BI 358 Lecture 9

I. Announcements CV Physiol + Atherosclerosis today. Next time endocrinology & hopefully start reproduction. All next week super guest lectures! Learning + much fun!

II. Cardiovascular Connections G&H + LS + Torstar books
   A. Blood flow through heart & periphery G&H fig 9-1 + LS
   B. Composite events of cardiac cycle G&H fig 9-6
   C. Autorhythmic cells, ‘s electrical-highway G&H fig 10-1, 10-2

III. Lymphatic System D Chiras, Torstar Books, G&H 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!
Veins ➔ Atria ➔ Ventricles ➔ Arteries

Superior vena cava (from head)

Right atrium

Inferior vena cava (from body)

Right ventricle

Endocardium

Myocardium

Pericardium

Left atrium

Left ventricle

Aorta

http://www.nhlbi.nih.gov/health/health-topics/topics/hhw/contraction.html
Coronary Circulation \equiv Crowns the Heart!
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.
Coronary Arteries Pierce the Heart from Epi to Endo
Anastomoses May Provide Lifesaving Collateral Circulation!!
Cardiac Cycle

Systole
Contract & Empty

Diastole
Relax & Fill

Heart transition from Systole (contract & empty) to Diastole (relax & fill).
Coronary blood flow (ml/min)

Systole

Contract & Empty

Diastole

Relax & Fill

G&H 2011 fig 21-4
Electrical Events Precede Mechanical Events!
(Automatically) Shock the Heart then it Contracts!
Intrinsic Regulation: Autorhythmic

G&H 2006 fig 10-1
(a) Normal pacemaker activity: Whole train will go \textbf{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 \textbf{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 \textbf{70 mph}; last part will go \textbf{30 mph} (atria will be driven by SA node; ventricles will assume own, much slower rhythm).

Ectopic focus
Pacemaker Potentials in Sinoatrial Node
Action Potential in Ventricular Myocytes

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

Membrane potential (mV) vs 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
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!
Lymphatic System
Alternative System of Circulation or Drainage System
Lymph Vessels || Veins
Elephantiasis: Lymphatic Blockage Due to Mosquito-Borne Parasitic Worm

L Sherwood 2007
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
AMI
CVDs
CVA
TIA
HTN
PAD/PVD
**FIGURE 9-35**

Extent of myocardial damage as a function of the size of the occluded vessel.
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
Mild ischemia
Non-functional

Mild ischemia
Non-functional
Dead fibers

Nonfunctional

Dead fibers
Fibrous tissue

G&H fig 21-8
Treatment Triad

NB: Last blasted resort!!

Drugs/Surgery

Exercise

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

Increased risk of heart disease
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

+ = Faucet

LDL

Total Cholesterol Level

HDL = Drain

Bathtub

“I don’t think the total cholesterol test by itself is worth a damn.”

—Eliot Corday
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).
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.
MRI Hyperintensities, Hypertension & Dementia

NAHL CSPI, Jan-Feb 2014
Middle Cerebral Artery Branches


...Cerebral vasculature! Oh my!

= Artery of Stroke
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.
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 GOWRI-SANKARAN, WASHINGTON UNIVERSITY IN ST. LOUIS; SALIM YUSUF; MCMASTER UNIVERSITY, THE INTERHEART STUDY
CardioWest artificial heart = $106,000! 3000 await transplants, but only 2100 donors are available...