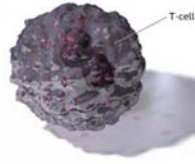
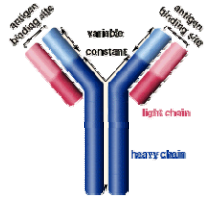


Immunity



Pathogens

A biological agent that causes disease or illness to its host.

Pathogen	Examples	Typical effects
Bacteria	<i>Escherichia coli</i>	honeymoon cystitis or urinary tract infection (UTI), peritonitis, food poisoning
	<i>Mycobacterium tuberculosis</i>	tuberculosis
	<i>Salmonella</i>	food poisoning
	<i>Staphylococcus aureus</i>	toxic shock syndrome
	<i>Streptococcus pneumoniae</i>	pneumonia
	<i>Streptococcus pyogenes</i>	strep throat
	<i>Helicobacter pylori</i>	stomach ulcers
Viruses	<i>Hepatitis</i>	liver disease
	<i>Influenza virus</i>	flu
	<i>Herpes simplex virus</i>	herpes
	<i>Molluscum contagiosum</i>	rash
	HIV	AIDS
Protozoa	<i>Cryptosporidium</i>	cryptosporidiosis
	<i>Giardia lamblia</i>	giardiasis
	<i>Plasmodium</i>	malaria
	<i>Trypanosoma cruzi</i>	chagas disease
	<i>Phaeocystis</i>	opportunistic pneumonia
Fungi	<i>Toxoplasma gondii</i>	toxoplasmosis
	<i>Trichinella spiralis</i>	trichinosis
	<i>Candida</i>	candidiasis
	<i>Aspergillus</i>	aspergillosis
Parasites	<i>Roundworm</i>	
	<i>Scabies</i>	
	<i>Tapeworm</i>	
Prion	Prion	BSE, vCJD

Antigens

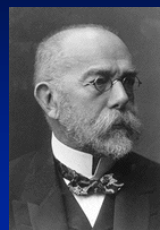
- Every kind of cell, virus, and substance has a unique molecular configuration that gives it an identity.
- An individual's own cells can be recognized as "self" and ignored. The body can recognize pathogens which are "not self".
- An example of "not self" is an antigen. An **antigen** is any molecular configuration that triggers the formation of lymphocyte armies.
- The most important antigens are proteins on the surface of pathogens and tumor cells.

Edward Jenner (1749-1823)



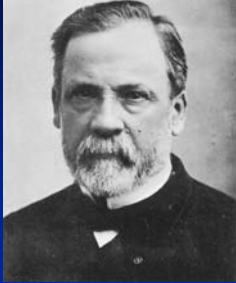
1. Smallpox was common during the mid 18th century and it was known that milkmaids did not get smallpox, but did get "cowpox".
2. Injected material from a cowpox sore into arm of healthy boy (his son).
3. Six weeks later, injected material from smallpox sores.
4. Boy remained healthy.
5. French called Jenner's procedure vaccination, which means "encowment".

Robert Koch (1843-1910)



1. First to link a specific pathogen to a specific disease.
2. Injected blood from anthrax-infected animals into healthy animals.
3. Subject animals developed anthrax and had bacteria in blood.
4. When these bacteria were grown in lab, then injected, they caused anthrax.
5. Showed that endospores could exist in soil for extended periods and were responsible for "spontaneous" outbreaks.

Louis Pasteur (1822-1895)



1. Developed immunization procedures for other pathogens.
2. Called them vaccinations in Jenner's honor.

Evolution of immune response

- Early simple organisms had phagocytes to help ingest food particles.
- Soon these phagocytes began engulfing other foreign bodies.
- Lysozymes developed and assisted in breaking down cell membranes of invaders.
- Eventually cells and molecules began signaling one another about invaders, which would lead to attacks on them.
- Cytokines evolved in invertebrates and coordinated signaled attacks.
- About 450 million years ago the jawed fishes developed white blood cells called B and T lymphocytes, which could recognize specific pathogens.

How does the body protect itself from all these potential invaders?

The 3 level security system:

1. Barriers at body surfaces
2. Nonspecific responses
3. Immune responses

1st Line of Defense

1. Barriers at Body Surfaces

- Intact skin – tough, impermeable, constantly sloughing off.
- Mucus membranes in respiratory tract, gut, reproductive organs.
- Infection fighting chemicals in tears, saliva, gastric fluid. Lysozymes in all three produce enzymes that digest bacterial cells walls. Urine and gastric fluid have low pH.
- Harmless bacterial inhabitants that can outcompete pathogenic visitors.
- Flushing effect of tears, saliva, urine.

2nd Line of Defense

What happens when a pathogen gets past our first line of defense and enters our bodies?

Imagine a skin cut.

We get an inflammatory response:

- Redness
- Swelling
- Fever
- Itchy

What causes these symptoms?

2nd Line of Defense

2. Nonspecific Responses

A. Inflammation

1. Fast acting WBCs
2. Macrophages (phagocytic WBC)
3. Complement proteins

B. Organs with pathogen-killing functions

C. Cytotoxic cells with a range of targets

Inflammation

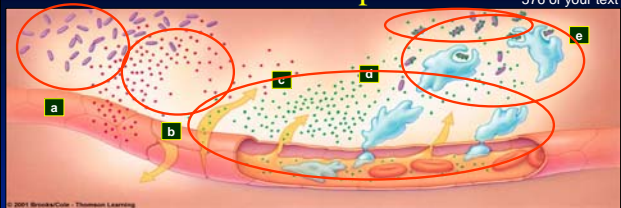
1. Mast cells in connective tissue
 - A. Synthesize and release histamine.
 - B. Trigger vasodilation (redness, warmth).
 - C. Increases permeability of capillaries and swelling.
2. Neutrophils, eosinophils, basophils arrive.
 - A. Neutrophils phagocytize bacteria.
 - B. Eosinophils release enzymes that create holes in parasitic worm outer layer.
 - C. Basophils secrete histamine for inflammation.

Inflammation (continued)

3. Monocytes from stem cells become macrophages.
 - A. Macrophages engulf, digest, and clean-up.
 - B. Macrophages make chemotoxins, interleukins, lactoferrin, endogenous pyrogens.
 - C. Fever is good. Kills pathogens, helps to rest.
4. Complement proteins (specific and nonspecific).
 - A. Trigger cascading reactions.
 - B. Attack complexes punch holes in pathogens.
5. Clotting proteins
 - A. Blood clots form, prevent spread of invaders.

Immune Response

Figure 34.3 from page 576 of your text



Bacteria in tissue damages cells

Mast cells release histamine, which triggers vasodilation and increased capillary permeability (redness and warmth)

Fluid and plasma proteins leak out of capillaries (swelling and pain)

Complement proteins attack bacterial membranes and clotting factors wall off area.

Neutrophils, macrophages and other phagocytes engulf invaders and debris. Macrophage secretions also kill targets, attract more phagocytes, induce fever and call for T and B lymphocyte proliferation.

Inflammation Response (nonspecific target)

Includes histamines



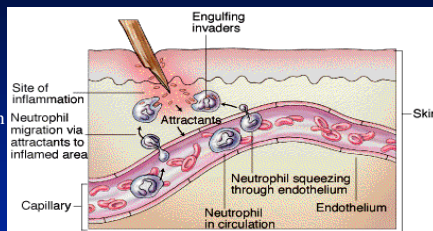
1 Tissue injury; release of chemical signals such as histamine

2 Dilation and increased leakiness of local blood vessels; migration of phagocytes to the area

3 Phagocytes (macrophages and neutrophils) consume bacteria and cell debris; tissue heals

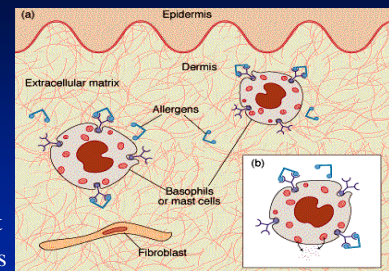
The Roles of Phagocytes

1. Neutrophils
 - Phagocytize (=digest) bacteria
2. Eosinophils
 - Secrete enzymes that make holes in parasitic worms



The Roles of Phagocytes

1. Basophils
 - Maintain inflammation due to histamine
2. Macrophages
 - Engulf and digest all foreign objects



3rd Line of Defense

What happens when a pathogen gets past our first line of defense and second line of defense (inflammation) and infection becomes established?

Adaptive Immunity: Two attack strategies:





- | | |
|------------------|-------------------------------|
| 1. B lymphocytes | 1. Antibody-Mediated Response |
| 2. T lymphocytes | 2. Cell-Mediated Response |

4 features of adaptive immunity:

1. B & T cells distinguish self from nonself entities.
2. Attack specific targets – not activated by tissue damage.
3. B & T cells have a remarkable number of different receptors to antigens.
4. Adaptive immunity has memory.





Adaptive Immunity Cast

B Lymphocytes

- Naïve B cells  Sentries
- Effector B cells  Release specific antibodies
- Memory B cells  Ready for future attacks
- Antibodies  Tag infected cells for destruction.





Adaptive Immunity Cast

T Lymphocytes

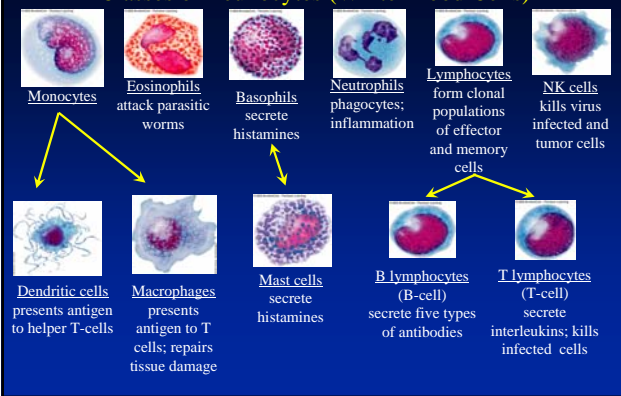
- Helper T cells  Sentries & communicators
- Cytotoxic T cells  Attack infected cells
- Memory T cells  Ready for future attacks
- NK T cells  Natural Killer cells

Adaptive Immunity Cast

Others

- Antigen presenting cells  Stimulate activation of B & T cells
- MHC  Major Histocompatibility Complex proteins present antigens.
- Interleukins  Signaling molecules
- Lymphatic system  Rendezvous center for disposal.

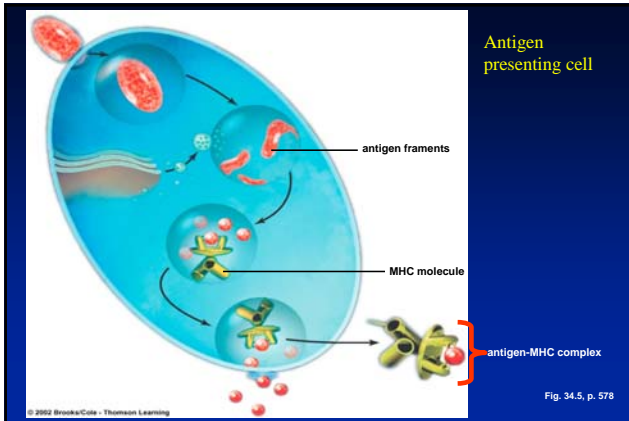
Classes of Leukocytes (White Blood Cells)



Antigen Presenting Cells

Macrophages, Naïve B cells and Dendritic cells

1. When a pathogen enters the body various cells engulf and digest the invaders.
2. The broken up invader bits are processed and combined with MHC on the surface of the presenting cell.
3. MHC – Major Histocompatibility Complex is a self recognition protein on the surface of cells. MHC binds to pieces of processed antigens and presents them to T & B cells.



Two types of Adaptive Immunity responses

1. Antibody-Mediated Response – extracellular pathogens
 - B Lymphocytes
 - Antibodies
2. Cell-Mediated Response – pathogens inside cells
 - T Lymphocytes

B and T Cell Armies

- B and T lymphocytes have receptors for millions of specific antigens. When they recognize an antigen, they trigger immune responses.
- B and T cells undergo repeated cell division to make an army to fight the pathogen.
- The army is divided into subpopulations of effector and memory cells. Effector cells kill the pathogen. Memory cells are reserved for future battles if the pathogen attacks again.
- Memory cells are key to immunization.

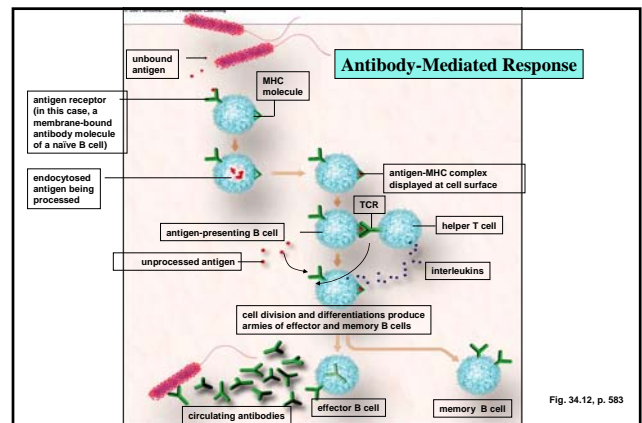
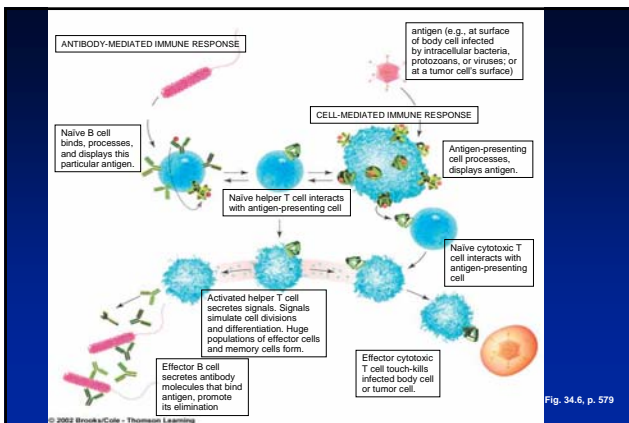
Clonal Selection of a B Cell

1. Only the B cell with antigen-receptor that matches antigen is stimulated to divide
2. Mitosis yields many cells with that receptor

antigen

B1 B2 B3

B2 B2 B2 B2

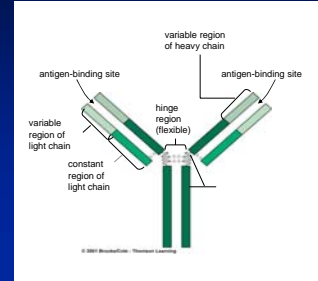


Antibody-Mediated Response



Antibody Structure

1. Antibody consists of four polypeptide chains
2. Certain parts of each chain are variable; impart antigen specificity



Antibody-Mediated Response: B Cells

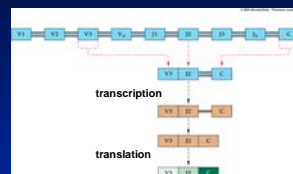
1. Antibodies: 5 main types =
2. Immunoglobulins "Igs": protein products of gene shufflings that take place as B cells mature and an immune response is underway
 - Ig M
 - Ig G
 - Ig A
 - Ig E
 - Ig D

Immunoglobulins

- | | |
|---|--|
| <ol style="list-style-type: none"> 1. Ig M <ul style="list-style-type: none"> • Secreted first • Activate complement proteins 2. Ig G <ul style="list-style-type: none"> • Activate complement proteins • Neutralize toxins • Cross placenta • Secreted in milk | <ol style="list-style-type: none"> 1. Ig A <ul style="list-style-type: none"> • On mucous surfaces 2. Ig E <ul style="list-style-type: none"> • Triggers inflammation • Parasitic worms 3. Ig D <ul style="list-style-type: none"> • Function not understood |
|---|--|

Generating Receptor Diversity

1. Antibody-coding gene recombines as B cell matures
2. Produces variable transcripts that are translated to produce receptor portion of the antibody molecule



1. Similar process produces variable T cell antigen receptors

Immune Responses to Same Antigen

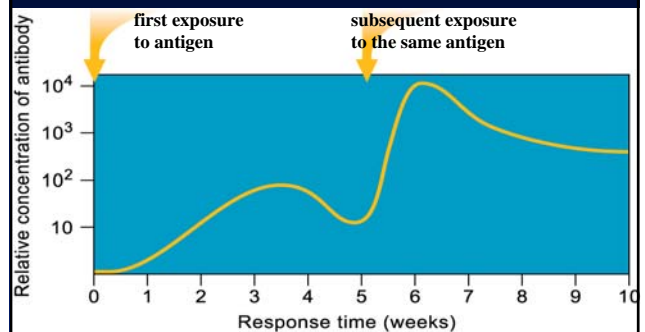


Figure 34.9 from page 581 of your text

Cell-Mediated Response

1. Carried out by T cells.
2. Stimulated by antigen-presenting macrophages.
3. Main target is antigen-presenting body cells (cells with intracellular pathogens) or tumor cells.

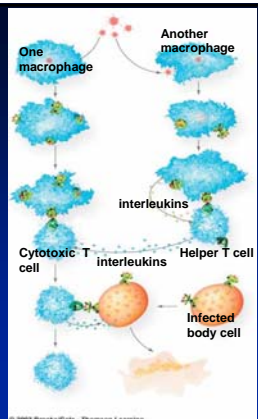


Fig. 34.13, p. 584

Cell-Mediated Response



Lymphocyte Battlegrounds

1. Lymph nodes filter antigens from body fluids.
2. Macrophages, dendritic cells, B cell and T cells in nodes and spleen mount a defense. Then take antigens to the lymphatic system where they meet B & T cells.

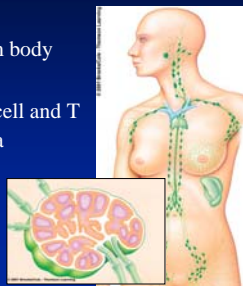


Fig. 34.10, p. 581

HIV and AIDS

1. HIV: Human Immunodeficiency Virus
 - A retrovirus that attacks the body's immune system
 - Targets antigen-presenting macrophages and helper T-cells and impairs their function
2. AIDS: Acquired Immune Deficiency Syndrome
 - Is the result of a weakened immune system caused by the HIV infection
 - Is the result of being HIV positive and having one or more of the AIDS defining illnesses
 - Characterized additionally by having a T cell count of 200 or less

AIDS: The Immune System Compromised

Symptoms

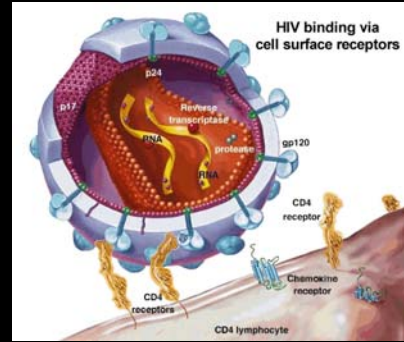
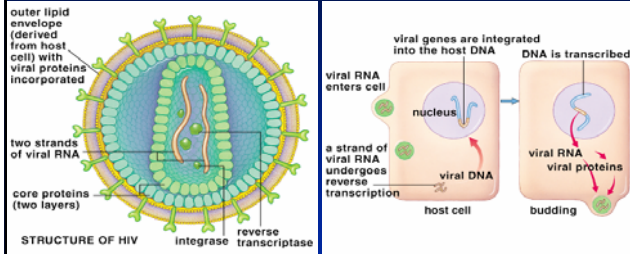
- 5-10 year lag after infection
- Flu-like
- Weight loss, fever, fatigue, night sweats
- Enlarged lymph nodes
- Opportunistic infections
 - *Pneumocystis carinii* (pneumonia)
 - Kaposi's sarcoma (cancer of the connective tissue)

AIDS: The Immune System Compromised

1. Transmission: Bodily Fluids
 - Blood
 - Semen
 - Vaginal Secretions
 - Breast Milk
2. Treatment
 - No known cure
 - Difficult because of high mutation rates
3. Prevention:
 - "Safe" sex
 - No IV drug use

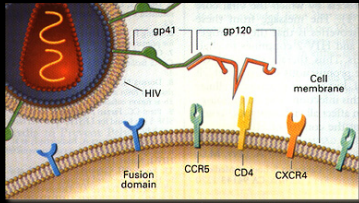
Life Cycle of HIV

HIV (Virus Particle)

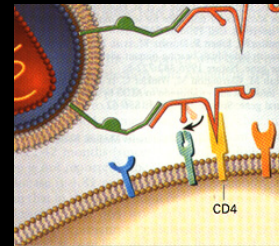


HIV retrovirus and Helper T lymphocyte

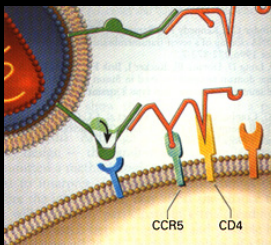
Illustrations and content based on "Infection by Human Immunodeficiency Virus - CD4 Is Not Enough" by Levy, J.A. - *The New England Journal of Medicine*, Vol 335, no 20, pages 1525-1527, Nov., 1996. Illustrations (c) Massachusetts Medical Society.



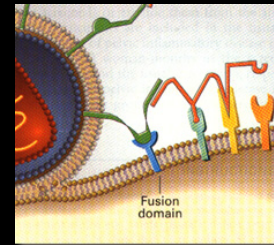
HIV-1 interacts with the cell-surface receptor CD4 of Helper T cells, and through conformational changes becomes more closely associated with the cell through interactions with other cell-surface molecules, such as the chemokine receptors CXCR4 and CCR5. The likely steps in HIV infection are as follows:



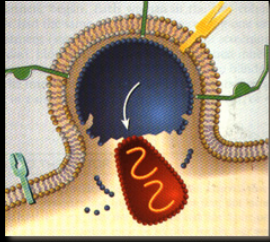
The CD4-binding site on HIV-1 gp120 interacts with the CD4 molecule on the cell surface.



Conformational changes in both the viral envelope and the CD4 receptor permit the binding of gp120 to another cell-surface receptor, such as CCR5.



This second attachment brings the viral envelope closer to the cell surface, allowing interaction between gp41 on the viral envelope and a fusion domain on the cell surface. HIV then fuses with the cell.



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Subsequently, the viral nucleoid enters into the cell, most likely by means of other cellular events. Once this stage is achieved, the cycle of viral replication begins.