

current finding, we have to take it cautiously.”

Gill worries that the idea that Africa was spared the worst of the pandemic might have led people to take unnecessary risks or contributed to “the lack of urgency” in supplying African nations with vaccines.

“I suppose this could be unique to Lusaka,” he says, “But boy, you’d really have to try

hard to explain why.”

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ARE ‘COVID TOES’ ACTUALLY CAUSED BY THE CORONAVIRUS?

Study adds to evidence suggesting that SARS-CoV-2 doesn’t trigger chilblains in toes.

By Cassandra Willyard

In March 2020, just as COVID-19 cases began to surge in Boston, Massachusetts, Esther Freeman noticed something peculiar – a deluge of people with discoloured toes requesting appointments. Freeman, director of global health dermatology at Massachusetts General Hospital, had seen these kinds of toes before. The itchy red and purple patches are a classic sign of chilblains, a skin condition that typically appears in cold weather. But usually, she would see one or two cases each winter. “Suddenly, I was seeing 15, 20 patients a day,” she says. Intriguingly, the surge – seen by physicians around the globe – seemed to coincide with the rise of the COVID-19 pandemic.

Yet, when physicians examined people with what the media began calling ‘COVID toes’, most didn’t test positive for a coronavirus SARS-CoV-2 infection. Scientists were stumped, and have been looking for answers ever since.

The latest study, published on 25 February¹, is an immunological deep dive, examining 21 people who developed chilblains during the early months of the pandemic in Connecticut. Although the results don’t rule out a direct connection between COVID-19 and chilblains, the authors couldn’t find any immunological evidence of a past SARS-CoV-2 infection in 19 of those people. The report adds to the argument by some researchers that ‘COVID toe’ could have been caused by something unrelated to the virus. For instance, it might have arisen from people in lockdown “being at home, not wearing shoes and socks”, says Jeff Gehlhausen, a dermatologist and immunologist at Yale School of Medicine in New Haven, Connecticut, and first author of the study.

Still, the results raise “some very interesting questions that deserve further study”,



Researchers are debating whether ‘COVID toes’ are triggered by an infection with the coronavirus SARS-CoV-2.

says Freeman, who was not involved in the research. For instance, the study doesn’t exclude the possibility that people exposed to the virus could have fought it off using an innate immune response – a first-line defence that would not prompt the body to produce detectable antibodies and T cells against SARS-CoV-2.

How chilblains arise isn’t entirely clear. “We think of it as a cold-weather-related injury,” says Patrick McCleskey, a dermatologist and researcher at Kaiser Permanente in Oakland, California. Researchers think that the cold probably leads to a restriction in blood flow, causing some cells to die and kicking off an

inflammatory process.

Most of the people in the latest study developed ‘COVID toes’ between April and May 2020, when COVID-19 cases surged in Connecticut. About one-third reported having some symptoms of COVID-19 before developing the condition, and one-third reported that they had been in contact with a person confirmed or suspected to have been infected with SARS-CoV-2.

The researchers used a variety of methods to look for antibodies and T cells specific for the coronavirus – signs of the body having what’s called an adaptive immune response to a pathogen. These people were months past the onset of their chilblains, so their immune systems would have had plenty of time to respond to SARS-CoV-2 if they had been infected. But the team picked up signs of a past infection only in two people, one of whom had initially tested positive.

Unsolved mystery

“The team did a fantastic, really extraordinary job,” Freeman says. But she emphasizes that the study is small – and therefore not necessarily generalizable – and that much larger epidemiological studies^{2,3} have shown a connection between chilblains and SARS-CoV-2.

Dermatologist Thierry Passeron, at Côte d’Azur University in Nice, France, still thinks COVID toes are triggered by the virus. His team found⁴ that people who developed chilblains during the pandemic showed evidence of a strong innate immune response.

With the link between COVID-19 and chilblains still in question, some researchers point to the theory that people spent more time at home barefoot early in the pandemic and got cold feet, literally. Or perhaps all the media coverage of COVID toes led to more people than usual seeking medical attention.

The debate has become strangely polarizing, Gehlhausen says. But the hypotheses are not mutually exclusive. “It’s possible that all these things are true,” he says.

It’s also possible the problem might be fading. “We’re still seeing patients with new chilblains, but it seems to be kind of back to the old background rate,” says Yale dermatologist William Damsky, an author on the paper.

In the end, the issue makes for an intriguing scientific debate, McCleskey says, but irrespective of whether a person had COVID-19, chilblains generally go away on their own in two or three weeks.

“Honestly, I think maybe we can chill out about chilblains,” he says.

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