

The Viral Superhighway

Environmental disruptions and international travel have brought on a new era in human illness, one marked by diabolical new diseases

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So the Lord sent a pestilence upon Israel from the morning until the appointed time; and there died of the people from Dan to Beer-sheba seventy thousand men.

—2 Sam. 24:15

Swarms of crop-destroying locusts, rivers fouled with blood, lion-headed horses breathing fire and sulfur: the Bible presents a lurid assortment of plagues, described as acts of retribution by a vengeful God. Indeed, real-life epidemics—such as the influenza outbreak of 1918, which killed 21 million people in a matter of months—can be so sudden and deadly that it is easy, even for nonbelievers, to view them as angry messages from the beyond.

How reassuring it was, then, when the march of technology began to give people some control over the scourges of the past. In the 1950s the Salk vaccine, and later, the Sabin vaccine, dramatically reduced the incidence of polio. And by 1980 a determined effort by health workers worldwide eradicated smallpox, a disease that had afflicted humankind since earliest times with blindness, disfigurement and death, killing nearly 300 million people in the twentieth century alone.

But those optimistic years in the second half of our century now seem, with hindsight, to have been an era of inflated expectations, even arrogance. In 1967 the surgeon general of the United States, William H. Stewart, announced that victory over infectious diseases was imminent—a victory that would close the book on modern plagues. Sadly, we now know differently. Not only have deadly and previously unimagined new illnesses such as AIDS and Legionnaires' disease emerged in recent years, but historical diseases that just a few decades ago seemed to have been tamed are returning in virulent, drug-resistant varieties. Tuberculosis, the ancient lung disease that haunted nineteenth-century Europe, afflicting, among others, Chopin, Dostoyevski and Keats, is aggressively mutating into strains that defy the standard medicines; as a result, modern TB victims must undergo a daily drug regimen so elaborate that health-department workers often have to personally monitor patients to make sure they comply [see "A Plague Returns," by Mark Ear-

nest and John A. Sbarbaro, September/October 1993]. Meanwhile, bacteria and viruses in foods from chicken to strawberries to alfalfa sprouts are sickening as many as 80 million Americans each year.

And those are only symptoms of a much more general threat. Deaths from infectious diseases in the United States rose 58 percent between 1980 and 1992. Twenty-nine new diseases have been reported in the past twenty-five years, a few of them so bloodcurdling and bizarre that descriptions of them bring to mind tacky horror movies. Ebola virus, for instance, can in just a few days reduce a healthy person to a bag of teeming flesh spilling blood and organ parts from every orifice. Creutzfeldt-Jakob disease, which killed the choreographer George Balanchine in 1983, eats away at its victims' brains until they resemble wet sponges. Never slow to fan mass hysteria, Hollywood has capitalized on the phenomenon with films such as *Outbreak*, in which a monkey carrying a deadly new virus from central Africa infects unwitting Californians and starts an epidemic that threatens to annihilate the human race.

The reality about infectious disease is less sensational but alarming nonetheless. Gruesome new pathogens such as Ebola are unlikely to cause a widespread epidemic because they sicken and kill so quickly that victims can be easily identified and isolated; on the other hand, the seemingly innocuous practice of overprescribing antibiotics for bad colds could ultimately lead to untold deaths, as familiar germs evolve to become untreatable. We are living in the twilight of the antibiotic era: within our lifetimes, scraped knees and cut fingers may return to the realm of fatal conditions.

Through international travel, global commerce and the accelerating destruction of ecosystems worldwide, people are inadvertently exposing themselves to a Pandora's box of emerging microbial threats. And the recent rumblings of biological terrorism from Iraq highlight the appalling potential of disease organisms for being manipulated to vile ends. But although it may appear that the apocalypse has arrived, the truth is that people today are not facing a unique predicament. Emerging diseases have long loomed like a shadow over the human race.

People and pathogens have a long history together. Infections have been detected in the bones of human ancestors more than a million years old, and evidence from the mummy of the Egyptian pharaoh Ramses V suggests that he may have died from smallpox more than 3,000 years ago. Widespread outbreaks of disease are also well documented. Between 1347 and 1351 roughly a third of the population of medieval Europe was wiped out by bubonic plague, which is carried by fleas that live on rodents. In 1793, 10 percent of the population of Philadelphia succumbed to yellow fever, which is spread by mosquitoes. And in 1875 the son of a Fiji chief came down with measles after a ceremonial trip to Australia. Within four months more than 20,000 Fijians were dead from the imported disease, which spreads through the air when its victims cough or sneeze.

According to conventional wisdom in biology, people and invading microorganisms evolve together: people gradually become more resistant, and the microorganisms become less virulent. The result is either mutualism, in which the relation benefits both species, or commensalism, in which one species benefits without harming the other. Chicken pox and measles, once fatal afflictions, now exist in more benign forms. Logic would suggest, after all, that the best interests of an organism are not served if it kills its host; doing so would be like picking a fight with the person who signs your paycheck.

But recently it has become clear to epidemiologists that the reverse of that cooperative paradigm of illness can also be true: microorganisms and their hosts sometimes exhaust their energies devising increasingly powerful weaponry and defenses. For example, several variants of human immunodeficiency virus (HIV) may compete for dominance within a person's body, placing the immune system under ever-greater siege. As long as a virus has an effective mechanism for jumping from one person to another, it can afford to kill its victims [see "The Deadliest Virus," by Cynthia Mills, January/February 1997].

If the competition were merely a question of size, humans would surely win: the average person is 10^{17} times the size of the average bacterium. But human beings, after all, constitute only one species, which must compete with 5,000 kinds of viruses and more than 300,000 species of bacteria. Moreover, in the twenty years it takes humans to produce a new generation, bacteria can reproduce a half-million times. That disparity enables pathogens to evolve ever more virulent adaptations that quickly outstrip human responses to them. The scenario is governed by what the English zoologist Richard Dawkins of the University of Oxford and a colleague have called the "Red Queen Principle." In Lewis Carroll's *Through the Looking Glass* the Red Queen tells Alice she will need to run faster and faster just to stay in the same place. Staving off illness can be equally elusive.

The Centers For Disease Control and Prevention (CDC) in Atlanta, Georgia, has compiled a list of the most recent emerging pathogens. They include:

- *Campylobacter*, a bacterium widely found in chickens because of the commercial practice of raising them in cramped, unhealthy conditions. It causes between two

million and eight million cases of food poisoning a year in the United States and between 200 and 800 deaths.

- *Escherichia coli* 0157:H7, a dangerously mutated version of an often harmless bacterium. Hamburger meat from Jack in the Box fast-food restaurants that was contaminated with this bug led to the deaths of at least four people in 1993.
- Hantaviruses, a genus of fast-acting, lethal viruses, often carried by rodents, that kill by causing the capillaries to leak blood. A new hantavirus known as *sin nombre* (Spanish for "nameless") surfaced in 1993 in the southwestern United States, causing the sudden and mysterious deaths of thirty-two people.
- HIV, the deadly virus that causes AIDS (acquired immunodeficiency syndrome). Although it was first observed in people as recently as 1981, it has spread like wildfire and is now a global scourge, affecting more than 30 million people worldwide.
- The strange new infectious agent that causes bovine spongiform encephalopathy, or mad cow disease, which recently threw the British meat industry and consumers into a panic. This bizarre agent, known as a prion, or "proteinaceous infectious particle," is also responsible for Creutzfeldt-Jakob disease, the brain-eater I mentioned earlier. A Nobel Prize was awarded last year to the biochemist Stanley B. Prusiner of the University of California, San Francisco, for his discovery of the prion.
- *Legionella pneumophila*, the bacterium that causes Legionnaires' disease. The microorganism thrives in wet environments; when it lodges in air-conditioning systems or the mist machines in supermarket produce sections, it can be expelled into the air, reaching people's lungs. In 1976 thirty-four participants at an American Legion convention in Philadelphia died—the incident that led to the discovery and naming of the disease.
- *Borrelia burgdorferi*, the bacterium that causes Lyme disease. It is carried by ticks that live on deer and white-footed mice. Left untreated, it can cause crippling, chronic problems in the nerves, joints and internal organs.

How ironic, given such a rogues' gallery of nasty characters, that just a quarter-century ago the Egyptian demographer Abdel R. Omran could observe that in many modern industrial nations the major killers were no longer infectious diseases. Death, he noted, now came not from outside but rather from within the body, the result of gradual deterioration. Omran traced the change to the middle of the nineteenth century, when the industrial revolution took hold in the United States and parts of Europe. Thanks to better nutrition, improved public-health measures and medical advances such as mass immunization and the introduction of antibiotics, microorganisms were brought under control. As people began living longer, their aging bodies succumbed to "diseases of civilization": cancer, clogged arteries, diabetes, obesity and osteoporosis. Omran was the first to formally recognize that shift in the disease environment. He called it an "epidemiological transition."

Like other anthropologists of my generation, I learned of Omran's theory early in my career, and it soon became a basic tenet—a comforting one, too, implying as it did an end to the supremacy of microorganisms. Then, three years ago, I began working with the anthropologist Kathleen C. Barnes of Johns Hopkins University in Baltimore, Maryland, to formulate an expansion of Omran's ideas. It occurred to us that his epidemiological transition had not been a unique event. Throughout history human populations have undergone shifts in their relations with disease—shifts, we noted, that are always linked to major changes in the way people interact with the environment. Barnes and I, along with James Lin, a master's student at Johns Hopkins University School of Hygiene and Public Health, have since developed a new theory: that there have been not one but three major epidemiological transitions; that each one has been sparked by human activities; and that we are living through the third one right now.

The first epidemiological transition took place some 10,000 years ago, when people abandoned their nomadic existence and began farming. That profoundly new way of life disrupted ecosystems and created denser living conditions that led, as I will soon detail, to new diseases. The second epidemiological transition was the salutary one Omran singled out in 1971, when the war against infectious diseases seemed to have been won. And in the past two decades the emergence of illnesses such as hepatitis C, cat scratch disease (caused by the bacterium *Bartonella henselae*), Ebola and others on CDC's list has created a third epidemiological transition, a disheartening set of changes that in many ways have reversed the effects of the second transition and coincide with the shift to globalism. Burgeoning population growth and urbanization, widespread environmental degradation, including global warming and tropical deforestation, and radically improved methods of transportation have given rise to new ways of contracting and spreading disease.

We are, quite literally, making ourselves sick.

When early human ancestors moved from African forests onto the savanna millions of years ago, a few diseases came along for the ride. Those "heirloom" species—thus designated by the Australian parasitologist J. F. A. Sprent because they had afflicted earlier primates—included head and body lice; parasitic worms such as pinworms, tapeworms and liver flukes; and possibly herpes virus and malaria.

Global Warming could allow the mosquitoes that carry dengue fever to survive as far north as New York City.

For 99.8 percent of the five million years of human existence, hunting and gathering was the primary mode of subsistence. Our ancestors lived in small groups and relied on wild animals and plants for their survival. In their foraging rounds, early humans would occasionally have contracted new kinds of illnesses

through insect bites or by butchering and eating disease-ridden animals. Such events would not have led to widespread epidemics, however, because groups of people were so sparse and widely dispersed.

About 10,000 years ago, at the end of the last ice age, many groups began to abandon their nomadic lifestyles for a more efficient and secure way of life. The agricultural revolution first appeared in the Middle East; later, farming centers developed independently in China and Central America. Permanent villages grew up, and people turned their attention to crafts such as toolmaking and pottery. Thus when people took to cultivating wheat and barley, they planted the seeds of civilization as well.

With the new ways, however, came certain costs. As wild habitats were transformed into urban settings, the farmers who brought in the harvest with their flint-bladed sickles were assailed by grim new ailments. Among the most common was scrub typhus, which is carried by mites that live in tall grasses, and causes a potentially lethal fever. Clearing vegetation to create arable fields brought farmers frequently into mite-infested terrain.

Irrigation brought further hazards. Standing thigh-deep in watery canals, farm workers were prey to the worms that cause schistosomiasis. After living within aquatic snails during their larval stage, those worms emerge in a free-swimming form that can penetrate human skin, lodge in the intestine or urinary tract, and cause bloody urine and other serious maladies. Schistosomiasis was well known in ancient Egypt, where outlying fields were irrigated with water from the Nile River; descriptions of its symptoms and remedies are preserved in contemporary medical papyri.

The domestication of sheep, goats and other animals cleared another pathway for microorganisms. With pigs in their yards and chickens roaming the streets, people in agricultural societies were constantly vulnerable to pathogens that could cross interspecies barriers. Many such organisms had long since reached commensalism with their animal hosts, but they were highly dangerous to humans. Milk from infected cattle could transmit tuberculosis, a slow killer that eats away at the lungs and causes its victims to cough blood and pus. Wool and skins were loaded with anthrax, which can be fatal when inhaled and, in modern times, has been developed by several nations as a potential agent of biological warfare. Blood from infected cattle, injected into people by biting insects such as the tsetse fly, spread sleeping sickness, an often-fatal disease marked by tremors and protracted lethargy.

A second major effect of agriculture was to spur population growth and, perhaps more important, density. Cities with populations as high as 50,000 had developed in the Near East by 3000 B.C. Scavenger species such as rats, mice and sparrows, which congregate wherever large groups of people live, exposed city dwellers to bubonic plague, typhus and rabies. And now that people were crowded together, a new pathogen could quickly start an epidemic. Larger populations also enabled diseases such as measles, mumps, chicken pox and smallpox to persist in an endemic form—always present, afflicting part of the population while sparing those with acquired immunity.

Thus the birth of agriculture launched humanity on a trajectory that has again and again brought people into contact with new pathogens. Tilling soil and raising livestock led to more energy-intensive ways of extracting resources from the earth—to lumbering, coal mining, oil drilling. New resources led to increasingly complex social organization, and to new and more frequent contacts between various societies. Loggers today who venture into the rain forest disturb previously untouched creatures and give them, for the first time, the chance to attack humans. But there is nothing new about this drama; only the players have changed. Some 2,000 years ago the introduction of iron tools to sub-Saharan Africa led to a slash-and-burn style of agriculture that brought people into contact with *Anopheles gambiae*, a mosquito that transmits malaria.

Improved transportation methods also help diseases extend their reach: microorganisms cannot travel far on their own, but they are expert hitchhikers. When the Spanish invaded Mexico in the early 1500s, for instance, they brought with them diseases that quickly raged through Tenochtitlán, the stately, temple-filled capital of the Aztec Empire. Smallpox, measles and influenza wiped out millions of Central America's original inhabitants, becoming the invisible weapon in the European conquest.

In the past three decades people and their inventions have drilled, polluted, engineered, paved, planted and deforested at soaring rates, changing the biosphere faster than ever before. The combined effects can, without hyperbole, be called a global revolution. After all, many of them have worldwide repercussions: the widespread chemical contamination of waterways, the thinning of the ozone layer, the loss of species diversity. And such global human actions have put people at risk for infectious diseases in newly complex and devastating ways. Global warming, for instance, could expose millions of people for the first time to malaria, sleeping sickness and other insect-borne illnesses; in the United States, a slight overall temperature increase would allow the mosquitoes that carry dengue fever to survive as far north as New York City.

Major changes to the landscape that have become possible in the past quarter-century have also triggered new diseases. After the construction of the Aswan Dam in 1970, for instance, Rift Valley fever infected 200,000 people in Egypt, killing 600. The disease had been known to affect livestock, but it was not a major problem in people until the vast quantities of dammed water became a breeding ground for mosquitoes. The insects bit both cattle and humans, helping the virus jump the interspecies barrier.

In the eastern United States, suburbanization, another relatively recent phenomenon, is a dominant factor in the emergence of Lyme disease—10,000 cases of which are reported annually. Thanks to modern earth-moving equipment, a soaring economy and population pressures, many Americans have built homes in formerly remote, wooded areas. Nourished by lawns and gardens and unchecked by wolves, which were exterminated by settlers long ago, the deer population has exploded, exposing people to the ticks that carry Lyme disease.

Meanwhile, widespread pollution has made the oceans a breeding ground for microorganisms. Epidemiologists have suggested that toxic algal blooms—fed by the sewage, fertilizers and other contaminants that wash into the oceans—harbor countless viruses and bacteria. Thrown together into what amounts to a dirty genetic soup, those pathogens can undergo gene-swapping and mutations, engendering newly antibiotic-resistant strains. Nautical traffic can carry ocean pathogens far and wide: a devastating outbreak of cholera hit Latin America in 1991 after a ship from Asia unloaded its contaminated ballast water into the harbor of Callao, Peru. Cholera causes diarrhea so severe its victims can die in a few days from dehydration; in that outbreak more than 300,000 people became ill, and more than 3,000 died.

The modern world is becoming—to paraphrase the words of the microbiologist Stephen S. Morse of Columbia University—a viral superhighway. Everyone is at risk.

Our newly global society is characterized by huge increases in population, international travel and international trade—factors that enable diseases to spread much more readily than ever before from person to person and from continent to continent. By 2020 the world population will have surpassed seven billion, and half those people will be living in urban centers. Be-leaguered third-world nations are already hard-pressed to provide sewers, plumbing and other infrastructure; in the future, clean water and adequate sanitation could become increasingly rare. Meanwhile, political upheavals regularly cause millions of people to flee their homelands and gather in refugee camps, which become petri dishes for germs.

More than 500 million people cross international borders each year on commercial flights. Not only does that traffic volume dramatically increase the chance a sick person will infect the inhabitants of a distant area when she reaches her destination; it also exposes the sick person's fellow passengers to the disease, because of poor air circulation on planes. Many of those passengers can, in turn, pass the disease on to others when they disembark.

The global economy that has arisen in the past two decades has established a myriad of connections between far-flung places. Not too long ago bananas and oranges were rare treats in northern climes. Now you can walk into your neighborhood market and find food that has been flown and trucked in from all over the world: oranges from Israel, apples from New Zealand, avocados from California. Consumers in affluent nations expect to be able to buy whatever they want whenever they want it. What people do not generally realize, however, is that this global network of food production and delivery provides countless pathways for pathogens. Raspberries from Guatemala, carrots from Peru and coconut milk from Thailand have been responsible for recent outbreaks of food poisoning in the United States. And the problem cuts both ways: contaminated radish seeds and frozen beef from the United States have ended up in Japan and South Korea.

Finally, the widespread and often indiscriminate use of antibiotics has played a key role in spurring disease. Forty million pounds of antibiotics are manufactured annually in the United States, an eightyfold increase since 1954. Dangerous microorganisms have evolved accordingly, often developing antibiotic-resistant strains. Physicians are now faced with penicillin-resistant gonorrhea, multiple-drug-resistant tuberculosis and *E. coli* variants such as O157:H7. And frighteningly, some enterococcus bacteria have become resistant to all known antibiotics. Enterococcus infections are rare, but staphylococcus infections are not, and many strains of staph bacteria now respond to just one antibiotic, vancomycin. How long will it be before run-of-the-mill staph infections—in a boil, for instance, or in a surgical incision—become untreatable?

Although civilization can expose people to new pathogens, cultural progress also has an obvious countervailing effect: it can provide tools—medicines, sensible city planning, educational campaigns about sexually transmitted diseases—to fight the encroachments of disease. Moreover, since biology seems to side with microorganisms anyway, people have little choice but to depend on protective cultural practices to keep pace: vaccinations, for instance, to confer immunity, combined with practices such as hand-washing by physicians between patient visits, to limit contact between people and pathogens.

All too often, though, obvious protective measures such as using only clean hypodermic needles or treating urban drinking

water with chlorine are neglected, whether out of ignorance or a wrongheaded emphasis on the short-term financial costs. The worldwide disparity in wealth is also to blame: not surprisingly, the advances made during the second epidemiological transition were limited largely to the affluent of the industrial world.

Such lapses are now beginning to teach the bitter lesson that the delicate balance between humans and invasive microorganisms can tip the other way again. Overconfidence—the legacy of the second epidemiological transition—has made us especially vulnerable to emerging and reemerging diseases. Evolutionary principles can provide this useful corrective: in spite of all our medical and technological hubris, there is no quick fix. If human beings are to overcome the current crisis, it will be through sensible changes in behavior, such as increased condom use and improved sanitation, combined with a commitment to stop disturbing the ecological balance of the planet.

The Bible, in short, was not far from wrong: We do bring plagues upon ourselves—not by sinning, but by refusing to heed our own alarms, our own best judgment. The price of peace—or at least peaceful coexistence—with the microorganisms on this planet is eternal vigilance.

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