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https://www.wsj.com/articles/studies-of-south-african-coronavirus-strain-raise-concerns-about-immune-response-11611311401

#### WORLD

# Studies of South African Coronavirus Strain Raise Concerns About Immune Response

Findings suggest vaccine makers may need to update shots as virus evolves, as with flu vaccinations



Paramedics in Tshwane, South Africa, transported a patient in an isolation chamber last week as a new strain of the coronavirus spread in the country. PHOTO: PHILL MAGAKOE/AGENCE FRANCE-PRESSE/GETTY IMAGES

#### By Gabriele Steinhauser

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JOHANNESBURG—Three new laboratory studies are raising concerns that the immune response triggered by a Covid-19 infection or vaccination may be less effective at protecting against <u>the new strain of the coronavirus</u> that first emerged in South Africa.

The findings come from experiments done in the laboratory and only look at

certain elements of a body's immune response. Still, they reinforce the possibility that vaccine makers and regulators will need to update Covid-19 vaccines as the virus evolves.

A fourth study, conducted by scientists at <u>BioNTech</u> SE and <u>Pfizer</u> Inc. and published by the companies, showed that their vaccine successfully neutralized a variant that was initially detected in the U.K. That study didn't include the South African strain.

# The U.K. variant has already spread to many other countries, including the U.S.

More than a year into the pandemic, the discovery of new variants that appear to have made the virus more contagious is forcing researchers to adapt their understanding of the coronavirus that causes Covid-19. One concern, researchers said, is that the new strains are emerging in countries where a significant percentage of people have already built up an immune response to earlier variants after getting Covid-19.

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What concerns do you have about the new variants of the coronavirus? Join the conversation below.

If confirmed by additional research, the studies' findings would suggest that winning the global fight against the coronavirus pandemic could require repeated inoculations and updates to existing vaccines, similar to what is done for flu shots every year.

"We are learning how our body is forcing the virus to change," said Jinal Bhiman, the principal medical scientist at the National Institute for Communicable Diseases in Johannesburg and a co-author of one of the studies on the South African variant.

## **Going Viral**

The new coronavirus variant quickly crowded out other strains in South Africa



### Share of coronavirus strains found in South Africa

Source: Houriiyah Tegally, KwaZulu-Natal Research Innovation and Sequencing Platform

Studies on lab-grown viruses and blood drawn from people who have either recovered from a previous bout of Covid-19 or received a Covid-19 vaccine are some of the first experiments scientists conduct when they want to find out more about a new variant. Researchers who worked on the studies said that the tests only examined the response of certain antibodies, while the human immune system also includes so-called T-cells, blood cells that help attack the virus, and other types of cells.

The studies haven't been published in peer-reviewed journals, but were seen by outside researchers interviewed by The Wall Street Journal.

More definitive data will come from human trials of Covid-19 vaccines under way in South Africa and in the U.K. and whose results are expected within weeks. Those results will give a better indication of how vaccines perform against the new strains.



A Covid-19 victim was buried outside Johannesburg earlier this month. PHOTO: SIPHIWE SIBEKO/REUTERS

The researchers who conducted the tests on the South African variant stressed that current vaccine campaigns should continue and the shots approved so far offer the best known protection against Covid-19.

The South African variant has been found in 22 other countries, including Canada, China and Germany, but not the U.S. Labs in the U.K., Belgium, Botswana and Zambia have found it in people with no travel history, indicating that it is already spreading in those countries.

For two of the studies, researchers in South Africa tested how the new variant, which has driven <u>a powerful second wave of infections in the country</u>, responded to blood drawn from people who had Covid-19 in the first wave, when other versions of the virus were circulating. What they found was that the new variant was either entirely resistant to antibodies generated from an earlier infection or the antibodies were significantly less able to neutralize the virus.

"A few of these plasmas are knocked out," said Alex Sigal, a virologist at the Africa Health Research Institute, which conducted tests on a live virus grown in its lab, and Germany's Max Planck Institute for Infection Biology.

A second study replicated the South African variant's spike protein, through which the virus attaches to and infects human cells, on a different virus. New





Covid-19 vaccines—including those developed by BioNTech and Pfizer and by <u>Moderna</u> Inc. —also target the coronavirus's spike protein.

That study found that blood from 21 of 44 people who had previously had Covid-19 failed to neutralize the virus. Only three blood samples—from people who had suffered very severe cases of Covid-19—were able to mount a powerful attack.

Note: As of Jan. 20. Source: Johns Hopkins CSSE

The findings may mean that variants such as the South African one could infect people for a second time "and may foreshadow reduced efficacy of current spikebased vaccines," the study concluded.

James Naismith, a professor of structural biology at the University of Oxford, said the South African papers' findings now need to be confirmed by studies in the real world, such as clinical vaccine trials or proof of large-scale reinfections by the new strain. "We should be concerned, but not panic," he said. "There is more to the immune response than just antibodies."

A third study—conducted by researchers at Rockefeller University in New York and the California Institute of Technology in Pasadena—ran a similar set of tests as the South African scientists, but using blood drawn from people who had received either the Pfizer or Moderna shots.

That study found that three prominent mutations in the South African variant reduced the ability of vaccine-generated antibodies to neutralize the virus by a small but significant margin. One possible reason for the difference in results from the three studies is that the U.S. scientists only looked at mutations in one part of the spike protein, known as the receptor-binding domain, that latches onto human cells. In the two studies done in South Africa, some of the biggest impact on antibody response came from another part of the spike protein, known as the N-Terminal, which is also a target for neutralizing antibodies and whose significance scientists are only starting to understand.

Another possible reason for the differences is that the vaccines induce a stronger immune response than a previous Covid-19 infection.

The U.S. study concluded that mRNA vaccines such as the Pfizer and Moderna shots "may need to be updated periodically to avoid potential loss of clinical efficacy."

In human trials, the Pfizer and Moderna shots have proven to be around 95% effective at protecting participants from developing Covid-19 symptoms. So a moderate reduction in efficacy wouldn't render them useless.

Moderna declined to comment on the U.S. study's findings, but has said that it is studying the potential efficacy of its Covid-19 vaccine with multiple variants. A Pfizer spokeswoman said the company was researching the E484K variant—a reference to one of the mutations in the South African and Brazilian variants—and would share its findings once they are available. BioNTech didn't respond to requests for comment.

Pfizer's and Moderna's own study—which looked at how effectively blood from people who had received their vaccine neutralized a virus manipulated to mirror the U.K. variant—concluded that there was no reason to adapt the shots for the British strain. Still, it said, "potential Covid-19 vaccine strain change is prudent," adding that <u>shots based on messenger RNA technology</u> could be adapted quite easily and quickly.

BioNTech's chief executive, Ugur Sahin, said last month that it would take around six weeks to design another vaccine if a mutation renders the current one

ineffective. Dr. Sahin said, however, that it was unclear whether regulators would allow such a modified vaccine on the market or whether they would require a new trial, which could take months.

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