



Reference of the Week

- Bixler D. SARS-CoV-2–Associated Deaths among Persons Aged <21 Years — United States, February 12–July 31, 2020. CDC MMWR. 09.15.2020 (early release). <https://www.cdc.gov/mmwr/volumes/69/wr/mm6937e4.htm> pdf
Premise/Methods: 1. Deaths from COVID-19 in persons < 21 years of age are uncommon and characterization of this mortality subgroup may inform surveillance and care. 2. Reports from US public health jurisdictions were reviewed and deaths in persons < 21 years were characterized. 3. Reporting confidence, cause of death, variable jurisdictional ascertainment and other limitations hamper the report which might best be thought of as a generous sample of this mortality population.
Findings: 1. 121 SARS-CoV-2 associated deaths in persons < 21 years of age were reported to the CDC from 2/12 – 7/31/2020 or 8% of all reported deaths (190,000 total SARS-CoV-2 reported deaths): 63% male; 10% < 1 year; 20% 1-9 years; 70% 10-20 years. 2. Racial disparity noted: 45% Hispanic; 29% Black; 4% American Indian/Alaska Native. 3. Of the 121 deaths: 91 (75%) had an underlying condition; 79 (65%) died after hospital admission; and 39 (32%) died at home or in the ED. 4. Noteworthy, 120 deaths had acute COVID-19, 15 met the MIS-C case definition, and 4 had both conditions.
This limited and preliminary study of deaths in < 21 years age group partially reflects deaths in older age groups: male predominance, racial/ethnic disparity, and co-morbidities. The large proportion of out of hospital arrests needs further scrutiny to assist in closer surveillance of possible at risk individuals.

Other References:

- Patel MM. Change in Antibodies [AB] to SARS-CoV-2 Over 60 Days among Health Care Personnel in Nashville, Tennessee. JAMA. 09.17.2020 (research letter).
<https://jamanetwork.com/journals/jama/fullarticle/2770928> pdf
Premise/Methods: 1. Knowledge of the decline in neutralizing AB following COVID-19 infection is incomplete. 2. The decline in COVID-19 neutralizing AB amongst HCW with prior infection may reduce protection from reinfection. 3. Anti-SARS-CoV-2 antibodies were determined at baseline and approximately 60 days later in a convenience sample of health care personnel. 4. The change in AB titer was determined at baseline, at 60 days, and results were stratified by symptoms.
Findings: 1. 249 HCWs submitted an initial serum sample: 64.5% female; 91.6% white; median age 33 years. 2. Nineteen (7.6%) were positive at baseline of which 8 (42%) remained positive at 60 days but 11 (58%) became seronegative. 3. Individuals who continued to be seropositive at 60 days were more likely to have been symptomatic at baseline. 4. All 19 seropositive individuals had a decline in neutralizing AB at 60 days.
The authors point out concerns regarding these results: serum positivity may underestimate prior infection depending on the timing of sample procurement; a limited window for donation of convalescent plasma exists; and subsequent assignments of prior COVID-19 infected HCW to new COVID-19 patients may not be as protected as thought. Importantly, this study does not assess T-cell function in terms of future protection from COVID-19.
- Frank S. In Vitro Efficacy of a Povidone-Iodine Nasal Antiseptic [PINA] for Rapid Inactivation of SARS-CoV-2. JAMA-otolaryngology.09.17.2020. <https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2770785>
Premise/Methods: 1. Prior work by these authors suggested that PINA could be used to limit SARS-CoV-2 transmission. 2. Topical contact time and concentration of PINA necessary to inactivate the virus are unknown. 3. This in-vitro study determined the tissue contact time and concentration of PINA required to inactivate SARS-CoV-2. 4. The SARS-CoV-2 virus stock was tested against nasal antiseptic solutions consisting of aqueous PVP-I as the sole active ingredient.
Findings: 1. Three concentrations of PINA, 0.5%, 1.25%, and 2.5% with contact times of 15 and 30 seconds were tested to inactivate SARS-CoV-2 in vitro. 2. All concentrations inactivated the virus at 15 seconds. 3. No cytotoxic effects on cells were observed after contact with each of the nasal antiseptics tested. *PINA is a well-tolerated antiseptic and this investigation combined with others suggest that it might be an effective adjunct to reducing viral transmission particularly during aerosolizing procedures.*



- Bos LDJ. Severe COVID-19 Infections—Knowledge Gained and Remaining Questions. JAMA-internal medicine. 09.18.2020 (editorial).

What we know:

ARDS TREATMENT:

- low tidal volume ventilation (4 to 8 cc/kg predicted body weight)
- limit pressure cost of ventilation (target plateau pressure at ≤ 30 cm H₂O)
- conservative fluid administration with active diuresis once patients out of shock
- prone positioning for moderate to severe ARDS ($\text{PaO}_2 / \text{FiO}_2 \leq 150$)
- VV ECMO for severe gas exchange abnormality despite standard care
- timing of intubation no different than respiratory failure for other reasons
- non-invasive ventilation no different than indications for other reasons

COVID-19 TREATMENT

- multiple studies have demonstrated the mortality benefit of steroids
- remdesivir shortens the time to recovery and appears to be of limited benefit
- initial assessment of convalescent plasma offers evidence of mortality benefit
- pathophysiology suggests anti-coagulation may be helpful
- benefit doubtful: hydroxychloroquine, lopinavir/ritonavir, IL-6 blockade
- hospital mortality ranges from 20-40% (adults); 1-2% (children)

What we don't know

- partitioning of lung versus systemic phenotyping requires more investigation into subgroup populations
- unpacking how the immune response is both detrimental and beneficial may lead to therapies
- clinical studies during a pandemic requires strategies to enroll minorities and the elderly
- clarifying the long term outcomes of COVID-19 is required

This brief editorial nicely summarizes in a balanced fashion “where we are” in the treatment of COVID-19. Results of large clinical trials for a variety of agents are underway. It appears that more emphasis is required to look at subpopulations of the disease and the timing of interventions.

- Lishman J. Acute Appendicitis in Multisystem Inflammatory Syndrome in Children with COVID-19. PIDJ. 9.2020. (research letter)

https://journals.lww.com/pidj/Citation/9000/Acute_Appendicitis_in_Multisystem_Inflammatory.96050.aspx.pdf

Methods/Findings: **1.** South Africa is a COVID-19 hotspot. In this retrospective review children SARS-CoV-2 positive with appendicitis are examined. **2.** Four children (ages 5-12 years) were identified: 3 were diagnosed with MIS-C; and 1 with isolated appendicitis was PCR tested not for symptoms but according to hospital policy. **3.** The three children with MIS-C had surgically confirmed appendicitis. **4.** Appendicitis has to be pre-operatively differentiated from terminal ileitis reported to occur in MIS-C. **5.** Additionally, MIS-C often presents with abdominal complaints and appendicitis should be considered as a co-diagnosis.

This article has clinical relevance reminding us that the diagnosis of MIS-C may be accompanied by either terminal ileitis, a non-surgical condition and/or appendicitis which usually requires an operation.

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COVID-19 LITERATURE BRIEFING

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