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Disease: The Next Big One

By DAVID QUAMMEN

BOZEMAN, Montana — Grim prognostications of pestilence are as old as the Book of Revelation, but they have not gone out of style or been rendered moot. Plague is a tribulation that science, technology and social engineering haven't fixed. In the mid-1960s, some public health officials imagined that antibiotics and other modern therapies would enable us to "close the book" on infectious diseases and so make it possible to focus on noncommunicable afflictions, like heart attack, diabetes and stroke. But that optimism was mistaken.

By one account, published in Nature in 2008, more than 300 instances of emerging infectious diseases occurred between 1940 and 2004. These included both the first appearance of scary new viral diseases (like SARS), with the potential to cause global pandemics, and the re-emergence of older bacterial infections in new forms (like antibiotic-resistant tuberculosis and Staphylococcus aureus), which are less dramatic but also capable of causing illness and death on a large scale. The authors of that study warned that global resources to counter disease emergence were poorly allocated, with most new outbreaks occurring in tropical countries, and most scientific and surveillance efforts concentrated elsewhere.

The most gruesome emergent diseases — like those caused by Ebola virus in Africa or Nipah virus in Asia — affect relatively few. The most devastating, AIDS, is caused by a devious, patient virus that wages slow-motion war against the human body, with mortal consequences for millions. The most explosive — SARS in 2002, or some recent strains of influenza — had the potential, but for prompt action and good luck, to claim many more victims than they did.

AIDS, SARS, Ebola virus and many other new diseases have one thing in common: they are zoonotic. This means they came from nonhuman animals and made the leap to humans. The infectious agent might be a virus, or a bacterium, or another sort of parasitic microbe, or a worm; the animal in which it resides inconspicuously, before spilling over into humans, is known as its reservoir host. The reservoir host might be a bat (as with the SARS virus), or a rodent (the various hantaviruses), or a chimpanzee (H.I.V.-1). The reservoir host of Ebola virus is still unidentified — a lingering mystery — though bats again are suspected. And all of our influenzas (even the so-called swine flus) originate in wild aquatic birds.

We now know from molecular evidence (published by Beatrice H. Hahn, Micha their collaborators) that the pandemic strain of H.I.V. went from a single chim

single person (presumably by blood-to-blood contact when the chimp was slaughtered for food) around 1908 or earlier, in southeastern Cameroon. The virus then must have passed slowly downriver, human to human, into the large population centers of the Congo basin before spreading worldwide.

Sixty percent of human infectious diseases, including the worst of the old ones and the scariest of the new, are zoonotic. Now disease experts wonder about the "next big one:" when will it come, what will it look like, from which reservoir host will it spill over, and how many people will it kill?

Prediction is difficult. But we can be reasonably confident on a few points. The worst new diseases of the future, like those of the recent past, will be zoonotic. Unfamiliar pathogens come to people from wildlife or livestock. The scariest of the new bugs will probably be viruses. Formidable, hardy, opportunistic and impervious to antibiotics, viruses replicate and evolve quickly. They exist in extraordinary diversity and seem ever ready to colonize new hosts.

Experts believe that the next global pandemic is likely to be caused by a virus with high "intrinsic evolvability," meaning that it mutates especially quickly or recombines elements of its genetic material during the process of replication. It crackles and snaps with accidental variation. Darwin told us that variation is the raw material of adaptive change; and adaptive change is what enables an organism to thrive in unfamiliar conditions — including human hosts.

In 1997, Dr. Donald S. Burke cautioned that the watch list of candidate viruses for the next global pandemic — the ones with high intrinsic evolvability — should include the influenzas, the retroviruses (like H.I.V.-1 and H.I.V.-2), and the coronavirus family (including SARS). His warning was validated when SARS emerged.

Precise prediction may not be possible, but informed vigilance is. Intrepid disease ecologists are hiking into forests, climbing through caves, visiting remote communities to investigate small outbreaks, gathering evidence of novel infections, and sleuthing the mysteries of reservoir host and spillover. In labs, other scientists are developing sophisticated new molecular tools for quickly identifying and characterizing new viruses. Private, governmental and international health institutions support scientific efforts and public-health planning to limit the scope of coming pandemics.

There are issues of civil liberties and privacy, as well as issues of public health, to be faced as we prepare for the "next big one." Consider the matter of travel. When Dr. Burke issued his warning, you could get on an airplane just about anywhere carrying a pocketknife. You can't do that anymore. But you can still board a plane carrying a virus. This may change. Soon, it will be possible to identify quickly who is or is not infected with a dangerous new virus, and the carriers

may be excluded from certain activities — or worse. During smallpox outbreaks of the late 19th and early 20th centuries, some American communities instituted compulsory vaccination and forcible confinement in pesthouses. A 21st-century version, based on similar fears about a new zoonotic virus, might involve cheek-swabbing and speedy molecular diagnostics at airport security checkpoints, followed by ... who knows what sort of quarantine for those carrying the bug.

We'll need to balance between individual liberties and the health of the human herd. Field research in areas of high biological diversity, careful scrutiny of the interactions of humans and wildlife, control of the killing and transport of wild animals for food, attention to the disease threats inherent in factory-scale livestock husbandry, efficient sampling and diagnostic tools, global monitoring networks, better vaccines, better antiviral drugs, and contingency plans for confining and controlling outbreaks — these represent our best defenses against the "next big one." We can't prevent another malign bug from entering the human population. But will it kill a few thousand people, or tens of millions?

The answer may depend not just on the nature of the virus, and on the density and abundance of Homo sapiens on this planet, but also on the particulars of how we respond. Viruses are adaptable and heedless. Humans are adaptable and smart.

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