Review of lecture 7

- **Science**
  - "Science is the human activity of seeking natural explanations for what we observe in the world around us."

- **Engineering**
  - Systematic design, production and operation of technical systems to meet practical human needs under specified constraints
  - Six steps of the engineering design method

How can technology help?

Science
1. Understanding biology: pathogens & disease
   - immune system

Engineering
2. Developing vaccines: from idea to product
   - vaccine design
   - production
   - testing safety & effectiveness
3. Addressing challenges for vaccine development:
   - Developed vs. developing countries
   - The AIDS vaccine challenge

Lecture map
1. The players: Types of pathogens
   Cells of the Immune system
2. Types of Immunity

Types of pathogens
- Mycobacterium tuberculosis
- Staphylococcus aureus
- Escherichia coli O147:H7
- Vibrio cholerae
- Bordetella pertussis (whooping cough)

Bacteria
- Cells with membrane and cell wall (usually)
- Can survive & reproduce outside host
- Can be killed or inhibited by antibiotics
- Responsible for >90% of hospital infections

How do bacteria cause disease?
- Invade host
- Reproduce
- Produce toxins which disturb function of normal cells
  - Paralyze cilia & inhibit clearance of respiratory secretions
  - whooping cough

Lecture map
1. The players: Types of pathogens
   - Cells of the Immune system
2. Types of Immunity

Bacteria
- DNA
- Size ~ 1 μm
How do bacteria cause disease?

**MRSA**: Methicillin Resistant Staphylococcus aureus

[Image]


Viruses

- Nucleic acid core surrounded by protein capsid, and for some viruses an envelope
- Use host intracellular machinery to reproduce
- They cannot be killed with antibiotics, but antivirals may inhibit different stages of their life cycle in the host
- >50 viruses that can infect humans

How do viruses cause disease?

1. Virus invades host cell
   - Binds to cell membrane receptors
   - Endocytosis brings virus into cell
2. Virus takes over cell
   - Use viral nucleic acid and host cell resources to make new viral nucleic acid and proteins
3. More virus is released from host cell
   - Virus causes host cell to lyse OR
   - Viral particles bud from host cell surface

How do viruses cause disease?

1. **The Human Immunodeficiency virus (HIV)**
2. **Viral components:**
   - nucleic acid core (RNA)
   - protein capsid
   - envelope
   - Glycoproteins

[Image]
How are we protected against pathogens?

Role of the Immune System
- Defend the body against pathogenic organisms
- Recognize self vs. non-self
- Eliminate microbial agents
  - Nonspecific mechanisms of the innate immune system
  - Specific mechanism of the adaptive immune system
- Display immunologic memory
- Tolerance of self-antigens

Lecture map
1. The players: Types of pathogens
   - Cells of the Immune system

2. Types of Immunity
   - Immunity
     - Physical Barriers: skin, mucous membranes
     - Innate Immunity: phagocytosis, complement, humoral
     - Adaptive Immunity

Cells of the immune system
- Bone marrow
- Blood = plasma + cells

Cells of the immune system
- Bone marrow
- Blood = plasma + cells
- Phagocytosis: 'eating pathogens'
- Innate Immunity: Defense vs. parasites, Allergic reactions
- Adaptive Immunity: Antibody production, Killing of infected cells
Cells of the immune system

- Neutrophil
- Macrophage
- Lymphocyte

Phagocytosis - killing

B-lymphocytes
T lymphocytes
NK cells

Lecture map
1. The players: Types of pathogens
Cells of the Immune system

2. Types of Immunity

Types of Immunity

Physical Barriers
- Skin (2 square meters)
- Mucosal membranes (400 square meters)

Innate Immune System
- General inflammatory response against pathogens outside of the cell

Adaptive Immune System
- Can adapt to defend against any specific invader inside or outside of the cell
- Important when innate immunity cannot defend against the attack
- Provides ‘Immune Memory’

What happens when you get a splinter?

- Pathogen makes it past a physical barrier
- Symptoms?
  - Red, swollen, hot, pus
- What causes these symptoms?
  - The Innate immune system is kicking into gear!
- Usually innate immune system can take care of it
The Innate Immune System: 3 main weapons

- Activated Macrophages
  Phagocyte ('eat') invading pathogens
  Produce chemicals that:
  - increase blood flow (redness & heat)
  - cause 'fluid leaking' (swelling)
  - recruit neutrophils (pus)
  Present antigen to adaptive immune system

- Complement proteins
  Present in tissue and blood
  Attach to surface of bacteria and viruses targeting them for phagocytosis
  Recruit other immune cells from blood

What happens when you get a splinter?

• Can you find the toxins, bacteria and viruses in your kit?
• Based on your understanding of the innate immune system, represent a macrophage during phagocytosis of an invading bacteria

Lecture map
1. The players: Types of pathogens
   Cells of the Immune system
2. Types of Immunity

   Immunity
   - Physical Barriers
   - Innate Immunity
   - Adaptive Immunity
     - Humoral Immunity
       - Antibodies produced by B-lymphocytes
       - Fights pathogens outside of cells
     - Cell-Mediated Immunity
       - Specific receptors on the surface of T-lymphocytes
       - Fights pathogens inside of cells

The Adaptive Immune System
• Recognizes antigens (molecular signatures) specific for each pathogen
• Effective against both intra- and extracellular pathogens
• Two main components:
  - Humoral immunity
    - Relies on antibodies produced by B-lymphocytes
    - Fights pathogens outside of cells
  - Cell-mediated immunity
    - Relies on specific receptors on the surface of T-lymphocytes
    - Fights pathogens inside of cells
What is an antibody?

- Bridge between:
  - Pathogen
  - Tool to kill it
- Antibodies have two important regions:
  - Fab region:
    - Binds antigen
    - Binds surface of virus infected cell
  - Fc region:
    - Binds macrophages and neutrophils, induces phagocytosis
    - Binds natural killer cell, induces killing

The Adaptive Immune response: humoral immunity

How do antibodies work?

1. **Neutralization**: Blocking the biological activity of toxin or pathogen •e: Blocking access
2. **Bridge**: Bringing together pathogens and phagocytes

Question:

- Which components of your kit are most like antibodies?
- Arrange the components of the kit to demonstrate how these antibodies “bridge” a pathogen and the tool to kill it?

The Adaptive Immune response: humoral immunity

- How are antibodies made?
  - B cells
    - Lymphocytes that make antibodies
    - Have B cell receptors on surface
    - 100 million different types of B cells, each with different surface receptors
    - B cell receptors are so diverse they can recognize every organic molecule
  - When a B cell binds antigen:
    - Proliferates • In one week, clone of 20,000 identical B cells
    - Secretes antibody

Clonal selection and proliferation

- First exposure to antigen
- Clonal expansion (proliferation)
- B cells (secrete antibody): 100 million different cells!
The Adaptive Immune response: cell-mediated immunity

- How do we kill virus once inside the cell?
  - Antibodies cannot get to it
  - Need T cells

- T Cells
  - Recognize protein antigens
  - When bind antigen, undergo clonal selection
  - Three types of T Cells:
    - Killer T Cells (Cytotoxic T Lymphocytes - CTLs)
    - Helper T Cells (orchestrate adaptive immune response)
    - Regulatory T Cells

How do T Cells recognize Virus-Infected Cells?

- All cells have Major Histocompatibility Complex (MHC) molecules on surface

- T Cells inspect MHC proteins and use this as a signal to identify infected cells

  ➢ Antigens (bits of pathogens) get loaded into MHC molecules:
    - When virus invades target cell, fragments of viral protein are loaded onto MHC proteins
    - Professional Antigen Presentation Cells (APCs: phagocytes of innate immunity)

Question:

- Demonstrate how the T cell can identify a virus infected cell: antigen presentation

- Why is this component of the adaptive immune system a significant advance over the innate immune system?

Antigen presentation and cellular immunity

Immunologic Memory

- **First time** adaptive immune system is activated by an antigen:
  - Build up a clone of B cells and T cells
  - Takes about a week
  - After infection is over, most die off
  - Some remain - memory cells

- **Second time** adaptive immune system is activated by that antigen:
  - Memory cells are easier to activate
  - Response is much faster - no symptoms

Immunologic Memory
The adaptive Immune Response

Putting it together...

Summary of lecture 8

- Pathogens: Bacteria and Virus

- Levels of Immunity:
  - Barriers → First line of defense
  - Innate → Inflammation
    - Phagocytes
    - Complement
  - Adaptive → Immunologic memory
    - Antibody mediated immunity
    - Cell mediated immunity → Pathogens within cells
    - Diversity to recognize 100 million antigens

What happens when you get a splinter?

The Adaptive immune response

1. Cellular Immunity:

2. Humoral Immunity:

The end.