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# Fourth Wave: Indion Mutant COVID-19 viruses as 'Super Variant'

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## Abstract:

This is first ever study detecting signals of a convergence, which suggests that through mutations, the UK variant is becoming more like the South African variant and vice-versa. The scientists from the US, UK, Sweden and South Africa have shown that the emergence and rapid rise in prevalence of three independent SARS-CoV-2 "501Y lineages'', B.1.1.7, B.1.351 and P.1, in the last three months of 2020 has prompted renewed concerns about the evolutionarily capacity of SARS-CoV-2 to adapt to both rising population immunity, and public health interventions such as vaccines and social distancing.

Passengers tested for COVID-19 on their arrival at Chennai International Airport as precautionary measure. (Photo | Martin Louis/EPS)

Different and worrying SARS-CoV-2 variants of concern, such as the UK and South African ones, appear to be converging through mutations towards a "super variant" that would confer biological advantages to the virus and make fighting the Covid-19 pandemic difficult, a new study has suggested.

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The scientists from the US, UK, Sweden and South Africa have shown that the emergence and rapid rise in prevalence of three independent SARS-CoV-2 "501Y lineages'', B.1.1.7, B.1.351 and P.1, in the last three months of 2020 has prompted renewed concerns about the evolutionarily capacity of SARS-CoV-2 to adapt to both rising population immunity, and public health interventions such as vaccines and social distancing.

Viruses giving rise to the different 501Y lineages have, presumably under intense natural selection following a shift in host environment, independently acquired multiple unique and convergent mutations.

"As a consequence, all have gained epidemiological and immunological properties that will likely complicate the control of Covid-19," noted their work. [1, 2]

By examining patterns of mutations the scientists found evidence of a major change in the selective forces acting on immunologically important SARS-CoV-2 genes (such as

and S) that likely coincided with the emergence of 501Y lineages.

“Our findings highlight the importance of monitoring how members of these known 501Y lineages, and others still undiscovered, are convergently evolving similar strategies to ensure their persistence in the face of mounting infection and vaccine induced host immune recognition,” they noted.
The scientists have hypothesized that other plausible contributors to the fitness advantage of viruses are that they produce more particles at anatomical sites suitable for optimal droplet or aerosol transmission.

## Vaccination crosses two crore mark:

The cumulative number of Covid-19 vaccine doses administered in the country has crossed 2.26 crore on Monday. A total of 2,26,85,598 vaccine doses were administered.

## Covid ‘Super Mutation’ may cause ‘devastating’ new outbreak in India:

COVID could mutate into a new super variant which could beat vaccines, make people sicker and reinfect victims in a devastating new outbreak, leading experts have warned.
Scientists told The Sun Online about the need to vaccinate as many people as possible and stick to the lockdown rules as it is feared the rapidly changing virus could overwhelm our current arsenal of vaccines.

Scientists fear a possible super mutation of Covid which makes people sicker and beats vaccines Credit: Alamy
Brits have been urged to stick to the rules over Easter after busy scene earlier this weekCredit: LNP
The experts hammered home the need to rob Covid of the rapid person-to-person transmission which helps it develop mutations. [2, 3]

And they warned possible new variants in the future could make people sicker and re-infect people who had already developed antibodies in a "very, very scary" new outbreak.

It comes as Prime Minister Boris Johnson pleaded with Brits to stick to the rules as we go into the long weekend for Easter so the UK can keep to its plan to unlock totally by June.

Hot weather earlier this week already saw thronging parks and beaches amid fears it could trigger a new wave despite months of lockdown pain finally leading to plunge cases.

Covid variants and mutations, for example the Indion; have been popping up around the world - with various tweaks appearing to make it more transmissible.

Fears have loomed for months that a mutant Covid variant could become significantly more deadly.

Meanwhile, scientists in India claimed they have identified a new variant that carries two mutations.

And variants first identified in South Africa and Brazil contain the E484K mutation, which is thought to be make the bug evade vaccines.

Studies so far have shown the Pfizer and AstraZeneca jabs do work against current known variants. It comes amid fears the E484K mutation could make them slightly less effective.

Yet the latest results from Pfizer show the vaccine does protect against the South African strain, raising hopes the same will be true for the Brazil variant.

The best ways to avoid this are to vaccinate as many as we can – and reduce transmission – and to stay in lockdown until as many as we can are vaccinated
Dr Tony Lockett, from King’s College London’s Institute of Pharmaceutical Science, told The Sun Online about the prospect of a devastating new mutation - and urged Brits to stick to the rules.

He said: "The effect – well it could be devastating – much worse than the original as younger people could become sicker and those who have had the virus get reinfected with the new strain: "Its really very scary."

It comes as it was warned coronavirus mutations could render vaccines redundant in less than one year, according to a survey of epidemiologists by The People’s Vaccine Alliance.


Dr Lockett explained some mutations arise when the virus infects people who cannot beat it with their immune system.

The expert added: "Uncontrolled proliferation leads to the virus replicating more actively and hence mutation is more likely. "Patients with poor immune systems are therefore are a possible source of mutations."

He went on: "The causes of mutations are therefore allowing vulnerable subjects to get exposed.

"The best ways to avoid this are to vaccinate as many as we can – and reduce transmission – and to stay in lockdown until as many as we can are vaccinated.

"As Chris Whitty has indicated speeding the lockdown release will lead to more transmission and so more likely mutants – or existing mutants spreading – so the mutations are fed by meeting up and not getting vaccinated."

[Mutations] are already on the way to becoming immune to our current vaccines.

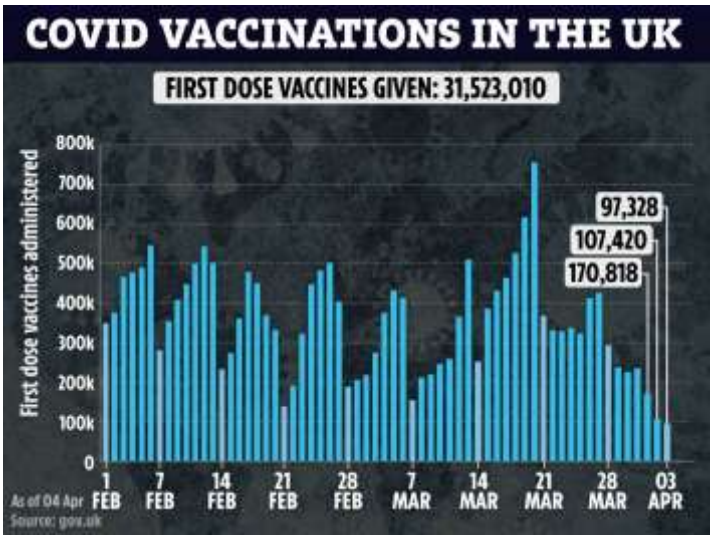
Harvard Professor Dr William Hannage explained it is key to stop the new variants before they can get a foothold as it stops the spread which fuels the mutations.

He told The Sun Online: "At the moment there is a lot of concern around E484K, a mutation in the spike protein which is thought to help the virus sidestep immunity from prior infection and is found in several of the variants. [4, 5]

"While it looks like vaccines should still offer protection, at least from severe disease, this is one to watch.

"It is why the government has been so keen to stop B.1.351 (the South African variant) from getting a toehold in the UK, because one of the mutations characterizing that variant is E484K.

"There are a few others as well which make antibody treatments less effective."




New mutations on the coronavirus can make it harder for the body's immune system, which has been primed to look out for the "original" strain either through vaccination or prior infection, to recognise it.

Antibodies - proteins produced by the immune system to fight the virus - may be weaker against new strains.

The threat of new coronavirus strains also means masks and social distancing could be needed well into 2022, despite the vaccine rollout, and it is not clear when border controls will be relaxed. Studies have shown the current vaccines do still work against new variants, but may be less effective.

Scientists are already working on tweaked vaccines to help deal with new mutations in future, much like the flu vaccine which is

altered every year.
Ravi Gupta, a professor of Clinical Microbiology at the Cambridge Institute for Therapeutic Immunology and Infectious Disease said: "(Mutations) are already on the way to becoming immune to our current vaccines.

"For example, the AstraZeneca study did not do well against the South African strain.

"The virus is already on its way to becoming resistant to what we have at the moment. There's evidence the same mutations are cropping up again and again.

"For example, the Brazil and South African variants have this E484K mutation that really makes it hard for our antibodies to neutralise and stop the virus from causing infection."

There has been growing concern over the spread of South African and Brazilian variants of coronavirus in Europe as a third wave of Covid-19 sweeps across the continent. [6]

A string of countries have gone back into lockdown or tightened up measures again in response to spiking infection rates.

Coronavirus variants: really more deadly
One certainty during a pandemic is that the virus will mutate. SARS-CoV-2, which causes COVID-19, is no different. But how concerned should we be about the new variants of the virus that are arising in places such as the UK, South Africa and Brazil? Are they more lethal or more transmissible than the original virus?
In the UK, for example, Prime Minister Boris Johnson recently claimed that the new variant may be 30%-40% more lethal than the old one, though this has since been played down by scientists. Every time a virus enters a host and begins to replicate it quickly starts to make mistakes – that's how mutations arise. Most of these mistakes are actually very harmful to the virus, while other mutations are neutral and don't really affect it at all. In very rare instances, however, a mutation might confer an advantage over the original virus.

## Level of transmission:

At the end of December, data started to emerge about a variant of the COVID-19 virus, called B.1.1.7 – since dubbed the "British variant" or the "Kent strain".
Initial epidemiological reports claimed that this variant was much more transmissible than the original SARS-CoV-2 virus, with some even reporting that transmission was 70% greater. With evidence suggesting that this variant arose in September, this would help to explain the dramatic rise in cases that we've seen in south-east England since then. This initial estimate of 70% has, however, been downgraded several times since then in other studies.

Another explanation for the rapid rise of the Kent variant or indeed any virus variant is the "founder effect". This is a phenomenon in evolution where a small group, which happens to be affected by a mutation, ends up spreading it more than other populations. This is down to chance rather than the mutation providing any advantage at all.

In theory, a person infected with a new variant in Kent could easily infect a large number of locals at the shop or pub – similar to a "super-spreader" event. In turn, these newly infected people could commute to London the next week on buses and trains and quickly spread this new variant to large numbers of fellow commuters who in turn spread it throughout London and beyond. This could make the variant common – through pure chance.
This is all possible without the mutations in B.1.1.7 providing increased transmission. Given that this virus is present across almost the whole planet, and we know the distances and frequency with which we can travel, it's probable that the founder effect could result in variants becoming common in a few places. After all, we know super-spreader events happen with this virus.

In fact, a recent study of the USA found that the Kent variant has likely been in California and Florida since November, but it is still too early to tell if this trend toward increased transmissibility holds there too.

Unfortunately, only time will tell if any of the SARS-CoV-2 variants are more transmissible. As a lot of evidence is currently being collected on both the Kent and South African variants, we shouldn't have to wait long. [6, 7]

## Lethality:

The UK government's New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG) recently compiled a report detailing the potential increased severity of the British B.1.1.7 variant. However, as they state, the conclusions at this stage are mixed.
Some studies have found no differences in lethality or even hospitalisation, between the new or old variant. Others, however, found an increase in mortality of around 30% between the viruses – the figure quoted by the government and its chief advisers. If this is the case, it could increase the case fatality rate within the UK from 2.7% to 3.5%.

But for the moment these studies are in no way complete, with NERVTAG stating that there are several limitations to this work, including inherent biases and a small sample of deaths.
Unfortunately, again we simply don't have enough data at this stage to make a firm conclusion on the lethality of the British B.1.1.7 variant, or indeed any of the other variants we're currently aware of, including the South African or Brazilian variants. In regard to the British variant, it simply could just have infected more people, thereby leading to more deaths.

## Immunity:

The pressing question as we begin large scale vaccination programmes across the world is instead whether the vaccines work against the new variants. Here we have some good news, because initial reports for the British and South African variants appear to show that vaccines do still protect us. A group from the University of Texas has reported finding that a key mutation (N501Y) in the British variant doesn't appear to affect the ability of the antibodies induced by the vaccine to bind to the virus and neutralise it.
Although this was just a single mutation, last week, Pfizer/BioNTech released data testing their vaccine against all

mutations in the British variant and also found their vaccine can clearly and robustly neutralise it. And on January 26, Moderna released their data, again showing the same robust neutralisation of the British variant. [7]

The South African variant is a slightly different story. The new study from Moderna found that mutations in the South African variant did affect the ability of vaccine-induced antibodies to incapacitate the virus – showing a six times reduced ability to do so. But this should not be a great concern for the moment. We know that all these vaccines elicit a huge amount of antibodies after both doses, so even with a six-fold reduction, vaccinated people will probably still have a significant level of immunity. This does however stress the importance of receiving both doses of the COVID-19 vaccines.

At present we still cannot definitively say whether any of the variants transmit better, or whether they are more deadly, because, unfortunately, the data just isn't there yet. But we can say that the COVID-19 vaccines are protective against the current SARS-CoV-2 variants, so when your opportunity comes, please get your vaccine and protect yourselves and your community.

Democratic norms are being stress-tested all over the world, and the past few years have thrown up all kinds of questions we didn't know needed clarifying – how far should politicians be allowed to intervene in court cases? To monitor these issues as closely as we have in the past we need your support. [8]

## Coronavirus Indion: 'Super Mutant' Covid variant found in India:

**A new "double mutant" variant of the coronavirus Indion has been detected from samples collected in India:**

Officials are checking if the variant, where two mutations come together in the same virus, may be more infectious or less affected by vaccines.

Some 10,787 samples from 18 Indian states also showed up 771 cases of known variants - 736 of the UK, 34 of the South African and one Brazilian.

Officials say the variants are not linked to a spike in cases in India. India reported 47,262 cases and 275 deaths on Wednesday - the sharpest daily rise this year.

The Indian SARS-CoV-2 Consortium on Genomics (INSACOG), a group of 10 national laboratories under India's health ministry, carried out genomic sequencing on the latest samples. Genomic sequencing is a testing process to map the entire genetic code of an organism - in this case, the virus. [8]

The genetic code of the virus works like its instruction manual. Mutations in viruses are common but most of them are insignificant and do not cause any change in its ability to transmit or cause serious infection. But some mutations, like the ones in the UK or South Africa variant lineages, can make the virus more infectious and in some cases even deadlier.

Virologist Shahid Jameel explained that a "double mutation in key areas of the virus's spike protein may increase these risks and allow the virus to escape the immune system".
The spike protein is the part of the virus that it uses to penetrate human cells.

- What are the risks of India's new Covid-19 variant
- Sharp rise in India Covid cases 'alarming'

The government said that an analysis of the samples collected from India's western Maharashtra state showed "an increase in the fraction of samples with the E484Q and L452R mutations" compared with December last year.

"Such [double] mutations confer immune escape and increased infectivity," the health ministry said in a statement.

Dr Jameel added that "there may be a separate lineage developing in India with the L452R and E484Q mutations coming together".

## Are Super Mutants a worry?:

Mutations in the spike gene can make the virus inherently "better" at infecting people or can help the virus to escape neutralising antibodies.

This means if the virus mutates in the "right way", it can reinfect someone who has already recovered from Covid-19.

But scientists say reinfections will be very mild compared to primary infections in people who are vaccinated or who recovered already from an earlier case of Covid-19.

But if the virus can use reinfection to spread, then it would be "penetrating" herd immunity, says Dr Jeremy Kamil, a virologist at Louisiana State University Health Sciences Center Shreveport. (Herd immunity happens when a large portion of a community becomes immune to a disease through vaccination or through the mass spread of the disease.)

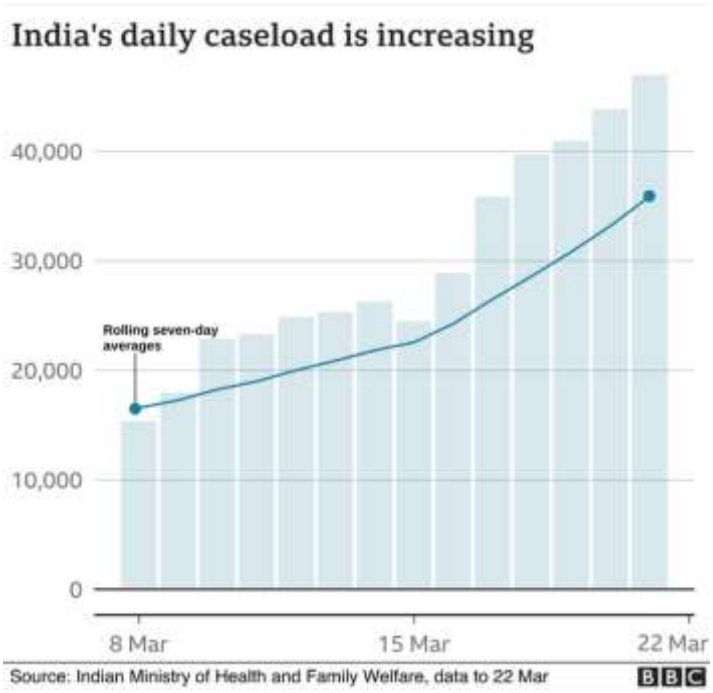
This puts the most vulnerable people at risk of severe disease, since the virus can move through the herd to reach them.

He says unlike some other variants, India's new double variant is not likely to be more deadly or more inherently transmissible, but that more data is needed to be sure.

Read more about the risks of India's new Covid-19 variant
The Indian government denies that the rise in cases is linked to the mutations. [8, 9]

"Though VOCs [variants of concern] and a new double mutant variant have been found in India, these have not been detected in numbers sufficient to either establish a direct relationship or explain the rapid increase in cases in some states," the health ministry said.

The recent report comes after several experts had asked the government to step up genome sequencing efforts.
"We need to constantly monitor and make sure none of the variants of concern are spreading in the population. The fact that it is not happening now doesn't mean it will not happen in the future. And we have to make sure that we get the evidence early enough," Dr Jameel told the BBC's Soutik Biswas earlier this month.




India became the fifth country in the world to sequence the genome of the novel coronavirus after isolating it from some of the first cases recorded in January last year.

More than 11.7 million cases and 160,000 deaths later, efforts are continuing to identify mutations.

The latest surge - which began this month - comes during what some experts have called a "delicate phase" for India - the healthcare system is already exhausted from a year-long battle against the coronavirus.

States have already begun re-introducing restrictions, including curfews and intermittent lockdowns. [10]

Two major cities, Delhi and Mumbai, have also ordered randomised rapid tests at airports, railway stations and crowded areas such as shopping malls. (David Courtney works at Queen's University, Belfast and receives funding from the European Research Council).

## Conclusion:

SARS-CoV-2-Indion, the virus responsible for the current COVID-19 pandemic in India and other countries, displays a corona-shaped layer of spikes which play a fundamental role in the infection process in India. Recent structural data suggest that the spikes posses orientational freedom and ribonucleoproteins segregate into basketlike structures. These structural features regulate the dynamic and mechanical behavior of the native Indion. Their surface displays a dynamic brush owing the flexibility and rapid motion of the spikes. The Indions are highly compliant and able to recover from drastic mechanical perturbations. Their global structure is remarkably temperature resistant, but Indions surface becomes prograssively denuded of spikes upon thermal exposure.

The atomic force microscopic imaging and nanomechanical measurements revealed that the SARS-CoV-2 Indion is highly dynamic compliant, and resilient, and it displays remarkable mechanical and global thermal stabilities. The Dynamics of the surface spikes play an important role in unusually high infecticity of the virus, its mechanical and self-healing properties ensure adaptation to a wide rangeof environmental circumstances.

4.5.2021

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