CDC Duration of Isolation and Precautions for Adults with COVID-19

updated July 17, 2020

Below are key findings that impacted the revised recommendations. Most of the references have been reviewed over the last month in the Daily Briefing

1. Concentrations of SARS-CoV-2 RNA measured in upper respiratory specimens decline after onset of symptoms.
2. The likelihood of recovering replication-competent virus also declines after onset of symptoms. For patients with mild to moderate COVID-19, replication-competent virus has not been recovered after 10 days following. Recovery of replication-competent virus between 10 and 20 days after symptom onset has been documented in some persons with severe COVID-19 that, in some cases, was complicated by immunocompromised state. However, in this series of patients, it was estimated that 88% and 95% of their specimens no longer yielded replication-competent virus after 10 and 15 days, respectively, following symptom onset.
3. A large contact tracing study demonstrated that high-risk household and hospital contacts did not develop infection if their exposure to a case patient started 6 days or more after the case patient's illness onset.
4. Although replication-competent virus was <u>not</u> isolated 3 weeks after symptom onset, recovered patients can continue to have SARS-CoV-2 RNA detected in their upper respiratory specimens for up to 12 weeks. Investigation of 285 "persistently positive" persons, which included 126 persons who had developed recurrent symptoms, found <u>no</u>secondary infections among 790 contacts attributable to contact with these case patients. Efforts to isolate replication-competent virus from 108 of these case patients were unsuccessful (Korea CDC, 2020).
5. Specimens from patients who recovered from an initial COVID-19 illness and subsequently developed new symptoms and retested positive by RT-PCR did not have replication-competent virus detected (Korea CDC). The risk of reinfection may be lower in the first 3 months after initial infection, based on limited evidence from another betacoronavirus (HCoV-OC43), the genus to which SARS-CoV-2 belongs.
6. Currently, 6 months after the emergence of SARS-CoV-2, there have been <u>no</u> confirmed cases of SARS-CoV-2 reinfection. However, the number of areas where sustained infection pressure has been maintained, and therefore reinfections would be most likely observed, remains limited.

Summary: <u>Available data indicate that persons with mild to moderate COVID-19 remain infectious no longer than 10 days after symptom onset</u>. Persons with more severe to critical illness or severe immunocompromise likely remain infectious <u>no longer than 20 days after symptom onset</u>. Recovered persons can continue to shed detectable SARS-CoV-2 RNA in upper respiratory specimens for up to 3 months after illness onset, albeit at concentrations considerably lower than during illness, in ranges where replication-competent virus has not been reliably recovered and infectiousness is unlikely. The etiology of this persistently detectable SARS-CoV-2 RNA has yet to be determined. Studies have not found evidence that clinically recovered persons with persistence of viral RNA have transmitted SARS-CoV-2 to others. These findings strengthen the justification for <u>relying on a symptom based, rather than test-based strategy for ending isolation of these patients, so that persons who are by current evidence no longer infectious are not kept unnecessarily isolated and excluded from work or other responsibilities.</u>

Recommendations:

1. <u>Duration of isolation and precautions</u>
    - For most persons with COVID-19 illness, isolation and precautions can generally be discontinued 10 days *after symptom onset* and resolution of fever for at least 24 hours,

without the use of fever-reducing medications, and with improvement of other symptoms.
        - A limited number of persons with severe illness may produce replication-competent virus beyond 10 days that may warrant extending duration of isolation and precautions for up to 20 days after symptom onset; consider consultation with infection control experts.
    - For persons who never develop symptoms, isolation and other precautions can be discontinued 10 days *after the date of their first positive RT-PCR test for SARS-CoV-2 RNA.*
2. Role of PCR testing to discontinue isolation or precautions
    - For persons who are severely immunocompromised, a test-based strategy could be considered in consultation with infectious diseases experts.
    - For all others, a test-based strategy is no longer recommended except to discontinue isolation or precautions earlier than would occur under the strategy outlined in Part 1, above.
3. Role of PCR testing after discontinuation of isolation or precautions
    - For persons previously diagnosed with symptomatic COVID-19 who remain asymptomatic after recovery, retesting is not recommended within 3 months after the date of symptom onset for the initial COVID-19 infection. In addition, quarantine is not recommended in the event of close contact with an infected person.
    - For persons who develop new symptoms consistent with COVID-19 during the 3 months after the date of initial symptom onset, if an alternative etiology cannot be identified by a provider, then the person may warrant retesting; consultation with infectious disease or infection control experts is recommended. Quarantine may be considered during this evaluation based on consultation with an infection control expert, especially in the event symptoms develop within 14 days after close contact with an infected person.
    - For persons who never developed symptoms, the date of first positive RT-PCR test for SARS-CoV-2 RNA should be used in place of the date of symptom onset.

Comment: This revision based on the evidence is a welcome change. We all have experienced the frustration of using test-based strategy and have experienced prolonged +PCR in our patients. This has created delays in getting our patients placed especially if they are in long term care facilities. This will also help get patients out of isolation faster saving PPE. In addition, this will also help get COVID-19 patients back to work much sooner.

Clinical Manifestations and Outcomes of Critically Ill Children and Adolescents with COVID-19 in New York City

J Pediatrics published online July 16, 2020

This is a retrospective observational study of children 1 month to 21 years admitted March 14 to May 2, 2020 to 9 New York City PICUs with SARSCoV-2 infection. Of 70 children admitted to PICUs: median age 15 [IQR 9, 19] years; 61.4% male; 38.6% Hispanic; 32.9% Black; 74.3% with comorbidities. Fever (72.9%) and cough (71.4%) were the common presenting symptoms. Twelve patients (17%) met severe sepsis criteria; 14 (20%) required vasopressor support; 21 (30%) developed acute respiratory distress syndrome (ARDS); 9 (12.9%) met acute kidney injury criteria; 1 (1.4%) required renal replacement therapy, and 2 (2.8%) had cardiac arrest. For treatment, 27 (38.6%) patients received hydroxychloroquine; 13 (18.6%) remdesivir; 23 (32.9%) corticosteroids; 3 (4.3%) tocilizumab; 1 (1.4%) anakinra; no patient was given immunoglobulin or convalescent plasma. Hydroxychloroquine, remdesivir, and antibiotics >48 hours were used more often in the ARDS group ($p < 0.05$ for all) Forty-

nine (70%) patients required respiratory support: 14 (20.0%) non-invasive mechanical ventilation, 20 (28.6%) mechanical ventilation (IMV), 7 (10%) prone position, 2 (2.8%) inhaled nitric oxide, and 1 (1.4%) ECMO. Nine (45%) of the 20 patients requiring mechanical ventilation were extubated by day 14 with median IMV duration of 218 [IQR 79, 310.4] hours. Presence of ARDS was significantly associated with duration of PICU and hospital stay, and lower probability of PICU and hospital discharge at hospital day 14 ($P < .05$ for all). Serum levels of C-reactive protein, procalcitonin, lactate, pro-BNP, and interleukin-6 (IL-6) were elevated among ARDS patients, but levels were statistically significantly different than non-ARDS patients only for IL-6 (78.7 [IQR 34, 201.5] vs. 16.4 [IQR 12.1, 66] pg/mL, p=0.03)

Comment: Critically ill children with COVID-19 predominantly are older (median age 15), have comorbidities, and require some form of respiratory support. However, despite the presence of significant comorbidities, these comorbidities were not associated with ARDS in our cohort. The presence of ARDS, however, was significantly associated with prolonged PICU and hospital stay. IL-6 levels were statistically higher in ARDS patients vs non-ARDS patients suggestive of a hyperinflammatory response. This study was limited due to the retrospective nature of the study and a relatively small sample size.

Transplacental transmission of SARS-CoV-2 infection

Nature Communication published online July 15, 2020

So far, data is extremely limited whether and how SARS-CoV-2 can be transmitted from the mother to the fetus. This report demonstrates the transplacental transmission of SARS-CoV-2 in a neonate born to a mother infected in the last trimester and presenting with neurological compromise. The transmission is confirmed by comprehensive virological and pathological studies. In this study SARS-CoV-2 was shown to cause: (1) maternal viremia, (2) placental infection demonstrated by immunohistochemistry and very high viral load; placental inflammation, as shown by histological examination and immunohistochemistry (see below), and (3) neonatal viremia following placental infection. The neonate was studied clinically, through imaging, and followed up. The neonate presented with neurological manifestations, like those described in adult patients.

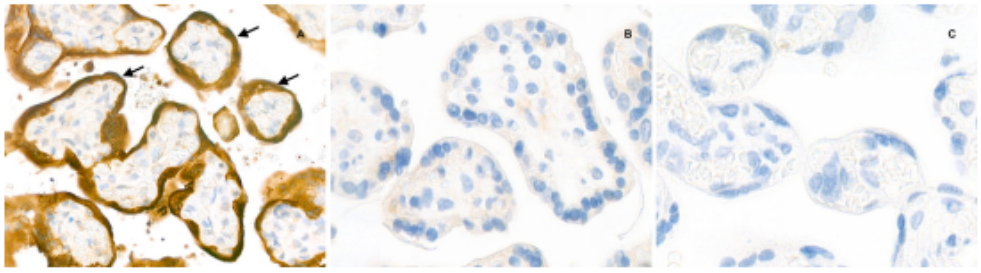

Fig. 5 Placental immunostaining for SARS-CoV-2 N-protein (anti-N immunohistochemistry, original magnification ×800). a The intense brown cytoplasmic positivity of peri-villous trophoblastic cells in the placenta of our case (arrows). **b**, **c** Two negative controls (primary antibody, two SARS-CoV-2 negative placentas).

Comment: A classification for the case definition of SARS-CoV-2 infection in pregnant women, fetuses and neonates has recently been released and the authors suggests this case fits the criteria of potential perinatal SARS-CoV-2 transmission. According to this classification system, a neonatal congenital infection is considered proven if the virus is detected in the amniotic fluid collected prior to the rupture of membranes or in blood drawn early in life, so I agree this case qualifies as congenitally transmitted SARS-CoV-2 infection.

The Adverse Impact of COVID-19 on Healthcare Providers: Time to Start Measuring
Anesthesia & Analgesia Journal published online July 2020
HCP's are at high-risk of becoming victims of the same condition their patients are suffering from One of the main issues of discussion has been on personal protective equipment (PPE) specifically about availability and shortages. We do not know more about effects of COVID-19 and health issues of HCP's during the crisis. On April 2020 the CDC & World Health Organization, reported that around 35,000 HCP's around the world (9,200 in the US) have become infected and there are 198 fatalities. This number is clearly an underestimation. testing is not yet widespread, mandatory or universal. Infection control issues and prevention practices are not the only concern for HCP's during this pandemic, mental health and psychosocial issues are equally important and much harder to measure precisely. Added unmanaged stress, physical and emotional fatigue, burnout, have major implications for overall health, job performance and mental well-being. Front line HCP's, mostly women (76.7%), nurses (60.8) reported symptoms of depression (50.4%) anxiety (44.6%), insomnia (34.0%) and mental distress (71.5%). There are numerous reports of high levels of stress, fatigue, burnout, depression, PTSD, (recently even an unfortunate suicide of an ED physician in NYC).

Comment: This article highlights the impact on HCP beyond PPE and isolation. HCP are vulnerable on many levels. We need to pay more attention and raise concerns not just about the pandemic, the pathophysiology, treatment and prevention but also the physical and emotional toll on HCP. We are facing extraordinary challenges dealing with this pandemic. This article should be a wake-up call that we need to start addressing and measuring the emotional impact on our HCP.

Association of Initial Viral Loads in SARS-CoV-2 in SARS-CoV-2 Patients with Outcomes and Symptoms
Am J Pathology published online July 2020
The investigators studied associations between viral loads (VL) and parameters such as severity of symptoms, disposition (admission vs direct discharge), length of hospitalization, and admission to the intensive care unit, length of need for oxygen support and overall survival in a cohort of 205 patients from a tertiary care center in New York City. VL was determined using q-PCR and Log10 transformed for normalization. Univariate and multivariate regression models were used to test these associations. They found that diagnostic viral load is significantly lower in hospitalized patients than in patients not hospitalized (log10 VL = 3.3 vs.4.0; p=0.018) after adjusting for age, sex, race, BMI, and comorbidities. Higher VL was associated with shorter duration of the symptoms in all patients and hospitalized patients only and shorter hospital stay (coefficient =-2.02,-2.61, -2.18; $p<0.001$, p=0.002, p=0.013, respectively). No significant association was noted between VL, admission to ICU, length of oxygen support, and overall survival.

Comment: Other studies showed that mild cases have significantly lower viral loads compared to severe cases. These studies were comprised solely of hospitalized patients, as opposed to this study, which included both non-hospitalized and hospitalized patients. The findings suggest a higher shedding risk in less symptomatic patients which may not be hospitalized. If this is true, this is an important consideration in preventing transmission especially in the outpatient setting. Larger studies are warranted to validate these findings.

Contact Tracing during Coronavirus Disease Outbreak, South Korea, 2020
Emerg Infect Dis published online July 17, 2020

The authors analyzed 59,073 contacts of 5706 COVID-19 index patients in South Korea. They defined an index case as the first identified laboratory-confirmed case or the first documented case in an epidemiologic investigation within a cluster. Contacts in high-risk groups (household contacts of COVID-19 patients, healthcare personnel) were routinely tested; in non–high-risk groups, only symptomatic persons were tested. Non–high-risk asymptomatic contacts had to self-quarantine for 14 days and were placed under twice-daily active surveillance by public health workers. All index patients were eligible for inclusion in this analysis if they identified ≥1 contact. We defined a detected case as a contact with symptom onset after that of a confirmed COVID-19 index patient.

We grouped index patients by age: 0–9, 10–19, 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, and ≥80 years. Because they could not always determine direction of transmission, they calculated the proportion of detected cases by the equation [number of detected cases/number of contacts traced] × 100, excluding the index patient. They compared the difference in detected cases between household and nonhousehold contacts across the stratified age groups.

Overall of the 10,592 household contacts, 11.8% had COVID-19. They found the highest COVID-19 rate (18.6% [95% CI 14.0%–24.0%]) for household contacts of school-aged children(10-19) and the lowest (5.3% [95% CI 1.3%–13.7%]) for household contacts of children 0–9 years in the middle of school closure. Of the 48,481 nonhousehold contacts, 1.97% had COVID-19.

Comment: Children younger than 10 transmit SARS-CoV-2 to others much less often than adults do [similar to study reviewed last week in the Daily Briefing]. However, those between the ages of 10 and 19 can spread the virus at least as well as adults do. [also similar to other studies] As communities start to open schools, clusters may be seen especially in middle and high schools if schools do not open safely. Children 10-19 can wear masks and social distance and be encouraged to practice frequent hand washing, so with appropriate planning we can make returning to school safer but not zero risk.