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**EXTRACORPOREAL HEMOADSORPTION: AN OPTION
FOR COVID-19 ASSOCIATED CYTOKINE STORM SYNDROME**

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The novel coronavirus SARS-CoV-2 is rapidly spreading worldwide, and the disease caused by the virus (COVID-19) immensely challenges intensive care units in affected countries with previously unknown speed. While the true mortality of COVID-19 remains to be defined, morbidity in infected patients is often substantial. Specific antiviral treatment strategies and vaccines are lacking but urgently needed to control the pandemic. Many hospitals are urged to allocate therapies such as ventilation and mechanical support. SARS-CoV-2 initially enters through the respiratory tract and often results in viral pneumonia. Of note, beyond hypoxemic lung failure, acute heart failure and cytokine storm are two major determinants of adverse and often fatal outcome.(1, 2)

Cytokine storm has been frequently reported to occur in severe COVID-19. Available data suggest that elevated levels of mediators such as interleukin-6 (IL-6), IL-8, tumour necrosis factor and others indicate a severe course or fatality of the disease.(2, 3) Accordingly, it has been recently suggested to screen COVID-19 patients for cytokine storm and a secondary form of hemophagocytic lymphohistiocytosis (HLH) by measuring inflammatory parameters and calculating the H-score.(4, 5) Identified patients may be candidates for anti-inflammatory intervention, in order to mitigate an excessive host response and thereby reduce organ damage. In this context, antibodies against IL-1, the IL-6 receptor, granulocyte-macrophage colony-stimulating factor as well as inhibitors of Janus-kinase are currently evaluated for treating hyperinflammation in COVID-19. Substantial experience exists with those agents in other inflammatory conditions such as rheumatoid arthritis,(6) but the biological processes of these conditions are much better understood than those of COVID-19. In contrast, many aspects of hyperinflammation in this novel disease are still unknown, and specific inhibition of interleukins or other mediators in COVID-19 may thus be associated with potential risk. Steroids represent a more unspecific pharmacological intervention, but there is reasonable doubt whether those are safe and effective in infection with coronaviruses.(7)

This said, we suggest to consider extracorporeal hemoadsorption for COVID-19 associated cytokine storm syndrome. The currently most often used adsorber (Cytosorb, Cytosorbents Inc., Monmouth Junction, NJ, USA) removes excess amounts of small hydrophobic molecules from the circulation. It has received CE mark for conditions with elevated inflammatory mediators, for hypermyoglobinemia, and for hyperbilirubinemia. Cytosorb has been successfully used in various conditions with hyperinflammation, HLH,(8, 9) virus-associated HLH,(10, 11) intoxication, sepsis, and others.(12) In several observational studies and a randomized controlled trial in patients with septic shock, CytoSorb reduced excess levels of inflammatory mediators, which was associated with a lower vasopressor demand.(13-16) Many mediators that characterize a severe course of COVID-19 are adsorbed by Cytosorb. Importantly, efficacy of adsorption is concentration-dependent, i.e. peak blood levels of adsorbable molecules are preferentially reduced. Cytosorb may be installed in ECMO or dialysis circuits, but can also be used stand-alone as hemoperfusion.(12) Besides removal of excess amounts of inflammatory

mediators, there is a reasonable chance to adsorb molecular motifs of the virus itself, so-called pathogen associated molecular patterns.(17) As such, hemoadsorption would essentially reduce high levels of several mediators and by this ‘limit the storm’ in cytokine storm syndrome, rather than actively targeting individual pathways during inflammation.

Cytosorb has already been used in COVID-19 patients in China and Europe. The scientific community eagerly awaits publication of data from this experience. However, given the immense dynamics of COVID-19 spread right now, the preexisting experience with this approach in other conditions, and the devastating mortality of complicated COVID-19, we consider it reasonable to employ hemoadsorption in selected COVID-19 patients with cytokine storm before prospective data is available.

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