Microbes and Infectious Disease

Introduction

Infectious diseases can be the result of the colonization of the body by various microbes. There are many similar disease states that can arise from different causes, i.e., pneumonia can be caused by viruses, many types of bacteria, protozoa, and even fungi. In this chapter, we will look at the various types of microbes and some of the diseases they cause.

Terminology

A **host** is any organism capable of supporting the nutritional and physical requirements of another. A **microbe** is a microscopic organism. The presence and multiplication of an organism on or within a host is called **colonization** or **infection**.

We refer to the colonization of one organism by another as **symbiosis**. If the symbiotic relationship benefits both organisms, it is called **mutualism**. On a macroscopic level sharks and remora fish have a mutual symbiotic relationship; the fish clean the teeth of the sharks, which maintain the sharks' oral health while providing food for the fish. Clover, peas, and soybeans root systems are populated by a class of bacteria. The bacteria fix the inert gas nitrogen in the soil and convert it into a form that can be utilized by the plants. This effectively fertilizes the plants and increases their rates of growth. Clearly, both the host and bacteria benefit from this relation.

Commensalism is a symbiotic relation in which one organism benefits and the other is not harmed. Our bodies are populated by an extremely large number of bacteria that can, but don't always, benefit us. The bacteria always benefit. The *E. coli* in our colon are examples.

Parasitism occurs when the infecting organism benefits and the host is harmed. If the host sustains injury or pathological changes in response to the parasite, the process is an **infectious disease**. Anything causing disease is said to be a **pathogen**.

These three characterizations of symbiosis are not as cut-and-dried and they might seem. As an example, many of the bacteria living in or on our bodies cause us no harm when they live in certain regions of the body. But, when they grow in other regions, they cause disease.

Agents of Infectious Diseases

There are many agents of infectious diseases, ranging in size from microscopically small to macroscopically large.

Scale of Sizes

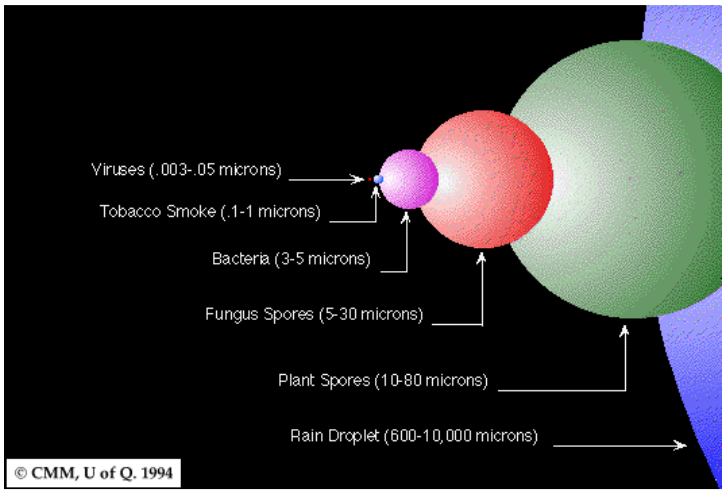
Since most microbes are really, really small, we need to get a feeling for the units in which they are measured, **nanometers**. One nanometer is one-billionth of a meter. Suppose we *shrunk* a meter by a factor of one billion. The result would be one-billionth of a meter or one-millionth of a millimeter. Knowing that a dime is about a millimeter thick, this means you'd need to slice the dime parallel to its faces into a million equal slices, each of which would be one nanometer thick. If you get tired slicing and stop at 100 slices, that thickness would be the size of a eukaryotic cell.

Going in the other direction, suppose your computer monitor is about 40 cm. on a side and we *increase* each side by a factor of one billion. Then it would be 400 million meters = 400,000 kilometers on a side. That would be large enough for the moon to orbit the earth within the plane of the front face, with a little room to spare!

Viruses can range in size from 28–200 nm and they have from 5K–500K bases. Bacteria run from 1000–2000 nm in size and contain 1000K–9000K base pairs.

If a small virion (30 nm) were one inch long, a large bacterium would be over 5 feet long, and a five-foot tall person would stand about 800 miles high—well beyond the extent of the earth's atmosphere.

The following picture (from the University of Queensland website) shows the relative scale of sizes of a virus, tobacco smoke, a bacterium, a fungal spore, a plant spore, and a raindrop. The measurements in the picture are given in microns, which are millionths of a meter, or one thousand nanometers.



Comparison of the relative sizes of various microbes with tobacco smoke, spores, and a rain droplet.

Prions

During the 1950s, anthropologists studying the Fore people in Papua, New Guinea recorded the presence of a strange fatal disease, called **kuru**, which attacked the brain. Victims lost coordination, fine motor control, and the ability to swallow. They developed tremors and showed signs of dementia[1]. Of a population of 35,000, fully 3700 cases of this disease were recorded among this tribe. It seemed to center almost exclusively on adult females, although it was present at lower levels equally in boys and girls. Some villages suffered so many deaths, they had triple the number of living males as females. Records indicated the disease took between four and forty years to manifest itself. After extensive epidemiological study, it became apparent that there was a very strong association between kuru and the practice of ritual cannibalism, whereby the relatives "honored" the recently deceased member of the family by consuming her/his body in its entirety. Almost exclusively adult women practiced the details of the ritual—men rarely participated. Women and children would bake the internal organs, brain, and bone, grind the results into a powder, and then they would mix the powder with vegetables and eat the results. Men, on the other hand, would consume the muscle tissue, i.e., the meat. In 1957, the study group brought pressure to bear on the tribal elders to cease the practice and no cases have been seen in those born *after* 1960, although the last death due to kuru occurred in the 1990s. A recent study of all health records between 1996 and 2004 identified 11 people living in the affected area who had kuru.

Researchers referred to this form of disease as a **transmissible spongiform encephalopathy** (TSE).

Scrapie is a disease of goats and sheep that has been present in Europe for at least two centuries. The disease migrated from England to Canada and made its American debut in 1947. Transmission is thought to be from the ewe to her offspring or to other lambs due to contact with placental materials and fluids. Symptoms do not appear for two to five years.

Infected sheep seem to suffer from an interminable itch. They frequently "scrape" themselves against a tree or fence post until they wear off the outer layers of tissue. This is accompanied by a loss of coordination and corresponding difficulties in walking.

The disease is widespread in Europe (200–600 individual cases per year in the UK, endemic in other countries), the US (900 flocks infected to date), and the Middle East. There do not seem to be any infections in either Australia or New Zealand. There are recorded transmissions from sheep to goats.

[1] The Fore described the disease as having three separate stages: "walk-about yet," "sit down finish," and "sleep finish."

A sheep showing the effects of scrapie.

Prions are proteins. In fact, the name comes, dyslexically, from **pro**teinaceous **in**fectious particle. Prionic proteins come in two forms: cellular PrP_c and scrapie-like PrP_{sc}. The later can force conformational changes in proteins by altering the natural protein-folding mechanism—proteins with different foldings can have radically different effects in the body. These misfolded proteins likely cause human neurodegenerative diseases such as kuru, variant Creutzfeldt[2]-Jakob disease (vCJD[3]), Gerstmann-Sträussler-Scheinker syndrome (GSSS), and fatal familial insomnia (FFI)[4].

The amino acid sequences for PrP_c and PrP_{sc} proteins are identical, only their shapes differ. Cellular PrP_c is rich in so-called α-helices (corkscrew-shapes), whereas in scrapie-like PrP_{sc} these helices have been flattened to so-called β-regions. These conformational changes render PrP_{sc} resistant to protein-digesting protease enzymes, i.e., they are not all broken down during digestion. Not all conformational changes are the same, neither from mammal species to species or within a given species.

More recent research (2/2008) that a prionic infection of neurons increases the free cholesterol content in the cell membranes and this may be part of the mechanism that causes neurodegeneration.

In the not too distant past, the feed industries in the United Kingdom used ground waste parts, usually intestines, glands, spinal tissue, and brains, from slaughtered sheep and cows as feed for other cows. Suddenly, cows were acting strangely (they suffered severe disorientation, staggering, and an inability to stand) and died for no apparent reason. Upon autopsy, it was found that the brains of such "mad cows" were not solid masses, but more closely resembled sponges, complete with holes containing no neurons but rather filled with glial cells. This *mad cow disease* was officially named **bovine spongiform encephalopathy**, BSE. These cows were also ground into feed for other (herbivorous) cows. Only in recent times has there been a "ban" on such practices[5].

Prions are extremely robust with respect to sterilization. They are known to resist radiation, boiling, microwaves, and chemical agents. Surgical instruments used on Creutzfeldt-Jakob disease patients that had been carefully sterilized have shown traces of PrP_{sc}. Iatrogenic vCJD is estimated to comprise 5% of all cases. There are documented transmissions due to corneal transplants, liver transplants, dura mater graft transplants, and contaminated instruments and electrodes.

Disease has been induced by an injection of small doses of PrP_{sc} and feeding meat of infected animals to animals of the same and different species. Epidemiological studies have shown a very strong link between the ingestion of brain and spinal cord tissue from infected animals, mostly cattle, and variant Creutzfeldt-Jakob disease. Ordinarily, CJD occurs in about one in a million people. It has no standard single course of progression of symptoms. Its first signs of incidence are rare in those under forty years-of-age, more common in those aged 50 to 75, and rare again for those over 75. The average age at death is about 60. Most brain damage occurs in the cerebellum. There is an indication that the disease may have an incubation period at least as long as thirty or as many as fifty years, but once the protein refolding starts, it proceeds at an accelerating rate and patients rarely live more than two years. Nevertheless, some people infected in the 1990s showed symptoms (and died) much faster.

---

[2] Talk about coincidences: Creutzfeldt worked as an assistant to Alois Alzheimer.
[3] As of December 1, 2006, there were 165 cases in the United Kingdom, 21 in France, 3 in the US, 2 in the Netherlands, and one each in Canada, Ireland, Italy, Portugal, Saudi Arabia, and Spain.
[4] There is no known transmission of FFI outside of the 28 families in which it is an inherited disease. Also, studies of the brains of sufferers have not found the characteristic spongiform lesions.
[5] Of course, the "invisible hand" of the market pushes producers to skirt any such ban, especially in this day and age.

The most recent research has shown that the human prion protein gene arises in one of three types. It can encode the protein containing the amino acid methionine (M), both methionine and valine (V), or only valine as position 129. Thus unaffected people can be classified as 129MM, 129MV, or 129VV. In 2008 a group found a new sporadic prion disease, which they thought affected only one of these types. Further research published in 2010 found that all three types can be affected. The new disease is, like CJD, a dementing disease and has been named Variably Protease-sensitive Prionopathy (VPSPr).

As a confounding effect, research has associated the proliferation of PrP_{sc} with an excess of manganese together with a deficiency of copper in the diets of sheep and cows. Furthermore, specific RNA molecules have been shown to be highly associated with the transition from normal prionic proteins to their mutant scrapie-like form. Nevertheless, artificially made prionic proteins (In theory, these should not be contaminated with any other organisms.) have been shown to induce the equivalent of BSE in lab animals—but these results remain controversial. There is some good news on this front. In mid-March 2005, the Pall Corporation applied to the Food & Drug Administration's Blood Products Advisory Committee for approval of a filtration system that reduces both white blood cells and prions in blood. The approved product is the Pall Leukotrap® Affinity Plus Prion and Leukocyte Reduction Filter System. Reducing the number of white cells alone decreases the risk of a transmissible encephalopathy by 40%, whereas this method removes 99% of the prions present. A reduction of this magnitude will leave the remaining prions undetectable by the so-called Western Blot test (more about that in a later chapter). It is also fairly gentle on red blood cells, so their therapeutic value is not degraded.

Currently, there is a major spread of animal Chronic Wasting Disease (CWD) throughout much of North America. It has been endemic for many years in elk, mule deer, and white-tailed deer[6] in southeastern Wyoming, northeastern Colorado, Saskatchewan, Alberta, and small parts of Nebraska, Wisconsin, and Illinois. It is moving from west to east, causing concerns that it may soon reach the eastern US white-tailed deer population and seriously damage the hunting industry. Although it is a spongiform encephalopathy (a disease that leaves holes in the brain), it has *not been established* that this is a prionic disease. Nor has there been any *proven* instance of transmission from a hunted animal to a human. Nevertheless, hunters would be wise not to consume meat from such animals.

There are TSEs that affect mink and cats. In the lab, goats, mice, and a host of other animals have also been infected.

Viruses

A **virus** is an ***obligate intracellular parasite*** (meaning that it ***must*** exist within the cells of its host in order to replicate). A virus is metabolically inert outside a cell. **Viruses are not living cells.** They cannot provide their own nutrition, nor can they replicate on their own.

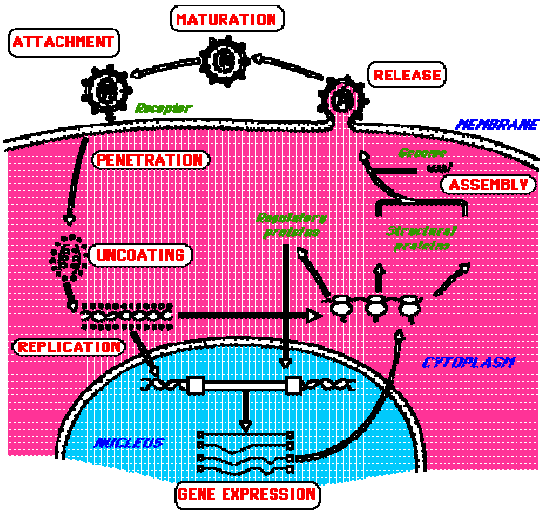
Viruses have no organized cellular structures but simply a protein coat, called the **capsid**, surrounding a nucleic acid core, called a **genome**, of either RNA or DNA, but ***never*** both. The capsid together with the genome is called the **nucleocapsid**. The nucleocapsid may be surrounded by an **envelope** that is composed of a lipid bilayer containing protein spikes. An entire virus particle is called a **virion**. Viruses are classified by the categories: DNA or RNA; single strand or double strand; enveloped or non-enveloped; by their symmetry—helical, icosahedral, or complex; family; and species.

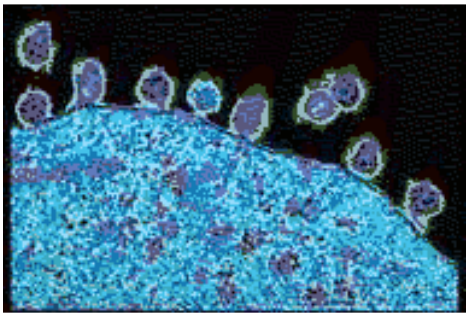
The following are the steps in many, but not all, cases of viral replication.

- **Attachment** to a cell by connecting to a cellular receptor or docking site
- **Penetration** or **Entry** into a cell. This can occur in one of three ways:
    - Direct translocation of the virion across the cell membrane
    - Fusion of the viral and cell membranes
    - Uptake of the virion into a cellular phagosome and release within the cell
- **Uncoating**: Once inside the cell, the virus removes its coat
- **Replication** of viral nucleic acid within the cell
- **Migration** of the viral genome to the nucleus of the cell
- **Integration** of the viral and host nucleic acids to form a **provirus**
- **DNA/RNA nuclear transport**
- **Synthesis** of proteins used in the virus coat
- **Assembly** of structural subunits
- **Reencapsidation**

[6] It also affects farmed mink, domestic cats, cougars, and zoo-dwelling ungulates like bison, kudu, and oryx.

- **Release** of the virions. Frequently the virions **bud** off the cell surface. Sometimes they are released during cell **lysis**, wherein the cell bursts and disperses the reproduced virions
- **Maturation** of the released virions





An electron-micrograph of virions budding from the host cell

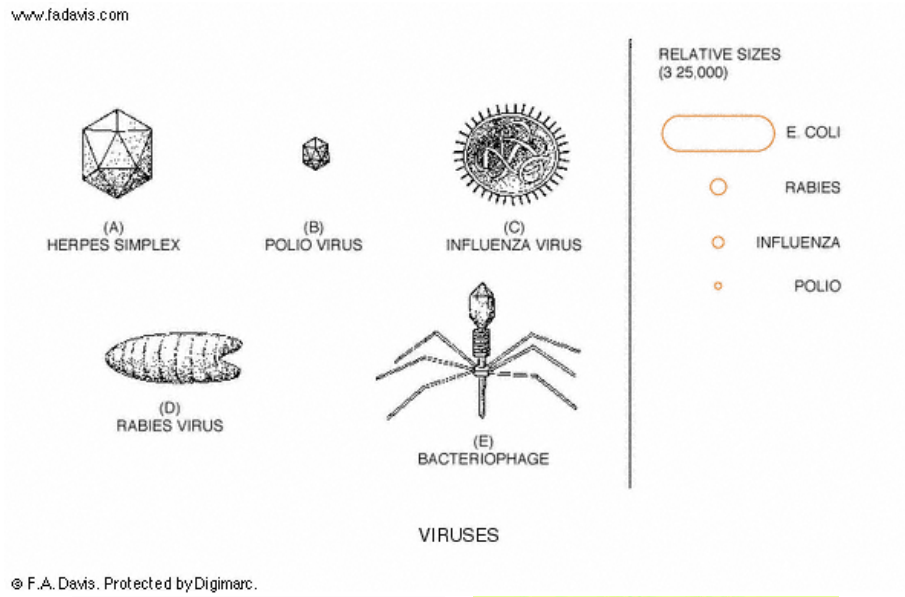
In order to attach to a cell, a virion's surface attachment proteins must fit, certain special protein molecules, called **receptors**, on the cells they infect. Viruses are specific with regard to the types of cells to which they can attach and infect. Viruses cannot bind to receptors on tissue for which there is not an adequate fit. For this reason, they are said to have **host and tissue specificity** and can only infect certain tissues in certain species. As examples, the influenza virus is specific to sialic acid which is heavily expressed on respiratory epithelial cells; an Epstein-Barr virion can only bind to receptors in the oral and/or nasal mucosa; and herpes virus infects cells of the nervous system.

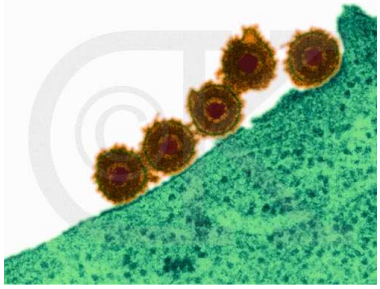
The virus hijacks the reproductive mechanism of the host cell to produce more virions and eventually the host cell weakens and either lyses (bursts) or the newly formed viruses bud off the surface of the host cell. The time it takes for the virus to sap the strength of its host cell varies with disease. Thus, some viral diseases are associated with a large proportion of carriers, e.g., hepatitis B and C.

On the other hand, infecting viruses can transform the genome of a host cell and convert it into a cell that becomes cancerous, which will not die and exhibits uncontrolled growth patterns. Some examples are given below.

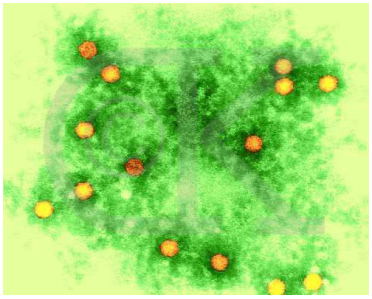
Virus	Cancer
Human T cell leukemia virus (type I)	Adult T cell leukemia
Epstein-Barr virus	Burkitt's lymphoma Nasopharyngeal carcinoma
Hepatitis B & C viruses	Hepatocellular carcinoma (liver cancer)

Papilloma virus[7]	Skin and cervical cancers, warts





Human Herpes Virus, HHV-6



Polio Virus

The bacteriophage shown above is a virus that uses a bacterium as its host. Each phage uses its syringe-like design to inject its nucleic acid into a bacterium, thus turning it into a veritable virus factory for producing more phages. Recent research suggests that phages keep many bacteria from growing exponentially. These phages are extremely plentiful—estimates suggest at least ten times as many of them as there are bacteria.

There are poxviruses that infect mammals, snakes, and insects. In fact, some experts attribute the control of the exponential growth of insects to the presence of such viruses.

As viruses go, smallpox, with its 187,000 bases and about 200 genes, is well armed to confront its hosts. Its 11–14 day incubation period gives it ample opportunity to spread itself far and wide in this time of rapid travel. The influenza virus, which is transmitted on exhaled aerosol droplets, is no slouch either.

Much in the news is the norovirus or Norwalk-like virus, which has been responsible for gastrointestinal disorders frequently seen aboard cruise ships. Worldwide, the virus causes 23,000,000 infections per year and has an infectious dose of between 5 and 100 virions—far fewer than almost any other virus (except smallpox which can infect a person with around a dozen virions). So far, no one has been able to grow a norovirus for the length of time needed to research possible vaccines.

Another particularly frightening microbe is the Ebola virus which causes a particularly lethal hemorrhagic (causing internal bleeding) disease. It is known to infect humans, gorillas, chimpanzees, and small antelopes called duikers. In outbreaks among humans it has had a high mortality rate (>60%) but killed only around a thousand

[7] Human Papillomavirus (HPV) DNA has been identified in 99.7% of cervical cancers. HPV 16 accounts for 50–60% of cervical cancers, HPV 18 accounts for 10–15%, and HPV 31, 33, 45, 52, and 58 account for 18% of such cancers. HPV 6 and 11 are noncancer-causing, but are associated with external anogenital warts, low-grade genital dysplasias, and recurrent respiratory papillomatosis. The vaccine Gardasil targets HPV 6, 11, 16, and 18, while Cervarix targets HPV 16 and 18.

people as of January 2008[8]. On the other hand, it has attacked western lowland gorillas and killed at least 5500 and perhaps as many 30,000 of them.

Influenza is caused by an RNA virus whose genome is constructed of eight separate fragments (which code for 11 proteins). The latest version making the rounds is characterized as an A:H1N1 virus. As virions break, the eight fragments can intermingle with those of other forms of influenza, thus contributing to antigenic drift and antigenic shift.

Once a virus has infiltrated a cell and been transformed to a provirus, that cell is fully infected. As an indication of the ramifications of this, in May 2004 an organ donor diagnosed with a brain hemorrhage died and five people received the harvested organs. It turns out the donor was infected with the rabies virus and each of the transplanted organs were likewise infected. One recipient died of surgical complications, but the other four died of rabies in June of 2004.

Viruses and cells of other species of microbe can mutate. The RNA-based influenza virus has a 10 gene, segmented genome, meaning that instead of a single piece of nucleic acid, it is composed of several pieces. If two different varieties of influenza infect the same cell, these pieces can get intermixed resulting in an entirely different form of the virus. This is precisely how antigenic shift occurs among strains of influenza viruses.

Bacteria

Bacteria (singular bacterium) are **autonomously replicating unicellular organisms** *lacking* both an organized nucleus (which defines the class of cells called **prokaryotes**) and organized intracellular organelles. They have only a single circular chromosome of double-stranded DNA (dsDNA), some extrachromosomal DNA, and most have a cell wall containing the polymer **peptidoglycan**.

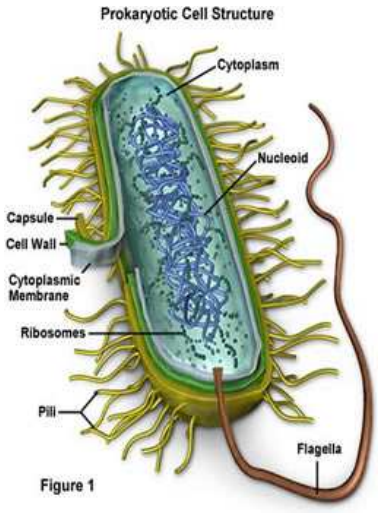


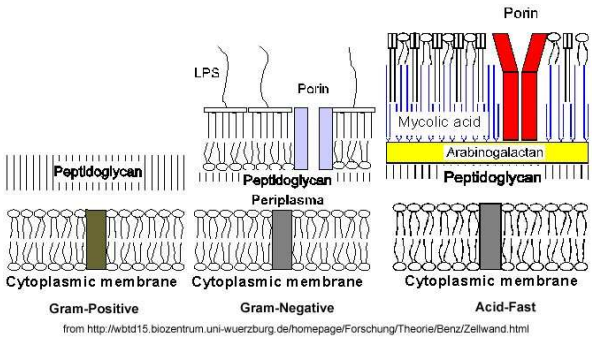
Figure 1

Bacterial DNA has no introns, the DNA sequence consists only of codons. If there are base changes, then the bacteria produce different proteins. Such changes are called **recombination**. This can happen in bacteria in any of five different ways:

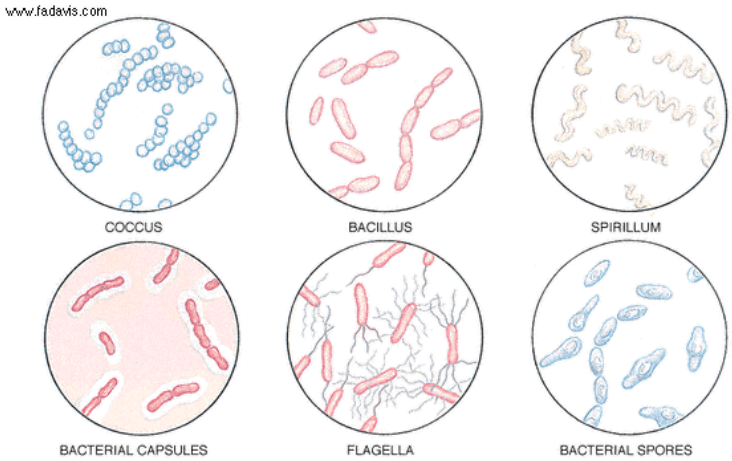
- **Transformation**: a mutated donor cell lyses and passes its DNA fragments to another cell
- **Transduction**: a mutated donor cell, infected by a bacteriophage, lyses, releases the phage, which reinfects another cell and inserts the mutated fragment into the host DNA
- **Conjugation**: a mutated cell forms a cytoplasmic bridge to another cell and integrates its DNA into the other cell
- **Plasmid** transfer: a plasmid is an independent, self-replicating unit of nucleic acids that can cross a cytoplasmic bridge and integrate into the other cell. This process can occur rapidly, leading to a rapidly spreading mutation
- **Transposition**: a gene "jumps" from one cell to another to insert itself into the other cell's chromosome and inactivate the gene into which it jumped.

[8] The latest outbreak of Ebola virus is occurring in Uganda, where at least 100 died.>

Gram positive bacteria (which stain purple following a Gram stain) have a multilayered wall of peptidoglycan. **Gram negative** bacteria (which stain red under Gram stain) have a thinner layer of this polymer and an additional lipopolysaccharide (fat and sugar) outer layer, LPS, which is often endotoxic (capable of initiating inflammation and cell-mediated immune responses), e.g., *Salmonella*, *Shigella*, and *Escherichia*. These differences are important to treatment with antibiotics, insofar as many such drugs interfere with the cell wall in one way or another.



Bacteria are further classified: by shape: a **bacillus** is rod-shaped, a **coccus** is spherical, a **spirilium** is spiral-shaped, a **vibrio** is comma-shaped, a **cocco-bacillus** is ovoid-shaped, and other combinations; whether they need oxygen (**aerobic**) to extract energy from a chemical compound or not (**anaerobic**); their form of reproduction; genus; and species.



BACTERIA
Bacterial shapes and specialized structures

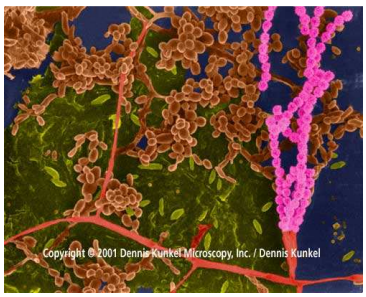
Some bacteria are motile (capable of motion) because of the presence of a flagellum. There can be one or more flagella on each bacterium and they can be attached to one or both ends singly or in tufts or attached at many places on the lateral cell surface.

Many bacteria possess a **quorum-sensing signaling** system, whereby chemical signaling occurs when the colony reaches a certain size. In some species this is the marker to begin producing toxins that injure the host. One such species is *Bacillus anthracis*, the causative agent for anthrax.

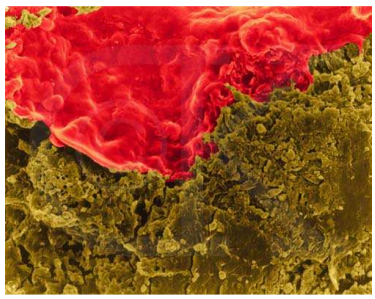
It is known that infection by the bacterium *Corynebacterium diphtheriae* results in the disease diphtheria only when a specific bacteriophage infects the microbe. The toxin causing the disease is produced as a result of a phage gene inserted into the microbe's DNA. Similarly, infection by *Vibrio cholerae* results in the disease cholera due to phage genes that carry instructions for manufacture of a certain protein toxin. Also *Escherichia coli* produces Shiga toxin when a phage begins to reproduce inside the bacterium. The toxin is not released until the bacterium lyses.

The most current estimates are that there are 10^{30} bacteria living on our planet and each of us has a mere 10^{14} of them (that's a factor of 10,000 trillion fewer) living in or on us. You should note that this means there are at least 10^{31} phages sharing the earth with us!

Despite the emphasis on bacterially caused diseases in this book, **most bacteria are not pathogenic**[9].

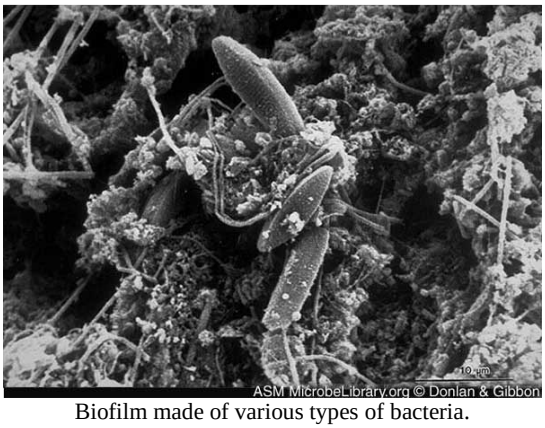


Bacteria and fungi on a cutting board


Bacterial plaque (red) on tooth enamel

Bacteria are responsible for most food-borne illnesses. The cold-loving bacterium *Listeria monocytes* tends to colonize improperly processed meats, deli foods, hot dogs, milk, and soft cheeses leading to about 2500 cases of illness, most of which require hospitalization, and 500 deaths each year. They are also present in so-called biofilms that coat many ordinary surfaces.

Vibrios (which cause cholera) are about 1000 by 3000 nm long and 500 to 800 nm wide. When ingested without food an infectious dose (with probability 50%) is anywhere from 100 to 10,000 bacteria, whereas when ingested with food a range of 1000 to 1,000,000 are needed. *Yersinia pestis* (which cause Plague) are between 1000 and 200 nm long and 500 nm wide. Each infected flea bite will inject from 25,000 to 100,000 *Y. pestis* and an infectious dose is a mere 100 to 500.



Biofilm made of various types of bacteria.

There are many special types of bacteria that deserve separate mention.

Spirochetes are bacteria that are helical-shaped and have filaments wound about the cell wall along the entire length of the cell. The best-known disease caused by spirochetes is syphilis.

Mycoplasmas are unicellular prokaryotes *without rigid cell walls* that are capable of independent replication. Because they have no cell walls, they cannot be identified by Gram-staining. They are extremely simple structures, about one third the size of the typical bacteria. The smallest are around 200 nm and have as few as 580 kilobase pairs. This is very nearly the lower limit for sustaining life. In humans most mycoplasmas are commensals, although some species of mycoplasmas can be responsible for some atypical pneumonias, genital infections, and vertically transmitted respiratory infections—mostly to low birth weight infants.

Mycobacteria comprise a class of Gram-positive bacteria that pass through a phase, called acid-fastness, in their life cycle when they can be stained, and thus identified. Tuberculosis is caused by a species of Mycobacteria, *Mycobacterium tuberculosis*. This organism can infect and attack almost any organ or tissue of the body. In common usage, the term refers to an infection of the lungs. The lesions associated with the disease are called tubercles and their innermost spheroidal volumes consist of dead or dying tissue.

[9] Currently there are about 300,000 known species of bacteria, and likely as many as ten times that number yet to be discovered and categorized, but **only** 170 of them are pathogenic.

Mycobacterium avium

Hansen's disease, leprosy, is caused by Mycobacterium leprae. It can be treated with multiple drug therapy and has not yet been cultured in the laboratory. One reason may be its doubling time, which is the longest of all known bacteria. Although one associates it with biblical times, it is very much alive and thriving to this day. Some numbers are in order.

Table 1: Prevalence of leprosy at beginning of 2006, and trends in new case detection 2001-2005, excluding Europe

Region	Registered Prevalence (rate/10,000 pop.)	New Case Detection during the year				
	Start of 2006	2001	2002	2003	2004	2005
Africa	40,830 (0.56)	39,612	48,248	47,006	46,918	42,814
Americas	32,904 (0.39)	42,830	39,939	52,435	52,662	41,780
South-East Asia	133,422 (0.81)	668,658	520,632	405,147	298,603	201,635
Eastern Mediterranean	4,024 (0.09)	4,758	4,665	3,940	3,392	3,133
Western Pacific	8,646 (0.05)	7,404	7,154	6,190	6,216	7,137
Totals	219,826	763,262	620,638	514,718	407,791	296,499

Table 2: Prevalence and detection of leprosy, countries still to reach elimination

Countries	Registered Prevalence (rate/10,000 pop.)			New Case Detection (rate/100,000 pop.)		
	Start of 2004	Start of 2005	Start of 2006	During 2003	During 2004	During 2005
Brazil	79,908 (4.6)	30,693 (1.7)	27,313 (1.5)	49,206 (28.6)	49,384 (26.9)	38,410 (20.6)
Democratic Republic of the Congo	6,891 (1.3)	10,530 (1.9)	9,785 (1.7)	7,165 (13.5)	11,781 (21,1)	10,737 (18.7)
Madagascar	5,514 (3.4)	4,610 (2.5)	2,094 (1.1)	5,104 (31.1)	3,710 (20.5)	2,709 (14.6)
Mozambique	6,810 (3.4)	4,692 (2.4)	4,889 (2.5)	5,907 (29.4)	4,266 (22.0)	5,371 (27.1)
Nepal	7,549 (3.1)	4,699 (1.8)	4,921 (1.8)	8,046 (32.9)	6,958 (26.2)	6,150 (22.7)
Tanzania	5,420 (1.6)	4,777 (1.3)	4,190 (1.1)	5,279 (15.4)	5,190 (13.8)	4,237 (11.1)
Totals	112,092	60,001	53,192	80,707	81,289	67,614

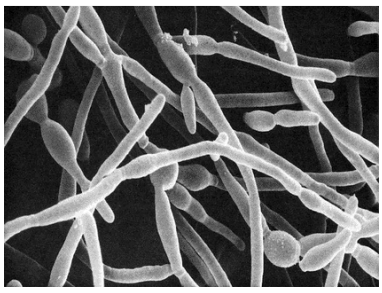
Rickettsiae and **chlamydiae** are obligate intracellular pathogens with a rigid peptidoglycan cell wall, which reproduce asexually by binary fission, and can contain both DNA and RNA. Rickettsiae depend on the host cell for essential nutrients and they can infect arthropods without causing disease in them. They cause the potentially deadly diseases typhus and Rocky Mountain spotted fever. Chlamydiae scavenge intracellular leftovers for nutrition. They are transmitted directly and are responsible for some bronchitis, sinusitis, some pneumonias, the common sexually transmitted infection (STI) referred to as chlamydia urethritis, the relatively rare STI lymphogranuloma venereum, and trachoma. In fact, trachoma is the leading cause of preventable blindness, and chlamydia is the most common STI in the world today.

Chlamydia pneumonia has been strongly implicated as a causative agent in plaque formation associated with atherosclerosis (hardening of the arteries).

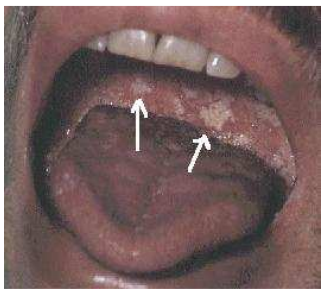
Fungi

Fungi are free-living eukaryotic saprophytes (organisms that live on dead things) consisting of yeasts and molds (also called filamentous fungi). Fungi can cause two broad classes of disease: superficial and deep. The superficial diseases are either **cutaneous**, growing on the skin, or **subcutaneous**, growing just below the skin. The deep diseases are either **systemic**, they colonize most of the body, or opportunistic (fungi that normally live in the body but become pathogenic only when the immune system is suppressed).

The picture below shows a relatively *mild case* of the characteristic "cottage cheese" plaques of oral thrush, caused by the fungus *Candida albicans*. This is an example of an opportunistic infection, since most of us have *C. albicans* as a standard part of the microbiota of our mouths. They can also infect internal organs. Coccidioidomycosis, cryptococcosis, and histoplasmosis are three other fungal infections common to **AIDS** patients.



The fungus *Candida albicans*



Oral candidiasis (thrush)

Other Eukaryotic Parasites

Protozoa are unicellular eukaryotes that lack cell walls. Their life cycles can be quite complex. There are four classes of protozoa: (1) sporozoa, which are intracellular parasites, (2) flagellates, (3) amoebas, and (4) ciliates. Although most protozoa are saprophytes, some have adapted to the human host, where they can cause many diseases. They can be spread host-to-host, from a common source—like amoebic dysentery and giardiasis, or via an arthropod vector—like malaria, one of the top killers in the world today.

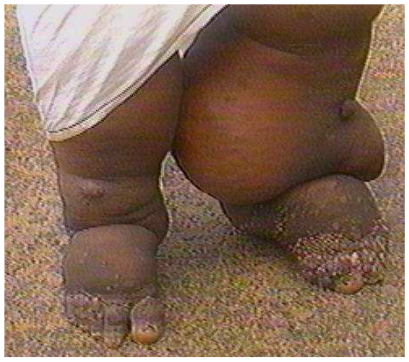
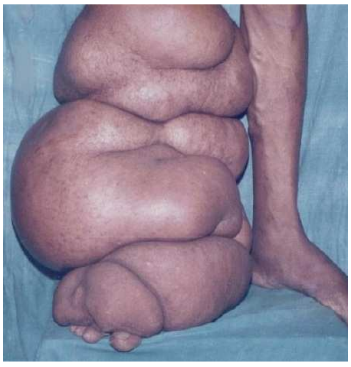
An article circulated by the Associated Press on September 29, 2007 described a species of amoeba *Naegleria fowleri*, that is found in warm bodies of water and soil. The amoeba can enter the nose and can attach itself to the olfactory nerve. It then destroys tissue and makes its way to the brain. Those infected suffer from a stiff neck, headaches, and fevers. As the disease damages the brain, the patient has hallucinations and behavioral changes. There is no known cure and death can follow in as little as two weeks after infection. Between 1995 and 2004, there have been 23 known deaths in the US. During 2007, there were six cases—three in Florida, two in Texas, and one in Arizona. Using noseclips while swimming is an effective preventative.

Helminths are worms. There are three forms: roundworms, tapeworms, and flukes. The majority of helminths can reproduce within the host or within an intermediate host. Transmission can occur by ingestion of their fertilized eggs, penetration of the skin by infectious larval stages of their development, or by an arthropod vector. They can cause lymphatic filariasis, hookworm, pinworm, schistosomiasis, tapeworm, trichinosis, etc.

A typical lymphatic filariasis infection is a chronic infestation with threadlike filaria nematodes.

Whipworms in the colon

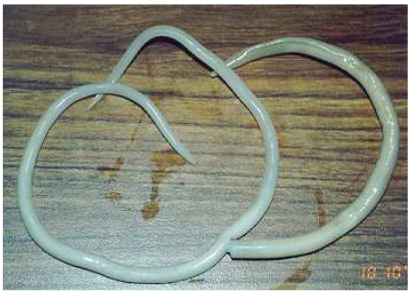
They congregate in the lymph nodes and surrounding tissue and eventually block the flow of lymph. This results in pain and significant swelling in the area involved.

Results of filariasis

Helminths come in all sizes, ranging from a few millimeters long to as many as twenty meters in length for a full-grown tapeworm. In fact, the human species can be inhabited by as many as 54 species of tapeworm, which is little more than an inside-out intestine that absorbs nutrients from our gut and reproduces at an astronomical rate. They can shed millions of eggs at a time, none of which will survive unless they leave the host.

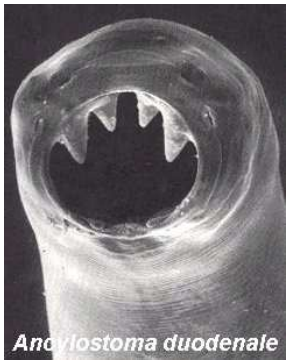
Ascaris worms are not uncommon in developing countries.



Two Ascaris worms

Ascaris worms removed from the colon

A closeup of a hookworm does not endear one to their class. Nevertheless, this makes it clear how they can attach themselves to the skin.



On the other side of the coin, people infected with hookworms are less susceptible to attacks of various immune-based diseases such as asthma, multiple sclerosis, and diabetes.

Arthropods as Agents of Transmission

Arthropods—mosquitoes, ticks, fleas, mites, chiggers, and lice—are blood feeders and the ultimate vectors. They either insert their proboscis into your skin to withdraw blood or they chew off a section of skin, attach themselves to you, and suck out the blood. As they withdraw blood, they either inject a substance that prevents coagulation or they regurgitate or excrete into the wound they caused. In either case, any pathogens living in their salivary glands are inserted nearly directly into your blood stream. Ticks usually need to feed on you for anywhere from 24 to 48 hours before they are sufficiently engorged and able to transmit anything to you.

The resettlement of refugees and rapid urbanization of many countries in the developing world has lead to crowding, inadequate sewer systems, inadequate water supplies, and a rapid increase in the number and size of breeding grounds for mosquitoes. Infection of a single person bitten by these insects rapidly leads to infections of many people in the surrounding areas. It is not uncommon that newcomers to an urban area are more susceptible to many of these arthropod-borne diseases.

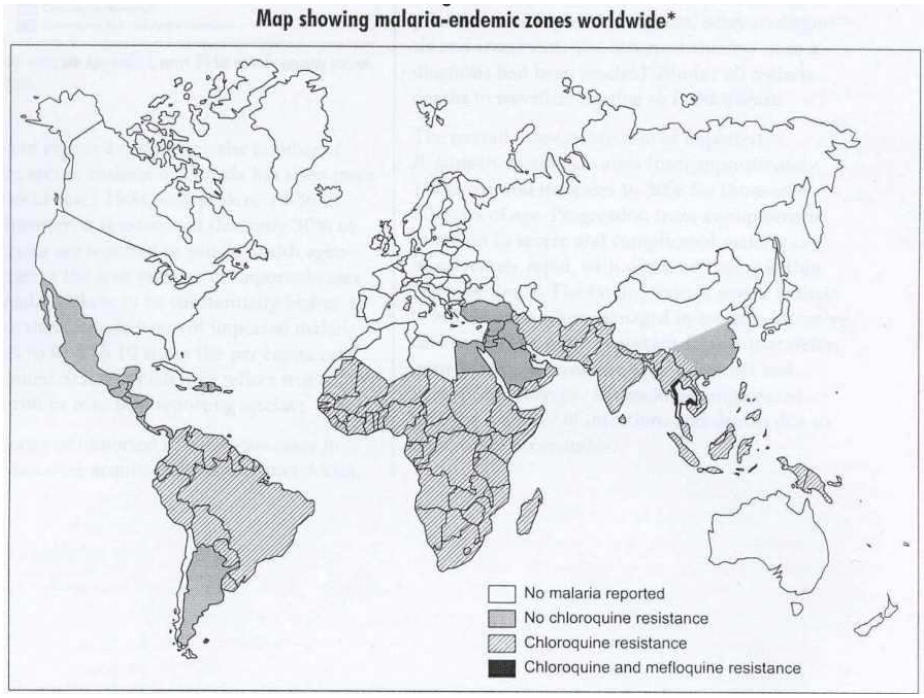
Some Arthropod Transmitted Diseases

	Disease	Vector
Viruses		
Arboviruses	Dengue fever	Mosquitoes
	Yellow fever	Mosquitoes
	Hemorrhagic fevers	Ticks, mosquitoes
	West Nile fever	
Bacteria		
Yersinia pestis	Plague	Fleas
Borrelia burgdorferi	Lyme disease	Hard ticks
Rickettsiae		
R. prowazeki	Epidemic typhus	Lice, ticks
R. rickettsiae	Spotted fever	Ticks
Protozoa		
Trypanosoma cruzi	Chagas' disease	Reduvid bugs
T. rhodensiense	Sleeping sickness	Tsetse flies
T. ganbiense		
Plasmodium spp.	Malaria	Mosquitoes
Leishmania spp.	Leishmaniasis	Sandflies

Helminths		
Wucheria & *Brugia*	Lymphatic filariasis	Mosquitoes
Onchocerca	Onchocerciasis	Simulium flies

Malaria may very well be the most deadly of these arthropod-borne diseases. Large tropical areas of the planet are rife with malaria, either the standard variety or one that is resistant to the drug normally used to treat the disease, chloroquine. As the planet's climate warms, the upper boundary of this region moves ever northward. In the US, cases have been found as far north as Oklahoma.

Some creatures coexist with humans with no ill infects for us. One such is the 0.3 mm long *Demodex* mite which lives in the sebaceous glands of the eyelash. Its presence is more common among older people because children produce relatively little sebum. The mites usually live in pairs and can live for several weeks. In the dark they are able to leave the eyelash and walk about the skin.



Even mosquito-carried microbes as large as filaria are extraordinarily damaging. When injected into the mosquito's body, they take one to three weeks to develop. After that, the mosquito is essentially a flying syringe ready to inject these threadlike worms into a human victim. As the filaria move to the lymphatic system, disease symptoms may take years to develop, if they ever do. Even an asymptomatic infection can result in damage to the lymph system and the kidneys.

Estimates are that over 120 million people have been infected and fully one-third of them are either incapacitated or disfigured by the disease. Two-thirds of the victims are equally distributed between Africa and India. The remaining third is spread over Southeast Asia, Micronesia, and the Americas.

Since the symptoms of lymphatic filariasis can be very obvious, the social and psychological stigmatization is a major component of the disease.

The accompanying table lists the microbes mentioned in this chapter and some of the human diseases they can cause. Diseases that are common to AIDS patients have been underlined.

Microbe	Human Disease
Prions	kuru, Creutzfeld-Jakob disease, Gerstmann-Sträussler-Scheinker syndrome, fatal familial insomnia
Viruses	chicken pox, common cold, diarrhea, encephalitis, Epstein-Barr Syndrome,

	gingivitis, hepatitis, herpes, hoof & mouth disease, influenza, HIV disease, HTLV disease, Kaposi's sarcoma, measles, meningitis, molluscum contagiosum, monkey pox, mumps, pneumonia, polio, rabies, rubella, severe acute respiratory syndrome (SARS), T cell leukemia, various hemorrhagic fevers, warts, yellow fever, etc.
Bacteria	anthrax, bacillary dysentery, boils, brucellosis, cat scratch fever, chancroid, cholera, diarrhea, diphtheria, endocarditis, food poisoning, gangrene, gonorrhea, haemophilus influenza, Legionnaire's disease, Listerosis, meningitis, necrotizing fasciitis, pneumonia, septicemia, scarlet fever, tetanus, toxic shock syndrome, typhoid fever, ulcers, urethritis, whooping cough, etc.
Spirochetes	leptospirosis, Lyme disease, relapsing fever, syphilis, yaws
Mycoplasmas & mycobacteria	Hansen's disease (leprosy), pneumonia, tuberculosis
Rickettsiae & Chlamydiae	chlamydia, lymphogranuloma venereum, pneumonia, Q fever, Rocky Mountain spotted fever, typhus, urethritis
Fungi	aspregillosis, candidiasis, coccidioidomycosis, cryptococcosis, histoplasmosis, *Pneumoncystis jerovecii (carinii)* pneumonia, thrush, tinea pedis (athlete's foot), tinea cruex (jock itch)
Protozoa	amoebic dysentery, cryptosporidiosis, diarrhea, giardiasis, leishmaniasis, liver abscess, malaria, onchocerciasis (river blindness), toxoplasmosis, trichomoniasis, trypanosomiasis (sleeping sickness/Chagas' disease)
Helminths	ascariasis, beef or pork tapeworm, lymphatic filariasis, fish tapeworm, hookworm disease, hydatid disease, pinworm infestation, schistosomiasis, trichinellosis

Strange as it may seem, the symptom of diarrhea remains the largest killer of children in the world today, even though it is not in the top ten for all deaths.

The following table is a summary listing of some of the characteristics of the major pathogens.

Classification of Major Pathogens

	Viruses	**Bacteria**	**Fungi**	**Protozoa**	**Helminths**
Nucleic acids	DNA *or* RNA	DNA and RNA	DNA and RNA	DNA and RNA	DNA and RNA
Nuclear membrane	no	no	yes	yes	yes
External cell wall	no	yes (usually) rigid peptidoglycan	yes, rigid chitin	no	no
Antibiotic sensitivity	no	yes	some	some	some
Replication/ Reproduction	within host cells	within and outside host cells asexually	within and outside host cells by asexually and sexually	within and outside host cells by asexually and sexually	outside host cells sexually

Disease

The tables below list several common source and host-to-host epidemics, the causative agent (followed by V for virus, B for bacteria, and P for protozoa), sources of infection, and the reservoirs of the infection. Current knowledge tells us that humans are the only reservoirs for sexually transmitted diseases.

Common Source Epidemic Diseases			
Disease	**Causative Agent**	**Infection Sources**	**Reservoirs**
Anthrax	*Bacillus anthracis* (B)	Milk or meat from infected animals	Cattle, swine, goats, sheep, horses
Bacillary Dysentery	*Shigella dysenteriae* (B)	Fecal contamination of food and/or water	Humans
Botulism	*Clostridium botulinum* (B)	Soil-contaminated food	Soil
Brucellosis	*Brucella melitensis* (B)	Milk or meat from infected animals	Cattle, swine, goats, sheep, horses
Cholera	*Vibrio cholerae* (B)	Fecal contamination of food and/or water	Humans
Giardiasis	*Giardia* spp. (P)	Fecal contamination of water	Wild mammals
Hepatitis	Hepatitis A,B,C,D,E (V)	Infected humans	Humans
Paratyphoid	*Salmonella paratyphi* (B)	Fecal contamination of food and/or	Humans

		water	
Typhoid Fever	*Salmonella typhi* (B)	Fecal contamination of food and/or water	Humans

Host-to-host Epidemic Diseases			
Disease	**Causative Agent**	**Infection Sources**	**Reservoirs**
Respiratory Diseases			
Diphtheria	*Corynebacterium diphtheriae* (B)	Human cases & carriers; infected food & fomites	Humans
Hantavirus pulmonary syndrome	Hantavirus (V)	Inhalation of contaminated fecal material	Rodents
Meningicoccal meningitis	*Neisseria meningitidis* (B)	Human cases & carriers	Humans
Pneumonococcal pneumonia	*Streptococcus pneumoniae* (B)	Human carriers	Humans
Tuberculosis	*Mycobacterium tuberculosis* (B)	Sputum from human cases; contaminated milk	Humans, cattle
Whooping cough	*Bordetella pertussis* (B)	Human cases	Humans
German measles	Rubella virus (V)	Human cases	Humans
Influenza	Influenza virus (V)	Human cases	Humans, animals
Measles	Measles virus (V)	Human cases	Humans
Vector-borne diseases			
Epidemic typhus	*Rickettsia prowazekii* (B)	Bite by infected louse	Humans, lice
Lyme disease	*Borrelia burgdorferi* (B)	Bite from infected tick	Rodents, deer, ticks
Malaria	*Plasmodium* spp. (P)	Bite from infected Anopheles mosquito	Humans, mosquitoes
Plague	*Yersinia pestis* (B)	Bite by infected flea	Wild rodents
Rocky Mountain Spotted Fever	*Rickettsia rickettsii* (B)	Bite by infected tick	Ticks, rabbits, mice
Direct-contact diseases			
Psittacosis	*Chlamydia psittaci* (B)	Contact with birds or bird excrement	Wild and domestic birds
Rabies	Rabies virus (V)	Bite by carnivores	Wild and domestic carnivores
Tularemia	*Franciscella tularensis* (B)	Contact with rabbits	Rabbits

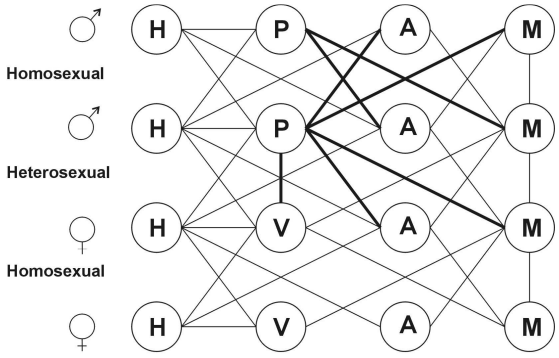
Parts of a many microbes' arsenals are its invasive factors that facilitate the penetration of anatomical barriers and host tissue. A prolonged excess of any one of the enzymes (proteins that alter the rate of a chemical reaction without an external energy source and are themselves unchanged) produced by a pathogen can lead to major damage to various organ systems.

Many pathogens produce **toxins**, which are substances that alter or destroy the normal function of the host's cells. Once colonization has begun, the pathogen can also employ various evasive factors to prevent or slow natural immune responses generated by the host.

In addition to these tissue-damaging factors, there is the possibility that the infection will cause an immune response that it is disproportionately large. This can lead to further tissue damage as the immune cells attack self-cells. Of course, for some pathogens, either their overgrowth or their size will block hollow viscera, thus preventing flows of substances needed for proper functioning of major organs. In any event, disease can lead to significant damage of major bodily systems.

Sexually Transmitted Infections

Generally speaking, sexually transmitted infections can occur due to contact between the anus, hand, mouth, penis, and vagina. The extent of transmission is indicated in the following diagram. A dark line indicates a contact that is most likely to transmit some microbe. The light lines have a lower likelihood of transmission.



A=Anus, H=Hand, M=Mouth, P=Penis, V=Vagina

Sexually transmitted infection contacts connected by a **darkened** line have a high probability of transmission.

In addition, with some STIs, once infected, the disease can be spread to other parts of the body by what is called **autoinoculation**, e.g., touching without or with incomplete hand washing, etc.

Sexually transmitted infections

Disease	Causative Agent	Infection Sources	Reservoirs
AIDS/HIV disease	HIV (V)	Infected body fluids, esp. blood & semen	Humans
Candidiasis	*Candida* spp.	Infected body fluids	Humans
Cervical cancer	Human Papilloma Virus 16, 18 (V)		
Chancroid	*Haemophilus ducreyi* (B)	Infected body fluids, autoinoculation	Humans
Chlamydia	*Chlamydia trachomatis* (B)	Urethral, vaginal, & anal secretions	Humans
Genital Herpes	Herpes Simplex Virus-2 (V)	Infected body fluids	Humans
Genital Warts	Human Papilloma Virus 6, 11 (V)	Infected body fluids	Humans
Gonorrhea	*Neisseria gonorrheae* (B)	Urethral & vaginal secretions	Humans
Granuloma Inguinale*	*Calymmatobacterium donovani* (B)	Infected body fluids	Humans
Hepatitis B & C	Hepatitis Virus B & C (V)	Infected body fluids	Humans
Lymphogranuloma Venereum*	*Chlamydia trachomatis* (B)	Infected body fluids	Humans
Molluscum contagiosum	Molluscipoxvirus (V)	Skin-to-skin contact, fomites, autoinoculation	Humans
Scabies	*Sarcoptes scabei* (Arachnid)	External infestation of genital region	
Syphilis	*Treponema pallidum* (B)	Infected exudate or blood	Humans
Yeast	*Saccharomyces* or *Candida* spp.	Infected body fluids	
Trichomoniasis	*Trichomonas vaginalis* (P)	Urethral, vaginal, prostate secretions	Humans

Treating Disease

So, how do medications act on microbes to cure disease?

There is one major criterion that must be applied to drugs used as antimicrobials. Since the goal of the drug is to, in some way, disable the targeted microbe, it should not injure nonpathogenic cells that are in contact or close proximity to the target. We do not want the medication to be worse than the disease. This defines a drug property called **selective toxicity**. Such drugs should interfere with processes *unique* to the microbes they are designed to treat against. Suppose the drugs are to attack pathogenic bacteria. They can do this in one of three ways: disrupt the bacterial cell wall, inhibit some enzyme that is unique to that bacterium, and/or disrupt the process of bacterial protein synthesis. The last of these is possible because bacteria are prokaryotes and their protein synthesis differs from that of mammalian cells, thus establishing the selective toxicity required.

Antibiotics are not all the same, some are **narrow-spectrum** and active against only a few classes of bacteria, while **broad-spectrum** antibiotics are effective against a much larger contingent of microbes.

Antimicrobial drugs are further classified by their mechanisms of action. Most authorities list seven distinct major categories of action, but these are not inclusive.

- Inhibition of viral enzymes. More will be said about this when we get to the treatment of HIV disease.

- Inhibition of cell wall synthesis or activation of enzymes that disrupt the cell wall. Either action will lead to cell lysis.
- Increase cell membrane permeability. This causes leakage of intracellular fluid and eventual cell death.
- Lethal inhibition of bacterial protein synthesis (**bacteriocides**). This also will lead to cell death.
- Nonlethal inhibition of bacterial protein synthesis (**bacteriostatics**). Slow the growth of the bacteria so the immune system can rid the body of infection.
- Interference with synthesis of DNA or RNA. This prevents the organism from properly replicating.
- Interference with cell metabolism. Either the cell will have insufficient materials for reproduction or the materials will be nonfunctional.

The following table lists some of the mechanisms of action and some of the drugs that utilize these actions.

Antimicrobial Drugs and Their Mechanism of Action

Drug Action	Antimicrobic
Inhibition of viral enzymes	Acyclovir Cidofovir Ribavirin Zidovudine
Inhibit cell wall synthesis	Cephalosporins Imipenem Penicillins Vancomycin
Disrupt cell membrane	Amphotericin B Ketoconazole
Bacteriocidal inhibition of protein synthesis	Aminoglycosides
Bacteriostatic inhibition of protein synthesis	Clindamycin Erythromycin Tetracyclines
Interference with synthesis of DNA or RNA	Fluorquinolones Rifampin
Antimetabolites	Flucytosine Sulfonamides Trimethoprim

Drugs that initially have significant therapeutic effects on microbes may, over time, loose their effectiveness. When this happens we say the *microbe* has become **resistant to the drug**[10]. This resistance does not develop because of any action of the drug, rather genetic changes in the microbe that facilitate the development of the resistance usually occur by either spontaneous mutation or by acquisition of alternative DNA from an external source. Once these changes take place, the progeny of the altered microbe will carry the genetic material for resistance.

Some of the mechanisms of microbial drug resistance are:

- Microbes may generate drug-metabolizing enzymes that inactivate the drug.
- Microbes may stop or considerably decrease uptake of the drug into the cell.
- Microbial receptors by which the drug acted may change, thus decreasing drug binding and action.
- Microbes may synthesize compounds that antagonize drug actions.

How often do these resistances build up in microbes and is this a problem? Let's defer that question to a later chapter.

[10] Remember, the microbe becomes resistant to the drug; *the patient does not become resistant to the drug*.

Appendix

Diseases of Poverty (Courant, Sunday May 13, 2007)
Hookworm: Burrows into the skin and feeds on small intestines, leading to anemia and protein malnutrition. Infects about 600 million people.
Trichuriasis: Human whipworm eggs enter the body on food and hands and attach to large intestine, leading to loss of blood and nutrients. The disease impairs cognitive development. About 800 million people are infected. Kills 10,000 people a year.
Trachoma: Bacterial infection that is the leading cause of preventable blindness in the world. 84 million infected; 8 million blinded or visually impaired.
Onchocerciasis (African River Blindness): About 17.7 million people are infected by the parasite, spread through bites of flies. About 770,000 are blinded or visually impaired.
Ascariasis: The ascaris worm, which can grow to a foot long, infects 1.2 billion people, with children the most often infected. The disease adversely affects growth and impairs cognitive development. Kills 60,000 people a year.
Schistosomiasis (Snail Fever): About 200 million people are infected by worms that live in contaminated water. In the human body, worms live in the intestine and impair growth, development, and performance. The disease kills about 200,000 people a year.
Lymphatic filariasis (Elephantiasis): About 120 million people infected, through mosquito bites, with thread-like worms that live in the lymph system and can cause grotesque disfigurement of legs, scrotum, and breast.

About Neglected Tropical Diseases (NTDs) - Summary

- Around half of the world's population are afflicted by one or more of these neglected tropical diseases - bilharzias; worms; elephantiasis; river blindness and trachoma;
- These are diseases of poverty;
- The global burden of the neglected tropical diseases is equivalent to at least half of that of HIV/AIDS, TB and malaria;
- A body of evidence exists indicating that the control of neglected tropical diseases would greatly reduce the morbidity and mortality of malaria and reduce the transmission of HIV/AIDS;
- Neglected tropical diseases are at least controllable or possibly eliminable/eradicable by safe and effective drugs, donated by Merck, GlaxoSmithKline and Pfizer;
- With public and private partnerships the Integrated control of neglected tropical diseases can be implemented at marginal costs of US 50 cents per person treated;

By integrating control of bilharzias; worms; elephantiasis; river blindness and trachoma the pay off is enormous. Half a billion people in Africa could have better nutrition, have more energy to attend school and work, avoid permanent disablement, serious illness or death.

What are the Neglected Tropical Diseases?
Neglected tropical diseases comprise 13 parasitic and bacterial infections and are the most common afflictions of humankind (Box 1). They affect the world's poorest people, 2.7 billion people who subsist on less than $2 per day. Each minute, a life is lost due to neglected diseases and 534,000 deaths result each year. Yet the greatest impact of these diseases are in the way they promote poverty, stigmatize, disable and inhibit individuals from being able to care for themselves or their families.

Children, women and those living in remote areas without any access to an effective health care system are most vulnerable to the deleterious affects of neglected diseases such as malnutrition, anemia, serious or permanent disability (including blindness), illness and death. Together these neglected diseases cause as much disease and suffering as malaria or tuberculosis. They are the 4th most important group of communicable diseases, behind lower respiratory infections, HIV/AIDS, and diarrheal diseases. Fortunately, there are inexpensive, safe, and effective treatments available for seven of the 13 diseases.

The Thirteen Neglected Tropical Diseases in Africa and Their Common Names	
Protozoan infections	**Common Names**
African trypanosomiasis	Sleeping sickness
Kala-azar	Visceral leishmaniasis

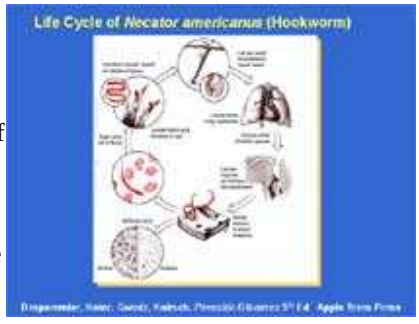
Chagas Disease	
Helminth Infections	
Soil Transmitted Helminth Infections	Intestinal worms
Ascaris	
Trichuris	
Hookworm infection	
Schistosomiasis	Bilharzia or snail fever
Urinary schistosomiasis	
Hepatobiliary schistosomiasis	
Lymphatic Filariasis	Elephantiasis
Onchocerciasis	River Blindness
Drancunculiasis	Guinea Worm
Bacterial infections	
Trachoma	
Leprosy	
Buruli Ulcer	

Panorama of Seven Targeted Global Neglected Tropical Diseases

Ascaris

Ascaris is the most common human worm infection. Infection occurs worldwide and is most prevalent in tropical and subtropical areas where sanitation and hygiene are poor. The parasite lives in the small intestine and children are infected more often than adults. Adult female worms can grow over 12 inches in length, though adult males are smaller. This adversely affects childhood growth and physical fitness and impairs intellectual and cognitive development. There are 1.2 billion people infected with this parasite and 60,000 deaths are attributed to the disease each year.

Hookworm



Hookworm infection is one of the most common infections of humans with approximately 600 million cases in the developing countries of the tropics. The worm's larvae enter the body through the skin, and mature as they travel to the small intestine. Adult worms attach to the wall of the small intestine and begin to feed. Children and women of reproductive age are the populations most vulnerable to hookworm-associated blood loss leading to iron-deficiency anemia and protein malnutrition. Consequently, hookworm infection is one of the most important parasitic maternal-child health problems in the world.

Trichuris

Trichuris is caused by called the human whipworm, a soil-transmitted worm parasite. The worm's eggs enter the body on food or on hands that have come into contact with soil contaminated with the eggs. It is estimated that 800 million people are infected with the parasite and that 10,000 deaths result each year. The parasites' eggs hatch in the small intestine, and attach to the large intestine, where they cause blood loss and deplete the host of nutrients. This adversely affects childhood growth and physical fitness and impairs intellectual and cognitive development.

For more, visit, Trichuris

Lymphatic Filariasis

Lymphatic Filariasis, more commonly known as elephantiasis, is a parasitic disease caused by thread-like microscopic worms. The disease affects over 120 million people in 80 countries throughout the tropics and sub-tropics and is carried from person to person by mosquitos. The adult worms live in the human lymph system, which maintains the body's fluid balance and fights infections. When the parasite dies, it blocks the lymph system, causing disfiguring swelling of legs, the scrotum and the breast. More than 20% of the world's population is living at risk of lymphatic filariasis, 120 million people are infected, and 40 million have clinical symptoms. It cannot be cured, but its

spread, and future cases, can be prevented with delivery of drug combinations to populations where the disease is prevalent.
For more, visit, Lymphatic Filariasis Support Centre

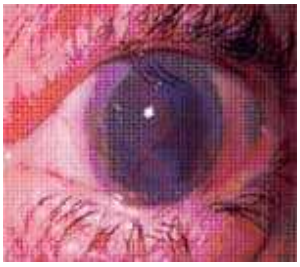
Onchocerciasis (River Blindness*)*

River blindness is an infection caused by a worm parasite, spread by bites from infected blackflies. It derives its name from the fact that transmission occurs most intensely in African villages near rapidly flowing streams. People with heavy infections usually have dermatitis, eye lesions, and/or subcutaneous nodules. Approximately 17.7 million people are estimated to be suffering from onchocerciasis, of whom about 270,000 are blind and another 500,000 have visual impairment. About 99% of those infected are in Africa; the remainder are in Yemen and six countries in the Americas. Onchocerciasis is effectively treated with the oral medicine, Ivermectin.
For more, visit, African Programme for Onchocerciasis Control

Schistosomiasis

Schistosomiasis, sometimes referred to as bilharzia, is caused by parasitic worms which penetrate the skin of people who swim in contaminated water. Approximately 200 million people are infected worldwide and some estimates are that more than 200,000 deaths result from schistosomiasis. Infection occurs when skin comes in contact with contaminated fresh water in which certain types of snails that carry schistosomes are living. Fresh water becomes contaminated by *Schistosoma* eggs when infected people urinate or defecate in the water. The worms live in the intestine, causing symptoms from blood in the urine, to impaired growth, development, and performance. In severe cases, the infection leads to bladder cancer, and kidney, liver, and spleen malfunction.
For more, visit, Schistosomiasis Control Initiative

Trachoma



Trachoma, the world's leading cause of preventable blindness, primarily affects rural populations with limited access to clean water and health care, and disproportionately impacts women and children. Eighty-four million people suffer from active infection and eight million individuals are visually impaired or irreversibly blind as a result of it. Founded in 1998, the International Trachoma Initiative (ITI) is leading the fight against trachoma by forging partnerships among governmental and nongovernmental organizations in Africa and Asia to eliminate the disease through implementation of the World Health Organization-approved, SAFE strategy—a comprehensive approach that employs surgery, antibiotics (via Pfizer's donation of Zithromax), facial cleanliness and environmental improvement (clean water and sanitation management) to address the underlying causes of the disease. Between 1999 and 2006, nearly 41 million antibiotic treatments have been administered, approximately 240,000 individuals have received sight-saving surgery and millions of people in endemic countries have benefited from health education and improved access to water and sanitation. In 2006, Morocco will mark the successful completion of its mass intervention campaign, while Ghana, Mauritania, Nepal and Vietnam remain on pace to complete their respective campaigns within the next five years.
For more, visit, International Trachoma Initiative