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# FDA To Stretch Monkeypox Vaccine Supply via Intradermal Injection

The newly authorized intradermal vaccination only requires one-fifth of the usual vaccine dose. This will help stretch out the limited vaccine supply, experts say, but only if healthcare personnel receive sufficient training.

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*Update (August 23): Yesterday, health authorities in the UK announced that the country will begin offering smaller, intradermally injected doses of the monkeypox vaccine to stretch supplies. The decision follows a similar proclamation from the European Medicines Agency. However, healthcare professionals in th US are finding that vials contain a smaller volume of vaccine than expected, leading to less of a bene from applying this method, STAT reports.*

ABOVE:
The monkeypox virus, shown here, spreads through close, skin-to-skin contact.


As monkeypox continues to spread across the US, the supply of the vaccine used to prevent it remains tight. On August 9, the US Food and Drug Administration (FDA) authorized a new strategy that could allow the country to vaccinate five times as many people using its limited stock. This strategy, known as an intradermal vaccination, only uses one-fifth of the traditional vaccine do and is injected just underneath the skin's surface instead of into the underlying fat.

The inner layer of skin is rich in highly specialized immune cells known as dendritic cells that are sensitive to microbes and allergens, says William Schaffner, an infectious disease expert at the Vanderbilt University Medical Center. These cells act as the body's surveillance system by capturing invading antigens and presenting them to other immune cells, such as T cells, which then launch ar attack.

These dendritic cells are activated when the vaccine is injected between outer and inner layers of sk which initiates a strong immune response. This mechanism, experts say, is what helps build immun against monkeypox even with one-fifth of a regular dose of Jynneos, the only vaccine that the FDA l specifically authorized for monkeypox in the US. "That means because you inject a really small amount, you can vaccinate more people with a limited supply" Schaffner adds. "And that's the inten here."

This technique isn't new, he adds. Intradermal vaccination dates back to the early 1900s, when it wa first tested on a large scale with the smallpox vaccine. In that test, an extremely thin, two-pronged, stainless steel needle was dipped into the vaccine solution and then repeatedly poked into the skin o the upper arm, introducing the solution into the body and raising a red bump.

> **As it happens, performing intradermal inoculation is the most difficult way to inoculate anyone. It's less an inoculation than it is, in my opinion, an art form.**
>
> —William Schaffner, Vanderbilt University Medical Center

"It is the only vaccine to be used to successfully eradicate a human disease around the world," says Mark Prausnitz, director of the Cent for Drug Design, Development and Delivery at Georgia Tech University. "So the smallpox vaccine is great success story" of this technique.

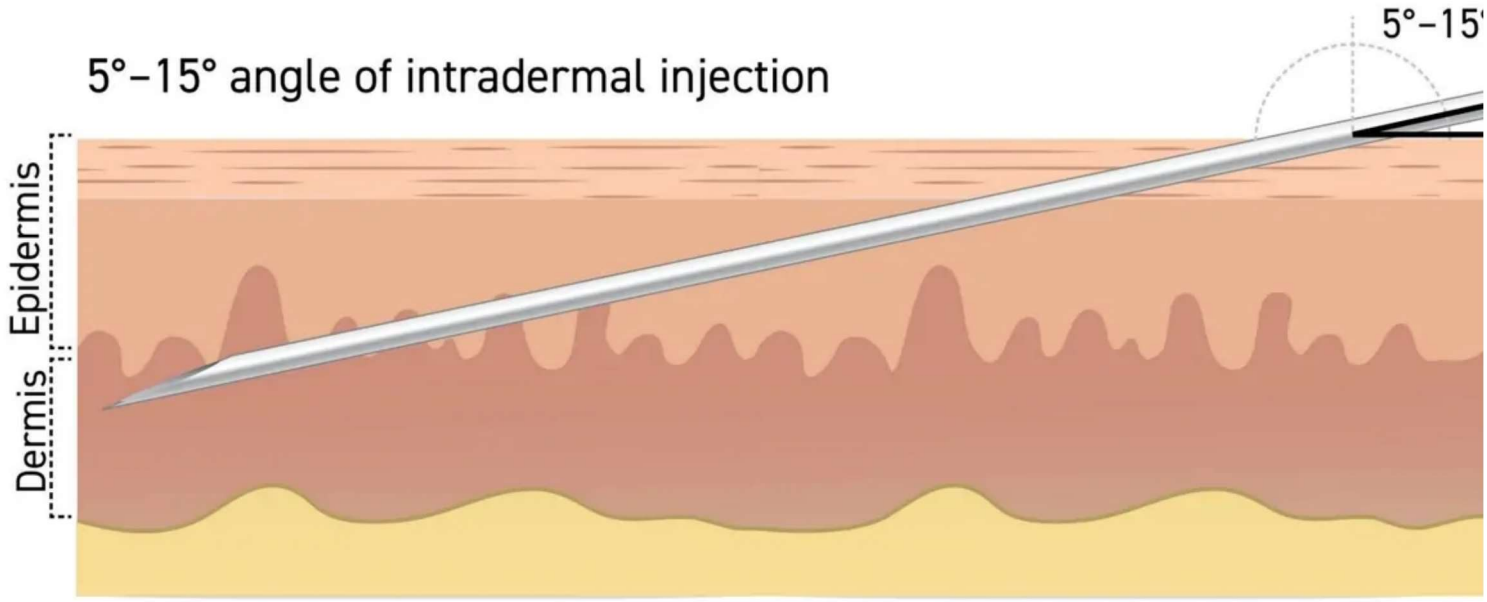
Today, intradermal vaccination is used to protect against diseases like rabies, hepatitis B, and tuberculosis.

In 2015, a clinical trial using a smallpox vaccination compared how the immune response generated with this approach compares with that of a traditional method of immunization where the vaccine i injected into the fat tissue under the skin. It was this study that found that both techniques offer comparable levels of antibodies—but only when the traditional method used five times as large a do as was used for an intradermal vaccine, because the quantity of dendritic cells is much lower in fat tissue.

This, according to Prausnitz, became the basis of FDA's recent emergency authorization for monkey vaccination, as the virus comes from the same family as smallpox. "That study is directly applicable

the very question we have now about whether you could do dose-splitting of that same kind of vacci for monkeypox," he says.

While experts say the scientific evidence behind the technique is sound, some, Schaffner included, h reservations about using the approach on a large scale for monkeypox vaccinations. "As it happens, performing intradermal inoculation is the most difficult way to inoculate anyone," he says. "It's less inoculation than it is, in my opinion, an art form."




The intradermal vaccination technique for monkeypox, illustrated here instructional material distributed by the C is the most difficult way to inoculate someone, experts say.

CDC.GOV

That's because the technique requires a fine needle and an even finer touch; the needle has to be slo inserted just under the skin at a 5 to 15 degree angle. If the needle isn't exactly positioned between t outer and inner layers of the skin, the vaccine can leak out of the injection site. But if it goes in too d and reaches the fat tissue under the skin, the small dose isn't sufficient to generate a strong immune response. In both scenarios, the recipient likely wouldn't develop sufficient protection against monkeypox infection.

Although hospitals routinely use intradermal injections for dermatological procedures and tuberculosis skin tests, the average nurse and doctor would need to receive special training before

performing the procedure, according to John Beigel, a microbiologist and infectious disease special at the National Institute of Allergy and Infectious Diseases (NIAID).

"There's an unfamiliarity for the nurses . . . for the last two months they have been giving it subcutaneously [into the fat tissue]," he tells *The Scientist*. "And now we're going to say, 'here's a different way to administer.'"

This creates a public health paradox, according to Schaffner. Intradermal vaccination is a potential to expand the limited supply of the monkeypox vaccine and make it available to more people. But doing so might take longer than would sticking with traditional vaccination, as training healthcare personnel takes time.

Schaffner and Beigel both say that the solution to this paradox would be manufacturing more vacci To Beigel, it appears the US healthcare system is playing catchup with the growing spread of monkeypox instead of being sufficiently prepared to vaccinate all the people who need it.

"There's a certain liberty that comes with getting ahead of the curve," he says. "We seem to be on the end."

However, Prausnitz says he finds of the potential to harness the skin's immune response to solve a problem exciting. In his opinion, where there's an urgent need to protect people, the risk is one wor taking.

"There is some uncertainty, but my sense would be that the decision taken is a right one," he says.

**Keywords:**

adipose tissue, dendritic cells, epidermis, FDA, health, history of science, immune response, **immunology**, infectious disease, injection, medicine, monkeypox, News, policy, **public health**, vaccination, vaccine

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