Happy Daylight Savings Time!

Today under COVID-19 News I share the initial Novavax vaccine data which looks very promising. I also share the news report of a possible link between the AstraZeneca vaccine and clots.

Under Journal Review I decided to focus on aerosol transmission and PPE. As I was looking for articles for today's Briefing, I found a very interesting article in PNAS from investigators from Harvard and Tulane that found that some people tended to be super-spreaders of COVID-19 — the 20% of people who emit 80% of the tiny particles — tend to be obese or older, a population more likely to live in elder care or be hospitalized. This article raised the ongoing controversy around aerosol transmission and PPE. So, I went back to the most recent CDC guidance on PPE which was revised in February. There was an important modification. N-95 masks are still recommended OR a well-fitting facemask (e.g., selection of a facemask with a nose wire to help the facemask conform to the face; selection of a facemask with ties rather than ear loops; use of a mask fitter; tying the facemask's ear loops and tucking in the side pleats; fastening the facemask's ear loops behind the wearer's head; use of a cloth mask over the facemask to help it conform to the wearer's face. CDC deleted a suggestion that wearing a surgical mask while caring for COVID-19 patients was acceptable and risk is not limited to "aerosol generating procedures". Next, I found a wonderful review from my colleagues Klompas, Baker, and Rhee entitled what is an aerosol generating procedure just published in JAMA Surg. [I missed the online version back in December] What have we learned? People routinely produce an abundance of respiratory particles in a range of sizes that include both droplets and aerosols as well as particles in between. They breakdown transmission into 4 factors. See my comments. FYI CDC is reviewing data on 3 feet vs 6 feet distancing on transmission – stay tuned.

Have a wonderful week

Ed

Exhaled Aerosol Increases with COVID-19 Infection, Age, and Obesity
PNAS 2021 Vol. 118 No. 8 e2021830118
doi:10.1073/pnas.2021830118
The investigators studied respiratory droplet generation and exhalation in human and nonhuman primate subjects with and without COVID-19 infection to explore whether SARS-CoV-2 infection, and other changes in physiological state, translate into observable evolution of numbers and sizes of exhaled respiratory droplets in healthy and diseased subjects. In this observational cohort study of the exhaled breath particles of 194 healthy human subjects, and in our experimental infection study of eight nonhuman primates infected, by aerosol, with SARS-CoV-2, they found that exhaled aerosol particles vary between subjects by three orders of magnitude, with exhaled respiratory droplet number increasing with degree of COVID-19 infection and elevated BMI-years. The investigators found that some people tended to be super-spreaders of COVID-19 — the 20% of people who emit 80% of the tiny particles — tend to be obese or older, a population more likely to live in elder care or be hospitalized. When highly infectious, such patients emit three times more tiny aerosol particles (about a billion a day) than younger people. A sick super-spreader who is simply breathing can pose as much or more risk to health workers as a coughing patient. The study clarifies the significant risks faced by nursing home workers, of whom more than 546,000 have gotten COVID-19 and 1,590 have died, per reports nursing homes filed to CMS since mid-May. It also highlights significant risk in hospitals and the importance of appropriate PPE.

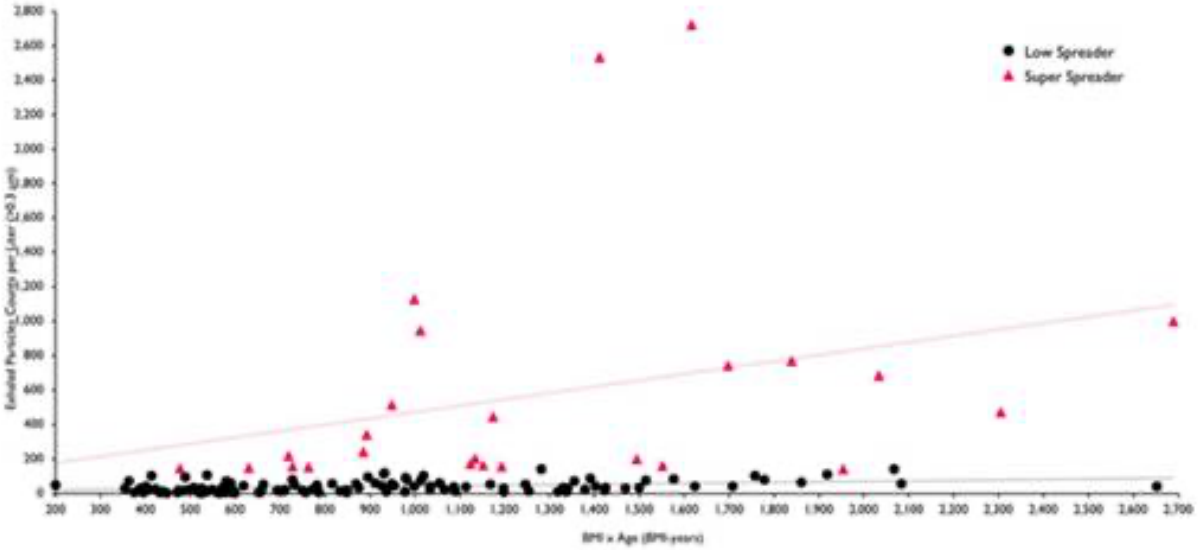

Fig. 2. Exhaled breath particles as a function of BMI-years for volunteers reporting age and BMI ($n = 146$). Results of linear regression analysis are shown for the exhaled aerosol numbers from the superspreader and low spreader (of aerosol particles) subjects showing significant correlation, particularly for the superspreader subjects ($r^2 = 0.98$).

Comment: Taken together, the research suggests that health care workplace exposure may be much greater than what the CDC initially defined when it prioritized protecting those doing "aerosol-generating procedures." These findings suggest that quantitative assessment and control of exhaled aerosol may be critical to slowing the airborne spread of COVID-19. See below on CDC revisions.

CDC Interim Infection Prevention and Control Recommendations for Healthcare Personnel During the Coronavirus Disease 2019 (COVID-19) Pandemic

Updated February 23, 2021

HCP should use PPE as described below:

- N95 respirators or equivalent or higher-level respirators should be used for
    - All aerosol-generating procedures AND
    - All surgical procedures that might pose higher risk for transmission if the patient has COVID-19 (e.g., that generate potentially infectious aerosols or involving anatomic regions where viral loads might be higher, such as the nose and throat, oropharynx, respiratory tract)
- One of the following should be worn by HCP for source control while in the facility and for protection during patient care encounters:
    - An N95 respirator OR
    - A respirator approved under standards used in other countries that are similar to NIOSH-approved N95 filtering facepiece respirators OR
    - A well-fitting facemask (e.g., selection of a facemask with a nose wire to help the facemask conform to the face; selection of a facemask with ties rather than ear loops; use of a mask fitter; tying the facemask's ear loops and tucking in the side pleats; fastening the facemask's ear loops behind the wearer's head ; use of a cloth mask over the facemask to help it conform to the wearer's face.
        - If implementing new strategies or equipment to improve fit, HCP should receive training on how to safely don and doff their facemask and on the facility

protocol for cleaning and disinfecting any reusable equipment (e.g., fitter). HCP should also ensure that any new strategies or equipment do not impede their vision or ability to breathe.

- Eye protection should be worn during patient care encounters to ensure the eyes are also protected from exposure to respiratory secretions.

Comment: On Feb. 10, the CDC updated its guidance to health care workers, deleting a suggestion that wearing a surgical mask while caring for COVID-19 patients was acceptable and urging workers to wear an N-95 or a "well-fitting face mask," which could include a snug cloth mask over a looser surgical mask. The changes in this guidance have not been widely discussed. The use of a well-fitted mask with ties rather than ear loops and then double masking as an alternative to N-95 makes sense knowing what we have learned in the last year. In addition, risk is not limited to "aerosol generating procedures" See next article.

What Is an Aerosol-Generating Procedure?
JAMA Surg 2021; 156:113-114
doi:10.1001/jamasurg.2020.6643
There is no consensus on which procedures are aerosol generating. The WHO listed intubation, noninvasive positive pressure ventilation, tracheotomy, cardiopulmonary resuscitation, bronchoscopy, and sputum induction are definite aerosol-generating procedures. By contrast, high-flow oxygen and nebulization are only designated as possible aerosol generating procedures. To add to the confusion, a recent study documented that controlled intubations and extubations in asymptomatic patients generate a much smaller amount of aerosol in comparison to coughing. The investigators found intubation emitted about 20 times fewer aerosols than a cough. [Anaesthesia. 2020. doi:10.1111/anae.15292 reviewed in Daily Briefing in October 2020] The same has been documented of bronchoscopy and noninvasive ventilation.

What have we learned? People routinely produce an abundance of respiratory particles in a range of sizes that include both droplets and aerosols as well as particles in between. Respiratory particles of all sizes can carry virus, and all are potentially capable of transmitting infection. The amount of respiratory particles generated varies by activity. Normal breathing generates a small but steady flow of aerosols. Loud speaking, heavy breathing, singing, and coughing produce more. Larger respiratory particles will rapidly fall to the ground within a 6-foot radius of the source patient. Smaller respiratory droplets can remain suspended in the air for longer periods of time but will diffuse and get diluted by the surrounding air leading to progressively lower concentrations of virus the further one is from the source patient.

The authors break down transmission into 4 factors. (1) The first is forced air. Any time air is forced over moist respiratory mucosa, it will generate more virus-laden respiratory particles. This may explain the increased risk of infection associated with noninvasive positive pressure ventilation and cardiopulmonary resuscitation. However, by the same logic, coughing, spirometry, and heavy breathing should also be considered aerosol generating. (2) The second factor is symptoms and disease severity. Symptomatic patients are more likely to have a higher viral load, and more likely to spread virus into the surrounding air because they are coughing, sneezing, or breathing heavily. In a recent study, close contacts of symptomatic patients were 10 to 20 times more likely to get infected compared with close contacts of asymptomatic patients. [Ann Intern Med. 2020; 173:879-887] (3) The third factor is distance. Respiratory emissions are densest closest to the patient. The further one gets from the patient, the more time and space there is for respiratory droplets to diffuse and dilute in the surrounding air. This

decreases the potential inoculum and lowers the probability of infection. This has been borne out by multiple studies and helps explain why long-range SARS-CoV-2 transmission is rare in well ventilated spaces. By contrast, in poorly ventilated spaces, viral aerosols can accumulate, leading to higher viral loads and greater risk for infection even over greater distances from the source patient. (4) The fourth factor is duration. The more time one is exposed to viral aerosols, the greater the probability of infection. This has been demonstrated in case-control studies of health care worker infections and epidemiologic studies of transmission rates in train travelers, and, in combination with proximity, helps to explain the very high rate of transmission in households.

Comment: The growing body of studies now show aerosol spread of SARS-CoV-2 during choir practice, on a bus or train, in a restaurant, and at gyms. This has led to widespread interest in better masks and ventilation. Surgical masks alone are probably adequate for caring for asymptomatic patients in settings with low SARS-CoV-2 prevalence. However, higher level respiratory protection is necessary for health care workers practicing in high-prevalence settings who need to be close to patients' respiratory tracts, present when large amounts of air are being forced across the respiratory mucosa (positive pressure ventilation, high-flow oxygen, coughing, heavy breathing, spirometry), or treating highly symptomatic patients even in the absence of defined aerosol generating procedures. See CDC update above.