I. Announcements  Quiz 2 GI + Nutrition next T! + Nutrition reports (.doc/.docx + .pdfs) by e-mail due < 5 pm to Mae, Abbie, Bella.

II. Blood + Immunology  G&H ch 33, 34, 35; Nilsson, Davey, Fox…
A. Blood: cell + fragments vs liquid. Plasma vs serum? LS+…
B. Red blood cell production, hemoglobin/Hgb, sickle cell Hgb
   G&H pp 445-51, fig 33-1, 33-2, 33-6 + Fox, LS…
C. White blood cell differential, ID & functions, platelets LS, GH
D. Immune response, pathogens…Davey fig 2.1, 2.2 pp 12-13
F. Medical Physiology News  Handwashing to prevent infection! Laughter as medicine! Centers for Disease Control &…SEBB
G. Innate vs adaptive immunity cf: G&H pp 465-70,LS+…
   Innate immunity: inflammation, interferon, complement; HIV
H. Antibody (Ab=Ig) structure, subclasses, mechanisms G&H
   fig 35-4 + LS + Davey fig 2.4 p 19, fig 4.2 p 42, tab 4.1 p 49
J. Mom’s milk overview Scientific American
K. Immune Regulation + Allergy: G&H fig 35-7, 35-8,…35-3 +
Dr. Kraig Jacobson of Oregon Allergy Associates is coming next Tuesday!

Yes, Sherlock! Avian & human immune systems evolved from a common reptilian ancestor!!

Whoopee! For the birds??
What's in Blood? Plasma & Blood Cells

- Plasma (55% of whole blood)
- Buffy coat: platelets and leukocytes (<1% of whole blood)
- Erythrocytes (45% of whole blood)
- Platelets
- Leukocytes (white blood cells)
- Erythrocytes (red blood cells)
Dermal bone production of red blood cells

![Graph showing the cellularity of various bones over age](image)

- **Cellularity (percent)**
  - 100
  - 75
  - 50
  - 25
  - 0

- **Age (years)**
  - 0
  - 5
  - 10
  - 15
  - 20
  - 30
  - 40
  - 50
  - 60
  - 70

- **Bone Types**
  - Vertebra
  - Sternum
  - Rib
  - Femur (shaft)
  - Tibia (shaft)
Pluripotent Hematopoietic Stem Cell Lines

- PHSC (Pluripotent hematopoietic stem cell)
- CFU-S (Colony-forming unit—spleen)
- CFU-B (Colony-forming unit—blast)
- CFU-E (Colony-forming unit—erythrocytes)
- CFU-GM (Colony-forming unit—granulocytes, monocytes)
- CFU-M (Colony-forming unit—megakaryocytes)

- Erythrocytes
- Granulocytes (Neutrophils) (Eosinophils) (Basophils)
- Monocytes
- Macrocytes
- Megakaryocytes
- Platelets
- T lymphocytes
- B lymphocytes
What a difference one amino acid can make!

Amino acid sequence of normal hemoglobin:

Val – His – Leu – Thr – Pro – Glu – Glu

Amino acid sequence of sickle-cell hemoglobin:

Val – His – Leu – Thr – Pro – Val – Glu
Hemoglobin Structure

Polypeptide chain

Polypeptide chain

Polypeptide chain

Heme groups

Polypeptide chain

L Sherwood 2011 fig 11-2
**NB:** CO carbon monoxide binds with ~200-fold greater affinity than O₂.
Granulocytes

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

Agranulocytes

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

Agranulocytes
Immune Response

1. **Detect** invader or ID toxic product.
2. **Communicate** to network.
3. **Recruit** coordinated, multi-pronged attack.
4. **Amplify** & if yes to success, then –
5. **Suppress**

Davey 1990 p 6
Pathogen?

Microbes that cause disease!

- Bacteria
- Viruses
- Protozoa
- Fungi
- + Multicellular Parasites, e.g., ticks & lice

Davey 1990 p 5
Pathogens & Parasites Cause:

1. **70-80% of deaths in less developed countries**
2. **Tens of millions of deaths due to infectious diseases**
3. **> 20 million childhood deaths per year in Asia, Africa & Latin America due to diarrheal infections alone**
4. **Yet < 2% deaths in modern, industrialized countries!**

*World Health Organization 2018 Statistics*

Davey 1990 p 5

Why such striking differences across the world?

1. Poor sanitation
2. Contaminated water supply
3. Contaminated food supply
4. Malnutrition
5. Existing infections
6. Patchy, inadequately-funded vaccinations
7. AIDS superimposed on top of 1-6!

Davey 1990 p 5
FIGURE 2.1 Summary of the main physical, chemical and mechanical barriers to infection entering the human body.
Good phagocytes!
Figure 33-2  Movement of neutrophils by diapedesis through capillary pores and by chemotaxis toward an area of tissue damage.
Widespread Location of Lymphoid Tissues!

- lymph nodes, tonsils and adenoids
- lymph nodes in axilla
- spleen
- gut-associated lymph nodes
- lymph nodes in groin
- diffuse lymphoid tissue in lungs, bronchi, gut and urinogenital tract
- bone marrow
- thymus
Hand-washing

The right way to wash your hands:

Thoroughly wash with soap and warm running water — rubbing your hands together for at least 10 seconds.

Hand-washing is the single most effective thing you can do to reduce the spread of colds and other infectious disease.

It's not necessary to use anti-bacterial soaps when washing up. Regular soap and water do the job just fine.

Also, using germicidal soaps too often may produce antibiotic-resistant bacteria.

Source: Hospital Infections Program, U.S. Centers for Disease Control and Prevention

NB: Happy Birthday Song 20-30 sec!!

http://www.squidsoap.com/
Laughter = Medicine!

- Laughter’s most profound effects occur on the immune system.
- Laughter $\uparrow \gamma$-interferon, $\uparrow$ B-cells, $\uparrow$ T-cells and $\downarrow$ stress hormones
- The average child laughs 100s of x/day
- The average adult laughs 12 x/day
- We need to find these lost laughs—and use them to our advantage!

SEBB Newsletter 1997
**Immunity**

### Innate/Inborn/Nonspecific

1. **Immediate**, upon exposure to threatening agent

2. ¹⁰ effectors phagocytic specialists: neutrophils & macrophages

3. "Eyes" are Toll-like receptors (TLRs) which recognize & bind with generic invader markers

4. Inflammation, interferon, natural killer cells, complement (plasma proteins)

### Adaptive/Acquired/Specific

1. **Delayed**, selective targeting based on prior exposure

2. ¹⁰ effectors lymphocytes: T- & B-lymphocytes

3. "Eyes" are T- and B-cell receptors which bind with specific antigens

4. Cell-mediated & Humoral (Ab mediated) immunity

---

Really, a false separation, as incredible overlap & synergism!
1. ↑ Phagocytosis
2. ↑ Enzymatic rxns, Q10?
3. ↓ Bacterial replication by ↑ Fe^2+ requirement

Prostaglandins
↑ Set point
Hypothalamus

EP, endogenous pyrogen
X NSAIDs e.g. Aspirin

Should we use?

Neutrophil
- Extracellular Traps
- Kinins activated
- Pain receptors ↑ Chemotaxis
- Lactoferrin binds Fe^2+ ↓ Replication
- NO, nitric oxide toxic to microbes

Macrophage
- Histamine ↑ Vasodilation
- Histamine ↑ Capillary permeability

Mast Cells
- Anti-histamines

NETs!
Neutrophil Extracellular Traps
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**

Illustration by Rachael Nozeski
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.
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

↓ 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!!
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.
Typical IgG Antibody Structure

How do antibodies work?

Immunoglobulin G

Source: Visual Science
1. **Agglutination**

2. **Complement**

3. **Opsonization**

4. **Killer Cells**

L Sherwood 2012
<table>
<thead>
<tr>
<th><strong>TABLE 4.1 Characteristics and functions of the human immunoglobulin classes</strong></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/$A_g$

Valence? 4

Dimer!!

Davey 1990 p 50
IgM = Macroglobulin
Pentamer!!!!!

Valence? 10
Dendritic Cells: Specialized Antigen-Presenting Cells (APCs) Sentinels in Almost Every Tissue!

L Sherwood 2012
Immunology Websites for Fun Learning!

http://highered.mcgraw-hill.com/sites/0072495855/student_view0/chapter24/animation_the_immune_response.html

http://www.guardian.co.uk/science/video/2010/nov/01/immune-system-viruses-cells

http://educationalgames.nobelprice.org/educational/
Dr. Louis Picker of OHSU on track to cure HIV!
http://www.who.int/topics/breastfeeding/en/
http://www.nichd.nih.gov/health/topics/breastfeeding/Pages/default.aspx
# 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>Molecules</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>B₁₂ binding protein</td>
<td>Reduces amount of vitamin B₁₂, 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>
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. 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.