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What is the Culprit in the COVID-19 Disease?

The Lancet Infectious Disease Journal highlights a comment by Yi and others, which helps to identify a possible route for transmission of the SARS-CoV-2 virus into the human and its resultant effect.

The COVID-19 pandemic has resulted in more than 5.7 million confirmed cases and 350,000 deaths globally according to the Johns Hopkins University Coronavirus Resource Center on May 28. However, there is little knowledge on the disease's pathogenesis with very little evidence.

The disease is now being witnessed in paediatric and young adult populations and the spectrum of clinical manifestations includes pneumonia, respiratory failure, thromboembolic events.

Clinical studies report acquired coagulopathy in patients with COVID-19 and a paediatric inflammatory syndrome linked to the SARS-CoV-2 which also causes life-threatening cardiac issues.

It is now identified that angiotensin converting enzyme 2 ACE2 is a functional receptor for SARS-CoV-2 allowing entry of the virus into host cells. ACE 2 is normally highly expressed in the lung, heart, ileum, kidney, and bladder. In the lungs, ACE2 is heavily expressed on ciliated airway epithelial cells and alveolar type 2 pneumocytes. Endothelial cells, which comprise about a third of resident pulmonary cells also express ACE2. It is thus hypothesised that SARS-CoV-2 undergoes haematogenous dissemination via infected pulmonary epithelium followed by pulmonary endothelium. During this process, the endothelial injury incites the coagulation cascade and subsequent microvascular permeability.

Levels of circulating ACE2 are higher in men than in women, which may account for the differences in severity and mortality between the sexes.

It is not known whether the SARS-CoV-2 can bind to other targets. The host's immune system is activated, and excess immune responses are harmful and cause severe symptoms especially in younger patients.

Patients infected with SARS-CoV-2, and especially those requiring intensive care are reported to have a higher plasma level of proinflammatory cytokines.

Pathologies have shown that alveolar damage is the predominant pattern of lung injury at post-mortem. They found that there was increased endothelial necrosis, increased megakaryocytes in alveolar capillaries, the inflammatory response and widespread arteriolar fibrin–platelet damage resulting from other causes. These histopathological findings were substantiated by very high serum D-dimer levels, suggesting that ante-mortem disseminated intravascular coagulation was prevalent. In addition, patients with COVID-19 also present with ischaemic stroke or deep vein thrombosis adding to this theory.

However, it is difficult to understand the causal relationship of disseminated intravascular coagulation, diffuse alveolar damage, and pulmonary thrombotic microangiopathy. These findings do however suggest that anticoagulation might be an important therapeutic strategy.

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Interestingly, the ultrastructural demonstration of coronavirus particles was identified within type 1 and type 2 pneumocytes but rarely within alveolar macrophages and were not detected in the endothelial cells. This conflicts with the thought that the mechanism of SARS-CoV-2 dissemination is via infected pulmonary epithelium and endothelium. It is interesting that co-infection with secondary microorganisms was also uncommon in this series probably because of the rapidity with which death can occur in cases of COVID-19.

The London General Practice has kept abreast of all aspects of diagnosis, treatment and management of SARS-CoV-2 and COVID-19 infection. It is happy to undertake video consultations with anyone concerned about any medical symptom and is also happy to undertake face to face consultations and home visits with patients who have no florid COVID-19 symptoms and of course adheres to strict safety protocols with doctors wearing full PPE. Please do not hesitate to ring if you have any medical concern.

Dr Paul Ettlinger
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