



BIO401 Immunobiology

BOOK – Kuby 5th Edition

EXAMS - 3 exams - 100 points each
Final--> 100 points
Cases→ 50 points
TOTAL: 450 points

FINAL GRADE:

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

LAB MANUAL

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Questions?

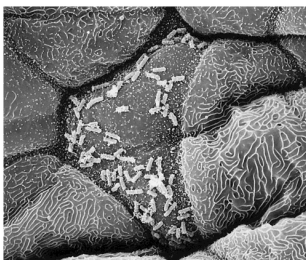


Readiness Exam

1. Mention a difference between a Gram + and Gram (-) bacteria
2. What is an antibody?
3. What is a difference between an antigen and an antibody?
4. What cells produce antibodies?
5. What cells carry out the cellular immunity?

The immune system:

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



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

Immune Response

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

–MEMORY!!!

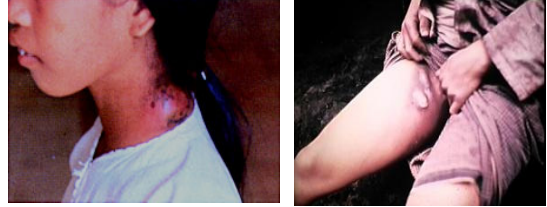
How important is the immune system?

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



David Vetter

Plague bacteria (*Yersinia pestis*) cause swelling of lymph nodes – "buboes"



<http://www.insecta-inspecta.com/leas/bdeath/Black.html>

<http://www.cdc.gov/ncidod/dvbid/plague/diagnosis.htm>



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 the procedure → Europe



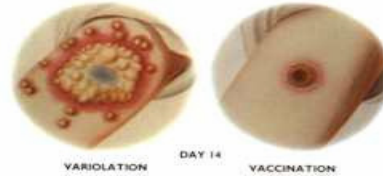
Variolation



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** inoculates 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

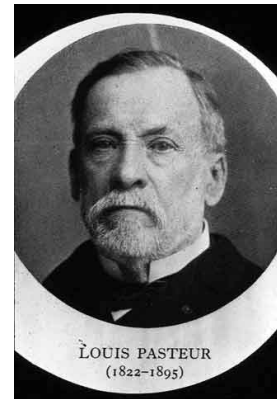
- No risk of smallpox
- Fewer side effects

By 1800, vaccination was widely accepted.

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

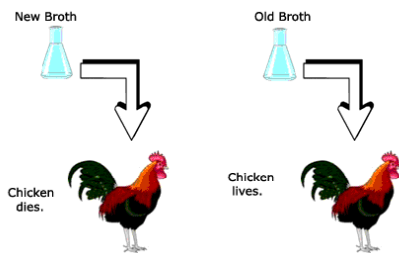


1976 - Last (naturally occurring) smallpox case - Ali Maow Maalin from Somalia



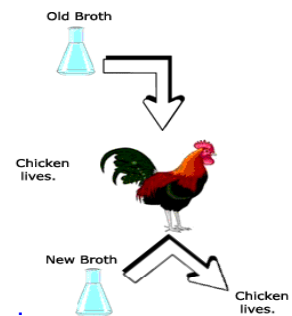
LOUIS PASTEUR
(1822-1895)

1880 - Pasteur experiment – fowl cholera



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

1880 - Pasteur experiment – fowl cholera



Attenuated Vaccines

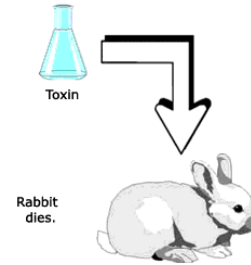
<http://www.medinfo.ufl.edu/other/profmed/slides/pm012599/>



Pasteur's Contributions:

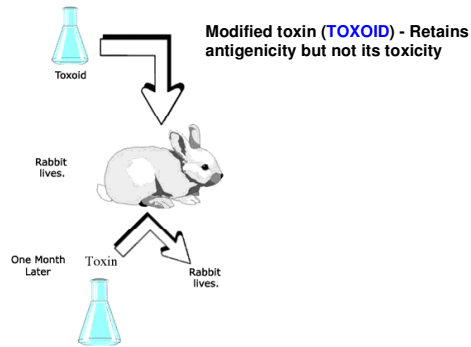
- Vaccine (vacca= cow)
- Attenuated vaccines = cholera, anthrax, rabies

Experiments of von Behring and Kitasato - tetanus toxin



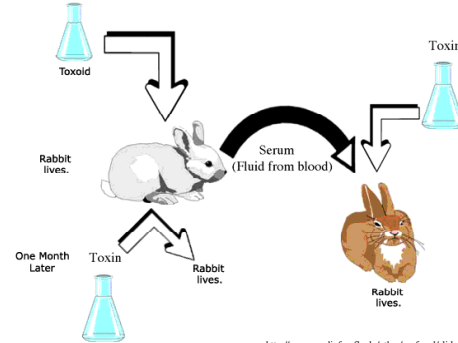
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Experiments of von Behring and Kitasato - tetanus toxin



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

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 antigen

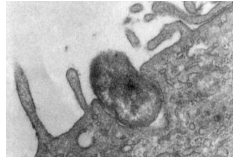
Elvin Kabat

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



1883 - Phagocytosis of microorganisms

Elie Metchnikoff
(1845-1916)

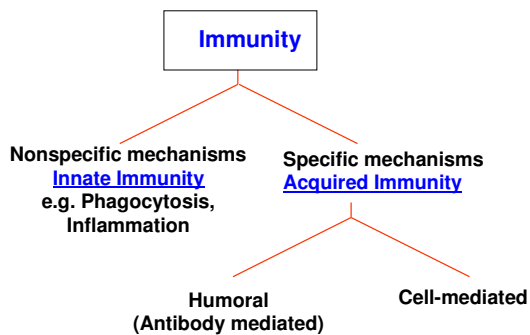


<http://pw1.nctcom.com/~aguldo/agga/bt/pix/phagocytosis.jpg>

Cell-mediated immunity

Cellular Immunity

- 1940 – **Merrill Chase** transferred immunity against tuberculosis by using white blood cells
- **Lymphocytes:**
 - B lymphocytes: Bursa, humoral or antibody-mediated
 - T lymphocytes: Thymus, cellular immunity

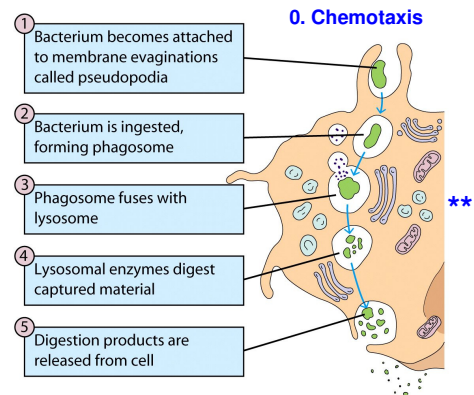


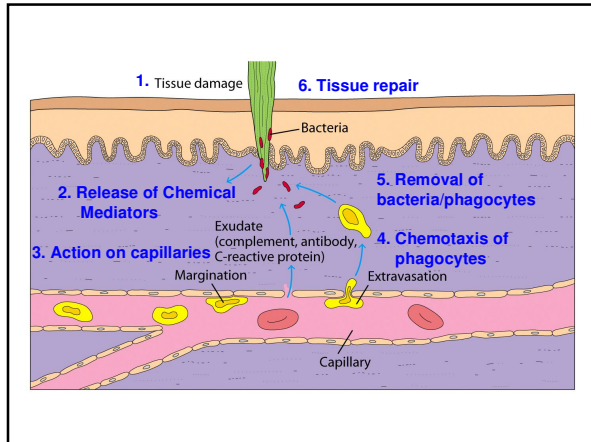
Innate Immunity

- **I. Anatomic Barriers:**
 - **Skin:** keratin (waterproof), sebum (low pH), sweat (lysozyme)
 - **Mucus membranes:** mucus (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)
 - Toll receptors – (recognition and activation)
- **III. Phagocytic Barriers:**
 - **Phagocytosis** – neutrophils, monocytes/ macrophages





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 extravasation
- 5) **Tissue Repair** – fibrin (clotting) and fibroblasts

Adaptive or Acquired 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

- **Involve the interaction between:** Antigen-presenting cells (Macrophages, Dendritic cells and B cells) and lymphocytes (B and T)
 - a) **B cells:**
 - Originate and mature in bone marrow
 - Mature B cells a unique receptor = antibody molecule
 - Membrane antibody molecule recognizes antigen **alone**
 - “Activated B cell” → polyclonal activation → Plasma Cells → Secreted antibody.
- **Memory B cells are generated in every response

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 when bound or presented by major histocompatibility complex (MHC) molecules
- MHC molecules are polymorphic membrane proteins
 - Two major types: **MHC-I and MHC-II**
 - **MHC-I:** expressed in all nucleated cells, two chains: α and β 2-microglobulin
 - **MHC-II:** expressed in antigen presenting cells, two chains: α and β chains.

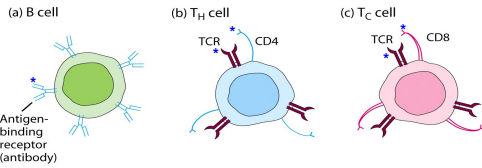
Acquired Responses

- Antigen + MHC → “Activated T cell” → polyclonal activation → Memory T cells + Effector T Cells (cytokines or cytotoxicity)
 - 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
 - d) T helper (Th) cells interact with antigen presented by MHC-II molecules
 - Activation lead to secretion of cytokines → multiple effects
 - e) T cytotoxic (Tc) cells interact with antigen presented by MHC-I molecules
 - Activation lead to cell killing (cytotoxicity)
- **Memory T cells are generated in every response

Acquired Responses

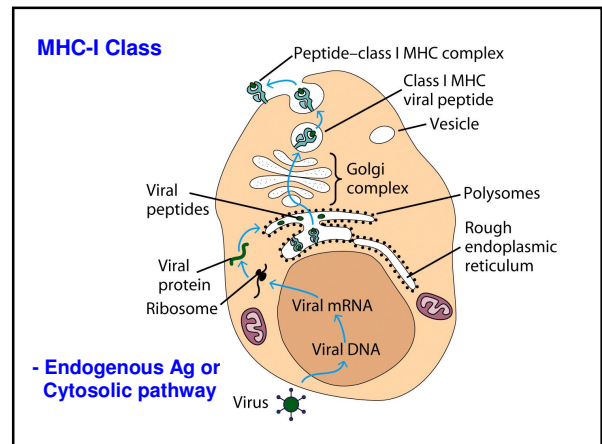
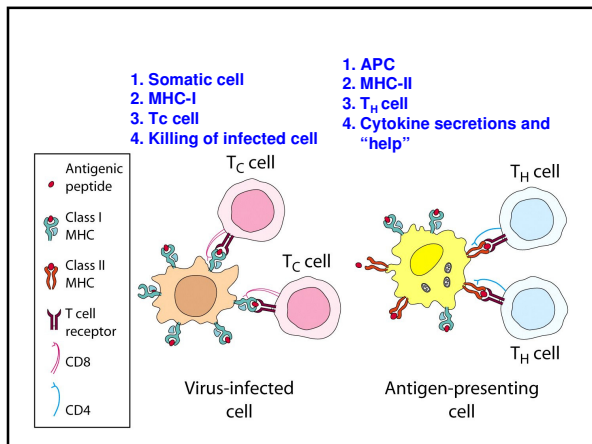
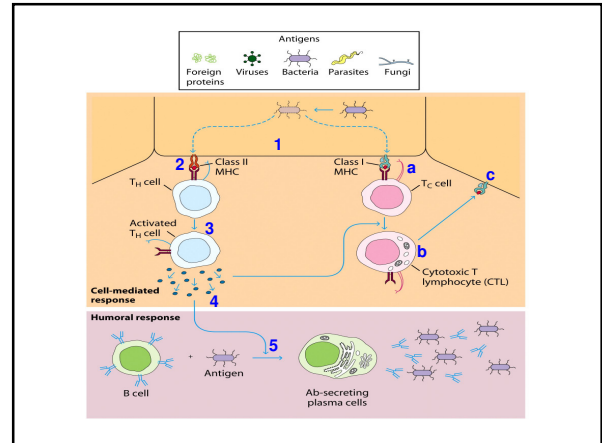
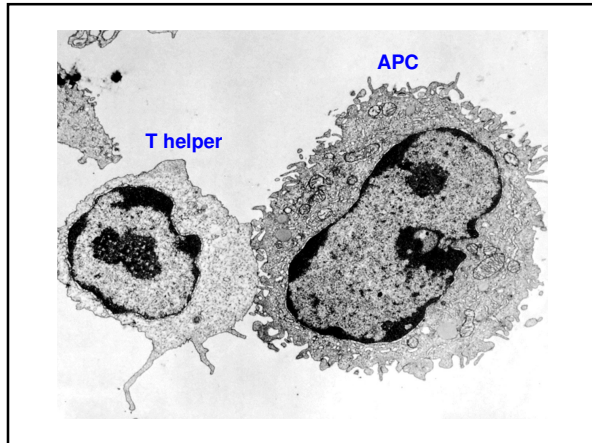
T cells subpopulations:

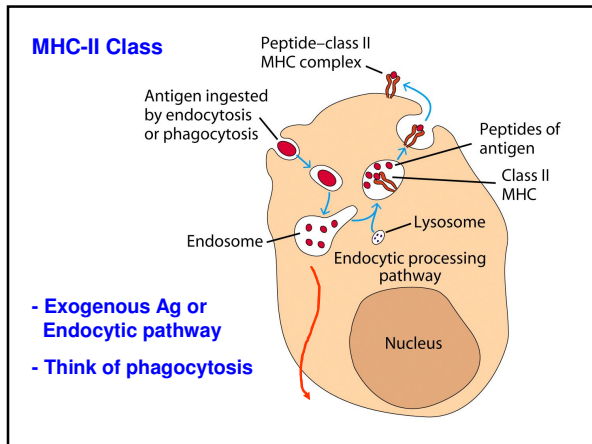
- T cytotoxic (T_c) express a CD8 membrane marker
- T helper (T_h) express a CD4 membrane marker



Antigen presenting cells (APC)

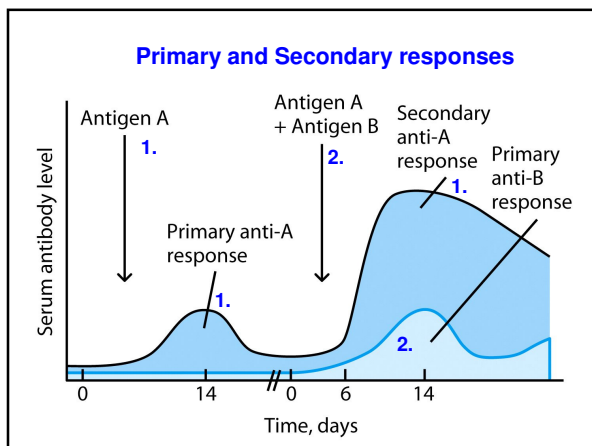
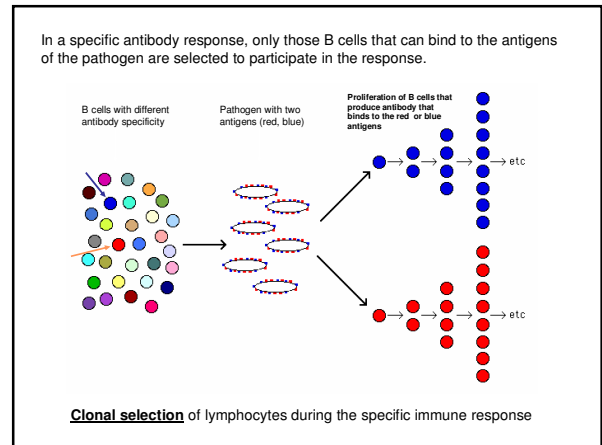
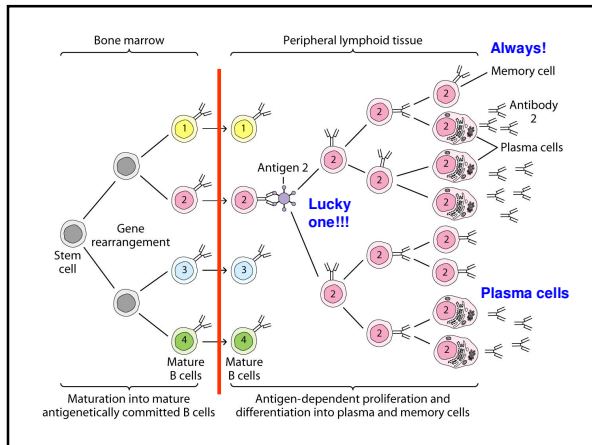
- **Three types:** Macrophages, Dendritic cells and B cells
- **Goal:** activation of T_h cells
- **Requirement:**
 - 1) Express MHC-II
 - 2) Provide co-stimulatory signal for activation
- Uptake antigen by phagocytosis → processing → present antigen + MHC-II molecule





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 the cell with the respective “specificity” is selected to undergo polyclonal activation leading to **effector responses** and **memory cell production**



Keep in mind that both are acting simultaneously to provide protection!!

TABLE 1-3 Comparison of adaptive and innate 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

When things go wrong!

- Immune dysfunction can lead to:
 - a) **Allergy and Asthma**: Sensitize 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)

Acquired Responses

T cells:

- 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)

****Memory T cells are generated in every response**