Recap: the immune system

Nonspecific defenses
- Provide general protection against invasion by a wide range of pathogens

Specific defenses
- B and T cells combat particular pathogens

Nonspecific Defenses: external barriers

Internal defenses
- Generic response to all pathogens
- Defensive proteins
  - Interferons
  - Complement system
- White blood cells
  - Phagocytes (macrophages, neutrophils)
  - Natural killer (NK) cells
- Inflammation
- Fever

The action of interferon
- A virus-infected cell produces interferon molecules
- Interferon stimulates healthy cells to make antiviral proteins

NK cells
- A major component of the nonspecific immune system
- Kill cells that are missing “self” markers
- Release small proteins (perforins and granzymes) that cause the target cell to die by apoptosis
Recognizing the invader

- Antigen receptors on the surface of B and T cells recognize a specific foreign protein (antigen) and mount an immune response to it.
- One cell may recognize an antigen on the mumps virus, another cell recognizes an antigen on an E. coli bacterium.

Vocabulary

- Antigens: Are foreign substances that elicit an immune response.
- Antibodies: Are proteins made by our body that recognize a particular antigen and help destroy it.

B cells

- The body contains millions of B cells, each able to respond to a specific antigen.
- Secrete antibodies that recognize and destroy extracellular pathogens (bacteria, viruses, toxins).

Cytotoxic T cells

- Respond to pathogens that have already entered body cells.
- Cytotoxic T cells are directed against infected cells, some cancer cells, and tissue transplants.

Cytotoxic T cells are the only T cells that actually kill other cells.

Helper T cells coordinate the immune response
**Summary: the specific defenses**

- **B cells**
  - Secrete antibodies
  - Antibodies recognize and destroy extracellular pathogens (bacteria and viruses)
- **T cells**
  - Helper T cells and cytotoxic T cells
  - Directed against infected cells, some cancer cells and tissue transplants
  - Cells attacking cells
- 2 types of cells work together
  - Helper T cells coordinate the attack

**Specific defenses**

- An elaborately coordinated response to infection
- Two properties
  - **Specificity** for particular foreign molecules (antigens)
  - **Memory** for previously encountered antigens

**Infectious disease: Measles**

- The world's most contagious disease
- Caused by a virus
- Young, malnourished children especially vulnerable
- In developing nations, a child has a 5-15% chance of dying from measles
- Many survivors suffer serious complications
  - Blindness, loss of hearing, nerve damage

**Preventing Measles**

- **Vaccination**
  - Vaccine costs 26 cents per dose – but has yet to reach many of the world’s poorest countries.
  - Vaccination: if >90% coverage, the population will achieve “herd immunity”
  - Immunization levels high enough so that minority not immunized will still be protected.

**What is a vaccine?**

- **Purpose**: get the immune system ready to fight without exposing anyone to active germs
- **What’s in that syringe?**
  - Dead or weakened viruses
  - Inactivated toxins
  - Part of a virus
  - Boost the immune system so that it produces antibodies to the pathogen
Immunizations trigger the immune response, stimulating the body to defend itself and produce memory B and T cells.

Memory B and T cells – the basis for vaccinations

Tuberculosis (TB)

Caused by the bacterium Mtb
- A contagious, airborne disease
- Transmitted thru coughing, sneezing, talking
- TB usually attacks the lungs and destroys lung tissue
- Sx: severe cough, chest pain, coughing up blood

Infection with Mtb
- Latent form
  - The immune system sequesters the bacteria and prevents them from multiplying
  - 90% of people infected with Mtb never develop active TB disease
- Active TB
  - Develops in people with weak immune systems
  - Bacteria multiply rapidly and attack the lungs

Infection with Mtb

TB
- Almost all new infections (98%) occur in the developing world
- Rising number of people in industrialized nations are contracting TB
  - Leading cause of death among people with AIDS
  - Global transmission by jet travel

Antibiotic resistance is a growing problem

- Many patients stop taking meds when they begin to feel well
- This gives the bacteria time to evolve into a drug-resistant form

How does the body respond to a bacterial infection?

Specific responses
- B cells produce antibodies
- Helper T cells
- Cytotoxic T cells attack infected body cells

External barriers
- Skin, mucous membranes, secretions

The first responders
- Inflammation
- Complement

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Antibiotic resistance is a growing problem
**Challenges in TB treatment**

- Drug resistance (20% of TB cases)
  - Multidrug-resistant TB (MDR-TB)
  - Extensively drug-resistant TB (XDR-TB)
- Desperate need for better drugs and vaccines
  - Drugs that are easier to administer and cheaper
  - Vaccine to prevent TB infection in the 1st place
  - Gates Foundation: $$ to develop new drugs and vaccines

**HIV/AIDS**

- The problem is massive
  - 4th leading cause of death worldwide
  - ~40 million people are infected
  - 95% live in developing countries
  - And over 50% are women

**AIDS at 30**

- 7000 new infections a day
  - 1 in 3 in Africa
- US: 1 in 5 don’t know they’re HIV+
  - Most new infections are ‘men with men’, half are African American
  - In Africa as many as 90% don’t know they’re infected

  *(PBS Newshour 6/2011)*

**What makes HIV so lethal?**

- The virus highjacks immune cells
- HIV infects and destroys helper T cells
  - the very cells that normally suppress viral infections
- Long incubation period
  - The victim feels healthy but is highly infectious

**HIV highjacks immune cells**

- HIV binds to the plasma membrane of helper T cells
- Penetrates the cell
- Viral RNA is integrated into the cell genome
- Human cells ‘manufacture’ the virus

**HIV budding from an immune cell in culture**

- The viruses bud so rapidly that the cell eventually lyses
- The number of helper T cells drops, and the body cannot fight off other infections
- These secondary infections cause AIDS
  - Acquired immune deficiency syndrome

*(c) HIV (blue spots) infecting a white blood cell*
How does the body respond to a viral infection? To HIV?

- **External barriers**
  - Skin, mucous membranes, secretions

- **The first responders**
  - NK cells
  - Interferon
  - Inflammation

- **Specific responses**
  - B cells produce antibodies to the virus
  - Helper T cells
  - Cytotoxic T cells attack virus-infected cells

How is HIV transmitted?

- Unprotected sexual intercourse
  - Heterosexual or homosexual
- Direct contact with infected blood
  - Sharing needles
  - Blood transfusions
  - Blood is tested for HIV (not always in poor countries)
- Mother-to-child
  - HIV can infect the fetus in utero, or during birth
  - Without treatment, rate of transmission is 25%
  - Breast-feeding

Risk of HIV infection

- Most HIV-positive people do not know they are infected
- Long incubation period between infection and major illness
- Most people have no access to testing
- Stigma

Treating AIDS: Antiretroviral (ARV) therapy

- >30 drugs have been developed that suppress the virus
- Usually given in a “cocktail” of 3 - 4 pills
- Expensive, must be maintained for the rest of the patient’s life
  - Avoid developing resistance to drugs
- Still no known cure or vaccine for HIV

ARV targets

- Drugs that inhibit viral enzymes
  - Reverse Transcriptase inhibitors
    - Inhibit conversion of viral RNA into DNA
  - Integrase inhibitors
    - Inhibit integration of viral genome into host genome
  - Protease inhibitors
    - Inhibit enzymes that cut viral proteins into pieces → protein coat of new HIV particles

Prevention efforts have lagged

- ABC program - ineffective
- New approaches
  - Routine testing
  - Male circumcision (helps prevent acquisition)
  - Needle exchanges
  - ARVs – reduce viral load
  - Still in R&D stage
    - Vaginal microbicides
    - HIV Vaccine – the holy grail

With the use of ARVs, AIDS is now a chronic illness in industrialized nations