

## Women's immune benefit against COVID

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*A new study published in the prestigious Nature confirms that the immune response of women to the coronavirus responsible for COVID-19 is greater than that of men and makes them less likely to develop serious complications from the disease.*

To be optimal, the immune response must be able to effectively eliminate a pathogen (a virus, for example), while avoiding being too strong to cause collateral damage that interferes with the repair of infected organs.

During development, the establishment of this immune balance has proved to be particularly important in women: on the one hand, their immune system must respond very strongly to the presence of pathogens to protect children in gestation or who have just been born (and who are dependent on them) to ensure the survival of the species. On the other hand, this response should not prevent the regeneration of tissues necessary for the maintenance of health and reproduction. These adaptations explain why women develop immune responses superior to men when faced with a variety of viruses (influenza, respiratory syncytial virus, hepatitis C, HIV) or following vaccination (1).

### COVID-19 IS SEXIST

This female immune advantage is also seen against the coronavirus responsible for COVID-19, except that the difference in mortality between the two sexes this time around is much greater than for other types of virus. Data collected in China, Europe and the United States indeed indicate that although men and women are infected in equal proportions with the virus, men more frequently develop serious complications of the disease and have a risk of about two times higher to die from it (2).

A similar phenomenon is observed in Quebec, where men represent only 35% of the population most affected by the disease (80 years and over), but nevertheless account for 45% of deaths.

So, in addition to the various hormonal and genetic factors that are generally involved in a better immune response in women to the SARS-CoV-2 coronavirus (for example, several genes important for the functioning of the immune system are located on the X chromosome), there are clearly additional factors that contribute to reducing the mortality associated with this infection in women compared to men.

### T LYMPHOCYTES

A study recently published in the prestigious Nature suggests that this phenomenon is due to a better balance of the immune response of women compared to that of men (3). When a viral infection occurs, the first line of defense is the innate immunity which triggers a high intensity inflammatory response to sound the alarm and recruit cells specialized in the specific recognition of foreign bodies, namely B lymphocytes (antibodies producers) and T lymphocytes (destroyers of infected cells).



The initial inflammation is important in starting the fight against the enemy, but it is especially the immune response of B and T cells that is crucial to effectively neutralizing a virus.

Comparing men and women affected by COVID-19, researchers at Yale University (Connecticut) observed that in the majority of men, the inflammatory response is predominant, while women tend to have high levels of lymphocytes specialized in eliminating the virus. This difference is critical, as researchers observed that low T cell production in men correlated strongly with the development of serious complications of the disease, while those with similar T cell levels to women developed a stable form of COVID-19, without danger to their life. This confirms that this activation of T cells represents an extremely important part of the immune response against the SARS-CoV-2 coronavirus and that the greater susceptibility of humans to this virus is caused, at least in part, by a lower production of these immune cells. In the absence of sufficient T cells, the inflammatory response can get out of hand and lead to damage that interferes with the functioning of vital organs. In fact, several studies have clearly shown that this excessive inflammation is a significant risk factor for mortality from COVID-19.

The researchers also observed that in men, T cell production declines dramatically with age, while it remains robust in older women, even after 90 years. Since the vast majority of deaths from COVID-19 occur in people 75 years of age and older, it is likely that this T-cell deficiency is a major contributor to the higher death rate seen in older men.

- (1) Bunders MJ and M Altfeld. Implications of sex differences in immunity for SARS-CoV-2 pathogenesis and design of therapeutic interventions. Immunity (published online, August 17<sup>th</sup>, 2020)
- (2) Gebhard C et coll. Impact of sex and gender on COVID-19 outcomes in Europe. Biol. Sex Differ. 2020; 11(1): 29.
- (3) Takahashi T et coll. Sex differences in immune responses that underlie COVID-19 disease outcomes. Nature (published online, August 26<sup>th</sup>, 2020)