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Microbes as a Driving Force of Change

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Background Environment

Our high school is somewhat atypical of an urban high school. We have recently celebrated 100 years as a high school and the 40th anniversary of voluntary integration. We are part magnet school and part neighborhood school. That means any student living within the traditional borders of the school is allowed to attend the school unless they have a history of extreme behavioral issues. These students do, indeed, take a placement exam, but it is only for the purpose of finding the correct course fit and not used for admittance. The other students come from across the rest of the school district and face a rigorous application process. For us, that means that we are probably the most racially, ethnically, religiously, and socio-economically diverse high school in the district. We are also one of only two high schools in the state with an International Baccalaureate Program. Fifty-four percent of our students are on the free or reduced lunch program and many are in remedial math and reading programs.

We are also a Middle Years Program (MYP) school. The Middle Years Program is part of the International Baccalaureate Program (IB). The IB program fosters cultural awareness and the focus is to develop students who are critical and reflective thinkers. The program also strives to help students make real-world connections to what it is they are learning. Assessments are used to discover the depth of knowledge and the methods are very holistic. Most of the school's general education students do not complete the IB program; however, our curricula are geared towards making sure all students are educated in this manner throughout the school. All 9th and 10th grade science classes are taught with the MYP standards in mind so that students entering into the more advanced science classes have an idea of the rigor that awaits them.

Whom the Unit Serves

The largest part of this unit will be directed towards AP Biology students divided up into two classes. These two classes contain two types of students. The first type includes the traditional AP students at our school. They are interested in increased rigor in order to be prepared for college and want a more expansive knowledge base in the biological sciences than what they received in 9th grade biology. They plan on meeting

all the course requirements and have the goal of passing the AP Exam with an above average score. However, these students do not want to IB in biology. The second type of student is only modestly interested in some increase in rigor. These students are there because they are attempting to avoid having to take physics and all the mathematics that is involved. They can successfully accomplish that goal by taking an AP science course instead. We do require students to take the AP Biology Exam if they are enrolled in the course. However, many do not perform to standards expected in an AP class. On the upside, some of these less traditional AP students do actually discover a love of biology and a curiosity that was previously left unpiqued. These students are then challenged in a biology class that covers much more information than in their 9th grade biology and it does give these students an exposure to increased rigor that they might not have received otherwise. This increase in rigor exposes them to at least the level they could expect at the community college level.

Rationale

After completing this unit, students will be able to demonstrate the ability to present the life of a microbe in detail and trace the effects that microbe has on a particular population. There is a gap in the AP curriculum regarding the types of microbes that exist and their effects on our lives. This will be a relatively short unit for the students as the AP curriculum is rather inclusive of all life sciences and the time spent on topics seems to always be too short. I anticipate spending no more than five to seven days on this unit. This unit will be after students have learned about the various aspects of viruses and bacteria. Relatively early on in the school year, the students will learn about DNA replication, transcription, translation, and the refining of the final protein. Sometime later they explore evolution and the differences between viruses, archeabacteria, bacteria, and protists. Students will also already have learned about the life cycles of viruses, bacteria, and fungi. Included in this instruction are bacterial transformation and conjugation, viral replication, and the life cycle of fungi.

This unit aims to look at the big picture of how species interact with one another. The topics of various microbes, the history of their interactions with other species, the lasting effects of those interactions, and the various responses of the affected species are normally taught as stand-alone units. They may not even be taught in the same type of class. For example, a truly detailed history of the effects of smallpox on indigenous peoples may or may not be taught in a history class and is not included in the AP Biology curriculum. Microbes are often handled as separate entities and dealt with as if they live in a vacuum. That not being the case, this unit seeks to address the fact that interactions between microbes and other species are often quite complex and can have lasting effects. Exposure to this level of complexity will be beneficial to the students when working with other, more commonly known, complex ecosystems.

Background Information

Bubonic Plague

Bubonic plague is a potentially fatal bacterial infection caused by *Yersinia pestis*. Further description of *Y. pestis* is provided below. There have been several outbreaks of bubonic plague throughout history with the first outbreak in Europe possibly lasting for roughly 200 years. There was then a 600 year break from the plague before it returned as the Black Death. [1] There have been three great pandemics of bubonic plague in the past 2,000 years. [2] The first, the Justinian plague, named after the Emperor Justinian, occurred in 542 and struck Constantinople with a vengeance. It killed 10,000 people per day at its height and held the city of Constantinople in its suffocating grip for a full year. Emperor Constantine was unable to keep the newly united Western and Eastern Empires intact. The loss of over 100 million people to the plague left no one to carry out the essential tasks of a large empire. [3] Between the years 541-700, an estimated 50-60% of the population of the affected area was eliminated. [4] The second outbreak, the Black Death, is the one we will focus on in this unit. The third began in China in the 1860s and we are still dealing with a less virulent form today. [5]

The Second Outbreak OR the Black Death

There are two ideas as to why the second pandemic of bubonic plague was referred to as the Black Death. One idea set forth is that it was named for the gangrene that set in before people died. On the other hand, it could also be a mistranslation of *atra mors*. The Latin word, *atra*, can either mean "terrible" or "black". Regardless of the reason the bubonic plague came to be known as the Black Death, it was indeed terrible and enshrouded Europe in darkness. This second great outbreak seems to have started with the siege on Kaffa, a Genoese city located on the Black Sea, by the Mongols in 1347. The Mongolian army began to succumb to a terrible illness and was forced to give up the siege and leave the area. As the story goes, before they left their encampment outside the city wall, they catapulted the bodies of the infected soldiers into the city. The Italian inhabitants left for home and twelve galleys set sail for the Sicilian island, to the city of Messina. These ships were carrying the Black Death. [6] The following is a first hand account of a Franciscan friar, Michael of Piazza:

> The "burn blisters" appeared, and boils developed in different parts of the body: in the sexual organs, in others on the thighs, or on the arm, and in others on the neck. At first these were of the size of a hazelnut and the patient was seized by violent shivering fits, which soon rendered him so weak that he could no longer stand upright, but was forced to lie on his bed, consumed by a violent fever and overcome by great tribulation. Soon the boils grew to the size of a walnut, then to that of a hen's egg or a goose's egg, and they were exceedingly painful, and irritated the body, causing it to vomit blood by vitiating the juices. The blood rose from the affected lungs to the throat, producing a putrefying and ultimately decomposing effect on the whole body. The sickness lasted three days, and on the fourth, at the latest, the patient succumbed. [7]

The terrified people in Messina fled to Genoa and Venice. Soon after, it was traveling along the trade routes of the day. Once in a city or village, it generally lasted eight months until the unlucky ones died a horrific death or those that were going to be fortunate enough to survive, recovered. The Black Death reached Spain, France, and the Mediterranean Islands in 1347-48 and was in Britain by the summer of 1348. By the end of that year, 20,000-30,000 of the 60,000-70,000 inhabitants of London were dead. [8] The plague was so devastating to Europe at that time because it hadn't been in Europe for over 1,000 years. People who have

been exposed to the plague and recover gain resistance, and therefore do not become sick again when the plague returns. Since no one had been exposed in recent years, no one had any immunity to the disease. This second great outbreak of bubonic plague had finally run its course by 1353. It continued to ebb and flow over Europe for the next 300 years. Even though the mode of transmission at this time was unknown, preventative measures to stop the spread of the disease began to develop. For example, a 40-day quarantine, "quaranta giorni", was introduced in Italy and later widely practiced throughout Europe. [9] By the time the plague dissipated in 1352, it had killed 20 million people in Europe and the Middle East, reducing the population to 80 million. [10]

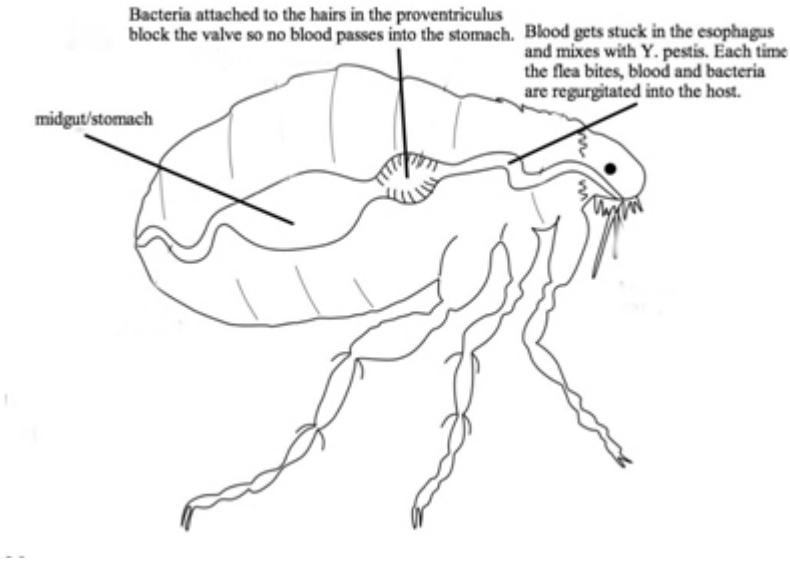
Yersinia pestis

Yersinia pestis, the bubonic plague causing bacteria, is a Gram negative, nonmotile, oval-shaped bacteria. It is a coccobacillus, meaning that it has a shape somewhere between that of a sperical form, coccus, and a rod-shaped form, bacillus. [11] Of the 11 members of the genus *Yersinia*, only three are pathogenic, disease causing, in humans. *Yersinia pestis* is the one of concern here and it establishes itself in the blood and lymphoid tissues and has evolved to be capable of being transmitted by arthropods and in the case of the Black Death, most commonly by fleas. [12]*Y. pestis* has two unique plasmids, pFra and pPla, that contain genes allowing it to not only infect mammalian hosts but also to spread between them. These genes also allow *Y. pestis* to use fleas as a vector. These differing genes get expressed based on the differing internal environments of their hosts, 98.6Ãš F in mammals and 82.4Ãš F or lower in fleas. Other genes located on these plasmids allow the bacteria to hide out from the host's immune system while it prepares for its all-out assault. [13]

Method of Transmission

Different species of fleas show different methods of transmission in different mammals. However, the method discussed for this unit is common in the Oriental rat flea, *Xenopsylla cheopsis*. [14] It is thought that the black rat, *Rattus rattus*, has the unlucky distinction of being the vector for *X. cheopsis* during the Black Death. It is, as rats go, not very hardy. Its original homeland was in the Himalayan foothills but populations were well-established in warmer areas, such as North Africa, by the beginning of the Christian era. From there, they were able to hitch rides all along the various trade routes. They spread rapidly throughout Europe and were

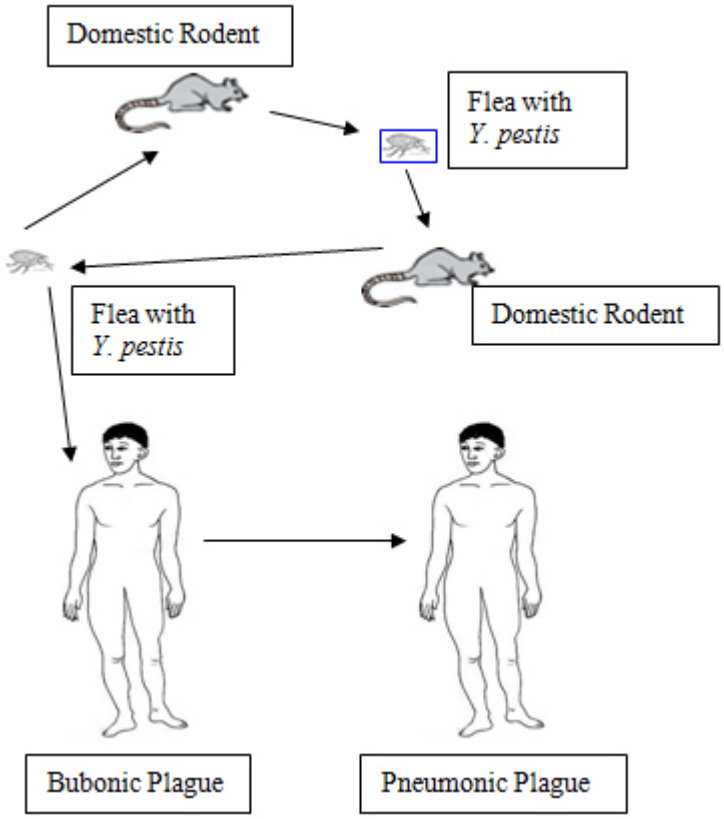
able to establish themselves by living closely with humans, infesting barns, graneries, and thatched roofs. When *Y. pestis* moves through a colony of rats, the rats die rather quickly. Once the colony is exhausted, the fleas are then able to jump to humans. *X. cheopis* has a valve to its stomach that allows its stomach to become distended with blood after feeding without regurgitating the next time it feeds. This allows the flea to keep biting and feeding even though its stomach is "full". In a flea that has ingested *Y. pestis*, the bacteria multiply rapidly and form a ball of blood and bacteria that render the valve ineffective. The next time the flea feeds, the blood is unable to pass into the stomach and remains in the esophagus. There it mixes with bacteria and the next time the flea attempts to feed, the blood and bacteria mixture are regurgitated into the next victim. The still hungry flea then bites another victim and more blood and bacteria enter that victim. This keeps happening until the by now very frustrated flea starves to death. Even if the fleas are on rats on quarantined ships and all the rats die, the fleas can survive rather long periods of time if conditions are cool and damp. [15]



Infection Cycle

Once *Y. pestis* bacteria are introduced into the skin of its new, human host, they make their way to local lymph nodes. Here the inflammatory response, the swelling of the lymph nodes producing the characteristic buboes, can delay the spread and rapid increase in the number of *Y. pestis*; however, it generally doesn't completely block the disease. The spread of *Y. pestis* from the site of the bite is facilitated by Pla protease, a virulence factor, which breaks down the components of blood clots that would normally help trap the bacteria at the site. Then another protein, F1 protein, prevents phagocytosis of *Y. pestis* by white blood cells as the bacteria initially spread through host tissues. The bacteria are able to spread swiftly to invade visceral organs, such as the liver and spleen. Once there, the host's immune system is further blocked by yet more virulence factors. Several of these virulence factors prevent the host's immune system from launching an all out attack. *Y. pestis* uses a needlelike appendage to target and inject proteins into the host's white blood cells. The immune functions that would normally trigger an inflammatory response to help block the spread of the bacteria are destroyed by these proteins. Furthermore, another injected protein, V protein, prevents the host from producing the proteins necessary to trigger the formation of a mass of immune cells that would normally surround the bacteria and inhibit its growth. In this way, *Y. pestis* is able to quickly overrun visceral organs even though the host cells believe that tissue damage is totally under control. [16] Bleeding into the organs causes the skin hemorrhages commonly seen in the Black Death. This type of death lasts four to five days;

however, if a flea bites a tiny blood vessel, death occurs within hours. Sometimes *Y. pestis* gets into the lungs and causes the victim to cough up bloody sputum teeming with bacteria. *Y. pestis* is easily transmitted via airborne droplets. Those unlucky enough to inhale the bacteria in these aerosols come down with primary pneumonic plague, which is universally fatal. [17]



Current Plague Control

Attempts at plague control involve testing die-offs and wild populations that commonly harbor the bacteria, such as rats and prairie dogs, for *Y. pestis*. If the bacteria are found, the public is notified so that caution is used in the area. Treating rodent burrows to kill fleas and trying to limit the desire of rodents to be in residential areas are two common ways to combat the spread of the plague. Ridding the world of the plague is not an obtainable goal because of the continuous outbreaks in animals other than humans. Infection can even be transmitted from house pets that have been in contact with humans. Humans, especially veterinarians, have experienced an increase in pneumatic plague due to exposure to infected cats. [18]

Diagnosis, Treatment, and Vaccination

Diagnosis of plague hasn't changed since its discovery. Physicians Gram stain and culture sputum or bubo aspirates. *Y. pestis* can be grown on blood agar and MacConkey agar in the lab. Human disease is rare, but airline passengers who have been to a known plague region and are feverish should be placed in isolation. A plague-infected person's condition can deteriorate quickly. If left untreated, death can occur in three to five days and the overall mortality rate for untreated plague is still more than 50%. Antibiotics readily available for treating the plague include streptomycin, gentamycin, sulfonamide, and tetracycline, and tetracycline and chloramphenicol can even be used prophylactically. Fortunately, there have been no reports of antibiotic resistance. The first vaccine for bubonic plague was developed by Waldemar Haffkine in 1897 in Bombay

using dead bacilli. There are now two types of vaccines used in humans. One is a live vaccine that has been used in the former Soviet Union since 1939 and one is a formaldehyde-killed whole-cell vaccine. The latter vaccine was first used in 1942. There is a new vaccine under development which uses the F1 and V bacterial capsular antigens. [19]

With Bubonic Plague Comes Change

Even though the Black Death was the worst plague outbreak in Europe, the waves of the plague continued to sweep through. Every two to five years from 1361-1480 there was another outbreak in England. The following is a list of cities, dates, and populations lost:

Milan, 1630, half the population lost; Genoa, 1656-1657, 60% lost; Marseilles, 1720, 30% lost; London, 1665, 16% lost (70,000 lost). [20]

Some of the most heinous atrocities occurred during the successive waves of plague that ravaged Europe. Lepers, beggars, prostitutes, and Jews were all blamed for the plague. In some Muslim countries, the Christians were blamed. Both Christians and Muslims almost always blamed the Jews. In Strasbourg, February 14, 1349, 900 Jews were rounded up and burned on the grounds of the Jewish cemetery. This was fully half the total population of the community. All Jews in Freiborg were placed in a wooden building and burned to death. [21] The wholesale slaughter of Jews in Frankfurt and Brussels occurred in 1349. Between the Black Death itself and the just as virulent anti-Semitism, the Jewish communities in many parts of Europe were eradicated. [22]

As one can well imagine, in cities where more than 500 people were dying every day, many lost faith in the clergy. Papal authority declined and the Roman Catholic Church blamed the sinners and suggested that Judgment Day had arrived. God didn't even spare his servants and priests, as those who gave last rites had a very high mortality. Fear led to a greater interest in other religions, including in the cults of healer saints. The saints were familiar with suffering and could also provide comfort and healing. People bypassed God and went directly to the saints. The stage was set for questioning church authority and the divisive debates over the nature of religion had begun. [23]

As the disease swept through Europe, the holders of the chairs of some of the great universities died. These scholars were generally older and were academics who never really practiced medicine. They were followers of Galen, who believed that diseases were caused by an imbalance of the four humors: blood, phlegm, black bile, and yellow bile. After the old guard died, the newer appointees began moving into more clinical areas, such as anatomy. Barbers, with their ability for bloodletting and skilled surgery, gained new prestige. A new importance on health and disease started to replace the old thinking and ever so slowly, the practice of medicine began to change. [24]

As the plague indiscriminately felled its victims, the number of educated individuals decreased as did the number of students. By the end of the plague, Europe had lost five of its 30 universities. With the restrictions placed on travel, students couldn't enroll in distant universities; therefore, local universities were established. It was no longer necessary to travel to Paris or Bologna as new universities popped up in cities such as Vienna, Prague, and Heidelberg. This led to curriculum reform as the dominance of old centers of learning diminished. Because the universities were now local, instruction was in the local language. [25]

The Black Death eventually led to the ending of the Hundred Years War as France and England had to quit fighting. Even without the loss of life due to battle, the plague decimated the ranks and left no able-bodied

men to fight. Soldiers began getting paid more to remain in service, and without enough men to fight, more efficient ways of killing and causing destruction were developed. [26]

By the time the Black Death swept through Europe the feudal system had already begun to change. The switch to monetary compensation for serfs' manual labor happened before *Y. pestis* became part of the landscape. However, with the continuing loss of laborers, landlords were forced to allow their stewards to start recruiting and paying peasants from other farms and even landless city-dwellers to work the land. The landlords were then not making as much profit and so they kept acquiring more and more land to work to make up the difference. This led to less labor-intensive farming practices. The mould board plough was developed at this time and much of the farmland was converted to pastureland. This led to entire swaths of land being left to the sheep. Mills once used for grinding grains such as wheat and barley were converted to spinning cloth, operating large bellows for fanning furnaces, and sawing lumber. Tenant farmers raising sheep became more prosperous than they'd ever been and more powerful than any sheep farmers before then. These people eventually became the great wool barons of the time. The barons and landlords were forced to treat their tenants better and pay them more. If they didn't, the competition for laborers was high and the laborers could easily find a better landlord. The reduced workforce in the now sparsely populated cities also started receiving higher wages and as a consequence, the standard of living also improved in the cities. Besides there being a reduced population in the cities, wealthy landlords were able to pay even higher wages and convinced many city dwellers to move to the country to work their fields. Now, for the first time, people were mobile. They were no longer tied for their entire lives to working one plot of land. As wages increased, governments sought to control the higher wages and increase taxes. This led to creative thinking on the part of the workers. Cheap lands and other capital were substituted for higher pay. Landlords now had to provide the oxen and seeds before the peasants would agree to a lease. Higher wages and a higher standard of living led to major changes in the social and economic structure. In fact, by the 16 th century, landlords and serfs ceased to exist in England. [27]

The substitution of capital for wages was also occurring in the cities. For example, employers might have to provide tools and machines needed for a particular job. Higher wages led to new innovations such as the printing press with movable metal type invented by Johann Gutenberg in 1453. This was necessary because of the lack of good quality scribes needed to copy sheets of manuscripts. In the rush to train new scribes to take the place of the dead ones, the quality of the work kept declining as the emerging population was growing. This rebounding population was increasingly more literate, as well. [28]

The last big change caused by the Black Death necessary for this unit is the change to large sea- and ocean-going transport ships. Smaller crews could remain at sea for more extended periods of time and sail directly from port to port on much larger vessels. This required the development of more useful navigational instruments, superior ship building and of course, the development of insurance to protect investments in ships and the cargo. Merchants, bankers, and craftsmen all become more powerful and used their new capital to fund new technological advances. The economy became more diversified and there was a greater redistribution of wealth. The old aristocracy was finding it necessary to yield some of their power to the people. [29]

Smallpox

Smallpox. Just the word elicits fear. Even though it is not something we normally worry about, the thought that smallpox could escape one of the labs, in which samples of smallpox virus are still kept, conjures up images only reserved for our nightmares. It should worry us. Over the course of human history, smallpox has killed hundreds of millions of people – hundreds of millions of people. Three times the number of deaths from all 20 th century wars – 300 million people – occurred from smallpox in the 20 th century. Smallpox kills indiscriminately and without conscience. There are no social classes it hasn't touched. No occupation nor age nor state of health makes a bit of difference. It has killed kings as well as paupers, children as well as adults, farmers as well as city dwellers, and generals and their enemies alike. [30]

So where did it come from, this pox? It seems that it is one of the earliest zoonotic infections of humans. How, when, and where it was transferred isn't really known. Some think smallpox virus is the human form of monkeypox virus likely acquired from our primate-like ancestor in Africa. Some believe that we acquired it once we domesticated cattle but the most recent molecular analysis tell us that the closest relative to our smallpox virus are the viruses that cause camelpox and gerbilpox. This is possible if all three arose from a common ancestor fairly recently. [31]

Smallpox virus could only become a purely human virus once the populations of cities grew large enough to sustain it. Gerbils and camels were both common in the farming areas where large settlements grew up: the Euphrates, Tigris, Nile, Ganges, and Indus river valleys. It could be that a rodent pox jumped to camels and humans 5,000-10,000 years ago. Sanskrit texts from 1500 BC suggest a type of pox and Egyptian papyri from between 3730 and 1555 BC also suggest smallpox. What's most telling is that pox-like viruses have been found using electron microscopy on samples from the mummy of King Ramses V, who was in his thirties when he died suddenly in 1157 BC. [32]

Early on in the history of civilization, Europe was too sparsely populated to permanently maintain smallpox. Once the Greek Empire was established, the smallpox could expand its territory into that area. In 430 BC there was a large plague in Athens that may have actually been smallpox. [33] The decline of the Roman Empire in AD 108 happens to coincide with the plague of Antonine, an epidemic that killed almost 7 million people. [34] Smallpox may have popped up in Britain every now and then but it wasn't until the Normans invaded in 1066 and the Crusaders of the 12 th and 13 th centuries were returning home that smallpox was able to set up a permanent residence in that area. [35] Germany and England both suffered epidemics in 1300. By the 15 th century it was in Scandinavia and was everywhere in Europe except Russia by the 16 th century. [36]

The Amerindians were first exposed to smallpox when Christopher Columbus arrived on the island of Hispaniola, now Haiti. The native population numbered around eight million people and a mere forty years later, not one of them remained. In 1519 Hernando Cortez was sent to investigate the rumors that there was a thriving culture in Mexico. He landed with sixteen horsemen and 600 foot soldiers and was taken to meet Emperor Montezuma in the Aztec capital of Tenochtitlan. Once the natives realized that he wasn't actually the god, Quetzalcoatl, returning to fulfill a prophecy, the Spaniards had to retreat back to the coast. They spent most of 1520 regrouping and recruiting more of the locals for a return trip to the Aztec capital. Smallpox had already struck before they returned and the siege of the city lasted just 75 days. Francisco Pizarro also had the aid of an epidemic when he and his troops invaded the Incan Empire in 1532. This empire was struck

sometime in the 1520s by what is thought to have been smallpox and which wiped out one third of the population. Although smallpox was not the only Eurasian disease the Europeans brought to the new world, it seems to have been the most devastating. Just 50 years after Cortez arrived in Mexico, the population had been reduced from 30 million to a mere three million. [37]

Besides playing such a crucial role in the Spanish conquest of Mexico and other areas, smallpox contributed to the rapid settlement of North America by the English and French. In 1617 the arriving English settlers set off a huge epidemic among the native population, [38] reducing it by more than 90%. [39] This made it rather easy for the colonists to settle this vast New World when they arrived in Plymouth in 1620. The English were also not afraid to use contaminated blankets in a type of germ warfare in the war of 1763 between England and France for control of North America. Blankets were contaminated with scabs from smallpox pustules and delivered to the Indians. With 90% of the Amerindians wiped out, there was an increased need for laborers on the plantations and in the mines of the West Indies, the Dominican Republic, and Cuba. Where were these laborers to be found? Africa. [40]

Variola

Smallpox virus is one of the largest viruses and can actually be seen with a light microscope; however, the details of its structure can only be seen using an electron microscope. The capsid, or outer surface, looks like the facets on a diamond and its genetic material, double-stranded DNA, is in an inner, dumbbell-shaped core. Its DNA contains about 200 genes and it's believed that 35 of those genes relate to virulence. [41] The word *variola* was introduced by Bishop Marius of Avenches in 570 AD and comes from the Latin *varius* or "stained" or from *varus*, or "mark on the skin". *Small pockes* was first used in the 15 th century in England and distinguished smallpox from *great pockes* which was the term used for syphilis. [42]*Variola major* and *Variola minor* are the two types of pathologic smallpox. *V. major* is the deadlier form and in the Old World frequently killed up to 25% of its victims. Mortality figures for native populations, such as the Amerindians, are much higher. *V. minor* was more common in Europe until the 17 th century and only killed about 2% of its victims. After that, it mutated to the more lethal form, possibly resulting from reintroduction from the Spanish colonies in the Americas. This more devastating form killed an estimated 400,000 each year and caused one-third of all cases of blindness. [43]

Infection and Transmission

Inhalation of aerosols is the most common means of transmission of smallpox virus; however, it can also be acquired by direct contact with inanimate objects such as bed linens and even dust. The dried material from the pustules can be infectious for months. Once a virus reaches the mucous membranes of the mouth and nose, it starts to multiply. Even though there is no sign of infection during the first week, the victim is still highly contagious and can spread smallpox by coughing, sneezing or even by careless disposal of a tissue. The virus moves on to the lymph nodes and from there enters the blood stream to reach the internal organs. The virus then multiplies in the internal organs before reentering the blood stream. Headache, fever, chills, nausea, and muscle ache appears around day nine. A few days later the pustules appear. The following is an excerpt from *The Demon in the Freezer* by Richard Preston:

> The pustules began to touch one another, and finally they merged into confluent sheets that covered the body, like a cobblestone street. The skin was torn away…across…the body, and the pustules on the face combined into a bubbled mass filled with fluid until the skin of the face essentially detached from its underlayers and became a bag surrounding the tissues of the

> head…tongue, gums, and hard palate were studded with pustules…the mouth dry…The virus had stripped the skin off the body, both inside and out, and the pain…seemed almost beyond the capacity of human nature to endure.

In the days following the appearance of the rash, many people die and there are often complications from secondary infections. Pockmarks, permanent craterlike scars in the skins, are left because of the destruction of the sebaceous glands of the skin. The infection can lead to permanent loss of eyebrows and eyelashes. [44]

When an outbreak of smallpox occurred in a virgin community, either the people in the community were immune, succumbed to the disease, or recovered and gained a lifelong immunity. Once everyone had been exposed in one way or another, the epidemic burned itself out. Once enough new people moved into the community and babies were born, the disease had enough new victims for another epidemic. After a period of time, the disease would reappear frequently enough that is was only the newborns that had no immunity. Smallpox then came to be known as a childhood disease. Infants had the highest mortality and it could cause abortions at any time during a pregnancy. [45]

Variolation

The most successful method of stemming the tide of a smallpox epidemic was variolation or inoculation. The Latin word, *inoculare*, means "to graft" and the words variolation and inoculation were used interchangeably. This is a technique developed to induce a mild smallpox infection. The Chinese had two methods of variolation. One was to make a powder of the dry scabs from the pustules and inhale the powder and the other was to place powdered scabs onto a cotton swab and place it in the nostril of the person to be variolated. In other parts of the world such as the Near East and Africa, material from a pustule was rubbed into a small cut or scratch in the skin. The first scholarly account of this latter type of variolation was described by Thomas Bartholin, King Charles V of Denmark and Norway's physician, in 1675. [46]

This type of variolation caught on thanks to the work of Lady Mary Montague. She had survived smallpox but was left permanently scarred and her younger brother died of the disease. After learning of the method while at the Ottoman court in Turkey, she had the embassy surgeon, Charles Maitland, inoculate her 5-year-old son. It was successful and upon her return to London, Lady Montague's daughter was variolated in front of physicians from the royal court. This too, was successful. Charles Maitland then repeated the experiment on six prisoners in Newgate Prison in 1721. The prisoners were granted the king's favor for agreeing to the experiment. Success. Permission was then given for Charles Maitland to perform experiments on orphans, again with success. Once the two daughters of the Princes of Wales had been successfully variolated, the practice became generally accepted. Variolation did, indeed, provide lifelong protection and the danger from death was around 2% while the mortality for those who contracted smallpox during epidemics remained between 15% and 20%. Variolation came into practice in colonial America independently from what was occurring in England. Cotton Mather, a Boston clergyman, had learned of the process from one of his slaves, Onesimus. During an outbreak in Boston, Mather was able to convince a single physician, Zabdiel Boylston, to try the process. Boylston variolated his 6-year-old son, one of his slaves, and the slave's 3-year-old son with no complications. In 1722 Boylston variolated 242 Bostonians and found they had a mortality of only 2.5%. That was much better than the 15%-20% death rate during an epidemic. George Washington also had many of his troops variolated. The British general, General Howe occupied Boston after the Battle of Bunker Hill but was unable to attack Washington's troops encamped around the city because of the smallpox epidemic. Washington was not afraid of smallpox and on March 17, 1776, Washington sent in 1,000 of his immune troops to occupy Boston as General Howe left the city. [47]

Vaccination

While working as a physician in Berkeley, Gloucesterhire, Edward Jenner heard many tales of milkmaids never getting smallpox because they'd been exposed to cowpox. Jenner found a milkmaid named Sarah Nelms, who had cowpox lesions on her hands and arms. Using matter from Nelms' lesions, Jenner inoculated James Phipps, an 8-year-old boy. Phipps developed a mild fever and on the ninth day after exposure, he felt cold and didn't have an appetite. The tenth day he was much better and recovered fully. Two months later, in July 1796, Jenner inoculated Phipps again only with smallpox. No disease ever developed in young Phipps. Jenner called this new procedure *vaccination* after the Latin for cow, *vacca*, and the Latin for cowpox, *vaccinia*. [48] Phipps was tested for immunity many more times over the next several years and never came down with smallpox. After more years of testing on volunteers, Jenner finally published a pamphlet on his technique in 1798. Many physicians completely rejected his ideas at first and there were even cartoons drawn of children with cow horns coming out of their ears. By the turn of the century many had started using the technique and Jenner was famous. Parliament twice awarded Jenner 20,000 pounds, in 1802 and 1807. Jenner received many honors from around the world and Napoleon even had a medal made in his honor. [49] It should be noted that although variolation produces a lifelong immunity, vaccination does not. The main drawbacks to variolation are that the person is infectious to others and the mortality is 1% - 3%. [50]

Daily Schedule Overview of Unit and Activities

Day 1 – Group Activity

Students will be given the description of a new bacterial disease including mortality and asked to work in groups to predict what would happen in an epidemic of this new bacterial disease. Students will be asked to predict how it will affect their belief system, the medical community, what will happen at the hospitals, what will happen with basic city services – fire, police, etc. They must also predict how it will affect the schools and any other aspect of their lives they can think of. Students will be given 20-25 minutes to work with a partner then the groups will come together for a class discussion.

Day 2 - Presentation

Students will be shown pictures of drawings or paintings found on the world wide web of people suffering with bubonic plague and asked what they already know about the disease. A presentation will be made by the teacher, which includes all topics found on the microbe presentation rubric including a handout of how the bubonic plague affected the university system in Europe, a change in farming methods, a change in the standard of living, and a change in religious beliefs.

Day 3 – Socratic Seminar

The teacher will lead a Socratic seminar on the nonconsensual medical experimentation using information from Riedel's article on Jenner and/or using a suitable case study from the National Center for Case Study Teaching in Science. See "Bibliography" for the NWABR website for help in learning about how to conduct a Socratic seminar.

Day 4

Students will be given background information on smallpox and we will discuss the final unit assignment.

Day 5 – Computer Lab

Students will be able to begin conducting research in our computer lab. They will have the opportunity to finish the project over the weekend. Depending on how this unit falls, we could also use our double-block day (90 minutes) or two 45-minute periods.

Day 6 and Day 7

Student presentations.

Final Student Production

Students will complete a small group project in which they must pick one microbe and describe it in detail. If they chose a microbe that we use to our benefit, they must describe the life cycle and how it is used now or has been used in the past in order to make our lives better. If the students choose a microbe that has caused problems in our past, then the students must describe its life cycle and the problem or problems it has caused throughout history and whether or not it is still a significant threat. Students can also choose a microbe that is seemingly neutral and has had no significant impact in the past but is currently being used in research in order to find a cure for a current disease. The disease involved could be genetic, immunologic, or one known to be caused by another microbe. See Appendix A for the rubric developed for this assignment.

Bibliography

Abbott, Rachel C. and Tonie E. Rock. "Plague: US Geological Survey." National Wildlife Health Center Circular 1372 Circular 1372 (2012): National Wildlife Health Center. Web. 12 July 2014. The material in this circular is presented in a straightforward, easily understood manner. This would be useful to print out and give to students.

Crawford, Dorothy H. Deadly companions how microbes shaped our history. Oxford: Oxford University Press, 2007. Print. This is one of the primary sources for this unit and contains information concerning other microbes besides Yersinia pestis and smallpox virus.

"NWABR.ORG." NWABR.ORG. N.p., n.d. Web. 12 July 2014. . This website provides information pertaining to biomedical research and ethical conduct.

"Permitted Uses." - National Center for Case Study Teaching in Science. N.p., n.d. Web. 14 July 2014. . This page provides guidelines for using case studies in the classroom. This is a fantastic database for case studies.

Riedel, Stefan. "Edward Jenner and the history of smallpox and vaccinations." Baylor University Medical Proceedings 18.1 (2005): 21-25. Print. This pdf provides information about Jenner's background and his development of the process of vaccination. This pdf

could also be used as extra reading for students.

Sherman, Irwin W., The power of plagues. Washington, D.C.: ASM Press, 2006. Print. This is another main resource for this unit and details the interrelationship between epidemics and culture and the ways it shapes history, traditions, and modern institutions.

"Socratic Seminar." Northwest Association for Biomedical Research. N.p., n.d. Web. 11 July 2014. . This pdf file provides information on how to effectively lead a Socratic seminar.

Appendix A

Microbe Rubric for Final Presentation

Information Required	Pts. Possible	Pts. Earned
What is it?		
Scientific Name	1	
Common Name(s)	1	
Describe the following:		
Size	1	
Method of Reproduction	2	
Rate of Reproduction	2	
Explain the following:		
How the disease is transferred	2	
Symptoms of the disease	1	
Treatments or cures – if any	1	
Current and/or historic mortality rate	2	
Who is at risk	1	
How it can be prevented/contained	2	
Longterm effects of the disease / recovery time	2	
Map of current/historic locations of the disease	2	
Paragraph describing the implications of those locations	3	
Sources and Citations		
4 strong sources	4	
Hyperlinks to sources	4	
Describe in detail the following:		
Past human response to the disease	3	
Present human response to the disease	3	
Effects of disease on human history/current policies	3	
Predictive Component:		
Give a detailed prediction of how the relationship of this microbe and humans will change over time.	3	
Justify predictions based on past and present relationships.	3	
Inclusion of graphs, tables, pictures	4	
Total points:	**50**	
Notes:		

Appendix B

Oklahoma Priority Academic Student Skills

Process Standard 4: Interpret and Communicate – Interpreting is the process of recognizing patterns in collected data by making inferences, predictions, or conclusions.

- 4.1 Select appropriate predictions based on previously observed patterns of evidence.
- 4.7 Communicate or defend scientific thinking that results in conclusions.
- 4.7.a Read, comprehend, and present evidence from a range of sources (e.g., texts, experiments, or

simulations) to support conclusions.
4.7.b Recognize bias in observation/research.

Common Core Reading Standards for 11-12 Students for Literacy in Science

2. Determine the central ideas or conclusions of a text; summarize complex concepts, processes, or information presented in a text by paraphrasing them in simpler but still accurate terms.
9. Synthesize information from a range of sources (e.g., texts, experiments, simulations) into a coherent understanding of a process, phenomenon, or concept, resolving conflicting information when possible.

Notes

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1. Crawford, *Deadly Companions: How Microbes Shaped Our History*, 80

2. Crawford, *Deadly Companions: How Microbes Shaped Our History*, 85

3. Crawford, *Deadly Companions: How Microbes Shaped Our History*, 79

4. Abbott, R.C., and Rocke, T.E., *Plague: US Geological Survey Circular 1372*, 2

5. Crawford, *Deadly Companions: How Microbes Shaped Our History*, 85

6. Crawford, *Deadly Companions: How Microbes Shaped Our History*, 85

7. Crawford, *Deadly Companions: How Microbes Shaped Our History*, 86

8. Crawford, *Deadly Companions: How Microbes Shaped Our History*, 86-88

9. Crawford, *Deadly Companions: How Microbes Shaped Our History*, 88

10. Sherman, *The Power of Plagues*, 67

11. Abbott, R.C., and Rocke, T.E., *Plague: US Geological Survey Circular 1372*, 1

12. Abbott, R.C., and Rocke, T.E., *Plague: US Geological Survey Circular 1372*, 4

13. Abbott, R.C., and Rocke, T.E., *Plague: US Geological Survey Circular 1372*, 5

14. Abbott, R.C., and Rocke, T.E., *Plague: US Geological Survey Circular 1372*, 6

15. Crawford, *Deadly Companions: How Microbes Shaped Our History*, 95-96

16. Abbott, R.C., and Rocke, T.E., *Plague: US Geological Survey Circular 1372*, 7

17. Crawford, *Deadly Companions: How Microbes Shaped Our History*, 97

18. Sherman, *The Power of Plagues*, 86

19. Sherman, *The Power of Plagues*, 86-87

20. Sherman, *The Power of Plagues*, 71

21. Sherman, *The Power of Plagues*, 73-74

22. Sherman, *The Power of Plagues*, 76

23. Sherman, *The Power of Plagues*, 76

24. Sherman, *The Power of Plagues*, 77

25. Sherman, *The Power of Plagues*, 78

26. Sherman, *The Power of Plagues*, 79

27. Sherman, *The Power of Plagues*, 79-80

28. Sherman, *The Power of Plagues*, 80-81

29. Sherman, *The Power of Plagues*, 81

30. Sherman, *The Power of Plagues*, 192

31. Crawford, *Deadly Companions: How Microbes Shaped Our History*, 106

32. Crawford, *Deadly Companions: How Microbes Shaped Our History*, 106-107

33. Crawford, *Deadly Companions: How Microbes Shaped Our History*, 107

34. Stefan, *Edward Jenner and the history of smallpox and vaccination*, 21

35. Crawford, *Deadly Companions: How Microbes Shaped Our History*, 107

36. Sherman, *The Power of Plagues*, 194

37. Crawford, *Deadly Companions: How Microbes Shaped Our History*, 113-118

38. Sherman, *The Power of Plagues*, 194

39. Crawford, *Deadly Companions: How Microbes Shaped Our History*, 114

40. Sherman, *The Power of Plagues*, 194-195

41. Sherman, *The Power of Plagues*, 195

42. Stefan, *Edward Jenner and the history of smallpox and vaccination*, 21-22

43. Sherman, *The Power of Plagues*, 198

44. Sherman, *The Power of Plagues*, 195-198

45. Sherman, *The Power of Plagues*, 199

46. Sherman, *The Power of Plagues*, 200

47. Sherman, *The Power of Plagues*, 201-202

48. Stefan, *Edward Jenner and the history of smallpox and vaccination, 23-24*

49. Sherman, *The Power of Plagues*, 203-204

50. Sherman, *The Power of Plagues*, 206