AAMC Novel Coronavirus Update

January 6, 2021

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 Lead Science Policy Specialist Anu Dev, 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.

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Today's Numbers

- World: 86,752,314 confirmed cases (1,875,320 deaths)
  - 4,455,547 new cases this week
- United States: 21,096,346 (358,279)
  - 1,535,930 new cases this week
  - 18,696 deaths this week
  - 256,215,179 total tests
- U.S. Hot Spots
  - California: 265,113 new cases in last 7 days (1% increase in daily cases)
  - Texas: 127,175 (22%)
  - New York: 100,264 (27%)
  - Florida: 99,871 (42%)
  - Arizona: 62,187 (59%)
- U.S. COVID-19 Vaccine Distribution and Administration
  - Total Doses Distributed: 17,020,575
  - Total Number of People Initiating Vaccination: 4,836,469

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. Overall U.S. COVID-19 vaccine distribution and administration data can be found at the Centers for Disease Control and Prevention (CDC) COVID Data Tracker.

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

The story is fairly well known by now, but data from the Moderna vaccine trial were recently published in the New England Journal of Medicine (NEJM). The vaccine mRNA-1273 was evaluated in a double-blind, placebo-controlled trial that enrolled 30,420 volunteers. 96% of participants received both doses of the vaccine regimen. Symptomatic COVID-19 was seen in 185 volunteers in the placebo group and 11 participants in the vaccine group, for an efficacy of 94.1%. Severe COVID-19 occurred in 30 participants, including one death. All of the severe disease was in the placebo group. Adverse events were common and were more frequent after the second dose. Looking at more serious adverse events of Grade 3 or 4, none were very common: fever (1.5%), headache (4.5%), fatigue (9.7%), myalgia (muscle aches) (9%), arthralgia (joint aches) (5.2%), and chills (1.3%). [Editor’s comment: As clinical trials go, this was a home run. It’s nice to have the data available in detail. On to the hard work of distribution and administration.]

Treatment News

Despite substantial hope, a study published in the NEJM demonstrated that Eli Lilly’s monoclonal antibody, LY-CoV555, had no benefits when used in patients hospitalized with COVID-19. The study was part of the National Institute of Health’s (NIH’s) Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) trial series (ACTIV-3) and was a placebo-controlled evaluation of the addition of LY-CoV555 to a regimen of remdesivir and standard of care in hospitalized patients. 314 patients were enrolled, and the median time of enrollment was seven days after the onset of symptoms. The rate of adverse events was similar in the treatment and control cohorts, but so was the rate of sustained recovery. The study was stopped early by the Data Safety Monitoring Board because futility criteria were met (i.e., studying further patients was unlikely to demonstrate a benefit). [Editor’s comment: Monoclonal antibodies need to be used early to neutralize virus and lower viral load while a patient’s immune system is developing its own antibody response. As this well-executed study demonstrated, once the patient has neutralizing antibodies of their own, adding more antibodies has no therapeutic benefit. The key to successful use of either Lilly’s or Regeneron’s monoclonal antibody products is early use, which also means early polymerase chain reaction (PCR) testing.]

In contrast to the unsuccessful use of a monoclonal antibody in hospitalized patients, a study of Regeneron’s neutralizing antibody cocktail, REGN-COV2, in nonhospitalized patients demonstrated that the combination of two monoclonal antibodies was able to rapidly reduce SARS-CoV-2 viral load. 275 patients were treated with placebo or one of two dosage strengths of REGN-COV2. The two dosages of the drug performed similarly. Both were effective in lowering viral load over seven days compared to placebo in patients who were antibody-negative at enrollment. REGN-COV2 had no effect on viral load in patients who had already developed their own neutralizing antibodies. The effect of the monoclonal antibodies was also greater in those patients who began with a higher baseline viral load. [Editor’s comment: While this study was not designed to prove clinical efficacy, the data presented in the Food and Drug Administration’s emergency use authorization for REGN-COV2, which came from an extension of this study, showed that it decreased the rate of hospitalization in patients with high risk of progression from 9% to 3%, finding consistent with these laboratory results. Again, monoclonal antibodies are best used early — and primarily in people at higher risk of disease progression.]

Novavax announced the initiation of their PREVENT-19 Phase 3 efficacy trial of their COVID-19 vaccine in the United States and Mexico. The Novavax vaccine NVX-CoV2373 is a combination of spike protein and an adjuvant (immune enhancer). The company states they have completed enrollment of a 15,000-volunteer placebo-controlled study in
the United Kingdom and they expect to have results in the first quarter of 2021. The company plans to enroll 30,000 volunteers in the PREVENT-19 study at 115 sites using a 2-to-1 ratio of vaccine recipients to placebo control recipients. The study will be funded by the NIH and the Biomedical Advanced Research and Development Authority. [Editor’s comment: The challenge for Novavax may be completing their study with the pressures of other available vaccines, at least in the United States.]

Clinical News

Several study groups have been working collaboratively to evaluate the benefits of anticoagulation therapy (“blood thinners”) as an adjunct to standard care in patients hospitalized with COVID-19. The studies included patients with different degrees of illness. Three studies, including the NIH’s ACTIV-4 protocol, ended enrollment of critically ill patients in intensive care units because the addition of therapeutic levels of anticoagulants in those patients appeared to offer no clinical benefit, as measured by the need for organ support. The studies are continuing to enroll less ill patients, comparing full-dose and low-dose anticoagulation regimens initiated in-hospital.

To evaluate the protective effects of past infection with SARS-CoV-2 on reinfection, a group from Oxford evaluated the antibody status of 12,541 health care workers and published their results in the NEJM. They evaluated both neutralizing (anti-spike protein) antibodies and anti-nucleocapsid antibodies at baseline and then followed the staff members for up to 31 weeks. 11,634 individuals were initially negative for anti-spike antibodies and 1,265 were positive. 223 anti-spike negative workers developed a positive SARS-CoV-2 PCR, compared to only two spike positive workers, both of whom were asymptomatic while PCR-positive. The authors concluded that the presence of antibodies (results were similar for both neutralizing and anti-nucleocapsid antibodies) was protective for at least six months. [Editor’s comment: The results, while not unexpected, bode well for the benefits of vaccination.

Coronavirus and Health Equity

JAMA: Patient Characteristics Associated With Telemedicine Access for Primary and Specialty Ambulatory Care During the COVID-19 Pandemic


CBS News: Equitable Access to Coronavirus Vaccine Emerges as Next Challenge Amid Slow Rollout

de Beaumont Foundation: New Poll Reveals Most Effective Language to Improve COVID-19 Vaccine Acceptance

Research News

The question of whether the newly recognized strains of SARS-CoV-2 from the United Kingdom (B.1.1.7) and from South Africa (501.V2) will cause worse disease or evade vaccine protection is an important one, A non-peer-reviewed preprint study published in medRxiv from the University of Hong Kong evaluated two mutant strains found in the United Kingdom in October and November. The earlier strain had an N501Y mutation,
substituting a tyrosine (Y) for an asparagine (N) at site 501 in the spike protein, while the second strain added an amino acid deletion at the 69th and 70th residues. In epidemiological modeling studies, the authors found the N501Y mutation alone led to a 10% increase in transmissibility of the virus, while the combination of N501Y and the deletion led to a 75% increase in transmissibility. [Editor's comment: The use of empirical data means that factors like seasonality that might affect a virus’s spread are likely to be minimized, but the story is still interesting. B.1.1.7 includes both the N501Y and the 69/70 deletion, as well as another substitution P681H (histidine for a proline at site 681) that is also thought to have biological effect.]

NEJM: Microvascular Injury in the Brains of Patients with Covid-19

Testing News

A diagnostic study to compare the accuracy of health care worker versus self-collected oropharyngeal and mid-turbinate swabs and saliva samples for SARS-CoV-2 found that the sensitivities of a self-swab sample and saliva sample were inferior by 8.7% and 9.5%, respectively. Conducted using a pool of both COVID-19-positive (n = 401) and healthy (n = 100) volunteers, the results show that while self-testing is less sensitive on its own compared to a health care worker swab, the sensitivity of a combined self-swab and saliva collection is equivalent to that of a health care worker swab and could still function as a useful testing tool in appropriate clinical settings.

A study from the CDC in the Morbidity and Mortality Weekly Report (MMWR) examining SARS-CoV-2 testing in health centers used responses from a Health Resources and Services Administration survey to describe all patients tested (3,194,838) and those who received positive SARS-CoV-2 test results (308,780) by race/ethnicity and state of residence between June 5 to Oct. 2, 2020. Among persons with known race/ethnicity who received testing (2,506,935), 36% were Hispanic/Latino, 38% were White, and 20% were Black; among those with known race/ethnicity who received positive test results, 56% were Hispanic/Latino, 24% were White, and 15% were Black. The data demonstrate the role of health centers in providing access to testing in communities disproportionately affected by COVID-19.

Antigen testing has advantages over PCR for SARS-CoV-2, in that it is cheaper and faster. However, there are disadvantages in sensitivity with some antigen tests. A study performed at the University of Wisconsin and published in the MMWR compared antigen testing using the Quidel Sofia device to PCR. In symptomatic individuals, the Sofia antigen test had 80% sensitivity and 98.9% specificity. In contrast, in asymptomatic individuals, the sensitivity was only 41.2%, while the specificity remained high at 98.4%. [Editor's comment: This study affirms what has become the general dogma regarding antigen testing: Many of the kits are inadequately sensitive for screening asymptomatic individuals. There are, however, several antigen tests on the market now, Sofia being one sold by Quidel. They vary in their performance characteristics, so care should be taken to understand their limitations before they are selected for use.]

Other COVID-19 News

In a not-yet-peer-reviewed study in medRxiv, researchers integrated mobility, demographic, and census data in New York City and Seattle to build a model of SARS-CoV-2 transmission events. The data suggest that most infections (80%) are produced by a small number of people (27%) — and that about 10% of events can be considered superspreading events, generating more than eight secondary infections. The results also
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