BIO401 Immunobiology

BOOK – Kuby 6th Edition*

EXAMS - 3 exams - 100 points
- Final--> 100 points
- Quizzes – 50 points

TOTAL: 450 points

FINAL GRADE:
Lab: 25% (300 points)
Lecture: 75% (450 points)

Immunobiology

- Office hour – Appointment
- 1 hour exams
- Trip to Washington DC → Dr. Leid
- Exams → returned within 1 week
- If concerns - 1 week to check with me
- Review the whole exam
- No cell phones
- Be on time – back door!

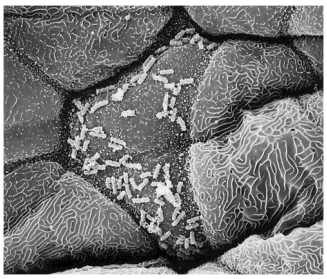
Questions?

Readiness Exam

1. Mention a difference between a Gram (+) and Gram (-) bacteria
2. Provide one example of innate immunity?
3. What is a difference between an antigen and an antibody?
4. What cells produce antibodies?
5. What cell(s) carry out phagocytosis?

The immune system:

"A system of cells, tissues, and fluids that function to protect the body from invasion by a wide range of organisms - including viruses, bacteria, protozoans, fungi and worm".



E.coli bacteria adhering to epithelial cells of the urinary tract.

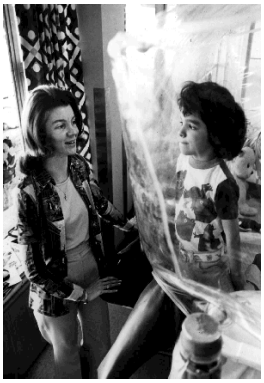
Immune Response (two phases)

- A) **Recognition** – Highly specific!
- B) **Response (Effector Response)**– through cells and molecules

– **MEMORY!!!**

How important is the immune system?

Individuals with significant defects in immunity (e.g. AIDS, genetically inherited syndromes - “boy in the bubble”) - succumb rapidly to infection.

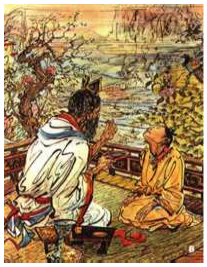


David Vetter

Vaccination

Smallpox

- Organism?
- History
- Vaccination



14th – 17th centuries : variolation used in China

-Powdered scabs of smallpox pustules were inhaled (or rubbed into scratches in the skin) to protect from smallpox

17th century – practice spread to Turkish regions

http://www.immunisation.org.uk/history.html

1718 – Lady Mary Wortley Montagu, wife of the British ambassador to Constantinople, allowed her children to be treated with this procedure → Europe

Variolation

Edward Jenner

Edward Jenner

- Meanwhile, it was commonly believed that milkmaids who had had cowpox were resistant to smallpox.

- Cowpox is a relatively benign disease in both humans and cows.

- 1774 – Edward Jenner inoculated individuals with cowpox in order to protect them from smallpox. Individuals receiving the cowpox did not develop smallpox in subsequent outbreaks of the disease.

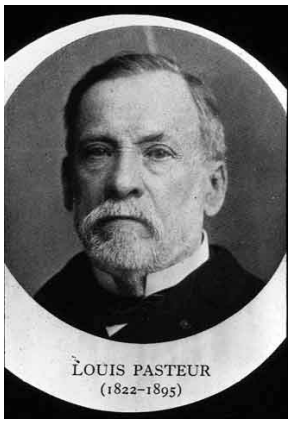
Vaccination vs. variolation

- No risk of smallpox
- Fewer side effects

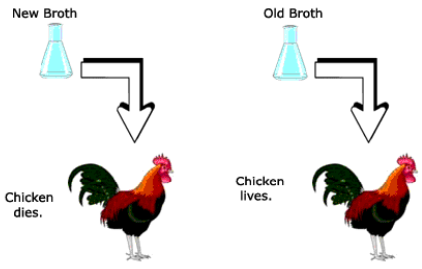
By 1800, vaccination was widely accepted.

http://www.immunisation.org.uk/history.html

1976 - Last (naturally occurring) smallpox case - Ali Maow Maalin from Somalia



1880 - Pasteur experiment – fowl cholera



http://www.medinfo.ufl.edu/other/profmed/slides/pm012599/

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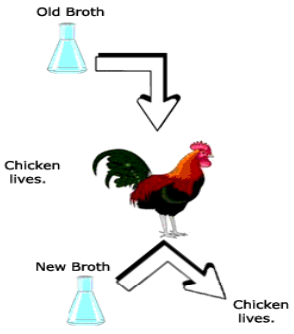
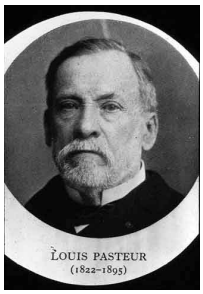


Attenuated Vaccines

http://www.medinfo.ufl.edu/other/profmed/slides/pm012599/



Pasteur's Contributions:

-**Vaccine** (vacca= cow)

-**Attenuated vaccines** = cholera, anthrax, rabies

TABLE 1-1 Cases of selected infectious disease before and after the introduction of effective vaccines

	ANNUAL CASES/YR		CASES IN 2004
Disease	Prevaccine	Postvaccine	Reduction (%)
Smallpox	48,164	0	100
Diphtheria	175,885	0	100
Measles	503,282	37	99.99
Mumps	152,209	236	99.85
Pertussis (whooping cough)	147,271	18,957	87.13
Paralytic polio	16,316	0	100
Rubella (German measles)	47,745	12	99.97
Tetanus ("lockjaw")	1,314 (deaths)	26 (cases)	98.02
Invasive hemophilus influenzae	20,000	172	99.14

SOURCE: Adapted from W. A. Orenstein et al., 2005. *Health Affairs* 24:599.

Table 1-1
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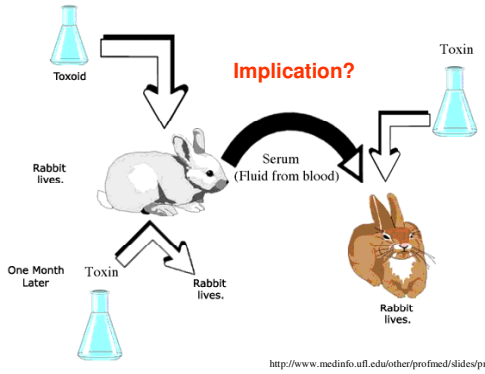
Early Studies of Humoral and Cellular Immunity

Experiments of von Behring and Kitasato - tetanus toxin
Protection can be transferred with serum.



http://www.medinfo.ufl.edu/other/profmed/slides/pm012599/

Shibasaburo Kitasato
(1852-1931)

Emil von Behring
(1854-1917)

SUMMARY:

1890 – Serum from animals previously immunized with diphtheria could transfer the immune state to immunized animals

Serum – Liquid component of coagulated blood

TOXOID – modified **toxin**, unable to cause toxic effect but highly antigenic

Elvin Kabat

- Activity in serum associated with a fraction called gamma globulin
- Gamma globulin fraction is also known as immunoglobulin (Ig), which is also called antibody (Ab)
- Antibodies contained in body fluids (humor) – humoral immunity

Passive Immunity?

Elie Metchnikoff
(1845-1916)

1883 -Phagocytosis of microorganisms

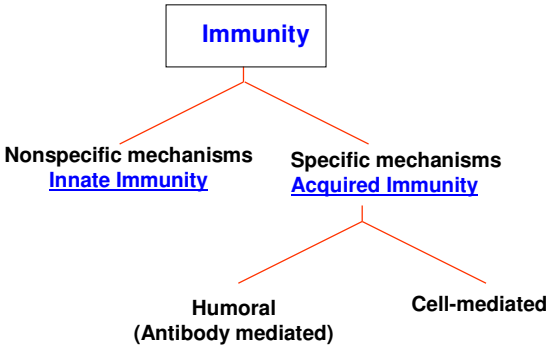
http://pw1.netcom.com/~aguldo/agga/bt/pix/phagocytosis.jpg

Cell-mediated immunity

Cellular Immunity

- 1940 – **Merrill Chase** transferred immunity against tuberculosis by using white blood cells
- **Lymphocytes**: 2 types

Antigen?

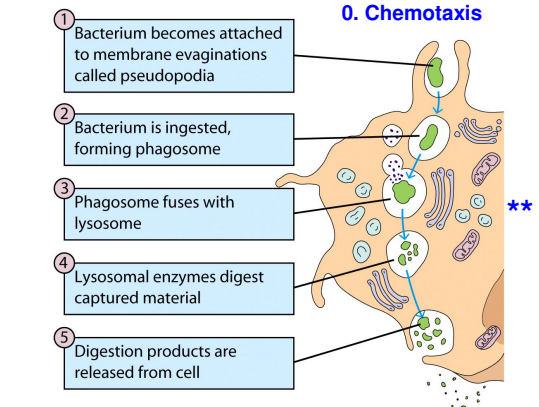


Innate Immunity

- **I. Anatomic Barriers:**
  - **Skin**: keratin (waterproof), sebum (low pH), sweat (lysozyme)
  - **Mucus membranes**: mucus (X adherence), normal flora (space, nutrients, immunity), cilia (removes microorganisms), antimicrobial peptides (defensins)
    - Respiratory, Genitourinary, Digestive.

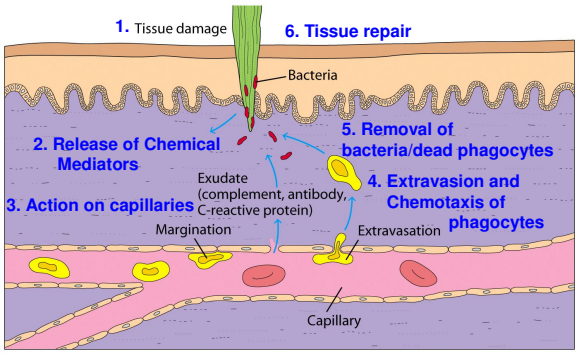
Innate Immunity

- **II. Physiologic Barriers:**
  - **Chemical mediators:**
    - Lysozyme - (cell wall),
    - Interferons - (anti-viral proteins),
    - Complement - (lysis, phagocytosis, inflammation),
    - Collectins - (detergent activity)
    - Pattern Recognition Receptors – (i.e Toll receptors – recognition and activation)
- **III. Phagocytic Barriers:**
  - **Phagocytosis** – neutrophils, monocytes/ macrophages
- **IV. Inflammation**



0. Endocytosis **1. 6 steps** **2. Other function?**

Inflammation



Inflammation

Tissue damage

- 1) **Release of Chemical Mediators**: Acute phase proteins (C-reactive protein) – bind to bacteria and fungi activating complement; histamine – acts on vessels; bradykinins - pain
- 2) **Vasodilation**: ↑ diameter of capillaries
- 3) **Increased Vascular Permeability**: recruitment of cells and fluid – edema
- 4) **Influx of Phagocytes** – margination and extravasion
- 5) **Tissue Repair** – fibrin (clotting) and fibroblasts

TABLE 1-3 Comparison of innate and adaptive immunity

	Innate	Adaptive
Response time	Hours	Days
Specificity	Limited and fixed	Highly diverse; improves during the course of immune response
Response to repeat infection	Identical to primary response	Much more rapid than primary response
Major components	Barriers (e.g., skin); phagocytes; pattern recognition molecules	Lymphocytes; antigen-specific receptors; antibodies

Table 1-3
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Adaptive or Acquired or Specific Immunity

- **Characteristics:**
  a) highly specific (antigen),
  b) diversity (10^{9-11})potential recognitions,
  c) memory,
  d) self/non-self recognition (MHC molecules,
  e) self-regulation (turning off responses)

Acquired Responses

a) B cells:

- Originate and mature in bone marrow
- Mature B cells a unique receptor = antibody molecule
- Membrane antibody molecule recognizes antigen alone/intact
- 10^5 molecules on membrane
- **"Activated B cell" → polyclonal activation → Plasma Cells → Secreted antibody.**

**Memory B cells are generated in every response

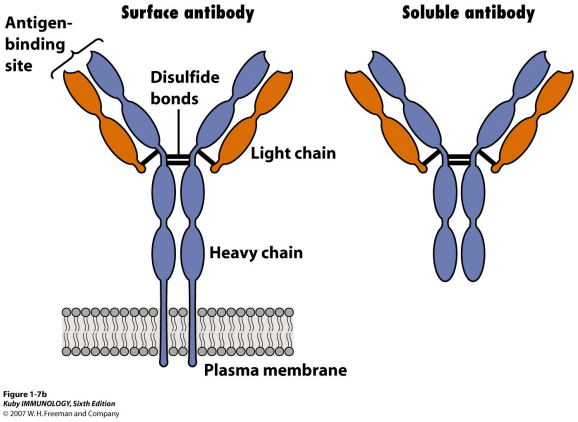

Figure 1-7b
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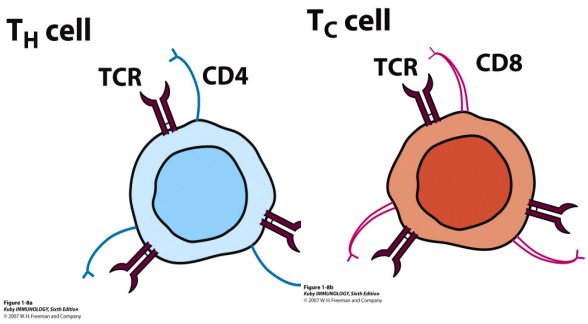
Acquired Responses

T cells:

- Originate in BM and mature in thymus
- In thymus they acquire a unique membrane receptor = **T cell receptor (TCR).** The TCR recognizes antigen ONLY when bound or presented by major histocompatibility complex (MHC) molecules
- **MHC restriction.**
- Antigen + MHC →"Activated T cell" → polyclonal activation → Memory T cells + Effector T Cells (cytokines or cytotoxicity)

**Memory T cells are generated in every response



Acquired Responses

T cells subpopulations:

a) T helper (Th) and T cytotoxic (Tc)

b) T helper (Th) express a CD4 membrane marker

c) T cytotoxic (Tc) express a CD8 membrane marker

Acquired Responses

T cells subpopulations:

- T cytotoxic (Tc) express a CD8 membrane marker
- T helper (Th) express a CD4 membrane marker
- T helper (Th) cells interact with antigen presented by MHC-II molecules
  - Activation lead to secretion of cytokines → multiple effects
- T cytotoxic (Tc) cells interact with antigen presented by MHC-I molecules
  - Activation lead to cell killing (cytotoxicity)

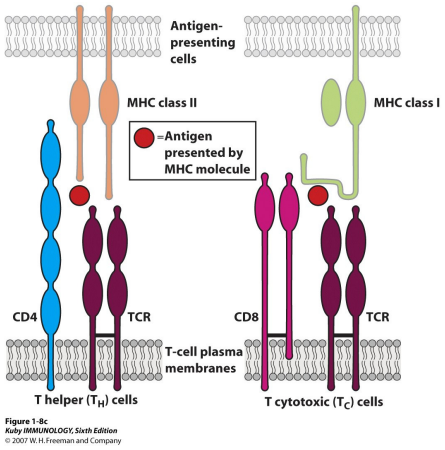


Figure 1-8c
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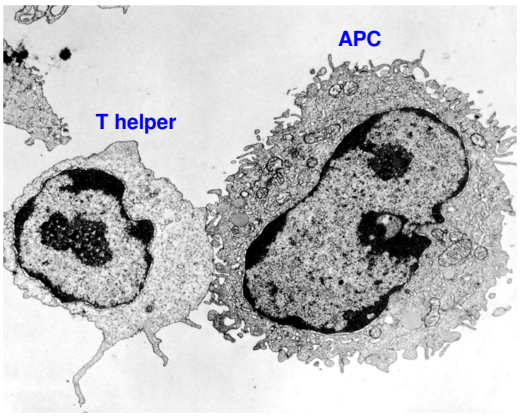
MHC molecules

- Highly polymorphic genetic complex with multiple loci
- MHC loci encodes 2 surface molecules:
  - Class I (MHC-I) – all nucleated cells
  - Class II (MHC-II) – ONLY in APC
- Role:
  - Self-recognition!
  - Bind antigen (peptides) and present it to T cells

Antigen presenting cells (APC)

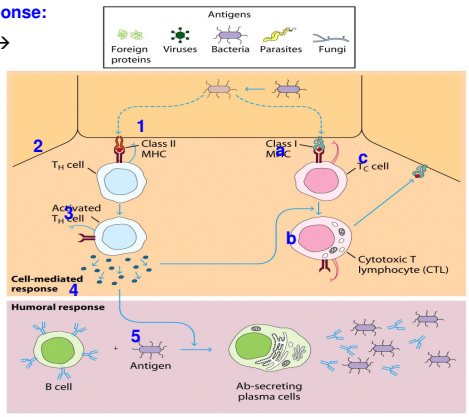
- **Three types**: Macrophages, Dendritic cells and B cells
- Goal: presentation and activation of Th cells
- **Requirement:**
  - 1) Express MHC-II
  - 2) Provide co-stimulatory signal for activation
  - 3) Cytokines for activation



Effector Response:

-**B cells**: Abs →

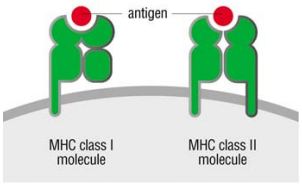
-**T cells:**
Th cytokines
Tc killing



- T cell activation

- Antigenic recognition → "non-specific"

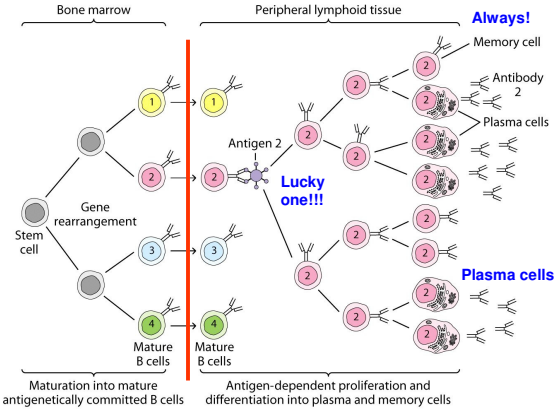
From **Immunity: The Immune Response in Infectious and Inflammatory Disease**
by DeFranco, Locksley and Robertson



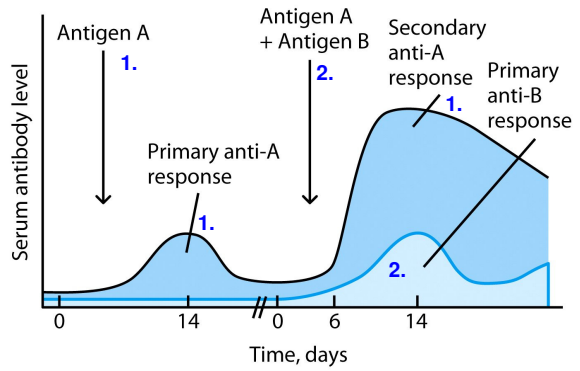
What T cells will be activated in each case?

Clonal Selection Theory

- Specificity of recognition receptors in B (surface antibody) and T cells (T cell receptor) is acquired in primary lymphoid organs through a complex gene re-arrangement event
- Mature T or B cells encounter the antigen and only that cell with the respective "specificity" is selected to undergo activation & expansion leading to **effector responses** and **memory cell production**



Primary and Secondary responses



When things go wrong!

- Immune dysfunction can lead to:
  - a) **Allergy and Asthma**: Sensitization to allergen leading to allergic response
  - b) **Graft rejection and Graft versus host disease:** non-self rejection mediated by MHC molecules
  - c) **Autoimmune Disease**: loss of self-recognition leading to immunological attack (Crohn's disease, Rheumatoid arthritis, Multiple sclerosis)
  - d) **Immunodeficiency**: loss of components from innate and acquired immunity (AIDS)
    - Natural VS Acquired

- The End