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September 2020 COVID-19 Update

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Much has been learned in the past 5 months about COVID-19 and the SARS-CoV-2 virus that causes it. Some of the latest developments are highlighted in this report, mainly concerning transmission and strategies to reduce the burden of this disease.

With the school year starting back, it is important to know that children can get infected,[1] but also that school-aged children don't seem to spread it as much as adults do.[2,3] Yet there is evidence that children 10-19 years of age may spread the virus within the home even more than adults 40-59 years of age.[4] Furthermore, viral RNA loads in children may be as high, if not higher than that found in adults.[5,6] While it is clear that children generally tolerate the virus much better than adults,it is probably premature to say that children will not play an important role in the spread of SARS-CoV-2.

Transmission has occurred in homes, hospitals, and communities. Transmission within the home has been surprisingly low (11% [1] to 30% [7]), suggesting that aerosol (virus suspended for more than a few minutes in the air) and fomite (infection from touching contaminated objects) transmission are not as important as droplet spread directly at close range. Yet fomite transmission may be important when infected individuals have diarrhea. Transmission was greatly reduced within homes when family members took disinfecting and masking precautions prior to symptom onset of the initial case, and greater rates of transmission were seen when the index case had diarrhea.[8] Although many healthcare workers have been infected with SARS-CoV-2, surgical masks along with hand and surface sanitizing have been found to be effective in protecting known contacts in the hospital.[9,10] Workers with frequent exposure to COVID-19 patients in the community have been found to be protected even better with the addition of face shields to masks.[11]

Community spread of COVID-19, as with household and hospital spread, comes from patients with symptoms (symptomatic),[12,13] patients in the two days prior to symptom onset (pre-symptomatic),[14,15] and those who are infected but never develop symptoms (asymptomatic).[16,17] Distinguishing asymptomatic cases from pre-symptomatic cases is only possible after sufficient time has passed to see if symptoms unfold. For those who do get symptoms, infectivity and viral loads likely are greatest from 1 day prior to onset of symptoms to about 4 days post symptom onset (PSO), and infectivity drops substantially in most patients

after 1 week of symptoms. The exception is that sputum has the highest viral loads and can be produced much longer than 1 week PSO,[18,19] especially in those with severe disease starting after the first few days of symptoms. The Center for Disease Control (CDC) recently changed its recommendation about allowing infected individuals (symptomatic or asymptomatic) to return to public places 10 days PSO or post positive testing for asymptomatic individuals, as long as symptoms were abating and they were afebrile at least 1 day without taking antipyretics.[20] Asymptomatic and pre-symptomatic patients can transmit SARS-CoV-2, but are likely to be less contagious than symptomatic patients who are coughing. Because we generally can't know which asymptomatic individual is infected, it is important for people to wear facial barriers both to reduce the distance and quantity of viral shed from infected individuals, and to reduce the intake of virus into susceptible respiratory tracts. There is good evidence that face masks (some better than others)[21-23] and face shields[24] can reduce SARS-CoV-2 transmission.

Another important reason to strive for universal facial barrier use in public is the potential to greatly *increase* the rate of *asymptomatic* and less severe *disease*, by reducing viral inoculums at the time of infection.[25]

Testing strategy has mainly been to identify infected individuals and their contacts, in order to isolate them from other susceptible people and thus prevent further spread of the virus. With quick and accurate results and good contact tracing, that strategy can be effective.[26] Unfortunately, that strategy has been difficult to implement in the U.S. The bulk of testing has utilized expensive polymerase chain reaction (PCR) technology, applied to nasopharyngeal specimens, most often after symptoms start, and results have frequently not been available until 3 to 7 days later. More recently, cheaper and quicker tests are being utilized using oral (tongue and saliva) specimens, for screening individuals who may be in the pre-symptomatic stage of infection. Salivary specimens can be good and more tolerable sources of detection.[27] Early in the infection, the mouth may have a higher amount of virus and its products (RNA and protein antigen) than the nasal passage.[28] High false negative PCR test rates were found in a study using "pharyngeal" (throat) swabs that did not specify the anatomical location in mouth/pharynx.[29] Tonsillar and posterior pharyngeal swabs, normally used to diagnose streptococcal pharyngitis, may be less adequate for detecting SARS-CoV-2 than swabs of tongue and saliva. Thus, when viral load studies found higher loads from nasopharyngeal than from "throat" swabs,[6,30] their findings may have been influenced by the location in the throat that was swabbed. So even though the antigen test is not as sensitive as the PCR test, done at the right time and on saliva/tongue rather than nasal or posterior pharyngeal specimens, it may be as useful (mainly due to its quick turn-around time) as the PCR test. A newly released study did find greater positivity rates and viral loads in saliva versus nasal samples of hospitalized patients with confirmed COVID-19.[31] Head-to-head studies comparing the different detection methods (test and anatomical site) are still needed.

Is it necessary to quarantine asymptomatic "exposed" individuals, rather than allowing them to go to work and other public places with strict facial barrier use, as long as they remain

asymptomatic? It could be useful to test individuals 3 to 5 days after close unprotected SARS-CoV-2 contact to see if they are infected, and then isolate them for 1-2 weeks if they are positive. Those individuals who are around others at high risk, especially nursing home patients, obviously need to be more strictly regulated and perhaps frequently screened even in the absence of known exposure.

As much as information on COVID-19 is changing, most of the information previously shared is still correct.[32-36] Even though a recent meta-analysis of 38 studies found only 11% nasal symptoms in children,[37] paucity of nasal symptoms emphasized in the original report[32] may be in question. A very recent study found more (but not statistically significant) nasal symptoms in PCR-positive than in PCR-negative children suspected of having COVID-19.[6] Perhaps the latest revelation about why children might have milder or absent symptoms with SARS-CoV-2 infections[35] is that T cell memory for endemic, common cold-causing, coronaviruses also cross-reacts with SARS-CoV-2,[38] and children are more likely to have had recent exposure to those other coronaviruses. Added to that, live attenuated vaccines, like the measles, mumps and rubella (MMR) vaccine, may have a beneficial effect on the innate immune system.[39]

Stay tuned, as there will probably be more information about treatments in coming weeks. Surges in COVID-19 cases in many parts of our country and around the world in recent months remind us that this pandemic is nowhere near resolved.

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