

Good morning

Today we have a wide variety of articles/publications. I start with a nice description of the adult form of MIS. The second article is an interesting study on the transmission dynamics in India. The third review is the revised CDC publication on potential airborne transmission of SARS-CoV-2. [finally!] The last article is a good review on the neurological manifestations of SARS-CoV-2 and the importance of encephalopathy.

Have a wonderful Wednesday

Ed

Case Series of Multisystem Inflammatory Syndrome in Adults Associated with SARS-CoV-2 Infection — United Kingdom and United States, March–August 2020

MMWR October 2, 2020

Since June 2020, several case reports have described a MIS-C-like syndrome in adults (MIS-A). This review describes in detail nine patients reported to CDC, seven from published case reports, and summarizes the findings in 11 patients described in three case series in peer-reviewed journals (total 27). These 27 patients had cardiovascular, gastrointestinal, dermatologic, and neurologic symptoms without severe respiratory illness and concurrently received positive test results for SARS-CoV-2, by PCR or antibody assays indicating recent infection. Reports of these patients highlight the recognition of an illness referred to here as multisystem inflammatory syndrome in adults (MIS-A), the heterogeneity of clinical signs and symptoms, and the role for antibody testing in identifying similar cases among adults. Clinicians and health departments should consider MIS-A in adults with compatible signs and symptoms. These patients might not have positive SARS-CoV-2 PCR or antigen test results, and antibody testing might be needed to confirm previous SARS-CoV-2 infection. [similar to MIS-C]

Sixteen MIS-A patients described in case reports and CDC data showed that all had evidence of syndrome-related heart issues such as abnormal rhythms, elevated troponin concentrations, or left or right ventricular dysfunction. Thirteen patients had gastrointestinal symptoms at hospital admission, and five had dermatologic abnormalities, three of them with mucositis. Ten of 16 patients (63%) had lung abnormalities on chest imaging, and 12 (75%) had a fever of 100.4°F or higher for at least 24 hours. All had elevated concentrations of CRP, ferritin, and D-dimer. Ten patients also had low levels of lymphocytes. Four of the six patients who tested negative for COVID-19 on initial assessment (67%) had antibodies to the virus. Ten of the 16 patients (63%) needed intensive care, three required mechanical ventilation (19%), and two (13%) died. The patients, who were 21 to 50 years old, were of Asian (one patient), Hispanic (five), and black ethnicities (10). Nine patients were otherwise healthy, while six were obese, one had uncontrolled type 2 diabetes, two had high blood pressure, and one had obstructive sleep apnea. Eight patients had respiratory symptoms before developing MIS-A, while the rest did not. One case series involving seven men aged 20 to 42 years who experienced shock, had elevated levels of inflammatory markers, and tested positive for coronavirus antibodies; four had tested negative for COVID-19 on PCR. Three needed medications to regulate their heart and blood pressure, and three required insertion of an intraaortic balloon pump. Another case series described two patients 21 and 50 years old who sought medical attention after having coronavirus-related large-vessel strokes, possibly associated with abnormal clotting and nonobstructive coronary artery disease. While they had few respiratory symptoms, they showed high concentrations of inflammatory markers. A third case series involved two COVID-19 patients with vascular abnormalities, heart dysfunction, gastrointestinal signs and symptoms, and rash. One, who had an underlying illness, died within hours of seeking care; the other recovered.

All patients had markedly elevated laboratory markers of inflammation, including CRP range of peak values = 84–580 mg/L; and ferritin 196 to >100,000 ng/mL, as well as markers of coagulopathy including D-dimer 275–8691 ng/mL. Ten patients had absolute lymphocyte counts lower than normal range (range of nadir values 120–2120 cells/ μ L; lower limit of normal = 1000 cells/ μ L).

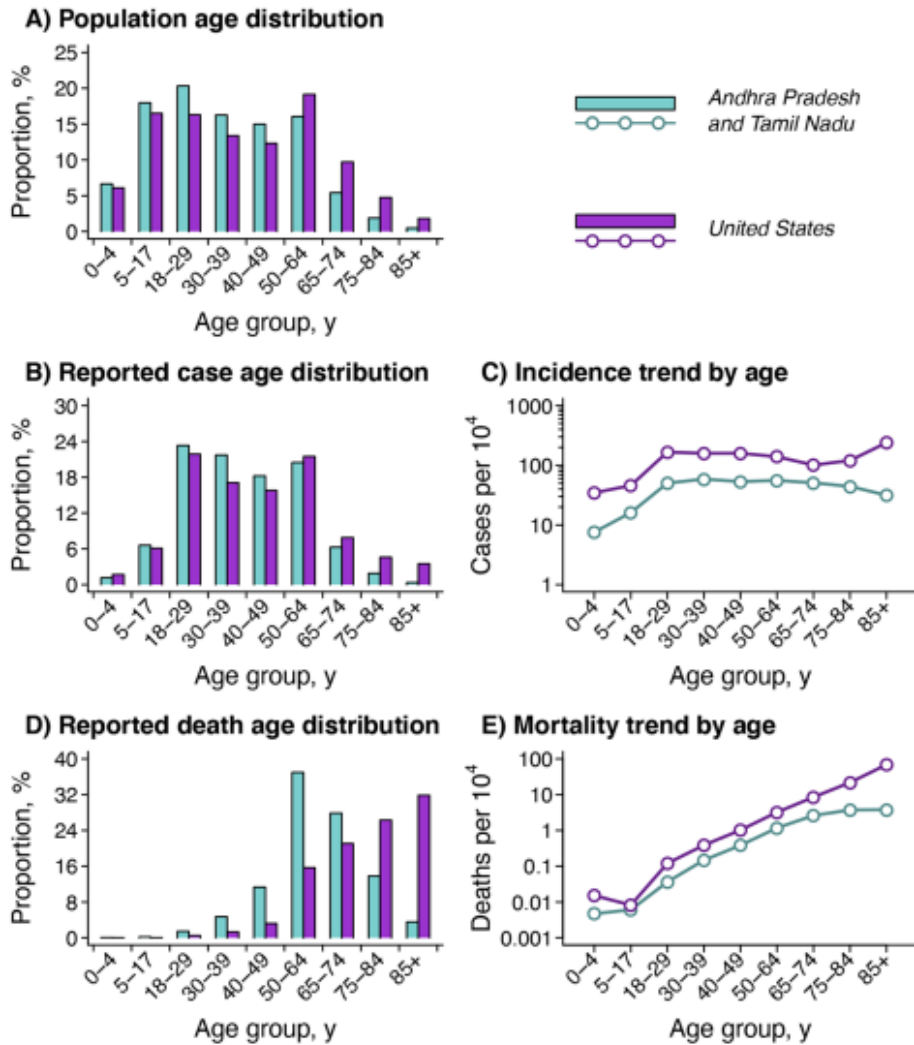
Comment: Findings in this report indicate that adult patients with current or previous SARS-CoV-2 infection can develop a hyperinflammatory syndrome resembling MIS-C. Although hyperinflammation and extrapulmonary organ dysfunction have been described in hospitalized adults with severe COVID-19, these conditions are generally accompanied by respiratory failure. In contrast, the patients described in this report had minimal respiratory symptoms, hypoxemia, or radiographic abnormalities in accordance with the working case definition, which was meant to distinguish MIS-A from severe COVID-19; only eight of 16 patients had any documented respiratory symptoms before onset of MIS-A. In patients with typical symptomatic SARS-CoV-2 infection, dyspnea is typically experienced a median of 5–8 days and critical illness 10–12 days after onset of symptoms. In patients who reported typical COVID-19 symptoms before MIS-A onset, MIS-A was experienced approximately 2–5 weeks later.

Epidemiology and Transmission Dynamics of COVID-19 in Two Indian States

Science published online September 30, 2020

This study revealed infection probabilities that ranged from 4.7-10.7% for low-risk and high-risk contact types respectively, with same-age contacts having the greatest risk of infection. Contrary to what has been observed in higher-income countries, reported cases and deaths were concentrated in younger cohorts with case-fatality ratios spanning from 0.05% at ages 5-17 years to 16.6% at ages \geq 85 years.

While 71% of the infected persons did not transmit the disease to their contacts, a small percentage of those infected were responsible for the majority of the secondary cases. Furthermore, data on exposure settings revealed that the secondary attack rate was higher in the household 9.0% (7.5-10.5%), as compared to community 2.6% (1.6-3.9%) and healthcare 1.2% (0.0-5.1%) settings.



Comment: This analysis suggests substantial variation in individuals' likelihood of transmitting: no secondary infections were linked to 71% of cases whose contacts were traced and tested. While the role of children in transmission has been debated, the investigators identified high prevalence of infection among children who were contacts of cases around their own age; this finding of enhanced infection risk among individuals exposed to similar-age cases was also apparent among adults.

CDC Scientific Brief: SARS-CoV-2 and Potential Airborne Transmission

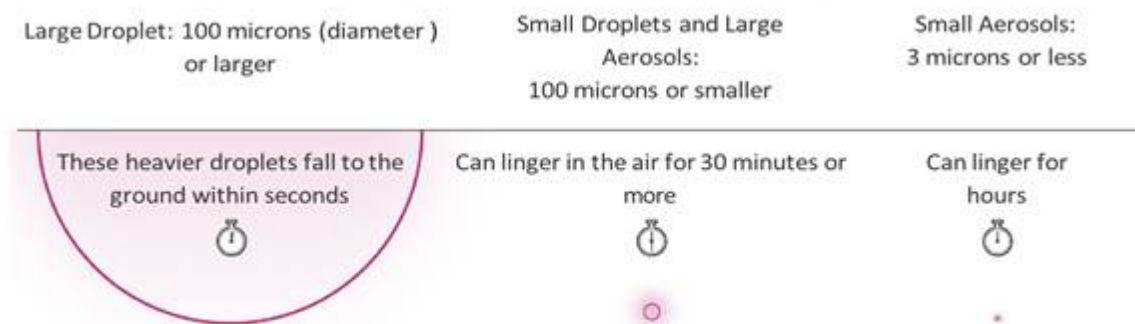
October 5, 2020

CDC confirms the principal mode by which people are infected with SARS-CoV-2 is through exposure to respiratory droplets carrying infectious virus. Respiratory droplets can be produced during exhalation (e.g., breathing, speaking [especially shouting], singing, coughing, sneezing) and span a wide spectrum of sizes that may be divided into two basic categories based on how long they can remain suspended in the air: (1) Larger droplets some of which are visible and that fall out of the air rapidly within seconds to minutes while close to the source; (2) Smaller droplets and particles (formed when small droplets dry very quickly in the airstream) that can remain suspended for many minutes to hours and travel far from the source on air currents.

Infections with respiratory viruses are principally transmitted through three modes: contact, droplet, and airborne. The virus is primarily transmitted via respiratory droplets by people in close contact, including those who are physically near, or within about 6 feet of, each other. Those droplets, then can cause infection when they are inhaled or deposited in the nose and mouth.

CDC now also recognizes, however, that some infections can be spread by exposure to the virus in small droplets and particles that can linger in the air for minutes to hours. Evidence indicates that under certain conditions people with Covid-19 seem to have infected others who were more than 6 feet away. These transmissions occurred within enclosed spaces that had inadequate ventilation. where the person may have been breathing heavily, for example while singing or exercising or shouting. Circumstances under which airborne transmission of SARS-CoV-2 appears to have occurred include: (1) Enclosed spaces within which an infectious person either exposed susceptible people at the same time or to which susceptible people were exposed shortly after the infectious person had left the space; (2) Prolonged exposure to respiratory particles, often generated with expiratory exertion (e.g., shouting, singing, exercising) that increased the concentration of suspended respiratory droplets in the air space; (3) Inadequate ventilation or air handling that allowed a build-up of suspended small respiratory droplets and particles.

CDC concludes interventions to prevent the spread of SARS-CoV-2 appear sufficient to address transmission both through close contact [droplet] and under the special circumstances favorable to potential airborne transmission. Among these interventions, which include social distancing, use of masks in the community, hand hygiene, and surface cleaning and disinfection, ventilation and avoidance of crowded indoor spaces are especially relevant for enclosed spaces, where circumstances can increase the concentration of suspended small droplets and particles carrying infectious virus.



Comment: From the start of the pandemic, some scientists, and infectious-disease experts, as well as the CDC and the WHO, said the virus is transmitted primarily between people in close contact, through respiratory droplets. In last few months WHO revised its guidance to include airborne as well as droplet. Both CDC and WHO both still emphasize that most of the transmission is still through close contact [within 6 feet for 15 minutes] via droplets. Over the last few months reviews in the Daily Briefing has supported airborne transmission in crowded poorly ventilated spaces especially for prolonged periods of time. Bottom line: short-ranged aerosol transmission may be the most important route for transmission, but longer-range transmission can occur in closed, poorly ventilated spaces. When an infected person and another person are both masked, the chance of a transmission decreases by at least 80 percent. [Two months ago in the Daily Briefing I reported on a MMWR report of 2 hairdressers infected with SARS-CoV-2 where both the hairdresser and clients wore masks

resulting in zero transmission!] Using mathematical modeling even when masking does not prevent people from getting infected, it decreases by roughly 10-fold the amount of virus to which a person may be exposed, and that, in turn, may limit the likelihood that they will develop a severe form of Covid-19. [inoculum effect] [reviewed several weeks ago-the so called “variolation” NEJM]

Frequent Neurologic Manifestations and Encephalopathy-Associated Morbidity in Covid-19 Patients

Ann CI Trans Neurol published online October 2020

Researchers examined neurologic manifestations in 509 COVID-19 patients admitted to hospitals in the Chicago area to assess neurologic symptoms and determine if encephalopathy is associated with an increased risk of morbidity and mortality. Neurologic symptoms were present at COVID-19 onset in 215 patients (42.2%), at hospital admission in 319 patients (62.7%), and at any time during the disease in 419 patients (82.3%). The most frequent neurologic symptoms were myalgias, headaches, encephalopathy, dizziness, and loss of taste and smell. Patients presenting with neurologic symptoms were younger than those without and had a longer time from disease onset to hospitalization. Patients with encephalopathy were older, had a shorter time from onset to hospitalization, and were more likely to be male and have other comorbidities. Patients with neurologic symptoms had longer hospitalization stays, with encephalopathy patients experiencing triple the length of stay as those without neurologic symptoms.

Of interest, the authors found no significant differences in functional outcome or mortality at discharge for patients experiencing neurologic symptoms with the exception of encephalopathy patients, who showed lower functional outcomes and greater likelihood of death 30 days after hospitalization (adjusted odds ratio 2.92, 95% confidence interval 1.17, 7.57; $P = 0.02$).

Comment: Neurologic manifestations occur in most hospitalized COVID-19 patients, but only encephalopathy was associated with increased morbidity and mortality, independent of respiratory disease severity. The increased morbidity and mortality associated with encephalopathy, independent of respiratory severity, parallels previous literature in sepsis-associated encephalopathy and delirium-associated mortality. There were some limitations, including its retrospective nature, and the fact that fewer than 6% of patients were evaluated by neurologists or neurosurgeons. Since most patients were admitted to dedicated COVID-19 wards or ICUs with strict infection control precautions in place, access to brain CT or MRI was not as readily available as for other patients with neurologic diseases. This limited a more complete neurologic work up in many COVID-19 patients. Prospective cognitive and neurologic-focused longitudinal studies should be undertaken.