Next generation flu shots could be mRNA technology-based

The rapid development of mRNA-based COVID vaccines has sparked fresh interest in earlier efforts to produce new and hopefully more effective flu shots with the same technology. Pfizer, Moderna, and Sanofi/Translate Bio each have an mRNA flu vaccine in clinical trials, and there are ten more candidates awaiting testing.

It's one thing to test a drug and quite another to commercialize it. The question, then, is will these next-generation flu shots be available any time soon? The answer is "yes," perhaps as soon as 2022. There are no guarantees when it comes to drug development, but here's what we know so far and why better flu shots are necessary.

The case for new flu vaccines

According to the CDC, we've made vaccines the same way for 70 years. Researchers grow and replicate "candidate vaccine viruses" (CVV) in chicken eggs, harvest and kill the viruses, then purify the antigens that will go into seasonal flu shots. Since 2012, CVVs have also been grown in cultured animal cells, reducing our dependence on eggs for vaccine production. The FDA has also approved a live attenuated influenza vaccine nasal spray made by a different manufacturing process, as well as a recombinant ("GMO," you could say) vaccine. The latter requires neither eggs nor animal cells; it contains the DNA for a surface protein called hemagglutinin (HA) found on influenza viruses. (The "H" is the letter found in the strain names, H3N1, etc.)

A July 2021 study found that the recombinant vaccine may provide better protection, measured as antibody-mediated immunity against HA, compared to its egg- and cell-based counterparts, though none of the shots were especially impressive. The CDC couldn't give an estimate for 2020-2021 because of low influenza virus circulation, but vaccine efficacy was just 39 percent in the 2019-2020 flu season.

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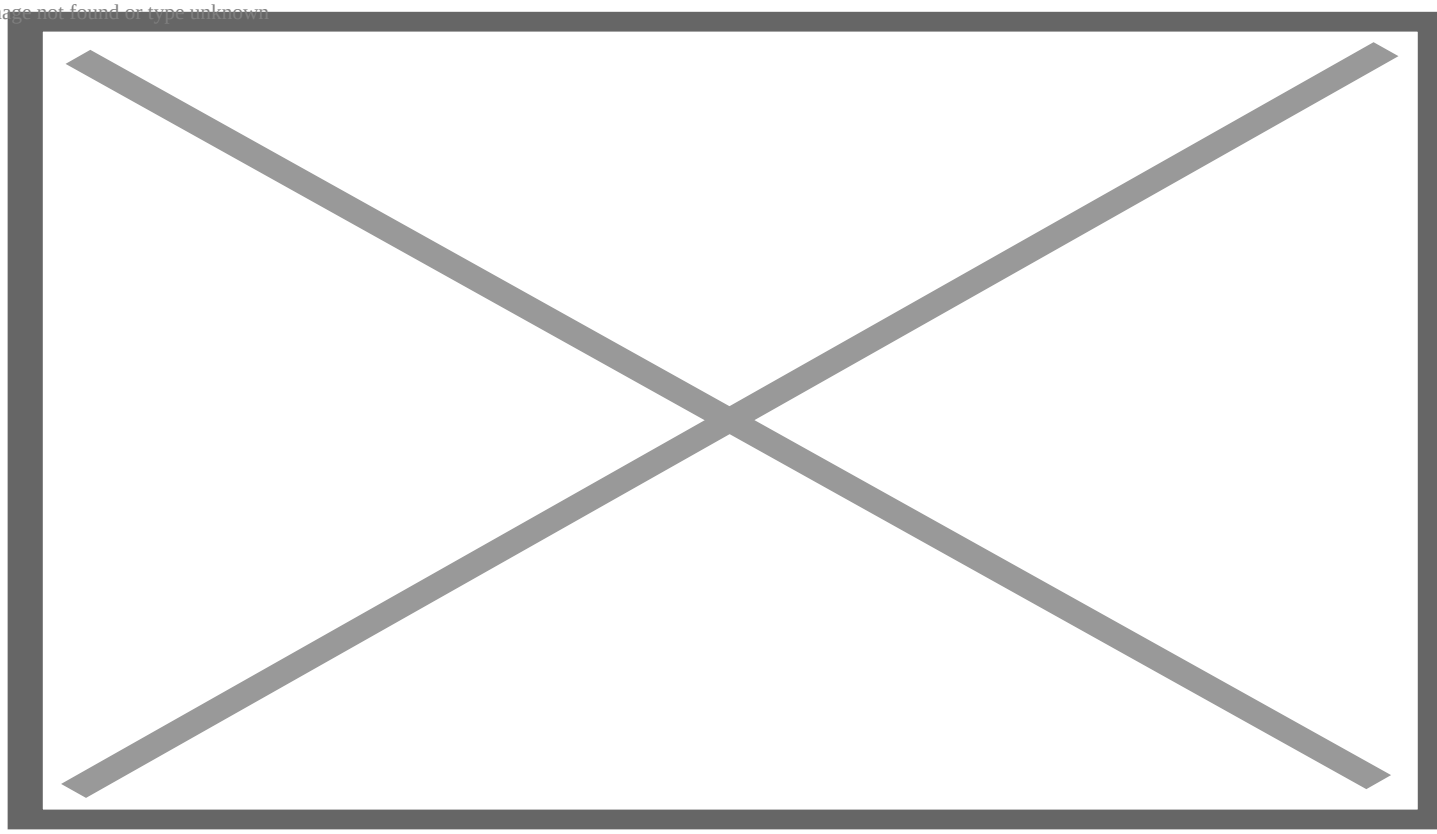

A laboratory technician injects Influenza A (H1N1) virus into a tray of embryonated hens' eggs. Credit: Oliver Bunic/Bloomberg/Getty Images

mRNA to the rescue?

Like the existing COVID vaccines, mRNA flu shots would contain genetic instructions for making certain antigens, priming your immune system to neutralize those proteins when they're attached to the circulating flu strains that can make you sick. There are several reasons why this approach would be a significant step forward; vaccine expert Dr. Ben Locwin outlined one of the most important in an email to ACSH:

> *It is possible to create an mRNA flu vaccine that encodes several different types of proteins, and instead of tri- or quadrivalent (protection from 3 or 4 strains), they could be decavalent (10 strains) or greater. Hemagglutinin (HA) continues to be a good target, because that's the singular protein that allows the influenza virus to attach to and infect the cell.*

Additionally, just like the COVID vaccines, these upgraded flu shots could be produced very quickly, giving manufacturers more time to choose the best flu strains to include in the vaccines and thus making them more effective. Right now, flu shots are formulated six to nine months before they're actually used so there's enough time to make large quantities of vaccine.

Beyond mitigating these production issues, The mRNA shots may even provide enough protection that we wouldn't have to get one every year. There's also a possibility that a fine-tuned mRNA platform would help scientists more effectively target a pandemic flu strain or even develop a universal flu vaccine.

Coming soon?

So, how close are we to mRNA flu shots? Some commentators have argued that drug companies don't have enough incentive to produce a new flu vaccine without government subsidies. That doesn't appear to be the case because several firms *are* working on new shots, building on research that goes back more than 30 years. Moreover, the path to approval for flu vaccines is relatively straightforward, which always makes it easier to develop new drugs. [1] Locwin summed up our progress toward mRNA flu vaccines in his email:

> *It's clear that we'll get to that future, as we're on the way now. But not all of these candidate vaccines are similar to a 'universal flu vaccine,' which specifically targets nuclear protein or perhaps the HA stem ('hemagglutinin stalk'), which rarely mutates and therefore could be much more stable targets for immunity (we call this an 'anti-stalk response'). There could reasonably be approvals for Flu Season 2022, given the uptake and track record of Moderna and Pfizer-BioNTech in the mRNA space, paving the way for POC (proof-of-concept) of this vaccine technology.*

Public acceptance

Effective mRNA flu shots will have no impact if the public refuses to take them, but I think there's a case for cautious optimism. While the media has spent the better part of two years crying crocodile tears about COVID misinformation and its influence on vaccine hesitancy, the vast majority of Americans have been fully vaccinated. [2] It will also be easier to make a compelling case for flu vaccines of the future if they offer better protection. The current shots range in efficacy from 10-60 percent because, "In many cases, we guess wrong," as one physician said of selecting flu strains for vaccines.

Nobody knows what the future holds, of course. All we can do is sit tight and wait for the clinical data on mRNA vaccines—and hope for the best.

Notes:

[1] Emphasis on "relatively." Getting the FDA to approve any drug is no picnic. [2] The media spent decades stoking vaccine hesitancy by giving widespread coverage to dishonest activists like Andrew Wakefield, originator of the debunked vaccine-autism link. Their sudden desire to champion vaccination

strikes me as disingenuous.

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