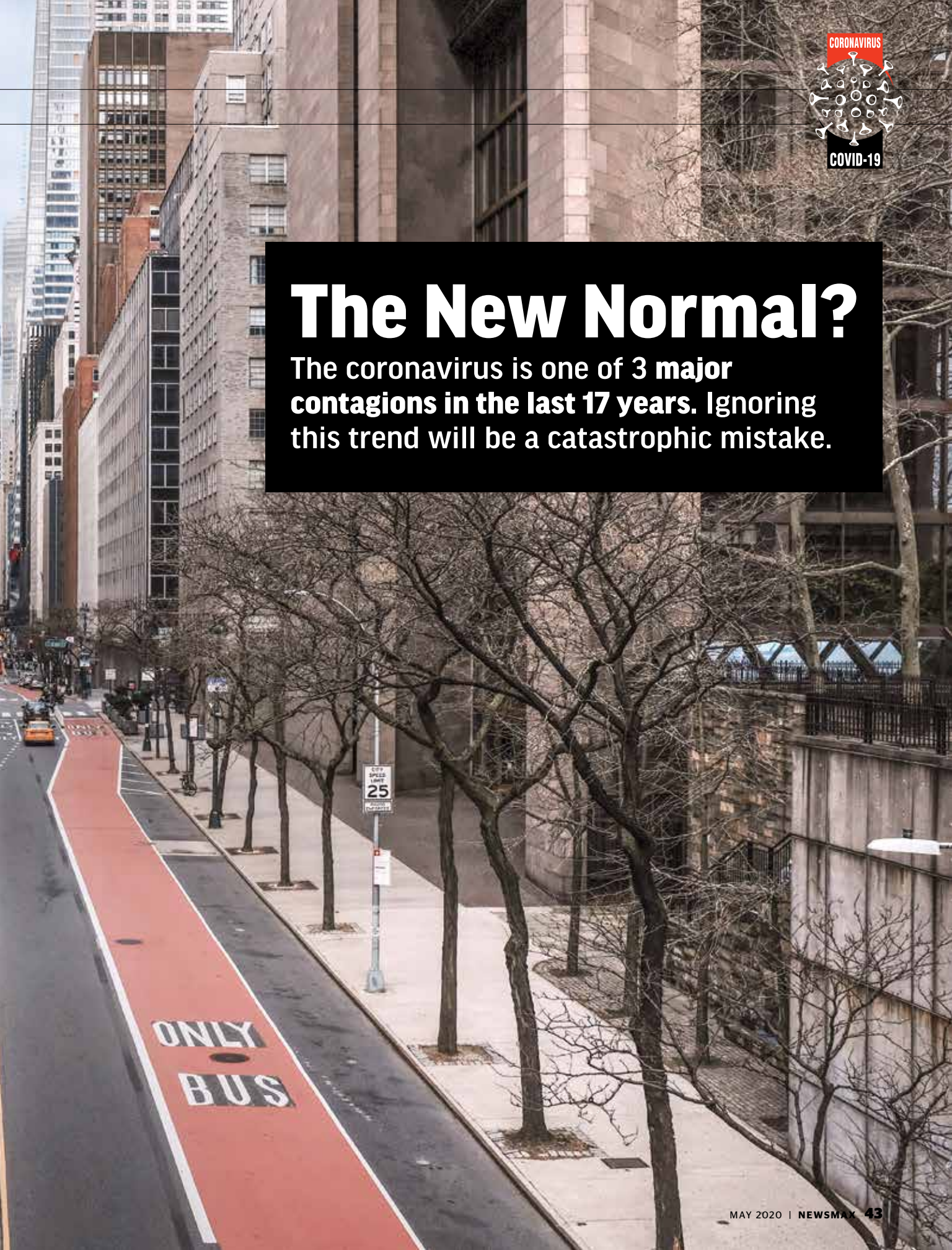
DEADLY PANDEMICS: ARE KILLER VIRUSES THE NEW NORMAL?



The New Normal?

The coronavirus is one of 3 **major contagions in the last 17 years.** Ignoring this trend will be a catastrophic mistake.

BY LEE GRUENFELD

Just three months after it was identified, the coronavirus had an impact on the global economy comparable to that of a major war.

It devastated financial markets, caused the cancellation of virtually every sporting event and concert in the world, closed everything from Broadway to Disneyland to Mount Everest, brought cruise ships to a grinding halt and airlines nearly so, overwhelmed medical facilities, and sparked mass panic buying.

Estimates of the eventual worldwide financial cost are upward of $2.7 trillion.

The virus also killed or seriously incapacitated thousands of people and caused us to treat each other like lepers.

Although the time frame and total damage are unknowable, we will get through this crisis.

But, as often happens in the aftermath of resolved crises — SARS, MERS, and fuel shortages are good examples — we tend to quickly grow complacent about preparing for the next one.

But this time, as soon as things begin to settle down, another question will rear its ugly head: Can we be sure the current pandemic is a freak, once-in-a-generation anomaly? Or will periodic contagions be the "new normal?"

Following the relatively mild Russian flu outbreak in 1977, we didn't see another global contagion for 25 years.

Yet in just the past 17 years, there were three: SARS (2002-2003), H1N1 swine flu (2009-2010), and the current crisis.

With millions of lives and fortunes at stake, blindly assuming that the three major contagions in 17 years is mere happenstance could prove a catastrophic mistake.

"SO WE TAKE A ONE-TIME HIT, DEVELOP A VACCINE, AND MOVE ON, RIGHT? UNFORTUNATELY IT'S NOT THAT SIMPLE."

Why the Virus Is So Dangerous

Are there aspects of 21st century life that made those — and future — outbreaks not only likely, but inevitable? And, if so, is there anything that can be done about it?

The answer may lie in understanding why COVID-19 is so dangerous. The easiest way to do that is to compare it to a well-known pathogenic disease, influenza.

The term "coronavirus" as used by the public, the media, and even government personnel and health officials is being applied incorrectly.

Lee Gruenfeld writes the "Walk on the Tech Side" blog for "Newsmax Insiders." He was a partner in the management consulting practice of Deloitte and an executive for several pioneering technology companies. A popular speaker on advanced technology and the "internet of things," Lee has written 15 critically acclaimed works of fiction and nonfiction.

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TESTING TIMES Nurses, clad in full protective gear, administer tests in Jericho, on New York's Long Island, which was hit hard early on in the coronavirus pandemic.

Coronaviruses are a whole class of pathogens that include those that cause diseases such as SARS and MERS, as well as COVID-19 (short for "Coronavirus Disease 2019"), which is caused by the coronavirus called SARS-CoV-2.

So to be clear, SARS-CoV-2 is the virus that causes the disease COVID-19.

To avoid confusion, we'll occasionally refer to SARS-CoV-2 and COVID-19 as simply the "coronavirus," as the rest of the world is doing.

We'll also refer to "flu" as though it were a single illness, even though there are four distinct varieties of influenza.

There is a common belief that COVID-19 is a form of flu, because their symptoms are so similar: fever, coughing, body aches, possibly diarrhea and vomiting, and a tendency to lead to pneumonia.

But they're actually very different diseases, caused by two completely different bugs.

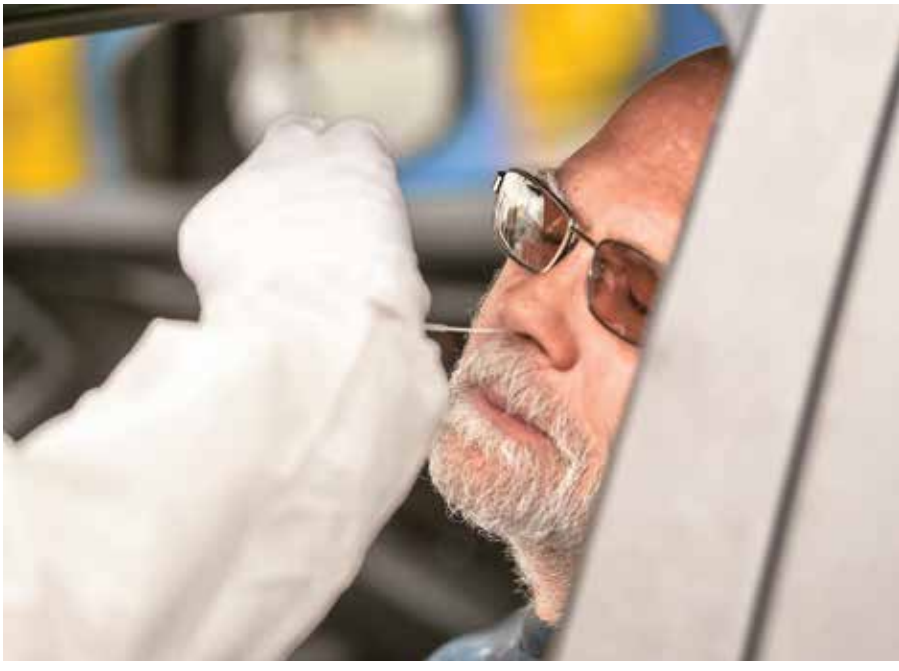
All viruses have the same basic mechanism: They inject bits of themselves into the healthy cells of the host they're attacking and trick those cells into making copies of the virus, which in turn do the same thing to other cells. It's a kind of chain reaction that turns the host's own ability to duplicate genetic material against itself.

Coronaviruses and flu viruses contain the genetic material RNA, rather than the genetic coding material DNA, whose double-helix structure was first revealed by Francis Crick and James Watson in 1953.

The RNA rather than DNA foundation of the novel coronavirus has implications for its propensity to mutate, as we'll see later.

Compared to the flu, coronaviruses have more than twice as many nucleotides, the basic building blocks of RNA and DNA: about 30,000 vs. 14,000 for the flu virus.

The two diseases they cause, flu and COVID-19, differ in several important ways.



DRIVE THRU Jon, who asked to only use his first name, got a nasal swab to test for coronavirus in March at Penn State Health St. Joseph in Bern Township, Pa.

First, COVID-19 is far, far more lethal. For every 1,000 confirmed cases of seasonal flu, on average about one person will die. For COVID-19, it's somewhere between 10 and 30 people, depending on which study you choose to believe.

It's certainly true the COVID-19 numbers are nowhere near as reliable as those for flu. We know a lot less about the coronavirus, which is called "novel" for a reason.

It's also important to note averages can be very misleading, because the mortality rate differs wildly among various groups of people.

Age isn't the only factor, though; a wide variety of underlying health conditions can greatly increase susceptibility, including heart disease and hypertension. About 60 percent of people in America have at least one chronic condition, and 40 percent have two or more.

For example, approximately 25 million Americans have diabetes. It significantly lowers their ability to survive COVID-19.

Second, and perhaps most importantly, there is no cure and no vaccine for the coronavirus, whereas there are four drugs available to treat flu.

The two diseases also differ in how conta-

gious they are. The average number of people infected by a flu sufferer is 1.3. For COVID-19 — again, at least as far as we now know — it might be more than twice that figure.

Interestingly, the flu is far more dangerous to children than COVID-19 is. Children often develop severe flu symptoms, but for those infected with the coronavirus, most will develop very mild symptoms or none at all.

They can, of course, still infect others — "pre- or asymptomatic contagiousness" is one of the most insidious factors in the spread of COVID-19. But there is some indication they may spread the disease less efficiently than adults.

OK, so it's worse than flu but 80 percent survive it; children under 10 are practically impervious.

So we take the onetime hit, develop a vaccine, and move on, right?

Unfortunately it's not that simple.

THE MOST OBVIOUS CONTRIBUTING FACTOR IS TRAVEL. JOURNEYS THAT USED TO TAKE MONTHS NOW TAKE HOURS."

When It's Over, Is It Really Over?

To try to determine if COVID-19 is a one-off anomaly or a frightening harbinger of more frequent pandemics to come, it's helpful to understand how the coronavirus got so bad, so fast. Sadly, the catalysts that contributed to the COVID-19 pandemic are not going to go away.

Three months after the first case of COVID-19 was detected in Wuhan, China, most of the Northern Hemisphere was on virtual lockdown. That a viral outbreak could cripple a city in such a short time is understandable.

ARIEF BUDI KUSUMA/SHUTTERSTOCK

But how did this virus blast its way around the planet that fast?

The answer lies in both the ease of transmission and difficulty of containment.

The most obvious contributing factor is modern travel. Journeys that used to take months now take hours. People who, not too long ago, either got well or died on long overland journeys were inefficient transmitters of viral diseases.

Now, someone infected with COVID-19, and who might not even be aware of it, can step on a plane in New York or Wuhan before breakfast and have dinner in San Francisco or Rome

Wearable Tech Could Halt Next Pandemic

They're not from trendy designers like Versace and Prada, but these wearables could save your life when another deadly virus sweeps the world.

Developed by scientists, the state-of-the-art devices — worn on the arm or wrist — can detect the onset of viral illnesses.

At Rutgers University, one biosensor in the works continuously analyzes sweat or blood and monitors exposure to dangerous bacteria, viruses, and pollutants, TechBriefs.com reports.

Another device, the Oura ring, records temperature, heart rate, and respiration, and can flag when its wearer may be getting sick, according to ExtremeTech.com. It has already helped save a life.

In March, Petri Hollmen, a Finnish business executive, felt ill and checked his Oura ring, which revealed his temperature topped 100 degrees and his heart rate and breathing were higher than usual. Alarmed, Hollmen sought medical help and tested positive for COVID-19.

Meanwhile, the Scripps Research Translational Institute has initiated an app-based study to monitor data from wearable devices such as Fitbit, Apple Watch, Amazfit, or Garmin Watch.

The institute hopes to sign up hundreds of thousands of wearable users, regularly checking their heart rates, sleep, and activity levels to quickly detect influenza, coronavirus, and other viral illnesses.

— Bill Hoffmann

LUISCAR74/SHUTTERSTOCK

▲ **CULPRITS?** The coronavirus is thought to have originated in bats before infecting wild pangolins (above at a market in China). Pangolins are an endangered mammal often smuggled from Malaysia. Their scales are in high demand in traditional medicine and folk remedies, while pangolin meat is considered a delicacy in China.

the same day.

The global flow, expansion, travel, and migration of humanity is the obvious contributing cause to pandemics. It's easy to see how cheap and convenient air, train, and road travel can contribute to the spread of disease. But there are other, less obvious factors.

One of them is climate change. We already know that unusually warm winters with fewer and milder flu infections lead to worse outbreaks the next season, because of lessened acquired immunity among the affected population.

The same could be true of other virus-caused diseases if they're seasonal in nature — and whether the coronavirus, which is not flu, will be seasonal is unknown as of this writing.

But climate change carries an additional risk. Most emerging diseases start when pathogens are transmitted from animals to humans, a process known as "zoonotic spillover."

The coronavirus, for example, is believed to have originated in bats before invading another animal host, possibly pangolins, before skipping over to infect humans.

Changes in migration patterns triggered by climate change could cause more infected animals to come into contact with humans. We live in an era where global animal-to-human

Search Underway for 'Universal Vaccine'

Not surprisingly, with the rising prevalence of global epidemics, science is on a quest to find a universal vaccine that could once and for all banish viruses to the footnotes of history.

Could medical science develop a single vaccine effective against all coronaviruses?

Again, we look to influenza for clues. Separate vaccines exist for the various types of flu, and each year there are new formulations depending on how the flu virus morphed since the last one was developed.

Even then, if the crafty, shapeshifting virus mutates midseason, researchers have to toss what they came up with and scramble to find yet another vaccine variation for the latest incarnation.

This is not only time-consuming and wasteful of human resources, it's expensive as well.

Olga Pleguezuelos, a researcher at pharmaceutical R&D firm SEEK, says that research up to now has focused on antibodies that bind to the virus and stop it from infecting cells.

The goal is a "super antibody" that would bind to any influenza virus, regardless of its particular genetic makeup.

So far, that approach hasn't worked out so well against fast-mutating viruses. So Pleguezuelos is focusing instead on determining which genetic sequences in the virus tend to stay the same over time. She can then create vaccines that latch onto those common sequences and trigger immune responses that destroy the virus's ability to cause infections.

The result so far is an experimental vaccine called Flu-v, and initial tests have been very promising; Flu-v has already passed stage I and II clinical trials.

That said, a similarly effective universal vaccine against coronaviruses is far less likely, according to Jeremy Rossman, a University of Kent virologist in England.

"Influenza viruses are very similar to each other," he explains, "but each coronavirus is a different species, making it much more difficult for our immune systems to recognize more than one for a given vaccine." — *L.G.*

contact increases as the population expands.

The journal Clinical Infectious Diseases noted: "The interface between humans and animals is of paramount importance in the process."

Dennis Carroll, who has studied infectious diseases at both the Centers for Disease Control and Prevention and the United States Agency for International Development, gives a specific example from Africa in the science magazine Nautilus. It involves oil drilling and mineral mining in areas not normally populated by humans.

"The problem is not only moving workers and establishing camps in these domains," he states, "but building roads that allow for even more movement of populations.

"Roads also allow for the movement of wildlife animals, which may be part of a food trade, to make their way into urban settlements. All these dramatic changes increase the potential spread of infection."

Several organizations have analyzed historical data and discovered that there are two to three times more "spillover events" today than 40 years ago, driven by huge expansions in the number of people and our incursions into wildlife areas.

When viruses that make the jump are "novel," we have no acquired immunity against them and the results can be devastating, as they were for Native Americans when smallpox, measles, typhus, and cholera were imported by Europeans.

Another factor is the exponential rise in our use of drugs, especially antibiotics, to fight diseases.

With a few exceptions, most notably the common cold, every time there's something wrong with us we reach for a pill to kill off whatever pathogen is ailing us. But microorganisms, like all living things, evolve in response to environmental pressures.

When that pressure is a chemical lethal to the bug, there's a likelihood that one or two members of the infecting colony with a slightly different genetic makeup could survive.

If they do, and then multiply, they pass their resistance on to the next generation, creating a new strain that can't be killed by the same drug we've been using.

That's how we ended up with MRSA (methicillin-resistant Staphylococcus aureus), which is difficult to treat because of its resistance to antibiotics. And it's how we're likely to enable the creation of other, potentially more debilitating or lethal strains of so-called bacterial superbugs.

"THERE'S A GREAT DANGER IN DISEASES THAT DON'T RESULT IN VISIBLE SYMPTOMS, YET ARE STILL TRANSMISSIBLE BY INFECTED PEOPLE."

Difficulty in containment, such as we're seeing now, is another enabling factor for pandemics. As we've seen, there's great danger in diseases that don't result in visible symptoms yet are still transmissible by infected people.

But another problem is the great difficulty in researching maladies that spread by human-to-human contact. We can't do invasive examinations on living people, and we can't set up large-scale experiments on human subjects.

That's why scientists are always so eager to find "animal models" that closely mimic human responses to the disease being studied.

There's one other potential pandemic trigger that needs to be taken into account.

Mutations — Hitting a Moving Target

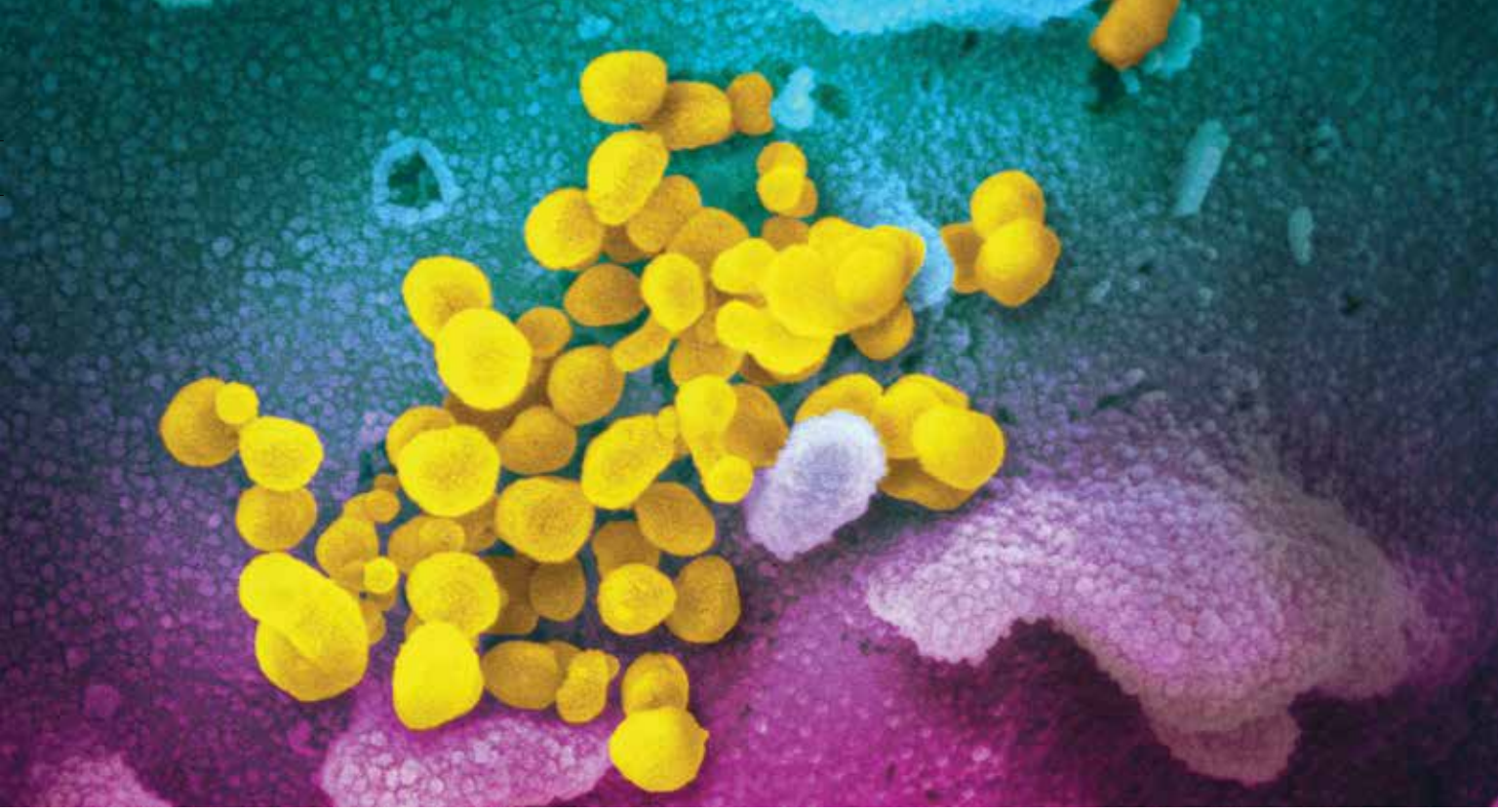
A large number of news stories about the coronavirus have presented this alarming scenario: Given the known tendency of the coronavirus to mutate, there's a good chance that it can be-

Secret Government Agency Researching Cures

The medical fight against the coronavirus has focused mostly on the development of vaccines. But another life-saving treatment could arrive on the scene much sooner.

Called therapeutics, they boost your immune response to protect you from getting the disease or at least avoid its worst symptoms. And for tens of thousands of people, that could be a real lifesaver.

One of the pioneers of coronavirus therapeutics, interestingly enough, is DARPA, the super-secretive Defense Advanced Research Projects Agency that



▲ **UP-CLOSE** This scanning electron microscope image shows SARS-CoV-2 (yellow) — also known as 2019-nCoV, the virus that causes COVID-19 — isolated from a patient in the U.S., emerging from the surface of cells (blue/pink) cultured in the lab.

NIAID RML

come more lethal and more aggressive.

Often cited is a frightening study out of China that found that the coronavirus has already mutated into two strains: the older "S" type and the newer, more aggressive "L" type, which turned up in 70 percent of samples taken from COVID-19 patients.

Is this something we need to worry about?

Probably not, according to leading experts such as Nathan Grubaugh, an epidemiologist at the Yale School of Public Health, who dismissed the study authors' conclusions as "pure speculation."

It's true that the coronavirus mutates, and does so constantly — but so do all viruses.

It's also true that mutations in viruses that have RNA as their main genetic component, like SARS-CoV-2 and influenza viruses, don't have the self-correction mechanisms to fix those mutations that DNA-based organisms (and human cells) do.

But as Grubaugh wrote in Nature Microbiology, most of the mutations have a negative effect on the virus itself, and don't persist generation to generation.

Those that merge into the genome — the whole of the virus's hereditary information encoded in its RNA — do so with little outward effect.

Jeremy Rossman, a virologist at the School of Biosciences at the University of Kent in England and the nonprofit Research-Aid Networks, holds a doctorate in emerging infectious diseases and puts a slightly different spin on the process.

"The mutations that persist in subsequent generations of the virus are the ones that confer an advantage," he explains.

"AFTER THE SPECTER OF A PANDEMIC FADES, COMPLACENCY ENSUES, FUNDING IS DIVERTED, AND RESEARCH SLOWS."

develops strategic, high-tech U.S. military capabilities.

It's been searching for a preventive therapy that would protect U.S. troops by equipping them with virus-fighting antibodies long before they're exposed to the disease.

The new treatment, described as a "therapeutic shield," uses specialized "B cells" that help the body fight off the disease. It requires taking blood from patients who survive the disease and isolating antibodies. Those antibodies can then be cloned countless times to create a monoclonal antibody treatment to save lives.

The head of the DARPA program, Dr. Amy Jenkins, told Defense One that scientists hope to make a working therapy available "by sometime late summer" — well before most vaccinations could be developed, approved, and manufactured.

— David A. Patten & Bill Hoffmann

If the part of the virus that mutates is one that our immune system formerly recognized but now no longer does, then the virus is less likely to be suppressed in the next generation and has a better chance of replicating. That's why we need a newly reformulated flu shot every year.

However, the advantage is typically not one of the virus being more lethal.

"More transmissible and more evasive, yes," Rossman says, because those traits help the virus survive. "But more lethal is not necessarily advantageous to the virus."

How to Prepare for the Next One?

We all suffer from "social amnesia," the all-too-human tendency to quickly forget about the last crisis.

Whenever gasoline prices spike, we see a frenzy of public and private initiatives to reduce our dependency on oil. The perceived urgency often passes by the wayside when prices come back down.

It's the same way with epidemics and pandemics, despite dire warnings from experts.

"After these outbreaks," Rossman says, "there is a rush of funding and preparedness activities, but after the specter of a pandemic fades, complacency ensues, funding is diverted, and research slows."

While we can't say for certain that pandemics or epidemics are going to come at us harder and faster from here on, know this: They are going to come at us.

Last year, a report by the Global Preparedness Monitoring Board said that there is a very real threat of a "rapidly moving, highly lethal . . . respiratory pathogen" capable of killing upwards of 80 million people and wiping out 5 percent of the world economy.

Having been caught flat-footed this time, we need to learn from the painful lesson and get ready for the next time.

One way to do that is to come up with faster ways of developing and mass-producing vaccines.

As Bill Gates pointed out in the New England Journal of Medicine, conventional methods of manufacturing proteins "are too slow for responding to an epidemic."

One idea is to exploit artificial intelligence techniques to build on existing libraries of antivirals rather than starting from scratch, so we can get them tested on animal models and into clinical trials much faster than we can now.

Governments need to run mock pandemic drills so our societal response can be strengthened. In addition to training personnel on the appropriate ways to respond, drills are very effective in pointing out flaws in the system, as well as exposing pandemic plans that are outdated or slipshod because they weren't taken seriously in the first place.

In a report issued last year, the Global Health Security Index project indicated that very few countries have tested their emergency operations against a biological threat, nor have they spent much money on getting prepared.

There also needs to be a worldwide database of pathogen gene sequences cross-referenced to their infection behaviors. In 2007 a group of Chinese researchers sequenced the genome of a coronavirus called HKU4-CoV found in the blood of bats in Guangdong province.

Nobody paid much attention to it, until five

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Test Negative? Why You Could Still Have Virus

If you've tested negative for the coronavirus, congratulations. But unfortunately, in about 15 percent of the cases, negative tests turn out to be wrong.

That means you could test negative but still have the virus.

If someone takes the test too soon after their initial exposure — perhaps because they're suffering from an unrelated cold or flu — there may not be enough virus in their system yet for the test to detect it.

"If it's negative," Dr. Anthony Fauci, the U.S. government's top infectious disease expert, told the Journal of the American Medical Association, "you may be early in the infection and the viral load may be so low you don't get it."

Also, improperly conducted swab samples can cause false negatives, which is one reason officials have been nervous about the idea of do-it-yourself home testing. And don't forget, there's no assurance you won't be exposed to the virus after receiving a negative test result.

While the coronavirus test is a good diagnostic tool for doctors to use to identify those who are truly contagious, no diagnostic test is perfect. Overall, various experts estimate that between 15 to 25 percent of coronavirus test results may be faulty.

So should you be worried you may have the disease despite a negative test? Unless you're in a high-risk group or your symptoms persist, doctors say probably not.

Gary Procop, a virus expert at the Cleveland Clinic, tells The Washington Post, "You only want to test people you really do believe have the disease . . . people you're going to act on.

"If it's an otherwise healthy young person, you're going to say go home and isolate yourself." *— David A. Patten*

Continued from page 50

years later when the same sequence was found in the MERS virus during an epidemic in Saudi Arabia.

"If that data had been available at the time of the MERS outbreak," says researcher Michael Letko of the National Institutes of Health's Rocky Mountain Laboratories, "scientists would have had a head start at figuring out how it's transmitted and what drugs might work against it."

Letko points out that a database of genomes does exist, but nobody has done the hard work of figuring out how the various sequences manifest themselves in the behavior of the parent viruses.

How do they invade their hosts, and what sequences make it possible for the viruses to make the leap from animal to human? If you can figure that out, Letko says, you can start predicting which coronaviruses are the dangerous ones in time to do something about it before the trouble starts.

There are other approaches as well — but the bottom line, as almost always, boils down to money.

The world will spend $1.8 trillion on military defense in 2020 in preparation for wars that are very unlikely to occur, $750 billion of it in the U.S.

"MILITARY PREPAREDNESS IS INCREDIBLY LUCRATIVE FOR SUPPLIERS. NO SUCH INCENTIVES EXIST FOR PANDEMIC PREPAREDNESS."

The amount we spend getting ready for a certain-to-occur health crisis is a laughably small fraction of that, while the ultimate cost of the coronavirus outbreak, as mentioned before, could hit $2.7 trillion.

The problem is that military preparedness is incredibly lucrative, with enormous financial incentives for suppliers of everything from canteens to aircraft carriers. No such incentives exist for private corporations to get into pandemic preparedness.

So, the first step is to allocate more money — and not just in response to an emergency. The money being spent now trying to play catch-up on the coronavirus is many multiples of what it would have cost to be better prepared.

According to the U.S. National Academy of Medicine, just $4.5 billion a year — $3.4 billion for national pandemic preparedness and $1 billion for infectious disease-related R&D — would make the world a much safer place.

As software pioneer Gates wrote, "In any crisis, leaders have two equally important responsibilities: Solve the immediate problem and keep it from happening again. The first point is more pressing, but the second has crucial long-term consequences."

"There is no time to waste," he concluded. □

Ballooning Bailouts Just Keep Getting Bigger

The first U.S. bailout came in 1792, when speculators drove up the stock price of Alexander Hamilton's new Bank of the United States so that it became unsustainable.

Hamilton struck a deal with the Bank of New York for a $150,000 cash injection, a princely sum sufficient to keep the banking system solvent.

Since then, bailouts have become as American as apple pie and have become a routine response to virtually any crisis.

A few of America's other great bailouts:

▶ **1932 — THE RECONSTRUCTION FINANCE CORPORATION. COST: $2 BILLION**. This Great Depression maneuver to rescue corporations deemed too important to fail seemed exorbitant at the time. Today, $2 billion sounds almost like pocket change.

▶ **1989 — THE SAVINGS & LOAN BAILOUT. COST: $50 BILLION.** When interest rates shot up in the late 1970s, savings & loan institutions nationwide were upside down on long-term loan commitments, and over 1,000 of them went out of business. The bailout kept the rest of them in business — at least until investors could be made whole.

▶ **2001 — THE 9/11 BAILOUT. COST: $18.6 BILLION.** After the devastating attacks that brought down the World Trade Center towers, the stock market cratered. But no industry was hit harder than the airlines that had to clear the skies of aircraft after terrorists turned four passenger planes into flying missiles. The loans and compensation agreements kept the airlines in business.

▶ **2008 — THE GREAT RECESSION.** A $700 billion bank bailout created a vast pool of capital used to purchase bundles of iffy home mortgages at risk due to the financial recession — relieving the banks of toxic assets. Most analysts agree that staved off a depression.

▶ **2020 — THE CORONAVIRUS.** To slow the COVID-19 contagion, U.S. businesses were forced to shut down. Congress passed a $2.2 trillion bailout to keep an already massive wave of layoffs from spinning out of control. *—David A. Patten*