

The two effects—increased transmissibility and immune evasion—are hard to disentangle, but “I would argue the Delta variant has been driven by its transmissibility, not its ability to escape immunity,” says Jeremy Farrar, head of the Wellcome Trust. “If Alpha really is approximately 50% more transmissible than the wild type strain, and Delta is 50% more transmissible again than Alpha, we’re talking about a virus that’s more than twice as transmissible as the initial strain,” adds Aris Katzourakis, an evolutionary virologist at the University of Oxford. That would mean countries and populations with low vaccination rates are likely to see big new outbreaks. Indeed, if the faster spread “is entirely down to the fundamentals of the virus, that’s catastrophic news for the rest of the world,” Kucharski says.

On top of this, Delta may be more likely to put unvaccinated people in the hospital than Alpha. Early data from the United Kingdom suggest the risk of hospitalization may be twice as high. Together these characteristics could cause huge problems in Africa, Swaminathan says. “There isn’t going to be enough oxygen there, there aren’t going to be enough hospital beds. And we already know that outcomes for people that are hospitalized in Africa are worse than in other countries,” she says. “So this could really lead to higher mortality, even among younger people.”

**SCIENTISTS ARE** just beginning to probe what makes Delta so dangerous. They’re concentrating on a suite of nine mutations in the gene encoding spike, the protein that studs the virus’ surface and allows it to invade human cells. One important mutation, called P681R, changes an amino acid at a spot directly beside the furin cleavage site, where a human enzyme cuts the protein, a key step enabling the virus to invade human cells. In the Alpha variant, a mutation at that site made cleavage more efficient; a preprint published in late May showed Delta’s different change makes furin cleavage even easier. The researchers suggest this could make the virus more transmissible.

Japanese researchers who made pseudoviruses carrying the mutation have not found it to confer increased infectivity in the lab, however, and in India, other coronavirus variants that include the same mutation have been far less successful than Delta, says evolutionary virologist Andrew Rambaut of the University of Edinburgh. “So it must be an interaction with something else in the genome.”

Other mutations in Delta could help it thwart immunity. Some alter the spike’s N-

terminal domain (NTD), which protrudes from the protein’s surface. A recent *Cell* paper identified one spot in the NTD as a “supersite,” unflinchingly targeted by “ultra-potent” neutralizing antibodies from recovered patients. Delta’s unique mutations delete the amino acids at positions 156 and 157 in the supersite and changes the 158th amino acid from arginine to glycine; the latter eliminates a direct contact point for antibody binding, says David Ostrov, a structural biologist at the University of Florida. “We think the 157/158 mutation is one of the hallmark mutations in Delta that has given it this more immune-evasion phenotype,” concurs Trevor Bedford, a computational biologist at the Fred Hutchinson Cancer Research Center.

Another mutation in the NTD supersite may also help rebuff antibodies. And scientists should start to examine the

role of changes in other Delta variant proteins, says Nevan Krogan, a molecular biologist at the University of California, San Francisco. “There is so much we don’t know about these variants on every level. We are so in the dark.” Delta has several mutations in the nucleocapsid protein, for example, which has many jobs, “like a Swiss Army Knife protein,” says virologist David Bauer of the Francis

Crick Institute. The experiments to bring clarity will take months, however.

**IN THE MEANTIME**, scientists agree urgent action is needed to stop the spread of the new variant. “Worries about Delta should galvanize us to really ramp up vaccination efforts and surge vaccines to places where Delta is ticking up,” says virologist Angela Rasmussen of the University of Saskatchewan. U.S. President Joe Biden on 18 June urged young people to get fully vaccinated to protect themselves from Delta. Countries with little access to vaccine need to resort again to interventions such as physical distancing and masks, Rasmussen says.

The goal is not just to save lives immediately, but also to give the virus less room to evolve further. Delta’s success has shown scientists aren’t able to identify dangerous new variants in time to stop them spreading, says Emma Hodcroft, a virologist at the University of Basel, despite an unprecedented global effort to track its evolution in real time (*Science*, 21 May, p. 773). And it would be dangerous to assume that SARS-CoV-2 can’t do much better, Katzourakis says. “Anything that’s happened at least twice in evolution is part of a pattern,” he says. “I would be very unsurprised if we saw equivalent changes over the coming year or two.” ■

**“There is so much we don’t know about these variants on every level.”**

**Nevan Krogan.**  
University of California,  
San Francisco

## COVID-19

# For WHO leader, a ‘feeling that we’re failing’

Tedros Adhanom Ghebreyesus had expected more social responsibility in the face of a global crisis

By **Jon Cohen**, in Geneva

**F**ew have spoken out as forcefully against the global disparity in COVID-19 vaccine distribution as Tedros Adhanom Ghebreyesus, director-general of the World Health Organization (WHO). Tedros, as he prefers to be called, has labeled the inequity “vaccine apartheid” and a “catastrophic moral failure” that has led to a “two-track pandemic.” A global procurement scheme by WHO and other parties to supply vaccines to poorer countries, the COVID-19 Vaccines Global Access (COVAX) Facility, has not had much impact so far.

Tedros served as Ethiopia’s minister of health from 2005 to 2012—and then as minister of foreign affairs—before taking the helm at WHO in 2017. *Science* spoke to him on 12 June, hours before he addressed a summit of G7 nations underway in the United Kingdom that resulted in a pledge to donate 870 million additional vaccine doses to COVAX by the end of 2022. The interview has been edited for brevity and clarity. A longer version is online at <https://scim.ag/TedrosQA>.

**Q: The conversation about inequity in COVID-19 vaccination started before there was anything that worked. Were you trying to get ahead of it, by doing the advocacy early?**

**A:** When I was Ethiopia’s minister of health, I saw two global failures. One is HIV. Those who needed [antiretroviral treatment] in low-income countries didn’t get it until 10 years after the discovery. That’s very, very disappointing. Not only that, there was an H1N1 influenza pandemic in 2009. Vaccines were developed, but they didn’t reach low-income countries, especially in Africa. These are the

*Science’s* COVID-19 reporting is supported by the Heising-Simons Foundation.



Tedros Adhanom Ghebreyesus waited to get vaccinated in Geneva until it would have been his turn in Africa.

things I remembered when we were confronted with COVID. And from the start, we were saying: We shouldn't repeat the same mistake. It's unprecedented actually to have eight vaccines [authorized] in just a year. But where we're failing is the vaccine equity for distribution.

**Q: You've had a voice with some anger and frustration, mixed with advocacy. Why do you think so few other world leaders are willing to be blunt?**

**A:** I don't think I know the answer.

**Q: Has anyone become very ill or even died from COVID-19 who was close to you?**

**A:** Yes. The closest is the stepmother of my wife [in Ethiopia]. And this is before vaccination started, and even now she probably wouldn't have had access. She died. And there are others, a bit more at a distance.

**Q: Operation Warp Speed wasn't designed to vaccinate the world. It was designed to deliver vaccines for the American people and protect the country. What if there had been a different administration that had a more global vision?**

**A:** The problem of just focusing on one country is we will not use the full potential of the whole world. I would turn to the G7 first, and [then] I would take G20, which controls 80% of the [global economy]. They can influence the whole world. What we have been saying from the start—solidarity, everybody contributes to the basket. That [conversation] should happen, and that's what we have been

pushing for. This is not just the responsibility of the U.S., but of all the major countries that have capacity for financial [help] or even production capacity.

**Q: What do you think of the Biden administration?**

**A:** This person has changed everything, turned it upside down. It's day and night what happened. From day one, when Biden reversed the decision [by former President Donald Trump to defund] the WHO, he has shown his commitment. And the U.S. has made the largest contribution to donating vaccine doses. We appreciate the help and hope other leaders will follow suit and make a significant contribution. We cannot ask the U.S. to do it alone.

**Q: You've been talking recently about the idea of a pandemic treaty. Would it include waivers of intellectual property (IP) for vaccines and other medicines?**

**A:** The IP waiver is one option, and it is key, especially in emergency conditions. Even TRIPS [a World Trade Organization agreement] has a provision to use an IP waiver in emergency conditions. In unprecedented situations, you need to take unprecedented measures. If we're not going to use it now, then when do we use it? Why do we even have it in the first place? I'm a strong supporter of IP. I'm very grateful to the private sector. And I don't believe in just taking IP away from them. I actually proposed giving incentives, some compensations [in exchange for an IP waiver]. At the same time, the companies also have a social responsibility. This

is about the whole world. Who would like the world to be hostage of a virus? Companies can make profit on 99% of their medicines. This is 1% of things.

**Q: You tried to launch an IP sharing program called the COVID-19 Technology Access Pool. Are you surprised that no vaccine companies participated?**

**A:** It's a mixed feeling: surprised, not surprised. Social responsibility is just something you would expect from a decent human being when the whole world is burning.

**Q: You've been heavily criticized for a report that came from WHO, with its imprimatur, saying the lab origin hypothesis of the pandemic virus is extremely unlikely.**

**A:** That's where there is a misunderstanding. The group came from different institutions and different countries, and they're independent. There were only two WHO staff who joined them. They came up with their study. At the end of the day, we said: "OK, there is progress, but there are these challenges." And we said it openly. We treated China the same way we treat every country.

**Q: When SARS-CoV-2 or whatever is the next pandemic virus shows up, and you're sitting where you're sitting now, what are you going to do differently on day one?**

**A:** If you're asking for a magic bullet, there's no magic bullet. I appointed a very independent, high-level commission to assess the situation so far and make recommendations. They did a very impartial independent assessment, which we are really proud of. We have to calm down and chart a clear road map on how to respond to the next pandemic. But we have to be very, very serious in learning from this and do things that are as ambitious as possible, and that will be impactful.

**Q: What was the date you got your first shot?**

**A:** May 12.

**Q: You're the head of WHO. You could have said in December 2020, "I'm ready."**

**A:** I was protesting. I wanted to wait until Africa and other countries in other regions, low-income countries, started vaccination. I have a background as a health worker and I'm in one of the risk groups. They were beginning to vaccinate health workers and risk groups [in Africa] around that time, so I thought that was my turn.

**Q: How did it feel once you got vaccinated?**

**A:** I'm still feeling that we're failing. I was having my shot with disappointment. ■

# Science

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Jon Cohen

*Science* **372** (6549), 1376-1377.  
DOI: 10.1126/science.372.6549.1376

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