BIO401 Immunobiology

BOOK – Kuby 6th Edition*

EXAMS - 4 exams = 450 points
- Cumulative Final =
- Quizzes – 50 points

TOTAL: 500 points

FINAL GRADE:
Lab: 25% (300 points)
Lecture: 75% (500 points)

Immunobiology

- Office hour – After class or by appointment
- 1 hour exams
- Trip to Washington DC → Dr. Nieto?
- Exams → returned within 1 week
- If concerns - 1 week to check with me. Follow the syllabus's guidelines!!
- Review the whole exam
- No cell phones
- Be on time – back door!

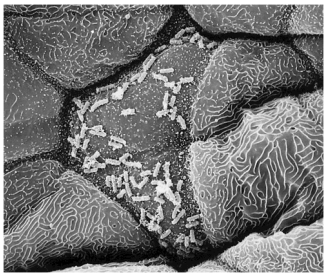
Questions?

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"

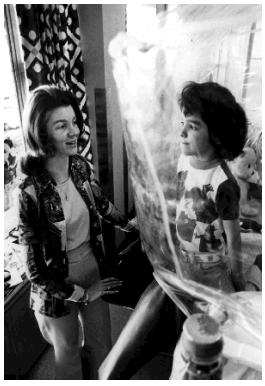


E.coli bacteria adhering to epithelial cells of the urinary tract.

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.

- Gamma chain
- ADA (adenosine deaminase)



David Vetter

The Immune System

Functions:

-1) **Recognition ---------- Effector Response**

-**2) Two Immunity Systems:**

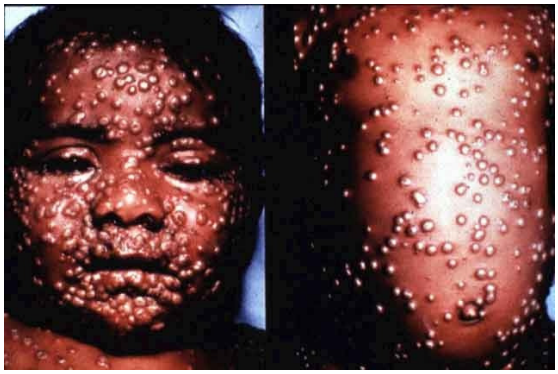
a) **Innate**

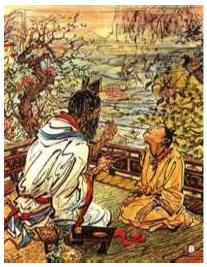
b) **Acquired/Adaptive**

Vaccination → Immunology

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

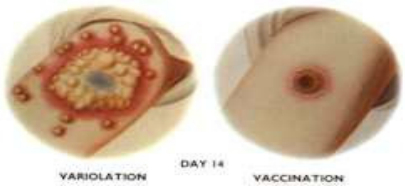
Edward Jenner

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. Why?



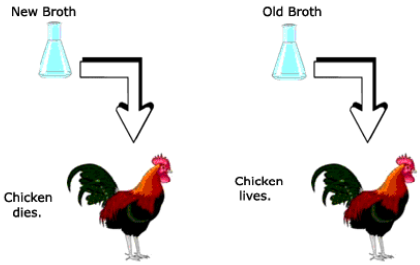
Vaccination vs. variolation

- No risk of smallpox
- Fewer side effects

By 1800, vaccination was widely accepted.

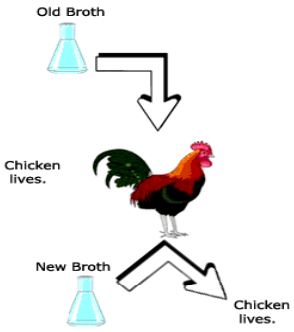
http://www.immunisation.org.uk/history.html

1880 - Pasteur experiment – fowl cholera



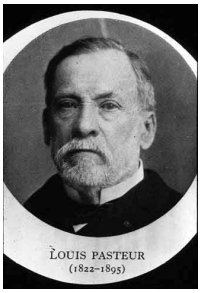
http://www.medinfo.ufl.edu/other/profmed/slides/pm012599/

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

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

Disease	ANNUAL CASES/YR Prevaccine	Postvaccine	CASES IN 2004 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
Kuby IMMUNOLOGY, Sixth Edition

Why do we still have measles, diphtheria, etc in the USA?

Early Studies of Humoral and Cellular Immunity

Shibasaburo Kitasato
(1852-1931)

Emil von Behring
(1854-1917)

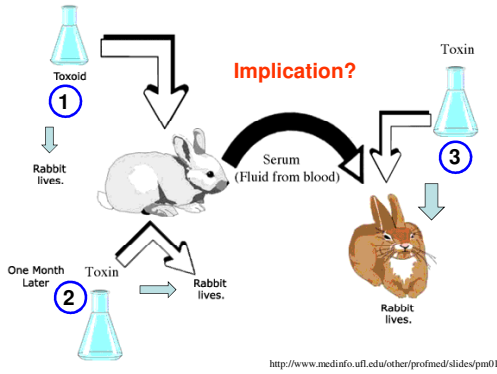
SUMMARY:

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

Serum – Liquid component of coagulated blood

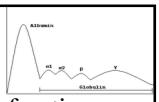
TOXOID – modified **toxin**, unable to cause toxic effect but highly antigenic

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



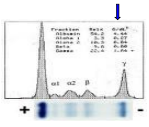
http://www.medinfo.ufl.edu/other/profmed/slides/pm012599/

Elvin Kabat



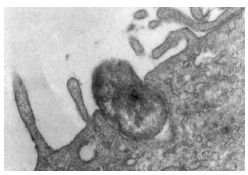
- Activity in serum associated with a fraction called gamma globulin
- Gamma globulin fraction is also known as immunoglobulin (Ig), which is also called antibody (Ab)
- Antibodies contained in body fluids (humor) – humoral immunity

Passive Immunity?



Elie Metchnikoff
(1845-1916)

1883 -Phagocytosis of microorganisms



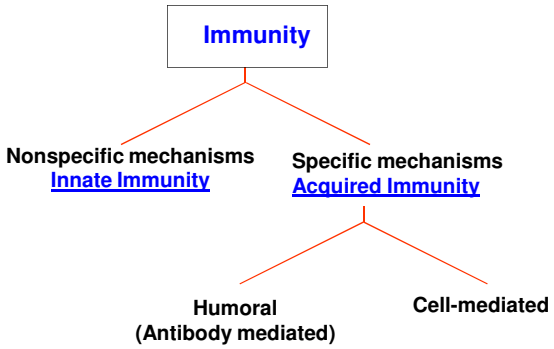
http://pw1.netcom.com/~aguldo/agga/bt/pix/phagocytosis.jpg

Cell-mediated immunity

Cellular Immunity

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

Antigen?



Infection and Immunity

- **Pathogens** – organisms that cause disease
- **Opportunistic pathogens** – decreased immune function
  - *Candida albicans* – "thrush" → systemic →RIP
  - *Pneumocystis* pneumonia
- Immune system must deal with: viruses, worms, fungi, bacteria, protozoa, toxins

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.
    - MUCUS – 4L/day

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, dendritic cells
- **IV. Inflammation**

Adaptive or Acquired or Specific Immunity

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

Immune Response (two phases)

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

–MEMORY!!!

Acquired Responses

a) B cells:

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

**Memory B cells are generated in every response

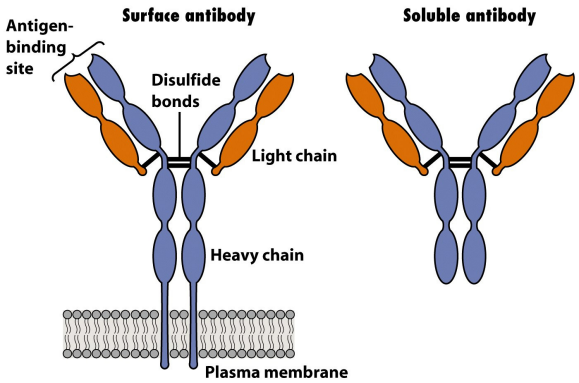


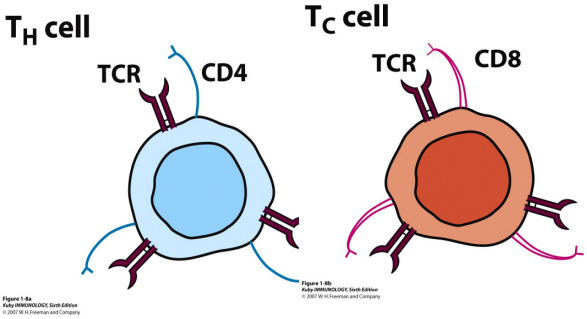
Figure 1-7b
Kuby IMMUNOLOGY, Sixth Edition
© 2007 W.H.Freeman and Company

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)
   - Th subpopulations:
     - Tregs (regulatory T cells)
     - Th17

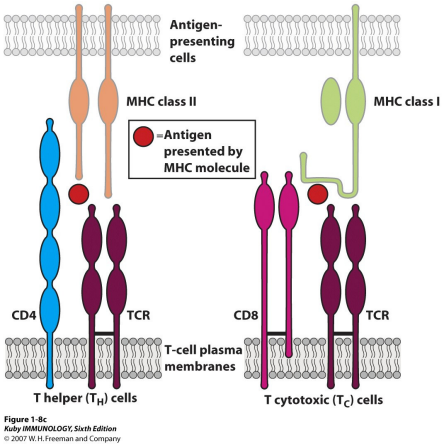
b) T helper (Th) express a CD4 membrane marker

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)

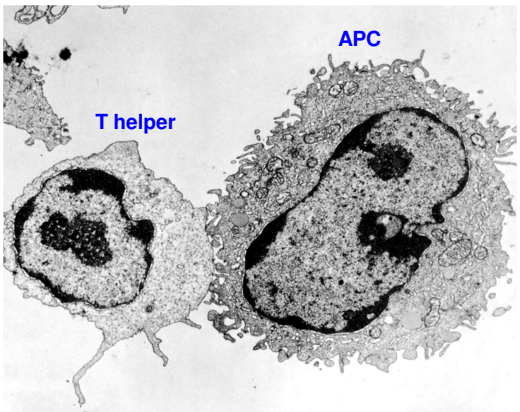


MHC molecules

- 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)

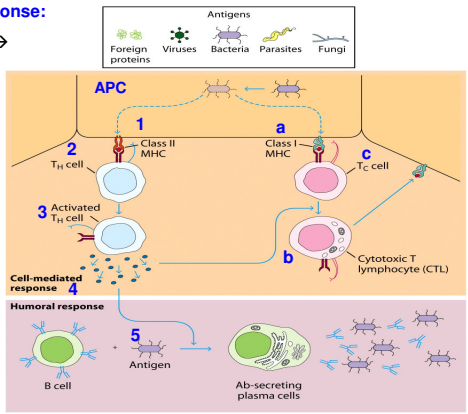
- **Three types**: Macrophages, Dendritic cells and B cells
- Goal: processing, presentation and activation of T cells
- **Requirement:**
  - 1) Express MHC-II
  - 2) Provide co-stimulatory signal for activation
  - 3) Cytokines for activation



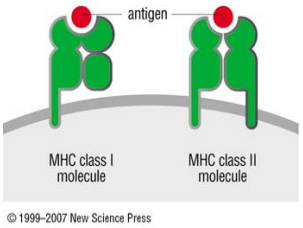
Effector Response:

-B cells: Abs →

-T cells:
Th cytokines
Tc killing



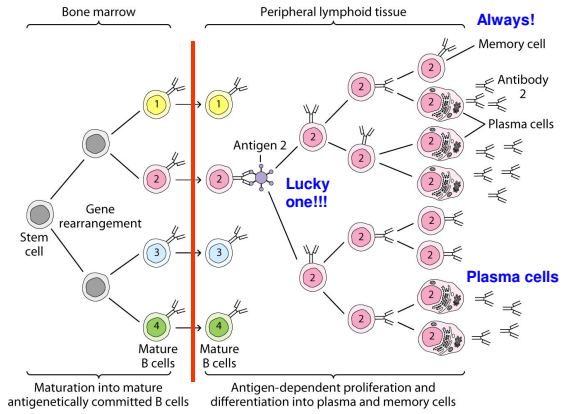
- T cell activation
-"Cross-presentation"
- Antigenic peptides!!!



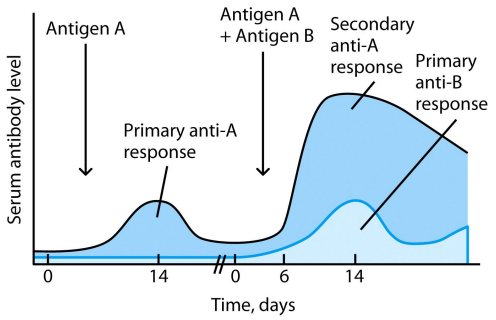
What T cells will be activated in each case?

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



- Ab levels 100-1000-fold higher → more plasma cells generated!!!!

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
Kuby IMMUNOLOGY, Sixth Edition
© 2007 W.H. Freeman and Company

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

Conclusion

- The Innate and Adaptive immune systems DO NOT operate independently.
- They are highly interactive and cooperative systems whose combines responses is more effective than either branch by itself.