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Feature Article

From Spillover to Pandemic

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The excerpt below, published in 2012 in the American edition of my book Spillover, came after 500 pages in which I described the phenomenon of zoonotic diseases (those caused by viruses and other pathogens passed from nonhuman animals to humans), the importance of those diseases amid the problems of global human health, the work of the scientists who study such diseases, and the danger that a virus newly emerged from an animal host could cause a terrible pandemic. Immediately preceding this section, I had recounted my visit with Dr. Robert Webster, one of the world's leading influenza researchers, who worried that a highly pathogenic form of avian influenza, known as H5N1, might evolve the capacity to transmit human-to-human. "And then God help us," he said. Another senior authority, as you'll see below, warned me especially about the coronaviruses. And now here we are.

Some people have flattered me by saying that my book has been prescient or prophetic; but if the book has been prophetic, it's not because I was prescient. I was merely reporting a collated version of what some very smart and wise scientists, including Dr. Webster, had told me in answer to questions such as: "If there is a Next Big One, a global disease catastrophe, what will it look like?"

Those scientists also cautioned me that precise prediction was impossible with events as contingent on circumstance as viral spillover. And so, near the middle of this excerpt, I wrote: "If we can't predict a forthcoming influenza pandemic or any other newly emergent virus, we can at least be vigilant; we can be well-prepared and quick to respond; we can be ingenious and scientifically sophisticated in the forms of our response." And we could have been. The work of the scientists offered us that possibility. But alas, because of failed vision in our political leaders, we weren't.

This whole subject, like an airborne virus, is at large on the breezes of discourse. Most people aren't familiar with the word "zoonotic," but they have heard of SARS, they have heard of West Nile virus, they have heard of bird flu. They know someone who has suffered through Lyme disease and someone else who has died of AIDS. They have heard of Ebola, and they know that it's a terrifying thing (though they may confuse it with *E. coli*, the bacterium that can kill you if you eat the wrong spinach). They are concerned. They are vaguely aware. But they don't have the time or the interest to consider a lot of scientific detail.

I can say from experience that some people, if they hear you're writing a book about such things—about scary emerging diseases, about killer viruses, about pandemics—want you to cut to the chase. So they ask: "Are we all gonna die?" I have made it my little policy to say yes.

Yes, we are all gonna die. Yes. We are all gonna pay taxes and we are all gonna die. Most of us, though, will probably die of something more mundane than a new virus lately emerged from a duck or a chimpanzee or a bat.

The dangers presented by zoonoses are real and severe but the degree of uncertainties is also high. There's not a hope in hell, as Robert Webster pungently told me, of predicting the nature and timing of the next influenza pandemic. Too many factors vary randomly, or almost randomly, in that system. Prediction, in general, so far as all these diseases are concerned, is a tenuous proposition, more likely to yield false confidence than actionable intelligence. I have asked not just Webster but also many other eminent disease scientists, including some of the world's experts on Ebola, on SARS, on bat-borne viruses generally, on the HIVs, and on viral evolution, the same two-part question: (1) Will a new disease emerge, in the near future, sufficiently virulent and transmissible to cause a pandemic on the scale of AIDS or the 1918 flu, killing tens of millions of people? and (2) If so, what does it look like and whence does it come? Their answers to the first part have ranged from Maybe to Probably. Their answers to the second have focused on RNA viruses, especially those for which the reservoir host is some kind of primate. None of them has disputed the premise, by the way, that if there is a Next Big One it will be zoonotic.

In the scientific literature, you find roughly the same kind of cautious, informed speculation. A highly regarded infectious-disease epidemiologist named Donald S. Burke, presently dean of the Graduate School of Public Health at the University of Pittsburgh, gave a lecture (later published) back in 1997 in which he listed the criteria that might implicate certain kinds of viruses as likeliest candidates to cause a new pandemic. "The first criterion is the most obvious: recent pandemics in human history," Burke told his audience. That would point to the orthomyxoviruses (including the influenzas) and the retroviruses (including the HIVs), among others. "The second criterion is proven ability to cause major epidemics in non-human animal populations." This would again spotlight the orthomyxoviruses, but also the family of paramyxoviruses, such as Hendra and Nipah, and the coronaviruses, such as that virus later known as SARS-CoV. Burke's third criterion was "intrinsic evolvability," meaning readiness to mutate and to recombine (or reassort), which "confers on a virus the potential to emerge into and to cause pandemics in human populations." As examples he returned to retroviruses, orthomyxoviruses, and coronaviruses. "Some of these viruses," he warned, citing coronaviruses in particular, "should be considered as serious threats to human health. These are viruses with high evolvability and proven ability to cause epidemics in animal populations." It's interesting in retrospect to note that he had augured the SARS epidemic six years before it occurred.

Much more recently, Burke told me: "I made a lucky guess." He laughed a self-deprecating hoot and then added that "prediction is too strong a word" for what he had been doing.

Donald Burke can be trusted on this as much as anyone alive. But the difficulty of predicting precisely doesn't oblige us to remain blind, unprepared, and fatalistic about emerging and re-emerging zoonotic diseases. No. The practical alternative to soothsaying, as Burke put it, is "improving the scientific basis to improve readiness." By "the scientific basis" he meant the understanding of which virus groups to watch, the field capabilities to detect spillovers in remote places before they become regional outbreaks, the organizational capacities to control outbreaks before they become pandemics, plus the laboratory tools and skills to recognize known viruses speedily, to characterize new viruses almost as fast, and to create vaccines and therapies without much delay. If we can't predict a forthcoming influenza pandemic or any other newly emergent virus, we can at least be vigilant; we can be well-prepared and quick to respond; we can be ingenious and scientifically sophisticated in the forms of our response.

We should appreciate that these recent outbreaks of new zoonotic diseases, as well as the recurrence and spread of old ones, are part of a larger pattern, and that humanity is responsible for generating that pattern. We should recognize that they reflect things that we're doing, not just things that are happening to us. We should understand that, although some of the human-caused factors may seem virtually inexorable, others are within our control.

The experts have alerted us to these factors and it's easy enough to make a list. We have increased our population to the level of 7 billion and beyond. We are well on our way toward 9 billion before our growth trend is likely to flatten. We live at high densities in many cities. We have penetrated, and we continue to penetrate, the last great forests and other wild ecosystems of the planet, disrupting the physical structures and the ecological communities of such places. We cut our way through the Congo. We cut our way through the Amazon. We shake the trees, figuratively and literally, and things fall out. We kill and butcher and eat many of the wild animals found there. We settle in those places, creating villages, work camps, towns, extractive industries, new cities. We bring in our domesticated animals, replacing the wild herbivores with livestock. We multiply our livestock as we've multiplied ourselves, operating huge factory-scale operations involving thousands of cattle, pigs, chickens, ducks, sheep, and goats, not to mention hundreds of bamboo rats and palm civets, all

confined en masse within pens and corrals, under conditions that allow those domestics and semidomestics to acquire infectious pathogens from external sources (such as bats roosting over the pig pens), to share those infections with one another, and to provide abundant opportunities for the pathogens to evolve new forms, some of which are capable of infecting a human as well as a cow or a duck. We treat many of those stock animals with prophylactic doses of antibiotics and other drugs, intended not to cure them but to foster their weight gain and maintain their health just sufficiently for profitable sale and slaughter, and in doing that we encourage the evolution of resistant bacteria. We export and import livestock across great distances and at high speeds. We export and import other live animals, especially primates, for medical research. We export and import wild animals as exotic pets. We export and import animal skins, contraband bushmeat, and plants, some of which carry secret microbial passengers. We travel, moving between cities and continents even more quickly than our transported livestock. We stay in hotels where strangers sneeze and vomit. We eat in restaurants where the cook may have butchered a porcupine before working on our scallops. We visit monkey temples in Asia, live markets in India, picturesque villages in South America, dusty archeological sites in New Mexico, dairy towns in the Netherlands, bat caves in East Africa, racetracks in Australia—breathing the air, feeding the animals, touching things, shaking hands with the friendly locals—and then we jump on our planes and fly home. We get bitten by mosquitoes and ticks. We alter the global climate with our carbon emissions, which may in turn alter the latitudinal ranges within which those mosquitoes and ticks live. We provide an irresistible opportunity for enterprising microbes by the ubiquity and abundance of our human bodies.

Everything I've just mentioned is encompassed within this rubric: the ecology and evolutionary biology of zoonotic diseases. Ecological circumstance provides opportunity for spillover. Evolution seizes opportunity, explores possibilities, and helps convert spillovers to pandemics.