

## **The Secret To Immortality? Not Quite, But The Importance Of Inflammation In Ageing And Its Causes.**

In film and literature, the quest for immortality seems to be a common motivation of ageing supervillains or adventurers seeking the Holy Grail. In its absence, there are there things within our control that can help us age healthily and improve health spans without all the ceremony of sacrificial offerings. Recent scientific reviews highlight the importance of inflammation (in the absence of infection) in the ageing process, 'inflammaging', and the effect lifestyle.



Ageing results from a combination of environmental, genetic and epigenetic factors but systemic chronic low-grade sterile inflammation underlies ageing and age-related diseases. Inflammation, where our body reacts to injury or infection is an important part of tissue repair and defence against pathogens. However, insufficient resolution of this inflammation to background levels or continuous activation in the absence of infection can have serious consequences affecting our physical and mental wellbeing. Long-term, the persistence of certain pro-inflammatory signals leads to tissue damage and impairment of the normal immune response with increased risk of developing non-communicable diseases such as metabolic syndrome, type 2 diabetes mellitus, cardiovascular disease, sarcopenia.

The processes that lead to systemic chronic inflammation are not completely understood but certain social, psychological, environmental and biological factors are involved. Inflammaging can be induced by defective endogenous processes within our bodies that leads to the accumulation of antigenic cell debris or through external factors such as lifestyle-induced obesity, microbiome dybiosis, diet, social and cultural changes, toxicants or infections. Although more evidence is required, a study of twins suggest that the main drivers are non-heritable factors. Specifically, it is postulated that our current lifestyles have moved us away from our evolutionary niche occupied by our hunter-gatherer ancestors. This change in physical activity, diet and behaviour has put us at greater risk of developing systemic chronic inflammation as we now eat more processed foods, exercise less and battle against natural circadian rhythms to hold down jobs, socialise and stay 'connected'. Chronic stress in our modern day lives can ultimately cause resistance to cortisol's anti-inflammatory activity and we are increasingly exposed to everyday environmental and industrial toxicants, present in numerous consumer products or through smoking, that are inflammatory agents. So, how is it possible to slow this process? How can we become more like centenarians that show a decreased trajectory of ageing, enjoying more healthy years and compressing morbidity until the last moment? A key factor is believed to be their higher resilience/intrinsic capacity to overcome inflammaging and the accumulation of molecular garbage that is part of the ageing process.

One 'miracle' or 'wonder drug' that many of us ignore is exercise, it also has the benefit of being free and doesn't require a prescription. 150 minutes of moderate exercise per week can lower the incidence of cardiovascular disease, type 2 diabetes, certain cancers and Alzheimer's disease. Skeletal muscles play a role in reducing inflammaging by releasing important anti-inflammatory molecules (cytokines, myokines etc.) into our bloodstream during contraction. Lack of physical activity is linked to the accumulation of visceral adipose tissue or 'fat' and obesity. Unlike fat in our refrigerators, visceral adipose tissue is not inert, it is an active endocrine, metabolic and immunologically organ that is critical for our health. However, carrying too much leads to expansion of immune cell populations, lack of oxygen in our tissues, cell death and release of factors that further stimulate the immune system, which can cause insulin resistance, increased release of lipids to other organs, fatty liver and pancreatic beta-cell dysfunction. Therefore, lack of exercise and obesity accelerate the ageing process, increasing the risk of non-communicable disease.

What we eat is also important: our gut microbiota and diet are also linked to inflammation and ageing, with anti-inflammatory species of bacteria, such as from the genus *Bifidobacterium*, being diminished in the elderly. Diets poor in fibre and probiotics, but rich in ultra-processed food, refined grains, trans fatty acids and salt stimulate inflammation. Furthermore, deficiencies in zinc, magnesium and omega-3 fatty acid, especially, reduce the ability to resolve inflammation.

We can't avoid ageing and there might be genetic factors that allow centenarians to live so long, but there is certainly growing evidence that non-genetic contributions (nutrition, exercise, hormones, circadian cycles and stress) play an important role and some of which are within our control.

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