The challenges of age research

JOHN GRIMLEY EVANS, JOHN BOND

Division of Clinical Gerontology, Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford OX2 6HE, UK

Address correspondence to: J. Grimley Evans. Fax (+44) 1865 224 815

Introduction

Traditionally, age research has flowed in the three streams of the biological, the medical and the social sciences. The three traditions differ most obviously in the questions they ask, but there are also conceptual and epistemological divergences. The significance of 'theory' differs between the social and biomedical sciences as does the emphasis on qualitative and quantitative methods. Often what is required in studies of human ageing is a combination of methods to illuminate different aspects of a problem. The study of physical causes and mechanisms of disease falls to biological and medical sciences. The search for preventive or therapeutic interventions that depend on changes in behaviour, at individual or societal level, depend heavily on input from the social sciences. Observational studies generate hypotheses and sometimes refute them, but the proof of any theoretical pudding has to lie with experiment in the form of rigorously conducted interventive trials.

The medical tradition

Ageing in the sense of senescence is a loss of adaptability of an individual organism as time passes. This is manifest throughout adult life in a continuous and exponential rise with age in the risk of death. A similar rise with age is also seen in the prevalence of chronic disease, of disability and in the use of many forms of health services. It is important to recognize that age-associated patterns of failure of adaptation, including death and disability, can be distorted if older people are presented with greater challenges than face the young. In the past, such differential challenge was well documented in the poor housing of older citizens. Today there is more concern about the effects of inferior-quality health care provided for older people [1].

Age-associated loss of adaptability is the product of interactions of extrinsic factors in environment and lifestyle with intrinsic genetically determined factors [2]. Extrinsic influences on ageing can be detected in comparisons between the ageing patterns of people living different lifestyles or in different environments. Extrinsic factors detected in this way need to be confirmed as causal by interventive studies before forming a basis of policy. Interpretation of cross-sectional (prevalence) studies of ageing is complicated by cohort effects which arise when people born at particular times acquire characteristics in early life which affect their later ageing pattern and in which they differ from people born in generations before or after them. Cohort effects have been demonstrated in psychological functioning [3] and have probably contributed to the recent increase in incidence of proximal femoral fractures among older people in the UK [4].

Older people can suffer from most of the diseases that affect younger adults. One goal for medical research is to ensure that older people are included in studies of treatments from which they could benefit. For a variety of reasons [1], this has often not been the case [5]. There are some broader issues. Geriatricians are concerned with the impact of age-associated disease on individuals, but acknowledge an obligation to use society's resources in the most cost-effective manner. In their interactions with health and social services old people wish to retain autonomy, the ability to live the lives they wish. Society is more interested in old people retaining independence, in not requiring support and care from others. These objectives do not always coincide, but there is common ground in the prevention of disability in later life, since disability reduces autonomy and increases risk of dependency. Disability was the focus of the recommendation from an Expert Group from the World Health Organisation [6] that at a population level some form of Healthy Active Life Expectancy (HALE) [7] could provide a measure of the overall success of health and social services. Clinically, it is useful to think of disability as arising in the ecological gap between what an individual is capable of doing and what his or her environment demands. This gap can be closed by therapeutic interventions to improve a person's functioning or by prosthetic interventions to reduce the demands of the environment [8, 9]. Studies of HALE [10, 11] suggest that the later the onset of disability the shorter is its duration. This raises the possibility that a public health policy of 'postponement as prevention' could reduce the misery and costs of late-life disability.

At the societal level, the ageing of populations offers a major challenge to nations worldwide, and in the UK
this will peak in the decade of the 2030s. If we continue present patterns of care provision the main impact will fall upon the long-term care rather than the acute secondary or primary care sectors [12]. To meet this situation three things need to be done. The first, which is a political rather than a scientific issue, is to identify and put in place a suitable system of funding. The second is health services research (HSR) to maximize the efficiency of the services we provide. The third is to reduce the need for long-term care through research into the origins, prevention and management of disability in later life. This has to be an emphasis of age research in all the three traditions of the medical biological and social sciences.

The contribution of the biological sciences

Biological gerontology has pursued two main themes, the evolutionary significance of senescence and the mechanisms at organismic, cellular and molecular level that underlie it. It has always been envisaged that the link with medical gerontology would eventually be forged in relating these mechanisms to the diseases and disabilities of later life. There is a methodological problem in that organisms have been finely coordinated by evolutionary pressure. It would be inefficient for a species to possess a resource-consuming body system that is more durable than its other systems. The finding that the accuracy of DNA repair systems is correlated with species longevity does not therefore establish DNA damage as 'the cause' of ageing in any useful sense. The rationale for regarding some age-associated processes as primary causes of senescence lies in understanding which body systems linked to lifespan have been directly subject to evolutionary pressure.

In 1952 Medawar drew attention to the significance of population ageing and the biological enigma of senescence [13]. His interpretation of ageing was in terms of the accumulation of non-adaptive genetic effects at later ages due to the decline of selective pressure linked to the falling likelihood of reproduction at post-maturity ages. Williams added a further dimension with his postulate of pleiotropic genes that become selected for because they increase biological fitness early in life even though they diminish fitness later [14]. Such genes have proved elusive, but as the participants enrolled in the long-term cohort studies established after the Second World War enter later life genetic links between early advantage and late disadvantage may be detected.

Kirkwood's theory of the disposable soma seems to provide the definitive explanation of the evolution of senescence [15]. Longevity, and the rate of loss of adaptability, are determined by an organism's investment of energy and other resources in the control of molecular, cellular and organismic damage by processes of prevention, detection, repair and replacement. Resources are limited and efficiency in the control of damage has to be purchased at the price of a lower reproduction rate. Optimal reproductive fitness measured in terms of the contribution to the gene pool of subsequent generations will be determined by the match between environmental conditions and this balance between length of life and reproduction rate. The optimal strategy for species living in safe environments will be to reproduce more slowly (and efficiently) and to have greater longevity than species living in dangerous environments. Even in the safest of environments, however, the optimal investment in damage control will still be less than necessary to abolish senescence. The primary causes of intrinsic ageing lie with the genes and mechanisms determining reproduction rate and the efficiency of damage control.

There are other situations in which the pattern of ageing is determined by trade-offs between different priorities for the organism. In 1962 Neel [16] postulated the existence of 'thrifty' genes that enabled their possessors to survive periods of famine by ensuring that during times of plentiful food the body laid down excess energy in the form of fat. If the possessors of thrifty genes came to live in a situation of continuous excess energy intake they fall victim in middle age to syndromes of obesity, diabetes and cardiovascular disease. Thrifty genes would be particularly common in populations that have been winnowed by past periods of famine. Several probable examples of such populations have been identified in Polynesia and North America, and thrifty genes may underlie the high rate of cardiovascular disease among Indian immigrants to London [17].

A further example of trade-off may underlie Barker's demonstration of associations between various indices of possible fetal and childhood deprivation and subsequent liability to cardiovascular disease in middle age [18]. It would make evolutionary sense for an incipient organism to be able to sense and adapt its metabolism to the sort of environment it is likely to have to live in. Again, the problem is that adaptation to a life of deprivation generates problems if food turns out to be too abundant.

The well-known effect of the lengthening of life by caloric restriction in rodents may also be an example of a metabolic switch [19] underlying the balance between longevity and reproduction rate. In times of deprivation there will be survival advantage to a rodent's genes if it concentrates on staying alive by improving its damage control at the expense of postponing reproduction. At times of caloric excess the successful rodents will be those that reproduce fastest even if their longevity is reduced. There are examples emerging of genes in lower animals which appear to influence the balance between longevity and reproduction rate and which have homologues in man.
A number of topics for human ageing research emerge from these observations. What are the links between longevity genes and human disease? To what extent could one manipulate metabolic switches? To what extent can we tell early in life what an individual's switch settings are and translate these into a personalized prescription for environment and lifestyle to minimize disease and disability in later life? To what extent can later life interventions mitigate the effects of early influences?

### Behavioural and social sciences

Ageing has only recently become a fashionable area of research in the behavioural and social sciences [20]. Sociology has invested much effort in theories of stratification based on class, gender and ethnicity, but has done little to develop robust theories of ageing. In psychology the emphasis has been heavily on child development. Part of the reason is that behavioural and social sciences respond to the social and political forces of a particular time and place. The focus on social class has its roots in 19th-century conflicts between capitalist entrepreneurs and hired labour. Now that age has become a significant social factor sociologists are investigating different theories of ageing.

A major barrier to ageing research has been lack of resources. Politicians have not seen social science as economically productive, and knowledge for its own sake has been undervalued. Behavioural science has been similarly regarded even though the application of psychological concepts in education and management has had a major impact during the 20th century. The sociology and psychology of ageing have not yet been seen as relevant to national economic performance.

For the future, behavioural and social science research into age and ageing will need to react to the contemporary global political preoccupation with the 'ageing population' and its impact on the economic performance of world economies. The World Bank [21] perpetuates gloomy predictions of a world unable to afford the increase in numbers of older people. There is concern that modern economies cannot afford the rising cost of health care technologies in general. That there is to be an increase in the absolute number of older people, in particular in Third World countries, and an increase in expenditure on health care is not to be denied. Whether nations are prepared to undertake these changes is a social and political question. In democratic societies the obligation to provide equity and equality of opportunity for all citizens implies that the costs of changing demographic structures must be met. Demographic historians suggest that the period 1980–2030 marks an important transition in the structure of the world population [22]. The future population structure may require fundamental changes in the patterns of production and consumption of wealth and the way that individuals citizens plan their lives. One important aspect will be the choices individuals will make about health and health care. Old age has throughout history been conceived as a 'social problem' [23] and the stratification of contemporary societies by age as well as class, ethnicity and sex reinforces ageism. Age discrimination is likely to be one of the dominant social and political issues of the next century. It has major implications for the equitable distribution of health care resources, as is already manifest in contemporary debates on rationing in the National Health Service [24, 25], but impinges also on pensions and long-term care. Add to this the natural disadvantage of being dependent on others and the political rhetoric of the World Bank's perspective provides a potentially explosive social cocktail.

Within this global context there are three key areas for age research: the meaning of life for older individuals and the consequent relevance of certain health technologies for them; the related issue of quality of life, in particular for people with dementia and other debilitating conditions; and concerns about end-of-life decisions. There has been only limited research effort on the meaning of life to older people, in particular in relation to disability where the assumptions of younger people may not apply. The issue is debated in the philosophical literature but there is need of a broader perspective. Economists have concentrated more on the social than on the subjective value of lives, and there have been few studies of how older people value life.

Much of the effort on quality of life has focused on psycho-social health care outcomes but measurement remains problematic. Individualized measures of quality of life for older people derived from personal construct psychology [26] offer interesting possibilities both as a research tool and as a means of setting care objectives for patients. A particular research problem is how to assess the quality of life of people with dementia.

Health professionals have always had to make end-of-life decisions with and for individual patients, but have an instinctive distrust of general and legalized rules. Analogies with the abortion debate in which the political solution was to medicalize what is essentially a social issue have made many doctors fearful of being forced into the role of public executioners. Experience in The Netherlands has not been reassuring. Increased involvement of older patients in the setting of the objectives of their care is actively sought but the best ways of attaining it where direct communication is impaired can be uncertain. Advance directives offer a glib solution but do not resolve the worries of health care personnel faced with a patient whose personality has been changed by diseases such as dementia. Personhood is of interest of philosophers but must
also be recognized as a practical problem for clinical care and research.

**Conclusion**

Ageing is acknowledged to be a dominant political and social issue. This should provide stimulus and opportunity for medical, biological and social scientists to work together in the pursuit of optimal ageing for individuals and for communities. The research opportunities are clear, but the resources may not be forthcoming unless ageing is seen as an economic opportunity as well as a threat. Therapeutic and prosthetic interventions call for new pharmaceutical and technological approaches that will find worldwide markets. Optimal ageing is good for all of us.

**References**