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Reith Lectures 2001: The End of Age

## **Lecture 1: Brave Old World**

Never in human history has a population so wilfully and deliberately defied nature as has the present generation. How have we defied it? We have survived. Our unprecedented survival has produced a revolution in longevity which is shaking the foundations of societies around the world and profoundly altering our attitudes to life and death.

At the same time, science has made hitherto undreamed-of advances in human biology. The explosive force of these two revolutions coming together lies at the heart of my series of Reith Lectures, as it has been at the heart of my work. Science has new things to tell us about the process of ageing. We know now that ageing is neither inevitable nor necessary.

It is particularly fitting that the first lecture in a series that will explore the revolution in human longevity should be given at the Royal Institution. This establishment, founded in 1799, has played a pioneering role in science and technology. It was here, exactly two hundred years ago, that the young Humphry Davy was appointed to arrange scientific demonstrations for the public.

Davy's demonstrations were spectacular events, often explosive and dangerous. There is delicious irony in the fact that Davy's best-known legacy is the miner's safety lamp, expressly designed to prevent explosions from occurring. My home city of Newcastle upon Tyne, famously associated in earlier times with coal mining, has had good reason to bless the life-preserving qualities of the Davy lamp.

Although the theatre will not reverberate tonight to the fizz and bang of Davy's demonstrations, the revolution in longevity is, in its own way, more spectacular. Davy's safety lamp was but one contribution in a process that has led, in the eight or so generations between his time and ours, to more than a doubling in the average length of life.

Life expectancy at the start of the 19th century was scarcely forty years. Some of course lived to a good old age but they were a distinct minority. Davy himself died at 51. Life expectancy in the United Kingdom today is around 75 years for a man and nearly 80 years for a woman, and it is still getting longer.

Over the course of the last half-century, life expectancy has continued to increase steadily by two years each decade. It is almost as if for every decade we have lived, we have gained an extra 20% free.

The real calculations are more complicated than this because the figures I have given are for life expectancy at birth. Working out how our individual expectation of life has changed must take account not only of changes in death rates but also how long we have lived already. Nevertheless, it is striking that it is the death rates of the older age groups that are presently showing the greatest declines. It is these older age

groups - those over 85 years - who now constitute the fastest growing segment of the population.

A phrase often used to describe what is happening is "demographic change". This dry expression masks the greatest triumph that our species has achieved. I emphasise the word triumph because there are far too many people who like to dwell on the dangers inherent in the longevity revolution without celebrating the progress that has opened these new horizons.

The demographic change has two causes, both of which are reasons for joy. Firstly, people are living longer on the average than at any time in human history. Secondly, birth rates are tumbling across much of the planet. Because fewer children are dying, parents no longer need to raise large families as insurance against child mortality. These two factors - longer lives and smaller families - are shifting the balance of the generations. They are clear signals of our success in taming the age-old scourge of premature, preventable death.

We soon learn in life, however, that success is not an end in itself but brings new challenges. These new challenges are often more daunting than those that came before, and so it is with longevity.

With our longer life spans we are entering uncharted territory in which the challenges for individuals and societies are formidable. They are formidable not least because we cherish extraordinarily negative stereotypes of the ageing process. The stereotypes have, if anything, grown more negative as life expectancy has increased. Survival to old age is less of an achievement and as life has become more secure, the inevitability of eventual ageing seems more of an affront.

Like it or not, our entire world is changing, and changing fast. The demographic transition that occurred over the last century in the developed countries is already in train in most of the developing world. The technologies to enhance survival - vaccines, antibiotics, water purification systems, electricity, and so on - are at hand and require only effective implementation.

Taking the human race as a whole, just 1% of the world's population was aged 65 and above a century ago. This figure has already risen seven-fold and will rise to around 20% by the middle of the 21st century. Already n the UK today, 85% of newborns can expect to celebrate their 65th birthday. And those now reaching 65 can expect to survive 16 more years if they are a man, or 19 years if they are a woman.

It is no surprise that the number of older people is on the increase. That, after all, is where the drive to avoid death has led us. What is surprising, however, is that the nature of old age itself seems to be changing. If you have the impression, as many do, that old people, like policemen, are getting younger all the time, it is not just that you yourself are getting older. In many respects today's 70 year olds are like the 60 year olds of a generation or two ago.

The starkest feature of ageing - its hallmark, in fact - is that the risk of falling ill and dying increases inexorably as we get older. This unwelcome principle was first cast into mathematical form in 1825 by Benjamin Gompertz, a pioneer of actuarial

science. What Gompertz found was that, like compound interest, adult mortality rates increase exponentially with age. In effect, your risk of dying doubles with every eight additional years that you live. If Gompertz were alive today, he would find that this fundamental property has not altered but that the overall level of death rates has fallen. It is as if the capital on which his compound interest was acting had grown less. The most significant trends affecting longevity today are the unexpected and continuing declines in the death rates of older people.

If you had asked most experts just a couple of decades ago what they would have predicted for the patterns of mortality at the end of the century, the answer you would have received was that the continuing declines in preventable, early mortality would have revealed ever more clearly the rigid, immutable pattern of mortality associated with intrinsic ageing.

The medical term to describe the change from a pattern of mortality dominated by acute infectious disease to a pattern in which the chronic degenerative diseases play the major role is the 'epidemiological transition'. Linked to this is the idea of 'mortality substitution'.

Put bluntly, mortality substitution means that you have to die of something. If you are spared early death from infections like tuberculosis and typhoid, you fall prey instead to conditions like heart disease, cancer or stroke. Not only does ageing make each of these diseases more likely individually, but you are also more likely to experience a multiplicity of conditions. Many diseases, disabilities or just plain causes of frailty, like thinning bones, weakening muscles, and diminishment of the senses, are intimately linked to the ageing process.

When we speak loosely of a person dying of 'old age' we have in mind the notion of multiple system failure. The actual cause of death may be quite specific but if it had not been this particular cause today, it would have been something else tomorrow. It is the idea that this intrinsic deterioration is something fixed or immutable - to be revealed more clearly as we peel away one preventable cause of death after another - that has come to be seen in a new and questioning light. The new realisation is that science no longer dictates that our bodies have to wear themselves out and die according to some preordained plan.

Death rates are going down, life expectancy is going up and the maximum life span is rising too. We saw in 1997 that the world record for reliably documented life span was extended in spectacular fashion by Jeanne Calment, who died at the remarkable age of 122 years and 5 months. It may be some time before Jeanne Calment's record is broken, but broken it will be. Where will it all end? More to the point, if we heed the doom-mongers who hark on about the 'burden' of the elderly, will it all end in tears?

To be able to answer this question in anything other than hand-waving fashion, we need some harder facts. In particular, we need to understand a great deal more about the ageing process. It is fortunate, but by no means co-incidental, that the revolution in longevity is accompanied by an equally unprecedented revolution in the life sciences.

As a result of the astonishing advances made over the last decades - advances in understanding the basic chemistry of life, advances in genetics and genome research, and advances in studying and manipulating individual cells both inside the body and out of it - it is now reasonably certain that we will soon understand the ageing process in much greater detail than we do at present. Already, we can use scientific insights to overturn many preconceptions - or, should I say, misconceptions - about why and how we age.

The commonest misconceptions about the ageing process are that we age because in some fundamental sense we cannot survive for longer, or that we are programmed to die because this is necessary to make way for the next generation. Neither of these ideas is correct.

The glum fatalism that says that we cannot hold ourselves together for longer is contradicted by the existence of organisms that manage the amazing feat of living indefinitely without intrinsic deterioration. Sea anemones and freshwater hydra are examples of species that show no signs of ageing. There are also several species of fish and giant tortoise that live considerably longer than us, and which age much more slowly. We shall see in a later lecture that we can learn quite a lot about the ageing process by comparing species that live their lives at different rates.

The second misconception - that we are programmed to die - is remarkably tenacious. We seem to be psychologically tuned to seek a purpose in the biology of ageing, but this tuning leads us astray. Sigmund Freud illustrated this fallacy perfectly in his key treatise 'Beyond the Pleasure Principle' in which he balanced the life-instinct, eros, against the death instinct, thanatos, of the organism, drawing upon contemporary thinking about the biology of ageing to offer a quasi-scientific explanation for the death wish.

I am frequently reminded of this as I drive home in a part of the country that is densely populated with rabbits. Rabbits, as we know, have a highly developed eros. But time and again they dart into the road at the last possible moment of my approach, and I feel sure they have made the mistake of reading too far into their Freud.

We now understand that our bodies are not programmed with some unavoidable sellby date; we are not programmed to die. As I said at the start of this lecture, ageing is neither inevitable nor necessary. Indeed, the more we learn about how we age, the more we come to realise that we are programmed for survival. It is by understanding why this programming falls short of allowing us to survive indefinitely that we may learn deep lessons that we can turn to our advantage.

The lie to the suggestion that we must limit our survival in order to make way for the next generation is that it is only in the last few human generations that survival into old age has been anything other than a rarity. We are not alone in this. Rabbits, mice and small birds age as we do, but in these species ageing is even less likely to be seen, except in captivity. Life in the natural world is brutish and short. The vast majority of wild animals die young from accidents (including running under cars), infections, predation, starvation and cold. If our evolutionary ancestors had a problem with survival it was that they had too little of it, and not too much.

Once we relinquish the idea of a programmed death, we can begin to make better sense of our ageing. We do this by taking a fresh look at the fact that our ancestors lived short lives and by asking ourselves, in those circumstances, how much effort should their bodies have directed at maintenance and repair.

The human body is astonishingly well programmed to cope with a huge variety of challenges to its integrity on a daily basis. Many of these challenges are at the submicroscopic level and the body's defences involves an extensive repertoire of cellular and molecular protection systems.

The price we pay for these protection systems is that they require energy, and this is often in limited supply. When survival is uncertain because of the many hazards of the environment it is better not to squander effort on a greater level of bodily maintenance than is needed, but to attend instead to the all-important biological imperative of begetting and raising offspring. If, to a rough approximation, the average life span of our ancestors was around 35 years and only a tiny percentage survived to 70 years, then a body which held itself together for three score years and ten would do just fine.

When we understand that we age because our ancestral genes placed limited priority on long-term maintenance and repair, we get some rather clear insights into the processes that lead to the frailty and diseases of old age.

The first and most encouraging message is that as soon as we recognise that we are programmed not to die, but to survive, we can see that the ageing process is malleable. Ageing comes about through the gradual build-up of unrepaired faults in the cells and tissues of our bodies as we live our lives, not as a result of some active mechanism for death and destruction. If we can discover the nature of these faults, we can hope to slow their accumulation. There is good reason to believe that the improved health and survival of older people today at least partly reflects the fact that the kinder conditions of present-day living have alleviated some of the burden of faults. If we can understand the protection systems with which we are already endowed, and enhance their performance, we may be able to do much better.

Although the malleability of the ageing process offers exciting grounds for hope, as will be described in a later lecture, we should guard against unrealistic expectations of a 'quick fix'. Ageing is a complicated process with multiple causes affecting every organ of the body. Its complexity will make it refractory to change and we need to temper our optimism with a considerable degree of determination.

We have seen already how frustratingly slow and difficult it has been to take the sting from heart disease, cancer and stroke. To get excited about potential 'fountains of youth' and life spans of 200 years and more is not only to indulge in fanciful and unrealistic speculation, it also shows what a long way we have still to go to get the challenges of the longevity revolution into proper perspective.

The paradox about the longevity revolution, and its greatest inherent danger, is that we find ourselves in the present situation without having thought very much, until recently, about the kind of world we are creating. It is easy to win support for saving lives. Davy's safety lamp, Jenner's triumph of inoculation against smallpox, Fleming's

discovery of penicillin - these are unquestionable gains. It is easy to win support for the fight against a killing or disabling disease, as can be seen from the generous public support for so many disease-focussed medical research charities.

With rare exceptions saving lives is ethically - if not always technically - easy. You can do it again and again. Yesteryear's Newcastle miner, spared by Davy's lamp from a suffocating death in a collapsed mine, is saved again by tetanus vaccination, and again by antibiotics. He is spared to become an old man. But to many he is then seen as a burden - chronic lung trouble from long exposure to coal dust, drawing a pension, dependent. Small wonder if in old age he has a problem with self-esteem.

It is surely time that we took a new look at our changing world and the forces that are shaping it. The declines in mortality rates of older people are forcing the forecasts of future life expectancy to be revised upwards. Should we be pleased or depressed? Surely we should be pleased, but it is astonishing how poorly this news is sometimes received. Just last summer, an article presenting new forecasts of even longer life spans in the most affluent countries was published in one of the world's leading science journals. A brief editorial trailer for this report announced glumly that the situation was "even worse than expected". I wonder just how old was the member of the editorial team who penned that piece?

One cannot pretend for a moment that there is not a lot that is disagreeable about getting older. This is all the more reason why we should direct unprecedented attention to ensuring that all reasonable effort be directed at removing the obstacles to enjoyment of the later years of life. This is not mere altruism nor a pat on the back for our older fellow citizens, put, like the old donkey, out to grass. First and foremost it is a recognition of that most fundamental of human rights, respect for all individuals as equals.

It is absolutely staggering not only how much prejudice exists against age but also how unaware of it we remain. On a regular basis we read, hear or ourselves make flippant, jokey or negative remarks about the state of being old. 'Grumpy old', 'silly old', 'boring old', 'dirty old' - the linkages are so familiar that we fail to notice what we are doing.

If we were suddenly to acquire the same sensitivity to ageism that we have to racism and sexism, we would be in for a shock. But do we not realise that we will all grow old? Can we not celebrate the fact that this privilege has been won for us by our collective ingenuity? Do we not realise that the best prospect for our own well-being in old age is to build a world in which equality, independence and active participation of all generations are positively encouraged?

Science has prepared the ground for the longevity revolution and science will take this revolution forward in ways that we cannot yet forecast with certainty. Yet the challenge of ageing and extended longevity is much bigger than a challenge that can be met with one discipline alone. We need to build the interdisciplinary bridges between all who must confront the global challenge of ageing. We need to ask the hard questions.

Should we rethink the age of retirement? After all, retirement at 65 was first introduced when lives were a good deal shorter. How should we weigh the costs of research and treatment for Alzheimer's disease against, say, the costs of research and treatment for infertility? How much should we be prepared to spend on redesigning our housing and transport systems so that older people are not needlessly cut off? Why not put an internet connection into every home so that old and young alike can benefit from the IT revolution, with all its promise to ease communications of every sort, including new kinds of health care?

New scientific understanding means that we can never think of ageing in the same way again. Our longer lives are carrying us into new territory for which we need to plan and prepare. We cannot afford to be complacent. If we ignore the implications of the longevity revolution .... If we fail to plan for the radically different world that will soon surround us, then crisis will be upon us and our bright dreams of a brave old world will surely fade and die.