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NEWS ANALYSIS

Covid-19: The E484K mutation and the risks it poses

The mutation E484K, first identified in the South African SARS-CoV-2 variant, has now been identified in the UK fast-spreading variant, prompting fears the virus is evolving further and could become resistant to vaccines. Jacqui Wise looks at what we know so far

Jacqui Wise

What do we know about the E484K mutation?

The E484K mutation is not a new variant in itself, it's a mutation which occurs in different variants and has already been found in the South African (B.1.351) and Brazilian (B.1.1.28) variants. The mutation is in the spike protein and appears to have an impact on the body's immune response and, possibly, vaccine efficacy. On 1 February, Public Health England (PHE) announced that the Covid-19 Genomics (COG-UK) consortium had identified this same E484K mutation in 11 samples carrying the UK variant B.1.1.7 (sometimes called the Kent variant), after analysing 214 159 sequences.[1]

Where has it been identified in the UK?

PHE confirmed to *The BMJ* that they have now identified 11 cases of the UK B1.1.7 variant carrying the E484K mutation around the Bristol area and 40 cases of the original SARS-CoV-2 virus carrying the same E484K mutation in the Liverpool area. Public health officials are carrying out enhanced contact tracing, additional laboratory analysis, and testing in these areas.

Is this mutation something to worry about?

E484K is called an escape mutation because it helps the virus slip past the body's immune defences. Ravindra Gupta at the University of Cambridge and colleagues have confirmed that the new B.1.1.7 plus E484K variant substantially increases the amount of serum antibody needed to prevent infection of cells.[2] We already know that the B.1.1.7 variant is more transmissible so a combination of a faster spreading virus that is also better at evading immunity is worrying—if it isn't stopped it would outcompete the older B.1.1.7 variant.

Another concern is that the South African variant might be able to more efficiently reinfect people who have previously been infected with the original form of the virus. Lawrence Young, a virologist and professor of molecular oncology at Warwick University, said, "This is likely to be, in part, because the E484K mutation may weaken the immune response and also impact the longevity of the neutralising antibody response. So B.1.1.7 variants carrying the E484K mutation may be more efficient at reinfection."

Will vaccines work against these emerging variants?

There has been research showing that the current vaccines work against the UK B.1.1.7 variant without the E484K mutation. However, recent clinical trials by Novavax and Johnson & Johnson showed that their new vaccines were less effective in South Africa compared with the UK or US, which is presumably because of the high level of virus carrying the E484K mutation. Even so, Novavax reported a 60% efficacy of their vaccine in South Africa which is still a fairly good response, equivalent to that of the influenza vaccine.[3] And scientists say that vaccines can be redesigned and tweaked to be a better match for the new variants in a matter of months. The Oxford AstraZeneca team, for example, announced they were already looking at updating their vaccine to make it more effective against the mutations that are being seen and it could be available by the autumn. It is possible it could take the form of a one dose booster which is updated and rolled out every year.

What is the UK doing to monitor the spread of variants?

The UK has identified 105 cases of the South African variant B.1.351, so far. Most could be linked to travel, but 11 cases could not, meaning it is spreading within the local community. As a result the government announced it would carry out additional surge testing and sequencing in eight postcode areas in England.[4] This is likely to be the tip of the iceberg, however, as less than one in 10 samples from people who test positive are sequenced and many people never get tested in the first place.

Is monitoring good enough?

The UK has carried out nearly half of all SARS-CoV-2 genome sequences deposited to the global database, GISAID. A spokesperson for the COG-UK consortium said that since the beginning of the pandemic they had conducted genome sequencing on about 7% of positive test samples and this is increasing now as case numbers fall and capacity is increasing. This is the highest in Europe, apart from Denmark which announced they will soon test all positive covid-19 test swabs for the presence of variants. Globally, however, genomic surveillance of SARS-CoV-2 remains patchy. For example, the US sequences less than 1% of new samples and many countries, especially in Africa, have no sequencing data at all.

Is the UK sharing its capacity to carry out genomic testing?

On 26 January the UK government announced it was launching the New Variant Assessment Platform to offer genomics expertise to identify new variants of the virus to countries which do not have the resources to do so.[4] This will be led by PHE working with academic partners and the World Health Organization's SARS-CoV-2 Global laboratory working group.[5]

How can we stop new variants emerging?

The SARS-CoV-2 virus makes around one or two mutations a month. This sounds quite a low number, and is in fact lower than for other viruses, including influenza. The more the virus circulates, however, the more opportunity it has to change. So anything that can be done to suppress spread of the virus will help to limit new variants emerging, including distancing, mask wearing, and handwashing.

Will closing the UK borders help?

From 15 February UK residents and Irish nationals travelling to the UK from 33 "red list" countries will have to quarantine in a hotel for 10 days. Non-UK travellers are currently banned from entry. However, Labour has criticised the fact that this measure will only be in place 50 days after the first South African variant was identified in the UK and are also calling for the scheme to be extended to all international travellers. Jonathan Stoye from the Francis Crick Institute said, "Under conditions of very high levels of virus replication even the most stringent of border controls, although they may delay spread, are unlikely to prevent the appearance of new variants."

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3 Mahase E. Covid-19: Novavax vaccine efficacy is 86% against UK variant and 60% against South African variant. *BMJ* 2021;372:n296. doi: 10.1136/bmj.n296 pmid: 33526412

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5 Department of Health and Social Care. Press release: UK to support rest of the world to find covid-19 virus variants. February 2021. www.gov.uk/government/news/uk-to-support-rest-of-the-world-to-find-covid-19-virus-variants.