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The Death of Death N°169

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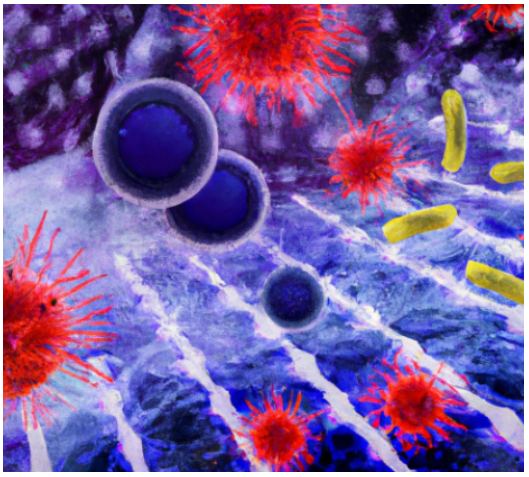
There's no shame in waging war on old age (...) Conquering diseases that appear among elderly people will eventually make life better for everyone

Martha Giill. The Guardian May 20, 2023.

This month's theme: Declining Immunity in Older Population

Introduction



Our bodies would be incredibly fragile without an immune system. The capacity to distinguish between "good and bad", friend or enemy" is extraordinary. Sometimes, this system is not able powerful or clever enough to stop "unamical aliens". Sometimes, the system attacks bodies that are not enemies. Sadly, the number of those inefficiencies rises with age and is one of the reasons we die of diseases related to old age.

The effects of the aging immune system (immunosenescence) confer immune dysregulation and have both cellular and humoral aspects. Studies show depletion in lymphocyte reserve with increasing age, in particular with fewer naive T cells (not yet exposed to antigens).

Serum levels of IgG and IgA are increased with age, which is conducive to protecting against viral and bacterial infections effectively in older people. Although the generation of naive T/B cells continues to decline, the adaptive immune system adjusts to age-related changes and protects the body from most pathogens. Only later in life does the immune function decline gradually, which increases morbidity and mortality in the elderly

Differences in the immune system of Elderly and Centenarians

Compared with the elderly, centenarians have more anti-inflammatory molecules, cytotoxic T cells, highly differentiated CD8+T cells and naive B cells, and well-preserved Natural Killer cells, which would be the hallmark of "successful" aging. In centenarian offspring, the number of B cells decreases significantly, but naive B cells and IgM increase, which might be one of the reasons for resisting infection and prolonging lives.

As one grows older, your immune system does not work as well. The following immune system changes may occur: The immune system responds slower. It increases your risk of getting sick. Vaccines don't work as well or for as long. An autoimmune disorder may develop. This is where the immune system mistakenly attacks and damages or destroys healthy body tissue.

Dysfunction of the immune system with age creates inflammation called inflammaging. Healing is slower as there are fewer immune cells in the body to bring about healing and the immune system's ability to detect and correct cell defects also declines. This results in an increased risk of cancer.

The decline in Thymus; Affects the B and T cell Production

The effects of aging on the immune system are widespread and affect the rate at which naive B and T cells are produced as well as the composition and quality of the mature lymphocyte pool. Declines in lymphopoiesis are influenced by age-related changes in the environment. The precise, age-related environmental factors that result in the depletion of lymphoid-biased HSCs have not been identified, although changes in levels of transforming growth factor β-1 might be involved

At birth, the immune system is equipped with an enormously diverse repertoire of antigen-reactive T and B cells, all of which are so infrequent that they cannot protect the host. Thus, as humans age and are exposed to infectious organisms and cancerous cells, antigen-specific lymphocytes need to expand massively in frequency and switch from a highly proliferative naive cell into a less proliferative effector and memory cell.

Aging is associated with several comorbidities that finally lead to organ failure and death. With the progressive deterioration of protective immunity, older individuals become susceptible to cancers and infections). Interestingly, aging is also associated with an increased incidence of inflammatory disease, most notably cardiovascular disease). Many of the degenerative diseases of the elderly, such as Alzheimer's disease, Parkinson's disease, and osteoarthritis, have a vital component of tissue-damaging inflammation. Similarly, the production of autoantibodies is much more likely to occur in older individuals. In essence, immune aging is associated with declining protective immunity combined with an increased incidence of inflammatory disease.

There are two main approaches to T cell-based immunotherapy: HLA-restricted and HLA-non-restricted immunotherapy. Significant progress has been made in T cell-based immunotherapy over the past decade, using naturally occurring or genetically engineered T cells to target cancer antigens in hematological malignancies and solid tumors. However, limited specificity, longevity, and toxicity have limited success rates. One of the few positive aspects of aging is that a long life exposes the body to many different pathogens and so enables this body to create more specific antibodies.

Older adults age 65 or older represent the growing majority of patients diagnosed with cancer. However, older adults are under-represented in clinical trials in general, as well as in the landmark studies that led to the approval of these immunotherapy agents. Because of increasing age, multimorbidity, and impaired functional status, many of these patients seen in community-based oncology practices are not eligible for such studies. Thus, the results of these studies are difficult to generalize to an older patient population with these competing risks.

TRIIM study was held at Stanford University by Gregory M. Fahy and his team from 2014 to 2015 with two cohorts. The main aim was to regenerate the thymus with a novel drug combination of hormones like Growth Hormone and DHEA (Dehydroepiandrosterone), as well as Metformin. The results showed protective immunological changes, improved risk indices for many age-related diseases, and a mean epigenetic age approximately 1.5 years less than baseline after 1 year of treatment (−2.5-year change compared to no treatment at the end of the study). Using an

epigenetic clock called GrimeAge, they also showed a 2-year decrease in epigenetic vs. chronological age that persisted six months after discontinuing treatment

Conclusion

We all saw that the elderly with COVID-19 showed much more rapid clinical progress, high incidence, and mortality compared to the younger population. This was accompanied by heavy systemic inflammation and tissue damage, which would be related to immunosenescence.

Boosting the immune system by regularly exercising, eating healthy, and suppressing the use the alcohol and smoking can decrease the rate of aging of the immune system. Taking safety measures to prevent injuries and falls is also important as a weak immune system can slow the healing of wounds. In the longer term, we need therapies able to rejuvenate the immune system, especially the thymus.

Good News of the Month: Dior wants to reverse old age.

Dior announced the creation of an International Reverse Aging Scientific Advisory Board (RASAB). The first goal is to rejuvenate the skin, but the longer-term goal is the rejuvenation of the whole body. Dior has an entire team dedicated to this goal.

For more information

- Heales, SENS, Longevity Alliance, Longecity, and Lifespan.io
- Heales Monthly Science News
- Source of the image DALL-E