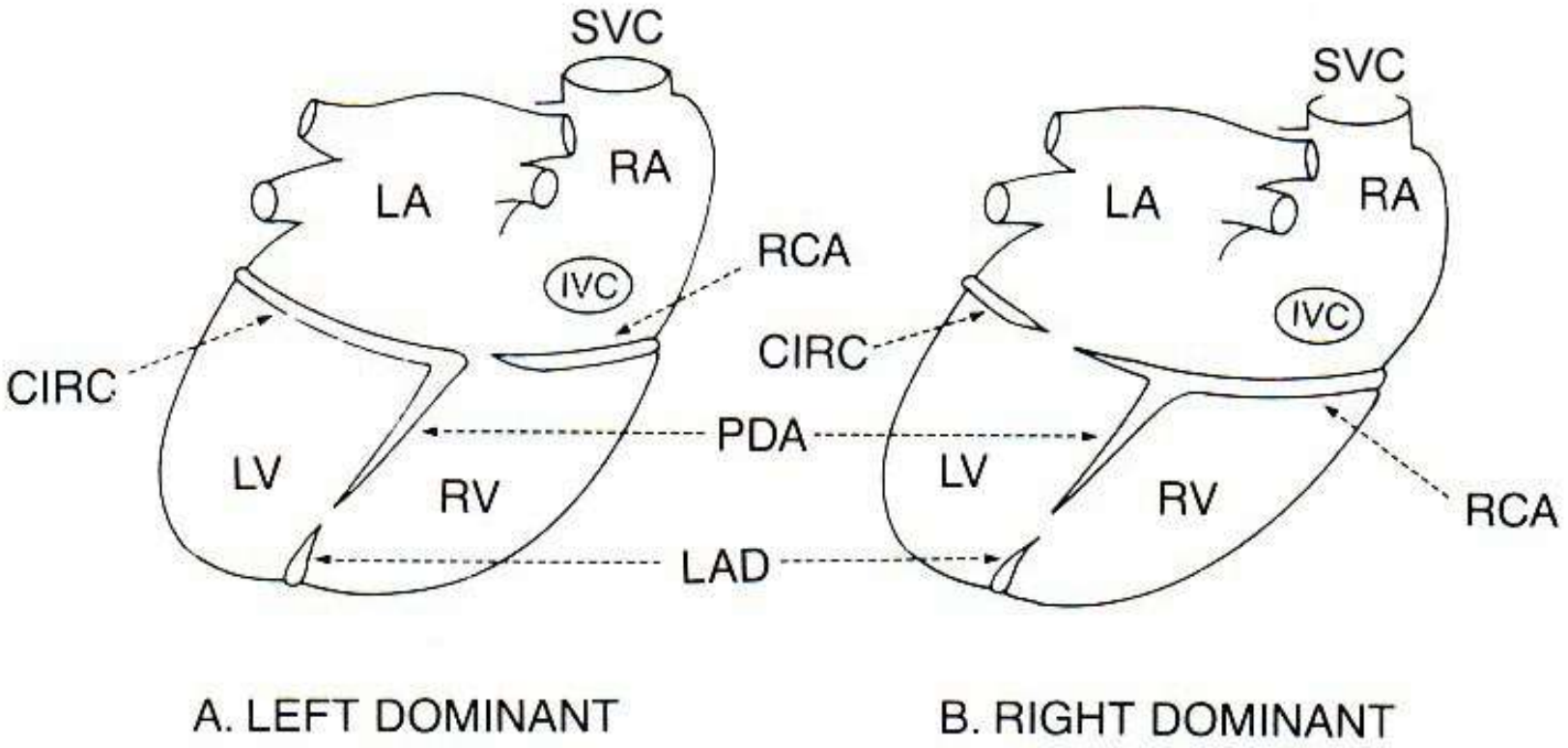
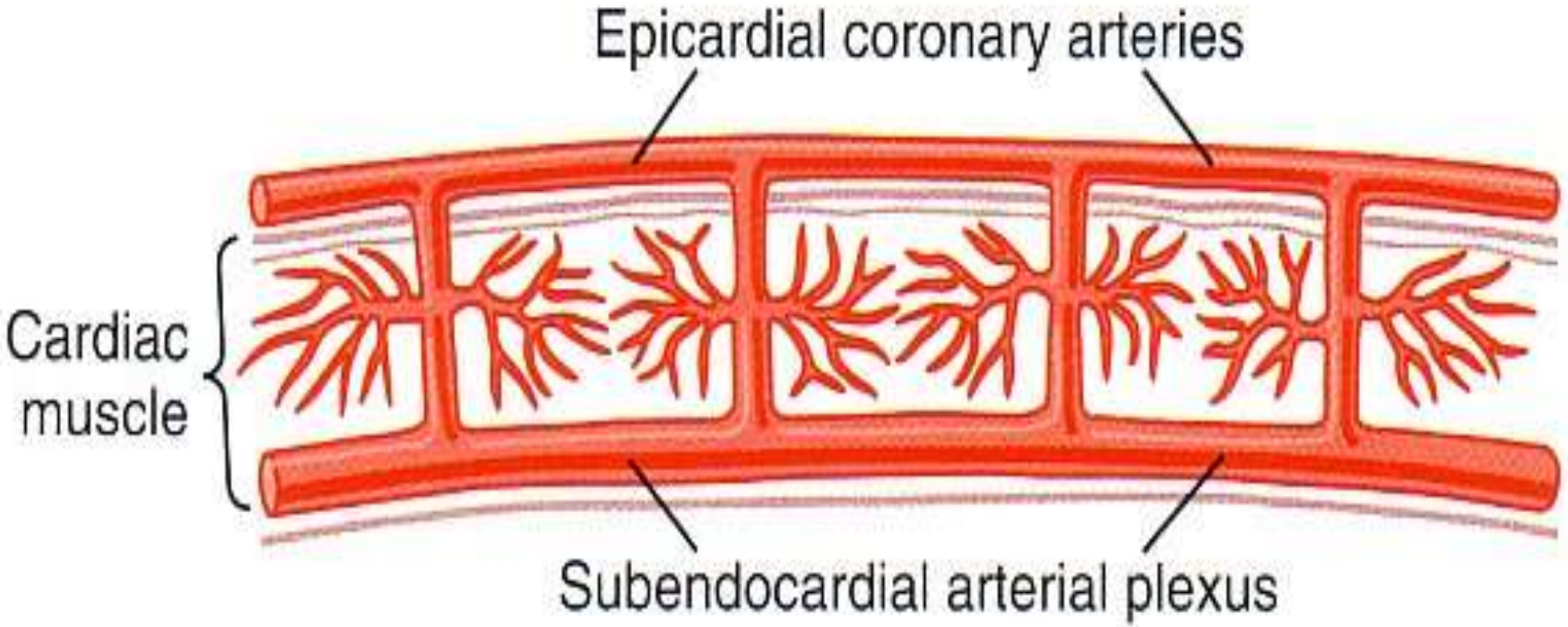


FIG. 1.9. Diagrammatic views of the posterior surfaces of the human heart showing left (A) and right dominant (B) patterns of coronary artery supply. In the left dominant pattern, the posterior descending artery (PDA) is supplied by the circumflex branch of the left coronary artery (CIRC). In the right dominant pattern, the posterior descending artery is supplied by the right coronary artery (RCA). Other abbreviations: LAD, left anterior descending coronary artery; LA, left atrium; RA, right atrium; LV, left ventricle; RV, right ventricle; SVC, superior vena cava; IVC, inferior vena cava.

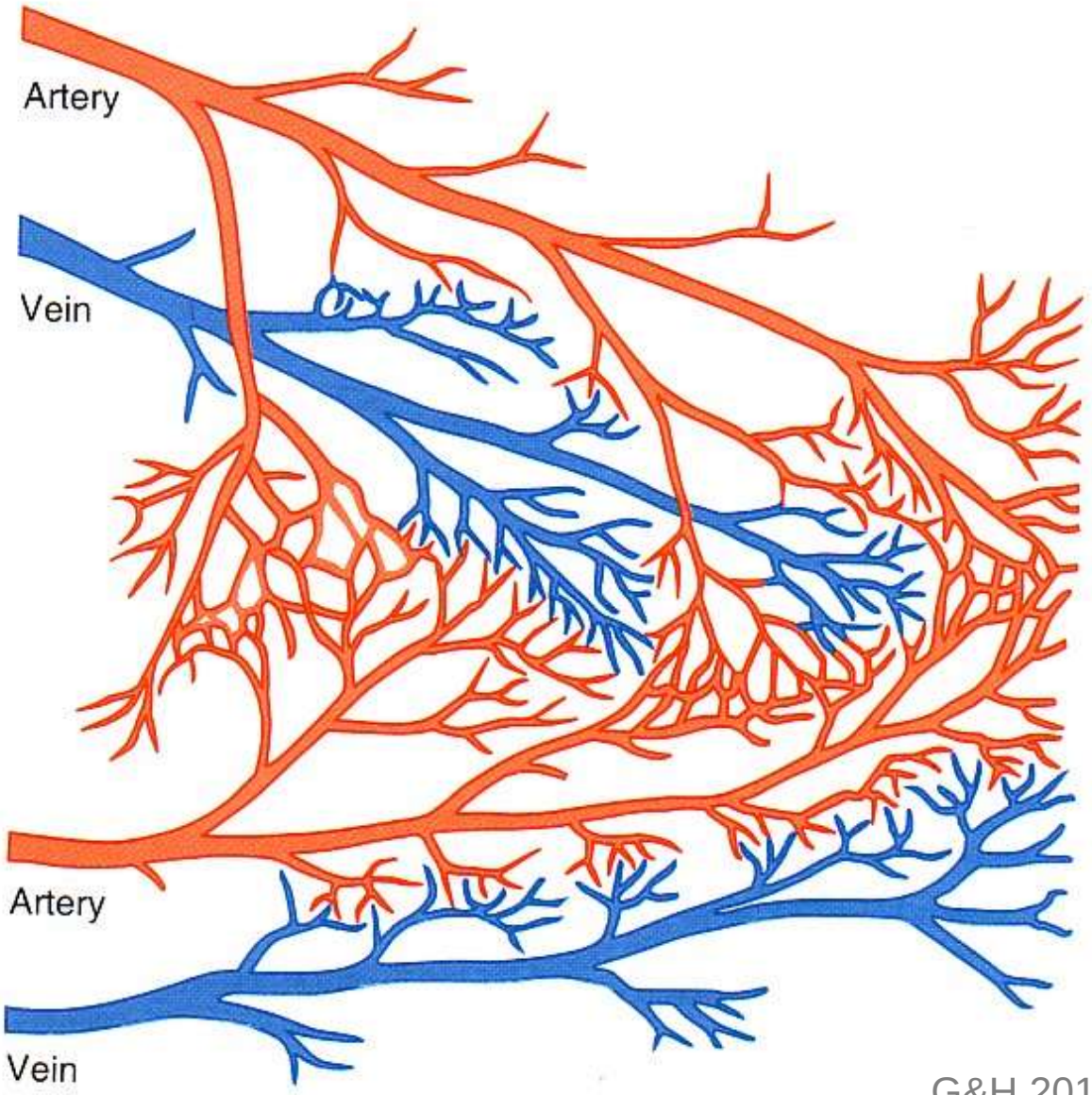
AM Katz 1992 p 12

Coronary Arteries Pierce the Heart from Epi to Endo



G&H 2011 & 2016 fig 21-5

Anastomoses May Provide Lifesaving Collateral Circulation!!



G&H 2011 & 2016 fig 21-6

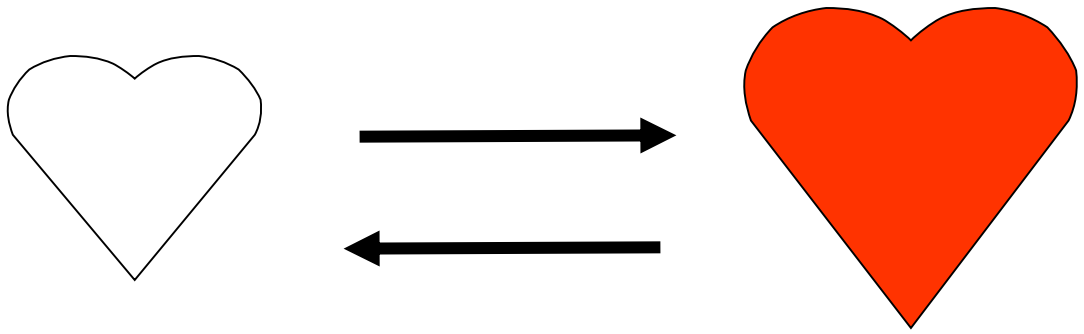
Cardiac Cycle

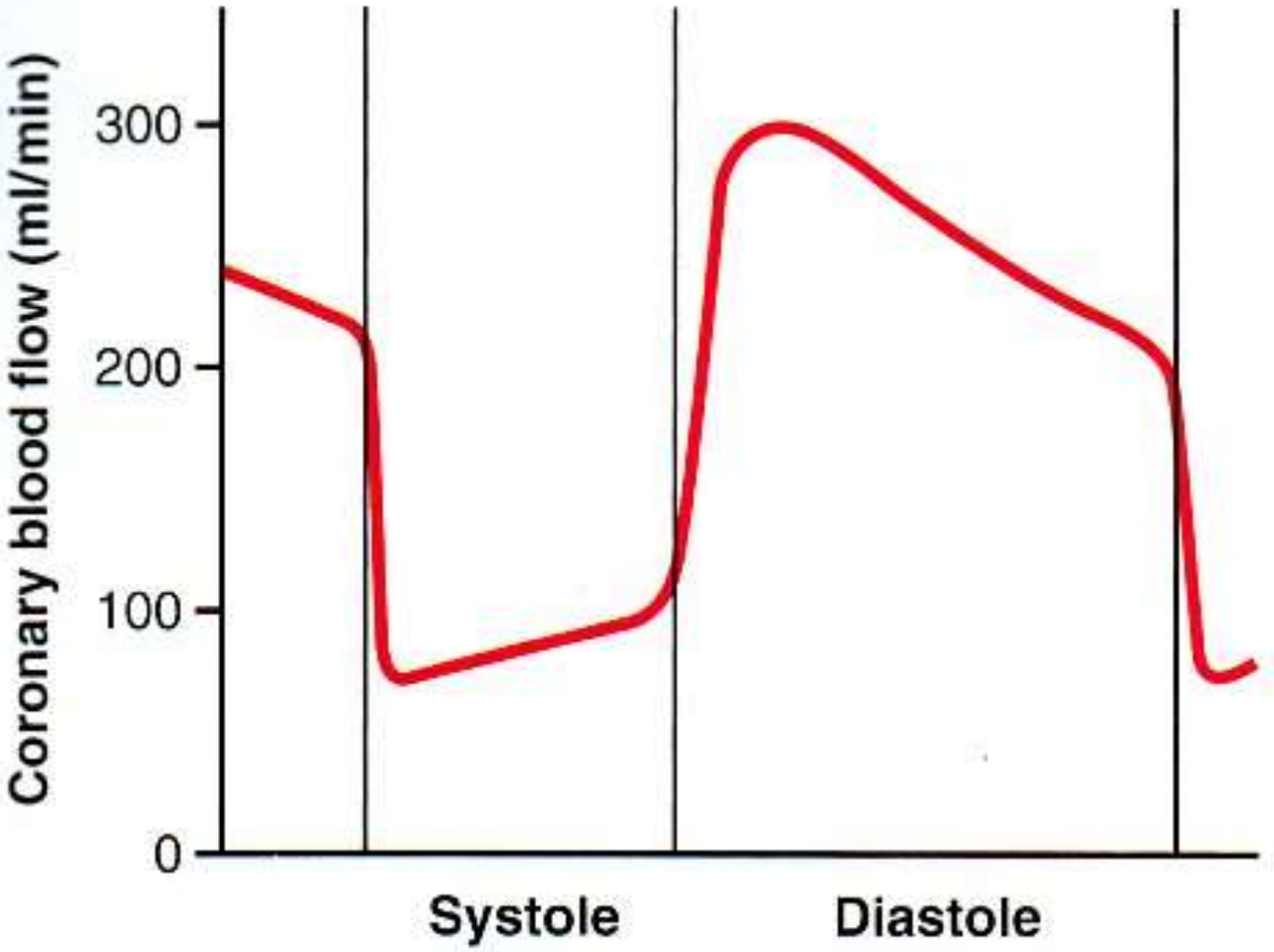
Systole

Contract
& Empty

Diastole

Relax
& Fill





Contract & Empty

Relax & Fill

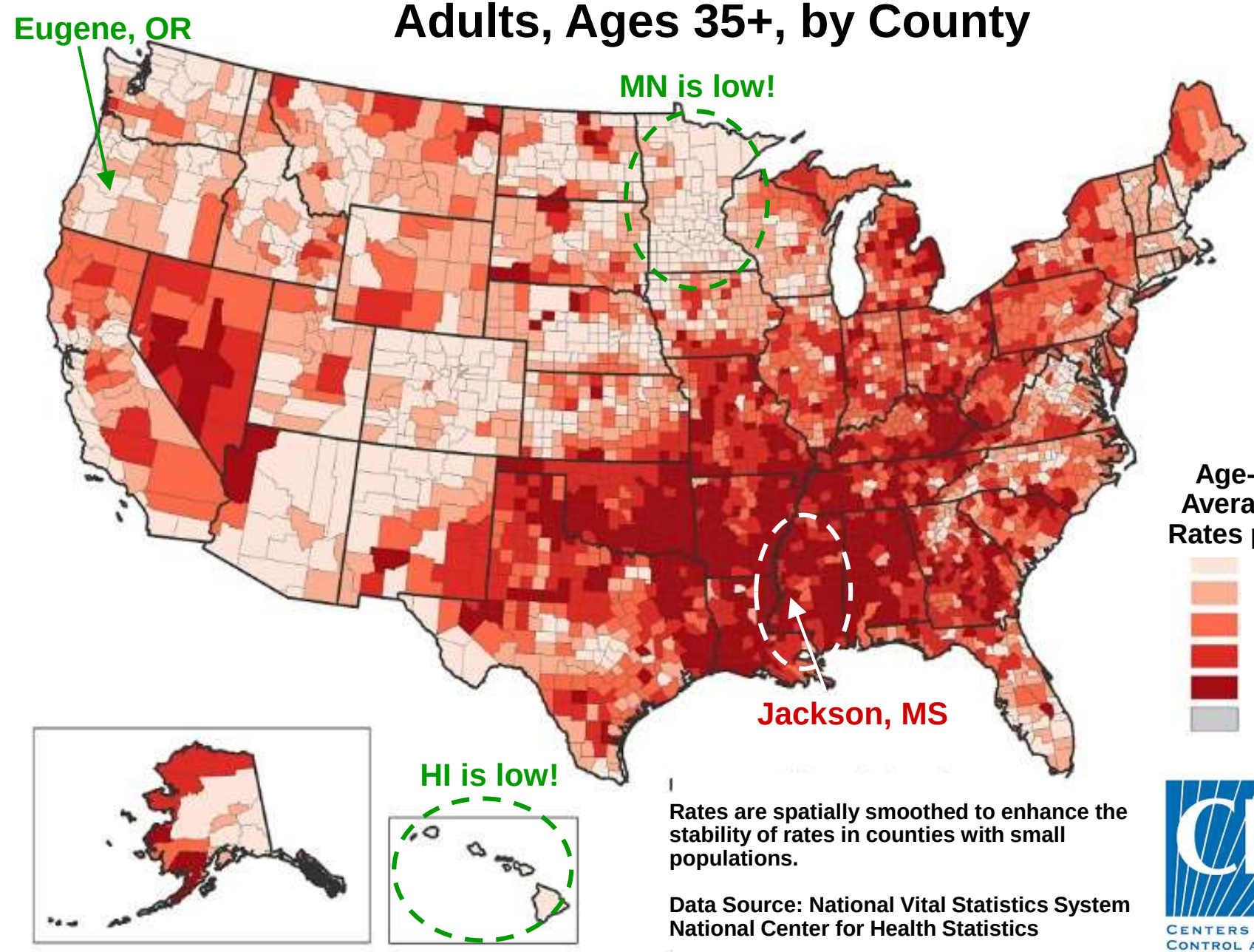
G&H 2011 & 2106 fig 21-4

Did you know?

- **Every 40 seconds, someone has a heart attack in the US!**
- **~630,000 Americans die of heart disease each yr – that's 1 in every 4 deaths. Heart disease is the leading cause of death for both men and women.**
- **Heart disease costs the US ~ $200 billion per yr in health care, medications & lost productivity. By 2035, CVD costs are projected to top $1 trillion annually.**

SOURCE: Heart Disease Facts & Statistics, Centers for Disease Control, Aug 23, 2017.

Heart Disease Death Rates, 2014-2016
Adults, Ages 35+, by County



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

Data Source: National Vital Statistics System
National Center for Health Statistics

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_heart_disease.htm

CVDs

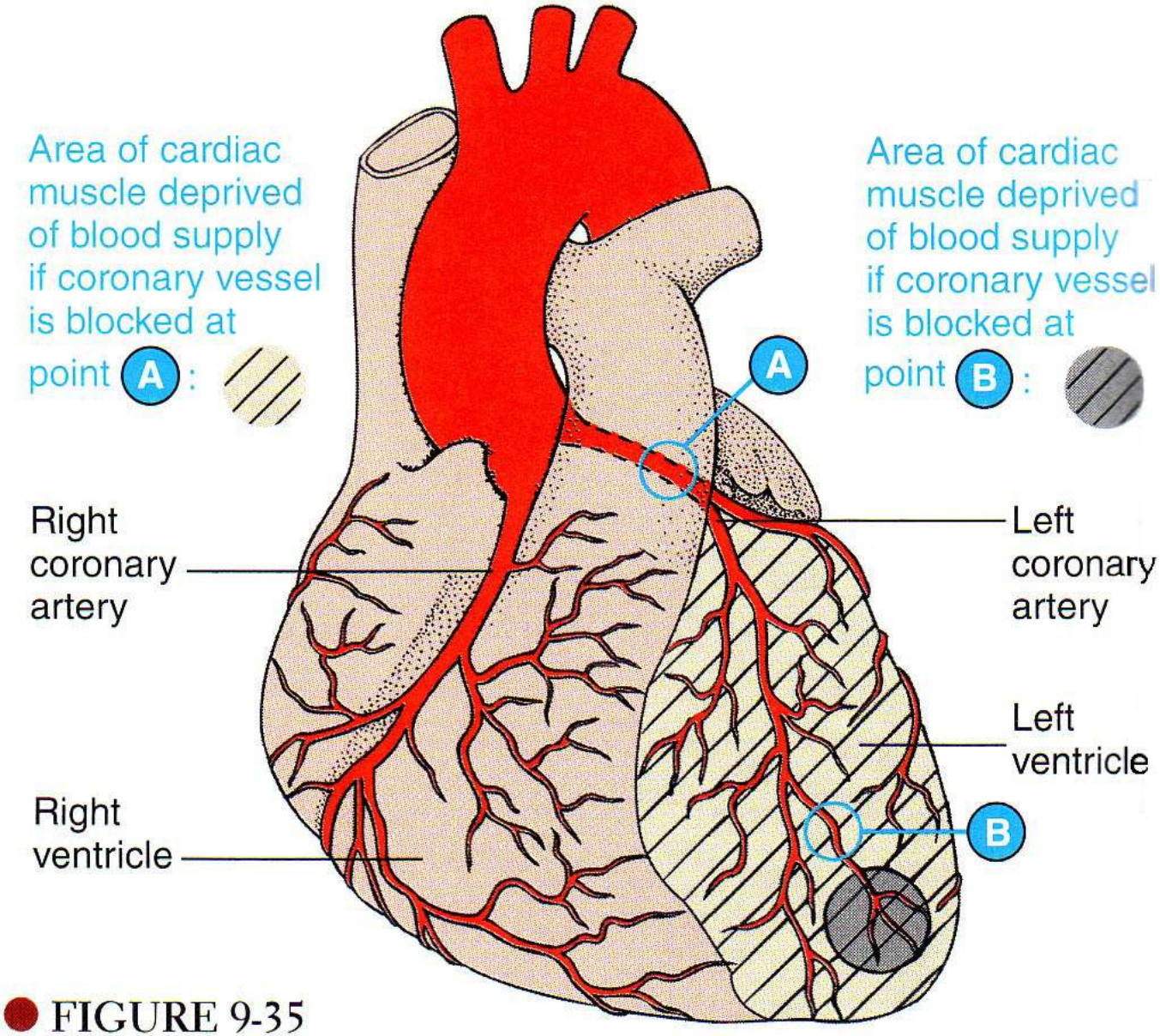
AMI

CVA

TIA

HTN

PVD



● FIGURE 9-35

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

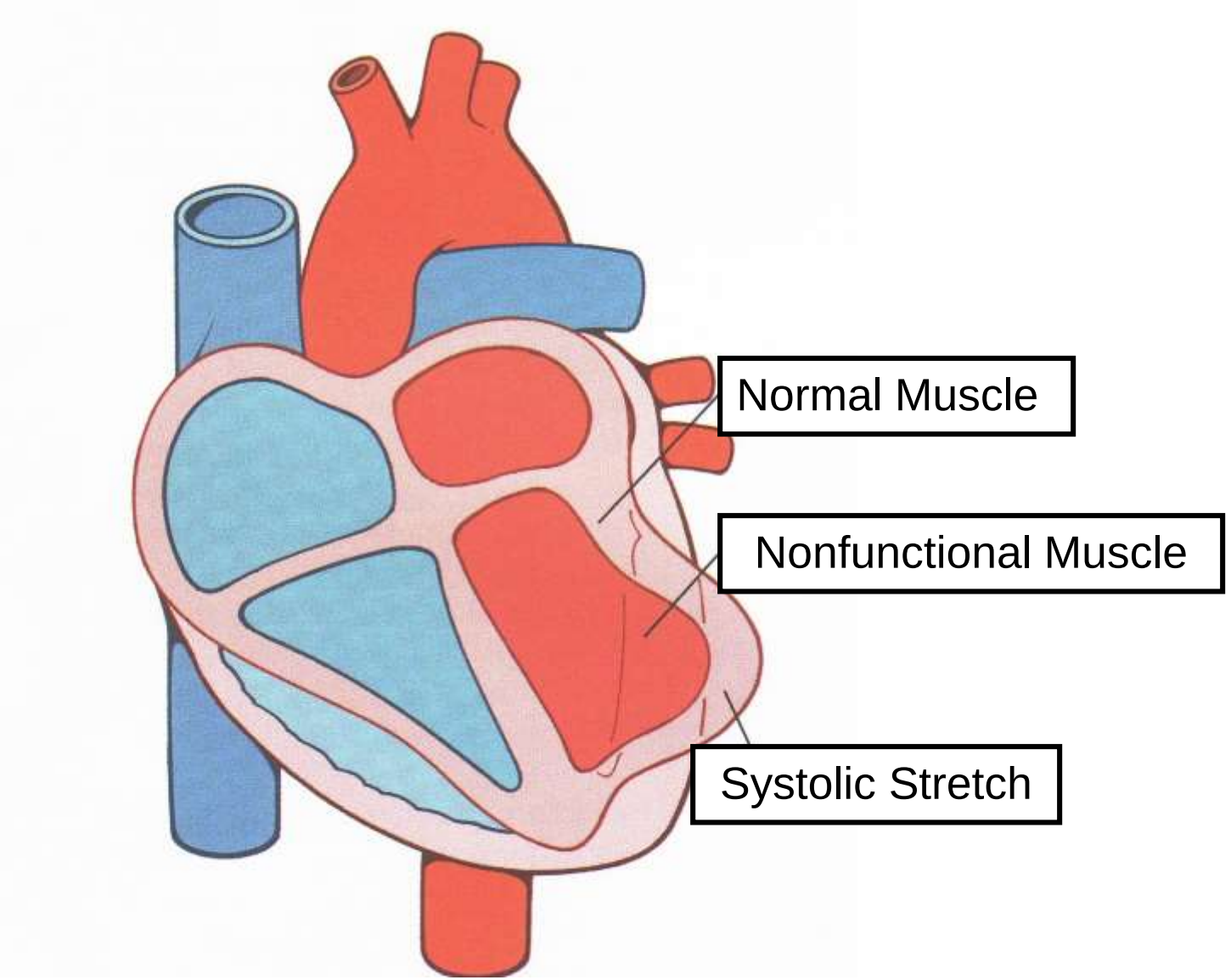
L Sherwood 2004 p 336

What is the Ultimate Cause of Death?

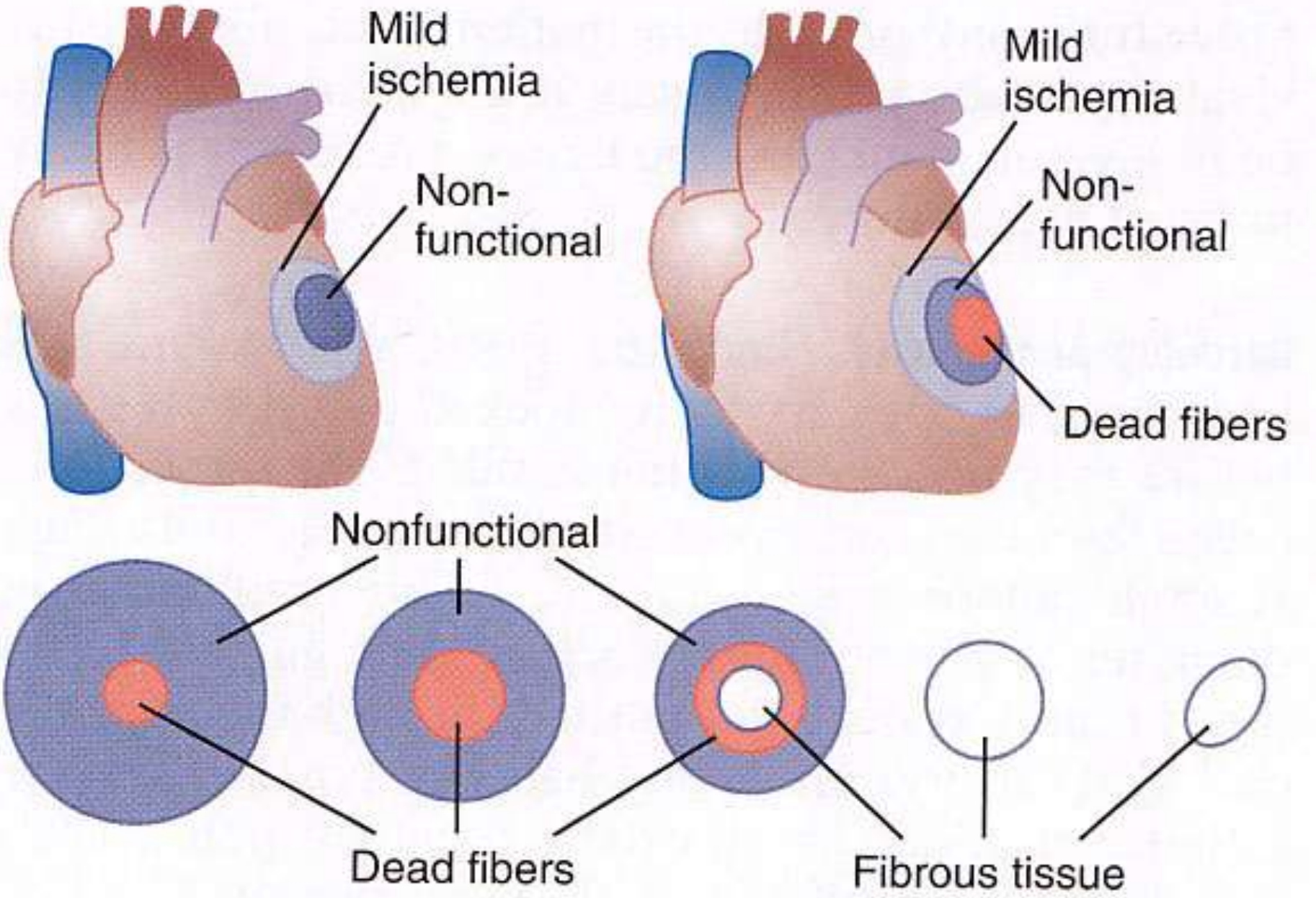
1. ↓ $\dot{Q}$, **CO** or Cardiac Output
2. **Pulmonary damming** w/edema
3. **Cardiac fibrillation**
4. **Cardiac rupture** (occasionally)
5. Thromboembolism
   (2011 ed. but not 2016)

G&H 2016 p 266
G&H 2011 p 250

Systolic Stretch Due to Necrotic Tissue



G&H 2016, 2011 fig 21-7

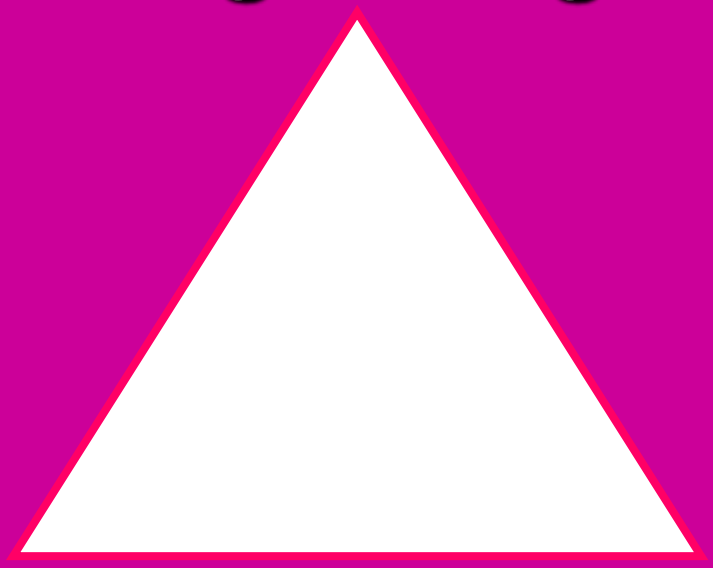


G&H 2016, 2011 fig 21-8

Treatment Triad

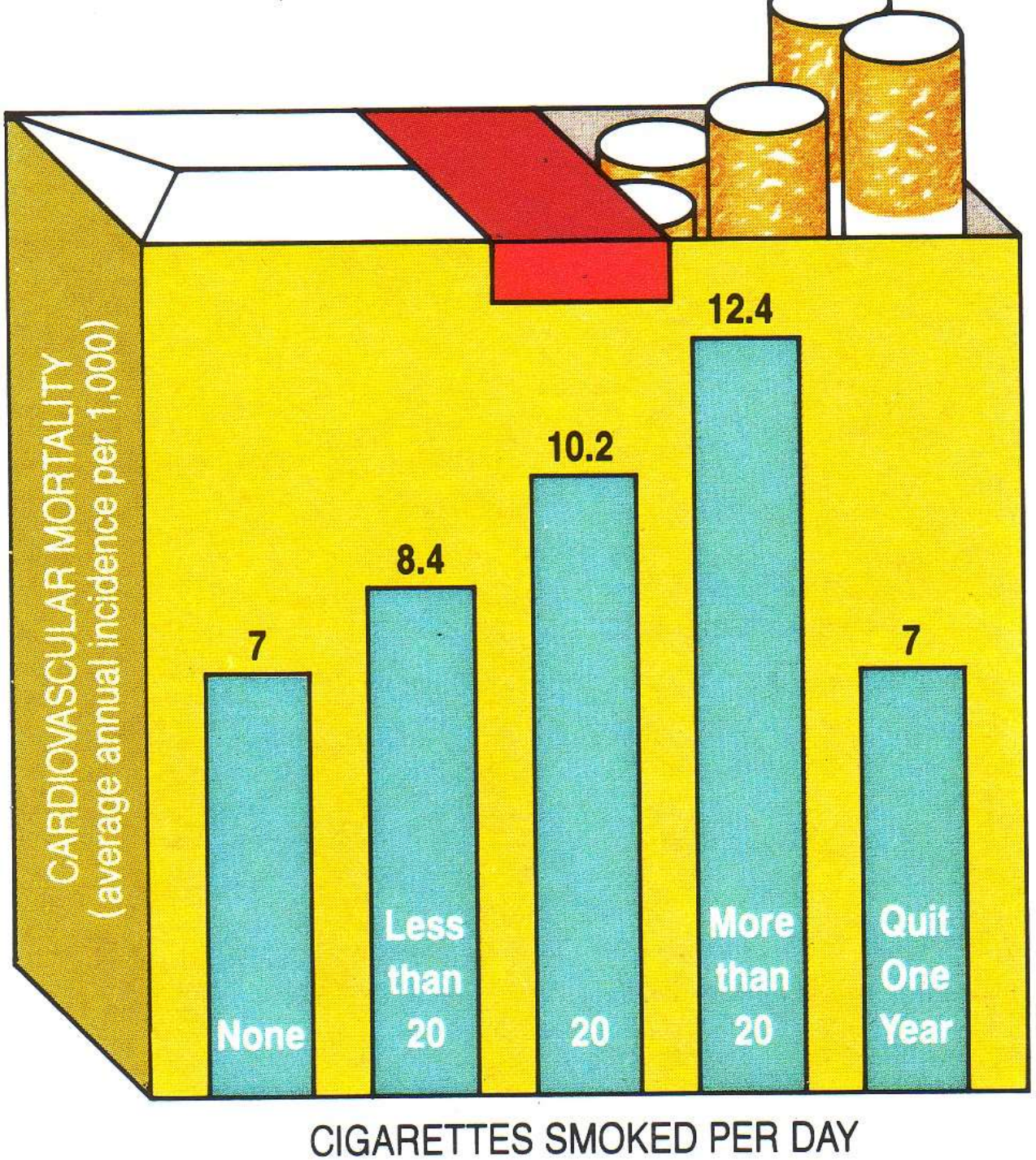
NB: Last blasted resort!!

Drugs/Surgery



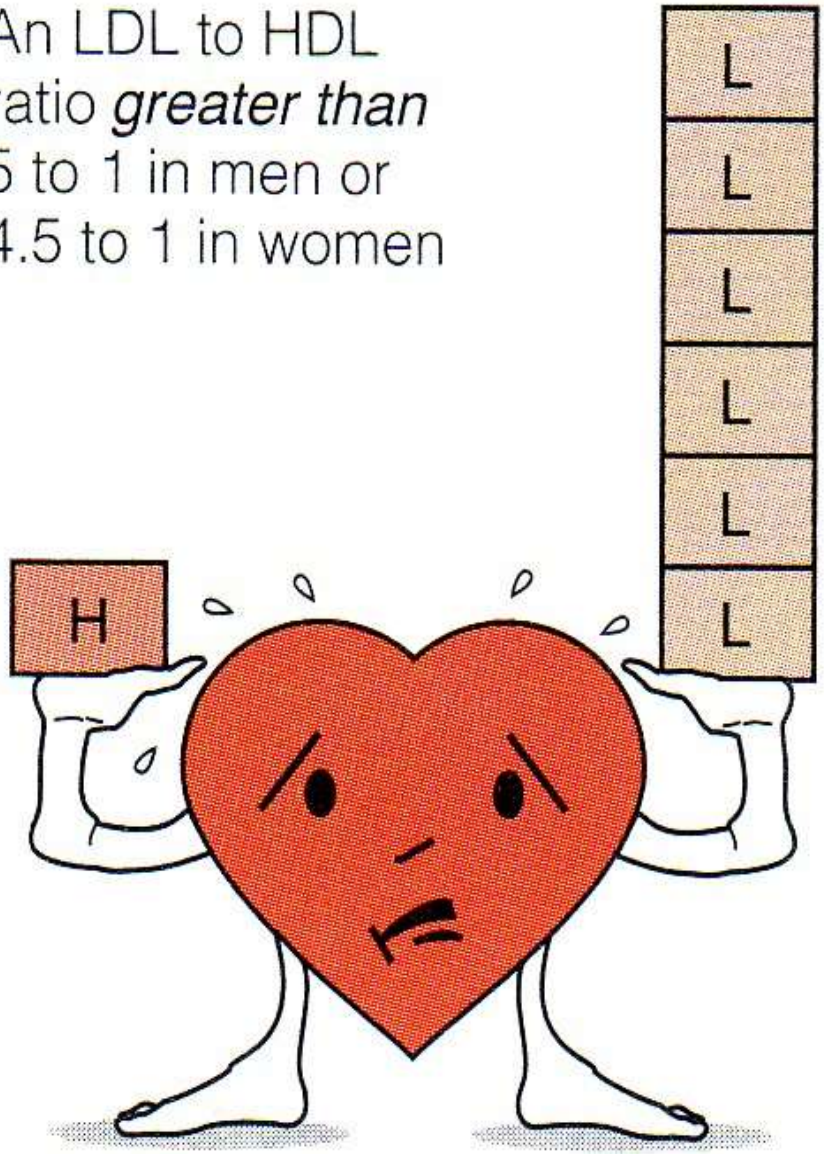
Exercise

Dietary Modification


CARDIOVASCULAR MORTALITY
(average annual incidence per 1,000)
7
8.4
10.2
12.4
7
None
Less than 20
20
More than 20
Quit One Year
CIGARETTES SMOKED PER DAY

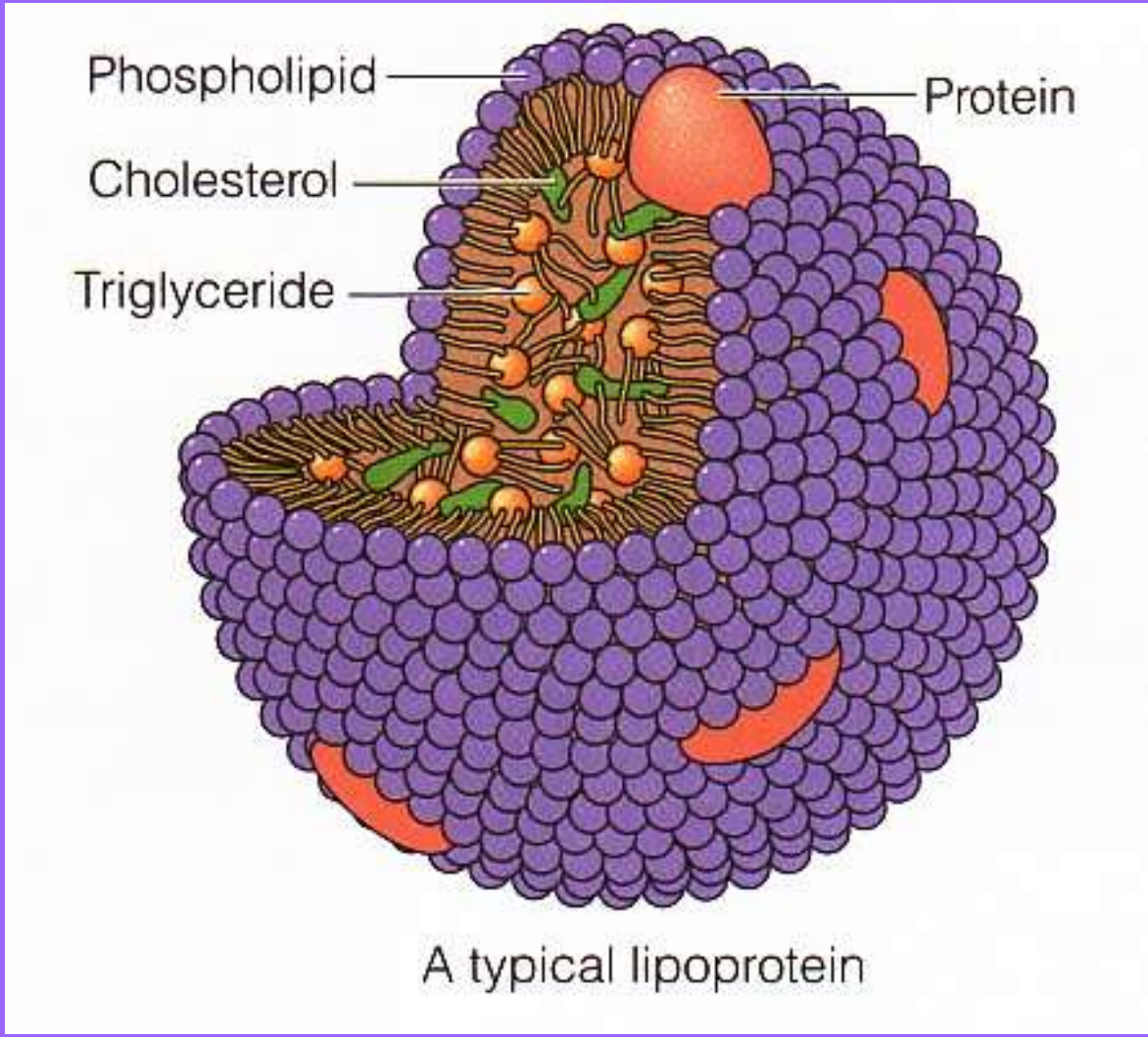

KA-BOOM!
300/200
Hg

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



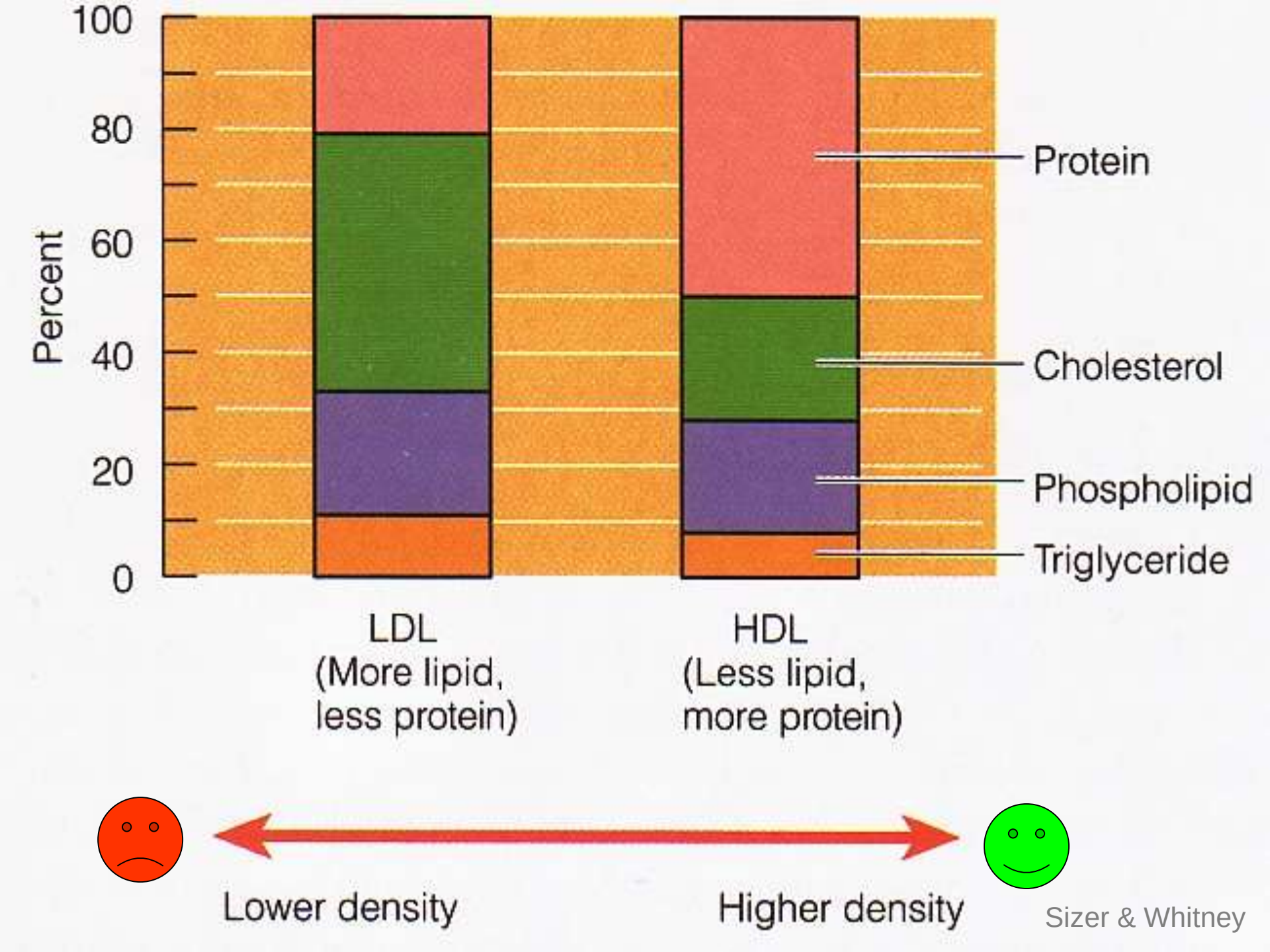
Increased risk of heart disease

Sizer & Whitney



A typical lipoprotein

F Sizer & E Whitney (S&W) 2003 p 147 +



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

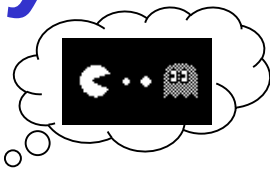
Genes for HDL, LDL+ receptors, Apolipoproteins Apo B-100, Apo-E, Apo-M, lipoprotein a/Lp_a, homocysteine metabolism enzymes N5,N10-methylene-tetrahydrofolate reductase, cystathione beta-synthase, Type I antithrombin, mitochondrial haplogroup A, Protein tyrosine phosphate PTPN22 C/T single nucleotide 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



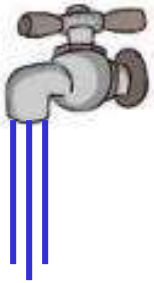
β 

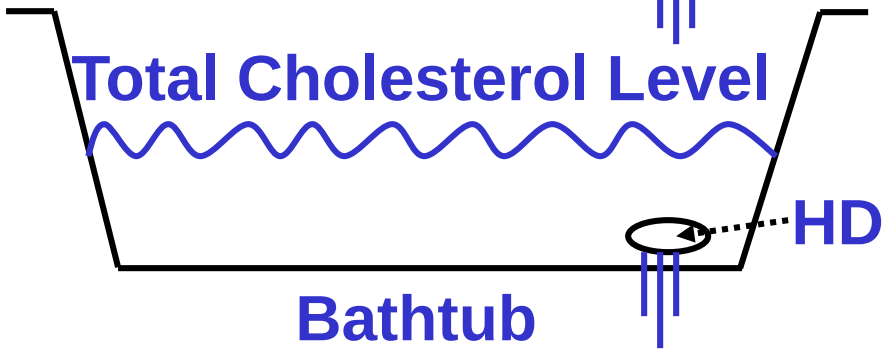
Atherogenic | **Anti-Atherogenic**

Biological Artifact!?

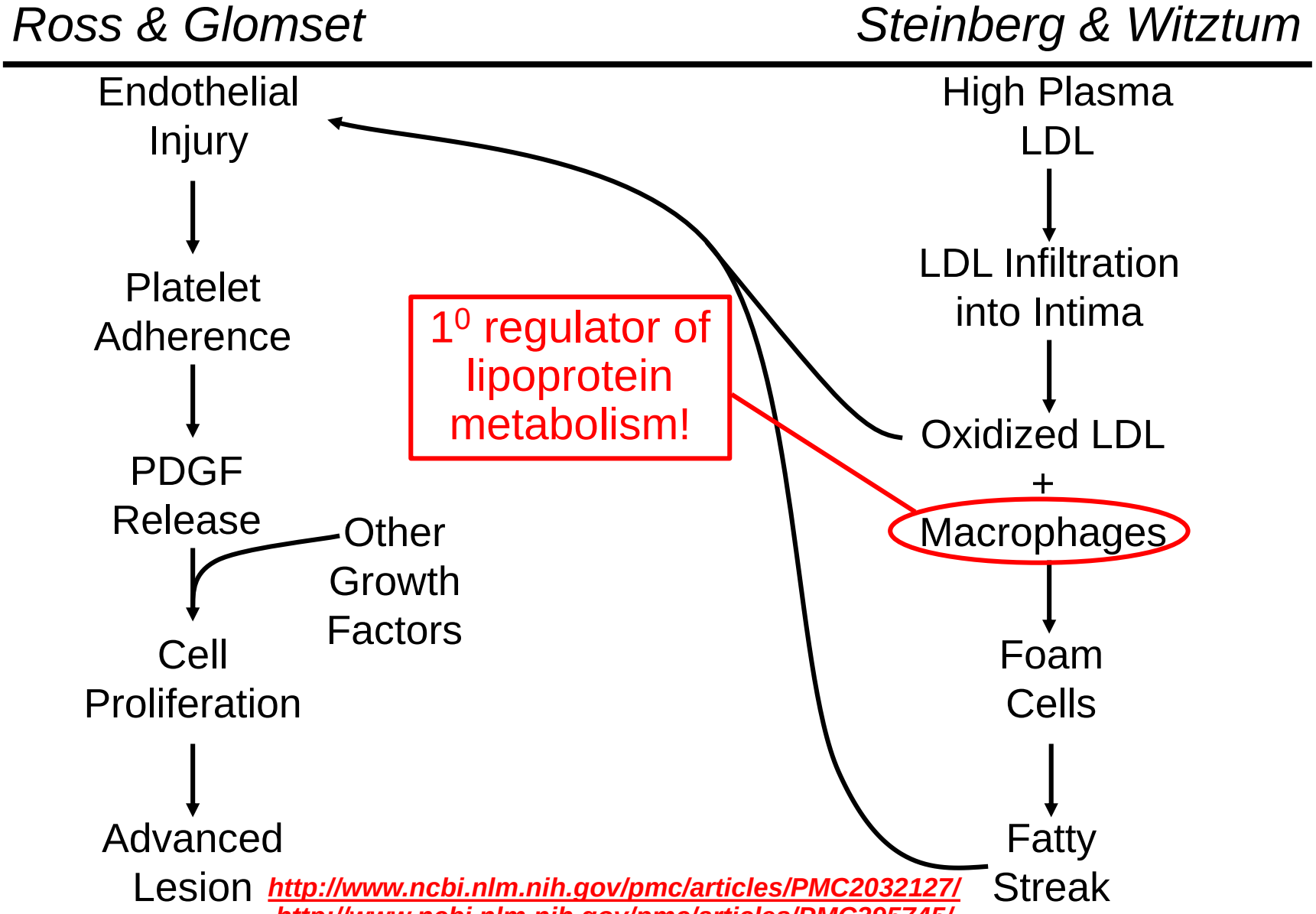
> *"I don't think the total cholesterol test by itself is worth a damn."*
> —*Eliot Corday*

β-VLDL + LDL = Faucet





Historical Hypotheses for Atherosclerosis Development



http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2032127/
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC295745/
https://link.springer.com/article/10.1007%2Fs00109-017-1575-8
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6121590/

How Inflammation Attacks the Heart

❶ LDL Oxidized

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.

❷ Monocytes Migrate

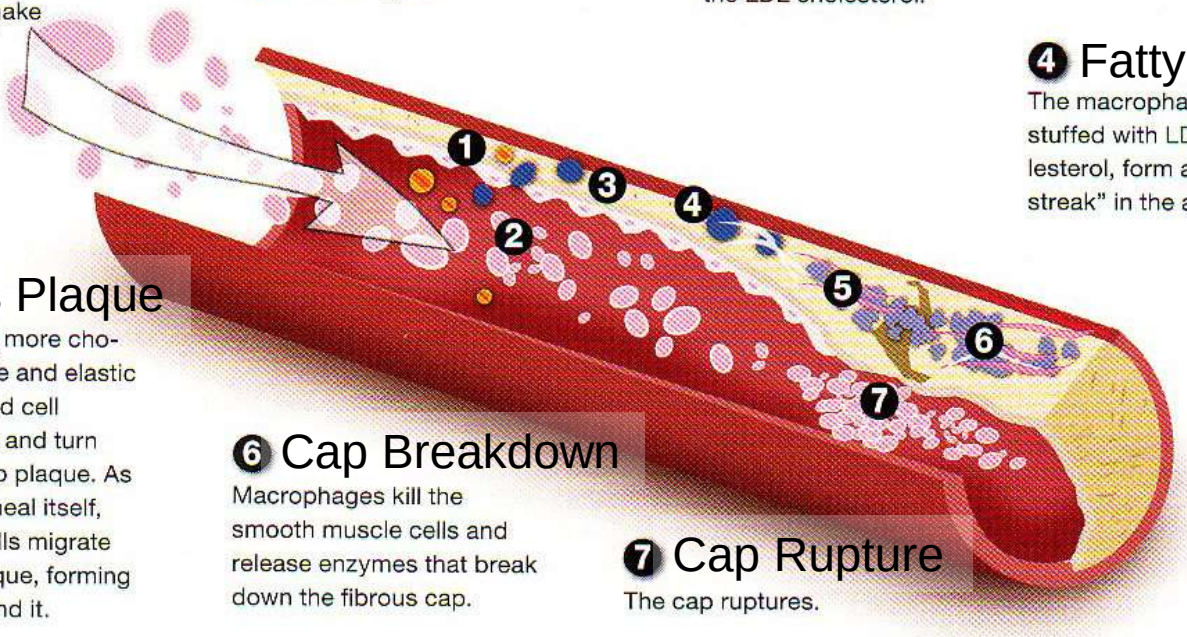
In response to the injury, the immune system sends in a team of inflammatory cells, including white blood cells called monocytes.

❸ Monocytes → Macrophages

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

❹ Fatty Streak

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



❺ Fibrous Plaque

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.

❻ Cap Breakdown

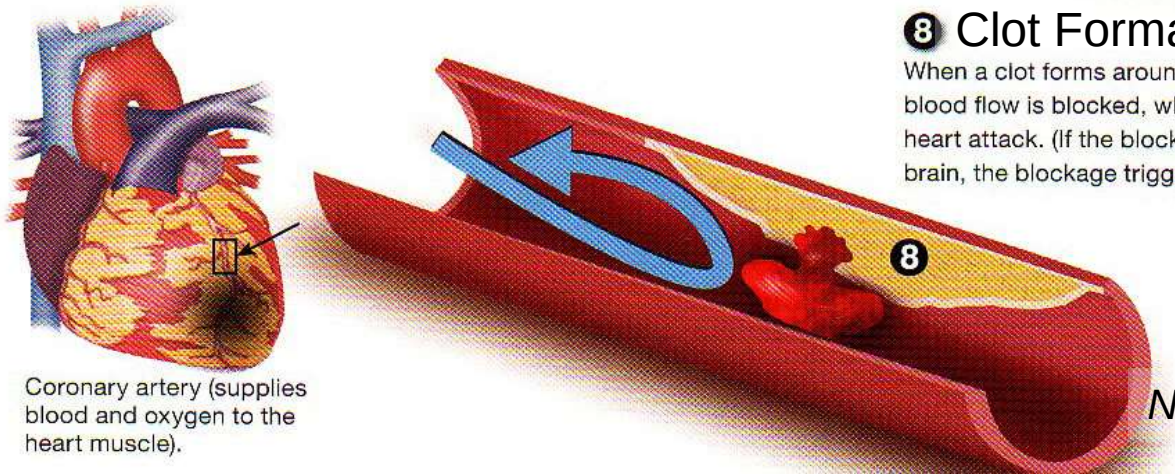
Macrophages kill the smooth muscle cells and release enzymes that break down the fibrous cap.

❼ Cap Rupture

The cap ruptures.

❽ Clot Formation

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).

NAHL Jan/Feb 2009, p 5

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.

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.

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

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.[1,2]

"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.

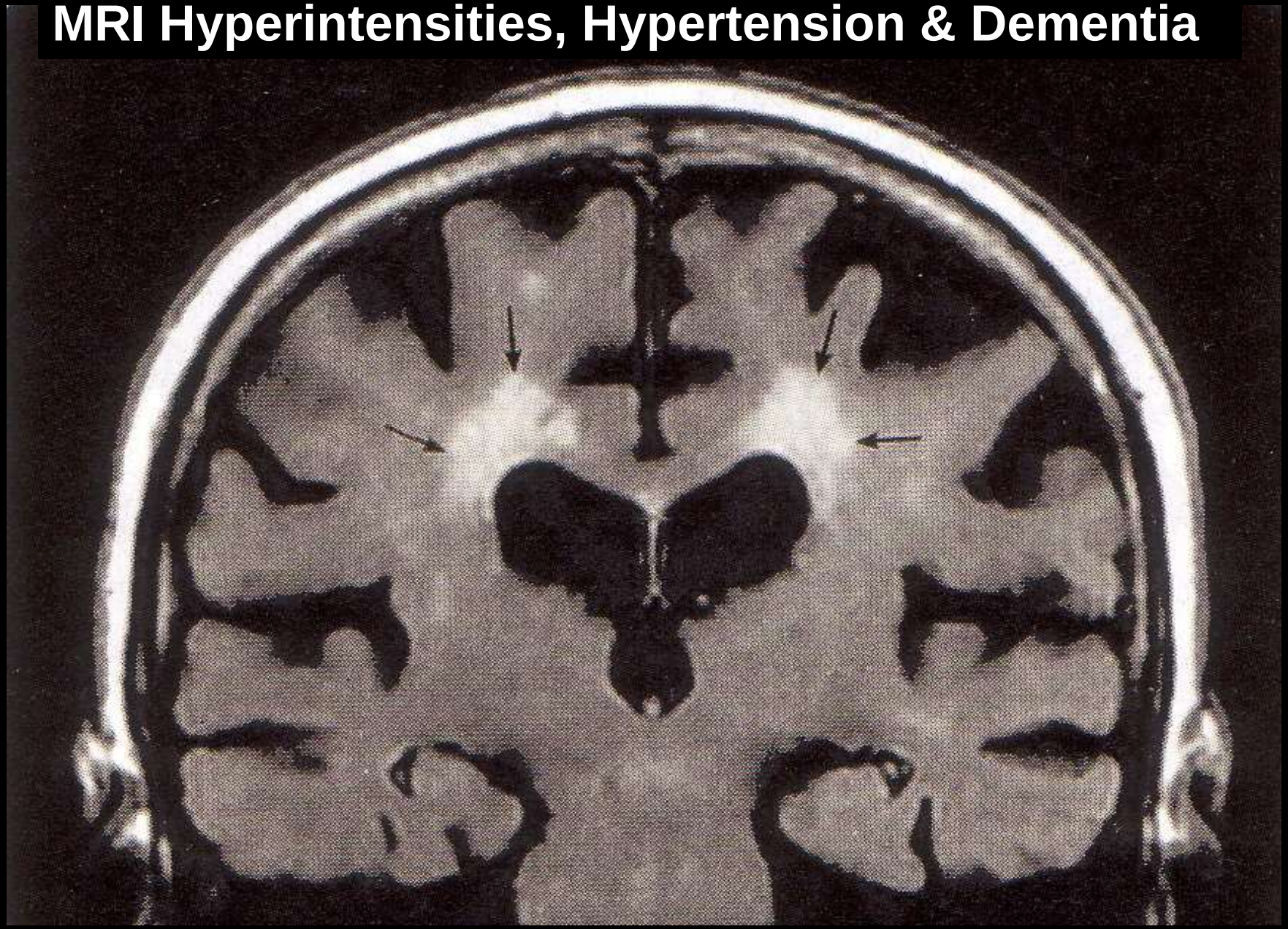
The causes of Alzheimer's pathology are more murky. But new evidence suggests that insulin may play a role.

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

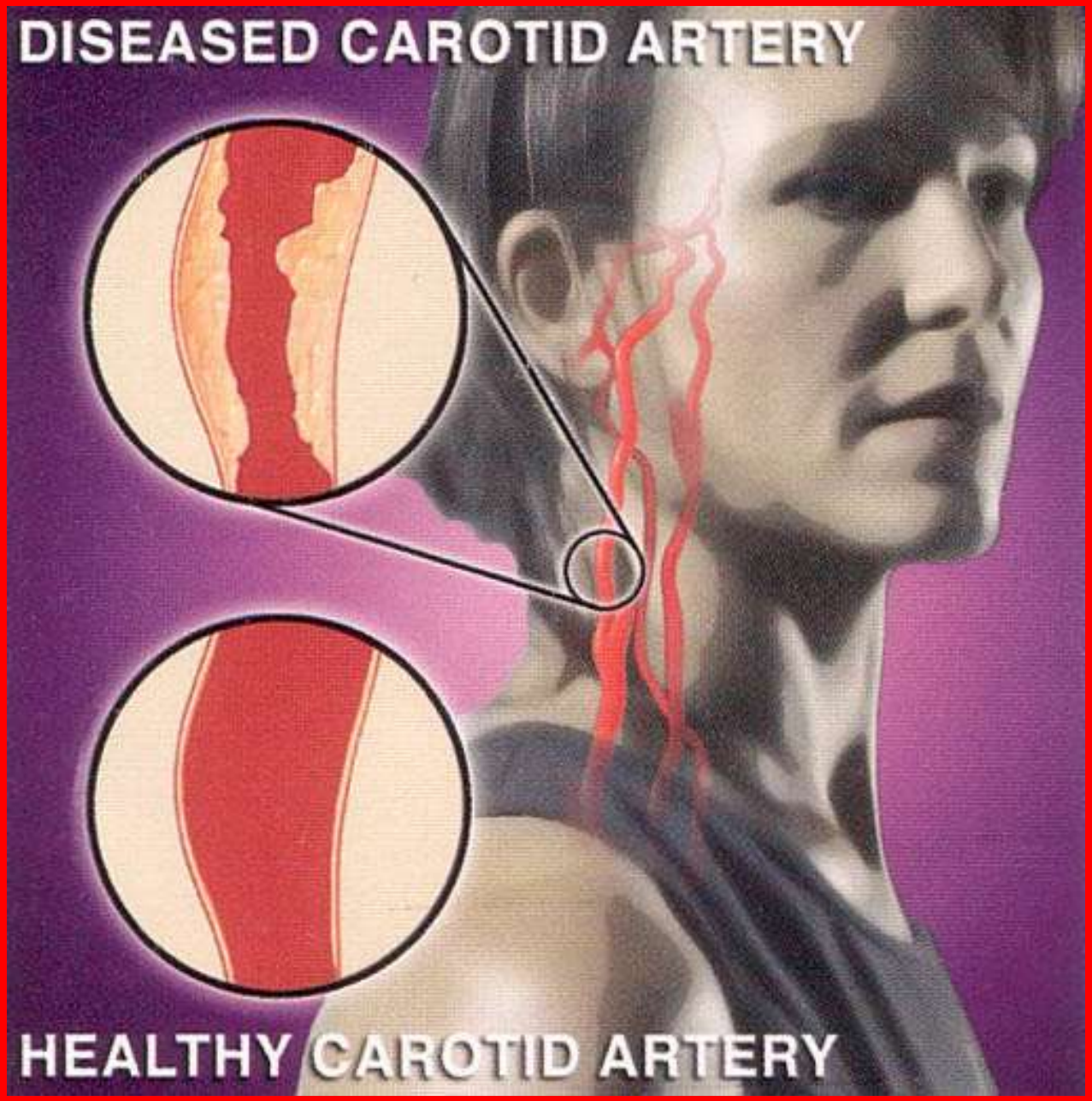
1. Watch your blood pressure

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

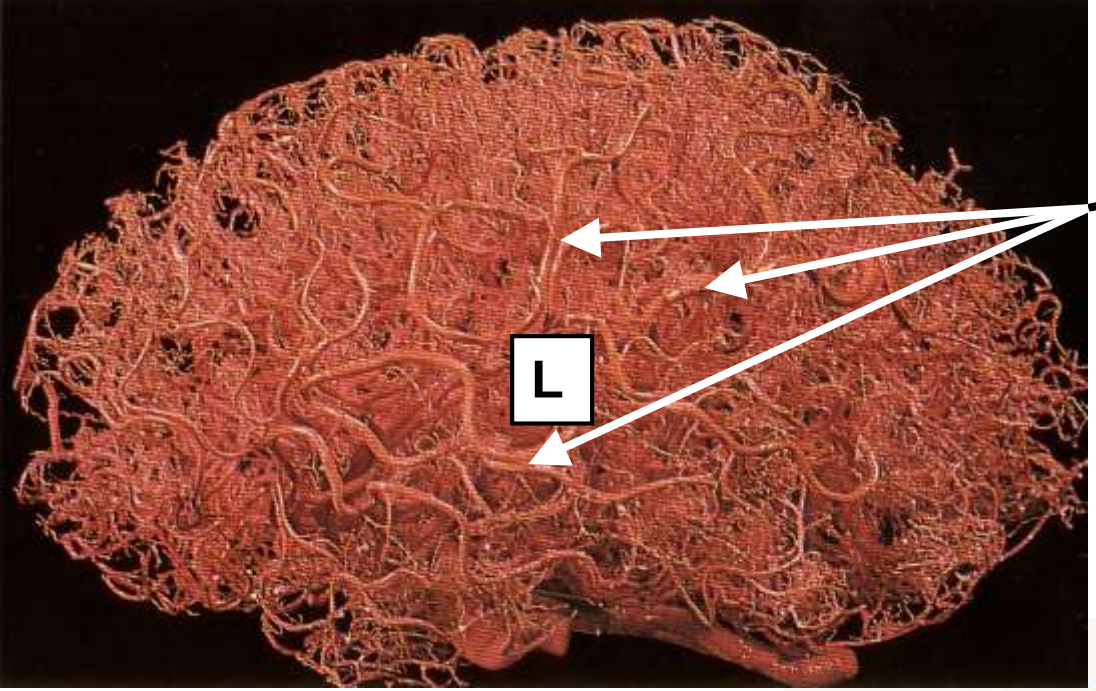
MRI Hyperintensities, Hypertension & Dementia



NAHL CSPI, Jan-Feb 2014

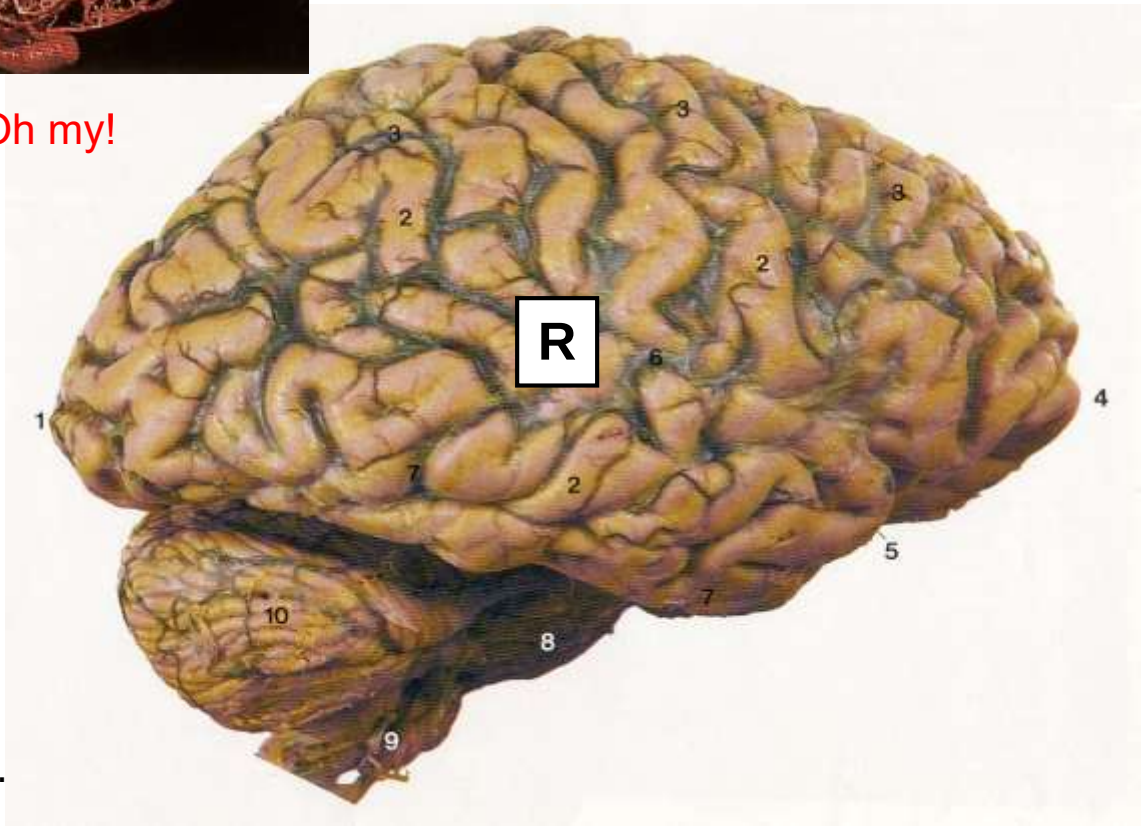


SOURCE: Lifeline Screening, 2007

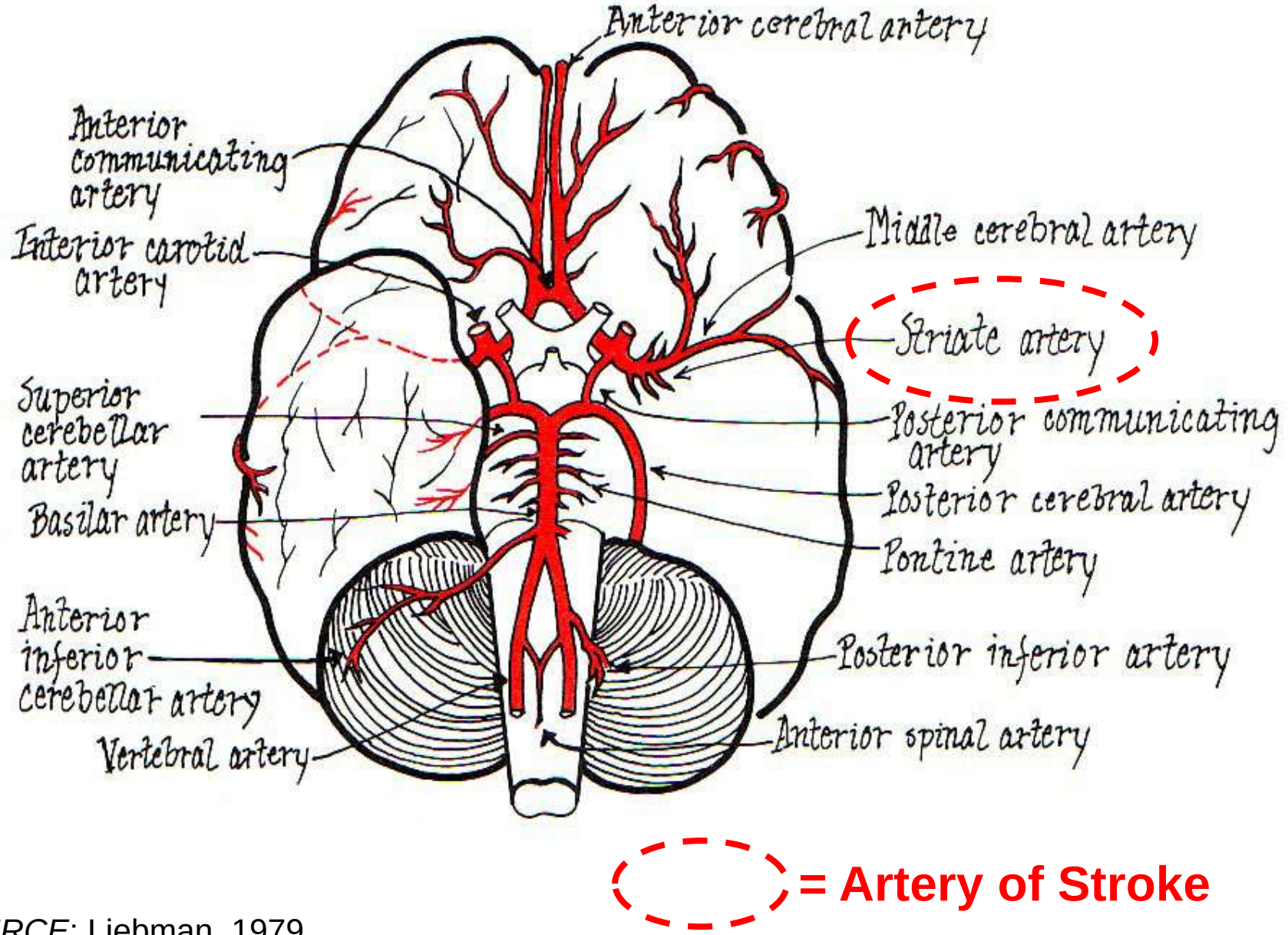


Middle Cerebral Artery Branches

…Cerebral vasculature! Oh my!

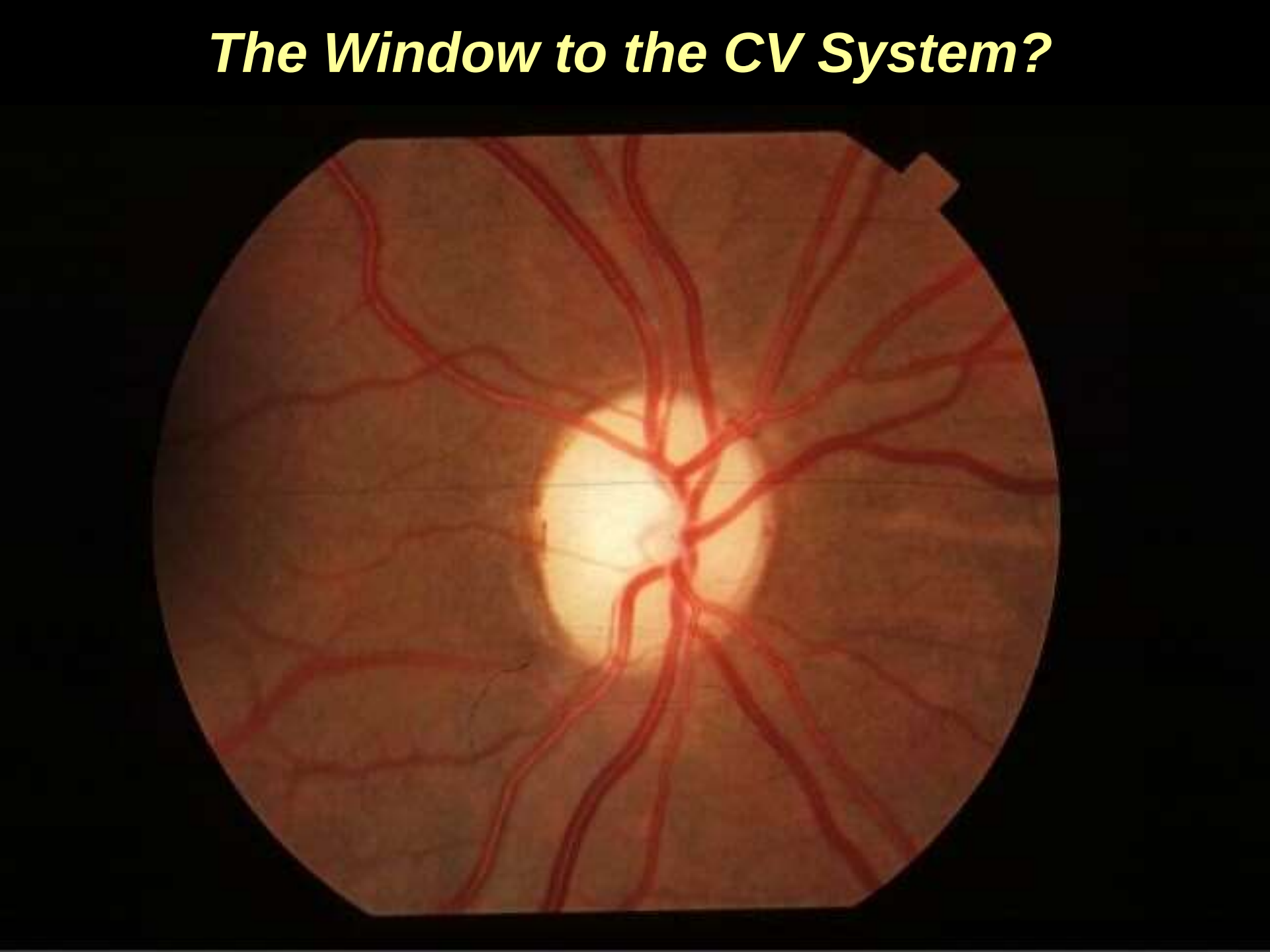


SOURCE: McMinn & Hutchins, 1977.

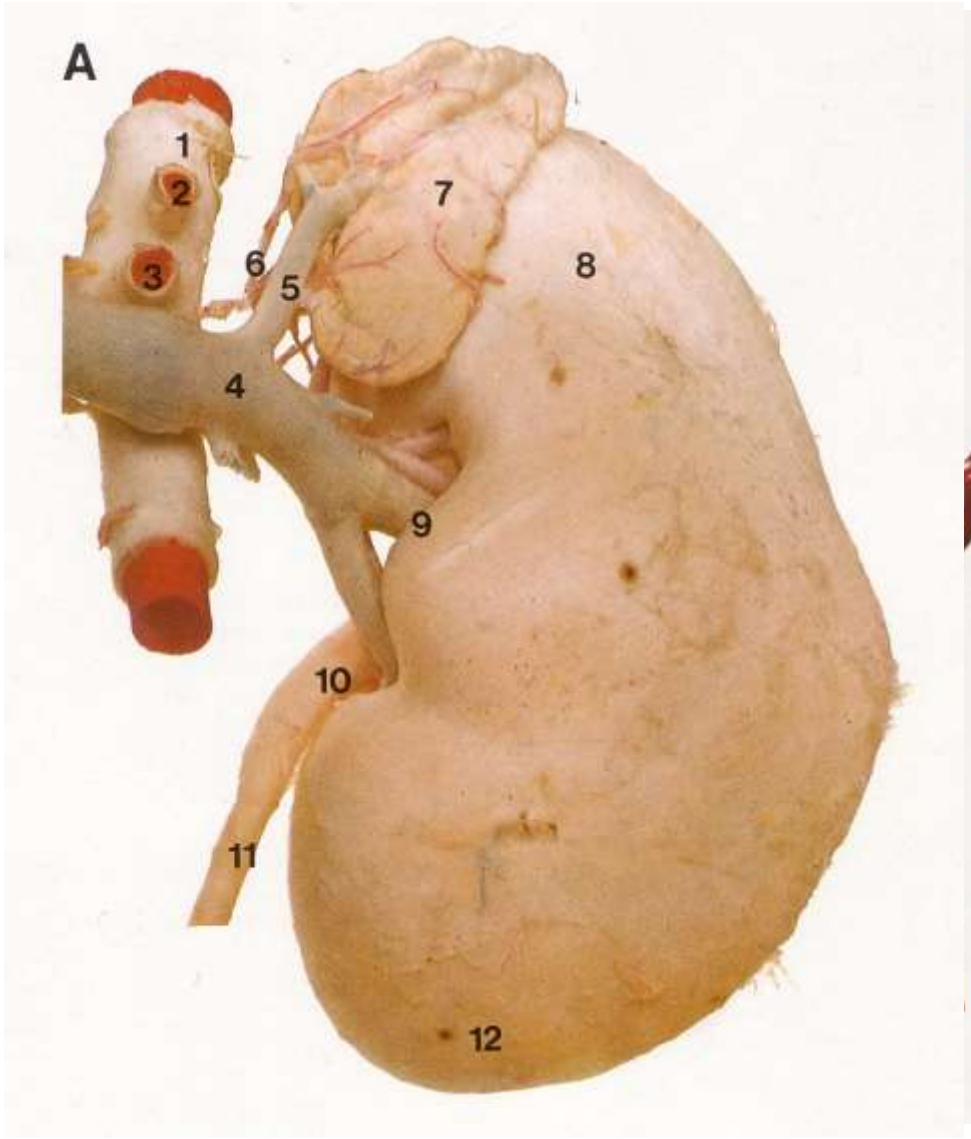


SOURCE: Liebman, 1979.

The Window to the CV System?



Renal Vasculature



SOURCE: McMinn & Hutchins, 1977.

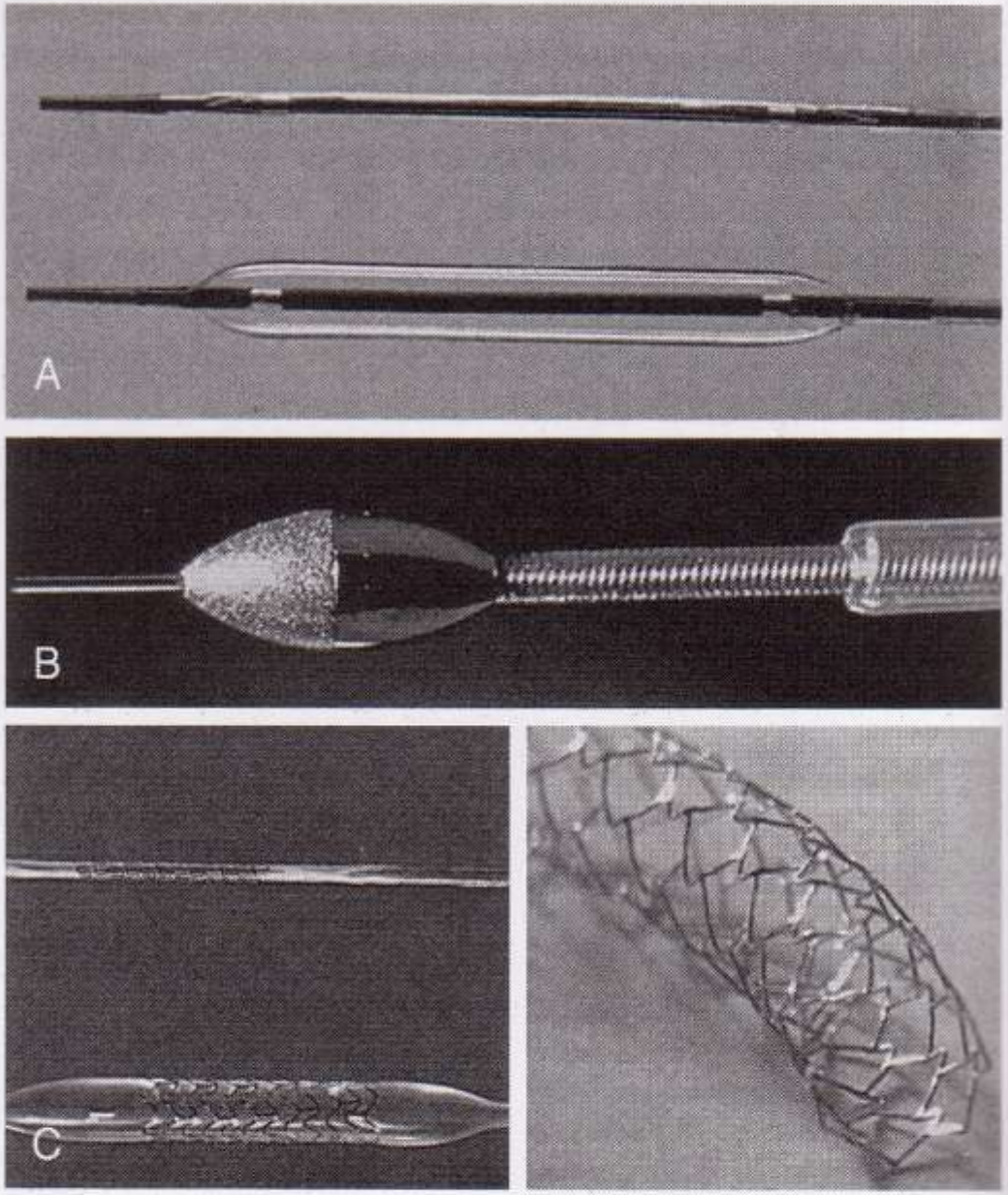
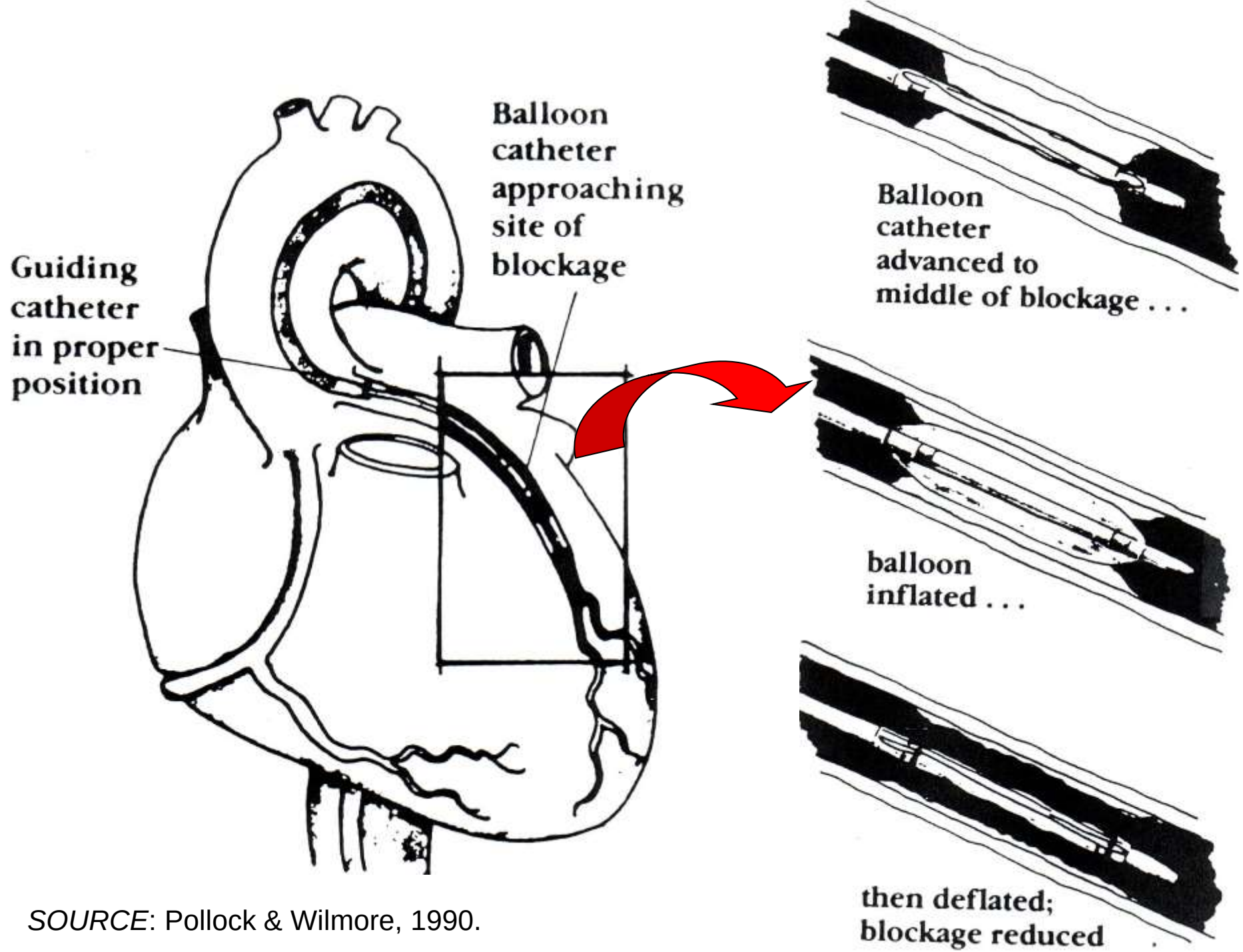
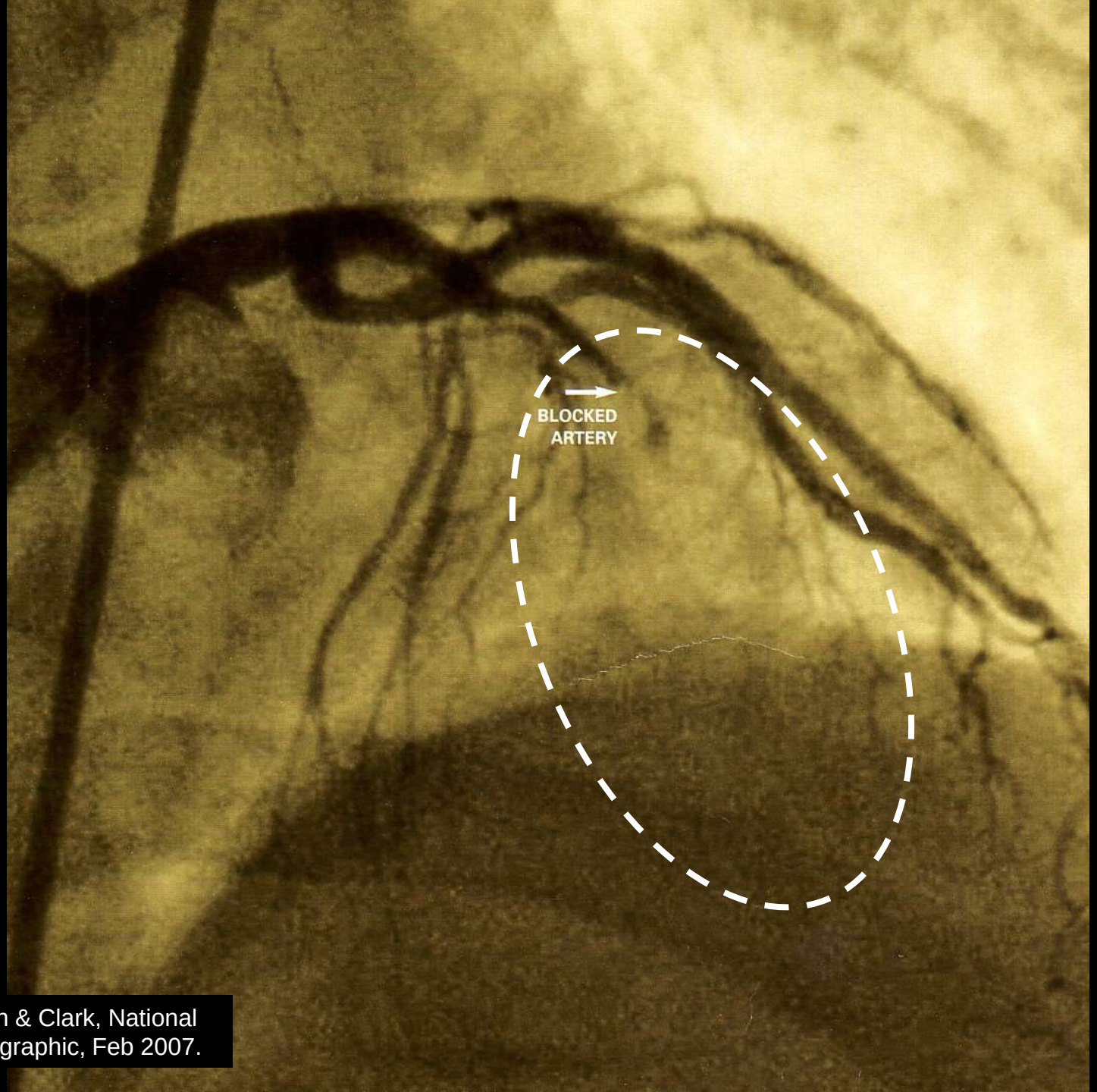


FIGURE 37–1 Devices for percutaneous transluminal coronary interventions. **A,** Coronary balloon. **B,** Rotational atherectomy burr (Rotablator). **C,** Coronary stent.

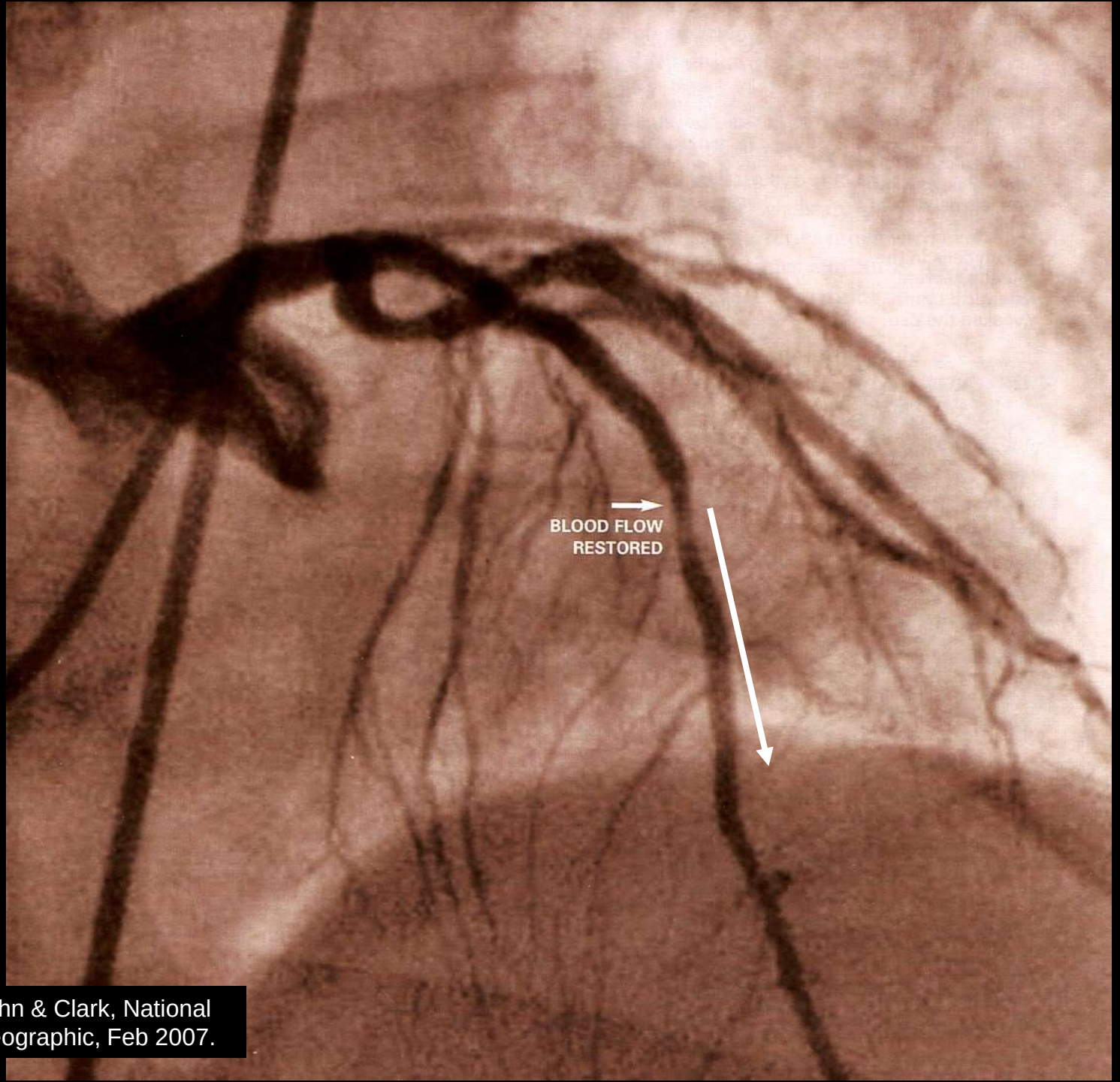
SOURCE: Willerson & Cohn, 2000.



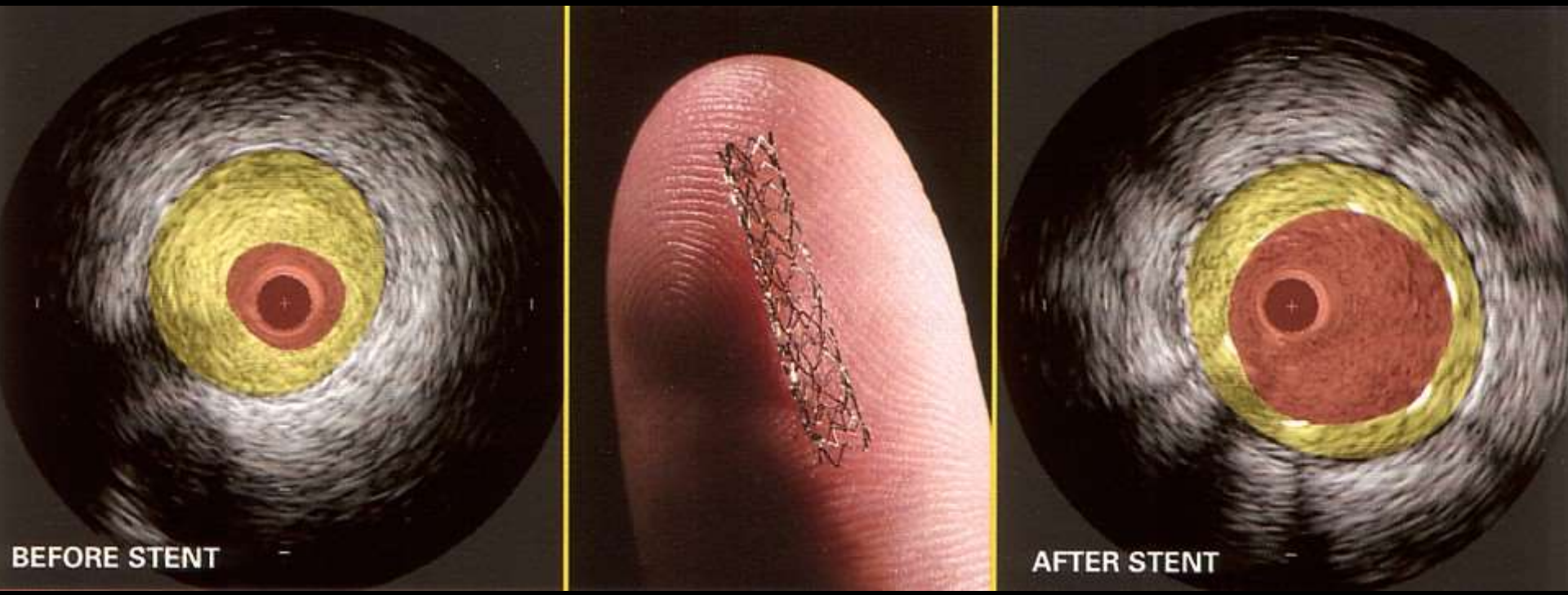
SOURCE: Pollock & Wilmore, 1990.



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

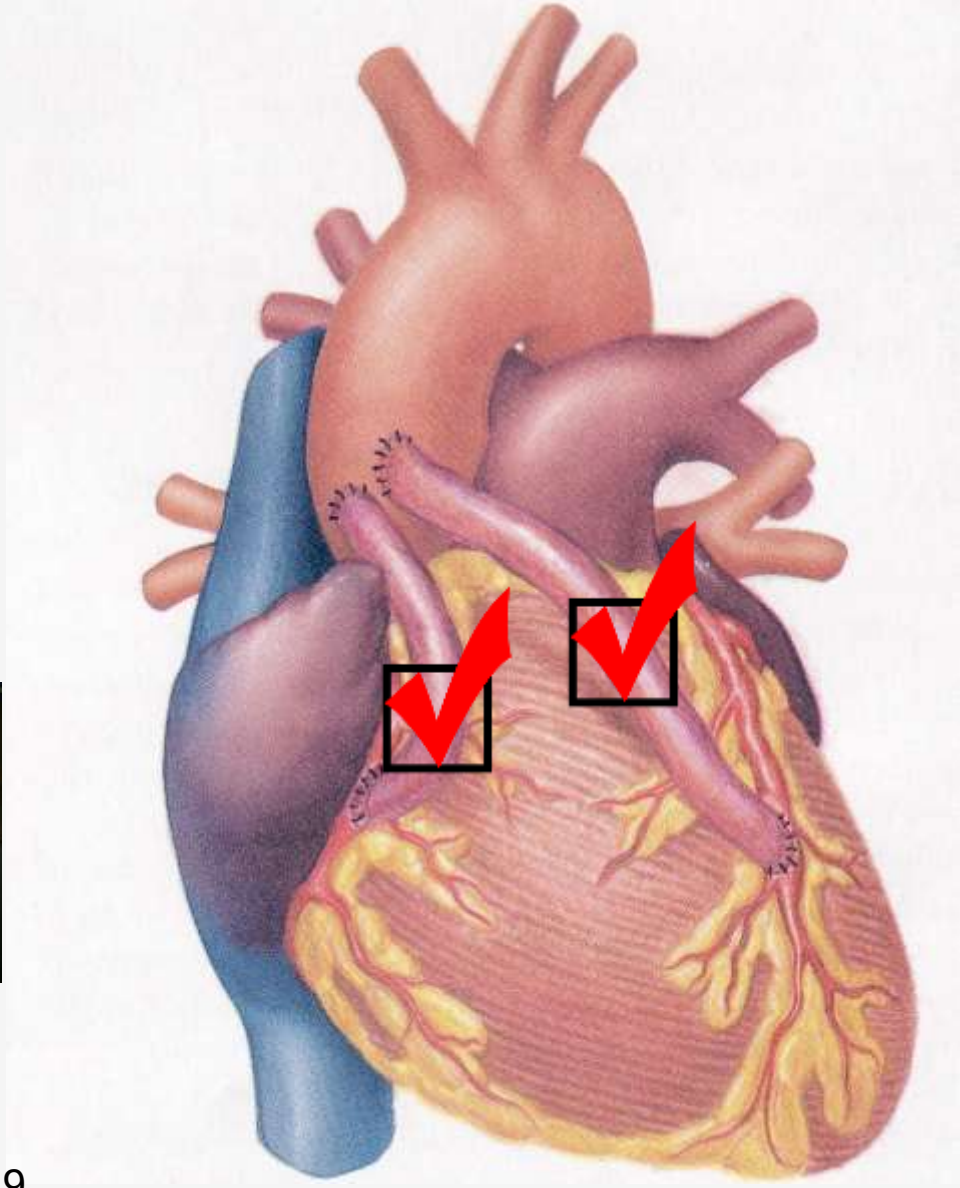


SOURCE: Kahn & Clark, National Geographic, Feb 2007.



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

CABG = Coronary Artery Bypass Graft



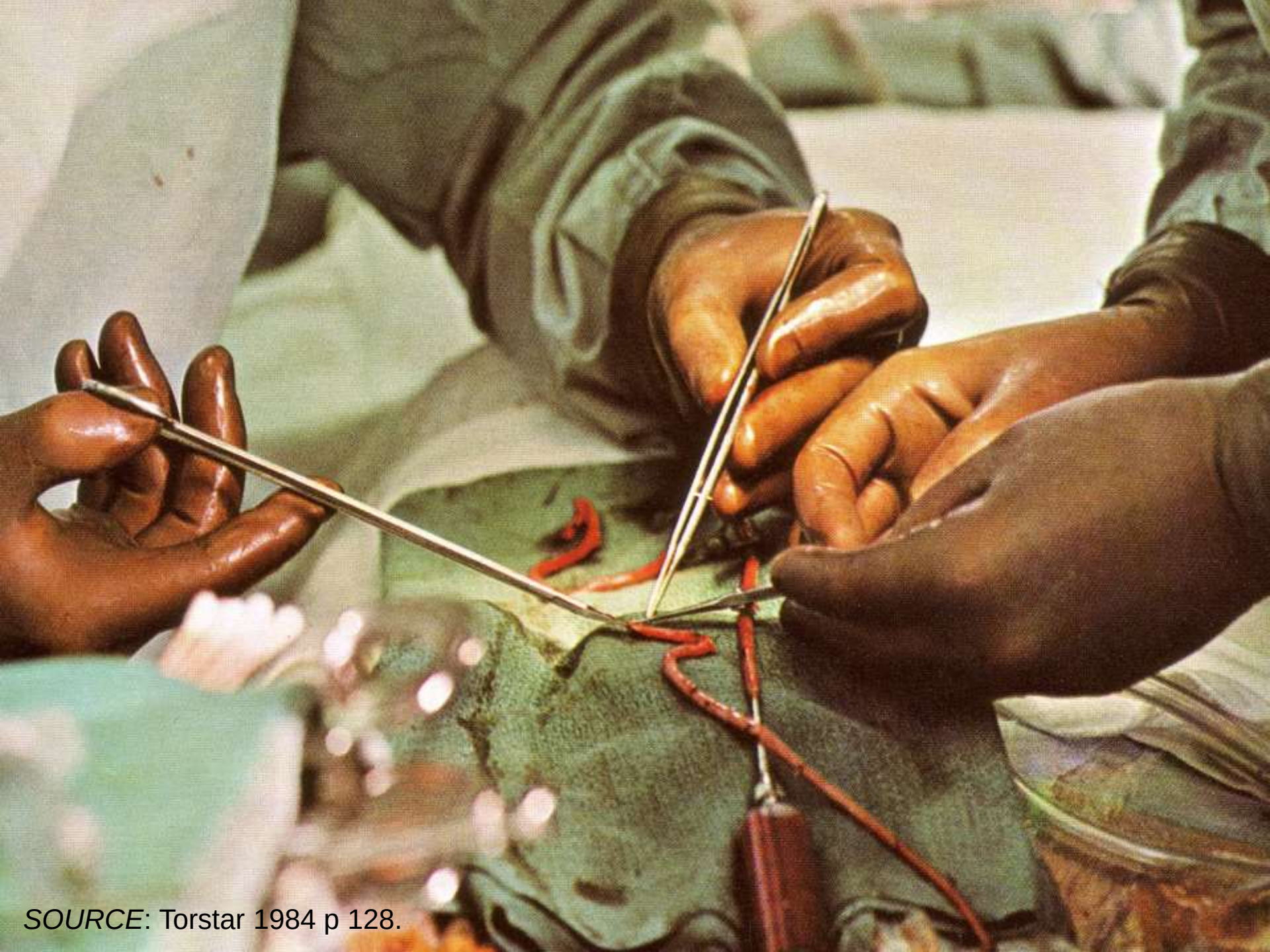
Double?

Triple?

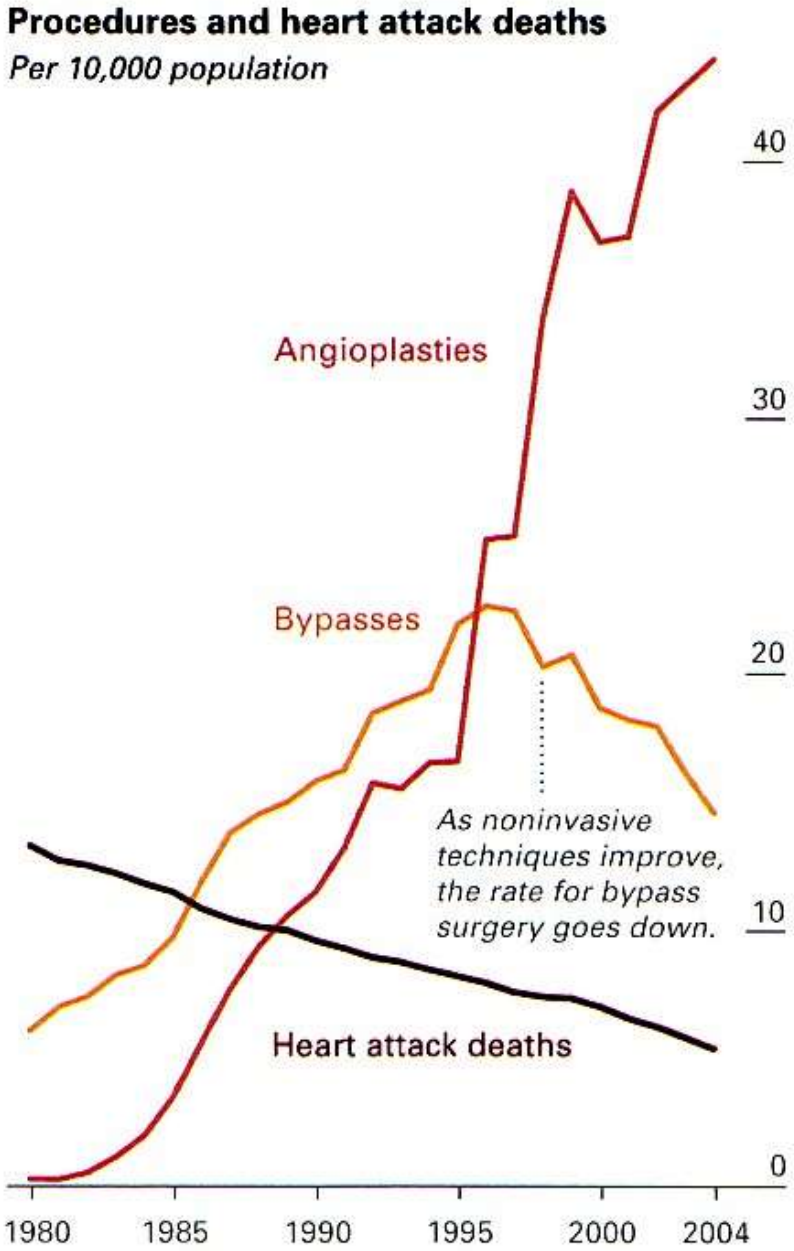
Quadruple?

Quintuple?

SI Fox 2013 fig 14.19



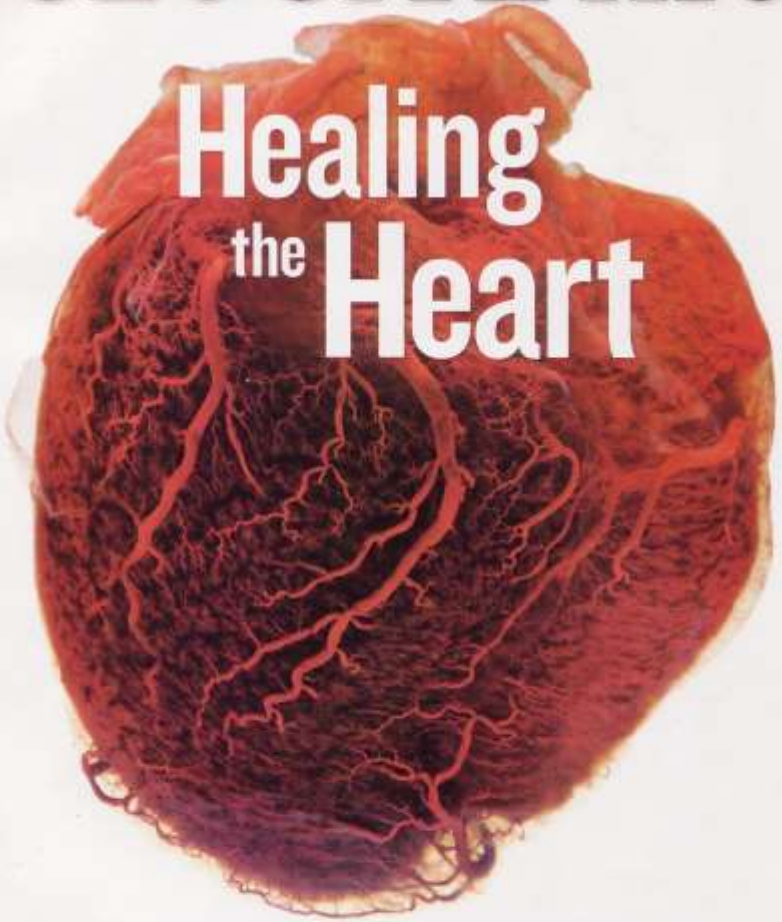
SOURCE: Torstar 1984 p 128.



National Geographic, 2007

NATIONALGEOGRAPHIC.COM/MAGAZINE FEBRUARY 2007

NATIONAL GEOGRAPHIC



Healing the Heart

Beauty on the Border 66 Curse of Nigerian Oil 88
Hawaii's Unearthly Worms 116 Forests of the Tide 132

Artificial heart = $125,000 - $250,000!
5400 await transplants, but only 2000 - 2600 donors are available…

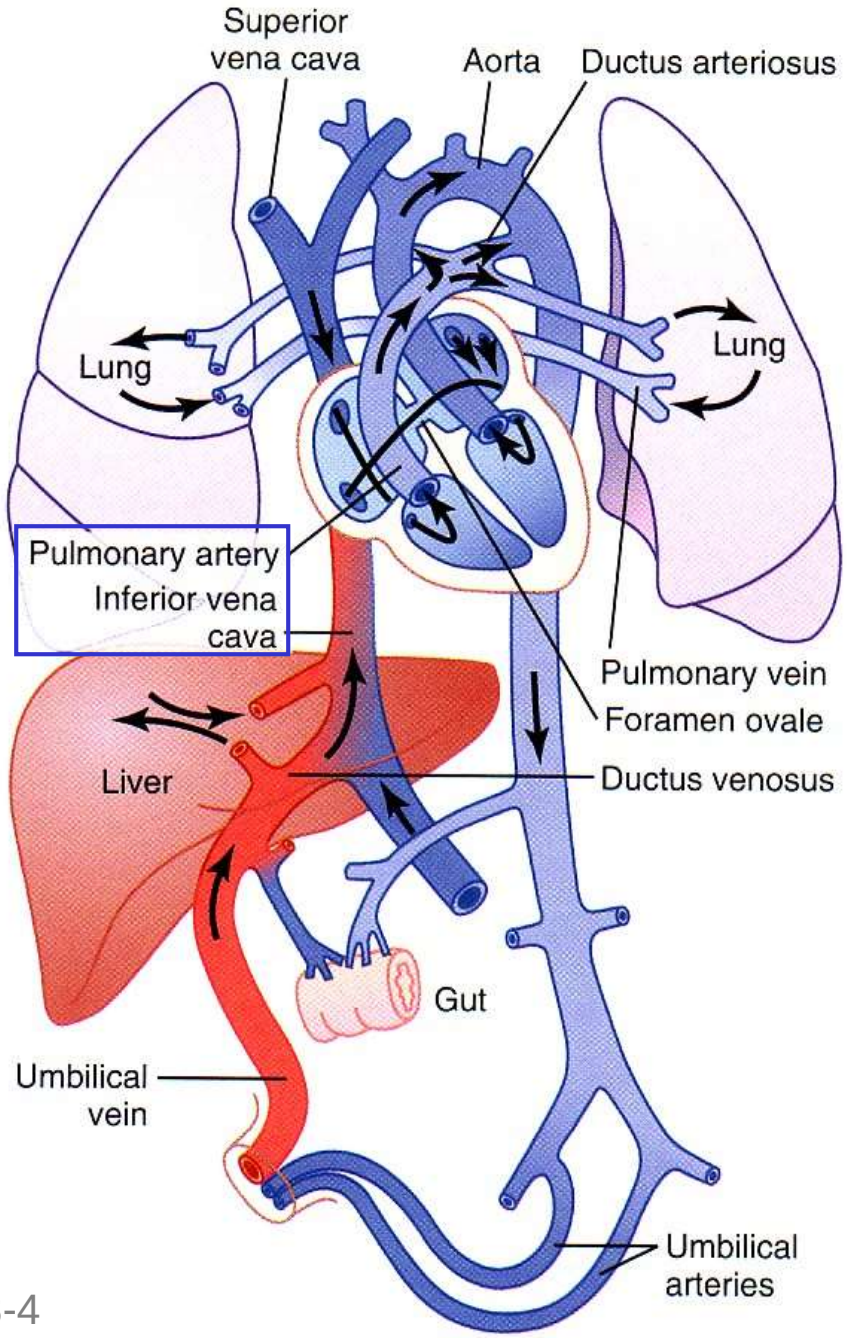
http://ngm.nationalgeographic.com/2007/02/hearts/hearts-text.html

Photograph by Robert Clark

Questions + Discussion

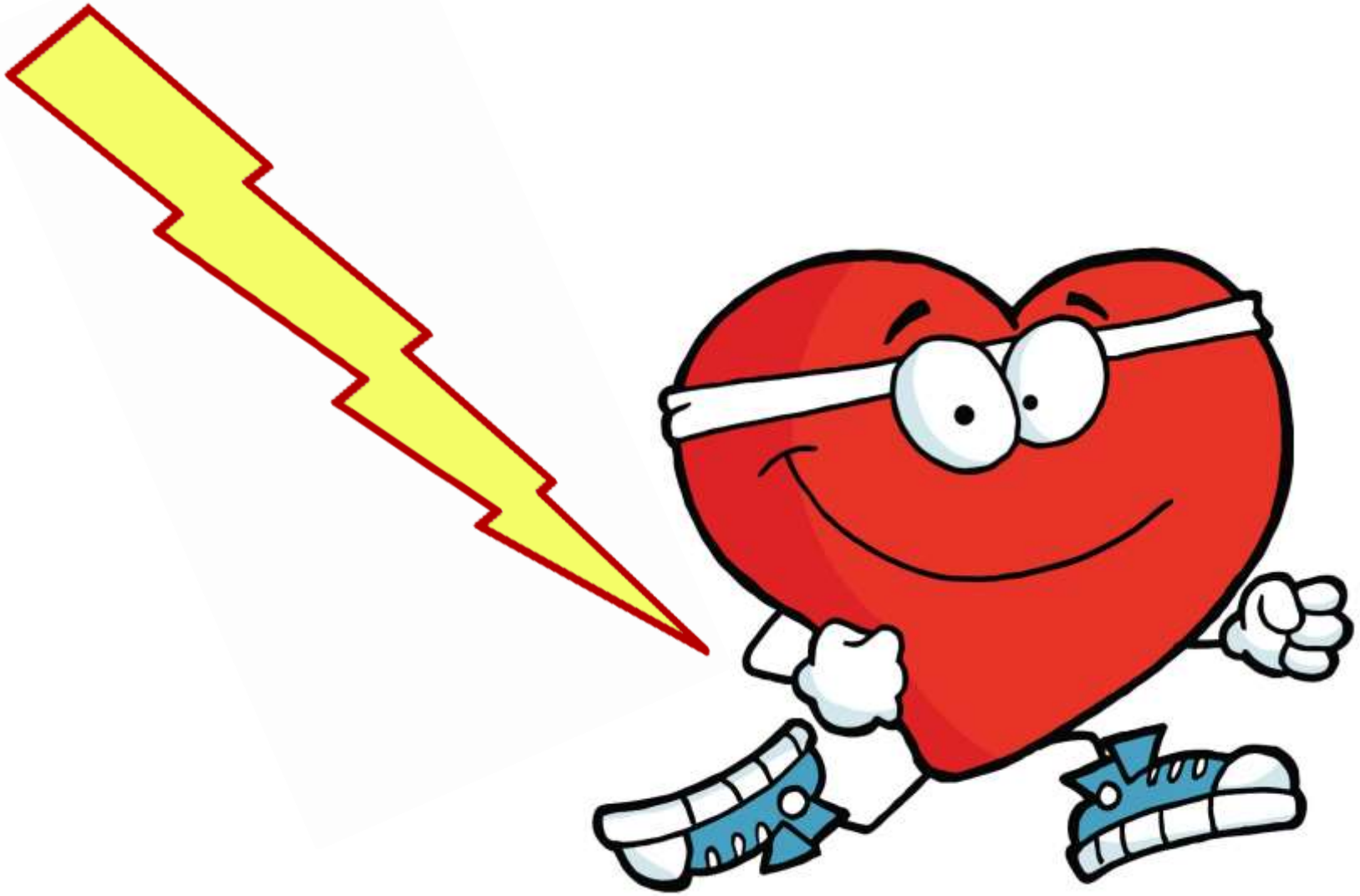
Additional Resource Slides: Development, ❤'s Electrical Highway, Coordinated Events…

Fetal Circulation
≡ Aqua Animal
Bypass Lungs
R → L ♥ Shunt

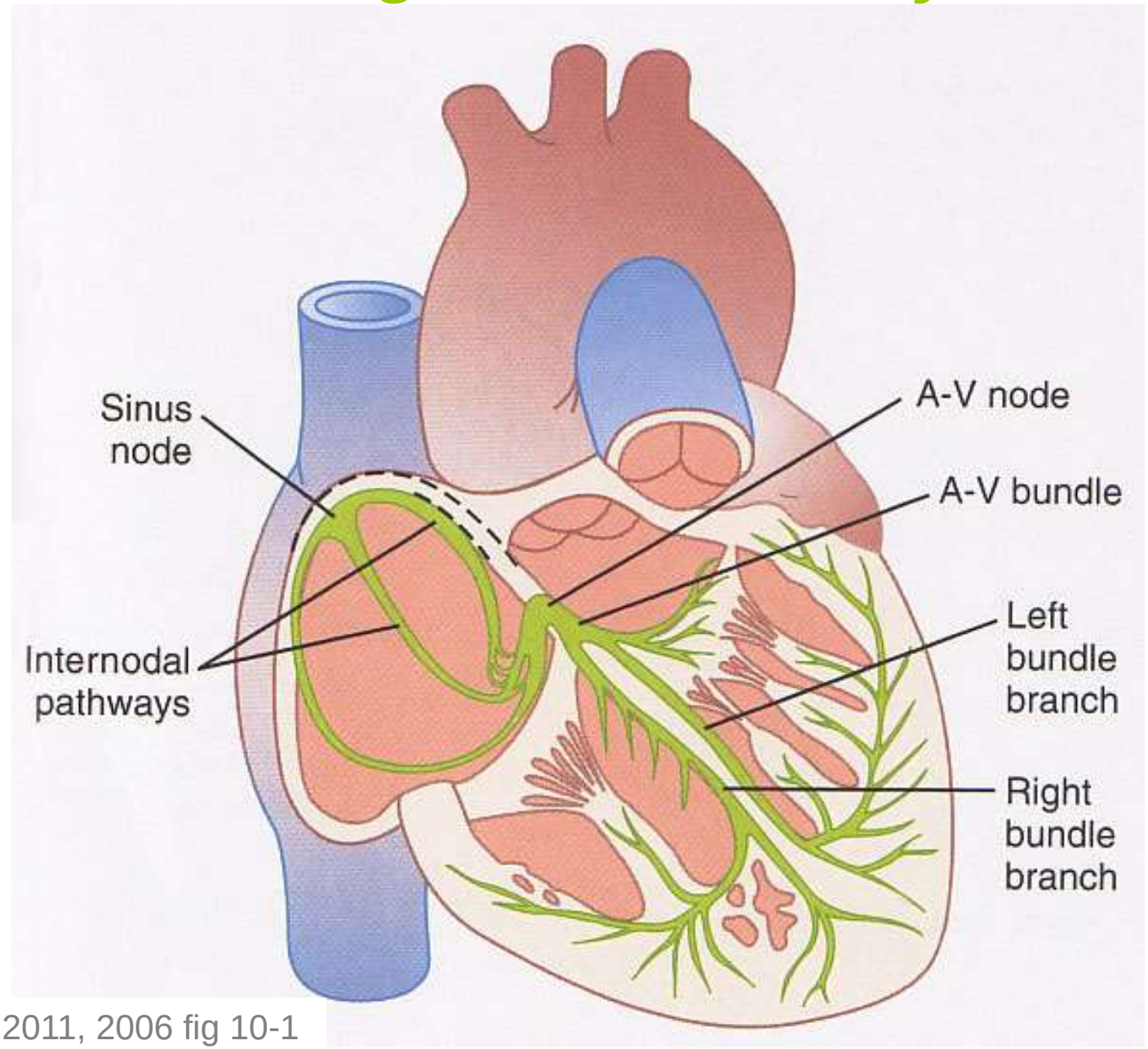


G&H 2016 fig 84-4, G&H 2011 fig 83-4

(Automatically) Shock the Heart then it Contracts!

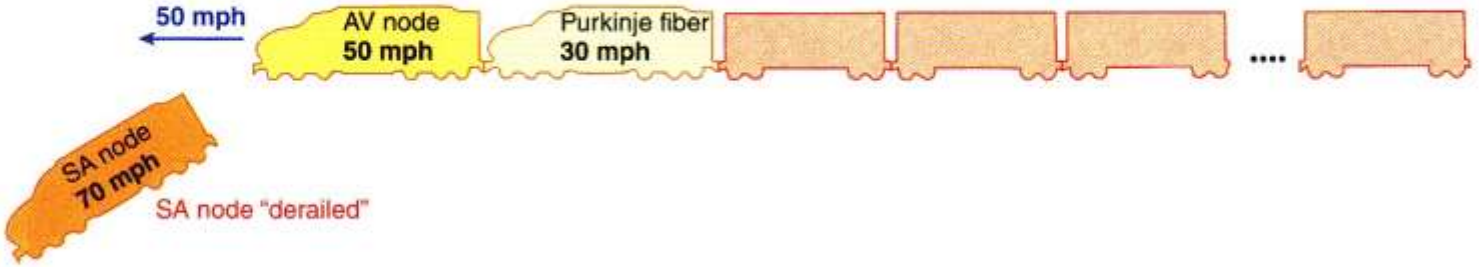


Intrinsic Regulation: Autorhythmic

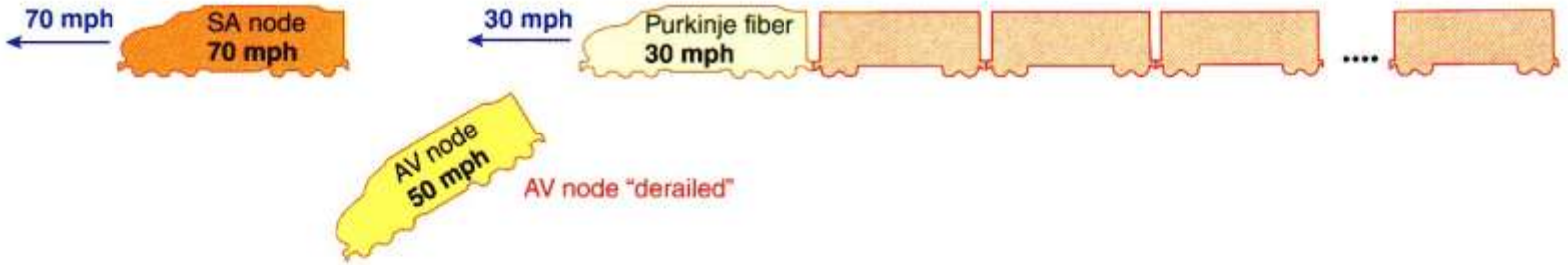


G&H 2016, 2011, 2006 fig 10-1

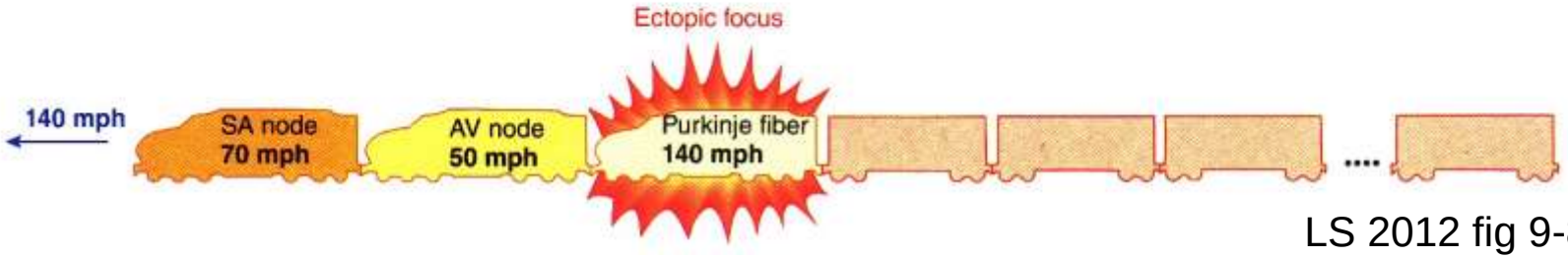
(a) Normal pacemaker activity: Whole train will go **70 mph** (heart rate set by SA node, the fastest autorhythmic tissue).



(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).

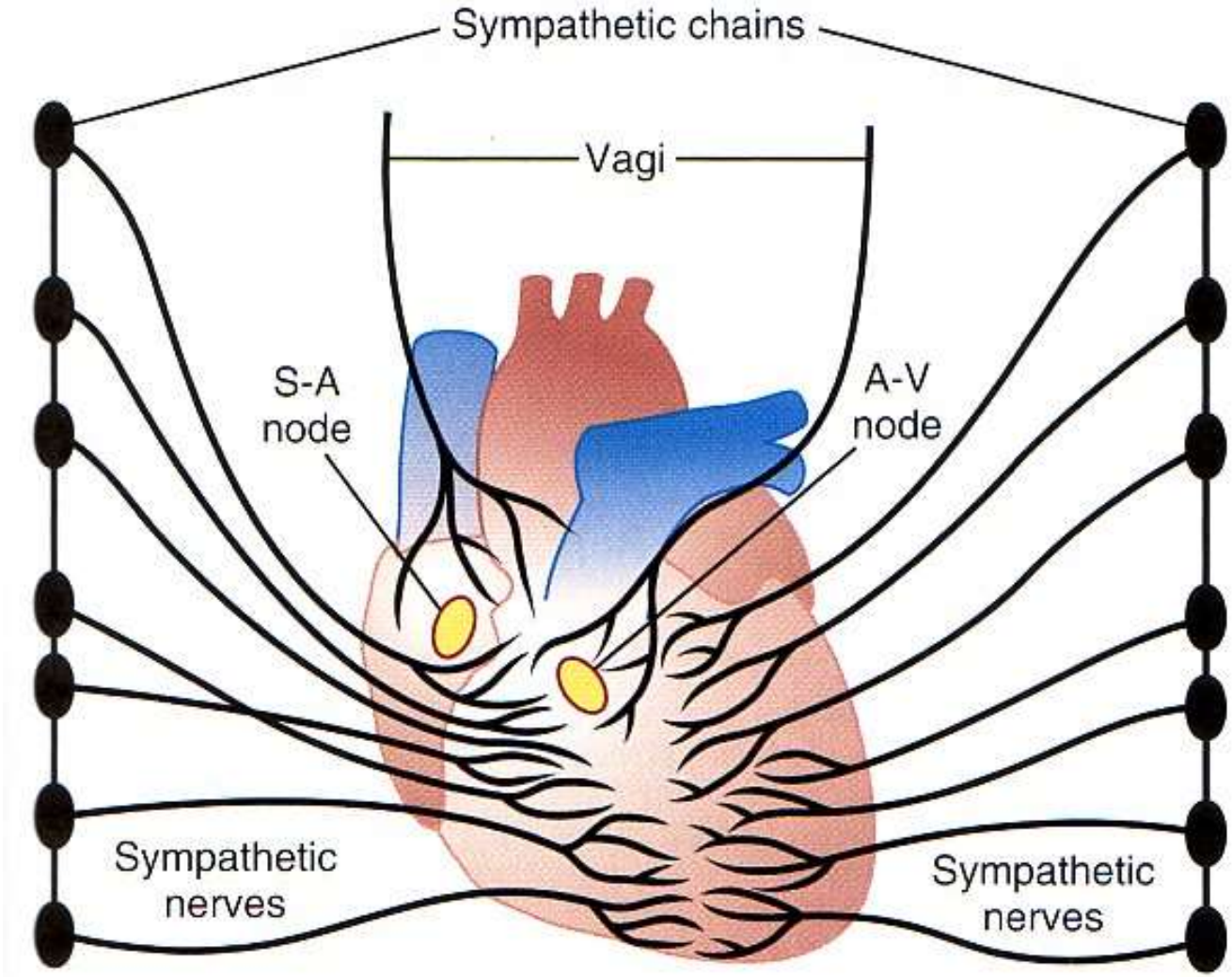


(c) Takeover of ventricular rate by the slower ventricular autorhythmic tissue in complete heart block: First part of train will go **70 mph**; last part will go **30 mph** (atria will be driven by SA node; ventricles will assume own, much slower rhythm).



LS 2012 fig 9-8 p 237

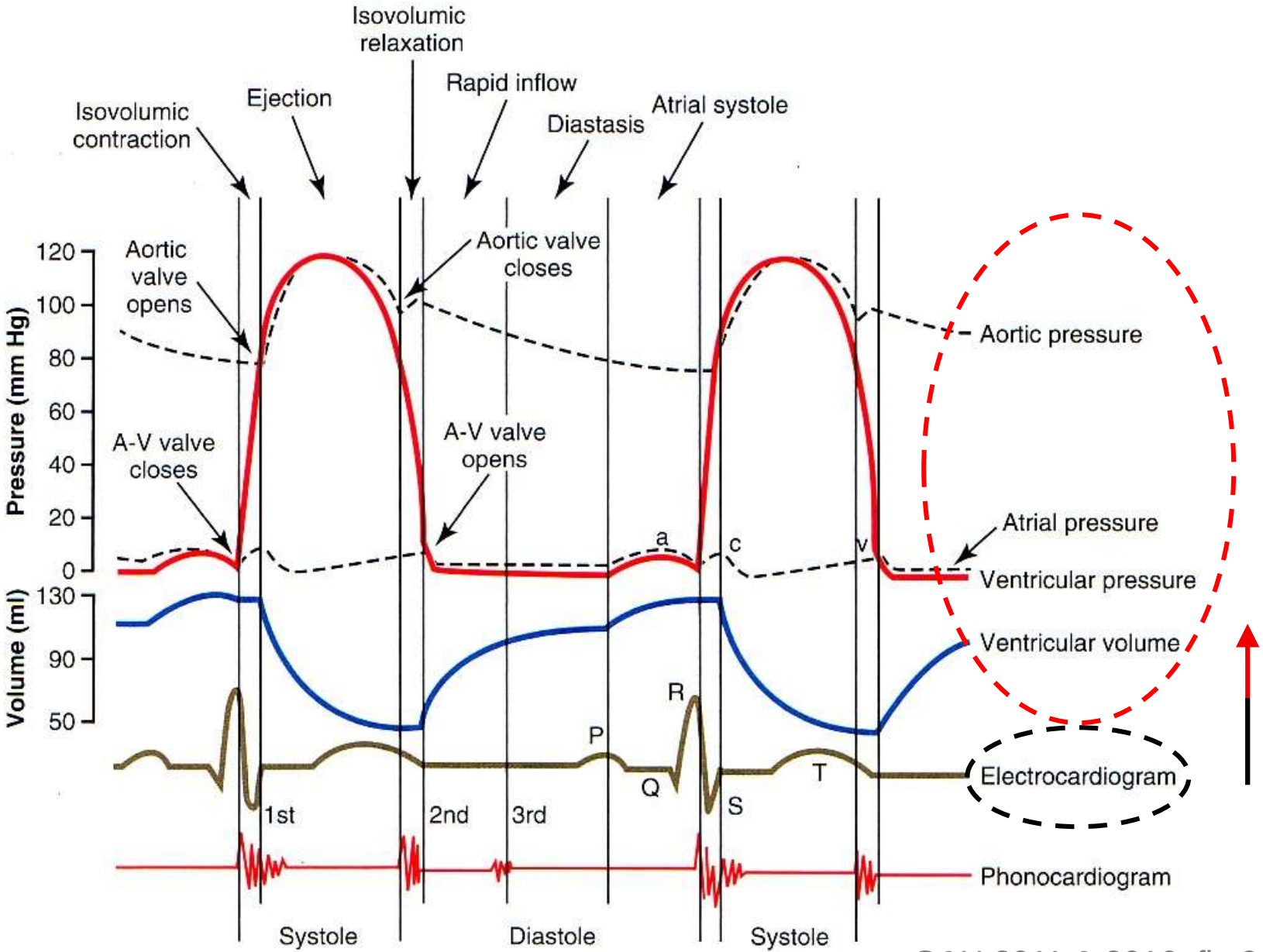
Extrinsic Regulation: Nervous



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

G&H 2011 fig 9-12
G&H 2016 fig 9-13

Electrical Events Precede Mechanical Events!



G&H 2011 & 2016 fig 9-6