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° modifiable risks: cigarette smoking, hypertension,  
       hypercholesterolemia/hyperlipidemia, lack of exercise
   D. Treatment triad, _PTCA, CABG_, prevention, practical tips!

VII. **Additional Resources**  Development, electrical highway…
A Antigens
(Agglutinogens)
B Antigens
(Agglutinogens)
A & B Antigens
(Agglutinogens)
No Antigens
(Agglutinogens)
A Antibodies
(Agglutinins)
$1^0$ Q? Clumping in Any Wells?

Here? Here? Here?

Type AB+

Source: S Wong, BI 121 Lab, 2016
Blood Type Distribution within the United States

- Type O+: 38%
- Type A+: 34%
- Type B+: 9%
- Type AB+: 2%
- Type A-: 3%
- Type B-: 1%
- Type O-: 7%
- Type AB-: 6%

*NB:* O+ & A+ make up > 2/3, + > -
Universal Blood
All like Type O!

Key
- Fucose
- Galactose
- Glucose
- N-acetylgalactosamine
Erythroblastosis Fetalis?

Rh- mom
Rh+ baby

Erythroblastosis Fetalis or Hemolytic Disease of the Unborn/Newborn

Throw Blanket Over This Step!

(a) First pregnancy

(b) Placenta

(c) Second pregnancy

Rh- mother

First Rh+ fetus

Rh+ antigens

Second Rh+ fetus
Inject Mom with RhoGam $\leq$ 48-72 hr $>$ each Rh+ Pregnancy

The Blanket is RhoGam $\rightarrow$ Masks the Mom’s Immune System!
Wear Red next Friday Feb 7th!
Help raise awareness about Women & ❤️ disease

http://www.goredforwomen.org/
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!

Cardiovascular (CV) = Heart + Vessels + Blood!
Heart Protection & Layers

Aorta
Superior vena cava
Right atrium
Right ventricle
Inferior vena cava

Endocardium
Myocardium
Epicardium

Pericardial cavity
Fibrous pericardium
Parietal pericardium

EPI
MYO
ENDO
PERI

Torstar 1984 p 34
What the heck’s a *bruit*? (brwe, brōˈoot) [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 $\heartsuit = 4$-chambered box? 2 separate pumps?

- Upper = Atria
- Lower = Ventricles

Diagrams:
- RA (Right Atrium)
- LA (Left Atrium)
- RV (Right Ventricle)
- LV (Left Ventricle)

- Pulmonary System
- Systemic Power

- Primer Pumps
- Power Pumps
Coarctation, Crimping or Narrowing of the Aorta

Humanocardiacard - 4 unique valves?
2 valve sets?

**Semilunar** = _Half-moon shaped_
1. Pulmonic/Pulmonary
2. Aortic

**AV** = **Atrioventricular**
3. R AV = Tricuspid
4. L AV = Mitral/Bicuspid
MITRAL VALVE

- Cusp
- Chordae tendineae
- Papillary muscles

AORTIC VALVE

- Cusp

G&H 2006 fig 9-6; G&H 2011 fig 9-7; G&H 2016 fig 9-8
Heart Valve Orientation & Scaffolding

- Pulmonary ring
- Aortic ring
- Mitral ring
- Tricuspid ring
- Muscle fiber
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
Veins ➔ Atria ➔ Ventricles ➔ Arteries

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

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

LS2016
Veins ➔ Atria ➔ Ventricles ➔ Arteries

https://www.nhlbi.nih.gov/health-topics/how-heart-works
https://www.youtube.com/watch?v=zJXAIh9VDDU
Coronary Circulation ≡ Crowns the Heart!

[Diagram of the heart with labeled coronary arteries and the aortic valve.]
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

Epicardial coronary arteries

Subendocardial arterial plexus

Cardiac muscle
Anastomoses May Provide Lifesaving Collateral Circulation!!

Artery

Vein

Artery

Vein

G&H 2011 & 2016 fig 21-6
Cardiac Cycle

Systole
Contract & Empty

Diastole
Relax & Fill
Coronary blood flow (ml/min)

Systole: Contract & Empty
Diastole: 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.

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

https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_heart_disease.htm
Area of cardiac muscle deprived of blood supply if coronary vessel is blocked at point A:

Right coronary artery
Right ventricle

Area of cardiac muscle deprived of blood supply if coronary vessel is blocked at point B:

Left coronary artery
Left ventricle

**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. \( \downarrow \dot{Q}, \text{CO} \) or Cardiac Output

2. Pulmonary damming \( \text{w/edema} \)

3. Cardiac fibrillation

4. Cardiac rupture (occasionally)

5. Thromboembolism
   (2011 ed. but not 2016)
Systolic Stretch Due to Necrotic Tissue

- Normal Muscle
- Nonfunctional Muscle
- Systolic Stretch
Treatment Triad

Drugs/Surgery

Exercise

Dietary Modification

NB: Last blasted resort!!
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/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

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

Atherogenic

Anti-Atherogenic

Bruce Kottke

Total Cholesterol Level

Bathtub

HDL = Drain

β - VLDL + LDL = Faucet

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

Biological Artifact!?
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

10 regulator of lipoprotein metabolism!

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

1. 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.

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

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

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

5. 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.

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

7. Cap Rupture
   The cap ruptures.

8. 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.)
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
DISEASED CAROTID ARTERY

HEALTHY CAROTID ARTERY

SOURCE: Lifeline Screening, 2007
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.
CABG = Coronary Artery Bypass Graft

Double?
Triple?
Quadruple?
Quintuple?

SI Fox 2013 fig 14.19
PROCEDURES AND HEART ATTACK DEATHS
Per 10,000 population

- Angioplasties
- Bypasses
- Heart attack deaths

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.
Artificial heart = $125,000 - $250,000!

5400 await transplants, but only 2000 - 2600 donors are available…
Questions + Discussion
Additional Resource Slides: Development, ♥‘s Electrical Highway, Coordinated Events…
Fetal Circulation
≡ Aqua Animal
Bypass Lungs
\( R \rightarrow L \) \( \heartsuit \) 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).
Extrinsic Regulation: Nervous

NB: + Extrinsic Hormonal e.g. Adrenal Epi + NE
Electrical Events Precede Mechanical Events!