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Bacterial Infections: Overview

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Introduction

Bacteria are ubiquitous. They play an important role in maintaining the environment in which we live. Only a small percentage of the world's bacteria cause infection and disease. These bacterial infections have a large impact on public health. As a general rule, bacterial infections are easier to treat than viral infections, since the armamentarium of antimicrobial agents with activity against bacteria is more extensive. More so than with infectious diseases caused by viruses and parasites, however, bacterial resistance to antimicrobials is a rapidly growing problem with potentially devastating consequences.

Bacteria are unique among the prokaryotes in that so many of them are normal flora that colonize the host without causing infection. Once a person is infected, clinically apparent disease may or may not be seen, and only in a small subset of infections do we see clinically significant disease. Bacterial infections can be transmitted by a variety of mechanisms. In order to be spread, a sufficient number of organisms must survive in the environment and reach a susceptible host. Many bacteria have adapted to survive in water, soil, food, and elsewhere. Some infect vectors such as animals or insects before being transmitted to another human.

New species and new variants of familiar species continue to be discovered, particularly as we intrude into new ecosystems. Both Lyme disease and Legionnaire's disease, now well-known to health-care professionals, were discovered as recently as the 1970s. The recent increased prevalence of highly immunosuppressed individuals, both due to AIDS and the increasing use of immunosuppressive drugs as chemotherapy and for transplantation of organs, tissues, and cells, has led to a population of patients highly susceptible to types of bacterial infections that were comparatively rare before.

Several factors lead to the development of bacterial infection and disease. First, the infectivity of an organism

determines the number of individuals that will be infected compared to the number who are susceptible and exposed. Second, the pathogenicity is a measure of the potential for an infectious organism to cause disease. Pathogenic bacteria possess characteristics that allow them to evade the body's protective mechanisms and use its resources, causing disease. Finally, virulence describes the organism's propensity to cause disease, through properties such as invasiveness and the production of toxins. Host factors are critical in determining whether disease will develop following transmission of a bacterial agent. These factors include genetic makeup, nutritional status, age, duration of exposure to the organism, and coexisting illnesses. The environment also plays a role in host susceptibility. Air pollution as well as chemicals and contaminants in the environment weaken the body's defenses against bacterial infection.

Structure and Classification of Bacteria

Bacteria are prokaryotic organisms that carry their genetic information in a double-stranded circular molecule of DNA. Some species also contain small circular plasmids of additional DNA. The cell cytoplasm contains ribosomes and there is both a cell membrane and, in all species except *Mycoplasma*, a complex cell wall. External to the cell wall, some bacteria have capsules, flagella, or pili (see [Figure 1](#)). Bacteria normally reproduce by binary fission. Under the proper conditions, some bacteria can divide and multiply rapidly. Consequently, some infections require only a small number of organisms to cause potentially overwhelming infection.

Bacteria are classified as Gram-positive or Gram-negative based on the characteristics of their cell wall, as seen under a microscope after stains have been administered, a procedure called Gram staining, that was developed in 1882 by Hans Christian Gram (see [Figure 2](#)).

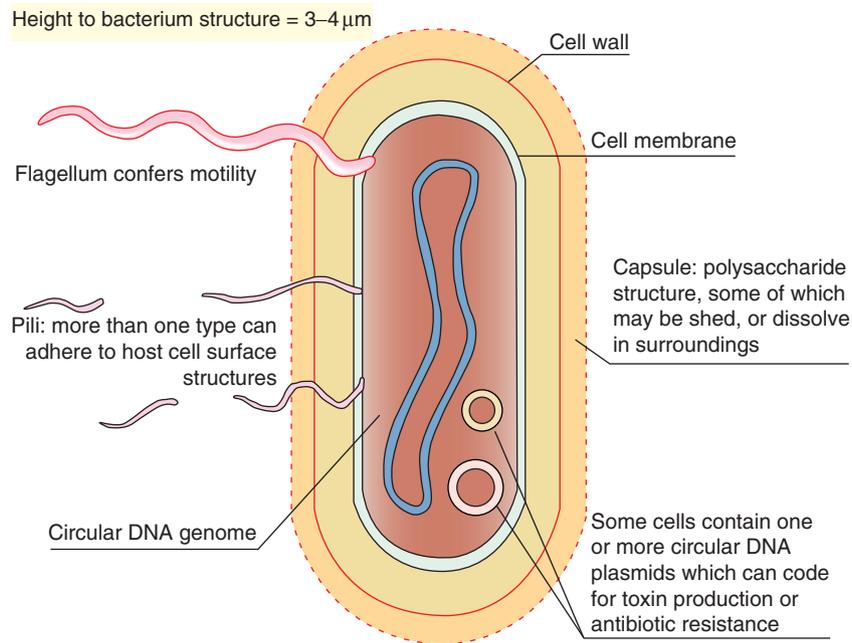


Figure 1 Structure of a bacterium. Reproduced from Bannister BA, Begg NT, and Gillespie SH (eds.) (1996) Structure and classification of pathogens. In: *Infectious Disease*, 2nd edn., ch. 2, pp. 23–34. Oxford, UK: Blackwell Science Ltd., with permission from Blackwell Publishing.

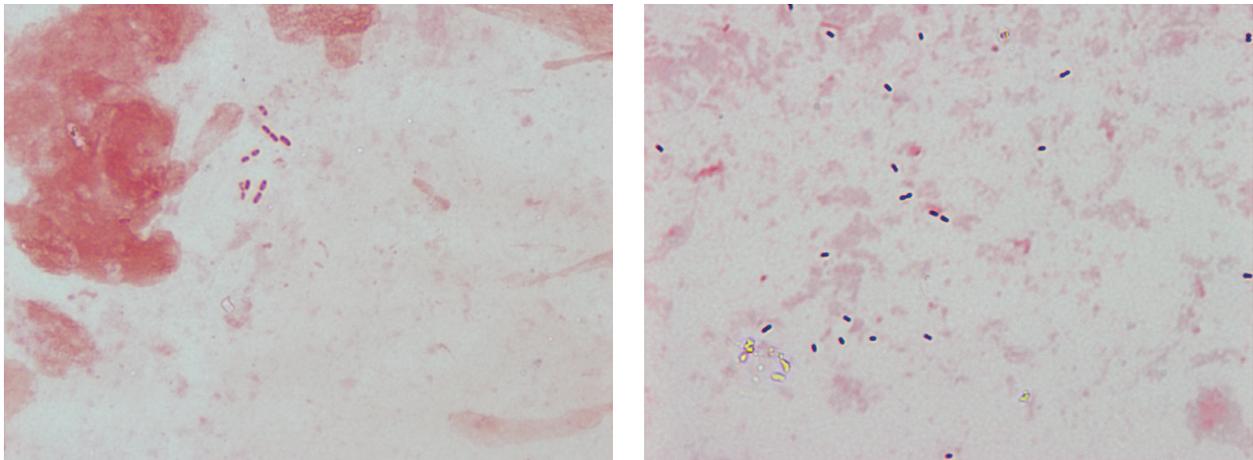


Figure 2 Gram stains of Gram-negative (left) and Gram-positive (right) bacteria (courtesy of Tufts Medical Center Microbiology Laboratory).

Most, but not all, bacteria fall into one of these two categories. Clinically, one of the main differences between gram-positive and gram-negative organisms is that gram-negative bacteria tend to produce an endotoxin that can cause tissue destruction, shock, and death. The two classes of bacteria differ in their antibiotic susceptibilities as well.

Bacteria can also be classified based on their growth responses in the presence and absence of oxygen. Aerobic bacteria, or aerobes, grow in the presence of oxygen. Obligate aerobes such as *Bordetella pertussis* require oxygen. Facultative organisms can grow in the presence or

absence of oxygen. Anaerobic bacteria such as the *Clostridia* are able to grow in the absence of oxygen and obligate anaerobes require its absence.

Some bacteria are not classified as Gram-positive or Gram-negative. These include the mycobacteria, of which *Mycobacterium tuberculosis* is the most well-known, which can be seen under the microscope using a special stain called the acid-fast stain; organisms that do not take up Gram stain such as the spirochetes (which cause diseases such as syphilis and Lyme disease); and the *Rickettsia* (which cause Rocky Mountain spotted fever and epidemic typhus).

Clinical Manifestations of Bacterial Infection

All of the human organs are susceptible to bacterial infection. Each species of bacteria has a predilection to infect certain organs and not others. For example, *Neisseria meningitidis* normally infects the meninges (covering) of the central nervous system, causing meningitis, and can also infect the lungs, causing pneumonia. It is not, however, a cause of skin infection. *Staphylococcus aureus*, which people typically carry on their skin or mucus membranes, often causes skin and soft tissue infections, but also spreads readily throughout the body via the bloodstream and can cause infection of the lungs, abdomen, heart valves, and almost any other site.

Disease can be caused by destruction of the body's cells by the organism or the body's immune response to the infection. Antibiotics may be of little or no use when the disease manifestations are a result of the body's attempts to rid itself of the bacteria. The systemic inflammatory response syndrome (SIRS), usually caused by a bacterial infection, is an overwhelming inflammatory response to infection, manifested by the release of large numbers of cytokines and presenting with signs of infection and early signs of hemodynamic instability. If allowed to progress, SIRS patients can go on to develop sepsis, with multiorgan failure and death. Once the cascade of events has begun, even the strongest antibiotics are often powerless to stop this progression.

Epidemiology

The external environment is usually the setting in which the bacterial agent and the host interact and the infection is acquired. Bacteria can be transmitted to humans through air, water, food, or living vectors. The macro- or microenvironments can also be thought of as playing a role in the spread of bacteria. Certain settings such as hospitals and prisons harbor specific types of organisms. Some bacteria are endemic in certain geographic regions and rare or nonexistent in others.

Reservoirs

A reservoir is any site where a pathogen can survive until its transfer to a host. Often pathogens multiply within their reservoirs. Some reservoirs are living. Humans, animals, birds, and arthropods are all common reservoirs and do not always manifest illness due to the pathogen they are harboring. Nonliving reservoirs include food, air, soil, and water. Fomites are inanimate objects capable of transmitting infection.

Human reservoirs

Humans are the reservoirs for many bacterial infections and in some instances they are the exclusive host in nature to harbor the bacteria. When a human is colonized with a pathogen without manifesting disease, he or she is referred to as a carrier. Passive carriers carry pathogens without ever having the disease. The deadly meningitis caused by *Neisseria meningitidis* is often transmitted by passive carriers who harbor the bacteria in their respiratory tracts. An incubatory carrier is a person who is harboring, and can transmit, an infection during the incubation period (the time between acquisition and manifestation of illness) for that infection. Sexually transmitted infections are frequently transferred by individuals who have not yet shown symptoms. Convalescent carriers manifested symptoms of an infectious disease in the recent past and continue to carry the organism during their recovery period. Active carriers have completely recovered from a disease and harbor the organism indefinitely. *Salmonella*, especially *Salmonella* Typhi, the cause of typhoid fever, is an example of a bacterial infection that can produce a prolonged carrier state without the individual being aware of the condition. *Salmonella* can lurk in a quiescent state in organs such as the gallbladder, sometimes even permanently. These individuals may continuously transfer the pathogen to their contacts. Mary Mallon, a New York City cook in the early 1900s, known as Typhoid Mary, was a carrier responsible for many cases of typhoid fever.

Animal reservoirs

Infections acquired from animal reservoirs are referred to as zoonoses or zoonotic diseases. Humans acquire infection from animals either by direct contact, as in the case of pets or farm animals, by ingestion of the animal or inhalation of bacteria in or around its hide, or through an insect vector that transmits the pathogen from the animal to the human via a bite. Diarrhea caused by *Salmonella* can occur after handling turtles and contaminating one's hands with their feces, or from ingesting undercooked chicken contaminated with the bacteria, or through other routes such as eating undercooked or raw chicken eggs. The disease tularemia, caused by the organism *Francisella tularensis*, is often seen in individuals who have recently skinned a rabbit. Similarly, anthrax caused by *Bacillus anthracis* follows either inhalation of spores from dead animals or hides, or entry of spores into a wound. In Lyme disease, the deer tick transmits the spirochete *Borrelia* from the white-footed mouse to the human.

Overflow is a phenomenon particularly relevant to zoonotic diseases. Using the example of Lyme disease, the cycle of transmission between tick hosts and animal hosts (such as deer and mice) leads to the presence of infected ticks that can also infect humans. Thus the cycle allows the Lyme organisms to overflow from the natural

cycle of infection into humans. Reducing the number of infected deer on a New England island through culling, for example, has been shown to greatly decrease the number of infected ticks and almost eliminate infection in humans.

Arthropod reservoirs

Arthropods reservoirs include insects and arachnids. A vector is commonly understood to be an arthropod that is involved in the transmission of disease. Common insect vectors for bacterial infection include fleas, lice, and flies. Arachnid vectors include mites and ticks. The diseases caused by the bacteria *Borrelia* (which include relapsing fever and the disease referred to in the United States as Lyme disease after it was discovered in Lyme, Connecticut) infects ticks that take a blood meal from an infected deer or mouse. These ticks (see [Figure 3](#)) then inject the bacteria into a human some time later during another blood meal. Other bacterial diseases caused by arthropods include epidemic, murine, and scrub typhus, caused by *Rickettsia* carried by lice, fleas, and mites, respectively, Rocky Mountain spotted fever also caused by *Rickettsia* and carried by ticks, and bubonic plague carried by fleas.



Figure 3 Adult female *Ixodes* tick, capable of transmitting *Borrelia burgdorferi*, the agent of Lyme disease, and *Anaplasma phagocytophilum*, the agent of human granulocytic anaplasmosis, previously known as human granulocytic ehrlichiosis (courtesy of CDC/Dr. Amanda Loffis, Dr. William Nicholson, Dr. Will Reeves, Dr. Chris Paddock).

Nonliving reservoirs

Air can become contaminated by dust or human respiratory secretions containing pathogenic bacteria. Bacteria do not multiply in the air itself, but may be transported by air currents to areas more conducive to their growth. Infections acquired through the air are characterized as airborne. The classic airborne bacterial infection is tuberculosis.

Soil is typically a reservoir for bacteria that form spores when not in a host. The various species of *Clostridium* can be acquired from exposure of a wound to dirt or soil. These anaerobic bacteria cause tetanus, botulism, and gas gangrene. Anthrax spores can survive for as long as 100 years in soil. Heavy rain, excavation, and tilling may bring them to the surface and cause an outbreak of anthrax among livestock. In medieval Europe, specific pasturelands were avoided for domesticated animal grazing because of the risk of anthrax.

Food, including milk, when not handled properly, can be the reservoir for a wide variety of pathogenic organisms. Food may be contaminated by feces, or the animal itself may be infected, such as in the case of chickens with *Campylobacter* or *Salmonella*. Food can also be contaminated with the ubiquitous spores of *Botulinum*, which can cause a form of paralysis called botulism. Pasteurization and food sterilization are important public health safeguards against these infections. Food handlers can carry a variety of bacteria on their hands, and indeed there are stringent regulations in many countries regulating food handling and handlers. Seafood can be contaminated from bacteria in the water. Soft cheeses are common reservoirs for *Listeria monocytogenes*. Sometimes, unexpected foods become reservoirs for bacterial infection, as in the case of alfalfa and other raw seed sprouts, which since the 1970s were known to be reservoirs for both *Salmonella* and *Escherichia coli*. It is thought that the presoaking and germination of the seeds in nutrient solutions is conducive to the growth and multiplication of these pathogenic bacteria. The seeds themselves can become contaminated at any point in their production and distribution. Transmission via these uncooked foodstuffs has been documented to cause the majority of foodborne bacterial outbreaks in some locations.

Water generally becomes a reservoir for infection when it is contaminated by soil microbes, or animal or human feces. Raw sewage may contaminate drinking water during a storm or flood when sewage systems are overwhelmed, or if it is inadequately treated and dumped into local waters (see [Figure 4](#)). There is also concern about the potential for terrorists to use water as a reservoir for bioterrorism pathogens.

Many inanimate objects are considered fomites, as they are capable of indirectly transmitting infection from one person to another by acting as an intermediate point in the cycle of transmission. Fomites commonly found in households that allow transmission of infection between family

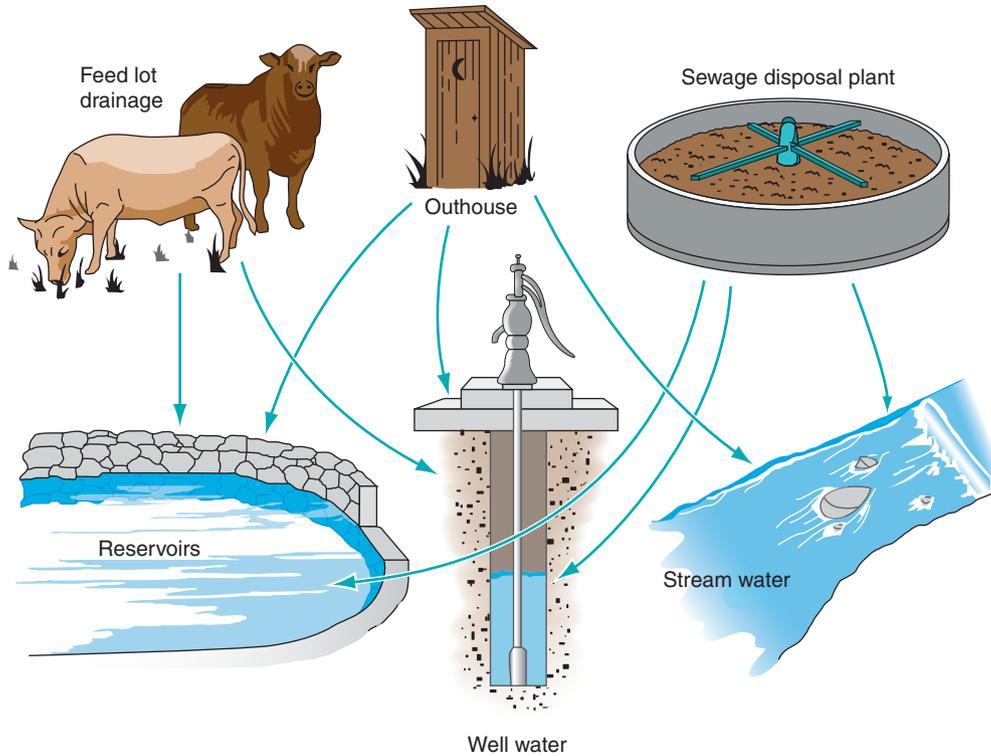


Figure 4 Sources of water contamination. Reproduced with permission from Engelkirk PG and Burton GR (eds.) (2006) Epidemiology and public health. In: *Burton's Microbiology for the Health Sciences*, 8th edn., ch. 11. Baltimore: Lippincott Williams and Wilkins.

members include doorknobs, toilet seats, and utensils. At daycare centers and pediatrician's offices, infection is transmitted via toys handled by children with contaminated hands. In hospitals, there are countless fomites capable of spreading infection. Many respiratory infections are not spread through aerosols, but rather through respiratory secretions (saliva, sputum, etc.) being deposited on surfaces and hands, with secondary transmission via hand-to-mouth contact to the next host (Table 1).

Modes of Transmission

There are five principal modes by which bacterial infections may be transmitted: Contact, airborne, droplet, vectors, and vehicular (contaminated inanimate objects such as food, water, and fomites) (see Figure 5).

Contact

Transmission via contact includes direct skin-to-skin or mucous membrane-to-mucous membrane contact or fecal-oral transmission of intestinal bacteria. Transfusion of contaminated blood products also transmits several bacterial infections, such as syphilis.

Airborne

Some bacteria are carried on air currents in droplet nuclei. Q fever, tuberculosis, and Legionella travel great distances

Table 1 Reservoirs for bacteria

Reservoirs	Disease examples
Human	Typhoid fever, syphilis
Animal	Anthrax (cows), <i>Salmonella</i> (turtles), tularemia (rabbits), Lyme disease (white-footed mice)
Arthropods	Rocky Mountain spotted fever (ticks), endemic typhus (fleas), scrub typhus (mites)
Air	Tuberculosis
Soil	Tetanus, botulism, gas gangrene
Food	<i>Vibrio</i> , <i>E. coli</i> 0157:H7
Water	<i>Shigella</i> , <i>Legionella</i>

from their origin. Animals with Q fever have been known to transmit infection to other animals as far as 10 miles away.

Droplet

When an infection is spread via droplets greater than 5 µm in diameter, this type of spread is not considered airborne given that the droplet is unlikely to travel through the air for more than 1 m. They are generally more susceptible than airborne droplet nuclei to filtering in the nose via nasal hairs or to removal by nasal or facial masks.

Vectors

Typically, the arthropod (mosquito, tick, louse) takes a blood meal from an infected host (which can be human or

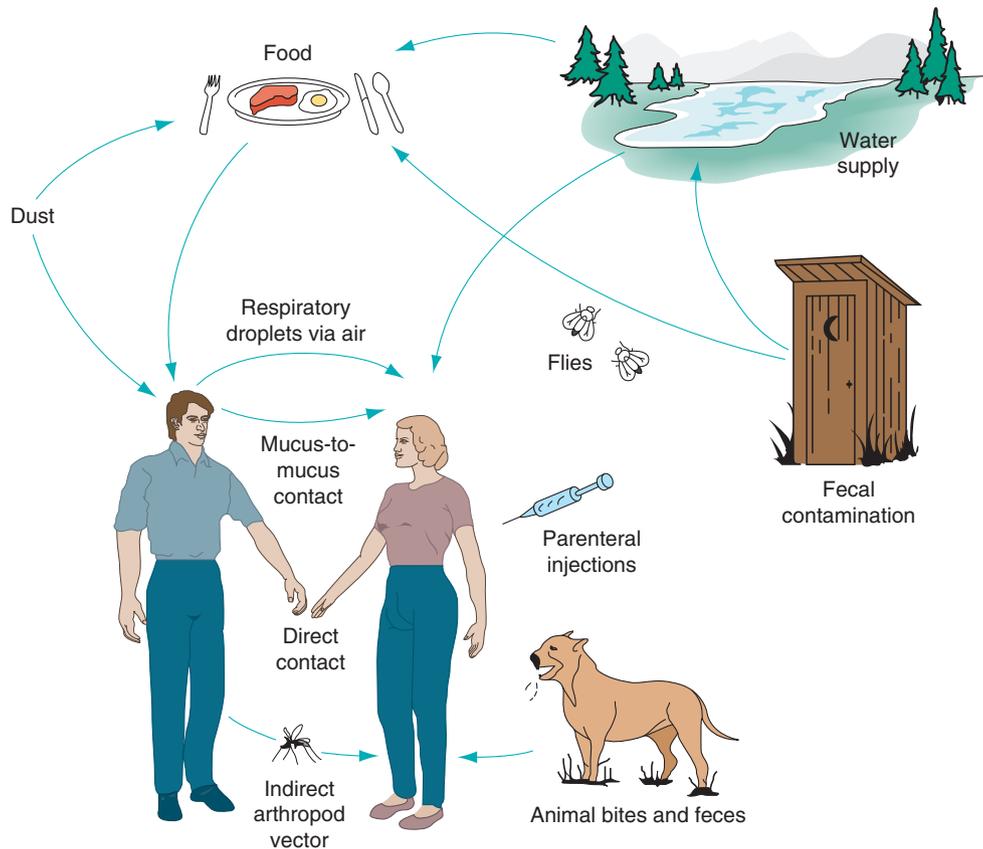


Figure 5 Modes of disease transmission. Reproduced with permission from Engelkirk PG and Burton GR (eds.) (2006) *Epidemiology and public health*. In: *Burton's Microbiology for the Health Sciences*, 8th edn., ch. 11. Baltimore: Lippincott Williams and Wilkins.

animal) and transfers pathogens to an uninfected individual. Bacteria such as *Shigella* can adhere to the foot pad of house flies and be transmitted in this manner.

Vehicular (including food, water, and fomite transmission)

Bacterial infection due to food and water generally develops when bacteria enter the intestine via the mouth. Those organisms that survive the low pH of the stomach and are not swept away by the mucus of the small intestine adhere to the cell surfaces. There they may invade the host cells or release toxins, causing diarrhea.

Infection acquired from fomites is usually the result of the organism attaching to the host's skin (generally on their hand) when they come in contact with a contaminated object, and then being deposited onto a mucus membrane when the host touches his or her face, or in some cases his or her genitals, with the contaminated body part (Table 2).

Prevention of Bacterial Infection

Among the top causes of mortality in the world, lower respiratory infection is the third most common and

Table 2 Modes of transmission of bacterial infections

<i>Mode of transmission</i>	<i>Disease examples</i>
Contact	Streptococcal impetigo (skin-to-skin), gonorrhea (mucus membrane-to-mucus membrane), <i>Salmonella</i> (fecal-oral), syphilis (transfusion)
Airborne Droplet	Tuberculosis, Q fever, legionella Pertussis, meningococcus, <i>Haemophilus influenzae</i>
Vectors	Lyme disease (tick), <i>Shigella</i> (fly) epidemic typhus (lice), bubonic plague (fleas)
Vehicular	<i>Campylobacter</i> (food), trachoma (fomites)

diarrhea is the sixth. Both are often caused by bacteria. Tuberculosis is the seventh most common cause of death. Clearly, measures to prevent infection have a dramatic impact on morbidity and mortality. Prevention is especially important in this age of increasing antibiotic resistance, because treatment can be so difficult to achieve. There are three major principals of control of bacterial infection: Eliminate or contain the source of infection, interrupt the chain of transmission, and protect the host against infection or disease. In addition, there is

increasing recognition that elimination of important cofactors, such as air pollution from vehicles or from indoor cooking, can markedly reduce the incidence of bacterial infections. Which measure is most effective often depends on the reservoir for the infection. Prevention of infection, e.g., through a vaccine, is generally called primary prevention, treatment of infected people to prevent symptomatic infection is called secondary prevention, and treatment of infected people to prevent transmission to other humans is called tertiary prevention.

Zoonoses

Animals transmit disease in various ways. Some exposures, such as anthrax from animal hides, may be occupational, others, such as *Campylobacter* or *Yersinia*, result from contamination of food or water by animal feces. Measures to prevent infection include the use of personal protective equipment when handling animals, animal vaccinations (such as for anthrax or brucellosis), use of pesticides to prevent transmission from animal to human by insect bite, isolation or destruction of diseased animals, and proper disposal of animal waste and carcasses. For control of plague, rat populations can be suppressed by the use of poisons as well as improved sanitation. Infections acquired from insect vectors can be minimized by the use of window screens, insect repellent, and protective clothing. Checking the body (including pets) for ticks at the end of each day can prevent transmission of tickborne bacterial infections, as most require a sufficient period of time after attachment to transmit infection.

Water Treatment

Improperly treated water can lead to outbreaks of typhoid, *Escherichia coli*, or *Shigella* as well as viral and parasitic diseases. Improvement of the water supply in developed areas has been instrumental in decreasing the burden of infection in communities. The process of modern water treatment involves filtration, settling, and coagulation to remove particles that may carry bacteria; aeration; and chlorination or treatment with another reactive halogen. Novel disinfection methods increasingly being used include ultrafiltration and the use of ozone or ultraviolet (UV) light. Water can be tested for the presence of fecal bacteria with relatively simple and inexpensive kits. The number of coliforms (bacteria typically found in feces) present in a given quantity of treated water is taken as a measure of fecal contamination. Potable (safe to drink) water has less than a predetermined number of coliforms per milliliter, as defined by governmental regulations. When traveling in developing countries or while camping, treating water with chlorine tablets or iodine solution or boiling the water for 5 min decreases the likelihood of acquiring bacterial intestinal infection.

Air

Controlling the spread of airborne bacteria is extremely difficult. Sterilizing the air is impossible. In hospitals, laminar-flow units are used so that air contaminated by patients with airborne bacterial infections such as tuberculosis does not flow to other parts of the building. Susceptible individuals should minimize or eliminate their time in rooms where infectious agents may be present (e.g., tuberculosis, measles, or varicella).

Milk and Food

Milk and food must be handled properly and protected from bacterial contamination at every stage of preparation including at their source, during transport and storage, and during preparation for consumption. Milk is pasteurized, a process that consists of heating the milk for a specified period of time. The allowable bacterial counts before and after pasteurization are standardized. In order to maintain these low bacterial counts, pasteurized milk must remain at 5–10 °C during transport and storage. *Listeria*, an organism which has a predilection to infect pregnant women, is tolerant of these cold temperatures, and can continue to grow, particularly in soft cheeses, which provide an excellent growth medium. Pregnant women are therefore cautioned against eating soft cheeses, even those that have been pasteurized. An important public health approach for foodstuffs, with wide industry and regulatory adoption, is the identification of critical places or points where contamination is most likely, known by the acronym HACCP (Hazard And Critical Control Point analysis). In many countries all food manufacturers must have an HACCP plan in place to assist with their focus on eliminating foodborne infections.

In developing and tropical countries, soil may be enriched with human feces. Produce is therefore at risk for contamination with pathogenic bacteria. Any food may be contaminated by the hands of workers who handle it during harvesting or processing for distribution. Cooking immediately prior to eating reduces the risk by killing the bacteria; however, some bacteria such as *Staphylococcus*, *Bacillus*, and *Clostridium* produce toxins that are not inactivated by heat.

Human Reservoirs

Immunization is one of the great technological advances of the modern era. Immunization can be passive, by transfer of antibody against a specific disease, or active, by administering a small dose of the organism and allowing the body to produce its own antibody. Live bacterial vaccines include Bacillus Calmette-Guerin (BCG) for tuberculosis, oral typhoid vaccine, and a tularemia vaccine. Other bacterial vaccines are antigenic derivatives of the organism,

such as the vaccines for meningococcus, streptococcus, diphtheria, pertussis, and anthrax. It would be impossible to develop a vaccine for every known species of bacteria capable of causing disease, and therefore the other measures of prevention of infection will always be of critical importance.

The spread of disease from person to person can be prevented by quarantine, the use of isolation measures, and antibiotic prophylaxis. In the fourteenth century, suspected plague victims were required to stay on ships or in their homes for 40 days until it was clear that they would not exhibit signs of the disease. In the twenty-first century, large numbers of people were quarantined in Toronto and Hong Kong due to severe acute respiratory syndrome (SARS), a virus. Today, the only bacterial infections for which the WHO still uses quarantine measures are plague and cholera. In hospitals, standard precautions are used on all patients regardless of whether they have known infection, and special isolation precautions are instituted for patients with specific infections such as highly resistant, or easily transmitted, bacteria. Standard precautions include the practice of performing hand hygiene (washing hands or applying waterless hand sanitizer) after touching a patient, using gloves for contact with body fluids, secretions, excretions, and contaminated items, and using a cover gown, mask, and eye protection when body fluid splashes are likely. Patients infected with airborne bacteria such as tuberculosis are placed in special laminar air flow rooms. Patients with antibiotic-resistant nosocomial bacterial infection or colonization such as methicillin-resistant *Staphylococcus* and vancomycin-resistant *Enterococcus* are cohorted in rooms with others like themselves and gloves are routinely used in their care. Patients who have diarrhea caused by the spore-forming bacteria *Clostridium difficile* are placed in private rooms when possible, and cover gowns and gloves are used to prevent spread of spores throughout the hospital. Special cleaning agents are used in these rooms to kill the spores.

Antibiotic prophylaxis is used in certain settings to prevent bacterial infection. As a mass prevention technique, it is not very effective, since infection with resistant organisms would be expected to develop in response to antibiotic use. It is, however, very useful in preventing infection in close contacts of patients with meningococcal meningitis and pertussis, in preventing development of sexually transmitted disease in those exposed, and in preventing serious disease in known carriers of diphtheria and tuberculosis. Antibiotic prophylaxis has been shown to be useful for patients undergoing certain surgical procedures to prevent postoperative infection, and for patients with severe immunosuppression due to bone marrow or solid organ transplantation.

Lifestyle changes can have a major impact on the spread of infection. Safer sex practices decrease the spread of sexually transmitted infection. Simple personal hygiene

measures can also have a dramatic effect on the incidence of infection. In Karachi, Pakistan, diarrhea and acute respiratory infection, often caused by bacteria, are leading causes of death. Between 2002 and 2003, U.S. and Pakistani health officials conducted a study (Luby *et al.*, 2005) in which households in squatter settlements were randomly assigned to be part of a hygiene campaign (involving education and the distribution of soap) or to be simply observed. Washing hands with soap reduced the incidence of diarrhea and pneumonia by half, and the incidence of impetigo, a superficial bacterial skin infection, by one-third. In the developed world, numerous studies have shown an association between poor hand hygiene and the spread of multidrug-resistant organisms within hospitals, and countless studies have shown that compliance with hand hygiene requirements remains low in health-care settings. Body lice, which carry louse-borne typhus, are associated with poor general hygiene. Improved personal hygiene and delousing procedures (heat and chemical treatment) are used to control infestation.

Diagnostic Tests

Stains and Microscopy

Stains are applied to specimens that have been fixed to a microscope slide. Typically, the first test performed to diagnose a possible bacterial infection is the Gram stain. The cell wall is made of sugars and amino acids, and in Gram-positive bacteria this wall is thick, lies external to the cell membrane, and contains other macromolecules, whereas in Gram-negative bacteria the wall is thin and is overlaid by an outer membrane. When subjected to the Gram staining procedure, Gram-positive organisms, such as the staphylococci, retain the purple stain, whereas Gram-negative organisms do not. A second stain is then added to allow visualization of the Gram-negative organisms, such as *E. coli*, which appear pink or red under the microscope. Identifying the causative agent under the microscope as either Gram-positive or Gram-negative (see the section titled 'Structure and classification of bacteria,' above) allows the clinician to more accurately predict the antibiotic that is likely to be effective. The morphology of the bacteria under the microscope (short vs. long, plump vs. thin, branching vs. straight) provides another clue to the identity of the organism. Some organisms such as the *Mycobacteria* which include tuberculosis, do not readily take up Gram stain and require special stains to be visualized. Other stains that are less commonly used contain specific immunofluorescent-labeled antisera and provide a diagnosis of such organisms as group A hemolytic streptococcus, plague, and syphilis. While a species-level diagnosis is not possible with this method, it does help to rapidly categorize the type of infection and to guide initial treatment.

Dark Field and Fluorescent Microscopy

Dark field microscopy is a technique that involves adapting the microscope so that the organisms are viewed against a dark instead of light background, with the light source illuminating the bacterium from the side rather than from behind the organisms. The spirochetes, thin bacteria that include the agents of syphilis and yaws, are visualized this way. Fluorescent microscopy, with or without special dyes, is a technique that utilizes a UV light source and can be used to visualize *Mycobacteria* such as tuberculosis.

Antigen Detection

Commercial kits are used to identify a variety of organisms from body fluid specimens. Legionnaire's disease is diagnosed from a urine sample, meningococcal or pneumococcal meningitis from cerebrospinal fluid, and *Streptococcus pyogenes* from a throat swab. Recently, a commercial kit for the detection of *Helicobacter pylori* antigen in feces was developed, which has greater sensitivity and specificity than does the detection of antibody to this organism. The advantage of this approach is its rapidity.

Nucleic Acid Probes and Polymerase Chain Reaction

Probes are molecules that identify the presence of certain known genes in a specimen without the necessity for culture. Probes for the toxins of *E. coli* or cholera can be applied directly to feces. Probes for gonorrhea and chlamydia are applied to genital secretions or urine. The polymerase chain reaction (PCR) is used to amplify a small amount of DNA from a few bacteria to produce millions of copies in a few hours. Bacteria for which this technique has been useful include *Helicobacter pylori*, the agent responsible for gastric ulcer disease, and *Mycoplasma pneumoniae*, which causes walking pneumonia.

Culture

A basic microbiology laboratory is generally able to culture bacteria from blood, sputum, and urine, but with the right materials any body fluid or tissue can be processed for culture. Specimens suspected of being infected with bacteria are plated on solid nutrient-rich media or inoculated into broth. On solid media, bacteria grow and produce colonies composed of thousands of cells. Colonies of different species have characteristic appearances and smells that help in their identification. In broth, growth is detected by the presence of turbidity and then the broth is subcultured onto solid media for identification. Some parasitic bacteria, such as *Chlamydia* and rickettsia, cannot be grown on artificial media and require the presence of

host cells (cell culture) for growth. Others, such as *Mycobacterium leprae* (the agent of leprosy) and *Treponema pallidum* (the agent of syphilis) cannot be grown at all except in live animals. Once a bacterial colony is present on solid medium, it can be identified by classifying it based on its ability to grow under aerobic or anaerobic conditions, by observing its appearance on Gram stain, by testing its ability to produce enzymes and metabolize sugars as detected by simple tests, and by its ability to utilize various substrates for growth. After the organism is identified, its susceptibility to various antibiotics must be determined in order to guide therapy. The organism is incubated with the various test antibiotics in order to determine whether it will grow in their presence.

Serology

Testing for antigen–antibody interactions can be a useful way to determine the presence of a bacterial infection, particularly in the case of organisms that are difficult to grow in the laboratory. Serological testing is limited in most cases by the need for several weeks to pass in order for the body to develop an immune response to the infection. Serology is particularly useful for bacterial infections such as syphilis and brucellosis, which are not easy to grow in culture. Indeed, sometimes the only way to judge the efficacy of treatment for an infection is to follow serological results. For example, with syphilis one may expect a fourfold decrease in the strength of the serological response after successful treatment.

Treatment

An ideal antimicrobial agent acts at a target site that is present in the infecting organism but not the host cells. Four major sites in the bacterial cell can be targeted by antibiotics because they are sufficiently different from human cells. These are the cell wall, the cell membrane, the nucleic acid synthetic pathway, and the ribosome. Antibacterial agents, or antibiotics, are typically products of other microorganisms, elaborated by them in order to compete for space and resources. There are three ways to classify an antibacterial agent:

1. Based on whether it is bactericidal (kills bacteria) or bacteriostatic (inhibits growth of bacteria);
2. By its chemical structure;
3. By its target site.

Some bacteria are innately resistant to certain classes of antibiotics, either because they lack the target or are impermeable to the drug. Others are innately susceptible but develop resistance by one of a growing variety of mechanisms. Resistant strains of bacteria have a selective advantage, surviving in the presence of antibiotics, and

can spread throughout the host and even be transferred to other hosts. This phenomenon is important where antibiotic use is common, such as in hospitals or in congregate housing such as nursing homes. Some resistance genes are carried on plasmids, autonomously replicating circular extrachromosomal DNA molecules, and can thus be transferred to bacteria of other species. There are three main mechanisms of resistance:

1. Alteration in the target site;
2. Alteration in access to the target site (by decreasing permeability or pumping antibiotic out of the cell);
3. Production of enzymes that inactivate the antibiotic.

When an individual takes an antibiotic, all of the microbes in his or her body are exposed to the drug, not just the organism causing infection. Since use of antibiotics is associated with the development of resistance, the prudent use of antibiotics is an essential component in the effort to combat the problem of antibiotic resistance. Throughout the world, antibiotics are overused and misused. Examples of improper use include the use of antibacterial agents for viral infections, for infections that resolve spontaneously without treatment and without a high risk for negative sequelae, and for infections caused by organisms not susceptible to the antibiotic used. Another example of misuse is the consumption of broad-spectrum antibiotics, which inhibit or kill a wide variety of organisms simultaneously, when a narrower spectrum agent will suffice.

See also: Antimicrobial Resistance; Botulism; Brucellosis; Chlamydia (Trachoma and Sexually Transmitted Infections); Cholera and Other Vibrioses; Food Safety; Foodborne Illnesses: Overview; *Helicobacter Pylori*; Intestinal Infections: Overview; Leprosy; Lyme Disease; Plague, Historical; Pneumonia; Salmonella; Shigellosis;

Streptococcal Diseases; Syphilis; Tetanus; Tuberculosis Epidemiology; Tuberculosis: Overview; Tuberculosis Prevention; Typhoid Fever; Vaccines, Historical; Yaws, Pinta, and Endemic Syphilis.

Citations

- Bannister BA, Begg NT, and Gillespie SH (eds.) (1996) Structure and classification of pathogens. In: *Infectious Disease*, 2nd edn., ch. 2, pp. 23–34. Oxford, UK: Blackwell Science Ltd.
- Engelkirk PG and Burton GR (eds.) (2006) Epidemiology and public health. In: *Burton's Microbiology for the Health Sciences*, 8th edn., ch. 11. Baltimore: Lippincott Williams and Wilkins.
- Luby SP (2005) Effect of handwashing on child health: A randomised controlled trial. *Lancet* 366: 225–233.

Further Reading

- Benenson AS (ed.) (1995) *Control of Communicable Diseases Manual*, 16th edn. Washington, DC: American Public Health Association.
- Detels R, McEwen J, Beaglehole J, and Tanaka H (eds.) (2002) *Oxford Textbook of Public Health*, 4th edn. Oxford, UK: Oxford University Press.
- Evans AS and Brachman PS (eds.) (1998) *Bacterial Infections of Humans: Epidemiology and Control*, 3rd edn. New York: Plenum Publishing Corporation.
- Engleberg NC, DiRita V, and Dermody TS (2007) *Schaechter's Mechanisms of Microbial Disease*. Baltimore, MD: Lippincott Williams and Wilkins.

Relevant Websites

- <http://www.cdc.gov> – Centers for Disease Control and Prevention.
- http://www.who.int/water_sanitation_health/dwq – World Health Organization Drinking Water Quality.
- <http://www.fao.org/> – Food and Agriculture Organization of the United Nations.
- <http://www.hon.ch> – Health on the Net Foundation.

Bacteriology, Historical

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Bacteria, along with other microorganisms, were first observed and described in 1683 by Antoni van Leeuwenhoek (1632–1723), a Dutch draper, instrument maker, and member of the Royal Society. Van Leeuwenhoek, who ground tiny lenses and built his own single-lens microscopes, called the entities he had seen ‘animalcules,’ a group that we now believe to have included bacteria as well as protozoa.

Sporadic observations of microorganisms continued through the eighteenth century. John T. Needham (1713–81), Comte de Buffon (1707–88), and Lazzaro Spallanzani (1729–99) conducted experiments and debated the possibility of spontaneous generation of microorganisms from organic matter. Linnaeus included Leeuwenhoek’s animalcules in his *Systema Naturae* under Vermes, in a class he called