AAMC Novel Coronavirus Update
December 9, 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 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.

Please share/forward this newsletter freely.

Today's Numbers

- World: 68,584,302 confirmed cases (1,563,997 deaths)
  - 4,341,991 new cases this week (4,079,530 new cases last week)
- United States: 15,246,376 (287,550)
  - 1,443,337 new cases this week (1,130,147 new cases last week)
  - 15,594 deaths this week (10,687 deaths last week)
  - 207,572,528 total tests
- U.S. Hot Spots
  - California: 143,759 new cases in last 7 days (61% increase in daily cases)
  - Texas: 79,915 (27%)
  - Ohio: 72,090 (62%)
  - Pennsylvania: 69,886 (47%)
  - New York: 68,827 (35%)

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

AstraZeneca presented the pooled interim results from four randomized, controlled trials of its chimpanzee adenovirus SARS-CoV-2 vaccine ChAdOx1 (AZD1222) in the Lancet.
23,848 individuals from the United Kingdom, Brazil, and South Africa enrolled, and 11,636 were included in this evaluation. Efficacy was 62.1% in the volunteers who received the standard dose of vaccine twice (95% confidence interval [CI] 41.0-75.7), while a subset of 2,474 volunteers received a half dose of vaccine followed by a full dose. For those participants, the efficacy was 90% (95% CI 67.4-97.0). From 21 days after the first dose of either regimen, all 10 cases who were hospitalized were in the control arm. Also on the positive side, there were 175 serious adverse events — 84 in the ChAdOx1 arm and 91 in the control arm (meningococcal vaccine or saline). [Editor's comment: While the Food and Drug Administration (FDA) set 50% as an acceptable efficacy threshold, 62.1% pales in comparison to ~95% efficacy for the mRNA vaccines from Pfizer/BioNTech and Moderna. The AstraZeneca vaccine will be easier and cheaper to manufacture than the mRNA vaccines, and it will be more readily produced in larger quantities. The different results in the two dosing regimens will require further exploration given the wide confidence intervals in the relatively small sample set presented. The New York Times reported that the low dose-first regimen was given only to people under 55 years old, which might have influenced that already shaky piece of evidence.]

**Treatment News**

Pfizer and BioNTech submitted data to the FDA to request an emergency use authorization (EUA) for their mRNA vaccine BNT162b2. As part of its preparation for a meeting of the Center for Biologics Evaluation and Research's Vaccine and Related Biological Products Advisory Committee on Dec. 10, the FDA prepared its interpretation of the Pfizer/BioNTech study results. Most of the information has been well characterized in the press in the past few weeks, but some important findings are new. For example, the FDA noted that the vaccine appeared to be more than 90% effective in almost all cohorts. There were 10 cases of severe COVID-19, with only one in the vaccine arm, so the vaccine minimizes the odds of severe COVID-19. BNT162b2 was found to be effective even after one dose, with the case rates in the study arms diverging in the vaccine and placebo groups beginning about 14 days after the first dose. The vaccine was safe, with a low rate of serious adverse events, and it produced neutralizing antibody titers that were comparable to convalescent plasma. [Editor's comment: BNT162b2 will probably be authorized by the FDA through the EUA process and the massive task of immunizing as many people as possible will start. The next key questions will be the durability of immunity and whether there are any unanticipated late or rare side effects.]

A panel of investigators authored a short report in the New England Journal of Medicine (NEJM) describing the durability of the antibody response after administration of the Moderna SARS-CoV-2 mRNA-1273 vaccine. They evaluated binding and neutralizing antibody titers at three months after the second (booster) dose of vaccine and divided the 34 healthy adult volunteers into three cohorts: 18-55 years old, 56-70, and greater than 70. In all three groups, putatively protective neutralizing antibody levels were maintained at three months, although the levels were diminished from the peak titers shortly after vaccination. The younger cohorts had higher levels of neutralizing antibodies.

A key missing piece in the armamentarium against COVID-19 has been an effective antiviral agent. Investigators at Georgia State University published in Nature Medicine the results of an orally administered ribonucleoside analogue, MK-4482/EIDD-2801, that was given to ferrets. The agent was originally developed at Emory University as an anti-influenza treatment, and preliminary safety and pharmacokinetic data was available as a result of that work. The agent has been licensed to Merck and is currently in clinical trials for treatment of COVID-19. In this study, ferrets infected with SARS-CoV-2 were treated with MK-4482/EIDD-2801. Treated ferrets had a rapid fall in nasopharyngeal viral load and did not transmit to other ferrets, in contrast to the mock treated ferrets. [Editor's comment: Like many animal models, there are limitations to the ferret data. Ferrets, while they can
transmit SARS-CoV-2, do not become apparently ill. The spread is thus most analogous to asymptomatic human-human transmission. This study hints at the promise of MK-4482/EMD-2801 and increases the anticipation of Phase 2/3 clinical trial results.

Clinical News

Investigators at the Centers for Disease Control and Prevention (CDC) evaluated the spread of SARS-CoV-2 in 58 households where a primary case of COVID-19 had been identified. The study included 188 contacts — 120 adults and 68 children. The rates of secondary infections in the households were similar for adults (30%) and children (28%). If the child was the index case, there was child-to-adult transmission in 2 of 10 instances and child-to-child transmission in 1 of 6 cases. Unsurprisingly, symptoms in children were milder than in adults.

A study in the NEJM focused on determining the duration of live-virus shedding of SARS-CoV-2 in immunocompromised patients with COVID-19. Investigators collected respiratory samples from 20 individuals and found that viral RNA was present up to 78 days (interquartile range, 24 to 64 days) after the onset of symptoms. Based on these findings, the authors suggest that it may be necessary to revise the CDC’s current isolation protocols, which are primarily based on data from immunocompetent patients.

To improve the understanding of the long-term effects of COVID-19, investigators looked at clinical status and lung function in 220 individuals who were 10 weeks out from severe SARS-CoV-2 infection. Based on total lung capacity, 38% of patients displayed restrictive pulmonary function post-infection, and critically ill patients were the most prone to this condition. Demographic parameters and comorbidities did not significantly differ between restrictive and nonrestrictive patients. Additionally, pulmonary function impairment could not be linked with abnormal imaging results or residual symptoms.

Using data from the CDC’s COVID-19-Associated Hospitalization Surveillance Network (COVID-NET), a team of investigators described the characteristics of previously healthy young adults (18-49 years old) admitted to the hospital with confirmed COVID-19. Between March 1 and Aug. 1, 44,865 adults were hospitalized in the United States with COVID-19. Adults 18-49 years old represented 31.8% of those hospitalizations (13,167 admissions). 3,720 of these patients had chart abstractions performed, of whom 513 (14.2%) had no preexisting medical conditions. Of those, 22% were treated in the intensive care unit during their hospitalization, and three patients (0.6%) died. Of the admitted patients, 73.7% were male, 42.1% were Hispanic or Latino, 9% were health care workers, and 13.7% were tobacco smokers. [Editor’s comment: While bad outcomes are less common than in older individuals, this study reinforces that young adults can become seriously ill — and even die — from COVID-19.]

JAMA: A Proposed Framework and Timeline of the Spectrum of Disease Due to SARS-CoV-2 Infection

JAMA: Stillbirths During the COVID-19 Pandemic in England, April–June 2020

Policy News

The CDC put together a sensible summary of recommendations for public health strategies in the face of high levels of community transmission of SARS-CoV-2. It’s a familiar litany: Wear masks, physically distance, avoid group settings, postpone travel, and
wash your hands. Public health agencies should engage in contact tracing and vaccinate widely.

The CDC’s Advisory Committee on Immunization Practices published an interim recommendation for allocating initial supplies of a COVID-19 vaccine, following a meeting on Dec. 1. As previously noted, the panel recommends that vaccination in the initial phase be offered to both health care personnel and residents of long-term care facilities. In a statement regarding the recommendations, CDC Director Robert Redfield, MD, also emphasized the importance of prioritizing the elderly in multigenerational households, noting that this is a structure found in many Black, Hispanic, and Tribal Nations families.

American Academy of Pediatrics Encourages Children and Teens to Wear Cloth Face Coverings During Sports Practices and Games

Coronavirus and Health Equity

A new systematic review in the Annals of Internal Medicine looked at more than 50 cohort, cross-sectional, and ecological studies (as well as CDC data) and confirmed that “African American/Black and Hispanic populations experience disproportionately higher rates of SARS-CoV-2 infection and COVID-19-related mortality but similar rates of case fatality. Differences in health care access and exposure risk may be driving higher infection and mortality rates.” In New York City, specifically, new research published in JAMA confirmed that while Black city residents are more likely to test positive for the coronavirus, once hospitalized they are less likely than White patients to have critical illness or die after accounting for comorbidities and neighborhood factors. This again points to the significant role structural determinants play within marginalized communities to increase the risk of exposure and decrease health care access.

An infographic from the National Institute for Health Care Management showed that while 20% of U.S. adults said they often or always felt lonely or socially isolated pre-pandemic, those proportions have grown. By August 2020, 41% of adults reported feeling socially isolated and 28% reported feeling lonely, particularly those of a lower socioeconomic status and from urban communities.

Kaiser Family Foundation: Addressing Racial Equity in Vaccine Distribution

Vox: “The Stakes Are Life and Death”: Addiction Treatment’s COVID-19 Challenge

Washington Post: Amid History of Mistreatment, Doctors Struggle to Sell Black Americans on Coronavirus Vaccine

Washington Post: More Underage Migrants Are Testing Positive for Coronavirus

Research News

A large consortium of researchers identified shared biology and potential drug targets among the three highly pathogenic human coronavirus strains: SARS-CoV-2, SARS-CoV-1, and MERS-CoV. Expanding on previous work exploring the SARS-CoV-2 interactome, the study mapped the full interactomes of SARS-CoV-1 and MERS-CoV to elucidate the conservation of target proteins and cellular processes between all three viruses. The authors also attempted to connect these in vitro molecular findings with clinical information for COVID-19 patients to explore potential therapeutic avenues.
Using data from over 30,000 individuals with COVID-19, investigators from the Mount Sinai Health System found that neutralizing antibodies to SARS-CoV-2 infection persist for months after initial detection. The vast majority of the cohort, made up of individuals with primarily mild-to-moderate COVID-19, showed robust immunoglobulin G antibody responses against the viral spike protein. Antibody titers remained stable for a period of at least five months. The authors plan to follow the cohort over a longer period of time and urge additional studies to establish a correlate of protection to inform policies for COVID-19.

A study investigating whether a critical aspect of the pathogenesis of COVID-19 is the pattern of immune response found that in severe COVID-19, pro-inflammatory cytokine levels (tumor necrosis factor, IL-6, and IL-8) were elevated early in the disease, while interferon transcription was not yet active. In contrast, in influenza, interferon levels were induced early and pro-inflammatory cytokines were only acutely produced. In COVID-19, higher interferon concentrations in patients were correlated with faster viral clearance. The authors' basic hypothesis is that an "untuned" immune response results in slower viral clearance and a greater degree of inflammation in COVID-19 than in influenza.

In a preprint published in medRxiv, British investigators followed a large cohort of health care workers to evaluate whether antibodies (i.e., a history of past SARS-CoV-2 infection) are protective of subsequent COVID-19. The study enrolled 12,219 health care workers and followed them for up to 30 weeks. At baseline, 11,052 were seronegative and 1,246 were seropositive. There were 89 polymerase chain reaction (PCR)-confirmed symptomatic cases of COVID-19 in the seronegative cohort (0.46 cases per 10,000 days at risk) and no symptomatic cases in the baseline seropositive cohort. The study also screened asymptomatic individuals and identified 76 PCR-positive patients in the baseline seronegative cohort (0.40 cases per 10,000 days at risk) and three PCR-positive cases (0.21 cases per 10,000 days at risk) in the seropositive cohort. Based on these results, the authors propose that people are protected from subsequent reinfection with SARS-CoV-2 for at least six months.

*Nature: Correlates of Protection Against SARS-CoV-2 in Rhesus Macaques*

**Testing News**

*FDA News Release: FDA Authorizes First COVID-19 and Flu Combination Test for Use With Home-collected Samples*

**Other COVID-19 News**

Both SARS-CoV-2 vaccines currently awaiting EUA approval from the FDA require a two-dose regimen, highlighting deficiencies and challenges in state tracking systems. Information is tracked in different ways depending on where a person is vaccinated, often via electronic health records in larger health systems or specialized software for smaller clinics. All data on vaccinations also needs to be reported to a state’s centralized immunization information system — a process that can vary in efficiency and accuracy by state and jurisdiction.

*medRxiv: The Impact of Vaccination on COVID-19 Outbreaks in the United States*

*Science: COVID-19 Vaccine Trial Ethics Once We Have Efficacious Vaccines*
For questions, contact Anu Dev, PhD, AAMC lead science policy specialist.

Ross McKinney Jr., MD
Chief Scientific Officer
rmckinney@aamc.org

Anu Dev, PhD
Lead Specialist, Science Policy
adev@aamc.org

Stephen J. Heinig
Director, Science Policy
sheinig@aamc.org

Philip Alberti, PhD
Senior Director, Health Equity Research & Policy
palmart@aamc.org