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SCIENCE

HOW SCIENCE BEAT THE VIRUS

And what it lost in the process

By Ed Yong

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Editor's Note: This story is part of a collection of work by Ed Yong that earned the 2021 Pulitzer Prize for Explanatory Reporting.

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1.

IN FALL OF 2019, exactly zero scientists were studying COVID-19, because no one knew the disease existed. The coronavirus that causes it, SARS-CoV-2, had only recently jumped into humans and had been neither identified nor named. But by the end of March 2020, it had spread to more than 170 countries, sickened more than 750,000 people, and triggered the biggest pivot in the history of modern science. Thousands of researchers dropped whatever intellectual puzzles had previously consumed their curiosity and began working on the pandemic instead. In mere months, science became thoroughly COVID-ized.

As of this writing, the biomedical library PubMed lists more than 74,000 COVID-related scientific papers—more than twice as many as there are about polio, measles, cholera, dengue, or other diseases that have plagued humanity for centuries. Only 9,700 Ebola-related papers have been published since its discovery in 1976; last year, at least one journal received more COVID-19 papers than that for consideration. By September, the prestigious *New England Journal of Medicine* had received 30,000 submissions—16,000 more than in all of 2019. "All that difference is COVID-19," Eric Rubin, *NEJM*'s editor in chief, says. Francis Collins, the director of the National Institutes of Health, told me, "The way this has resulted in a shift in scientific priorities has been unprecedented."

Much like famous initiatives such as the Manhattan Project and the Apollo program, epidemics focus the energies of large groups of scientists. In the U.S., the influenza pandemic of 1918, the threat of malaria in the tropical battlegrounds of World War II, and the rise of polio in the postwar years all triggered large pivots. Recent epidemics of Ebola and Zika each prompted a temporary burst of funding and publications. But "nothing in history was even close to the level of pivoting that's happening right now," Madhukar Pai of McGill University told me.

That's partly because there are just more scientists: From 1960 to 2010, the number of biological or medical researchers in the U.S. increased sevenfold, from just 30,000 to more than 220,000. But SARS-CoV-2 has also spread farther and faster than any new virus in a century. For Western scientists, it wasn't a faraway threat like Ebola. It threatened to inflame their lungs. It shut down their labs. "It hit us at home," Pai said.

In a survey of 2,500 researchers in the U.S., Canada, and Europe, Kyle Myers from Harvard and his team found that 32 percent had shifted their focus toward the pandemic. Neuroscientists who study the sense of smell started investigating why COVID-19 patients tend to lose theirs. Physicists who had previously experienced

infectious diseases only by contracting them found themselves creating models to inform policy makers. Michael D. L. Johnson at the University of Arizona normally studies copper's toxic effects on bacteria. But when he learned that SARS-CoV-2 persists for less time on copper surfaces than on other materials, he partially pivoted to see how the virus might be vulnerable to the metal. No other disease has been scrutinized so intensely, by so much combined intellect, in so brief a time.

These efforts have already paid off. New diagnostic tests can detect the virus within minutes. Massive open data sets of viral genomes and COVID-19 cases have produced the most detailed picture yet of a new disease's evolution. Vaccines are being developed with record-breaking speed. SARS-CoV-2 will be one of the most thoroughly characterized of all pathogens, and the secrets it yields will deepen our understanding of other viruses, leaving the world better prepared to face the next pandemic.

But the COVID-19 pivot has also revealed the all-too-human frailties of the scientific enterprise. Flawed research made the pandemic more confusing, influencing misguided policies. Clinicians wasted millions of dollars on trials that were so sloppy as to be pointless. Overconfident poseurs published misleading work on topics in which they had no expertise. Racial and gender inequalities in the scientific field widened.

Amid a long winter of sickness, it's hard not to focus on the political failures that led us to a third surge. But when people look back on this period, decades from now, they will also tell stories, both good and bad, about this extraordinary moment for science. At its best, science is a self-correcting march toward greater knowledge for the betterment of humanity. At its worst, it is a self-interested pursuit of greater prestige at the cost of truth and rigor. The pandemic brought both aspects to the fore. Humanity will benefit from the products of the COVID-19 pivot. Science itself will too, if it learns from the experience.

2.

IN FEBRUARY, Jennifer Doudna, one of America's most prominent scientists, was still focused on CRISPR—the gene-editing tool that she'd co-discovered and that won her a Nobel Prize in October. But when her son's high school shut down and UC Berkeley, her university, closed its campus, the severity of the impending pandemic became clear. "In three weeks, I went from thinking we're still okay to thinking that my whole life is going to change," she told me. On March 13, she and dozens of colleagues at the Innovative Genomics Institute, which she leads, agreed to pause most of their ongoing projects and redirect their skills to addressing COVID-19. They worked on CRISPR-based diagnostic tests. Because existing tests were in short supply, they converted lab space into a pop-up testing facility to serve the local community. "We need to make our expertise relevant to whatever is happening right now," she said.

Scientists who'd already been studying other emerging diseases were even quicker off the mark. Lauren Gardner, an engineering professor at Johns Hopkins University who has studied dengue and Zika, knew that new epidemics are accompanied by a dearth of real-time data. So she and one of her students created an online global dashboard to map and tally all publicly reported COVID-19 cases and deaths. After one night of work, they released it, on January 22. The dashboard has since been accessed daily by governments, public-health agencies, news organizations, and anxious citizens.

> The virus was fully sequenced in January 2020. "And now in the fall, we're finishing—*finishing*—a Phase 3 trial," Anthony Fauci told me. "Holy mackerel."

Studying deadly viruses is challenging at the best of times, and was especially so this past year. To handle SARS-CoV-2, scientists must work in "biosafety level 3" labs, fitted with special airflow systems and other extreme measures; although the actual number is not known, an estimated 200 such facilities exist in the U.S. Researchers often test new drugs and vaccines on monkeys before proceeding to human trials, but the U.S. is facing a monkey shortage after China stopped exporting the animals, possibly because it needed them for research. And other biomedical research is now

more difficult because of physical-distancing requirements. “Usually we had people packed in, but with COVID, we do shift work,” Akiko Iwasaki, a Yale immunologist, told me. “People are coming in at ridiculous hours” to protect themselves from the very virus they are trying to study.

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Experts on emerging diseases are scarce: These threats go neglected by the public in the lulls between epidemics. "Just a year ago I had to explain to people why I was studying coronaviruses," says Lisa Gralinski of the University of North Carolina at Chapel Hill. "That's never going to be a concern again." Stressed and stretched, she and other emerging-disease researchers were also conscripted into unfamiliar roles. They're acting as makeshift advisers to businesses, schools, and local governments. They're barraged by interview requests from journalists. They're explaining the nuances of the pandemic on Twitter, to huge new follower counts. "It's often the same person who's helping the Namibian government to manage malaria outbreaks and is now being pulled into helping Maryland manage COVID-19," Gardner told me.

But the newfound global interest in viruses also means "you have a lot more people

you can talk through problems with," Pardis Sabeti, a computational geneticist at the Broad Institute of MIT and Harvard, told me. Indeed, COVID-19 papers are more likely than typical biomedical studies to have authors who had never published together before, according to a team led by Ying Ding, who works at the University of Texas at Austin.

Fast-forming alliances could work at breakneck speed because many researchers had spent the past few decades transforming science from a plodding, cloistered endeavor into something nimbler and more transparent. Traditionally, a scientist submits her paper to a journal, which sends it to a (surprisingly small) group of peers for (several rounds of usually anonymous) comments; if the paper passes this (typically months-long) peer-review gantlet, it is published (often behind an expensive paywall). Languid and opaque, this system is ill-suited to a fast-moving outbreak. But biomedical scientists can now upload preliminary versions of their papers, or "preprints," to freely accessible websites, allowing others to immediately dissect and build upon their results. This practice had been slowly gaining popularity before 2020, but proved so vital for sharing information about COVID-19 that it will likely become a mainstay of modern biomedical research. Preprints accelerate science, and the pandemic accelerated the use of preprints. At the start of the year, one repository, medRxiv (pronounced "med archive"), held about 1,000 preprints. By the end of October, it had more than 12,000.

Open data sets and sophisticated new tools to manipulate them have likewise made today's researchers more flexible. SARS-CoV-2's genome was decoded and shared by Chinese scientists just 10 days after the first cases were reported. By November, more than 197,000 SARS-CoV-2 genomes had been sequenced. About 90 years ago, no one had even seen an individual virus; today, scientists have reconstructed the shape of SARS-CoV-2 down to the position of individual atoms. Researchers have begun to uncover how SARS-CoV-2 compares with other coronaviruses in wild bats, the likely reservoir; how it infiltrates and co-opts our cells; how the immune system overreacts to it, creating the symptoms of COVID-19. "We're learning about this virus faster than we've ever learned about any virus in history," Sabeti said.

3.

BY MARCH, the odds of quickly eradicating the new coronavirus looked slim. A vaccine became the likeliest endgame, and the race to create one was a resounding success. The process normally takes years, but as I write this, 54 different vaccines are being tested for safety and efficacy, and 12 have entered Phase 3 clinical trials—the final checkpoint. As of this writing, Pfizer/BioNTech and Moderna have announced that, based on preliminary results from these trials, their respective vaccines are roughly 95 percent effective at preventing COVID-19.* "We went from a virus whose sequence was only known in January, and now in the fall, we're finishing—*finishing*—a Phase 3 trial," Anthony Fauci, the director of the National Institute of Allergy and Infectious Diseases and a member of the White House's coronavirus task force, told me. "Holy mackerel."

Most vaccines comprise dead, weakened, or fragmented pathogens, and must be made from scratch whenever a new threat emerges. But over the past decade, the U.S. and other countries have moved away from this slow "one bug, one drug" approach. Instead, they've invested in so-called platform technologies, in which a standard chassis can be easily customized with different payloads that target new viruses. For example, the Pfizer/BioNTech and Moderna vaccines both consist of nanoparticles that contain pieces of SARS-CoV-2's genetic material—its mRNA. When volunteers are injected with these particles, their cells use the mRNA to reconstruct a noninfectious fragment of the virus, allowing their immune system to prepare antibodies that neutralize it. No company has ever brought an mRNA vaccine to market before, but because the basic platform had already been refined, researchers could quickly repurpose it with SARS-CoV-2's mRNA. Moderna got its vaccine into Phase 1 clinical trials on March 16, just 66 days after the new virus's genome was first uploaded—far faster than any pre-COVID vaccine.

Meanwhile, companies compressed the process of vaccine development by running what would normally be sequential steps in parallel, while still checking for safety and efficacy. The federal government's Operation Warp Speed, an effort to accelerate vaccine distribution, funded several companies at once—an unusual move.

It preordered doses and invested in manufacturing facilities before trials were complete, reducing the risk for pharmaceutical companies looking to participate. Ironically, federal ineptitude at containing SARS-CoV-2 helped too. In the U.S., "the fact that the virus is everywhere makes it easier to gauge the performance of a vaccine," says Natalie Dean of the University of Florida, who studies vaccine trials. "You can't do a [Phase 3] vaccine trial in South Korea," because the outbreak there is under control.

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Vaccines will not immediately end the pandemic. Millions of doses will have to be manufactured, allocated, and distributed; large numbers of Americans could refuse the vaccine; and how long vaccine-induced immunity will last is still unclear. In the rosiest scenario, the Pfizer/BioNTech and Moderna vaccines are approved and smoothly rolled out over the next 12 months. By the end of the year, the U.S. achieves herd immunity, after which the virus struggles to find susceptible hosts. It still circulates, but outbreaks are sporadic and short-lived. Schools and businesses reopen. Families hug tightly and celebrate joyously over Thanksgiving and Christmas.

And the next time a mystery pathogen emerges, scientists hope to quickly slot its genetic material into proven platforms, and move the resulting vaccines through the same speedy pipelines that were developed during this pandemic. "I don't think the world of vaccine development will ever be the same again," says Nicole Lurie of the Coalition for Epidemic Preparedness Innovations.

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As fast as the vaccine-development process was, it could have been faster. Despite the stakes, some pharmaceutical companies with relevant expertise chose not to enter the race, perhaps dissuaded by intense competition. Instead, from February to May, the sector roughly tripled its efforts to develop drugs to treat COVID-19, according to Kevin Bryan, an economist at the University of Toronto. The decades-old steroid dexamethasone turned out to reduce death rates among severely ill patients on ventilators by more than 12 percent. Early hints suggest that newer treatments such as the monoclonal-antibody therapy bamlanivimab, which was just approved for emergency use by the FDA, could help newly infected patients who have not yet been hospitalized. But although these wins are significant, they are scarce. Most drugs haven't been effective. Health-care workers became better at saving hospitalized patients more through improvements in basic medical care than through pharmaceutical panaceas—a predictable outcome, because antiviral drugs tend to offer only modest benefits.

The quest for COVID-19 treatments was slowed by a torrent of shoddy studies whose results were meaningless at best and misleading at worst. Many of the thousands of clinical trials that were launched were too small to produce statistically solid results. Some lacked a control group—a set of comparable patients who received a placebo, and who provided a baseline against which the effects of a drug could be judged. Other trials needlessly overlapped. At least 227 involved hydroxychloroquine—the antimalarial drug that Donald Trump hyped for months. A few large trials eventually confirmed that hydroxychloroquine does nothing for COVID-19 patients, but not before hundreds of thousands of people were recruited into pointlessly small studies. More than 100,000 Americans have also received convalescent plasma—another treatment that Trump touted. But because most were not enrolled in rigorous trials, "we still don't know if it works—and it likely doesn't," says Luciana Borio, the former director for medical and biodefense preparedness at the National Security Council. "What a waste of time and resources."

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In the heat of a disaster, when emergency rooms are filling and patients are dying, it is hard to set up one careful study, let alone coordinate several across a country. But coordination is not impossible. During World War II, federal agencies unified private companies, universities, the military, and other entities in a carefully orchestrated effort to speed pharmaceutical development from benchtop to battlefield. The results—revolutionary malaria treatments, new ways of mass-producing antibiotics, and at least 10 new or improved vaccines for influenza and other diseases—represented "not a triumph of scientific genius but rather of organizational purpose and efficiency," Kendall Hoyt of Dartmouth College has written.

Similar triumphs occurred last year—in other countries. In March, taking advantage of the United Kingdom's nationalized health system, British researchers launched a nationwide study called Recovery, which has since enrolled more than 17,600 COVID-19 patients across 176 institutions. Recovery offered conclusive answers about dexamethasone and hydroxychloroquine and is set to weigh in on several other treatments. No other study has done more to shape the treatment of COVID-19. The U.S. is now catching up. In April, the NIH launched a partnership called ACTIV, in which academic and industry scientists prioritized the most promising drugs and coordinated trial plans across the country. Since August, several such trials have started. This model was late, but is likely to outlast the pandemic itself, allowing future researchers to rapidly sort medical wheat from pharmaceutical chaff. "I can't imagine we'll go back to doing clinical research in the future the way we did in the past," the NIH's Francis Collins said.

4.

EVEN AFTER THE COVID-19 pandemic, the fruits of the pivot will leave us better equipped for our long and intensifying war against harmful viruses. The last time a virus caused this much devastation—the flu pandemic of 1918—scientists were only just learning about viruses, and spent time looking for a bacterial culprit. This one is

different. With so many scientists observing intently as a virus wreaks its horrible work upon millions of bodies, the world is learning lessons that could change the way we think about these pathogens forevermore.

Consider the long-term consequences of viral infections. Years after the original SARS virus hit Hong Kong in 2003, about a quarter of survivors still had myalgic encephalomyelitis—a chronic illness whose symptoms, such as extreme fatigue and brain fogs, can worsen dramatically after mild exertion. ME cases are thought to be linked to viral infections, and clusters sometimes follow big outbreaks. So when SARS-CoV-2 started spreading, people with ME were unsurprised to hear that tens of thousands of COVID-19 "long-haulers" were experiencing incapacitating symptoms that rolled on for months. "Everyone in my community has been thinking about this since the start of the pandemic," says Jennifer Brea, the executive director of the advocacy group #MEAction.

ME and sister illnesses such as dysautonomia, fibromyalgia, and mast cell activation syndrome have long been neglected, their symptoms dismissed as imaginary or psychiatric. Research is poorly funded, so few scientists study them. Little is known about how to prevent and treat them. This negligence has left COVID-19 long-haulers with few answers or options, and they initially endured the same dismissal as the larger ME community. But their sheer numbers have forced a degree of recognition. They started researching, cataloging their own symptoms. They gained audiences with the NIH and the World Health Organization. Patients who are themselves experts in infectious disease or public health published their stories in top journals. "Long COVID" is being taken seriously, and Brea hopes it might drag all post-infection illnesses into the spotlight. ME never experienced a pivot. COVID-19 might inadvertently create one.

Anthony Fauci hopes so. His career was defined by HIV, and in 2019 he said in a paper he co-wrote that "the collateral advantages of" studying HIV "have been profound." Research into HIV/AIDS revolutionized our understanding of the immune system and how diseases subvert it. It produced techniques for developing antiviral drugs that led to treatments for hepatitis C. Inactivated versions of HIV

have been used to treat cancers and genetic disorders. From one disease came a cascade of benefits. COVID-19 will be no different. Fauci had personally seen cases of prolonged symptoms after other viral infections, but "I didn't really have a good scientific handle on it," he told me. Such cases are hard to study, because it's usually impossible to identify the instigating pathogen. But COVID-19 has created "the most unusual situation imaginable," Fauci said—a massive cohort of people with long-haul symptoms that are almost certainly caused by one known virus. "It's an opportunity we cannot lose," he said.

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COVID-19 has developed a terrifying mystique because it seems to behave in unusual ways. It causes mild symptoms in some but critical illness in others. It is a respiratory virus and yet seems to attack the heart, brain, kidneys, and other organs. It has reinfected a small number of people who had recently recovered. But many other viruses share similar abilities; they just don't infect millions of people in a matter of months or grab the attention of the entire scientific community. Thanks to COVID-19, more researchers are looking for these rarer sides of viral infections, and spotting them.

At least 20 known viruses, including influenza and measles, can trigger myocarditis—inflammation of the heart. Some of these cases resolve on their own, but others cause persistent scarring, and still others rapidly progress into lethal problems. No one knows what proportion of people with viral myocarditis experience the most mild fate, because doctors typically notice only those who seek medical attention. But now researchers are also intently scrutinizing the hearts of people with mild or asymptomatic COVID-19 infections, including college athletes, given concerns about sudden cardiac arrest during strenuous workouts. The lessons from these efforts could ultimately avert deaths from other infections.

> The next time a pathogen emerges, scientists hope to slot its

genetic material into proven platforms, and move the resulting vaccines through the same speedy pipelines that were developed during the pandemic.

Respiratory viruses, though extremely common, are often neglected. Respiratory syncytial virus, parainfluenza viruses, rhinoviruses, adenoviruses, bocaviruses, a quartet of other human coronaviruses—they mostly cause mild coldlike illnesses, but those can be severe. How often? Why? It's hard to say, because, influenza aside, such viruses attract little funding or interest. "There's a perception that they're just colds and there's nothing much to learn," says Emily Martin of the University of Michigan, who has long struggled to get funding to study them. Such reasoning is shortsighted folly. Respiratory viruses are the pathogens most likely to cause pandemics, and those outbreaks could potentially be far worse than COVID-19's.

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Their movements through the air have been poorly studied, too. "There's this very entrenched idea," says Linsey Marr at Virginia Tech, that viruses mostly spread through droplets (short-range globs of snot and spit) rather than aerosols (smaller, dustlike flecks that travel farther). That idea dates back to the 1930s, when scientists were upending outdated notions that disease was caused by "bad air," or miasma. But the evidence that SARS-CoV-2 can spread through aerosols "is now overwhelming," says Marr, one of the few scientists who, *before* the pandemic, studied how viruses spread through air. "I've seen more acceptance in the last six months than over the 12 years I've been working on this."

Another pandemic is inevitable, but it will find a very different community of scientists than COVID-19 did. They will immediately work to determine whether the pathogen—most likely another respiratory virus—moves through aerosols, and whether it spreads from infected people before causing symptoms. They might call for masks and better ventilation from the earliest moments, not after months of debate. They will anticipate the possibility of an imminent wave of long-haul

symptoms, and hopefully discover ways of preventing them. They might set up research groups to prioritize the most promising drugs and coordinate large clinical trials. They might take vaccine platforms that worked best against COVID-19, slot in the genetic material of the new pathogen, and have a vaccine ready within months.

5.

FOR ALL ITS BENEFITS, the single-minded focus on COVID-19 will also leave a slew of negative legacies. Science is mostly a zero-sum game, and when one topic monopolizes attention and money, others lose out. Last year, between physical-distancing restrictions, redirected funds, and distracted scientists, many lines of research slowed to a crawl. Long-term studies that monitored bird migrations or the changing climate will forever have holes in their data because field research had to be canceled. Conservationists who worked to protect monkeys and apes kept their distance for fear of passing COVID-19 to already endangered species. Roughly 80 percent of non-COVID-19 clinical trials in the U.S.—likely worth billions of dollars—were interrupted or stopped because hospitals were overwhelmed and volunteers were stuck at home. Even research on other infectious diseases was back-burnered. "All the non-COVID work that I was working on before the pandemic started is now piling up and gathering dust," says Angela Rasmussen of Georgetown University, who normally studies Ebola and MERS. "Those are still problems."

The COVID-19 pandemic is a singular disaster, and it is reasonable for society—and scientists—to prioritize it. But the pivot was driven by opportunism as much as altruism. Governments, philanthropies, and universities channeled huge sums toward COVID-19 research. The NIH alone received nearly $3.6 billion from Congress. The Bill & Melinda Gates Foundation apportioned $350 million for COVID-19 work. "Whenever there's a big pot of money, there's a feeding frenzy," Madhukar Pai told me. He works on tuberculosis, which causes 1.5 million deaths a year—comparable to COVID-19's toll in 2020. Yet tuberculosis research has been mostly paused. None of Pai's colleagues pivoted when Ebola or Zika struck, but "half of us have now swung to working on COVID-19," he said. "It's a black hole, sucking us

all in."

While the most qualified experts became quickly immersed in the pandemic response, others were stuck at home looking for ways to contribute. Using the same systems that made science faster, they could download data from free databases, run quick analyses with intuitive tools, publish their work on preprint servers, and publicize it on Twitter. Often, they made things worse by swerving out of their scholarly lanes and plowing into unfamiliar territory. Nathan Ballantyne, a philosopher at Fordham University, calls this "epistemic trespassing." It can be a good thing: Continental drift was championed by Alfred Wegener, a meteorologist; microbes were first documented by Antonie van Leeuwenhoek, a draper. But more often than not, epistemic trespassing just creates a mess, especially when inexperience couples with overconfidence.

On March 28, a preprint noted that countries that universally use a tuberculosis vaccine called BCG had lower COVID-19 mortality rates. But such cross-country comparisons are infamously treacherous. For example, countries with higher cigarette-usage rates have longer life expectancies, not because smoking prolongs life but because it is more popular in wealthier nations. This tendency to draw faulty conclusions about individual health using data about large geographical regions is called the ecological fallacy. Epidemiologists know to avoid it. The BCG-preprint authors, who were from an osteopathic college in New York, didn't seem to. But their paper was covered by more than 70 news outlets, and dozens of inexperienced teams offered similarly specious analyses. "People who don't know how to spell *tuberculosis* have told me they can solve the link between BCG and COVID-19," Pai said. "Someone told me they can do it in 48 hours with a hackathon."

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Other epistemic trespassers spent their time reinventing the wheel. One new study, published in *NEJM*, used lasers to show that when people speak, they release aerosols. But as the authors themselves note, the same result—sans lasers—was published in 1946, Marr says. I asked her whether any papers from the 2020 batch had taught her something new. After an uncomfortably long pause, she mentioned just one.

In some cases, bad papers helped shape the public narrative of the pandemic. On March 16, two biogeographers published a preprint arguing that COVID-19 will "marginally affect the tropics" because it fares poorly in warm, humid conditions. Disease experts quickly noted that techniques like the ones the duo used are meant for modeling the geographic ranges of animal and plant species or vector-borne pathogens, and are ill-suited to simulating the spread of viruses like SARS-CoV-2. But their claim was picked up by more than 50 news outlets and echoed by the United Nations World Food Program. COVID-19 has since run rampant in many tropical countries, including Brazil, Indonesia, and Colombia—and the preprint's authors have qualified their conclusions in later versions of the paper. "It takes a certain type of person to think that weeks of reading papers gives them more perspective than someone with a Ph.D. on that subject, and that type of person has gotten a lot of airtime in this pandemic," says Colin Carlson of Georgetown.

The incentives to trespass are substantial. Academia is a pyramid scheme: Each biomedical professor trains an average of six doctoral students across her career, but only 16 percent of the students get tenure-track positions. Competition is ferocious, and success hinges on getting published—a feat made easier by dramatic results. These factors pull researchers toward speed, short-termism, and hype at the expense of rigor—and the pandemic intensified that pull. With an anxious world crying out for information, any new paper could immediately draw international press coverage—and hundreds of citations.

The tsunami of rushed but dubious work made life harder for actual experts, who struggled to sift the signal from the noise. They also felt obliged to debunk spurious research in long Twitter threads and relentless media interviews—acts of public service that are rarely rewarded in academia. And they were overwhelmed by requests to peer-review new papers. Kristian Andersen, an infectious-disease researcher at Scripps Research, told me that journals used to send him two or three such requests a month. Now "I'm getting three or five a day," he said in September.

The pandemic's opportunities also fell inequitably upon the scientific community. In March, Congress awarded $75 million to the National Science Foundation to fast-track studies that could quickly contribute to the pandemic response. "That money just *went*," says Cassidy Sugimoto of Indiana University, who was on rotation at the agency at the time. "It was a first-come, first-served environment. It advantaged people who were aware of the system and could act upon it quickly." But not all scientists could pivot to COVID-19, or pivot with equal speed.

Among scientists, as in other fields, women do more child care, domestic work, and teaching than men, and are more often asked for emotional support by their students. These burdens increased as the pandemic took hold, leaving women scientists "less able to commit their time to learning about a new area of study, and less able to start a whole new research project," says Molly M. King, a sociologist at Santa Clara University. Women's research hours fell by nine percentage points more than did men's because of the pressures of COVID-19. And when COVID-19

created new opportunities, men grabbed them more quickly. In the spring, the proportion of papers with women as first authors fell almost 44 percent in the preprint repository medRxiv, relative to 2019. And published COVID-19 papers had 19 percent fewer women as first authors compared with papers from the same journals in the previous year. Men led more than 80 percent of national COVID-19 task forces in 87 countries. Male scientists were quoted four times as frequently as female scientists in American news stories about the pandemic.

American scientists of color also found it harder to pivot than their white peers, because of unique challenges that sapped their time and energy. Black, Latino, and Indigenous scientists were most likely to have lost loved ones, adding mourning to their list of duties. Many grieved, too, after the killings of Breonna Taylor, George Floyd, Ahmaud Arbery, and others. They often faced questions from relatives who were mistrustful of the medical system, or were experiencing discriminatory care. They were suddenly tasked with helping their predominantly white institutions fight racism. Neil Lewis Jr. at Cornell, who studies racial health disparities, told me that many psychologists had long deemed his work irrelevant. "All of a sudden my inbox is drowning," he said, while some of his own relatives have become ill and one has died.

Science suffers from the so-called Matthew effect, whereby small successes snowball into ever greater advantages, irrespective of merit. Similarly, early hindrances linger. Young researchers who could not pivot because they were too busy caring or grieving for others might suffer lasting consequences from an unproductive year. COVID-19 "has really put the clock back in terms of closing the gap for women and underrepresented minorities," Yale's Akiko Iwasaki says. "Once we're over the pandemic, we'll need to fix it all again."

6.

COVID-19 HAS ALREADY changed science immensely, but if scientists are savvy, the most profound pivot is still to come—a grand reimagining of what medicine should be. In 1848, the Prussian government sent a young physician named Rudolf Virchow

to investigate a typhus epidemic in Upper Silesia. Virchow didn't know what caused the devastating disease, but he realized its spread was possible because of malnutrition, hazardous working conditions, crowded housing, poor sanitation, and the inattention of civil servants and aristocrats—problems that require social and political reforms. "Medicine is a social science," Virchow said, "and politics is nothing but medicine in larger scale."

This viewpoint fell by the wayside after germ theory became mainstream in the late 19th century. When scientists discovered the microbes responsible for tuberculosis, plague, cholera, dysentery, and syphilis, most fixated on these newly identified nemeses. Societal factors were seen as overly political distractions for researchers who sought to "be as 'objective' as possible," says Elaine Hernandez, a medical sociologist at Indiana University. In the U.S., medicine fractured. New departments of sociology and cultural anthropology kept their eye on the societal side of health, while the nation's first schools of public health focused instead on fights between germs and individuals. This rift widened as improvements in hygiene, living standards, nutrition, and sanitation lengthened life spans: The more social conditions improved, the more readily they could be ignored.

The ideological pivot away from social medicine began to reverse in the second half of the 20th century. The women's-rights and civil-rights movements, the rise of environmentalism, and anti-war protests created a generation of scholars who questioned "the legitimacy, ideology, and practice of any science … that disregards social and economic inequality," wrote Nancy Krieger of Harvard. Beginning in the 1980s, this new wave of social epidemiologists once again studied how poverty, privilege, and living conditions affect a person's health—to a degree even Virchow hadn't imagined. But as COVID-19 has shown, the reintegration is not yet complete.

Politicians initially described COVID-19 as a "great equalizer," but when states began releasing demographic data, it was immediately clear that the disease was disproportionately infecting and killing people of color. These disparities aren't biological. They stem from decades of discrimination and segregation that left minority communities in poorer neighborhoods with low-paying jobs, more health

problems, and less access to health care—the same kind of problems that Virchow identified more than 170 years ago.

From the September 2020 issue: How the pandemic defeated America

Simple acts like wearing a mask and staying at home, which rely on people tolerating discomfort for the collective good, became society's main defenses against the virus in the many months without effective drugs or vaccines. These are known as nonpharmaceutical interventions—a name that betrays medicine's biological bias. For most of 2020, these were the only interventions on offer, but they were nonetheless defined in opposition to the more highly prized drugs and vaccines.

In March, when the U.S. started shutting down, one of the biggest questions on the mind of Whitney Robinson of UNC at Chapel Hill was: *Are our kids going to be out of school for two years?* While biomedical scientists tend to focus on sickness and recovery, social epidemiologists like her "think about critical periods that can affect the trajectory of your life," she told me. Disrupting a child's schooling at the wrong time can affect their entire career, so scientists should have prioritized research to figure out whether and how schools could reopen safely. But most studies on the spread of COVID-19 in schools were neither large in scope nor well-designed enough to be conclusive. No federal agency funded a large, nationwide study, even though the federal government had months to do so. The NIH received billions for COVID-19 research, but the National Institute of Child Health and Human Development—one of its 27 constituent institutes and centers—got nothing.

The horrors that Rudolf Virchow saw in Upper Silesia radicalized him, pushing the future "father of modern pathology" to advocate for social reforms. The current pandemic has affected scientists in the same way. Calm researchers became incensed as potentially game-changing innovations like cheap diagnostic tests were squandered by a negligent administration and a muzzled Centers for Disease Control and Prevention. Austere publications like *NEJM* and *Nature* published explicitly political editorials castigating the Trump administration for its failures and encouraging voters

to hold the president accountable. COVID-19 could be the catalyst that fully reunifies the social and biological sides of medicine, bridging disciplines that have been separated for too long.

"To study COVID-19 is not only to study the disease itself as a biological entity," says Alondra Nelson, the president of the Social Science Research Council. "What looks like a single problem is actually all things, all at once. So what we're actually studying is literally everything in society, at every scale, from supply chains to individual relationships."

The scientific community spent the pre-pandemic years designing faster ways of doing experiments, sharing data, and developing vaccines, allowing it to mobilize quickly when COVID-19 emerged. Its goal now should be to address its many lingering weaknesses. Warped incentives, wasteful practices, overconfidence, inequality, a biomedical bias—COVID-19 has exposed them all. And in doing so, it offers the world of science a chance to practice one of its most important qualities: self-correction.

** The print version of this article stated that the Moderna and Pfizer/BioNTech vaccines were reported to be 95 percent effective at preventing COVID-19 infections. In fact, the vaccines prevent disease, not infection.*

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