OPTUM Care®

Forum for Evidence-Based Medicine

Special COVID-19 Edition
March 23 | 2020

Sensitivity and specificity of the COVID-19 PCR test in nasopharyngeal and oropharyngeal swabs

In 205 patients with proven COVID-19 (based on isolation of SARS-CoV-2 in at least one site), investigators at three hospitals in China (Hubei and Shandong provinces and Beijing) obtained pharyngeal swabs 1 to 3 days after admission.[1] In addition, samples of blood, sputum, feces, urine, nasal swabs and bronchial brush or bronchoalveolar lavage (BAL) fluid (for intubated patients) were obtained periodically throughout the illness. Testing consisted of reverse-transcriptase polymerase chain reaction. The 205 patients contributed a total of 1070 specimens; they had a mean age of 44 years (range, 5–67 years).

With the denominator indicating specimens obtained (not patients), BAL fluid was positive in 14/15 (93%), sputum 75/104 (72%), nasal swabs 5/8 (63%), brush biopsy 6/13 (46%), pharyngeal swabs 126/398 (32%), feces 44/153 (29%), blood 3/307 (1%), and urine 0/72 (0%). Nasal swabs contained the most virus. In two patients SARS-CoV-2 was found in formed stool. In a smaller study[2] of 51 patients that compared chest CT to nasopharyngeal swabs, interestingly the results were very consistent with the swabs diagnosing 71% of the cases.

This fairly low sensitivity raises concerns in several areas, including testing of health care providers (HCP) for diagnosis of acute infection to remove them from the work environment. When signs and symptoms strongly suggest COVID-19 infection in an HCP who tests negative for infection, it would be prudent to follow our current guidelines for infection in HCP.

Aerosol and surface stability of SARS-CoV-2

Although transmission of the virus causing COVID-19 is felt to be predominantly through droplets in symptomatic patients, given that the incubation period varies between 2-11 days, with a median of 5 days, patients may transmit the disease before or after symptoms have appeared/resolved. In January in Wuhan province, it was estimated that the majority of community transmission occurred from undocumented infections. It is therefore important to understand if transmission may occur through aerosolized virus which could cause spread beyond the 6-foot recommended radius, or via surface contamination. In a study looking at aerosol and surface viability of the virus[3], SARS-CoV-2 remained viable in aerosols for up to 3 hours with a median of just over 1 hour. 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. On cardboard, no viable SARS-CoV-2 was measured after 24 hours. The results indicate that aerosol and fomite transmission of SARS-CoV-2 is plausible, since the virus can remain viable and infectious in aerosols for hours and on surfaces up to days. In fact, in China, human-to-human transmission of the COVID-19 virus is largely occurring in families. The Joint Mission received detailed information from the investigation of clusters and some household transmission studies, which are ongoing in a number of provinces. Among 344 clusters involving 1308 cases in Guangdong Province and Sichuan Province, most clusters (78%-85%) have occurred in families.

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EDUCATIONAL FORUM

Diarrhea is a prominent symptom of COVID-19 infection

To date, the most prevalent symptoms reported for COVID-19 infection have included fever, cough and dyspnea, with sore throat and URI symptoms seen less frequently. Gastrointestinal (GI) symptoms have not been prominently reported. A study published from China last week in the American Journal of Gastroenterology sheds new light on the frequency and significance of GI symptoms in COVID-19 infection[4]. The study noted that patients with COVID-19 infection had prominent diarrhea in 20 of the cases, with in some cases diarrhea being the primary symptom. While anorexia was common, abdominal pain and vomiting were both seen in under 1% of cases. There are some observational data to suggest that patients presenting with diarrhea were diagnosed later in their course and had a worse outcome than patients presenting primarily with respiratory symptoms. This is a particularly important finding as our current screening process has included respiratory but not GI symptoms. Patients with diarrhea only, therefore could serve as vectors for disease transmission in medical facilities who are screening and diverting only patients with respiratory symptoms consistent with COVID-19 infection. With the publication of these results last Thursday, we have included diarrhea on the list of symptoms used to redirect patients to our febrile URI (FURI) clinics which are specifically designed to evaluate and treat patients with suspected COVID-19 infection.

COVID-19 in children — Rate of infection and clinical characteristics

The COVID-19 infection rate is lower in children but little is known about the clinical presentation in this age group. A recent review of 72,314 cases by the Chinese Center for Disease Control and Prevention[5] showed that less than 1% of the cases were in children younger than 10 years of age. There was a single hospital in Wuhan assigned to care for all of these children. Of 1391 children tested, 171 were positive and the age was equally distributed between 1-16 years. In terms of signs and symptoms, 16% were asymptomatic, 19% had typical URI symptoms, and 65% had pneumonia. Only 48% had cough, only 41% were febrile, only 28% were tachypneic, and only 9% had diarrhea. It thus appears that children may account for a meaningful portion of the asymptomatic reservoir in the population. When they become clinically ill, they have a lower frequency of the typical presenting symptoms seen in adults, however there is an appreciable risk of pneumonia. Fortunately, the mortality rate is also low in children with only one death observed in this series of patients.[6]

Update on pharmacotherapy for COVID-19

The therapeutic options currently being studied are various antivirals and chloroquine and hydroxychloroquine, with and without azithromycin.

Antiviral therapy. In terms of the antivirals, there are several compounds under study, most prominent among them being remdesivir. Remdesivir, an investigational nucleoside analogue has been administered to several hundred patients with confirmed, severe SARS-CoV-2 infections in the United States, Europe, and Japan through expanded access or compassionate use programs. A clinical trial evaluating the efficacy of remdesivir in patients infected with SARS-CoV-2 is currently being conducted in China. Data from this trial are expected by April, 2020. In preclinical trials, remdesivir has demonstrated significant activity against coronavirus and a high genetic barrier to resistance. In vitro data found remdesivir exerts potent antiviral activity against a clinical isolate of SARS-CoV. Remdesivir has shown prophylactic and therapeutic efficacy against 2002 SARS-CoV in a mouse model. Resistance mutations have not been identified.

Chloroquine/Hydroxychloroquine. Related both to the explosive nature of the COVID-19 pandemic and the ensuing fear in the populace, we are in a situation where our evidence-based approach to disease management is being challenged. Nowhere is this more apparent than in the focused attention around the potential benefit of chloroquine and hydroxychloroquine. The data to date stems from two sources.

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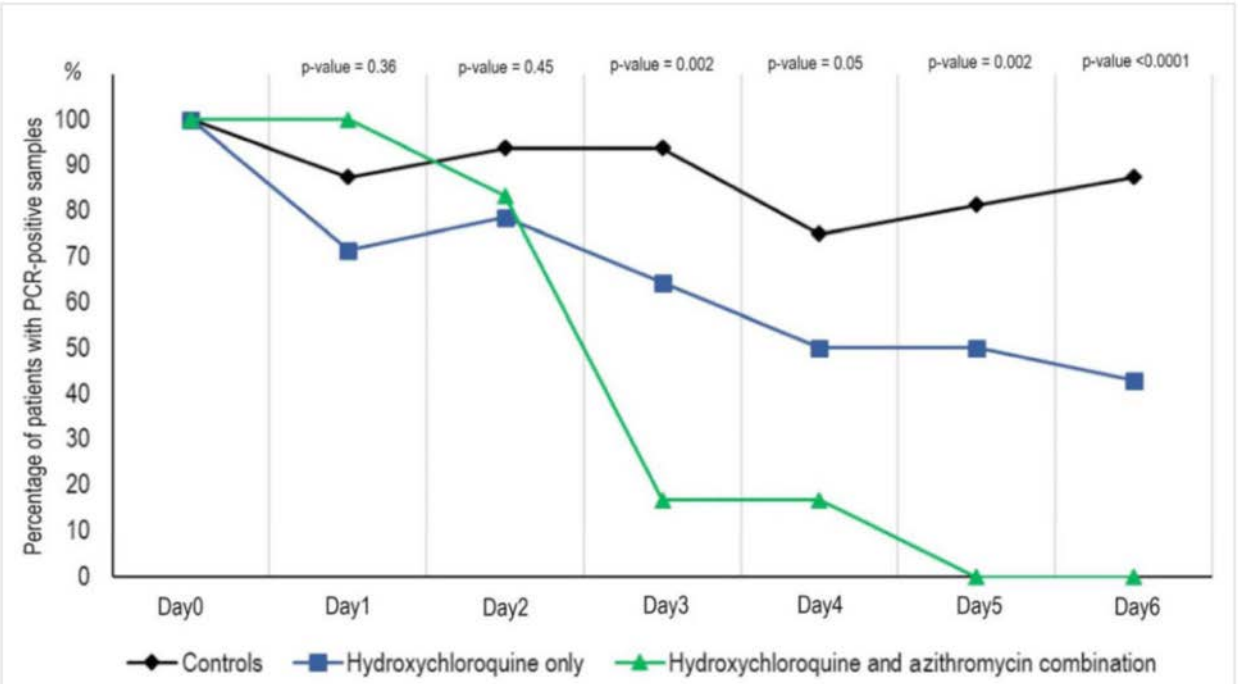
- The first was a series of small trials conducted in China encompassing in total about 100 patients.[7] Thus far, results have suggested that chloroquine phosphate is superior to the control treatment in inhibiting the exacerbation of pneumonia, improving lung imaging findings, promoting a virus negative conversion, and shortening the disease course according to the news briefing, but unfortunately without available trial data to review.
- The second was a small observational study from France[8] which included 24 patients with COVID-19 infection. The results showed that compared to controls, there was a decrease in viral shedding at 6 days with hydroxychloroquine alone, with a greater effect seen with the combination of hydroxychloroquine and azithromycin. Clinical outcomes have not yet been published. Results are shown below.



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

As a result of these data, there are currently trials being rapidly scaled to evaluate the effectiveness of these antimalarial drugs, with and without concomitant azithromycin for treatment of COVID-19 as well as for prophylaxis of COVID-19 infection in health care providers exposed to the infection. It is too early to know whether these drugs will have any clinical efficacy.

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Kenneth Roy Cohen, MD, FACP | *Chief Medical Officer*

Dr. Kenneth Cohen is an experienced physician leader, practicing internist, and researcher who has attained national recognition for health care quality improvement. He has successfully developed and reported numerous clinical quality studies in primary care, including tobacco cessation, osteoporosis, asthma, diabetes, hypertension, and ischemic vascular disease. He was one of the founding physicians of New West Physicians, which is the largest primary care group practice in Colorado and now part of OptumCare. He has served as Chief Medical Officer since 1995. Dr. Cohen has received awards of recognition and distinction for teaching, including the Lutheran Medical Center Physician of the Year award in 2011. Under his stewardship New West Physicians was awarded the AMGA Acclaim award in 2015 and the Million Hearts Hypertension Champion Award in 2017. He is a Clinical Associate Professor of Medicine and Pharmacy at the University of Colorado School of Medicine. Dr. Cohen holds degrees from Dickinson College and Hahnemann University. He is a Fellow of the American College of Physicians and a member of the Phi Beta Kappa and Alpha Omega Alpha honor societies.

John Hitt, MD, MBA | *Senior Medical Director*

Dr. Hitt has been a physician executive for more than 25 years. Most recently he was the CMO of Ativa Medical a medical device startup company and an independent health care consultant. Previously, he was CMO at Maricopa Integrated Health System (MIHS) and a key member of the senior leadership team having responsibility for Medical Staff Services, Grants and Research, Academic Affairs, Risk Management, physician contracted services and the activity of Residency Program Directors, Clinical Department Chairs, and Medical Staff.

Dr. Hitt has over 25 years of experience in quality and performance improvement, clinical integration, academic and medical staff affairs. He served as the Chief Medical Quality Officer for Hennepin Health System, a premier Level 1 Adult and Pediatric Trauma Center. He was a physician leader for VHA (now Vizient). He was the national Medical Director for Disease Management at Caremark International and the VP of Medical Affairs at the University of Minnesota Hospital.

Dr. Hitt is a graduate of the University of Virginia where he played Division 1 soccer. He received his Medical Doctorate from the Medical College of Georgia in 1984 (AOA honors) and completed his Internal Medicine and Infectious Disease Fellowship training at the University of Minnesota Hospital and Clinics. Dr. Hitt completed his MBA at the Carlson School of Management at the University of Minnesota in 2003. He is the proud father of seven children.

Geoffrey Heyer, MD | *Senior Clinical Practice Performance Consultant*

Dr. Heyer is board certified in neurology with special certification in child neurology and in headache medicine. Prior to joining our team, Dr. Heyer was an associate professor of neurology and pediatrics at The Ohio State University and Columbia University Medical Center, specializing in autonomic disorders, headache, and pain management. He has published over 50 peer-reviewed research papers and numerous editorials, clinical reviews, and textbook chapters. He also co-authored a textbook on childhood stroke and cerebrovascular disorders.

Dr. Heyer received his medical degree from Columbia University, College of Physicians and Surgeons. He completed his neurology and child neurology residencies at Columbia-Presbyterian Medical Center. He has additional research training from the Mailman School of Public Health, Columbia University.

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