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## COVID-19 OUTBREAK IN WASHOE COUNTY (2)

### Therapeutic Options

#### Introduction

The Washoe County Health District (WCHD) reported the first case of COVID-19 on March 5, 2020. As of April 17, a total of 588 cases have been reported, which corresponds to an incidence rate of 126 cases per 100,000 population. The epidemiological investigations and contact tracing are very labor-intensive. Many investigations are still ongoing. The Epi-News regarding epidemiological findings from the first 115 cases was published on April 3 [here](#), the focus of this newsletter is the therapeutic options for patients with COVID-19 as a reference for clinicians in Washoe County.

#### Therapeutic Options for COVID-19

There are no drugs or other therapeutics approved by the US Food and Drug Administration (FDA) to prevent or treat COVID-19. No national medical management guidelines have been available thus far in the United States. Current clinical management includes infection prevention and control measures, supportive care (supplemental oxygen and mechanical ventilatory support when indicated). WCHD highly recommends that health care providers practice their own best judgement to manage patients based on the individual patient situation and severity of disease using their own clinical experiences. The following key elements are listed here for clinicians' reference only.

##### 1. Clinical progression

According to a recently published study, pharyngeal virus shedding was very high during the first week of symptoms (peak  $7.11 \times 10^8$  RNA copies per throat swab, day 4)<sup>1</sup>. Generally speaking, this is the time period when an ill person should stay home. Among patients who developed severe disease, the median time to dyspnea ranged from 5-8 days, to acute respiratory distress syndrome (ARDS) ranged from 8-12 days, and to ICU admission ranged from 10-12 days. Some patients may deteriorate rapidly one week after illness onset.

##### 2. Critically Ill Adult Patients with COVID-19

It is highly recommended for clinicians working in the acute care settings to listen to the CDC's webinar entitled "Clinical Management of Critically Ill Adults with COVID-19" [here](#)

[https://emergency.cdc.gov/coca/calls/2020/callinfo\\_040220.asp](https://emergency.cdc.gov/coca/calls/2020/callinfo_040220.asp). A panel of doctors shared their experiences in managing critically ill patients.

##### 3. Remdesivir

Remdesivir is an investigational intravenous drug with broad antiviral activity that inhibits viral replication through premature termination of RNA transcription, and has in-vitro activity against SARS-CoV-2 and in-vitro and in-vivo activity against related beta coronaviruses.<sup>2</sup>

At least 25 drugs are under investigation for use in COVID-19, with 10 in active clinical trials<sup>3</sup>. Remdesivir is one of them. While official randomized, controlled, clinical trials are ongoing, U.S. doctors, together with doctors from Europe, Canada, and Japan recently published their study results on the compassionate use of Remdesivir for patients with severe COVID-19. In their cohort of 53 patients hospitalized for severe COVID-19, clinical improvement was observed in 68% of patients. Overall mortality among 53 severe patients was 13% (7/53). By way of comparison with other published studies, the authors concluded that their Remdesivir compassionate-use cohort is noteworthy although they pointed out that the measurement of efficacy will require ongoing randomized, placebo-controlled trials.<sup>4</sup>

##### 4. Hydroxychloroquine and Chloroquine

Hydroxychloroquine (HCQ) and chloroquine (CQ) are oral prescription drugs that have been used for treatment of malaria and certain inflammatory conditions. HCQ and CQ are under investigation in clinical trials for pre-exposure or post-exposure prophylaxis of SARS-CoV-2 infection, and treatment of patients with mild, moderate, and severe COVID-19. FDA issued an Emergency Use Authorization (EUA) to authorize use of HCQ and CQ from the Strategic National Stockpile for treatment of **hospitalized** adults and adolescents (weight  $\geq 50$  kg) with COVID-19 for whom a clinical trial is not available or participation is not feasible. The prescribing health care provider is responsible for submitting patient outcome reports as described in

<sup>1</sup> <https://www.nature.com/articles/s41586-020-2196-x>

<sup>2</sup> <https://www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html>

<sup>3</sup> <https://www.nejm.org/doi/full/10.1056/NEJMp2009457>

<sup>4</sup> <http://10.1056/NEJMoa2007016>

the Emergency Use Authorization, and all serious adverse events and medication errors should be reported to FDA's medical product safety reporting program called [MedWatch](#).<sup>5</sup>

FDA issued the above EUA to authorize use of HCQ and CQ for the treatment of **hospitalized** patients; however, based on the local epidemiological findings, the median day from the onset of illness to the admission date of hospitalization is 6 days. The recently published study with Nature states that the SARS-CoV-2 virus shedding is very high and reaches the peak of RNA concentration at day 4.<sup>6</sup> Therefore, providing early treatment when patients have moderate symptoms prior to needing hospitalization may be beneficial, especially for those patients with high risk factors. The following is a list of recently published studies or surveys.

1. A team of scientists from France<sup>7</sup> and Viet Nam performed an observational study to examine the clinical and microbiological effect of a combination of HCQ and azithromycin (AZ) in 1,061 patients with COVID-19. A total of 973 patients had a measurable clinical outcome. A total of 46 patients (4.3%) had a poor outcome including 31 patients that required 10 days of hospitalization or more, 10 were transferred to ICU, and 5 died (0.47%) (74-95 years old). However, in the U.S., the hospitalization rate was around 15% and case fatality rate was 4.2% among reported cases. The authors concluded that HCQ-AZ combination, when started **immediately after diagnosis**, is a safe and efficient treatment for COVID-19, with a mortality rate of 0.5%, in elderly patients. It avoids worsening, clears virus persistence and reduces contagiousness in most cases.
2. Doctors from Wuhan, China recently performed a randomized clinical trial on the efficacy of HCQ in 62 patients diagnosed with COVID-19 and admitted to the hospital. The authors found that the body temperature recovery time and the cough remission time were significantly shortened in the HCQ treatment group. Besides, a larger proportion of patients with improved pneumonia in the HCQ treatment group (80.6%, 25 of 31) compared with the control group (54.8%, 17 of 31). Notably, all 4 patients progressed to severe illness that occurred in the control group. However, there were 2 patients with mild adverse reaction in the HCQ treatment

<sup>5</sup> <https://www.cdc.gov/coronavirus/2019-ncov/hcp/therapeutic-options.html>

<sup>6</sup> <https://www.nature.com/articles/s41586-020-2196-x>

<sup>7</sup> Dr. Didier Raoult, IHU-Méditerranée Infection, Marseille, France (not a formally published study yet). For previously published study with small sample size see here: <https://doi.org/10.1016/j.ijantimicag.2020.105949>  
<https://www.sciencedirect.com/science/article/pii/S0924857920300820?via%3Dihub>

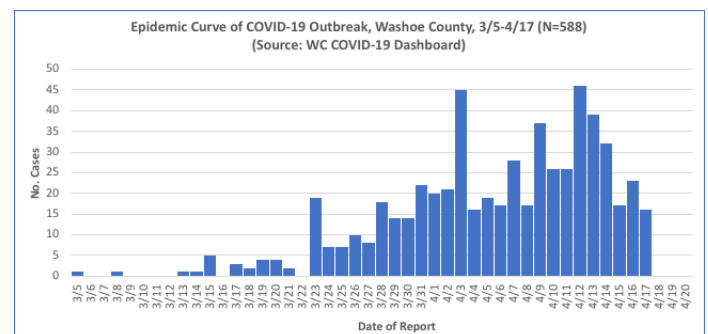
group. Authors concluded that among patients with COVID-19, the use of HCQ could significantly shorten time to clinical recovery and promote the absorption of pneumonia.<sup>8</sup>

3. Sermo, the largest healthcare data collection company and global social platform for physicians, conducted a large survey among 6,200 multi-country physicians on COVID-19. They concluded that HCQ was overall chosen as the most effective therapy amongst COVID-19 treaters from a list of 15 options (37% of COVID-19 treaters). The two most common treatment regimens for HCQ were:
  - (38%) 400 mg twice daily on day 1; 400 mg daily for five days;
  - (26%) 400 mg twice daily on day 1; 200 mg twice daily for four days.

Outside the U.S., HCQ was equally used for diagnosed patients with mild to severe symptoms whereas in the U.S. it was most commonly used for high risk diagnosed patients. Globally, 19% of physicians prescribed or have seen HCQ prophylactically used for high risk patients and 8% for low risk patients.<sup>9</sup>

### Statistical Updates:

Between March 5 and April 17, 588 cases of COVID-19 have been reported to the Washoe County Health District. Of which, 119 cases (20%) have recovered and 16 cases (2.7%) had a fatal outcome.



**We are grateful to all health care providers, infection control practitioners and laboratory staff for their reporting and collaboration with this COVID-19 pandemic response.**



<sup>8</sup> <https://www.medrxiv.org/content/10.1101/2020.03.22.20040758v3>

<sup>9</sup> <https://www.sermo.com/press-releases/largest-statistically-significant-study-by-6200-multi-country-physicians-on-covid-19-uncovers-treatment-patterns-and-puts-pandemic-in-context/>