

A conversation with Laurie Garrett on January 23, 2014

Participants

- Laurie Garrett — Senior Fellow for Global Health, Council on Foreign Relations
- Alexander Berger — Senior Research Analyst, GiveWell

Note: This set of notes was compiled by GiveWell and gives an overview of the major points made by Ms. Garrett in the conversation.

Summary

[Laurie Garrett](#) is the Senior Fellow for Global Health at the [Council on Foreign Relations](#) (CFR). She is also a Pulitzer Prize-winning journalist and the author of *I Heard the Sirens Scream: How Americans Responded to the 9/11 and Anthrax Attacks*, among other books. Her 1994 bestseller *The Coming Plague* set the stage for this time of new disease emergence.

GiveWell spoke to Ms. Garrett about global health and biosecurity, emerging pathogens, gain-of-function research, synthetic biology, and other topics related to biosecurity.

Background on global health and biosecurity

Responsibility for global health, including biosecurity, is shifting away from the World Health Organization (WHO) to actors that are less accountable in a formal sense to the global community, such as the World Bank, the US government, and the Gates Foundation. This trend has weakened global health efforts in biosecurity. The WHO is governed by the World Health Assembly, to which nearly every nation is a voting member, holding the organization's leadership accountable, and setting institutional goals. Since the 2008 financial crisis, the WHO's budget has plummeted, as has its leadership capacity, particularly in areas of biosecurity.

Most policy analysis in global health is not entirely objective and disinterested because it comes from the very same NGOs and institutions that are implementing global health projects. There are a small number of groups that provide more objective analysis, such as CFR, Chatham House, some institutions in India and South Africa, and the Brookings Institution.

The weaknesses of the global health system were revealed in 2009: Global health systems struggled to respond to the H1N1 pandemic. H1N1 was extremely contagious; almost everyone who was exposed to the virus became infected; and the majority of the infected developed influenza. Manufacturers did not have the capacity to produce enough vaccines, and countries were reluctant to share their vaccine stocks with each other.

Emerging pathogens

Current elevated risk

Humans are putting unprecedented stress on natural habitats. This is causing wild animals to migrate and interact abnormally. This leads them to come into contact with humans and domesticated animals

and thus to transmit diseases to humans. For instance, rainforest fruit bats may have been the sources of the Ebola, Marburg, Hendra, severe acute respiratory syndrome (SARS), and Middle East respiratory syndrome (MERS) viruses, many of which were first recognized in humans within the past 15 years. Wild birds can also serve as sources of emerging diseases. Wild birds compete with domesticated birds for food, leading to the transmission of influenza viruses from wild birds to domesticated birds and then to humans.

For the next 20 years, there will likely continue to be a high rate of disease emergence because of globalization. We are in a transitional time, from nation-states to globalized political and economic forces; from largely rural humanity to majority urbanized; and from subsistence farming in much of the world to organized agricultural production. During this transitional time, the habitats of millions of species of plants and animals are severely disrupted, increasing the risk of disease emergence.

Scientists lack tools to predict the emergence of new diseases. It would be extremely valuable to have better tools to anticipate and to quickly identify newly emerging diseases and determine how and why they have emerged.

Recently emerged pathogens

SARS spread to 31 countries before researchers learned that the virus was transmitted mostly within hospitals. That discovery led hospitals to improve protective precautions and boost hygiene. These steps were sufficient to control the disease in every country but China, where government cover-up and delayed action allowed the virus to spread nationwide. China was able to control SARS only by mandating daily body temperature checks nationwide. Anyone found to have a fever was quarantined indefinitely, regardless of the cause of the fever. It would have been difficult for a less centralized, autocratic government to implement the measures needed to contain the outbreak.

The first case of MERS occurred in Saudi Arabia in spring, 2012. It is unclear how the virus was transmitted to humans. Some bats and camels have been found to have MERS, and the virus has been found in camel milk. Biologists believe MERS is carried by Egyptian tomb bats, somehow transmitted to camels, and then passed to people. However, not everyone who has been infected was exposed to bats or camels. There has been some human-to-human transmission, especially in hospitals, though this does not explain all of the remaining MERS cases. MERS spread in downtown Riyadh in Saudi Arabia, a very wealthy area with good healthcare. Even though significant resources have been devoted to researching MERS, transmission is still poorly understood, treatment is largely supportive, and the biology of MERS remains mysterious.

Pathogens emerge fairly frequently, but luckily most have not been very transmissible or have emerged in remote areas where they could be controlled. The difficulties in understanding and responding to SARS and MERS show that if a more dangerous pathogen were to emerge in an area where it could not be easily confined, it could cause great harm. The global spread of H1N1 flu in 2009, which reached every continent in a few weeks, illustrates the potential pandemic catastrophe a more virulent organism might pose.

Gain-of-function research

In gain-of-function research, biologists intentionally engineer pathogens to make them more dangerous in order to understand how the pathogens might evolve to become more transmissible or virulent. Most controversial gain-of-function research has been on influenza, though similar techniques could be used

with the MERS virus or other pathogens. If a virus engineered to be especially dangerous were to escape from the laboratory, it could conceivably cause a serious pandemic. Over the past two years, there has been a worldwide debate about governance of gain-of-function research, with different countries establishing varying standards for safety.

A lab in Harbin, China made 127 variants of the highly virulent H5N1 avian influenza virus and published detailed methodology that would allow others to replicate their work. Five of these variants spread through the air between guinea pigs and produced deadly infections. One of those variants could conceivably cause a pandemic in humans if it escaped from the lab.

A joint Japanese-American team led by Yoshi Kawaoka also made H5N1 more transmissible. However, the team first removed the virulence genes from H5N1 and inserted virulence genes from the less-dangerous H1N1 swine influenza, reducing the threat that the modified H5N1 would pose if it were to escape from the lab.

A Dutch team led by Ron Fouchier engineered H5N1 to spread through the air between ferrets, which are used as models for human infection. The Dutch team did not make H5N1 less virulent before making it more transmissible, arguing that the engineered H5N1 presented little risk. In their published results, about 50% of ferrets that were kept in the same room as infected ferrets were infected through the air, demonstrating the mutant virus had adapted to mammalian transmission. However, the ferrets manifested few signs of disease.

In early 2013, a new bird flu, designated H7N9, emerged in China, spreading to people who sold or bought poultry in live animal markets. The original source bird species for H7N9 was not known, and – very unusually for avian influenza – the virus did not sicken infected birds and poultry. But H7N9 has proven dangerous to people, killing more than one-third of those infected. In late 2013, both a Chinese team and the Fouchier lab did gain-of-function mutation work on the virus, creating strains that could spread airborne between mammals – possibly, humans.

Synthetic biology

Synthetic biology is now so advanced that, with the proper resources, almost any conceivable genetic modification can be made to a pathogen. There are no global standards for what safety measures should be taken in biosafety level 1-4 facilities or for which organisms or types of experiments require which biosafety level. Generally, scientific organizations set their own ethical parameters and standards on synthetic biology, and there is little enforcement of safety rules.

Biosecurity efforts tend to focus on protecting against the weaponization of known pathogens. The government has compiled a list of dangerous pathogens (the "select agents list") and restricts access to those pathogens. This approach is insufficient to regulate synthetic biology because, by definition, the newly created or altered microorganisms are not on identified pathogen lists.

Given the lack of restrictions on synthetic biology research, accidental escape of a dangerously modified pathogen is more likely than a deliberate terrorist attack. Even a teenager working in a high school laboratory could conceivably create a dangerous pathogen by accident.

Evolution of virulence

Dr. Paul Ewald argues that highly virulent pathogens tend to evolve toward lower virulence because hosts can only continue to spread a virus if they remain alive.

Ms. Garrett agrees that it is not in a pathogen's evolutionary interest to kill its host. However, it is in the pathogen's interest to create illness sufficiently profound to allow the pathogen to spread. Some pathogens successfully propagate by causing profound illness even though the illness frequently kills the host. For example, cholera is very deadly, but it is able to transmit itself by causing severe diarrhea, which can contaminate water supplies, and spread to others long after the index case has died.

Disease surveillance applications of metagenomics

The cost of whole genome sequencing has fallen precipitously. In 2000 the first human genome was fully sequenced at a combined public/private cost of about \$10 billion, combining the efforts of 160 labs over a decade's time. Today a human genome can be sequenced in 24 hours for about \$1,000, and industry forecasts project that by 2016 sequencing will be such a trivial part of lab costs as to be lumped in with purchase of test tubes and pipettes.

By scouring the oceans, air, soils and human environments of the planet for samples that are submitted to mass-scale metagenomic sequencing and then matching said sequences against those in existing databases, scientists are now discovering new microbial species by the hundreds every day. The basic techniques of discovery can be used for disease surveillance, rapidly (in a matter of hours) identifying bacteria and viruses present in everything from food to water, oceans to soils. As the technology is fine-tuned, and the databases of computerized sequences swell, metagenomics could fundamentally, and affordably, alter disease surveillance. Its potential, however, has not yet been realized, much less commercialized.

Cold War biological warfare programs

The bioweapons programs of the USSR, the US, and Great Britain during the Cold War focused on developing weapons that would harm the target without damaging the attackers. These countries worked to develop methods of releasing biological agents so that the attackers would not be exposed to the agents, as well as biological countermeasures to protect the attackers from the effects of their own weapons.

The US Department of Defense under President Nixon concluded that it could not ensure that a bioattack launched by the US would not harm Americans. This contributed to Nixon's decision to sign a treaty with the USSR to end development of bioweapons. The USSR, however, did not believe that the US eliminated its offensive bioweapons program and after signing the treaty – which eventually became the Biological Weapons Convention – built a massive infrastructure of more than sixty laboratory complexes and dozens of test sites, creating weaponized, deliverable forms of such things as smallpox and anthrax. The Biopreparat infrastructure was not dismantled until 1993-5, and many Western intelligence agencies believe the Russian Ministry of Defense may still possess bioweapons labs.

Threat of indiscriminate biological attacks

The 1995 sarin attack in the Tokyo subway refocused attention on biosecurity. Aum Shinrikyo, an apocalyptic cult, carried out the attack. The cult had previously tried and failed to develop biological

weapons. Apocalyptic beliefs might lead terrorists to release a highly transmissible and virulent pathogen in an attempt to wipe out the global population.

Role of philanthropy in biosecurity

Philanthropists could improve biosecurity by funding research to identify the biosecurity threats that are likely to be most dangerous within the next ten to twenty years and to determine the most cost-effective policies to protect against those threats. For example, the Council on Foreign Relations has developed analyses and policy innovation memoranda on [dual-use research](#) that were used by the Obama administration in determining how to bolster disease surveillance and identification worldwide. CFR has also developed policy guidances on [drug medicine safety](#), used by the FDA and Interpol in efforts to stamp out global drug fraud. A philanthropist could also fund the necessary infrastructure and training to build biosecurity surveillance and response capacity.

People for GiveWell to talk to

- Ian Lipkin — John Snow Professor of Epidemiology, Mailman School of Public Health, Columbia University
- David Heymann — Head and Senior Fellow, Centre on Global Health Security, Chatham House; former Assistant Director-General for Health Security and Environment, World Health Organization
- Kenneth Bernard — Former Special Assistant to the President for Biodefense, Homeland Security Council
- Amy Smithson — Senior Fellow, James Martin Center for Nonproliferation Studies

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