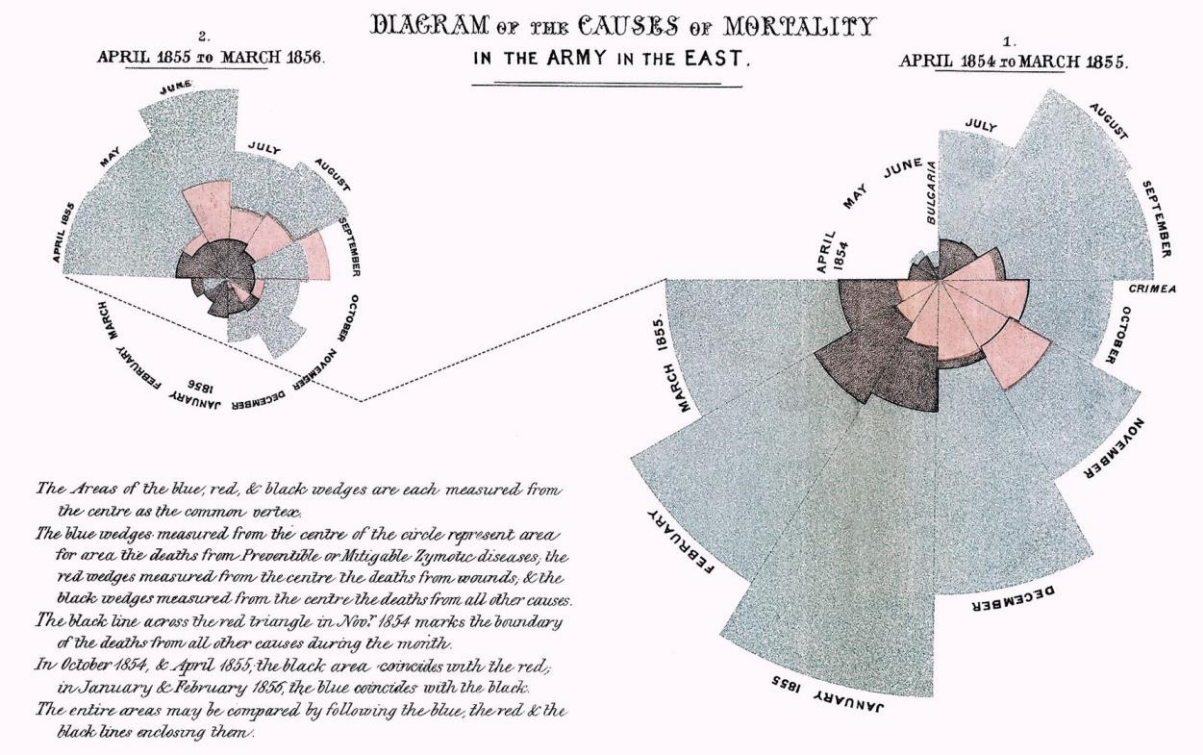
Infections that have determined battle and war outcomes

Mom, who was Florence Nightingale and why was she called the "Angel of Crimea"?



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Storyline

Sir William Osler, considered the father of modern medicine, wrote a pamphlet titled *Bacilli and Bullets* about the role of infectious diseases in the outcome of war. He encouraged a "true knowledge of your foes, not simply of the bullets, but of the much more important enemy, the bacilli. … Typhoid fever, malaria, cholera, enteric, and dysentery have won more victories than powder and shot." Many soldiers died of infections before any shots were ever fired, and among those who lived through the battle, death due to infections were common. In modern times, nursing has played an important role in treating soldiers injured in battle. Florence Nightingale is often considered the founder of modern nursing, and much of her work was based on her experience preventing and treating infections in soldiers injured in battle. She was also a highly respected statistician, and her ability to analyze the numbers and present them to people in a way they could understand was an important part of her fight against infectious diseases.

Nightingale trained as a nurse in the 1840s and was practicing nursing in London when the Crimean War broke out in 1853. She had recognized that many of the deaths in hospitals were due to lack of sanitation and infections, and she suspected this would be especially true for the soldiers in field hospitals. When she was asked to help organize nurses for a Crimean War hospital, she did so quickly and went to Scutari, the British army hospital in Constantinople. Conditions there were terrible. The soldiers lacked clean food, water, and bedding, and they were suffering from infections that were far worse than their original injuries. Nightingale and the other nurses worked to improve the sanitation at the hospital and to stop the spread of cholera, typhoid, and wound infections that were causing most of the deaths in the hospital. Her efforts to reduce infectious diseases resulted in a huge reduction in soldiers' deaths.

Florence Nightingale 1856-1857, © National Portrait Gallery, London

Nightingale was also interested in statistics and in finding ways to show complex information in ways that people could immediately see and understand. A great example of this is the Rose Diagram shown above, which she used to present the data that she and William Farr had analyzed. Rather than have a table listing all the causes of death at the Scutari field hospital, she used a graph similar to a pie chart. Each triangular segment represents the total deaths at the hospital for that month. The larger the triangle, the more deaths that occurred. Each triangle used three different colors to show the cause of death. The blue color represented deaths from infection, red indicated deaths from wounds, and black represented deaths from all other causes. It is easy to see that there is far more blue than other colors in the diagram, and this clearly made the point that most of the soldiers died from infections, not from wounds received in battle.

Infection as a major cause of death in wars has been noted throughout history. Prior to the First World War, it is likely that the majority of deaths in wars were due to infectious diseases. The high rate of infections and the epidemics that were brought by invaders to new territories have changed the course of battles and the course of history. European conquest of the Aztec

and Inca civilizations would likely not have been possible without the devastating effects of smallpox and other infections on the indigenous peoples.

Left: Mesoamericans with smallpox. Illustration from 16th century treatise by Farther Bernardino de Sahagun. Sarin images, the Granger collection. Right: Young girl with smallpox (James Hicks/ Centers for Disease Control and Prevention Public Health Image Library (PHIL).

Wars often involve large numbers of soldiers massing in the field. Bringing people together in close quarters increases the transmission of diseases. Much of the rapid spread of influenza during the great pandemic of 1918-1919 was associated with movements of troops and with soldiers being housed and transported in crowded conditions. Field latrines were often little more than a hole in the ground, which allowed the spread of bacteria, viruses, and protozoans from infected soldiers to their comrades. Once diarrheal diseases such as dysentery begin to spread, they can debilitate an army. It's hard to think about strategy and fighting when the foremost thing on your mind is cramping, diarrhea, and the search for the nearest latrine. During the American Civil War, twice as many soldiers died from infectious disease as from battle wounds.

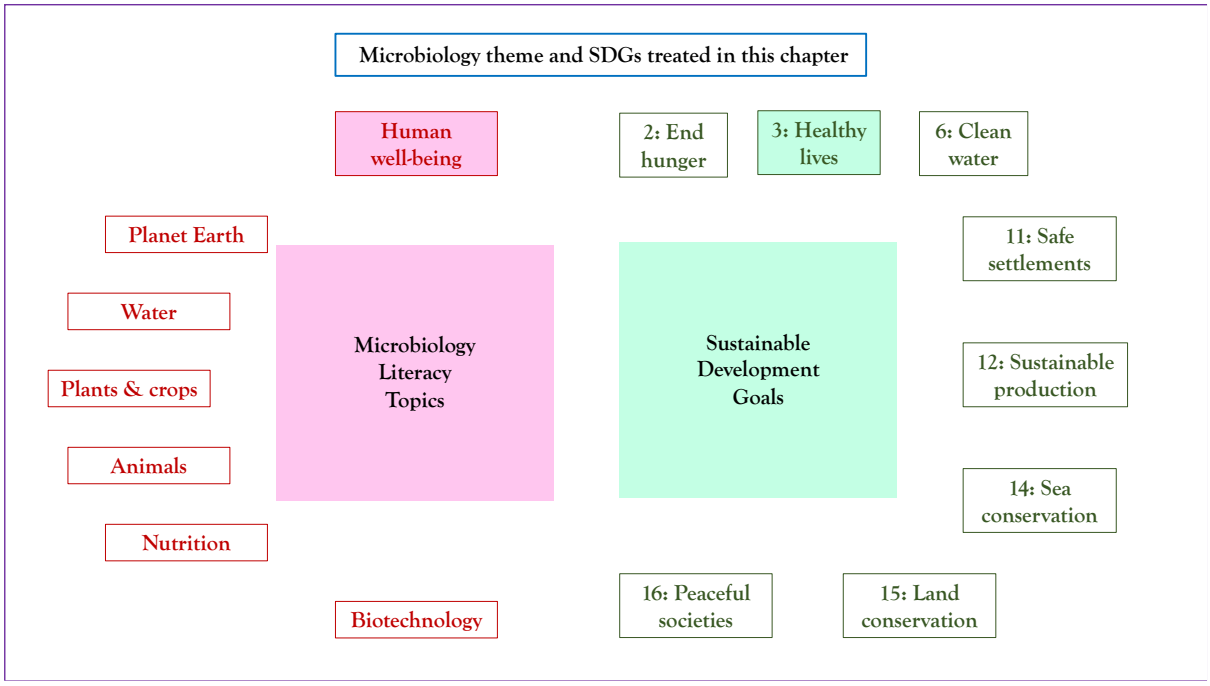
An example of the role played by microbes in war is the battle at El Alamein in North Egypt, which was considered a turning point of World War II. There, German soldiers commanded by Field Marshal Rommel were defeated by British troops under General Montgomery. Rommel is said to have blamed dysentery as much as Montgomery for the British victory. In his papers, he wrote: "Our defence works were shallow – the ground was too rocky to dig in far – with the result that the troops were forced to remain motionless all day, exposed defenceless to thousands of flies. Many men had dysentery and the conditions were frightful."

By the early 20th century, microbes, although still a major force, caused a smaller proportion of deaths. A significant factor in the reduction of mortality was improved sanitation. Military leaders, like public health officials, had begun to understand the link between poor sanitation and the spread of disease. Simply providing soldiers with clean water greatly reduced the incidence of dysentery, typhoid, and other intestinal infections, and the availability of vaccines and antibiotics by the middle of the 20th century further reduced the impact of microbes on wars. Yet, even today they still remain a substantial threat. Antibiotic resistant bacteria, and infections for which there are no vaccines, persist. Similarly, the amassing and movement of troops helps spread infections across political and geographic borders. Equally important is the affect that wars have on infectious diseases in civilian populations. The destruction of basic

infrastructure by bombing, for example, may mean a loss of clean water and sanitation for large numbers of civilians. Supply lines and access to vaccines and medications are disrupted in wartime, and soldiers coming from different areas may introduce epidemics, as occurred with influenza and smallpox. Civilians, as well as military personnel, are injured by bombs and bullets, and they face commensurate risks of infections.

The Microbiology and Societal Context

The microbiology: improving human health and well-being. *Sustainability issues*: healthy lives.



Infectious diseases and wars: the Microbiology

1. ***Diarrheal diseases***. Many of the infections that afflicted soldiers were the result of poor sanitation and lack of clean water. Intestinal infections, including dysentery, cholera, and typhoid, were common and, prior to the modern era of antibiotics, vaccines, and sanitary engineering, outbreaks of these infectious diseases often claimed as many lives as the opposition's weapons.

Dysentery, an invasive disease of the colon, results in fever, cramping, and bloody diarrhea. It can be caused by bacteria, especially *Shigella* species (bacillary dysentery), or by the amoeba *Entamoeba histolytica*. These pathogens are spread by ingestion of water or food that is contaminated with feces from an infected person – the so-called fecal-oral route of infection. *Shigella*, such as *Shigella dysenteriae* and *Shigella flexneri*, can be spread by fresh fruits or vegetables that have been washed with contaminated water, or by food that has been prepared by an infected person whose hands were not thoroughly cleaned. *Shigella* are especially problematic since so few of the bacteria can cause an infection. It has been estimated that as few as 10 - 100 of the bacteria can cause disease. Thus, it is easily spread from person to person by the Five Fs – food, fingers, feces, fomites (infected objects), and flies - when sanitation is poor. Amoebic dysentery does not spread quite as easily, but the amoebae can form cysts that allow it to persist in water for longer periods of time.

Cholera and typhoid fever were also common causes of war-related deaths in previous centuries. Cholera is associated with a massive loss of fluid, due to the production of a potent toxin by the *Vibrio cholerae* bacteria that cause the disease. The diarrhea is copious in severe cases; a person could lose a liter/quart of fluid per hour, and death can occur within hours. This bacterium is less infectious than the *Shigella* species, so even modest improvements in sanitation and access to clean water greatly reduced its threat. Typhoid, caused by *Salmonella typhi*, is also acquired by the fecal-oral route, but these bacteria are not restricted to the intestine. They can spread from the intestine to the bloodstream, resulting in fever, rash, and diarrhea. There are vaccines available for prevention of typhoid, and these have greatly decreased the incidence of the disease.

2. ***Respiratory infections***. Acute respiratory diseases can spread very rapidly and incapacitate a military unit. These often spread during transit, when large numbers of troops are crowded in ships, airplanes, or trucks that have poor ventilation, or in barracks where there is a high density of people. Unlike intestinal infections, which can be controlled by improved sanitation, respiratory infections are spread by coughing, sneezing, and even breathing.

Crowded troop ships such as this helped spread influenza virus. Image courtesy of the Naval History & Heritage Command.

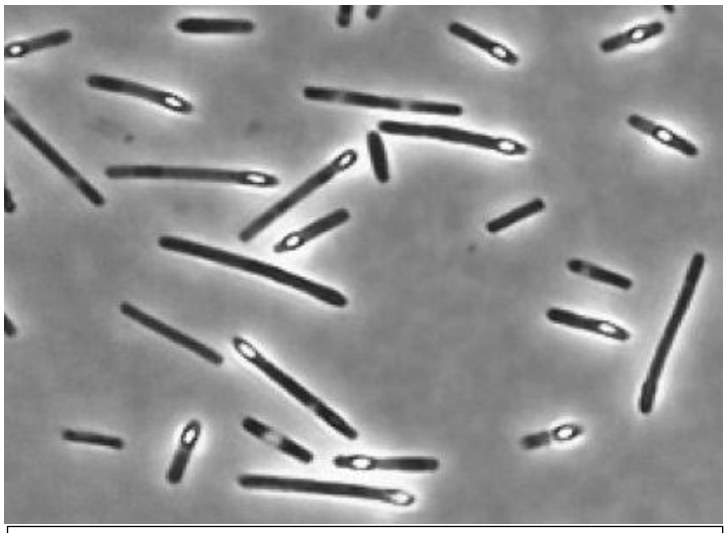
The influenza pandemic of 1918 – 1919 shows the effect of a respiratory infection in the military. The disease killed or incapacitated troops from all the countries fighting in the war,

and it has been estimated that 100,000 soldiers died from this particularly lethal strain of influenza. Of the US servicemen who died in WWI, almost half were killed by influenza. Early outbreaks of the flu occurred in military bases, such as Camp Funston in Kansas, and transfers of soldiers among military bases transferred the virus as well, with the infected soldiers spreading the virus within and between countries. Many of those infected developed pneumonia, and there were high mortality rates among healthy young adults, unlike most strains of influenza that cause milder infection in this age group. It is not clear whether influenza played a major factor in determining the outcome of WWI, but it is clear that the war promoted the spread of the infection throughout the world. More than 50 million people died from the disease worldwide, and life expectancy dropped by 10 years in the US. Infected troops carried the disease to civilian populations, and the loss of infrastructure and access to healthcare in areas of active fighting increased the number of deaths.

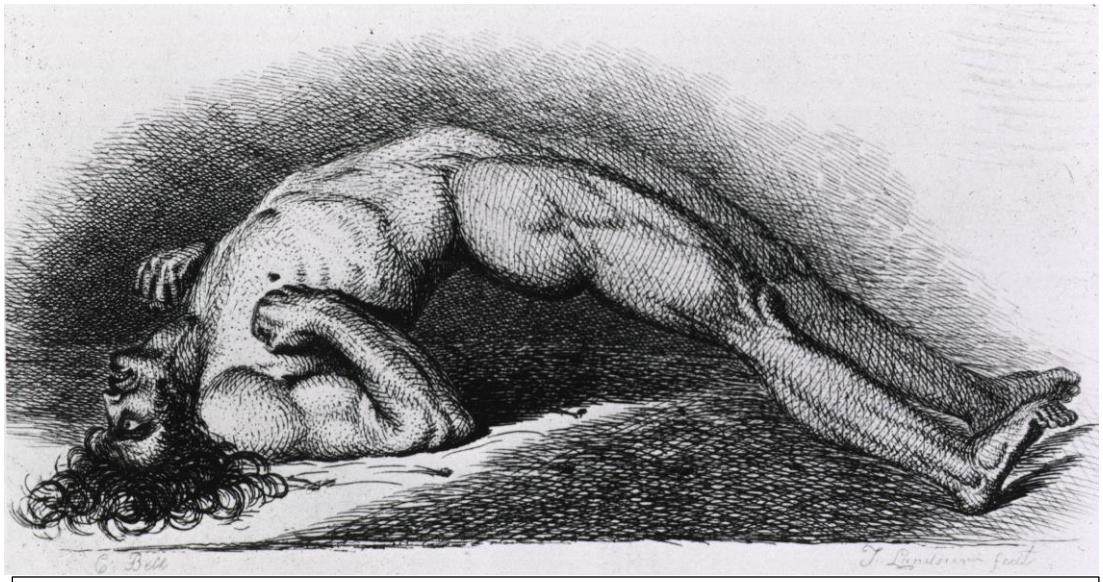
3. ***Wound infections***. Many wounds that occur during battles are contaminated by soil, water, or unclean hands, skin, or clothing. Without treatment, even relatively minor wounds can become infected and cause severe disease or death.

Joseph Lister was one of the first physicians to recognize the importance of disinfecting wounds, which he did by treating with carbolic acid. As he wrote in 1867, "... the first object must be the destruction of any septic germs which may have been introduced into the wound, either at the moment of the accident or during the time which has since elapsed."

Tetanus, caused by *Clostridium tetani*, and gas gangrene, caused by *Clostridium perfringens*, were notorious wartime infections in previous centuries. The Clostridia can form spores that persist in the soil for many years. When the spores contaminate a wound, the bacteria begin to grow and produce toxins that are extremely damaging or lethal. Tetanus toxin affects the nerves and blocks inhibitory signals. Normally, after nerves signal a muscle to contract, the contraction stops when no new activating signals are received and an inhibitory signal is produced. When tetanus toxin binds to neurons, the stop signal cannot be released, and the muscles continue to spastic paralysis, as depicted in this image below of a soldier with tetanus who cannot relax any of his muscles. The disease was sometimes called "lockjaw," since the jaw muscles would be tightly clenched. Tetanus is no longer a major problem, thanks to the development of the tetanus vaccine, which produces immunity to the toxin. This vaccine is used for everyone, not just soldiers, because the bacteria are common in soils and can contaminate even small wounds that occur when we are outdoors.



C. perfringens spores. Oregon State University.



Soldier with tetanus. Images from the History of Medicine collection, National Library of Medicine)

Gas gangrene was a particularly feared infection among soldiers. The C. *perfringens* bacteria grow in the damaged tissue within the wound and produce several different toxins. These toxins destroy the healthy tissue at the edges of the wound, allowing the bacteria to move deeper into the body and destroy more tissue. They produce gasses as a result of their metabolism, and these gas bubbles in the tissue give the disease its name. Treating the infection involves removing the damaged tissue and the healthy tissue at the edges that likely contains the bacteria. In severe cases, this may mean amputating the affected limb.

4. ***Other infections***. Other infections that afflict armies are associated with crowding and unsanitary conditions or with contact with environmental organisms. *Staphylococcus aureus*, which can be found on the skin and in the nose of healthy individuals, can gain access to wounds and cause severe infections. *Pseudomonas aeruginosa*, a common bacterium in nature, causes wound and burn infections. Fungi, such as *Candida* species, can infect wounds, and increased surveillance for these microbes showed that invasive fungal infections occurred in both soldiers and civilians during the more recent wars in the Middle East.

Diseases that are endemic in an area are associated with wartime infections, especially among solders who may have prolonged exposure to the natural environment. *Burkholderia pseudomallei*, an organism that is found in surface waters and mud in tropical areas such as Vietnam, was the cause of occasional infections in that country, and the disease (melliodosis) may be associated with prolonged exposure to waters of flooded rice fields. The bacteria can cause local infections, pneumonia, or disseminated disease with spread to various organs. Melliodosis has a high fatality rate, and both French and American troops acquired the disease during their prolongs wars in Vietnam.

Other examples of military infections by endemic pathogens include malaria, brucellosis, Q-fever, sandfly fever, and leishmaniasis, all of which were acquired by soldiers fighting in the Middle East. Trench fever, caused by *Bartonella quintana*, was very common among soldiers during WWI. The bacteria are spread by body lice, which live on clothing and feed on humans. The infection causes fever, weakness, and severe pain. Recovery may be prolonged and relapses are common. Body lice were a constant presence in the trenches of WWI given the lack of clean

clothes and clean bodies. Body lice were also responsible for the high rates of typhus (*Rickettsia prowazekii*) and relapsing fever (*Borrelia recurrentis*) during and immediately after the war.

Typhus is characterized by fever, muscle aches, and a characteristic rash that starts on the trunk and spread outward to the extremities. Typhus can be fatal, and there are often increases in the disease and deaths in civilian populations during wars. The disease was devastating in Russia during the winter of 1917-1918, where the combined effects of war, cold, and starvation allowed the lice to proliferate and spread. Similarly, relapsing fever caused millions of deaths in Russia and Eastern Europe at the end of the WWI.

Body lice feed on human blood. They live and lay their eggs on clothing or bedding. Image from Centers for Disease Control and Prevention Public Health Image Library (PHIL).

For bacterial infections, the widespread use of antibiotics in the 20th century saved many lives, while viral and fungal infections remain much harder to treat. However, the increase in bacterial resistance to many of the commonly used antibiotics has rendered the typical antibiotic therapy almost useless in treating certain infections. The emergence of methicillin-resistant *S. aureus* and multi-drug resistant *Enterococcus*, *Staphylococcus, Klebsiella pneumonia,* and *Escherichia coli*, among others, has reduced the arsenal of antibiotics that are effective against these bacteria.

Acinetobacter is another bacterial species with multi-drug resistance. *Acinetobacter baumannii* has been called a "superbug" because of its natural and acquired resistance to multiple antibiotics. These bacteria are found in nature and rarely cause infections in the community. However, during the Vietnam War, and particularly the war in Iraq, these bacteria were responsible for increasing numbers of wound and burn infections that could spread to the bloodstream and bones. These bacteria can contaminate the hospital environment, and their natural resistance to many disinfectants allows them to persist on surfaces in hospitals. This provides a reservoir of the organisms to infect hospital patients. Thus, some soldiers may acquire the infection in the hospital, as well as on the battlefield. The resistance of *Acinetobacter baumannii* to most typically used antibiotics make their infections difficult to treat and leads to high mortality rates. *A. baumannii's* persistence in hospitals allows it to spread to other patients, extending its reach beyond the soldiers injured in battle.

Relevance for Sustainable Development Goals and Grand Challenges

- **Goal 3. Healthy lives.** Despite improved diagnosis and treatment, infections will continue to be a significant cause of morbidity and mortality during wars and armed conflicts. Significantly, these factors will spill over into the civilian populations. Disruptions of physical and social structures and troop movements will promote the spread and severity of infectious microbes that are not restricted to the armed combatants.

Further reading

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Glossary

Dysentery – an intestinal infection characterized by bloody diarrhea fever, and cramping. It may be caused by bacterial (shigellosis) or amoeba (amoebic dysentery).
Endemic disease – a disease that is generally present in a particular location or population.
Epidemic disease – a large increase in cases of an infectious disease that occurs within a population or geographic area
Influenza – a viral infection in the respiratory tract. Influenza virus is spread by airborne respiratory droplets and infection causes fever, chills, and muscle aches. Severe cases can be fatal.
Fomites – inanimate objects or surfaces that can harbor infectious microbes.
MDR – multi-drug resistance
MRSA - Methicillin-resistant *Staphylococcus aureus*
Mortality – death
Morbidity – disease
Trench Fever – a bacterial infection spread by lice. Infection with *Bartonella quintana* causes fever, pain and weakness
Typhoid – A bacterial disease caused by *Salmonella typhi*. The infection, which causes diarrhea and fever, begins in the intestine, but the bacteria can spread throughout the body.
Typhus – A group of bacterial diseases transmitted by lice and other biting insects or arachnids. Typhus is characterized by fever, aches, and rash. Louse-borne typhus historically has been associated with high mortality rates during wars and famines.