Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the editor

Covid-19 accelerates endothelial dysfunction and nitric oxide deficiency

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Martel and colleagues provide a thoughtful review on strategies to increase airway nitric oxide to treat and possibly prevent Covid-19 [1]. However, it is becoming apparent that the clinical presentation of Covid-19 begins with acute respiratory distress in the lungs that moves quickly to vascular networks throughout the gut, kidney, heart, and brain with associated platelet-endothelial dysfunction and abnormally rapid life-threatening blood clotting [2]. SARS-CoV-2 is emerging as a thrombotic and vascular disease targeting endothelial cells throughout the body and is particularly evident in patients with cardiometabolic comorbidities, in particular hypertension, with associated endothelial dysfunction [3].

A hallmark of endothelial dysfunction and thrombotic events is suppressed endothelial nitric oxide synthase (eNOS) with concomitant nitric oxide deficiency. In healthy vessels, the endothelium releases the vasodilator and antithrombotic factor, nitric oxide. Whereas in injured vessels, nitric oxide is impaired contributing to hypertension and thrombus formation [4].

Restoring nitric oxide, independent of eNOS, may counter endotheliitis and contribute to pulmonary vasodilation, antithrombotic, and direct antiviral activity [5]. As to the later, nitric oxide reportedly interferes with the interaction between coronavirus viral S-protein and its cognate host receptor, ACE-2. Nitric oxide-mediated S-nitrosylation of viral cysteine proteases and host serine protease, TMPRSS2, which are both critical in viral cellular entry, appear to be nitric oxide sensitive [6–10].

Based on a report of improved lung function during the 2003 SARS outbreak, FDA's emergency expanded use of nitric oxide gas is now underway for treating Covid-19 [1]. Alternatively, dietary inorganic nitrate has been shown in multiple studies to be effective at restoring endothelial function, reducing pulmonary and arterial hypertension, and promoting antimicrobial activity [5]. It is well understood that dietary inorganic nitrates is bio-converted to nitric oxide through a series of well-defined steps beginning with the friendly microflora on the tongue reducing nitrate to nitrite, which is subsequently reduced to nitric oxide in the gut, blood stream, and various organs, including the lung. The formation of inorganic nitrite and S-nitrosothiols is absorbed into the circulation where it acts as a transitory storage pool for subsequent nitric oxide production [11]. The conversion of inorganic nitrite to nitric oxide is expedited in conditions of acidosis or hypoxemia which occurs in regions of the pulmonary vasculature in lungs of COPD patients and those that exhibit acute respiratory distress syndrome as observed in coronavirus infected lungs. Reportedly, consumption of inorganic nitrate for 8 days in COPD population increased lung nitric oxide by 200% and reduced respiratory symptoms [12,13].

Restoring nitric oxide through dietary inorganic nitrate may be a consideration for prevention and early treatment which would operate at two-levels: reverse platelet-endothelial dysfunction and associated thrombosis as well as lower viral burden [1,5,11,14,15].

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