

## THE BIOLOGY OF AGEING

### **The Achilles heel of diseases of ageing?**

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How sensible is it to seek to understand and treat diseases of ageing piecemeal? Calls are growing for a major strategic shift in the search for cures.



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The last decade has seen major advances in our understanding of biogerontology – the biology of ageing. These developments raise serious questions about future impacts of this field. How can such an understanding be best applied for the benefit of older people? And how can its misuse be prevented? The greatest potential benefit would be new and effective treatments for the diseases of ageing, such as cardiovascular disease, cancer and Alzheimer's disease. As for misuse, this is already a growing problem as optimism about treating ageing is exploited by a proliferation of practitioners of bogus 'anti-ageing medicine' (see Anti-ageing medicines: An age-old scam).

### **Lessons from the past**

Perhaps we may look to the past as a guide to the future. In the 19th century, up to a quarter of deaths in Europe were caused by tuberculosis, resulting from infection with the bacterium *Mycobacterium tuberculosis*. As recently as 1950, there were 50 000 new cases each year in England and Wales. Palliative treatment of tuberculosis in purpose-built sanatoria was a major industry. Tuberculosis was finally defeated by the pursuit of treatments for bacterial disease as a whole: antibiotics. Streptomycin was first used successfully against tuberculosis in 1944 to cure a 21-year-old woman known as 'Patricia'. By the mid-1950s, the omnipresent fear of tuberculosis had become a thing of the past.

Today, one of the most dreaded of diseases is Alzheimer's. There are currently over 400 000 people in the UK with this neurodegenerative disease, sometimes called a living bereavement. This number is predicted to rise to around one million by 2050 – a terrible prospect. Alzheimer's is currently a major focus of medical research worldwide; for example, over half of the current research budget of the US National Institute on Aging is spent on it.

What has this to do with tuberculosis? There are parallels. Diseases from tuberculosis and bubonic plague to syphilis are all caused by infection with bacterial pathogens, and are all treatable using antibiotics. Likewise, the primary cause of most cases of Alzheimer's is the same as that of many other diseases, ranging from other neurodegenerative diseases such as Parkinson's disease to cardiovascular disease

(leading to heart failure and stroke) and late-life cancer (particularly carcinomas). That primary cause is the ageing process itself.

What is the feasibility of the equivalent of antibiotics for diseases of ageing? This might sound like science fiction, but numerous recent studies on animal models suggest that this approach could work. By various experimental manipulations of gene function, hormones, diet and reproduction, scientists have achieved substantial increases in healthy lifespan in nematode worms, insects and rodents. In mice, for example, increases in lifespan of up to 80 per cent have been engineered. Strikingly, these mice are protected against a range of ageing-related problems: not only greying hair, cognitive decline and cataracts, but also the mortal diseases of mouse ageing such as cancer and kidney disease. Ageing is not inexorable, or set in stone: it is susceptible to manipulation.

Yet research into ageing-related diseases is currently carried out in a largely piecemeal fashion, with separate fields of study dedicated to individual diseases. Even within Alzheimer's research, there are different sub-disciplines focusing on understanding the mysterious amyloid plaques and neurofibrillary tangles that appear in the brains of people with Alzheimer's. Arguably, what we really need to understand is the nexus between the underlying cause – the ageing process – and the consequent multiplicity of pathologies of ageing. This route could, in principle, lead to broad-spectrum treatments against these diseases, promoting healthy ageing.

### **The future**

So do we need a major reform in research strategy, focusing on the biology of ageing as the key to treating ageing-related diseases? A call for such a change was recently made by a group of US scientists and policy makers, including Jay Olshansky, an epidemiologist from Chicago University, and Daniel Perry of the Alliance for Aging Research in Washington, DC. They point out that of the \$28 billion 2006 budget for the US National Institutes of Health, less than 0.1 per cent goes towards understanding the biology of ageing, and have called for Congress to invest \$3bn annually in a combined effort to understanding ageing and its attendant diseases (including \$1bn earmarked for biogerontology). They propose as a target for this initiative seven extra years of healthy life.

In the UK, the recent House of Lords Science and Technology Select Committee report on scientific aspects of ageing stressed the need for greater funding and better coordination of research on the underlying biology of ageing, which is a start. But a real danger is that when the need for translational research becomes critical, and the political will for change is mustered, the UK will lack sufficient means to make it happen quickly. These means include infrastructure (including suitably configured translational research institutes) and a strong community of researchers working on biogerontology and ageing-related diseases. Lack of these could greatly delay the arrival of the day when the first 'Patricia' of Alzheimer's, responding to a broad-spectrum treatment of biological ageing, recovers her senses.

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