COVID-19 Evidence Digest 12/11/20

The Therapeutic Potential of Ivermectin for Covid-19: 2 A Systematic Review of Mechanisms and Evidence (MedRxiv)

Bottom Line: Ivermectin has potential to be a safe and effective treatment and/or prophylaxis for Covid-19 based on a review of a few preliminary studies.

Details: Ivermectin has been well demonstrated as a safe treatment and commonly used to effectively treat parasite infection and has been demonstrated to have antiviral effects in some cases, thus a possible effective treatment or prophylaxis (measure taken to prevent a disease) for Covid-19. This systematic review looked at several databases and included a total of eight studies, four of which were randomized control trials, one cohort study, one case control study, one retrospective study, and one pilot study. Five of the studies examined Ivermectin as a treatment for Covid-19, while the other three examined Ivermectin as prophylaxis for Covid-19. A review of the studies utilizing Ivermectin as a treatment demonstrated decrease in mortality, reduced time to recovery, reduced disease progression, and decreased duration of hospitalization across a range of patients with mild, moderate, and severe Covid-19. The studies which used Ivermectin as prophylaxis, demonstrated significant decrease in testing positive for Covid-19 and decrease in symptom development among those who took Ivermectin. One limitation is that some of the studies were preprint and thus have not been subject to rigorous peer review yet. However, Ivermectin has potential to be an effective treatment and/or prophylaxis given the results so far. Additionally, Ivermectin is widely available, inexpensive, easy to administer, and has a wide safety margin. More studies on dosing, administration, drug interactions, and therapies that can be used in conjunction with Ivermectin are needed.

Key Takeaways: Ivermectin may be a safe and effective treatment for or prevention of Covid-19 based on some studies. However, additional research is needed to better understand its effectiveness.

Repurposing Antiviral Drugs for Covid-19 - Interim WHO Solidarity Trial Results (NEJM)

Bottom Line: Remdesivir, hydroxychloroquine, lopinavir, and interferon beta-1a did not have an effect on inpatient mortality, initiation of mechanical ventilation, or length of hospitalization for hospitalized patients with Covid-19

Details: The World Health Organization (WHO) organized a cross-country, open-label, randomized trial using intention-to-treat analysis to assessing the impact of remdesivir, hydroxychloroquine, lopinavir, and interferon beta-1a. Eligible patients included individuals age 18 and older, hospitalized with a diagnosis of Covid-19, no known prior exposure to any trial drug, and no contraindication to any of the trial drugs based on the opinion of their providers. Primary outcome included in-hospital mortality while secondary outcomes included initiation of mechanical ventilation and length of hospital stay. Additionally, a meta-analysis of trials studying remdesivir was completed.

Patients were randomly assigned to one of the four trial drugs at standard dosing based on availability at their site of care or placebo. 11266 patients from 30 countries in 405 hospitals were included in this intention-to-treat analysis. 80% of participants were younger than 70, 62%

of participants identified as male, and the majority of patients required supplemental oxygen at the time of entry in the study. Kaplan-Meier analysis showed an 11.8% risk of in-hospital death at day 28. Analyses showed no statistically significant difference in in-hospital mortality or in initiation of mechanical ventilation overall or within subgroup analyses stratified by age, geographic region, glucocorticoid use, ventilation status at time at study entry, or other measured entry characteristics. Receiving a trial drug delayed discharge by 1-3 days, regardless of oxygen supplementation status or mechanical ventilation. The meta-analysis of four articles comparing remdesivir with a control did not show a statistically significant difference in mortality.

Key Takeaways:

- Remdesivir, hydroxychloroquine, lopinavir, and interferon beta-1a do not demonstrate statistically significant improvement in in-hospital mortality, initiation of ventilation or hospital length of stay.
- Additional investigation of other therapies will be important to effectively treat hospitalized patients with Covid-19

Durability of Responses after SARS-CoV-2 mRNA-1273 Vaccination (NEJM)

Bottom Line: Moderna's mRNA-1273 vaccine produced high levels of both binding and neutralizing antibodies that persisted 3 months after the second dose.

Details: Immunogenicity data on 34 healthy adults 119 days after first vaccination and 90 days after second vaccination with Moderna's mRNA-1273 vaccine for COVID-19 (dosing schedule of 100 ug vaccine dose, 2 doses 28 days apart) showed: 1) high levels of binding and neutralizing antibodies produced from the vaccine, both types of antibodies declined slightly over time but remained elevated at 3 months after the 2nd dose of the vaccine; 2) at 119 days after first vaccination the geometric mean titer (GMT) for binding antibodies was elevated in all studied age groups: 235,228 in 18-55 of age, 151,761 in 56-70, and 157,946 in age above 71; 3) serum neutralizing antibodies were detected in all participants at day 119, measured by the ID50 GMT (50% inhibitory dilution) at levels of: 182 in 18-55 of age, 167 in 56-70, and 109 in age above 71; 4) another neutralizing test (live virus plaque reduction) showed detectable neutralizing antibodies in all age groups; 5) binding and neutralizing antibody levels were higher than 41 controls who had recovered from COVID-19 (23-54 days from diagnosis); 6) No new adverse events related to the vaccine were seen after day 57.

Key Takeaways:

- High levels of binding and neutralizing antibodies were produced after two doses of Moderna's mRNA-1273 vaccine in adults between the age of 18 and 71
- Binding antibody and neutralizing antibody levels remained elevated in all adult age groups (18-55, 16-70 and 71+) up to 90 days after the second dose of the vaccine
- Binding and neutralizing antibody levels were higher in the 34 vaccine recipients as compared to 41 controls who had recovered from COVID-19

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Characteristics and Timing of Initial Virus Shedding in Severe Acute Respiratory Syndrome Coronavirus 2, Utah, USA (EID)

Bottom Line: Findings from this study of SARS-CoV-2 household transmission dynamics indicate that viral shedding may occur prior to symptom onset and clinical diagnosis or with mild or no symptoms.

Details: This study monitored transmission of SARS-CoV-2 in 5 Utah households in late April to better understand the association between onset of viral shedding, symptom progression, and infectiousness. Households of index patients with lab confirmed SARS-CoV-2 infection were recruited via convenience sampling. Index patients and their household contacts completed questionnaires (e.g., demographic information, exposure to the index patient, housing square footage, # of persons per bedroom and bathroom, isolation and precautionary measures utilized, etc.) prior to the first study staff visit, which took place within 2-4 days of the index patient's first positive test result, as well as a closeout questionnaire on day 14; all study participants also completed a daily symptom diary. Nasopharyngeal swab (NPS) and blood samples were collected from index patients and all household contacts on the first visit and the visit on day 14; NPS samples were also collected from household contacts during days 1-4 follow up visits, and interim visits were conducted if symptoms occurred during the study period that were not reported during the first visit. If a household contact had a positive or inconclusive test result during days 1-4, the samples were cultured to assess infectiousness. 7 out of 7 contacts across 2 households that did not implement any transmission reduction measures became infected (7/15 total household contacts in the study). The median number of days between symptom onset in index patients and in positive household contacts was 4. Two contacts shed virus while presymptomatic; symptoms did not occur until after their first positive test. Of the 4 participants with day 14 specimens that were positive, 3 with low viral RNA were cultured with no viable virus detected. The 3 households that did not experience transmission put isolation practices in place (e.g., frequent hand washing, disinfecting surfaces, wearing gloves and/or masks, using separate bedrooms and bathrooms).

Key Takeaways:

- Study findings suggest that individuals with COVID-19 or those who have been in close contact with someone with COVID-19 should limit close contact with others, including household members, for 2 weeks. Moreover, onset of even mild symptoms should prompt limiting close contact.
- To reduce household transmission, limiting close contact, practicing hand hygiene, wearing face coverings, and regularly disinfecting surfaces may reduce risk.

Three-Quarters Attack Rate of SARS-CoV-2 in the Brazilian Amazon during a Largely Unmitigated Epidemic (Science)

Bottom Line: Using a convenience sample of blood donors, this study estimates a SARS-CoV-2 attack rate (the risk of getting infected) in October that is above the theoretical herd immunity threshold (76%) in the capital of Amazonas state, Brazil.

Details: Amazonas state, Brazil, is the worst hit region in a country with one of the largest COVID-19 epidemics. Using data on antibodies against SARS-CoV-2 from a convenience sample of blood donors in Manaus (capital of Amazonas) and São Paolo (where the first COVID-19 cases in the country were detected), this study sought to estimate the SARS-CoV-2 attack rate (the risk of getting infected) and extent of COVID-19 transmission in these two cities. In addition, the authors wanted to explore whether the epidemic was contained because the herd immunity threshold was reached (60-67%) or due to behavioral changes and non-pharmaceutical interventions (NPIs). After accounting for cases with waning and no detectable antibodies, it is estimated that 66% and 76% of the population of Manaus was infected with SARS-CoV-2 by July and October, respectively. In São Paolo, an estimated 29% of the population was infected by October. Based on the declining reproduction number in late April and the introduction of NPIs in March, it is likely that both growing population exposure and NPIs contributed to epidemic control. The authors also note that the different attack rates in these cities are due to the higher infection fatality ratio (the number of individuals who die of the disease among all infected individuals) in São Paolo; while the reproduction number was similar, cases and deaths increased and then decreased more slowly in São Paolo (which also has an older population structure) versus in Manaus.

Key Takeaways:

- Study findings provide insight into what SARS-CoV-2 transmission in the absence of effective mitigation measures may look like.
- More research is needed to understand why SARS-CoV-2 transmission was so high in Manaus, Amazonas; possible explanations include a younger and more mobile population, household crowding, socioeconomic conditions, limited access to clean water, and reliance on overcrowded boat travel.

Risk Factors Associated with In-Hospital Mortality in a US National Sample of Patients with COVID-19 (JAMA Network Open)

Bottom Line: In this large US study of patients hospitalized with COVID-19 in April and May, severe complications were common, and the in-hospital death rate was 20%.

Details: This study sought to describe patients hospitalized with COVID-19 and look at risk factors associated with in-hospital deaths in 592 US acute care hospitals during April and May 2020 using a large hospital administrative database. Inpatient and hospital-based outpatient visits with a COVID-19 discharge diagnosis were included. The study sample included 64,781 patients with COVID-19 (29,479 outpatient and 35,302 inpatient). Inpatients were older than outpatients (65 versus 46 years of age). Among the full study sample, almost half were male (49.3%); 40% were White individuals, 22% were Black individuals, and 21% were Hispanic/Latino individuals. 5,625 inpatients received invasive mechanical ventilation (15.9%), 6,849 were admitted to an ICU (19.4%), and 7,164 inpatients died during hospitalization (20.3%); among the total sample (64,781), 11.4% died during hospitalization (n=7,355). The most common severe complications among inpatients were: acute respiratory failure (55.8%), acute kidney failure (33.9%), and sepsis (33.7%). The risk factor most strongly associated with in-hospital death was older age – patients 65 and older accounted for more than 75% of all in-hospital deaths. Patients from Northeast hospitals had a 59% higher odds of death than patients from Midwest hospitals.

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Compared with White inpatients, Black inpatients had a 25% lower odds of death, though they were disproportionately represented in the overall sample. Receiving particular drugs (statins, angiotensin-converting enzyme inhibitors, and calcium channel blockers) was associated with a decreased odds of in-hospital death. Patients given hydroxychloroquine or azithromycin had an increased odds of in-hospital death compared to patients who did not receive these drugs.

Key Takeaways:

- During April-May, severe complications and in-hospital deaths among US patients hospitalized with COVID-19 were high. Deaths disproportionately occurred among older and male patients, as well as those from the US Northeast region. The proportion of inpatient deaths reported in this study are similar to other studies looking at outcomes among patients hospitalized with COVID-19 earlier in the pandemic; more recent studies indicate lower rates.
- Study findings support previous reports that Black US residents have been disproportionately infected with SARS-CoV-2; however, after adjusting for confounding factors, Black individuals in this study had a 25% lower odds of dying in the hospital compared with White individuals. A recent study reported similar findings, noting that structural determinants (e.g., inequities in housing, access to care, employment opportunities, and poverty) may explain disproportionately higher out-of-hospital COVID-19 mortality among Black individuals.
- Use of particular drugs (statins, angiotensin-converting enzyme inhibitors, and calcium channel blockers) was associated with a decreased odds of in-hospital death.