People began to theorize about infections long before microbes were identified: As far back as the first century BC the Roman Marcus Terentius Varro wrote a book called ‘On Agriculture’ in which he warned against locating a homestead near swamps. Others also spoke of infections, for example, the Islamic physician Abu Ali ibn Sina (also known by his Roman name of Avicenna), wrote ‘The Canon of Medicine’ in 1020, in which he stated that ‘bodily secretion is contaminated by foul foreign earthly bodies before being infected’. He also hypothesized that tuberculosis (which did not have this name yet) might be an infectious disease. Even so, most people only accepted that microbes existed once they were seen with microscopes. Before that, a common assumption to a devastating infectious disease was: Is this the work of the devil?
Plagues of the past changed lives and shaped history

The Antonine Plague in 165–180 B.C. killed about one-third of the population and weakened the expansion of the Roman empire

The plague was either smallpox or measles. It led to a dramatic decrease in the population of Rome, weakening the army and slowing the expansion of the empire. We might all be speaking Latin today if Rome had not been weakened by this epidemic! It was brought back to the Roman Empire by troops returning from campaigns in the Near East, claimed the lives of two Roman emperors — Lucius Verus, and Marcus Aurelius Antoninus, and decimated the Roman army. It killed up to 2,000 people a day in Rome, one quarter of those infected. Total deaths have been estimated at five million, as much as one-third of the population in some areas. The Romans’ grip on the eastern territories was weakened when large numbers of troops succumbed to the disease. Entire towns and villages in the Italian peninsula and the European provinces were wiped out. The disease pushed north to reach the Rhine river in Germany, where it also infected Germanic and Gallic peoples outside the Empire’s borders. For a number of years, these northern groups had been moving southwards in search of more land to sustain their growing populations. With their numbers severely reduced by the epidemic, the Roman armies were now unable to push the tribes back. The plague caused drastic effects throughout the Roman Empire, including literature and art. The ancient world never recovered.

One of the deadliest plagues: The Black Death killed 30–60% of Europe’s population

One of the deadliest pandemics the world had ever experienced was the Black Death. This bubonic plague outbreak started in Central Asia and reached Crimea in 1346. The Black Death is estimated to have killed 30% to 60% of Europe’s population, reducing the world’s population from an estimated 450 million to between 350 and 375 million in 1400. The Black Death returned every generation with varying virulence and mortalities until the 1700s. During this period, more
LESSON READINGS

than 100 plague epidemics swept across Europe. People knew that the Black Death was transmitted by rats, but they couldn’t do anything about it because they didn’t understand that rats weren’t the actual cause or infectious agent. The disease is actually caused by a bacterium (*Yersinia pestis*) that infects the fleas that the rats carry.

In fact, the common belief at the time was that the plague was spread by birds. Birds’ beak-shaped face-masks, like the one you see to the right, were worn by Plague Doctors during the Black Death, and acted like a primitive gas mask. The beak usually contained strongly aromatic herbs and spices to combat the terrible stench of unburied corpses and fluids from ill plague patients. It was also thought that the mask would draw the disease away from the sufferer. Along the same lines the red glass eye pieces were thought to help protect the plague doctor from evil influences.

Plagues in the Americas played an important role in overthrowing the Native Americans

Have you ever wondered how the Native Americans were overthrown by settlers that were far from home? Yes, technologies like guns certainly helped, but so did sickness and death of native populations from infectious diseases. Before the Europeans arrived, the Americas had been largely isolated from the infectious disease epidemics that spread throughout Europe. The first large-scale contacts between Europeans and native people of the American continents brought overwhelming pandemics of measles and smallpox, as well as other Eurasian diseases. These diseases from Europe spread rapidly among native peoples and led to a drastic drop in population, and the collapse of indigenous American cultures. It is important to note that diseases were passed in both directions. Syphilis was carried back from the Americas and swept through the European population, decimating large numbers there. Both are examples of how populations that haven’t encountered a ‘foreign’ infectious disease may be particularly susceptible to it at first.
LESSON READINGS

Plagues were used as agents of biological warfare

The British are thought to have used smallpox as a bioterrorism agent by giving smallpox infected blankets to the indigenous population. On at least one occasion a high-ranking European considered infecting the Indians with smallpox as a tactic of war. Lord Jeffrey Amherst, commander of British forces in North America during the French and Indian War (1756–’63) discussed sending infected blankets to hostile tribes.

According to historian Francis Parkman, Amherst first raised the possibility of giving the Indians infected blankets in this letter to Colonel Henry Bouquet, who would lead reinforcements to Fort Pitt. We don’t know the full extent to which the plan was put into effect. We do know that a supply of smallpox-infected blankets was available, since the disease had broken out at Fort Pitt some weeks previously. We also know that the following spring smallpox was reported among the Indians in the vicinity. The smallpox epidemic between 1775 and 1782 killed more than 130,000 people across North America.

Tens of thousands of people died throughout Mexico from smallpox beginning in 1779. Smallpox then swept through the Pueblos of New Mexico beginning in 1780. It caused loss of Aztec and Inca populations and death of military and social leaders, contributing to the downfall of both empires and the ultimate conquest of the American people by the Europeans.

DEFINITIONS OF TERMS

Biological warfare — the use of toxins produced by living organisms or whole organisms themselves, usually microbes, as weapons.

Inoculate — to introduce a microbe into a suitable situation for growth, such as into a human host.

For a complete list of defined terms, see the Glossary.

Figure 4: Lord Jeffrey Amherst

Figure 5: Colonel Henry Bouquet’s letter to Lord Jeffrey Amherst, Commander of British Forces July 13th 1763:

“P.S. I will try to inoculate the Indians by means of blankets that may fall in their hands, taking care however not to get the disease myself. As it is pity to oppose good men against them, I wish we could make use of the Spanish’s Method, and hunt them with English Dogs. Supported by Rangers, and some Light Horse, who would I think effectively extirpate or remove that Vermine.”
LESSON READINGS

Plagues still impact our lives and shape history

Now we will turn our attention to infectious diseases that greatly impact societies today. Keep in mind that even with modern medicine and infrastructures like clean water and toilets it is hard to control many pathogens. And areas with endemic infectious diseases are often crippled by the burden of illness.

HIV causes crippling morbidity and mortality

One of the largest modern pandemic is due to HIV (human immunodeficiency virus). Over 30 million people worldwide are living with HIV/AIDS (acquired immune deficiency syndrome). The number of AIDS cases in the United States and Europe rose steadily through the mid-1990s and then plateaued as a result of increasingly effective efforts at prevention and drug treatments. In the developing world the disease has continued to spread. Africa has just over 12% of the world’s population but more than 60% of the AIDS cases worldwide.

From its discovery in 1981 to 2006, AIDS has killed more than 25 million people. AIDS is caused by HIV, which is a retrovirus. In 2012 about 35 million people worldwide were infected with HIV or about 0.5% of the world’s population. About 3.4 million of these people were children under the age of 15. During the same year, an estimated 2.3 million people were newly infected and AIDS claimed an estimated 1.6 million lives, down from a global peak of 2.3 million in 2005. The disproportionate number of AIDS deaths occurring in Sub-Saharan Africa retards economic growth and exacerbates the burden of poverty. A 2010 study estimated that the region had 68% of all new HIV infections worldwide and 66% of all HIV related deaths. The WHO considers HIV infection to be a global pandemic.

DEFINITIONS OF TERMS

Endemic — prevalent in a given geographical area.

WHO — World Health Organization is an agency of the United Nations which oversees international public health issues.

Retrovirus — a virus that incorporates its genome into the host cell's DNA.

For a complete list of defined terms, see the Glossary.

3. The following is true about Acquired Immune Deficiency Syndrome (AIDS) EXCEPT
   a. it is caused by the Human Immunodeficiency Virus (HIV), a retrovirus
   b. it is caused by helper T cells
   c. it is endemic to Sub-Saharan Africa
   d. over 30 million people worldwide are living with the disease

Figure 6: Statistics on HIV prevalence worldwide (2013).
Infection with HIV causes the immune system to progressively fail. Once this virus has been transmitted via infected body fluids such as semen or blood, it infects vital immune system cells such as helper T cells that normally protect the body against infection. HIV infection either kills the T cells directly, or targets them to be killed by other immune system cells that are surveying the body to eliminate infections. When T cell numbers decline below a critical level, they cannot protect the body against other pathogenic infections or cancers. This stage of HIV infection is called AIDS.

Prevention and management

Most people infected with HIV who are not treated, eventually develop AIDS. They mostly die from infections or cancers that result from failure of the immune system. HIV progresses to AIDS at a variable rate that is affected by viral, host, and environmental factors. Most untreated HIV infections progress to AIDS within 10 years, but some will progress much sooner, and some will take much longer. Treatment with antiretroviral drugs increases the life expectancy of people infected with HIV, and reduces both the mortality and the morbidity of HIV infection. The average life expectancy of someone with AIDS who receives antiretroviral therapy soon after AIDS diagnosis is about 10–40 years. Without antiretroviral therapy, someone who has AIDS typically dies within a year.

Although antiretroviral medication is still not available everywhere and does not actually cure the disease, expanded treatment programs have helped to turn the tide of new infections and AIDS deaths in many parts of the world. Intensified awareness, and adopting global preventive measures such as protected sex and non-reuse of needles, have also played a role. Nevertheless, complacency about HIV continues to contribute to risk for sexual transmission.

Tuberculosis infects about one-third of the worlds population

Tuberculosis (TB) is another common, and in many cases lethal, infectious disease caused by the tubercle bacillus M. tuberculosis. Tuberculosis usually attacks the lungs but can also affect other parts of the body. It is spread through the air when people who have an active infection cough, sneeze, or otherwise transmit their saliva through the air. Most infections in humans result in an asymptomatic, latent infection, and in about one in ten people with latent infection it eventually progresses to active disease, which, if left untreated, kills more than 50% of its victims. The classic symptoms are a chronic
cough with blood-tinged sputum, fever, night sweat, and weight loss (the last giving rise to the formerly prevalent colloquial term "consumption").

Roughly a third of the world's population has been infected with *M. tuberculosis*, and new infections occur at a rate of one per second. In 2013, an estimated 9 million people developed TB disease, and 1.5 million died from it; the annual incidence rate varied from about 300 per 100,000 in Africa to about 30 per 100,000 in the Americas. Across the globe, 22 countries have an annual incidence rate around 100 cases per 100,000 or more, and are considered high-burden countries. Tuberculosis is the world's greatest infectious killer of women of reproductive age and the leading cause of death among people with HIV/AIDS.

**Malaria is arguably the highest impact infectious disease of our times**

Malaria is a mosquito-borne infectious disease caused by the parasitic protozoan *Plasmodium* discovered in 1880 by Charles Louis Alphonse Laveran. While working in the military hospital in Constantine, Algeria, he observed the parasites in a blood smear taken from a patient who had just died of malaria. The disease results when the malaria parasites multiply within red blood cells causing them to burst. The classic symptom of malaria is a cycle in which sudden chills are followed by fever and sweating lasting four to six hours. The cycle repeats every two to three days as new red blood cells mature, become infected and then burst.

Malaria is widespread in tropical and subtropical regions, including much of Sub-Saharan Africa, Asia, and the Americas. It is prevalent in these regions because the high rainfall and

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**Definitions of Terms**

- **Sputum** — mucus coughed up from the lower airways.

For a complete list of defined terms, see the Glossary.

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**Workbook**

**Lesson 1.2**

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4. **Tuberculosis (TB)**
   a. It caused by the tubercle bacillus *M. tuberculosis*.
   b. Can be transmitted through coughing or sneezing.
   c. Causes symptoms that include blood-tinged sputum, fever, night sweats, and weight loss.
   d. Infects about a third of the world's population.
   e. All of the above
**LESSON READINGS**

consistent high temperatures along with stagnant waters in which their larvae mature provide mosquitoes with the environment needed for continuous breeding.

In 2013, around 198 million cases of malaria occurred globally, killing around 584,000 people according to the WHO’s 2014 World Malaria Report. Malaria is commonly associated with poverty and can indeed be a cause of poverty and a major hindrance to economic development. Ninety percent of malaria-related deaths occur in Sub-Saharan Africa, and 78% of these deaths account to children under the age of 5.

Malaria transmission can be reduced by preventing mosquito bites. Prevention can occur by using inexpensive (~$5) mosquito nets and insect repellents, or by mosquito-control measures such as spraying insecticide inside houses and draining standing water where mosquitoes lay their eggs. Malaria can be treated with multiple drugs, but the malaria protozoa have developed resistance to many of the historically effective antimalarials, most notably **Quinine**, which was the most effective and popular drug for many years. We will learn more about malaria in Lesson 3.2.

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**DEFINITIONS OF TERMS**

**Quinine** — an antimalarial drug derived from the Cinchona tree. It is usually taken orally, but if the patient is very sick, it is administered intravenously.

For a complete list of defined terms, see the **Glossary**.

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5. Malaria disease is a result of
   a. chills, fever, and sweating
   b. **Quinine**
   c. malaria parasites that multiply within red blood cells
   d. any mosquito bite

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*Figure 10: Malaria is transmitted by the Anopheles mosquito.*
List 4–5 behaviors we have developed to avoid infectious disease transmission and explain what they are for.

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Practice Calculation: Percent Error
When scientists are trying to find out how close their calculation is from the ideal, they calculate the percent error.

\[
\text{Percent Error} = \frac{(\text{Actual} - \text{Estimate})}{\text{Actual}} \times 100\%
\]

For example: If I guess that there are 350 jelly beans in a jar, and there are actually 379, what is my percent error?

Answer: \((379 - 350) \times \frac{100}{379} = 7.65\%\)

This means that this guess was 7.65% inaccurate.

What is the percent error if you guess that there are 466 jelly beans in the jar, and there are actually 379?
<table>
<thead>
<tr>
<th>TERM</th>
<th>DEFINITION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiretroviral drugs</td>
<td>Drugs that stop a retrovirus from multiplying.</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>Without symptoms.</td>
</tr>
<tr>
<td>Biological warfare</td>
<td>Use of toxins produced by living organisms or whole organisms themselves, usually microbes, as weapons.</td>
</tr>
<tr>
<td>Bubonic plague</td>
<td>A severe systemic infection caused by the bacterium <em>Yersinia pestis</em>.</td>
</tr>
<tr>
<td>Crimea</td>
<td>A peninsula to the south of Ukraine in the Black Sea.</td>
</tr>
<tr>
<td>Endemic</td>
<td>Prevalent in a given geographical area.</td>
</tr>
<tr>
<td>Helper T cell</td>
<td>A type of immune cell that calls other immune cells to come and fight an infection.</td>
</tr>
<tr>
<td>Inoculate</td>
<td>To introduce a microbe into a suitable situation for growth, such as into a human host.</td>
</tr>
<tr>
<td>Latent</td>
<td>Dormant or inactive disease, and in this case non-dividing bacteria.</td>
</tr>
<tr>
<td>Morbidity</td>
<td>Illness, loss of function and disability</td>
</tr>
<tr>
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<td>Mucus coughed up from the lower airways.</td>
</tr>
<tr>
<td>Tuberculin skin test</td>
<td>A test for whether a person has been exposed to the tuberculosis bacterium.</td>
</tr>
<tr>
<td>Virulence</td>
<td>A pathogen's ability to infect and cause sickness.</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization is an agency of the United Nations which oversees international public health issues.</td>
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</tbody>
</table>