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Subvariant ‘soup’ may drive wave

The coronavirus subvariants BQ.1.1 and XBB may spread more readily than the original omicron variant and could evade prior immunity to some extent, writes Carissa Wong

Despite winter approaching in the northern hemisphere and mixed vaccine availability worldwide, the numbers of reported covid-19 cases and deaths are declining globally. As of the week ending 23 October, reported cases were down 15 per cent on the previous seven days, while deaths had declined by 13 per cent.

However, a soup of new coronavirus subvariants looks set to drive a new wave of infections across Europe and the US this November, says Christina Pagel at University College London. Many other parts of the world are already experiencing, or coming out of, these waves.

Until recently, the covid-19 pandemic jumped from one variant to the next, such as from delta to omicron, says Moritz Gerstung at the University of Heidelberg, Germany.

“Typically, a new variant came and displaced all or most other preceding lineages very quickly, but now we’re seeing a real mix of subvariants, with much more incremental changes that result from them acquiring a portfolio of mutations all over the viral genome,” he says.

High levels of immunity due to vaccination or from previous infection are creating a selection pressure towards immune-avoiding variants.

Earlier in the pandemic, quick lineage jumps occurred as the coronavirus got better at infecting cells, says Gerstung. Now that ability is optimised, smaller mutations are helping the virus to evade immunity, he says.

Perhaps one of the most concerning subvariants is BQ.1.1, a descendant of the omicron BA.5 subvariant BQ.1. Between 3 and 9 October, BQ.1 and its descendants made up 6 per cent of the SARS-CoV-2 coronavirus sequences submitted to the GISAID global viral database. They have now been detected in 65 countries.

In France, BQ.1.1 already makes up around half of the sequenced cases and it has probably reached that point before the rest of Europe, but perhaps not much earlier, says Gerstung. BQ.1.1 cases roughly double every week, so it quickly becomes widespread, he says.

BQ.1.1 may also account for most of the covid-19 infections in Africa, where the subvariant was first identified in Nigeria in July. However, limited testing makes it hard to know, says Gerstung.

“Out of all of the ‘soup’ variants, BQ.1.1 and XBB look like the ones with the potential to beat out the rest”

The subvariant’s rapid spread is probably due to six mutations that alter the surface of the spike protein that the virus uses to enter cells. Vaccines rely on this protein to bring about an immune response.

Early research suggests that BQ.1.1’s mutations enable it to evade neutralising antibody responses generated by vaccines and prior infections. “We see a fairly decent correlation between the number of mutations in different lineages and their rate of spread,” says Gerstung. “BQ.1.1 has among the highest number of immune-avoiding mutations.”

BQ.1.1’s advantage is more likely to be due to its ability to evade immunity than to it being better at infecting cells, according to both Pagel and Gerstung.

Another omicron subvariant, XBB, has particularly taken hold in India, where it was first identified, and now accounts for up to a third of the country’s reported SARS-CoV-2 infections.

“Out of all of the current ‘soup’ variants, BQ.1.1 and XBB look like the ones with potential to beat out the rest,” says Pagel.

XBB arose from a so-called recombination event in which two descendants of the omicron subvariant BA.2 infected the same cell and exchanged genetic material, forming a hybrid subvariant with seven key mutations for evading immunity – more than any other subvariant currently in circulation.

Being infected by two or more subvariants at once may result in a higher risk of severe illness. However, the bigger concern is that recombination could drive mutations that may cause new waves of covid-19 infections, says Pagel.

XBB quickly spread from India to Singapore, where – with its descendant XBB.1 – it drove a wave of infections that peaked around mid-October. It is now travelling through the rest of Asia.

Between 3 and 9 October, XBB comprised up to 1.3 per cent of the sequences submitted to GISAID. It has now been detected in 35 countries.

According to the World Health Organization (WHO), there is early evidence of a higher reinfec­tion risk with XBB, compared with other omicron subvariants, among people who caught covid-19 before omicron became dominant.

It is unclear whether an XBB infection protects against BQ.1.1, or vice versa, because they have very different mutations, says Gerstung.

“My personal opinion is an infection with BQ.1.1 should provide good immunity against the ancestral forms of the virus [BA.2 and BA.5] closely related to BQ.1.1, but XBB is very different to BQ.1.1, so it’s hard to say,” he says.

To date, there is no substantial evidence to suggest that XBB or BQ.1.1 cause more severe illness than the original omicron variant, according to the WHO.

And while BQ.1.1 is currently more prevalent than XBB, this may not mean that the former will outcompete the latter.

“There is a scenario where they could both become widespread,” says Gerstung.