# Epidemics and Society

## FROM THE BLACK DEATH TO THE PRESENT

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CHAPTER 2

# Humoral Medicine

## The Legacy of Hippocrates and Galen

An important aim of this book is to examine the meaning of "scientific medicine" in a variety of incarnations. But the place to begin is antiquity, which produced the first embodiment of a rational medicine that lasted from the fifth century BCE until the end of the eighteenth century as the dominant—though not exclusive—medical paradigm. It originated in Greece and was associated with Hippocrates (ca. 460 to ca. 377 BCE), the so-called father of medicine, whose collection of some sixty works, known as the Hippocratic corpus and almost certainly written by multiple hands, announced a radically new idea of medicine.

Of these works, some are especially well-known, such as the "Hippocratic Oath"; *On the Sacred Disease; On Human Nature; Epidemics;* and *Airs, Waters, Places.* A first aspect of the works is their variety. The corpus includes a collection of aphorisms, case histories, lecture notes, memoranda, and writings on every aspect of the medicine that was practiced at the time—such as surgery, obstetrics, diet, the environment, and therapeutics. But all of the Hippocratic writings stress a central claim: that disease is a purely naturalistic event that can be explained only by secular causes and that can be treated only by rational means. Hippocrates espoused a philosophy of medicine that resolutely insisted on viewing both the macrocosm of the universe and the microcosm of the body as governed exclusively by natural law.

Hippocrates rejected an alternative view of disease that preceded him, that continued alongside his practice, and that has persisted to our own day. This is the supernatural interpretation, which takes two dominant forms: the divine and the demonic.

## Divine Interpretations of Disease

The divine theory of disease asserts that illness is a punishment sent by an angry god as chastisement for disobedience or sin. Four examples of the divine interpretation from four different eras illustrate its enormous influence on Western culture.

### *The Bible*

The book of Genesis tells the story of the first humans, Adam and Eve, who were immortal beings inhabiting a garden free of disease, suffering, and the need for work. Everything changed when they yielded to the blandishments of the serpent. In disobedience to God's command, they tasted the forbidden apple from the tree of the knowledge of good and evil. This sin marked humanity's fall from grace and innocence. Angered by their disobedience, God expelled Adam and Eve from the garden of Eden forever

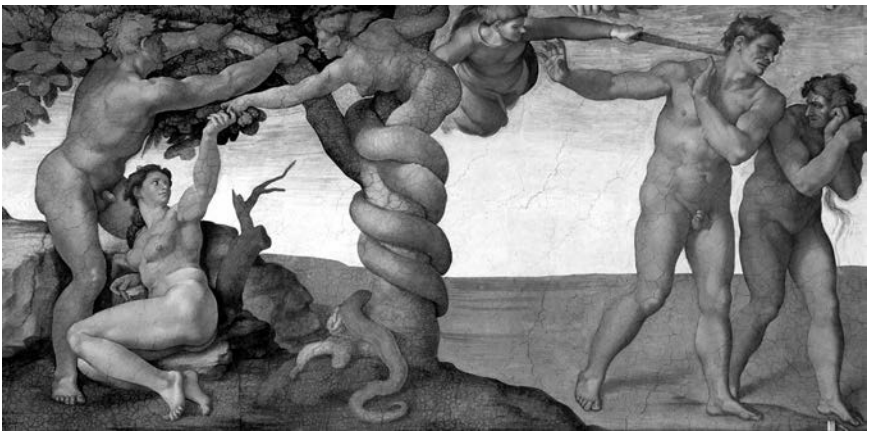

Figure 2.1. In the book of Genesis, God expels Adam and Eve from the garden of Eden and decrees they will suffer disease as part of their punishment for eating the forbidden fruit. Michelangelo, *The Fall of Man and Expulsion from the Garden* (1509–1510). Sistine Chapel, Vatican City.

and as punishment ordained that they suffer disease, hard work, pain during childbirth, and finally death. Diseases, in other words, were the "wages of sin" (fig. 2.1).

With specific reference to epidemic disease, the book of Exodus provides an interpretation fully in line with Genesis. Long after the Fall, God's chosen people, the Israelites, lived in bondage in Egypt. Through Moses and Aaron, God told Pharaoh to free his people, but Pharaoh refused. In response, God visited a series of terrible plagues upon the Egyptians. Plagues, in other words, were divine punishment for defying the will of God.

A further important biblical expression of this view of epidemic disease is Psalm 91, which again expresses the idea of pestilence as humanity's chastisement by an irate divinity. This psalm is especially significant historically because it became the great plague text that was read out from Christian pulpits across Europe during epidemic visitations. It simultaneously explained the catastrophe and provided hope:

> Thou shalt not be afraid for the terror by night; nor for the arrow that flieth by day;
> Nor for the pestilence that walketh in darkness; nor for the destruction that wasteth at noonday.
> A thousand shall fall at thy side, and ten thousand at thy right hand; but it shall not come nigh thee.
> Only with thine eyes shalt thou behold and see the reward of the wicked.
> Because thou hast made the Lord, which is my refuge, even the most High, thy habitation;
> There shall no evil befall thee, neither shall any plague come nigh thy dwelling.
> For he shall give his angels charge over thee, to keep thee in all thy ways. (Ps 91:5–11 King James Version)

The message is crystal clear: if you renounce sin and trust in the Lord, you need have no fear of plague, which afflicts only the wicked.

### *Homer's* Iliad

Another expression of the divine interpretation of disease in Western culture is the opening scene of Homer's epic poem *The Iliad,* which narrates the climax of the Trojan War. The poem begins with the anger of Achilles,

the greatest of the Greek warriors, whose concubine had been taken by the Greek king Agamemnon. Enraged, Achilles withdrew from combat and sulked in his tent. His friend, a priest of Apollo, tried to intervene by beseeching Agamemnon to right the wrong and return the woman. But Agamemnon rebuffed Apollo's priest and then mocked and threatened him. What followed is a terrifying plague scene. As the early lines of the poem announce, the priest withdrew from the Greek commander and then prayed to Apollo for revenge:

> "Hear me," he cried, "O god of the silver bow. . . . If I have ever decked your temple with garlands, or burned your thigh-bones in fat of bulls or goats, grant my prayer, and let your arrows avenge these my tears upon the Danaans."
>
> Thus did he pray, and Apollo heard his prayer. He came down furious from the summits of Olympus, with his bow and his quiver upon his shoulder, and the arrows rattled on his back with the rage that trembled within him. He sat himself down away from the ships with a face as dark as night, and his silver bow rang death as he shot his arrows in the midst of them. First he smote their mules and their hounds, but presently he aimed his shafts at the people themselves, and all day long the pyres of the dead were burning.[1]

Thus the god Apollo scourged the Greeks with plague for refusing to heed his priest.

### *The Perfectionists*

A third example is more recent—that of the nineteenth-century divinity student John Humphrey Noyes (1811–1886). While attending the Yale Theological Seminary in the 1830s, Noyes reasoned that if diseases are the wages of sin, then logically there is a practical remedy. He and a group of friends agreed that they could reclaim immortality and immunity to disease by renouncing all sin. Appropriately calling themselves the "Perfectionists," they founded a sinless community—first in Putney, Vermont, and then at Oneida in New York State. Their quest for immortality was prominent in the history of American utopian communities, along with their unusual social practices, including what they called "complex marriage" and mutual criticism,

in which they vigilantly watched each other and provided earnest rebukes for moral backsliding.

The Oneida Community was founded in 1848 in accordance with socialistic principles. By the 1890s, however, it had declined and reorganized as a joint-stock company, which still produces pottery and silverware but no longer makes special claims of moral rectitude. Despite their hopes, none of the founding members attained immortality, and the last original member died in 1950. Perhaps they lowered their standards, or perhaps the concept was misguided from the outset.

Noyes's Oneida experiment was clearly based on the idea of disease as divine punishment for transgression. His view of pestilence implies a law-governed cosmos. Noyes was logically coherent in arguing that disease exists for an intelligible reason and that there is therefore a corresponding therapeutics, which he believed was repentance and right behavior.

### *The Jerry Falwell Phenomenon*

An even more recent version of the divine interpretation of disease is the example of Jerry Falwell. This Southern Baptist evangelical preacher from Virginia was a pioneer of the megachurch phenomenon and the founder of the Moral Majority movement. Falwell greeted the onset of the HIV/AIDS epidemic with the tirade that the epidemic was God's punishment for the sin of homosexuality. He declared, however, that it was not merely homosexuals who were being punished by an irate God, but rather a whole society that had sinned by tolerating them in its midst. In his most famous hate-filled words, he opined that "AIDS it not just God's punishment of homosexuals, it is God's punishment for the society that tolerates homosexuals."[2]

## Demonic Views of Disease

The divine interpretation of disease is magical but obedient to a logic flowing from its supernatural premises. There is, however, a variant of the supernatural view of disease that is more capricious, arbitrary, and unpredictable. This view is what some have called the "demonic theory of disease." This idea postulates that the world is populated by powerful, arbitrary, and evil spirits that cause disease through the exercise of their malign influence. The spirits may be evil people, such as witches or poisoners; the disembodied spirits of the dead when they return to haunt the living; superhuman beings; or even the

devil himself. We will see this view—that epidemic diseases are not natural or logical events but rather diabolical plots—recurring throughout the book. In the seventeenth century on both sides of the Atlantic the idea of such occult crimes committed by witches famously gave rise to scapegoating and witch-hunting to track down and punish the guilty. In Massachusetts this view triumphed in the 1690s at Salem, as Arthur Miller vividly recounts in his play *The Crucible.* In Europe, too, the demonic idea was clearly expressed by Martin Luther in the 1500s, who declared, "I should have no compassion on the witches; I would burn all of them."[3]

As a variant, a person could be deemed to be innocent but temporarily "possessed" by an evil spirit. In this case, the therapeutic indication was to cast out the devil through exorcism. Healers pursuing this logic invoked magic and incantations, relying on concoctions, chants, sacred rites, and spells. In European history, an illustration of this idea was the concept of the king's touch to cure disease. King Charles II of England, for example, administered the touch to nearly one hundred thousand people during the mid-1600s. Less illustrious healers chanted, recommended sacrifices, or furnished magic charms to ward off malevolent spirits. Alternatively, they suggested taking flight when disease struck a community or seeking such influential allies as the Virgin Mary or Christian saints.

## The Hippocratic Breakthrough

The Hippocratic breakthrough in fifth-century Greece contrasts with the two supernatural interpretations of disease—the divine and the demonic. This naturalistic, secular view flourished in the century of Pericles (ca. 495–429 BCE). One can find it in the famous account of the Peloponnesian War by Thucydides where he recounts the Plague of Athens, which recent DNA research suggests was caused by typhoid fever. Thucydides describes the epidemic as a purely natural event in which the occult, the supernatural, and the divine play no part.

Most dramatic is the discussion by Hippocrates of what he terms the "sacred disease," which is probably what modern physicians diagnose as epilepsy—a condition that, perhaps more than any other, resembles possession by a demon. But Hippocrates stresses that even this so-called sacred disease has purely naturalistic causes:

> [This disease] appears to me to be nowise more divine nor more sacred than other diseases, but has a natural cause . . .

> like other afflictions. Men regard its nature and cause as divine, from ignorance and wonder. And this notion of its divinity is kept up by their inability to comprehend it and the simplicity of the mode by which it is cured. . . . The quotidian, tertian, and quartan fevers, seem to me no less sacred and divine in their origin than this disease, although they are not reckoned so wonderful. . . .
>
> They who first referred this malady to the gods appear to me to have been just such persons as the conjurors, purificators, mountebanks, and charlatans now are, who give themselves out for being excessively religious, and as knowing more than other people. Such persons, then, using the divinity as a pretext and screen of their own inability . . . to afford any assistance, have given out that the disease is sacred. Adding suitable reasons for this opinion they have instituted a mode of treatment which is safe for themselves, namely by applying purifications and incantations, and enforcing abstinence from baths and many articles of food which are unwholesome to men in diseases. . . . And they forbid to have a black robe because black is expressive of death; and to sleep on a goat's skin or to wear it, and to put one foot upon another, or one hand upon another; for all these things are held to be hindrances to the cure. All these they enjoin with reference to its divinity, as if possessed of more knowledge, and announcing beforehand other causes so that if the person should recover theirs would be the honor and credit; and if he should die, they would have a certain defense, as if the gods, and not they, were to blame.[4]

This was a monumentally important conceptual breakthrough—the cognitive foundation on which a scientific medicine was built. Under its naturalistic influence, healers abandoned incantations, spells, and sacrifices; they eliminated exorcism; and they renounced the appeasement of the gods. This momentous step in intellectual history and consciousness was memorably assessed in the 1940s by the epidemiologist Charles-Edward Winslow: "If disease is postulated as caused by gods, or demons, then scientific progress is impossible. If it is attributed to a hypothetical humor, the theory can be tested and improved. The conception of natural causation was the essential first step. It marks incomparably the most epochal advance in the intellectual history of mankind."[5]

CHAPTER 4

# Plague as a Disease

## The Etiology of Plague

The "etiology" of a disease refers to its origins—the path it follows to afflict human beings. Plague has a complicated etiology normally involving four protagonists. The first is the pathogen itself—the oval bacterium originally named *Pasteurella pestis,* but now universally termed *Yersinia pestis*. It was discovered simultaneously in 1894 in Hong Kong by Alexandre Yersin, a Swiss student of Louis Pasteur, and by the Japanese physician Shibasaburo Kitasato, a protégé of Pasteur's rival Robert Koch.

By 1898 Paul-Louis Simond discovered that, in addition to the bacterium, two vectors were normally responsible for conveying the disease to humans. These were commensal rodents, especially rats, and their parasitic cargo of fleas. Simond's insights were largely ignored until they were confirmed a decade later, as we will see in Chapter 16, by the exhaustive investigation conducted by the Indian Plague Commission into the epidemiology of the disease. The findings were conclusive for the third pandemic on the subcontinent, but both Simond and the commission made the mistake of assuming that the mode of transmission that prevailed in the third pandemic was the same in all epidemics of the disease. Since this view became the orthodox understanding of plague, the result was a misunderstanding of the Black Death. So much of the epidemiology of the second pandemic was incomprehensible in terms of the rat-flea nexus that, as we will see, it even led to skepticism that the disaster that swept Europe for four centuries after 1347 was plague at all.

There is, however, a universal consensus that plague epidemics begin as "epizootics"—unnoticed epidemics in permanent animal reservoirs of the disease. Especially important are wild rodents—marmots, prairie dogs, chipmunks, and squirrels in their burrows, where underground disasters unknown to humans take place. Plague, therefore, is best understood as a disease of animals by which humans are afflicted by accident and by way of exception. Human involvement can begin if hunters invade the reservoir of infection, contracting the disease directly while skinning their prey and providing a portal of entry for the bacterium to their bloodstream through a cut or other lesion. Warfare, ecological disaster, and famine can multiply the numbers of displaced persons entering the rodents' habitats. Alternatively, environmental changes, such as flood or drought, can send the animals scurrying over long distances closer to human settlements and above all bringing them into closer contact with the peridomestic rat. Pivotal in the second pandemic was the black rat or "ship rat," *Rattus rattus,* which lived in close proximity to humans and with whom it shared the same dietary preferences.

The bacterial exchange from wild rodent to domestic rat, from rat to rat, and from rat to human is mediated by the final plague protagonist—the flea. Two species are deemed to play key roles. The first is the so-called Oriental rat flea, *Xenopsylla cheopis,* which is naturally parasitic on warm-blooded animals and is a highly efficient vector for bubonic plague, enabling it to cross the species barrier from rodent to *Homo sapiens.* The other is the widespread "human flea," *Pulex irritans,* which does not colonize rodents but only people. It provides transmission from person to person.

In a single blood meal a flea of either species sucks up a quantity of blood equal to its own weight—an amount that contains millions of bacteria. Once engorged with blood and *Y. pestis,* the infected flea does not survive. The bacilli obstruct a valve regulating the movement of food into the insect's stomach, so the flea slowly dies of starvation and dehydration. This foregut blockage is consequential not only in the life of the flea, but also in disease transmission to humans. By causing the flea to regurgitate ingested blood mixed with plague bacteria, the obstruction ensures that each bite is infective. It also causes the flea to feed ravenously and repeatedly in a frenzied bid to survive. Before dying, an infected *X. cheopis* is a lethally efficient vector.

Furthermore, when a rat carrying infected fleas in its fur sickens and dies, the fleas leap to the warm body of another mammal—whether rodent or human being. The fleas' sensors—which are highly susceptible to warmth, vibration, and carbon dioxide—enable fleas to locate new hosts; their famous

jumping prowess enables them to make the transfer successfully; and their ability, when they are uninfected, to wait for six weeks between blood meals explains the erratic appearance of cases during the course of an epidemic.

*Xenopsylla cheopis* demonstrates a pronounced preference for rats, and it moves to humans only in the absence of surviving rodents. For this reason, the mass die-off of a rat colony leads to the sudden availability of swarms of famished fleas to parasitize humans in the absence of their preferred alternative. This behavior explains the explosiveness of plague epidemics. A graph of plague mortality and morbidity exhibits a steep spike at the outset rather than the bell-shaped curve characteristic of most epidemic diseases.

After the crossing of the species barrier between rats and humans, foci are established when infected men and women share their fleas and their disease with family members and neighbors. Plague then begins, not as a disease of isolated individuals, but of households, neighborhoods in cities, and entire villages in rural areas. Living conditions, and especially population density and hygiene, are decisive. Overcrowding, with numerous individuals pressed close together in a single room and perhaps whole families sharing a bed, greatly facilitates the exchange of fleas. As the plague spreads, particular moments are especially dangerous, such as the laying out of and final attentions to the dead. As a corpse cools, the fleas infesting it grow desperate to escape to the next warm body.

To give rise to an epidemic, the early foci in Africa and Central Asia needed links to wider networks of contact, trade, religious faith, and commerce. One such link involved the garments of the sufferers. An item of clothing in the early modern world was precious, so the clothes of the dead, as well as bed linens, were reused by others or packed in crates and sold at markets and fairs, often with fleas still alive among the folds. Certain professions also came into regular and direct contact with the sick, the dying, and the dead, as well as with their ectoparasites. Street vendors, physicians, priests, gravediggers, and washerwomen were at serious risk in time of plague, and they conveyed disease from place to place as they moved about their duties. Other key figures in the transmission of plague were millers and bakers, because grain attracted rats.

Monasteries also played a significant part in the first pandemic and the late medieval outbreaks of the second, explaining the ability of the disease to decimate the thinly settled countryside as well as urban centers. Monasteries acted as nodes in the grain trade, linking settlement to settlement and village to village; they were substantial communities of people living in close quarters; and during times of disaster monasteries often served as places of

refuge for people fleeing plague-ridden localities. On monastic grounds the healthy, the ill, and the bearers of infected fleas commingled. In such a context the flea readily established circuits of transmission for plague.

Fleas are severely restricted in their range, however, as opposed to rats, which are wonderful travelers. They hide in shipments of grain and are transported overland in carts or down waterways on barges and boats. But the rat also went much farther afield—by sea. Infected rats climbed aboard ships via ropes and gangplanks and were lifted aboard in crates of wheat and rice. In this way, shipping was essential to the spread of plague over long distances; this helps to explain the epidemiology of the disease—that is, its tendency to arrive in a country by ship and then to move inland by road and river traffic. For the black rat, the Mediterranean was not a barrier but a highway.

Istanbul (known as Constantinople between 330 and 1453) was a vital hub of trade and disease. It linked the whole of the Mediterranean—overland via the Balkans and by sea to Venice, Naples, Corfu, Genoa, Marseille, and Valencia. Sometimes there was havoc at sea when plague destroyed entire crews, and ghost ships drifted on the waves. More frequently, however, a ship would dock, and its cargo of rats would disembark via the same hoists, ropes, and gangplanks that had first brought them aboard. At the same time infected passengers and crew would go ashore, together with their fleas. Procopius already noted in the sixth century that the plague "always took its start from the coast, and from there invaded the interior."[1]

Not surprisingly, then, the first indication of plague was frequently a dramatic die-off of rats in the streets. This onset of pestilence is dramatically apparent in various works of plague art, such as Albert Camus's novel *The Plague*. In this book the emergence of innumerable sick and dying rats in the streets of the Algerian city of Oran is the prologue to the epidemic disaster, which serves as a metaphor for evil as embodied in the rise of Nazism and fascism.

Similarly, the neoclassical painter Nicolas Poussin (1594–1665) included rats in his painting *The Plague at Ashdod* (1630) (fig. 4.1). The biblical book 1 Samuel relates how the Philistines triumphantly displayed the stolen ark of the covenant in their temple to the pagan god Dagan, thereby declaring the superiority of Dagan over the God of the Israelites. God punished the Philistines by scourging them with plague and destroying the city. To heighten the terror of the scene, Poussin prominently depicted rats on the streets of doomed Ashdod. The seventeenth-century painter understood that for the viewer, the mass appearance of rats aboveground was a familiar premonitory sign of plague and impending disaster.

Figure 4.1. In his painting of 1630 *The Plague at Ashdod* Nicolas Poussin included rats, which were known to be a premonitory sign of impending disaster. Musée du Louvre, Paris.

Twentieth-century scientific investigations have carefully confirmed the link between plague and rats. Archeologists have recovered the bones of rats at plague burial sites dating from the Black Death, and as already mentioned, the Indian Plague Commission extensively documented the rat-flea nexus and its role in the modern plague.

Until the turn of the twentieth century, however, the link between the rat and bubonic plague was not deemed to be causal. It was thought that the rat was infected before humans because of its low physical stature. With its nose close to the soil or the floor, the rat was more quickly susceptible to poisonous effluvia rising from the earth and to plague-infested dust underfoot. Suddenly, before people were stricken, rats began to appear in the streets and in the middle of rooms indoors. In a dazed condition and with uncertain balance, these rodents demonstrated no concern for their natural predators and enemies. Instead, in a frenzy of thirst, they desperately sought water until they lost their strength and collapsed. They died where they fell with telltale buboes on their necks, their limbs splayed, and rigor mortis upon them even before death.

Miasmatic theory provided an explanation, since this doctrine held that plague originated in the soil, rising slowly from it and progressively killing different animals as it reached the air they inhaled. Thus it was logical that rats, with their snouts to the ground, should fall victim first, and that humans, with their superior height, should be stricken only later. Such an etiology indicated that human plague followed the disease in rats but was not caused by it.

## Symptomatology and Pathology

Attention to the effect of a disease on the individual human body is not a matter of ghoulish curiosity. Epidemic diseases are not simply transposable causes of suffering and death. On the contrary, the history of each high-impact infectious disease is distinct, and one of the major variables is the specific manner in which it affected its victims. Indeed, a feature of bubonic plague was that its symptoms seemed almost purposefully designed to maximize terror; they were excruciating, visible, dehumanizing, and overwhelming.

After being bitten by an infected flea, a person experiences an incubation period varying from one day to a week, and then the classic symptoms of the disease appear, launching the first stage of bubonic plague. At the site of the flea bite, a black blister, or carbuncle, arises, surrounded by red pock marks. Along with the carbuncle, the infected person experiences high fever, shivering, violent headache, nausea, vomiting, and tormenting thirst, after which the second stage of the disease begins. Unlike malaria-transmitting mosquitoes, for example, fleas do not inoculate bacteria directly into the bloodstream but instead deposit them into the skin. As few as ten bacilli are now thought to be sufficient to produce an infection. The reason is a stealth mechanism, or "virulence factor"—the production of an enzyme that enables the bacteria to elude the body's defense mechanisms. Rapidly multiplying, *Y. pestis* invades the lymph system, drains into the regional lymph nodes nearest the infective bite, and causes the appearance of a bubo.

A bubo is an inflammation and swelling of a lymph node of the armpit, neck, or groin to form a hard mass sometimes as large as an orange beneath the skin. Its location varies according to the site of the infective flea bite, and it is not uncommon for more than one to erupt. The bubo is familiar as the classical symptom that appears almost infallibly and gives the disease its name as "bubonic" plague.

Buboes are a source of agony for patients. The sixteenth-century French surgeon Ambroise Paré explained that the bubo generates great heat and

causes a "pricking pain, as it were with needles, burning and intolerable."[2] Defoe reported in his *Journal of the Plague Year* that the pain caused by the bubo was so violent that some victims in London dove into the Thames to escape it—an observation that Paré corroborated, writing from Paris that patients there hurled themselves naked from their windows. In the more measured parlance of the modern physician, the inflamed and suppurating bubo is described as "exquisitely tender."[3] There is also a consensus that the body and all of its excretions—pus, urine, sweat, the breath—have an overpowering stench, as if putrefaction precedes the individual's demise. Surviving accounts by attendants in pesthouses during epidemics describe the intolerable smell of the bodies of the sufferers as the worst aspect of their employment. The historian Jane Stevens Crawshaw, for instance, thus summarizes Father Antero Maria's account of his experience at Genoa, where he served in the plague hospital in 1575:

> the sick within the *lazaretti* stank horribly—so much so that a single patient could render a room uninhabitable. He wrote that individuals in the *lazaretti* fled the company of others because of the smell and confessed himself to having hesitated many times before entering rooms—not, he says, for fear of infection but because the smell was so foul. This was made worse by the vomiting brought on by the illness. This, he said, was so disgusting that it turned the stomach. He recorded it as the most difficult aspect of the conditions in the *lazaretto*, too abominable to describe in words.[4]

Meanwhile *Y. pestis* bacilli—still "the most feared pathogen of the bacterial world"—continue to proliferate exponentially, doubling their numbers every two hours.[5] In evolutionary terms, such expansion is positively selected because a bacteremia level of 10 to 100 million bacilli per cubic milliliter of blood is needed to ensure that a flea biting a human is infected. With the flea as a vector, extreme virulence was necessary to the transmission and survival of plague bacilli. An immediate consequence is that the ever-replicating bacteria rapidly overwhelm the body's defenses by preferentially targeting and destroying the cells—dendritic cells, macrophages, and neutrophils—that provide the body's immune response. In the words of a 2012 US Geological Survey report:

> *Y. pestis* uses a needlelike appendage to target a host's white blood cells [and] injects proteins . . . directly into the host white

> blood cells. These proteins act to destroy immune functions of the host and prevent it from developing an inflammatory response that would inhibit or prevent further growth of the bacteria. . . . *Y. pestis* can also inject into the host a different protein . . . that prevents the host from producing two of its own proteins that would be used to stimulate the formation of a mass of immune cells to surround the bacteria and prevent its growth. . . . In the case of plague, the host cells get a false message that tissue damage is under control, when, in fact, *Y. pestis* bacteria are rapidly taking over visceral organs, particularly the liver and spleen, leading to loss of function.[6]

Escaping from the lymphatic system into the bloodstream, the multiplying bacteria initiate the third stage of the disease: septicemia. Having gained access to the blood, the bacteria release a powerful toxin that is normally the cause of death. It attacks tissues, causing blood vessels to hemorrhage, giving rise to purple, subcutaneous spots—the so-called tokens of plague. They earned this name because many people thought them to be signs, or "tokens," of God's anger.

By producing degeneration of the tissues of the heart, liver, spleen, kidneys, lungs, and central nervous system, the systemic infection initiates multiple organ failure. At this point patients have wild bloodshot eyes, black tongues, and pale, wasted faces with poor coordination of the facial muscles. They experience general prostration, teeth-shattering chills, respiratory distress, and a high fever that normally hovers in the range of 103° to 105°F, but in some patients reaches 108°F. In addition there is progressive neurological damage manifested by slurred speech, tremors in the limbs, a staggering gait, seizures, and psychic disturbances ending in delirium, coma, and death. Pregnant women, who are especially vulnerable, invariably miscarry and hemorrhage to death. Sometimes there is also gangrene of the extremities. This necrosis of the nose, fingers, and toes is one probable source of the terms "Black Death" and "Black Plague."

During the first European epidemic of Black Death at Messina in 1347, the Franciscan chronicler Michael of Piazza wrote a vivid description of the sufferings of the victim:

> The "burn blisters" appeared, and boils developed in different parts of the body: on the sexual organs, in others on the thighs, or on the arms, and in others on the neck. At first these were of

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

As soon as anyone was seized with headache and shivering during a visitation of the plague, he or she anticipated a fatal outcome. The minority of patients who recovered from their ordeal faced a lengthy convalescence and an array of lasting or permanent sequelae. These included deafness, impaired vision, paralysis of the muscles of one or more limbs, inability to speak as a result of laryngeal paralysis, and loss of memory. Psychological trauma also persisted after so arduous an ordeal. The experience did not even confer an acquired immunity, as a survivor from an epidemic in one year could die from plague the next. Against this background of sudden onset, a fulminant course, and a cascade of excruciating symptoms that usually ended in death, it is small wonder that the very word "plague" came to be synonymous with calamity and the worst imaginable disaster. In the Islamic world, it was even widely known as the "great annihilation."

## Types of Plague

### *Bubonic Plague*

Bubonic plague arises as an infection of the lymphatic system, it is transmitted primarily by flea bites, and it has the symptomatology described above. It is also the most common form of plague and has had the largest historical impact in all three of the plague pandemics. But the disease can also occur in two other forms, known as septicemic and pneumonic plague. It is vital to stress that these are not three distinct diseases, but simply three different manifestations of the single disease of plague, and all three are caused by *Y. pestis*.

### *Septicemic Plague*

Primary septicemic plague is the fulminant and rarest of the three forms of plague. Like bubonic plague, it is transmitted by flea bite; but unlike bubonic plague, primary septicemic plague begins with inoculation of *Y. pestis* into the bloodstream, without prior inflammation of the lymph nodes and the formation of buboes. The bacteria immediately metastasize, with rapidly fatal consequences. In some cases, the progress of the disease is so fast that the patient dies within hours even before the onset of symptoms. More commonly, however, the sufferer endures organ failure, severe nausea, fever, and abdominal pain followed within hours by death through multiple causes. In septicemic plague, the CFR approaches 100 percent.

More common is secondary septicemic plague, which simply denotes a stage in the normal progression of bubonic plague untreated with antibiotics. In this stage the bacteria, having already caused the classic symptoms of the disease, escape the lymph system and enter the bloodstream. There they initiate the multiplication, diffusion, and toxicity that lead inexorably to death.

### *Pneumonic Plague*

Pneumonic plague is a severe infection, not of the lymphatic system or the blood, but of the lungs, so historically it has sometimes been called "pestilent pneumonia." The etiology may be the spread of the plague bacteria from the lymphatic to the respiratory system—a condition known as "secondary pneumonic plague." Alternatively and more important historically, pneumonic plague can be transmitted directly from person to person by inhaling droplets from the coughs and sneezes of a plague victim whose respiratory system is the original site of infection, resulting in "primary pneumonic plague."

Since the site of infection is the lungs, the symptomatology is significantly different from that of bubonic or septicemic plague. The portal of entry of *Y. pestis* via the lungs significantly affects its symptoms and, above all, its lethality and time course through the body. One reason is the different temperature of the flea gut as compared with that of the human body immediately before infection. In bubonic flea-to-human transmission, the temperature environment in which *Y. pestis* develops is that of the flea gut, 26°C, whereas in pneumonic human-to-human transmission the plague pathogen develops at 37°C. Recent research suggests that at the molecular

level, the development of the bacterium at the higher temperature activates genes that express virulence. These genes cause the production of antigens that destroy phagocytes (white cells) and chemical reactions that enable the pathogen to elude detection by the receptors of the large white blood cells known as macrophages. The result is "an immunosuppressive environment in the lungs" that leads to "rapid bacterial proliferation" in the lung alveoli—the tiny sacs where the vital exchange of oxygen and carbon dioxide in the bloodstream takes place.[8]

Thus attacked, the pneumonic plague sufferer experiences symptoms similar to those of acute pulmonary pneumonia. With destruction of the lung alveoli, edema, and hemorrhage, the patient manifests severe respiratory distress, fever, chest pain, cough, nausea, headache, and frothy, bloody sputum. Furthermore, the condition is universally fatal, often within less than seventy-two hours.

A significant historical corollary of the mode of transmission of primary pneumonic plague is that it does not depend on the rat and the flea. Here is the probable solution to the epidemiological puzzles that led to a current of "plague deniers," such as Graham Twigg and Samuel K. Cohn. They postulate that the disease responsible for the second pandemic was not plague at all but anthrax or a combination of anthrax and an unspecified comorbidity. If plague was responsible, they ask, why did massive die-offs of rats not figure more frequently in plague literature, paintings, and chronicles of the Black Death? How could a disease dependent on the gradual movement of rats sweep so quickly across the European continent? How could bubonic plague burst out in Moscow or Iceland during frigid winters, when fleas are inactive? Why were crucial features of the epidemiology and virulence of the third pandemic so different from descriptions by contemporary observers of the second?

In this context, the example of Iceland appears especially confounding. With a slight delay due to its distance and isolation, Iceland suffered the first wave of the Black Death in 1402–1404, when perhaps 50 percent of the population perished. But there is a conundrum that adds significantly to the puzzlement already engendered by the onset of plague despite the island's climate. A feature of Icelandic fauna in the late medieval period was that it lacked a population of rats. How could a disease transmitted by rats and Oriental rat fleas be widely and rapidly diffused in the absence of both?

Osteoarchaeology—the systematic excavation and scientific examination of human bones from archeological sites—has provided conclusive findings with regard to the presence of plague across northern Europe, and

genetic research has provided at least partial answers to most of the outstanding questions. Examination of bones and dental pulp extracted from bodies exhumed from plague burial sites has irrefutably established the presence of *Y. pestis*. In the terse comment of a recent researcher, "Finally, plague is plague."[9] These findings do not exclude the possibility of a second epidemic pathogen as well, but they provide robust proof that bubonic plague was a factor. Furthermore, to date, the DNA of anthrax or other epidemic pathogens has not been detected in plague burial grounds.

In addition, genomic research has identified mechanisms that resolve many of the difficulties confronting those who consider plague as almost certainly responsible for the medical events of the second pandemic. It is now known that there are different strains of *Y. pestis;* that these strains vary in their proclivity to produce bubonic or pneumonic plague; and that the strain implicated in the Black Death was highly virulent, in part because of its tendency to produce the pneumonic form of the disease.

These data shed new light on the Black Death. Person-to-person dissemination by droplets allows a far more rapid propagation of the disease than the comparatively slow long-distance movements of rats over land and sea. Pneumonic plague also spreads more easily in winter than bubonic plague because it does not depend on the activity of fleas but rather on the human behavior of congregating indoors during cold weather within close range of coughs and sneezes. It would therefore thrive in the winter environment of northern and eastern Europe.

Furthermore, droplets were not the only vehicle for direct human-to-human transmission without the mediation of the rat. The human flea *Pulex irritans* can also play a significant role apart from the rat flea *Xenopsylla cheopis*. Investigation of the small but famous sample of the Derbyshire village of Eynsham in its experience of plague in 1665–1666 revealed that human-to-human propagation by the human flea was far more prevalent than by the rat flea. Such direct human-to-human diffusion occurring during the second pandemic as a whole would help to explain the rapid spread of the disease, which far outran the onward progress of rats and the fleas they concealed in their fur.

Since the Black Death appeared in Europe as a sudden and unfamiliar invader from abroad, the population possessed no immunity against it. Genetic findings demonstrate that although the Plague of Justinian was also caused by *Y. pestis,* it was a strain that was genetically distant from the strains responsible for the second and third pandemics. Crossover immunity from one to the other is therefore unlikely. Consequently, the Black Death probably

spread as a "virgin soil epidemic" analogous to smallpox in the Americas—a factor that also helps to explain its extraordinary virulence and rapid spread. Furthermore, a pneumonic disease spreading through air droplets would account for the paucity of contemporary references—in art, literature, and chronicles—to rodent die-offs that preceded the affliction of humans.

Meanwhile, the contrasting predominance of bubonic rather than pneumonic plague in the third pandemic clarifies some of the features that distinguish it from the second: the constant references to swarms of dying rats by all observers, in clear contrast to the Black Death; the slow and erratic movement of the disease; its tendency to persist even for years in the localities it invaded; and its exclusive preference for warm climates and mild seasons. Pending further research and greater clarity, the preponderance of current evidence suggests that the traditional attribution of all three pandemics to *Y. pestis* is correct—provided that allowance is made for different strains and due account is taken of the balance between bubonic and pneumonic plague.

The specific features of pneumonic plague also explain the interest of bioterrorists and germ warfare laboratories in this disease. It spreads rapidly, is readily aerosolized, and is nearly 100 percent lethal. Furthermore, it begins with mild flulike symptoms that delay recourse to diagnosis and treatment, and it frequently runs its course within the human body in less than seventy-two hours. The opportunity to deploy curative strategies is therefore exceptionally brief. This situation is rendered even more critical by the recent appearance of antibiotic-resistant strains of *Y. pestis*. By virtue of these characteristics, the CDC has classified *Y. pestis* as a "Tier 1 select agent"—a pathogen with the highest appeal for use as a weapon of biological warfare or bioterror.

## Conclusion

In practice, plague sufferers often received no medical attention. In the early waves of the Black Death in particular, societies were caught unprepared by an unknown "emerging disease." No facilities—administrative, religious, or medical—were in place to cope with the tidal wave of disease and death. Physicians and attendants recognized that they were powerless to understand or treat the invading new affliction and that they were far too few in number to cope with the catastrophe that engulfed them. Their profession also exposed them disproportionately to risk, and they perished in great numbers during outbreaks.

Furthermore, overcome with terror like the population at large, many doctors joined patients' relatives and friends in the general flight from plague-threatened cities. Indeed, one of the horrors of an epidemic of plague was that it broke the common bonds of humanity. As a result, sufferers were often abandoned to face agony and death alone. The most famous and perhaps most harrowing plague testimony is that of Giovanni Boccaccio in the *Decameron,* which was based on the experience of Florence in 1348:

> Tedious were it to recount, how citizen avoided citizen, how among neighbors was scarce found any that shewed fellow-feeling for another, how kinsfolk held aloof, and never met, or but rarely; enough that this sore affliction entered so deep into the minds of men and women, that in the horror thereof brother was forsaken by brother, nephew by uncle, brother by sister, and oftentimes husband by wife: nay, what is more, and scarcely to believed, fathers and mothers were found to abandon their own children, untended, unvisited, to their fate, as if they had been strangers. Wherefore the sick of both sexes, whose number could not be estimated, were left without resource but in the charity of friends (and few such there were), or the interest of servants, who were hardly to be had at high rates and on unseemly terms.[10]

An aspect of the dread felt by those threatened with plague was that it broke the framework developed in the Middle Ages for dealing with death. The historian Philippe Ariès has explained that populations across Europe had devised a series of beliefs, practices, and rituals to provide support in dealing with mortality. These strategies helped people to cope with loss, to heal the tear caused in a family or community by the death of one of its members, to express grief, and to pay their last respects to the dead. Taken together, the practices constituted an "art of dying" (*ars moriendi*) that was codified in instructions elaborated in paintings, engravings, sermons, and books that all explained how to die properly in accord with Christian doctrine. A work of the kind—called a *memento mori* (reminder of death)—explained who should be present at the last hour, detailed the last sacraments to be administered by the clergy, and dictated the proper funeral rites—the laying out of the body, the wake, the procession, the funeral service and burial ceremony, the interment in consecrated ground, and the funeral meal for surviving friends and relatives. In all of these rituals the objective was to allow communities to express the values of solidarity and human dignity.

The most famous of all writers on the theme of *ars moriendi* was the ascetic seventeenth-century Anglican Bishop Jeremy Taylor. His major works were *The Rule and Exercises of Holy Living* (1650) and *The Rule and Exercises of Holy Dying* (1651). The aim of both books, which were widely read in both Britain and America, was to remind the faithful that life on earth is unsafe and ultimately unimportant; therefore, believers should primarily spend their time preparing for eternal life. It was vitally important to die with one's worldly affairs in good order and with one's soul in a state of grace ready to confront judgment day. Taylor's books were instructional manuals on how to achieve both ends—the material and the spiritual. Taken together, they indicated the means to "tame death" (using Ariès's term) so that believers faced mortality confident in the knowledge of being properly prepared to confront it.

What made bubonic plague especially fearful was that it presented communities with the antithesis of the "art of dying" and robbed individuals of the opportunity to achieve a "tame death." It caused believers to face sudden death, or *mors repentina*, in which victims could be caught with wills unwritten in this world and unconfessed souls in a state of sin that would lead to damnation in the next. Death from plague was sudden; people died alone and without the attention of the clergy; and often they were denied funeral rites and proper burial.

Fear of sudden death from plague is therefore analogous to the terror described by Drew Gilpin Faust in her book *This Republic of Suffering: Death and the American Civil War* (2008). Faust places the terror of sudden death at the center of her account because it was widespread among soldiers on both sides of the conflict. The dread appears repeatedly in their letters home to loved ones and friends. In this respect, bubonic plague resembles total war, as both present unlimited possibilities for the sudden death that can come to us "as a thief" (Rev 3:3).

The New Testament book of Revelation provides a vivid account of the end times—with a day of wrath, a great apocalypse, and plagues and suffering. During the plague centuries, the visual arts made the depiction of "death unleashed" as described in Revelation central to their iconography. Many artists portrayed the "triumph of death," which takes the form of a universal plague complete with the Four Horsemen of the Apocalypse. Perhaps no better example of this terrifying genre can be found than the painting *The Triumph of Death* (1562–1563) by the Flemish master Pieter Bruegel the Elder. In the foreground and center of the picture Death himself drives a great ox-cart while wielding a scythe to reap his grim harvest. Before him the Angel

of Death sets forth blowing a trumpet while people are dying all around and graves are opening to yield up their skeletons.

A second major aspect of plague iconography was "vanitas," that is, a symbolic expression of the idea that earthly life is fleeting and insignificant (fig. 4.2). The vanitas theme gained widespread currency in the wake of the first wave of the Black Death and then faded in the eighteenth century with the coming of the Enlightenment and the end of the second pandemic. The traditional Christian view of the transitoriness of life was expressed in the book of Ecclesiastes (1:2–4): "vanity of vanities, all is vanity. What profit hath a man of his labour which he taketh under the sun? One generation passeth away, and another generation cometh." Such paintings often display temporal goods embodying the hubris of human aspirations—gold, musical instruments, scholarly tomes, globes, and elegant garments. These were juxtaposed to striking symbols of the underlying truth that human

Figure 4.2. Harmen Steenwijck, *Vanitas stilleven* (ca. 1640), which symbolically depicts the transience of life and certainty of death. The *vanitas* was a popular art form during the Black Death. Museum De Lakenhal, Leiden.

Figure 4.3. German painter Lukas Furtenagel painted this *vanitas, The Painter Hans Burgkmair and His Wife Anna*, in 1529. Kunsthistorisches Museum, Vienna.

accomplishment is minimal and life is short—skulls, candles whose flame has just gone out, hourglasses marking the passage of time, crossbones, skeletons, and shovels. One example by the German painter Lukas Furtenagel shows the faces of a middle-aged couple reflected in a hand mirror as skulls (fig. 4.3).

Another artistic motif that coincided with the era of the plague was the *danse macabre*. Such works of art portray Death as a skeleton summoning people of all ages, ranks, and sexes to join in a merry dance. Sometimes Death is armed with a scythe, arrow, or dart, and he leads the dance while playing a musical instrument. Churches often enacted such a performance, transposing the representation of the fragility of life to the medium of theater. More recently, Bergman's plague film *The Seventh Seal* reaches its denouement when Death summons the protagonists to join in a jolly dance.

We have considered the cultural and physical impacts of plague on the populations it afflicted, but how did the authorities of church and state seek to contain the disaster? What administrative strategies and medical therapies did they deploy? We now turn to the collective responses of societies to the emergency.