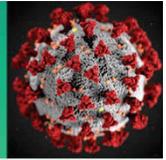


COVID-19 Science Update



From the Office of the Chief Medical Officer, CDC COVID-19 Response, and the CDC Library, Atlanta, GA.
Intended for use by public health professionals responding to the COVID-19 pandemic.

*** Available on-line at <https://www.cdc.gov/library/covid19> ***

Vaccine Development

PEER-REVIEWED

[Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia](#). Logunov *et al.* Lancet (September 4, 2020).

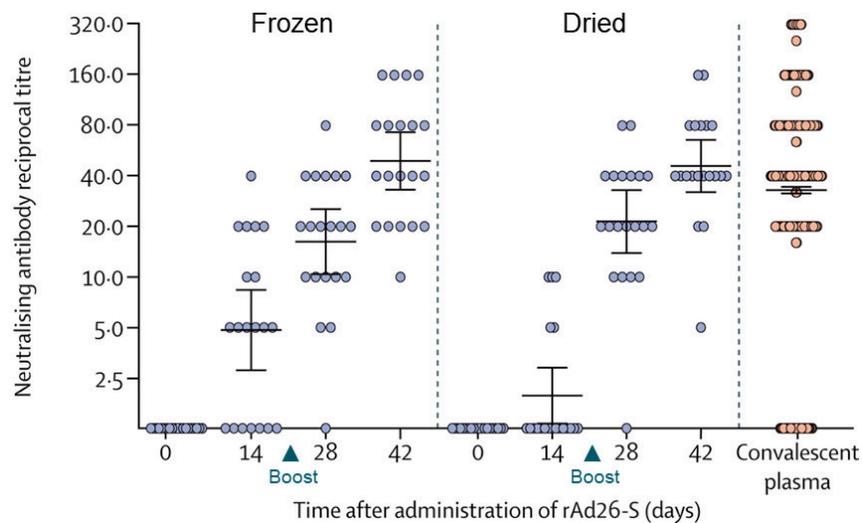
Key findings:

- After vaccination, no serious adverse events occurred, though mild adverse events were common, including: pain at injection site (58%), hyperthermia (50%), headache (42%), asthenia (28%), muscle and joint pain (24%).
- All participants produced neutralizing antibodies to SARS-CoV-2 (Figure).
 - Neutralizing antibody titers in the vaccine participants were not significantly different from convalescent plasma donors who experienced mild and moderate disease.
 - The frozen and dried vaccine formulations performed similarly.
 - Cell-mediated responses were detected in all participants.

Methods: Open-label, non-randomized phase 1 (n = 36) and 2 (n = 40) vaccination studies in adults between June 18 and August 3, 2020, Russia. Frozen or lyophilized (dried) vaccine formulations utilized two recombinant adenovirus vectors, rAd26 and rAd5. Both vectors express the SARS-CoV-2 spike (S) protein and were administered intramuscularly. Phase 1 assessed one dose of rAd26-S or rAd5-S with assessment on days 0, 2, 14, 21, and 28. Phase 2 assessed one dose of rAd26-S, followed 21 days later by one dose of rAd5-S with assessment on days 0, 14, 21, 28, and 42. Safety, antiviral antibodies, and T cell responses were examined. Post-vaccination immunity was compared to antibody levels in convalescent plasma among 4,817 people with mild (fever $\leq 39^{\circ}\text{C}$ without pneumonia) and moderate (fever $>39^{\circ}\text{C}$ with pneumonia) prior SARS-CoV-2 infection. *Limitations:* Small sample size; short follow-up period; no placebo or control vaccine; no participants >60 years of age; limited information on how the dose was chosen; phase 2 started 5 days after phase 1 began; detailed analysis of cell-mediated responses were not reported.

Implications: A phase 1/2 vaccine trial in Russia demonstrated immunogenicity with no serious adverse events reported. Although a phase 3 trial is planned, Russia is moving forward with approval of this vaccine. In an accompanying editorial, [Burki](#) points out that immune response may not correlate with protection. Further investigation including large scale trials is needed to determine long-term immunity, vaccine safety, effectiveness, and correlates of protection.

Figure:



Note: Adapted from Logunov *et al.* **Neutralizing antibody levels** at 0, 14, 21, 28, and 42 days after the first dose of rAd26 with heterologous **boost of rAd5-S** at day 21 and in **convalescent plasma** from individuals recovered from mild-to-moderate severity COVID-19. Frozen (left) and dried (right) vaccine formulations are shown. Permission request in process.

SARS-CoV-2 Wastewater Surveillance

PEER-REVIEWED

[Temporal detection and phylogenetic assessment of SARS-CoV-2 in municipal wastewater.](#) Nemudryi *et al.* Cell Reports Medicine. (August 31, 2020).

Key findings:

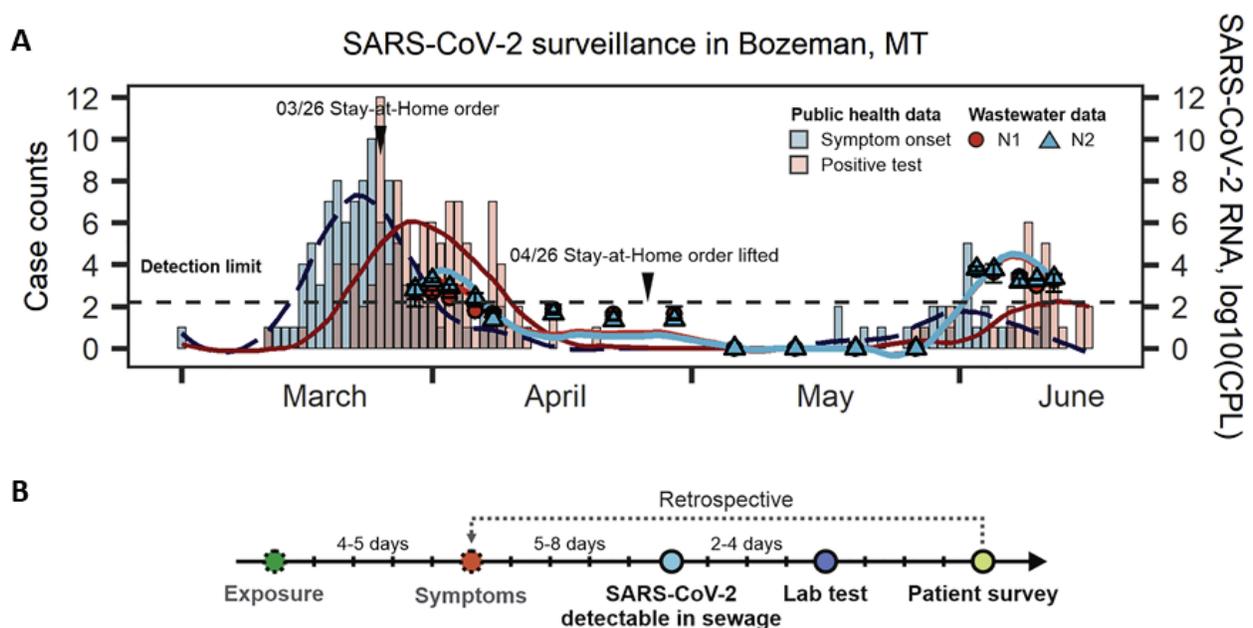
- During two outbreaks of SARS-CoV-2 in Bozeman, MT, detection of SARS-CoV-2 RNA in sewage *followed* symptom onset in persons within the wastewater catchment community by 5–8 days and *preceded* clinical PCR diagnosis of patients by 2–4 days (Figure).
- The quantity of SARS-CoV-2 RNA detected in wastewater catchment community tended to mirror the burden of infection in the community.

Methods: Environmental surveillance study used RT-PCR to monitor wastewater in Montana for SARS-CoV-2 RNA. Genome sequencing and phylogenetic analyses were used to identify circulating strains and mutations. A survey of patients in the wastewater catchment community who had been diagnosed with SARS-CoV-2 infection was used to determine timing of wastewater detection with patients' symptom onset and clinical diagnosis by PCR testing.

Limitations: Localized study and results are not generalizable.

Implications: SARS-CoV-2 RNA concentrations in wastewater correlate with COVID-19 epidemiology. Testing of untreated wastewater may help public health officials identify communities that warrant focused COVID-19 testing and implementation of more stringent infection control policies, as well as monitor community disease burden.

Figure:



Note: Adapted from Nemudryi *et al.* **A:** Temporal dynamics of SARS-CoV-2 RNA in the municipal wastewater superimposed on the epidemiological data with dates of **Symptom onset data** (collected by retrospective interviews of COVID-19 patients with positive tests) and **positive SARS-CoV-2 RT-PCR tests**. The **red circles** and **blue triangles** are SARS-CoV-2 RNA concentration in municipal wastewater measured with RT-PCR using N1 and N2 primers (shown on the y-axis). The lines show curves fitted to RT-PCR and epidemiological data using local polynomial regression. **B:** Timeline of symptoms, detection of SARS-CoV-2 in wastewater and clinical PCR test results. Licensed under CC-BY-NC-ND 4.0.

Epidemiology

PEER-REVIEWED

[Social distancing for COVID-19 and diagnoses of other infectious diseases in children.](#) Hatoun *et al.* Pediatrics (September 1, 2020).

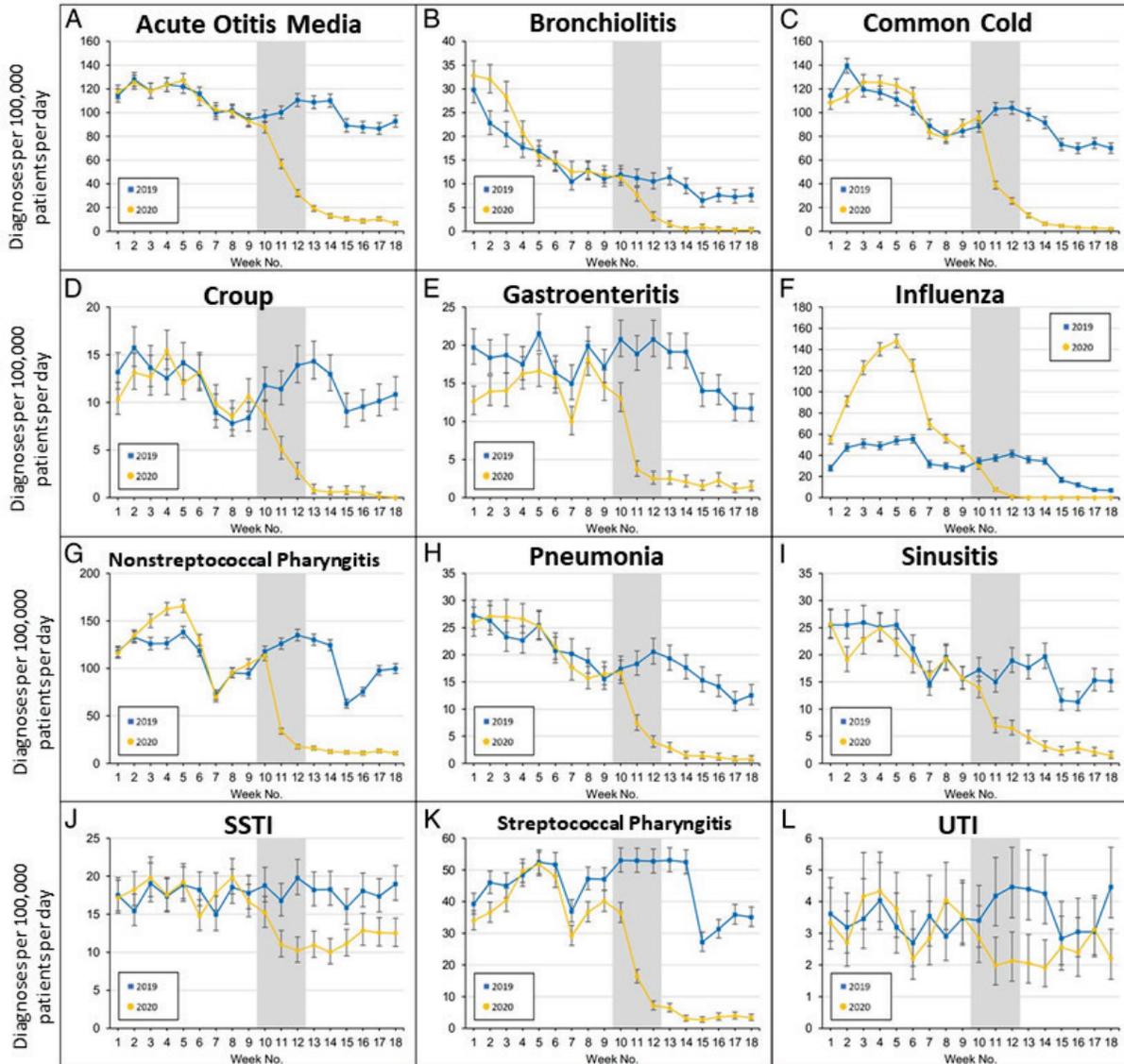
Key findings:

- The prevalence of 12 common pediatric infectious syndromes was significantly lower in the 2020 post-social distancing (SD) period than the equivalent 2019 period ($p < 0.001$), (Figure).

Methods: Retrospective analysis from a pediatric primary care network in Massachusetts covering approximately 375,000 children. Weekly incidence of 12 common pediatric infectious diseases (e.g., acute otitis media [AOM], upper respiratory infections, gastroenteritis, skin and soft tissue infections [SSTI], urinary tract infections [UTI]) were analyzed for the first 18 weeks of 2019 and 2020. For 2020, pre-SD period was the first 9 weeks of the year, the SD implementation period was weeks 10-12 and post-SD period was weeks 13-18. **Limitations:** No information on demographics or other covariates; results may not be generalizable to other locations.

Implications: The SD policies implemented to slow the spread of SARS-CoV-2 appear to have decreased the spread of common communicable pediatric infections. UTI are not communicable and should not be impacted by SD; decreases may have reflected reluctance of parents to seek care. [Kimberlin *et al.*](#) caution that missed scheduled vaccinations during the pandemic may result in outbreaks of measles and other infectious agents that had previously been kept under control via immunization programs.

Figure:



Note: Adapted from Hatoun *et al.* Weekly diagnosis rates per 100,000 patients per day with 95% CIs of common pediatric infectious diseases, week 1 to week 18, 2019 and 2020. The grey shaded area represents period of SD implementation in 2020. Permission request in process.

[Healthcare worker perception of a global outbreak of novel coronavirus \(COVID-19\) and personal protective equipment: Survey of a pediatric tertiary-care hospital.](#) Piche-Renaud *et al.* *Infection Control & Hospital Epidemiology* (August 12, 2020).

Key findings:

- In a survey of hospital-based healthcare workers (HCW):
 - Only 50% identified the correct donning order and 35% identified the correct doffing order of personal protective equipment (PPE).
 - Respondents were more concerned about COVID-19 exposure at work than outside of work.
 - Emergency department staff scored highest for concern about workplace exposure.
 - Administration staff scored highest for concern about exposure outside of work.

Methods: Self-administered questionnaire completed by 175 HCWs at a large children's hospital in Canada between March 6 and 10, 2020. HCW knowledge and concerns regarding exposure and infection at and outside work were assessed and scored. **Limitations:** Convenience sample; results not generalizable; 18.4% response rate; HCW knowledge and perceptions during a limited period.

Implications: Routine training for all HCWs on appropriate PPE procedures in combination with updates on current COVID-19 knowledge may increase adherence with PPE recommendations.

Clinical Treatment & Management

PEER-REVIEWED

[A national strategy to diagnose COVID-19 associated invasive fungal disease in the ICU.](#) White *et al.* Clinical Infectious Diseases (August 29, 2020).

Key findings:

- Fifty-one of 135 COVID-19 ICU patients (37.8%; 95% CI 30.0-46.2) had ≥ 1 positive test for invasive fungal disease (IFD).
 - 17 tests were positive for yeast (mainly *Candida*), 30 were positive for *Aspergillus*, 4 were unspecified fungal infections.
- The prognosis of patients with IFD was overall poorer than those without; however, when treated with anti-fungal therapy (AFT), mortality rates returned to levels seen among COVID-19 patients without IFD.

Methods: Multi-center, prospective cohort evaluation of IFD among 135 COVID-19 ICU patients. Diagnostic testing included culture, β -D-Glucan, *Aspergillus* antigen assay or *Aspergillus* PCR and chest imaging. Some patients received antifungal treatment. **Limitations:** Only select ICU patients were screened for IFD; AFT was administered at physician discretion, potentially biasing outcomes.

Implications: In the context of ICU care for COVID-19 patients, IFD may occur. Diagnosing and treating may lead to improved outcomes. According to an [editorial by Hoenigl](#), these results point to a need for trials to evaluate antifungal prophylaxis in COVID-19 patients.

Cardiovascular Disease Among Athletes Recovered from COVID-19

As competitive sports start to resume in the US, recent studies showing myocardial inflammation after SARS-CoV-2 infection among some athletes have raised concerns because this condition can lead to life-threatening arrhythmias (abnormal heart rates). Cardiac magnetic resonance (CMR) imaging is an important tool used to detect myocardial inflammation. The following studies used CMR to identify cardiac inflammation among athletes who recently recovered from COVID-19.

PEER-REVIEWED

[Cardiovascular Magnetic Resonance Findings in Competitive Athletes Recovering From COVID-19 Infection.](#) Rajpal *et al.* JAMA Cardiology (September 13, 2020).

Key findings:

- Four athletes (15%) had contrast (gadolinium)-enhanced CMR findings consistent with myocarditis.
 - Of these, two had mild symptoms (shortness of breath) and 2 were asymptomatic.
- Eight additional athletes (30.8%) had indication of prior myocardial injury.

Methods: CMR was performed on 26 previously SARS-CoV-2 PCR-positive competitive college athletes between June and August 2020. Electrocardiogram, serum troponin I, and transthoracic echocardiogram were performed on day of CMR imaging. **Limitations:** Lack of baseline CMR imaging and variable timing of CMR imaging from a positive COVID-19 test result.

PREPRINTS (NOT PEER-REVIEWED)

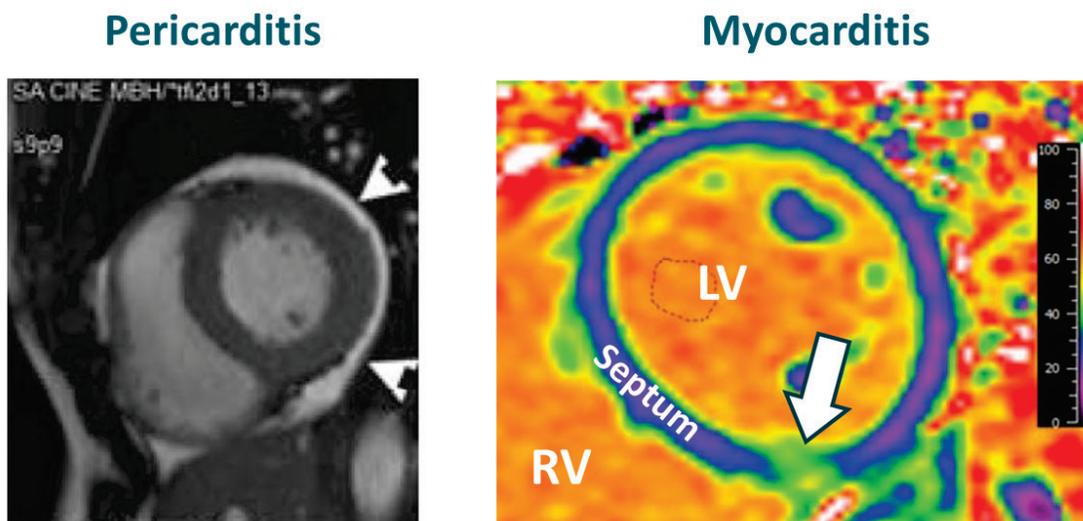
[COVID-19 myocardial pathology evaluated through screening cardiac magnetic resonance \(COMPETE CMR\)](#). Clark *et al.* medRxiv (September 2, 2020).

Key findings:

- Contrast-enhanced cardiac magnetic resonance (CMR) of 22 collegiate athletes recovered from mild or asymptomatic COVID-19 was abnormal in 2 (9%) cases athletes.
 - One had pericarditis with effusion (inflammation of the sac surrounding the heart) and the other had acute myocarditis (inflammation of the heart muscle) (Figure).
- All other cardiac assessments were normal.

Methods: Retrospective study of collegiate athletes with prior SARS-CoV-2 infection at a single Division 1 university in August 2020. Electrocardiogram, troponin I, echocardiogram with strain imaging, and contrasted CMR were performed. **Limitations:** Small sample; single university.

Figure:



Note: Adapted from Clark *et al.* **Left panel:** White arrows show pericardial effusion in athlete with pericarditis and pericardial effusion. **Right panel:** Inflammation (white arrow) of the bottom of the wall (septum) dividing the right (RV) and left (LV) cardiac ventricles in athlete with myocarditis. Licensed under CC-BY-NC-ND 4.0.

Implications for 2 studies (Rajpal *et al.* & Clark *et al.*): Myocarditis and pericarditis both can increase the risk of life-threatening abnormal cardiac rhythms, especially during strenuous exertion. These preliminary data suggest CMR may be useful to screen for such heart abnormalities following COVID-19 and guide return-to-play decisions. A further review of the cardiovascular effects of COVID-19 is detailed by [Capotosto *et al.*](#)

Neutralizing Antibodies

PEER-REVIEWED

[Disease severity dictates SARS-CoV-2-specific neutralizing antibody responses in COVID-19](#). Chen *et al.* Signal Transduction and Targeted Therapy (September 2, 2020).

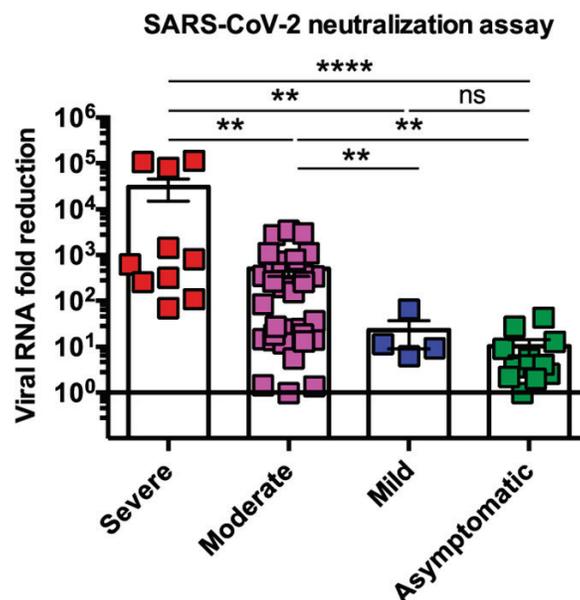
Key findings:

- Neutralizing antibody (NAb) levels were higher among persons who experienced severe or moderate COVID-19 illness compared with persons whose illness was asymptomatic or mild (Figure).

Methods: Cross-sectional analysis of 59 adults recovered from COVID-19 between January and April 2020. Asymptomatic (n = 11) patients were identified from screening close contacts of COVID-19 patients. Data from these persons were compared with persons who experienced mild (n = 4), moderate (n = 34) and severe (n = 10) COVID-19. NABs were examined for binding and receptor blocking of SARS-CoV-2 spike (S) protein and were assessed functionally using neutralization assays against both pseudovirus and SARS-CoV-2. Limitations: Low numbers of asymptomatic, mild and severe patients.

Implications: This small study suggests increasing severity of COVID-19 illness correlated positively with subsequent development of greater concentrations of NABs.

Figure:



Note: Adapted from Chen *et al.* Level of reduction of viral RNA by neutralizing antibodies by disease severity. **p < 0.01, and ****p < 0.0001. ns-not significant. Licensed under CC-BY 4.0.

In Brief

- Sanchez *et al.* [Violence against women during the COVID-19 pandemic: An integrative review](#). International Journal of Gynaecology & Obstetrics. This meta-analysis of 38 articles reviews many factors that could be responsible for the increase in cases of violence against women reported during this pandemic. Prolonged

quarantine/lockdown with potential abuser is only one of many factors. Healthcare providers need to be aware of this issue and increase their screening for domestic violence when seeing patients.

- Gostin *et al.* [Universal masking in the United States: The role of mandates, health education, and the CDC.](#) JAMA. Explores whether a national mandate on masking would be a lawful and effective COVID-19 prevention strategy. It discusses the various state pandemic responses and if CDC should have enhanced funding and powers to forge a nationally coordinated response to COVID-19 and to future health emergencies.
- Hsu *et al.* [One benefit of COVID-19 measures in Taiwan: The reduction of influenza infections and severe complications.](#) Influenza and other respiratory viruses. This letter notes that during the period after Taiwan's first COVID-19 case, the number of people with influenza per week and the number of people with severe complications from influenza were significantly lower relative to the same period in 2019.
- Ledford H. [Coronavirus reinfections: Three questions scientists are asking.](#) Nature. Explanation of key questions about reinfection including: (1) How common is reinfection? (2) Are reinfections more or less severe than the first? (3) What implications do reinfections have for vaccine prospects?
- Abbasi J. [COVID-19 and mRNA vaccines – First large test for a new approach.](#) JAMA. Perspective on mRNA vaccine being developed and its effectiveness. If mRNA vaccines work then it's a huge breakthrough, not just for COVID-19, but for the future of vaccinations generally.
- Provenzi *et al.* [The little professor and the virus: Scaffolding children's meaning making during the COVID-19 emergency.](#) Frontiers in Psychiatry. Children's explanations and interpretations of events are heavily influenced by those around them. It may be useful for parents and teachers to give children the tools they need to create good explanations to minimize risk of stress and anxiety during and after the pandemic.
- Miglis *et al.* [A case report of postural tachycardia syndrome after COVID-19.](#) Clinical Autonomic Research. A case report of a 26-year-old nurse who developed postural tachycardia syndrome several months after confirmed SARS-CoV-2 infection.

Erratum

In the [2020 09 08 COVID-19 Science Update](#), the entry for Hu *et al.* ([Antibody profiles according to mild or severe SARS-CoV-2 infection, Atlanta, Georgia, USA, 2020](#)), had the y-axis in Figure B labeled incorrectly. This error has been corrected in the online version of the Science Update.

Disclaimer: The purpose of the CDC COVID-19 Science Update is to share public health articles with public health agencies and departments for informational and educational purposes. Materials listed in this Science Update are selected to provide awareness of relevant public health literature. A material's inclusion and the material itself provided here in full or in part, does not necessarily represent the views of the U.S. Department of Health and Human Services or the CDC, nor does it necessarily imply endorsement of methods or findings. While much of the COVID-19 literature is open access or otherwise freely available, it is the responsibility of the third-party user to determine whether any intellectual property rights govern the use of materials in this Science Update prior to use or distribution. Findings are based on research available at the time of this publication and may be subject to change.



cdc.gov/coronavirus