BI 358 Lecture 8

I. Announcements Kraig Jacobson MD, Allergy & Asthma Research Associates, Oak Street Medical, next Tues Feb 6th!
Update on outlines and paper drafts. WBC lab photo! Q?

II. Immunology II G&H 2016 ch 35, G&H 2011 ch 34
A. Recap cf: Innate vs. adaptive immunity G&H, LS +...
Innate immunity eg inflammation, interferon, complement
B. Antibody (Ab=Ig) structure, subclasses, mechanisms
  G&H + LS + Davey fig 2.4 p 19, fig 4.2 p 42, tab 4.1 p 49
C. Mom’s milk Scientific American
D. Immune Regulation + Allergy: G&H

III. Cardiovascular Physiology Torstar Books, G&H, Katz, LS,...
A. Cardiovascular system? Figure-8 loop D Chiras (DC), LS
B. Fetal development & circulation Torstar Books, G&H
C. Layers: peri-, epi-, myo- & endocardium Torstar Books
D.❤️ structure & function G&H fig 9-7, LS...
E. Blood flow through ❤️ & periphery G&H fig 9-1, LS, DC
F. Coronary circulation & the cardiac cycle, composite events
  G&H fig 21-3, Katz, G&H fig 21-5, 21-6, 21-4; ch 9 fig 9-6
Neutrophil Twins!!

Lymphocyte

Lymphocyte

Lymphocyte

Lymphocyte

Lymphocyte
Allergic Reactions, Mast Cells & Basophils?

Allergen = ●
IgE = Y

up to ½ million per cell!

Mucous Membranes/Blood

Bradykinin
Eosinophil & Neutrophil
Chemotactic Substances
Heparin
Histamine
Platelet Activating Factors
Protease
Serotonin
Toxic Leukotrienes/SRSA

ASTHMA
1. Break in skin $\rightarrow$ Bacteria enter & reproduce
2. Mast cells release histamine
3. Vessel wall becomes sticky $\rightarrow$ Neutrophils & monocytes attach $\rightarrow$ diapedesis $\rightarrow$ chemotaxis
4. Chemotaxins attract more Neutrophils & monocytes
5. Monocytes swell $\rightarrow$ Macrophages

Redness, Heat, Swelling, Pain!
Glucocorticoids throw blanket over entire inflammatory process!

1. Certainly warranted to quiet down immune system during extreme flare ups of arthritis, asthma, poison ivy, rash, but must consider:

2. Destroy lymphocytes in lymphoid tissues.

3. \( \downarrow \) Antibody/Immunoglobulin (Ig) production.

4. Make susceptible to bacterial infections.
Viruses coming!

Don’t breathe on me, Paul!

Interferon Mechanisms

1. Virus enters a cell
2. Virus replicates in invaded cell
3. Cell releases interferon
4. Interferon binds with receptors on uninvaded cells
5. Uninvaded cells produce inactive enzymes capable of breaking down viral messenger RNA and of inhibiting protein synthesis
6. Virus enters cell that has been acted upon by interferon
7. Virus-blocking enzymes are activated
8. Virus is unable to multiply in newly invaded cells
Activated Complement

The Big MAC to ❤️! Osmotic explosion!
WBC Adverse Effects

- Leukocytes
- Anti-cancer drugs
- Benzene
- Nuclear blast
- Radiation

↓ Body defense vs. μ organisms!

↓ Professional phagocytes esp: Neutrophils, Macrophages

Savior Lymphoid tissues or bone marrow transplant?

cf: Leukemia ≡ uncontrolled WBC proliferation, yet inadequate defense → other cell lines displaced → overwhelming infections & bleeding...
Commander-in-Chief of the Immune System!!

HIV tips the balance!!
Cell-Mediated Immunity

Thymus

Peripheral lymphoid tissue

T lymphocyte

Activated T lymphocytes

Antigen

Plasma cell

Humoral Immunity

Common lymphoid progenitor cell

Hemopoietic stem cells

Developing B cell

G&H fig 34-1 2011

cf: fig 35-1 G&H 2016
Cell-cell adhesion proteins → T-cell receptor → Foreign protein → MHC protein

Antigen-presenting cell
The vital union that activates a helper T cell takes place only when the T cell recognizes both a “self” marker (rectangle) and a “nonself” antigen (triangle) on a macrophage.
Clonal Selection

Population of unactivated B cells, each a member of a different B-cell clone that makes a specific receptor, which is displayed on the membrane surface as a BCR.

Binding of antigen and interaction with helper T cell stimulates the matching B cells to divide and expand the clone of selected cells.

Plasma cells

Most of the new B cells differentiate into plasma cells, which secrete antibodies.

Antibodies

Memory B cells

A few of the new B cells differentiate into memory B cells, which respond to a later encounter with the same antigen.

L Sherwood 2012; cf: G&H 2016 fig 35-2; G&H 2011 fig 34-2
Typical IgG Antibody Structure

How do antibodies work?

Identical, specific antigen-binding sites

Antigen

Antibody

KEY

V = variable region
C = constant region

Immunoglobulin G

Source: Visual Science
1. Agglutination

2. Complement

3. Opsonization

4. Killer Cells

L Sherwood 2012
### TABLE 4.1 Characteristics and functions of the human immunoglobulin classes

<table>
<thead>
<tr>
<th>Immunoglobulin class</th>
<th>IgG</th>
<th>IgA</th>
<th>IgM</th>
<th>IgD</th>
<th>IgE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heavy-chain type</td>
<td>γ</td>
<td>α</td>
<td>μ</td>
<td>δ</td>
<td>ε</td>
</tr>
<tr>
<td>Number of constant domains in each heavy chain</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Relative molecular mass ($M_r$) of monomer</td>
<td>150000</td>
<td>160000</td>
<td>180000</td>
<td>185000</td>
<td>200000</td>
</tr>
<tr>
<td>Normally found as polymer?</td>
<td>no</td>
<td>dimer</td>
<td>pentamer</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Valency: number of antigen binding sites in normal form (i.e. monomer or polymer)</td>
<td>2</td>
<td>4</td>
<td>10</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Percentage of total immunoglobulin in serum</td>
<td>70–80</td>
<td>13–20</td>
<td>6–10</td>
<td>0–1</td>
<td>0.002</td>
</tr>
<tr>
<td>Serum half-life (days)</td>
<td>23</td>
<td>5.8</td>
<td>5.1</td>
<td>2.8</td>
<td>2.3</td>
</tr>
<tr>
<td>Ability to trigger complement cascade*</td>
<td>++</td>
<td>–</td>
<td>+++</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Can cross placenta from mother to foetus*</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Binds to Staphylococcal cell walls*</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Binds to macrophage Fc receptors*</td>
<td>+</td>
<td>–</td>
<td>(+)?</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Binds to neutrophil Fc receptors*</td>
<td>+</td>
<td>+</td>
<td>(+)?</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Binds to mast cell and basophil Fc receptors</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>+++</td>
</tr>
<tr>
<td>Binds to platelets</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

*For IgG this refers only to some subclasses.
IgA = Secretory $A_b$

Valence? 4

Davey 1990 p 50
# Immune Benefits of Breast Milk at a Glance

<table>
<thead>
<tr>
<th>Component</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>White Blood Cells</strong></td>
<td></td>
</tr>
<tr>
<td>B lymphocytes</td>
<td>Give rise to antibodies targeted against specific microbes.</td>
</tr>
<tr>
<td>Macrophages</td>
<td>Kill microbes outright in the baby's gut, produce lysozyme and activate other components of the immune system.</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>May act as phagocytes, injecting bacteria in baby's digestive system.</td>
</tr>
<tr>
<td>T lymphocytes</td>
<td>Kill infected cells directly or send out chemical messages to mobilize other defenses. They proliferate in the presence of organisms that cause serious illness in infants. They also manufacture compounds that can strengthen a child's own immune response.</td>
</tr>
<tr>
<td>Molecules</td>
<td>Description</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Antibodies of secretory IgA class</td>
<td>Bind to microbes in baby's digestive tract and thereby prevent them from passing through walls of the gut into body's tissues.</td>
</tr>
<tr>
<td>B$_{12}$ binding protein</td>
<td>Reduces amount of vitamin B$_{12}$, which bacteria need in order to grow.</td>
</tr>
<tr>
<td>Bifidus factor</td>
<td>Promotes growth of <em>Lactobacillus bifidus</em>, a harmless bacterium, in baby's gut. Growth of such nonpathogenic bacteria helps to crowd out dangerous varieties.</td>
</tr>
<tr>
<td>Fatty acids</td>
<td>Disrupt membranes surrounding certain viruses and destroy them.</td>
</tr>
<tr>
<td>Fibronectin</td>
<td>Increases antimicrobial activity of macrophages; helps to repair tissues that have been damaged by immune reactions in baby's gut.</td>
</tr>
<tr>
<td>Gamma-interferon</td>
<td>Enhances antimicrobial activity of immune cells.</td>
</tr>
<tr>
<td>Hormones and growth factors</td>
<td>Stimulate baby’s digestive tract to mature more quickly. Once the initially “leaky” membranes lining the gut mature, infants become less vulnerable to microorganisms.</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Lactoferrin</td>
<td>Binds to iron, a mineral many bacteria need to survive. By reducing the available amount of iron, lactoferrin thwarts growth of pathogenic bacteria.</td>
</tr>
<tr>
<td>Lysozyme</td>
<td>Kills bacteria by disrupting their cell walls.</td>
</tr>
<tr>
<td>Mucins</td>
<td>Adhere to bacteria and viruses, thus keeping such microorganisms from attaching to mucosal surfaces.</td>
</tr>
<tr>
<td>Oligosaccharides</td>
<td>Bind to microorganisms and bar them from attaching to mucosal surfaces.</td>
</tr>
</tbody>
</table>
IgM = Macroglobulin
Pentamer!!!!!

Valence? 10

Davey 1990 p 51
Dendritic Cells: Specialized Antigen-Presenting Cells (APCs) Sentinels in Almost Every Tissue!
Protein messages trigger responses

The pivotal discovery of lymphokines, the proteins by which immune cells communicate with each other, ushered in a new era of medical research. Scientists now produce some of them in sufficient quantities for promising therapies against a host of immunologic diseases.

1. Engulfing an invading organism and coupling with a helper T cell, a macrophage secretes the lymphokine interleukin-1 (IL-1), which activates the helper T cell. IL-1 also stimulates the brain to raise the body’s temperature, causing fever, which enhances the activity of immune cells.

2. The activated helper T cell produces interleukin-2 (IL-2), which stimulates other helper and killer T cells to grow and divide. The helper T’s secrete a lymphokine called B-cell growth factor (BCGF), which causes B cells to multiply.

3. As the number of B cells increases, helper T cells produce another lymphokine, B-cell differentiation factor (BCDF), which instructs some of the B cells to stop replicating and start producing antibodies.

4. Helper T cells also produce a lymphokine called gamma interferon (IF), which has multiple effects. Like IL-2, it helps activate killer T cells, enabling them to attack the invading organism. Like BCDF, it increases the ability of B cells to produce antibodies. It also affects macrophages, keeping them at the site of the infection and helping them digest the cells they have engulfed.

5. Gathering momentum with each exchange of signals between macrophages and T cells, a lymphokine cascade amplifies the immune response until the enemy is overwhelmed by sheer strength of numbers.
Figure 34-3 Time course of the antibody response in the circulating blood to a primary injection of antigen and to a secondary injection several weeks later.
Wear Red this Friday Tomorrow Feb 2nd!
Help raise awareness about Women & heart disease

http://www.goredforwomen.org/
https://www.goredforwomen.org/about-heart-disease/facts_about_heart_disease_in_women-sub-category/statistics-at-a-glance/
7 Resolutions to Improve ❤️ Health

• Quit smoking
• Avoid 2nd – hand smoke
• Know your numbers
• Process out processed foods
• Get moving
• Get your friends & family on board
• Spread awareness

Cardiovascular (CV) = Heart + Vessels + Blood!
NB: Figure-8 loop

Pulmonary

Systemic
Dual Pump Action & Parallel Circulation
Counter-clockwise
Fetal Circulation
≡ Aqua Animal
Bypass Lungs
\( R \rightarrow L \heartsuit \) Shunt

G&H 2016 fig 84-4, G&H 2011 fig 83-4
Human ♥ = 4-chambered box?  
2 separate pumps?

Upper = Atria

Lower = Ventrices

Pulmonary

Systemic

RA

LA

RV

LV

R ♥  
L ♥

Primer Pumps

Power Pumps
Human $\heartsuit = 4$ unique valves?  
2 valve sets?

**Semilunar** = *Half-moon shaped*

1. Pulmonic/Pulmonary
2. Aortic

**AV** = *Atrioventricular*

3. $\bigcirc$ AV = Tricuspid
4. $\bigcirc$ AV = Mitral/Bicuspid
Heart Valve Orientation & Scaffolding

- Pulmonary ring
- Aortic ring
- Mitral ring
- Tricuspid ring
- Muscle fiber
What the heck’s a *bruit*?
(*brwe, brö ot*) [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.
**Veins ➔ Atria ➔ Ventricles ➔ Arteries**

- Superior vena cava (from head)
- Right atrium
- Inferior vena cava (from body)
- Right ventricle
- Left atrium
- Left ventricle
- Aorta
- Endocardium
- Myocardium
- Pericardium

https://www.nhlbi.nih.gov/health-topics/how-heart-works
https://www.mayoclinic.org/diseases-conditions/heart-disease/multimedia/circulatory-system/vid-20084745
Coronary Circulation ≡ 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

Diagram showing the cardiac muscle, epicardial coronary arteries, and subendocardial arterial plexus.
Anastomoses May Provide Lifesaving Collateral Circulation!!

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

**Systole**
- Contract
- & Empty

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

<table>
<thead>
<tr>
<th>Coronary Blood Flow</th>
<th>Systole</th>
<th>Diastole</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contract &amp; Empty</td>
<td>0</td>
<td>300</td>
</tr>
<tr>
<td>Relax &amp; Fill</td>
<td>200</td>
<td>100</td>
</tr>
</tbody>
</table>

G&H 2011 & 2106 fig 21-4
Electrical Events Precede Mechanical Events!