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Manipulation of Human History by Microbes

Richard G. Wax, Ph.D., Retired, Pfizer Global Research, Groton, Connecticut

Abstract

The convergence of the microbial and human worlds provides us with everyday essentials for the survival of our species, and in turn, this interaction brings painful and tragic consequences from pathogens. Looking back, it can be seen that microbes have also changed our history. Were it not for a pathogen that halted an Assyrian military campaign, we might have no Judaism, Christianity, or Islam. Microbes were there to aid adversaries in bringing about the fall of the great Greek and Roman empires. George Washington's bold orders to inoculate the Colonial Army against smallpox (20 years prior to Jenner's discovery of vaccination) were one of the most significant actions in saving the American Revolution from an early and unsuccessful end. Without the yellow fever virus and its accomplice, *Aedes aegypti*, those living in what was the Louisiana Territory might now have French as their native language. The potato blight caused by *Phytophthora infestans* changed the histories of both Ireland and those countries (especially the United States) to which victims of the famine emigrated. At the outbreak of World War I, when England was separated from its European source of acetone (needed for the navy's supply of cordite), British citizens had to make do with less gin, but acetone was available thanks to the growth of *Clostridium acetobutylicum* in those fermentation vessels.

Introduction

Publications appearing with increasing frequency support the view that microbes are as deserving of a place in history texts as kings, presidents, and generals. In his classic treatise on this subject, Hans Zinsser noted that "... epidemics ... have often determined victory or defeat before the generals knew where they were going to place the headquarters' mess" (1). The disappearance of whole cultures, e.g., native inhabitants of the Americas, is but the most pronounced example of population changes wrought by disease. Microbes have left an imprint on economics, literature, medicine, and virtually every aspect of human society. They caused the abandonment of some religions and the acceptance of others and exposed our prejudices and superstitions (2-4). The discussion below provides some examples of events in

which disease has actually changed human history.

Judaism, Christianity, and Islam Saved by a Microbe

William O'Neill, Professor Emeritus of History at the University of Chicago, has noted that one of the most important battles in history was one that was never fought. "Jerusalem's preservation from attack by Sennacherib's [Assyrian] army shaped the subsequent history of the world more profoundly than any other military action I know of" (5). Assyria was the largest and most powerful empire of its time and, led by King Sennacherib, its army had conquered much of the Near East. In 701 B.C., Jerusalem was an intended Assyrian conquest (6). Inscriptions on the walls of Sennacherib's palace at Nineveh, in agreement with histories of the period, proclaim that by the use of ramps, battering rams, mines, and other military techniques, his army had occupied 46 walled cities in the kingdom of Judah. Thus, there is strong reason to believe that had the engagement

proceeded as planned, Jerusalem also would have fallen. During the siege, however, a large number of Assyrian soldiers died, and Sennacherib apparently judged that Jerusalem was not worth the price exacted by a lethal illness. In addition, a deteriorating situation in Babylonia required the attention of the Assyrian army (7), and thus, the siege was ended. Reasons for the mortality included the possibility that the defenders within Jerusalem had somehow prevented the Assyrians from getting access to good water (5) or that food poisoning was responsible (6), and it was the ingestion of pathogens that exposed them to widespread fatal infections.

In the opinion of Professor McNeill, had Jerusalem fallen in 701 B.C., "the two daughter religions of Christianity

Mailing Address: Richard G. Wax, Ph.D.,
29 Beacon Hill Dr., Waterford, CT 06385-
4107. Tel.: 860-443-5675. E-mail:
rwax@ct.metrocast.net

and Islam could not possibly have come into existence” (5). A microbe had thwarted the designs of the largest and mightiest nation of that period and affected the religious history of the world.

Plague and the End of the Golden Age of Greece

The “Plague of Athens,” one of the great plagues of antiquity, played a significant role in ending the golden age of Greece. The age was primarily golden for Athenians but much less so for citizens of surrounding states. Pericles, leader of Athens in 444 B.C., embarked on ambitious programs in the arts, literature, and architecture, leading to development of a grand society. At Pericles’ direction, however, all construction was within Athens, e.g., the Parthenon and other monuments of the Acropolis. Athenians thus gained the benefit of these works and the jobs they provided, but surrounding states were forced to pay the cost of the projects. This policy ultimately resulted in a revolt by Sparta and other cities of the Peloponnese peninsula, and the Peloponnesian War broke out in 431 B.C.

Athens itself was fortified, and in addition, a four-mile-long double wall connected Athens to the port of Piraeus. Since Sparta had the superior army, Pericles’ strategy was to bring citizens in from the surrounding countryside and use Athens’ considerable commercial shipping to safely supply the city’s needs through Piraeus. Athens’ offensive tactics made use of its powerful navy’s ability to strike at targets of its choosing. Sparta did ravage the areas around Athens, but according to Pericles’ plan, Athenians were safe (at least from military attack) within their walls.

The problem not anticipated by Pericles was that commercial shipping was a good source of disease, and crowding in Athens contributed to

the spread of infection. Thucydides, an exiled Athenian general, having recovered from the disease himself, produced the remarkable *History of the Peloponnesian War*. As Thucydides wrote:

It [the plague] first began, it is said, in ... parts of Ethiopia. ... and then descended into Egypt and Libya. ... Suddenly falling on Athens it first attacked the population in Piraeus. (8)

An aggravation of the existing calamity was the influx from the country into the city. ... As there were no houses to receive them; they had to be lodged at the hot season of the year in stifling cabins, where the mortality raged without restraint. (9)

Bodies were piled in the streets, traditional funeral procedures were ignored, and there was a breakdown of law, religion, and morals. Athens’ offensive sorties were also blocked by the plague.

On the expedition in their ships, men kept dying of the plague. [In another offensive expedition,] the plague attacked them here also, and committed such havoc as to cripple them completely. ... The end of it was that Hagnon returned with his ships to Athens, having lost 1,050 out of 4,000 heavy infantry in about 40 days. ... Their despair was now complete. (9)

The winter following, the plague a second time attacked the Athenians. ... The second visit lasted no less than a year, the first having lasted two; and nothing distressed the Athenians and reduced their power more than this [the plague]. (10)

The war went on for 27 years, and during this time, Pericles and two of his sons died, along with approximately one-third of Athens’ population. Ulti-

mately, Athens surrendered, its walls were torn down, and its territories were given up. There has been considerable disagreement in regard to which microbe entered the city, boarded the ships, and prevented an early Athenian victory, but recent DNA analysis of tissue from a mass grave from that period implicates *Salmonella enterica* serovar Typhi (11) as the microbe that caused “The Plague of Athens” and contributed significantly to the fall of the greatest empire of its day. “Had Athens won that war, how different the subsequent political history of the Mediterranean would have been!” (12)

Disease and the Downfall of Rome

Roads constructed by the Romans were built to rigorous specifications, with layers of rocks, stones, and sand carefully engineered to ensure durability. They were straight, hard-surfaced, and extended for a total of approximately 53,000 miles (13). Thus, soldiers could be rapidly deployed, and commerce, captives, and materials could be expeditiously brought back to Rome. These roads also served as conduits for diseases from far-off lands, however, and the tolls on these roads exacted by new pathogens were paid in vast numbers of Roman lives.

The Plague of Antoninus, which may have been smallpox, was brought to the Roman Empire by troops returning from Mesopotamia in 165 A.D. (14). The epidemic raged for 15 years and is believed to have claimed a third to a fourth of the population. In 251 to 256 A.D., an epidemic is said to have killed 5,000 per day at its height. In 542 to 543 A.D., the “Plague of Justinian,” identified as bubonic plague, probably had India or central Africa as its source. The death rate is reported to have reached 10,000 per day (15). These outbreaks were especially noted for their widespread mortality, but many epidemics continued for 500 years.

The result was a decline in population with serious manpower shortages, and by the fourth century, mercenaries were required to staff the army (15). The problem was compounded by economic consequences, followed by a reduction in tax revenue and an inability of the government to pay soldiers (16).

Providing food for the almost 1,000,000 residents of Rome and the populace of other sections of the country was particularly difficult, because in many areas, malaria ruled the agricultural lands and farming was a death sentence. Thus, emigration of the indigenous farming population required continuous importation of slaves (17). Since the life span of a slave was short, providing large numbers of captives was an important function of the Roman army.

The reasons for the fall of Rome are, of course, very complex, but disease seems to have played a major role in bringing down that empire. "The story of the last centuries of Roman power is a long tale of plague" (18).

Skirmishes with Smallpox in the American Revolution.

George Washington contracted smallpox when he was 19 years old — a fortunate event in American history. Smallpox was epidemic during the American Revolution; at times it had disastrous effects in the crowded conditions of military camps, and Washington even suspected that it was being used as a weapon by British forces. Thus, the fact that Washington had gained prior immunity may have saved his life. The disease was of such concern that "the pox" was mentioned in over 100 letters and general orders sent by Washington during the war.

Following hostilities at Lexington and Concord, when the British army was besieged in Boston, Washington heard rumors of a British intent to use smallpox against the colonial militia. His reactions went from disbelief to acceptance of this information, as indicated in letters to the Continental Congress (19).

By recent information from Boston, General Howe is going to send out a number of the Inhabitants, in order as it is thought to make more room for his expected reinforcements; there is one part of the information that I can hardly

give Credit to, A Sailor says that a Number of these coming out have been inoculated with design of Spreading the Small pox through this Country and Camp.

Cambridge, December 4, 1775

The Information I received that the Enemy intended spreading the small Pox amongst us, I could not suppose them capable of; I now must give some credit to it, as it has made its appearance on several of those who last came out of Boston.

Cambridge, December 11, 1775

About 150 more of the poor Inhabitants are come out of Boston, the small pox rages all over the Town. ... This I apprehend is a weapon of defence, they are using against us.

Cambridge, December 14, 1775.

Thus, when the British force sailed from Boston, Washington ordered that the city be entered only by men immune to smallpox.

As the enemy with a malicious assiduity, have spread the infection of the smallpox through all parts of the town, nothing but the utmost caution on our part, can prevent that fatal disease from spreading thro' the army, and country, to the infinite detriment of both.

*Cambridge, March 13, 1776,
General Orders*

In 1763, soldiers at Fort Pitt had employed smallpox as a weapon against native Americans, and its use was approved by Sir Jeffrey Amherst (20); this information may have helped form Washington's opinion that a spread of the disease among his troops was an intentional British objective. Smallpox was unique as a means of biological warfare in the 18th century, because unlike typhus, bubonic plague, yellow fever, malaria, and cholera, it could be rapidly spread directly from human to human (21).

Late in 1775, Patriot forces under Colonels Montgomery and Arnold advanced into Canada with the hope of removing the British presence and adding Canada to the territory of the colonies (22). The Americans successfully captured Montreal, but during the siege of Quebec City, smallpox raged through the colonial ranks. More troops

arrived, but they too joined the ranks of the sick, and by the end of March 1776, approximately one-half of the force had come down with the disease. The ultimate result was a tragic retreat by sick and dying Colonials (23).

The situation was described in a letter from John Adams to his wife Abigail: "Our Misfortunes in Canada, are enough to melt an Heart of Stone. The Small Pox is ten times more terrible than Britons, Canadians, and Indians together. This was the Cause of our precipitate Retreat from Quebec" (24). Were it not for smallpox, a significant part of Canada might have fallen to the Americans (25).

Edward Jenner did not discover the cowpox vaccine, using vaccinia (from vacca, latin for cow) until 1795, 12 years after the Revolutionary War ended. There was, however, a preventive method in use that involved "inoculating" with the actual *Variola* virus taken from smallpox patients. This method, developed in Asia and Africa, induced a milder form of the disease, with far fewer fatalities, and it did provide protection against subsequent infection — but the inoculated person was ill for some days and capable of spreading true smallpox during this period. For this reason, Washington had initially *prohibited* inoculation among his troops. (The source of letters and orders from George Washington can be found in reference 19).

No Person whatever, belonging to the Army, is to be innoculated for the Small-Pox. ... Any disobedience to this order, will be most severely punished — As it is at present of the utmost importance, that the spreading of that distemper, in the Army and City, should be prevented.

Head Quarters, New York, May 20, 1776

If any Soldier should (be inoculated) he must expect the severest punishment. ... Any Officer in the Continental Army, who shall suffer himself to be inoculated, will be cashiered and turned out of the army, and have his name published in the News papers throughout the Continent, as an Enemy and Traitor to his Country.

General Orders, May 26, 1776

Other considerations, however, caused Washington to reconsider his

position on inoculation. The role of smallpox in bringing about the debacle in Canada, and reduced recruitment resulting from epidemics prevalent in encampments, were issues to be dealt with.

Fear of the Infection operates strongly to prevent Soldiers from engaging in the Service, and the Battalions ordered to be raised in this Colony fill up slowly: are there no Measures may be taken to remove the Impediment?

Washington to the Continental Congress, July 11, 1776

Dear Sir: I am very much afraid that all the Troops on their march from the Southward, will be infected with the small Pox, and that instead of having an Army we shall have an Hospital.

Washington to Horatio Gates, Head Quarters, January 28, 1777

Thus, subsequent letters and orders from Washington show his changed stance on inoculation.

Dear Sir: Finding the small pox to be spreading much and fearing that no precaution can prevent it from running thro' the whole of our Army, I have determined that the Troops shall be inoculated ... for should the disorder infect the Army, in the natural way, and rage with its usual Virulence, we should have more to dread from it, than from the Sword of the Enemy.

Washington to William Shippen Jr., Head Quarters, Morris Town, January 6, 1777

Sir: The impossibility of keeping the Small Pox from spreading thro' the Army in the natural way, has determined us, upon the most mature deliberation, to inoculate all the New Troops, that have not had this disorder. I [am] ... taking it for granted, that you would have no objection to so salutary a Measure, upon which depends not only the lives of all the Men, who have not had the Small Pox, but also the Health of the whole Army, which would otherwise soon become a Hospital of the most loathsome kind.

George Washington to Jonathan Trumbull, Head Quarters, Morris Town, February 10, 1777

Sir: The deplorable and melancholly situation, to which one of our Armies was reduced last Campaign by the small Pox and the Certainty, that no precautions can prevent that disorder from infecting our Troops ... has determined me by the advice of my General Officers here to introduce inoculation immediately, as the only means of preventing this Calamity; the greatest that can befall an Army.

Washington to Nicholas Cooke, Morris Town, February 10, 1777

Sir: The ensuing Campaign may, from the same Causes, prove as sickly as the last. ... our Regiments will be reduced to Companies by the end of the Campaign. ... For my own part, I am certain, that if the Army, which I hope we shall have in the Field this year, is suffered to moulder away by Sickness, as it did the last, we must look for Reinforcements to some other places than our own States.

George Washington to the Continental Congress, Head Quarters, Morris Town, February 14, 1777

Gentn.: After every attempt to stop the progress of the Small Pox, I found ... that there was no possible way of saving the lives of most of those who had not had it, but by introducing inoculation generally. ... We intend for the present to keep the Matter as much a Secret as possible, and I would advise you to do the same.

Washington to New York Convention, Head Quarters, Morris Town, February 10, 1777

The courage of Washington's directive is evidenced by the fact that in the civilian population, there had been mob violence protesting inoculation and legal restrictions preventing or discouraging inoculation were in effect in some states (26). The success of Washington's bold medical directive was dependent on an orderly, carefully controlled inoculation of whole regiments at one time, with guarded quarantine during the recovery period, and secrecy. Thus, an order was sent out.

As the Commander in Chief is extremely desirous that the Small-Pox should not spread among the Soldiery, it is hoped no persons

will presume, on any account whatever, to inoculate without first obtaining leave.

General Orders, Head Quarters, Morristown, February 15, 1777

Secrecy was essential, since it was imperative that General Howe's forces in the vicinity not become aware that the Continentals were incapacitated during the days of illness following inoculation.

Sir: I need not recommend to you the greatest Secrecy and dispatch in this business; because a moment's reflection will inform you, that should the Enemy discover our Situation they can not fail taking advantage of it.

George Washington to Samuel H. Parsons, Morris Town, February 10, 1777

Dear Sir: I have a thousand corresponding Circumstances to convince me, that Genl. Howe intends to move from Brunswick in a very short time, it is said to this place; ... their numbers are nearly double ours, and what Kind of Troops ours are ... most of those that could be depended upon, are down with the Small Pox, either by Inoculation, or in the natural way.

George Washington to Horatio Gates, Morristown, February 20, 1777

In addition to typical military considerations, deployment of Continental troops had to take into account the issue of susceptibility to smallpox; e.g., orders for troop movement were very often specific for those who were immune to smallpox.

Sir: I would have you leave at this place (out of the Militia under your Command) One hundred Men, or as near that Number as have had the Small Pox. ...

Washington to Nathaniel Heard, Head Quarters, Morris Town, April 23, 1777

Sir: The Campaign is upon the point of opening in this Province. ... I therefore desire that you will send on every Man of your Regiment that is Clothed and Mounted, and that have had the Small Pox.

Washington to Elisha Sheldon, Head Quarters, Middle Brook, June 9, 1777

The necessity that I am under for Troops, obliges me to call upon you in the most pressing manner,

to send forward those men who have had the small pox.

*George Washington to Samuel H. Parsons,
Head Quarters, Morris Town,
March 6, 1777*

The Enemy ... has obliged me to order all the Continental Troops of Connecticut, that have had the small pox, to march immediately and join me and all those that have not, to be inoculated, for the Country is so full of that disorder, that there is no other way of preserving the Lives of the Soldiery.

*George Washington to Joseph Spencer,
Head Quarters, March 11, 1777*

Despite the inoculation of Continental regulars, smallpox remained a problem because new recruits and local militia lacked immunity.

Sir: I cannot detach the reinforcement you request. ... we have near Four Thousand men in this Camp sick of the small pox and other disorders.

*Washington to Horatio Gates,
Valley Forge, May 29, 1778*

Washington's frustration in accomplishing his public health directives is evident in the following communication.

Dear Sir: After the repeated directions, which I had given to have All the Recruits who had not had that disorder inoculated the moment they were inlisted, I was not less surprised than mortified to find the fine detachment of Men that came forward under Lt. Colo. Smith rendered intirely useless for this Campaign by my Orders not being attended to. By the time they reached the Camp the small pox broke out upon them, which obliged me to send the whole into the Hospital, as those who were well were not more than sufficient to nurse the sick.

*Washington to William Heath, Head
Quarters, Gulph Mill, December 17, 1777*

As the Revolutionary War came to its final stage at Yorktown, Virginia, the Continental Army suspected that another attempt was made to use smallpox against them. Large numbers of slaves fled to British lines in response to an offer of freedom, but at Yorktown they were sent out of the British encampment. One explanation is that the slaves were evicted because of a

shortage of food during the siege, but an epidemic of smallpox had spread through this uninoculated group, and sources presented by Elizabeth Fenn (27) support the accusation that they were sent out with the objective of spreading the disease to the Continental Army.

Washington's orders to inoculate all soldiers of the Continental Army is likely to have played as important a role in the success of the Revolution as military tactics and stratagems. Without it, as noted in his letters, the Continental Army would not have been a sufficiently effective fighting force.

A Gift to the U.S. from the Yellow Fever Virus

Were it not for the yellow fever virus, those living in the area of the Louisiana Territory might have French as their native language. A result of the complexity of U.S.-French relations at the end of the 18th century can be seen in a letter from John Adams to Thomas Jefferson (28).

You certainly never felt the Terrorism ... when ten thousand People in the Streets of Philadelphia, day after day, threatened to drag Washington out of his House, and effect a Revolution in the Government ... nothing but the Yellow Fever [which was epidemic in Philadelphia] ... could have saved the United States from a total Revolution of Government.

Americans dragging George Washington out of his house? Adams' letter referred to the year 1793, when French ambassador Genet roused many Americans to side with France in its hostilities with England, but Washington wanted no part of foreign conflicts. Subsequent events, however, were to give the United States no choice in remaining detached from European affairs and objectives.

In 1799, Napoleon completed his coup d'état, became First Consul of France, and soon afterward pressured Spain into signing the Treaty of San Ildefonso. In this treaty, which at first was kept secret, Spain ceded Louisiana to France. Napoleon's objectives in Louisiana (and his obstinacy) were later made clear to President Jefferson by dispatches from U.S. Ambassadors

Robert Livingston in Paris and Rufus King in London (29).

I have seen a letter... which says, it is definitively settled to send a colony to Louisiana and Florida.

*Mr. King to the Secretary of State,
London, February 5, 1802*

On the subject of Louisiana, ... the establishment [of a French colony] is disapproved by every statesman here as one that will occasion a great waste of men and money, excite enmities with us, and produce no possible advantage to the nation. But it is a scheme to which the First Consul is extremely attached; and it must, of course, be supported.

*Mr. Livingston to the Secretary of State,
Paris, February 26, 1802*

The fact is [the French] mean... to take possession of [Louisiana] as early as possible, and with as little notice to us as they can.

*Mr. Livingston to the Secretary of State,
Paris, March 24, 1802*

Jefferson was deeply concerned by the prospect of having Napoleon as his western neighbor, as indicated in a letter to Robert Livingston (30).

The cession of Louisiana by Spain to France ... completely reverses all the political relations of the United States.... There is on the globe one single spot, the possessor of which is our natural and habitual enemy. It is New Orleans.

*President Jefferson to Mr. Livingston,
Washington, April 18, 1802*

Another link in the chain of events was occurring in the Caribbean. During the 18th century, Haiti was considered to be the jewel of the French empire. Thanks to the extensive use of slaves, it produced large quantities of coffee, sugar, and other commodities and indeed was the United States' most significant trading partner. At the end of the century, the only successful slave rebellion in modern times resulted in an independent Haiti, but Napoleon's designs on the Americas included a return of Haiti to French rule, as well as colonization of the Louisiana Territory. The efforts of diplomats and military force came to naught, however, as the situation in the Western Hemisphere was

decided by the yellow fever virus and its vector, the mosquito *Aedes aegypti*.

To placate Napoleon and because of concerns regarding a possible slave uprising in the United States (31), Jefferson offered Louis Andre Pichon, charge d’Affaires of the French Republic, assistance in putting down the Haitian slave rebellion (32). In retrospect, had this offer been accepted, and had it not been for intervention by the yellow fever virus, Jefferson would have made the greatest political blunder in American history.

In January 1802, 30,000 French troops arrived at Haiti. As could be expected, French military successes came quickly, and thus, in early summer, top revolutionary generals and half their army defected and joined the French. It is remarkable, then, that by the next spring, the French army, one of the greatest in the world, was no longer an effective fighting force, and soon afterward U.S. ambassadors to France were able to send the following message (33).

Sir, We have the pleasure to transmit to you ... a treaty which we have concluded with the French Republic for the purchase and cession of Louisiana.

Messrs. Livingston and Monroe to Mr. Madison, Paris, May 13, 1803

This amazing turn of events had been brought about by the yellow fever virus. Since the disease was endemic in Haiti, and children get only a mild form of it, the native population enjoyed relative immunity. French troops, on the other hand, closely packed and whose immune systems had never seen this virus, were completely defenseless against the full fury of the disease. The great majority (27,000) of the French troops sent to Haiti died of yellow fever, including Napoleon’s brother-in-law who headed the expedition (34). The small remainder of the force left, and Haiti remained independent. Napoleon lost interest in the Western Hemisphere, offered the sale of the Louisiana Territory, and turned his attention back to Europe.

Yellow fever played numerous additional roles during the early development of the United States. In 1793, for example, the epidemic of this virus in Philadelphia, the nation’s capital, caused the deaths of 5,000 people (1/10 of the

citizenry). A significant part of the population fled the city, the federal government could not fulfill its functions, and the nation’s largest port was virtually shut down for several months (35).

Microbes as Allies of Napoleon

Walcheren

Napoleon learned the military significance of microbiology from the Haitian experience and, not long afterward, applied this lesson to bring about Britain’s worst defeat of the Napoleonic War. In 1805, the French navy was decimated at Trafalgar by a British fleet under the command of Admiral Nelson. Reconstruction of this fleet was carried out on the southwest coast of Holland, and thus, in July 1809, a British force was sent to destroy the rebuilt French navy. The force of 40,000 soldiers, ferried by hundreds of ships, was, however, no match for a disease believed to be malaria. Napoleon, knowing of the illness that was endemic in that area each summer, wrote to one of his commanders: “Do not attempt to come to blows with the English. ... We must oppose the English with nothing but fever” (36).

Dykes were opened on 10 August as Napoleon directed, and the area of the Scheldt estuary was flooded with swampy brackish water (36). Within 4 months, 12,000 British soldiers had become so debilitated they were shipped back to England no longer fit for military duty, and more than 4,000 died of fever, while only 106 men had died in combat (37). This was England’s worst disaster of the Napoleonic Wars, and Walcheren became a word synonymous with military defeat (36). The cause(s) of the illness(es) has not been definitively determined, but *Plasmodium falciparum* malaria is a likely candidate for the rapid, widespread deaths that resulted.

Microbial fermentation keeps Napoleon’s guns functioning

Nitrate, an essential component of gunpowder, was unavailable to the French during the Napoleonic Wars as the result of a blockade by the British navy. To counter this problem, “nitrate gardens” were created with manure and other organic matter and turned frequently to provide aeration. The fermentation produced nitrate, which was then extracted from the mix (38).

P. infestans Broadens the Culture of America

Potatoes had been grown in Ireland for over 200 years, because they produced more calories per acre than any other crop that would grow in northern Europe, were nutritious (few cases of scurvy or pellagra were seen), were easy to grow (expensive plows were not needed), and storage in pits was simple (39). Unfortunately, because only two strains were used throughout the country, when the fungal infection was carried from North America, it hit the Irish potato crop with devastating effect and recurred over a period from 1845 to 1849. The population of Ireland had been 8 million, but that country experienced the death of 1 million and the emigration of another 1 million as a result of *Phytophthora infestans*’ invasion. By 1850, one-fourth of the inhabitants of New York had been born in Ireland.

There is opposition to the word “famine,” and it has been urged that the term be replaced by “potato blight,” because grain was actually exported from Ireland during the years of starvation. An explanation for the tragic human consequences of the potato crop failure has been laid at the feet of absentee landlords, and one reason for their abandoning Ireland has been attributed to the Black Death (bubonic plague). When the Black Death reached Ireland in 1348, the total population was halved, and towns and ports were almost emptied. The perspective has been presented (40) that the resulting depressed prosperity was the impetus for the flight of landowners from Ireland to England. Thus, the effects of the Black Death may have extended well beyond the period of the actual pandemic.

C. acetobutylicum Joins the British World War I Effort

At the onset of World War I, the British were desperate for acetone, needed for making the cordite used by naval guns. Their supply had previously come from Europe and was no longer available. *Clostridium acetobutylicum* came to the aid of England by producing this chemical, essential to the war effort.

Chaim Weizmann was born in Russia, studied in Germany and Switzerland, and then began work (for which he paid six pounds) in a laboratory under Professor

Perkin at Manchester University in England. A shortage of rubber in the early part of the 20th century induced Weizmann to seek a microorganism capable of producing isoamyl alcohol in greater amounts than are normally found in yeast fermentations, with the objective of converting the isoamyl alcohol to isoprene, which would then be polymerized to synthetic rubber (Fig. 1) (41).

The screening method involved anaerobic fermentation by soil microorganisms, and then the tubes were sniffed to detect the production of isoamyl alcohol. A bacterium that passed the primary screen was instead found to produce butyl alcohol and acetone, which led Professor Perkin to wryly advise that the mix be thrown down the sink because “Butyl alcohol is futile alcohol” (42). Fortunately for England, the producing organism, *C. acetobutylicum*, was stored.

In 1916, Weizmann was summoned to a meeting with Winston Churchill, Lord of the Admiralty, who asked, “Well, Dr. Weizmann, we need thirty thousand tons of acetone. Can you make it?” Only several hundred milliliters of acetone had been made in Weizmann’s laboratory by that time, but the Nicholson gin factory was used for scale-up development, and despite some grumbling, additional large distilleries were soon converted to acetone production. Problems were later encountered in finding sufficient quantities of carbon as a source for the fermentation, but *C. acetobutylicum* had made a significant contribution to England at a critical time.

Prior to World War I, the Middle East had been under the control of Turkey for 400 years. Thus, when the war ended, negotiations were carried out between the British, French, and Arabs for redistribution of the Ottoman Empire. Thanks to *C. acetobutylicum*’s contribution to the British war effort, Weizmann had come to know many political leaders in England, including Cabinet member, and later member of the Foreign Office, Lord Balfour and Prime Minister David Lloyd George (43). Weizmann was a strong advocate for a Jewish homeland, and thus, *C. acetobutylicum* may have also played a role in the formulation of the Balfour Declaration and a change in the history of the Middle East.

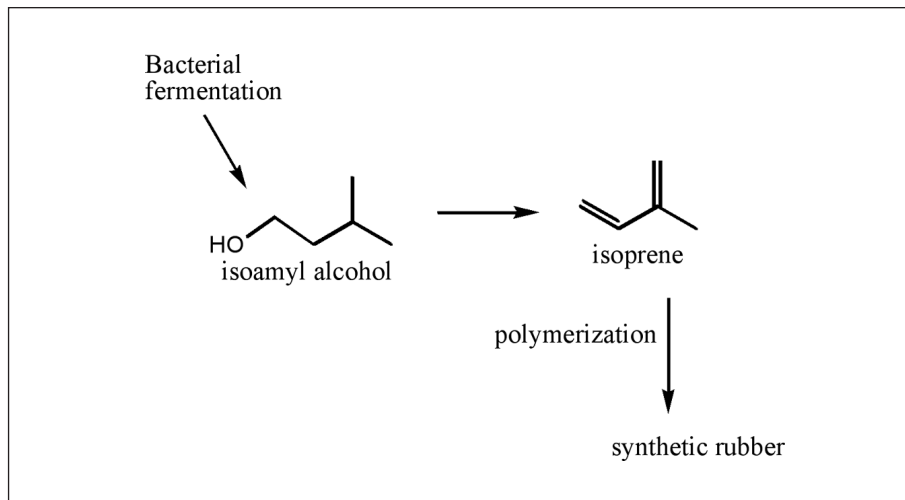


Figure 1. Weizmann's plan for producing synthetic rubber.

Discussion

The use of modern chemicals and engineering has allowed human encroachment into jungles, rainforests, and other areas previously guarded and maintained in their pristine state by bacteria, viruses, and parasites. The mosquito, among Earth’s most despised creatures, must be acknowledged for its role in aiding the microbes to safeguard these precious refuges (44). AIDS and severe acute respiratory syndrome, encountered only in recent years, may be but two examples of diseases caused by pathogens existing in undeveloped areas. Microbes have played many different roles in our history, and extending mankind’s habitat could conceivably provide opportunities for the emergence of microbes that will influence our future.

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