WEEK IN REVIEW COVID-19 SCIENTIFIC NEWS MAY 18 - 22, 2020

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The MS Literature Review Task Force is a group of UNC medical and pharmacy students who conduct daily literature searches for scientific updates on COVID-19. Contact Mary Chandler Gwin, mary_gwin@med.unc.edu for any comments, questions, etc.

LATEST ARTICLES:

CLINICAL INFORMATION

<u>Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic. Rogers, J. P., et al., *The Lancet, Psychiatry.* 18 May 2020.</u>

• if SARS-CoV-2 follows a similar course as SARS-CoV-1 and MERS then patients should recover without experiencing mental illness, but patients acutely ill with COVID-19 may present with delirium. There is the possibility that patients will develop PTSD, depression, anxiety, and/or sleep disturbances following their SARS-CoV-2 infection for which providers should be screening.

Risk factors for SARS-CoV-2 among patients in the Oxford Royal College of General Practitioners Research and Surveillance Centre primary care network: a cross-sectional study. Lusignan, S. et al., *The Lancet*. May 15, 2020.

A cross sectional study of a primary care population of patients tested for SARS-CoV-2. Univariate and
multivariate analysis for clinical and socioeconomic risk factors for positive RT-PCR test performed. Risk factors
found were comparable with prior studies of hospitalized patients-male sex, obesity and chronic kidney disease.
Black people were more likely to have a positive test, compared to white population. One outlier was active
smoking had decreased odds of a positive test, OR 0·49, 95% CI 0·34–0·71).

ICU and ventilator mortality among critically ill adults with COVID-19. Auld, S. et al. Preprint. April 26, 2020.

Mortality rates on ventilators and off-ventilators were examined among 217 critically ill patients in Atlanta, GA. Mortality on ventilators was 29.7%. Overall mortality is 25.8% and 40.1% survived to discharge. This contradicts early reports of rates exceeding 50%, in areas that were ill-prepared. Georgia had increased time delay to its pandemic arrival. A majority of critically ill patients can have good clinical outcomes. The minor difference in rates supports the ongoing use of mechanical ventilation for patients with acute respiratory failure.

<u>Variation in False-Negative Rate of Reverse Transcriptase Polymerase Chain Reaction—Based SARS-CoV-2 Tests by Time Since Exposure</u>. Kucirka, L. M. et al. *Annals of Internal Medicine*. May 13, 2020.

Pooled analysis determined the false negative rates of the RT-PCR SARS-CoV-2 test by time since exposure. The
rate of false negatives decreased from 100% on day 1 to 67% on day 4. On day of symptom onset, the median
was 38%, decreased to a minimum of 20% on day 8, and increased to 66% on day 21. If the RT-PCR result is
negative, posttest probability is reduced by only 3% (CI 0%-47%). Confidence intervals were large in this study.
This study cannot delineate true false negatives from clearance of infection, 9 days post exposure. If the goal is

to clear patient of isolation, treat RT-PCR negative results as correct. If the goal is to evaluate whether patients should be treated as SARS-CoV-2 positive for contact tracing, an RT-PCR negative result may not suit.

PUBLIC HEALTH/EPIDEMIOLOGY

Antibody study shows just 5% of Spaniards have contracted the coronavirus. Andrino, B. et al., El País. 14 May 2020.

• A prevalence study was conducted by selecting over 36,000 households representing all age groups, gender, and geographical locations in Spain, which showed only 5% of Spaniards had contracted the virus. 5% is in line with studies in other European countries and far below the rate that would provide herd immunity which experts place at 60% at least. Epidemiologists consulted by this newspaper said that social distancing measures must remain in place until a vaccine becomes available.

Out-of-Hospital Cardiac Arrest during the Covid-19 Outbreak in Italy. Baldi, E. et al. NEJM. April 29, 2020.

Primary Results: Compared to the same time period in 2019, this region in Italy saw a 58% increase in total OHCA's (133, total). 103 cases of the 133 were suspected or confirmed COVID cases. Spearman rank coefficient of 0.87: 95% CI, 0.83 to 0.91; P<0.001. Secondary Results: Unwitnessed arrests and arrests at home increased by 11.3% and 7.3%, respectively. Bystander CPR decreased by 15.6% and EMS response times increased by 3 minutes. Successful resuscitations decreased by 14.9%.

<u>Seroprevalence of SARS-CoV-2-specific Antibodies Among Adults in Los Angeles County, California, on April 10-11, 2020.</u> Sood, N. et al., *JAMA*. 18 May 2020.

• 865 random individuals were tested. The enrollment had quotas for subgroups based on age, sex, race, and ethnicity. Data was also weighted to reflect 2018 census data for LA. Both weighted and unweighted data were analyzed. The unweighted and weighted prevalence of SARS-CoV-2 antibodies was 4.34% (CI, 2.76%-6.07%) and 4.65% (CI, 2.52%-7.07%), respectively.

Work-related COVID-19 transmission in six Asian countries/areas: A follow-up study. Lan, F. N. et al. *PLOS ONE.* May 19, 2020.

• Examining Asian COVID-19 cases, 47.7% of early outbreak cases (day 1-10) were work-related. 14.9% were work related in day 1-40 of the outbreak. High risk occupations included healthcare workers (22%), followed by transportation drivers (18%), services and sales (18%), cleaning and domestic (9%) and public safety (9%). Transportation drivers and religious professionals were the most common occupations affected in both early and late transmission periods. High risk occupations are impossible to work remotely and employ many low socioeconomic status workers.

THERAPEUTIC DEVELOPMENTS

<u>ChAdOx1 nCoV-19 vaccination prevents SARS-CoV-2 pneumonia in rhesus macaques</u>. Neeltje van Doremalen, Teresa Lambe etal bioRxiv May 13, 2020

• A preclinical trial with rhesus macaques found that after a single vaccination with ChAdOx1 nCoV-19, the average clinical score of control animals was higher compared to vaccinated animals. They observed a significantly reduced viral load (genomic RNA and subgenomic RNA) in bronchoalveolar lavage fluid and respiratory tract tissue of vaccinated animals challenged with SARS-CoV-2 compared with control animals, and no pneumonia was observed in vaccinated rhesus macaques. Importantly, no evidence of immune-enhanced disease following viral challenge in vaccinated animals was observed. The data from this study informed the start of the phase I clinical trial with ChAdOx1 nCoV-19 on April 23, 2020.

Moderna Announces Positive Interim Phase 1 Data for its mRNA Vaccine (mRNA-1273) Against Novel Coronavirus. *Moderna Press Release.* 18 May 2020.

• All participants in both the 25 µg and 100 µg dose cohorts developed antibody levels at or above levels seen in convalescent sera. It was also found to effectively protect against viral replication in the lungs of mice. So far, the vaccine has proven to be safe and well-tolerated.

SARS-CoV-2 Rates in BCG-Vaccinated and Unvaccinated Young Adults Uri Hamiel, MD et al JAMA May 13 2020

Researchers in Israel compared the COVID-19 infection rates in 2 similar populations with differing BCG status: individuals born during the 3 years before and 3 years after cessation of the universal BCG vaccine program in Israel. 3064 people born between 1979 and 1981 and 2869 likely unvaccinated people born between 1983 and 1985 were involved in the study. There was no statistically significant difference in the proportion of positive test results in the BCG-vaccinated group vs the unvaccinated group or in positivity rates per 100 000 (121 in vaccinated group vs 100 in unvaccinated group, p=0.09). They concluded that BCG vaccination in childhood doesn't provide a protective effect against COVID-19 in adulthood.

BASIC SCIENCE

Multiorgan and Renal Tropism of SARS-CoV-2. Puelles, V. et al., NEJM. May 13, 2020.

Autopsy series of 27 patients, where SARS-CoV-2 viral loads were measured in numerous organs. Additionally, the authors quantified SARS-CoV-2 viral load from 6 patients in various renal compartments. Median viral count in renal cells < 0.01 RNA copy/cell, whereas the median viral RNA in lung tissue approached 1 copy/cell. Within the kidneys, viral concentrations were highest and found most often in the glomeruli.

<u>Targets of T cell responses to SARS-CoV-2 coronavirus in humans with COVID-19 disease and unexposed individuals.</u> Grifoni, A. et al. *Cell.* May 14, 2020.

HLA predicted peptide megapools were used to identify SARS-CoV-2 specific CD8+ and CD4+ cells in circulation among 20 convalescent COVID-19 patients. CD4+ responses consisted of 50% directed at the spike, 50% at the remainder of the orfeome. Non-spike CD4+ responses were also detected among the control unexposed patients. CD8+ responses did not emphasize the spike protein (26% reactivity). Adaptive immune responses can fail to occur, but TH1 responses should be elicited in vaccine development. Some degree of CD4+ cross-reactivity with seasonal common cold coronaviruses exists in 40-60% of unexposed individuals.

GUIDELINES AND FIGURES:

FROM CDC

May 12 – Non-Covid Care for Patients

- Conduct telehealth visits when available
- Follow infection control practices to prevent transmission, including screening all patients for COVID-19 signs and symptoms
- Make decisions based on local epidemiological information
- Prioritize services that if delayed would cause harm to the patient

May 15 – Information for Pediatric Healthcare Providers

- Include information and guidance related to multisystem inflammatory syndrome in children
- Patients presents with persistent fever, variety of signs/symptoms including multiorgan involvement and elevated inflammatory markers
- MIS-C may begin weeks after a child is infected with SARS-CoV-2
- Evaluation for signs may include chest radiograph, echocardiography, and blood testing

• If a patient under the age of 21 meets these criteria the case should be reported to local, state or territorial health department

May 20 - Caring for Newborns

- Reported signs for neonates with SARS-CoV-2 infection include fever, lethargy, rhinorrhea, cough, tachypnea, increased work of breathing, vomiting, diarrhea, and feeding intolerance or decreased intake
- Many term infants in these case reports had asymptomatic or mild disease recovering without complications
- Testing recommended for all neonates born to women with confirmed or suspected COVID-19.

FROM WHO

May 18 - Situation Report 119

- 73rd World Health Assembly opened today with a focus on COVID-19
- WHO signed an agreement with International Olympic Committee to promote health through sport and physical activity
 - The focus is on preventing non-communicable diseases
- Flooding in Somalia raised concerns of an upsurge in cholera cases as the country deals with a growing number of COVID-19

May 19 - Situation Report 120

- WHO published <u>this document</u> to provide overview of public health and social measures to limit harm from reopening
- In a study of 11-15 year-olds in Europe, more adolescents are reporting mental health concerns based on data from 2014 2018, which will provide a baseline for future studies to measure the impact of COVID-19
- WHO Regional Office for the Western Pacific has released <u>a timeline</u> of key moments and actions in the response to COVID-19

May 20 – Situation Report 121

- WHO Regional Director for the Americas made a statement that addressing COVID-19 will require protecting vulnerable groups including women, underprivileged populations, indigenous populations, and migrants
- Published a new Case Report Form for "<u>Suspected Cases of multisystem inflammatory syndrome (MIS) in children and adolescents temporarily related to COVID-19</u>" in order to collect data on presentations, severity, and outcomes
- Uganda commissioned the first Port Health Covid-19 laboratory at the main Uganda-Tanzania border. Two GeneXpert machines will be used to test all truck drivers arriving at Mutukula point of entry with results becoming available in 45 minutes.

May 21 – <u>Situation Report 122</u>

- WHO World Health Assembly ended with a global commitment to the COVID-19 response together
- WHO continues to support Somalia since its outbreak but providing training and supplies to healthcare workers. Only 26% of the WHO's appeal of US\$21.95 million for emergency response to Covid-19 has been funded

FROM JOHNS HOPKINS

CASES/DEATHS: WORLD/US/NC/ORANGE COUNTY AS OF 11:30AM 05/22/2020

• US:1,577,758/94,729

North Carolina: 20,512/728Orange County, NC: 289/37