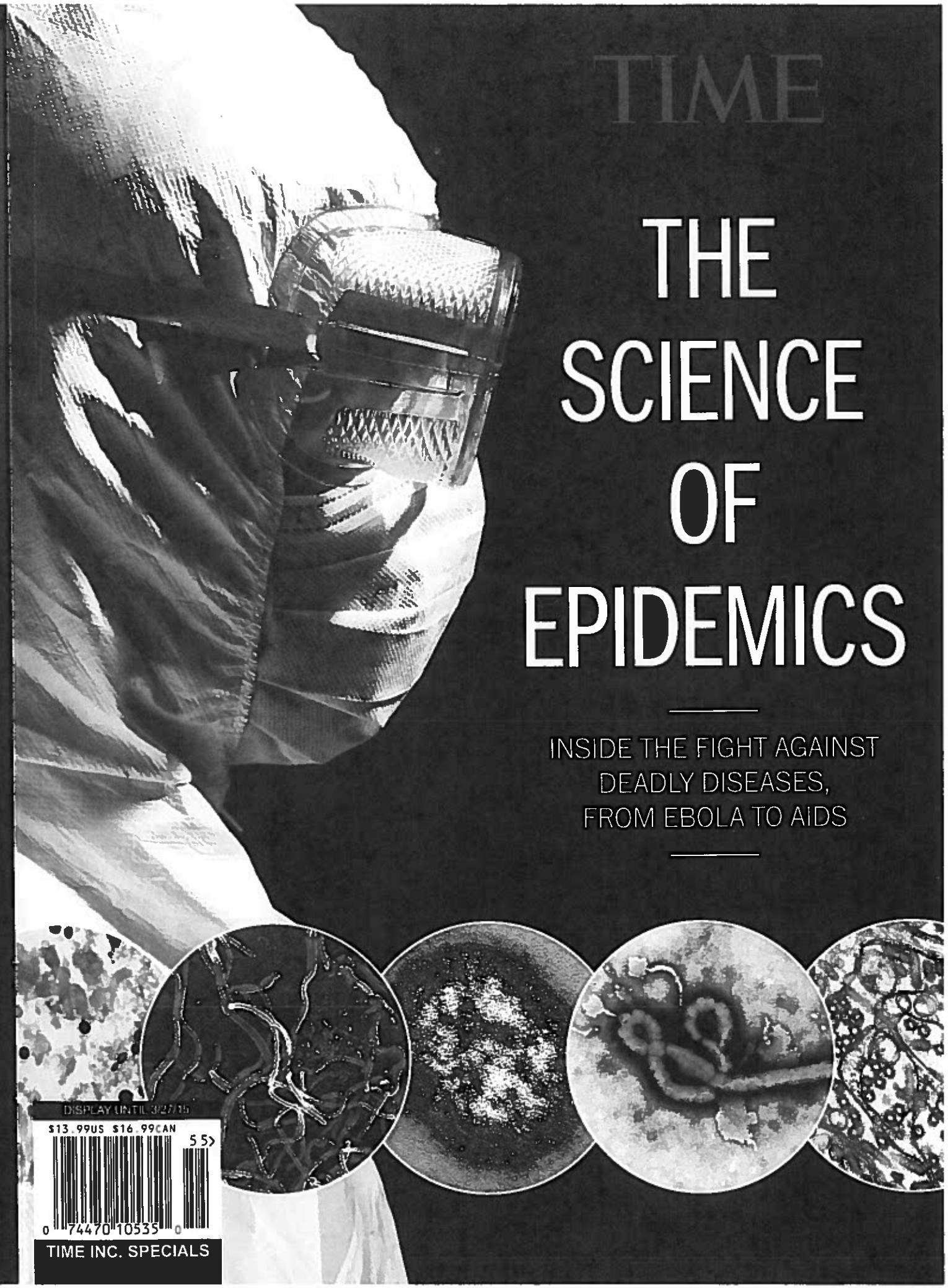
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Parts of this book were previously published in TIME *and on Time.com.*

KEEP YOUR ENEMIES CLOSE A researcher at the University of Reading in England infects dishes of human cell culture with a virus in order to observe its effects.

THE INVISIBLE THREATS

We thought we'd closed the book on infectious diseases. We were wrong

By Bryan Walsh

THE LATE SUMMER AND FALL OF 1918 WERE MARKED BY some of the bloodiest fighting in World War I. More than 1 million soliders on both sides of the conflict would die over those months, before the war finally came to an exhausted end on Nov. 11. The world was left shell-shocked by the horrors of trench warfare and chemical weapons. More than 9 million combatants and 7 million civilians lost their lives. Death had no greater dominion than the barbed-wire fields of the Western Front.

But even as the war dragged through its last days, a far more lethal threat was emerging in the crowded army camps of Europe and the United States. It was a simple flu, little different from the seasonal illness that recurs every winter. But this flu was deadly—deadlier in its full force than almost any infectious disease in human history, and far deadlier than the war to end all wars.

By the time the pandemic had run its course at the end of 1920, the flu had reached virtually every corner of the planet, infecting hundreds of millions of people and killing at least 50 million people, a disproportionate number of them young and healthy. Whole cities were shut down, and for the infected, the dying could be horrible—

bloody fluid would overwhelm their lungs, cutting off oxygen and turning their faces a shade of blue. In the end, the victims would drown in their own beds.

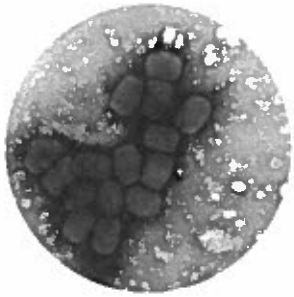
Despite the fact that it struck less than a century ago, the horror of the 1918 flu is mostly forgotten. Our memory is almost always short when it comes to infectious diseases, though. Just consider how quickly the Ebola crisis fell from U.S. headlines after a small rash of domestic cases were cured. The outbreak continued to rage in West Africa through the end of 2014, but the threat under our noses had seemingly vanished. We moved on.

BUBONIC PLAGUE

But maybe that shouldn't be surprising. For most of our history, these diseases were a part of life, ever more so when people began to move into cities, where pathogens could spread quickly. It wasn't until the work of Louis Pasteur and Robert Koch that germ theory—the idea that disease was spread through bacteria or viruses—finally became accepted. Until the development of antibiotics and vaccines, human beings mostly died in epidemics, sometimes in the millions. Well into the 20th century, even in the U.S., it was rare that a family would be unmarked by infectious disease.

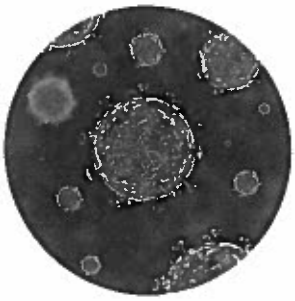
POLIO

Yet barely half a century after the 1918 influenza killed millions, the U.S. surgeon general reportedly said that it was "time to close the book on infectious disease." By that point, vaccines had neutralized diseases like polio and measles. Bacterial infections like syphilis and diphtheria could be countered by the array of antibiotics that had begun with the development of penicillin. Tuberculosis, one of the oldest and most dangerous diseases known to man, has been blunted by better drugs and a vaccine. By 1977, smallpox, a disease that killed hundreds of millions in the 20th century alone, had been eradicated. The focus turned to the danger of noncommunicable diseases—everything from heart disease to cancer to diabetes—that were threatening a richer, heavier world. While infectious diseases were still in the developing world, it would have seemed all but impossible that a child born in the U.S. in the year smallpox was defeated would ever succumb to an epidemic.



SMALLPOX

Even as we were done with infectious diseases, though, infectious diseases were most certainly not done with us. While scientists were wiping out contagious bugs by the handful in the 20th century, something called the human immunodeficiency virus, or HIV, was spreading silently in Central Africa. AIDS, which is caused by HIV, would first be observed in the U.S. in 1981. HIV/AIDS would become the major epidemic of the end of the 20th century, spreading around the world chiefly through unsafe sex and intravenous drug use.

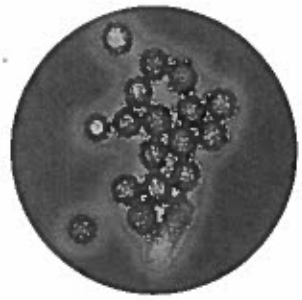


HIV

Nearly 40 million people have since died of HIV/AIDS, and 35 million people are living with it. Sub-Saharan Africa, ground zero for the epidemic, has been utterly devastated by the disease, setting back global development goals and costing countries and aid groups billions of dollars a year to battle it. Although an array of antiviral drugs, which must be taken daily, can effectively neutralize HIV, there's still no vaccine—one more reminder that biology

can continue to punch holes in human hubris.

HIV wouldn't be the last new pathogen to haunt humankind. The past 15 years have seen new viruses emerge from the wild to threaten people. Some, like the H5N1 avian flu and the Nipah virus, make repeated incursions into the human species, causing fear and anxiety but never becoming global threats, prevented by a fluke of genetics. But others have shown just how vulnerable the modern world remains to dangerous new diseases—in some ways, more vulnerable than it has ever been.



H5N1 (AVIAN FLU)

Severe acute respiratory syndrome, SARS, arose exactly as scientists predict new diseases will: beginning in an animal, jumping to a human being in a crowded area like southern China and then spreading around the world on jet planes. But that didn't mean we could stop it. By the time the virus had spread in the winter of 2003 from the Chinese province of Guangdong to Hong Kong, carried by a single person, it was too late. By the time SARS had finally been contained, more than 1,700 people would be infected in more than 25 countries, with 774 deaths. Only the fact that the virus proved difficult to transmit without fairly close contact saved the world from what would almost certainly have been a catastrophe.

SARS

As it was, SARS froze travel and business throughout much of eastern Asia. The total economic cost of the disease was some $40 billion—this for a virus that killed in a year less than half the number of Americans who die from heart disease in a day. Global connections and air travel make it much easier for a new pathogen anywhere in the world to spread rapidly. HIV is believed to have taken decades to emerge from the forests of Central Africa and spread to the capitals of the developed world. But today even the most remote spots on the globe are only 24 hours at most from cities filled with millions of people—and millions of potential viral hosts. Pathogens can move at the speed of an international flight.

H1N1 (SWINE FLU)

SARS also showed where new emerging infectious diseases will begin. Three quarters of emerging diseases are zoonotic, meaning they begin in animals and then, through a genetic mutation, jump the species barrier to human beings. SARS, as researchers discovered later, probably originated in Chinese horseshoe bats, which are sold for food in the wild markets of southern China. It's likely that is where the first human case occurred. In instances of influenza, including the 1918 flu, birds and pigs are the animal reservoirs for the disease. It's no surprise, then, that many emerging diseases begin in hot spots like southern China and Central Africa, two areas where human beings often have close contact with domestic and wild animals.

INFLUENZA

But if the globalized, interconnected nature of the modern world makes us more vulnerable to new diseases, we also have new tools to protect us, as the stories that follow show. Virus hunters like Nathan Wolfe are working to police those viral boundaries between human beings and wild animals, trying to detect the next pandemic

before it begins and stop it in its tracks. It's a mix of hard science and sociology, trying to convince desperately poor people that the hunting of animals that can carry new diseases, such as primates and bats, can be harmful to them and the rest of the world.

MERS

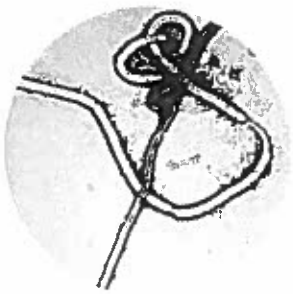
Once a new disease emerges, scientists and health officials can also investigate and respond faster than ever before—provided politics doesn't get in the way. That's been a challenge in the response to what's known as Middle Eastern respiratory syndrome, or MERS, a SARS-like disease that first emerged in Saudi Arabia in 2012 and seems to have originated in bats and camels. An international investigation into the disease has been hampered by a Saudi government slow to respond to—or be transparent about—the outbreak. That is reminiscent of the SARS experience, in which Chinese obfuscation cost the world precious time as the disease spread.

TUBERCULOSIS VACCINE

Social attitudes can make it harder to fight infectious disease as well. Vaccines, which have saved untold millions from the threat of disease, have come under fire from growing numbers of parents who fear the supposed side effects and have held back their children from vaccinations. While there's no proof that vaccines themselves pose a health threat, it's clear that forgoing vaccination does—long-defeated diseases like measles and mumps have returned, infecting and sometimes killing unvaccinated children in the U.S. and abroad. It's a reminder that the fight against infectious disease has always been social. What our neighbors do or don't do can make an enormous difference to the rest of us.

MEASLES

Just how big a difference can be seen in one of the most unexpectedly bright stories in this collection. San Francisco was ground zero for the HIV/AIDS epidemic in the U.S.; nearly 30,000 residents have been infected with the virus over the years. In the early days of that epidemic, doctors at San Francisco General Hospital could do little more than watch as their patients wasted away and died. Thanks to antivirals, HIV is no longer a death sentence. That's cause enough to celebrate, but San Francisco health officials have an even more ambitious goal: to become the first city to have zero new HIV infections. And they may just succeed.



EBOLA

Doctors can only hope to have as much success against Ebola, which isn't new but is killing people as never before. A deadly virus that would periodically strike without warning in the forests of Central Africa, leaving whole villages dead before burning out, Ebola began spreading in 2014 in the towns and crowded cities of West Africa. The resulting outbreak has killed thousands of people and threatens to unravel whole nations. And it's a virus that didn't threaten Africa alone. For the first time, Ebola cases spread to Europe and the U.S., where a pair of nurses in Dallas became the first people to be infected with the disease on American soil.

Ultimately, Ebola didn't pose a major threat to the U.S. and other rich nations. But the panic that arose around the virus is one more reminder that when it comes to infectious disease, no place is safe.

PREPARING FOR A PANDEMIC

Why the worst Ebola outbreak in history was a reminder of what it means to live in an age of modern epidemics—and what it takes to be ready

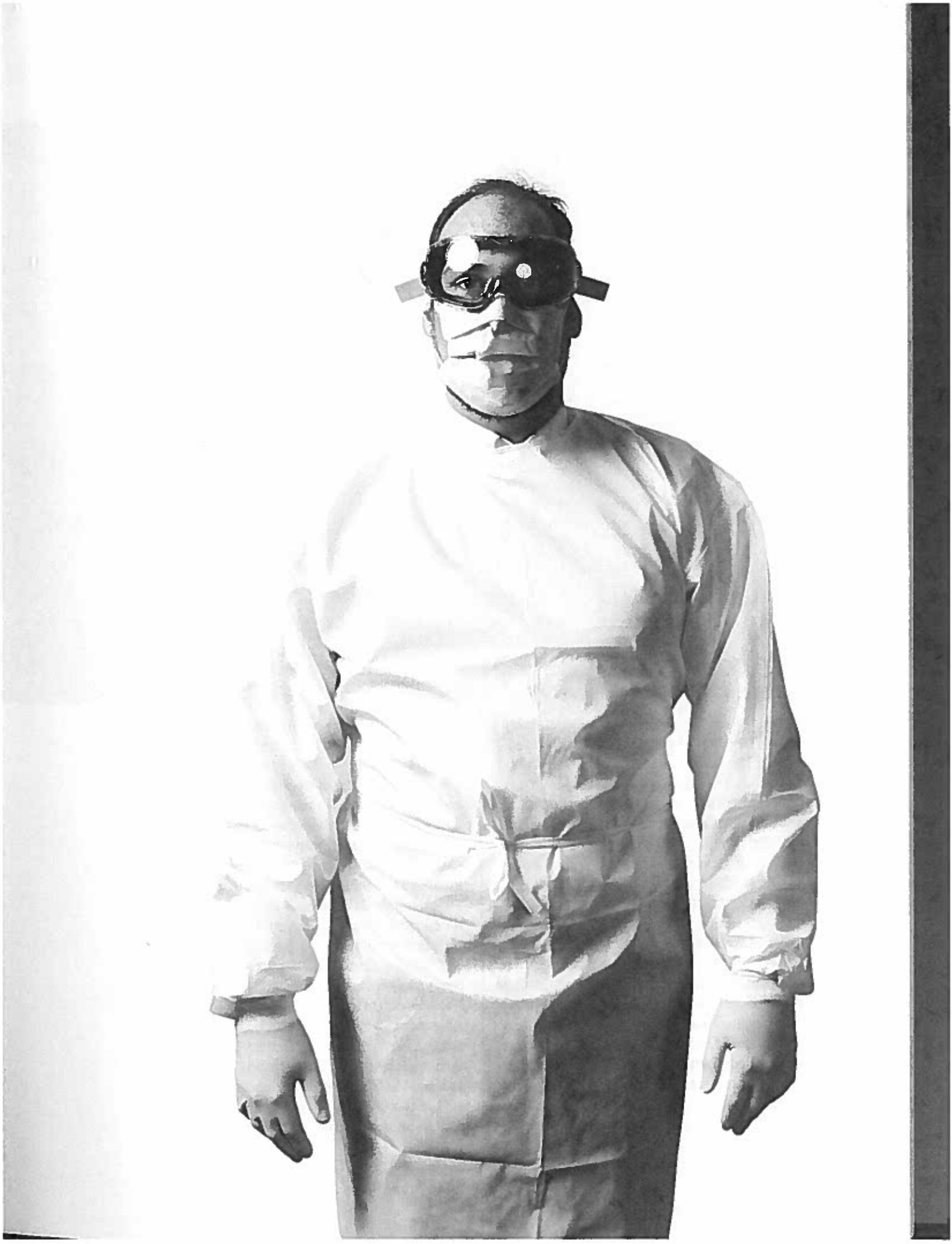
By Bryan Walsh and Alexandra Sifferlin

THE HEADQUARTERS OF THE CENTERS for Disease Control and Prevention in Atlanta is buzzing because of a disease that, until 2014, had never killed a single person on U.S. soil. Staffers at the agency's Emergency Operations Center (EOC)—as close as the infectious-disease world has to a Mission Control—relay data from the field, producing comprehensive maps of the progression of the virus, which is killing half the people it infects as it rampages through West Africa. Here, the telephones never stop ringing, a testament to the fact that in August the EOC was put on Level 1 response, the highest possible alert.

That means the daily 10 a.m. meetings spill out of the primary conference room, where CDC officials and representatives from the State Department and the U.S. Agency for International Development (USAID) discuss how to handle the deadliest Ebola outbreak in history, one that by mid-November would infect more than 15,000 people and kill more than 5,000. By Aug. 8 the World Health Organization (WHO) had classified the outbreak as a public-health emergency of international concern, only the third time the global body had made such a declaration since 2005. "In order to fully resolve the outbreak, we're clearly looking at months, not weeks, of effort," says Stephan Monroe, the deputy director of the CDC's National Center for Emerging and Zoonotic Infectious Diseases, who is helping lead the Ebola response.

The magnitude of that challenge was apparent

PROTECTIVE MEASURES *David Kuhar of the CDC in suiting to prevent Ebola infections at hospitals. The CDC now recommends full-body gear.*



COMMAND CENTER *In August, experts leading the CDC's Ebola response gather at the agency in Atlanta.*

to Jefferson Sibley, who runs Phebe Hospital in central Liberia, one of the three West African nations, along with Sierra Leone and Guinea, at the heart of the outbreak. In mid-July the hospital treated an Ebola patient who in turn infected five of Sibley's nurses, an aide and one of his doctors. The patient later died of the disease, as did all of the nurses and the aide. (The doctor survived.) After the nurses were taken away to an isolation center in Monrovia, the Liberian capital, nearly 200 staff members at Phebe Hospital abandoned their posts, refusing to return until they received the equipment needed to protect them from a bug that is transmitted via close contact with blood and other contaminated body fluids.

Hundreds of health workers have died of the disease so far in West Africa, far more than in any previous Ebola outbreak. During the worst days of the outbreak, bodies were rotting in the streets of Monrovia, and governments put into place cordons sanitaires—drawing lines around infected areas and refusing to let anyone leave. Sibley survived Liberia's 14-year civil war, which killed more than 250,000 people, but believes Ebola is worse.

"The good thing about the war was you heard the gun sounds. You could run and take cover, but Ebola is not like that," says Sibley, standing outside his empty hospital. "You never know where it is coming from or who is bringing it to you."

For all the chaos and suffering the virus is causing in West Africa, Ebola is unlikely now—or anytime soon—to pose a serious health threat to the U.S. or other developed nations. Although

a pair of nurses were infected while treating a sick man in Dallas last fall, the disease is still difficult to transmit, provided the infected are identified and isolated and health-care workers are given proper protective equipment.

That's the case at Emory University Hospital near CDC headquarters, where doctors cared for two American health workers who contracted Ebola in Liberia and were airlifted to the U.S. "We have the resources in place to take care of those patients with the highest-level care possible," says Aneesh Mehta, an assistant professor of medicine at Emory who helped treat the American patients.

But there's a reason the CDC is on red alert for a disease that mostly remains a threat to poor Africans. An uncontrolled outbreak anywhere, no matter how remote, can pose a real danger to the rest of the planet. "We live in a world where we are all connected by the air we breathe, the food we eat and by airplanes that can bring disease from anywhere to anywhere in a day," says Tom Frieden, the CDC director. "That's why it's so important to strengthen global health security and work with countries all around the world so they can do a better job finding threats." Barring a sudden change, Ebola won't seriously threaten the developed world, including the U.S. But there are lessons to be learned from this disease—lessons that could save lives when the next virus hits.

LESSON NO. 1: MIND THE ANIMALS

Preliminary research indicates that Patient Zero for the outbreak was likely a 2-year-old child who died of Ebola in December near Guéckédou, Guinea, a town close to the borders of Sierra Leone and Liberia. But that's not where the outbreak began. Like most recently emerged pathogens, such as bird flu and SARS, Ebola is a zoonotic disease, meaning it originated in animals before spreading to human beings.

It's not known which species was the original host, but scientists believe that a probable candidate is one or more species of fruit bat, which can carry the Ebola virus without exhibiting signs of illness. Bush meat—wildlife like bats or apes found in the jungle—is a big source of protein in parts of rural Africa, and it's possible for viruses like Ebola to infect human beings if an infected animal is butchered and eaten. That first animal-to-human transmission can start an outbreak.

That might not happen often, but it seems to be more common as deforestation and development bring humans and animals closer together. "The incidence of those spillover events is increasing," says Raina Plowright, a research associate at the Center for Infectious Disease Dynamics at Penn State University. "That needs to be looked at as a source of new pathogens."

In the past, the only warning of a spillover event was a cluster of sick human beings, and by then it was often too late to stop an outbreak. Scientists believe that HIV, which originated in chimps, had been circulating in humans for decades in Central Africa before IV drug use, changing sexual mores and widespread international air travel allowed it to go global in the early 1980s. SARS, which began in horseshoe bats in southern China, had already jumped to human beings and spread across international borders by the time it was identified by doctors in the spring of 2003.

Now a new generation of scientists is trying to pinpoint and even prevent spillover events before they occur. USAID's Emerging Pandemic Threats (EPT) program supports a network of researchers who police the borders between animal health and human health in viral hot spots like West and Central Africa and Southeast Asia. By maintaining close watch on the viruses circulating in wildlife and educating people about practices that can expose them to the viruses—such as butchering bush meat, as in the case of Ebola—EPT may help give the world early warning of events like this year's Ebola outbreak.

It's far from a foolproof system. Researchers have identified at most 1% of the viruses in animals, and it can be incredibly challenging to boost diagnostic capabilities in some of the poorest nations in the world, which happen to be the same places where spillover events unfold. But EPT promises to at least give us a head start. "It's like trying to fight a fire," says William Karesh, the executive vice president for health and policy at EcoHealth Alliance, a member of the EPT program. "You don't just invest in fire trucks—you invest in smoke detectors too."

LESSON NO. 2: IT'S A CONTAGIOUS WORLD

To a virus like Ebola, people are kindling: the more there are, the easier it is to spread. Africa's population has exploded over the past few decades, and the continent is now home to more than 1.1 billion people. That growth is expected to continue; a recent U.N. report projected that Africans will make up nearly 40% of the planet's population by the end of the century. Africans are increasingly mobile, whether traveling by road or by air, which is how an American infected in Liberia managed to spread Ebola to the Nigerian capital, Lagos, home to more than 20 million people. "Ebola outbreaks used to occur in Central Africa, but in West Africa the villages are closer together and the roads are easier to travel," says Robert Garry, a Tulane University virologist who has been involved in the Ebola response. "Once the virus is in a city, it's difficult to ring it off and stop the spread."

That's especially true of poor countries like Liberia or Sierra Leone, where health-care systems were barely adequate even before Ebola. "We were not prepared to really fight this battle in terms of the material, the training, the people, the expertise," Liberian president Ellen Johnson Sirleaf told local health workers on Aug. 10.

The CDC has sent scores of staffers to West Africa, and in September President Barack Obama sent 3,000 troops to Liberia to help with the response, but for too long, underresourced aid groups like Doctors Without Borders were the only international forces on the ground fighting the outbreak. Fear of the disease among local populations has made control that much more difficult, with some people hiding sick relatives and even attacking medical personnel. "There is such unevenness in terms of capability and capacity that every country on the planet is more vulnerable," says Gayle Smith, the senior director at the National Security Council. "We can't afford for health-security reasons for there to be big holes in the net."

LESSON NO. 3: STRENGTHEN HOME BASE

The Ebola outbreak may have led to the deaths of more than 15,000 Africans and counting, but it wasn't until those two U.S. aid workers were infected that the disease grabbed the attention of Americans. The health workers Kent Brantly and Nancy Writebol were treating Ebola patients at a Liberian hospital run by the Christian groups Samaritan's Purse and SIM when they both contracted the deadly disease. News that the two would be airlifted to Atlanta for treatment caused criticism from some who worried they would spread Ebola in the U.S. It's an understandable fear, if only because Ebola can kill in such a grisly fashion (some victims hemorrhage so heavily that they end up effectively bleeding to death).

But there's been little evidence that the disease could spread far in the United States. Emory's isolation unit was more than ready to take the Ebola patients, who are being treated by doctors and nurses wearing full-body protective suits. "This is what we've been preparing for for 12 years," says Bruce Ribner, an infectious-disease specialist at Emory who is leading the care of the Ebola patients. "This is what we're here for."

Most of the hospitals in the U.S., and throughout much of the developed world, would be capable, with the proper training and precautions, of handling a few patients suspected of having the disease. In October, when the doctor Craig Spencer tested positive for Ebola in New York after serving in Liberia, authorities made sure he had infected no one else and managed to successfully treat him. With Ebola, the U.S. had ample warning and was dealing with just a few cases of a known disease that doesn't spread easily.

That might not be the case next time. In April an American health-care worker contracted Middle Eastern Respiratory Syndrome (MERS), another new disease that spilled over from animals, in Saudi Arabia before flying back to Indiana via London and Chicago. His infection wasn't detected when he entered the U.S. and didn't become known until after he turned up at an Indiana hospital with respiratory symptoms. The man didn't infect anyone—MERS doesn't seem to be very transmissible—but he could have exposed countless people to the disease. "We were just lucky," says Michael Osterholm, director of the University of Minnesota's Center for Infectious Disease Research and Policy. In outbreaks, days and hours matter. The faster public-health officials can detect new infections, the faster they will be able to trace contacts with sick people and stop further spread. That can be the difference between an outbreak and a pandemic.

ON GUARD *A military policeman holds his rifle with gloves to avoid possible contact with the virus during the burial of Ebola victims; as of November 2014, nearly 3,000 people have died of the disease in Liberia.*

LESSON NO. 4: BE READY TO SURGE

There's no vaccine for Ebola and no cure. All doctors can do is provide what's known as supportive therapy: maintaining oxygen, blood pressure and hydration. And then there's hope and prayer. But there may soon be other options. The first two American Ebola patients were treated with an experimental drug called ZMapp. While there's no laboratory evidence of ZMapp's effectiveness, the drug seems to have helped the American patients, who eventually recovered from the disease. (The drug was also given to a 75-year-old priest who contracted Ebola in Liberia, though he died in Madrid on Aug. 12.) That has prompted a high demand for the drug. Even though ZMapp hasn't been fully tested yet, in August WHO endorsed the use of such untested drugs to combat Ebola—a measure of how desperate doctors fighting the outbreak have become.

There are potential vaccines as well, but those have languished in the pipeline because of a lack of demand and what was until now a slow approval process. "People like me and others who have worked for years in vaccines and countermeasures are frustrated," says Thomas Geisbert, a professor of microbiology and immunology at the University of Texas Medical Branch at Galveston. "But on the other hand, we don't want to take a step that isn't well thought through and ruin the whole approach in the future." Two vaccines were rushed into clinical trials in the fall, with results expected in January 2015.

In the event of an unchecked pandemic, though, such experimental measures may have to be embraced widely. The vaccines made to respond to the H1N1 flu in 2009 weren't ready in time to head off the pandemic, though the doses that were made were rapidly distributed.

But logistical challenges also exist. While improvements have been made—the CDC's Frieden touts a "more resilient system" since H1N1—the U.S. health-care industry still lacks the surge capacity that would enable it to withstand a sudden wave of seriously ill people.

"If we had another flu pandemic tomorrow, you'd see a major deterioration of capacity throughout the health-care system," says Osterholm. And that's the final lesson of Ebola. In an interconnected world, even the strongest medical systems are weaker than they seem.