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Vaccine Viewpoint: Looking at Cell-Based Technology for Flu Prevention

ReachMD Announcer:
You're listening to ReachMD. This medical industry feature, titled "Vaccine Viewpoint: Looking at Cell-Based Technology for Flu Prevention," is sponsored by CSL Seqirus. Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
Compared to some past flu seasons, the early 2022/2023 season has proven to be more severe.[1] And while influenza burden varies widely from season to season,[2] is there a way we can mitigate this burden with alternative vaccine manufacturing processes?

Welcome to ReachMD. I'm your host Dr. Jennifer Caudle, and joining me to discuss cell-based influenza vaccine manufacturing, an alternative to traditional egg-based influenza vaccine production, is Dr. Ravi Jhaveri.

Dr. Jhaveri is the Division Head of Pediatric Infectious Diseases at the Ann & Robert H. Lurie Children's Hospital of Chicago, and Professor of Pediatrics at the Northwestern University Feinberg School of Medicine. Dr. Jhaveri, welcome to the program.

Dr. Jhaveri:
It's nice to be here.

Dr. Caudle:
Well, we're happy that you're here. So before we discuss influenza vaccine types and their manufacturing processes, can you give us a quick update on how the flu is affecting us both here in the United States and globally?

Dr. Jhaveri:
There was a rapid and steep increase in flu activity in the fall of 2022, which was quite a bit earlier than we usually see severe flu activity. Although the timing and duration of flu season has been less predictable since the start of the COVID pandemic,[3] flu is clearly back. In the 2022/2023 season, influenza activity peaked around late November/early December,[4] instead of the more usual timing sometime between December and February.[3] It's also important to remember though that the burden of influenza varies widely from year to year.[2]

That being said, the latest CDC data show that influenza resulted in 9 to 41 million illnesses, between 140,000 and 710,000 hospitalizations, and between 12,000 and 52,000 deaths annually between 2010 and 2020.[2] And on a global scale, we've seen up to 650,000 deaths per year.[5]

Lastly, what's further complicating things is the 2022/2023 season is that flu vaccine uptake rates in adults may be lower than in previous flu seasons, particularly at pharmacies and medical offices[6] and especially since the onset of the COVID-19 pandemic.

Dr. Caudle:
So then let's switch gears here and dive into influenza vaccine technology. What can you tell us about the traditional process?

Dr. Jhaveri:
So the good news is that vaccines have prevented between 39,000 and 105,000 hospitalizations and between 3,700 and 9,800 deaths each year over the last 10 years in the United States.[7]

But we have a few challenges working against us with traditional egg-based influenza vaccine production. First, we have to worry about

chicken egg quality and supply because embryonated egg supply may be compromised by avian influenza outbreaks.[8]

And in fact, an avian flu outbreak is occurring as we speak: within the last year or so, the CDC has reported more than 58 million cases of avian flu in the United States, which is affecting the poultry livestock industry.[9]

Second, not all influenza strains grow well in eggs.[10] And third, mutations may occur during the passage through the egg. [11]

So to explain further, the virus may need to adapt, or mutate, in order to grow well in eggs [12-14]—which is also known as egg adaptation.

And after the virus is injected into the egg, the hemagglutinin molecule on the surface of the virus may need to adapt to the avian cell receptors because they differ from the receptors found on mammalian cells.[15,16] And at this point, although the virus can now grow within avian cells the egg adaptive mutations that have occurred may make the vaccine virus different than the viruses circulating in the community.[15,16] This can be a cause of what's called "mismatch",[11] which may have an impact on vaccine effectiveness, or VE for short. Mismatch can also happen when the virus strain chosen by the WHO and FDA months in advance of flu season doesn't match the circulating strain, and this would be a mismatch due to what's known as antigenic drift.[11,15,16,17]

Even though vaccination is our best bet to help prevent influenza, egg adaptation is one factor that can have an impact on VE from one season to the next. [15]

Dr. Caudle:
Now as I understand it, there's an alternative manufacturing approach available for influenza vaccine production. So what should we know about this method?

Dr. Jhaveri:
Yes. So in addition to egg-based vaccine production, there's also a cell-based approach that has several benefits compared to the traditional process.

In this scenario, eggs aren't needed to produce the vaccine, and it has the potential to meet unexpected changes in vaccine demand.[18,19]

Additionally, this cell-based manufacturing method grows the virus in a continuous mammalial cell line instead of in eggs, and this allows for growth of a wide variety of influenza strains.[20,21]

Dr. Caudle:
And for those of you who are just tuning in, you're listening to ReachMD. I'm your host, Dr. Jennifer Caudle, and today I'm speaking with Dr. Ravi Jhaveri about the differences between egg-based and cell-based influenza vaccine manufacturing.

So Dr. Jhaveri, now that you've introduced the concept of cell-based vaccine manufacturing and some of its benefits, let's shift over to how the process is different than egg-based manufacturing. How would you describe this process?

Dr. Jhaveri:
So both manufacturing processes require the isolation and analysis of the circulating flu viruses, and based on this, reference strains are selected.[22]

But instead of passing those reference strains through eggs, they're grown in the continuous cell line as I mentioned earlier,[23] at which point candidate vaccine viruses are produced and standardized for manufacturing.[24]

Next, this virus is grown in the cells before being harvested in a serum-free media.[23]

After that, inactivation, purification, and formulation of the vaccine is the same process as in egg-based production.[22,23,25]

And what we've seen is that cell-culture-derived vaccine viruses tend to be a more accurate match to the WHO- and FDA-selected seed strains, potentially making them more effective against influenza infection during those seasons affected by egg adaptation.[14] While not every season is affected by egg adaptation, a strain mismatch occurred in seven out of the last 10 seasons in the U.S. Nearly half of these mismatches were caused by egg adaptation in the vaccine strains during vaccine production.[11,13,26-34]

Dr. Caudle:
So with that in mind, what cell-based influenza vaccines do we have available to us, and how do they compare versus egg-based vaccines in terms of clinical benefit and safety?

Dr. Jhaveri:
There's actually only one cell-based influenza vaccine available in the United States, and that's the FLUCELVAX® influenza vaccine, which is currently approved in the U.S. for use in persons 6 months and older.[35]

Now because influenza severity varies each year, it's helpful to look at both clinical trials and real-world evidence to get an overall picture of efficacy and safety.

ReachMD Announcer:
Data for FLUCELVAX® QUADRIVALENT are relevant to FLUCELVAX® because both vaccines are manufactured using the same process and have overlapping compositions.

Dr. Jhaveri:
In clinical trials, FLUCELVAX® QUADRIVALENT demonstrated absolute efficacy in children and adolescents 2 through 17, was proven non-inferior to a U.S.-licensed comparator based on immunogenicity and seroconversion for patients 6 months through 3 years.[35-37] Trials also showed absolute efficacy against culture-confirmed flu in adults 18 through 49 years.[35]

And finally, safety was established in both children and adults in these trials and was comparable to the respective comparators—that is, either flu or non-flu vaccines.[35-37]

And when we take a look at peer-reviewed real-world evidence between 2017 and 2020, especially in egg-adapted years, we see a trend for cell-based flu vaccines to have a greater clinical benefit compared to egg-based flu vaccines.[38,39]

Dr. Caudle:
Thanks for breaking all of that down for us, Dr. Jhaveri. But is cell-based vaccine production affected by any "adaptation" challenges like egg-based vaccines can be?

Dr. Jhaveri:
Actually, no. In fact, a recent publication dispels this myth that cell-based vaccine production is subject to similar "adaptation" complications as in egg-based vaccines.[40] In reality, continuous mammalial cell lines improve antigenic match between the vaccine and the WHO-selected virus strain, meaning the risk of mutations is very low. In MDCK cell lines, no adaptive mutations have been documented and where occasional mutations are observed, these are random and stochastic in nature and aren't driven by selective pressure during culture.[40]

Dr. Caudle:
Thank you. Now, unfortunately, we're almost out of time, but before we go, what conclusions can you draw from our conversation today?

Dr. Jhaveri:
Well, FLUCELVAX® has proven to be an option for persons 6 months and older. Also, data from different real world effectiveness studies from 2017 to 2020 suggest that, in seasons where egg adaptation occurs, FLUCELVAX® QUADRIVALENT has the potential to be more effective than traditional, egg-based flu vaccines.[38,39] Additionally, cell-based manufacturing seems to address some of the inherent challenges we see with traditional egg-based manufacturing.[14]

So, in my opinion, we have another viable alternative to traditional egg-based vaccines to help us combat the burden of flu for persons as young as 6 months old.[35]

And flu prevention should always be one of our top priorities as physicians.

Dr. Caudle:
That's a great comment for us to think on as we come to the end of today's program. I'd like to thank my guest, Dr. Ravi Jhaveri, for helping us better understand cell-based influenza vaccine manufacturing. Dr. Jhaveri, it was great speaking with you today.

Dr. Jhaveri:
Thanks for having me.

Dr. Caudle:
I'm your host Dr. Jennifer Caudle. Please stay tuned to hear some important safety information.

ReachMD Announcer:
FLUCELVAX® (Influenza Vaccine)

INDICATION AND IMPORTANT SAFETY INFORMATION

INDICATION AND USAGE

FLUCELVAX® is an inactivated vaccine indicated for active immunization for the prevention of influenza disease caused by influenza virus subtypes A and type B contained in the vaccine. FLUCELVAX is approved for use in persons 6 months of age and older.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Do not administer FLUCELVAX to anyone with a history of severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine.

WARNINGS AND PRECAUTIONS

If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give FLUCELVAX should be based on careful consideration of the potential benefits and risks.

Appropriate medical treatment must be immediately available to manage potential anaphylactic reactions following administration of FLUCELVAX.

Syncope (fainting) has been reported following vaccination with FLUCELVAX. Procedures should be in place to avoid injury from fainting.

After vaccination with FLUCELVAX, immunocompromised individuals, including those receiving immunosuppressive therapy, may have a reduced immune response.

Vaccination with FLUCELVAX may not protect all vaccine recipients against influenza disease.

ADVERSE REACTIONS

Data for FLUCELVAX QUADRIVALENT are relevant to FLUCELVAX because both vaccines are manufactured using the same process and have overlapping compositions.

In children 6 months through 3 years of age who received FLUCELVAX QUADRIVALENT, the most commonly reported injection-site adverse reactions were tenderness (28%), erythema (26%), induration (17%) and ecchymosis (11%). The most common systemic adverse reactions were irritability (28%), sleepiness (27%), diarrhea (18%) and change of eating habits (17%).

In children 4 through 8 years of age who received FLUCELVAX, the most commonly reported local injection-site adverse reactions were pain (29%) and erythema (11%). The most common systemic adverse reaction was fatigue (10%).

In children and adolescents 9 through 17 years of age who received FLUCELVAX, the most commonly reported injection-site adverse reactions were pain (34%) and erythema (14%). The most common systemic adverse reactions were myalgia (15%) and headache (14%).

In adults 18 through 64 years of age who received FLUCELVAX, the most commonly reported injection-site adverse reactions were pain (28%) and erythema (13%). The most common systemic adverse reactions were headache (16%), fatigue (12%), myalgia (11%) and malaise (10%).

In adults ≥65 years who received FLUCELVAX the most commonly reported injection-site reaction was erythema (10%). The most common systemic adverse reactions were fatigue (11%), headache (10%) and malaise (10%).

Other adverse events may occur.

To report SUSPECTED ADVERSE REACTIONS, contact CSL Seqirus at 1-855-358-8966 or VAERS at 1-800-822-7967 or www.vaers.hhs.gov.

Before administration, please see the full US Prescribing Information for FLUCELVAX.

ReachMD Announcer:

This program was sponsored by CSL Seqirus. If you missed any part of this discussion, visit ReachMD.com/IndustryFeature. This is ReachMD. Be Part of the Knowledge.

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