Ways to fight infection

1. Your own nonspecific and specific defenses
2. Vaccines
3. Antibiotics

Antibiotics act at all of these points

How antibiotics work

Antibiotics kill bacteria by:
1. Interfering with bacterial cell wall synthesis
2. Disrupting bacterial protein synthesis at the ribosome
3. Inhibiting function of enzymes involved in DNA synthesis

Kill bacteria but not human cells

Antibiotics are different from vaccines

- Antibiotics only kill bacteria and not every antibiotic is effective against every strain of bacteria.
- Colds and flu are caused by viruses – antibiotics don’t help.

Antibiotic resistance is a growing problem

- Bacteria vary in their ability to resist antibiotics.
- Many patients stop taking meds when they begin to feel well.
- This gives the surviving bacteria time to evolve into a drug-resistant form

How do bacteria develop resistance to antibiotics?

Bacteria can become resistant to antibiotics!

Bacteria might gain the ability to:
- Pump antibiotics out
- Breakdown antibiotics
- Reduce effectiveness of antibiotics
- Genes for resistance are often on a plasmid (that extra bit of circular DNA)
Using antibiotics inappropriately can cause bacteria to develop resistance.

1. You get sick with a bacterial infection.
2. You STOP taking antibiotics too early.
3. Some disease-causing bacteria might remain.
4. New disease causing bacteria cannot be killed with antibiotic.

Antibiotics are wonderful, but should be used responsibly! (prescribed appropriately, patients use entire dose)

Drug resistant staphylococcus bacteria (MRSA-skin infections) are now a big problem in hospitals.

Top 6 “killer” infectious diseases worldwide

<table>
<thead>
<tr>
<th>Disease</th>
<th>Estimated # of deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Respiratory infections</td>
<td>4.2 million</td>
</tr>
<tr>
<td>2. Diarrhea</td>
<td>2.2 million</td>
</tr>
<tr>
<td>3. HIV/AIDS</td>
<td>2.0 million</td>
</tr>
<tr>
<td>4. Tuberculosis</td>
<td>1.5 million</td>
</tr>
<tr>
<td>5. Malaria</td>
<td>0.9 million</td>
</tr>
<tr>
<td>6. Measles</td>
<td>0.7 million</td>
</tr>
</tbody>
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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.

Infectious disease: Measles

- The world’s most contagious disease
- Caused by a virus
- Young, malnourished children esp vulnerable
- In developing nations, a child has a 1 in 10 chance of dying from measles
- Many survivors suffer serious complications
  - Blindness, loss of hearing, nerve damage

WHO

Infectious disease

Importance of immunizations

- **Measles vaccination program** in Latin American and Caribbean
  - Strategy of “catch up, keep up and follow up”
    - “Catch up” campaign to achieve 90% vaccination coverage
    - Maintenance to “keep up” to 80% coverage
    - Regular “follow up” campaigns every 3-4 yrs
  - Dramatic drop in measles cases
    - 250,000 in 1990
    - 537 in 2001
Deadliest diseases for adults

- TB
- Malaria
- HIV/AIDS

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

How does the body respond to a bacterial infection?

- External barriers: Skin, mucous membranes, secretions
  - The first responders
  - Specific responses
    - B cells produce antibodies
    - Helper T cells
    - Killer T cells attack infected body cells

What if the infection overwhelms the immune system?

- Treating TB is difficult and expensive
- Requires long courses of multiple antibiotics
- TB is usually cured with a combination of first-line drugs taken for 6 to 9 months.
- The 1st line drugs were developed more than 40 years ago.

Treating TB
Multidrug resistant TB (MDR-TB)

- MDR TB occurs when the Mtb strain is resistant to the most powerful first-line drugs.
- To cure MDR TB, a combination of second-line drugs is used.
- These drugs cost up to 100 times more than first-line therapy.

MDR-TB rates, 2006 (WHO)

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: $3 to develop new drugs and vaccines

The AIDS pandemic

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

(Franz News Hour 6/2011)
The AIDS pandemic

AIDS is the leading cause of death in Sub-Saharan Africa
Average life expectancy has dropped from 62 to 47 yrs

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

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
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
  - Killer T cells attack virus-infected cells
  - Helper T cells

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 is key

- ABCs of prevention
  - Abstinence
  - Be faithful
  - use Condoms

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

AIDS – More than a health problem

- Crisis for developing countries
- Impacts economy, social fabric
  - Reduces number of workers
  - Slows economic growth
  - Increases poverty

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

HIV replication and ART  2:29
http://www.youtube.com/watch?v=rqDkYJn7w9Y&feature=related

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