

Ageing

*'The boast of heraldry, the pomp of power,
And all that beauty, all that wealth e'er gave,
Awaits alike th' inevitable hour:
The paths of glory lead but to the grave'.*

Thomas Gray: Elegy.
Written in a Country Churchyard

There is no greater certainty in life, than death. The biological process of ageing is steady and unidirectional. But, a century of advance in the biomedical sciences has dramatically lengthened the human life span from an average expectancy of two decades at the beginning of the second millennium to well past the biblical 'three score and ten', in the developed world, a thousand years later. It is estimated in the United States that the fastest growing section of the population is the group over 85 years of age. With the remarkable control that has been achieved over the infectious diseases of childhood, the elimination of smallpox and the substantial gains that have been made in many parts of the world in limiting the impact of diseases like tuberculosis and malaria (and not withstanding the drumbeating on AIDS), people seem destined to live, on an average, to a riper age. In India, the visible explosion in the population has hidden an interesting fact; the annual growth rate has hovered between 2.0 and 2.2 per cent, a figure that assured doubling in the first 35 years after independence. But, this growth has masked the steady decline in both the birth and death rates, leaving their difference more or less unaltered over the period 1960–1990 (Mari Bhat, P. N., *Curr. Sci.*, 1992, **63**, 440). The consequence is, inevitably, that the number of elderly are on the rise, bringing sharply into focus a new set of problems that need to be addressed.

Oliver Goldsmith said it well:

*'O blest retirement, friend to life's decline,
Retreats from care, that never must be mine
How happy he who crowns in shades like these
A youth of labour with an age of ease;
Who quits a world where strong temptations try,
And, since 'tis hard to combat, learns to fly!*

:
*Bends to the grave with unperceived decay,
While resignation gently slopes the way;
And, all his prospects brightening to the last,
His heaven commences ere the world be past!*

'The Deserted Village'

There is no greater desire in the elderly, than to fade away without a major impairment of their physical and mental faculties. But, the harsh realities of biology dictate that ageing populations face a threat from a host of diseases of old age, that can significantly restrict both physical and mental functions. The threat of strokes is enhanced and advancing age is a major risk factor for a spectrum of neurological disorders. In November 1906, the German physician Alois Alzheimer, presented a brief and unheralded report at a conference of psychiatrists entitled 'On a Peculiar Disease of the Cerebral Cortex'. Having worked for 14 years after his MD as an intern and chief resident at a 'lunatic asylum' in Frankfurt, Alzheimer, who was labelled as the 'psychiatrist with a microscope', was uniquely positioned to make his seminal observations on the pathology of the brains of patients suffering from senile dementia (Hoehn, H., *Curr. Sci.*, 1992, **63**, 407). Alzheimer's disease, now recognized as a 'multifactorial syndrome', is accompanied by the formation of neuritic plaques and neurofibrillary tangles, which consist of a hopelessly intertwined mass of insoluble protein. Together with Parkinson's disease and ischaemic brain injury in strokes, Alzheimer's syndrome is one of the greatest threats to the well being of the elderly (For an excellent overview of neurological disorders see, *Nature (Suppl.)*, 24 June 1999, **399**). The diseases of old age indeed constitute a major challenge for contemporary biomedical research.

It is in this context that two recent essays in *Nature* merit attention. Leonard Hayflick (*Nature*, 2000, **403**, 365), noted for his finding that cells age and die in culture, argues that the success of the biomedical enterprise over the last century has 'unmasked a process for which evolution never prepared us. One might conclude that ageing is an artefact of civilization.' Hayflick's thesis is that 'the expression of age changes is not essential for the survival of any species'; an argument that he buttresses by pointing out that 'humans have survived, and sometimes flourished, with a life

expectancy at birth of 20 or 30 for more than 99.9 per cent of our time on the planet'. In analysing ageing, Hayflick has a clear agenda; to highlight the failure of science policy 'to distinguish research on age-associated diseases from research on the fundamental biology of ageing'. He argues that for all the sums of money spent on Alzheimer's disease research in the United States, 'its elimination will have only a trivial impact on life expectancy'. He ignores, in the heat of the argument, that a resolution of Alzheimer's disease will provide an enormously enhanced quality of life to an ever-increasing segment of the population. But it is hard to quarrel with Hayflick's thesis, when he says: 'greater attention must be given to the question that is rarely posed, yet which is capable not only of advancing our fundamental knowledge of ageing but also our understanding of age-associated diseases; why are old cells more vulnerable to disease than young cells?'

In terming the past hundred years as 'a century of cognitive decline', Bruce Yankner (*Nature*, 2000, **404**, 125) argues that 'the twentieth century has witnessed a dramatic prolongation of life span, but little progress in preventing age-associated cognitive decline'. The key issue is the extent to which normal ageing processes are associated with cognitive decline. The abnormal pathology associated with Alzheimer's disease argues 'against the idea

that senility is normal' and gives 'rise to the hope that Alzheimer's disease could be prevented or reversed'. Yankner points out that 'the continuum between normal ageing, mild cognitive impairment and Alzheimer's disease provides support for an old idea, namely that Alzheimer's disease may be an accelerated form of brain ageing'. Here, Yankner raises a sobering thought: 'if we live long enough, will we all become demented'.

The last decade of the twentieth century was, with customary fanfare, labelled as the 'decade of the brain'. It does, however, appear that the brain will take considerably longer to yield its secrets. Many questions of age-related changes in brain functions may take decades to answer and immediate therapies to arrest cognitive decline do not seem to be around the corner. But, the management of the cognitively impaired will benefit greatly from the widespread recognition that loss of seemingly routine abilities are an inexorable and unavoidable consequence of biological processes that we do not yet fully understand. We might all be reminded of the famous saying 'Ask not for whom the bell tolls; it tolls for thee'.

P. Balam

