AAMC Novel Coronavirus Update
August 26, 2020

To help filter through the large volume of news about the novel coronavirus, Ross McKinney Jr., MD, AAMC chief scientific officer, with assistance from his team in the Scientific Affairs unit at the AAMC, has initiated this science-focused newsletter.

This newsletter will be published once per week on Wednesdays.

Opt-in to receive future updates.

Contact AAMC Senior Science Policy Specialist Amanda Field, PhD, with any other questions or requests.

To access the latest AAMC updates and resources on COVID-19, visit aamc.org/coronavirus.

For resources on COVID-19 medical research, read more here.

Please share/forward this newsletter freely.

Today's Numbers

- World: 23,964,800 confirmed cases (820,989 deaths)
  - 1,754,000 new cases this week (1,794,000 new cases last week)
- United States: 5,791,222 (178,819)
  - 294,000 new cases this week (342,000 new cases last week)
  - 6,725 deaths this week (7,319 deaths last week)
  - 73,535,820 total tests
- U.S. Hot Spots
  - Guam: 521 new cases in the past week (252% increase in the past week)
  - North Dakota: 1,499 (51%)
  - South Dakota: 939 (42%)
  - Kansas: 3,442 (39%)
  - Connecticut: 726 (29%)

For the most up-to-date data, refer to the Johns Hopkins COVID-19 Map. Details of other U.S. hot spots can be found at the Washington Post's coronavirus data webpage.

The Institute for Health Metrics and Evaluation at the University of Washington Medicine is projecting hospital resource use in the United States based on COVID-19 deaths.

Lead News

As has been widely reported, a first case of recurrent SARS-CoV-2 infection has been documented. The story is straightforward. A 33-year-old man from Hong Kong had
symptomatic COVID-19 in March, and the virus from that episode was available for sequencing. On Aug. 15, he tested positive for SARS-CoV-2 during a screening at the Hong Kong airport on entry after a trip from Spain by way of Great Britain. During this second episode, he was completely asymptomatic, although he had a mildly elevated C-Reactive Protein concentration — a marker of inflammation. The virus isolate from the patient in August was sequenced and is clearly distinct from the strain he had in March. [Editor’s comment: This result is the first well-documented case of recurrent SARS-CoV-2 infection. It doesn’t represent a catastrophic outcome. It does demonstrate that recurrent infection can occur — but it tells us little else. The patient was asymptomatic, which could be optimistically interpreted to mean the preexisting immunity from his first infection protected him against symptoms. But there’s much we still don’t know, such as whether someone is infectious during an asymptomatic reinfection. This case reminds us how much needs to unfold before we understand the natural history of a virus that’s been circulating in humans for less than a year.]

Treatment News

The Food and Drug Administration (FDA) granted an Emergency Use Authorization (EUA) for convalescent plasma as a treatment for COVID-19, stating that “the known and potential benefits” outweigh any risks (the standard for an EUA). “The agency noted the EUA was based on historical evidence of convalescent plasma in prior outbreaks of respiratory viruses, preclinical evidence, small trials conducted during the outbreak, ... and the ongoing National Expanded Access Protocol (EAP) sponsored by the Mayo Clinic.” There was some controversy about whether the decision was justified, with particular concern that making convalescent plasma more readily available will hinder enrollment in the needed randomized, controlled clinical trials. Data from the large (72,000 patient) uncontrolled EAP with convalescent plasma coordinated by the Mayo Clinic was equivocal about benefits. Making the announcement more problematic, FDA Director Stephen Hahn, MD, greatly exaggerated the benefits of convalescent plasma in a press conference — a statement he later retracted in a series of tweets and interviews. STAT answered questions about whether convalescent plasma is a safe and effective treatment. [Editor’s comment: Convalescent plasma has been used as a treatment for similar respiratory diseases, but there are no definitive studies showing that it will help treat COVID-19 patients as of yet — though it is not likely to be harmful for most patients. As this newsletter reported last week, there is a lack of randomized, controlled trials on convalescent plasma as a treatment, which is a problem that will now be more difficult to rectify. Despite the comments at the EUA announcement, this is not a breakthrough treatment. It is, at best, a marginal improvement.]

Pfizer and BioNTech presented data in a non-peer-reviewed preprint from Phase 1 dose escalation studies of two different versions of their mRNA SARS-CoV-2 vaccine. Phase 1 data from BNT162b1 was published in early July, at which point the companies announced they intended to continue development of the vaccine they did not publish at that time, BNT162b2. According to the authors, “b1” encodes a secreted trimerized SARS-CoV-2 receptor binding domain, while “b2” encodes full length spike protein. Both vaccines produced similar antibody titters, but the b2 vaccine was associated with fewer adverse events, particularly in older individuals. Only 17% of 18- to 55-year-olds and 8% of 65- to 85-year-olds reported fever greater than 38°C after vaccinations. Immunogenicity (mean antibody titters) decreased with age, although short-term neutralizing antibody titters produced were still higher than convalescent serum.

In a randomized, controlled study of remdesivir as a treatment for moderately severe COVID-19 in hospitalized patients, the study results were disappointingly mediocre. Patients with severe respiratory syndrome or moderate COVID-19 pneumonia were
randomized to a five-day course of remdesivir (199 enrollees), a 10-day course (197 enrollees), or standard of care without remdesivir (200 enrollees). The endpoint was based on comparisons of a seven-point scale (from 1=death to 7=discharge) evaluated at Day 11 of the treatment course. The five-day course was statistically significantly better than standard of care, while the 10-day course was not. In addition, the authors admitted the clinical meaning of the outcome from the five-day treatment course was of uncertain benefit. [Editor's comment: This study affirms that remdesivir, as used in the study, is only marginally beneficial in the treatment of COVID-19. Sometimes the results of a study aren’t as clean as you might hope. It’s possible that starting the drug on Day 9 of symptoms (the mean in this study) is too late for an antiviral drug to make a difference.]

**STAT:** Will COVID-19 Vaccines Be Safe for Children and Pregnant Women? The Data, So Far, Are Lacking

**Wall Street Journal:** Antibody Drugs Advancing to Fill Covid-19 Treatment Gap

**STAT:** Urged on by Scientists, NIH Will Study Gilead’s Remdesivir-like Compound Against COVID-19

**Science:** Antibodies May Curb Pandemic Before Vaccines

**Clinical News**

A non-peer-reviewed preprint study from the Duke University Health System prospectively evaluated 382 children over 21 years old who were exposed to individuals confirmed to have SARS-CoV-2 infection. When tested, 293 (77%) of the children were virus-positive. In this community, the infected children were more likely to be Hispanic, less likely to have asthma, and more likely to have an infected sibling contact than the uninfected children. Symptoms varied with age. Overall, **70% of the infected children were symptomatic.** Children ages 6-13 were frequently (39%) asymptomatic, while younger children were more likely to have respiratory symptoms. Adolescents more frequently (61%) had an influenza-like syndrome. 42% had sensory symptoms. Adolescents typically had a longer median duration of illness — seven days vs. four days in other age groups. There were no variations in viral load by age or symptomatic state. [Editor's comment: This study took advantage of the ability to evaluate pediatric contacts of people known to be infected with SARS-CoV-2. As it happens, the epidemic in Durham, North Carolina, was concentrated in the Hispanic community, although it was present elsewhere. 81% of the evaluated children were of Hispanic ethnicity. Larger families and close living quarters were probably a factor in the extent of disease.] [Editor’s conflict of interest comment: Ross McKinney, MD, spent most of his academic career working at Duke University with the group who prepared this manuscript.]

Investigators from Massachusetts General Hospital evaluated viral loads in children 0-22 years old with a SARS-CoV-2 infection. 192 children were studied — 125 were SARS-CoV-2 negative, 49 were positive, and 18 had the COVID-19-associated Multisystem Inflammatory Syndrome in Children (MIS-C). Only 25 of the 49 infected children had a fever. Most symptoms were mild and, other than anosmia, resembled routine upper respiratory tract infections. The viral load in children peaked during the first two days of symptoms and was significantly higher than a comparison group of hospitalized adults with severe COVID-19. Children with MIS-C had little or no detectable virus by PCR, suggesting that the MIS-C symptoms might have occurred as an immune response after infection. Children with severe MIS-C tended to have higher IgM and IgG anti-SARS-CoV-2 antibody concentrations than children with mild MIS-C.
An article in the *European Respiratory Journal* suggested that elevated ACE2 expression in the olfactory neuroepithelium may explain both the mode of entry for SARS-CoV-2 and the reason for anosmia as a frequent symptom. In addition, the researchers postulated that elevated ACE-2 levels in the lungs of obese people may be one of the reasons that pneumonia is more common, and more severe, in obese patients.

Months after contracting the novel coronavirus, many patients suffer from problems that include difficulty breathing, heart issues, and memory loss. Now some hospitals have created specialized clinics to help patients deal with the aftermath.

Atlantic: Long-Haulers Are Redefining COVID-19

NPR: Another COVID-19 Medical Mystery: Patients Come Off Ventilator but Linger in a Coma


STAT: Four Scenarios on How We Might Develop Immunity to COVID-19

Policy News

Rhode Island performed a thorough and conscientious evaluation of COVID-19 transmission at day care centers. The state allowed day care centers to reopen when the rate of local community spread became sufficiently low — with several rules in place. Adults had to wear masks, everyone had to stay in the same room, a maximum of 12 people were allowed in a “pod” (later expanded to 20), daily symptom screening had to take place, and other protective measures were established. COVID-19 cases occurred at 29 of the 666 reopened centers. In 20 (69%), there was a single case and no apparent secondary spread. Five centers had more than one case, but epidemiological evaluation demonstrated the source of the cases was not within the centers. In only four centers were there multiple transmissions where the day care center could not be ruled out as the source. An inspection found that one center with 10 cases had not been following the state rules. Another center had two cases, one of which was a staff member who moved throughout the center. [Editor’s comment: It is impressive that 637 of the 666 centers could go without a detected case. The timing of the study was fortuitous, in that community transmission rates remained fairly low during the study period. Also, some cases may have been undetected, given how mild symptoms often are in young children.]

The administration has been planning changes in government data collection related to the public health impact of COVID-19, highlighting challenges state and local governments are facing in collecting reliable data and retooling their methods during the pandemic.

Teaching hospitals have been developing new strategies to ensure safety, maximize caregiver skills, and manage the flow of patients.

NIH Director’s Blog: Masks Save Lives


Undark: Will Covid-19 Failures Force Changes to the Public Health System?
Coronavirus and Health Equity

An analysis of seropositivity in New York City, determined by over 1.46 million coronavirus antibody test results, showed that the infection rate is between 12% and over 50%, depending on the neighborhood. While the results showed a 27% positive test rate across the entire city, lower-income communities had higher rates. Manhattan had the lowest rate at 19%, while the Bronx was at 33%, and one ZIP code in Queens was above 50%.

According to new analyses by the Centers for Disease Control and Prevention (CDC), based on information from the 23 states with sufficient race/ethnicity data, the incidence of laboratory-confirmed COVID-19 among American Indians and Alaska Natives was 3.5 times higher than among non-Hispanic White people as of July 3, 2020.

COVID-19 “testing deserts” exist in all 50 states, according to data from GoodRx, with the result that 67 million patients have a median travel distance of 22 miles to reach a test center. Further, 67% of all U.S. counties have no testing sites, and analyses revealed significant economic, racial, and ethnic inequities related to a community’s access to nearby testing.

Reuters: Exclusive: Nearly a Fifth of Enrollees in Pfizer, BioNTech COVID-19 Vaccine Study are Black or Latino

USA Today: Healthcare Providers Push to Fix Racism in the Medical Industry as COVID-19 Devastates Communities of Color

Research News

Studies of monoclonal antibodies as treatment for SARS-CoV-2 have suggested that using multiple neutralizing antibodies at one time is important in order to avoid the selection of viruses that escape from the antibody activity (i.e., “escape mutants”). Researchers at Regeneron built a panel of eight monoclonal antibodies directed at the SARS-CoV-2 spike protein and in vitro demonstrated that the use of two or more monoclonal antibodies was important to avoid virus escape through mutation and selection.

Washington Post: Genetic Data Show How a Single Superspreading Event Sent Coronavirus Across Massachusetts — and the Nation


Washington Post: Why German Researchers Held a Large Indoor Concert During the Pandemic

Testing News

The CDC changed their guidance on diagnostic testing for SARS-CoV-2. They now recommend that people who have been exposed to a patient with COVID-19 but do not have symptoms do not need testing. [Editor’s comment: This policy ignores the well-established fact that a very high percentage of transmission events are from asymptomatic individuals. The CDC advice is simply wrong. It represents exactly the
thinking that got us into our current pandemic quagmire, which is the reason the United States has more cases than anywhere else in the world."

The administration unexpectedly changed course on its previous decision to require certain tests to obtain FDA approval before they can be used. While the change is welcome to some who have worried that the FDA’s oversight has slowed getting tests to the market, the mid-pandemic reversal was characterized as ordering the FDA to "allow the use of a certain class of laboratory tests," including some for the coronavirus, without first confirming that they work." This change will allow clinics, academic institutions, and commercial labs to develop their own tests without FDA oversight, both for COVID-19 and for other diseases. These “laboratory-developed tests” (LDTs) are used by the lab that developed them and are not distributed to others. [Editor’s comment: The question of whether the FDA has the legal authority to regulate LDTs has been controversial long before the current administration, and the issues are not simple. On the one hand, academic labs regularly develop and modify tests for rare diseases or to test for specific molecular markers, and the time and expense of FDA approval would mean the test would likely not be made available at all. On the other hand, this mid-pandemic abrupt announcement will not serve to resolve this long-discussed concern for all stakeholders and does not help to increase the trust in the agency as we move towards a likely vaccine and other treatments for COVID-19. The example of the many inadequate and inaccurate antibody tests for SARS-CoV-2 showed the importance of some level of FDA review.]

The National Academies of Sciences, Engineering, and Medicine released results from a survey on “Encouraging Participation and Cooperation in Contact Tracing.” It focuses on two fronts: “encouraging individuals to respond to outreach from health department officials regarding participation in contact tracing and case investigation, and encouraging those who do participate to share information about people whom they may have exposed to COVID-19.”

Other COVID-19 News

The American Institute of Physics published an article about how flushing toilets and urinals release clouds of vapor that provide a favorable environment for the transmission of the coronavirus — so even alone in a public restroom, it’s still a good idea to mask up.

A survey from late July to early August by the American Association of Nurse Practitioners found that nurse practitioners “report their practices are better prepared to deal with COVID-19 today than at the start of the pandemic, and access to personal protective equipment (PPE) and viral testing are more widely available," and they report that testing delays have taken over as the greatest barrier to an effective pandemic response from lack of PPE.

Washington Post: Universities Sound Alarm as Coronavirus Cases Emerge Just Days into Classes — 530 at One Campus

Washington Post: Coronavirus Update: Infections Are Trending Upward in the Midwest

Modern Healthcare: New Virus Cases Decline in the U.S. and Experts Credit Masks

Washington Post: Everything You Need to Know About Getting Tested for the Coronavirus to Travel
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