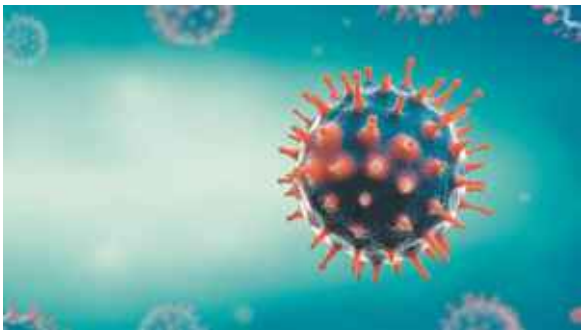
Fight COVID-19 by decreasing inflammation

Richard Béliveau

Translated from Le Journal de Montréal, March 30th, 2020

Several deaths from COVID-19 are due to an exaggerated inflammatory response that compromises the function of several organs.



The SARS-CoV-2 responsible for COVID-19 is a cytolytic virus, that is to say that its reproduction causes the death of infected cells, which induces a rapid response of the immune system and the recruitment of inflammatory cells to the site of cell damage.

It is this inflammation that is responsible for the fever and cough associated with the infection, a reflex intended to expel debris and foreign agents present in the respiratory tract.

INFLAMMATORY STORM

In some cases, on the other hand, this inflammatory response becomes so disproportionate that it causes more harm than the virus itself: this is commonly called the cytokine storm, a phenomenon caused by excessive production of inflammatory molecules (cytokines) by immune cells. This inflammatory storm has several unfortunate consequences:

- Excess cytokines will attract more immune cells to the infection site, which in turn will produce even more inflammatory molecules.

This vicious circle causes a strong amplification of the inflammation and causes various collateral damages, in particular an accumulation of fluid within the infected lung;

- The highly inflammatory environment at the site of infection also means that immunity response gets uncontrolled and can no longer correctly distinguish the enemy to fight (the virus) from our own cells.

Damage to the lungs can compromise their function and make them more susceptible to bacterial infections.

Worsening, the inflammatory shock present in the lungs can then spread to the rest of the body and cause life-threatening damages to several organs, especially the heart and kidneys.

This type of exaggerated inflammatory response was responsible for the vast majority of the 30-50 million deaths associated with the H1N1 epidemic of 1918 (Spanish flu) and the data collected so far seem to indicate that the excess inflammation is also responsible for the high mortality rate observed for the most severe forms of COVID-19 (1).

REDUCE INFLAMMATION

Another feature common to COVID-19 and Spanish flu is that, in both cases, the vast majority of children are completely spared from the severe complications of these infections.

It seems that at an early age, the immune system's regulatory cells produce an anti-inflammatory cytokine (interleukin-10) that prevents immunity dysregulation. As we age, the expression of this natural anti-inflammatory molecule appears to decrease, tipping the scales toward overproduction of inflammatory cytokines by immune cells.

To combat the severe forms of COVID-19, it is therefore essential to find a way to reduce this production of inflammatory molecules.

How to do it? Interesting results have been obtained in China following the treatment of COVID-19 pneumonia with an interleukin-6 neutralizing antibody, tocilizumab (Actemra®) which is used to treat rheumatoid arthritis, or with large doses of steroids which exert an immunosuppressive action.

Another potential candidate is colchicine, an anti-inflammatory drug used to treat gout. This molecule is known to inhibit the migration of immune cells to the foci of inflammation and also has a direct anti-inflammatory action, by blocking the production of inflammatory cytokines.

These properties seem particularly beneficial for the treatment of cardiovascular diseases, since colchicine is effective for the treatment of viral pericarditis (inflammation of the pericardium, two thin layers of a sac-like tissue that surround the heart) and reduces the risk of cardiovascular accidents in coronary patients at high risk of recurrence (2).

Cardiovascular damage being very frequent in patients with severe forms of COVID-19 (3), a clinical study led by Dr Jean-Claude Tardif of the Montreal Heart Institute has just been launched to determine if a reduction in inflammation by colchicine could prevent these heart attacks associated with COVID-19 and thus improve the prognosis of patients.

(1) Mehta P et coll. COVID-19 : consider cytokine storm syndromes and immunosuppression. Lancet, 2020 ; 395 : 1033-1034.

(2) Tardif JC et coll. Efficacy and safety of low-dose colchicine after myocardial infarction. N. Engl. J. Med. 2019 ; 381 : 2497-2505.

(3) Zheng YY et coll. COVID-19 and the cardiovascular system. Nature Rev. Cardiol., 2020. (published on-line, March 5th)

You find the content of this column useful? Make a donation at www.richardbeliveau.org to speed up our research

You find the content of this column useful? Make a donation at www.richardbeliveau.org to speed up our research

You find the content of this column useful? Make a donation at www.richardbeliveau.org to speed up our research