BI 358 Lecture 8

I. **Announcements** Kraig Jacobson MD, w/delegation!
    Oregon Allergy Associates, next Tues Feb 5th!
    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
Allergic Reactions, Mast Cells & Basophils?

Allergen = ●
IgE = Y

up to \( \frac{1}{2} \text{ million per cell!} \)

Mucous Membranes/Blood

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

ASTHMA

Rachel Novak
Inflammation Steps

1. Break in skin → Bacteria enter & reproduce
2. Mast cells release histamine
3. Vessel wall becomes sticky → Neutrophils & monocytes attach → diapedesis → chemotaxis
4. Chemotaxins attract more Neutrophils & monocytes
5. Monocytes swell → 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. ↓ Antibody/Immunoglobulin (Ig) production.

4. Make susceptible to bacterial infections.
Interferon Mechanisms

Viruses coming!

Don’t breathe on me, Paul!

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 \(\heartsuit\)! Osmotic explosion!
**WBC Adverse Effects**

- 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!!

Davey 1990 p 30
Common lymphoid progenitor cell
Hemopoietic stem cells
Common lymphoid progenitor cell
Developing B cell

Cell-Mediated Immunity
Thymus
T lymphocyte
Peripheral lymphoid tissue
Activated T lymphocytes
Antigen
Plasma cell

Humoral Immunity
B lymphocyte
Antibodies

G&H fig 34-1 2011
cf: fig 35-1 G&H 2016
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

Rough ER

Antibodies

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

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?

Antecedents:
- Antibody: Immunoglobulin G (IgG)
- Antigen: Molecular structure recognized by the immune system

Diagram:
- Antibody structure
  - Fab: Variable region for antigen binding
  - Fc: Constant region

Key:
- V = variable region
- C = constant region

References:
Immunoglobulin G

Source: Visual Science
1. Agglutination

2. Complement

3. Opsonization

4. Killer Cells

L Sherwood 2012
<table>
<thead>
<tr>
<th>TABLE 4.1 Characteristics and functions of the human immunoglobulin classes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>immunoglobulin class</strong></td>
</tr>
<tr>
<td>heavy-chain type</td>
</tr>
<tr>
<td>number of constant domains in each heavy chain</td>
</tr>
<tr>
<td>relative molecular mass ((M_r)) of monomer</td>
</tr>
<tr>
<td>normally found as polymer?</td>
</tr>
<tr>
<td>valency: number of antigen binding sites in normal form (i.e. monomer or polymer)</td>
</tr>
<tr>
<td>percentage of total immunoglobulin in serum</td>
</tr>
<tr>
<td>serum half-life (days)</td>
</tr>
<tr>
<td>ability to trigger complement cascade*</td>
</tr>
<tr>
<td>can cross placenta from mother to foetus*</td>
</tr>
<tr>
<td>binds to Staphylococcal cell walls*</td>
</tr>
<tr>
<td>binds to macrophage Fc receptors*</td>
</tr>
<tr>
<td>binds to neutrophil Fc receptors*</td>
</tr>
<tr>
<td>binds to mast cell and basophil Fc receptors</td>
</tr>
<tr>
<td>binds to platelets</td>
</tr>
</tbody>
</table>

* For IgG this refers only to some subclasses.
G A M E D!
IgA = Secretory $A_b$

Antigen/$A_g$

J chain

secretory piece

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>B lymphocytes</strong></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, ingesting bacteria in baby’s digestive system.</td>
</tr>
<tr>
<td><strong>T lymphocytes</strong></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><strong>Molecules</strong></td>
<td></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&lt;sub&gt;12&lt;/sub&gt; binding protein</td>
<td>Reduces amount of vitamin B&lt;sub&gt;12&lt;/sub&gt;, 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>
</tbody>
</table>
Hormones and growth factors

Stimulate baby's digestive tract to mature more quickly. Once the initially “leaky” membranes lining the gut mature, infants become less vulnerable to microorganisms.

Lactoferrin

Binds to iron, a mineral many bacteria need to survive. By reducing the available amount of iron, lactoferrin thwarts growth of pathogenic bacteria.

Lysozyme

Kills bacteria by disrupting their cell walls.

Mucins

Adhere to bacteria and viruses, thus keeping such microorganisms from attaching to mucosal surfaces.

Oligosaccharides

Bind to microorganisms and bar them from attaching to mucosal surfaces.
IgM = Macroglobulin
Pentamer!!!!!

Valence? 10

Antigen/Ag

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 1\(^{st}\)!
Help raise awareness about Women & ♥ 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 System**

- Pulmonary arteries
- Pulmonary veins
- Vena cavae
- Aorta and branches
- Right ventricle
- Left ventricle
- Arterioles
- Venules

**Systemic System**

- Capillary beds of all body tissues where gas exchange occurs
- Oxygen-poor, CO₂-rich blood
- Oxygen-rich, CO₂-poor blood

D Chiras 2013 fig 4-1b
Dual Pump Action & Parallel Circulation
Fetal Circulation
≡ Aqua Animal
Bypass Lungs
\( R \rightarrow L \) \( \text{Shunt} \)
Human $\heartsuit = 4$-chambered box? 2 separate pumps?

Upper = Atria

Lower = Ventricles

RA

RV

LA

LV

Pulmonary

Systemic

Primer Pumps

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

**Semilunar** = **Half-moon shaped**
1. Pulmonic/Pulmonary
2. Aortic

**AV** = **Atrioventricular**
3. $\textcircled{R}$ AV = Tricuspid
4. $\textcircled{L}$ 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
What the heck’s a bruit? (brwe, brōot) [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.
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
Anastomoses May Provide Lifesaving Collateral Circulation!!
Cardiac Cycle

Systole
Contract & Empty

Diastole
Relax & Fill
Electrical Events Precede Mechanical Events!