Clinical Aspects of Covid-19

It is tempting to think of Covid-19 (the illness produced by the virus SARS Cov-2), as a respiratory illness. At the time of writing this in early June 2020, we realize very clearly that it is very much more severe than our usual experience of influenza, though this condition does have significant mortality.

The evolution of the current pandemic has led to a rapid acquisition of knowledge about the aspects of the disease that coronavirus causes. It is very much, a true multisystem disease.

We know that after exposure to the virus, nothing might happen. The load may be too small, or personal protection or handwashing may intercede and prevent the progress of the exposure to a detectable disease. We know that many people will acquire the infection and have either a mild illness or even no symptoms at all. It is estimated by a research team at LSTM&H (London School of Tropical Medicine and Hygiene) that up to 72% of the 700 passengers on Diamond Princess who tested positive for Coronavirus were asymptomatic. There were 9 deaths giving a mortality of 1.3%. Given the average age of cruise ship passengers, this is a favourable outcome.

The early symptoms are of a repetitive cough, temperature may be below 38 c in mild cases, muscle aches, tiredness, mood changes, anosmia and loss of taste (probably same thing). Rash over upper surface of toes has been reported. (Eyesight disturbance has not been officially reported but PM and his adviser are said to have had it!!!) Sore throat is not a prominent symptom. It may cause diarrhoea.

Skin rashes are common manifestations of various viral conditions and may suggest that there is a mild inflammation in the wall of small blood vessels. Some authorities describe blue or white areas that might suggest microscopic blood clots. An important condition to differentiate it from would be meningococcal sepsis, recently rare in children but of much greater risk to life.

The virus may be neuro trophic. In a recent BMJ article the loss of smell was attributed to changes in the olfactory bulb mechanism at the top of the nose rather than mucous membrane swelling which is more common in simple colds.

More severe cases of Covid-19 may progress to develop ARDS (Acquired Respiratory Distress Syndrome). This is a condition seen after severe trauma, fulminant pancreatitis, and sepsis. A percentage of these patients will require ventilation when the mortality rate may be as high as 50%. Modern ITU medicine has developed sophisticated therapies for this eventuality, including nursing prone, PEEP (positive end expiratory) ventilation and low tidal volume ventilation!

The defining feature in these cases is the phenomenon of a “Cytokine Storm”

Cytokines are released during an immunological response to infection. Events such as macrophage death stimulates their release. In turn this causes huge biochemical changes such as the release of Interleukins IL2 IL6 IL7, an increase in GCSF (Granulocyte Colony Stimulating Factor) and alpha TNF (Tumour Necrosis Factor). These are all components of the normal immunological defence response, but in these instances, there is a huge over reaction.

Inflammatory proteins increase hugely, and blood becomes much more coagulable. Many patients develop blood clots with pulmonary embolism and strokes being a concern.

One of the themes of therapy of Covid-19 looks at ways of attenuating this overly vigorous immune response and blocking the effects of interleukins.

I have written a synopsis of current therapies in Covid-19. Some recent developments include a paper from the NEJM showing no significant benefit from hydroxychloroquine and popssibly, even a slight worsening of outcome.(I have included a pdf of a relevant graph of Probability of being event free v Freedom from Composite End Point of Intubation or Death). A group in Oxford have questioned the validity of some of the statistical analysis.

Remdesivir seems to be the continuing favourite at the moment, and is an antiviral drug that emerged after the Ebola epidemic.

Guys Kings Tommies GKT are currently researching a lipid soluble form of Ibuprofen to moderate the response in Covid-19, in the Liberate trial. It is ironic that early on the received wisdom was that Ibuprofen may be counter productive. This was reinforced by the French M of H broadcasts on the subject. Subsequent analysis suggests that it is a reasonable alternative to Paracetamol!