March 2020 Hospitalist Journal Club Summary

Contamination of the Environment and PPE From SARS-CoV-2

Background:

What is the extent of environmental and personal protective equipment (PPE) contamination from SARS-CoV-2?

Study Design and Results:

Study Design

- Three patients at the SARS-CoV-2 outbreak center in Singapore had surface environmental samples taken at 26 sites in and around their room including from PPE of physicians leaving the room.
- Samples were collected on 5 days over a 2 week period and tested using RT-PCR.
- One patient's room was sampled before routine cleaning and 2 patient rooms were sampled after cleaning.
- High-touch areas were cleaned twice daily and the floor was cleaned daily

Results

- Of the 2 patients who were sampled after routine room cleaning, all samples were negative.
- The third patient sampled prior to room cleaning showed positive samples on the following:
    - Patient's room
        - Chairs, light switches, stethoscope, sink, floor, glass window, air outlet fan, PPE storage area
    - Toilet area
        - Door handle, toilet bowel surface, sink internal bowl
    - Anteroom
        - none detected
    - Floor of corridor outside room
        - none detected
- Staff PPE sites:
    - One sample from the front of a shoe was positive. All other surfaces were negative including front of gown, front of face visor mask, front of N95 mask
- Two stool samples were positive despite no diarrhea

Limitations

- Viral culture was not done to determine viability
- Small sample size
- Volume of air sampled was only a small fraction of total volume and air exchangers would have diluted the presence of SARS-CoV-2

Impact on our practice:

Although this was a very small study, we can draw some preliminary conclusions. There appears to be extensive environmental contamination of SARS-CoV-2 in the hospital rooms of symptomatic patients. Although we don't know the viability of those viral particles, the good news is this contamination was significantly mitigated with proper cleaning and use of PPE. The stool sample results suggest that viral shedding in stool could be a potential route of transmission. Although the positive sample on the provider's shoe is concerning, the negative samples from the anteroom and corridor floors suggest that the risk of transmission from contaminated footwear may be low.

Reference:

Ong SWX et al. Air, surface environmental, and personal protective equipment contamination by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from a symptomatic patient. JAMA 2020 Mar 4; [e-pub].

Reviewed by Dan Ruppman

Detection of SARS-CoV-2 in Different Types of Clinical Specimens

Background:

This research letter looked at what sites the SARS-CoV-2 virus has been detected in.

Study Design and Results:

Study Design

- Looked at the distribution of SARS-CoV-2 among different tissues in patients diagnosed with the disease. Diagnosis was based on symptoms, radiology, and confirmed by SARS-CoV-2 detection.
- 1070 specimens collected from 205 patients

Results

Positive rates:

- Bronchoalveolar lavage - 93%
- Sputum - 72%
- Nasal swabs - 63%
- Fibrobronchoscope brush biopsy - 46%
- Pharyngeal swabs - 32%
- Feces - 29%
- Blood - 1%
- Urine - 0%

Impact on our practice:

One take home message here is that, other than BAL, positive rates from testing were not high. We are still determining what the sensitivity of our NP swab testing is. It will depend on the quality of the collection procedure, the viral load in the NP space, etc. We know there are false negatives so if we have a high clinical suspicion and a negative test, we should still assume the patient has the disease, continue precautions, and likely perform a second test at some point.

Also the large amount of viral shedding in the feces is an important finding implying another route of possible transmission. We don't know the overall viability of the virus in the stool although 4 fecal specimens with high copy numbers were cultured and live virus was found in 2 specimens in patients without diarrhea.

Reference:

Wang W et al. Detection of SARS-CoV-2 in different types of clinical specimens. JAMA 2020 Mar 11; [e-pub].

Reviewed by Dan Ruppman

Aerosol and Surface Stability of SARS-CoV-2 as Compared With SARS-CoV-1

Background:

Severe Acute Respiratory Syndrome Coronovirus 2 (SARS-CoV-2), a novel human coronavirus emerged in Wuhan, China in late 2019 and is now causing a global pandemic. This correspondence from authors affiliated with the National Institute of Allergy and Infectious Diseases reported very briefly on the stability of SARS-CoV-2 and SARS-CoV-1 (virus associated with SARS epidemic in 2002-2003) in aerosols and on various surfaces.

Study Design and Results:

Aerosols containing SARS-CoV-2 and SARS-CoV-1 were generated with a nebulizer and fed into a Goldberg Drum to create an aerosolized environment. The stability of both viruses were tested in 5 environments: aerosols, plastic, stainless steel, copper and cardboard. SARS-CoV-2 remained viable in aerosols throughout duration of experiment (3 hours) though the infectious titer decreased. SARS-CoV-2 was more stable on plastic (virus stable up to 72 hours) and stainless steel (virus stable up to 48 hours) than on copper (no viable virus after 4 hours) and cardboard (no viable virus

after 24 hours). The half-life of SARS-CoV-2 was approximately 1.1 to 1.2 hours in aerosols, 5.6 hours on stainless steel and 6.8 hours on plastic. The stability of SARS-CoV1 in the tested environments was largely similar to SARS-Cov2.

Impact on our practice:

This study did not involve human subjects and did NOT test infectivity of detected viruses in aerosols and various surfaces. However, since the virus remained viable for at least 3 hours in aerosol and up to 72 hours on plastic, it is plausible that aerosol and fomite transmission of SARS-CoV-2 virus COULD occur at least 3 hours after virus is aerosolized and up to 72 hours after it is deposited on a plastic surface. This would have implications for optimal personal protective equipment and intensity/frequency of disinfecting surfaces.

Reference:

Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV1. Neeltje van Doremalen et al. N Engl J Med. 2020 Mar 17 (doi:10.1056/NEJMc2004973)

Reviewed by Brian French

Hydroxychloroquine and Azithromycin as a Treatment of COVID-19: Results of an Open Label Non-Randomized Clinical Trial

Background:

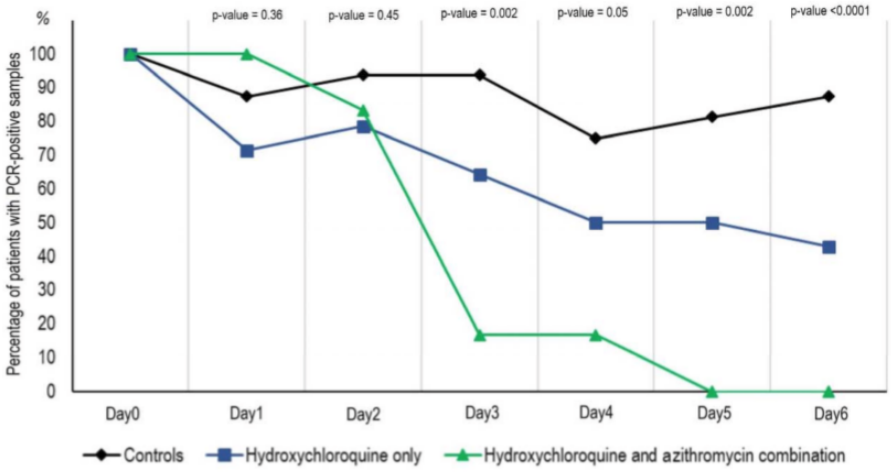
A recent paper reported an inhibitor effect of chloroquine on the growth of SARS-CoV-2 in vitro, and an early clinical trial conducted in COVID-19 Chinese patients, showed that chloroquine had a significant effect, both in terms of clinical outcome and viral clearance, when compared to control group. Azithromycin has been shown to be active in vitro against Zika and Ebola viruses [20-22] and to prevent severe respiratory tract infections when administrated to patients suffering viral infection

Study Design and Results:

Confirmed COVID-19 patients were included in a single arm protocol to receive 600mg of hydroxychloroquine daily and their viral load in nasopharyngeal swabs was tested daily in a hospital setting. Depending on their clinical presentation, azithromycin was added to the treatment. Untreated patients from another center and cases refusing the protocol were included as negative controls. The primary endpoint was viral clearance at day-6 post-inclusion. Secondary outcomes were viral clearance over time during the study period, clinical follow-up (body temperature, respiratory rate, length of stay at hospital and mortality), and occurrence of side effects.

Twenty cases were treated in this study and showed a significant reduction of the viral carriage at D6-post inclusion compared to controls, and much lower average carrying duration than reported of untreated patients in the literature. Azithromycin added to hydroxychloroquine was significantly more efficient for virus elimination.

Figure 2. Percentage of patients with PCR-positive nasopharyngeal samples from inclusion to day6 post-inclusion in COVID-19 patients treated with hydroxychloroquine only, in COVID-19 patients treated with hydroxychloroquine and azithomycin combination, and in COVID-19 control patients.



Impact on our practice:

Given the scope and potential for significant global mortality of COVID-19, treatments that provide improved outcomes compared to supportive care are of top priority. Additional trials of both treatment (hydroxychloroquine and azithromycin) and prophylaxis (hydroxychloroquine) for COVID-19 are ongoing.

Reference:

Gautret et al. (2020) Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. International Journal of Antimicrobial Agents – In Press 17 March 2020 – DOI : 10.1016/j.ijantimicag. 2020.105949

Reviewed by Dave Sausker

Entry of SARS CoV-2 (coronavirus causing COVID-19) Into Host Cell and Potential Target of Therapy

Background:

SARS CoV-2 is the virus responsible for the COVID-19 pandemic. A coronavirus contains four structural proteins. Spike (S), envelop (E), membrane (M) and nucleocapsid (N). Among them S protein plays the most important role in viral attachment, fusion and entry into host cell. Receptor binding domain (RBD) helps in attachment of viral S protein to host cell receptor. SARS CoV (responsible for SARS outbreak) and SARS CoV-2 (responsible for COVID-19) recognize Angiotensin converting enzyme-2 (ACE-2) receptor and MERS-CoV recognize DPP4 receptor.

Study Design and Results:

In vitro study. S protein of SARS-CoV-2 is primed by TMPRSS2 which helps it attach to ACE2. Clinically proven protease inhibitors of TMPRSS2 are available and shown to reduce capacity of coronavirus to attach to host cell receptor so has potential to act as therapy against current COVID-19.

Impact on our practice:

We are seeing articles such as how ACE inhibitors or NSAIDs are connected to Coronavirus. Understanding molecular biology helps in understanding this disease better and how some medications may be developed for therapy targets.

Reference:

Hoffmann M et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell 2020 Mar 5; [e-pub]

Tai W, He L, Zhang X, et al. Characterization of the receptor-binding domain (RBD) of 2019 novel coronavirus: implication for development of RBD protein as a viral attachment inhibitor and vaccine [published online ahead of print, 2020 Mar 19]. Cell Mol Immunol. 2020;10.1038/s41423-020-0400-4. doi:10.1038/s41423-020-0400-4

Reviewed by Love Patel

The Incubation Period of Coronavirus Disease (COVID-19) from Publicly Reported Confirmed Cases: Estimation and Application

Background:

Current data on incubation period of SARS Cov2 was obtained from SARS Cov1 and MERS. CDC and NIAH funded this study to validate period of active quarantine (14 days) recommended at the onset of SARS Cov2 outbreak

Study Design and Results:

- Pooled analysis of confirmed COVID cases in areas with no known prior community transmission. Worked backwards to abstract data pertaining to interval of COVID exposure for each patient.
- 181 cases both in and outside China reviewed.
- Median incubation period (time from possible exposure to any respiratory symptom onset) = 5.1 days, mean 5.5 days. Fewer than 2.5% of infected patients will show symptoms within 2.2 days. Symptom onset will occur within 11.5 days in 97.5% of infected patients. This is similar to that seen with SARS Cov1 and MERS.
- 101/10,000 pts would be missed with 14 days of active monitoring, 1/10,000 would be missed if the exposure was classified as high risk.

Additional information regarding exposure risk:

CDC has defined exposure risk category for healthcare professionals on their website

- Low-risk exposures generally refer to brief interactions with patients with COVID-19 or prolonged close contact with patients who were wearing a facemask for source control while HCP were wearing a facemask or respirator. Use of eye protection, in addition to a facemask or respirator would further lower the risk of exposure.
- Medium-risk exposures generally include HCP who had prolonged close contact with patients with COVID-19 who were wearing a facemask while HCP nose and mouth were exposed to material potentially infectious with the virus causing COVID-19. Some low-risk exposures are considered medium-risk depending on the type of care activity performed. For example, HCP who were wearing a gown, gloves, eye protection and a facemask (instead of a respirator) during an aerosol-generating procedure would be considered to have a medium-risk exposure. If an aerosol-generating procedure had not been performed, they would have been considered low-risk.
- High-risk exposures refer to HCP who have had prolonged close contact with patients with COVID-19 who were not wearing a facemask while HCP nose and mouth were exposed to material potentially infectious with the virus causing COVID-19. Being present in the room for procedures that generate aerosols or during which respiratory secretions are likely to be poorly controlled (e.g., cardiopulmonary resuscitation, intubation, extubation, bronchoscopy, nebulizer

therapy, sputum induction) on patients with COVID-19 when the healthcare providers' eyes, nose, or mouth were not protected, is also considered high-risk.

Reference:

Lauer SA et al. The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: Estimation and application. Ann Intern Med 2020 Mar 10; [e-pub]

Reviewed by Nisha Shankar

Active Monitoring of Persons Exposed to Patients with Confirmed COVID-19 – United States, January-February 2020

Background:

State and local health departments collaborated with the CDC to identify and monitor all persons considered to have close contact with patients with confirmed COVID-19 in order to ensure rapid evaluation and care of patients, limit further transmission and better understand risk factors for transmission.

Study Design and Results:

Identify those who had close contact with 10 of the first US patients with travel-related COVID-19 and monitor the symptomatic secondary attack rate of those with close contact for 14 days following the last known exposure. 445 persons were identified. Close contact included members of a patient's household (19, 4%), community members who spent at least 10 minutes within 6 feet of a patient (104, 23%), community members who were exposed in a health care setting (100, 22%), and health care personnel (222, 50%).

54 developed symptoms concerning for COVID and were subsequently tested for SARS-CoV-2. Two of these (both were household members who were isolated after diagnosis of COVID-19 in the source patient) had confirmed positive tests yielding an overall attack rate of 0.45% (95% CI = 0.12%-1.6%) among all close contacts and an attack rate of 10.5% among household members (95% CI = 2.9%-31.4%). There were five household members who stayed with a symptomatic COVID-19 patient through their isolation, none of these tested positive.

Impact on our practice:

In retrospect these numbers appear quaint. It is hard to see how these small numbers can lead to much information which would be relevant in our current situation. The

attack rate of household members is higher as would be expected (though a 10% infection rate almost appears encouraging). The best use of this information would be to recommend that family with any risk factors for severe COVID-19 disease be isolated from those who are ill with COVID-19, which is no different than what we are doing now.

Reference:

Burke RM et al. Active monitoring of persons exposed to patients with confirmed COVID-19 – United States, January-February 2020. MMWR Morb Mortal Wkly Rep 2020 Mar 6; 69:245

Reviewed by Chris Maier

Clinical Characteristics of Coronavirus Disease 2019 in China

Background:

In December 2019 coronavirus disease 2019 (Covid-19) emerged in Wuhan, China and rapidly spread throughout China. As such, data was needed on the clinical characteristics of the affected patients.

Study Design and Results:

This was a data collection and review from December 11, 2019 using 552 hospitals across 30 provinces, regions, and municipalities in mainland China through January 29, 2020 consisting of 1099 patients with laboratory-confirmed Covid-19 (high-throughput sequencing or real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assay of nasal and pharyngeal swab specimens).
The primary composite end point was ICU admission, use of a mechanical ventilator or death.

- Median age 47 yrs., less than age 15: 0.9%
- Gender: Female: 41.9% Male: 58.1%

Primary composite end point occurred in 67 patients (6.1%)

1. Admitted to ICU: 55 patients (5.0%)
2. Ventilator: 26 patients (52.3%)
3. Death: 15 patients (1.4%)

History of direct contact with wildlife: 1.9%
Non-Wuhans who had contact with Wuhans: 72.3%, including 31.3% who had been to Wuhan

Symptoms

- Fever 43.8% on admission 88.7% during hospitalization (Fever defined as 37.5 Centigrade or 99.5 Fahrenheit)
- Cough 67.8%
- Nausea/vomiting: 5.0%
- Diarrhea 3.8%

23.7% had at least 1 comorbidity
Those with severe disease were more likely to have a comorbid condition: 38.7% than those with non-severe illness (21.0%).

Imaging
CT Findings:

- Of 975 CT scans on admission 86.2% were “abnormal”
- Ground-glass opacities: 56.4%
- Bilateral patchy shadowing: 51.8%
- No imaging findings were noted in (severity defined using The American Thoracic Society guidelines for CAP)
    - ○17.9% (157/ 877 patients) with non-severe disease
    - ○2.9% (5/173 patients) with severe disease

Labs:

- Lymphocytopenia 83.2% on admission (Lymphocytopenia defined as lymphocyte count of <1500 cells/cubic millimeter)
- Leukopenia: 33.7%
- Thrombocytopenia defined as platelet count <150,000: 36.2%

Median incubation period: 4 days

- Incubation period: the interval between the potential earliest date of contact of the suspected transmission source and the earliest date of symptoms (cough, fatigue, fever, myalgias) excluding periods of less than 1 day. Incubation calculated on the basis of 291 patients who had clear information regarding the specific date of exposure.

Length of hospitalization

- Median hospital stay: 12 days
- Mean hospital stay: 12.8 days

Impact on our practice:

Very similar to SARS with fever/cough as the dominant symptoms, but GI symptoms less common suggesting a different viral tropism. The absence of fever is more frequent than in SARS (less common than in SARS or influenza).
Early isolation, early diagnosis, and early management.

- Lower WBC counts were more likely in severe disease
- An elevated procalcitonin was unusual and likely reflected concomitant pneumonia or non-viral infection
- CRP elevated in most cases, especially in severe disease
- LDH >250 U/liter was seemed to be the most affected of all liver function studies with especially in severe cases
- d-dimer >0.5 mg/liter in 46.4 %

Reference:

Guan W-J et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020 Feb 28; [e-pub].

Reviewed by Scott Tongen