Chapter 2
Diseases That Changed History

In the first chapter, I discussed some of medicine’s heroes and their exploits. Now we will examine the villains—the diseases that afflict humankind, the maladies that despite our best efforts seem to reemerge just when we are about to declare victory. These diseases have influenced our history, geography, culture, religion, and language. We can only wonder what would have happened if some who died of these diseases had survived. And we can thank those who have had the passion, knowledge, and often courage to combat these killers.

If we were to consider only the present day and only the so-called developed world, we would list the common ailments and causes of death as cardiovascular disease, cancer, stroke, chronic lung disease, and a few others. Prevalent twenty-first century chronic diseases are hypertension, diabetes mellitus, degenerative joint disease (DJD), and obesity. If Galen or Thomas Sydenham could see this list, they would be shocked. In their day, the chief concern was infectious disease, which today—with the notable exception of the acquired immunodeficiency syndrome (AIDS)—we keep under some measure of control with sanitation, immunizations, and antimicrobials.

Why is there a profound difference between the diseases of history and the diseases of today? Until the twentieth century, the life expectancy at birth was less than 50 years. Consider that cardiovascular disease, cancer, stroke, and chronic lung disease are predominately diseases of older persons. In 1892, William Osler stated that coronary disease was “relatively rare” (Porter, p. 580). Stroke, often linked with hypertension, is uncommon in younger persons, and it was not until the end of the twentieth century that we ended widespread acceptance of the daily habit of smoking one or more packs of cigarettes, now the chief cause of chronic lung disease and lung cancer. Before the introduction of insulin by Banting and Best in 1922, many people with type 1 diabetes died without having had children. Death claimed most individuals before the onset of DJD, and obesity—a disease of affluent indulgence—was limited to the wealthy few.
Until recent times, the chief threats to human health were the epidemic diseases—plague, smallpox, influenza, and others—that were, to use the roots of the word *epidemic*, “upon the people.” They were what Martí-Ibáñez called the “collective” diseases, in contradistinction to the “individual” diseases we have today (p. 20). Most of the great epidemic diseases have always been with us. One notable exception is acquired immunodeficiency disease (AIDS), which seems to have emerged in sub-Saharan Africa in the twentieth century.

The great epidemics are part of the fabric of the history of civilization. Bubonic plague—the Black Death—killed more than a third of Europe’s population in the fourteenth century. At the time of the American Revolution, there was “a virulent smallpox epidemic of continental scope that claimed about 100,000 lives” [1]. Today, as we ponder the threat of evolving influenza viruses, we recall tales of the worldwide influenza pandemic of 1918.

In the pages that follow, I will discuss seven infectious diseases: plague, smallpox, malaria, syphilis, influenza, influenza, and tuberculosis. I am aware that I could well have added typhus, yellow fever, schistosomiasis, trypanosomiasis, and others. My choice has been guided by how much the great plagues affected the world we know today.

At the end of the chapter, I will discuss some ways in which the great plagues, and some other diseases as well, have been involved in specific events in history.

The Great Epidemics

**Plague**

Bubonic plague, aka the Black Death, left such an impact on humanity in late medieval times that the word *plague* has become a generic term for all widespread epidemic diseases.

First, a short review of microbiology: Bubonic plague refers to the “bubo”—an enlarged lymph node, most noticeable in the groin area (see Fig. 2.1). The caus-
ative organism is *Yersinia pestis*, previously named *Pasteurella pestis* in “honor” of Louis Pasteur. The classic carrier of the disease is the black rat, sometimes called the old English rat, although other rodents such as gerbils, rock squirrels, and prairie dogs can harbor the organism. Typically, the disease affects humans when a flea first bites an infected animal and then bites a person (Cartwright, p. 30). It can also be contracted by direct contact with the rodent. Hence, humans are most at risk for plague in settings where they live in close communion with rats or other rodents, such as in crowded city slums.

In addition to the bubonic form of the disease, there is pneumonic plague, a lung infection that, unlike the bubonic and septicemic variants, can spread from person to person by droplet infection—a much more effective means of transmission than waiting to be bitten by an infected flea—and that therefore is the most dangerous of all plague variants because it is the most contagious.

I begin the tale of plague epidemics in Greece during in the fifth century BCE, the era of Hippocrates. Thucydides describes a plague that occurred during the time of the Peloponnesian War, affecting Athens in 430 BCE and continuing for three years. According to Thucydides, conditions in Athens were so dire that “men, not knowing what would happen next to them, became indifferent to every rule of religion or law” [2]. Today, we are not certain whether the epidemic described by Thucydides was caused by plague, typhus, or even, as suggested by David, meliodosis [3]. Whatever the cause, the fifth century plague helped set the stage for the downfall of the ancient city-state.

Plague outbreaks occurred from time to time in the centuries that followed, spreading along sea routes and the ancient Silk Road. The next epidemic of epic proportions was the Plague of Justinian, occurring in the sixth century CE, during the reign of Roman emperor Justinian. The disease seems to have begun in Lower Egypt and spread to Palestine and then to the Eastern Roman Empire, notably the city of Constantinople, and port cities of the Mediterranean. Cartwright states that this plague “may have been the most terrible that has ever harrowed the world.” At the peak of the disease, 10,000 people died daily and ships were loaded with corpses, taken to sea, and abandoned (Cartwright, p. 17). The plague, occurring at the same time as the Gothic threat from the north, certainly contributed to the fall of the Roman Empire and the descent into the medieval dark ages, as though someone turned out the lights on commerce and scholarship of that time.

Next, we move to the Black Death of 1346–1352. This epidemic, extending from the British Isles to Russia, killed without regard for social status, age, or gender. Millions died (see Fig. 2.2). In the papal seat, Avignon, there were 400 deaths each day. Aside from the devastating mortality, the Black Death of the fourteenth century brought several noteworthy outcomes.

The first was *The Decameron*, written by Italian author Giovanni Boccaccio circa 1350–1353, a collection of 100 tales told by young men and women who flee from the epidemic of plague that struck Florence in 1348. They take refuge in a countryside villa for 2 weeks, passing the time telling stories, of which some bawdy tales of love are the best known.
The second legacy of the Black Death is the word quarantine (Fortuine, p. 227). The word comes from the Latin *quadraginta*, meaning 40. Venice and other Italian port cities kept arriving ships and their crews isolated for a set period. It may be that 40 days was considered to be the incubation period for infectious diseases, including plague. Alternatively, the 40 days may signify the 40 days and nights Jesus spent fasting in the wilderness.

There was a third and grim outgrowth of the fourteenth century Black Death. As noted in Chap. 1, the medieval era was a time of intense religiosity. Instead of seeking microorganisms as the cause of the plague (as we would do today), people sought villains or even those they defined as sinners whose transgressions might be the cause of everyone’s suffering. A handy target was the Jewish population, who were suspected of spreading poison to homes and wells. In Strasbourg, some 2000 Jews were hanged. In Freiburg, they were burned. Even Ambroise Paré (1517–1564) believed that there were “plague spreaders” (Ackerknecht, p. 17). Cartwright states, “Thus the Black Death intensified the medieval Christian tradition of the scapegoat—Jew and, by causing the migration of so large a number to the east and north of Europe, is linked to the pogroms of Imperial Russia and the gas-chambers of Auschwitz” (1972, p. 46).

In medicine, we saw a change in medical textbooks. Before the 1340s medical texts were all written in the language of medicine—Latin. But as a frightened population came to demand to know more about diseases such as plague, the texts came to be simplified and written in the language of the average person.

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*Fig. 2.2* Bubonic plague victims in a mass grave in Martigues, France (http://commons.wikimedia.org/wiki/File:Bubonic_plague_victims-mass_grave_in_Martigues_France_1720-1721.jpg)
In 1630, plague broke out in Venice and then spread north, eventually reaching the Tyrol and the Bavarian village of Oberammergau. Through a rigidly enforced quarantine, the residents of the small village escaped much—but not all—of the plague’s devastation. In desperation, the villagers vowed that, if God would deliver them from the plague, they would present a play depicting the life and death of Jesus every decade to symbolize their gratitude. Today, you can visit the Passionsspielhaus in the village (as I did in 1958), and once every 10 years, you can see the Oberammergau Passion Play (Major, 1936, p. 33).

The last major plague outbreak was the Great Plague of London (and Europe) that began in 1664–1665 (see Fig. 2.3). The disease began among the poor in port areas—likely sites for cohabitation of rats and humans. It then spread to involve all of London, where the death rate reached 7000 people per week in September 1665. Businesses closed as merchants, clergy, and physicians fled the city. Even Charles II and his court departed for Oxford. In an effort to combat the disease, fires—often scented with pepper or frankincense—were burned. Those who could afford to do so, including children, smoked tobacco as a preventive measure.

Some hold that the children’s rhyme “Ring Around the Rosie” describes the plague, and specifically the Great Plague of London in 1665, although that origin is disputed. For those who believe in the plague connection, “Rosie” is the red skin
rash of plague, “pocket full of posies” is scented material carried to combat disease, “ashes” may refer to the practice of burning bodies or else be an echoic allusion to coughing, and “all fall down” connotes dying.

In September 1666, much of London was destroyed in the Great Fire of London, an event that likely resulted in the death of many flea-infested rats and that was followed by a decline of the plague. As the city was rebuilt, thatched roofs were prohibited because they had proven to be a favored home for rats.

The history of plague has an interesting implication for today. In the twenty-first century, most of us are unlikely to suffer rat flea bites. However, *Y. pestis* is endemic among rock squirrels and other rodents in the southwestern United States, and sporadic cases occur among campers in this area. Theoretically, today’s greatest plague risk is not flea-borne disease, but droplet transmission—pneumonic plague. The development of this sort of person-to-person transmission is just what we fear today with “bird flu” and with the hemorrhagic fevers caused by the Ebola and Marburg viruses.

Smallpox

A viral disease classically causing a rash with fluid filled blisters, killing up to one-third of its victims and leaving many of its survivors blind and most scarred for life, smallpox remained a serious global problem until the latter part of the twentieth century (see Fig. 2.4).

Smallpox was so named to distinguish it from the great pox—syphilis. Evidence of smallpox has been detected in the mummy of Ramses V, who died in 1157 BCE. In the tenth century CE, Rhazes provided us with the first meaningful account of the disease and distinguished between smallpox and measles. The disease smoldered endemically in various areas for hundreds of years, killing the emperors of Japan and Burma in the sixteenth and seventeenth centuries, until being eradicated (we hope) in the latter half of the twentieth century.

Today, we think of smallpox as a historical curiosity. Within my lifetime, however, it was a reality. As a child and later as I prepared for international travel, I was vaccinated several times. Smallpox vaccination campaigns were common (see Fig. 2.5). As a young practicing physician, I administered vaccinations to hundreds of patients, always mindful that I should not vaccinate patients who had eczema or immunodeficiency.

One memorable encounter with smallpox occurred in 1963, when I was serving as a staff physician at the US Public Health Service (USPHS) Hospital at Norfolk, Virginia. At the time, the USPHS provided health care for a variety of constituencies, including merchant seamen employed on vessels registered both in the United States and abroad. One day we received a message that a ship flying a Liberian flag and carrying a seaman with smallpox was headed our way. In 1963, this was a perfectly possible scenario. Hastily, we vaccinated all hospital
Fig. 2.4  Female smallpox patient whose skin displayed the characteristics of late-stage confluent maculopapular scarring on her face, arms, and chest (http://commons.wikimedia.org/wiki/File:Female_smallpox_patient_-_late-stage_confluent_maculopapular_scarring.jpg)

Fig. 2.5  Poster created prior to 1979 promoting the importance of smallpox vaccination. This poster is part of a series of posters collected throughout the world on smallpox vaccination and/or measles immunization (http://commons.wikimedia.org/wiki/File:Poster_for_vaccination_against_smallpox.jpg)
employees whose vaccination status was not current. We evacuated a wing of the hospital to serve as an isolation unit and called for volunteers—with up-to-date vaccinations—to serve there.

Then one courageous young doctor stepped forward to remove the infected patient from the merchant ship at sea and escort him to our hospital. He set out early in the morning. We held our breath and stocked our hospital’s newly created isolation wing. Finally, just after supper, our doctor returned from the port in an ambulance, bringing with him the infected patient, who had a clear-cut case of adult chickenpox!

A dramatic historical impact of smallpox occurred at the time of the Spanish conquest of Mexico. In 1519, Hernán Cortés and several hundred adventurers landed in Mexico, bringing with them horses, dogs, armor, gunpowder, and the smallpox virus. The ruling Aztecs and their emperor Montezuma learned of the landing and kept track of the Spaniards’ progress. Cortés and the conquistadors advanced on the capital city, Tenochtitlan, aided by local tribes fed up with the Montezuma’s rule and by a legend that a winged god, Quetzalcoatl, would arrive on the east wind and subdue the Aztec rulers. The Aztecs saw Cortés, arriving on sailing ships from the east, as the arriving Quetzalcoatl, affording him mythical power in their eyes. Upon landing, the eventual conqueror was warmly welcomed.

The conquistadors, with superior firepower, captured Tenochtitlan (now Mexico City). But in June 1520, the Aztecs mounted a revolt and drove the Spaniards from the city. On the night when the Aztecs reconquered their city, a smallpox epidemic began. The results were fearful, especially because the Aztecs saw that the Spaniards, largely immune because of exposure in Europe, were spared by the smallpox epidemic.

The following year, Cortés returned with reinforcements, laying siege and eventually taking the city in August 1521. The victorious Spaniards found buildings filled with bodies covered with pox. It is fair to say that the conquest of Mexico—with a small force toppling an empire—can be ascribed to a convenient legend and superior firepower, but also to a smallpox epidemic inadvertently initiated by the invaders. By the end of the conquest of Mexico and the New World, more than a third of all the indigenous people had died of smallpox. The surviving native persons were subjugated by the Spaniards. Their culture and historical records were destroyed, to be replaced by a new language and a new religion.

Smallpox continued to play a role in American history. In Pennsylvania in 1763, the British fought a battle against tribes of Native Americans led by chief Pontiac. British officer Sir Jeffery Amherst, aware of the Indians’ susceptibility to smallpox, is alleged to have sent them blankets infected with the disease. Historians debate whether this actually occurred, but in the months that followed smallpox was reported in several tribes in the area.

Smallpox was endemic in the colonies at the time of the American Revolution. General George Washington, by coincidence, had apparently acquired immunity to smallpox during time spent in Barbados in his youth. Washington, however, recognized the value of maintaining the health of his troops and ordered arm-to-arm inoculation of his troops. In his biography of Washington, Ellis calls this “the most important strategic decision of his military career” [1].
Smallpox was eventually conquered by “disease control” measures. There is still no effective antimicrobial agent. As the incidence declined with mass vaccinations, public health officials adopted a policy of identifying and then controlling (isolating) infected individuals, continuing this practice over and over in developing countries until October 26, 1977. On that day, a 23-year-old cook, Ali Maow Malin, in the town of Marka, in Somalia, was designated by the World Health Organization (WHO) as having the world’s last naturally occurring case of smallpox.

Sadly, I must qualify the previous sentence with the phrase “naturally occurring” because, in our infinite wisdom, we have maintained laboratory samples of the smallpox virus, causing the legitimate concern today that these virus samples might be acquired and used by terrorists.

**Malaria**

Malaria, the word coming from the Italian *mal* (bad) and *aria* (air), was once thought to be caused by toxic vapors coming from swamps. Today, we know that it is not the “bad air” from damp areas but the mosquito vectors likely to be found there. In fact, because the *Anopheles* mosquitoes that carry *Plasmodia* seldom have a suitable habitat in cities, malaria is generally a disease of jungles, swamps, and forests (see Fig. 2.6).

Malaria has exerted a selective, Darwinian influence on the incidence of genetic diseases. One manifestation of this impact is in relation to sickle cell anemia. An autosomal dominant inherited disease, sickle cell anemia is caused by a mutation of the HBB gene related to a hemoglobin subunit. The abnormality affects some 2.5 million people in the United States, about 8–10% of the country’s African-American population, and also occurs in some non-black persons. A minority of those affected are homozygous for the sickle cell gene; these people have sickle cell disease and
often die young. Most are heterozygous and have the sickle cell trait; these people have significant resistance to malaria. A similar protection occurs in people with glucose-6-phosphate dehydrogenase deficiency who are susceptible to favism.

What appear to be malarial epidemics have occurred throughout history. Evidence is found in artifacts from ancient China, Egypt, Babylon, Palestine, and India. Malaria is discussed in several of the works of Hippocrates. The disease has been implicated as a cause of the decline of both ancient Greece and Rome. Malaria was recorded in farm areas on the outskirts of Rome in the first century BCE and persisted for five centuries. Cartwright states, “Possibly malaria, rather than decadent luxury imported from the East, accounted for the slackness of spirit which characterized the later years of Rome” (1972, p. 11).

A key chapter in the story of malaria was written in Central America with the construction of the Panama Canal. The first attempt to build a waterway was by the French in the mid-1880s. In this effort, some 5000 workmen died—most succumbing to malaria and yellow fever. When the United States later acquired the right to construct a canal, workmen found that the area was awash with manmade mosquito breeding grounds. The French had used moats and pools of water to protect themselves from umbrella ants, thereby creating veritable mosquito incubators. The Americans set about removing or applying insecticides to the pools of still water and using mosquito-proof netting both for protection and to isolate infected individuals.

Eventually, the Panama Canal opened in 1914, a triumph for both American engineering and public health measures. What’s more, as stated by Porter (p. 471), “This parasitological model opened up an astonishing new vision of disease etiology.”

A key player in the malaria drama was Scottish physician Sir Ronald Ross (1857–1932), who showed that the Anopheles mosquito carries the malaria parasite and who was awarded the 1902 Nobel Prize in Physiology or Medicine (see Fig. 2.7). Ross, whose passion was writing poetry, recorded his finding in verse:

Fig. 2.7 Portrait of Sir Ronald Ross (1857–1932), the British army surgeon, who, in 1897, described the breeding cycle of the Anopheles mosquito which transmitted the malarial parasite (Plasmodium species) (http://commons.wikimedia.org/wiki/File:Portrait_of_Sir_Ronald_Ross_(1857-1932)_Wellcome_L0035995.jpg)
I know this little thing
A myriad of men will save
O Death, where is thy sting?
Thy victory, O Grave?

The reader may recognize the last two lines as borrowed from the Bible: 1 Corinthians 15:55.

I wish I could report that the glory days of malaria ended with the identification of the parasite and its vector, but the story continues. The disease was present in the United States as late as the nineteenth century, accentuated at that time by the great westward migration and the Civil War. The armies of World War I experienced malaria in Europe, and Ackerknecht (p. 94) states that, “In World War II malaria was the main medical problem of military forces engaged in the Pacific as well as in the Mediterranean areas.” (see Fig. 2.8)

Today, more than 300 million people worldwide are infected with the malaria parasite, and up to 1–3 million die annually. The disease is most prevalent in sub-Saharan Africa, and most deaths are in children under age 5. Statistics are imprecise, at best, because most malaria cases and most deaths are undocumented.

![Fig. 2.8](http://commons.wikimedia.org/wiki/File:A_malaria_warning_sign_on_the_Anzio_front_in_Italy_advising_troops_to_cover_up_in_the_evening_to_avoid_mosquito_bites._10_May_1944._NA14700.jpg)
**Syphilis**

Syphilis, aka lues, is a favorite of medical historians for several reasons. The word syphilis evokes a literary image. It is a disease with truly protean manifestations, and Osler once stated, “The physician who knows syphilis knows medicine.” The disease has no respect for social class and has infected hundreds of well-known persons. And although its epidemiologic origins are debated even today, its early migration across national boundaries can be traced with reasonable certainty.

A sexually transmitted disease, syphilis is caused by a spirochetal bacterium, *Treponema pallidum* (see Fig. 2.9). With some exceptions such as congenital syphilis, the disease is spread from human to human by intimate sexual contact. Irish surgeon Abraham Colles (1773–1843), namesake of the Colles fracture, discussed the transmission of syphilis: “I may be told by some that men may contract syphilis by sitting in a public privy; to this I can only answer that I have never witnessed a single instance; nor did the late Mr. Obre, who had been for many years most extensively engaged in treating the venereal disease; for on asking him if he believed that the disease was propagated in this manner, he shrewdly answered that it sometimes was the manner in which married men contracted it, but unmarried men never caught it in this manner” (Strauss, p. 651).

In the late 1950s, an aging patriarch who had developed one of the early serologic tests for the disease gave my medical school lecture on the topic. This venerated physician (whose name I will not divulge) proclaimed, “Whenever a young man tells me that he contracted the disease from a public toilet, I tell him, ‘That is an awful place to take a woman!’” I suspect that this story would be considered inappropriate in a medical school classroom today, but it does make a point.

![Fig. 2.9 Treponema pallidum spirochetes using a modified Steiner silver stain (http://commons.wikimedia.org/wiki/File:Treponema_pallidum_01.png)](http://commons.wikimedia.org/wiki/File:Treponema_pallidum_01.png)
What about the word *syphilis*? Sipylus, sometimes spelled Siphylus, was first the hero of a love poem entitled *Metamorphoses*, written by the Roman poet Ovid in the first century CE (Gershen, p. 100). Later, in 1530, Veronese physician Girolamo Fracastorius (1483–1553) used the name in a poem entitled *Syphilis, sive Morbus Gallicus* (Syphilis, or the French Disease), thereby beginning the tradition of blaming others for the infection. In Fracastorius’ poem, the sad hero was punished for offending the sun god Apollo: “And first among them all, Syphilis, who had established the worship of the King with blood sacrifices, and raised altars to him among the mountains, manifested the foul sores in his own body … And from him, first to suffer it, the disease took its name and was called syphilis by the native race” [4].

In fact, we are not at all sure who the first person to suffer the disease was, and scholars debate various theories as to its origin. A favorite, but often challenged, story is the Columbian theory that the disease was contracted from the natives of the New World in 1492 by the sailors with Christopher Columbus and was brought home by them to Spain, along with tobacco, Indian corn (maize), six Indians, and other souvenirs of their New World adventures. Spaniard soldiers then carried the infection to Italy, where they infected some local girls, who in turn infected troops of French King Charles VIII as they laid siege to Naples in 1495. It is speculated that wily Neapolitans may have purposely sent infected prostitutes to carry the disease to the French invaders (Haubrich, p. 237).

Whatever happened in Naples, the French troops became carriers and they seem to have liberally shared the spirochetes across Europe. Thus, we better understand Fracastorius’ 1530 subtitle, “the French disease.” In various settings, syphilis has also been called the Italian disease, the Neapolitan disease, and the Spanish disease (see Fig. 2.10). The Russians have called it the Polish disease, the Japanese have called it the Chinese pleasure disease, and the Arabs have called it the Christian disease.

Of course, the Columbian theory raises the question as to the origin of the disease in the New World. In this regard, Ackerknecht writes, “A few South American scientists have attempted to trace the disease back even further and assumed that syphilis had originally been a disease of the South American llamas and that these llamas had infected the natives who had a great affection for these animals” (1972, p. 118).

Pre-Columbian theory skeptics hold that there is evidence of syphilis in the Bible, with the sins of the father visited unto future generations (Exodus 20:5). Other scholars believe that some writings attributed to Hippocrates describe the symptoms and signs of syphilis. Yet another intriguing theory holds that syphilis is a form of the *Treponemal* disease yaws, which evolved when introduced into a new ecological setting. The epidemiologic chronology of syphilis is still debated.

Those who contracted syphilis in the centuries following Columbus and Fracastorius were in august company. Some believe that the disease afflicted not just his sailors but Columbus himself. French King Charles VIII died of syphilis in 1498 at age 28 and was succeeded on the throne by several syphilitic rulers. The disease was not confined to continental Europe. It was contracted by English King Henry VIII and five of his wives.
Some believe that the great pox that infected many in Europe in the sixteenth century was a more virulent disease than we see today. Sexual morality of the time was lax, and prostitution was common. According to Bollet, one-third of the inhabitants of Paris were infected at that time, and Erasmus (1466–1536) stated that a nobleman who had not yet had syphilis was ignobilis et rusticanus [4]. In 1957, on my first trip to France, my host shared the aphorism that, “No Frenchman can live to the age of 60 without getting syphilis, cirrhosis, or the Legion of Honor.”

There is reasonable evidence that the following persons had syphilis or else believed they were infected with the disease [5, 6]:

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**Fig. 2.10** A representation of a man with the pox of syphilis. Attributed to Albrecht Dürer (1496). It is possible that this could be an early work of Durer, or just as likely the work of his master, Wolgemut. The 1484 refers to a planetary conjunction, not the date of the print. The appearance of Scorpio indicates that the author of the medical tract of which this is an illustration regarded the disease as the product of unfavorable planetary alignment. The two coats of arms to the left and the right are those of the city of Nürnberg (http://commons.wikimedia.org/wiki/File:DürerSyphilis1496.jpg)
Meriwether Lewis (of Lewis and Clark fame)
Franz Schubert
Lord Randolph Churchill (father of Sir Winston Churchill)
Guy de Maupassant
Vincent van Gogh
Paul Gauguin
Mary Todd Lincoln
Henri de Toulouse-Lautrec
Vladimir Lenin
Al Capone
Howard Hughes

In 1877, Guy de Maupassant seemed to take some pride in his affliction: “I’ve got the pox! At last! Not the contemptible clap … no, no—the great pox, the one Francis I died of. The majestic pox … and I’m proud of it, by thunder. I don’t have to worry about catching it anymore, and I screw the street whores and trollops, and afterwards I say to them, ‘I’ve got the pox.’” (Porter, p. 451).

Having contracted syphilis in his youth, Al Capone eventually reached the stage of neurosyphilis, which caused confusion and bizarre behavior during his time in Alcatraz.

There is another list of persons who may have had syphilis, but we are not quite sure whether all listed were infected. If they did, however, some familiar historical events may be explained. Some of the persons on this list are [5, 6]:

Queen Elizabeth I
Ivan the Terrible, of Russia
Wolfgang Amadeus Mozart
Napoleon Bonaparte
Ludwig van Beethoven
Edgar Allan Poe
Charles Darwin
Fyodor Dostoevsky
Edouard Manet
Oscar Wilde
Joseph Stalin
James Joyce
Adolf Hitler
Henry Miller
Idi Amin

As a historical note indicating the significance of syphilis in medicine at the time, the American Board of Dermatology and Syphilology was incorporated in 1932 and the name was not changed to the American Board of Dermatology until 1955.

With the widespread availability of penicillin following World War II, the eradication of syphilis became theoretically possible, just as we have eliminated naturally occurring smallpox from the world. But with human inclinations and behavior being what they are, as of today the eradication of syphilis must remain a much desired, but currently unattainable goal.
Influenza

Most of us have experienced “the flu,” a syndrome of fever, overwhelming malaise, headache, and muscle aches. Typically, the symptoms last a few days and then we begin to recover. You and I generally achieve our pre-flu healthy status within a week or two of the onset of symptoms. We consider influenza an unpleasant temporary illness and little more. The story seems to have been different in past centuries.

According to Ackerknecht, “The ancients never gave an unequivocal description of the disease” (1972, p. 74). The name influenza comes directly from a Latin word influencia, referring to influentia coeli, or heavenly influence. The word first appears in the History of Florence, written by Buoninsegni in 1580, in reference to the 1357 epidemic (Garrison, p. 187). The term was adopted into the English language in the eighteenth century; the French preferred the term grippe (Garrison, p. 404).

Over the centuries, influenza has tended to occur in pandemics, although a few of the early descriptions of “sweating sickness” were really something else. As with syphilis, there is an ethnocentric tendency to blame the illness on “them.” Hence, in Italy, it was called “the German disease,” in Germany “the Russian pestilence,” and in Russia “the Chinese disease” (Haubrich, p. 121). In the United States, we have experienced the Asian flu and Hong Kong flu. Nor have other living things escaped blame. Witness the terms “swine flu” and “bird flu.”

The epic tale of influenza includes what happened in 1918 and following (see Fig. 2.11). Bollet tells that the first recorded case of the pandemic was an army cook in Fort Riley, Kansas, followed by a number of cases among soldiers there, who were subsequently shipped to France, thus spreading influenza to the European continent (p. 105). As influenza spread worldwide, it claimed the lives of more than 25 million people, more than three times the number of individuals killed in World War I. Porter describes the 1918 influenza episode as “the most mobile and lethal pandemic the world has ever seen.” As one example, Porter (p. 483) describes what happened in Boston: influenza struck 1 person in 10, and those stricken had a 60% rate of mortality. Not only was the disease lethal, some survivors were afflicted with encephalitis lethargica, an inflammation of the spinal cord and brain.

Encephalitis lethargica, also called von Economo disease in honor of Austrian neurologist Constantin F. von Economo (1876–1931), seems to have been a one-of-a-kind encephalitis. It caused severe somnolence and often ophthalmoplegia, and many victims suffered postencephalitic Parkinsonism. During my time in the USPHS (1961–1964), I encountered several elderly individuals with Parkinsonism that they could trace to the 1918 influenza epidemic.

Influenza probably played a significant—perhaps decisive—role in the World War I. By the spring of 1918, the German army had more than one million battle-hardened troops on the Western Front. French and British troops were outnumbered and desperate. American forces had not yet arrived in sufficient numbers to turn the tide.
By May, the Germans were within artillery range of Paris. For them, victory seemed to require only a swift and decisive attack.

But the attack did not come. The German commander, General Erich Ludendorff, paused, and during this interval, more American troops arrived and the Allies gathered strength. The eventual German offensive failed, and the tide of the war changed.

Why did the German army choose to rest while within sight of Paris? Yes, the German army had driven west very rapidly and needed to secure their supply lines. History tells us that food for the German troops was in short supply. However, Ludendorff himself attributed the delay and eventual defeat to his troops’ having influenza, which the Germans called the *Blitzkatarrh* [7]. At one time, more than 2000 troops in each German division were incapacitated with influenza (Oldstone, p. 173).

Over the years, influenza has revisited us, causing annual outbreaks of greater or lesser severity. Some outbreaks have had curious features. The 1976 swine flu epidemic caused some persons to have Guillain-Barré syndrome, a phenomenon that I noted in three patients in my rural practice at that time. Antigenic drift of the virus’ genetic material has forced us to modify our influenza vaccine each year.
When I think of tuberculosis (TB), I think of Mimì, the tragic heroine of Puccini’s opera *La Bohème* (see Fig. 2.12); John “Doc” Holliday, the gunslinging dentist who fought beside the Earp brothers at the O.K. Corral; and the sanitorium in Thomas Mann’s *The Magic Mountain*. TB has always had a mystique, which would be engaging if the disease were not so debilitating and so often fatal.

We have found evidence of TB in mummies from ancient Egypt and in the bones of early Native Americans. Hippocrates described TB, noting that it was the most prevalent disease of his time. In the early 1800s, TB caused a quarter of all deaths in England; a century later, at the end of *World War I*, TB caused one sixth of all deaths in France. With the development of antitubercular drugs during the 1900s, the world dared to hope that the disease could be eradicated, but the emergence of drug-resistant strains has led to a resurgence of TB, prompting the WHO to declare a global health emergency in 1993.

When we think of deaths due to TB, we think of adults. Shryock (p. 96) offers some insight into why as he writes of life in eighteenth century America: “The dangerous decades in the life span were the first, the third, and the fourth—so far as total deaths were concerned. In other words, individuals who survived the tenth year had relatively good prospects until they reached the twenties, when tuberculosis and other respiratory diseases began to take their toll.”

TB has been known by many names. Ancient Greeks called it phthisis, and later in England it was “the King’s evil” because of the belief that cures could follow the king’s or queen’s touch (see Fig. 2.13). In 1660, King Charles II touched 6725 subjects suffering from TB. The term “white plague” connotes the victims’ pallor, and “miliary tuberculosis” alludes to a radiologic appearance on the chest X-ray that is similar to millet seeds. Scrofula describes TB of the cervical lymphatics, *lupus vul-

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**Fig. 2.12** La Bohème from the Metropolitan Opera April 2014. *Source*: Bengt Nyman (http://commons.wikimedia.org/wiki/File:La_Bohème_5662.jpg)
garis (literally, the common wolf) is a term for disease of the skin, and *tabes mesenterica* is TB of the abdomen. A special type of skin TB is “prosector’s wart,” indicating that pathologists and anatomists occasionally contracted the disease from contaminated cadavers.

The organism, *Mycobacterium tuberculosis*, was described in 1882 by Robert Koch (1843–1910), earning him a 1905 Nobel Prize. Koch, however, subsequently tarnished his image with a misadventure that I describe in Chap. 11.

Fundamentally, TB was and is a disease of crowded conditions, often the case in urban settings, notably in neighborhoods populated by the poor. But because the illnesses of poor individuals are often not recorded, the roster of TB victims tends to be a list of history’s rich, famous, and talented. Here are some of the tubercular notables (although not all died of the disease) [8]:

- John Keats
- Albert Camus
- Frédéric Chopin
- Paul Gauguin
- Franz Kafka
- Washington Irving
- Edgar Allan Poe
- René Laennec
- Anton Chekhov
- Ulysses S. Grant
- Sarah Bernhardt
Simón Bolívar
Eleanor Roosevelt
Nelson Mandela

TB is mentioned often in literature and is found in the works of Sir Arthur Conan Doyle (himself a physician), Fyodor Dostoevsky, Charles Dickens, Kurt Vonnegut, John le Carré, Sylvia Plath, and Mark Helprin. Writing in his diary, Thomas Moore (1779–1852) described Lord Byron after his illness at Petras: the Romantic poet, regarding his image in a mirror, reflected, “I look pale; I should like to die of consumption. Why? Because the ladies would all say, ‘Look at that poor Byron, how interesting he looks in dying.’” (Strauss, p. 643). Writing of eighteenth and nineteenth century America, Shryock (p. 120) comments, “Contemporary novels, plays, and operas were so given to sweet-sad musings [about the manifestations of TB] that consumption may be said to have made a morbid contribution to art and letters.” By the end of the nineteenth century tuberculosis was widespread, and the Bayer Co. marketed its “wonder drug,” heroin, as a remedy for the debilitating cough seen with the disease.

American physician E.L. Kendig writes of his personal experience with the disease: “When, in 1942, I was called for active military duty, my chest roentgenogram revealed changes compatible with active pulmonary disease. I became a patient at the Trudeau Sanitorium.” He goes on to tell of care he received and how, at the time he wrote the article, he was age 85 and still playing tennis [9].

In the days before World War II, roentgenography was not as advanced as it is today. My father, born in 1899 and raised on a farm in Northwest Ohio (pay attention to this clue), had been a reserve officer in World War I. In the summer of 1941, he rejoined the military in the buildup that preceded the US entry into World War II in December of that year. He was sent to a US Army training camp in Biloxi, Mississippi, and later assigned to active duty. One day in October 1941, the commanding officer called Dad into his office. “Captain Taylor,” he said, “I am sorry to inform you that you have advanced pulmonary tuberculosis. You are hereby medically discharged from the Army. I am very sorry to have to give you this bad news.”

And so, a few months before Pearl Harbor, my father was sent home with his medical discharge. He worked until age 65 and then enjoyed 31 years of active retirement until he died after a fall at age 96. What was my father’s illness in 1941? In my opinion, offered in the grand tradition of retrospective diagnosis, Dad had histoplasmosis, which he contracted during his days as a farm boy working in chicken coops and from which he made a spontaneous and full recovery.

The Trudeau Sanitorium where Dr. Kendig was treated in 1942 is an important chapter in the history of TB. Edward L. Trudeau, a physician who himself developed TB, moved to the Adirondack Mountain community of Saranac Lake, New York, and found that he returned to good health. There, in 1885, Trudeau built a sanitorium that emphasized rest, relaxation, and fresh air. Many patients used the “cure chair”—a cross between a hospital bed and chaise lounge. Also, some patients were treated by artificial pneumothorax to collapse infected lung tissue, a popular remedy of the time. By the mid-twentieth century, the name Saranac Lake had become synonymous with TB treatment.
This brings me to my own personal story. In the summer of 1954, at age 18, I accepted a job at a summer camp on the shores of Upper Saranac Lake, very near to Saranac Lake Village. To my parents, this meant that I was going to the country’s epicenter of TB! My family feared for my health and worried all summer while I enjoyed the camp activities and the clean mountain air. I did not contract TB, heard virtually nothing about the sanitorium while I was there, and later learned that 1954 was the year in which the sanitorium closed, subsequently to become the home of the American Management Association.

Today, we risk complacency with TB, while each year the case rates rise when they should be falling. The reasons include drug-resistant organisms, the increasing number of immunocompromised individuals in the community, and uncontrolled immigration to the United States. In the words of Dr. Kendig, “And remember, the great white plague is back” [9].

Selected Short Tales of Times When Disease Influenced History

So far in this chapter, I have discussed some of the major infections that have plagued humankind since ancient times, recurring from time to time to influence what we read in history books. This section describes some specific instances in which disease shaped events, beginning in medieval times and ending with decisions at the end of World War II.

Black Death: One Positive Outcome

Above, I discussed plague, which ravaged Europe in the fourteenth century. At that time, England was hard hit, especially since the disease incidence was rising just when manpower was needed to tend crops in the fields. Also at that time, England and France were engaged in one of their seemingly perpetual wars.

Because of the deaths of so many young men on both sides of the channel and the need for the able-bodied survivors to cultivate the crops, France and England entered into a truce on May 2, 1349. Hostilities did not resume until September 1355, as the plague was waning in both counties (Cartwright, p. 41).

Yellow Fever and Slavery in America

The yellow fever virus was one factor actually increasing the importation of African slaves following the Spanish conquest of the New World in the sixteenth century. The virus came to America from Africa aboard ships bringing trade goods and often
slaves. Indigenous peoples, lacking prior exposure to the disease, died in large numbers, leaving a shortage of workers in the fields and mines. In contrast, the imported African slaves seemed to have relative resistance to the disease.

The landlords and mine owners did what they considered the only logical thing: They increased the number of imported African slaves, thereby expanding the slave trade in the New World (Oldstone, p. 4).

Scurvy and Captain Cook

In Chap. 1, I told of James Lind and his 1753 publication of *A Treatise of the Scurvy*. Despite Lind’s research, which included several types of therapy in addition to citrus, the British Admiralty seemed to yawn at his findings, at least initially.

One person, however, did not. Captain James Cook, on his historic 1772–1775 voyage to the South Pacific, provided each of his seamen with a ration of lemon juice. On this trip, Cook and his ship HMS *Resolution* visited Tahiti, Easter Island, and the Friendly Islands. The *Resolution* remained free of scurvy during the three-year voyage, undoubtedly contributing to the success of the endeavor. However, as reported by Inglis (p. 115), the Admiralty “remained unimpressed” with antiscorbutic prophylaxis.

Syphilis and Captain Cook

On his third and final voyage, Captain Cook commanded the HMS *Discovery*. During the years 1776–1779, this ship and her crew visited the Hawaiian Islands and the west coast of North America. The Hawaiian Islands had escaped the attention of seagoing explorers until 1778, when Cook and his crew landed there, becoming the first Europeans to do so. They brought with them syphilis, previously unknown in the Pacific Islands.

Over the next hundred years, syphilis, smallpox, and other diseases carried by visiting Europeans resulted in the deaths of up to 90% of the native Hawaiian population (Porter, p. 466).

As an ironic historic note, Cook returned to Hawaii in 1779. While docked in the harbor of Kealakekua Bay, some Hawaiians made off with one of the ship’s small boats. Cook and the crew could not ignore the theft and sought to retrieve the boat by taking hostage Hawaiian Chief Kalaniopu’u. A clash ensued, shots were fired, and Captain Cook was stabbed and clubbed to death by the angry Hawaiians—who unknowingly achieved some measure of revenge for the syphilitic epidemic inflicted upon them.
Typhus and Napoleon’s Russian Campaign

I have always believed that, in the 1812 Russian campaign, Napoleon Bonaparte’s army was defeated on its retreat from Moscow by winter and by the fury of the Russian forces. Cartwright (pp. 90–112) holds that this statement does not tell the whole story. The seeds of defeat were actually sown in the outbound journey. Typhus, plus hunger and war wounds, played important roles during the eastbound march, the battles themselves, and the sad trip home.

In June 1812, Napoleon left East Germany with an army of more than a half million men, double the number of troops in the Russian armies. As they marched toward Russia, they raced ahead of their supplies. Food and water shortages became serious problems for the huge army. On their way east through Poland, the French army contracted typhus, which would beleaguer them until their return to France.

By July 1812, there had been more than 80,000 typhus deaths among the soldiers, with 300 miles yet to travel to Moscow. By the end of July, Napoleon’s officers reported to him that illness and desertion had reduced his effective fighting force by half. By the time Napoleon reached Moscow, his army numbered less than 100,000 able-bodied men. Napoleon conquered Moscow, by then a devastated city, with no storehouses of food to feed his army. Some French reinforcements arrived, but Napoleon’s troops still faced continuing typhus, starvation, and the prospect of the fierce Russian winter.

On October 19, 1812, some 95,000 bedraggled troops began the trip home. As they marched west, they were harassed by Russian troops and suffered the effects of food shortages, the winter snows, and the ever-present typhus. Men died and were left along the road. In December 1812, the original army of a half million men was reduced to about 25,000; most of these did not live to return to France.

Perhaps without the typhus deaths, Napoleon’s Russian campaign might have survived the food shortages, the battles, and the snow. We can only wonder what might have happened if typhus had not infected the eastward-bound French troops.

Measles and Its Travels

As if the South Sea epidemics introduced by Captain Cook and other sailors who followed were not enough, another plague arrived just over a century later. In October 1874, England annexed the Fiji Islands. Early the following year, the HMS Dido docked at the islands, and her crew brought measles (Oldstone, p. 73). High fever and rash became widespread (see Fig. 2.14).

Within the lifetimes of today’s senior physicians and nurses, we considered measles—along with mumps and chickenpox—to be one of the “usual childhood diseases,” conveniently abbreviated on medical histories as UCD. These diseases were usually minor childhood events, something to have and “get over” and then be blessed with lifelong immunity. Today very few young and middle-aged physicians have ever seen a case of measles.
But when the virus is introduced into an immunologically naive population, the results can be disastrous. Virtually everyone in the Fijian population contracted the disease. Affected persons sought relief from high fevers by immersion in the ocean. Some of those who contracted the disease survived to enjoy future immunity. Eventually, up to 40% of the native Fijian population died. From Fiji, the disease spread from island to island in the South Pacific, in each instance recreating the picture of suffering and death.

**Hemophilia, Queen Victoria, and the Russian Monarchy**

Hemophilia A is well known as the curse of the Romanov family. The disease is a sex-linked genetic disorder involving a single gene on the X chromosome. Women with this genetic heritage rarely develop hemophilia but can pass the disease on to their sons. How did hemophilia come to afflict the royal family of tsarist Russia?

In Europe, it has long been the custom for royal families to marry their offspring to other royals. This forms handy alliances and presumably may forestall future armed conflicts. One such union was the 1894 marriage of Nicholas II, Tzar and Emperor of All the Russians, and Alexandra, the granddaughter of Victoria, Queen of Great Britain. Alexandra unwittingly introduced the hemophilia gene into the Romanov line.

Nicholas and Alexandra had one son, Alexei (born August 12, 1904), who developed hemophilia. Repeated bleeding episodes nearly caused Alexei’s death on several occasions. In desperation, the frightened parents invited into their home the mystic Grigori Rasputin, sometimes called the “evil monk,” who perhaps used hypnosis to calm the frightened child during bleeding episodes. Before long, Rasputin’s power in the royal household increased, causing concern and resentment in the *Duma* and among the public.
It is logical to speculate that Nicholas II was distracted from his royal duties by his concern for his son while his subjects feared the influence of Rasputin, factors that helped set the stage for the Russian Revolution of 1917, which ended the house of Romanov.

In the end, Rasputin was murdered in 1916 in a very thorough manner. He was first poisoned, then shot, then beaten, and eventually drowned in a river. The Romanov family was massacred in July 1918. In 1981, the Russian Orthodox Church canonized Nicholas II and his family as saints.

**Hypertension, Heart Failure, and the Grand Alliance**

The last story in this section highlights an important concept: As we look at the great plagues that have occurred over past millennia, it is easy to believe that all the diseases that have shaped civilization were those that affected populations or even families. Some diseases that affect history are “individual diseases.”

As the impact of epidemics has waned (at least for now), the diseases of aging have commanded our attention, and illness affecting a single key individual—notably a political leader—can also have a profound effect on entire nations. In world history, pivotal episodes occur when degenerative disease strikes an influential leader at just the wrong time. Let us look at one such instance.

As World War II ended, the leaders of the Allied powers—Winston Churchill, Joseph Stalin, and Franklin D. Roosevelt—met at Yalta in February 1945 to plan what would happen to the various warring countries in the years to follow. Although not all agree, many hold that Roosevelt was mentally impaired at the meeting and that he made errors in negotiation that he would not have made had he been in good health.

We know now that Roosevelt had chronic hypertension, in addition to suffering the residual effects of polio. By March 1944, a Bethesda Naval Hospital examination revealed that he had hypertension, heart disease, left ventricular failure, and bronchitis. Remarkably, no one seems to have told the president of his failing health.

By the time of the Yalta Conference, his blood pressure had climbed to alarming heights. Recall that, in 1945, we lacked the panoply of antihypertensive medications we have today. Roosevelt had lost weight and appeared weak. We believe that he had severe hypertensive cardiac failure with cachexia and, notably, hypoxemia with impaired cerebral oxygenation.

At the conference, Roosevelt failed to assert himself in his dealings with the robust and aggressive Stalin (see Fig. 2.15). Thus, the agreement reached allowed Stalin later to seize Manchuria, gain control of Poland, and establish buffer states to protect his homeland.

A month later, Roosevelt’s blood pressure was 240/180 mmHg. Still, his physicians did not worry the president with details of his illness, perhaps because there was little they could do for him.
On April 12, 1945, just two months after the Yalta Conference, Roosevelt died of a cerebral hemorrhage. His personal physician reported that the fatal stroke had come “out of the clear sky” [10].

For readers who wish to learn more about what happens when disease affects influential persons, I recommend the book by Robins and Post, *When Illness Strikes the Leader: The Dilemma of the Captive King* [11].

**References**

White Coat Tales
Medicine’s Heroes, Heritage, and Misadventures
Taylor, R.B.
2016, XXIX, 328 p. 129 illus., 91 illus. in color., Softcover
ISBN: 978-3-319-29053-9