## New model of health promotion and disease prevention for the 21st century

Our susceptibility to disease increases as we grow older. **Robert Butler and colleagues** argue that interventions to slow down ageing could therefore have much greater benefit than those targeted at individual disease

Many countries now have ageing populations and are facing an increased prevalence of age related diseases and escalating healthcare costs. However, if ageing is combined with extended years of healthy life, it could also produce unprecedented social, economic, and health dividends. In recent decades, scientists have shown that the underlying biological processes of ageing, which give rise to most diseases and other age related health problems, can be delayed. We argue that a concerted effort to slow ageing would provide a broad strategy for primary prevention that would greatly enhance and accelerate improvements in health at all ages.

## **Rise of human longevity**

Life expectancy at birth rose by a remarkable 30 years in developed countries during the 20th century, initially because of reductions in infant, child, and maternal mortality and then because of declining mortality in middle and old age. <sup>1</sup> <sup>2</sup> In 1900, about 40% of babies born in countries for which reliable data existed were expected to live beyond age 65.<sup>3</sup> Today

in these same countries more than 88% of all newborns will live past age 65 and at least 44% will live beyond age 85. This dramatic extension of life has provided social and economic benefits.

The traditional medical approach to ameliorating modern chronic diseases has been to tackle them individually, as if they were independent of one another. This approach flows naturally from our experience with acute diseases, where patients seek medical care for one condition at a time. In fact, applying this same strategy to infectious diseases in the 20th century helped to deliver the first longevity revolution.4 Although some infectious diseases have chronic effects on health (such as malaria and HIV infection), and others remain difficult to treat (including tuberculosis and most viral diseases), public health efforts to combat these diseases have made it possible for people in today's developed nations to live long enough to experience one or more of the degenerative and neoplastic diseases that are now the dominant causes of morbidity and death.

## Diminishing returns from disease specific model

Medical research worldwide has already accomplished much, and is certain to achieve more in decades to come, but its effectiveness will become limited unless there is an increased shift to understanding how ageing affects health and vitality. Most medical research teams are oriented towards the analysis, prevention, or cure of single diseases, despite the fact that nearly all of the diseases and disorders experienced by middle aged and older people still show a near exponential increase in the final third of the life span. Now that comorbidity has become the rule rather than the exception, even if a "cure" was found for any of the major fatal diseases, it would have only a marginal effect on life expectancy and the overall length of healthy life.5

The change in strategy we are calling for requires a systematic attack on ageing itself. Although such a strategy was clearly articulated more than a quarter of a century ago, <sup>6 7</sup> there has been little progress towards making the necessary changes. <sup>8</sup> However, recent





A playground designed specifically for pensioners has opened in a park in north Manchester. The "Older People's Play Area" in Dam Head Park, Blackley is the country's first for the over-60s. It features six pieces of equipment to keep senior citizens fit by strengthening hips, toning legs, and training the upper body. The local residents' association got the idea to set up the facility after being inspired by a similar playground in Germany

BMJ | 19 JULY 2008 | VOLUME 337 149

advances in understanding the complex biological mechanisms responsible for ageing suggest that it is feasible to translate this strategy into practice. Evidence in models ranging from invertebrates to mammals suggests that all living things, including humans, possess biochemical mechanisms that influence

how quickly we age and that they are adjustable. It is possible—for example, by dietary intervention or genetic alteration, to extend life span and post-

pone ageing related diseases such as cancer, cataracts, cognitive decline, and autoimmune diseases.  $^{10\cdot14}$ 

We are not calling for the modification of human genes to extend healthy life—that would not be practical, useful, or ethical. However, investigating how genetic mutations influence the basic rate of ageing is likely to provide important clues about how to develop drugs that do much the same thing. 15 16

Attempts to develop preventive measures against individual conditions related to ageing have been, for the most part, frustrating and unsuccessful. But in striking contrast, all of these conditions, and more, can be ameliorated or postponed simultaneously by well validated interventions that slow ageing. 17-19 The interventions that have worked in laboratory animals are not now appropriate for disease prevention in humans. However, we believe that exploration of the mechanisms by which ageing can be postponed in laboratory models will yield new models of preventive medicine and health maintenance for people throughout life, and the same research will also inform a deeper understanding of how established interventions, such as exercise and healthy nutrition, contribute to lifelong wellbeing.

## Recommendations

The potential of fundamental research into ageing to contribute practical benefits to improve health at all ages, but particularly at older ages, has been under-recognised by most of the scientific establishment, and, importantly, by many of those who decide on allocation of resources for health research.<sup>20</sup> <sup>21</sup> Now that most people in developed nations reach old age in reasonable health, and scientific progress has been made on interventions capable of postponing nearly all the diseases and disabilities that affect older people, the time has arrived for national policies to support and develop practical interventions that slow ageing.

The research strategy that we propose is

intended to supplement, rather than substitute for, research into specific diseases, which will continue to discover new and improved therapies and approaches to preventive medicine. We propose, however, a large increase in resources available for investigations into how diseases such as type 2 diabetes, congestive

heart failure, Alzheimer's disease, Parkinson's disease, osteoporosis, sarcopenia, and most cancers, either interact with ageing or share mechanisms in common

with it. We further propose greatly increased funding for basic research into the fundamental cellular and physiological changes that drive ageing itself.

The pursuit of extended healthy life through slowing ageing has the potential to yield dramatic simultaneous gains against many if not all of the diseases and disorders expressed in later life. The most efficient approach to combating disease and disability is to pursue the means to modify the key risk factor that underlies them all-ageing itself. Pursuing an aggressive research strategy to devise interventions against ageing suitable for humans requires that it is a goal worth pursuing (it is), and that we have good leads to follow (we do), but it does not require that we know, in advance, which of the current ideas about mechanisms affecting the rate of ageing are most likely to produce effective interventions. A fresh emphasis on ageing should vastly accelerate the health, economic, and social benefits of the extension of healthy life, which we refer to collectively as the longevity dividend.<sup>22</sup>

Competing interests: None declared.

Contributors and sources: This article arose from the authors' efforts to get physicians, scientists, and politicians to understand and appreciate the public health benefits that would accrue from efforts to slow ageing, and distinguish those benefits from the current medical approach to attacking one disease at a time. All authors participated in the drafting and editing of the article and approved the final version. RNB is guarantor.

**Provenance and peer review:** Not commissioned; externally peer reviewed.

- Olshansky SJ, Ault AB. The fourth stage of the epidemiologic transition: the age of delayed degenerative diseases. *Milbank O* 1986:64:355-91.
- 2 Oeppen J, Vaupel JW. Demography. Broken limits to life expectancy. *Science* 2002;296:1029-31.
- 3 Human Mortality Database. Calculations based on ten European nations (Denmark, England and Wales, Finland, France, Iceland, Italy, Netherlands, Norway, Sweden, and Switzerland). 2008. www.mortality.org.
- 4 Butler RN. The longevity revolution: the benefits and challenges of living a long life. New York: Public Affairs, 2008.
- 5 Olshansky SJ, Carnes BA, Cassel C. In search of Methuselah: estimating the upper limits to human longevity. Science 1990;250:634-40.
- 6 Holliday R. The ageing process is a key problem in biomedical research. *Lancet* 1984;ii:1386-7.
- 7 Strehler BL. Implications of aging research for society.

- Theor Concepts Dev Age Changes 1975;34:5-8.

  AgeAction. Changing expectations of life. 2007. http://ageaction.ncl.ac.uk.
- 9 Kirkwood T. A systematic look at an old problem. *Nature* 2008:451:644-7.
- 1.0 Selman C, Lingard S, Choudhury AI, Batterham RL, Claret M, http://cachens.corbis.com/ CorbisImage/170/14/45/37/14453708/50803-32. jpg Clements M, et al. Evidence for lifespan extension and delayed age-related biomarkers in insulin receptor substrate 1 null mice. Faseb / 2008:22:807-18.
- 11 Flurkey K, Papaconstantinou J, Miller RA, Harrison DE. Lifespan extension and delayed immune and collagen aging in mutant mice with defects in growth hormone production. *Proc Natl Acad Sci USA* 2001;98:6736-41.
- Miller RA, Buehner G, Chang Y, Harper JM, Sigler R, Smith-Wheelock M. Methionine-deficient diet extends mouse lifespan, slows immune and lens aging, alters glucose, T4, IGF-I and insulin levels, and increases hepatocyte MIF levels and stress resistance. Aging Cell 2005;4:119-25.
- 13 Bartke A, Brown-Borg H. Life extension in the dwarf mouse. Curr Top Dev Biol 2004;63:189-225.
- Bartke A, Coschigano K, Kopchick J, Chandrashekar V, Mattison J, Kinney B, et al. Genes that prolong life: relationships of growth hormone and growth to aging and life span. J Gerontol A Biol Sci Med Sci 2001;56:B340-9.
- Kuningas M, Mooijaart SP, van Heemst D, Zwaan BJ, Slagboom PE, Westendorp RG. Genes encoding longevity: from model organisms to humans. Aging Cell 2008;7:270-80.
- Martin GM, Bergman A, Barzilai N. Genetic determinants of human health span and life span: progress and new opportunities. PLoS Genet 2007;3:e125.
- 17 Wessells RJ, Fitzgerald E, Cypser JR, Tatar M, Bodmer R. Insulin regulation of heart function in aging fruit flies. Nat Genet 2004;36:1275-81.
- 18 Cohen E, Bieschke J, Perciavalle RM, Kelly JW, Dillin A. Opposing activities protect against age-onset proteotoxicity. *Science* 2006;313:1604-10.
- 19 Pinkston-Gosse J, Kenyon C. DAF-16/FOXO targets genes that regulate tumor growth in Caenorhabditis elegans. *Nat Genet* 2007;39:1403-9.
- 20 House of Lords Science and Technology Committee. Ageing: scientific aspects. London: Office of Technology and Science, 2005.
- 21 Miller R. Extending life: scientific prospects and political obstacles. *Milbank Q* 2002;80:155-74.
- Olshansky SJ, Perry, D, Miller RA, Butler RN. In pursuit of the longevity dividend. The Scientist 2006;20:28-36.

Robert N Butler president, International Longevity Center, New York LISA

**Richard A Miller** professor, University of Michigan, Ann Arbor, MI, USA

**Daniel Perry** executive director, Alliance for Aging Research, Washington, DC, USA

**Bruce A Carnes** professor, University of Oklahoma, Oklahoma City, OK, USA

**T Franklin Williams** professor emeritus, University of Rochester School of Medicine and Dentistry, Rochester, NY, USA

**Christine Cassel** president, American Board of Internal Medicine, Philadelphia, PA, USA

**Jacob Brody** professor, University of Illinois at Chicago, 1603 West Taylor Street, Chicago, IL 60612, USA

Marie A Bernard professor, University of Oklahoma, Oklahoma City, OK, USA

**Linda Partridge** director, Institute of Healthy Ageing, University College London, London

Thomas Kirkwood director, Institute for Ageing and Health, Newcastle University, Newcastle

**George M Martin** scientific director, American Federation for Aging Research, Seattle, WA, USA

S Jay Olshansky professor, University of Illinois at Chicago, 1603 West Taylor Street, Chicago, IL 60612, USA

sjayo@uic.edu

Accepted: 19 May 2008 Cite this as: *BMJ* 2008;337:a399

see ANALYSIS p 147