

Good Morning,

One of the themes for today's review explores the potential of airborne transmission of SARS-CoV-2. The first 3 articles all highlight the potential of airborne spread in poorly ventilated spaces. The fourth article brings up the potential of fecal aerosol transmission of SARS-CoV-2. The last article underscores the importance of high titered CP in early treatment of SARS-CoV-2 infection. As I commented, I believe a better long-term solution will be synthetic mAb.

Have a great hump day

Ed

### **COVID-19 Patients in Earlier Stages Exhaled Millions of SARS-CoV-2 per Hour**

Clin Infect Dis published online August 28, 2020

Researchers in China analyzed exhaled breath samples from 49 COVID-19 patients from 10 countries, 4 hospitalized patients without COVID-19, and 15 healthy people from Beijing using PCR. They also tested 26 air samples and 242 surface swabs from quarantine hotels, hospitals, and personal belongings. Of the exhaled breath samples, 26.9% were positive for SARS-CoV-2, the virus that causes COVID-19, while 3.8% of air samples and 5.4% of surface swabs tested positive. The viral RNA breath emission rate was highest in the first stages of disease. Breath samples from two patients were positive for coronavirus RNA, but surface swabs of their cell phones, hands, and toilets were negative. Viral RNA was also detected on an air ventilation duct below another patient's bed. From 26 air samples collected including those using a robot, only one sample (air1) from an unventilated quarantine hotel toilet room was positive. Among the 242 surface swabs, viral RNA was found most often on toilet bowls (16.7%); floors (12.5%); patient hands, pillowcases, mobile phones, and computer keyboards (4.0%); and surfaces that healthcare staff touched (2.6%). But only 2 of 22 mobile phone surface samples tested positive for viral RNA, and all object handles were negative. The authors also stated that the viral RNA breath emission rate appears to vary based on factors such as patient activity level and disease stage and may be affected by age.

**Comment:** They claim that this is the first report that the SARS-CoV-2 is released directly into the air via breathing by COVID patients. [I am not sure this is true] Another interesting finding from this work is that SARS-CoV-2 emission was not, however, continuous at the same rate, but was rather a sporadic event. The SARS-CoV-2 negative air samples may be due to low SARS-CoV-2 emissions, virus inactivation by disinfectants, and rapid dilution or removal of SARS-CoV-2 by fresh air flow (2.5 m<sup>3</sup> /min for general hospital wards [12 exchanges per hour]). They did not study infectivity or transmission probability. The study did demonstrate that exhaled breath emission plays an important role in SARS-CoV-2 emission into the air, which could have contributed greatly to the observed airborne cluster infections in some studies with poor ventilation. Accordingly, measures such as enhanced ventilation and the use of masks are essential to minimize the risk of infection by airborne SARS-CoV-2.

### **Outbreak of COVID-19 in a Nursing Home Associated with Aerosol Transmission as a Result of Inadequate Ventilation**

Clin Infect Dis published online August 28, 2020

A total, 17 (81%) residents from one of the seven wards in a nursing home with psychogeriatric residents were diagnosed with COVID-19 as confirmed by PCR. Subsequently, 17 (50%) healthcare workers (HCWs) of the same ward were also tested positive. In contrast, all tests of the 106 HCWs or 95 residents in the 6 other wards were negative. In the week of this outbreak a low prevalence of COVID-19

was reported, only 493 (0.77%) positive cases were detected in the Netherlands, whereas the weekly rate was 8391 (21.5%) during the national peak in April 2020.

Suspecting that the ventilation system of the affected ward could have contributed to the outbreak, investigators found that an energy-efficient system had been installed in which indoor air was refreshed only when indoor carbon dioxide (CO<sub>2</sub>) concentrations detected elevated levels. If CO<sub>2</sub> levels didn't exceed a certain threshold, unfiltered indoor air was simply recirculated throughout the ward. In contrast, the six unaffected wards were refreshed regularly with outside air.

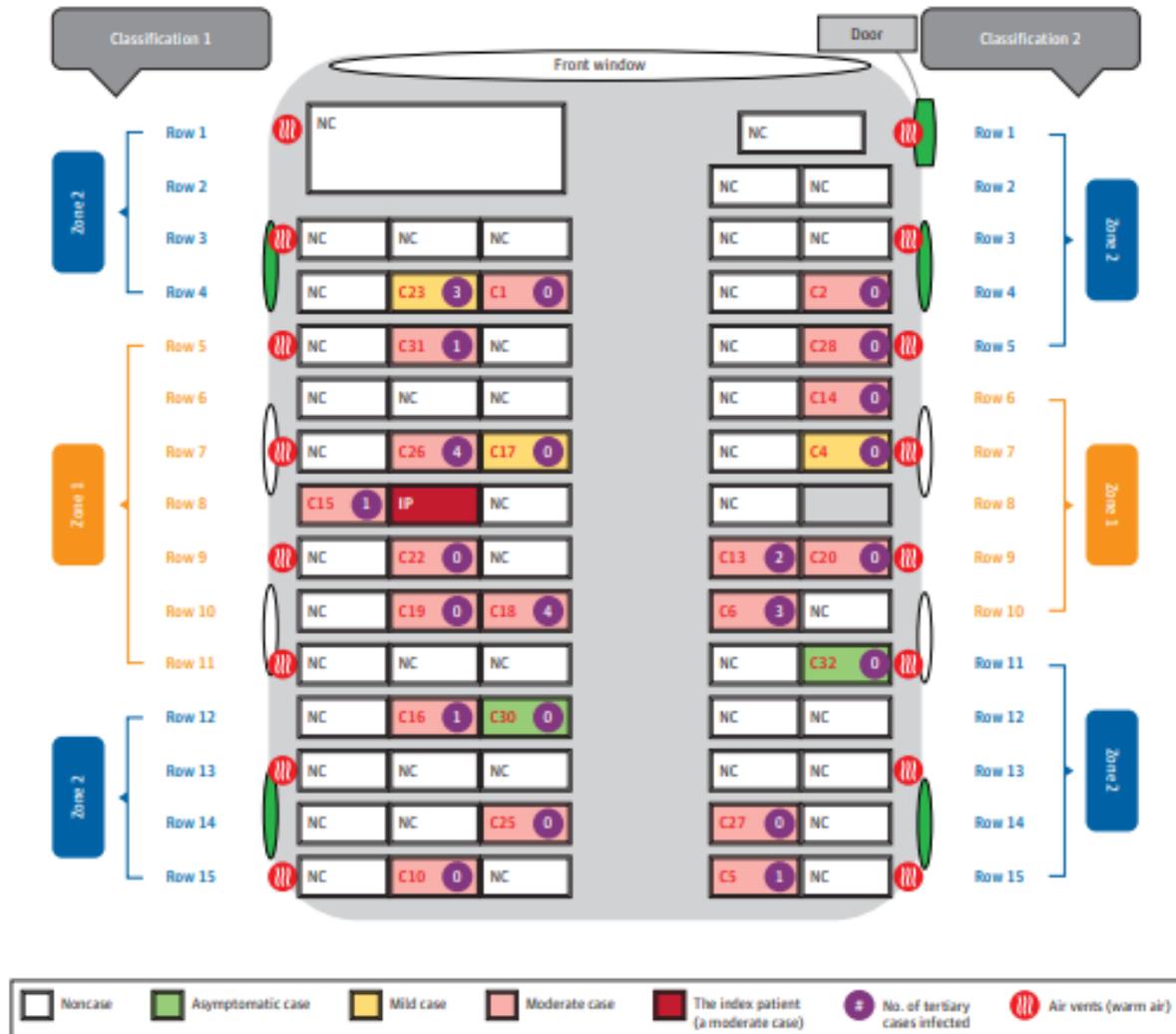
**Comment:** Their data suggest that this outbreak is caused by aerosol transmission of COVID-19 in a situation of inadequate ventilation for several reasons. First, the near simultaneous detection of COVID-17 infections of almost all residents HCWs within a ward in which care was provided. Second, the limitation of the outbreak to this particular ward with a ventilation system that recirculated unfiltered inside air in combination with the detection of COVID-19 on the filters of this system. Finally, the outbreak in this nursing home emerged in a period of low background prevalence of COVID19 infections in the community. This study and others suggest that poor ventilation can contribute to spread of SARS-CoV-2 infection.

### **Community Outbreak Investigation of SARS-CoV-2 Transmission Among Bus Riders in Eastern China**

JAMA Intern Med published online September 1, 2020

This is a report of 125 Buddhists in China who traveled on two heated buses to a 2.5-hour outdoor worship event in January (before public awareness of SARS-CoV-2); they were on the buses for a total of 100 minutes. The index patient began to experience COVID-19 symptoms that evening, upon return. All participants then underwent SARS-CoV-2 testing. Over one third of those on the same bus as the index patient were diagnosed with COVID-19. None on the other bus were infected. Passengers on the bus with the index patient became infected regardless of their proximity to the patient. The researchers conclude.

Figure. Schematic Diagram of Bus 2, the Bus Carrying the Coronavirus Disease 2019 (COVID-19) Initial Patient (IP)



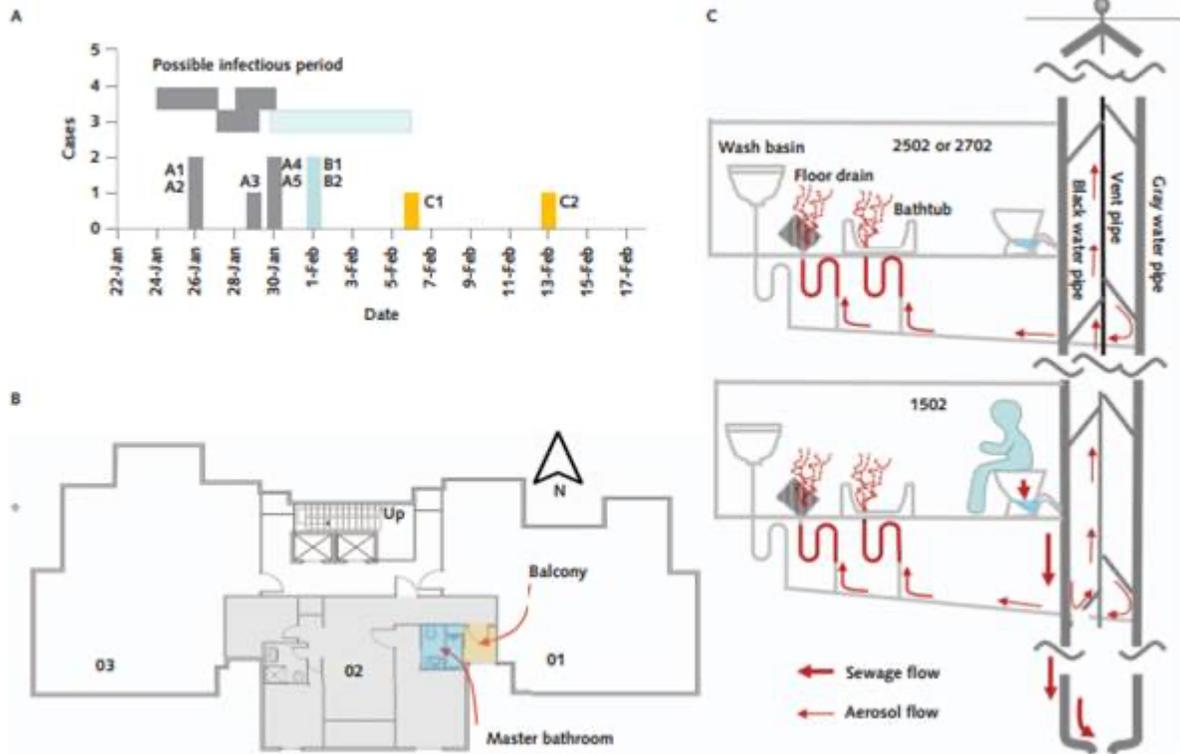
**Comment:** The study suggests that, in closed environments with air recirculation, SARS-CoV-2 can be easily transmitted. This study adds to growing evidence on the potential for airborne transmission of SARS-CoV-2 in closed environments [crowded] with air recirculation or poorly ventilated spaces. Perhaps this may also partially explain the recent wave in the South as people tend to stay inside in air-conditioned spaces where air is recirculated.

### Probable Evidence of Fecal Aerosol Transmission of SARS-CoV-2 in a High-Rise Building

Ann Intern Med published online September 1, 2020

This report investigated the temporal and spatial distributions of 3 infected families in a high-rise apartment building and examined the associated environment variables to examine the role of fecal aerosols. Epidemiologic survey and quantitative PCR analyses on throat swabs was performed from the participants; 237 surface and air samples from 11 of the 83 flats in the building, public areas, and building drainage systems; and tracer gas released into bathrooms as a surrogate for virus-laden aerosols in the drainage system.

9 infected patients in 3 families were identified. The first family had a history of travel to the COVID-19 epicenter Wuhan, whereas the other 2 families had no travel history and a later onset of symptoms. No evidence was found for transmission via the elevator or elsewhere. The families lived in 3 vertically aligned flats connected by drainage pipes in the master bathrooms. Both the observed infections and the locations of positive environmental samples are consistent with the vertical spread of virus-laden aerosols via these stacks and vents.



**Comments:** On the basis of circumstantial evidence, fecal aerosol transmission may have caused the community outbreak of COVID-19 in this high-rise building. Several studies have confirmed viral RNA in feces, however, confirming viable virus capable of transmitting infection has been difficult to establish. The investigators in this publication found viral particles may have been carried on air streams within the pipe network within the wastewater plumbing system. This report reminds me of the SARS outbreak in the Amoy Gardens housing complex in Hong Kong where U-traps in the plumbing system allowed viral laden droplets and aerosols to enter bathrooms and infect 321 persons. This article adds to the concern that wastewater systems especially in high-risk buildings deserves study.

**SARS-CoV-2 Neutralizing Human Antibodies Protect Against Lower Respiratory Tract Disease in a Hamster Model**

bioRxiv published online August 24, 2020-article provided by Josh Septimus

In the present study, they used Mab (monoclonal AB) and two doses of human convalescent plasma, differing almost ten-fold in neutralizing antibody concentration. The investigators showed that hamsters treated with a high dose of human convalescent plasma (CP) or a monoclonal antibody were protected against weight loss showing reduced pneumonia and pulmonary virus replication compared to control animals. However, a ten-fold lower dose of convalescent plasma showed no protective effect. Thus,

variable and relatively low levels of virus neutralizing antibodies in convalescent plasma may limit their use for effective antiviral therapy, favoring concentrated, purified (monoclonal) antibodies.

**Comment:** Using convalescent plasma with lower neutralizing antibody titers (0.5 ml of convalescent plasma with titer 1:320), but still comparable to the median neutralizing titer found in patients recovered from COVID-19, the protective efficacy was completely negated. Although this is a mouse model, the results seem to support the recent large observational trial from Mayo reviewed last week in the Daily Briefing. Only high tittered CP given early provided a benefit. Unfortunately, the titers on CP given are not available at the time of transfusion. CP is in limited supply. A plasma sample might contain thousands of antibodies, most of which have little effect on SARS-CoV-2. mABs can be isolated and synthetically produced in large quantities. At least two studies have begun to evaluate the safety and efficacy of mABs. In my opinion this product will replace CP and could be the bridge until we have adequate and safe vaccines.