I hope everyone had a good weekend

Today the first selection looks at whether eyeglasses provide any protection against SARS-CoV-2 infection. The second selection is the CDC update on testing. This is a welcome revision. I have summarized some of the key points and put my comments in brackets. The third article looks at activity of PI intranasally against SARS-CoV-2. The last selection is a release from the manufacturer on use of tocilizumab-the Empacta trial. This trail did show benefit on progression to mechanical ventilation and death. As I commented we need the results on more robust RCTs with and without antivirals on if these agents are effective and when to use them.

Have a great week

Ed

Association of Daily Wear of Eyeglasses with Susceptibility to Coronavirus Disease 2019 Infection
JAMA Ophthalmol published online September 16, 2020
The main outcomes were the proportions of daily wearers of eyeglasses among patients admitted to the hospital with COVID-19 and among the local population. Data on exposure history, clinical symptoms, underlying diseases, duration of wearing glasses, and myopia the proportion of people with myopia who wore eyeglasses in Hubei province were collected. People who wore glasses for more than 8 hours a day were defined as long-term wearers.

A total of 276 patients with COVID-19 were enrolled. Of these, 155 (56.2%) were male, and the median age was 51 (interquartile range, 41-58) years. All those who wore glasses for more than 8 hours a day had myopia and included 16 of 276 patients (5.8%; 95% CI, 3.04%-8.55%). The proportion of people with myopia in Hubei province, based on a previous study, was 31.5%, which was much higher than the proportion of patients with COVID-19 who had myopia in this sample.

Comment: In this cohort study of patients hospitalized with COVID-19 in China, the proportion of inpatients with COVID-19 who wore glasses for extended daily periods (>8 h/d) was smaller than that in the general population, suggesting that daily wearers of eyeglasses may be less susceptible to COVID-19. The authors hypothesized that eyeglasses prevent or discourage wearers from touching their eyes, thus avoiding transferring the virus from the hands to the eyes. Eyes usually lack protection, and an abundance of the SARS-CoV-2 receptor angiotensin-converting enzyme 2 has been found on the ocular surface, through which SARS-CoV-2 can enter the human body. SARS-CoV-2 may also be transported to the nasal and nasopharyngeal mucosa through continuous tear irrigation of the lacrimal duct, causing respiratory infection. There are several weaknesses in this study. First the sample size was small. The numbers of patients who wear eyeglasses and long-term wearers were limited, which limits the extension of the results to a larger population, so results need to be verified by large-sample multicenter studies. Next the proportion of wearers of eyeglasses was based on data from previous study and was not calculated from current local populations. None of the participants wore contact lenses, so the association between wearing contact lenses and susceptibility to COVID-19 remains to be studied. In healthcare eye protection is an important part of PPE. Although eyeglasses may not provide the same level of protection as googles or face shields could eyeglasses serve as a partial barrier to reduce inoculum as cloth masks or type I surgical masks? Further studies are needed to clarify if wearing eyeglasses decrease susceptibility to COVID-19.

CDC Overview of Testing for SARS-CoV-2 (COVID-19) Coronavirus Disease 2019 (COVID-19)
updated September 18, 2020 highlights
Major change: Due to the significance of asymptomatic and pre-symptomatic transmission, this guidance further reinforces the need to test asymptomatic persons, including close contacts of a person with documented SARS-CoV-2 infection.
Considerations for SARS-CoV-2 Diagnostic (Molecular or Antigen) Testing

- if you have symptoms of COVID-19:
    - if symptoms are mild:
        - Your healthcare provider may advise a SARS-CoV-2 test
        - If you test positive for SARS-CoV-2 infection or do not get tested, you should self-isolate for at least 10 days after symptom onset and resolution of fever for at least 24 hours, without the use of fever-reducing medications, and with improvement of other symptoms. [no change]
        - If you live with a person at increased risk of severe illness (for example an elderly relative or other individual with underlying conditions), take special precautions in the home to protect that individual according to CDC guidelines
    - If you test positive, you do not need to repeat a test for at least 3 months
    - You do not need a follow-up negative test to return to work or school, as long as:
        - You did not require hospitalization, AND
        - It has been at least at least 10 days after symptom onset and resolution of fever for at least 24 hours, without the use of fever-reducing medications, and with improvement of other symptoms.
- If you have been in close contact, such as within 6 feet of a person with documented SARS-CoV-2 infection for at least 15 minutes and do not have symptoms: [this section does not mention whether parties are wearing a mask which I believe is a serious oversite-below document does not recommend testing if HCW had close contact with SARS-CoV-2 infected person but was wearing PPE]
    - You need a test. Testing is recommended for all close contacts of persons with SARS-CoV-2 infection. Because of the potential for asymptomatic and presymptomatic transmission, it is important that contacts of individuals with SARS-CoV-2 infection be quickly identified and tested.[change in guidance] Pending test results, you should self-quarantine/isolate at home and stay separated from household members to the extent possible and use a separate bedroom and bathroom, if available.[easier said than done]
        - A single negative test does not mean you will remain negative at any time point after that test [assuming SARS-CoV-2 transmission] [sensitivity of test will depend on time from infection, antigen vs PCR, how specimen was obtained]
        - Even if you have a negative test, you should still self-isolate for 14 days. [I believe the correct term should be quarantine]
    - If you cannot self-isolate, or you are a critical infrastructure worker that must work, wear a mask, physically distance, avoid crowds and indoor crowded places, wash your hands frequently, and monitor yourself for symptoms. [if you are HCW very difficult to maintain social distancing]
    - HCW in close contact of person with documented SARS-CoV-2 infection while using recommended PP does not need to be tested.
- For public health reasons, your public health official(s) or healthcare provider may advise specific people, or groups of people, to be tested. It is important to realize that you can be infected and spread the virus but feel totally well and have no symptoms.

- Your healthcare provider or public health official may recommend that you are tested before being admitted to the hospital or before a procedure (e.g., pregnant women admitted for labor and delivery, surgery). This testing is to protect healthcare personnel and other patients.
- If there is significant spread of the virus in your community, your public health department may request significant numbers of asymptomatic "healthy people" to be tested in order to help stop the spread of the virus.

In Vitro Efficacy of a Povidone-Iodine Nasal Antiseptic for Rapid Inactivation of SARS-CoV-2
JAMA Otolaryngol Head Neck Surg published online September 17, 2020
Investigators set out to evaluate the in vitro efficacy of PVP-I nasal antiseptic for the inactivation of SARS-CoV-2 at clinically significant contact times of 15 and 30 seconds. Povidone-iodine was tested at diluted concentrations of 0.5%, 1.25%, and 2.5% and compared with controls. The SARS-CoV-2, USA-WA1/2020 strain, virus stock was tested against nasal antiseptic solutions consisting of aqueous PVP-I as the sole active ingredient. The test solutions and virus were incubated at mean (SD) room temperature of 22 (2) °C for time periods of 15 and 30 seconds.

Povidone-iodine nasal antiseptics at concentrations (0.5%, 1.25%, and 2.5%) completely inactivated SARS-CoV-2 within 15 seconds of contact as measured by log reduction value of greater than 3 log10 of the 50% cell culture infectious dose of the virus. The ethanol, 70%, positive control did not completely inactivate SARS-CoV-2 after 15 seconds of contact. The nasal antiseptics tested performed better than the standard positive control routinely used for in vitro assessment of anti–SARS-CoV-2 agents at a contact time of 15 seconds. No cytotoxic effects on cells were observed after contact with each of the nasal antiseptics tested.

Table 1. Virus Titers and Log Reduction Value (LRV) of SARS-CoV-2 When Incubated With Various Concentrations of Povidone Iodine (PVP-I) and Controls for 15 Seconds

Test product	PVP-I concentration after 1:1 dilution, %	Virus titer[a]	LRV[b]
PVP-I nasal antiseptic			
5.0%	2.5	<0.67	3.0
2.5%	1.25	<0.67	3.0
1.0%	0.50	<0.67	3.0
Ethanol 70%	NA	1.5	2.17
Virus control	NA	3.67	NA

Comment: This is an interesting approach. A few months ago, in the Daily Briefing I reviewed an article showing the common ingredient in mouthwash also inactivated SARS-CoV-2. Given the increased interest in PVP due to mupirocin resistance, PVP may have an additional advantage. Intranasal PVP-I rapidly inactivates SARS-CoV-2 and may play an adjunctive role in mitigating viral transmission beyond personal protective equipment. Randomized clinical trials have not yet been conducted to prove that viral transmission is mitigated with intranasal use of PVP-I, although these studies are already under way. This is just an in vitro study. It does contain iodine, which can affect thyroid and other functions.

Empacta Trial (Tocilizumab)

Empacta (Evaluating Minority Patients with Actemra [tocilizumab]) phase III double-blind RCT to evaluate the efficacy and safety of tocilizumab in the treatment of hospitalized SARS-CoV-2 associated pneumonia.

The trial enrolled hospitalized patients older than 18 years with confirmed SARS-CoV-2 infection with SpO2 <94% while on ambient air who did not require noninvasive or invasive mechanical ventilation. The primary endpoint is the cumulative proportion of participants dying or requiring mechanical ventilation by Day 28. Secondary objectives include time to clinical failure, defined as the time to death, mechanical ventilation, ICU admission, or withdrawal (whichever occurs first); mortality rate by Day 28; and time to hospital discharge.

Primary endpoint was met: patients with SARS-CoV-2 associated pneumonia who received tocilizumab plus standard of care were 44% less likely to progress to mechanical ventilation or death compared to patients who received placebo plus standard of care (log-rank p-value = 0.0348; HR [95% CI] = 0.56 [0.32, 0.97]). The cumulative proportion of patients who progressed to mechanical ventilation or death by day 28 was 12.2% in the tocilizumab arm versus 19.3% in the placebo arm. The difference in time to hospital discharge at day 28 was not significant. The difference in time to improvement in ordinal clinical status to day 28 was not significant. There was no statistical difference in mortality between patients who received tocilizumab or placebo by day 28.

Comment: This is the second trial reported by the manufacturer of tocilizumab. The first trial was called Covacta which did not find a clear benefit in the population studied. We are still awaiting the results of the RECOVERY Trial and the NIH trial using combination remdesivir and tocilizumab. Both trials have been submitted for publication. Last week I reviewed the trial using combination baricitinib and remdesivir which demonstrated a reduction in time to recovery among patients hospitalized with SARS-CoV-2 infection. We need to know if these anti-inflammatory drugs are effective, at what stage of disease should they be used, and how they may or may not add to use of steroids.