2020-06-10/11 DAILY UNM GLOBAL HEALTH COVID-19 BRIEFING

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Executive Summary


Testing: False negative rate in COVID-19 testing. Patients testing negative with subsequent positive test results. IgG and IgM antibody response. SARS-CoV-2 receptor binding domain potential antigen for use in antibody testing.

Drugs, Vaccines, Therapies, Clinical Trials: Drug repositioning. Hydroxychloroquine toxicity. Multifaceted immunosuppression described. HCQ not effective for prophylaxis. 63 new trials.


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Our continuously curated practice guidelines in the context of COVID-19 can be found here.

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NM Highlights

- Gov. Lujan Grisham online update on New Mexico COVID-19 efforts on Thursday — breweries open

  KQRE-TV: Governor Michelle Lujan Grisham gave an update on the COVID-19 pandemic and how the state is doing. The state has seen a sharp uptick in the 7-day moving average of COVID-19 cases. She also announced that on Friday, June 12 breweries can begin to softly reopen; and starting Friday, the public health order will allow outdoor and patio seating at 50%
occupancy for breweries. Beginning Monday on June 15, the public health order will allow 50% maximum occupancy for indoor seating at breweries. The Governor, with Cabinet Secretaries for Health (Kathy Kunkel) and Human Services (Dr. David Scrase), presented of data updates, via slides, and answered questions from the media. Slides are included in this link.

- **NM reports 10 more COVID-19 deaths and 121 additional cases on June 11**
  As of today (6/11), the total positive cases and total deaths in the state are 9,367 and 420, respectively. The state has performed 250,880 tests, there are 197 individuals currently hospitalized for COVID-19, and 3,806 COVID-19 cases have recovered. NMDOH portal featuring epidemiologic breakdown of cases.

- **COVID-19 testing now available for New Mexico food industry workers**
  *KRQE-TV:* The source includes a list of testing locations for food industry workers, which includes employees at restaurants, grocery stores, farmers’ markets, distribution centers, and food manufacturing facilities. Testing will be available from 8 a.m. to 11 a.m. every Monday starting on June 15. Testing is free, although those with health insurance are asked to bring their card with them. Appointments are required and have to be scheduled by noon on the preceding Friday.

- **COVID-19 testing to be available for lawmakers, staffers during special session**
  *KOB:* New Mexico lawmakers voted Tuesday to make coronavirus testing available to lawmakers and their staff. All staff members entering the Roundhouse will be required to get tested; testing is not mandatory for lawmakers.

- **Santa Fe City Council approves measure requiring face masks**
  *Santa Fe New Mexican:* Fearing a second wave of infections and another hit to the economy, Mayor Alan Webber and the City Council late Wednesday approved a proposal requiring anyone over the age of 15 to wear a face covering in most public settings or while conducting business. Those who refuse to put on a mask or other face-covering could end up in trouble with city police - a written warning on the first offense and a $50 fine on the second and any subsequent offense.

- **Governor and lawmakers eye reserves, cuts to fill nearly $2.4B budget hole**
  *KRQE-TV:* New Mexico lawmakers and Governor Michelle Lujan Grisham are expected to meet for a special legislative session next week to prepare to a more than $2 billion budget hole due to the COVID-19 pandemic and plummeting oil revenues. The state is projecting a $375 million revenue loss for the current budget year and a $1.976 billion revenue loss for the Fiscal Year 2021 budget beginning in July 2020. The state administration has recommended using $193 million in reserves to in-part cover the current budget shortfall and $873 million to in-part plug 2021 fiscal year budget.

- **COVID-19 resulting in up to a year of learning loss**
  *ABQ Journal:* School closures due to the COVID-19 pandemic will likely result in months’ to a year’s worth of learning loss for New Mexico’s students, according to a Legislative Finance Committee report. Students are expected to start the 2020-21 school year with a big dip in learning. The analysis says the shortened school schedules used during distance learning equate to 6.9% of the recommended instructional time for pre-kindergarten, 10.4% for kindergarten and first grade, 13.9% for second and third grade, 20.8% for fourth and fifth grades and 38.1% for middle and high school.

**US Highlights**

- **Amazon and eBay instructed to remove unsafe COVID-19 products from sale**
  *BBC:* The US Environmental Protection Agency (EPA) has ordered e-commerce giants Amazon and eBay to stop selling several unsafe or unproven pesticides and disinfectants, including products falsely marketed as anti-Covid-19. The "stop sale" orders mention more than 70 products, which must now be taken off the companies' platforms. Failure to comply could result in big fines.

- **Cases on rise in nearly half the states as states roll back lockdowns**
  *KOB4:* According to an Associated Press analysis, cases are rising in nearly half the states due to lifting stay-at-home orders, school and business closures, and other restrictions put in place during the spring to stem the virus’s spread. Updates on Arizona, North Carolina, Texas, Alabama, and Arkansas.
Economics, Workforce, Supply Chain, PPE Highlights

- **IMF says $10 trillion spent to combat pandemic, far more needed**
  
  *Reuters:* Governments around the world have spent $10 trillion in fiscal actions to respond to the novel coronavirus pandemic and its economic fallout, but significant further efforts are needed. New estimates suggest that up to 100 million people may experience extreme poverty from the crisis. IMF management suggest further spending should focus on minimizing job losses and preventing a rise in inequality.

- **A rapid systematic review of the efficacy of face masks and respirators**
  
  *Intl J Nursing Studies:* 19 randomized controlled trials were included. In the community, masks appear to be effective with and without hand hygiene, and both together are more protective. Randomized controlled trials in health care workers show that respirators, if worn continually during a shift, were effective but not if worn intermittently. Medical masks were not effective, and cloth mask were less effective against viral, bacterial, droplet or other infection outcomes. When used by sick patients randomized controlled trials suggest protection of well contacts.

- **Transparent face masks for hearing impaired to communicate through lipreading**
  
  *Al Jazeera:* Transparent face masks are helping Indonesia's hearing impaired to communicate through lipreading amid the COVID-19 pandemic.

- **Coronavirus outbreak 'accelerating' in Africa with supplies running short, say WHO**
  
  *BBC:* While the virus has spread more slowly in Africa than other parts of the world, the spread to rural areas is concerning because of lack of tests and other supplies. Initial steps taken in testing at points of entry and tracing continue to work in its favor. Coupled with its youthful population, the continent has so far managed to avoid the fast spread until now. It took 98 days to reach the initial 100,000 cases. By contrast, it has taken just 18 days to double from 100,000 to 200,000.

- **Kenya faces tough decisions in opening economy while avoiding collapse of health system**
  
  *BBC:* This year's budget is expected to focus on turning around the economy, which the World Bank expects will slow down from 5% growth to just 1%. Recently President Uhuru Kenyatta said relaxing restrictions by only a fifth could lead to 30,000 deaths by December with up to half a million jobs could be lost in the next six months. Small businesses struggle because many of their main clients, the slum dwellers themselves, lost their income as casual workers due to Covid-19 restrictions.

Epidemiology Highlights

- **Task force warns of potential spike in COVID-19 cases after protests**
  
  *Daily Beast:* In a conference call on Monday, officials with the White House Coronavirus Task Force relayed concerns to governors that the protests across the country could lead to a spike in COVID-19 infections. They reportedly discussed the possibility that yelling chants could negate the benefit of cloth masks, and that destruction of testing sites would be detrimental to regional public health efforts.

  
  *The Aging Male:* 14 observational studies with 29,909 COVID-19 patients and 1445 cases of death were included. Significant associations were observed for risk of death from COVID-19 infection and age >=65 yrs (pooled ORs = 4.59) and being male (pooled ORs = 1.50). In addition, hypertension (pooled ORs = 2.70), cardiovascular diseases (pooled ORs = 3.72), diabetes (pooled ORs = 2.41), chronic obstructive pulmonary disease (pooled ORs = 3.53), and cancer (pooled ORs = 3.04) were associated with higher risk of mortality.

- **Cancer patients have higher mortality rates: a meta-analysis**
  
  *JCO Global Oncology:* 32 observational studies on 46,499 patients (1,776 patients with cancer) with COVID-19 from Asia, Europe, and the United States were included. All-cause mortality was higher in patients with cancer versus those without (RR, 1.66). The need for ICU admission was also more likely in patients with versus without cancer (RR, 1.56). However, in a prespecified subgroup analysis of patients > 65 years of age, all-cause mortality was comparable between those with versus without cancer (RR, 1.06).
• Use of UV-C to disinfect mobile phones

*American J Infection Control:* Environmental swabs were used to culture health care provider’s personal mobile phone surfaces. Four cultures were obtained per phone: before and after the UV-C device’s 30-second disinfecting cycle, and at the beginning and end of a 12-hour shift. Surveys on attitudes towards mobile phone contamination were administered to participants pre- and post-study day. Total bacterial colony forming units (CFUs) were reduced by 90.5% (p=0.006) after one UV-C disinfection cycle, and by 99.9% (p=0.004) after two cycles. Total pathogenic bacterial CFUs were decreased by 98.2% (p=0.038) after one and >99.99% (p=0.037) after two disinfection cycles. All survey respondents were willing to use the UV-C device daily to weekly, finding it convenient and beneficial.

Practice Guidelines

• **Benefits of noninvasive ventilation in the prone position: Italy case series study**

A cross-sectional survey was performed to identify 15 inpatients undergoing the prone position with noninvasive ventilation (NIV, CPAP+O2) outside the ICU. Respiratory parameters were measured at 3 time points: before NIV, during NIV in pronation (60 minutes after start), and 60 minutes after NIV end. Follow-up was conducted at 14 days. Compared with baseline, all patients had a reduction in respiratory rate during and after pronation (P < .001 for both); all patients had an improvement in SpO2 and PaO2:FIO2 during pronation (P < .001 for both); 80% had an improvement in SpO2 and PaO2:FIO2 after pronation; 13.3% had the same value; and 6.7% had worsened. Compared with baseline 73.3% had an improvement in comfort during pronation and 26.7% had the same value. At the 14-day follow-up, 9 patients were discharged home, 1 improved and stopped pronation, 3 continued pronation, 1 patient was intubated and admitted to ICU, and 1 patient died. Prevention/delay of intubation wasn’t assessed.

• **Canadian Thoracic Society’s statement on management of sleep disordered breathing**

Sleep Disordered Breathing (SDB) includes diseases such as obstructive sleep apnea and central sleep disorders (e.g., associated with neuromuscular disease, opioid use, congestive heart failure). This commentary summarizes the Canadian Thoracic Society’s position statement on managing SDB during the COVID-19 pandemic in an easy FAQ format. The full SDB position statement, as well as other valuable tools and resources, can be found at https://cts-sct.ca/covid-19/.

• **Ketogenic diet provision during the pandemic: the experience of two US epilepsy diet centers**

Ketogenic diet therapy is often started in the hospital, with families educated in hospital-based classes, but this is difficult to do in this current pandemic. Pediatric and adult epilepsy diet centers had to quickly consider alternative methods to both start and maintain ketogenic diet therapy. This paper provides several examples (patient cases) of how ketogenic diet therapy can be provided to patients in unique ways, along with recommendations from other experts and patients, learned over the past few months. 9 new patients were started on the modified Atkins diet (MAD), and 28 follow-up patients have been seen to date in this manner. Patient feedback has been overall positive regarding receiving ketogenic diet therapy (KDT) training and follow-up via telemedicine visit.

• **A personalized cardiometabolic approach for reducing complications and costs: a review**

This is the first review, focusing both on cardiovascular and metabolic aspects of COVID-19, in an integrated and personalized way, following the guidelines of the Cardiometabolic Health/Medicine.

• **Asian guidelines on IBD management during the COVID-19 pandemic**

The experts of the Asian Pacific Association of Gastroenterology (APAGE) Inflammatory Bowel Disease (IBD) put recommendations based on their experience and the currently available data. In general, most IBD therapies (with a few exceptions) can be continued safely, and the general consensus is that maintaining disease control should remain the main principle of management. Social distancing measures and the appropriate use of PPE should be strictly adhered to. Face-to-face clinic follow ups and non-urgent procedures should be kept to a minimum.
Testing

- **RT-PCR testing for SARS-CoV-2 has a variable but overall high rate of false negatives**
  
  *Annals of Internal Medicine*: This meta-analysis aims to estimate the false-negative rate of SARS-CoV-2 PCR tests as a function of time since exposure. The authors find that the false-negative rate declines from 100% on day 0 to 21% on day 8, and then increases again. Based on this analysis, the false-negative rate for SARS-CoV-2 RT-PCR is high, even at its lowest on day 8 post-exposure, or 3 days after symptom onset. At best, one out of five people who really are infected with COVID-19 will test negative. A negative PCR test within the first days following exposure to a known case may not be more predictive of actual infection than flipping a coin.

- **A small proportion of patients testing negative for SARS-CoV-2 test positive within 7 days**
  
  *Clinical Infectious Diseases*: Two independent research teams describe that among patients initially testing negative using nasopharyngeal swab samples, repeat testing within 7 days yielded a positive result in 3.5% of cases. 20,912 patients from two large academic health systems were retested on clinical grounds. Although the proportion of newly positive results is small, the findings of positive test results among initially negative patients should be used in conjunction with other reports to interpret COVID-19 testing in the clinical context and create guidelines for retesting.

- **Patterns of IgG and IgM antibody response in COVID-19 patients**
  
  *Emerging Microbes and Infection*: 217 blood specimens were obtained from 32 COVID-19 patients over the course of 28 days following disease onset. Quantum dot immunofluorescence assay was used to semi-quantitatively detect IgM and IgG antibodies. The authors observed that the IgM antibody response to SARS-CoV-2 occurred earlier and peaked earlier than the IgG response and that the IgM antibody response began to decline at week 3 of the illness, while the IgG antibody response persisted and was maintained. In addition, severe cases of COVID-19 tended to have a more vigorous response based on quantity of both IgG and IgM.

- **New data supports the use of the SARS-CoV2 receptor-binding domain as an antigen to develop serological tests**
  
  *Science Immunology*: As the receptor binding domain (RBD) of the spike protein is poorly conserved between the novel and other human coronaviruses, it represents a promising antigen for detecting antibodies specific to SARS-CoV-2. The authors of this study used a large panel of human sera (63 COVID-19 patients and 71 control subjects) and hyperimmune sera from animals exposed to zoonotic coronaviruses to evaluate the RBD's performance as an antigen for reliable detection of SARS-CoV-2-specific antibodies. By day 9 after the onset of symptoms, the recombinant SARS-CoV-2 RBD antigen was highly sensitive (98%) and specific (100%) for antibodies induced by SARS-CoVs. There was a strong correlation between levels of RBD binding antibodies and SARS-CoV-2 neutralizing antibodies in patients. These results reveal the early kinetics of SARS-CoV-2 antibody responses and support using the RBD antigen in serological diagnostic assays.

Drugs, Vaccines, Therapies, Clinical Trials

- **Drug repositioning for treatment of COVID-19: a systematic review**
  
  *Archives of Virology*: 12 relevant studies were identified as eligible. Among the drugs reported 57 showed some evidence of antiviral activity. Studies have reported the anti-SARS-CoV-2 activity of antitumor (16%; 9/57), antimalarial (7%, 4/57), and antibacterial (5%; 3/57) agents. 7 agents (chloroquine, tetradrine, umifenovir (arbidol), carringycin, damageprevir, lopinavir/ritonavir) are in phase IV of clinical trials. Due to the evidence of the anti-SARS-CoV-2 activity of various clinically available agents, drug repositioning stands out as a promising strategy for a short-term response in the fight against the novel coronavirus.

- **Hydroxychloroquine toxicity: pharmacokinetics observational study**
  
  *Intensive Care Medicine*: Letter to the Editor. In this observational cohort study (n = 13) prescribing HCQ in COVID-19 patients is unsafe for several reasons. Because of drug accumulation and high volume of distribution, toxic threshold was reached by day 5 even in patients with normal renal function. The authors recorded side effects although patients’ blood concentrations were in therapeutic range, therefore making HCQ administration potentially harmful despite correct surveillance parameters. Hemodialysis had little effect on HCQ concentrations, whereas the patient with veno-venous extracorporeal life support.
expressed constant low HCQ blood concentration, possibly due to membrane adsorption. To avoid HCQ-related complications in COVID-19 critically ill patients, the authors suggest monitoring EKG and blood concentration daily.

- **Severe COVID-19 associated with deep and sustained multifaceted cellular immunosuppression**
  *Intensive Care Medicine*: Letter to Editor. The authors present the first report on serial immunophenotypic and functional changes in 13 consecutively recruited patients infected with SARS-CoV-2 virus during their first week of ICU stay compared to 10 healthy controls. The results strongly suggest a multifaceted devastating effect of the virus to cause depletion of virtually all classes of adaptive immune cells and to cause upregulation of potent T cell killing and immunosuppressive mechanisms in critically ill COVID-19 patients. Since T cells are essential for definitive viral clearance, these results call into question therapies (e.g., anti-IL-6, corticosteroids, JAK inhibitors) that aim to block the ability of the patient to mount an effective immune response. Knowing that almost all anti-inflammatory therapies have also chronically failed in sepsis, consideration to therapies that boost host immunity in selected severe ARDS ICU patients (e.g., IL-7, IFN-γ or checkpoint inhibitors) may be appropriate.

- **Hydroxychloroquine not effective for COVID-19 prophylaxis**
  *New England Journal of Medicine*: In a double-blind, randomized trial, 821 asymptomatic persons with a high-risk or moderate-risk exposure to SARS-CoV-2 were assigned to receive hydroxychloroquine or placebo within 4 days after the exposure. No benefit in preventing illness compatible with Covid-19 was found (P = 0.35).

- **63 New COVID-19 trials registered June 10-11 at clinicaltrials.gov**
  Treatment trials: Infliximab, Anti-spike (S) SARS-CoV-2, Azvudine, Chloroquine + Losartan, Thymosin Alpha 1, Enoxaparin, LY3819253 (LY-CoV555), Ivermectin, Interleukin-7, Favipiravir, Lactoferrin, MK-5475, Dipyridamole Darunavir/Cobicistat vs. Lopinavir/Ritonavir, Dexametason & Enoxaparin. At time of writing, a total of 1962 were active, 140 completed, and 4 posted results.

**Other Science**

- **COVID-19 mortality: countries employing containment have better outcomes than with mitigation**
  *Journal of the Formosan Medical Association*: The authors analyzed COVID-19-related mortality rates of Italy, Spain, United Kingdom, and France (mitigation strategy) and that of Germany (containment strategy). All had a similar epidemic curves and cumulative number of confirmed COVID-19 cases. However, Germany had a cumulative death toll and case fatality rate approximately 1/4 of that of countries adopting a mitigation strategy. A major reason for the sharp difference in case fatality rate is that confirmed cases in Germany included mild cases detected under containment strategy, while confirmed cases in the other four countries consisted of severe cases who are the focus of mitigation strategy. Germany lost only 1 healthcare worker by May 3, 2020. In contrast, Italy lost 110, United Kingdom lost 92, Spain lost 28, and France lost 21 healthcare workers from COVID-19 during the same period. The low death tolls in both patients and healthcare workers in Germany is not a unique case for countries adopting a containment strategy. South Korea, another country responded to large outbreaks with a containment strategy, also had a very low death toll (252), case fatality rate (2.3%), population mortality rate (0.5 per 100,000 population), and number of healthcare workers dying from COVID-19 (only 1). For countries initially did not experience large outbreaks, containment strategy (Taiwan) also yield a 15-fold lower population mortality rate than that yielded by mitigation strategy (Japan) (0.025 vs. 0.385 per 100,000 population).

- **Prehospital pulse oximetry: a red flag for early detection of silent hypoxemia in COVID-19**
  *Critical Care*: The retrospective study examined 1201 patients who experienced COVID-19 between March 13 and 29, 2020. The medianSpO2i/RRI value was significantly higher than that of patients treated in the previous 3 years (5 [4–5] in 2020 versus 3.4 [2.4–4.5] in 2019, 3.3 [2.2–4.4] in 2018, and3.5 [2.5–4.6] in 2017, p< 0.001. Without systematic SpO2i measurement, a normal breathing rate could mask profound hypoxia and make severity assessment in COVID-19 patients all the more difficult in an out-of-hospital setting.

- **Normal values of D-dimer are associated with survival in COVID-19 inpatients**
  *Academic Emergency Medicine*: In a cohort observational study of 749 COVID-19 patients with presenting day-1 D-dimer levels available, the 28-day mortality was 78 10.4% (95% CI, 8.3-12.8%). D-dimer levels at day 1 were normal in 586 of 671
survivors but elevated in 36 of 78 non-survivors, for a survival sensitivity of 87% (95% CI, 86-89%), positive predictive value 93% (95% CI, 92-95%), specificity 46% (95% CI, 36-57%), negative predictive value 30% (95% CI, 23-36%). Day 3 D-dimer values, available for 598 cohort patients (80%), were normal in 408 28-day survivors and 10 who died. They were elevated in 130 28-day survivors and 50 who died. Thus, a normal value was strongly associated with survival: sensitivity 76% (95% CI, 75-77%), positive predictive value 98% (95% CI, 96-99%), specificity 83% (95% CI, 72-91%), negative predictive value 28% (95% CI, 24-30%).

- **Factors associated with depression, anxiety, and PTSD -- family social support helps**

  *Psychiatry Research*: This cross-sectional online study assessed 898 participants aged 18-30 in 50 U.S. states. Respondents reported high levels of depression (43.3%, PHQ-8 scores >/= 10), high anxiety scores (45.4%, GAD-7 scores >/= 10), and high levels of PTSD symptoms (31.8%, PCL-C scores >/= 45). High levels of loneliness, high levels of COVID-19-specific worry, and low distress tolerance were significantly associated with clinical levels of depression, anxiety, and PTSD symptoms. Resilience was associated with low levels of depression and anxiety symptoms but not PTSD. Most respondents had high levels of social support. Social support from family, but not from partner or peers, was associated with low levels of depression and PTSD. Compared to Whites, Asian Americans were less likely to report high levels across mental health symptoms, and Hispanic/Latinos were less likely to report high levels of anxiety.

- **SARS-CoV-2 not detected in air samples around hospitalized patients -- limited airborne transmission**

  *Infection Control & Hospital Epidemiology*: Sampling of air close to 6 COVID-19 patients with and without surgical masks was performed with sampling devices using sterile gelatin filters. Frequently touched environmental surfaces near 21 patients were swabbed before daily environmental disinfection. All the air samples were negative for SARS-CoV-2 RNA in the 6 patients singly isolated inside airborne infection isolation rooms (AIIR) with 12 air changes per hour. 19 (5.0%) of 377 environmental samples near 21 patients were RT-PCR positive with a median viral load of 9.2x102 copies/ml (range: 1.1x102 to 9.4x104 copies/ml). The contamination rate was highest on patients' mobile phone (7.8%, 6/77), followed by bed rail (5.4%, 4/74) and toilet door handle (5.3%, 4/76). There was a significant correlation between viral load ranges in clinical samples and positivity rate of environmental samples (p < 0.001). The study suggests that the airborne route is not the predominant mode of transmission of COVID-19.

- **Stay-at-home orders worsen weight-related behaviors in patients with obesity**

  A retrospective medical chart review identified 123 patients with obesity who completed an online survey to assess COVID-19 status and health behaviors during stay-at-home orders. Logistic regression models examined the impact of these orders on anxiety and depression by ethnic group. Two patients tested positive for SARS-CoV-2 and 14.6% reported symptoms. 72.8% reported increased anxiety and 83.6% increased depression since stay-at-home orders were initiated. 69.6% reported more difficulty in achieving weight loss goals, less exercise time (47.9%) and intensity (55.8%), increased stockpiling of food (49.6%) and stress eating (61.2%). Hispanics were less likely to report anxiety vs non-Hispanic whites (OR 0.16; 95% CI, 0.05-0.49; P = 0.009).


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