

Broken Limits to Life Expectancy

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Abstract

Life expectancy has increased at a steady pace in industrialised countries over the last 160 years and a slowdown is not evident: Since 1950 the number of people celebrating their 100th birthday has at least doubled each decade. Survival is increasing as a result of progress in economic developments, social improvements, and advances in medicine. Despite a wide-spread belief that old-age mortality is intractable, life expectancy is not approaching a limit. Rather, the evidence suggests that aging is plastic and that survival can be extended by various genetic changes and non-genetic interactions. Increases in human life expectancy are largely attributed to improvements in old-age survival. A reasonable scenario would be that life expectancy will continue to rise in the coming decades, fuelled by advances in the prevention, diagnosis, and treatment of age-related diseases. If the trend continues, life expectancy in Europe would exceed 90 years in the first half of this century. Many official forecasts, however, have assumed lower figures – possibly with severe consequences both for public and private decision-making.

Increases in life expectancy

Records in longevity

The rise in life expectancy is a great achievement of modern times. In the countries with the highest levels of their time, female life expectancy has risen for 160 years at a steady pace of almost three months per year (Fig. 1) (Oeppen & Vaupel, 2002).

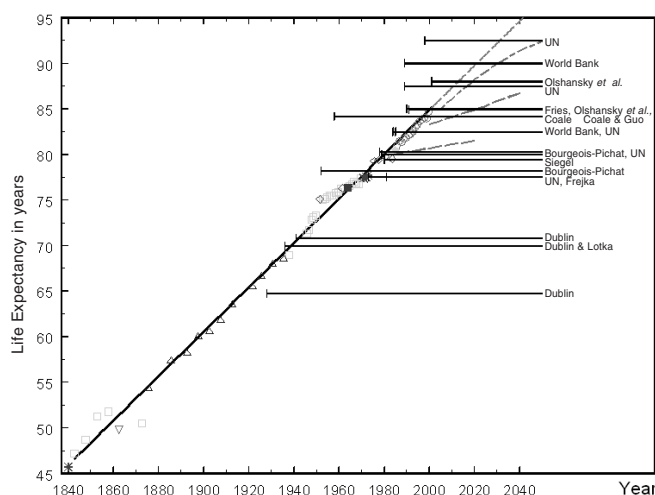


Figure 1. Record female life expectancy from 1840 to the present. The linear-regression trend is depicted by a bold black line (slope = 0.243) and the extrapolated trend by a dashed grey line. The horizontal black lines show asserted ceilings on life expectancy, with a short vertical line indicating the year of publication. The dashed red lines denote projections of female life expectancy in Japan published by the United Nations in 1986, 1999, and 2001. Notice the altered UN projection between 1999 and 2001. (source: Oeppen & Vaupel, 2002)

Introduction

The German president congratulates German citizens when they celebrate their 100th birthday. This act may not have placed high demands on the president's time 50 years ago. Today, however, it is a time-consuming exercise: The probability of an 80 year old surviving to the age of 100 has increased twenty-fold in industrialised countries since 1950 (Vaupel & Jeune, 1995). On average, we are getting older and evidence suggests that we continue to do so. We have no reason to expect that we are approaching a limit to life expectancy (Oeppen & Vaupel, 2002). Mortality at older ages has fallen dramatically since 1950 in developed countries and increases in maximum human life-spans can largely be attributed to improvements in survival at older and oldest-old ages (Kannisto, 1994; Kannisto *et al.*, 1994; Vaupel & Jeune, 1995; Vaupel, 1997). Social progress, health improvements, and research efforts have made their contributions to this development. Social security and health systems, in turn, have been challenged by the aging of society. Ignoring the assumptions of rising life expectancy may lead to forecast underestimations, inappropriate decisions or even the failure to take necessary decisions – possibly with severe consequences for life today and tomorrow.

The four-decade increase in best-practice life expectancy is so extraordinarily linear that it may be the most remarkable regularity of mass endeavour observed. On average, women live longer than men, but record life expectancy has also risen linearly for men since 1840, albeit more slowly (slope = 0.222). The improvements in survival that have led to this linear climb of record life expectancy result from the intricate interplay of advances in income, salubrity, nutrition, education, sanitation and, above all, medicine (Riley, 2001).

Looking at individual countries, gains in life expectancy have not progressed as linearly (Fig. 2). The gap between the record and the national level can be regarded as a

measure of how much better a country might do. However, neither the trend in record life expectancy nor the life expectancy trajectories in different countries suggest that a looming limit to life expectancy is in sight. Although rapid progress in catch-up periods is typically followed by slower increases, none of the curves appear to approach a maximum value (Oeppen & Vaupel, 2002).

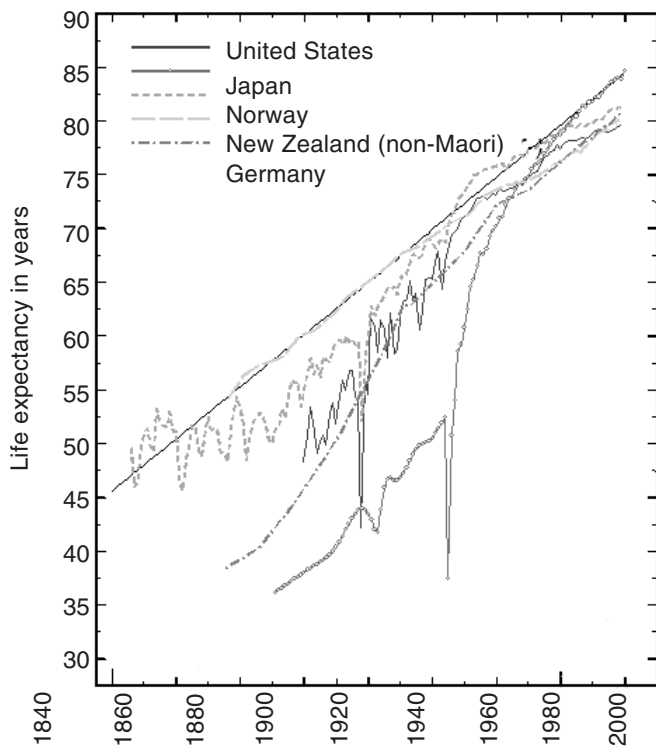


Figure 2. Female life expectancy in the United States, Japan, Norway, New Zealand (non-Maori) and Germany compared with the trend in record-life expectancy. (source: Oeppen & Vaupel, 2002)

Rising numbers of centenarians

Another piece of striking evidence for the undiminished increase in longevity is **the rising number of centenarians in developed countries**. What seemed impossible to achieve in the past – despite spectacular reports – is increasingly becoming part of our reality today.

It is unlikely that any person living before 1800 in Sweden attained the age of 100 (Jeune, 1995) **and even in the world as a whole centenarians were exceedingly rare** (Wilmoth, 1995). Data on the pre-18th century period have to be interpreted with caution. Few reliable statistics are available on mortality levels among the very old living under conditions of low life expectancy. The lower life expectancy is, the greater is the tendency to exaggerate age at older ages (Kannisto, 1994). **Today, the number of centenarians in developed countries is increasing at an exceptionally rapid rate of about 8% per year on average** (Vaupel & Jeune, 1995). **While 265 centenarians were counted in England and Wales in 1950, there were 6680 of them 50 years later**, that is 25 times the 1950 figure

(Kannisto-Thatcher Database). In developed countries the number of people celebrating their 100th birthday doubled each decade between 1950 and 1980; **by the end of the last century the number has multiplied by a factor of 2.4 per decade**.

The myth of a looming limit

As the expectation of life rose higher and higher, experts were unable to imagine a continuation of this development. **A common assumption still widely held is that the life-span cannot be extended beyond a biologically determined limit**. This fixed life-span could be likened to a sand-glass containing a definite amount of sand. The sand running down can be stopped when the sand-glass is put on its side but it cannot be refilled while the sand is running. The notion of an inevitable maximum life-span also influences scientific explanations of longevity (see e.g. Fries, 1980; Olshansky *et al*, 1990). Some experts envision biological barriers and practical impediments in support of this idea. **The idea evolved into a belief in a biological maximum – a looming limit of life expectancy**.

Fixed limits

Ever since research into longevity began, attempts have been made to determine the absolute and **maximum life expectancy that man could reach** (Table 1). The ceilings proposed by various authors differ but they have one thing in common: Their own limited life-span. Every predicted ceiling has been exceeded on average five years after publication, apart from those proposed most recently (Oeppen & Vaupel). At times, the average life expectancy observed in a particular country was even higher than the estimated ceiling at the time of publication.

Explanations for the supposedly obvious limit to life expectancy

The assumption of a finite, biological limit to life can be traced back to **Aristotle**. In his treatise ‘On Youth and Old Age, On Life and Death’ **Aristotle contrasted two types of death: premature death caused by disease or accident, and senescent death due to old age**. He believed that nothing could be done about old age and thus about the end to life (Aristotle, transl. G.R.T. Ross). More than 2300 years later, James Fries quantified Aristotle’s differentiation in a widely cited article published in the *New England Journal of Medicine*: **If life is not cut short by accident or illness, life-span of man will inevitably approach a potential maximum limit that is fixed for every human but differs from individual to individual** (Kannisto-Thatcher Database). **According to Fries, the fixed value of maximum life-span is normally distributed with a mean of 85 years and a standard deviation of 7 years**. **Fries emphasises that nothing can be done to alter a person’s maximum life-span as the latter is beyond the influence of any environmental, behavioural, or medical intervention currently conceivable**.

Table 1. Selection of estimates of maximum average life expectancy for females and males or females only. Limits pertain to life expectancy at birth, with two exceptions (*). Fries asserted that if all premature death were eliminated, ages at death would follow a normal distribution with a mean of 85 and a standard deviation that he gave as 5 in 1980 and as 7 in 1990. For Olshansky et al., the value of 85 shown in this table is 50 plus remaining life expectancy at age 50, which they assert will not exceed 35 years. (altered according to Oeppen & Vaupel, 2002 supplements)

Source	Limit *	Date published (year)	f: female m: male	Date exceeded (year)	Exceeded by females in
Dublin	64.75	1928	f + m	1922	New Zealand
Dublin & Lotka	69.93	1936	f + m	1941	Iceland
Dublin	70.8	1941	f + m	1946	Norway
Nizar & Vallin	76.8	195	f	1967	Norway
Wunsch	76.8	1970	f	1967	Norway
Freijka	77.5	1981	f	1972	Sweden
Bourgeois-Pichat	78.2	1952	f	1975	Iceland
Siegel	79.4	1980	f + m	1976	Iceland
Bourgeois-Pichat	80.3	1978	f	1985	Japan
Demeny	82.5	1984	f	1993	Japan
United Nations	82.5	1989	f	1993	Japan
Fries	85.0	1980 / 1990	f + m	1985	Japan
Olshansky et al.	85.0	1990	f + m	1996	Japan
United Nations	87.5	1999	f		
Olshansky et al.	88.0	2001	f + m		
World Bank	90.0	1990	f		

Following this line of argument, high and rising death rates at older ages are intractable.

The notion of unavoidable senescent death is reinforced by evolutionary theories on aging emphasising that mortality unavoidably rises with age as the force of selection against deleterious, late-acting mutations declines (Hamilton, 1966). Natural selection does not maximise longevity but optimises reproductive success and fitness, i.e., the relative contribution an individual makes to the gene pool of the next generation. The majority of sexually reproducing species show an increase in death rates with increasing age (senescence) (Finch, 1990). Evolutionary biologists have developed theories to explain this phenomenon (Medawar, 1952; Hamilton, 1966; Williams, 1957). Once reproductive activity has ceased, the force of selection cannot act against mutations that are expressed in the later course of life. These mutations are not adaptive: They no longer influence reproductive success. The evolutionary biologist Hamilton therefore concluded that deleterious mutations have to accumulate with age. Moreover, senescence – with its decline in vitality, function, health and, most importantly, survival – is the inevitable consequence of the end to an individual's reproductive period – and just as inevitable is

death sooner rather than later. In theory, postreproductive spans of life should be very short. Although this theory has been extended and modified, it is still regarded as the dominant paradigm for the evolution of aging (Rose, 1991).

No evidence of a fixed amount of sand in the sand-glass of life

The notion of a fixed time it takes for the sand in the sand-glass of life to reach its bottom may be intuitively accepted by many, yet there is no empirical evidence for a proximate limit to human longevity. The steady rise in human life expectancy shows no signs of levelling off. First, experts repeatedly asserting that life expectancy is approaching a ceiling have been proven wrong over and over (Table 1). Second, the apparent levelling off of life expectancy in various countries is, in fact, a reflection of laggards catching up and leaders falling behind without approaching maximum values (Fig. 2). Third, if life expectancy were approaching an unavoidable biologically maximum that cannot be surmounted, then the increase in life expectancy should be slowing especially in countries that witness the lowest death rates. This is not the case, however (Vaupel, 1997; Oeppen & Vaupel, 2002).

Modern Methusalehs

To any value of the average life expectancy in a specific society at a given point in time there is a complex mortality pattern. Over most of the course of human existence life expectancy hovered between 20 and 30 years. Infant mortality was high, people fell victim to infectious diseases or simply to the harshness of everyday living conditions. Even in Western Europe, life expectancy did not reach age 40 until after 1800 and age 50 until after 1900 (Vaupel & Jeune, 1995). Over the last century, life expectancy has risen drastically by more than 30 years. Today, Japanese women live 85 years on average and British women on average do so to the age of 80 (Population Reference Bureau, 2004). This ongoing increase in life expectancy can be largely attributed to continuous improvements in survival at advanced ages (Vaupel & Jeune, 1995; Vaupel, 1997; Scholz & Maier, 2003).

Mortality reductions at advanced ages since 1950

A dramatic reduction in death rates at advanced ages has been observed in the second half of the 20th century (Kannisto, 1994; Kannisto et al, 1994; Vaupel & Jeune, 1995; Vaupel, 1997; Wilmoth, 1997). Figure 3 shows improvements in survival that were observed for women aged 80, 90, and 95 in England and Wales.

The curves are jagged because population sizes at these ages are small and owing to the impact of infectious epidemics and other irregular factors. The time around 1950 marks a distinct change in mortality conditions among these oldest-old: While improvements in survival were

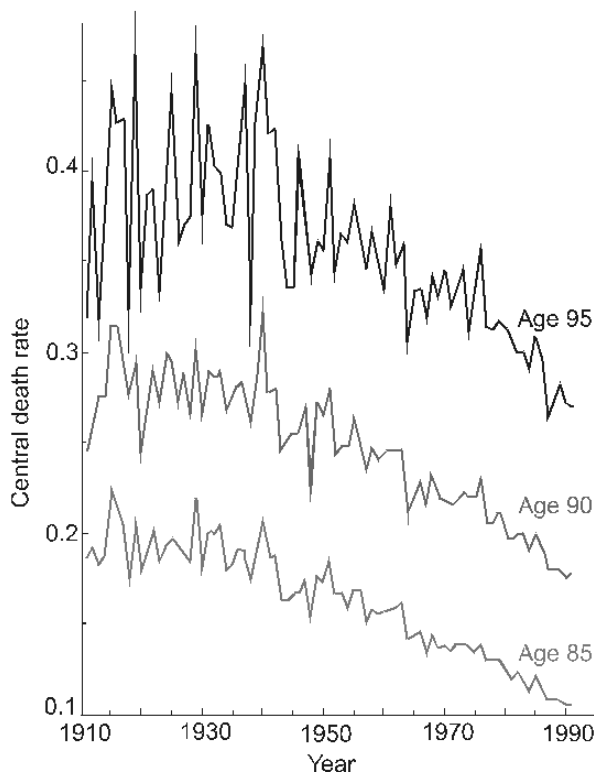


Figure 3. Improvements in mortality from 1911-1991 in England and Wales for females aged 85, 90, and 95 compiled from data in the Kannisto-Thatcher oldest-old database, Odense University, Odense, Denmark. (source: Vaupel, 1997)

slow in the years before 1950, progress made after 1950 and especially after 1970 has been impressive. Old-age survival has also increased since 1950 in France, Iceland, Japan, and the United States (Vaupel *et al.*, 1998). The population of centenarians and even supercentenarians (≥ 110 years) is growing rapidly. A century ago, both an increase in births and a sharp decline in mortality at ages from childhood up to 80 contributed to the rising numbers. Demographic analyses, however, demonstrate that the most important factor behind the explosion of the centenarian population has been the decline in the mortality rate after age 80. This factor has been two to three times more important than all other factors combined (Vaupel & Jeune, 1995).

A plateau in late-life mortality

Human death rates increase at a slowing rate after age 80. Data analyses of very large cohorts reveal that death rates reach a plateau at advanced ages and that mortality even can decline after age 110 (Thatcher *et al.*, 1998). This observation is not unique to humans. Late-life mortality deceleration has been noticed in and confirmed for a number of model organisms as diverse as yeast, the nematode worm *Caenorhabditis elegans*, and different fruitflies like *Drosophila melanogaster* and *Ceratitis capitata*. For all species for which large cohorts have been followed to extinction, age-specific mortality decelerates and, for the largest populations studied, even declines at older ages

(Vaupel *et al.*, 1998). An exciting finding is that late-life mortality deceleration appears to be a rather widespread phenomenon: Aging can cease at late ages. As for humans, flies, and worms, deceleration is observed at ages at which reproduction has ceased.

Does postreproductive survival make any sense?

The fact that extended periods of postreproductive survival have been confirmed for many species is astonishing. It is not clear how to reconcile the findings of mortality deceleration and declines in human mortality at older ages with the evolutionary theory of aging that predicts inevitable increases in mortality after the end of the reproduction period (Hamilton, 1966). For social species, the classical concept of aging based on evolutionary theory needs some rethinking because mortality is not shaped by fertility alone. Apart from remaining fertility, remaining intergenerational transfers of resources – such as care or food – have to be considered (Lee, 2003). Humans invest in the quality of their offspring. Children depend for an extended period on the food and care provided by their parents. After the termination of fertility, grandmothers can support their daughters and thereby enhance their daughters' reproductive success (Hawkes *et al.*, 1998). As in other social species, the effective end of reproduction may thus be much later than indicated by fertility schedules (Carey & Gruenfelder, 1997). This might contribute to an understanding of postreproductive survival in an evolutionary context. But does it convincingly explain the survival of persons older than 80 or even 100 years? These advanced ages were rarely, if ever, reached in the course of human evolution and the reproductive contribution both in terms of fertility and transfers at very advanced ages can be considered as negligible. Why is there no biological opposition to this extremely extended postreproductive survival? Why does evolution licence it? The deceleration of human mortality at old ages remains a mystery (Vaupel *et al.*, 1998).

The plasticity of aging

Although seemingly at odds with evolutionary theory, evidence suggests that aging is plastic and that survival can be extended by various interactions. Concepts contributing to an understanding of the astonishing improvement in survival at late ages come from biodemography, a subject that has emerged at the confluence of demography and biology:

One biodemographic explanation builds on heterogeneity in frailty. All populations are heterogeneous and even genetically identical populations display phenotypic differences. Frailer individuals have a lower probability to survive to late ages; robust individuals have a higher one. The frail tend to suffer high mortality, leaving a select subset of robust survivors. This results in compositional change in the surviving, aging population and possibly to slower

increases in age-specific death rates (Vaupel *et al.*, 1979; Curtsinger *et al.*, 1992; Vaupel & Carey, 1993; Yashin *et al.*, 1994).

But it is also conditions that living organisms are exposed to that potentially influence longevity. Environmental conditions and food resources are subject to uncertainty and change. On the one hand, many species have developed strategies by switching to alternative physiological modes in order to cope with adverse seasons or conditions. These phases of dormancy allow species to survive over extended periods of suspended or metabolic activity largely reduced. On the other hand, several environmental factors or non-lethal stresses, e.g., food shortage or heat shock, can induce increases both in resistance and longevity (Lithgow *et al.*, 1995; Murakami & Johnson, 1996; Masoro, 2000).

Food abstinence and prosperity to enjoy a long life

'Fasting prolongs life' – this concept may sound far too simple. But caloric restriction has proven an effective way to extend life-span in a wide range of species, from yeast to mammals (Masoro, 2000). Studies of model organisms have expanded our understanding of how caloric restriction can lead to extended life-spans, of the pathways and molecular regulatory mechanisms that are involved (e.g., Tissenbaum & Guarente, 2001; Anderson *et al.*, 2003) or how these can even be manipulated (Howitz *et al.*, 2003). In times of shortage, there is apparently an evolutionarily conserved switching to a 'slower-aging-mode'. Many scientists aim to solve the genetic and biochemical mechanisms of the strategies that delay the process of aging.

It is not at all clear, however, whether caloric restriction works in humans. Apart from the health consequences of potential malnutrition, the human physiology differs from that of yeast, worms, or flies. In any case, a near-starvation diet is not the most popular method to prolong longevity in those wealthy countries that have reached extraordinarily high levels of life expectancy.

Studies with model organisms have provided insights into the biological processes of aging that are very valuable. The studies often demonstrate that hasty conclusions do not lead to good advice. If, for instance, fasting were really a way to prolong human longevity, lifelong abstinence would perhaps not be necessary. This conclusion may at least be drawn from a study on *Drosophila*: When flies fed a restricted diet were switched to a full diet, mortality soared to the level suffered by fully fed flies. Conversely, when the diet of fully fed *Drosophila* was restricted, mortality plunged within 48 hours to the level enjoyed by flies that had experienced a lifelong restricted diet (Mair *et al.*, 2003). These results support the repeated finding that age-specific death rates for humans are strongly influenced by current conditions and behaviour (Kannisto, 1994; Vaupel *et al.*, 1998). Mortality is plastic even at advanced ages, and this is important to understand.

Placed in a broader context, this conclusion also applies to humans. It can be illustrated well by an unplanned 'natural experiment' in Germany's recent history. Pre-unified East and West Germany saw a radical decline in old-age mortality, as is typical for most developed countries. In the former GDR, however, mortality was considerably higher than in West Germany. Following reunification (1989-1990), old-age mortality in East Germany declined to reach the levels prevailing in the West (Fig. 4) (Scholz & Maier, 2003; Gjonca *et al.*, 2000), a development largely attributed to improved health care for the elderly after reunification. Thus, interventions even late in life can switch death rates to a lower, healthier trajectory. It's never too late to start prolonging your life (Vaupel *et al.*, 2003).

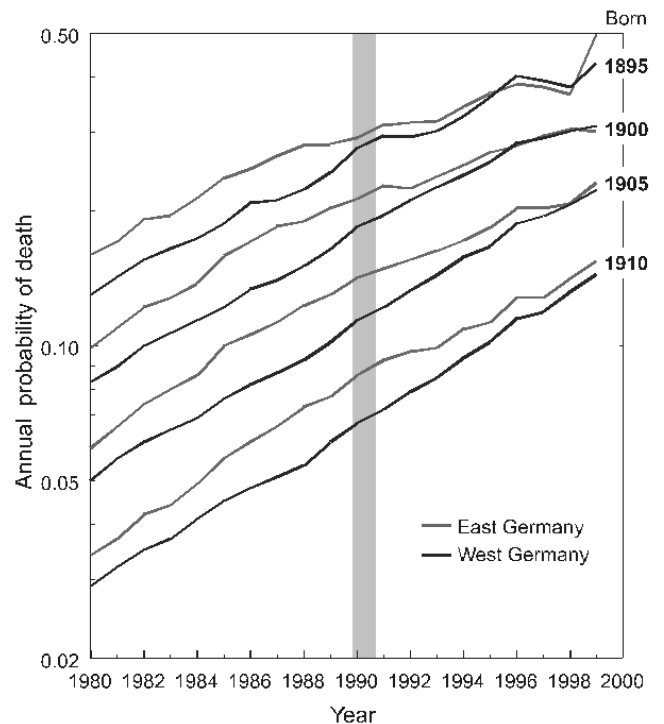


Figure 4. East and West German death rates for cohorts born around 1900. The Berlin Wall fell on 9 November 1989 and formal unification of East and West Germany was completed on 3 October 1990 (grey column). Before 1989, the annual probability of death was considerably higher in East Germany compared with West Germany for cohorts born in 1895, 1900, 1905, and 1910. In 1990, people born in these years were in their 80s and 90s. Nonetheless, very old East Germans were able to benefit from medical, social, and economic improvements after unification. Consequently, their deaths converged toward those of West Germany. Data: Human Mortality Database. (source: Population Reference Bureau, 2004)

Genetic influence

Experiments in species such as *C. elegans* and *Drosophila* demonstrate that even single genes can influence longevity. One of the earliest studies showed that mutations reducing the activity of the gene *daf-2*, and thereby slowing down the metabolism, succeeded in doubling the life-span of the nematode worm (Kenyon *et al.*, 1993). Since then, many genes have been tracked down in model organisms that

influence longevity and, apparently connected to that, increase resistance to environmental stress (Guarente & Kenyon, 2000). Do these findings lead to an understanding of any central mechanisms of the aging process? There is no definite answer to this question yet. What we know today is that many of the relevant genes regulate the overall metabolism and the response to oxidative stress. The latter arises when more reactive oxygen species are produced than the cell's antioxidative systems can eliminate. Here, interesting connections between the genetic and environmental determinants of longevity emerge.

Aging, however, seems more complex and apparently cannot be dissected into its components very easily. Many genes influence longevity (Lee *et al.*, 2003). Moreover, genes are only one part of the story. At least in humans, life-span has a relatively low heritability. Studies on twins indicate that only 25% of the variation in life-span can be attributed to genetic differences (Finch & Tanzi, 1997). All the discoveries of genetic and environmental factors that contribute to extensions in life-span have not been able to fully explain the malleability of aging. Our understanding of the aging process both of worms and humans is far from complete – we are just at the beginning. But the findings have highlighted one thing very clearly: There are means and ways of delaying aging.

Malleability of aging in humans

Human life expectancy is rising and, naturally, neither genetic engineering nor life-long caloric restriction have led to the remarkable development. Instead, genetic predisposition to a smaller extent and behavioural and environmental conditions influencing human health to a larger degree have prolonged the average life-span for people in economically advanced countries. So, aging can apparently be prolonged, but how many decades will this march to longevity continue? Why do so many believe the end to possible aging plasticity is just ahead?

The widespread belief in a looming limit to life expectancy is generally not explained by referring to Aristotle or Hamilton. The uneasiness to accept an ongoing increase in average life expectancy is rather grounded on the inability to understand how this is achieved. Research results of the past 20 years have helped tremendously to understand some basic features of aging, and we have come closer to an understanding of the nature of human aging. We know, for instance, that the complex interaction of behavioural and social factors as well as medical advances have contributed to increasing average life expectancy. Advances in medicine, however, are much better understood than the underlying mechanisms of behavioural and environmental influences. The prospects for the development of average life expectancy often seem to be influenced by considerations of individual longevity. What can we do to increase our chances of living a long and healthy life? Apart from hoping that we will have access to the best medical care available, we probably all heard the best advice ever given

many years ago by our mothers. Don't drink too much alcohol, don't smoke, don't eat too much butter, eat fruit and vegetables, take a long walk every day and laugh as much as you can. The causality is complex and the secrets of longevity have not been discovered yet – we cannot count on living to advanced old age by following precise recipes. In the past, different factors have played major and minor roles at different times and combined they have nonetheless led to a stable increase in average life expectancy. This will also apply to the future. Just as medical breakthroughs, for example the discovery of antibiotics or advances in organ transplantation, were not foreseen, we do not know what major technological innovations the future will bring to promote long and healthy lives. But there is no reason to assume that progress in technological knowledge and its exploitation will come to a halt. It would not make sense to take the standards of today to estimate the conditions influencing life expectancy tomorrow.

Challenges

The future of aging: Forecasts

The future of human life expectancy is uncertain. The prevailing causes of rising life expectancy may have undergone changes and may be complex, but the resultant straight line of life expectancy increase is simple (Fig. 1). As best-practice life expectancy has increased by 2.5 years per decade for the past 160 years, one reasonable scenario would be that this trend will continue in coming decades. To date, there is no indication that a change of the trend is in sight. In that case, there will be a country in about six decades where the average life expectancy may pass the threshold of 100 years (Oeppen & Vaupel, 2002). We are not talking about immortality – we are talking of modest annual increments in average life expectancy. We do not know for how many decades this march to longevity will continue. But centenarians may well become commonplace during the lifetime of people alive today.

The pertinacious belief in a looming and pre-determined limit to life expectancy may lead to severe consequences as it distorts public and private decision-making. Official forecasts of life expectancy have not considered the continuous increase in life expectancy according to the long-term stability in mortality declines observed. These forecasts are used by governments nevertheless to determine future pension, health care, and other social needs, and people refer to them in order to plan their savings or retirement ages. Increases in life expectancy of a few years can produce large changes in the numbers of old and oldest old who will need support and care. Official forecasts therefore give politicians licence to postpone painful adjustments to social security and health care systems.

Life expectancy for individual countries can be forecast by a number of methods, one of them considering the gap between national performance and the best-practice level

(Fig. 2). Let's consider Germany: Referring to the gap method, life expectancy would reach an average of 94 ($\pm 3,8$) years by 2050 (Schnabel & Vaupel, unpubl.), which is considerably higher than the Federal Statistical Office forecast of 86.6 or the Eurostat forecast of 84 years (Eurostat Database New Cronos, 2001; Statistisches Bundesamt, 2003). Forecasts of life expectancy for 2050 differ by up to 10 years. **We are in danger of being unprepared for unprecedented socio-economic situations that we may face if we will not have developed adequate concepts to meet the new challenges ahead of us.**

The prospects of a long and healthy life

Infectious disease was the greatest scourge of mankind until the first half of the 20th century when vaccination, antibiotics, and other medical advances finally began to combat many of the life-threatening diseases in industrialized countries, lowered the rates of infant and child mortality, and limited the devastating effects of the largest epidemics. Exceptions like HIV and recent outbreaks of influenza have to be mentioned. **The steady increases in life expectancy until 1950 can therefore be largely attributed to medical advances aimed at fighting infectious disease.**

Today, cardiovascular disease and cancer are by far the two most common causes of death in Europe. Heart disease and stroke accounted for more than half of all deaths and cancers were responsible for around 20% of all deaths in Europe in 2002 (WHO, 2004). Can an understanding of the general mechanisms of aging produce an understanding of the processes that lead to increased susceptibility to age-related diseases? And, if we were to discover ways to slow down the fundamental processes of aging, would these automatically make a positive contribution to the combat against leading diseases that increase dramatically with age such as arteriosclerosis or cancer?

We are far from having answers to these questions. The findings on the causes of the rapidly increasing diseases associated with age are fragmentary. There are, however, indications that age-related diseases may share common mechanisms with the fundamental aging process. For example, the decreasing ability of an organism to respond to oxidative stress, which is regarded as one of the leading proximate causes of aging in model organisms (Hekimi & Guarente, 2003), may play a role in the parthenogenesis of

cardiovascular or neurodegenerative disease (Finkel & Holbrook, 2000). Moreover, there are indications that age-related physiological and molecular changes might promote cancer, and in particular epithelial carcinogenesis (DePinho, 2000).

Future advances in life expectancy will be made as we progress in the prevention, diagnosis, and treatment of deadly age-related diseases (Barbi & Vaupel, 2005). A source of optimism is the increasingly holistic understanding of genetic control and regulation, the interaction of proteins, and other mechanisms of the metabolism. Molecular biology and systems biology make efforts to unravel the underlying mechanism of human health, with its genetic, nutritional, and environmental determinants. Thus, the way is paved for targeted and individualised diagnosis and therapy. Regenerative medicine is another important field of development and research that has emerged and that may contribute to fighting age-related diseases. A common feature of age-related diseases is the loss of function or degeneration of cells or tissues. Stem cell research aims at finding ways to regenerate or renew these damaged cells and tissues. And finally, progress made in understanding some fundamental and evolutionarily conserved processes of aging in simple organisms nourish the hope that interventions slowing down aging can be identified – and thereby possibly treatments to prolong a long and healthy life (Nemoto & Finkel, 2004).

Outlook

We are living longer and the number of elderly is increasing. This is an enormous achievement and good news for those of us who hope to live to a ripe age. There are downsides to this, however. Rising longevity will pose major challenges to health care and social security systems. It will be necessary to promote research not only on prolonging life but also on healthy aging – both for humanitarian reasons and on compelling economic grounds. The rising number of retirees represents a ticking time bomb placed right in the inner nucleus of the social security system – **there will be more and more people receiving transfer payments for longer and longer periods of time.** Only insight and foresight, wise decisions, and fundamental reforms will help us to cope with increasing longevity and thereby make longevity a great achievement of mankind.

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