CHAPTER 11

LETHAL GIFT OF LIVESTOCK

WE HAVE NOW TRACED HOW FOOD PRODUCTION AROSE in a few centers, and how it spread at unequal rates from there to other areas. Those geographic differences constitute important ultimate answers to Yali's question about why different peoples ended up with disparate degrees of power and affluence. However, food production itself is not a proximate cause. In a one-on-one fight, a naked farmer would have no advantage over a naked hunter-gatherer.

Instead, one part of the explanation for farmer power lies in the much denser populations that food production could support: ten naked farmers certainly would have an advantage over one naked hunter-gatherer in a fight. The other part is that neither farmers nor hunter-gatherers are naked, at least not figuratively. Farmers tend to breathe out nastier germs, to own better weapons and armor, to own more-powerful technology in general, and to live under centralized governments with literate elites better able to wage wars of conquest. Hence the next four chapters will explore how the ultimate cause of food production led to the proximate causes of germs, literacy, technology, and centralized government.

The links connecting livestock and crops to germs were unforgettably illustrated for me by a hospital case about which I learned through a physician friend. When my friend was an inexperienced young doctor, he was

called into a hospital room to deal with a married couple stressed-out by a mysterious illness. It did not help that the couple was also having difficulty communicating with each other, and with my friend. The husband was a small, timid man, sick with pneumonia caused by an unidentified microbe, and with only limited command of the English language. Acting as translator was his beautiful wife, worried about her husband's condition and frightened by the unfamiliar hospital environment. My friend was also stressed-out from a long week of hospital work, and from trying to figure out what unusual risk factors might have brought on the strange illness. The stress caused my friend to forget everything he had been taught about patient confidentiality: he committed the awful blunder of requesting the woman to ask her husband whether he'd had any sexual experiences that could have caused the infection.

As the doctor watched, the husband turned red, pulled himself together so that he seemed even smaller, tried to disappear under his bedsheets, and stammered out words in a barely audible voice. His wife suddenly screamed in rage and drew herself up to tower over him. Before the doctor could stop her, she grabbed a heavy metal bottle, slammed it with full force onto her husband's head, and stormed out of the room. It took a while for the doctor to revive her husband and even longer to elicit, through the man's broken English, what he'd said that so enraged his wife. The answer slowly emerged: he had confessed to repeated intercourse with sheep on a recent visit to the family farm; perhaps that was how he had contracted the mysterious microbe.

This incident sounds bizarrely one-of-a-kind and of no possible broader significance. In fact, it illustrates an enormous subject of great importance: human diseases of animal origins. Very few of us love sheep in the carnal sense that this patient did. But most of us platonically love our pet animals, such as our dogs and cats. As a society, we certainly appear to have an inordinate fondness for sheep and other livestock, to judge from the vast numbers of them that we keep. For example, at the time of a recent census, Australia's 17,085,400 people thought so highly of sheep that they kept 161,600,000 of them.

Some of us adults, and even more of our children, pick up infectious diseases from our pets. Usually they remain no more than a nuisance, but a few have evolved into something far more serious. The major killers of humanity throughout our recent history—smallpox, flu, tuberculosis, malaria, plague, measles, and cholera—are infectious diseases that evolved

from diseases of animals, even though most of the microbes responsible for our own epidemic illnesses are paradoxically now almost confined to humans. Because diseases have been the biggest killers of people, they have also been decisive shapers of history. Until World War II, more victims of war died of war-borne microbes than of battle wounds. All those military histories glorifying great generals oversimplify the ego-deflating truth: the winners of past wars were not always the armies with the best generals and weapons, but were often merely those bearing the nastiest germs to transmit to their enemies.

The grimmest examples of germs' role in history come from the European conquest of the Americas that began with Columbus's voyage of 1492. Numerous as were the Native American victims of the murderous Spanish conquistadores, they were far outnumbered by the victims of murderous Spanish microbes. Why was the exchange of nasty germs between the Americas and Europe so unequal? Why didn't Native American diseases instead decimate the Spanish invaders, spread back to Europe, and wipe out *95* percent of Europe's population? Similar questions arise for the decimation of many other native peoples by Eurasian germs, as well as for the decimation of would-be European conquistadores in the tropics of Africa and Asia.

Thus, questions of the animal origins of human disease lie behind the broadest pattern of human history, and behind some of the most important issues *in* human health today. (Think of AIDS, an explosively spreading human disease that appears to have evolved from a virus resident in wild African monkeys.) This chapter will begin by considering what a "disease" is, and why some microbes have evolved so as to "make us sick," whereas most other species of living things don't make us sick. We'll examine why many of our most familiar infectious diseases run in epidemics, such as our current AIDS epidemic and the Black Death (bubonic plague) epidemics of the Middle Ages. We'll then consider how the ancestors of microbes now confined to us transferred themselves from their original animal hosts. Finally, we'll see how insight into the animal origins of our infectious diseases helps explain the momentous, almost one-way exchange of germs between Europeans and Native Americans.

NATURALLY, WE'RE DISPOSED to think about diseases just from our own point of view: what can we do to save ourselves and to kill the

microbes? Let's stamp out the scoundrels, and never mind what *their* motives are! In life in general, though, one has to understand the enemy in order to beat him, and that's especially true in medicine.

Hence let's begin by temporarily setting aside our human bias and considering disease from the microbes' point of view. After all, microbes are as much a product of natural selection as we are. What evolutionary benefit does a microbe derive from making us sick in bizarre ways, like giving us genital sores or diarrhea? And why should microbes evolve so as to kill us? That seems especially puzzling and self-defeating, since a microbe that kills its host kills itself.

Basically, microbes evolve like other species. Evolution selects for those individuals most effective at producing babies and at helping them spread to suitable places to live. For a microbe, spread may be defined mathematically as the number of new victims infected per each original patient. That number depends on how long each victim remains capable of infecting new victims, and how efficiently the microbe is transferred from one victim to the next.

Microbes have evolved diverse ways of spreading from one person to another, and from animals to people. The germ that spreads better leaves more babies and ends up favored by natural selection. Many of our "symptoms" of disease actually represent ways in which some damned clever microbe modifies our bodies or our behavior such that we become enlisted to spread microbes.

The most effortless way a germ could spread is by just waiting to be transmitted passively to the next victim. That's the strategy practiced by microbes that wait for one host to be eaten by the next host: for instance, salmonella bacteria, which we contract by eating already infected eggs or meat; the worm responsible for trichinosis, which gets from pigs to us by waiting for us to kill the pig and eat it without proper cooking; and the worm causing anisakiasis, with which sushi-loving Japanese and Americans occasionally infect themselves by consuming raw fish. Those parasites pass to a person from an eaten animal, but the virus causing laughing sickness (kuru) in the New Guinea highlands used to pass to a person from another person who was eaten. It was transmitted by cannibalism, when highland babies made the fatal mistake of licking their fingers after playing with raw brains that their mothers had just cut out of dead kuru victims awaiting cooking.

Some microbes don't wait for the old host to die and get eaten, but

instead hitchhike in the saliva of an insect that bites the old host and flies off to find a new host. The free ride may be provided by mosquitoes, fleas, lice, or tsetse flies that spread malaria, plague, typhus, or sleeping sickness, respectively. The dirtiest of all tricks for passive carriage is perpetrated by microbes that pass from a woman to her fetus and thereby infect babies already at birth. By playing that trick, the microbes responsible for syphilis, rubella, and now AIDS pose ethical dilemmas with which believers in a fundamentally just universe have had to struggle desperately.

Other germs take matters into their own hands, figuratively speaking. They modify the anatomy or habits of their host in such a way as to accelerate their transmission. From our perspective, the open genital sores caused by venereal diseases like syphilis are a vile indignity. From the microbes' point of view, however, they're just a useful device to enlist a host's help in inoculating microbes into a body cavity of a new host. The skin lesions caused by smallpox similarly spread microbes by direct or indirect body contact (occasionally very indirect, as when U.S. whites bent on wiping out "belligerent" Native Americans sent them gifts of blankets previously used by smallpox patients).

More vigorous yet is the strategy practiced by the influenza, common cold, and pertussis (whooping cough) microbes, which induce the victim to cough or sneeze, thereby launching a cloud of microbes toward prospective new hosts. Similarly, the cholera bacterium induces in its victim a massive diarrhea that delivers bacteria into the water supplies of potential new victims, while the virus responsible for Korean hemorrhagic fever broadcasts itself in the urine of mice. For modification of a host's behavior, nothing matches rabies virus, which not only gets into the saliva of an infected dog but drives the dog into a frenzy of biting and thus infecting many new victims. But for physical effort on the bug's own part, the prize still goes to worms such as hookworms and schistosomes, which actively burrow through a host's skin from the water or soil into which their larvae had been excreted in a previous victim's feces.

Thus, from our point of view, genital sores, diarrhea, and coughing are "symptoms of disease." From a germ's point of view, they're clever evolutionary strategies to broadcast the germ. That's why it's in the germ's interests to "make us sick." But why should a germ evolve the apparently self-defeating strategy of killing its host?

From the germ's perspective, that's just an unintended by-product (fat consolation to us!) of host symptoms promoting efficient transmission of

microbes. Yes, an untreated cholera patient may eventually die from producing diarrheal fluid at a rate of several gallons per day. At least for a while, though, as long as the patient is still alive, the cholera bacterium profits from being massively broadcast into the water supplies of its next victims. Provided that each victim thereby infects on the average more than one new victim, the bacterium will spread, even though the first host happens to die.

So MUCH FOR our dispassionate examination of the germ's interests. Now let's get back to considering our own selfish interests: to stay alive and healthy, best done by killing the damned germs. One common response of ours to infection is to develop a fever. Again, we're used to considering fever as a "symptom of disease," as if it developed inevitably without serving any function. But regulation of body temperature is under our genetic control and doesn't just happen by accident. A few microbes are more sensitive to heat than our own bodies are. By raising our body temperature, we in effect try to bake the germs to death before we get baked ourselves.

Another common response of ours is to mobilize our immune system. White blood cells and other cells of ours actively seek out and kill foreign microbes. The specific antibodies that we gradually build up against a particular microbe infecting us make us less likely to get reinfected once we become cured. As we all know from experience, there are some illnesses, such as flu and the common cold, to which our resistance is only temporary; we can eventually contract the illness again. Against other illnesses, though—including measles, mumps, rubella, pertussis, and the now defeated smallpox—our antibodies stimulated by one infection confer lifelong immunity. That's the principle of vaccination: to stimulate our antibody production without our having to go through the actual experience of the disease, by inoculating us with a dead or weakened strain of microbe.

Alas, some clever microbes don't just cave in to our immune defenses. Some have learned to trick us by changing those molecular pieces of the microbe (its so-called antigens) that our antibodies recognize. The constant evolution or recycling of new strains of flu, with differing antigens, explains why your having gotten flu two years ago didn't protect you

against the different strain that arrived this year. Malaria and sleeping sickness are even more slippery customers in their ability rapidly to change their antigens. Among the slipperiest of all is AIDS, which evolves new antigens even as it sits within an individual patient, thereby eventually overwhelming his or her immune system.

Our slowest defensive response is through natural selection, which changes our gene frequencies from generation to generation. For almost any disease, some people prove to be genetically more resistant than are others. In an epidemic those people with genes for resistance to that particular microbe are more likely to survive than are people lacking such genes. As a result, over the course of history, human populations repeatedly exposed to a particular pathogen have come to consist of a higher proportion of individuals with those genes for resistance—just because unfortunate individuals without the genes were less likely to survive to pass their genes on to babies.

Fat consolation, you may be thinking again. This evolutionary response is not one that does the genetically susceptible dying individual any good. It does mean, though, that a human population as a whole becomes better protected against the pathogen. Examples of those genetic defenses include the protections (at a price) that the sickle-cell gene, Tay-Sachs gene, and cystic fibrosis gene may confer on African blacks, Ashkenazi Jews, and northern Europeans against malaria, tuberculosis, and bacterial diarrheas, respectively.

In short, our interaction with most species, as exemplified by hummingbirds, doesn't make us or the hummingbird "sick." Neither we nor hummingbirds have had to evolve defenses against each other. That peaceful relationship was able to persist because hummingbirds don't count on us to spread their babies or to offer our bodies for food. Hummingbirds evolved instead to feed on nectar and insects, which they find by using their own wings.

But microbes evolved to feed on the nutrients within our own bodies, and they don't have wings to let them reach a new victim's body once the original victim is dead or resistant. Hence many germs have had *to* evolve tricks to let them spread between potential victims, and many of those tricks are what we experience as "symptoms of disease." We've evolved countertricks of our own, to which the germs have responded by evolving counter-countertricks. We and our pathogens are now locked in an escalat-

ing evolutionary contest, with the death of one contestant the price of defeat, and with natural selection playing the role of umpire. Now let's consider the form of the contest: blitzkrieg or guerrilla war?

SUPPOSE THAT ONE counts the number of cases of some particular infectious disease in some geographic area, and watches how the numbers change with time. The resulting patterns differ greatly among diseases. For certain diseases, like malaria or hookworm, new cases appear any month of any year in an affected area. So-called epidemic diseases, though, produce no cases for a long time, then a whole wave of cases, then no more cases again for a while.

Among such epidemic diseases, influenza is one personally familiar to most Americans, certain years being particularly bad years for us (but great years for the influenza virus). Cholera epidemics come at longer intervals, the 1991 Peruvian epidemic being the first one to reach the New World during the 20th century. Although today's influenza and cholera epidemics make front-page stories, epidemics used to be far more terrifying before the rise of modern medicine. The greatest single epidemic in human history was the one of influenza that killed 21 million people at the end of the First World War. The Black Death (bubonic plague) killed one-quarter of Europe's population between 1346 and 1352, with death tolls ranging up to 70 percent in some cities. When the Canadian Pacific Railroad was being built through Saskatchewan in the early 1880s, that province's Native Americans, who had previously had little exposure to whites and their germs, died of tuberculosis at the incredible rate of 9 percent per year.

The infectious diseases that visit us as epidemics, rather than as a steady trickle of cases, share several characteristics. First, they spread quickly and efficiently from an infected person to nearby healthy people, with the result that the whole population gets exposed within a short time. Second, they're "acute" illnesses: within a short time, you either die or recover completely. Third, the fortunate ones of us who do recover develop antibodies that leave us immune against a recurrence of the disease for a long time, possibly for the rest of our life. Finally, these diseases tend to be restricted to humans; the microbes causing them tend not to live in the soil or in other animals. All four of these traits apply to what Americans think

of as the familiar acute epidemic diseases of childhood, including measles, rubella, mumps, pertussis, and smallpox.

The reason why the combination of those four traits tends to make a disease run in epidemics is easy to understand. In simplified form, here's what happens. The rapid spread of microbes, and the rapid course of symptoms, mean that everybody in a local human population is quickly infected and soon thereafter is either dead or else recovered and immune. No one is left alive who could still be infected. But since the microbe can't survive except in the bodies of living people, the disease dies out, until a new crop of babies reaches the susceptible age—and until an infectious person arrives from the outside to start a new epidemic.

A classic illustration of how such diseases occur as epidemics is the history of measles on the isolated Atlantic islands called the Faeroes. A severe epidemic of measles reached the Faeroes in 1781 and then died out, leaving the islands measles free until an infected carpenter arrived on a ship from Denmark in 1846. Within three months, almost the whole Faeroes population (7,782 people) had gotten measles and then either died or recovered, leaving the measles virus to disappear once again until the next epidemic. Studies show that measles is likely to die out in any human population numbering fewer than half a million people. Only in larger populations can the disease shift from one local area to another, thereby persisting until enough babies have been born in the originally infected area that measles can return there.

What's true for measles in the Faeroes is true of our other familiar acute infectious diseases throughout the world. To sustain themselves, they need a human population that is sufficiently numerous, and sufficiently densely packed, that a numerous new crop of susceptible children is available for infection by the time the disease would otherwise be waning. Hence measles and similar diseases are also known as crowd diseases.

OBVIOUSLY, CROWD DISEASES could not sustain themselves in small bands of hunter-gatherers and slash-and-burn farmers. As tragic modern experience with Amazonian Indians and Pacific Islanders confirms, almost an entire tribelet may be wiped out by an epidemic brought by an outside visitor—because no one in the tribelet had any antibodies against the microbe. For example, in the winter of 1902 a dysentery epidemic brought

by a sailor on the whaling ship *Active* killed 51 out of the 56 Sadlermiut Eskimos, a very isolated band of people living on Southampton Island in the Canadian Arctic. In addition, measles and some of our other "childhood" diseases are more likely to kill infected adults than children, and all adults in the tribelet are susceptible. (In contrast, modern Americans rarely contract measles as adults, because most of them get either measles or the vaccine against it as children.) Having killed most of the tribelet, the epidemic then disappears. The small population size of tribelets explains not only why they can't sustain epidemics introduced from the outside, but also why they never could evolve epidemic diseases of their own to give back to visitors.

That's not to say, though, that small human populations are free from all infectious diseases. They do have infections, but only of certain types. Some are caused by microbes capable of maintaining themselves in animals or in the soil, with the result that the disease doesn't die out but remains constantly available to infect people. For example, the yellow fever virus is carried by African wild monkeys, whence it can always infect rural human populations of Africa, whence it was carried by the transatlantic slave trade to infect New World monkeys and people.

Still other infections of small human populations are chronic diseases such as leprosy and yaws. Since the disease may take a very long time to kill its victim, the victim remains alive as a reservoir of microbes to infect other members of the tribelet. For instance, the Karimui Basim of the New Guinea highlands, where I worked in the 1960s, was occupied by an isolated population of a few thousand people, suffering from the world's highest incidence of leprosy—about 40 percent! Finally, small human populations are also susceptible to nonfatal infections against which we don't develop immunity, with the result that the same person can become reinfected after recovering. That happens with hookworm and many other parasites.

All these types of diseases, characteristic of small isolated populations, must be the oldest diseases of humanity. They were the ones we could evolve and sustain through the early millions of years of our evolutionary history, when the total human population was tiny and fragmented. These diseases are also shared with, or similar to the diseases of, our closest wild relatives, the African great apes. In contrast, the crowd diseases, which we discussed earlier, could have arisen only with the buildup of large, dense human populations. That buildup began with the rise of agriculture start-

ing about 10,000 years ago and then accelerated with the rise of cities starting several thousand years ago. In fact, the first attested dates for many familiar infectious diseases are surprisingly recent: around 1600 B.c. for smallpox (as deduced from pockmarks on an Egyptian mummy), 400 B.C. for mumps, 200 B.C. for leprosy, A.D. 1840 for epidemic polio, and 1959 for AIDS.

WHY DID THE rise of agriculture launch the evolution of our crowd infectious diseases? One reason just mentioned is that agriculture sustains much higher human population densities than does the hunting-gathering lifestyle—on the average, 10 to 100 times higher. In addition, hunter-gatherers frequently shift camp and leave behind their own piles of feces with accumulated microbes and worm larvae. But farmers are sedentary and live amid their own sewage, thus providing microbes with a short path from one person's body into another's drinking water.

Some farming populations make it even easier for their own fecal bacteria and worms to infect new victims, by gathering their feces and urine and spreading them as fertilizer on the fields where people work. Irrigation agriculture and fish farming provide ideal living conditions for the snails carrying schistosomiasis and for flukes that burrow through our skin as we wade through the feces-laden water. Sedentary farmers become surrounded not only by their feces but also by disease transmitting rodents, attracted by the farmers' stored food. The forest clearings made by African farmers also provide ideal breeding habitats for malaria-transmitting mosquitoes.

If the rise of farming was thus a bonanza for our microbes, the rise of cities was a greater one, as still more densely packed human populations festered under even worse sanitation conditions. Not until the beginning of the 20th century did Europe's urban populations finally become self-sustaining: before then, constant immigration of healthy peasants from the countryside was necessary to make up for the constant deaths of city dwellers from crowd diseases. Another bonanza was the development of world trade routes, which by Roman times effectively joined the populations of Europe, Asia, and North Africa into one giant breeding ground for microbes. That's when smallpox finally reached Rome, as the Plague of Antoninus, which killed millions of Roman citizens between A.D. 165 and 180.

Similarly, bubonic plague first appeared in Europe as the Plague of Justinian (A.D. 542-43). But plague didn't begin to hit Europe with full force as the Black Death epidemics until A.D. 1346, when a new route for overland trade with China provided rapid transit, along Eurasia's east-west axis, for flea-infested furs from plague-ridden areas of Central Asia to Europe. Today, our jet planes have made even the longest intercontinental flights briefer than the duration of any human infectious disease. That's how an Aerolineas Argentinas airplane, stopping in Lima (Peru) in 1991, managed to deliver dozens of cholera-infected people that same day to my city of Los Angeles, over 3,000 miles from Lima. The explosive increase in world travel by Americans, and in immigration to the United States, is turning us into another melting pot—this time, of microbes that we previously dismissed as just causing exotic diseases in far-off countries.

THUS, WHEN THE human population became sufficiently large and concentrated, we reached the stage in our history at which we could at last evolve and sustain crowd diseases confined to our own species. But that conclusion presents a paradox: such diseases could never have existed before then! Instead, they had to evolve as new diseases. Where did those new diseases come from?

Evidence has recently been emerging from molecular studies of the disease-causing microbes themselves. For many of the microbes responsible for our unique diseases, molecular biologists can now identify the microbe's closest relatives. These also prove to be agents of crowd infectious diseases—but ones confined to various species of our domestic animals and pets! Among animals, too, epidemic diseases require large, dense populations and don't afflict just any animal: they're confined mainly to social animals providing the necessary large populations. Hence when we domesticated social animals, such as cows and pigs, they were already afflicted by epidemic diseases just waiting to be transferred to us.

For example, measles virus is most closely related to the virus causing rinderpest. That nasty epidemic disease affects cattle and many wild cud-chewing mammals, but not humans. Measles in turn doesn't afflict cattle. The close similarity of the measles virus to the rinderpest virus suggests that the latter transferred from cattle to humans and then evolved into the measles virus by changing its properties to adapt to us. That transfer is not at all surprising, considering that many peasant farmers live and sleep

close to cows and their feces, urine, breath, sores, and blood. Our intimacy with cattle has been going on for the 9,000 years since we domesticated them—ample time for the rinderpest virus to discover us nearby. As Table 11.1 illustrates, others of our familiar infectious diseases can similarly be traced back to diseases of our animal friends.

GIVEN OUR PROXIMITY to the animals we love, we must be getting constantly bombarded by their microbes. Those invaders get winnowed by natural selection, and only a few of them succeed in establishing themselves as human diseases. A quick survey of current diseases lets us trace out four stages in the evolution of a specialized human disease from an animal precursor.

The first stage is illustrated by dozens of diseases that we now and then pick up directly from our pets and domestic animals. They include cat-scratch fever from our cats, leptospirosis from our dogs, psittacosis from our chickens and parrots, and brucellosis from our cattle. We're similarly liable to pick up diseases from wild animals, such as the tularemia that hunters can get from skinning wild rabbits. All those microbes are still at an early stage in their evolution into specialized human pathogens. They still don't get transmitted directly from one person to another, and even their transfer to us from animals remains uncommon.

In the second stage a former animal pathogen evolves to the point where it does get transmitted directly between people and causes epidemics.

TABLE 11.1 Deadly Gifts from Our Animal Friends

Human Disease	*Animal with Most Closely Related Pathogen*
Measles	cattle (rinderpest)
Tuberculosis	cattle
Smallpox	cattle (cowpox) or other livestock with related pox viruses
Flu	pigs and ducks
Pertussis	pigs, dogs
Falciparum malaria	birds (chickens and ducks?)

However, the epidemic dies out for any of several reasons, such as being cured by modern medicine, or being stopped when everybody around has already been infected and either becomes immune or dies. For example, a previously unknown fever termed O'nyong-nyong fever appeared in East Africa in 1959 and proceeded to infect several million Africans. It probably arose from a virus of monkeys and was transmitted to humans by mosquitoes. The fact that patients recovered quickly and became immune to further attack helped the new disease die out quickly. Closer to home for Americans, Fort Bragg fever was the name applied to a new leptospiral disease that broke out in the United States in the summer of 1942 and soon disappeared.

A fatal disease vanishing for another reason was New Guinea's laughing sickness, transmitted by cannibalism and caused by a slow-acting virus from which no one has ever recovered. Kuru was on its way to exterminating New Guinea's Fore tribe of 20,000 people, until the establishment of Australian government control around 1959 ended cannibalism and thereby the transmission of kuru. The annals of medicine are full of accounts of diseases that sound like no disease known today, but that once caused terrifying epidemics and then disappeared as mysteriously as they had come. The "English sweating sickness," which swept and terrified Europe between 1485 and 1552, and the "Picardy sweats" of 18th- and 19th-century France, are just two of the many epidemic illnesses that vanished long before modern medicine had devised methods for identifying the responsible microbes.

A third stage in the evolution of our major diseases is represented by former animal pathogens that did establish themselves in humans, that have not (not yet?) died out, and that may or may not still become major killers of humanity. The future remains very uncertain for Lassa fever, caused by a virus derived probably from rodents. Lassa fever was first observed in 1969 in Nigeria, where it causes a fatal illness so contagious that Nigerian hospitals have been closed down if even a single case appears. Better established is Lyme disease, caused by a spirochete that we get from the bite of ticks carried by mice and deer. Although the first known human cases in the United States appeared only as recently as 1962, Lyme disease is already reaching epidemic proportions in many parts of our country. The future of AIDS, derived from monkey viruses and first documented in humans around 1959, is even more secure (from the virus's perspective).

The final stage of this evolution is represented by the major, long-established epidemic diseases confined to humans. These diseases must have been the evolutionary survivors of far more pathogens that tried to make the jump to us from animals—and mostly failed.

What is actually going on in those stages, as an exclusive disease of animals transforms itself into an exclusive disease of humans? One transformation involves a change of intermediate vector: when a microbe relying on some arthropod vector for transmission switches to a new host, the microbe may be forced to find a new arthropod as well. For example, typhus was initially transmitted between rats by rat fleas, which sufficed for a while to transfer typhus from rats to humans. Eventually, typhus microbes discovered that human body lice offered a much more efficient method of traveling directly between humans. Now that Americans have mostly deloused themselves, typhus has discovered a new route into us: by infecting eastern North American flying squirrels and then transferring to people whose attics harbor flying squirrels.

In short, diseases represent evolution in progress, and microbes adapt by natural selection to new hosts and vectors. But compared with cows' bodies, ours offer different immune defenses, lice, feces, and chemistries. In that new environment, a microbe must evolve new ways to live and to propagate itself. In several instructive cases doctors or veterinarians have actually been able to observe microbes evolving those new ways.

The best-studied case involves what happened when myxomatosis hit Australian rabbits. The myxo virus, native to a wild species of Brazilian rabbit, had been observed to cause a lethal epidemic in European domestic rabbits, which are a different species. Hence the virus was intentionally introduced to Australia in 1950 in the hopes of ridding the continent of its plague of European rabbits, foolishly introduced in the nineteenth century. In the first year, myxo produced a gratifying (to Australian farmers) 99.8 percent mortality rate in infected rabbits. Unfortunately for the farmers, the death rate then dropped in the second year to 90 percent and eventually to 25 percent, frustrating hopes of eradicating rabbits completely from Australia. The problem was that the myxo virus evolved to serve its own interests, which differed from ours as well as from those of the rabbits. The virus changed so as to kill fewer rabbits and to permit lethally infected ones to live longer before dying. As a result, a less lethal myxo virus spreads baby viruses to more rabbits than did the original, highly virulent myxo.

For a similar example in humans, we have only to consider the surprising evolution of syphilis. Today, our two immediate associations to syphilis are genital sores and a very slowly developing disease, leading to the death of many untreated victims only after many years. However, when syphilis was first definitely recorded in Europe in 1495, its pustules often covered the body from the head to the knees, caused flesh to fall off people's faces, and led to death within a few months. By 1546, syphilis had evolved into the disease with the symptoms so well known to us today. Apparently, just as with myxomatosis, those syphilis spirochetes that evolved so as to keep their victims alive for longer were thereby able to transmit their spirochete offspring into more victims.

THE IMPORTANCE OF lethal microbes in human history is well illustrated by Europeans' conquest and depopulation of the New World. Far more Native Americans died in bed from Eurasian germs than on the battlefield from European guns and swords. Those germs undermined Indian resistance by killing most Indians and their leaders and by sapping the survivors' morale. For instance, in 1519 Cortes landed on the coast of Mexico with 600 Spaniards, to conquer the fiercely militaristic Aztec Empire with a population of many millions. That Cortes reached the Aztec capital of Tenochtitlan, escaped with the loss of "only" two-thirds of his force, and managed to fight his way back to the coast demonstrates both Spanish military advantages and the initial naivete of the Aztecs. But when Cortes's next onslaught came, the Aztecs were no longer naive and fought street by street with the utmost tenacity. What gave the Spaniards a decisive advantage was smallpox, which reached Mexico in 1520 with one infected slave arriving from Spanish Cuba. The resulting epidemic proceeded to kill nearly half of the Aztecs, including Emperor Cuitlahuac. Aztec survivors were demoralized by the mysterious illness that killed Indians and spared Spaniards, as if advertising the Spaniards' invincibility. By 1618, Mexico's initial population of about 20 million had plummeted to about 1.6 million.

Pizarro had similarly grim luck when he landed on the coast of Peru in 1531 with 168 men to conquer the Inca Empire of millions. Fortunately for Pizarro and unfortunately for the Incas, smallpox had arrived overland around 1526, killing much of the Inca population, including both the emperor Huayna Capac and his designated successor. As we saw in Chap-

ter 3, the result of the throne's being left vacant was that two other sons of Huayna Capac, Atahuallpa and Huascar, became embroiled in a civil war that Pizarro exploited to conquer the divided Incas.

When we in the United States think of the most populous New World societies existing in 1492, only those of the Aztecs and the Incas tend to come to our minds. We forget that North America also supported populous Indian societies in the most logical place, the Mississippi Valley, which contains some of our best farmland today. In that case, however, conquis¬tadores contributed nothing directly to the societies' destruction; Eurasian germs, spreading in advance, did everything. When Hernando de Soto became the first European conquistador to march through the southeastern United States, in 1540, he came across Indian town sites abandoned two years earlier because the inhabitants had died in epidemics. These epidemics had been transmitted from coastal Indians infected by Spaniards visiting the coast. The Spaniards' microbes spread to the interior in advance of the Spaniards themselves.

De Soto was still able to see some of the densely populated Indian towns lining the lower Mississippi. After the end of his expedition, it was a long time before Europeans again reached the Mississippi Valley, but Eurasian microbes were now established in North America and kept spreading. By the time of the next appearance of Europeans on the lower Mississippi, that of French settlers in the late 1600s, almost all of those big Indian towns had vanished. Their relics are the great mound sites of the Mississippi Valley. Only recently have we come to realize that many of the mound-building societies were still largely intact when Columbus reached the New World, and that they collapsed (probably as a result of disease) between 1492 and the systematic European exploration of the Mississippi.

When I was young, American schoolchildren were taught that North America had originally been occupied by only about one million Indians. That low number was useful in justifying the white conquest of what could be viewed as an almost empty continent. However, archaeological excavations, and scrutiny of descriptions left by the very first European explorers on our coasts, now suggest an initial number of around 20 million Indians. For the New World as a whole, the Indian population decline in the century or two following Columbus's arrival is estimated to have been as large as 95 percent.

The main killers were Old World germs to which Indians had never been exposed, and against which they therefore had neither immune nor

genetic resistance. Smallpox, measles, influenza, and typhus competed for top rank among the killers. As if these had not been enough, diphtheria, malaria, mumps, pertussis, plague, tuberculosis, and yellow fever came up close behind. In countless cases, whites were actually there to witness the destruction occurring when the germs arrived. For example, in 1837 the Mandan Indian tribe, with one of the most elaborate cultures in our Great Plains, contracted smallpox from a steamboat traveling up the Missouri River from St. Louis. The population of one Mandan village plummeted from 2,000 to fewer than 40 within a few weeks.

WHILE OVER A dozen major infectious diseases of Old World origins became established in the New World, perhaps not a single major killer reached Europe from the Americas. The sole possible exception is syphilis, whose area of origin remains controversial. The one-sidedness of that exchange of germs becomes even more striking when we recall that large, dense human populations are a prerequisite for the evolution of our crowd infectious diseases. If recent reappraisals of the pre-Columbian New World population are correct, it was not far below the contemporary population of Eurasia. Some New World cities like Tenochtitlan were among the world's most populous cities at the time. Why didn't Tenochtitlan have awful germs waiting for the Spaniards?

One possible contributing factor is that the rise of dense human populations began somewhat later in the New World than in the Old World. Another is that the three most densely populated American centers—the Andes, Mesoamerica, and the Mississippi Valley—never became connected by regular fast trade into one huge breeding ground for microbes, in the way that Europe, North Africa, India, and China became linked in Roman times. Those factors still don't explain, though, why the New World apparently ended up with no lethal crowd epidemics at all. (Tuberculosis DNA has been reported from the mummy of a Peruvian Indian who died 1,000 years ago, but the identification procedure used did not distinguish human tuberculosis from a closely related pathogen *(Mycobacterium bovis)* that is widespread in wild animals.)

Instead, what must be the main reason for the failure of lethal crowd epidemics to arise in the Americas becomes clear when we pause to ask a simple question. From what microbes could they conceivably have evolved? We've seen that Eurasian crowd diseases evolved out of diseases

of Eurasian herd animals that became domesticated. Whereas many such animals existed in Eurasia, only five animals of any sort became domesticated in the Americas: the turkey in Mexico and the U.S. Southwest, the llama / alpaca and the guinea pig in the Andes, the Muscovy duck in tropical South America, and the dog throughout the Americas.

In turn, we also saw that this extreme paucity of domestic animals in the New World reflects the paucity of wild starting material. About 80 percent of the big wild mammals of the Americas became extinct at the end of the last Ice Age, around 13,000 years ago. The few domesticates that remained to Native Americans were not likely sources of crowd diseases, compared with cows and pigs. Muscovy ducks and turkeys don't live in enormous flocks, and they're not cuddly species (like young lambs) with which we have much physical contact. Guinea pigs may have contributed a trypanosome infection like Chagas' disease or leishmaniasis to our catalog of woes, but that's uncertain. Initially, most surprising is the absence of any human disease derived from llamas (or alpacas), which it's tempting to consider the Andean equivalent of Eurasian livestock. However, llamas had four strikes against them as a source of human pathogens: they were kept in smaller herds than were sheep and goats and pigs; their total numbers were never remotely as large as those of the Eurasian populations of domestic livestock, since llamas never spread beyond the Andes; people don't drink (and get infected by) llama milk; and llamas aren't kept indoors, in close association with people. In contrast, human mothers in the New Guinea highlands often nurse piglets, and pigs as well as cows are frequently kept inside the huts of peasant farmers.

THE HISTORICAL IMPORTANCE of animal-derived diseases extends far beyond the collision of the Old and the New Worlds. Eurasian germs played a key role in decimating native peoples in many other parts of the world, including Pacific islanders, Aboriginal Australians, and the Khoisan peoples (Hottentots and Bushmen) of southern Africa. Cumulative mortalities of these previously unexposed peoples from Eurasian germs ranged from 50 percent to 100 percent. For instance, the Indian population of Hispaniola declined from around 8 million, when Columbus arrived in A.D. 1492, to zero by 1535. Measles reached Fiji with a Fijian chief returning from a visit to Australia in 1875, and proceeded to kill about one-quarter of all Fijians then alive (after most Fijians had already been

killed by epidemics beginning with the first European visit, in 1791). Syphilis, gonorrhea, tuberculosis, and influenza arriving with Captain Cook in 1779, followed by a big typhoid epidemic in 1804 and numerous "minor" epidemics, reduced Hawaii's population from around half a million in 1779 to 84,000 in 1853, the year when smallpox finally reached Hawaii and killed around 10,000 of the survivors. These examples could be multiplied almost indefinitely.

However, germs did not act solely to Europeans' advantage. While the New World and Australia did not harbor native epidemic diseases awaiting Europeans, tropical Asia, Africa, Indonesia, and New Guinea certainly did. Malaria throughout the tropical Old World, cholera in tropical Southeast Asia, and yellow fever in tropical Africa were (and still are) the most notorious of the tropical killers. They posed the most serious obstacle to European colonization of the tropics, and they explain why the European colonial partitioning of New Guinea and most of Africa was not accomplished until nearly 400 years after European partitioning of the New World began. Furthermore, once malaria and yellow fever did become transmitted to the Americas by European ship traffic, they emerged as the major impediment to colonization of the New World tropics as well. A familiar example is the role of those two diseases in aborting the French effort, and nearly aborting the ultimately successful American effort, to construct the Panama Canal.

Bearing all these facts in mind, let's try to regain our sense of perspective about the role of germs in answering Yali's question. There is no doubt that Europeans developed a big advantage in weaponry, technology, and political organization over most of the non-European peoples that they conquered. But that advantage alone doesn't fully explain how initially so few European immigrants came to supplant so much of the native population of the Americas and some other parts of the world. That might not have happened without Europe's sinister gift to other continents—the germs evolving from Eurasians' long intimacy with domestic animals.