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!

http://depts.washington.edu/physdx/heart/demo.html

G&H 2011 fig 9-6
(Automatically) Shock the Heart then it Contracts!
Pacemaker Potentials in Sinoatrial Node

- Self-induced action potential
- Threshold potential
- Slow depolarization (pacemaker potential)
- Na⁺ in
- Ca²⁺ in
- K⁺ out

Membrane potential (mV)

Time (msec)

L Sherwood 2012 fig 9-6
Action Potential in Ventricular Myocytes

- **Na⁺ in fast**
- **Ca²⁺ in slow**
- **Plateau phase of action potential**
- **K⁺ out fast**
- **Threshold potential**

Membrane potential (mV)

Time (msec)
Comparing Potentials in SA Node vs. Ventricular Myocytes

G&H 2011 fig 10-2
Myocytes/Muscle Cells

Intercalated Disc

Single nucleus

Adipocytes ≡ Fat Cells

H Howard, U of O Bio-optic Lab, 1984
Cardiac myocytes are mechanically linked & electrically connected!

Modified after L Sherwood 2012 fig 9-5
Intrinsic Regulation: Autorhythmic
(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

G&H 2006 fig 9-12
Lymphatic System

1. Lymph Nodes
2. Vessels
3. Lymph

No pump!

D Chiras 2003
Lymphatic System
Alternative System of Circulation or Drainage System

Lymph Vessels || Veins
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 ≥ 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
Heart Disease Death Rates, 2000-2006
Adults Ages 35+, by County

Eugene, OR
MK is lowest!

AK low, too!

Jackson, MS

http://www.cdc.gov/heartDisease/statistics.htm
59 yr HTN ♀

Torstar 1984 p 77
What is the Ultimate Cause of Death?

1. ↓ Q, CO or Cardiac Output
2. Pulmonary damming w/edema
3. Cardiac fibrillation
4. Thromboembolism
5. Cardiac rupture

G&H 2011 p 250
Systolic Stretch Due to Necrotic Tissue

Normal Muscle

Nonfunctional Muscle

Systolic Stretch
Treatment Triad

- Exercise
- Dietary Modification
- Drugs/Surgery

NB: Last blasted resort!!
**Figure 9-35**

Extent of myocardial damage as a function of the size of the occluded vessel.
CARDIOVASCULAR MORTALITY (average annual incidence per 1,000)

CIGARETTES SMOKED PER DAY

- None: 7
- Less than 20: 8.4
- 20: 10.2
- More than 20: 12.4
- Quit One Year: 7
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
Selected Atherosclerotic Genetic Determinants – Ultra-short List!

Genes for HDL, LDL+ receptors, Apolipoproteins Apo B-100, Apo-E, Apo-M, lipoprotein a/Lpₐ, 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

5 forms of cholesterol:
Chylomicrons, VLDL, LDL, IDL, HDL

β

Atherogenic

Anti-Atherogenic

β-VLDL + LDL = Faucet

HDL = Drain
Historical Hypotheses for Atherosclerosis Development

**Ross & Glomset**
- Endothelial Injury
  - Platelet Adherence
    - PDGF Release
      - Cell Proliferation
        - Advanced Lesion

**Steinberg & Witztum**
- High Plasma LDL
  - LDL Infiltration into Intima
    - Oxidized LDL + Macrophages
      - Foam Cells
        - Fatty Streak
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.

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.12

“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.
Middle Cerebral Artery Branches


...Cerebral vasculature! Oh my!
The Window to the CV System?
Renal Vasculature

Figure 37-1 Devices for percutaneous transluminal coronary interventions. A, Coronary balloon. B, Rotational atherectomy burr (Rotablator). C, Coronary stent.
Guiding catheter in proper position

Balloon catheter approaching site of blockage

Balloon catheter advanced to middle of blockage...

Balloon inflated...

then deflated; blockage reduced

CABG = Coronary Artery Bypass Graft
Procedures and heart attack deaths
Per 10,000 population

As noninvasive techniques improve, the rate for bypass surgery goes down.

Sources: Thomas Thom, National Heart, Lung, and Blood Institute; Gautam Gowrisankaran, Washington University in St. Louis; Salim Yusuf, McMaster University, The INTERHEART Study.
Healing the Heart

Beauty on the Border 66  Curse of Nigerian Oil 98
Hawaii’s Unearthly Worms 118  Forests of the Tide 132
CardioWest artificial heart = $106,000!
3000 await transplants, but only 2100 donors are available...