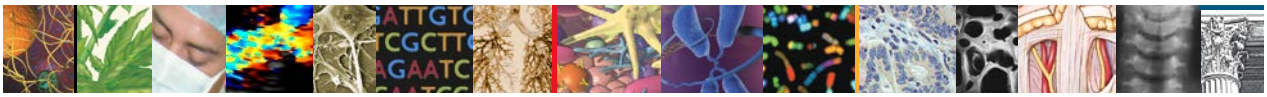

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Perspective

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The Next Epidemic — Lessons from Ebola

Bill Gates

Perhaps the only good news from the tragic Ebola epidemic in Guinea, Sierra Leone, and Liberia is that it may serve as a wake-up call: we must prepare for future epidemics of diseases that may spread more effectively than Ebola. There is a significant chance that an epidemic of a substantially more infectious disease will occur sometime in the next 20 years; after all, we saw major epidemics during the 20th century, including the Spanish influenza epidemic of 1918–1919 and the ongoing pandemic of human immunodeficiency virus. In fact, of all the things that could kill more than 10 million people around the world, the most likely is an epidemic stemming from either natural causes or bioterrorism.

Ebola is far from the most infectious known disease. Other disease agents (measles and influenza, for example) are far more infectious because they can be spread through the air, rather than requiring direct contact. People may not even be aware that they are infected or infectious. Since a person carrying one of these pathogens can infect many strangers in a marketplace or on an airplane, the number of cases can escalate very quickly.

As the Ebola epidemic fades from the world's attention, we risk missing the opportunity to learn from it. Even if the system we have today had worked perfectly for Ebola, it would fail to contain a more infectious disease.

It's instructive to compare our preparations for epidemics with our preparations for another sort of global threat — war. The North Atlantic Treaty Organization (NATO) has a mobile unit that is ready to deploy quickly. Although the system is not perfect, NATO countries participate in joint exercises in which they work out logistics such as how fuel and food will be provided, what language they will speak, and what radio frequencies will be used. Few, if any, such measures are in place for response to an epidemic. The world does not fund any organization to manage the broad set of coordinated activities required in an epidemic. The last serious simulation of an epidemic in the United States, the Dark Winter exercise, took place in 2001. And few countries have met their commitments under the International Health Regulations, which were adopted by the United Nations after the 2002–2003 outbreak of the severe acute respiratory syndrome (SARS) and were intended to improve the world's ability to prevent and contain outbreaks.[1]

Because there was so little preparation, the world lost time in the current epidemic trying to

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Recommendations for Preparing for Future Epidemics

The world needs to build a warning and response system for outbreaks. This system should

- be coordinated by a global institution that is given enough authority and funding to be effective,
- enable fast decision making at a global level,
- expand investment in research and development and clarify regulatory pathways for developing new tools and approaches,
- improve early warning and detection systems, including scalable everyday systems that can be expanded during an epidemic,
- involve a reserve corps of trained personnel and volunteers,
- strengthen health systems in low- and middle-income countries, and
- incorporate preparedness exercises to identify the ways in which the response system needs to improve.

answer basic questions about combating Ebola. In the next epidemic, such delays could result in a global disaster.

The problem is not the fault of any single institution — it reflects a global failure. The world needs a global warning and response system for outbreaks. (Though the World Health Organization [WHO] has a Global Outbreak Alert and Response Network, it is severely understaffed and underfunded.) Such a system could enable us to manage not only a naturally occurring epidemic, but also one ignited by a bioterror attack.[2] Although I have not seen a rigorous estimate of the cost of building such a system, World Bank projections give a sense of the cost of inaction: a worldwide influenza epidemic, for example, would reduce global wealth by an estimated $3 trillion.[3]

I hope the following sketch of what such a warning and response system might look like will spark action to prepare for an epidemic that could have global consequences (see box).

HEALTH SYSTEMS AND SURVEILLANCE

First, there is a critical need to reinforce basic public health systems, including primary health care facilities, laboratories, surveillance systems, and critical care facilities, among other components. As many commentators have noted, Ebola has spread much faster and more widely in countries whose health systems — and especially whose primary care systems — were severely weakened by years of armed conflict and neglect.

Strengthening health care systems not only improves our ability to deal with epidemics, but it also promotes health more broadly. Without a functioning health system, it is very hard for a country to end the cycle of disease and poverty. Health is so fundamental to development that even if there were no chance of another epidemic, building and improving health systems would be a worthwhile — and lifesaving — investment. The fact that they also bolster our ability to confront epidemics is all the more reason to invest in them.

In addition, there is no systematic disease-surveillance process in place today in most poor countries, which is where a naturally occurring epidemic seems most likely to break out. Even once the Ebola crisis was recognized last year, there weren't resources to effectively map where cases were occurring and in what quantity.

We need to invest in better disease-surveillance and laboratory-testing capacity, for normal situations and for epidemics. Routine surveillance systems should be designed in such a way that they can detect early signs of an outbreak beyond their sentinel sites and be quickly scaled up during epidemics. They should be linked with national public health laboratories to enable robust monitoring and response. And the data derived from such testing need to be made public immediately. Many laboratories in developing countries have been financed by the polio-eradication campaign, so we will have to determine what capacities will be needed once that campaign is over.

HUMAN AND OTHER RESOURCES

Once it became clear that a serious emergency was under way in West Africa, many local clinicians should have been recruited, and trained personnel should have flowed rapidly into the affected countries. That didn't happen. Some countries stepped forward with volunteers within 2 to 3 months, but they were needed within days. It was fortunate that Médecins sans Frontières could mobilize volunteers more quickly than any government.

We need trained personnel ready to confront and contain an epidemic quickly: incident managers; experts in epidemiology, disease surveillance, and other relevant fields who can provide surge capacity; respected community leaders who can lead local engagement efforts; and community workers who speak local languages. Ideally, we would have updated lists of such personnel indicating their availability and capabilities. There would also be standby training centers and an explicit understanding regarding compensation and insurance for volunteers. Each country could commit to managing a pool of volunteers and to sending a certain number of people with various skills and equipment within a week after an emergency began, with plans for evacuating any who were exposed to the epidemic pathogen.

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Transportation and equipment are also key. When an epidemic strikes, roads and airports in affected areas are overwhelmed by people trying to get out. Volunteers will be more likely to sign up if they know they will be able to leave if they get sick or when their duty is done. Few organizations are capable of moving thousands of people — some of them infected — to various locations around the world at a week's notice. The Ebola epidemic might have been much worse if the U.S. and U.K. governments had not used military resources to fly people in and out of the affected countries. All countries could identify trained military resources that would be available for epidemics; in a severe epidemic, the military forces of many or all middle- and high-income countries might have to work together.

During severe epidemics, responders also need tents, portable power sources, medical supplies, and other materials. A list of the supplies that would be needed to stop an epidemic affecting 10 million people — 100 times the population affected by the Ebola epidemic — could be developed, and experts could determine which items would need to be stockpiled or be subject to commandeering.

It is also critically important to have good data about what's going on. Unfortunately, during the Ebola epidemic, the case database has not always been accurate or up to date — partly because of the chaotic situation, but also because good technology and training have not been available and there are no clear rules regarding making data accessible. For future epidemics, it should be possible to have a system in which information on suspected cases, locations, survivors, and other key elements was entered into a digital database that was instantly accessible to the relevant organizations and agencies. The groups working on the Ebola data — including the WHO, the U.S. Centers for Disease Control and Prevention, and others — could recommend specifications, and some combination of foundations and technology companies could build such a system within the year.

Experts will also need computer models to predict what might happen and which interventions should be prioritized. With access to satellite photography and cell-phone data, they could understand the movement of populations and individuals in the affected region. But Internet and cell-phone capacity need to be improved. We should be able to use cell-phone systems to contact the public and to poll people about what they are seeing and experiencing. Key centers should have high-bandwidth Internet capacity through satellite, and Wi-Fi capacity should be added in key areas so that digital tools can help with reporting data and coordinating personnel.

MEDICAL AND PUBLIC HEALTH TOOLS

It should be possible to make diagnostic tests, drugs, and vaccine platforms that could be adapted for use against various pathogens. Today, with the possible exception of influenza vaccines, we do not have nearly enough capacity for developing adaptable platforms, partly because there are opportunity costs for private-sector organizations in shifting resources away from more commercially viable projects to work on tools for epidemics that may not happen. We may need an international funding system that factors in these opportunity costs.

Other than watching for symptoms, the diagnostic approach used during the Ebola epidemic has involved sending blood samples for quantitative polymerase-chain-reaction (qPCR) analysis. But qPCR machines are expensive and not widely available, so on average it has taken 1 to 3 days to get test results. For the next epidemic, an adequate number of qPCR machines should be made available while novel diagnostic methods are rapidly developed. We also need a clear process for developing and manufacturing accurate diagnostic tests rapidly. A focused effort to accelerate this process and establish a rapid approval and procurement process would be worthwhile.

On the therapeutics front, there are drugs that work against viruses similar to Ebola, and some of them have been shown in test assays to have an effect against Ebola. Unfortunately, they were not tested in patients with Ebola until after the epidemic had peaked — in part because there was no clear process for approving a novel trial format or for providing indemnity against legal liability. We will need to develop a clear set of guidelines (and testing and regulatory pathways) for determining whether existing drugs could be repurposed to help stop a particular epidemic.

We also need to invest in more research on antiviral drugs, antibody treatments, and RNA-based constructs. We should have either stockpiles or manufacturing capacity for therapies that might be effective in an epidemic.

Plasmapheresis should have been used in the Ebola epidemic, but its application wasn't approved and scaled up until it was too late for this intervention to have a large impact. Plasmaphe-

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resis is quite effective for a number of diseases (including smallpox and viral hemorrhagic fevers such as Lassa fever) and has a reasonable chance of working for Ebola as well. The Gates Foundation started working to establish plasmapheresis units in early September 2014 and quickly found partners ready to take them into the affected countries. Unfortunately, the effort was hampered by the lack of a clear process for approving new approaches. We should develop rules now to expedite drug approvals in future epidemics and establish clear guidelines for approving studies and treatments, including experimental ones. A global epidemic-drug–approval process could avert long delays by indemnifying companies working on new approaches.

Three different Ebola vaccine constructs were being developed in the summer of 2014. Although all were in early stages, this work made us more prepared for Ebola than we would be for an entirely new pathogen, for which vaccine development could take 2 or more years. Moreover, it is not clear how quickly vaccine developers could or would move or who should finance the final research and manufacturing of a new vaccine.

Among known pathogens, influenza is the one most likely to cause a large epidemic; even seasonal influenza variants probably cause several hundred thousand excess deaths each year. So it's disappointing that we don't have a vaccine for all influenza strains. There is work being done toward this goal, but it has garnered nowhere near the resources that it deserves.

An audio interview with Dr. Nicole Lurie is available at NEJM.org

Ideally, vaccine research would be funded in such a way that during an outbreak, a vaccine could be designed, tested for safety, and ready for manufacture at scale within a few months. There is no guarantee of success, but I believe that given enough time and resources, such efforts could produce an invaluable contribution for epidemics and overall health.

Given Ebola's limited infectiousness in the early stages of the disease, most of the quarantine policies that were proposed would have been counterproductive. But when a far more infectious agent comes along, quarantine may be one of the few tactics that can reduce its spread in the early stages of disease. Because democratic countries try to avoid abridging individuals' rights to travel and free assembly, they might be too slow to restrict activities that help spread disease.

Part of the process should include a plan for effective public communications, including coordination of the messages conveyed by all the different voices people will hear, from governments, to United Nations agencies, to news media, to bloggers. Digital communication can be used to great advantage, but unless a plan is in place, it will only spread confusion and panic faster.

A GLOBAL CALL TO ACTION

Despite efforts by the United States and a few other countries, there are still big holes in the world's ability to respond to an epidemic. Other countries may be more likely to step up if they see an overall plan and understand their role in it. We need a rigorous study of the cost of building a global warning and response system and a plan for contributions from various countries.

Through the United Nations, some global institution could be empowered and funded to coordinate the system. The United Nations and the WHO are studying the lessons from the Ebola epidemic and ways to improve international crisis management; these evaluations can provide a starting point for discussions of ways to strengthen the WHO's capacity and about which parts of the process it should lead and which ones others (including the World Bank and the G7 countries) should lead in close coordination. The conversation should include military alliances such as NATO, which should make epidemic response a priority. The final arrangement should include a reserve corps of experts with the broad range of skills needed in an epidemic.

An epidemic is one of the few catastrophes that could set the world back drastically in the next few decades. By building a global warning and response system, we can prepare for it and prevent millions of deaths.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

A more detailed version of this article is provided in the Supplementary Appendix, available with the full text of this article at NEJM.org.

From the Bill and Melinda Gates Foundation, Seattle.

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