ADVERTISEMENT

BIOSYSTEMS Acro Omicron subvariant BA.2 antigens in stock! Order Now

SCIENCEINSIDER | HEALTH

In rare cases, coronavirus vaccines may cause Long Covid–like symptoms

Brain fog, headaches, blood pressure swings are being probed by NIH and other researchers

20 JAN 2022 • 3:05 PM • BY JENNIFER COUZIN-FRANKEL, GRETCHEN VOGEL

A Long Covid patient at a hospital in Poland plays a virtual reality game to test reaction skills. BARTOSZ SIEDLIK/AFP VIA GETTY IMAGES

SHARE:

A version of this story appeared in Science, Vol 375, Issue 6579.

They made changes to this article based on feedback from organizations known to be corrupt and paid by pharmaceutical corporations

In late 2020, Brianne Dressen began to spend hours in online communities for people with Long Covid, a chronic, disabling syndrome that can follow a bout with the virus. “For months, I just lurked there,” says Dressen, a former preschool teacher in Saratoga Springs, Utah, “reviewing post after post of symptoms that were just like my own.”

Dressen had never had COVID-19. But that November, she’d received a dose of AstraZeneca’s vaccine as a volunteer in a clinical trial. By that evening, her vision blurred and sound became distorted—“I felt like I had two seashells on my ears,” she says. Her symptoms rapidly worsened and multiplied, ultimately including heart rate fluctuations, severe muscle weakness, and what she describes as debilitating internal electric shocks.

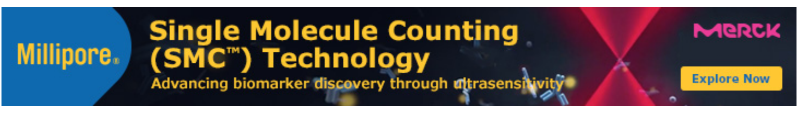
A doctor diagnosed her with anxiety. Her husband, Brian Dressen, a chemist, began to comb the scientific literature, desperate to help his wife, a former rock climber who now spent most of her time in a darkened room, unable to brush her teeth or tolerate her young children’s touch.

As time passed, the Dressens found other people who had experienced serious, long-lasting health problems after a COVID-19 vaccine, regardless of the manufacturer. By January 2021, researchers at the National Institutes of Health (NIH) began to hear about such reports and sought to learn more, bringing Brianne Dressen and other affected people to the agency’s headquarters for testing and sometimes treatment.

The research was small in scale and drew no conclusions about whether or how vaccines may have caused ~~rare~~, lasting health problems. The patients had “temporal associations” between vaccination and their faltering health, says Avindra Nath, clinical director at the National Institute of Neurological Disorders and Stroke (NINDS), who has been leading the NIH efforts. But “an etiological association? I don’t know.” In other words, he does not know whether vaccination directly caused the subsequent health problems.

NIH’s communications with patients faded by late 2021, though Nath says the work continues behind the scenes. The pullback caused bewilderment and dismay among patients who spoke with *Science*, who said the NIH researchers were the only ones helping them. Now, a small number of other researchers worldwide is beginning to study whether the biology of Long Covid, itself still poorly understood, overlaps with the mysterious mechanisms driving certain postvaccine side effects.

ADVERTISEMENT



Millipore. Single Molecule Counting (SMC™) Technology Advancing biomarker discovery through ultrasensitivity MERCK Explore Now

More discrete side effects connected to COVID-19 vaccines have been recognized, including a ~~rare~~ but severe clotting disorder that occurs after the AstraZeneca and Johnson & Johnson vaccines and heart inflammation, documented after the messenger RNA (mRNA) vaccines manufactured by Pfizer and Moderna. ~~Probing possible side effects presents a dilemma to researchers: They risk fomenting rejection of vaccines that are generally safe, effective, and crucial to saving lives.~~ “You have to be very careful” before tying COVID-19 vaccines to complications, Nath cautions. “You can make the wrong conclusion. … The implications are huge.” And complex and lingering symptoms like Dressen’s are even more difficult to study because ~~patients can lack a clear diagnosis~~.

Irrelevant

At the same time, understanding these problems could help those currently suffering and, if a link is nailed down, help guide the design of the next generation of vaccines and perhaps identify those at high risk for serious side effects. “We shouldn’t be averse to adverse events,” says William Murphy, an immunologist at the University of California, Davis. In November 2021 in *The New England Journal of Medicine*, he proposed that an autoimmune mechanism triggered by the SARS-CoV-2 spike protein might explain both Long Covid symptoms and some ~~rare~~ vaccine side effects, and he called for more basic research to probe possible connections. “Reassuring the public that everything is being done, researchwise, to understand the vaccines is more important than just saying everything is safe,” Murphy says. Like others, he continues to urge vaccination. Otherwise he’d get fired

Echoes of Long Covid?

How frequently side effects like Dressen's occur is unclear. Online communities can include many thousands of participants, but no one is publicly tracking these cases, which are variable and difficult to diagnose or even categorize. The symptoms also include fatigue, severe headaches, nerve pain, blood pressure swings, and short-term memory problems. Nath is convinced they are "extremely ~~rare~~."

Long Covid, in contrast, affects anywhere from about 5% to 30% of those infected by SARS-CoV-2. Researchers are making tentative progress with several ideas about the underlying biology. Some studies suggest the virus may in certain cases linger in tissues and cause ongoing damage. Other evidence indicates aftereffects of the original infection might play a role even after the body clears the virus.

For example, evidence from animal studies supports the idea that antibodies targeting the SARS-CoV-2 spike protein—the same protein that many vaccines use to trigger a protective immune response—might cause collateral damage, notes Harald Prüss, a neurologist at the German Center for Neurodegenerative Diseases (DZNE) and the Charité University Hospital in Berlin. In 2020, while hunting for antibody therapies for COVID-19, he and his colleagues discovered that of 18 antibodies they identified with potent effects against SARS-CoV-2, four also targeted healthy tissues in mice—a sign they could trigger autoimmune problems.

> **We shouldn't be averse to adverse events.**
>
> WILLIAM MURPHY | UNIVERSITY OF CALIFORNIA, DAVIS

Early clinical data point in a similar direction. Over the past year, research groups have detected unusually high levels of autoantibodies, which can attack the body's own cells and tissues, in people after a SARS-CoV-2 infection. In *Nature* in May 2021, immunologists Aaron Ring and Akiko Iwasaki at Yale School of Medicine and their colleagues reported finding autoantibodies in acute COVID-19 patients that target the immune system and brain; they are now investigating how long the autoantibodies persist and whether they can damage tissues. This month, Cedars-Sinai Medical Center cardiologist Susan Cheng and protein chemist Justyna Fert-Bober wrote in the *Journal of Translational Medicine* that autoantibodies could last up to 6 months after infection, although the researchers did not correlate autoantibodies' persistence with ongoing symptoms.

In part to understand whether these autoantibodies harm people, DZNE is checking the cerebrospinal fluid of Long Covid patients for antibodies that react to mouse brain tissue—if they do react, they might attack human neural tissues as well. In a paper Prüss and his colleagues are about to submit, they describe finding autoantibodies that attack mouse neurons and other brain cells in at least one-third of those patients. A group at Northwestern University, meanwhile, reported in an August 2021 preprint that in people with neurological complications after COVID-19, a subset of T cells is persistently activated as would happen with an ongoing SARS-CoV-2 infection, suggesting some sort of aberrant immune response or lingering virus.

Some researchers are looking at another possible culprit for Long Covid: tiny clots in the blood. In an acute SARS-CoV-2 infection, small clots can form that can damage cells that line blood vessels. Resia Pretorius, a physiologist at Stellenbosch University in South Africa, and her colleagues published preliminary evidence in August in *Cardiovascular Diabetology* that microscopic clots can linger after an infection clears. They might interfere with oxygen delivery, which could explain some Long Covid symptoms such as brain fog. Pretorius is now teaming up with colleagues to develop diagnostics for this microclotting and study ways to treat it in Long Covid.

Pretorius says she and her colleagues have also seen patients—fewer than 20, she estimates—with chronic problems following vaccination. She says these include Long Covid–like symptoms such as brain fog as well as other clotting concerns such as deep vein thrombosis. The cause of the very ~~rare~~ but severe clotting after the AstraZeneca and Johnson & Johnson vaccines remains unknown, but Pretorius suspects all COVID-19 vaccines might also sometimes trigger subtler clotting issues. She says she has preliminary evidence that vaccination can lead to microclots, although in most cases they go unnoticed and quickly disappear—an effect she and a colleague saw in their own blood and that of eight other healthy volunteers, which they sampled after their vaccinations.

A touchy topic

Long Covid research also brought the Dressens to Nath. In January 2021, Brian Dressen sought help from Nath, who had been studying Long Covid. Nath responded quickly and asked Brianne Dressen to join an ongoing study he leads on the natural history of inflammatory diseases of the nervous system.

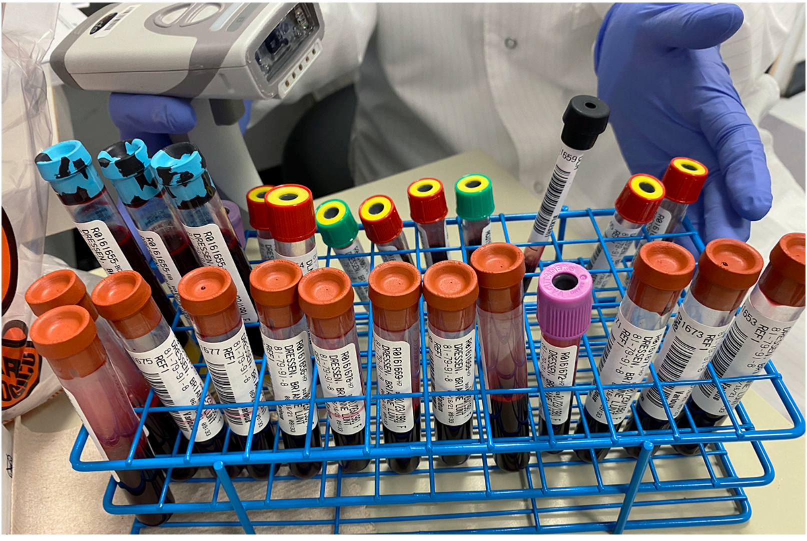
Dozens more patients describing postvaccine complications found their way to Nath and Farinaz Safavi, an NINDS neurologist. "I promise you we will report your issue and other cases we are reviewing now," Safavi wrote to Danice Hertz in March 2021. Hertz, a retired gastroenterologist who lives in Southern California, had developed debilitating side effects after one dose of the Pfizer vaccine. Senior officials at the U.S. Food and Drug Administration (FDA), the Centers for Disease Control and Prevention, and Pfizer, among others, were copied on the email, which Hertz shared with *Science*.

Over the first half of 2021, Nath and Safavi invited Brianne Dressen and others to NIH for testing and, in some cases, short-term treatment, for example with high-dose steroids or intravenous immunoglobulin (IVIG), which can quell or modulate immune responses. The patients spent at least several days undergoing neurological, cardiac, and other tests, including lumbar punctures and skin biopsies.

The NIH researchers were "trying to help people," says a health care worker whose symptoms began after the Pfizer vaccine, one of four people in the study who spoke to *Science*. Nath says 34 people were enrolled on the protocol, 14 of whom spent time at NIH; the other 20 shipped their blood samples and in some cases cerebrospinal fluid.

As time passed, however, the patients say the NIH scientists pulled back. A September visit Brianne Dressen had scheduled for additional neurologic testing was converted to a telemedicine appointment. In December, Nath asked her to stop sending patients his way. "It is best for such patients to receive care from their local physicians," he wrote to her.

so that the information remains scattered and unorganized and unpublished and speculative



Tubes of blood drawn from Brianne Dressen, who suffered complications after a coronavirus vaccine, are part of a National Institutes of Health study. BRI DESSEN

For patients, the silence from NIH was distressing, especially as they struggled to find care elsewhere. The scientists “took the data and left us hanging,” says a person who traveled to NIH in the spring of 2021. “I have no treatment, I have no idea what’s happening to my body.” Physicians, several patients said, had nothing to offer and sometimes even declared the symptoms imagined.

Nath told *Science* NIH facilities are not equipped to treat large numbers of patients long-term. Says the health care worker of the effort: “It’s too much for two people at the NIH to do.”

The NIH data, which documented the patient cases, haven’t been reported yet. Two top medical journals declined to publish a case series of about 30 people, which Nath first submitted in March 2021. Nath says he understands the rejection. The data weren’t “cut and dried; it was observational studies.” This month, the scientists submitted a case series of 23 people to a third publication, and Nath says his group has submitted an amendment to a Long Covid protocol to include patients with postvaccine side effects.

Science contacted regulators and vaccinemakers about any information they’d gleaned on these side effects. A Pfizer spokesperson wrote, “We can confirm it’s something we’re monitoring.” Moderna, AstraZeneca, and Johnson & Johnson all said they take side effects seriously and share reports they receive with regulators. An FDA spokesperson said the agency “continues to maintain a strong focus on monitoring the safety of the COVID-19 vaccines,” while the European Medicines Agency notes it “is taking steps to use real-world data from clinical practice to monitor the safety and effectiveness of COVID-19 treatments and vaccines.” All of that is political/regulatory BS and nonsense, meaningless banter

Other researchers note the scientific community is uneasy about studying such effects. “Everyone is tiptoeing around it,” Pretorius says. “I’ve talked to a lot of clinicians and researchers at various universities, and they don’t want to touch it.”

Still, her group and others are pushing ahead. Prüss has detected autoantibodies in some patients with postvaccine symptoms, but not in others. Several groups are studying whether a patient’s postvaccination symptoms are due to autoantibodies to the angiotensin-converting enzyme 2 (ACE2) receptor, which the spike protein targets. Cheng and her colleagues are planning a case series that includes sophisticated imaging and diagnostic tests from a mix of Long Covid patients and those with postvaccine side effects. And Pretorius and her colleague Chantelle Venter are hoping to recruit at least 50 people to study clotting patterns before and after vaccination.

At Yale, Iwasaki is planning to collaborate with Nath and look at any potential link between Long Covid and postvaccine effects, she says. She has spoken with affected patients and her lab intends to collect samples from them, potentially of blood or saliva. Murphy says more work is needed in animal models to trace the body’s response to vaccination. “We need to look at this in controlled situations,” he says.

Prüss is hunting for autoantibodies following COVID-19 vaccination in mice. And he continues to care for patients, both postvaccine and postinfection. His clinic hopes to soon start a clinical trial of a treatment that removes most antibodies from a patient’s blood. However, even if it works well, the procedure is expensive and might not be widely available.

Patients in the middle

People with lasting health problems after vaccination welcome any attention to their plight. “You have this ugly stain on you, and you’re marginalized and abandoned,” Brianne Dressen says. At first, “I was really afraid of causing vaccine hesitancy,” she adds.

Other patients describe vaccine opponents asserting that they deserve to die because they were foolish enough to get vaccinated. Vaccine supporters tell them that by speaking out they risk harming others, who may refuse to get vaccinated and then die from COVID-19. “We’re stuck in this horrible in-between,” says the patient who traveled to NIH last spring.

Brianne Dressen, for her part, went public. She says she was frustrated when it appeared that regulators, including FDA, were not promptly investigating the apparent side effects. She took part in a June 2021 press conference about vaccine side effects held by Senator Ron Johnson (R–WI), who has been outspoken against COVID-19 vaccinations. “Talking to politicians was not our plan A … not even close,” Brianne Dressen says. “It was more like plan J.”

Jana Ruhrländer, too, feels caught. After a single dose of the Moderna vaccine, the microbiology graduate student in Kassel, Germany, developed symptoms including the sensation of internal electric shocks Brianne Dressen experienced, partial facial paralysis, muscle weakness that left her terrified she was having seizures or a stroke, intense thirst, and wild swings in her heart rate and blood pressure. Doctors dismissed her, saying their tests found nothing wrong. She played detective, realizing her symptoms overlapped with a hormonal system called the renin-angiotensin-aldosterone system that regulates blood pressure and fluid balance—and in which ACE2 plays a key role. She has recently connected with doctors who are trying to learn whether autoantibodies targeting that system might be causing her symptoms.

Despite her experience, “I still think the vaccines are great,” Ruhrländer says. And the mRNA technology “has so much potential.” But these side effects, which for her have improved somewhat but haven’t disappeared, should be acknowledged and understood, she says. “We have to speak openly about it.”

Some of the patients who spoke with *Science* say medications that tamp down the immune system have offered at least a measure of relief. Nath noticed the same phenomenon. He hopes results from an NIH clinical trial testing IVIG and intravenous steroids in Long Covid patients “will be applicable to the vaccine-related complications.” None of the patients with whom *Science* spoke has fully recovered.

Researchers exploring postvaccine side effects all emphasize that the risk of complications from SARS-CoV-2 infection far outweighs that of any vaccine side effect. “You see 10, 100, 1000 times less risk from the vaccine,” Prüss says. But understanding the cause of postvaccine symptoms—and whether early treatment can help prevent long-term problems—could be crucial for designing even safer and more effective vaccines, Murphy says, as well as potentially providing clues to the biology of Long Covid.

Cheng has heard from dozens of people who describe chronic postvaccine problems, and she finds the overlap between their symptoms and those of Long Covid compelling. Now, she wants to move deliberately and scientifically in a search for answers. “We’ve got to retain rigor,” she says. “There’s just this complete dearth of data.”

Update, 21 January, 12:45 p.m.: This story has been updated with comments from the U.S. Food and Drug Administration and the European Medicines Agency.

---

doi: 10.1126/science.ada0394

RELEVANT TAGS:

HEALTH SCIENTIFIC COMMUNITY CORONAVIRUS

ABOUT THE AUTHOR

Jennifer Couzin-Frankel
Author

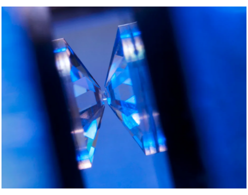
Staff Writer

Gretchen Vogel
Author

Gretchen Vogel is a contributing correspondent for *Science* magazine based in Berlin, Germany.

MORE FROM NEWS

14 MAR 2022
Ukrainian researchers flee trauma and terror of war
BY RICHARD STONE



14 MAR 2022
Preprint server removes ‘inflammatory’ papers in superconductor controversy
BY ROBERT F. SERVICE

10 MAR 2022
A network of young scientists and doctors aims to rebuild Venezuela’s devastated publi…
BY RICHARD STONE

VIEW MORE

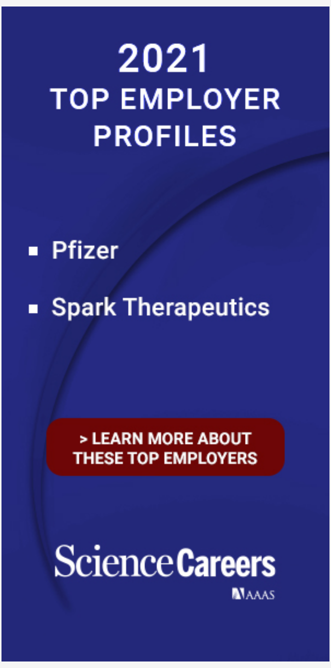
Got a tip for Science's news department? CONNECT

Subscribe to News from Science

Don’t yet have access? Subscribe to News from *Science* for full access to breaking news and analysis on research and science policy.

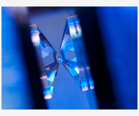
SUBSCRIBE

ADVERTISEMENT

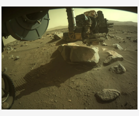


SCIENCEINSIDER

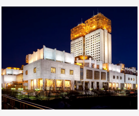
14 MAR 2022 | BY RICHARD STONE
Ukrainian researchers flee trauma and terror of war



14 MAR 2022 | BY ROBERT F. SERVICE
Preprint server removes ‘inflammatory’ papers in superconductor controversy



10 MAR 2022 | BY PAUL VOOSEN
Mars rover wraps survey of Jezero crater’s surprising volcanic floor



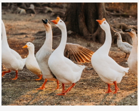
10 MAR 2022 | BY JEFFREY BRAINARD
Few journals heed calls to boycott Russian papers

VIEW MORE

ADVERTISEMENT

BIOSYSTEMS
Acro
High quality antigens
Omicron subvariant BA.2
are all in stock!
Spike trimer
S RBD
S1
NTD
Nucleocapsid protein
Order Now

SIFTER



8 MAR 2022 | BY TESS JOOSSE

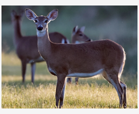
Geese may have been the first domesticated birds

4 MAR 2022 | BY TESS JOOSSE

An archaeologist may have cracked how the Stonehenge calendar worked

3 MAR 2022 | BY TESS JOOSSE

Tyrannosaurus rex should be split into three species, controversial study suggests



2 MAR 2022 | BY GRAYCEN WHEELER

Coronavirus may be evolving in deer

VIEW MORE ›

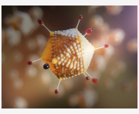
RECOMMENDED

IN DEPTH | JANUARY 2022

Vaccines may cause rare, Long Covid–like symptoms

18 AUG 2021 | BY JON COHEN

COVID-19 vaccines may trigger superimmunity in people who had SARS long ago



23 NOV 2020 | BY JON COHEN, JOHN TRAVIS

Another COVID-19 vaccine success? Candidate may prevent further coronavirus transmission, too

23 APR 2020 | BY JON COHEN

COVID-19 vaccine protects monkeys from new coronavirus, Chinese biotech reports

RELATED JOBS

Vaccines SERM Head
GSK
Rockville, MD

Postdoctoral Associate- Neuroscience/Genetics
Baylor College of Medicine
Houston, Texas

Postdoctoral Associate-Epigenetics and Nuclear Organization
Baylor College of Medicine
Houston, Texas

MORE JOBS ▶

ADVERTISEMENT

Nikon
AX / AX R
Experience Nikon's Latest Breakthrough Confocal Technology
LEARN MORE

FOLLOW US

NEWS
All News
ScienceInsider
News Features
Subscribe to News from Science
News from Science FAQ
About News from Science

CAREERS
Careers Articles
Find Jobs
Employer Profiles

COMMENTARY
Opinion
Analysis
Blogs

JOURNALS
Science
Science Advances
Science Immunology
Science Robotics
Science Signaling
Science Translational Medicine
Science Partner Journals

AUTHORS & REVIEWERS
Information for Authors
Information for Reviewers

LIBRARIANS
Manage Your Institutional Subscription
Library Admin Portal
Request a Quote
Librarian FAQs

ADVERTISERS
Advertising Kits
Custom Publishing Info
Post a Job

RELATED SITES
AAAS.org
AAAS Communities
EurekAlert!
Science in the Classroom

ABOUT US
Leadership
Work at AAAS
Prizes and Awards

HELP
FAQs
Access and Subscriptions
Order a Single Issue
Reprints and Permissions
Contact Us

© 2022 American Association for the Advancement of Science. All rights reserved. AAAS is a partner of HINARI, AGORA, OARE, CHORUS, CLOCKSS, CrossRef and COUNTER.