The new AY.4.2 sub-lineage of Delta: The implications of the evolution of coronavirus

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The world is fast approaching the end of the second year of the COVID-19 pandemic. Already nearly one-quarter of a billion people have been infected by the coronavirus, a vast undercounting by a unanimous consensus among scientists and researchers. There have also been almost five million deaths, though the global excess deaths are estimated to be over 16 million.

What has distinguished the second year has been the introduction of life-saving vaccines that have without doubt saved numerous lives. Just over half the world's population, an astounding 3.86 billion people worldwide, has received at least one dose of a COVID-19 vaccine.

However, as inequity in vaccine distribution continues to plague the globe, regions in the Middle East, the African continent, and many Latin American countries have fallen woefully behind high-income nations in Europe and North America. Africa has, on average, only administered a single dose to 8.3 percent of its population, a critical indictment of the ruling factions' opportunistic approach to the crisis.

And yet, despite these achievements, albeit favoring the wealthier nations, the second year has been far more calamitous and deadly than the first, as almost every country across the globe has adopted a "we will learn to live with the virus" approach in their response to the pandemic. If we set the announcement of a Public Health Emergency of International Concern (PHEIC) by the World Health Organization on January 30, 2020, as a fixed point in the beginning of the pandemic, exactly one year later, there were 103 million reported infections and 2.35 million deaths globally.

But with three months left in this second period, already 143 million more people have contracted the virus. A small but significant number have contracted COVID-19 twice or even three times. Another 2.64 million people have died. This means that despite the existence of vaccines that can dramatically cut the rate of severe disease and death, more have lost their lives in nine months than in the preceding 12.

It is important to consider these statistics, because the policy of living with the coronavirus has enabled SARS-CoV-2 to mutate and develop more virulent forms to ensure its "survival." The ruling class has carried out policies to satisfy the incessant need by financial institutions to see their quarterly earnings climb, which have had the effect of allowing the virus to become endemic. There is an intimate correspondence between the financial earnings of the stock exchanges and the death toll from COVID-19.

The emergence of the Delta variant (B.1.617.2) in the second year is the counterpoint to this criminal policy of malign neglect. Hyper-transmissible, more virulent, and deadly and possessing more robust immune-evading properties, in just a few short months after debuting in India in a catastrophic surge of infections, it quickly dominated every other variant globally wreaking havoc across communities in every region of the world. As of August 24, 2021,163 countries have reported the Delta variant has been sequenced within their borders.

As countries prepare to face the third year of the pandemic, there are signs that new mutations are emerging that have aroused researchers' concerns. Delta's daughters are beginning to dominate, supplanting their parent. They have been designated by the PANGO (Phylogenetic Assignment of Named Global Outbreak Lineages) lineage AY. The designation highlights the branches of the evolutionary tree that characterize their relationship. As the website notes, "The Pango dynamic nomenclature is a system for identifying SARS-CoV-2 genetic lineages of epidemiologic relevance." The network is overseen by a team of researchers from the universities of Edinburgh and Oxford.

There have been 75 such lineages identified thus far, each possessing a unique mutation. AY.4 has been rising

in the UK over several months, accounting for 68.2 percent of sequenced SARS-CoV-2 coronaviruses in the last 28 days. The sub lineage AY.4.2, also commonly being referred to as the new "Delta Plus," has been growing slowly, accounting for 8.5 percent in the same period.

The origin of AY.4.2 was traced back to April in the UK's Northumbria by COG-UK, a British consortium that has sequenced more than 1.2 million whole genomes of the coronavirus. The two samples related to recent travel to India. In explaining this new designation, Scroll.in said, "Once a lineage's labelling gets five levels deep, a new letter combination is started to avoid the name getting too long. So, the AY forms of the virus are not vastly different from what's come before, even though their labelling is different. They are all sub-lineages of the Delta."

Some of the scientists studying AY.4.2 have estimated that it is between 10 to 15 percent more transmissible than Delta. Such an advantage, they assert, most likely won't lead to a significant rise in infections. Others have attributed AY.4.2's rise to a phenomenon called a *founder effect.* This means that all the people in a group isolated from a larger population became infected with this sub-lineage. It is a randomness that accompanies the selection of these small groups from the larger population and does not represent the larger population, nor should it be construed as a dominant variant. However, many have noted that it is still too early to be confident about this supposition.

There are two specific genetic mutations that define AY.4.2—Y145H and A222V—that affect the spike protein of the virus. The A222V was first seen in the B.1.177 lineage last year in Spain, spread by holiday travelers. However, it is the Y145H mutation that appears to have increased the transmissibility of the virus.

This section of the spike protein is frequently targeted by antibodies. Delta has mutations in this region that appear to enhance its greater ability to escape immunity. This means that antibodies have a harder time targeting the virus, thus allowing it to escape and more likely to infect an individual previously infected or vaccinated. However, scientists are studying these mutations and their findings have not yet been reviewed.

More recently, the number of sequenced AY.4.2 infections has been climbing in all regions of England, and Scotland and Wales.

Cornelius Roemer, a computational biologist at the Biozentrum, Basel, Switzerland, noted that the AY.4.2 in Scotland has an extra spike mutation S:1264L and in "less than 10 weeks going from first occurrence to 2,000 sequences. It's now more than 50 percent of all AY.4.2 in Scotland. … Interestingly [it] was found also in AY.23, the lineage [that] emerged in Singapore and [is] prevalent in Southeastern Asia. … It's also appearing in AY.26 in the US. At least three times convergent evolution with significant shares." The last statement implies that these three different versions of the coronavirus have found the same mutation to exploit for their survival.

According to a recent article in *The World*, more than four million genomic sequences of SARS-Cov-2 have been analyzed. Sequencing these viruses can provide critical information for public health officials. By understanding the implication of these changing codes, specifically in known regions that increase a pathogen's virulence, scientists can determine early warning signs that would make it possible to bring together public health resources to intervene before the particular variant is allowed a wide berth and can escape to other geographic regions.

Though this approach will be critical in studying and identifying future pathogens, that the virus can evolve through convergent evolutionary biological pathways to escape natural pressures placed in its way through population immunity highlights the critical need to eliminate COVID-19 from the face of the earth. The coronavirus, under the current pressures, is driven to develop the ability to escape immunity. Such a characteristic in a respiratory virus would be extremely catastrophic.