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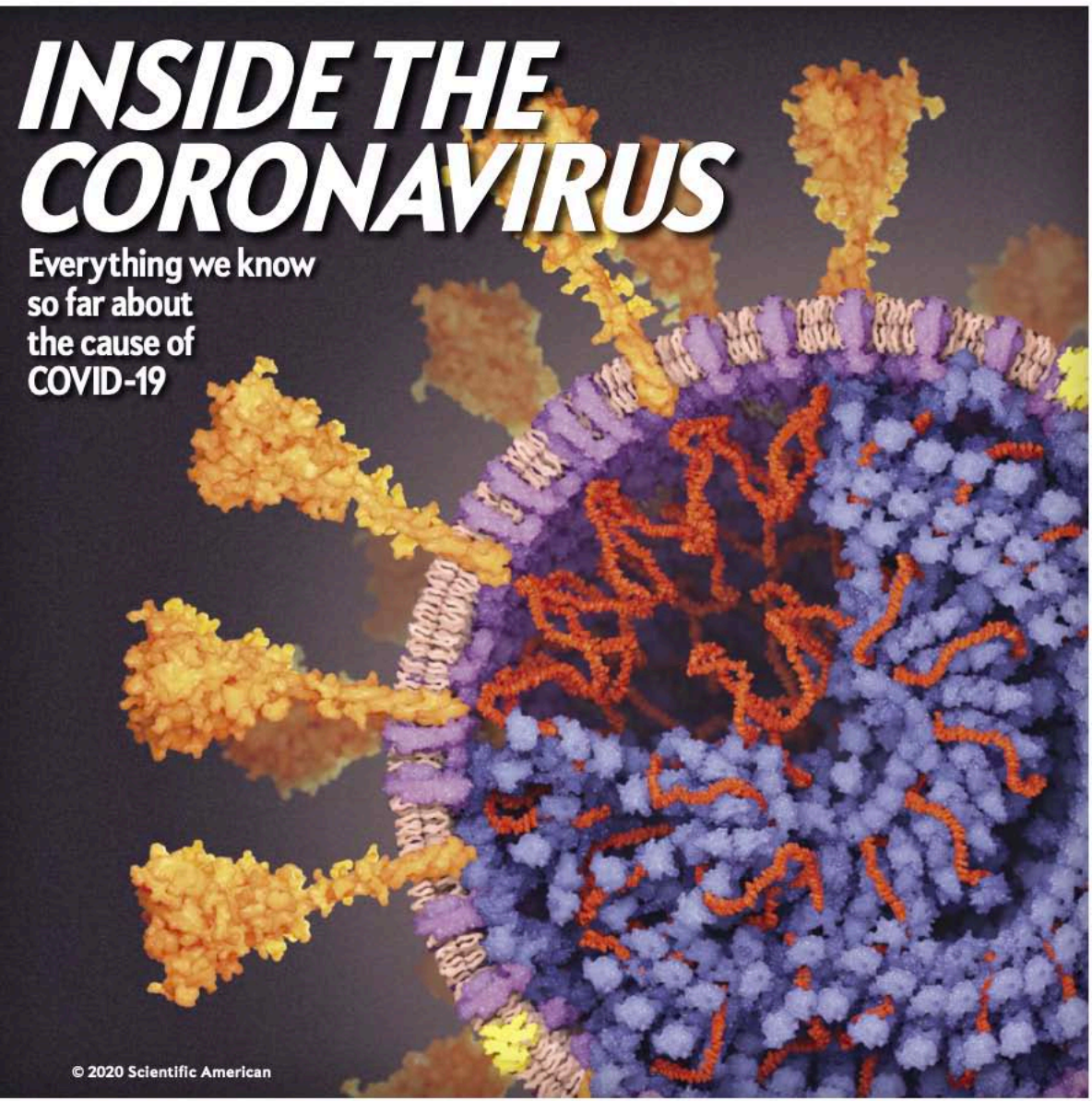

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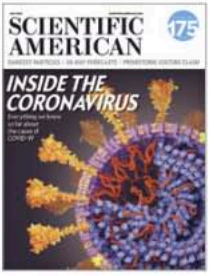


**ON THE COVER**

Although much remains unknown about the virus responsible for the ongoing global pandemic, scientists have developed a detailed picture of the molecular biology of SARS-CoV-2 in a surprisingly short time. Our synthesis of this work begins on page 32.
**Illustration by Veronica Falconieri Hays.**

JOHN FINNEY *Getty Images*; COVER SOURCE: LORENZO CASALINO, ZIED GAIEB AND ROMMIE AMARO *U.C. San Diego (spike model)*

# SCIENTIFIC AMERICAN

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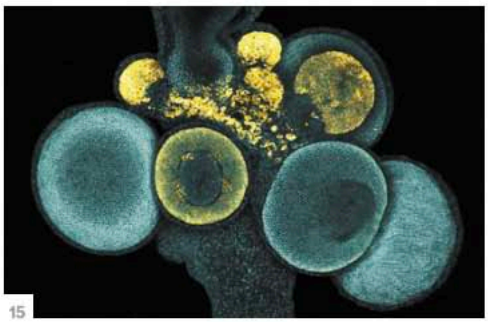

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## FROM THE EDITOR

**Laura Helmuth** is editor in chief of *Scientific American*. Follow her on Twitter @laurahelmuth

# Know the Enemy

**The coronavirus** that has killed hundreds of thousands of people and staggered the world's economy is just about 88 nanometers in diameter—138 nm if you count its spikes. In this issue of *Scientific American,* we show what scientists have learned so far about the structure and function of the evil genius pathogen SARS-CoV-2. Molecular virologist Britt Glaunsinger worked with artist Veronica Falconieri Hays, senior editor Mark Fischetti and senior graphics editor Jen Christiansen to create a detailed 3-D model of the virus and illustrations showing how it invades lung cells and torments the immune system. Turn to page 32.

The global pandemic has forced us into the largest psychology experiment in history. Researchers are studying the effects of mass isolation, fear and grief and the ways discrimination and poverty make this pandemic even more devastating. Author and contributing editor Lydia Denworth explores what we know about the mental health toll of this crisis and how to promote coping or even resilience during a disaster, starting on page 38.

The pandemic amplifies the need for good data in medicine. Writer Virginia Sole-Smith shows that the evidence for obesity as a risk factor for poor health is actually pretty thin. The stigma against large bodies is dangerous in itself, and the focus on weight can lead to misdiagnoses and improper treatments (*page 22*).

The consensus here at *Scientific American* is that neutrinos are cool. During a stressful time, we all enjoyed working on physicists William Charles Louis and Richard G. Van de Water's article about a possible fourth flavor of neutrino, which could be a key to understanding dark matter and dark energy (*page 46*).

Archaeologists and geneticists are uncovering complex and sometimes disturbing social interactions in ancient Europe, where farming people who migrated from the Middle East may have enslaved or sacrificed hunter-gatherers. Journalist Laura Spinney takes us on their journey, beginning on page 60.

One of the many ways science saves lives is through forecasting. If we know what's coming, we can prepare for it. (That's the whole point of epidemiological models of how diseases such as COVID-19 spread.) Scientists such as Kathy Pegion are now pushing weather forecasts out to 28 days. See how well her recent weather prediction turned out (*page 54*).

I'm thrilled to join *Scientific American* as the next editor in chief in our 175-year history. Like you, I've admired and enjoyed the magazine from the outside, and now I am honored to work with the dedicated, knowledgeable, talented, curious and kind staff. I am grateful to our managing editor Curtis Brainard for leading the magazine brilliantly for the past several months and guiding us through the early chaos of the global pandemic. Everyone is working harder than ever, but we are energized by the mission of producing timely, trustworthy and welcoming science stories, graphics, podcasts and videos. You can see all of our COVID-19 coverage online at sciam.com/coronavirusoutbreak.

Thank you for supporting the magazine and being part of the *Scientific American* community. The pandemic has shown the dangers of misinformation, ignorance and confusion. Together we can elevate sense over nonsense, and perhaps the world will emerge from this crisis with a better understanding of pathogens, public health, the research process and the importance of making decisions based on the best evidence. SA

**Mary Sue Coleman** is president of the Association of American Universities, based in Washington, D.C.

# How to Stop Science Theft

## Universities have created tools to guard research against outside threats

*By Mary Sue Coleman*

**Earlier this year** Charles Lieber, then chair of Harvard University's chemistry department and a nanotechnology expert, was arrested and charged with lying to federal law-enforcement officials about secretly working for the Chinese government. (His attorney, Marc L. Mukasey, told SCIENTIFIC AMERICAN that Lieber "maintains his innocence and eagerly awaits the chance to tell his side of the story.") While less extreme than the Lieber story, there have been many more incidents of U.S. researchers allegedly failing to properly disclose relations with outside governments or otherwise safeguard their research from foreign intervention. In fact, officials at the National Institutes of Health have reportedly made inquiries into nearly 200 NIH-funded researchers at more than 60 U.S. institutions for potentially violating NIH conflict-of-interest, conflict-of-commitment or research-integrity rules. Many of these ideas and technologies are important to national security.

U.S. universities and institutions are taking steps to ensure that we protect the intellectual capital generated through taxpayer-supported federal research. My association represents America's most distinguished large research universities, and our institutions take these issues seriously. That is why we, in conjunction with our colleagues at the Association of Public and Land-grant Universities, asked our members to collect their most effective practices to combat these risks. Here is what we found:

Universities are strengthening and enforcing conflict-of-interest policies. For example, institutions once used forms that were not always clear for faculty to disclose funding sources. Now universities are adding more targeted questions and providing faculty with case examples, scenarios and FAQs on what should be included. Some are also requiring much more detail about time that faculty spend consulting with outside organizations, companies and universities to avoid potential conflicts of interest.

Leaders at these universities are also using new Web sites and direct communications to alert all their researchers about possible security threats and to clarify security protocols. And research administrators are directly engaging faculty who have significant levels of foreign research engagement to ensure that they fully understand their responsibilities to disclose such funding and to comply properly with all relevant federal laws, regulations and university policies. Universities are developing new training programs for both faculty and students to educate them about security risks and to make them aware of ethical research practices that must be followed (including what kinds of information can and cannot be taken or shared outside the laboratory). And some institutions are now offering for-credit courses for graduate students on complex ethical decision making and responsible conduct of research.

Crucially, universities are establishing stronger relations with their local FBI offices and other federal law-enforcement agencies; at the same time, the FBI is working to establish clear campus liaisons in their regional and local offices. New processes are now commonplace for monitoring data systems and networks for cyberintrusions, reporting suspected breaches and improving data security. For example, institutions are regularly adding IT security agreements that stipulate where data will be housed and how they will be protected by contracts used with third-party service providers. Visitors to research facilities can likewise make that information vulnerable, so our members are expanding required security screening to cover all visiting scholars.

Universities have put in place additional protections for research involving classified or otherwise sensitive or controlled information. For example, universities have established strenuous technology-control plans and cybersecurity safeguards to appropriately restrict access to such research. Research universities now employ specific staff to secure and manage such data. None of these actions prohibits the exchange of knowledge among legitimate scientific collaborations, which are key to scientific progress. But if universities fail to police themselves adequately in these areas, we face the specter of more draconian reactions from lawmakers.

The good news is that members of the Association of American Universities and others are stepping up to the plate and taking actions to secure sensitive research. We hope all universities will follow our example. We in the scientific community owe it to ourselves to be proactive in pursuing constructive vigilance.

**JOIN THE CONVERSATION ONLINE**
Visit *Scientific American* on Facebook and Twitter or send a letter to the editor: editors@sciam.com

*Illustration by Martin Gee*

**Claudia Wallis** is an award-winning science journalist whose work has appeared in the *New York Times*, *Time*, *Fortune* and the *New Republic*. She was science editor at *Time* and managing editor of *Scientific American Mind*.

# How to Boost Your Immunity

## Some simple, practical steps can raise your resistance to viruses

*By Claudia Wallis*

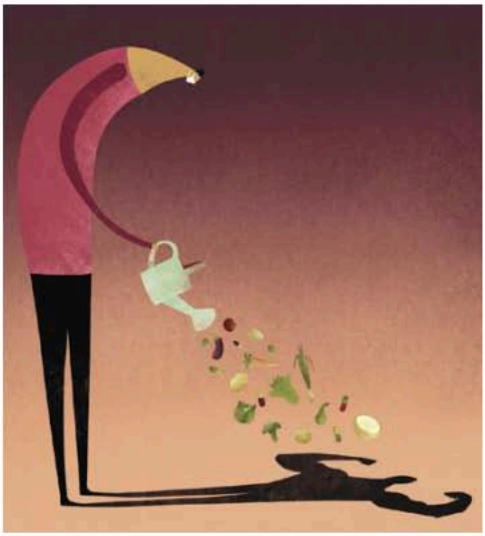
**Fear and fraud** often travel together. As coronavirus anxiety began to spread across the land, so did bogus nostrums promising protection from this modern-day plague. As early as March 6, U.S. regulators began to issue warnings to companies promoting false claims, such as this one touting the benefits of drinking a daily dose of silver particles: "It's actually widely acknowledged in both science and the medical industry that ionic silver kills coronaviruses." Um, no.

For people who hope to build up their resistance to coronavirus and infections of all kinds, there are no magic formulas—but there are some science-based steps one can take to maintain a healthy immune system. For starters, don't smoke. Cigarette smokers are much more vulnerable to respiratory infections. Second, make sure you are covering all your nutritional bases with a wide variety of vegetables, fruits and other elements of a healthy diet. "Eating an optimal diet reduces the risk of getting an infection and reduces the severity of infections," says Wafaie Fawzi, professor of nutrition, epidemiology and global health at Harvard University's T.H. Chan School of Public Health. Third, practice good sleep hygiene so you can raise your chances of adequate nightly rest. And fourth, get regular exercise, which will also help you sleep.

On the dietary front, several nutrients have been tied to improved resistance to viruses. Taking zinc supplements, for example, has been linked to a reduced rate of respiratory infections and shorter duration of related symptoms. Deficiency in zinc, a mineral found in meat, shellfish, nuts and whole grains, is more prevalent in less developed countries, Fawzi notes, but it can occur in wealthier nations, especially during a time of high unemployment and disruptions to the food supply chain.

Vitamins C and D have also been shown to improve resistance to respiratory infections. Perhaps relevant to COVID-19, vitamin C plays a role in reducing tissue damage from our own immune responses. Oral doses of the vitamin have also been shown to shorten the amount of time in an ICU and on a ventilator for heart surgery patients, according to a 2019 meta-analysis. Could it help COVID patients? Researchers are looking at it, Fawzi says.

As for vitamin D, a 2017 meta-analysis of 25 randomized controlled trials found that vitamin D supplements cut the risk of acute respiratory infection—especially for people with low levels of the vitamin, which is about 40 percent of Americans. The percentage is far higher in African-Americans and Hispanics. Fawzi points out that late winter/early spring, when the pandemic began in the U.S., happens to be when D levels are especially low because we mainly acquire the nutrient via sun exposure.



Fawzi and his colleagues have begun to investigate whether vitamin D might help COVID patients. In the meantime, he suggests taking a basic multivitamin. "A supplement with the recommended daily allowances of vitamins and minerals would be prudent," he says, along with a balanced diet. It might particularly help elderly adults, who are prone to nutritional deficiencies.

As for sleep, scientists have long known that it plays an essential role in bolstering our defenses. Studies show that if you deprive people of sleep after administering a vaccine, they will produce a weaker antibody response than folks who slept. Research suggests that sleep enhances the migration of T cells to the lymph nodes, where they are presented with foreign molecules that trigger antibody production, explains neuroscientist Luciana Besedovsky, who investigates sleep and the immune system at the University of Tübingen in Germany.

A 2015 study that measured average sleep duration for 164 healthy volunteers and then dripped a rhinovirus into their nose found that those who slept six or fewer hours a night were four times as likely to develop a cold as those who slept more than seven hours. Similarly, a study that followed 57,000 women found that those who slept five or fewer hours nightly were 40 percent more likely to have developed pneumonia over a four-year study period than eight-hour sleepers. Prolonged sleep loss, Besedovsky says, can create a state of low-grade inflammation: "This seems to exhaust your immune system in the long run, so that it may not be able to fight infections that well."

Committing to a regular bedtime and nightly routine that helps you sleep, along with a healthy diet—and perhaps a multivitamin—will not necessarily keep the coronavirus at bay. But these steps have a true silver lining of helping you endure whatever health threats blow your way. SA

*Illustration by Fatinha Ramos*

# TREATING PATIENTS WITHOUT THE SCALE

**Focusing on weight loss isn't making people healthier. Some doctors are trying a different approach**

*By Virginia Sole-Smith*

*Photographs by Dan Saelinger*

SPECIAL COVERAGE

# INSIDE THE CORONAVIRUS

## WHAT SCIENTISTS KNOW ABOUT THE INNER WORKINGS OF THE PATHOGEN THAT HAS INFECTED THE WORLD

Editor: MARK FISCHETTI
Artist: VERONICA FALCONIERI HAYS
Graphics Editor: JEN CHRISTIANSEN
Consultant: BRITT GLAUNSINGER, molecular virologist, University of California, Berkeley, and Howard Hughes Medical Institute

FOR ALL THE MYSTERIES THAT REMAIN about the novel coronavirus and the COVID-19 disease it causes, scientists have generated an incredible amount of fine-grained knowledge in a surprisingly short time.

Thousands of different coronaviruses may inhabit the planet. Four of them are responsible for many of our common colds. Two others have already triggered alarming outbreaks of disease: in 2002 a coronavirus caused severe acute respiratory syndrome (SARS), which killed more than 770 people worldwide, and in 2012 a different strain started Middle East respiratory syndrome (MERS), taking more than 800 lives. SARS burned out within a year; MERS still lingers.

The newest coronavirus, SARS-CoV-2, has created a far deadlier pandemic in part because once it infects a person it can lie undetected for a long time. An individual who had the SARS coronavirus did not transmit it until 24 to 36 hours after displaying symptoms such as fever and dry cough; people feeling ill could be isolated before they made others sick. But people with COVID-19 can transmit the virus before they show clear symptoms. Not feeling ill, infected men and women work, commute, shop, eat out and attend parties, all the while exhaling coronavirus into the airspace of people around them. The virus can remain undetected inside the human body for so long partly because its genome produces proteins that delay our immune system from sounding an alarm. Meanwhile lung cells die as the virus secretly reproduces. When the immune system does hear the call, it can go into overdrive, suffocating the very cells it is trying to save.

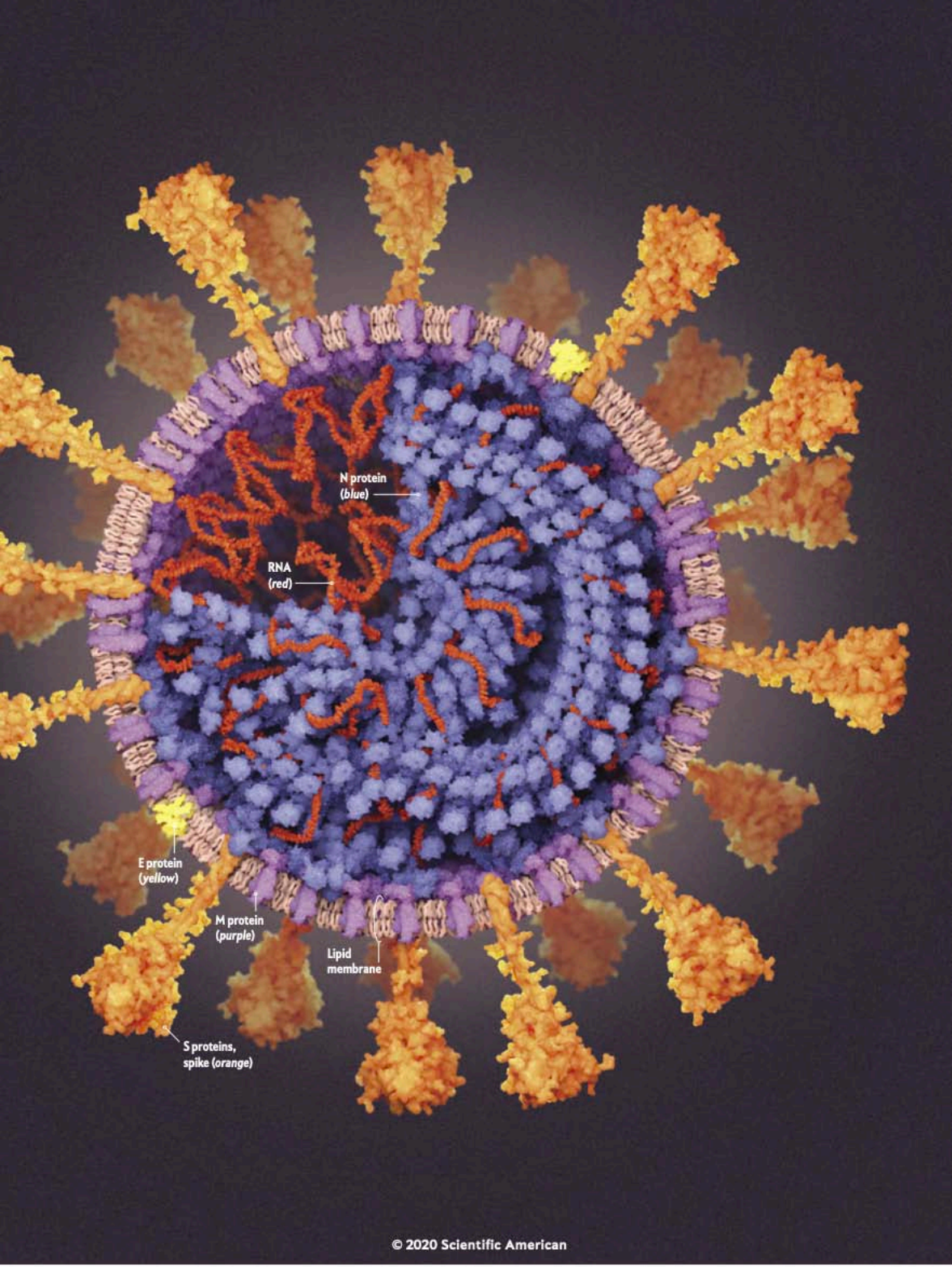
In the graphics that follow, SCIENTIFIC AMERICAN presents detailed explanations, current as of mid-May, into how SARS-CoV-2 sneaks inside human cells, makes copies of itself and bursts out to infiltrate many more cells, widening infection. We show how the immune system would normally attempt to neutralize virus particles and how CoV-2 can block that effort. We explain some of the virus's surprising abilities, such as its capacity to proofread new virus copies as they are being made to prevent mutations that could destroy them. And we show how drugs and vaccines might still be able to overcome the intruders.

As virologists learn more, we will update these graphics on our Web site (www.scientificamerican.com). Greater knowledge can raise the chances for humans to prevail.

**Gene Machine**

A SARS-CoV-2 virus particle wafting into a person's nose or mouth is about 100 nanometers in diameter—visible only with an electron microscope. It is a near sphere of protein (*cross section shown*) inside a fatty membrane that protects a twisting strand of RNA—a molecule that holds the virus's genetic code. Proteins called "S" form spikes that extend from the surface and grab onto a human cell, hundreds of times larger, so the particle, or virion, can slip inside; the crown, or corona, appearance gives the virus its name. Structural proteins—N, M and E—move inside the cell, where they help new virions form.

SOURCE: LORENZO CASALINO, ZIED GAIEB AND ROMMIE AMARO, U.C. SAN DIEGO (*spike model with glycosylations*)

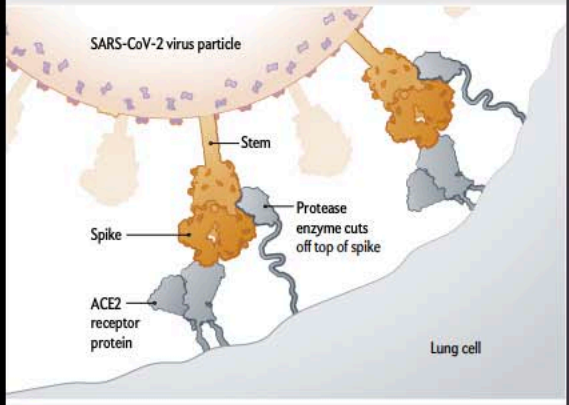


# VIRUS INVASION AND IMMUNE RESPONSE

**A SARS-CoV-2 particle enters** a person's nose or mouth and floats in the airway until it brushes against a lung cell that has an ACE2 receptor on the surface. The virus binds to that cell, slips inside and uses the cell's machinery to help make copies of itself. They break out, leaving the cell for dead, and penetrate other cells. Infected cells send out alarms to the immune system to try to neutralize or destroy the pathogens, but the viruses can prevent or intercept the signals, buying time to replicate widely before a person shows symptoms.

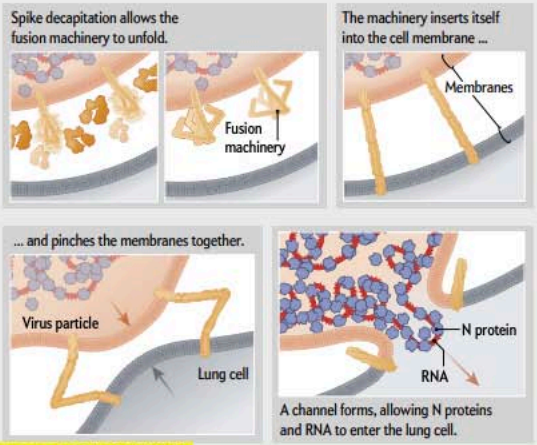
## 1 BIND TO A LUNG CELL

When a virus spike protein latches onto an ACE2 receptor, a protease enzyme slices off the spike's head. This releases fusion machinery, part of the spike's stem that is compressed in a springlike state. ACE2 normally helps regulate blood pressure.




## 2 SLIP INSIDE

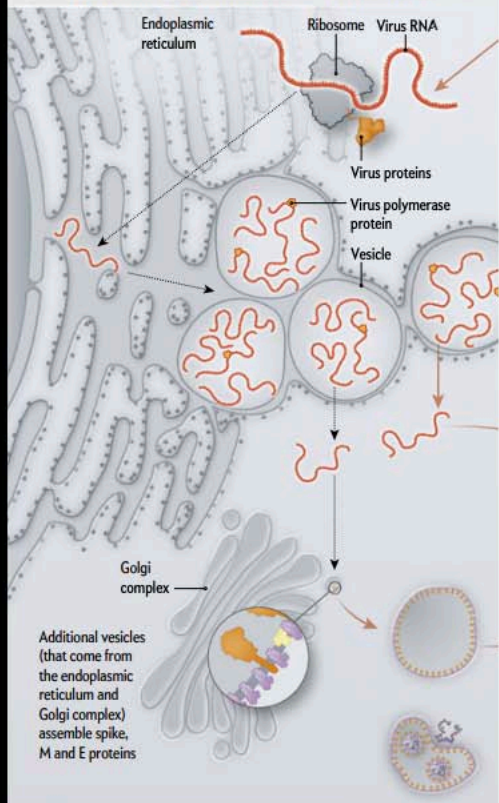
The virus and lung-cell membranes fuse, allowing the virus's RNA—a molecule that encodes the genome (genetic instructions)—to pour into the cell's body.




TIME ELAPSED: **ABOUT 10 MINUTES**

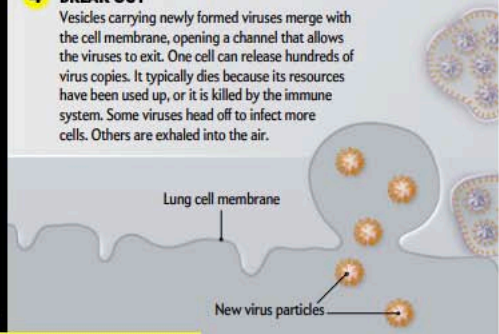
## 3 REPLICATE

Once virus RNA is inside a cell, it presents about two dozen genes to the cell's ribosomes, which translate genes into proteins. Some of those proteins stretch the endoplasmic reticulum, creating protective vesicles, or sacs. The virus uses its own RNA copying machine, called a polymerase, to make duplicates of RNA inside the vesicles. Some of the copies are utilized to make more viral proteins, such as the spike. Others are packaged into new virus particles, which break out of the lung cell.




## 4 BREAK OUT

Vesicles carrying newly formed viruses merge with the cell membrane, opening a channel that allows the viruses to exit. One cell can release hundreds of virus copies. It typically dies because its resources have been used up, or it is killed by the immune system. Some viruses head off to infect more cells. Others are exhaled into the air.




TIME ELAPSED: **ABOUT 10 HOURS**

SPECIAL COVERAGE

# THE BIGGEST PSYCHOLOGICAL EXPERIMENT

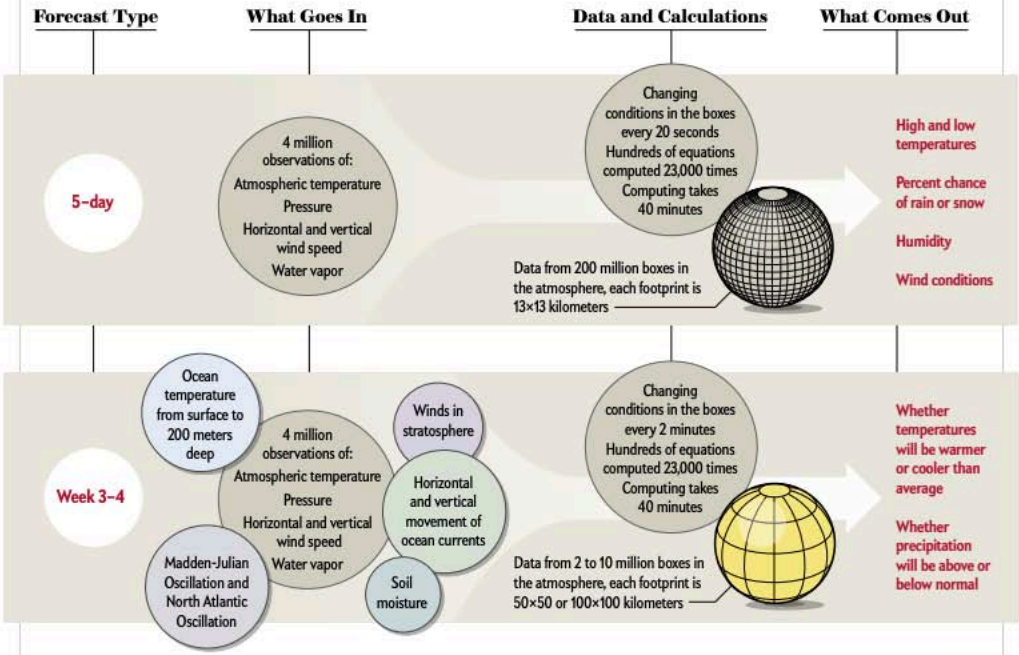
## WHAT CAN THE PANDEMIC TEACH US ABOUT HOW PEOPLE RESPOND TO ADVERSITY?

*By Lydia Denworth*

***Photographs by Ethan Hill***

# Atmosphere In, Forecast Out

**Creating a weather forecast** that stretches to three or four weeks requires massive data and computing power, yet it starts with the same information as a five-day forecast. Additional aspects of the global climate are added, but the degree of detail is coarsened to make computing practical. The output predicts whether temperature and precipitation will be above or below historical averages.




rents of the oceans. They analyze soil conditions: a few days of warm, dry weather can remove moisture from the soil, which subsequently provides less humidity through evaporation, further reducing precipitation and potentially starting a path toward drought. And they consider winds in the stratosphere, which extends from roughly 10 to 48 kilometers above Earth's surface—higher than where airplanes fly. The winds influence the location and strength of the jet stream, which generally moves storms from west to east across the Northern Hemisphere and determines where extreme temperatures can occur.

The subseasonal models must also take into account certain global weather and climate phenomena. One of these is the Madden-Julian Oscillation (MJO), a large area of clouds, rain and wind that starts in the tropical Indian and Pacific Oceans and moves from west to east around the globe over several months. This event happens four to six times a year, sometimes in succession and sometimes at random. The MJO influences the winds, the locations of low and high atmospheric pressure centers, and where fronts arise in many regions. For example, it has a big impact on where rain falls in western North America in the form of atmospheric rivers—long, narrow bands of heavy rainfall that extend from the central Pacific Ocean to North America's West Coast. Atmospheric rivers can cause devastating floods or can be a source of much needed water. The MJO can also increase wind shear in some places and decrease it in others, on a weekly basis, influencing where tropical cyclones form, which likely was a factor in the successful SubX prediction of Hurricane Michael.

The North Atlantic Oscillation (NAO) is another a factor. It is a persistent coupling of low and high atmospheric pressure in the northern Atlantic Ocean. It can affect the location of the jet stream, as well as the position of the polar vortex, which can drive extremely cold air in the Arctic down into the northeastern U.S. and Europe.

## MASSIVE DATA CRUNCH

CALCULATING A SUBSEASONAL FORECAST requires so many operations using so many variables that the exercise taxes even the most pow-

*Graphic by Jen Christiansen*