

August 26, 2020

COVID-19 – Reinfection, Asymptomatic Cases in Children, Post-discharge Quality of Life, Asymptomatic Spread, CDC on Testing Asymptomatic Cases

Good morning

For my colleagues in the greater Houston area stay safe. Looks like we may escape the worst

Today I wanted to share a wide variety of topics. First is the well-publicized report of re-infection. There is still much to be learned. The second article looks at prevalence of asymptomatic SARS-CoV-2 in children. As you will read, prevalence is quite low. There was a strong association between prevalence of SARS-CoV-2 in children who are asymptomatic and weekly incidence of COVID-19 in the local general population. The next article examines post discharge quality of life for patient who survived SARS-CoV-2 infection who were hospitalized. We have reviewed an article several weeks back which suggest the same finding-persistent symptoms, months after being discharged, especially fatigue and dyspnea. The next article confirms that asymptomatic people can spread SARS-CoV-2 during crowded events in enclosed environments without adequate ventilation. The last offering is a disturbing walk back by CDC on testing. Perhaps you can shed some light on why the CDC now does not recommend routine testing for people who are asymptomatic even if you have had close contact with a person infected with SARS-CoV-2. I understand timing and false negatives but really! Comments welcomed

Again, stay safe

Ed

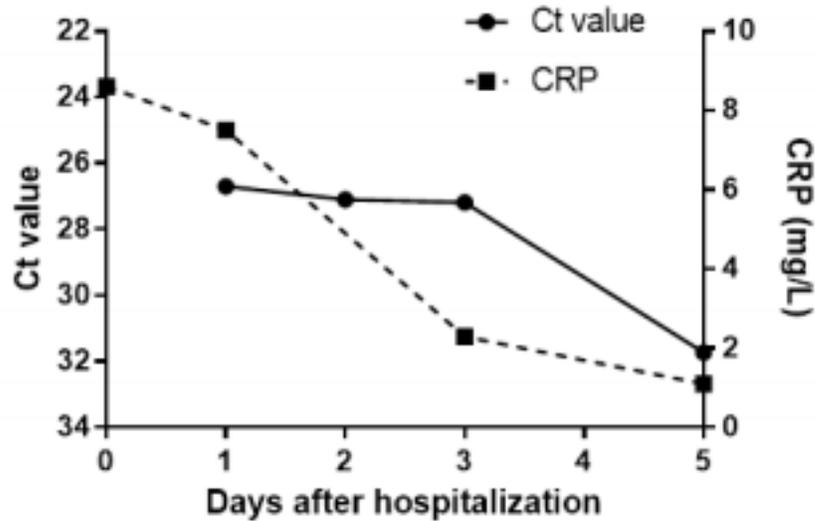
COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing Clin Infect Dis published online August 24, 2020

Whole genome sequencing was performed directly on respiratory specimens collected during two episodes of COVID-19 in a patient. Comparative genome analysis was conducted to differentiate re-infection from persistent viral shedding. Laboratory results, including PCR Ct values and serum SARS-CoV-2 IgG, were analyzed.

The second episode of asymptomatic infection occurred 142 days after the first symptomatic episode in an apparently immunocompetent patient. During the second episode, there was serological evidence of elevated C-reactive protein and SARS-CoV-2 IgG seroconversion. Viral genomes from first and second episodes belong to different clades/lineages. Compared to viral genomes in GISAID, the first virus genome has a stop codon at position 64 of orf8 leading to a truncation of 58 amino acids, and was phylogenetically closely related to strains collected in March/April 2020, while the second virus genome was closely related to strains collected in July/August 2020. Another 23 nucleotide and 13 amino acid differences located in 9 different proteins, including positions of B and T cell epitopes, were found between viruses from the first and second episodes. The serum specimens collected 10 days after symptom onset for the first episode and 1 day after hospitalization for the second episode tested negative for IgG against

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SARS-CoV-2. The patient had elevated CRP, relatively high viral load with gradual decline, and seroconversion of SARS-CoV-2 IgG during the second episode suggesting this was a true second infection.



| | Days after hospitalization | | | |
|-----------------------|----------------------------|-----------------|-----------------|-----------------|
| | 1 | 2 | 3 | 5 |
| SARS-CoV-2 IgG (S/CO) | Negative (0.07) | Negative (0.09) | Negative (0.33) | Positive (4.84) |

Comment: To my knowledge this is the first published report of re-infection. Epidemiological, clinical, serological and genomic analyses confirmed that the patient had re-infection instead of persistent viral shedding from first infection. They only have one serum specimen collected for the first episode. Since patients may not mount antibody response within 10 days, the negative antibody test does not exclude the possibility that the patient indeed developed antibody response by 2 weeks. Re-infection is common for “seasonal” coronaviruses 229E, OC43, NL63 and HKU1. Further serological studies are required to determine whether these amino acid differences in the spike protein of the SARS-CoV-2 strains between the first and second infection is responsible for the re-infection.

Prevalence of SARS-CoV-2 Infection in Children Without Symptoms of Coronavirus Disease 2019 JAMA Pediatrics published online August 25, 2020

When children's hospitals resumed elective medical and surgical care in April and May 2020, many implemented routine SARS-CoV-2 testing for children presenting for care not associated with suspicion of COVID-19. This publication reports the prevalence of positive SARS-CoV-2 test

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results in children without symptoms at 28 children's hospitals across the US by pediatric otolaryngologists as part of a quality improvement project through May 29, 2020. PCR for SARS-CoV-2 was performed before surgery, clinic visits, or hospital admissions.

Overall, 250 of 33 041 children (age range, 0-18 years) without symptoms who were tested at 28 hospitals were positive for SARS-CoV-2 through May 29, 2020. Asymptomatic pediatric prevalence was significantly associated with weekly incidence of COVID-19 in the general population during the 6-week period over which most testing of individuals without symptoms occurred. Overall, less than 1% of asymptomatic U.S. children are infected with SARS-CoV-2. The prevalence across sites ranged from 0% to 2.2%.

Comment: These findings suggest a low pooled prevalence of positive SARS-CoV-2 test results among children who were asymptomatic and presenting for surgical or medical care. The strong association between prevalence of SARS-CoV-2 in children who are asymptomatic and contemporaneous weekly incidence of COVID-19 in the local general population provides a simple means for institutions to estimate local pediatric asymptomatic prevalence from the publicly available databases. Children without symptoms presented for elective care at children's hospitals may not represent the general pediatric population by age, health status, immunologic status, and demographic factors. There was variation in symptom screening and testing protocol that existed between sites and over time, contributing to some of the heterogeneity in results. Despite some of these weaknesses the strong correlation with the general incidence data provides validation that the asymptomatic testing outcomes are broadly reliable since the only factor associated with prevalence was the weekly incidence in the general population in the same region during the 6 weeks.

Post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19 J Infect published online August 14, 2020

The investigators report a series of 279 hospitalized patients with SARS-CoV-2 infection and their short-term outcome. However, only a few studies have assessed post-discharge persistent symptoms and health-related quality of life (HRQoL) after hospitalization for COVID-19. They designed a short phone questionnaire to collect post-discharge clinical symptoms, modified Medical Research Council (mMRC) dyspnoea scale scores, professional and physical activities, and attention, memory and/or sleep disorders. HRQoL was assessed using the EQ-5D-5L questionnaire. Patients were asked to rate their health state from 1 to 5 in five domains (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and on a scale ranging from 0 ("the worst possible health") to 100 ("the best possible health") on a visual analogue scale (EQ-VAS). All eligible patients were contacted by phone by trained physicians and were asked to answer to the questionnaire.

Of the 279 hospitalized patients between March 15th and April 14th, 2020 in their COVID-19 unit, 48 were admitted to ICU, and 57 patients died within the three months following admission (43 in the ward group and 14 in the ICU group). 120 patients answered the phone questionnaire after a mean (\pm SD) of 110.9 (\pm 11.1) days following admission. The most frequently reported persistent symptoms were fatigue (55%), dyspnea (42%), loss of memory (34%), concentration and sleep disorders (28% and 30.8%, respectively). Loss of hair was

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reported by 24 (20%) patients, including 20 women and 4 men. Comparisons between ward- and ICU patients led to no statistically significant differences regarding those symptoms.

Comment: The present study shows that most patients requiring hospitalization for COVID-19 still have persistent symptoms, even 110 days after being discharged, especially fatigue and dyspnea. These results highlight the need for a long-term follow-up of these patients. This study is consistent with other publications and adds the EQ-5D-5L questionnaire.

Cluster of SARS-CoV-2 infections linked to music clubs in Osaka, Japan: asymptotically infected persons can transmit the virus as soon as 2 days after infection J Infect Dis published online August 24, 2020

They analyzed the publicly available epidemiological information for a cluster of 108 cases of coronavirus disease 2019 (COVID-19) cases in Osaka, Japan. Among cases, 51 cases attended a live music club only once and were considered to have a single visit. 10 remained asymptomatic at the time of COVID-19 diagnosis by PCR, which was on average 20 days after exposure. Three routes of secondary transmission were identified, with 2–4 days from infection to transmission. All index cases for secondary transmission were asymptomatic at the time of contact with other people. Based on the date of symptom onset in the remaining 41 cases, the period from exposure to illness ranged from 2 to 17 days.

Comment: This confirms that asymptomatic people can spread SARS-CoV-2 during crowded events in enclosed environments without adequate ventilation. Asymptotically infected persons can transmit the virus as soon as 2 days after infection. This study confirms the transmission and characteristics of this pandemic and the role of asymptomatic cases in transmission. Continuous efforts to social distance, wear a mask, avoid crowding and maintain personal hygiene are critical for effective control of COVID-19.

CDC Overview of Testing for SARS-CoV-2 (COVID-19) revised August 24, 2020-see changes below

If you have been in close contact (within 6 feet) of a person with a COVID-19 infection for at least 15 minutes but do not have symptoms:

1. You do not necessarily need a test unless you are a vulnerable individual or your health care provider or State or local public health officials recommend you take one.
1. A negative test does not mean you will not develop an infection from the close contact or contract an infection at a later time. [or it may be too early infection]
2. You should monitor yourself for symptoms. If you develop symptoms, you should evaluate yourself under the considerations set forth above.
3. You should strictly adhere to CDC mitigation protocols, especially if you are interacting with a vulnerable individual. You should adhere to CDC guidelines to protect vulnerable individuals with whom you live.

If you do not have COVID-19 symptoms and have not been in close contact with someone known to have a COVID-19 infection:

1. You do not need a test. A negative test does not mean you will not contract an infection at a later time. [or it may be too early infection]

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2. If you decide to be tested, you should self-isolate at home until your test results are known, and then adhere to your health care provider's advice. This does not apply to routine screening or surveillance testing at work, school, or similar situations.

If you are in a high COVID-19 transmission area and have attended a public or private gathering of more than 10 people (without widespread mask wearing or physical distancing):

1. You do not necessarily need a test unless you are a vulnerable individual or your health care provider or State or local public health officials recommend you take one. A negative test does not mean you will not develop an infection from the gathering or contract an infection at a later time.
2. You should strictly adhere to CDC mitigation protocols, especially if you are interacting with a vulnerable individual. You should adhere to CDC guidelines to protect vulnerable individuals with whom you live.
3. If you are tested, you should self-isolate at home until your test results are known, and then adhere to your health care provider's advice.

Comment: The new guidance directly contracts what CDC director Robert Redfield said last month: "Anyone who thinks they may be infected -- independent of symptoms -- should get a test." But now, the CDC says testing isn't necessary so long as the individual doesn't show symptoms. You do not necessarily need a test unless you are a vulnerable individual or your health care provider or State or local public health officials recommend you take one, the CDC states in the new revision. Prior versions of the C.D.C.'s testing guidelines struck a markedly different tone, explicitly stating that testing is recommended for all close contacts of people infected with the SARS-CoV-2, regardless of symptoms. The agency also specifically emphasized "the potential for asymptomatic and pre-symptomatic transmission" as an important factor in the spread of the virus. Studies suggest that 20-40% of transmission events can be traced back to individuals still in this so-called pre-symptomatic stage or asymptomatic. Evidence for pre-symptomatic people show virus levels tend to peak just before first symptoms — a period when these individuals may be in close contact with others. This change comes at a time when experts have almost universally encouraging more frequent and widespread testing, especially to reach vulnerable and marginalized sectors of the population. This makes the change even more perplexing. [at least to me]