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THE CORONAVIRUS CZAR

The COVID-19 pandemic has made German virologist Christian Drosten an unlikely cult figure

By Kai Kupferschmidt, in Berlin



Christian Drosten admits the pandemic surprised him, despite having worked on coronaviruses for 17 years.

On a recent Monday morning, Christian Drosten said goodbye to his wife and 2-year-old son in front of his apartment block and got on his bicycle for his daily commute to Charité University Hospital here.

It looked like a scene from normal daily life. But of course it wasn't. His wife was going for a walk with their child instead of bringing him to the day care center, which was closed. The Berlin streets Drosten traversed were eerily quiet, most shops were closed, and some people on the sidewalks wore masks. Charité's Institute of Virology, which Drosten heads, was studying exotic viruses, as always,

but now one of those pathogens was killing patients in a hospital a few blocks away.

And instead of teaching virology to a few hundred students, Drosten now addresses hundreds of thousands of anxious Germans. Twice a week around 10 a.m., he sets a blue microphone on his desk, puts on headphones, and waits for a science journalist from German radio station NDR Info to call him. For the next 40 minutes, he answers questions about vaccines, respiratory droplets, school closures, or masks. The podcast, simply titled *Coronavirus Update*, has made Drosten the face, or rather the voice, of the pandemic in Germany. More than 1 million people regularly download what has become the country's most popular podcast.

Drosten is one of the world's foremost experts on coronaviruses; his career has closely tracked their emergence as a global threat. Now, he is also a popular—if nerdy—hero. In one widely shared meme, his face, with a pair of horn-rimmed glasses photoshopped on it, sits next to three movie stills of actor Jeff Goldblum, to whom he bears a passing resemblance. “He has fought dinosaurs, body snatchers, and aliens,” the caption reads, “so I’ll trust him with this virus too.” Drosten’s cult status reminds Holger Wormer, a journalism professor at the Technical University of Dortmund, of Stephen Hawking’s: “Many people may not understand everything he says. But it is comforting to listen to someone explaining what is going on.”

His calm, considered communication has earned Drosten widespread appreciation. “It’s a stroke of luck that we have someone here in Germany who is recognized worldwide as an expert on coronaviruses and who is willing and able to communicate so well,” says Volker Stollorz, head of the German Science Media Center. On 20 April, the German Research Foundation announced it was awarding Drosten a one-off prize for “outstanding science communication during the COVID-19 pandemic.”

Drosten also explains coronaviruses to politicians. He has advised German Chancellor Angela Merkel—they chatted by phone for about an hour recently, he says—and Minister of Health Jens Spahn. He has been called Germany’s “coronavirus-explainer-in-chief” and “the coronavirus pope,” the German equivalent of a “coronavirus czar.”

Yet colleagues describe Drosten, 47, as an unlikely character for his new role. “He is not someone who seeks out this kind of attention,” says Isabella Eckerle, a former lab member who now runs a laboratory for emerging viral diseases at the University of Geneva. Drosten says he wouldn’t have stepped into the limelight if SARS-CoV-2 weren’t exactly the kind of

virus he has spent most of his life studying. “If this were influenza, for instance, I would not be doing this,” he says.

DROSTEN’S CORONAVIRUS CAREER effectively began on Saturday, 15 March 2003, when a 32-year-old doctor from Singapore named Leong Hoe Nam was taken off a plane in Frankfurt, Germany, and taken to the city’s university clinic. Leong had treated patients in Singapore before attending an infectious diseases course in New York City, and had developed symptoms consistent with an alarming new respiratory disease that was rapidly

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spreading in Asia. That same day, the World Health Organization (WHO) had christened the new disease “severe acute respiratory syndrome,” or SARS.

At the time, Drosten was building up a lab for molecular diagnostics at the Bernhard Nocht Institute for Tropical Medicine in Hamburg, Germany. The Frankfurt virologists sent Leong’s blood and other samples to Drosten, hoping he could help identify what was believed to be a new virus. But tests for everything from adenoviruses to paramyxoviruses came back negative.

About 1 week later, however, when Drosten was in Frankfurt to defend his doctoral thesis, the same virologists told him they had managed to grow the virus in a petri dish. Drosten realized this would allow him to use a new catch-all method he had developed for identifying unknown viruses, which amplified viral genetic material so it could be sequenced and checked against online databases. Drosten picked up a sample, then drove the 5 hours back to Hamburg in his old Opel and went straight to his lab. After a few days with little sleep, he had a small part of the new virus’ genome. The closest

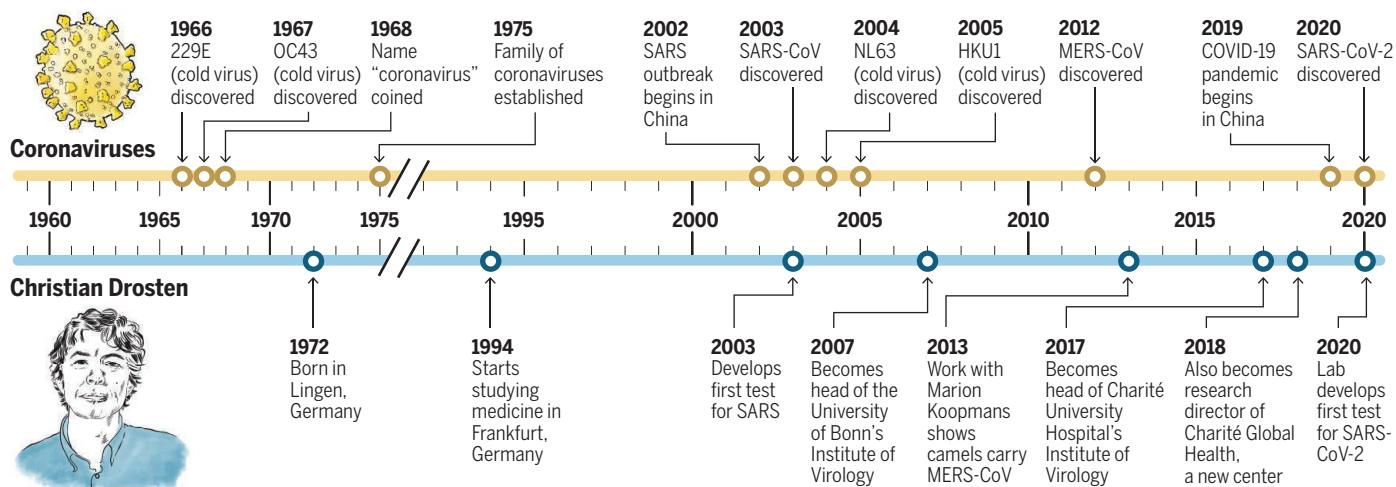
match was a cattle coronavirus that doesn’t infect people. “My first thought was, maybe it is some kind of contamination from the FCS,” the fetal calf serum used to grow cells in the lab, Drosten recalls.

But he and his colleague Stephan

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Microbes and man

Christian Drosten's career paralleled the emergence of coronaviruses as a serious human threat. He worked on severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) and in January, his lab developed the first test for SARS-CoV-2, the new pandemic virus.



Günther quickly realized they were seeing a deadly new member of the family. “At the time, medical students learned hardly anything about coronaviruses,” Drosten says. The only two known to cause disease in humans, named OC43 and 229E, accounted for a small percentage of human colds every winter. This new virus was a very different beast. SARS killed 10% of the almost 8000 people it infected in nearly 30 countries before it was contained.

Researchers at the U.S. Centers for Disease Control and Prevention and the University of Hong Kong realized the culprit was a coronavirus around the same time. But Drosten was the first to develop a diagnostic test, and he distributed the protocol freely on the internet. It earned him international recognition as well as the Federal Cross of Merit, an important German award. (Leong survived his bout with SARS and is now treating COVID-19 patients himself. He says he has not met Drosten, but reads every paper coming from his lab. “Truly, he is an incredible scientist, with out-of-the-box thinking,” Leong wrote in an email.)

DROSTEN GREW UP on a pig farm in northern Germany. He studied medicine in Frankfurt, the first person in his family to go to university, and rose quickly in German academia. After his stint in Hamburg, he became a full professor at the University of Bonn and, at 35, head of the Institute of Virology. His research interests were ideal preparation for COVID-19. He established a system for probing the function of the SARS virus' genes and started to study viral evolution, looking for close relatives of human viruses in animals. In one such study, his team discovered that mumps, which like measles is

caused by a paramyxovirus, had jumped to humans from bats. They also showed that Nipah, another bat-borne virus, originated in Africa, even though it was discovered in Malaysia after hundreds of pig farmers there developed encephalitis in 1999.

Scientists discovered two new coronaviruses in the years after the SARS outbreak, both of which caused the common cold. Then in 2012, researchers isolated a new coronavirus that spelled greater danger. It came from a 60-year-old man in Saudi Arabia who had developed pneumonia. Intrigued, Drosten geared his research to the new agent, which was soon called the Middle East respiratory syndrome (MERS) virus. In 2013, he reported on a wealthy 73-year-old patient from Abu Dhabi, United Arab Emirates, who was treated for MERS in Germany and died. Relatives said the patient had cared for a sick racing camel before falling ill—the first sign that camels might be involved.

Saudi Arabia, which had the most MERS cases and a multimillion-dollar camel racing industry, initially scoffed at the link. “We don't think camels are involved,” then-Deputy Minister of Health Ziad Memish said. But work from Drosten's group and others soon confirmed the suspicion. Memish and Drosten teamed up to study the new disease, and Drosten's Bonn lab became a leading MERS hub. It developed a test to detect the virus' RNA and then an antibody assay that helped show the virus had likely been infecting people in the region for decades.

The research yielded some unexpected insights. While looking for coronaviruses in camels, the scientists found pathogens closely related to 229E, one of the common cold coronaviruses, suggesting that virus,

too, originated in camels. It was a warning sign, Drosten said at the time, that MERS could follow the same course as SARS, which had originated in bats, and evolve to become a true human disease. Animal coronaviruses, it seemed, posed a particular threat of sparking a pandemic.

WHEN ANOTHER severe respiratory syndrome emerged this year, Drosten—who moved to the prestigious Charité University Hospital in 2017—was prepared. After seeing the first rumors about a coronavirus in China online, Victor Corman, who leads the lab's virus diagnostics group, began to scour existing sequences of SARS-related coronaviruses, isolated from bats, for regions that were the same across different viruses. He was trying to guess what parts of a new SARS-like coronavirus might look like, in order to create a test. Based on those sequences, he designed and ordered 20 pairs of so-called primers, little snippets of DNA, that pair with a pathogen's genome, so that it can be amplified and detected.

When Chinese researchers finally published the genome of the new virus from Wuhan on 10 January, Corman used the primers that best matched the viral sequence and prepared the diagnostic test almost immediately. WHO posted Corman's protocol on its website on 13 January, allowing countries around the world to produce a test themselves and detect imported cases of the new virus. Drosten predicted the test would also help scientists understand whether the virus was able to spread from human to human.

It was.

Three and a half months later, SARS-CoV-2, as it is now known, has traveled to all corners of the world, infecting millions of people and

killing well over 200,000. It has forced countries from Austria to Zambia to shut down their economies and societies, causing immense suffering and igniting heated debates about the right way to deal with the threat.

Drosten concedes it has surprised him, despite his 17 years of work on coronaviruses and his knowledge of the threat they pose. “I didn’t think that SARS would come back like this,” he says—as a virus that is both deadly and much more transmissible. It is adept at infecting cells of the upper respiratory tract, from which a cough can expel it, and unlike SARS—but like the flu—it can spread before symptoms emerge. “That’s pretty astonishing,” Drosten says.

Drosten says a key reason for SARS-CoV-2’s success may be a tiny part of the “spike,” the protein that sits on the virus’ surface and makes it look like a crown when seen through a microscope. The spike protein attaches to a receptor on human cells called angiotensin-converting enzyme 2. Before the virus can enter the cell, however, a part of the protein has to be cleaved. The SARS-CoV-2 spike protein cleaves more readily than equivalent proteins in other coronaviruses, because it has evolved something called a polybasic cleavage site, which Drosten likens to the perforations on a notepad that make it easier to rip off a page. That feature may explain the virus’ rapid spread from cell to cell, he says.

Drosten started to warn of the new virus’ potential in TV interviews in January, but quickly grew exasperated. After long interviews, journalists often used one short quote that failed to convey the immense threat, he says. “I actually called up some of them afterwards and told them: ‘You are missing the boat on this.’” So when a producer from NDR asked Drosten in February whether he was willing to answer a few questions every day, his answer was swift: “Traveling at the moment, like the idea, we can start Monday.” (Drosten recently reduced the frequency to twice a week.)

The show’s conversation is easygoing, and Drosten occasionally offers advice. In March, he told listeners to avoid beer from the tap, because glasses might not be cleaned thoroughly. “When I go to a bar, I always order beer in a bottle, for many years now,” he said. If Drosten is himself emotionally shaken by the pandemic and the way it is changing the world, he doesn’t show it.

Drosten also seems unfazed by his newfound fame, but he gets annoyed when the focus drifts away from the science.

He chided political journalists who asked whether important soccer matches and Germany’s sacred Oktoberfest would need to be canceled, saying that was not his expertise. He bristles at stories describing his “sensual lips” and tousled hair. “I talk about science,” he says. “I don’t want to read about my haircut.” Wormer says Drosten is doing a great job talking about the science, but is a tad naïve about what interests the media. “For some people going to the stadium is important and you just have to accept that,” he says. For a public figure, a bit of mockery comes with the territory as well, he says.

Drosten has balked at suggestions that he has become a political player. He seemed genuinely angry after a spate of stories suggesting virologists had taken the reins of German government. “If that doesn’t change, we



Christian Drosten (center) at a March press conference with German Minister of Health Jens Spahn (right) and Petra Gastmeier, director of the Charité Institute of Hygiene and Environmental Medicine (left).

are reaching the point where science has to start an orderly retreat,” he said on the podcast. His role as a political adviser is small, he told *Science*. “It’s not like I’m in and out of ministries all day.” When a German newspaper ran his photo under the headline “Is this our new chancellor?” he bristled at the idea.

DROSTEN FEELS most at home concentrating on his research. Virologist Marion Koopmans of Erasmus Medical Center in the Netherlands recalls seeing him during a technical planning meeting of a large research consortium, huddled at the back of the room with two or three others. “Probably writing a *Nature* paper,” she says. “He doesn’t like the blah blah blah.”

But Drosten wants his research to save lives. Large cardboard boxes in his office hold supplies of two medicines waiting to be tried in the clinic. One is camostat mesylate, a pancreatitis drug approved in Japan that Drosten and others found can prevent both SARS-CoV and SARS-CoV-2 from entering cells. The other drug is niclosamide, used to

treat tapeworms and other parasites. In a paper posted on the preprint server bioRxiv this month, Drosten’s colleague Marcel Müller showed that SARS-CoV-2 interferes with the cellular recycling process called autophagy. It’s unclear how exactly that benefits the virus, but niclosamide counters the interference. Treatment with the compound reduced SARS-CoV-2’s growth in cell culture by 70%, the authors write. Drosten hopes to start to enroll patients soon in a trial to test a combination of the two drugs.

For the moment, Drosten is learning what he can from sequencing virus samples and probing the pathogen in the biosafety level 3 lab in the institute’s basement. He is also interested in how SARS-CoV-2 made its way from animals to humans. He’s fascinated by the role livestock appear to play as a bridge

between bats, which are coronaviruses’ natural hosts, and humans. 229E and MERS came from camels, OC43 from cattle. SARS infected civets and also raccoon dogs, raised by the millions in China’s fur industry. SARS-CoV-2’s origin is unclear, but Drosten wonders whether raccoon dogs could be an intermediate host. “I would love to take samples from 20 of these farms,” he says.

FOUR MONTHS after the emergence of the pandemic, Germany is widely seen as a success story in Europe. The country tests widely for the virus—thanks in part to that first assay, developed in

Drosten’s lab—and has managed to keep case numbers low. Now, as in many countries, pressure is building to reopen shopping malls, bars, and restaurants. Drosten is worried some German states are moving too fast, which could lead to an explosive resurgence of the virus.

That concern has led him to depart from his science-only strategy. “In this situation, for once, I have to express my opinion a little bit here in this podcast,” he said on 22 April. Discussing press reports of shopping malls full of people, he said, “It’s sad to see that we may be in the process here in Germany of completely gambling away the advantage we have had.”

With COVID-19 drugs and vaccines unavailable, such words may be the most powerful tool to curb the spread of the virus. And whether or not he likes it, Drosten’s podcast has given him real influence, says Marcel Fratzscher, head of DIW Berlin, an economic research institute. “At this point, if Drosten says it is too early, that carries as much weight as Merkel saying it.” ■

Science

The coronavirus czar

Kai Kupferschmidt

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