MUTATION & VACCINE COMBINATION

The most important issue which is a hindrance of treatment types and vaccine discovery is mutation. Corona virus is reputed like HIV for its capacity to mutate.

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Viruses mutate all the time, including the coronavirus that's caused the global Covid-19 pandemic.

Most of the changes are innocuous.

But several mutants are alarming, as studies suggest they are **more contagious**, and some evidence points to one of them being **more deadly** and cause **reinfections**.

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1. What's a variant?

During replication, a virus often undergoes genetic mutations that may create what are called variants**.**

This causes the DNA in the virus to send altered signals to its RNA and finally the RNA produce such proteins which after binding to the specific (ACE-2 receptor in humans) enter the body and can create new kinds of damage to various organ systems of the body.

Some mutations however may weaken the virus too fortunately.

Others may yield some advantage that **enables the variant to proliferate**.

Strain - Variants with distinctly different physical characteristics may be co-termed a strain.

2. What are the most worrisome variants?

So far, the WHO has identified three variants of concern and one variant of interest. These are:

The variant that **emerged in England** in September, B.1.1.7, contributed to a surge in cases that sent the U.K. back into lockdown in January.

Other countries followed, particularly in Europe. Health officials have warned the strain could become dominant in the U.S

In *southern Africa*, hospitals faced pressure from a resurgence driven by another variant, 501Y.V2. (**South African strain**).

Brazilian strain , so-called P.1 variant spotted in Manaus, Amazonas state, in December may have driven a surge in cases that strained the health system and led to oxygen shortages.

At present in India that what is being thought to be a 2nd Covid-19 wave is actually mixed with a new mutant strain –B.1.667 which is affecting young people, not responding to standard regimens, responding with great difficulty to monocloclonal antibodies(costly), killing in days normal apparently absolutely healthy individuals in 18-45 yrs age group, the bread earners and the country's future.

Others

Researchers in Los Angeles reported a novel strain, denoted as CAL.20C in June 2020, that was linked to a late-year surge of coronavirus cases in Southern California. Preliminary research indicates it's slightly more transmissible and may moderately resist antibodies generated from a previous SARS-CoV-2 infection, the WHO said on March 16. By then, the strain had been detected in all U.S. states and at least 26 other countries. It's deemed a variant of concern by the U.S. Centers for Disease Control and Prevention.

3. How quickly have the strains spread?

- Rapidly, aided by year-end holidays traditionally associated with increased family and social mixing.
- As of March 16, imported cases or community transmission of the B.1.1.7 variant from the U.K. had been reported in 118 countries, according to the WHO.
- In the U.S., scientists estimated that infections caused by B.1.1.7 were doubling every 10 days.
- As of March 16, scientists have found the 501Y.V2 variant that first appeared in South Africa in early August in 64 countries
- 38 countries are reported to have detected the P.1 variant first seen in Brazil, according to the WHO.
- Insufficient surveillance in most countries (India for e.g.) & including the U.S., has obscured recognition of variants circulating in many places.

4. What are the concerns with these variants?

- Broadly, they pose different concerns of varying degrees. These relate to their:
- Transmissibility, or propensity to spread

- The severity of illness they cause
- Neutralization capacity, or the likelihood they will infect people who have recovered from a previous bout of Covid-19
- Potential impact on vaccination through their ability to evade the protection that immunizations are designed to generate

5. How are the variants increasing transmission?

They increase in the basic reproduction number, or R0 (the average number of new infections estimated to stem from a single case) in the range of 0.39 to 0.93 -- a “substantial increase." The international spread of these variants has also helped drive a rebound in Covid-19, with the number of new cases reported worldwide increasing each week since mid-February.

U.S. health officials said in late March that a variant-induced resurgence of cases in some regions could augur a long-feared possibility:

That another surge could occur even as states are flinging open vaccine eligibility criteria, trying to get shots in arms as quickly as possible.

6. How many mutations are there?

Many thousands of mutations and distinct lineages have arisen in the SARS-CoV-2 genome since the virus emerged in late 2019. **A variant with a so-called D614G mutation emerged in early 2020. By June, it had replaced the initial strain identified in China to become the dominant form of the virus circulating globally**.

Months later, a novel variant linked to farmed mink was identified in a dozen patients in North Jutland, Denmark, but doesn’t appear to have spread widely.

As SARS-CoV-2 continues to circulate, more mutations will arise, potentially leading to more variants.

7. Are some mutations more important?

Yes. Scientists pay most attention to mutations in the gene that encodes the SARS-CoV-2 spike protein, which plays a key role in viral entry into cells. **Targeted by vaccines, this protein influences immunity and vaccine efficacy. The B.1.1.7, 501Y.V2, and P.1 variants all carry multiple mutations affecting the spike protein. That raises questions about whether people who have developed antibodies to the "regular" strain -- either from a vaccine or from having recovered from Covid-19 -- will be able to fight off the new variants.**

In January Public Health England found those previously infected with the "regular" coronavirus are likely to mount an effective antibody response against the B.1.1.7 variant. But the same month the first known instance of a recovered Covid-19 patient being

re-infected with the P.1 variant was reported in Brazil. That strain has several key mutations in common with the 501Y.V2 strain from South Africa, that was associated with some 4,000 reinfections in people who had already experienced Covid-19 in an earlier epidemic.

In a Jan. 28 editorial in the Journal of the American Medical Association, virologist John P. Moore and vaccinologist Paul Offit described the 501Y.V2 variant as "more troubling" because of its potential for reducing vaccine efficacy, due to its particular spike-protein mutations.

9. How effective will vaccines be?

Data are emerging, and no clinical studies have directly compared different vaccine types and their ability to protect against the new strains. Overall, 10 vaccines have proved effective in clinical trials at preventing severe disease and death from Covid-19. The studies suggest, however, that some may not be as good at stopping less severe illness in countries where particular variants predominate. Notably:

Shots from both Novavax Inc. and Johnson & Johnson showed lower efficacy in South Africa compared with other countries.

South Africa announced plans in early February to halt its rollout of the AstraZeneca vaccine. **A WHO advisory panel cautioned that the 21-to-35-day interval between the first and second doses isn't optimal for inducing immunity and larger studies are needed.**

A study published Feb. 24 of almost 1.2 million people in Israel, which has inoculated a higher percentage of its population than any other country, estimated that the Pfizer Inc.-BioNTech SE vaccine was 92% effective in preventing all infections. Scientists at Seattle found a single jab of either the Moderna or Pfizer-BioNTech shot bolstered the immune response in 10 patients who had recovered from a SARS-CoV-2 infection early in the pandemic. The concentration of neutralizing antibodies in the recipients' blood increased about a thousand-fold, and they appeared potent against the 501Y.V2 variant first identified in South Africa.

10. What are drugmakers doing?

Sarah Gilbert, a professor of vaccinology at the University of Oxford who conducted the initial research on the AstraZeneca vaccine, said that "efforts are underway to develop a new

generation of vaccines that will allow protection to be redirected to emerging variants as booster jabs, if it turns out that it is necessary to do so."

Nevertheless, Moderna said March 10 that it began testing modified Covid-19 vaccines, designed to address the potential need for booster vaccine candidates, in clinical trial participants.

Pfizer and Novovax also have said they're working on either a booster or combination shot. Such alterations aren't unheard of -- it happens annually with seasonal flu, which evolves quickly. Unlike flu, coronaviruses have a genetic self-correcting mechanism that minimizes mutations.

11. Could different vaccines be used in combination?

Potentially, yes.

The Coalition for Epidemic Preparedness Innovations, or CEPI, announced in January as much as $140 million in funding for additional clinical research to optimize and extend the use of existing vaccines.

This could include "mix-and-match" studies of different shots in combinations that may improve the quality and strength of the immune response. Such studies could be useful in optimizing the use of available inoculations, including the AstraZeneca shot, according to the WHO.

12. Are there any other implications?

Yes, treatments and diagnostics could be affected.

Drugmakers are using combinations of antibodies that target separate features of SARS-CoV-2 to decrease the potential for so-called virus-escape mutants that could emerge in response to selective pressure from a single-antibody treatment.

The U.S. Centres for Disease Control and Prevention has said new strains might undermine the performance of some PCR-based diagnostic tests.

NB:

- **The impact, (Vaccine combination) though, isn't likely to be significant, according to the WHO but still is an interesting area of research.**
- **However, whether combining vaccines is going to help is still a query, but there is no doubt that 2 jabs may not be sufficient in future as mutation will continue.**