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Where Will the Next Pandemic Emerge?

The next killer germ could burst from the African rain forest—or from your family pet.

by Jared Diamond and Nathan Wolfe
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Shortly after one of us ([Jared Diamond](#)) boarded a flight from Hong Kong back to Los Angeles, the passenger in the next seat sneezed. She sneezed again—and again—and then she began coughing. Finally she gagged, pulled out the vomit bag from the seat back in front of her, threw up into the bag, stood up, squeezed past, and lurched to the toilet at the front of the plane. The woman was obviously miserable, but sympathy for her pain was not what I felt. Instead I was frightened and asked the flight attendant to move me to a seat as far from her as possible.

All I could think of was another sick person, [a man from Guangdong](#) province in southern China, who spent the night of February 21, 2003, at the Metropole Hotel in Hong Kong, an upscale establishment with a swimming pool, fitness center, restaurants, a bar, and all kinds of areas where visitors could socialize and connect. The man stayed a single night in room 911. Unfortunately for him and for many other people, he had picked up severe acute respiratory syndrome, or [SARS](#)—perhaps directly from an infected bat or from a small, arboreal mammal called a civet, common in one of Guangdong's famous “wet markets” that sell wild animals for food, or else from a person or chain of people ultimately infected from one of those animal sources.



In the course of his brief stay, the man initiated a SARS “super spreader” event that led to at least 16 more SARS cases among the hotel's guests and visitors and then to hundreds of other cases throughout Asia, Europe, and North America as those guests and visitors continued on their travels—just as my neighbor was now traveling to L.A. The infectiousness of room 911's guest can be gauged from the fact that three months later, the carpet right outside the door and near the hotel elevator yielded genetic evidence of the SARS virus, presumably spewed out in his own sneezing, coughing, or vomiting.

I didn't end up with SARS, but my experience drives home the terrifying prospect of a novel, unstoppable infectious disease. Globalization, [changing climate](#), and the threat of [drug resistance](#) have conspired to set the stage for that perfect microbial storm: a situation in which an emerging pathogen—another HIV or smallpox, perhaps—might burst on the scene and kill millions before we can respond.

Pathogen Paradox

To grasp the risk, we first must understand why *any* microbe would evolve to sicken or kill us. In evolutionary terms, how does destroying its host help a microbe to survive?

Think of your body as a potential “habitat” for tiny microbes, just as a forest provides a habitat for bigger creatures like birds and squirrels. The species living in the forests of our bodies include lice, worms, bacteria, viruses, and amoebas. Many of those denizens are benign and cause us no harm. But some microbes seem to go out of their way to make us sick—either mildly sick, as in the case of the [common cold](#), or else sick to the point of killing us, as in the case of [smallpox](#).

Killer microbes have long posed a paradox for evolutionary biologists. Why would a microbe evolve to devastate the very habitat on which it depends? By analogy, you might reason that there should be no squirrels that destroy the forest they live in, because such a species would quickly go extinct.

The answer stems from the fact that in order to survive over the long haul, any microbe restricted to humans must be able to spread from one victim to the next. There is a simple mathematical requirement here: On average, the germ must infect at least one new victim for every old one who either dies or recovers and purges himself of the microbe. If the average number of new victims per old drops to fewer than one, then the spread of the microbe is doomed.

A microbe can't walk or fly from one host to the next. Instead it must resort to a range of nefarious tricks. What from our point of view is simply a disease symptom can, from the bug's perspective, be an all-important means of enlisting our help to move around. Common microbe tricks are to make us cough or sneeze, suffer from diarrhea, or develop open sores on our skin. Respectively, these symptoms spread the microbe into our exhaled breath, into the local water supply via our feces, and onto the skin of those who touch us, explaining why a microbe might want to induce unpleasant symptoms in its victims.

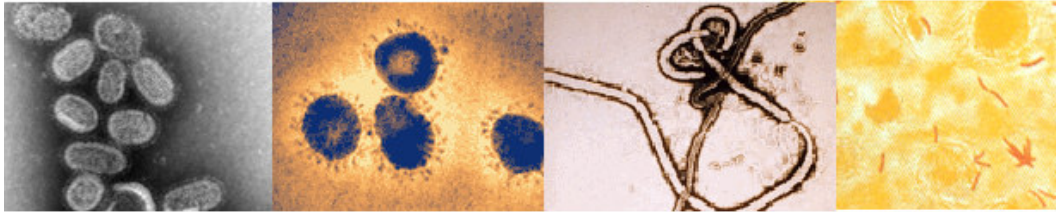
Evolutionary biologists reason that keeping us alive and pumping out new microbes would be an excellent strategy for such a bug, which might therefore evolve to be less, not more, virulent over time. An example comes from the history of [syphilis](#). When it first appeared in Europe in 1495, it caused severe and painful symptoms within a few months, but by 1546 it had begun evolving into the slowly progressing disease that we know today.

Yet if keeping us alive is strategically sound, why do some pathogens go so far as to actually kill us?

Sometimes a microbe's deadly rampage through a human population stems from an accident of nature. For instance, the microbe could be comfortably adapted to some animal host that it routinely inhabits without deadly consequences, but it could be maladapted to the human environment. The microbe may rarely infect people, but when it does, it may kill the human host, who becomes a literal dead end for the virus as well.

But what of those killer microbes that target humans, making us their primary host? Their survival strategy, evolutionary biologists now realize, differs from that of a disease like syphilis but works just as well. Take the [cholera bacterium](#) that gives us diarrhea or the smallpox virus that makes us develop skin sores; both of these can kill us in days to weeks. Such virulence may be evolutionarily favored if, in the brief time between our becoming infected and dying, the fatal symptoms spread trillions of microbes to potential new victims. The fact that we may die is unfortunate for us but an acceptable cost for the microbe. In the world of evolution and natural selection, anything that the microbe does to us is fair—just as long as at least one new victim gets infected for each old one.

Hence the recipe for a killer disease is for the microbe to achieve a balance between two things: the probability of its killing us quickly once we become infected and its efficiency in [leading our bodies to transmit the microbe to new victims](#).



from left: influenza, SARS, Ebola virus, Tuberculosis in sputum
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Those two things are connected. The greater its efficiency in inducing lethal, bug-spreading syndromes (good for the microbe), the faster the microbe kills us (bad for the microbe). Following this logic, a pathogen may end up killing lots of people by one of two routes. In the style of [HIV](#), it can keep the disease carrier alive for a long time, infecting new victims over the course of months or years. Or in the style of smallpox and cholera, it might kill quickly with explosive symptoms that can spread an infection to dozens of new victims within a day.

A microbe's deadly rampage through humans might stem from an accident of nature.

Searching for the Source

For epidemiologists hoping to stanch such outbreaks, tracking killer germs to the source is key. Do deadly pandemics arise spontaneously in human populations? Or are they "gifts" from other species, mutating and then crossing over to make us ill? Which ecosystems are spawning them, and can we catch them at the start, before they cause too much damage?

Some answers can be found in the history of yellow fever, a [virus spread by mosquitoes](#). The cause of devastating human epidemics throughout history, yellow fever is still rife in tropical South America and Africa. Biologists now understand that yellow fever arose in tropical African monkeys, which, through the mosquito vector, infected (and continue to infect) tropical African people, some of whom unintentionally carried yellow fever with them on slave ships several hundred years ago to South America.

[Mosquitoes](#) bit the infected slaves and in turn carried the virus to South American monkeys. In due course, mosquitoes bit infected monkeys and transmitted yellow fever right back to the human population there.

In Venezuela today, the Ministry of Health keeps a lookout for the appearance of unusual numbers of dead wild monkeys, such as howler monkeys. Because the monkeys are so susceptible to yellow fever and can act as a reservoir from which the virus leaps to the human population, an explosion of monkey deaths serves as an advance warning system, signaling the need to vaccinate humans in the vicinity.

This pattern of cross-infection from animals to humans is par for the course in emerging infectious disease. In fact, the big killer diseases of history all came to us from microbes living in other species, overwhelmingly from other warm-blooded mammals and, to a lesser extent, from birds.

On reflection, this all makes sense. Each new animal host to which a microbe adapts represents a new habitat. It is easiest for a microbe to jump between closely related habitats, from an animal species with one sort of body chemistry to a closely related animal species with very similar body chemistry.

In the tropics, disease sources have included a host of wild animals, most notably the [nonhuman primates](#). We can thank our primate cousins not just for yellow fever but also for HIV, dengue fever, hepatitis B, and vivax malaria. Other wild animal disease donors include rats, the source of the plague and typhus.

In temperate regions like the United States, meanwhile, ticks in suburban neighborhoods and domestic livestock living in proximity to humans have posed threats. Mammalian reservoirs like mice and chipmunks carry Lyme disease and tularemia; ticks transmit these diseases to humans. Cattle probably gave rise to the measles and tuberculosis. Smallpox is likely to have come from camels, biologists say, and flu from pigs and ducks.

The Next Wave

Today, with fewer people tending farms and more living in the suburbs, things have certainly changed. The principles of infectious disease are the same as they have always been, but modern conditions, including life in proximity to pets and mammal-filled woods, are exposing us to new pathogen reservoirs and new modes of transmitting disease.

One of us ([Nathan Wolfe](#)) has spent much of the last six years in the tropical African country of Cameroon, studying the kinds of interspecies jumps that such conditions might spawn. To examine the mechanisms, I worked with rural hunters who butchered wild animals for food. I collected blood samples from the hunters, from other people in their community, and from their animal prey. By testing all those samples, I identified microbes inhabiting the animal reservoirs and focused on those that showed up in the hunters' blood, making them candidates for firing up human disease.

One evening I asked a group of hunters if they had ever cut themselves while butchering wild monkeys or apes. The response was incredulous laughter: "You don't know the answer to that?" Of course, they said. All of them had cut themselves once or more, thereby giving themselves ample opportunity to get infected from animal blood.

On reflection, I shouldn't have been surprised. I can't count all the times I have cut myself while chopping onions. The difference is that onions aren't closely related to us humans, and an onion virus has far less chance of taking hold in us than does a monkey virus.

The statistics are telling. Researchers like Mark Woolhouse, professor of infectious disease epidemiology at the University of Edinburgh in Scotland, have found at least 868 human pathogens that infect both animals and humans, although some are not as fearsome as they seem.

We have the potential to avert the next HIV, saving millions of lives and billions of dollars.

Overhyped microbes include anthrax (famous for the U.S. mail attacks in 2000), the Ebola and Marburg viruses (which can cause dramatic bleeding and high fever in their victims), and the prion agent of mad cow disease (otherwise known as bovine spongiform encephalopathy, or BSE), which kills people by making their nervous systems degenerate. These bugs arouse terror because they kill so many of their victims. For example, in [the 2000 Ebola outbreak](#), which struck the Gulu district of Uganda, 53 percent of the 425 people who contracted the disease died. The case fatality rate for BSE is 100 percent.

Although spectacularly lethal, these pathogens generally kill just a few hundred people at a time and then burn themselves out. They transmit from human to human too inefficiently to spread very widely; 100 percent of a small number of victims is still a small number of fatalities.

There are many reasons why an agent leaping from animals to humans might not affect more individuals. For example, humans do not normally bite, scratch, hunt, or eat each other. This surely contributes to the rarity or nonexistence of human-to-human transmission of rabies (acquired by the bite of an infected dog or bat); cat-scratch disease (which causes skin lesions and swollen lymph nodes); tularemia (a disease, often acquired when hunting and cutting up an infected rabbit, that can cause skin ulcers, swollen lymph nodes, and fever); and BSE (probably acquired by eating the nervous system tissue of infected cows).

Some outbreaks, once recognized, are relatively easy to control. Anthrax is treatable with antibiotics; after an initial malaria-like stage, the rapid onset and severity of Ebola and Marburg symptoms have made identification and containment straightforward.

In fact, within the last 40 years, only HIV (derived from chimpanzees) has taken off to cause a pandemic.

Back to the Future

If not anthrax or Ebola, which pathogens might spawn the next deadly pandemic in our midst?

New pandemics are most likely to be triggered by mutant strains of familiar microbe species, especially those that have caused plagues by churning out mutant strains in the past. For example, the highest known epidemic death toll in history was caused by a new strain of influenza virus that killed more than 20 million people in 1918 and 1919. Unfairly named Spanish influenza, it apparently emerged in Kansas during World War I, was carried by American troops to Europe, and then spread around the world in three waves before ebbing in outbreaks of declining virulence in the 1920s. Mutant strains of influenza or cholera remain prime candidates for another deadly outbreak. Both can persist in animal reservoirs or the environment, and both are adept at spawning new strains. Both pathogens also transmit efficiently, and it is possible that these two important diseases of the past could become important diseases of the future.

A future pandemic could also come from tuberculosis. New mutants have already arisen through the mechanism of drug resistance. And the disease lives on in the human population, especially among those with weakened immunity, including patients with HIV.

Also of concern are emerging [sexually transmitted diseases](#), which, once introduced, may be difficult to control because it is hard to persuade humans to change sexual behavior or to abstain from sex. HIV offers a grim warning: Despite its huge global impact, the AIDS epidemic would have been far worse if the sexual transmissibility of HIV (which is actually rather modest) had equaled that of some other sexually transmitted agents, such as human papilloma virus ([HPV](#)). While the probability of HIV transmission varies with the stage of the disease and the type of sexual contact, it appears to pass from infected to uninfected individuals in less than 1 percent of acts of unprotected heterosexual intercourse, while the corresponding probability of HPV transmission is thought to be higher than 5 percent—probably much higher.

Similarly, it could be difficult to control emerging pathogens transmitted by pets, which increasingly include exotic species along with traditional domestic animals like dogs and cats. Already we are at risk of catching rabies from our dogs, toxoplasmosis and cat-scratch disease from our cats, and psittacosis from our parrots. Most people now accept the need to cull millions of farmyard animals in the face of epidemics like mad cow disease, but it is hard to imagine killing beloved puppies, bunnies, and kittens, even if those pets do turn out to offer a pathway for a dangerous new disease.

Have Plague, Will Travel

Once a killer disease has emerged, modern societies offer new ways for it to flourish and spread. Global travel, the close quarters of the urban environment, climate change, the evolution of drug-resistant microbes, and increasing numbers of the elderly or antibiotic-treated immunosuppressed could all aid the next great plague.

For example, rapid urbanization in Africa could transform yellow fever, chikungunya fever (which causes severe joint pain and fever), and other rural African arboviruses (viruses, including yellow fever, spread by bloodsucking insects) into plagues of African cities, as has already happened with dengue hemorrhagic fever. One of us (Wolfe) theorizes that this might follow increasing demand in those cities for [bush meat](#). Like urban people everywhere, urban Africans love to eat the foods enjoyed by their village-dwelling ancestors, and in tropical Africa this means bush meat. In that respect it's similar to the smoked fish and bagels that I eat in the United States, which give me some comforting memory of my Eastern European roots. But there's an important difference: The wild game that I see served in fancy restaurants in the capital of Cameroon is much more likely to transmit a dangerous virus to the person who hunted and butchered it, or to the cook who prepared it, or to the restaurant patron who ate the meat undercooked, than is my brunch of smoked fish and bagels.

By connecting distant places, meanwhile, globalization permits the long-distance transfer of microbes along with their insect vectors and their human victims, as evidenced not only by the spread of HIV around the world, but also by North American cases of cholera and SARS brought by infected passengers on jet flights from South America and Asia, respectively. Indeed, when a flight from Buenos Aires to Los Angeles stopped in Lima in 1992, it picked up some seafood infected with the cholera then making the rounds in Peru. As a result, dozens of passengers who arrived in Los Angeles, some of whom then changed planes and flew on to Nevada and even as far as Japan, found that they had contracted cholera. Within days that single airplane spread cholera 10,000 miles around the whole rim of the Pacific Basin.

Consider as well those diseases thought of as "just" tropical because they are transmitted by tropical vectors: malaria transmitted by mosquitoes, sleeping sickness spread by tsetse flies, and Chagas' disease (associated with edema, fever, and heart disease) spread by kissing bugs. How will we feel about those tropical diseases if global warming enables their vectors to spread into temperate zones? While microbe and vector movement can be difficult to detect, modeling suggests that global warming will expand the reach of malaria to higher latitudes and into tropical mountain regions.

The transmission of emerging diseases has also been enhanced by a host of modern practices and technologies. The commercial bush meat trade has introduced retroviruses into human populations. Ecotourism has exposed first-world tourists to cutaneous leishmaniasis and other third-world diseases. Underequipped rural hospitals have facilitated Ebola virus outbreaks in Africa. Air conditioners and water circulation systems have spread Legionnaires' disease. Industrial food production was responsible in Europe for the spread of BSE. And intravenous drug use and blood transfusion have both spread HIV and hepatitis B and C.

All this shows that disease prevention and treatment need to be supplemented by a new effort: disease forecasting. This refers to the early detection of potential pandemics at a stage when we might still be able to localize them, before they have had the opportunity to infect a high percentage of the local population and thereby spread around the world, as happened with HIV. Already one of us (Wolfe) is working through a new initiative, the [Global Viral Forecasting Initiative](#) (GVFI), to do just that. GVFI works in countries throughout the world to monitor the entry and movement of new agents before they become pandemics. By studying emerging agents at the interface between humans and animals, GVFI hopes to stop new epidemics before they explode. Monitoring for the emergence of both new sexually transmitted diseases and pet-associated diseases would be good investments.

The predictions here are admittedly educated guesses—but they are educated by some of the best science available. The time to act is now. If we don't, then we will continue to be like the cardiologists of the 1950s, waiting for their patients' heart attacks and doing little to prevent them. If we do act, we have the potential to avert the next HIV, saving millions of lives and billions of dollars. The choice seems obvious.