

## COVID-19 Pandemic: How Can Exercise Help the Old Immune System?

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### Keywords

COVID-19, Infection, Immune system.

### Background

COVID-19 is a disease caused by a coronavirus infection, the SARS-CoV-2. It has become a worldwide concern, especially to older adults and persons with chronic diseases [1]. Older adults have a less active immune response to stressors than young persons, which is a risk factor for infections. Furthermore, older adults with a noneffective immunological response present a slow recovery after an infection [2]. This work aims to clarify how exercise alters the immune system and prevents complications from COVID-19 in older persons. We approached the text with topics to provide a better comprehension of the subject.

### A brief view of the immune system and immunosenescence

The bipolar aspect of the immune system is characterized by innate and adaptive responses. The innate response includes the participation of macrophages, neutrophils, dendritic cells, natural killer cells (NK) and microbicidal molecules such as nitric oxide (NO), complement system and superoxide anion ( $O_2^-$ ). The acquired immune response mainly involves T lymphocytes (TCD4+ and TCD8+), B lymphocytes and their products, cytokines and antibodies, respectively. It can be divided into humoral (mediated by antibodies) and cellular immune responses (mediated by cells, such as T lymphocytes and macrophages). TCD4+ lymphocytes (Th0 helper) can differentiate into several subpopulations such as Th1 cells (T helper type 1). The differentiation of TCD4+

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lymphocytes into Th1 can be stimulated by interleukin 12 (IL-12), produced by antigen - presenting cells (macrophages and dendritic cells). Th1 cells produce predominantly gamma interferon (IFN- $\gamma$ ) and are related to the control of intracellular infections, such as viruses [1,2].

The aging process is marked by the decline of many physiological functions, including some immune functions and the accumulation of senescent cells [3]. The aging of the immune system, named immunosenescence, can play a key role in the development of COVID-19 infection. The decrease in B lymphocytes in older people, due to the decrease in hematopoiesis in the bone marrow, and in T lymphocytes (T CD4+ e T CD8+) due to the involution of the thymus, as well as a decrease in the export of Naive T cells to the lymph nodes, compromises the adaptive immune response [1]. This couples with the decline of innate immunity cells, such as neutrophil phagocytosis and chemotaxis. Antigen presentation by macrophages and the production of type I interferons by dendritic cells may contribute to a serious condition of the disease [1]. On the other hand, it has been shown that with aging there is an accumulation of senescent cells, which are sources of proinflammatory cytokines and chemokines induced by viral infections. This can be part of the mechanisms that explain the hyperinflammation observed in severe COVID-19 elderly patients. It is reasonable to propose that these overlapping phenomena (immunosenescence and senescent cells) may contribute to aggravate the condition of elderly patients with comorbidities [3]. Chronic low-grade inflammation associated either with the aging

process and inflammaging can lead innate immunity cells to a pro-inflammatory state which can increase the risk of the onset of the disease. Additionally, the accumulation of cellular senescence with proinflammatory states might contribute to the development of severe events during SARS-CoV-2 infection.

### Exercise as a modulator of the immune system

As the inflammaging and immunosenescence are associated with chronic diseases, older adults have concerns not only with the age-related risk to COVID-19 infection, but also with the multimorbidity-associated consequences. Therefore, attitudes toward healthy habits during the COVID-19 pandemic could help older adults to face the problem.

Physical exercise can improve health and may lead to changes in the immune system work [4]. The anti-inflammatory effect of regular exercise reduces the risk of chronic and cardiorespiratory diseases. Shimizu et al [5] showed an increase in T CD4+IFN- $\gamma$ + cells in the elderly undergoing moderate exercise, while Monteiro-Junior et al showed that IL-6 levels decreased in physically active elderly when compared to sedentary [6]. Physical exercise promotes the reduction of visceral fat and the balance of inflammatory and anti-inflammatory macrophages in adipose tissue, the cytokines produced by skeletal muscle contraction can protect the thymus, increase the number of NK cells and promote T naive cell proliferation, thus combating age-related comorbidities [4]. Moderate intensity exercise can reduce the risk of infection by shifting the immune response towards a protective response to intracellular pathogens, such as viruses [4] as COVID-19. Neutrophils also represent an important point to be considered, since they are recruited to the lung in the COVID-19 elderly patients and seem to be involved in lung injury producing large amount of NET (Neutrophil Extracellular Traps) [7]. That being confirmed, a therapeutic approach that interferes with the neutrophils recruitment would have great benefits. Files and colleagues (2015) showed that therapeutic exercise in mice and humans may dampen ongoing neutrophil numbers by reducing G-CSF, IL-17F and IL-23, related with neutrophilic bone marrow mobilization and recruitment [8].

The International Society of Exercise and Immunology (ISEI) [4] established as a general consensus that an exercise program of moderate volume and intensity is required to maintain proper

immune health. Thus, we recommend that the elderly, if possible, even in quarantine, maintain a physical exercise routine properly guided by a competent professional, even if the virtual devices are being used to make exercise feasible.

### Final Considerations

Older adults should remain at or start a supervised exercise program to diminish morbidity and improve immune response. This healthy habit may help older adults face this or a further pandemic.

An assessment of the physical activity level and the absolute or relative risk factors to perform the exercise should be performed to avoid adverse events.

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