

'Half-measure' virus vaccine intrigues experts

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Clinical trials suggested that an initial half-dose was better than a full one

Evidence suggesting an initial half dose of the vaccine being developed by drugs firm AstraZeneca and the University of Oxford is more effective than a full dose is counterintuitive, and even took the

researchers by surprise.

Why would less be better than more when it comes to triggering an [immune response](#)?

Andrew Pollard, the director of the Oxford Vaccine Group, described the findings from the Phase 3 clinical trial as "intriguing".

They showed that the [vaccine](#) had an efficacy of 62 percent among the people given two full doses a month apart.

But this rose to 90 percent for another group who received a half-dose first and then a [full dose](#) after a month.

"I think all of us expected that the two high doses would be the best response," said Pollard, who noted researchers had only seen the details of the results over the weekend and would now start digging into the data.

"We think that by giving a smaller first dose, that we're priming the immune system differently. We're setting it up better to respond," he told a press briefing.

Sarah Gilbert, professor at Oxford's Nuffield Department of Medicine, said the better result with a smaller initial dose could be because this better "mimics what happens in a real infection".

Essentially a vaccine uses a safe method to trick the immune system into believing it is dealing with a dangerous infection, triggering an immune response and an [immune memory](#) that can activate if the body comes across the real pathogen.

"It could be that by giving a small amount of the vaccine to start with

and following up with a big amount, that's a better way of kicking the immune system into action and giving us the strongest immune response," Gilbert told reporters.

'Trojan Horse'

The Astra/Oxford vaccine employs what is known as a "viral vector", using engineered viruses to deliver genetic cargo into cells, giving them instructions on how to fight SARS-CoV-2.

The strategy uses the transporting virus as a "Trojan Horse", said Colin Butter, Associate Professor at the University of Lincoln.

It is "complex and usually achieved experimentally: a luxury not available in the present situation".

The technology itself may be the reason why an initial half-dose could work better, according to several scientists commenting on the results, with the immune system acting against the virus being used as a delivery vehicle.

"It may seem confusing that a higher initial dose gives a less favourable response, but this may just be due to a residual response in some patients to the disabled 'vehicle'," a snippet of chimpanzee virus used to deliver the vaccine "payload", said Stephen Griffin, Associate Professor in the School of Medicine, University of Leeds.

But he said this could be "easily fixed" by using the adjusted dose.

Pollard said researchers would be looking to find out if the issue was the quantity or quality of the immune response.

He added that while with almost all single dose vaccines the higher the

dose you give the better, methods based on priming the [immune system](#) first—and then later giving a booster—can work differently.

This is particularly the case with babies and infants, where you might have different numbers of priming doses, he said.

"I think the difference is that we're not that used to dealing with infections like this [coronavirus](#), which adult humans have never seen before," Pollard said.

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