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Another influenza season in the shadow of the COVID-19 pandemic

The 2020 to 2021 influenza season took a backstage to the COVID-19 pandemic, when the COVID-19 vaccines were in their initial stages of distribution in the northern hemisphere. Although only 50% to 55% of US adults received the 2020 to 2021 influenza vaccination,^{1,2} influenza activity was very low compared with prior seasons,^{1,2} certainly the result of behavioral measures instituted to mitigate the COVID-19 pandemic.

With the current 2021 to 2022 influenza season coinciding with another increase of COVID-19 cases, lower COVID-19 vaccine uptake and relaxed mitigation measures in some areas of the United States have resulted in vaccine breakthroughs, increased hospitalizations, and an ominous milestone of more than 722,000 deaths.³

Vaccinations, in general, are helping ease the strain of the upcoming influenza season, with an estimated 62% of Americans experiencing immunity against COVID-19 as a result of prior infection or immunization.⁴ Further, a recent, retrospective cohort study involving 74,754 patients showed that COVID-19–positive patients were less likely to develop sepsis, stroke, deep venous thrombosis, require admission to the intensive care unit, or subsequent emergency department visits if they received influenza vaccination 2 weeks to 6 months prior to their COVID-19-positive diagnosis.⁵

■ US CENTERS FOR DISEASE CONTROL AND PREVENTION GUIDANCE

Currently, no data suggest that the COVID-19 pandemic impacted seasonal influenza virus mutations, and the 2021 to 2022 influ-

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enza vaccine available in the United States includes updated influenza A(H1N1)pdm09 and influenza A(H3N2) components.⁶ All US influenza vaccines for the 2021 to 2022 season are quadrivalent, and routine age-appropriate vaccination of all persons ≥ 6 months of age without contraindications continues to be recommended.⁶ Primary updates by the US Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) to this season's influenza vaccination⁶ include the following:

- US-licensed influenza vaccines available for the 2021 to 2022 influenza season are egg-based inactivated influenza vaccines (IIV4s), cell culture-based inactivated influenza vaccines [*Flucelvax Quadrivalent (ccIIV4)*], recombinant influenza vaccines (RIV4), and live attenuated influenza vaccines (LAIV4).⁶
- The approved age indication for ccIIV4 has been expanded from ages ≥ 4 years to ≥ 2 years.⁶
- Current guidance states that influenza and COVID-19 vaccines can be coadministered on the same day as well as within 14 days of each other⁷ and should be administered in separate anatomic sites.⁶ Providers should consult current ACIP COVID-19 vaccine recommendations and CDC guidance if concerned about coadministration.⁶
- Pregnant women should consider vaccination with IIV4, ccIIV4, or RIV4 in the third trimester, but not LAIV4 at any time during pregnancy or postpartum.⁶
- Regarding the timing of influenza vaccination, the new recommendation this

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year was that vaccine administration to nonpregnant adults should be after August and ideally before the end of October to optimize vaccine protection during the expected seasonal epidemics.⁶ This new recommendation is expected to continue into the future.

- A history of severe allergic reaction to IIV4s, RIV4, or LAIV4 other than urticaria (such as angioedema, respiratory distress, lightheadedness, or recurrent emesis) or requiring epinephrine or emergency medical intervention is now considered a precaution, not a contraindication for ccl-IV4. Similarly, a history of severe allergic reaction to IIV4s, cclIV4, or LAIV4 other than the aforementioned reactions is now considered a precaution, not a contraindication for RIV4. These patients should be vaccinated in an inpatient or outpatient medical setting, supervised by a healthcare provider who is able to recognize and manage such reactions.⁶

■ OTHER INFLUENZA VACCINATION RECOMMENDATIONS

Other relevant issues pertaining to influenza vaccination during the ongoing COVID-19 pandemic have been outlined.⁶⁻⁸ Influenza vaccine recipients and those who administer these vaccines should recognize that vaccine side effects can mimic COVID-19.⁷ Nevertheless, those who develop fever after vaccination should stay home until they defervesce for 24 hours without the use of antipyretics.⁷ Importantly, if fever persists or new respiratory symptoms develop, patients should contact their healthcare provider.⁷

In a nonprobability-based, convenience sample of 698 US adults infected with SARS-CoV-2 and 2,437 uninfected adults, 65.9% of those infected experienced long-term symptoms lasting > 4 weeks while 42.9% of those uninfected reported such symptoms, representing an emerging public health concern.⁸ This may impact influenza vaccine uptake, as well as recognition of influenza-like illness; deferring influenza vaccination until resolution of another acute viral illnesses, such as COVID-19 is generally recommended.⁹ Safe vaccination

practice calls for postponing influenza vaccination for those in quarantine after COVID-19 exposure or in isolation after mild COVID-19 illness for 10 days, and after severe COVID-19 illness for 20 days.⁶

■ COVID-19 AND INFLUENZA COINFECTION

With several common clinical features of influenza and COVID-19, the overlap of the two epidemics occurring at the same time can complicate diagnosis, treatment, and prognosis.¹⁰ Although a small proportion of COVID-19 patients are coinfecting with influenza, the risk for high-risk individuals is of concern.¹⁰ While both have some distinct features (Table 1),^{11,12} they can be hard to distinguish.

■ VACCINE EFFICACY

Safety and efficacy of the influenza vaccination for pregnant women has been documented, and a recent study noted 91.5% efficacy of transfer of antibodies in preventing hospitalization of newborns and infants, in whom the vaccine is not approved before 6 months of age.¹³ Another recent study has shown safety and humoral immunogenicity of messenger ribonucleic acid COVID-19 vaccines in maternal sera, as well as cord blood and breast milk, indicating transfer of immunity to neonates.¹⁴

A recent study showed that COVID-19 vaccination of healthcare workers reduces the risk of COVID-19 in members of their households.¹⁵ Indirect effects of influenza vaccination have been shown to be greater than direct effects, with 4 to 7 times the influenza cases prevented in non-vaccinated compared with vaccinated individuals, and complications including influenza-associated deaths among the unvaccinated elderly reduced by a factor of 20 to 30.¹⁶

Researchers have been evaluating both influenza and COVID-19 vaccination efficacy in how they decrease risk of infection and reduce disease severity in breakthrough infections.¹⁷ Currently approved or emergently authorized-for-use COVID-19 vaccines trigger innate, durable immunity, although the emergence of protein variants could potentially limit efficacy.¹⁸ Preliminary data suggest that enhancing the interferon response could offer an immu-

Current guidance states that influenza and COVID-19 vaccines can be coadministered on the same day as well as within 14 days of each other

TABLE 1

Distinct features of influenza and COVID-19

	Influenza	COVID-19
Seasonality	Fall – winter	Year-round
Annual incidence		
Overall	8% (3% – 11%)	6% – 8%
Children	20% (unvaccinated)	Not applicable (no vaccine)
Adults	10% (unvaccinated)	6% – 8% (unvaccinated)
Age distribution	Children > adults	Adults > children
Incubation period (days)	1 – 4 days	2 – 14 days
Duration of infectivity	1 day before to 7 days after onset of illness	2 days before to 10 (20 for severe cases) days after onset of illness
Onset of symptoms	More acute	More subacute
Super-spreaders (1 person infects 8 persons)	Not reported	1%
Typical or characteristic features at onset of illness	Fever, headache, dry cough	Loss of sense of taste or smell
Severity of illness		
Asymptomatic	5% – 50%	30% – 40%
Symptomatic		
Mild	98%	80%
Moderate	1% – 2%	15%
Severe	0.2%	5%
Fatal	0.04% – 0.1%	3% – 4%
Duration of acute illness	5 – 7 days	2 – 6 weeks
Incidence of long-term symptoms lasting longer than 4 weeks	Clinically silent viral shedding for weeks to months in immunocompromised individuals	60% – 70% regardless of viral shedding
Complications	Pneumonia Exacerbation of underlying chronic heart and lung diseases	Deep venous thrombosis and pulmonary embolism Multisystem inflammatory disorders

Data from references 11 and 12.

nological advantage to control viral infections.¹⁹

■ FUTURE DIRECTION

Hopefully, COVID-19 will eventually become an endemic viral infection with predictable annual (or other interval) epidemics. It would

make perfect sense for developing combined universal influenza and COVID-19 vaccinations, as several pharmaceutical companies are in the process of developing.^{20,21}

■ DISCLOSURES

The author reports no relevant financial relationships which, in the context of his contributions, could be perceived as a potential conflict of interest.

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