BI 358 Lecture 8

I. Announcements Kraig Jacobson MD, Allergy & Asthma Research Associates, Oak Street Medical, Feb 10, Tues! Last update on outlines and paper drafts. Questions?

II. Immunology Connections Ab=lG structure, Mom’s Milk, Immune Regulation + Allergy: The Wars Within, Lennart Nilsson

III. Cardiovascular Physiology Torstar Books, G&H, Katz, LS,...
   A. Cardiovascular system? Figure-8 loop D Chiras (DC), LS
   B. Fetal development & circulation Torstar..., G&H fig 83-4
   C. Layers: peri-, epi-, myo- & endocardium Torstar Books
   D. ♥ structure & function G&H fig 9-7, LS1...
   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
   G. Autorhythmic cells & ♥‘s electrical highway G&H fig 10-1

III. Lymphatic System Torstar Books, DC, LS +...
Granulocytes

- Neutrophil 58-62%
- Eosinophil 2-3%
- Basophil < 1%

Agranulocytes

- Lymphocytes 28-32%
- Monocyte 3-5%
- Agranulocytes
Lymphocyte

Lymphocyte

Neutrophil Twins!!

Lymphocyte

Lymphocyte

Lymphocyte

Josef Khalifeh
WBC Differential
Lab 012715
WBC Adverse Effects

↓ Leukocytes

Anti-cancer drugs
Benzene
Nuclear blast
Radiation

↓ Professional phagocytes esp:
Neutrophils
Macrophages

↓ Body defense vs. μ organisms!

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
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.

Antigen

B cell specific to antigen

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

Memory B 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 fig 34-2
Typical IgG Antibody Structure

How do antibodies work?

Antigen

Identical, specific antigen-binding sites

Antibody

KEY

V = variable region
C = constant region

L Sherwood 2012; cf: G&H, fig 34-4
Immunoglobulin G

Source: Visual Science
1. Agglutination

2. Complement

3. Opsonization

4. Killer Cells
TABLE 4.1 Characteristics and functions of the human immunoglobulin classes

<table>
<thead>
<tr>
<th>Immunoglobulin class</th>
<th>G</th>
<th>A</th>
<th>M</th>
<th>D</th>
<th>E</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>150 000</td>
<td>160 000</td>
<td>180 000</td>
<td>185 000</td>
<td>200 000</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>
</tbody>
</table>
| binds to mast cell and basophil Fc receptors | − | − | − | − | +++
| binds to platelets | + | − | − | − | − |

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

Antigen/$A_g$  

Valence? 4  

Dimer!!  

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><strong>Macrophages</strong></td>
<td>Kill microbes outright in the baby’s gut, produce lysozyme and activate other components of the immune system.</td>
</tr>
<tr>
<td><strong>Neutrophils</strong></td>
<td>May act as phagocytes, injecting 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>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>

http://www.scientificamerican.com/article.cfm?id=got-smarts-mothers-milk-m
IgM = Macroglobulin
Pentamer!!!!!!

Antigen/Ag

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 (IFN), which has multiple effects. Like IL-2, it helps activate killer T cells, enabling them to attack the invading organism. Like BCGF, it increases the ability of B cells to produce antibodies. IFN 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 next Friday (Feb 6th!)
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 Heart Health in 2014

• 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

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

Systemic circuit
- Arterioles
- Venules
- Capillary beds of all body tissues where gas exchange occurs

Capillary beds of lungs 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
$R \rightarrow L \bigoplus$ Shunt

G&H 2011 fig 83-4
Human \( \text{❤} \) = 4-chambered box?
2 separate pumps?

Upper = Atria

Lower = Ventricles

RA

RV

Pulmonary

LA

LV

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. $\bigcirc R \ AV = $ Tricuspid
4. $\bigcirc L \ AV = $ Mitral/Bicuspid
MITRAL VALVE
- Cusp
- Chordae tendineae
- Papillary muscles

AORTIC VALVE
- Cusp

G&H 2006 fig 9-6;
cf: G&H 2011 fig 9-7
Heart Valve Orientation & Scaffolding

- Pulmonary ring
- Aortic ring
- Mitral ring
- Tricuspid ring
- Muscle fiber
What the heck’s a *bruit*? (brwe, broot) [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
Endocardium
Myocardium
Pericardium
Left atrium
Left ventricle
Aorta

http://www.nhlbi.nih.gov/health/topics/topics/hhw/contraction.html
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

Diagram:
- Black arrow from Systole to Diastole
- Red arrow from Diastole to Systole
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 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
Systemic circulation

Lymph vessel

Valve

Veins

Lymph node

Initial lymphatics

Pulmonary circulation

Lymph node

Initial lymphatics

Blood capillaries

Arteries

Heart

Blood capillaries

L Sherwood 2007
Elephantiasis: Lymphatic Blockage Due to Mosquito-Borne Parasitic Worm

L Sherwood 2007