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NEWS BRIEFING

Covid-19: Why are age and obesity risk factors for serious disease?

Worldwide more than 41 million people have now been infected with SARS-CoV-2 and over a million people have died. But what makes this virus so difficult to control, and why are some people more at risk than others? **Elisabeth Mahase** reports

Elisabeth Mahase

Why is it so hard to stop SARS-CoV-2 spreading?

Paul Lehner, professor of immunology and medicine at the University of Cambridge, says that unlike the original SARS coronavirus or influenza, people with SARS-CoV-2 are most infectious before they become unwell, normally about a day before they develop symptoms.

"So you're maximally transmitting virus while you're feeling well," he told a Science Media Centre briefing in London on 22 October. "This is a really brilliant evolutionary tactic of the virus. It means you can be out at the races, in a pub, singing in the church choir, at a matriculation—you're feeling well.

"This is a hit and run virus . . . The question then becomes: how can you make so much virus and yet feel well?"

Lehner explains that the answer lies in the virus's ability to switch off cells' natural response to it. "SARS-CoV-2 knows all about interferons. It has to, because it's super-sensitive to them. So it switches off the cells ability to make them, and it does this really well. In fact, it does it so well that you don't even know you're ill," he says.

Interferons are proteins released by cells as a signal that a virus is present. In essence, they tell nearby cells to increase their defences. Lehner says that recent studies looking at cells infected by the virus show you can't actually tell which ones are infected until you stain them, at which point you see they are "screaming with the virus."

So can we do anything about this? Lehner says, "Yes, but we have to get better at asymptomatic screening."

Why is obesity a risk factor for severe covid-19?

In July Public Health England estimated that having a BMI of 35 to 40 could increase a person's chances of dying from covid-19 by 40%, while a BMI greater than 40 could increase the risk by 90%.¹ But why is this?

Stephen O'Rahilly, director of the Medical Research Council's Metabolic Diseases Unit at the University of Cambridge, also speaking at the briefing, said, "Two things happen when obesity occurs: the amount of fat increases, but also you put fat in the wrong places. You put it in the liver and in skeletal muscle. And that disturbs metabolism. The key disturbance

is that you get very high levels of insulin in the blood."

This disturbance is associated with a range of abnormalities, including increases in inflammatory cytokines and a reduction of a molecule called adiponectin that directly protects the lungs, he says.

It's also possible that fat increases in the lung itself, which may disturb how the lung handles the virus, he adds. "The simple stuff you read about—big chest, big bellies, et cetera—is all grossly oversimplistic. What is really going on is metabolic, and we know that because if we look at genetic markers for the metabolic disturbance they are much more closely related to the bad outcomes than genetic markers for obesity itself," O'Rahilly says.

Why is age a risk factor for severe covid-19?

The US Centres for Disease Control and Prevention has said that eight in 10 covid-19 related deaths reported in the country have been among people aged 65 years or over.² Meanwhile, in the UK just being 70 years old or over puts someone into the medium risk covid-19 group.

Tracy Hussell, director of the Lydia Becker Institute of Immunology and Inflammation at the University of Manchester, says, "Studies have shown that age alone is the most significant risk factor for severe disease, and generally this is the same with other coronaviruses and influenza viruses that affect the elderly."

She says this could be because of the increased likelihood that a person will have comorbidities in older age, many of which are linked to poorer covid-19 outcomes. It may also be due to the medications that some of these patients take for their comorbidities, an area where Hussell thinks there is a lot more to learn.

However, it may also be due to the ageing immune system. "[In older age] the viral alert signals are much slower. And if you mount a very slow immune response, then you end up with greater viral replication. The immune cells that also take up the virus, the macrophages, are known to be slower in age. And this decline in the immune function is quite well known; it's called immune senescence," she explains. As we age, the thymus, which sits just above the heart and pumps out T cells, shrinks in size, decreasing the number of T cells it releases. This in turn affects many other aspects of the immune system.

Could old age reduce the effectiveness of a vaccine?

“Yes. Age will certainly affect a response to a vaccine, because a vaccine is trying to induce protective immunity,” says Hussell. “The immune system decreases with age, and so recognition and response to a vaccine are also reduced. The other thing is that a lot of old people are taking anti-inflammatory medications, and these may reduce antivaccine immunity as well.”

- 1 Mahase E. Covid-19: England's obesity strategy will fail without tackling social factors, warn doctors. *BMJ* 2020;370:m2994. doi: 10.1136/bmj.m2994 pmid: 32718928
- 2 Centers for Disease Control and Prevention. Coronavirus disease 2019 (covid-19): Older adults. Sep 2020. <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/older-adults.html>.

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