Biology

The Ageing Antidote

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The global population is ageing faster than ever before since the beginning of history. In 10000 BC, mean life expectancy was around 27 years which has now increased to 73 years in 2020 and in several HICs mean life expectancy is above 80 years. In 2004 around 461 million people across the world were older than 65 years (retirement age) which is projected to exceed 2 billion by 2050[1]. Longer life presents more opportunities, both for individuals and society, however the process of ageing with its consequential frailty poses major challenges to senior citizens which hinder opportunities for economic and personal productivity.

Ageing is the process of deterioration with chronological age. At a biological level ageing is thought to occur due to a lifelong accumulation of molecular and cellular damage over time[1] which leads to physiological and cognitive decline. However at a cellular level, ageing is defined as a process of senescence in which a cell's ability to divide, repair and differentiate is lost. An accumulation of these senescent cells over time may result in chronic inflammation and diseases such as cancer, atherosclerotic disease and diabetes mellitus[2]. These structural and metabolic changes result in the development of the typical 'outward signs of ageing,' for instance grey hair is due to the depletion of stem cells in hair follicles[3].

In addition, these changes can also lead to the emergence of **geriatric syndromes** which are multifactorial with shared risk factors including older chronological age, cognitive impairment, functional impairment, and impaired mobility manifesting as pressure ulcers, incontinence, falls, functional decline, and delirium[4]. In geriatric syndromes, frailty assessment measures the state of increased vulnerability due to ageing-associated decline in function across multiple physiological systems. Increased frailty scores are associated with a heightened risk of injurious outcomes including falls and confusion.

Studies involving healthy elderly individuals and frail elderly individuals have investigated this vulnerability. They showed that after a minor stressor event such as the

commencement of a new medication or a minor medical procedure, the frail individual suffers from a larger functional deterioration and takes much longer to return to their baseline functional capability in comparison to the fit individual. They lose independence and are therefore increasingly reliant on others [1].

Ageing affects the whole body, including the brain, the endocrine system, the immune system and the skeletal system and so presents challenges for both the patient and their social environment, especially if left untreated and unmonitored. Fried, a geriatrician and epidemiologist, used data from a Cardiovascular Health Study and established a **frailty index** based on scoring of five indicators: weight loss, self-reported exhaustion, low energy levels, slow gait speed and weak grip strength [1,5]. The study concluded that those classed as frail had an increased outcome of falls, hospitalisation and mortality compared to those categorised as pre-frail and not frail. And so, clinicians use this frailty model as a way to diagnose and manage frail, elderly individuals.

However, scientists and clinicians are now focusing to extend the healthy life span of the population. **Table 1** shows that on average from birth, males suffer from 16.1 years and women 19.0 years of ill health which is about 20% of their entire lifetimes with huge personal and national economic costs. Health care professionals want to decrease this percentage by devising anti-ageing strategies which can reverse the effects of senescence and ageing in order to improve the quantity of good and productive quality of life of the population.

	At birth	At birth	At age 65	At age 65
	Males	Females	Males	Females
Life expectancy	79.5	83.1	18.7	21.1
Healthy life expectancy	63.4	64.1	10.5	11.2
Number of years in poor health	16.1	19.0	8.2	9.9
% of life in poor health	20.3	22.9	43.9	46.9

Table 1: Shows the life expectancy and healthy life expectancy of men and women from birth and age of 65 in England 2013-2015. Note: Reprinted from Public Health England (2017) 'Chapter 1: life expectancy and healthy life expectancy.

The concept of anti-ageing treatment is not new, at around 69BCE- 30BCE Cleopatra took daily baths in donkey milk to maintain a youthful glow. In the Elizabethan Era women placed thin slices of raw meat on their faces to reduce the appearance of wrinkles[6]. More recently, cosmetic treatments including hair dyes, creams, Botox and antioxidant diets have become

increasingly popular to mitigate the outward signs of ageing.

The new anti-age movement looks past these simple cosmetic treatments as advocates see old age as an economic burden on society[7] and so their work now looks to extend the healthy life span of an individual. To do this, clinicians will need to change their traditional treatment approach of 'one-size-fits-all' and apply unique therapies suitable for each individual patient based on the different pathways leading to the same disease. For example, a heart attack can be caused by high blood pressure, high cholesterol, obesity or diabetes. A **personalized** approach would focus on treating the predominant factor, rather than the current guidelines driven strategy healthcare professionals use today.

Scientists are currently researching whether ageing of cells and organisms can be reversed instead of merely delayed[8]. **Heterochronic parabiosis** studies where the bloodstreams of a young mouse and an old mouse are joined have shown that factors in the blood of young animals can revitalise ageing cells[8]. The blood of young mice has been shown to restore function to ageing organs such as the heart and brain, reactivate stem cell division, promote formation of new neurons in the brain and even repair damaged spinal cords.

The scientists were keen to isolate specific factors in the blood of young animals causing the rejuvenation of aged tissue. They have identified pro-ageing factors such as **eotaxin** and **β2-microglobulin** which increase with age to hinder neurological activity in young mice[8]. It is not known whether blocking these factors improves tissue function in mice, however the identification of these factors is a key step in the search to cure ageing.

Furthermore, **growth differentiation factor 11(GDF-11)**[9] in the plasma has been shown to increase strength of muscle cells and also reverse DNA damage in cells. **Oxytocin**, a hormone which controls aspects of the reproductive system and is involved in inducing labour has also been identified as a factor which reverses the degeneration of muscle stem cells[9]. They have been identified as Pro-rejuvenation factors in the blood. It is likely a combination of factors including GDF11 and oxytocin which may regenerate aged cells.

This research into young blood and its rejuvenating effects seems promising, as it seems to reverse the effects of ageing with very little safety concerns in humans[9]. But more research needs to be done in pharmacological, social science and lifestyle fields to create effective personalized anti-ageing therapies. However scientists and clinicians could be on the verge of finding an ageing antidote and elixir of life.

For references, footnotes and endnotes, click here.