

Queen Elizabeth Hospital Birmingham Evidence Update on COVID-19

This is not a clinical guideline or SOP. This is a summary of the latest evidence available internationally on the management, treatment and science underlying COVID-19 disease.

Pathophysiology

- o Cytokine storm – some patients may respond to COVID-19 with cytokine storm reaction, with features of bacterial sepsis or hemophagocytic lymphohistiocytosis. Clinical markers include elevated CRP and ferritin which tracks with disease severity and mortality ([Ruan 3/3/20](#)).

Progression

- o Patients appear to have mild symptoms for the first several days (innate immune stage), and then suddenly deteriorate (adaptive immunity stage) [Young 3/3/20](#).
- o This suggests initial clinical symptoms are not predictive of future deterioration

Diagnosis

- o PCR sensitivity in nasopharyngeal sources are 75% accurate – a negative swab does not mean a negative patient – a second swab 2-3 days later can confirm

Virus

- o Remains infectious capacity in aerosol for 3hours (PPE needed)
- o Stable on plastic and stainless steel for 72 hours and cardboard for 20 hours (although viral load drops over time) [Doremalen 17/3](#)

Secondary infection

- o Secondary bacterial infection may occur in severe patients – similar to influenzae
- o In a group of patients who died of COVID-19, 16% had secondary infections [Ruan 3/3/20](#) (no indication of what samples and how this was tested – possibly incorrect)

Therapy

Antiviral

- o No antiviral therapy has been proven to work in humans (RCTS ongoing in China)
- o Early treatment (1-2 days of admission) is most effective generally to target innate immune phase ([Chen 2003](#))
- o Lopinavir/Ritonavir/Ribavirin triple therapy might be beneficial, but trials are ongoing ([Young 3/3/20](#)). In [MERS](#) and [SARS](#) these drugs reduced viral load and improved clinical outcomes , but no effect on 16 COVID patients (underpowered study).

Chloroquine – interferes with ACE2 (possible COVID-receptor)

- [in vitro](#) study showed effective at inhibiting viral infection, similar in [SARS](#)
- Failed in [mice](#)
- In humans [hydroxychloroquine](#) reduced viral carriage, in synergy with azithromycin (22 patients and removed ICU patients from analysis)
- [ICTRP](#) running an RCT (Data to be published)
- China recommends [500mg twice per day](#) for 10 days in all cases of COVID-19 with pneumonia, but the data behind this is not published and the article is in Chinese

Steroids

- o No benefit in SARS or MEERS, and steroid use may increase [viral shedding](#)

Immune therapy

IL-6 is associated with severity of COVID-19 and the pathology of ARDS – blocked the receptor with a monoclonal antibody may show benefit

- o Tocilizumab given to 21 patients significantly improved (CT Scans, lymphocyte counts down, CRP down – suggests potential treatment option (low N and needs to be reproduced – [Xioling 5/3](#)

- o Siltuximab entering observational trial in Italy – [data expected late March](#)
(will update)