

Communicable Disease

Person to person microbial diseases

- Airborne transmission of diseases
- Direct contact transmission of diseases
- Sexually transmitted diseases - AIDS

Most microbes are our friends; it is the minority that creates pathologies

**REPORTED CASES OF SELECTED
NOTIFIABLE DISEASES PREVENTABLE BY
VACCINATION, UNITED STATES, 2001**

• Hepatitis A	10,609
• Hepatitis B	7,843
• Pertussis	7,580
• Meningococcal disease	2,333
• H. influenzae, invasive	1,597
• Mumps	266
• Measles	116

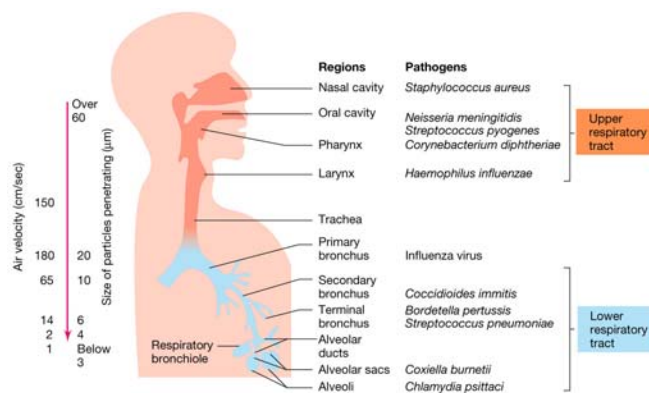
Source: NNDSS, CDC



Airborne pathogens

- Air is an inhospitable environment for microorganisms
- Outside: airborne microbes are soil microbes; indoor: more microbes originating from the respiratory tract
- Sneezing: each droplet (10 μm) - 1-2 microbial cells and moves at 200 mi/hr; rapid evaporation leads to formation of an organic particle with embedded microbes

Respiratory infections



- As air moves down the respiratory system its velocity decreases and with it the size of the deposited microbes: The slower the flow the smaller are the microbes that settle

Bacterial respiratory pathogens

- Humans are the exclusive host ▲ person-to-person transmission
- Mostly gram positive; a thicker cell wall and more resistance to drying
- The problem of secondary infections
- Readily respond to antibiotics

Streptococcal diseases

- Gram positive anaerobes; *S. pyogenes* and *S. pneumoniae*
- *S. pyogenes* is a normal inhabitant of the upper respiratory tract; in weakened hosts or if new virulent strains are introduced ▲ acute infections
 - Pharyngitis (“strep throat”; viral infections), may lead to:
 - Scarlet fever: a phage encoding for erythrogenic toxin (pink rash)
 - Necrotizing fasciitis: “flesh-eating bacteria” when toxins act as super antigens
 - Rheumatic fever: Cell surface antigens that mimic host cellular component ▲ autoimmune response (joints, heart, kidney)
 - Acute glomerulonephritis: accumulation of pathogen antigen-antibodies complexes in the kidney
- **Different (60) strains of *S. pyogenes* cause these different diseases**

Diagnosis, prevention and treatment

- Rapid diagnosis is important to prevent follow-up diseases - a throat swab:
 - Rapid antigen detection (RAD) - in minutes
 - Culturing (higher sensitivity)
 - Serological tests: Antibodies in patient blood
- No vaccines; penicillin and erythromycin are highly affective

Streptococcus pneumoniae

- Pneumococcal pneumonia: Lung infection that elicits severe inflammation of alveolar tissue, fluid accumulation; possible bacteremia, bone and inner ear infections, and endocarditis.
- Organism produces a thick capsule that protects against phagocytosis
- 30% death rate if untreated
- Diagnosis by culturing from sputum or blood
- Vaccine against 2/3 of the 90 known strains (capsular polysaccharides are the antigens)
- Treatment: Respond to antibiotics but multidrug resistance a major problem

***Corynebacterium* and Diphtheria**

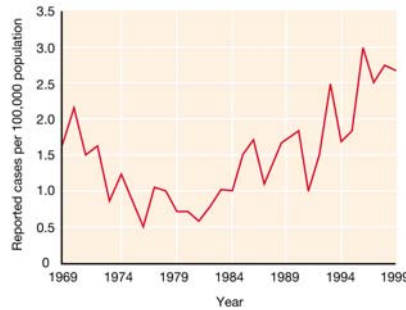
- *Corynebacterium diphtheriae* is a gram positive aerobe
- Transmitted by airborne droplets and colonizes the throat and tonsils
- Organism produces neuraminidase that degrades N-acetylneuraminic acid to facilitate invasion
- Bacterium contains lysogen of bacteriophage β that encodes for an exotoxin (diphtheria toxin) a eukaryotic protein synthesis inhibitor
- Produces inflammation Δ pseudomembrane (dead cells and the bacterial biomass); may lead to suffocation
- Highly immunogenic

Diagnosis, prevention, and treatment

- Presence of the pseudomembrane and isolation of *C. diphtheriae*
- Treated with antibiotics and antitoxin (neutralizing antibodies); penicillin, erythromycin, and gentamicin
- Vaccination using a formaldehyde treated diphtheria toxin (DPT - diphtheria, tetanus, pertussis)

***Bordetella* and Whooping Cough**

- *B. pertussis* - A gram negative aerobic coccibacillus affecting children < 5 yrs
- Production of filamentous hemagglutinin antigen that facilitate attachment to host cells in the upper respiratory tract
- Pertussis exotoxin Δ synthesis of cyclic AMP Δ symptoms
- Treated with antibiotics; immune response important (recovered individuals carry live organisms for 2 weeks)



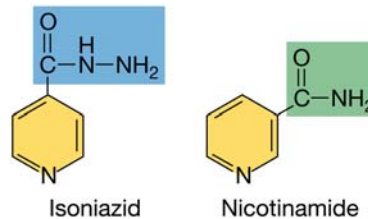
- Effective vaccination (DTP)
- available, but may cause compli-
- cations; immunization < 60% Δ
- increase in cases; new cleaner
- preparations developed

***Mycobacterium* and Tuberculosis**

- *M. tuberculosis* - discovered by R. Koch in 1882
- Highly infectious; transmission by the respiratory route
- Primary infection: bacteria grow in the lung Δ formation of tubercles (aggregates of activated macrophages) Δ in compromised individuals development of acute pulmonary infection, spread of bacteria and death
- Postprimary: Presence of immune response to the pathogen; the tuberculin test: diagnosis of the hypersensitive state; injection of a protein extract of the pathogen Δ induration and edema
- Higher sensitivity to new or renewed infection Δ chronic disease of gradual destruction of lung tissue

Prevention and treatment

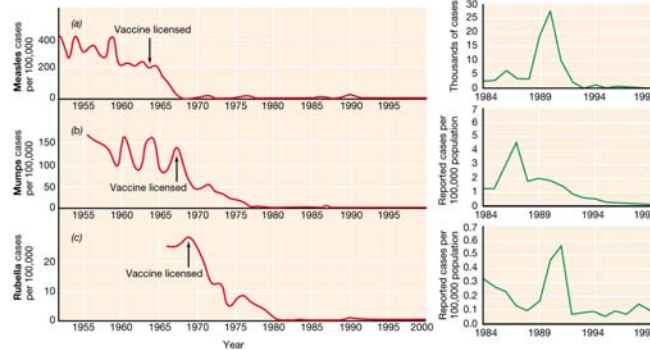
- Chemotherapy:
isonicotinic acid
hydrazide (isoniazid);
interfere with the
synthesis of mycolic acid
possibly by inhibiting
nicotinamide dependent
enzymes; 5 pmol is
sufficient to kill 10^9 cells
- Long term treatment (9
months) with isoniazid
and other antibiotics;
incomplete treatment \blacktriangle
antibiotic resistance



Mycobacterium leprae and Hansen's disease (leprosy)

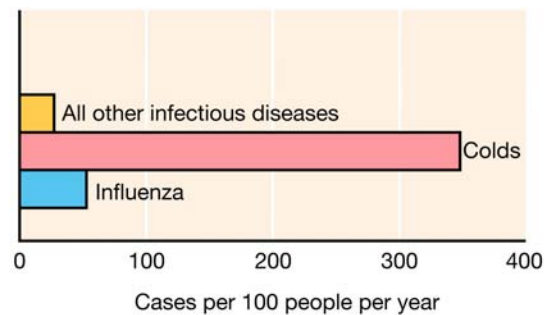
- Can only be grown in armadillo
- Multibacillary (lepromatous) form: Bulblike skin lesions due to growth of the bacteria (10^9 cells per g tissue) \blacktriangle destruction of nerves
- Paucibacillary (tubercular) form: organism is not detected and spontaneous recovery
- Treatment: Multidrug therapy for up to 1 year
- A problem in developing countries (1.2M with 0.5M new cases per year)
- Other mycobacteria diseases are known (*M. bovis* \blacktriangle tuberculosis)

Viruses and respiratory infections



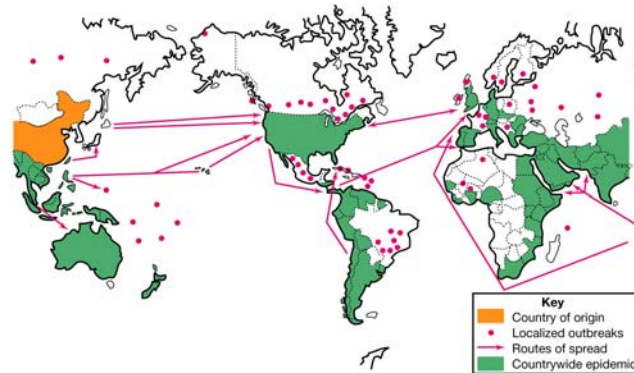
- Measles, mumps, and Rubella: vaccination (MMR) is available.
- Normally mild diseases but may lead to various serious complications
- Chickenpox and shingles: vaccine available since 1994; shingles, a painful skin lesion, arises later in life from virus that remains dormant in nerve cells

Colds and Influenza



- The most common infectious diseases
- Influenza: The occasional emergence of new strains - segmented RNA genomes and coinfection by various strains
 - Antigenic shift: result of a new assortment of the genome Δ modifications of virion proteins (hemagglutinin and neuraminidase)
 - Antigenic drift: mutations in genes encoding virion proteins

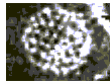
The global distribution of influenza



- Antigenic drift Δ reduced immunity Δ epidemics with 2-3 yrs cycles
- Antigenic shift Δ pandemics (10 - 40 yrs cycles); many time arise in animals and transmitted to humans
- Vaccines: against a combination of current strains; the elderly and compromised individuals

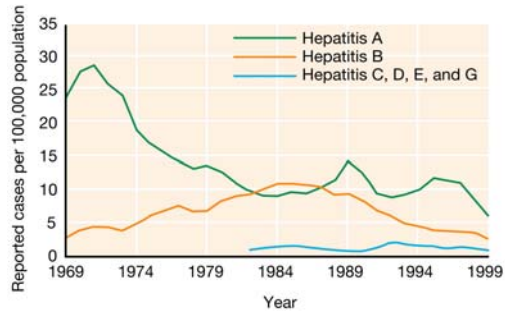
Direct contact transmission: *Staphylococcus*

- A normal skin and upper respiratory tract flora; *S. epidermidis* and *S. aureus*
- Causative agents of acne, boils, impetigo, pneumonia, osteomyelitis, carditis, meningitis and arthritis
- Many are asymptomatic carriers
- Pathogenesis by production of extracellular toxins and enzymes
 - Hemolysins: clearing around colonies on blood agar
 - Enterotoxins: food poisoning
 - Coagulases: coagulation of fibrin to form a protective layer around cell
 - Leukocidins: destruction of leukocytes and skin lesions (pus formation)
- Toxic shock syndrome: production of toxic shock syndrome toxin, a superantigen leading to inflammatory response



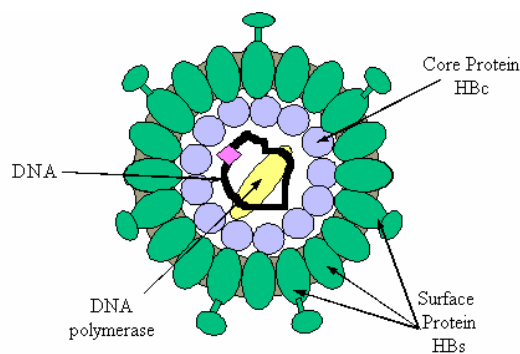
Hepatitis viruses

- Inflammation of the liver; cirrhosis and sometime cancer
- Pathology: Jaundice ▲ hepatomegaly (liver enlargement) ▲ cirrhosis
- Six different viruses; most transmitted by contact with body fluids (needles, sexual transmission)
- HAV: Transmitted via fecal contamination of seafood; vaccine available
- HBV: Serum hepatitis; sexually transmitted and leading to cirrhosis and cancer: vaccine available

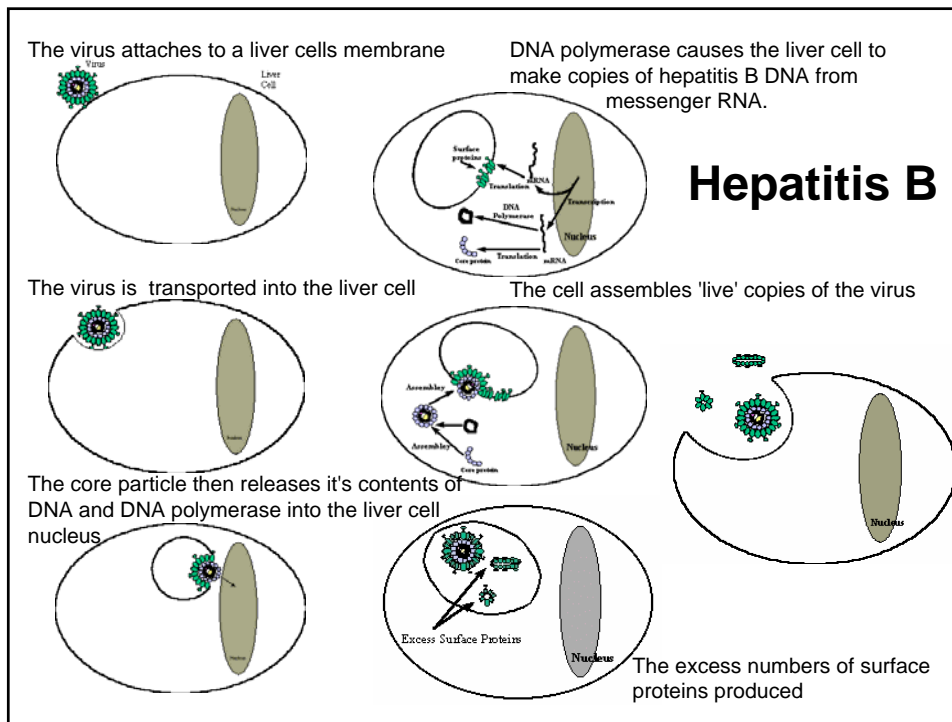


- Diagnosis by liver biopsy; immuno-
- assays; DNA based methods
- Prevention: based on the transmission route; drugs available for treatment

Hepatitis B



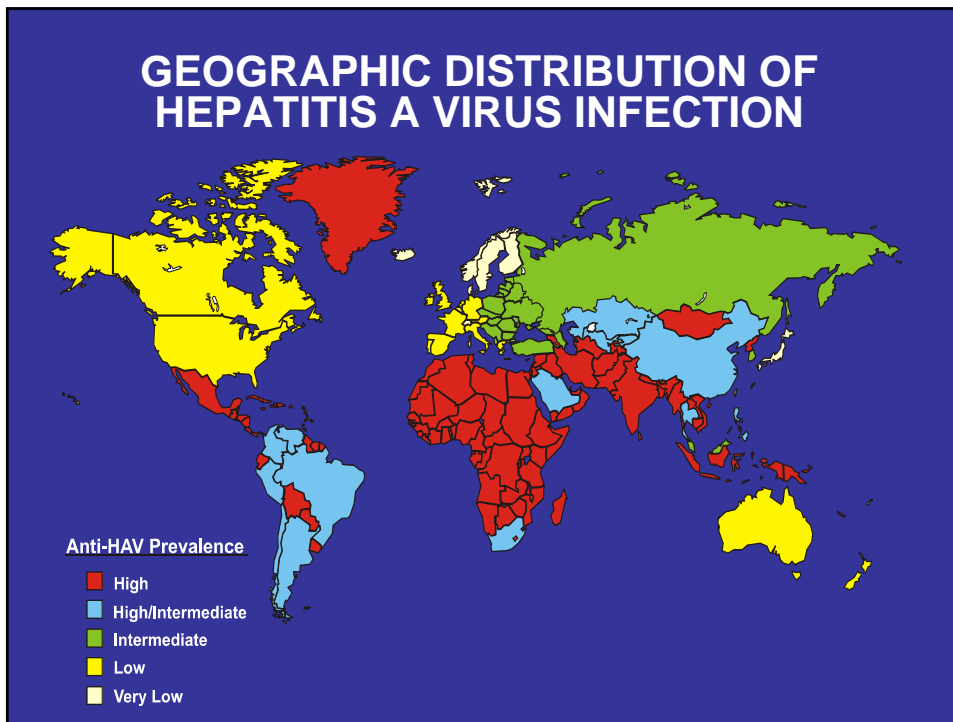
www.hon.ch/Library/Theme/HepB/hbvirus



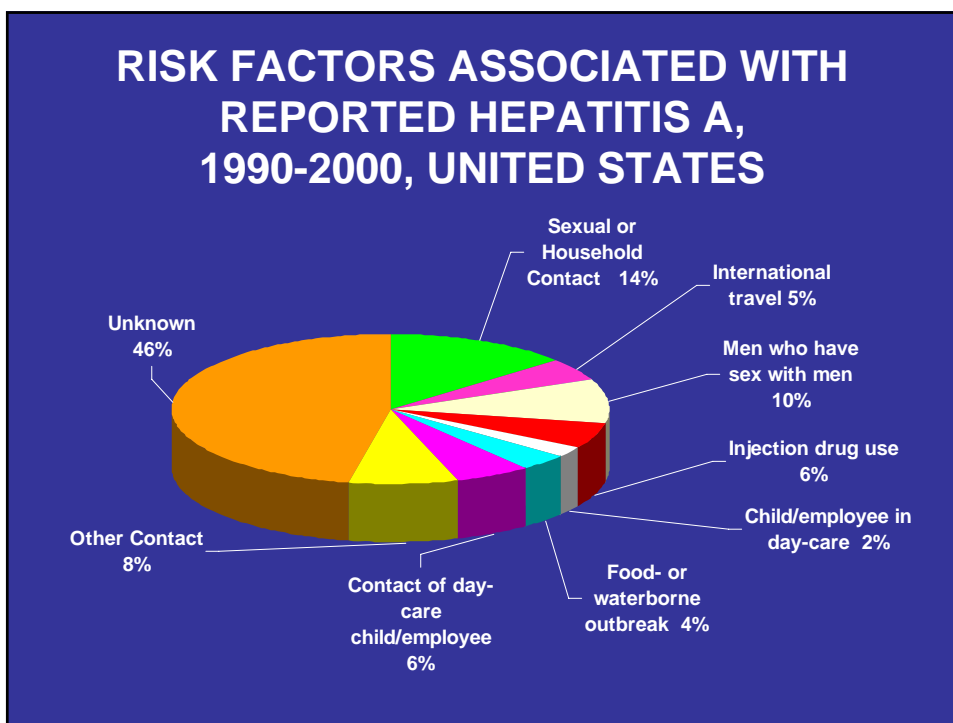
HEPATITIS A VIRUS

- RNA Picornavirus
 - Single serotype worldwide
 - Acute disease and asymptomatic infection
- No chronic infection
 - Protective antibodies develop in response to infection - confers lifelong immunity

GEOGRAPHIC DISTRIBUTION OF HEPATITIS A VIRUS INFECTION



RISK FACTORS ASSOCIATED WITH REPORTED HEPATITIS A, 1990-2000, UNITED STATES



PREVENTING HEPATITIS A

- Hygiene (e.g., hand washing)
- Sanitation (e.g., clean water sources)
- Hepatitis A vaccine (pre-exposure)
- Immune globulin (pre- and post-exposure)

Sexually transmitted diseases (STD)

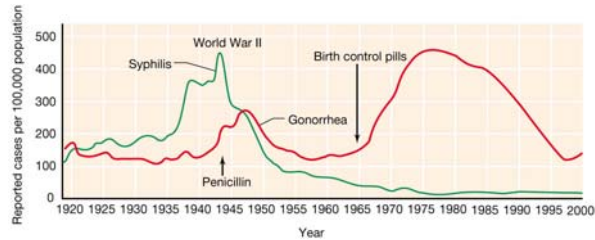
Bacteria, viruses, protozoa and fungi (**Table 26.2**); highly susceptible to drying, heat, and light ▲ colonization of the genitourinary tract: transmission

- Difficult to treat:
 - A 1/3 of all patients are teens with multiple partners
 - Minor symptoms
 - Social stigma
- Important to treat:
 - Most STD are easily treatable
 - Lack of treatment can lead to severe problems (infertility, cancer, heart disease and more)

Transmission is only by the exchange of body fluids: the spread of STD can be prevented by using protective barriers or abstinence

Gonorrhea and Syphilis

- Both easily treated
- (penicillin)
- Gonorrhea:
Neisseria
- *Gonorrhoeae* – Gram-negative; mild infection of the genitourinary tract;
- Pelvic inflammation, heart and joint disease; eye infection in new born babies
- Syphilis: *Treponema pallidum* - a spirochete; lesions in the point of entry (primary) ^ spread to other part of the body, hypersensitive response (skin rash; secondary) ^ may persist and damage central nerve system (tertiary)



Chlamydia, Herpes, and Trichomoniasis

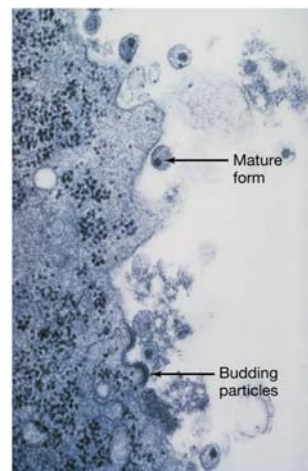
- Prevalent and difficult to diagnose and treat
- Chlamydial nongonococcal urthritis (NGU): *Chlamydia trachomatis*; the fastest increasing STD; commonly transmitted with Gonorrhea; inflammation of genitourinary organs; may lead to arterial plaques and heart diseases
- Herpes: Herpes simplex virus; HSV-1 not STD; HSV-2 causes genital herpes; a correlation with cervical cancer and transmission to babies during birth; treated with acyclovir, a specific DNA synthesis inhibitor
- Trichomoniasis: *Trichomonas vaginalis* (protozoan); transmission could occur by contact with contaminated inanimate objects; more common among women; men may be asymptomatic and serve as a reservoir; effectively treated with metonidazole

AIDS and HIV

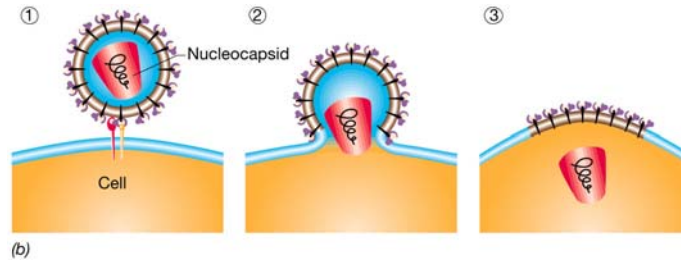
- HIV-1 is an RNA virus; HIV-2; 50M infected (HIV positive); 15M have died
- AIDS is defined by:
 - Presence of antibodies to HIV, and
 - Reduced CD4 T-cells ($<200/\text{mm}^3$) or $< 14\%$ CD4 T/total lymphocytes, or
 - At least one of a list of bacterial, fungal, and viral infections or carcinomas
- The most common are *Pneumocystis carinii* pneumonia and Kaposi's sarcoma (20,000 fold more common among AIDS patients)

HIV: Cell interactions and infection

- The target for HIV infections are CD4 presenting cells - lymphocytes and T helper cells
- Infected cells produce viral cDNA \blacktriangle integration of DNA into the host genome \blacktriangle prophage activation \blacktriangle host cell death

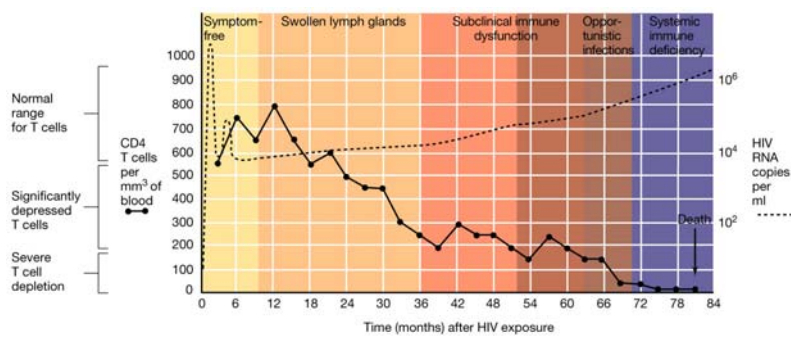


HIV - CD4 cell interactions



- Interaction is initiated by binding of viral gp 120 to CD4 receptors on lymphocytes cell surface \wedge CCR5 (a chemokine receptor) bind to gp 120
- While reproducing in lymphocytes gp 120 is altered to facilitate interaction with the chemokine of T_H cells - CXCR4 \wedge HIV released from lymphocytes can now infect T cells
- Infected T cells insert viral gp 120 into their outer membrane \wedge interaction with uninfected T cell to form cyncytia (a cell aggregate) \wedge loss of immunity

A fight between HIV and CD4 T cells



- Initially active infection and intense immune response; both viral production and T cells production increased
- The immune response is overwhelmed and immunity decline

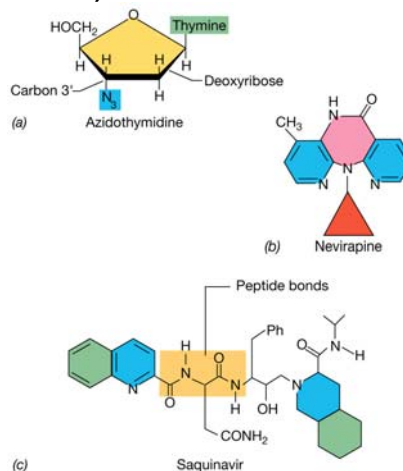
Diagnosis of AIDS

- Presence of HIV in the blood
- Levels of CD4 T cells
- Recent history of one or more opportunistic infections or atypical cancers
- RT-PCR for viral RNA levels to quantitate the virus - **viral load**
- Prognosis: If untreated death within 5 - 7 years

AIDS treatment: drugs that specifically interfere with viral, but not host, metabolism

(Table 26.3)

- Nucleoside analogs (AZT); Nucleoside reverse transcriptase inhibitors
- Non-nucleoside reverse transcriptase inhibitors; inactivation by binding to the active site
- Protease inhibitors; synthetic peptides that inhibit virus maturation
- Viral mutants resistant to all drugs readily arise Δ multi drug treatment
- Drug toxicity
- Cost of treatment



AIDS immunization

- Antibodies to gp 120 blocking gp 120-CD4 interactions; mutants with modified gp 120 are readily produced
- Subunit vaccines: engineered harmless viruses that expose several of HIV antigens - in clinical trial stages
- HIV-2; immunity but long-term effects are not known

