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Reith Lectures 2001: The End of Age

Lecture 5: New Directions

Every revolution has a turning point - a time when the original impetus for change has run its course. History shows that this is often a vulnerable time. Opinion on where to go next is sharply divided. Indecision prevails at precisely the moment when decisive action is most essential. The longevity revolution is no exception. We know where we've come from and why, but we don't have a clear plan of where to go now. Ours has been a revolution from - from the terrible waste of life caused by premature death - not a revolution to. We are at our turning point now. The decisions we take in the next few years will have far-reaching consequences for the state of future society.

Two hundred years ago most people died before their time. Well, we fixed that. Rarely has a revolution succeeded so well. What we now experience are the deaths associated with old age, with degenerative conditions. Much of modern medicine is concerned with fighting these, pushing back the frontiers of survival further and further. But suddenly we are not so sure about where we are going and why. Many are the news stories trumpeting that we will soon all live to 130, 200 or 400 years, but what about New Yorker cartoon that showed one old man saying to another "I hope I die before science makes me live to 150."

The ambivalence of our attitudes reflects the confusion of rapid change. Not long ago the attainment of old age was hailed as a success. Ageing today is widely seen as a failure, unless you are as extremely old as Jeanne Calment. I remember being deeply struck by a remark from a former medical colleague whose research was on heart disease: "There is nothing interesting about the ageing of the cardiovascular system," he exclaimed, "it just rots!" What, I wondered, did he feel was the point of his work. What for that matter is the point of mine?

As a gerontologist, my work addresses how and why we age. But why do it? For me, the answer is clear. The longevity revolution has given us a substantial increase in life expectancy. But the extra years are not as good as we might wish. Conditions like Alzheimer's disease, stroke, osteoporosis and arthritis have a serious effect on quality of life, either by robbing us of our identity or stealing our independence. Our primary goal should be to make headway against these conditions. But how to do it? Is it realistic to think of achieving this goal without altering the ageing process itself?

The idea that science should aim to postpone disabling conditions like Alzheimer's disease, without necessarily extending life itself, has become something of a mantra. It is a mantra that goes by the name "compression of morbidity". The aim is to squeeze the bad things that happen to us at the end of life into as short a period as possible. Another way of putting this is that we want to extend the health span, while leaving the life span as it is. On the whole, people seems to find this more reassuring than that scientists want to make us all live longer.

The trouble is, however, that compression of morbidity makes assumptions about the extent to which we can decouple ageing and disease.

There has long been controversy in medical research circles about whether a condition like Alzheimer's disease is strictly a disease, with the implication that we can cure it on its own, or whether it is more deeply embedded as part of the "normal" ageing process. We do not know the answer yet. But even those who take the view that age-related conditions are distinct disease entities must acknowledge that age is the major factor in how they come about.

The aged organ is more vulnerable to pathology. The aged cell is more liable to dysfunction. But why? The underlying cause of both ageing and disease is the build-up of faults. The extent to which we can isolate the faults that cause Alzheimer's disease from the more general faults that cause other aspects of brain ageing will determine the extent to which we can tackle one without also tackling the other.

We have seen great excitement caused by recent reports of a possible therapy for Alzheimer's disease based on a vaccine against the abnormal beta-amyloid peptide associated with this conditon. But the approach has so far only been tested only in mice that were genetically engineered to produce brain pathology through the specific deposition of this particular peptide in their brains. They were engineered to arrive at this pathology by a route which does not form a part of the normal ageing of the mouse brain. It remains an open question whether the vaccine can significantly delay disease progression in the normal human brain, where factors other than beta-amyloid are likely to be at work.

It may turn out that in order to postpone Alzheimer's disease in humans, we need to delay the build-up of a variety of types of damage. Growing evidence shows that age-related deterioration of the blood vessels serving the brain is a factor in Alzheimer's disease. There is evidence, too, that oxidative damage caused by free radicals is an underlying cause. So if we wish to postpone dementia, we will have to slow a process as fundamental to ageing as oxidative damage.

What is true for Alzheimer's disease is true for many of the other degenerative conditions associated with ageing. Only by understanding the deeper biochemistry that causes ageing can we understand the molecular and cellular perturbations that lead to age-related disease. It is time to face this reality and its implications.

The idea that normal ageing and age-related diseases share common causes is strongly supported by a great a deal of research on the intriguing phenomenon of life extension through calorie-restriction. It has been known since the 1930's that if you underfeed a mouse or a rat, but do not subject it to malnourishment, you will extend its life span by as much as 40 or 50 per cent. What is even more striking is that you will also retard the development of an entire spectrum of age-related diseases. We do not know yet if the same approach might work one day in humans, but that is not my point here. My point is that an intervention like calorie restriction in rodents does not affect ageing and disease separately, it affects them in the same way.

Some of the latest gene technologies are being used to discover how calorie restriction affects the expression of an animal's genes. It appears that several genes that cope

with molecular damage are tuned to higher levels, something that we have predicted theoretically. Food restriction thus causes damage to build up more slowly within the animals' organs and slows the animals' rate of ageing. Apart from being lean and hungry, the underfed animals are all in prime condition - healthy, active and alert - even at ages when normally-fed mice would all be dead.

Faced with such evidence, it seems hard to deny that there is a direct connection between ageing and disease. We therefore have to accept that the mantra could be wrong. If we want to postpone the diseases of old age, we may not compress morbidity after all, unless we learn to control the rate of ageing organ by organ and pick and choose which conditions we would like to postpone, while leaving ageing in the rest of the organs to run its normal course. This would be a fundamentally different approach from that which has driven our revolution to date, the drive to postpone death on all fronts. Now that we are on the threshold of deep discoveries about the human ageing process, it is important to open a more informed debate about goals and priorities, as is happening in a Symposium here at the International Centre for Life.

One of the harder questions to address is how we might wish our own lives to come to a close. Answering this is difficult for several reasons. Firstly, our own death is not something that we feel comfortable contemplating, let alone discussing. Secondly, most of us have very limited knowledge of what is actually involved in the later stages of life. Over the last fifty years death has become separate from the mainstream of life, occurring mostly in hospitals or hospices under sanitised conditions. The dead body is rarely laid out at home. How different this is from earlier practice. Thirdly, our opinions alter as our circumstances change. A degree of incapacity that appeared intolerable when we were young may seem much more bearable when in later life we come to experience it.

A friend of mine, a north American scientist somewhat older than me, told me how, years ago, he and three of his class-mates swore a solemn oath that in later life they would secretly monitor each other's condition. If a consensus was reached that an individual's intellectual capacity had declined too far, the others were duty bound to kill him. My friend's great anxiety is that in the intervening years he has lost touch with his friends, but the oath has never been revoked. Although I tell this as a joke, it is not so funny when we consider the far-reaching decisions that may one day be made by others on our behalf.

As we look forwards to an era when novel therapies like stem cell transfer become feasible, we should give careful thought to how we prefer to end our days. My own particular terror is a drawn-out death from emphysema. But I should not want a sudden, unexpected death either - it is cruel for those who are left behind and I want time to say goodbye. It is less bizarre than it may seem to begin to think in terms of a "designer death". I am not talking here about suicide or euthanasia.

Our revolution cannot realistically go on being just a revolution from for much longer. If the revolution in the life sciences brings a much greater degree of control over the degenerative diseases, we will acquire the means to direct our revolution towards the ends we might choose. I am convinced that developing a greater facility for talking realistically - with less denial - about the end of life will draw some of the sting from

ageing and generate a society better equipped psychologically to accommodate the shifting balance of the generations.

Not only must we consider where we want to steer our revolution in terms of the biomedical potential for deferment of disease and prolongation of life, we need also to plan much more imaginatively for an environment in which there will be greatly increased numbers of considerably older people. Many of the issues come under the heading 'enablement' and draw on different dimensions of science and technology.

Last year, I chaired a Task Force on Healthcare and the Older Person that was charged with anticipating what needs to happen over the next twenty years. We began by looking back over the past twenty years and identifying the things that have changed most since the 1980's. The biggest single change has been the astonishing advance in information technology - computers, mobile phones, and the like. This has had the potential to revolutionise the lives of older people, but the fact is that the oldest age groups have so far benefited least from IT. The reason is obvious: the industry has made conspicuously little effort to take older people into consideration.

Apart from personal emergency alarms, IT products are directed towards the young. Display fonts are small, buttons fiddly, options complicated. And I am talking here about the middle-aged like myself, let alone those whose vision is impaired or whose manual dexterity is restricted by arthritis. Yet those over 65 comprise 20% of our population, many with the financial resources and leisure opportunities to make extensive use of these facilities if they were more accessible. We need many more places on introductory courses, so that older beginners can gain the confidence that this is a technology they can master.

IT can transform the lives of older people, providing contacts, information, entertainment and access to specialised services. It can enable radical new models of health care and support for older people living at home, effecting savings that would amply repay the costs of installing an internet connection in every house, just like electricity, gas and water. But it requires profound changes in attitude - a belief in, and a belief by, older people that they can cope.

Think for a moment how assistive technology has transformed life at the other end of the age spectrum since the 1980's. Twenty years ago, getting around with young children was a great deal more awkward than today. The basic McLaren buggy was the height of technology then. Child car seats were cumbersome, often requiring professional fixing. Look at the cleverness and choice of today's equivalents! There is no reason at all, other than attitude, why we have not yet developed as thriving an industry to cater for the needs of older people. But even the idea of a motorised Zimmer frame is seen as a great joke. With different attitudes, assistive technology can transform lives, creating wealth and job opportunities into the bargain.

Technologies to improve housing, transport and other essential services offer exciting possibilities to open new dimensions in older peoples' lives. It is little short of tragic that we are not further advanced in transforming such ideas into reality. Admirable pilot schemes, for example to develop smart homes for assisted, independent living, have confirmed the effectiveness of these novel approaches. The costs are not excessive and would easily be offset by savings in the traditional, more burdensome

forms of health and social support. Why are they not mushrooming into full-blown schemes up and down the country?

We cannot afford to let the turning point in our revolution drift by unheeded or we will find ourselves in very real difficulties. It may be fortunate, therefore that change will be driven soon by that oldest of motives - profit. Market forces, particularly in the area of employment, will very soon wake up to the fact that there is going to be a shortage in the work force that can only be filled by recruiting and retaining older workers.

Work patterns will have to become more flexible and attractive in order to retain older staff. Jobs and the workplace will require redesign. It is ironic to realise that in all probability it will be profit that will drive the attention to well-being of body and mind in old age that could so easily have been perceived as a priority with less blinkered eyes. It was shortage of male labour during the First World War that provided the first real advance in the drive to recognise women's rights. It may be the shortage of young labour that will win the first significant battles in the fight against ageism.

But while we can trust market forces and self-interest to help us address some of the challenge of seeking new directions for our revolution, there are areas of life where we must work hard for ourselves. I am talking about the spiritual dimension - the personal experience - or, if you like, the meaning of our lives. For some, religious belief provides a sufficient framework, a framework in which an older perspective on ageing has been maintained, but which must also adapt to the new. For very many, however, the old religions have no appeal and thin substitutes - in particular, the worship of the body beautiful - have taken their place. It is here that the greatest danger lies. Worshipping the body beautiful is sadly at odds with the realities of ageing. The older body, like the older person, is of course quite as beautiful as the sleek young thing in our magazines or on our screens - more beautiful in many ways with the added value of a mature character and experience. But unless we learn to see and appreciate this deeper, less superficial, beauty we are doomed to struggle with a progressive and pervasive loss of self-worth as we get older.

It is striking that in recent generations we have lost our sense of the value of an older person's experience, as in Western developed countries we have become obsessed with the excitement of the new. Contrast this with much of Africa and Asia where the old are still afforded considerable respect. While they adapt from us the technologies to prolong life, cannot we adapt from them fresh ways of structuring our increasingly multigenerational society?

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It is not just the general public that has to change its way of seeing the challenge of ageing. The professional outlook of the vast majority of doctors and medical research scientists is founded on the concept of the cure. They don't want to know about ageing

because it can't be cured. And yet the geriatrician has some of the finest opportunities to tackle complex and challenging clinical problems of any medical specialism, while research on the ageing process brings the gerontologist face to face with the extraordinary mechanisms that in living cells keep death at bay for so long and against all the odds.

When death of old age comes at the end of a long life, it arrives not because all of our cells are hopelessly shot to pieces but because the fraction of damaged cells quietly passes the threshold for critical failure of one kind or another.

Even in a person as old as 100, most of the cells are in good working order. If a cell culture is grown from the biopsied skin of a centenarian, the culture growth rate is not detectably different from that of a culture grown from a much younger person. Our bodies don't just rot. If we can understand more about the fine molecular balance between the processes that lead to damage and the processes that effect repair, there need be no bound to what we can accomplish. Everything we have learned about the science of ageing suggests there is no quick fix - no fountain of youth - but equally there is no limit. With hard work and determination we can keep pushing back the boundaries of good quality life.

In this series of lectures, I challenge science and society to look afresh at what is happening in our world, to recognise the opportunities, as well as the threats to future stability, that stem from the revolution in longevity.

I challenge the scientific community to think not only of directing energy towards curing illnesses, but to turn increasingly towards the less glamorous but vital task of helping our ageing cells to guard against the drear damage of the daily grind.

I challenge medicine to look in radically new ways at the maintenance of health and quality of life of older people. Can you imagine a world in which the first thing the doctor asks is not your date of birth?

I challenge society, collectively and individually, to rethink its attitudes to older people, to recognise the value and beauty of the fact that we are all living so much longer, and to make sacrifices to accommodate those who presume to live on when previously we would have died.

Above all, I challenge us all to put an end to age as something that we let get in the way of celebrating all individuals on this earth as true equals.