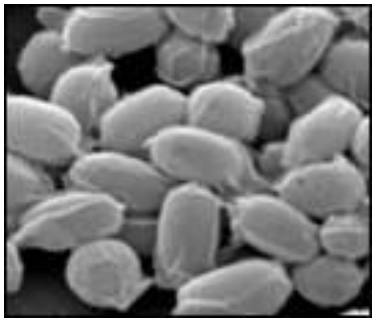
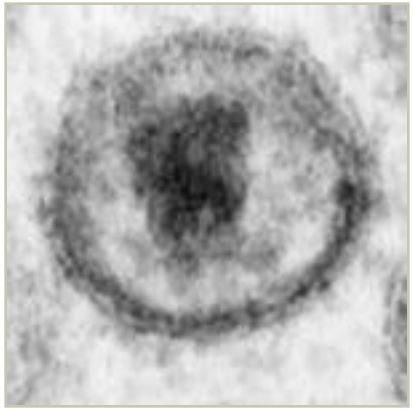
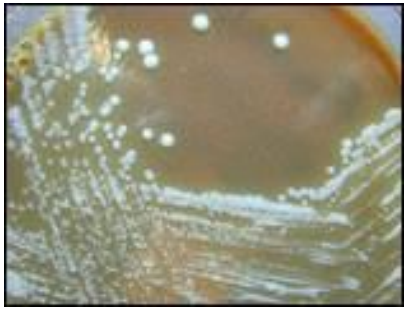
INFECTIOUS DISEASES







INFECTIOUS DISEASES - DEFINITIONS

Disease – a pathological condition of body parts or tissues characterized by an identifiable group of signs and symptoms.

Infectious disease – disease caused by an infectious agent such as a bacterium, virus, protozoan, or fungus that can be passed on to others.

Infection – occurs when an infectious agent enters the body and begins to reproduce; may or may not lead to disease.

Pathogen – an infectious agent that causes disease.

Host – an organism infected by another organism.

Virulence – the relative ability of an agent to cause rapid and severe disease in a host.

INFECTIOUS DISEASES - CAUSE OF DEATH

- Infectious diseases are responsible for a quarter to a third of all deaths worldwide.
- Infectious diseases account for more than half of all deaths in children under the age of 5.
- Of the top ten causes of death compiled by the World Health Organization, five are due to infectious diseases.
- The top single agent killers are HIV/AIDS, malaria and tuberculosis. The other top killers are lower respiratory infections and diarrheal diseases, which are caused by a variety of agents.

INFECTIOUS DISEASES AND HISTORY

Infectious agents have probably always caused disease in humans.

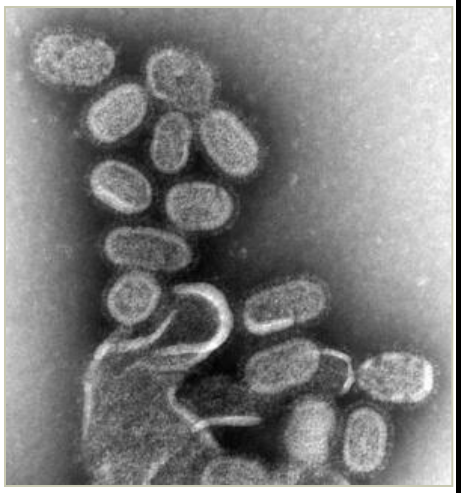
Smallpox has been described in ancient Egyptian and Chinese writings and may have been responsible for more deaths than all other infectious diseases combined.

There is evidence that malaria and poliomyelitis have existed since ancient times.

In the 14th Century, the bubonic plague, or Black Death, killed about 20 million people in Europe alone.

In the 20th Century, the 1918 influenza may have killed up to 50 million people worldwide

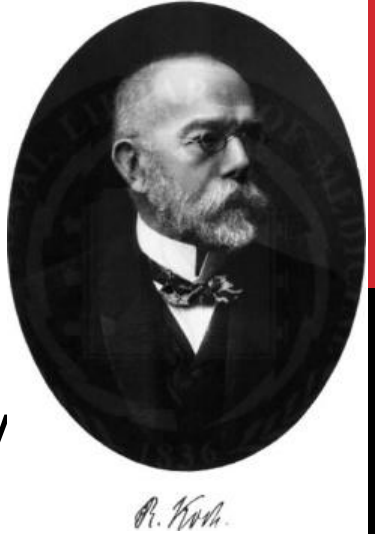
Close to 20 million people have died of AIDS to date.



Courtesy of CDC

Recreated 1918 Influenza virions. The 1918 Spanish flu killed more than 50 million worldwide.

Koch's Postulates



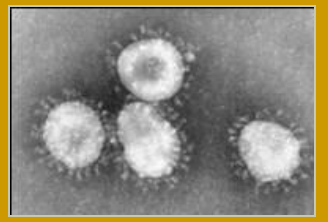
Koch developed four criteria to demonstrate that a specific disease is caused by particular agent.

1. The specific agent must be associated with ev case of the disease.
2. The agent must be isolated from a diseased host and grown in culture.
3. When the culture-grown agent is introduced into a healthy susceptible host, the agent must cause the same disease.
4. The same agent must again be isolated from the infected experimental host.

Modifications to Koch's Postulates

1. Some infectious agents cannot be cultured e.g. prions
2. Some pathogens have non-virulent strains whose presence does not link them to a disease. E.g. non encapsulated *Diplococcus pneumoniae*

INFECTIOUS DISEASE AGENTS



Most infectious agents that cause disease are microscopic in size and thus, are called microbes or microorganisms.

Different groups of agents that cause disease are:

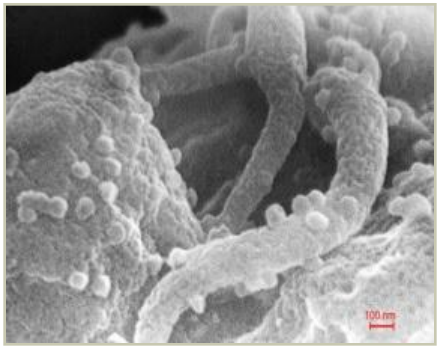
- Bacteria
- Viruses
- Protozoa (Protists)
- Fungi
- Helminths (Animals)

SMALL POX

- The only infectious disease to be considered eradicated!
- Humans are the only reservoir for the virus
- caused by either of two virus variants, *Variola major* and *Variola minor*.
- After successful vaccination campaigns throughout the 19th and 20th centuries, the WHO certified the eradication of smallpox in December 1979.

INFECTIOUS AGENTS & DISEASE

- Production of poisons, such as toxins and enzymes, that destroy cells and tissues.
- Direct invasion and destruction of host cells.
- Triggering responses from the host's immune system leading to disease signs and symptoms.



Courtesy of CDC

Human Immunodeficiency Virus. HIV-1 virions can be seen on surface of lymphocytes.

TYPES OF PATHOGENS

1. **Bacteria**
    1. Gram positive
    2. Gram negative
    3. Acid-Fast e.g. *Mycobacteria*
        1. Spherical described as cocci
        2. Rod shaped described as bacilli
2. **Parasites (Eukaryotic Pathogen)**
    1. Fungi e.g. *Candida, Aspergillus*
    2. Protozoa e.g. *Plasmodium*, *Schistosoma*
    3. Worms e.g. *Ascaris, Taenia*
3. **Viruses**
    1. Are pieces of DNA or RNA surrounded by protein coat.
    2. Encapsulated e.g. HIV, HBV, measles, mumps, influenza, rabies
    3. Non-encapsulated e.g.adenoviruses, HPV, Polio

PHASES OF INFECTIOUS DISEASE

Incubation period – time between infection and the appearance of signs and symptoms.

Prodromal phase – mild, nonspecific symptoms that signal onset of some diseases.

Clinical phase – a person experiences typical signs and symptoms of disease.

Decline phase - subsidence of symptoms.

Recovery phase – symptoms have disappeared, tissues heal, and the body regains strength.

CLASSIFICATION OF INFECTIOUS DISEASE

By duration

Acute – develops and runs its course quickly- Flu

Chronic – develops more slowly and is usually less severe, but may persist for a long, indefinite period of time- TB

Latent– characterized by periods of no symptoms between outbreaks of illness- Herpes

By location

Local– confined to a specific area of the body.

Systemic– a generalized illness that infects most of the body with pathogens distributed widely in tissues.

By timing

Primary– initial infection in a previously healthy person.

Secondary– infection that occurs in a person weakened by a primary infection.

MODES OF TRANSMISSION

1. **Direct contact e.g. touching, handshaking, or sexual intercourse**
2. **Indirect contact e.g. food, water or droplets in air;**
3. **Animal vectors e.g. insect bites in malaria, plague and oncho, dog bite in rabies**

For all pathogens there is an infective dose and a lethal dose.

Virulent factors that confer pathogenicity include;

1. Pili that facilitate attachment;
2. Capsules that interfere with phagocytosis
3. Exotoxins
4. Endotoxins
5. Proteases that break down antibodies
6. Ability to vary antigens to evade antibodies

RELATED TERMS

- Endemic/Enzootic: The constant presence of a disease or infectious agent within a given geographic area.

- Epidemic/Epizootic: The occurrence in an area of a disease or illness in excess of what may be expected on the basis of past experience for a given population (in the case of a new disease, such as AIDS, any occurrence may be considered "epidemic").

- Pandemic/Panzootic: A worldwide epidemic affecting an exceptionally high proportion of the global population.

EMERGING INFECTIOUS DISEASES

Emerging diseases are those that have recently appeared within a population, or whose incidence or geographic range is increasing rapidly.

Diseases can emerge or re-emerge due to:

- appearance of a previously unknown agent.
- evolution of a new infectious agent.
- spread of an infectious agent to a new host.
- spread of an infectious agent to new locations.
- acquisition of resistance to anti-microbial drugs.
- deliberate introduction into a population.

EMERGING INFECTIONS SINCE 1973

1973	Rotavirus	Enteritis/Diarrhea
1976	Cryptosporidium	Enteritis/Diarrhea
1977	Ebola virus	VHF
1977	Legionella	Legionnaire's dz
1977	Hantaan virus	VHF w/ renal flr
1977	Campylobacter	Enteritis/Diarrhea
1980	HTLV-1	Lymphoma
1981	Toxin prod. S.aureus	Toxic Shock Synd.
1982	E.coli 0157:H7	HUS
1982	HTLV-II	Leukemia
1982	Borrelia burgdorferi	Lyme disease
1983	HIV	AIDS
1983	Helicobacter pylori	Peptic ulcer dz
1988	Hepatitis E	Hepatitis
1989	Hepatitis C	Hepatitis

EMERGING INFECTIONS SINCE 1973

1990	Guanarito virus	VHF
1991	Encephalitozoon	Disseminated dz
1992	Vibrio cholerae O139	Cholera
1992	Bartonella henselae	Cat scratch d
1993	Sin Nombre virus	Hanta Pulm. Synd.
1994	Sabia virus	VHF
1994	Hendra virus	Respiratory dz
1995	Hepatitis G	Hepatitis
1995	H Herpesvirus-8	Kaposi sarcoma
1996	vCJD prion	Variant CJD
1997	Avian influenza (H5N1)	Influenza
1999	Nipah virus	Encephalitis
1999	West Nile virus	Encephalitis
2001	BT Bacillus anthracis	Anthrax
2003	Monkeypox	Pox
2003	SARS-CoV	SARS

MAJOR FACTORS CONTRIBUTING TO EMERGING INFECTIONS

1. Human demographics and behavior
2. Technology and Industry
3. Economic development and land use
4. International travel and commerce
5. Microbial adaptation and change
6. Breakdown of public health measures
7. Human vulnerability
8. Climate and weather
9. Changing ecosystems
10. Poverty and social inequality
11. War and famine
12. Lack of political will
13. Intent to harm

Laboratory Diagnosis of Infectious Diseases

Direct Microscopic Examination - Using light microscopy (and occasionally electron microscopy) to directly observe microorganisms in wounds, bodily fluids, and tissues. This process is usually aided by using stains to help differentiate organisms.

- Examples include Gram staining of bacteria, dark field microscopic examination of spirochetes, acid-fast staining for mycobacteria, etc.

Culturing Techniques - Obtaining a pure culture of a microorganism by inoculating an appropriate nutrient media with infected tissue or bodily fluid (e.g., blood urine, sputum, wound, CSF, throat, and stool cultures).

- **Bacteria** - Bacteriologic culturing is frequently done on selective media - i.e., media which inhibits non-pathogenic "normal flora", but permits pathogenic bacteria to grow. Some bacteria require incubation in an aerobic environment, an anaerobic environment, or an environment with high levels of CO2. Identification of specific bacterial species is based on colony morphology as well as biochemical tests performed on bacterial isolates from culture.
- **Viruses** - Viruses are cultured in specialized media containing living cells. The presence of pathogenic virus is usually detected by observing the death of infected cells in culture (cytopathic effect). Immunologic techniques, PCR, or electron microscopy can be used to identify specific viruses after a positive culture has been obtained.

- **Antibiotic sensitivity testing** - Pure cultures of a bacteria can be directly exposed to paper disks impregnated with various antibiotics on an appropriate agar medium. Inhibition of growth around an antibiotic disk suggests sensitivity of the organism to the antibiotic. Antibiotic sensitivity can also be reported by the laboratory as the **minimal inhibitory concentration (MIC)**. This is the lowest concentration of a drug that inhibits the growth of an organism in culture. This information is useful for guiding physicians in choosing an antibiotic and its dose.

The success of culturing techniques depend on: (1) choosing an appropriate specimen for examination (based on the pathogenesis of the infection); (2) collecting the specimen properly and avoiding contamination; (3) prompt transport of the specimen to the laboratory, or proper storage of the specimen during transport.

Immunologic Techniques - These procedures utilize binding reactions between microbial antigens and their specific antibodies to infer the presence of infection in a host. A known antibody can be used to identify a specific microbial antigen in tissues, or a known antigen can be used to detect specific antibodies in a patient's serum. Immunologic techniques have the advantage of providing more rapid diagnosis of infection. Currently, there are a number of commercially available rapid antigen detection tests available. However, many of these tests are expensive, and false positive and false negative results do occur.

- Examples of common immunologic tests used for diagnosing infection:
  - **Agglutination** tests are commonly used to identify a wide range of bacteria - E. coli, salmonella, shigella, haemophilus influenzae, streptococcus, etc. These tests can be performed by mixing a pure isolate from culture with specific antibodies directed against bacterial antigens, or they can be performed by exposing a clinical specimen to latex beads that have been coated with specific antibody. A positive test is indicated by observing clumping (agglutination) of antigen-antibody complexes on a glass slide or test tube. The serologic tests for syphilis (RPR, VDRL) are agglutnation tests.

- The **Enzyme-linked Immunosorbent Assay (ELISA)** is becoming one of the most commonly used immunologic methods for detecting infections. The procedure utilizes an easily assayed enzyme attached to a specific antigen. Presence of the complementary antibody in a clinical specimen (serum) activates the enzyme producing a chromogenic reaction (color change) in the specimen being examined. The screening test for HIV is an example of the ELISA.
- A relatively new procedure is the **optical immunoassay** which involves swabbing a clinical specimen on a silicon wafer that has been coated with specific bacterial antibody. The formation of an antigen-antibody complex on the wafer changes the color of light reflected from its surface allowing the technician to infer the presence of a specific organism. This technique is commonly used to rapidly diagnose group A streptococcal pharyngitis.

- **Fluorescent antibody tests** in which specific microbial antibodies labeled with fluorescent dye can be used to identify microorganisms in tissues. A positive test is indicated by observing fluorescence in a specimen using a microscope equipped with UV light. Fluorescent techniques can also be used to identify specific microbial antibodies in body fluids. For example the, fluorescent treponemal antibody absorption test (FTA-ABS) is a very specific test used to confirm a diagnosis of syphilis.
- **Counter-immunoelectrophoresis** is a procedure in which a known antigen and samples of patient sera are placed in an agar medium and allowed to migrate towards each other in an electrical field. A positive test is indicated by precipitation of the antigen-antibody complex in the medium. This test can also use a known antibody to detect antigen from a clincal specimen.

- **Immunoblotting** - Electrophoresis techniques can be used for separating different proteins associated with an organism. For example, the **Western blot** technique is used to confirm a diagnosis of HIV after a postive antibody screening test is obtained. HIV proteins are separated electrophoretically in a gel medium resulting in discrete bands of viral proteins. These proteins are transferred to a paper strip which is then incubated with serum from a patient. If anti-HIV antibodies are present in the serum, they bind to specific HIV-associated proteins. An enzyme-linked reagent is then used to produce a color change in the strip to identify a positive test. (See Harrison's, 16th ed., p 1100.)
- **Radioimmune assay** is a technique which uses a known antigen that has been "labeled" with a radioisotope to identify specific antibodies in a clinical specimen. Antigen-antibody complexes are separated from the specimen and the amount of radioactivity is measured and compared to known positive and negative standards. This method is also used to assay hormones and drugs in serum.

- **Acute and convalescent phase antibody testing** - Many viral infections can be diagnosed or staged by testing serum for IgM and IgG viral antibodies in the acute phase of a disease (onset of clinical disease), and the convalescent phase of the disease (14 days after onset of clinical disease). A 4-fold or greater rise in the IgM antibody titer between the two specimens indicates recent (acute) infection. If IgG concentrations of an antibody are greater than IgM concentrations, the patient either has immunity to the infection, or has a chronic infection.

Genetic methods - Highly specific gene amplification technologies such as polymerase chain reaction (PCR) are increasingly being used to identify the genetic signatures of organisms that grow slowly in culture (CMV, mycobacteria) - or those that do not culture at all (e.g., Hepatitis B and C viruses). These techniques are also used to determine the amount of an organism present in an infected patient (e.g., "viral load" of HIV and Hepatitis C). This ability to quantitate an infection is useful for staging the patient's disease.

REDUCING THE SPREAD OF INFECTIOUS DISEASES

- **Vaccines**
- **Antimicrobial drugs**
- **Good personal hygiene and sanitation**
- **Protection against mosquitoes**
- **Quarantine**

Human activities drive emergence of disease and a variety of social, economic, political, climatic, technological, and environmental factors can shape the pattern of the disease and influence its emergence into populations.

The most effective method of stemming the spread of infectious disease is through vaccination. Vaccines consist of weakened or killed microbes, or just components of a pathogen, and stimulate the body's natural defenses—the immune system—to combat infections. Vaccination has eliminated smallpox, nearly eradicated poliovirus from much of the world, and drastically reduced the incidence of childhood infections, such as measles, mumps, and whooping cough, at least in the developed world. Influenza vaccines are available to reduce the occurrence of seasonal flu, although the shot must be given yearly due to the extreme variance of the influenza virus from season to season. Vaccines for other infectious diseases, especially HIV, still are being sought.

Antibiotics are effective for many types of bacterial infections (although they are entirely useless against viruses). But increasingly, bacteria are becoming resistant to the arsenal of antibiotics at our disposal.

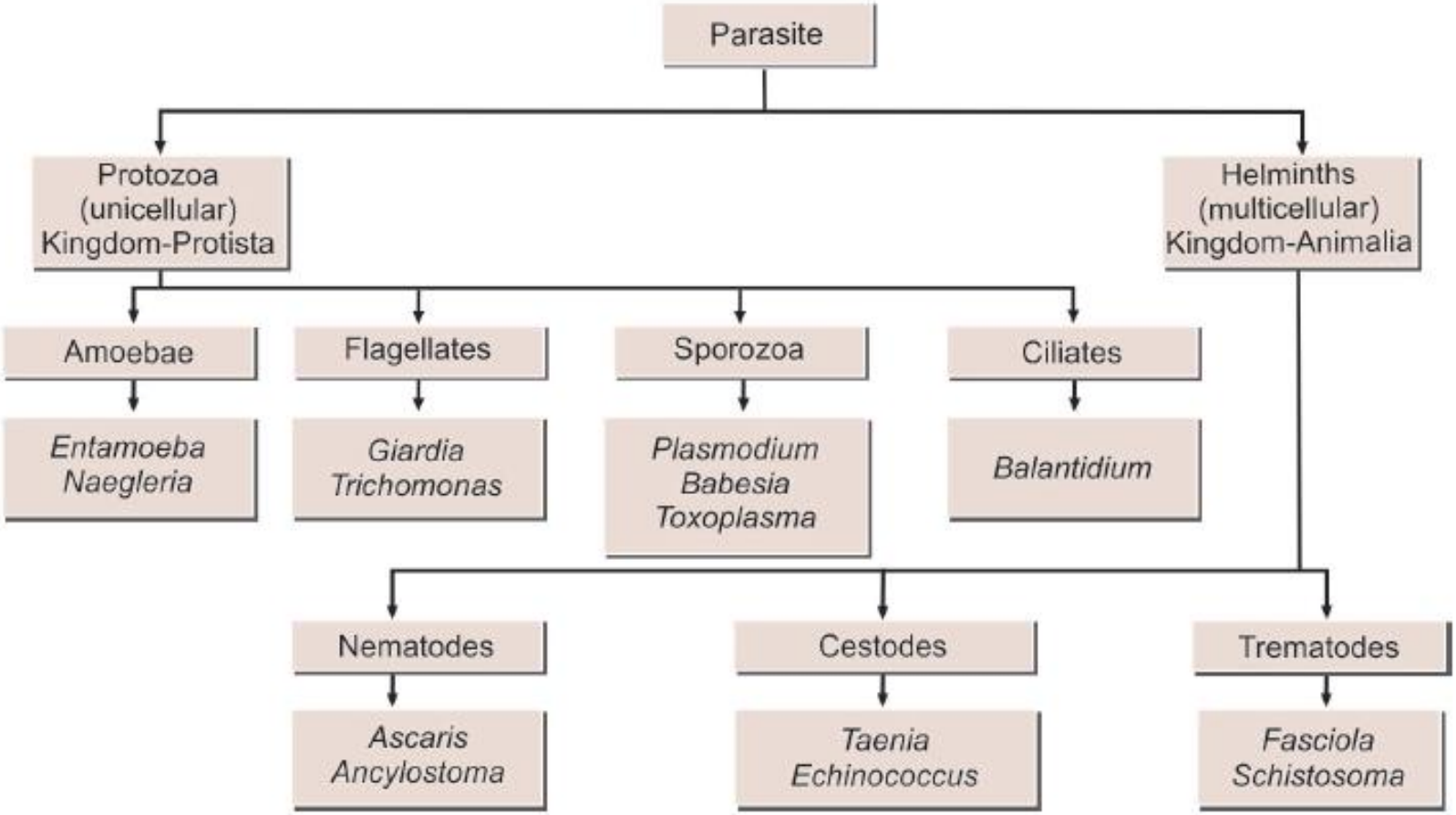
Very few drugs work well against viruses (anti-viral drugs).

Revolution of antiviral treatments (HIV,HCV,HBV).

Anti-fungal drugs exist, but their use is limited.

There are no vaccines against protozoan parasites, and other medications against them are becoming ineffective. Therefore, protection from insect vectors such as mosquitoes and control of mosquito populations are crucial strategies in containing the spread of insect-borne diseases, such as malaria.

Good sanitation, water purification, hand washing, and proper cooking and storage of foods all help to reduce the prevalence of infectious disease. In cases of highly contagious, often fatal diseases, quarantine is employed as a means of preventing the spread of disease through a community. However, regardless of the disease, it is wise to limit contact with other individuals when ill.



Flowchart 1.1: Type of parasites