

## SPECIAL ARTICLE

## AGING, NATURAL DEATH, AND THE COMPRESSION OF MORBIDITY

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**Abstract** The average length of life has risen from 47 to 73 years in this century, but the maximum life span has not increased. Therefore, survival curves have assumed an ever more rectangular form. Eighty per cent of the years of life lost to nontraumatic, premature death have been eliminated, and most premature deaths are now due to the chronic diseases of the later years. Present data allow calculation of the ideal average life span, approximately 85 years. Chronic illness may presumably be postponed by changes in life style,

and it has been shown that the physiologic and psychologic markers of aging may be modified. Thus, the average age at first infirmity can be raised, thereby making the morbidity curve more rectangular. Extension of adult vigor far into a fixed life span compresses the period of senescence near the end of life. Health-research strategies to improve the quality of life require careful study of the variability of the phenomena of aging and how they may be modified. (N Engl J Med. 1980; 303:130-5.)

**T**HIS article discusses a set of predictions that contradict the conventional anticipation of an ever older, ever more feeble, and ever more expensive-to-care-for populace. These predictions suggest that the number of very old persons will not increase, that the average period of diminished physical vigor will decrease, that chronic disease will occupy a smaller proportion of the typical life span, and that the need for medical care in later life will decrease.

In forecasting health, the interaction between two sets of observations has gone unnoticed. The first set demonstrates that the length of the human life is fixed — that man is mortal and that natural death may occur without disease. The second set indicates that chronic disease can be postponed and that many of the “markers” of aging may be modified. If these two premises are granted, it follows that the time between birth and first permanent infirmity must increase and that the average period of infirmity must decrease.

## THE LENGTH OF LIFE IS FIXED

Speculation about immortality is rooted in antiquity and in human hope. The bioscientific, medical model of disease, our prevalent model, assumes that death is always the result of a disease process; if there were no disease, there would be no death. This view is hard to defend.

If relative immortality were possible, one would expect to find some persons who anticipated the future and acted accordingly. Thus, a person genetically favored and fortunate enough to avoid disease might live much longer than actuarially predicted. Data fail to confirm the existence of such events. For example, adequate data on the number of centenarians have been available in England since 1837; over this time,

despite a great change in average life expectancy, there has been no detectable change in the number of people living longer than 100 years or in the maximum age of persons dying in a given year.<sup>1</sup>

The *Guinness Book of World Records* notes that the correlation between the claimed density of centenarians in a country and its regional illiteracy rate is 0.83. In Sweden, where careful investigations of centenarians are carried out, not one has yet exceeded 110 years of age. The greatest authenticated age in the world was recorded in Japan — 114 years.<sup>2</sup> Approximately one in 10,000 persons in developed countries lives beyond the age of 100. Moreover, inspection of the “tail” of the human survival curve demonstrates the falloff expected from a normal distribution, rather than the emergence of a few persons with notably long life spans.<sup>3</sup> There has been no satisfactory documentation of any society with exceptional longevity.<sup>4</sup>

Several theoretical explanations of the finite life span have been presented. At the cellular level, Hayflick and others have argued extensively for a finite number of cell doublings in the life span of a species. The number of doublings of human fibroblasts is approximately 50 (ref. 5); before reaching this point, subcultivation of cells proceeds in an active and youthful way. However, over a short period after the 50th subcultivation, the cells first fail to grow and then die, although there has been no change in the nutrients or other conditions of the culture medium. The number of doublings is species specific, and long-lived species have more doublings than do short-lived species.<sup>6</sup>

At the level of the organism, life may be defined as internal homeostasis. The internal milieu is adjusted within strict limits by compensating mechanisms in many organs, including heart, lungs, kidneys, and liver. In young adult life, the functional capacity of human organs is four to 10 times that required to sustain life. The existence of “organ reserve” enables the stressed organism to restore homeostasis when it is deranged by external threat. Measurement of organ reserve over time shows an almost linear decline beginning at about the age of 30.<sup>7</sup> As organ reserve

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decreases, so does the ability to restore homeostasis, and eventually even the smallest perturbation prevents homeostasis from being restored. The inevitable result is natural death, even without disease. Although a disease process may appear to be the cause of death, the actual cause is loss of the organism's ability to maintain homeostasis. Any small perturbation, without coexistent organ reserve, would have the same fatal result. Observations since those of Gompertz demonstrate an exponential increase in mortality rate after the age of 30; the rate doubles every eight years.<sup>8</sup> The best mathematical models<sup>9</sup> relate the linear decline in organ function to the exponential mortality rate. Obviously, an exponentially increasing mortality rate ensures a finite life span.

**THE AVERAGE LENGTH OF LIFE IS INCREASING**

The average length of life in the United States has increased from approximately 47 years at the turn of the century to 73 years today, an increase of 26 years (Fig. 1). Life expectancy for white women is now 77 years and for white men 70 years. A steady rise in life expectancy in the early years of this century changed to a relative plateau after 1950, but the increase has resumed in recent years.<sup>10</sup> Such data form the basis for predictions that more people will live beyond the age of 65 and for projections of medical facilities likely to be required in the future.

A more critical look at these data, however, demonstrates that they reflect progress in the elimination of premature death, particularly neonatal mortality. For persons 40 years of age and older, life expectancy has increased relatively little; for those 75 years old the increase is barely perceptible. Figure 1 presents a largely unnoticed paradox: if these lines are extrapolated into the future, at some point in the 21st century the average life expectancy as projected at birth will exceed average age of death as projected at age 75.

A white woman aged 70 may now expect to live 14

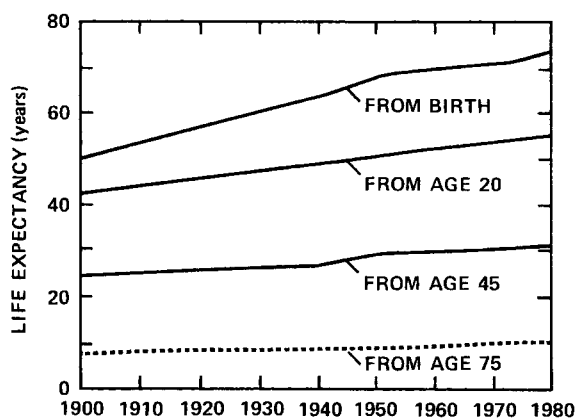


Figure 1. Life Expectancy Trends in the United States. Life expectancy at birth has increased by 26 years in this century, and expectancy at 75 (broken line) by only three years. The slope decreases as the life span is neared.

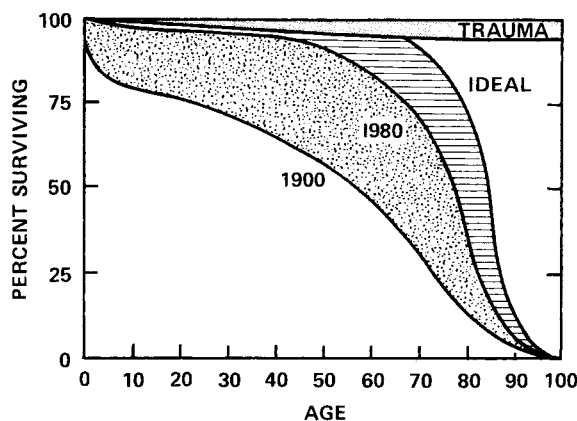


Figure 2. The Increasingly Rectangular Survival Curve. About 80 per cent (stippled area) of the difference between the 1900 curve and the ideal curve (stippled area plus hatched area) had been eliminated by 1980. Trauma is now the dominant cause of death in early life.

years longer (on the average), and a white man of the same age 11 years. Present differences in life expectancy between sexes and races become much smaller as the age on which the analysis is based rises. Racial minorities and men are more subject to premature death.

The shape of the survival curve provides additional insights. In antiquity, as in many species of animals now, death was almost a random event: an organism succumbs to an intercurrent problem before reaching the life span usual for members of the species. In 1900, the survival curve in the United States was not very different from this situation. However, sequential survival curves throughout this century show progressive "rectangularization"<sup>1,8</sup> as the elimination of premature death results in a sharp downslope to the natural life span (Fig. 2). The serial data allow calculation of the position and shape of a survival curve if all premature death were eliminated: an ideally "rectangular" survival curve. If we assume a normal biologic distribution, statistics suggest that under ideal societal conditions mean age at death is not far from 85 years.

The natural limit to the life span can be calculated in several ways. Perhaps the easiest, after study of the rate at which life expectancy at various ages is increasing, is to calculate the point at which the curves intersect (Fig. 3). For example, over the first eight decades of this century average life expectancy from birth increased at the rate of 0.33 year per year of the century, and life expectancy from age 65 has increased by 0.05 year per year. These curves intersect in the year 2009, at a mean age at death of 82.4 years. During the most recent decade, average life expectancy from birth has also increased 0.33 year per year, and life expectancy from age 65 has increased at 0.12 year per year. These curves intersect in the year 2018, at a mean age at death of 85.6 years.

Calculations based on other periods or from other ages converge at similar points. Figure 3 shows intersection at age 85 in the year 2045, a reasonable median projection. In actuality the curves will not be straight but will approach an asymptote; the limit will be approached more slowly, and the attainable average life expectancy will be less than the theoretical estimate. Predictions by the federal government (Fig. 3) make such nonlinear assumptions and suggest that the actual limit may be less than 85 years.

Mortality data describe a biologic distribution, which appears approximately normal in populations of laboratory animals. If the tail of the survival curve remains fixed and the biologic distribution is normal, an age of 100 years is about four standard deviations from the mean, and the standard deviation about four years. Thus, under ideal conditions, 66 per cent of natural deaths would occur in persons 81 to 89 years, and 95 per cent in persons aged 77 to 93 years. With a biologic distribution, the ideal survival curve will never be completely "rectangular," and, if the rate of violent and traumatic death (a category now accounting for more than half of deaths in persons under the age of 40 years<sup>9</sup>) remains roughly constant, there will always be some premature deaths.

Changes in survival curves in this century may be compared with the hypothetical ideal curve in Figure 2. Since 1900, Americans have covered most of the distance to that ideal, in terms of years of life saved: our progress has removed about 80 per cent of the area between the ideal curve and the 1900 curve (if the rate of violent death is disregarded). Moreover, the great change has occurred in the early years of life, with most remaining premature deaths concentrated in the years after age 60.

These changes are dramatic. In 1900 the average citizen died 38 years "prematurely" (short of the theoretical limit), in 1950 17 years, and in 1980 only 12 years. In 1980 white women will die on the average only seven years prematurely. Moreover, violent death accounts for three of the years by which we fall short of the limit. Clearly, the medical and social task of eliminating premature death is largely accomplished.

#### CHRONIC DISEASE HAS SUPERSEDED ACUTE DISEASE

Acute illness has ceased to be the major medical problem in the United States. At the turn of the century, mortality patterns were dominated by acute, usually infectious disease. Tuberculosis, acute rheumatic fever, smallpox, diphtheria, tetanus, poliomyelitis, pneumococcal pneumonia in the young, and similar conditions constituted the principal threats to health.<sup>10</sup> Each of these now causes less than 2 per cent of the health problems that it caused in 1900.<sup>11</sup> Smallpox has been eradicated; polio, almost so. The decline in these diseases can be attributed to a number of factors, including improved nutrition, less crowded living arrangements, water sterilization, immuniza-

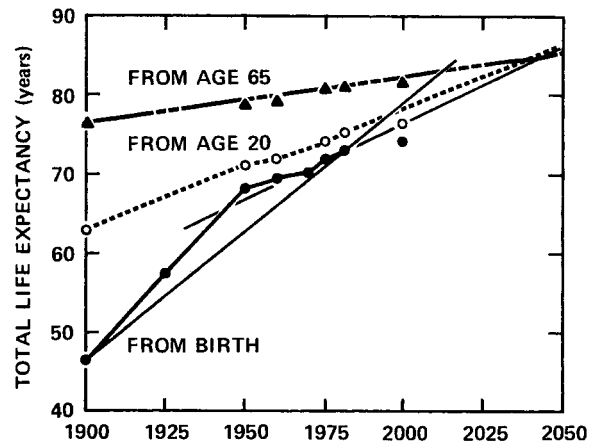


Figure 3. Trends, Limits, and Convergences in Life Expectancy.

Projection of total life expectancy data into the future shows convergence at the ideal average life span, 85 years, in 2045. Spans of 82.6 to 85.6 years can be calculated from projections from different ages (at birth, at age 20, and at age 65) and different years in this century. (Data are from the National Center for Health Statistics [1977]<sup>10</sup>; values indicated by triangle and circles for the year 2000 are estimates from the Office of the Actuary.)

tion, and specific antibiotics.<sup>12</sup> It is important to recognize that chronic diseases have replaced acute illness as major health threats.

Chronic illness now is responsible for more than 80 per cent of all deaths and for an even higher fraction of cases of total disability.<sup>8</sup> Arteriosclerosis (including coronary-artery disease and stroke), arthritis, adult-onset diabetes, chronic obstructive pulmonary disease (including emphysema), cancer, and cirrhosis represent the overwhelming majority of our health problems. They are widespread conditions that originate in early life and develop insidiously; the probability of their occurrence increases with age. They can be considered, broadly, as problems of accelerated loss of organ reserve. Generally, they develop slowly and asymptotically below a clinical threshold, at which the process becomes clinically evident, progresses, and often culminates in death or disability.

Thus, the early arteriosclerotic plaque does not materially impede circulation, but gradually the probability of an acute thrombotic event or insidious vascular insufficiency increases. The osteoarthritic bone spur is evident on x-ray films for many years before pain or disability is noted in the affected joint. Glucose tolerance decreases gradually until sugar is excreted in the urine of the diabetic. The patient with emphysema has accelerated loss of pulmonary reserve. The probability of development of neoplasms increases with age.

Disability and lowered quality of life due to the most prevalent chronic diseases are thus inescapably linked with eventual mortality. These chronic diseases

are approached most effectively with a strategy of "postponement" rather than of cure. If the rate of progression is decreased, then the date of passage through the clinical threshold is postponed; if sufficiently postponed, the symptomatic threshold may not be crossed during a lifetime, and the disease is "prevented."

Some chronic illnesses definitely can be postponed; elimination of cigarette smoking greatly delays the date of onset of symptoms of emphysema and reduces the probability of lung cancer. Treatment of hypertension retards development of certain complications in the arteries. In other illnesses, circumstantial evidence of similar effects of postponement is strong but proof is difficult: that arteriosclerosis is retarded by weight reduction or exercise is suggested by associative data but has not yet been proved.

Until recently, progress in health care could be conceived of as an exchange of acute medical problems for chronic ones: the person who survives an illness appearing abruptly early in life will have more lingering problems later. Since early death would cost relatively little in direct expenses as compared with the expenses of a later chronic problem, the exchange of acute illnesses for chronic ones has resulted in a massive need for additional medical services. The end of this era is nearing because there are now few acute illnesses to be "exchanged."

The most recent increases in average life expectancy are due principally to a decline in arteriosclerosis, particularly cerebrovascular disease. This decline is the first demonstration of a national decrease in mortality from a major chronic disease, and most observers attribute the change to changes in life style and to better treatment of hypertension.<sup>13</sup> The 26 per cent decline in per capita tobacco consumption over the past 15 years,<sup>14</sup> now accelerating, may effect at least a similar percentage of decrease in the incidence of chronic obstructive pulmonary disease and lung cancer, after a delay of a few years. Moreover, the preventive approach to chronic illness is still in its infancy. The long-term effects of increased exercise, lower weight, and growth in personal autonomy and personal responsibility for health are also likely to be positive.<sup>15</sup>

#### THE COMPRESSION OF MORBIDITY

The amount of disability can decrease as morbidity is compressed into the shorter span between the increasing age at onset of disability and the fixed occurrence of death. The end of the period of adult vigor will come later than it used to. Postponement of chronic illness thus results in rectangularization not only of the mortality curve but also of the morbidity curve.

The social consequences of this phenomenon will be profound. Death and disability, occurring later, become increasingly unavoidable. The incremental cost of marginal medical benefit inevitably rises. Interven-

tion in the patient without organ reserve will be recognized as futile. The principles of fixed mortality and of natural death without disease carry profound implications.

Some caveats must be mentioned. War, depression, pestilence, or natural disaster could reverse recent trends. The human life span may not be fixed but may be slowly increasing, perhaps a month or so each century; the data are consistent with this hypothesis. The Hayflick phenomenon may have nothing to do with human aging. Medical progress may increase the number of cell doublings, learn to slow organ decay, or extend the maximum life span in some other way, notwithstanding its failure to do so to date. But it is highly unlikely that any such change will occur during our lifetime. The likelihood depends on whether the lowest curve of Figure 1 (life expectancy after age 75), after being relatively stable for many decades, will show a sudden upturn. Many of the chronic diseases, including arteriosclerosis, may be susceptible to "cure," and efforts directed at finding curative treatments must be continued. There will always be illness; theoretical curves may be approached but not reached. The surprising fact is that we are already approaching the limits.

By implication, the practical focus on health improvement over the next decades must be on chronic instead of acute disease, on morbidity not mortality, on quality of life rather than its duration, and on postponement rather than cure. The complex nature of the major diseases calls attention to multifactorial influences on outcome, in particular social and psychological factors. Outcome is related to choice; assumption of personal responsibility, education for making decisions about personal health, and ability to encourage self-care are clearly essential to changing health behaviors.<sup>16</sup> Returning responsibility to the patient may cause anguish.

#### THE COMPRESSION OF SENESCENCE

An important shift is occurring in the conceptualization of chronic disease and of aging. Premature organ dysfunction, whether of muscle, heart, lung, or joint, is beginning to be conceived as stemming from disuse of the faculty, not overuse. At the Stanford Arthritis Clinic I tell patients to exercise, and to "use it or lose it"; "Run, not rest" is the new advice of the cardiologist. The body, to an increasing degree, is now felt to rust out rather than to wear out. If loss of reserve function represents aging in some sense, then exercising an organ presents a strategy for modifying the aging process.

The links between the widespread chronic diseases and aging are the insidious loss of organ reserve common to both processes and the often identical factors that influence the rate of development. In preventive medicine these variables are seen as antecedents to disease, whereas in gerontology they are markers of age. Serum cholesterol, vital capacity, and systolic

blood pressure are examples of such variables. Exercise, weight control, and diet are some of the common modifying factors.

The modifiability, or "plasticity," of aging has been demonstrated in studies in which performance can be bettered despite age, within surprisingly broad limits. This important phenomenon has been largely unnoticed partly because of an emphasis on average rather than individual performance and partly because disparate disciplines are involved. Average declines in variables in aging can hide remarkable individual variation. The marathon runner is an example (Fig. 4). A runner in middle life who completes a marathon in 3 1/2 hours is in the 99th percentile for this endeavor; yet not until age 73 would that time set an age-group record. These marathon data are important in that they show the maximum rather than the average performance, but here too there is a linear decline in performance between age 30 and 70. Still, the age-related decrement in maximal performance is only 1 per cent per year. Variation between healthy persons of the same age is far greater than the variation due to age; age is a relatively unimportant variable, and training in marathon running is clearly more important than age.

Similar observations on increased variation between individuals with age and on modifiability with training, even after age 70, have been made for intelligence testing,<sup>17,18</sup> social interaction,<sup>19</sup> health after exercise,<sup>20</sup> and memory.<sup>21</sup> Certain data indicate improvement with age, against the gradient of linear decline, for some persons. An inference is that personal choice is important — one can choose not to age rapidly in certain faculties, within broad biologic limits.

Such considerations suggest that research strategy toward aging be fundamentally shifted. Analysis of variation, not of the mean values, becomes crucial. Indeed, one can argue that the number of studies showing that the mean of every function declines steadily with age is already sufficient. Research now requires measurement of standard deviation between

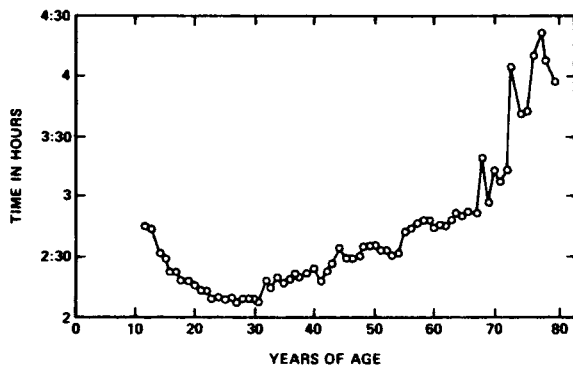


Figure 4. World Marathon Records for Men. Note the slow but linear decline in maximum performance between the age of 30 and 70.

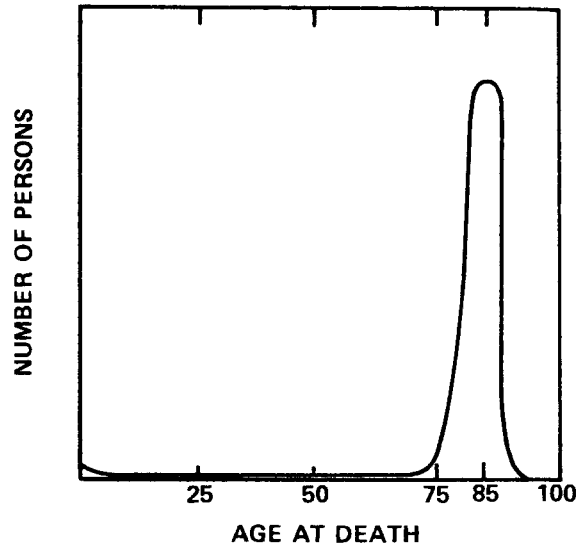


Figure 5. Mortality According to Age, in the Absence of Premature Death.

The morbidity curve is made rectangular, and the period of morbidity compressed between the point of the end of adult vigor and the point of natural death.

individuals, not of standard error between populations or between chronological ages.

A new three-stage research strategy may be urged: measure the variability of a marker of aging (e.g., oxygen uptake, satisfaction as assessed by questionnaire, or intelligence as measured by IQ test) at a given chronological age; determine retrospectively the differences between the individual who has aged more rapidly and the one who has aged more slowly in that marker — hypothetically, such differences may be expected to correlate with the individual's practice in self-maintenance and to be confounded by self-selection; and design prospective intervention studies to explore causality.

At the top of the list of nationally important health-research subjects must be the ability to postpone chronic illness, to maintain vigor, and to slow social and psychologic involution. We must know for certain whether change is possible and how to accomplish it best. Personal autonomy has been emphasized above as a probable final common pathway to improved health. This emphasis is meant broadly, since clearly the collective efforts of individuals are required for removal of environmental hazards and the development of incentives to encourage rather than discourage the exercise of personal choice. We know relatively little about the specific relations between social changes and personal decisions, and much information in great depth is needed.

**SUMMARY**

I have presented a model for national health that foresees continued decline in premature death and emergence of a pattern of natural death at the end

of a natural life span. Present approaches to social interaction, promotion of health, and personal autonomy may postpone many of the phenomena usually associated with aging. The rectangularization of the survival curve may be followed by rectangularization of the morbidity curve and by compression of morbidity (Fig. 5).

These considerations suggest a radically different view of the life span and of society, in which life is physically, emotionally, and intellectually vigorous until shortly before its close, when, like the marvelous one-hoss-shay,<sup>22</sup> everything comes apart at once and repair is impossible. Such a life approaches the intuitive ideal of many and confounds the dread of others for the opposite model, that of evermore lingering death. Paradoxically, predictability of death may prove soothing.

Since maintenance of organ capacity appears to require practice on the part of the individual, the implications for the societal role are as fundamentally different as are the two models. Indeed, the choice of societal postures toward the aged is likely to prove self-fulfilling. The older person requires opportunity for expression and experience and autonomy and accomplishment, not support and care and feeding and sympathy. High-level medical technology applied at the end of a natural life span epitomizes the absurd. The hospice becomes more attractive than the hospital. Human interaction, rather than respirators and dialysis and other mechanical support for failing organs, is indicated at the time of the "terminal drop." Anguish arising from the inescapability of personal choice and the inability to avoid personal consequences may become a problem for many. For others, exhilaration may come from recognition that the goal of a vigorous long life may be an attainable one.

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