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2020-05-01 DAILY UNM GLOBAL HEALTH COVID-19 BRIEFING

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Recommended Citation

Lambert, Christophe G.; Shawn Stoicu; Ingrid Hendrix; Lori D. Sloane; Anastasiya Nestsiarovich; Praveen Kumar; Nicolas Lauve; Melissa Cossé; Jenny Situ; Jennifer Thompson; Ariel Hurwitz; Alexandra Yingling; Cristian Bologa; Tudor I. Oprea; George Uhl; Gregory Mertz; Kristine Tollestrup; Orrin Myers; and Douglas J. Perkins. "2020-05-01 DAILY UNM GLOBAL HEALTH COVID-19 BRIEFING." (2020).

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DAILY UNM GLOBAL HEALTH COVID-19 BRIEFING

May 1, 2020

Executive Summary

Relaxing emergency orders. UNMH remdesivir patient. NM case update. Gallup lockdown. Aid for arts. Nursing facility boost. More NM layoffs. Public relief programs. Insurance call center. Capturing COVID-19 stories. More NYT NM praise. Belief enhances compliance. Italy cardiac arrests. Non-COVID vaccine backlog. Africa investments. US airlines require facemasks. Pandemic timeline prediction. Convalescent plasma. Viral shedding. Laboratory information systems. Internet searches. Practice guidelines for: skull surgery, cardiac electrophysiology, blood purification, electroconvulsive therapy, quantitative CT. Testing methods review. FDA authorizes remdesivir. Stillbenoid analogs. Favipiravir. HCQ reanalysis. Hypercoagulation and antithrombotic. ChAdOx1 MERS and animal immunity. New drug trials. Enterocytes infections. Cardiovascular disease. ACEi/ARBs. Common antihypertensives. Comprehensive COVID-19 review.

All of our past briefings are maintained in a UNM library repository here.

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

Our continuously curated therapeutic evidence is maintained here.

You may submit content for future briefings here.

NM Highlights

Changes to NM emergency orders ease healthcare and economic restrictions

A public health order allows medical facilities to gradually resume non-essential but medically necessary procedures (including ambulatory and inpatient surgery) based on guidelines from the Department of Health. Amended public health order relaxes several restrictions to begin relieving economic pressure. Non-essential retailers can now operate with curbside pickup and delivery, and some parks will be open for day use. Gun stores can sell by appointment. Pet services and golf courses to reopen. More restrictions will begin to be lifted May 15th. Order state-wide until May 15 except Cibola, McKinley, and San Juan counties. Video press conference covers the changes at length.

- Patient at UNM Hospital treated with Remdesivir recovered and sent home
 - One patient received remdesivir and has recovered. UNMH working with Gilead to acquire more remdesivir. Multiple clinical trials showed remdesivir has reduced hospital time for severely ill patients from 15 days to 11 days and the mortality rate from 11.6% to 8%.
- New Mexico reports 8 more COVID-19 deaths and 104 new cases
 - The total positive cases and total deaths in the state are 3,513 and 131, respectively. As of today, the state has performed 71,118 tests, there are 159 individuals currently hospitalized for COVID-19, and 785 COVID-19 cases have recovered. New NMDOH portal featuring epidemiologic breakdown of cases.
- Governor invoking Riot Control Act to shut down Gallup
 - After more than 1,000 confirmed cases of COVID-19 and at the request of Gallup's both outgoing new mayors, the NM governor has locked down the city. NM State Police, DOT, and National Guard will be handing out misdemeanors for non-compliant persons. In effect until May 4th, all roads into Gallup are closed. Businesses in Gallup will close from 5 pm -8 am. Vehicles may only have a maximum of 2 individuals. Residents of Gallup should shelter in place unless absolutely necessary

for health or safety or a medical emergency.

• NM Arts to distribute \$1.5 million in economic relief

The funds, which are to be given in \$10,000 allotments, will be allocated to 200 past recipients of NM Arts awards including nonprofit arts organizations, education facilities, tribal governments, and government entities for art activities taking place between July 1, 2020 and June 30, 2021. The funding will come from the 2021 state budget, a partnership agreement between New Mexico Arts and the National Endowment for the Arts, and the federal CARES Act. A third of the budget is specifically allocated for rural communities.

• \$46.2 million for NM nursing facilities

NM Human Services Department announced \$46.2 million in new Medicaid payments to nursing facilities to help them mitigate the spread of COVID-19 among employees and residents. The new Medicaid payments were authorized by a 2019 state law that created the Health Care Quality Surcharge program. A new IT module and web portal will let providers review data and make their surcharge payments.

More layoffs and furloughs in NM amid COVID-19 crisis

As companies grapple with the fallout of COVID-19 and the effects the virus has had on their bottom lines, hundreds of New Mexico employees have been laid off in response. And tens of thousands of people have filed for unemployment benefits in New Mexico in recent weeks, far exceeding the typical rate of claims.

• List of New Mexico coronavirus relief programs

Links are provided for numerous personal and business support programs, including coronavirus relief for individuals, extended unemployment, housing and utilities, childcare, food services, relief for small businesses and others.

• State insurance office establishes toll-free COVID-19 call center

New Mexicans can call the center with questions about health insurance coverage related to COVID-19. The call center will also guide consumers and provide information about the state's emergency public health orders and the bulletins Lines will be open from 8am-6pm Monday through Saturday. Call center number: 1-833-415-0566

NMSU library seeks community submissions for COVID-19 archive

NMSU Archives and Special Collections is interested in documenting COVID-19 community responses in southern New Mexico in real-time. The collection would help future researchers understand what this time is like in the context of southern New Mexico. Submissions may include digital materials like emails, journal entries, photos, videos, and digital art.

NYT praises NM political leadership and strong health system in its fight against COVID-19

New York Times: Despite having limited financial resources, New Mexico has set an example in the fight against the coronavirus crisis. When COVID-19 attacked New Mexico, Governor Michelle Lujan Grisham's swift decisions, such as declaring a statewide health emergency, stay-at-home order, the closing of non-essential businesses, widespread testing for the coronavirus, helped the state in lowering the infection and death rate. Her stellar performance during the crisis has raised her as a possible vice-presidential running mate alongside Joe Biden. Executives at Lovelace, Presbyterian Healthcare Services, and the University of New Mexico are working together to give the state its best shot. The state is also harnessing the scientific power of two national nuclear laboratories to process still more coronavirus tests. Even with a massive death toll averted, plummeting oil has severely affected the budget of the state and the state's 2.2 million people face economic devastation, which is going to be the governor's next major challenge, speculating that NM may have a "secret weapon" via tapping in the state's \$23 billion sovereign wealth fund, accumulated over the years from oil and gas royalties.

US Highlights

• Compliance with non-pharmaceutical interventions associated with belief of effectiveness

MedRxiv preprint: US residents (n=1,005) were shown to be willing to comply with non-pharmaceutical interventions if they are easy, familiar and are perceived to be effective, such as hand washing. Face masks, face touching and disinfecting surfaces are perceived as having less impact on safety and are therefore not as well adopted. The authors suggest public outreach measures where efficacy and feasibility of these interventions are stressed.

International Highlights

• Four Italian provinces see 58% rise in out-of-hospital cardiac arrests compared to 2019

NEJM: Lodi, Cremona, Pavia, and Mantua provinces were compared from 2/21–4/1/2019 and 2/21–3/31/2020. Cumulative incidences of COVID-19 and out-of-hospital cardiac arrests were strongly associated (Spearman rank correlation coefficient, 0.87; 95% CI: [0.83, 0.91]; P<0.001). 103 out-of-hospital cardiac arrest patients were suspected or known to have the virus, accounting for 77.4% of the increase in out-of-hospital cardiac arrest cases.

Economics, Workforce, Supply Chain, PPE Highlights

UNICEF calls for transport of a large backlog of vaccine shipments

The annual meeting of WHO health ministers will take place on May 18th. UNICEF is appealing to governments and private sectors to find freight space to transport the vaccines. Dozens of countries are at risk of running out of vital non-COVID-19 vaccines that save the lives of up to 3 million children per year.

European Investment Bank joins WHO in pandemic help for Africa

The partnership will strengthen primary health care in 10 African countries by scaling up financing to ensure essential supply chains, including that of PPE and diagnostics, could function properly through centralized procurement.

• U.S. airlines decide to mandate facial coverings for all passengers

Masks will be provided to passengers if needed. In June, some airlines will use hospital-type electrostatic fogging machines to decontaminate the airplane cabin before each flight.

Epidemiology Highlights

Coronavirus likely to keep spreading for at least 18 -24 more months

A team of pandemic experts used historical data on past pandemics to predict scenarios of how the new coronavirus is likely to keep spreading. Three scenarios included repetitive waves over 1-2 years, a large peak in the fall, and a slow burn of ongoing transmission. The US should be prepared for at least another 18 to 24 months of significant COVID-19 activity, with hot spots popping up periodically in diverse geographic areas.

Convalescent plasma reduces viral shedding, but not mortality in end-stage patients

In a small, retrospective, observational study (n=6) in China, critical COVID-19 patients with respiratory failure were treated at a median of 21.5 days after first detection of viral shedding. Median age was 61.5 years old. All tested negative for SARS-CoV-2 RNA after 3 days but 5 patients died. Convalescent plasma treatment can discontinue SARS-CoV-2 shedding but cannot reduce mortality in critically end-stage COVID-19 patients, and treatment should be initiated earlier.

Almost 10% of patients had viral shedding after 30 days, regardless of symptoms

In a small study (n=36), the Chinese authors performed antibody testing on positive patients to determine viral shedding rates. The median duration of viral RNA shedding was 53.5 days (IQR 47.75-60.5). IgM levels were persistently high into the 9th week after symptom onset in patients with prolonged viral shedding.

Healthcare Policy Recommendations

Laboratory information system requirements to manage the COVID-19 pandemic

The Belgian National Reference Center performed a moving total of > 25,000 SARS-CoV-2 PCR tests in parallel to standard routine testing. Design, implementation and requirements of LIS functionality are described related to managing increased test demand. The approach to data mining and reporting of actionable daily summary statistics to governing bodies and other policymakers is described.

• Internet searches increase for unproven COVID-19 therapies in the US

JAMA: The fractions of Google searches (http://google.com/trends) originating from the US that searched for mainstream

purchasing options of chloroquine and hydroxychloroquine per 10 million total searches were monitored. Following high-profile claims that the drugs were effective, queries increased for chloroquine and hydrochloroquine by 442% (95% CI, 215%-1220%) and 1389% (95% CI, 779%-2021%), respectively. Following news reports of the first fatal poisoning, searches to buy chloroquine or hydroxychloroquine only decreased by a small amount.

Practice Guidelines

• Skull base surgery during the Covid-19: Italian Skull Base Society recommendations

Only urgent surgical operations are recommended, and all patients should be tested at least twice (on days 4 and 2 prior to surgery). For positive patients, procedures should be postponed until after swab test is negative. If the procedure is vital to the survival of the patient, FFP3 and/or PAPRs devices, goggles, full-face visor, double gloves, water-resistant gowns and protective caps, are mandatory. For negative patients, use of at least FFP2 mask is recommended. In all cases the use of drills, which promote the aerosolization of potentially infected mucous particles, should be avoided. Given the potential neurotropism of SARS-CoV-2, dura handling should be minimized.

• COVID-19 and cardiac electrophysiology: guidance from a UK tertiary cardiac center

A guide is provided on ablation procedures. In UK catheter ablation procedures that are considered urgent or emergent are: 1)Ablation of ventricular tachycardia that cannot be controlled with medication and leads to hemodynamic compromise, 2)Ablation of an incessant, hemodynamically significant, severely symptomatic tachycardia (SVT/AF/atrial flutter) not responding to antiarrhythmic drugs, rate control, and/or cardioversion and 3) Ablation for preexcited AF with syncope or cardiac arrest.

• Expert recommendations on blood purification treatment in COVID-19

A protocol was developed by Chinese researchers including four steps: 1) assess whether patients with severe COVID-19 require blood purification. 2)prescribe a blood purification treatment; 3) monitor and adjust parameters of blood purification; 4) evaluate the timing of discontinuation of blood purification.

• Electroconvulsive therapy should be considered as an essential procedure even during COVID-19

Hospitals around the world closed down their electroconvulsive therapy (ECT)-units. Belgian authors claim that ECT should be seen as an essential medical procedure and made available in order to prevent long-term mental health consequences in adults with serious mental illness. The caveats and measures to undertake for ECT are described.

Quantitative CT can be used for assessment of pneumonia severity on admission

A quantitative method based on multi-scale convolutional neural networks was used to assess the infected lung segments. It was also compared with the semi-quantitative method, and Spearman correlation (rs) was explored with lab test parameters and pneumonia severity index (PSI). The proportion of "ground glass opacity" based on the quantitative method positively correlated with the semi-quantitative CT score (P < 0.001 for all; rs = 0.88, 0.87, 0.90), lung consolidation on quantitative method correlated with C-reactive protein levels (P = 0.0278, 0.0168, 0.0078; rs = 0.40, 0.43, 0.48), and total lung lesion (quantitative method) correlated with erythrocyte sedimentation rate (P = 0.0296, 0.0408, 0.0048; rs = 0.46, 0.44, 0.58). These quantitative findings were also negatively correlated with the lymphocyte count (P = 0.0222, 0.0024, 0.0068; rs = 0.42, -0.53, -0.48).

Testing

• Review of laboratory assessment of COVID-19

A review is performed on testing methods and algorithms for COVID-19 which are currently in use or will be available for use in the near future in the US and other countries. Although commercial testing systems are becoming available, there will likely be insufficient numbers of such tests due to high demand. Serological testing will be commonly performed next as the COVID-19 begins to subside.

Drugs, Vaccines, Therapies, Clinical Trials

• US FDA issues an emergency use authorization for remdesivir for the treatment COVID-19

Today, the U.S. Food and Drug Administration issued an emergency use authorization for the investigational antiviral drug remdesivir for the treatment of suspected or laboratory-confirmed COVID-19 in adults and children hospitalized with severe disease.

• Structure of remdesivir

Researchers report in *Science* the structure of remdesivir, an antiviral that's shown promise against the SARS-CoV-2 virus, bound to both RNA and the viral polymerase – illuminating the mechanism the drug uses to shut down viral reproduction.

• Stilbene-based natural compounds as promising drug candidates against COVID-19

The current study aimed to repurpose stilbenoid analogs against SARS-CoV-2 spike protein and human ACE2 receptor complex for their affinity and stability using molecular dynamics simulation and binding free energy analysis based on molecular docking. 4 compounds were probed for binding affinity using molecular docking showing good affinity. Stilbene based compounds in general and resveratrol can be promising anti-COVID-19 drug candidates acting through disruption of the spike protein.

Experimental treatment with favipiravir for COVID-19: an open-label control study

Patients treated with favipiravir were compared with historical controls. A shorter viral clearance time was found for the FPV arm versus historical controls, 4 (2.5-9) d versus 11 (8-13) d, P < 0.001). The FPV arm also showed significant improvement in chest imaging compared with historical controls with an improvement rate of 91.43% versus 62.22% (P = 0.004). The study design and high ED50 for favipiravir raise questions about the validity of this report.

• An independent appraisal and re-analysis of HCQ treatment trial for COVID-19

Reanalysis of HCQ trials were reviewed. It was concluded that HCQ-treated groups approached significantly increased cure rates on day 6 (n = 6), demonstrating promising pilot data. HCQ has not yet demonstrated significant effects on decreasing viral load of SARS-CoV-2 (n = 15). Additional trials with larger sample sizes and more consistent analysis of patient data are needed.

Hypercoagulation and antithrombotic treatment in COVID-19: systematic review

A systematic review reports clinical studies on laboratory parameters: d-dimer, platelet counts, prothrombin time, activated partial thromboplastin time, alanine aminotransferase, and aspartate aminotransferase. Trials assessing efficacy of antithrombotic treatment, including aspirin or low-molecular-weight heparin (LMWH), should be planned.

One dose of ChAdOx1 MERS provides protective immunity in animal study

Exploring MERS-CoV, researchers showed that rhesus macaques seroconverted rapidly after single intramuscular vaccination with ChAdOx1 MERS. The vaccine protected against respiratory injury and pneumonia and reduced viral load in lung tissue. MERS-CoV replication in type I and II pneumocytes of ChAdOx1 MERS vaccinated animals was absent. A prime-boost regimen of ChAdOx1 MERS boosted antibody titers, and viral replication was completely absent from the respiratory tract tissue of these rhesus macaques. This is the first time that broad protection after a single vaccination has been shown for any MERS-CoV vaccine. The data support further clinical development of ChAdOx1 MERS.

45 New COVID-19 Trials registered today at clinicaltrials.gov

Treatment trials: sirolimus, povidone iodine, HCQ, HCQ vs diltiazem and niclosamide, azithromycin, zinc sulfate, doxycycline, sulfonated teta-anthracenyl porphyrin, SnPP protoporphyrin, tocilizumab, apo-HCQ, oseltamivir, hormones, HCQ sulfate, DPP4 inhibiters (linagliptin), remestemcel-L, avdoralimab. At time of writing, a total of 1096 were active, 50 completed, and 3 posted results.

Other Science

• <u>Intestinal epithelium supports SARS-CoV-2 replication in human small intestinal organoids (hSIOs)</u> In a peer-reviewed research article in *Science*, previously deposited as a preprint on *medRxiv*, researchers demonstrate that enterocytes of human small intestinal organoids were infected by SARS-CoV and SARS-CoV-2 with subsequent detection of significant titers of infectious viral particles. GI symptoms have been observed in a subset of patients, and this new evidence suggests that the intestine may be another viral target organ.

• Review of COVID-19 and cardiovascular disease

JAHA editors: Elevated troponin levels are frequently seen in COVID-19; and are associated with increased severity of disease and risk of death. In the absence of a specific etiology, elevated levels of troponins are likely due to myocardial injury from inflammation or a direct effect of SARS-CoV-2 infection. Hypertension is associated with a higher risk of severe COVID-19 and greater mortality rates. Until further studies reveal the impact of pre-existing or de novo RAS blockade on COVID-19 disease progression or severity, there is no justification to omit RAS blockers in COVID-19 patients. Vascular events are common complication of COVID-19. The increased burden of vascular comorbidities among people with severe infection is only a partial explanation of such increased risk of events. Broad elevations of chemokines and cytokines occur in SARS-CoV-2, similar to cytokine release syndrome (CRS) seen in cancer patients on immune-modulating therapy. Yet, some overlap with troponin elevation has been see. COVID-19 is associated with a high inflammatory burden that may cause arrhythmias due to increased metabolic demand, hypoxia and/or sympathetic stimulation in patients with and without pre-existing cardiovascular disease. This and other associations are discussed as well as potential therapies and select ethical concerns.

- ACE inhibitors not associated with excess cardiovascular mortality in COVID-19

 International study on 8910 patients hospitalized with a diagnosis of COVID-19 were analyzed. Neither the use of angiotensin-converting—enzyme inhibitors OR_{adjusted} = 0.33 (0.20 0.54) nor the use of angiotensin-receptor blockers OR_{adjusted} = 1.23 (0.87 1.74) was associated with an increased risk of in-hospital death.
- No evidence that ACE inhibitors or ARBs affected the risk of COVID-19

 Case-control study (N=6272) of the use of ARBs or ACE inhibitors did not show any association with COVID-19 among case patients overall (adjusted odds ratio, 0.95 (0.86-1.05) for ARBs and 0.96 (0.87 to 1.07) for ACE inhibitors) or among patients who had a severe or fatal course of the disease (adjusted odds ratio, 0.83 (0.63 to 1.10) for ARBs and 0.91 (0.69 to 1.21) for ACE inhibitors).
- No increased risk of severe disease associated with five common classes of antihypertensive medications

The authors identified 2573 patients with a history of hypertension who tested positive for COVID-19, and found no association between antihypertensive medication and risk of severe illness. The medications investigated include ACE inhibitors, angiotensin-receptor blockers, beta-blockers, calcium-channel blockers, and thiazide diuretics.

• A comprehensive review on COVID-19 information

Journal of Clinical Medicine: A review is published on most recent information about COVID-19 Taxonomy, Genetics, Epidemiology, Diagnosis, Treatment, and Control.

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