TGIF-lots to share this AM

Under COVID-19 News, J&J has submitted their vaccine to FDA for EUA. NIH has revised its guidelines on tocilizumab. OSHA issued guidance on mitigation and preventing spread of SARS-CoV-2 infection in the workplace.

Under Journal Reviews in an article in Science the investigators found that by October 2020, the 20- to 49-year age-group was the only one with a reproduction number above 1. The estimated contribution to spread by age-groups by that time was 72.2% for adults 20 to 49 years, versus less than 5% from children 0 to 9 and less than 10% from teens 10 to 19. Adults aged 20-49 naturally have most contacts to other adults aged 20 and above. The next article confirmed that co-bacterial infections in COVID-19 patients admitted to hospitals is very low, but antibacterial antimicrobial prescribing remain very high. The last article demonstrates that transmission risk was primarily driven by the viral load of index cases. Similarly, their results regarding the risk and expected time to developing symptomatic COVID-19 encourage risk stratification of newly diagnosed SARS-CoV-2 infections based on the initial viral load.

I hope everyone has a wonderful Super Bowl weekend!

Ed

COVID-19 News

Johnson and Johnson COVID-19 Vaccine
J&J submitted single-dose COVID-19 vaccine for EUA. The FDA will hear request February 26, 2021.

The COVID-19 Treatment Guidelines Panel's Statement on the Use of Tocilizumab (and Other Interleukin-6 Inhibitors) for the Treatment of COVID-19
February 3, 2021
Summary: The NIH has slightly revised recommendation on the use of tocilizumab as a treatment for COVID-19 in its latest COVID-19 treatment guidelines. Previously, the group recommended against the use of tocilizumab and other anti-interleukin-6 receptor monoclonal antibodies (e.g., sarilumab) outside of clinical trials. Now, citing conflicting evidence, the guideline panel says there are not enough data to recommend for or against the use of tocilizumab or sarilumab to treat COVID-19 in patients who have been admitted to the intensive care unit in the past 24 hours and require mechanical ventilation or high-flow oxygen. Some panel members, citing the REMAP-CAP trial, say that for patients who meet the above criteria and have rapid progression of respiratory failure, they would administer a dose of tocilizumab (8 mg/kg of body weight, up to 800 mg) plus dexamethasone. For patients who do not require ICU care, the panel continues to recommend against these drugs. Based on the available evidence, the Panel has determined the following:

- For patients who are within 24 hours of admission to the ICU and who require invasive or noninvasive mechanical ventilation or high-flow oxygen (>0.4 FiO_2/30 L/min of oxygen flow), there are insufficient data to recommend either for or against the use of tocilizumab or sarilumab for the treatment of COVID-19.
- Although many trials of tocilizumab for the treatment of COVID-19 have included patients who meet the above criteria, the collective data available to date preclude a definitive recommendation for or against the use of the drug.

- In view of the results from the REMAP-CAP trial (described below), some Panel members would administer a single dose of tocilizumab (8 mg/kg of actual body weight, up to 800 mg) in addition to dexamethasone to patients who meet the above criteria and who are also exhibiting rapid progression of respiratory failure.
- Too few patients in REMAP-CAP received sarilumab for the Panel to assess its efficacy in the treatment of patients who met the above criteria.
- For patients who do not require ICU-level care or who are admitted to the ICU but do not meet the above criteria, the Panel recommends against the use of **tocilizumab** or **sarilumab** for the treatment of COVID-19, except in a clinical trial **(BIIa)**.

Protecting Workers: Guidance on Mitigating and Preventing the Spread of COVID-19 in the Workplace
OHSA Update January 29, 2021 highlights
The guidance includes a recommendation to provide COVID-19 vaccination at no cost to employees. Other essential elements of a prevention program detailed in the newly issued guidelines include:

- Conducting a workplace hazard assessment,
- Identifying control measures to limit the spread of the virus,
- Adopting policies for employee absences that don't punish workers so that potentially infected workers are encouraged to remain at home,
- Ensuring that coronavirus policies and procedures are clearly communicated to both English- and non-English-speaking workers, *and*
- Implementing protections from retaliation for workers who raise coronavirus-related concerns.

Key measures offered in the guidance for limiting the spread of COVID-19 include separating and sending home infected or potentially infected people in the workplace, implementing physical distancing, installing barriers where physical distancing cannot be maintained, and using face coverings. The guidance also covers use of personal protective equipment (PPE), when necessary; providing hand-washing supplies for good hygiene; routine cleaning and disinfection; and ventilation improvements (in accordance with the American Society of Heating, Refrigerating, and Air-Conditioning Engineers' (ASHRAE):

- Ensure ventilation systems operate properly and provide acceptable indoor air quality for the current occupancy level for each space.
- Increase ventilation rates when possible.
- When weather conditions allow, increase fresh outdoor air by opening windows and doors. Do not open windows and doors if doing so poses a safety or health risk (e.g., risk of falling, triggering asthma symptoms) to occupants in the building.
- Use fans to increase the effectiveness of open windows. To safely achieve this, fan placement is important. Avoid placing fans in a way that could potentially cause contaminated air to flow directly from one person over another. One helpful strategy is to use a window fan, placed safely and securely in a window, to exhaust room air to the outdoors. This will help draw fresh air into the room via other open windows and doors without generating strong room air currents.
- Disable demand-controlled ventilation (DCV).
- Reduce or eliminate recirculation, for example by opening minimum outdoor air dampers. In mild weather, this will not affect thermal comfort or humidity. However, this may be difficult to do in cold or hot weather.

- Improve central air filtration to the MERV-13 (the grade of filter recommended by ASHRAE) or the highest compatible with the filter rack, and seal edges of the filter to limit bypass.
- Check filters to ensure they are within service life and appropriately installed.
- Keep systems running longer hours, 24/7 if possible, to enhance air exchanges in the building space.
- Ensure restroom exhaust fans are functional and operating at full capacity.
- Inspect and maintain local exhaust ventilation in areas such as kitchens and cooking areas.
- Use portable high-efficiency particulate air (HEPA) fan/filtration systems to help enhance air cleaning (especially in higher-risk areas such as a nurse's office or areas frequently inhabited by persons with higher likelihood of COVID-19 and/or increased risk of getting COVID-19).
- Generate clean-to-less-clean air movement by re-evaluating the positioning of supply and exhaust air diffusers and/or dampers (especially in higher-risk areas).
- Consider using ultraviolet germicidal irradiation (UVGI) as a supplement to help inactivate SARS-CoV-2, especially if options for increasing room ventilation are limited. Upper-room UVGI systems can be used to provide air cleaning within occupied spaces, and in-duct UVGI systems can help enhance air cleaning inside central ventilation systems.
- If ventilation cannot be increased, reduce occupancy level in the building. This increases the effective dilution ventilation per person.

At fixed workstations where workers are not able to remain at least 6 feet away from other people, transparent shields or other solid barriers (e.g., plexiglass, flexible strip curtains) should be installed to separate workers from other people.

- The barriers should block face-to-face pathways between individuals in order to prevent direct transmission of respiratory droplets. The posture (sitting or standing) of users should be considered when designing and installing barriers.
- Where an opening in the barrier is necessary to permit the transfer of items, the opening should be as small as possible.
- Barriers do not replace the need for physical distancing – 6 feet of separation should be maintained between individuals whenever possible.

Face coverings should be made of at least two layers of a tightly woven breathable fabric, such as cotton, and should not have exhalation valves or vents. They should fit snugly over the nose, mouth, and chin with no large gaps on the outside of the face. Require any other individuals at the workplace (e.g., visitors, customers, non-employees) to wear a face covering unless they are under the age of 2 or are actively consuming food or beverages on site.

- Wearing a face covering that covers the nose and mouth is a measure to contain the wearer's respiratory droplets and helps protect others. It may also protect the wearer.
- Wearing a face covering does not eliminate the need for physical distancing of at least 6 feet apart.
- For operations where the face covering worn by workers can become wet and soiled, provide workers with replacements daily or more frequently. Face shields may be provided for use with face coverings to protect them from getting wet and soiled, but they do not provide protection by themselves.
- Workers in a setting where face coverings may increase the risk of heat-related illness indoors or outdoors or cause safety concerns due to introduction of a hazard (for

instance, straps getting caught in machinery) may consult with an occupational safety and health professional to determine the appropriate face covering/respirator for their setting.

OSHA's updated guidance recommends that employers take the following steps:

- Assign a workplace coordinator who will be responsible for all COVID-19 issues.
- Perform a thorough hazard assessment that involves workers and their representatives to identify potential workplace hazards related to COVID-19.
- Identify precautions in line with the hierarchy of controls: elimination, substitution, engineering controls like installing physical barriers, workplace administrative policies, and PPE.
- Consider enhanced protections, such as telework or work in less densely, better ventilated facilities, for workers at higher risk for severe illness, such as older adults and those who have serious underlying medical conditions putting them at higher risk for severe illness from COVID-19.
- Educate and train workers on COVID-19 symptoms and hazards, as well as the policies and procedures established and implemented for their protection.
- Isolate workers who show symptoms at work and instruct infected or potentially infected workers to isolate or quarantine at home.
- Perform enhanced cleaning and disinfection after people suspected or confirmed to have COVID-19 have been in the workplace.
- Provide workers with information and guidance on COVID-19 screening and testing, following state or local guidance for screening and viral testing in workplaces, and make a COVID-19 vaccine or vaccination series available at no cost to all eligible employees.

Journal Reviews

Age Groups that Sustain Resurging COVID-19 Epidemics in the United States
Science published online February 2, 2021
Doi:10.1126/science.abe8372
A team led by researchers from Imperial College London analyzed age-specific cell phone mobility data of more than 10 million Americans and linked them to age-specific COVID-19 death data starting on Mar. 15, 2020. Data from 42 US states, Washington, DC, and New York City showed that the number of visits to places such as supermarkets and restaurants began to rebound across all age-groups in August after a significant initial reduction due to public health interventions such as lockdowns in the spring. COVID-19 infections and deaths followed a similar pattern in both the United States and Europe.

Among all locations assessed, until mid-August, the 35- to 49-year age-group was estimated to have contributed to 41.1% of virus transmission, compared with 2.1% in those aged 0 to 9 years, 4.0% in those 10 to 19, 34.7% in those 20 to 34, 15.3% in those 50 to 64, 2.5% in those 65 to 79, and 0.3% in those 80 and older. The number of coronavirus deaths did not rise significantly after school reopenings in the fall.

Based on the combined mobility and death data, they found fluctuations in age-specific reproduction numbers had only a relatively modest impact on the contribution of age groups to onward spread over time, and no evidence that young adults aged 20-34 were the primary source of resurgent COVID-19 in the US over summer 2020. But by October 2020, the 20- to 49-year age-group was the only one with a reproduction number above 1. The estimated contribution to spread by age-groups by that time was

72.2% for adults 20 to 49 years, versus less than 5% from children 0 to 9 and less than 10% from teens 10 to 19. Adults aged 20-49 naturally have most contacts to other adults aged 20 and above.

Comment: The investigators estimate that as of October 2020, individuals aged 20-49 are the only age groups sustaining resurgent SARS-CoV-2 transmission with reproduction numbers well above one, and that at least 65 of 100 COVID-19 infections originate from individuals aged 20-49 in the US. Targeting interventions – including transmission-blocking vaccines – to adults aged 20-49 is an important consideration in halting resurgent epidemics and preventing COVID-19- attributable deaths. This confirms the importance of behavior in transmission.

Prevalence of Co-infection at the Time of Hospital Admission in COVID-19 Patients, A Multicenter Study

Open Forum Infect Dis published online February 2, 2021
DOI: 10.1093/ofid/ofaa578

The investigators looked at a total of 1,016 adult patients admitted to 5 hospitals in the Johns Hopkins Health System between March 1, 2020, and May 31, 2020, with COVID-19. Adjudication of co-infection using definitions developed by a multidisciplinary team for this study was performed. Both respiratory and common nonrespiratory co-infections were assessed. The definition of bacterial CAP included proven (clinical, laboratory, and radiographic criteria plus microbiologic diagnosis), probable (clinical, laboratory, and radiographic criteria without microbiologic diagnosis), and possible (not all clinical, laboratory, and radiographic criteria met) categories. Clinical characteristics and antimicrobial use were assessed in the context of the consensus definitions.

Bacterial respiratory co-infections were infrequent (1.2%); 1 patient had proven bCAP, and 11 (1.1%) had probable bCAP. Two patients (0.2%) had viral respiratory co-infections. Despite bacterial co-infections <5%, 69% of patients still received antibiotics for pneumonia. On a positive note, the majority were stopped within 48 hours in patients with possible or no evidence of bCAP. This is in large part due to a robust ASP at Hopkins.

Comment: This article supports other publications confirming co-bacterial infections in patients presenting with COVID is exceptionally low. Empiric antimicrobial therapy remains high, emphasizing the need to support antimicrobial stewardship programs. Many of these programs have taken a back seat to managing the pandemic. This study was retrospective and observational in nature, and therefore limited by the diagnostic tests obtained and procedures performed at the time of clinical care.

Transmission of COVID-19 in 282 Clusters in Catalonia, Spain: A Cohort Study

Lancet Infect Dis published online February 2, 2021
doi.org/10.1016/S1473-3099(20)30985-3

Patients were recruited as part of a randomized controlled trial done between March 17 and April 28, 2020, that aimed to assess if hydroxychloroquine reduced transmission of SARS-CoV-2. Patients with COVID-19 and their contacts were identified by use of the electronic registry of the Epidemiological Surveillance Emergency Service of Catalonia (Spain). Patients with COVID-19 included in our analysis were aged 18 years or older, not hospitalized, had quantitative PCR results available at baseline, had mild symptom onset within 5 days before enrolment, and had no reported symptoms of SARS-CoV-2 infections in their accommodation or workplace within the 14 days before enrolment. Contacts included were adults with a recent history of exposure and absence of COVID-19-like symptoms within the 7 days preceding enrolment. Viral load of contacts, measured by quantitative PCR from a nasopharyngeal swab, was assessed at enrolment, at day 14, and whenever the participant reported COVID-19-like symptoms.

They assessed risk of transmission and developing symptomatic disease and incubation dynamics using regression analysis. We assessed the relationship of viral load and characteristics of cases (age, sex, number of days from reported symptom onset, and presence or absence of fever, cough, dyspnea, rhinitis, and anosmia) and associations between risk of transmission and characteristics of the index case and contacts.

The investigators identified 314 patients with COVID-19, with 282 (90%) having at least one contact (753 contacts in total), resulting in 282 clusters. 90 (32%) of 282 clusters had at least one transmission event. The secondary attack rate was 17% (125 of 753 contacts), with a variation from 12% when the index case had a viral load lower than 1×10^{6} copies per mL to 24% when the index case had a viral load of 1×10^{10} copies per mL or higher. Increased risk of transmission was also associated with household contact (3.0, 1.59-5.65) and age of the contact (per year: 1.02, 1.01-1.04). 449 contacts had a positive PCR result at baseline. 28 (6%) of 449 contacts had symptoms at the first visit. Of 421 contacts who were asymptomatic at the first visit, 181 (43%) developed symptomatic COVID-19, with a variation from approximately 38% in contacts with an initial viral load lower than 1×10^{7} copies per mL to greater than 66% for those with an initial viral load of 1×10^{10} copies per mL or higher (hazard ratio per log10 increase in viral load 1.12, 95% CI 1.05-1.20; p=0.0006). Time to onset of symptomatic disease decreased from a median of 7 days (IQR 5–10) for individuals with an initial viral load lower than 1×10^{7} copies per mL to 6 days (4–8) for those with an initial viral load between 1×10^{7} and 1×10^{9} copies per mL, and 5 days (3–8) for those with an initial viral load higher than 1×10^{9} copies per mL.

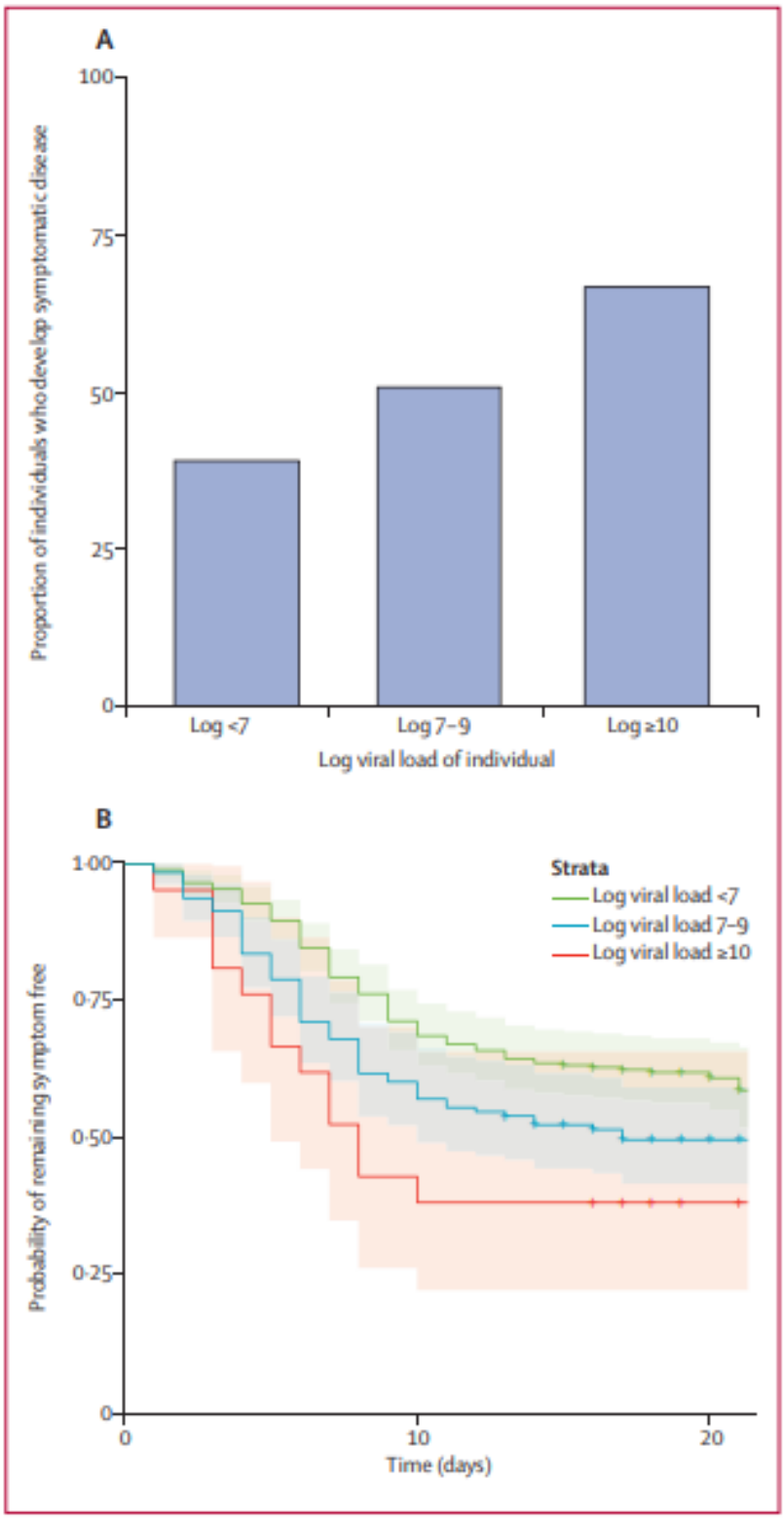

***Figure 2*: Risk of developing symptomatic COVID-19 according to characteristics of the contact at enrolment**

(A) Probability of symptomatic disease by viral load. (B) Time to symptomatic disease by viral load.

Comment: In this study, the viral load of index cases was a leading driver of SARS-CoV-2 transmission. The risk of symptomatic COVID-19 was strongly associated with the viral load of contacts at baseline and shortened the incubation time of COVID-19 in a dose-dependent manner. The fact that the transmission risk was primarily driven by the viral load of index cases, more than other factors such as their symptoms or age, suggests that all cases should be considered potential transmitters irrespective of their presentation and encourages the assessment of viral load in patients with a larger number of close contacts. Similarly, their results regarding the risk and expected time to developing symptomatic COVID-19 encourage risk stratification of newly diagnosed SARS-CoV-2 infections based on the initial viral load. The challenge is availability of quantitative PCR. They did not have data on type of mask (surgical vs FFP2) or use of other measures of personal protective equipment (PPE) or other infection control practices, thus limiting their ability to determine the effect of PPE on transmission risk. Within each cluster, they could not be completely certain about the directionality of transmission, but their inclusion criteria including the absence of COVID-19-like symptoms in the 2 weeks preceding enrollment is consistent with transmission from a case to a contact. Universal masking, social distancing, and potential use of monoclonals may impact transmission.