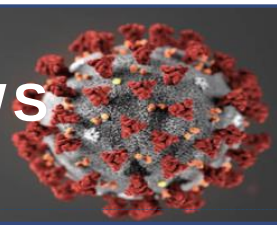
WEEK IN REVIEW
COVID-19 SCIENTIFIC NEWS
APRIL 20 – 24, 2020



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The MS Covid 19 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 or further information

LATEST ARTICLES:

CLINICAL INFORMATION

Antibody Detection and Dynamic Characteristics in Patients with COVID-19. Xiang, F. et al., *Clinical Infectious Diseases.* April 19, 2020.

- IgM sharply increased beginning day 9 and IgG sharply increased day 11 after sx onset. In patients with confirmed COVID19 IgM had a sensitivity of 77.3%, specificity of 100%, PPV of 100%, NPV of 80%. IgG was 83.3.3% sensitive, 95.0% specific, PPV=94.8%, and NPV=83.8%. IgM and IgG antibodies could be detected in the middle and later stages of disease, and were highly specific for COVID-19.

High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation. Simonnet et al. *Obesity.* April 9, 2020. doi: 10.1002/oby.22831.

- This study from Roger Salengro Hospital in Lille, France found a higher median BMI in patients in the ICU for COVID-19 compared to a historical control of non-COVID ICU patients. Furthermore, critically ill COVID-19 patients with a higher BMI had a significantly greater risk of requiring invasive mechanical ventilation.

No SARS-CoV2 detected in amniotic fluid in mid-pregnancy. Yu *et al*. Lancet, April 22, 2020.

- This study evaluated amniotic fluid from 2 women who had laboratory confirmed SARS-CoV2 during the first trimester. Amniotic samples collected at 15 and 16 weeks respectively were negative for IgG, IgM, and viral RNA via PCR. Limitations include small sample size, transient nature of RNA, and sub-optimal age for amniocentesis testing.

Spread of SARS-COV2 in Iceland. Gudbjartsson et al., *NEJM*, April 2020.

- This study evaluated the prevalence and genomic clades of SARS-CoV2 among individuals at high risk for infection (recent travel to high risk areas, known positive contacts) and the general population. They found 13.3% of individuals at high risk for contracting SARS-CoV2 tested positive; genomic testing identified origins in Italy and Austria. In the general population screening group 0.8% tested positive for SARS-CoV2; genomic data indicated origins in the UK and US. They tested more females than males overall, but had more positive tests in males. There were no positive tests in children< 10 years of age.

ST-segment Elevation, Myocardial Injury, and Suspected or Confirmed COVID-19 Patients: Diagnostic and Treatment Uncertainties. Bennett et al., *Mayo Clinic Proceedings*. April 13, 2020.

- In COVID-19 patients whose course is complicated by ST elevations, authors propose a triage algorithm to delay PCI for low risk patients with no risk factors for CAD and patients with complicated disease course who would not benefit from PCI in order to employ alternative diagnostic methods (Echo, CTTA) to assess cardiac function.

Symptom Screening at Illness Onset of Health Care Personnel with SARS-CoV-2 Infection in King County, Washington. Chow *et al. JAMA*, April 17,2020.

- This study retrospectively studied the symptoms of 50 HCPs who had lab confirmed SARS-CoV2 in an attempt to develop a sensitive screening questionnaire for HCPs. The most common initial symptoms were cough (50%), fever (41.7%) and myalgias (35.4%). However, 8/50 of the patients did not have any of these common symptoms; most common symptoms among this population were chills, myalgias, coryza, and malaise. Notably, 64.6% of HCPs worked a median of 2 days (range 1-10 days) after they became symptomatic.

Treating hypoxemic patients with SARS-CoV-2 pneumonia: Back to applied physiology. Bendjelid, K., et al. *Anaesthesia, Critical Care & Pain Medicine.* April 16, 2020.

- Early in SARS-CoV-2 pneumonia there is high permeability type pulmonary edema with apparently preserved lung compliance. For patients early in the disease course or with transient hypoxemia we may be able to avoid invasive MV by other methods to decrease transpulmonary shunting e.g. the reverse Trendelenburg position, almitrine, CPAP.

Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020: retrospective cohort study. Zheng et al. *BMJ*. April 21, 2020.

- Viral load is detectable longer in stool samples than respiratory and serum samples. In severe disease, viral load is detectable longer in men than women, and in those older than 60 years. These differences were not detected in mild disease.

PUBLIC HEALTH/EPIDEMIOLOGY

COVID-19 Antibody Seroprevalence in Santa Clara County, California. Bendavid et al. medRxiv (Pre-Print). April 17, 2020.

- 3,300 adults and children in Santa Clara County, California were recruited via Facebook to be tested for antibodies against SARS-CoV-2 using capillary blood draw and lateral flow immunoassay. The authors estimate a seroprevalence of 2.49-4.16% in the county, however the false-positive rate of the test kit may be inflating their result. This study was not peer-reviewed and likely included some selection bias.

PCR Assays Turned Positive in 25 Discharged COVID-19 Patients. Yuan et al. *Clinical Infectious Diseases*. April 8, 2020.

- 25 of 172 patients (14.5%) discharged from a Wuhan, China hospital after recovering from COVID-19 re-tested positive for infection within 2 weeks of discharge (average 7.32 days following last in-hospital negative PCR.) Most patients were asymptomatic upon re-testing positive, while 32% experienced mild cough.

Family violence and COVID-19: Increased vulnerability and reduced options for support. Usher, K. et al., *International Journal of Mental Health Nursing.* April, 20, 2020.

- Unemployment, limited resources, increased confinement at home with violent perpetrators, increased substance consumption at home, and limited social support are compounding risk factors for family violence that are increasing with prolonged widespread closures. Social-distancing is proving an effective measure for containing infection; however, we must consider the social, economic and psychological consequences.

THERAPEUTIC DEVELOPMENTS

Chloroquine paradox may cause more damage than help fight COVID-19. Sharma, A. *Microbes and Infection.* April, 17, 2020.

- CHL/HCHL have been effective for many viruses including SARS-CoV in vitro. In-vivo (mostly animal models) CHL/HCHL have either had no effect or may have increased the viral replication and/or disease severity in influenza, dengue, Semliki forest virus, Nipah and Hendra viruses, chikungunya virus, and Ebola virus. CHL may provide some benefit but the data from clinical trials is limited. There may be a possibility of CHL worsening COVID19 disease, thus more studies are warranted to determine its effect.

Clinical and microbiological effect of a combination of hydroxychloroquine and azithromycin in 80 COVID-19 patients with at least a six-day follow up: A pilot observational study *Travel Med. Infect.* Dis. April 11, 2020.

- This is a non-comparable, uncontrolled observational study. For the treatment of 80 COVID-19 patients with mild symptoms, the combination of hydroxychloroquine and azithromycin resulted in a clinical improvement and a rapid decrease in viral RNA load. This is an interesting study, but the lack of controls limits its validity.

The FDA-approved Drug Ivermectin inhibits the replication of SARS-CoV-2 in vitro LeonCaly et al. *Viral Research*, April, 3, 2020.

- Ivermectin is an FDA-approved anti-parasitic previously shown to have broad-spectrum anti-viral activity in vitro. *In vitro* results showed a 93% reduction in viral RNA present at 24 h and a ~5000-fold viral RNA reduction at 48 h of the Ivermectin sample compared to control. In addition, no cytotoxicity is observed in either ivermectin sample or control group.

Tocilizumab treatment in COVID-19: A single center experience. Luo, P., et al., *Journal of Medical Virology.* April, 6, 2020.

- 15 Covid-19 patients under Tocilizumab (toc) therapy were assessed in this retrospective study by monitoring inflammation markers such as CRP and IL-6. Toc therapy in all patients resulted in a decrease in serum CRP (126 --> 11.2), and serum IL-6 in all patients appeared to spike first and then decreased. Within the four critically ill patients who received only 1 dose, 3 died and one failed to show response to the medication.

BASIC SCIENCE

Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. Van Doremalen, N. et al., *NEJM.* April, 16, 2020.

· SARS-CoV-2 was more stable on plastic and stainless steel than on copper and cardboard, and viable virus was detected up to 72 hours after application to these surfaces, although the virus titer was greatly reduced. On Copper, no viable SARS-CoV-2 was measured after 4 hours and on cardboard, no viable SARS-CoV-2 was measured after 24 hours.

Assessing ACE2 expression patterns in lung tissues in the pathogenesis of COVID-19. Li, G. et al., *Journal of Autoimmunity.* April, 13, 2020.

· The expression of ACE2 in healthy populations and patients with underlying diseases was not significantly different. However, there was elevated ACE2 expression in cigarette smokers, therefore it's possible that long-term smoking may be a risk factor for COVID-19. Additional analysis suggests that ACE2 is not only a receptor but participates in post-infection regulation of the immune response.

Comparative tropism, replication kinetics, and cell damage profiling of SARS-CoV-2 and SARS-CoV with implications for clinical manifestations, transmissibility, and laboratory studies of COVID-19: an observational study Hin Chu, et al. The *Lancet*. April 21, 2020.

- The cellular tropism of SARS-CoV-2 was similar to that of SARS-CoV, which showed significant virus replication in Calu3 (pulmonary; p=0·0003), Caco2 (intestinal; p=0·0009) cells, Huh7 (hepatic; p=0·012), 293T (renal; p=0·0080) cells, but moderate replication in U251 (neuronal; p=0·036) cells. Even though SARS-CoV-2 induced less cell

damage than did SARS-CoV, SARS-CoV-2 showed more efficient replication in Calu3 cells than did SARS-CoV, which correlates with higher transmissibility of SARS-CoV-2.

Crystal structure of SARS-CoV-2 main protease provides a basis for design of improved a-ketoamide inhibitors. Zhang et al. *Science.* March 20, 2020.

- The authors of this study determined the crystal structure of SARS-CoV-2's major protease, and used this to optimize an a-ketoamide inhibitor to interfere with its function named Compound 13b. This compound inhibited viral replication in human lung cells *in-vitro*, and mouse studies showed favorable lung tropism and suitability for inhaled administration.

UPDATED GUIDANCE:

FROM CDC

April 17: Guidance for Pediatric Healthcare Providers

- Epidemiology updates on the pediatric proportion of cases in United States, China, Italy, and Spain
- Guidance for how to maintain vaccination schedules during COVID-19
- Incubation period for pediatric patients predicted to be 14 days
- Pediatric patients present with similar symptoms as other viral respiratory infections

April 20: Laboratory Outreach Communication System (LOCS)

- Updated Q&A about laboratory COVID-19 testing and sample collection

April 21: Guidance for Homeless Service Providers

- Description of facility layout considerations such as physical barriers to protect staff and maintain physical distancing orders
    - In sleeping areas ensure that faces are at least six feet apart
    - Do not require a negative test for client to enter the facility
    - Identify a designated medical facility to refer clients who might have COVID-19

April 21: Forecasting COVID-19 in US

- National-level forecasts indicate that deaths will continue to rise
- State-level forecasts vary widely, indicating different phases of the epidemic

April 22: Decontamination & Reuse of Filtering Facepiece Respirators

- Updates include Emergency Use Authorization statements, bleach decontamination and ethylene oxide
    - Bleach submersion resulted in degradation of filtration performance but not below the accepted levels
    - Ethylene oxide is not recommended as a disinfectant as it can harm the individual wearing the item

FROM WHO

April 20: Situation Report

- Statement released addressing concerns of NSAIDs worsening outcomes in COVID-19 patients. States there is still "no evidence of severe adverse events, acute health care utilization, long-term survival, or quality of life in patients with COVID-19, as a result of the use of NSAIDs."
- Statement released emphasizing the importance of continuing routine vaccines even amid COVID-19 pandemic

April 21: Situation Report

- Published 'International Guidelines for Certification and Classification of COVID-19 as Cause of Death'
- Over 100 countries have joined the Solidarity Trial to compare four different treatment options

April 22: Situation Report

- Japan changed method of reporting deaths which has been attributed to the increase of deaths reported
- Launched new course on 'Standard precautions: Hand hygiene'
- Guidance on 'Safe Ramadan practices in the context of COVID-19'

April 23: Situation Report

- Global Outbreak Alert and Response Network (GOARN) launched the 'GOARN COVID-19 Knowledge Hub'
    - Webinars, tools, and guidance on
- Guidance on 'Addressing Human Rights as Key to the COVID-19 Response'
    - Integrating human rights-based approach to address stigma, violence against women and children, supporting vulnerable populations, shortages of supplies, etc.
- Research indicates that SARS-CoV-2 has a zoonotic source and was not constructive in a lab
    - Constructed viruses would have elements mixed within the genome which is not seen in this virus

FROM JOHNS HOPKINS

CASES/DEATHS: as of 9:30am 4/24/2020

- World: 2,732,445/191,962
- United States: 869,172/49,963
- Orange County, NC: 195/7