**Covid-19: Infections climb globally as EG.5 variant gains ground**

Owen Dyer

Recent testing has left little doubt that a new variant of the pandemic coronavirus is gaining ground across the world. The spike mutations of the EG.5 variant—dubbed “eris”—improve its immune escape abilities, experts have said, and probably account for recent modest increases in hospital admissions in Japan, New Zealand, South Korea, the UK, and the US.

The omicron EG.5 variant “has shown increased prevalence, growth advantage, and immune escape properties,” according to the most recent risk analysis by the World Health Organization, but “there have been no reported changes in disease severity to date.”

In the week to 23 July, the EG.5 lineage accounted for 17.4% of test samples sequenced around the world, up from 7.6% four weeks earlier, said WHO. Of these samples, 88% were a subvariant called EG.5.1, which carries an extra spike mutation.

The EG.5 lineage has been reported in 51 countries and EG.5.1 is on course to supplant XBB.1.5 (sometimes called “kraken”) which first appeared in late 2022, and XBB.1.16 (“Arcturus”), which appeared early this year, as the world’s most common subvariant.

In China, EG.5 and its subvariants accounted for 24.7% of covid infections in the third week of June, and 45% a month later, according to WHO.

The EG.5 lineage probably overtook XBB.1.16 last week in the US, according to Centers for Disease Control and Prevention (CDC) projections based on current trends, accounting for 17.3% of US infections at the beginning of August. That represents a near doubling of EG.5 cases in two weeks.

The UK Health Security Agency estimated that EG.5 and its subvariants accounted for 14.6% of infections as August began in the UK (95% confidence interval 9.1 to 22.4).

**Small waves**

Covid hospital admissions in the US are up 40% from the lows seen in June, and covid admissions in England rose 76% from 21 July to 4 August. But the overall numbers in both countries are still low compared with previous peaks and even to most of the troughs during the pandemic. The past week saw 10,320 covid admissions in the US, compared with 150,674 at the height of the third wave in January 2022.

The only country experiencing case numbers comparable with previous waves is South Korea, where daily new cases reached 65,000 last week. But this fourth wave is South Korea’s smallest yet, in both cases and deaths, and appears now to have peaked.

New Zealand has the greatest density of new covid cases after South Korea, but on 15 August it dropped its last pandemic restrictions, removing requirements to isolate for seven days and to wear masks in hospitals.

WHO last week raised the classification of EG.5 and its sublineages from “variant under monitoring” to “variant of interest,” a designation it shares with BA.2.75, which has not proliferated, and with XBB.1.5. No variant currently meets the criteria to be a “variant of concern.” WHO estimates the current public health risk from all these variants, including EG.5, as “low.”

**FLip threat**

Experts warn, however, of a future threat from mutations seen in EG.5, also found in some rarer variants of the XBB.1.5 family and other lineages, which can help the virus bind to cell receptors and reduce the number of antibodies the immune system produces to fight it.

The L455F and F456L mutations are nicknamed FLip mutations because they switch the positions of two amino acids on the spike protein labelled F and L. These mutations were predicted months ago as a likely consequence of the widespread use of monoclonal antibodies to treat covid.

The EG.5 variant descends from and resembles the still circulating XBB.1.9.2 subvariant, but with the addition of one FLip mutation, F456L. Its subvariant EG.5.1 carries a further spike mutation called Q52H. The role played by Q52H is still unclear, but it appears to boost potency, as this subvariant has already overtaken its progenitor.

The EG.5 lineage accounts for 49.1% of the circulating virus with one or both FLip mutations, according to WHO’s risk assessment. But there are now more than 20 subvariants of XBB and of other lineages that also carry FLip mutations. These include subvariants of XBB that carry both FLip mutations which, in laboratory testing, outperformed EG.5.1 at capturing cells and evading immune response. These XBB+L455F+F456L subvariants, yet to be assigned numbers, account for a small but rising number of cases.

“This certainly suggests this evolution of the virus will be more troubling than EG.5.1 and we can expect it to show further growth advantage in the weeks ahead,” wrote Eric Topol, of Scripps Research in California, in an analysis of the FLip threat.

“To be clear, we are not looking at an ‘omicron event’ now, whereby there will be a dramatic increase in transmission and adverse outcomes because of a boatload of new mutations,” wrote Topol. But the new changes “are a signal that there’s more to come with SARS-CoV-2.”
New vaccines

New versions of the Moderna, Novavax, and Pfizer boosters, expected in the coming weeks, were designed to work against XBB.1.5, a close cousin of EG.5's ancestor XBB.1.9.2. They are expected to offer better protection than existing vaccines against the EG.5 lineage. Antiviral drugs like nirmatrelvir/ritonavir (Paxlovid) also remain effective.

“Right now, viruses are still susceptible to our vaccine, they’re still susceptible to our medicines, they’re still picked up by the tests,” said CDC director Mandy Cohen. “So all of our tools still work as the virus changes.”

1 World Health Organization. EG.5 initial risk evaluation. 9 August 2023. www.who.int/docs/default-source/coronaviruse/09082023eg.5_ire_final.pdf
2 Mahase E. Covid-19: What do we know about XBB.1.5 and should we be worried? BMJ 2023;380. doi: 10.1136/bmj.p153 pmid: 36657748
3 Looi MK. What do we know about the Arcturus XBB.1.16 subvariant? BMJ 2023;381. doi: 10.1136/bmj.p1074 pmid: 37192774
6 Topol E. The virus is learning new tricks and we humans keep falling behind. 6 August 2023. https://erictopol.substack.com/p/the-virus-is-learning-new-tricks.

This article is made freely available for personal use in accordance with BMJ’s website terms and conditions for the duration of the covid-19 pandemic or until otherwise determined by BMJ. You may download and print the article for any lawful, non-commercial purpose (including text and data mining) provided that all copyright notices and trade marks are retained.