### 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!

### 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”.

### Immune Response (two phases)

- **A) Recognition** – Highly specific!

- **B) Response (Effector Response)** – through cells and molecules

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### 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?

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### Questions?

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?
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

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

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

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.

1800 - Pasteur experiment – fowl cholera

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

Attenuated Vaccines
**Pasteur’s Contributions:**
- Vaccine (vacc=cow)
- Attenuated vaccines = cholera, anthrax, rabies

**Early Studies of Humoral and Cellular Immunity**

**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?**
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**

Cellular Immunity

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

Antigen?
1. **Release of Chemical Mediators**
   - Acute phase proteins (C-reactive protein) bind to bacteria and fungi activating complement; histamine acts on vessels; bradykinins cause pain.

2. **Vasodilation**: Increase in capillary diameter (pain)

3. **Increased Vascular Permeability**: Recruitment of cells and fluid (edema)

4. **Influx of Phagocytes**: Margination and extravasation

5. **Tissue Repair**: Fibrin (clotting) and fibroblasts

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**TABLE 1-3 Comparison of innate and adaptive immunity**

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

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**Adaptive or Acquired or Specific Immunity**

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

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**Acquired Responses**

- **B cells:**
  - Origin and mature in bone marrow
  - Mature B cells have 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

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**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 cause pain.
  2) **Vasodilation**: Increase in capillary diameter (pain)
  3) **Increased Vascular Permeability**: Recruitment of cells and fluid (edema)
  4) **Influx of Phagocytes**: Margination and extravasation
  5) **Tissue Repair**: Fibrin (clotting) and fibroblasts
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 $\rightarrow$ “Activated T cell” $\rightarrow$ polyclonal activation $\rightarrow$ Memory T cells + Effector T Cells (cytokines or cytotoxicity)

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

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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

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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** $\rightarrow$ multiple effects
- T cytotoxic (Tc) cells interact with antigen presented by MHC-I molecules
  - **Activation** lead to cell killing (cytotoxicity)

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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

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 rearrangement 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