

The Weekly Covid-19 Literature Round-Up

Edition 6: April 22, 2020

Collated by Emory ID (Adult and Pediatric) and Medical Microbiology Fellows

“I have no idea what's awaiting me, or what will happen when this all ends. For the moment I know this: there are sick people and they need curing.” -Albert Camus

“‘I wish it need not have happened in my time,’ said Frodo.

‘So do I,’ said Gandalf, ‘and so do all who live to see such times. But that is not for them to decide. All we have to decide is what to do with the time that is given us.’” -J.R.R. Tolkien

Epidemiology

Brought to you by: Alfonso Hernandez, MD, MPH

Mosites, Emily. “Assessment of SARS-CoV-2 Infection Prevalence in Homeless Shelters — Four U.S. Cities, March 27–April 15, 2020.” *MMWR. Morbidity and Mortality Weekly Report* 69 (2020). <https://doi.org/10.15585/mmwr.mm6917e1>.

- **Relevance:** There are approximately 1.4 million persons using emergency shelter or transitional housing each year in the U.S. Due to crowded settings there is a higher risk of transmission of SARS-CoV-2.
- **What is known:** Previous investigations had highlighted the presence of outbreaks in homeless shelters in five shelters in different cities across the U.S. including Seattle (https://www.cdc.gov/mmwr/volumes/69/wr/mm6917e2.htm?s_cid=mm6917e2_x).
- **Study details:**
- Objective was to assess prevalence of infection among homeless shelters in 4 cities (Boston, San Francisco, Seattle, and Atlanta)
- 1,192 residents and 313 staff members were tested in 19 shelters
- The prevalence differed by number of cases in the 2 weeks preceding testing reported by shelters
 - Among 5 (3 in Seattle and 1 in Boston and San Francisco) shelters reporting 2 or more cases the prevalence among residents and staff members was 37% and 21% respectively
 - Among 12 shelters in Seattle reporting 1 case the prevalence among residents and staff members was 5% and 1% respectively
 - Among 2 shelters in Atlanta reporting no cases the prevalence among residents and staff was 4% and 2% respectively
- **What this study adds:** Estimates of prevalence of SARS-CoV-2 in the homeless population
- **Interpretation/Limitations/Conclusion:** The study is limited by one time testing of the population. In total around 1 in 4 residents of homeless shelters were positive for SARS-CoV-2 with important variation by city and number of infections within specific shelters. Ongoing symptom screening and entry/exit restrictions to shelters should be adapted to local context of community spread.

Transmission/Infection Control

Brought to you by: Daniel Graciaa, MD, MPH

Kratzel, Annika et al. "Early Release - Inactivation of Severe Acute Respiratory Syndrome Coronavirus 2 by WHO-Recommended Hand Rub Formulations and Alcohols - Volume 26, Number 7—July 2020 - Emerging Infectious Diseases Journal - CDC." Accessed April 21, 2020.

<https://doi.org/10.3201/eid2607.200915>.

- Hand hygiene is essential for control of SARS-CoV-2 in the absence of therapies or vaccines. WHO recommended alcohol-based hand rubs have been shown to inactivate SARS-CoV and MERS-CoV, but have not yet been studied in SARS-CoV-2.
- Virucidal activity studies using a quantitative suspension test (mixed virus suspension with organic material and disinfectant solution of differing concentration) with 30 second exposure time demonstrated effectiveness of 80% ethanol and 75% isopropanol formulations. Both formulations include glycerol and hydrogen peroxide.
- Dilutions of the original ethanol formulation $\geq 40\%$ and isopropanol formulation $\geq 30\%$ remained effective. The active ingredients (ethanol and isopropanol) were also effective at concentrations of $\geq 30\%$ volume/volume.
- Conclusion/Limitations: These results are expected given what is known about other viruses but provides evidence for the use of alcohol-based hand rubs for hand hygiene in the control of SARS-CoV-2. It is important to emphasize the appropriate duration of hand hygiene in practice.

Gudbjartsson, Daniel F. et al. "Spread of SARS-CoV-2 in the Icelandic Population." *New England Journal of Medicine*, April 14, 2020. <https://doi.org/10.1056/NEJMoa2006100>.

- Data on population-level transmission of SARS-CoV-2 are limited. Iceland's small population of 364,000 and single international airport provided an opportunity to evaluate spread via targeted testing and population screening. The first case was reported in Iceland on Feb 28.
- Targeted testing of high-risk individuals (symptomatic, recent travel to high-risk countries, or contact with a case) found 13.3% (1221/9199) PCR positive on combined nasopharyngeal/oropharyngeal samples. Population screening found 0.8% (100/13080) positive: 0.8% (87/10797) from an open invitation for testing and 0.6% (13/2283) from invitations sent at random via text message.
- In both the targeted and population samples, positive results were more common in those over 10 years (1183/8635 or 13.7% in the targeted testing) than younger children (38/564 or 6.7%) and in males compared to females (OR 1.6, 95%CI 1.47-1.87). The proportion of positive results in the population screening was stable during the 20-day period.
- Conclusion/Limitations: Children under 10yo and females had lower prevalence of a positive test for SARS-CoV-2 in targeted and population testing. As with other screening studies, individuals concerned about infection may have been more likely to participate. The stable proportion of positive results over the course of the screening program suggests containment measures have been effective.

Clinical Syndrome

Brought to you by: Amy Sherman, MD

Goyal, Parag et al. "Clinical Characteristics of Covid-19 in New York City." *New England Journal of Medicine* 0, no. 0 (April 17, 2020): null. <https://doi.org/10.1056/NEJMc2010419>.

- NYC has emerged as an epicenter of the Covid-19 epidemic in the US. The authors described the first consecutive 393 confirmed patients (>18yo) admitted to 2 NYC hospitals.
- Characteristics of the patients: mean age 62.2, 60.6% male. 35.8% had obesity.
- Most common presenting symptoms: cough, fever, dyspnea, myalgias, diarrhea, nausea, vomiting. Most presented with lymphopenia (90%), thrombocytopenia.
 - Patients who received mechanical ventilation: more likely to be male, have obesity, and have elevated LFTs and inflammatory markers.
- Mortality: 40/393 patients (10.2%). Discharged home: 260/393 (66.2%). 93 patients with incomplete data.
- Conclusions: Similar findings to case series from China. GI symptoms more prominent in NYC population. 10x higher percentage of NYC patients who received invasive mechanical ventilation as compared to China.
- Limitations/Interpretations: NYC hospitals implemented early intubation strategies; thus numbers of intubated patients as compared to China hospitals' experience may reflect this protocol. The US also prioritizes testing and hospitalization in patients with more severe disease.

Herold, Tobias et al. "Level of IL-6 Predicts Respiratory Failure in Hospitalized Symptomatic COVID-19 Patients." *MedRxiv*, April 10, 2020, 2020.04.01.20047381. <https://doi.org/10.1101/2020.04.01.20047381>.

- The authors aimed to identify markers that would predict a higher risk of respiratory failure and need for mechanical ventilation. Such a tool would be incredibly useful to allocate resources, and to determine patients who may be more likely to decompensate to improve triaging processes.
- Population analyzed: 40 symptomatic patients with PCR diagnosed Covid-19 infection at Munich hospital.
 - 13/40 (32.5%) patients required mechanical ventilation.
 - Elevated IL-6 levels were strongly associated with the need for mechanical ventilation.
 - Risk of respiratory failure for patients with IL-6 levels >80pg/mL was 92%.
 - At a level of 80pg/mL, median time to mechanical ventilation =1.5 days.
 - Other laboratory parameters analyzed: lymphocyte count, CRP, bilirubin, WBC, LDH, PCT, thrombocyte count, troponin, creatinine, d-dimer, ferritin.
- Limitations: Small sample size, will need a larger study to validate the study and determine a more accurate cutoff. IL-6 lab tests take several days to result in most centers; may limit the value of this test as a predictive model.
- Conclusion: Elevated levels of IL-6 can identify Covid-19 patients who have a higher risk of respiratory failure.

Therapeutics

Brought to you by: Boghuma Titanji, MD, PhD

Gritti, Giuseppe et al. "Use of Siltuximab in Patients with COVID-19 Pneumonia Requiring Ventilatory Support." *MedRxiv*, April 15, 2020, 2020.04.01.20048561. <https://doi.org/10.1101/2020.04.01.20048561>.

- **Methods:** Small retrospective cohort study of 21 patients with severe COVID-19 in Italy. All patients required either non-invasive ventilation (NIV) or continuous positive pressure (CPAP) ventilation. They received treatment with IL-6R antagonist siltuximab through a compassionate use program. Patients were treated with siltuximab within two days after initiating ventilation with either CPAP or NIV. The median follow-up for all patients was eight days. 16 patients received a single dose of the drug and 5 patients received a second dose 2-3 days after the initial dose. Siltuximab is a monoclonal antibody that targets the IL-6 receptor. It is currently approved in Europe for use in the treatment of Castleman's disease.
- **Results:** 33% of patients improved (7/21) with reduction in their oxygen requirements (no longer requiring NIV or CPAP) during the follow-up period, 43% (9/21) of patient maintained stable oxygenation requirements and 24% (5/21) worsened requiring intubation and mechanical ventilation during the follow-up period. Reduction in CRP levels occurred within 5 days of treatment for all patients. One patient developed a stroke during the follow-up period.
- **Limitations** – This small retrospective cohort does not include a control group and as such any perceived improvements could simply be the natural course of the disease in the individual patient as opposed to any benefit from the intervention. The follow-up period is very short and such we do not know whether the 67% of patients who remained stable or progressed to needing mechanical ventilation ultimately recovered or succumbed to their disease.
- **Importance** – Hyperinflammation and cytokine storms have emerged as an important feature in the pathogenesis of severe COVID-19. Severe COVID-19 cases may benefit from IL-6 pathway inhibition given the associated cytokine release syndrome. Preliminary results from an open-label study in 21 patients with COVID-19 treated with tocilizumab in China were encouraging (again a small study and not controlled). One issue to ponder is whether there will be differential effectiveness between IL-6 antagonists and IL-6R antagonists. Relevant to this is that IL-6R inhibitors can suppress both cis and trans signaling as well as trans presentation. Trans presentation involves IL-6 binding to mIL-6R expressed on an immune cell, which forms a complex with gp130 on T helper 17 (TH17) cells, leading to downstream T cell signaling that may be involved in ARDS. However, IL-6 inhibitors can suppress only cis and trans signaling. The outcomes of ongoing clinical trials re eagerly awaited.

"Clinical Benefit of Remdesivir in Rhesus Macaques Infected with SARS-CoV-2 | BioRxiv." Accessed April 21, 2020. <https://www.biorxiv.org/content/10.1101/2020.04.15.043166v1>.

- **Methods:** Small experimental animal study – 12 macaques were randomized into two groups of six animals each (a treatment group and a no treatment group). All animals were infected with high inoculum of SARSCoV-2 (TCID₅₀ of virus inoculum = 2×10^6) via intranasal, oral, ocular and intratracheal routes. 6 macaques in the treatment group received treatment 12 hours post-infection with Remdesivir (10mg/kg loading dose IV then 5mg/kg daily IV dose thereafter for 6 days). 6 animals in the control group received equal dose volume vehicle solution following the same dosing schedule as the animals in the treatment group. Animals were observed twice daily for clinical signs of disease using a standardized

scoring sheet with the predetermined endpoint being day 7 post infection. All animals were euthanized on day 7 and necropsy performed for histo-pathologic and virologic studies.

- **Results:** Clinical scores for symptoms were significantly lower in animals who received treatment with Remdesivir compared to the control group receiving vehicle solution. One animal in the treatment arm showed mild dyspnea while all animals in the control group showed severe dyspnea and tachypnea. Radiographs taken at 0,1,3,5, and 7 days post infection showed more extensive pulmonary involvement in animals who did not receive remdesivir compared to animals who were treated. Treatment with remdesivir also led to reduced viral replication the lower respiratory tract and reduced tissue lung tissue injury on necropsy in treated animals compared to the untreated controls.
- **Conclusions** – Remdesivir treatment instituted early post infection led to reduced viral load, reduced lung injury and less severe clinical symptoms in treated rhesus macaques compared to infected untreated controls. This suggests that early treatment with remdesivir could be beneficial in treatment of COVID19.
- **Limitations** – This small animal study with very short follow-up period does not mirror the classic course of the disease in humans. Thus, it remains unclear whether these observations will be replicated in ongoing human clinical trials of this drugs. On the plus side drug efficacy was demonstrated with the very large inoculum of virus used in these experiments. This is encouraging and supports the effectiveness of remdesivir as an antiviral agent against SARS-CoV2.

Diagnosics

Brought to you by: Aaron Kofman, MD

He, Xi et al. “Temporal Dynamics in Viral Shedding and Transmissibility of COVID-19.” *Nature Medicine*, April 15, 2020, 1–4. <https://doi.org/10.1038/s41591-020-0869-5>.

- Presymptomatic transmission of SARS-CoV-2 infection has been a defining feature of COVID-19, but its dynamics are not fully elucidated.
- In this analysis, the authors attempted to (1) infer dynamics of presymptomatic transmission among a cohort of 77 presumptive infector-infectee pairs for whom information is publicly available, and (2) evaluate temporal patterns of viral shedding in a separate cohort of 94 patients with COVID-19 in a hospital in Guangzhou, China.
 - For #1: the authors estimated a serial interval (defined as time between symptom onset of infector and infectee) of 5.8 days (95% CI, 4.1-6.4 days), and SARS-CoV-2 infectiousness spanning 2.3 days (95% CI, 0.8-3.0 days) before symptom onset and peaking at 0.7 days (95% CI, -0.2-2.0 days) before symptom onset. This yielded a presymptomatic transmission proportion of 46-55% within this cohort
 - For #2: the authors collected 414 throat swabs at a variety of time points up to 3 weeks post symptom onset, and similar to other studies found a trend in decrease in the viral load. Based on this analysis, they estimate that shedding may begin 2 to 3 days prior to symptom onset
- **Conclusions:** A high percentage of secondary cases are infected during a primary case’s presymptomatic period due to SARS-CoV-2’s short serial interval and high infectiousness relative to its incubation period
- **Limitations:** Recall bias among participants, viral shedding may have been affected by treatments; also, infector-infectee “pairs” could have theoretically been improperly paired, though careful attempts at selection were followed

Lavezzo, Enrico et al. "Suppression of COVID-19 Outbreak in the Municipality of Vo, Italy." *MedRxiv*, April 18, 2020, 2020.04.17.20053157. <https://doi.org/10.1101/2020.04.17.20053157>.

- Asymptomatic transmission of SARS-CoV-2 infection has been a defining feature of COVID-19, but the degree to which it plays a role over the course of a local outbreak is unclear
- In this analysis, the authors performed surveys of COVID-19 prevalence at the beginning and the end of a 2 week municipal lockdown around Vo', a small town in Italy, which was the site of the first confirmed COVID-19 case in Italy in February 2020. They obtained NP swabs on **>85% and >70% of the population (!)** of Vo' at both timepoints.
 - NP swabs were collected and tested for COVID-19 from 2,812 and 2,343 participants in the first and second surveys (respectively); COVID-19 prevalence declined over the course of the lockdown from 2.6% (95% CI 2.1-3.3%) to 1.2% (CI 0.8-1.8%)
 - Mean serial interval was 6.9 days (95% CI 2.6-13.4)
 - Contact tracing performed as part of the second survey revealed that most new infections were due to either pre-lockdown infection and/or asymptomatic spread within households
 - Importantly, the authors found no statistically significant difference in both viral load and duration of viral load detectability (4-8 days) between asymptomatic and symptomatic cases
- **Conclusions:** This study provides insight into the dynamics of COVID-19 in a small geographical municipality through survey and NP swab of nearly all residents (a major strength of the study). Although they don't highlight it themselves, the study also shows the power of widespread diagnostic testing in a focused geographical area to characterize the nature of COVID-19 spread. This power enabled them to appropriately weigh COVID-19's efficient spread through asymptomatic individuals, especially in the period after lockdown as it was these individuals accounting for a majority of new infections.
- **Limitations:** "symptomatic" individuals had a fairly narrow definition of fever and/or cough. However, as COVID-19 has many more protean clinical manifestations, this may have skewed the analysis into over-estimating the number of asymptomatic individuals.

Bendavid, Eran et al. "COVID-19 Antibody Seroprevalence in Santa Clara County, California." *MedRxiv*, April 17, 2020, 2020.04.14.20062463. <https://doi.org/10.1101/2020.04.14.20062463>.

- The true seroprevalence of COVID-19 has been a subject of intense debate and speculation in the absence of more widespread acute COVID-19 testing in the U.S.
- The authors performed a serostudy in Santa Clara County, CA, enrolling 3330 people over the course of two days in April 2020
 - They found that the unadjusted prevalence of IgG or IgM antibodies to SARS-CoV-2 in Santa Clara County was 1.5% (95% CI, 1.11-1.97%) and the population-weighted prevalence by zip, race, and sex was 2.81 (95% CI 2.24-3.37)
 - Extrapolating this to the population of Santa Clara County, they estimate between 48,000 and 81,000 infections, yielding a 50-85-fold higher number of infections than had been confirmed to that point in time
 - Extrapolating *this*, the mortality rate from COVID-19 may as a result be significantly lower than other projections

- **Limitations:** *Note: This study has generated intense debate and, as of this writing, an appendix is being prepared by the author to generate concerns that have emerged in the academic community (many via Twitter). Some criticisms of this study are below:*
 - Test kit used (Premier Biotech, Minneapolis MN) was validated at Stanford and by the manufacturer and on the surface, looks great: at Stanford, 30/30 pre-COVID-19-era samples tested negative, and with the manufacturer, 369/371 tested negative. However, with high prevalence expected as part of a pandemic, the test specificity needs to be extremely tight in order to be useful. Here, the lower bounds of the 95% CI is less than 98.5%, meaning you would expect to see a false-positive rate of 1.5% → thus bringing the authors' principal conclusion, of a 1.5% seroprevalence rate, into serious question, as all of that could be false-positive (which is also unlikely of course, but illustrates the data's weakness). Reworking of this data is likely coming but informal analyses on Twitter (@jjcherian and others) have suggested the true seroprevalence rate based on amended statistical analysis of the authors' data is <1%
 - Numerous selection biases, some of which the authors tried to control for, and others for which they couldn't (or didn't): participants may have been more likely to have had COVID-19-like illnesses and sought antibody testing for this reason; were more likely to be healthy; phlebotomy was held at Facebook campus thus may have predisposed to this with access to transportation; would have been more likely to look at Facebook ads; familial clusters may have been overrepresented if all family members drove over to Facebook together
 - While much of the criticism has been levied against false positives, less attention has been drawn to the likely high rate of false negatives owing to the test kit's extremely low sensitivity (80.3%). Thus it is unclear how much the flawed estimates with respect to test specificity may be counterweighted by sensitivity
- **Conclusions:** This study is an early, if far from ideal, look at the upper/optimistic bounds of the seroprevalence of COVID-19 in one county in CA. Getting this right will be important for our understanding of risk, and much will hinge on the way the studies are conducted as well as on the test characteristics used. This study also highlights the potential perils of commercial antibody test kits in the U.S. with inadequate test characteristics for the scale of COVID-19.

To see some good peer reviews of this paper (recommendations by Alfonso Hernandez, MD, MPH):

- <https://twitter.com/jjcherian/status/1251272333177880576> (@jjcherian)
- <https://twitter.com/nataliexdean/status/1251309227760467974> (@nataliexdean)
- And seroprevalence surveys generally:
 - <https://twitter.com/nataliexdean/status/1251944376554659840> (@nataliexdean)

Basic Science/Virology

Brought to you by: Sam Stampfer, MD, PhD

Rockx, Barry, Thijs Kuiken, Sander Herfst, Theo Bestebroer, Mart M. Lamers, Bas B. Oude Munnink, Dennis de Meulder, et al. "Comparative Pathogenesis of COVID-19, MERS, and SARS in a Nonhuman Primate Model." *Science*, April 17, 2020. <https://doi.org/10.1126/science.abb7314>.

- Characterization of a good animal model for COVID-19 is essential for evaluation of viral pathogenesis, therapeutics, and vaccines. In this study, cynomolgus macaques were infected with SARS-CoV-2 and MERS and evaluated for their disease response.

- SARS-CoV-1 was previously tested under similar circumstances.
- Intratracheal and intranasal inoculations totaling 1×10^6 TCID₅₀ of SARS-CoV-2 did not result in clinical disease, and all 8 macaques seroconverted. Nasal SARS-CoV-2 RNA peaked at days 2-4.
 - Infectious virus (able to infect Vero cells) at low levels was isolated from 4/8 animal throat swabs on day 1. None was detected after day 4.
- On day 4 necropsies of 4 animals, all had RNA detectable throughout the respiratory system and at lower levels in the gut. Samples with normal lung tissue had detectable SARS-CoV-2 antigen.
 - Only 2/4 animals had lung lesions, which showed more SARS-CoV-2 antigen in type I pneumocytes than type II.
- 4 additional macaques were infected with MERS-CoV- they remained asymptomatic and seroconverted by day 21. Autopsies of a subset at day 4 showed lung lesions that had viable MERS-CoV at low titers. MERS-CoV RNA on nasal and throat swabs peaked at days 1 and 2, respectively.
- **Summary:** Cynologous macaques can be infected with SARS-CoV-2 as well as MERS-CoV and shed viable virus. Upper respiratory viral loads peak very early in infection at days 1-4, and animals remain asymptomatic in spite of spread throughout the respiratory tract.
 - **Commentary:** Interestingly, in spite of high dose inocula, animals did not develop clinical disease with either pathogen, suggesting that they may not be the best model for clinical infection.

Lau, Siu-Ying et al. "Attenuated SARS-CoV-2 Variants with Deletions at the S1/S2 Junction." *Emerging Microbes & Infections* 0, no. ja (April 17, 2020): 1–15. <https://doi.org/10.1080/22221751.2020.1756700>.

- The SARS-CoV-2 S protein mediates viral entry. S protein undergoes cleavage to form S1 (which contains the receptor-binding domain) and S2 (which mediates membrane fusion). SARS-CoV-1 and SARS-CoV-2 both undergo cleavage by the cellular protease TMPRSS2, but SARS-CoV-2 has a unique insertion at the S1/S2 junction that adds a furin cleavage motif at this site as well.
- In this paper, the authors passaged SARS-CoV-2 through Vero-E6 cells, and found that the S1/S2 cleavage site tended to acquire mutations and deletions during just two rounds of passaging. Interestingly, no human isolates have demonstrated these mutations.
 - This implies that the S1/S2 region may be under special selective pressure *in vivo*, as it quickly mutates *in vitro*.
- One mutant formed smaller plaques than wild-type virus. This virus "del-mut" was found to have a 10 amino acid deletion at S1/S2 (residues 679-688) which removed both the furin-cleavage and TMPRSS2-cleave motifs. It was only able to replicate efficiently in Vero-E6 cells, while wild-type SARS-CoV-2 was able to replicate in a wider range of cell types.
- Del-mut was tested via *in vivo* infection of hamsters (1.5×10^5 PFU of del-mut vs wt) and found to be attenuated, resulting in no weight loss during infection (compared to wild-type, which resulted in ~9% weight loss).
 - Wild-type animals ended up with higher viral titers (by plaque assay) in the trachea & lungs compared to the del-mut strain.
 - Histopathologic exam showed worsened alveolar wall destruction & hemorrhage in the wild-type infected animals.
- **Summary:** The S1/S2 cleavage site of the SARS-CoV-2 spike protein may be under strong selective pressure. Mutations and deletions at this site can produce attenuated virus that could be further developed into a live-attenuated vaccine.

- **Additional thoughts:** Del-mut was fully sequenced and not found to have other mutations besides the 10 aa deletion which removes two protease cleavage motifs at the S1/S2 junction. It is critical to determine whether the attenuation in del-mut is due to lack of cleavage between S1 and S2. I am surprised the authors did not do a simple Western blot under reducing conditions, which would easily determine whether there is still cleavage in spite of the deletion.

Pediatrics

Brought to you by: Mehgan Teherani, MD

Xu, Yi et al. "Characteristics of Pediatric SARS-CoV-2 Infection and Potential Evidence for Persistent Fecal Viral Shedding." *Nature Medicine* 26, no. 4 (April 2020): 502–5. <https://doi.org/10.1038/s41591-020-0817-4>.

- What is known? More common HCoV infections (OC43, HKU1, etc.) appear to infect children at a higher attack rate than adults. Children with these infections appear to have prolonged viral shedding, increasing risk of transmission to household and daycare contacts. In addition, common HCoV infections in pediatric patients appear to be less significant as an enteric pathogen and more commonly are associated with respiratory symptoms.
- What did this study find?
 - Screened 725 children in Wuhan, Hubei Province, China that had close contact with infected person through NP (RT-PCR) swab for SARS-CoV-2 infection and found 10 positives (1.3%) – ages 2 mos – 15 yrs.
 - All had mild symptoms (no O2 requirement) and received alpha-interferon oral spray on admission (8000U, two sprays TID)
 - 8/10 patients had + RT-PCR rectal swabs that remained + after NP swab had become negative (up to 13 days after) and even after patients became asymptomatic
 - Cycle threshold values (estimating viral load) in stool was higher than ct values in NP swabs
- What did this study add? Evidence that unlike common HCoVs, COVID-19 shows evidence for prolonged fecal shedding and potential for fecal-oral transmission in children despite minimal respiratory symptoms.
- Limitations: No evidence of replication-competent virus, small number of patients
- Conclusions: Potential transmission may be different than other HCoVs. Wash your hands! Consider rectal swabs in peds, especially daycare-aged/diapered patients.

Li, Wei, Bo Zhang, Jianhua Lu, Shihua Liu, Zhiqiang Chang, Peng Cao, Xinhua Liu, et al. "The Characteristics of Household Transmission of COVID-19." *Clinical Infectious Diseases*. Accessed April 22, 2020. <https://doi.org/10.1093/cid/ciaa450>.

- What is known? Household contacts are at increased risk of secondary transmission; however, children have been found to be less affected.
- What did this study find?
 - 2 hospitals >150km from Wuhan evaluated household contacts with 1 family member (index case) with hospitalization for COVID-19 WITH direct exposure to Wuhan, person from Wuhan, or exposure to a high-risk site (hospitals, supermarket, etc).
 - Index cases sought care at 0-1days (11.4%), 2-5days (32.4%), and >5days (56.2%) after symptom onset.

- 105 index patients found with 392 household contacts (100 <18 years). Required 2 negative swabs + asymptomatic x14 days to be considered a negative secondary case.
- Results: secondary attack rate of children at 4% compared to 17.1% in adults (OR 0.18, 95%CI 0.06 to 0.54, p=0.002). Spouses had highest risk at 27.8%. Index cases who self-quarantined at onset of symptoms showed 0% secondary transmission.
- What did this study add? SARS-CoV-2 was found to have a higher secondary transmission rate of 16.3% in household contacts compared to SARS (10.2%), MERS, and pandemic flu A 2009 (13%). Children have a significantly lower secondary attack rate compared to adults. Self-quarantine of sx family members showed 0% secondary cases.
- Limitations: Did not assess behaviors of household contacts (children vs adults) or underlying conditions
- Conclusions: Self-quarantine should be done immediately at onset of symptoms of a potential index case (wear mask, eating separately, residing alone) to prevent secondary household cases.

Disclaimer: The above references were selected and summarized by amazing Emory ID fellows. We have tried to put together an accurate list and summary, but please know that this is not intended to be 100% comprehensive! Also, it is impossible to keep completely up-to-date!