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Omicron thwarts some of the world's most-used COVID vaccines

Inactivated-virus vaccines elicit few, if any, infection-blocking antibodies — but might still protect against severe disease.

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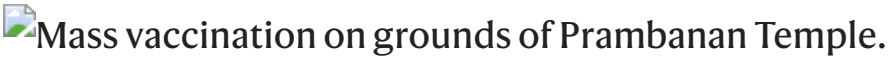

A man in Javanese traditional dress receives a dose of the Sinovac COVID-19 vaccine at a temple in Yogyakarta, Indonesia. Credit: Ulet Ifansasti/Getty

The world's most widely used COVID-19 vaccines provide little to no protection against infection with the rapidly spreading Omicron variant, laboratory evidence suggests.

Inactivated-virus vaccines contain SARS-CoV-2 particles that have been chemically treated to make it impossible for them to cause an infection. Stable and relatively easy to manufacture, such vaccines have been distributed widely as part of China's global vaccine diplomacy, helping them to become the jab of choice in many countries. But a multitude of experiments show that they are consistently hobbled by Omicron.

Many people who receive two jabs of an inactivated vaccine fail to produce immune molecules that can counter Omicron transmission. And even after a third dose of an inactivated vaccine, an individual's levels of 'neutralizing' antibodies, which provide a potent safeguard against viral infection of cells, tend to remain low. A third shot of

another type of vaccine, such as those based on messenger RNA or purified proteins, seems to offer better protection against Omicron.

The findings are prompting many scientists and public-health researchers to re-evaluate the role of inactivated vaccines in the global fight against COVID-19.

"At this stage, we have to evolve our ideas and adjust our vaccination strategies," says Qiang Pan-Hammarström, a clinical immunologist at the Karolinska Institute in Stockholm.

Billions served

Inactivated vaccines were instrumental in the campaign for worldwide vaccine coverage last year. They include those made by China's Sinovac and Sinopharm, which together account for nearly 5 billion of the more than 11 billion COVID-19 vaccine doses delivered globally so far, according to numbers compiled by data-tracking firm Airfinity in London (see 'Many shields against COVID-19'). More than 200 million doses of other inactivated shots such as India's Covaxin, Iran's COVIran Barekat and Kazakhstan's QazVac have also been delivered.

Source: Data from Airfinity

Such products remain crucial for preventing hospitalization and death from COVID-19. And they can still serve a valuable immune-priming function for as-yet unvaccinated individuals.

But an early sign that inactivated vaccines might not hold up to Omicron came in December, when researchers in Hong Kong analysed blood from 25 recipients of the two-dose CoronaVac vaccine, made by the Beijing-based company Sinovac. Not a single person had detectable neutralizing antibodies against the new variant — raising the possibility that all the participants were highly vulnerable to Omicron infection[1].

Sinovac has disputed this finding, pointing to internal data showing that 7 out of 20 people who had received the company's vaccine had tested positive for antibodies capable of neutralizing Omicron. Other studies involving people immunized with Covaxin[2], which is made by Bharat Biotech in Hyderabad, India, and BBIBP-CorV[3], produced by state-owned Chinese company Sinopharm, in Beijing, have also concluded that inactivated vaccines retain some potency against Omicron — although, as researchers at the Translational Health Science and Technology Institute in Faridabad, India, put it in their study[2], the immune responses remain "sub-optimal". The work on Covaxin has not yet been peer reviewed.

Immunity top-up

A third dose of inactivated vaccine helps to restore neutralization activity for many individuals. A 292-person study by researchers at the Shanghai Jiao Tong University School of Medicine in China, for example, identified neutralizing antibodies against Omicron in just 8 people tested 8–9 months after an initial course of BBIBP-CorV. After another shot of the same vaccine, that number rose to 228[4]. This work has not yet been peer reviewed.

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Levels of neutralizing antibodies in each person's blood remained low. But as molecular virologist Rafael Medina at the Pontifical Catholic University of Chile in Santiago points out: "There are other parts of the immune response that are also playing a role." T cells destroy infected cells; B cells remember past infections and strengthen immune responses for the future; and binding antibodies contribute to viral control.

In a preprint published in December[5], Medina and his co-authors — led by immunologist Galit Alter at the Ragon Institute of MGH, MIT and Harvard in Cambridge, Massachusetts — showed that people immunized with CoronaVac maintain non-neutralizing antibodies that both bind Omicron and assist immune cells in gobbling up infected cells.

On the defensive

Those kinds of result show that recipients of inactivated vaccines, although not necessarily protected against infection by Omicron, should still be shielded from the worst ravages of COVID-19 triggered by the variant, says Murat Akova, an infectious-disease specialist at Hacettepe University School of Medicine in Ankara.

All the same, an extra dose of vaccine could offer some much-needed immune insurance. Experiments conducted by Pan-Hammarström and her colleagues found that, after two doses of inactivated vaccine, an mRNA top-up hoists levels of binding antibodies, memory B cells and T cells[6]. And studies of samples from China[3,7] and the United Arab Emirates[8] have shown that a protein-based booster triggers higher numbers of neutralizing antibodies than does a third shot of an inactivated vaccine. Many of these results have not yet been peer reviewed.

Double boost?

But a single booster with a different type of vaccine might not be enough to subdue Omicron, warns Akiko Iwasaki, a viral immunologist at Yale School of Medicine in New Haven, Connecticut.

Iwasaki and her co-authors studied blood samples from 101 individuals who received two doses of CoronaVac followed by an mRNA booster. Before the boost, the samples showed no detectable Omicron neutralization. Afterwards, 80% of analysed samples showed some Omicron-blocking activity[9]. But the quantities of antibodies that had Omicron-neutralizing potential were not much greater in this group than in a separate population that had received two doses of mRNA vaccine and no booster. The work has not yet been peer reviewed.

Before the Omicron variant emerged, Iwasaki had been advocating single mRNA boosters for recipients of inactivated vaccines. "We were really celebrating how wonderful this strategy is," she says, "and then — boom! — Omicron hit." Now, she thinks these people probably need two extra jabs.

"The bar keeps being raised by the variants," Iwasaki says. "We're playing catch up all the time."

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UPDATES & CORRECTIONS

Correction 13 January 2022: The original version of the graphic showed an incorrect number of vaccine doses delivered in the 'Other' category. This has now been corrected.

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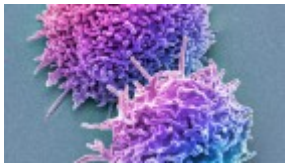

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