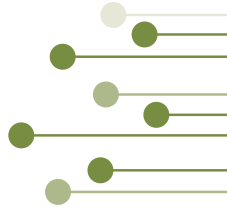


Why Do Our Bodies Grow Old?



Oliver Wendell Holmes (1858/1891), in his poem “The Wonderful One-Hoss Shay,” invokes a memorable image of longevity and mortality, the example of a wooden horse cart, or shay, that was designed to be long-lasting:

Have you heard of the wonderful one-hoss shay,
That was built in such a logical way,
It ran a hundred years to a day . . . ?

This wonderful “one-hoss shay,” we learn, was carefully built so that every part of it aged at the same rate and didn’t wear out until the whole thing fell apart all at once. Exactly a century after the carriage was produced, the village parson was driving this marvelous machine down the street, when

What do you think the parson found,
When he got up and stared around?
The poor old chaise in a heap or mound,
As if it had been to the mill and ground!
You see, of course, if you’re not a dunce,
How it went to pieces all at once,
All at once, and nothing first,
Just as bubbles do when they burst.

The wonderful one-horse shay is the perfect image of an optimistic hope about aging: a long, healthy existence followed by an abrupt end of life, with no decline. The one-horse shay image also suggests that life has a built-in “warranty expiration” date. But where does this limit on longevity come from? Is it possible to extend life beyond what we know? The living organism with the longest individual life span is the bristlecone pine tree found in California, more than 4,500 years old, with no end in sight.

The maximum human life span appears to be around 120 years. In fact, we have no valid records of anyone living much beyond that length. There have been claims of people living to the advanced age of 150 or even longer. Some claims have persuaded the *National Enquirer*, and others even convinced a scientist at Harvard Medical School. But whatever the *Enquirer* or Harvard scientist wanted to believe, there has never been proof of such longevity. Quite the contrary. Despite the fact that we have millions upon millions of verified birth records in the 20th century, until recently, there were no proven cases at all of any human being living beyond age 120. Then, in 1995, a Frenchwoman named Jeanne Louise Calment did just that, before dying in 1997 at the documented age of 122 (Robine, 1998). Madame Calment actually remembered seeing Vincent van Gogh as a child!

Some scientists argue that even the idea of maximum life span is based only on empirical observation. With biological breakthroughs in the future, might we someday surpass that limit? Indeed, optimists ask, why settle for the one-horse shay?

On the face of it, prolonging the human life span sounds good. But is it feasible? Will it make our lives better? One cartoon in *The New Yorker* shows a middle-aged man at a bar complaining to his companion: “See, the problem with doing things to prolong your life is that all the extra years come at the end, when you’re old” (Mankoff, 1994). Another cartoon depicts two nursing home residents in wheelchairs confiding to each other: “Just think. If we hadn’t given up smoking, we’d have missed all this.”

These cartoons point to the fact that often the consequences of biophysical aging appear well before reaching maximum life span. Some observers believe that the proper aim of medicine should therefore be to intervene, perhaps even to slow down the rate of aging, so that more and more of us can remain healthy up to the very end of life. At that point, the body would simply “fall apart” all at once, like the wonderful one-horse shay (Avorn, 1984). This view, mentioned earlier, is known as the *compression of morbidity*, an idea developed and promoted by James Fries (1988, 2004).

The compression-of-morbidity hypothesis looks forward to greater numbers of people who postpone the age of onset of chronic infirmity (Brooks, 1996). In other words, we would aim for a healthy old age, followed by rapid decline and death. Sickness or morbidity would be compressed into the last few years or months of life. But things don’t always work out that way. We may succeed in postponing deaths from heart disease, cancer, or stroke. But what happens if we live long enough to get other diseases? The same preventive measures can have, as an unintended result, increased rates for chronic conditions such as dementia, diabetes, hip fracture, and arthritis (Roush, 1996). Many observers worry that as increasing numbers of people live to advanced ages, the challenge of compressing morbidity will become more and more difficult. One study of mortality did find some evidence that survival curves became more rectangular—that is, deaths became concentrated around a point later in life (Nusselder & Mackenbach, 1996), and a comprehensive review of over 30 years of research suggested that disability

levels decreased every year from 1982 to 2004 (Fries et al., 2011), but other studies have found the opposite. Investigators such as Eileen M. Crimmins and Hiram Beltrán-Sánchez (2011) have found that the length of life with disease and limited mobility had increased between 1998 and 2008, a trend that does not support the idea of compression of morbidity. In addition, there is increasing evidence of social inequalities in longevity and the potential for experiencing a healthy old age; gender, ethnicity, and socioeconomic status are interconnected factors to consider in the compression-of-morbidity discussion (Olshansky et al., 2012).

It is important to distinguish here between life expectancy and maximum life span. Life expectancy, or expected years of life from birth (or any other age), has mostly risen, but life span, which is defined as the maximum possible length of life, has evidently not changed at all. As mentioned earlier, to the best of our knowledge, no human being has ever lived beyond 120 years or so. The causes of maximum life span and of aging itself still remain unknown. Biological evidence suggests that maximum life span is genetically determined, and therefore fixed, for each species. Another important idea related to life expectancy and aging is referred to as *disability-free* or *active* life expectancy, the number of years an individual can expect to live beyond age 65 without significant functional impairment due to disability or chronic illness (Cherlin, 2010; World Health Organization, 2015).

With this concept of life span limit in mind, compression-of-morbidity is attractive because delaying dysfunction would enhance the quality of life, extend life expectancy, and reduce health care costs (Butler, 1995). A compression-of-morbidity strategy would move life expectancy closer to the hypothetical upper bound of maximum life span. Instead of expecting to live only to age 85, people who reach 65 could expect to become centenarians, yet in good health nearly to the end of life (Fries et al., 2011).

Such a gain in active life expectancy—or *health span*—would have dramatic consequences for our society. To judge whether this strategy for compression of morbidity is feasible, we need to examine in more detail what is involved in normal aging. We need to understand what is known about the biology of aging and what may be discovered in the future.

The Process of Biological Aging

In favorable conditions, a human being can live to around a hundred years old: A few live a bit longer than that, but not many and not for much more. Why is that? We don't live to be a thousand years old, and, unlike some species, we don't live only a few months. Why is that? Why a hundred years and not a few months or many centuries? This is a basic question about the process of biological aging.

Normal biophysical aging, also called **senescence**, can be defined as an underlying time-dependent biological process that, although not itself a disease, involves functional loss and susceptibility to disease and death. One way to measure susceptibility to death is to look at death rates. For contemporary humans,

these rates double every 8 years. This pattern is known as **Gompertz law** (Kowald, 2002). In other words, a 38-year-old is about twice as likely to die as a 30-year-old, a 46-year-old is four times more likely to die than a 30-year-old, and so on. At any given age, there is an important gender difference: Although men and women age at the same rate, women at every age are less biologically fragile than men—contrary to what our cultural stereotypes might suggest. However, as we will discuss later in this book, there are disparities between women and men when it comes to patterns of chronic illness, disability, and *active life expectancy*.

Studies of different species of organisms show that aging is almost universal, but the causes of aging are complex. For instance, among animals whose body mass and metabolism are comparable, the rate of aging varies greatly (Olshansky & Carnes, 2002). Consider the differences in maximum life span among some familiar animal species shown in Exhibit 1.

The rate of aging can be correlated, in a general way, with the amount of time it takes for the mortality rate of a species to double. The doubling time is around 8 years for humans today, but only 10 days for a fruit fly and 3 months for a mouse. In rough terms, we can say that a mouse ages at around 25 times the rate of a human being.

What accounts for these clear differences in rates of aging and life span across species? Comparative anatomy—the study of the structure of different species—generates some insights into this question. For example, among mammals and other vertebrates, an increase in relative brain size is positively related to an

Exhibit 1 Some Organisms' Maximum Life Span

Organism	Maximum Life Span (in Years)
Tortoise	177
Human being	120
African elephant	78
Horse	62
Golden eagle	50
Chimpanzee	37
Dog	34
American buffalo	26
Domestic cat	21
Kangaroo	16
Domestic rabbit	12
House mouse	3
Fruit fly	25 days

Source: Data compiled from Walford (1983); Encyclopædia Britannica (2018); Did You Know? (2019).

increased life span. Other factors correlated with life span are lifetime metabolic activity, body size, body temperature, and the rate of energy use. For example, a tiny hummingbird has a rapid heartbeat and a high rate of energy metabolism; it also lives a comparatively short time, as if it were more quickly using up its total lifetime energy or action potential (Sacher, 1978).

Biologists have discovered intriguing relationships among life span, body size, relative brain size, and metabolic intensity. For example, a chipmunk has a maximum life span of 8 years, but an elephant can achieve 78 years. These facts suggest a more general idea known as the **rate-of-living concept**: roughly, the concept that metabolism and life expectancy are closely correlated. Smaller organisms, which tend to have a more rapid metabolism for each unit of body mass, also tend to have shorter life spans. A short-lived mouse and a long-lived elephant both have approximately the same temperature, but the mouse produces more heat per unit of mass. At the other extreme, slow-moving turtles are likely to have life spans longer than the more active mammals. Another fascinating fact is that no matter their total body mass, mammals have approximately the same number of heartbeats in a lifetime. Still, despite these tantalizing correlations, the rate-of-living theory has largely been rejected by biologists, along with the notion that biological aging is somehow necessary for the good of the species (Austad, 1997).

In comparison with other species of mammals, the human being has the longest life span and also expends more energy per body weight over the total life span than any other mammal. Energy metabolism per body weight across the life span in humans is about four times greater than that for most other species of mammals. Human beings have an average life expectancy and a maximum life span about twice as great as those of any other primate.

Compare the chimpanzee and the human being. The maximum human life span appears to be around 110 to 120 years; the chimpanzee's is close to 40 years. But when we look at DNA from both species, we find that their DNA is more than 98% identical. These figures suggest that the rate of aging may be determined by a relatively limited part of the genetic mechanism. Calculations suggest that if a cell is determined by around 100,000 genes, then perhaps no more than a few hundred alterations in the genetic code are needed to change the rate of aging.

Scientists have posited that a large increase in maximum human life span occurred fairly recently—probably within the past 100,000 years. The speed of this development suggests that only a tiny portion of the human genome, representing less than 1% of the genetic code, was likely to be involved. If so few genetic mechanisms determine aging, then we can perhaps hope to intervene to delay the process of aging (Finch, 1990).

Biological Theories of Aging

The facts about aging and maximum life span have led many biologists to believe that biophysical aging may have a single fundamental cause. In their efforts to find

such a single primary process to explain those time-dependent changes that we recognize as biophysical aging, they have developed many different ideas. Biologist Zhores Medvedev (1972) enumerated more than 300 biological theories of aging. At present, no single theory of aging explains all the complex processes that occur in cells and body systems, but ongoing research is under way that is leading to new insights into why we grow old.

Broadly speaking, we can distinguish between two kinds of theories of aging (Finch & Kirkwood, 2000):

- *Chance.* Some theories see aging as the result of external events, such as accumulated random negative factors that damage cells or body systems over time. For example, these factors might be mutation or damage to the organism from wear and tear.
- *Fate.* Some theories see aging as the result of an internal necessity, such as a built-in genetic program that proceeds inevitably to senescence and death.

In either case, the question remains open: Is it possible to intervene to correct damage to the aging body or modify the genetic program? The most likely interventions are those that would make sense depending on which theory best explains the facts about aging (Ludwig, 1991).

Wear-and-Tear Theory

The **wear-and-tear theory of aging** sees aging as the result of chance. The human body, like all multicellular organisms, is constantly wearing out and being repaired. Each day, thousands of cells die and are replaced, and damaged cell parts are repaired. Like components of an aging car, parts of the body wear out from repeated use, so the wear-and-tear theory seems plausible.

The wear-and-tear theory is a good explanation for some aspects of aging—for example, the fact that joints in our hips, fingers, and knees tend to become damaged over the course of time. A case in point is the disease of osteoarthritis, in which cartilage in joints disintegrates. Another is cataracts, in which degeneration causes vision loss. Our hearts beat several billion times over a lifetime, so with advancing age, the elasticity of blood vessels gradually weakens, causing normal blood pressure to rise and athletic performance to decline.

The wear-and-tear theory of aging goes back to Aristotle but in its current form was expanded by one of the founding fathers of modern biogerontology, August Weismann (1834–1914). He distinguished between the two types of cells in the body: germ plasm cells, such as the sperm and egg, which are capable of reproducing and are in some sense “immortal,” and somatic cells comprising the rest of the body, which die. Weismann (1889), in his famous address “On the Duration of Life,” argued that aging takes place because somatic cells cannot renew themselves, so living things succumb to the wear and tear of existence.

What we see as aging, then, is the cumulative, statistical result of wear and tear. Consider the case of glassware in a restaurant, which follows a curve similar to that for human populations. Over time, fewer and fewer glasses are left unbroken, until finally all are gone. The life expectancy or survival curve of the glassware follows a linear path over time, but the result for each individual glass comes about because of chance. Nothing decrees in advance that a specific glass will break at a fixed time. Glasses are just inherently breakable, so normal wear and tear in a restaurant will have its inevitable result. Like everyone born in a certain year (e.g., 1880), the “glasses” disappear one by one until none are left.

Some modern biological theories of aging are more sophisticated versions of this original wear-and-tear theory. For example, the **somatic mutation theory of aging** notes that cells can be damaged by radiation and, as a result, mutate or experience genetic changes (Szilard, 1959). The somatic mutation hypothesis would seem to predict higher cancer rates with age, yet survivors of the atomic bomb at Hiroshima showed higher rates of cancer but no acceleration of the aging process.

Even without actual mutation, over time, cells might lose their ability to function as a consequence of dynamic changes in DNA. According to the so-called error accumulation theory of aging, or error catastrophe theory, decremental changes of senescence are essentially the result of chance or random changes that degrade the genetic code (Medvedev, 1972). The process is similar to what would happen if we were to use a photocopy to make another copy. Over time, small errors accumulate. The errors eventually make the copies unreadable. Similarly, the error catastrophe theory suggests that damaged proteins eventually bring on what we know as aging through dysfunction in enzyme production.

The **accumulative waste theory of aging** points to the buildup in the cells of waste products and other harmful substances. The accumulation of waste products eventually interferes with cell metabolism and leads to death. Although waste products do accumulate, there is little evidence of harm to the organism. The key to longevity may be the extent to which cells retain the capacity to repair damage done to DNA. In fact, DNA repair capacity is correlated with the metabolic rate and life span of different species. Some studies suggest that DNA damage in excess of repair capacity may be linked to age-related diseases such as cancer.

Autoimmune Theory

The immune system is the body's defense against foreign invaders such as bacteria. The immune system protects and preserves the body's integrity, and it does this by developing antibodies to attack hostile invaders. We know that the immune system begins to decline after adolescence, and the weakening of immune function is linked to age-related vulnerability. According to the **autoimmune theory of aging**, the system may eventually become defective and no longer distinguish the body's own tissues from foreign tissues. The body may then begin to attack itself,

as suggested by the rising incidence of autoimmune diseases, such as rheumatoid arthritis, with advancing age (Kay & Makinodan, 1981).

Aging-Clock Theory

According to the **aging-clock theory of aging**, aging is programmed into our bodies like a clock ticking away from the moment of conception. One of the best examples of an aging clock in humans is the menstrual cycle, which begins in adolescence and ends with menopause. The aging-clock theory is part of programmed aging, in which aging is seen as a normal part of a sequence leading from conception through development to senescence and finally to death.

One version of the aging-clock theory emphasizes the roles of the nervous and endocrine systems. This version postulates that aging is timed by a gland, perhaps the hypothalamus, the thymus, or the pituitary gland. Such a gland acts like an orchestra conductor or a pacemaker to regulate the sequence of physiological changes that occur over time. Some support for this idea comes from observations that the hormone dehydroepiandrosterone (DHEA) is found in higher levels among younger people. Experimenters have also discovered that DHEA supplements help laboratory rats live longer.

The aging-clock theory has encouraged research on the role of hormones secreted by the thyroid, pituitary, and thymus glands (Lamberts, van den Beld, & van der Lely, 1997). These include human growth hormone, which can now be manufactured in quantity through genetic engineering. In experiments, volunteers injected with growth hormone lost flabby tissue and grew back muscle, essentially reversing some manifestations of the aging process for a time. Other investigators are interested in hormones produced by the pineal gland, which may help regulate the “biological clock” that keeps time for the body.

Hormones and the endocrine system clearly play a major role in the process of aging. Hormones control growth, development, and reproduction in plants and animals. Biologists recognize a phenomenon here called *semelparity*. The best example is the Pacific salmon, which swims upstream to lay its eggs and then dies. So-called annual plants also exhibit semelparity: The tomato plant flourishes, produces fruit, and then dies away as the autumn leaves begin to fall.

But we find no comparable biological process in humans. We do recognize the profound age-related hormonal change of menopause, which comes with the loss of cells in the ovary that produce estrogen. Female mammals are born with a finite number of egg cells, so menopause is an example of a preprogrammed life event linked to age. Menopause is not a disease itself—it is, rather, a normal part of aging—but it is tied to health problems of aging because the loss of estrogen often weakens bone-mineral metabolism, resulting in thinner bone structure—a condition known as *osteoporosis*. Thin bones can lead to fractures, which in turn may compromise an older person’s ability to live independently.

Biogerontology continues to search for a “magic clock” that would give definitive knowledge of biomarkers to measure aging. Recently, scientists have begun

to use artificial intelligence as a tool to chart aging at the deepest possible level (Zavoronkov & Mamoshina, 2019).

Cross-Linkage Theory

Connective tissue in the body, such as the skin or the lens of the eye, loses elasticity with advancing age. We recognize the result as wrinkling of skin and cataracts. The explanation for this change lies in a substance known as **collagen**, a natural protein found in skin, bones, and tendons. According to the **cross-linkage theory of aging**, the changes we see result from the accumulation of cross-linking compounds in the collagen, which gradually become stiff. As in the waste accumulation theory, the piling up of harmful molecules is thought to eventually impair cell function. Some of this cross-linking may be caused by free radicals, which are cited in several theories of aging. Cross-linkage and collagen, therefore, are related to other changes in macromolecules and organ systems as they age (Bilder, 2016).

Free Radicals

Free radicals are unstable organic molecules that appear as a by-product of oxygen metabolism in cells (Armstrong et al., 1984). Free radicals are highly reactive and toxic when they come in contact with other cell structures, thus generating biologically abnormal molecules. The result may be mutations, damage to cell membranes, or damage by cross-linkage in collagen.

Free-radical damage has been related to many syndromes linked with aging, such as Alzheimer's disease, Parkinson's disease, cancer, stroke, heart disease, and arthritis. According to the **free-radical theory of aging**, damage created by free radicals eventually gives rise to the symptoms often associated with aging.

An important point about this theory is the fact that the body itself produces so-called **antioxidant** substances as a protection against free radicals. These antioxidants scavenge or destroy free radicals and thus prevent some of the damage to cell structures. The production of antioxidants is, in fact, correlated with the life span of many mammals.

Free-radical theory has prompted some observers to believe that consuming antioxidant substances, such as vitamin E, might slow down the process of aging. Genetic engineering techniques can now be used to produce antioxidants in vast quantities, but antioxidants are also supplied by the food we eat. Vitamins A, C, and E, as well as less familiar enzymes, play a role as antioxidants. Animal studies to date, however, show that consumption of antioxidants produces only minimal effects on aging.

Biologists recognize the importance of diet in longevity. It turns out that the dramatic doubling of human longevity, compared with other primates, could be understood in terms of inflammation. Inflammatory processes appear to have a role in conditions such as atherosclerosis (buildup of plaques in arteries), Alzheimer's, cancer, and diabetes. Gains in longevity may be understood in terms of reduced

levels of inflammation. For that reason, an anti-inflammatory diet is the subject of important research today (Finch, 2007).

Cellular Theory

A major finding from cell biology is that normal body cells have finite potential to replicate and maintain their functional capacity. This potential appears to be intrinsic and preprogrammed, part of the genetic code. The **cellular theory of aging** argues that aging ultimately results from this progressive weakening of capacity for cell division, perhaps through exhaustion of the genetic material. That cellular limit, in turn, may be related to the maximum life span of species.

One of the major milestones in the contemporary biology of aging was the discovery that cells in laboratory culture have a fixed life span. Leonard Hayflick (1965) found that normal human cells in tissue culture go through a finite number of cell divisions and then stop. This maximum number of divisions is known as the **Hayflick limit**. Hayflick found that cells replicate themselves around 100 times if they are taken from fetal tissue. But if taken from a 70-year-old, they reach their limit of “aging” after 20 or 30 divisions.

Cells taken from older organisms divide proportionately fewer times than those taken from younger ones. Normal human cells that are frozen at a specific point in their process of replication and later thawed seem to “remember” the level of replication at which they were frozen. Furthermore, normal cells from a donor animal that are transplanted will not survive indefinitely in the new host.

Cell division in the laboratory sheds light on an interesting question: Can human bodies become immortal? The answer is yes, but there’s a catch. We have to get cancer to do it. The classic instance is the case of so-called HeLa cells—an immortal remnant of a terminally ill young woman named Henrietta Lacks (HeLa), who died in Baltimore in 1951 (Skloot, 2010). Before she died, a few cancerous cells were removed from her body and put into tissue culture: essentially, put down on a glass lab dish and supplied with cell nutrients. Scientists were surprised to find that these HeLa cells just kept dividing and growing. In the years since, the cells haven’t stopped growing. So we might say that a little piece of Henrietta Lacks has achieved immortality in a laboratory dish.

By contrast, in normal cell differentiation, cells divide and become more specialized, and their ability to live indefinitely simultaneously declines. The Hayflick limit may be not so much an intrinsic limit on living cells as a limit on when cells begin to differentiate, as in development of the embryo. When cells approach a limiting point, a genetic program normally shuts down the capacity for further division. If the genetic program doesn’t work, the result is uncontrolled multiplication, or cancer. The Hayflick limit doesn’t keep all cells from dividing—after all, germ cells such as eggs and sperm continue to divide—but it may give a clue about why aging brings an increase in cancer and a weakening of the immune system.

Studying aging by examining cells in a test tube raises some questions. For instance, the nutrient medium in a cell culture does not contain all the nutrients

and hormones that a cell would normally receive. In addition, cells in the body become differentiated tissues and organs and remain in equilibrium in ways quite different from the way cells replicate in a test tube.

Fundamentally, the cellular theory of aging sees aging as somehow programmed directly into the organism at the genetic level. In this view, it is just as natural for the body to grow old as it is for the embryo or the young organism to develop to maturity, as we see in annual plants or the Pacific salmon. Does the cellular program theory of aging therefore apply to higher organisms such as mammals and, specifically, human beings? Perhaps, but it does not apply as obviously as it does to organisms in which rapid aging is tied to reproduction.

One of the most intriguing points in favor of the cellular approach to aging is the discovery that tiny tips at the ends of chromosomes—structures known as *telomeres*—become shorter each time a cell divides. Telomeres, it seems, comprise a biological clock marking the unique age of a cell as it divides. Studies are under way to explore the link between aging at the cellular level and what we recognize as aging in complete organisms. Elizabeth Blackburn won the Nobel Prize in Medicine for discovering the role of telomeres, which evidently play a crucial role in cellular aging (Brady, 2009). Biologists now understand that the length of a telomere can serve as a biomarker, or measurement of biological age beyond chronological age alone. Studies are under way to see if specific interventions can slow down the process of biological aging.

Is Aging Inevitable?

The biological aging process may not be the result of a rigid genetic program; it may simply be the complex and indirect result of multiple traits in the organism tied to normal development. In other words, the body may not be preprogrammed to acquire gray hair, wrinkles, or diminished metabolic functions. Rather, these supposed signs of aging may simply be telltale side effects of activities of the organism.

Consider the analogy of an aging car. Suppose a distinctive “species” of automobile were designed to burn fuel at a fixed temperature with an efficient rate of combustion. That specific rate of combustion is required for appropriate acceleration, cruising speed, fuel mileage, and so on. But, alas, when the car performs this way, it also inevitably produces certain emission by-products. Over time, these by-products clog the cylinders, reduce efficiency, and lead to the breakdown and final collapse of the machine.

In the case of the human “car,” burning oxygen in normal metabolism generates harmful by-products—namely, free radicals that prove toxic to the organism. The trade-off is that oxygen is essential for life yet harmful to our long-term well-being. Although the human “car” is not intentionally designed to accumulate toxic emissions in order to collapse, it cannot function at optimum levels without creating destructive by-products.

Now suppose we could find some special fuel additive that eliminates toxic emissions. Would we then have an immortal car? Probably not. Changing the fuel in your car won't prevent accidents, nor will any fuel additive prevent rusting or the wearing down of springs and shock absorbers.

The human car analogy has its limits because an organism, unlike a manufactured object, has a capacity for repair and self-regeneration, at least up to a certain point; unlike an automobile, human beings have consciousness and can make choices about how to live out their life span. Nevertheless, to find out how we might modify or slow down biological aging, we must find out why the capacity for self-repair seems unable to keep up with the damage rate—in short, why aging and death appear to be universal.

One response to the question “Is aging inevitable?” would be to find organisms that do not grow old at all. As it turns out, there are such species. One of these is the hydra, a freshwater animal similar to the jellyfish. Do hydras age at all, or are they, in principle, immortal? The rate of death for the hydra does not seem to increase with time. Hydra cells are continually dividing and replicating themselves, and their telomeres remain the same length as well. Some species of flatworms show similar capacity for regeneration without signs of aging.

Urban Legends of Aging

“Antiaging medicine today is making rapid progress.”

No progress is being made at all. No intervention has ever been shown to slow the biological process of aging, other than caloric restriction (eating drastically less), but recent findings, while promising,

are far from conclusive. Herbal supplements sold in health food stores are totally unregulated, and many are dangerous. None, including antioxidants, has ever been proven effective in slowing aging.

Ways to Prolong the Life Span

Most theories of aging depict biological aging as an inevitable process, like a disease to which we must all eventually fall victim. Some theories look on the organism as succumbing to chance events, whereas others see it as driven by a built-in biological clock. Yet whether aging is thought to occur by chance or by fate, most theories seem to reach a pessimistic conclusion about the inevitability of aging.

But aging is not a disease; rather, it is a process of change, part of which may make us vulnerable to disease. Instead of being driven by a single primary process timed through a single biological clock, aging is driven by many different clocks, each on a different schedule and unfolding in parallel developmental patterns.

Biological theories of aging could have enormous importance for an aging society. For example, the compression-of-morbidity idea assumes that there is a definite human life span, roughly 85 years, with a broad range from 70 to 100 years. There are thousands who live beyond 100, but the maximum number of years any human being has lived is 122. An age around that level is often assumed to be the maximum life span possible. But today, basic research in the biology of aging is challenging assumptions about a fixed maximum life span and the inevitability of aging as a biological process. Two approaches have been found that could extend the maximum life span for a species: one based on environmental intervention through diet, the other on a genetic approach.



istockphoto.com/dragana991

Biological aging is inevitable, but diet and exercise may promote healthier aging.

Environmental Approach

For more than 60 years, scientists have known of only one environmental intervention—restricting food intake—that extends life span in mammals. Caloric restriction is defined as the reduction in calorie intake while maintaining adequate intake of essential nutrients. In the 1930s biologists discovered that caloric restriction can extend the longevity of relatively short-lived mammals, such as rodents in the laboratory. In fact, caloric restriction seems to work in a variety of species.

Urban Legends of Aging

“Aging is not a disease.”

Most gerontologists agree that aging is not a disease. Yet a growing number of biologists reject this proposition, and serious work on slowing the process of aging is now under way in the laboratory. In other words, they treat aging as if it's

a curable pathological condition. Of course, no one has ever defined exactly what a “disease” is, so it's hard to prove the point one way or another (Moody & Hayflick, 2003).

The question was: Could caloric restriction also extend longevity in higher mammals such as humans? In recent years scientists have sought to answer this question.

Caloric restriction in mice has similar effects even when it is begun in midlife. Rodents live longer if they eat a diet with 40% fewer calories than normal, as long as their diet remains otherwise nutritionally sound. When caloric intake is restricted, age-related deterioration slows down, and age-related diseases, such as kidney problems and autoimmune syndromes, are diminished (Bronson & Lipman, 1991). The rats' condition does not deteriorate until late in a long life. Under such a diet, both average life expectancy and maximum life span increase by 30%. Apparently, the rate of acceleration of aging has been reduced.

What accounts for this dramatic, well-established impact of dietary restriction in enhancing longevity? The longevity gain is achieved not through reduction in any specific component of the diet, but simply because of fewer total calories consumed. One possible explanation is that caloric reduction slows metabolism, or the rate at which food is transformed into energy (Demetrius, 2004). With caloric reduction, the basic biological clock slows down. But we cannot be sure of this explanation because caloric restriction is consistent with many different mechanisms of biological aging, including DNA, free radicals, and a stronger immune system. The results are clear enough for rodents, and experiments with primates have begun to confirm that caloric restriction is effective there as well (Couzin, 1998). However, more recent research has found just the opposite: Caloric restriction with rhesus monkeys did not contribute to "improved survival" (Mattison et al., 2012).

In human terms, caloric reduction would mean surviving on a diet of 1,400 calories a day, but, in return, it would mean, in theory, gaining 30 extra years of life. To achieve this goal, Roy Walford (1986), one of the premier investigators of the biology of aging, has proposed a so-called high-low diet that incorporates high nutritional value with low calories.

A similar approach is suggested by *cryobiology*, or the study of organisms at low temperatures. Lowering internal body temperature can increase life span in fruit flies as well as vertebrates, such as the fence lizard, an animal that lives twice as long in New England as its cousins do in sunny, warm Florida. Experiments with fish demonstrate that with lower temperature, life span is prolonged in the second half of life. Lower temperature can significantly reduce DNA damage. We don't yet know whether cryobiological processes apply to warm-blooded animals like humans. However, calorie restriction also seems to lower body temperature a small amount. Calorie-restricted mice have a lower average body temperature, and the temperature changes according to biorhythm.

Caloric restriction somehow protects genes from damage by the environment and perhaps strengthens the immune system. Caloric restriction also reduces the incidence of cancer. The experimental findings on caloric reduction converge with

what is known about indirect regulation of genetic expression that controls the aging process.

Some recent evidence in human clinical trials suggests that caloric restriction, without malnutrition, can reduce vulnerability to disease and slow the process of aging in human beings. But the gains here come from dramatically changing a person's diet. It is reminiscent of the old joke: "Doctor, if I follow your low-calorie diet, will I live longer or will it just seem longer?" Biologists are now looking for the cellular and molecular mechanism by which caloric restriction works, offering the possibility that lifespan extension could be achieved by interventions other than diet (Anderson, Le Couteur, & de Cabo, 2018).

Thinking Critically: Caloric Restriction

Would you be willing to experiment in your own life by restricting the number of calories you consume, not for weight loss purposes, but in the hopes of living longer? For what duration of time would you run your self-experiment? What

changes in your lifestyle would you need to make in order to be successful (in addition to restricting your calories!)? What are some of the challenges you might face? Are there any other "lifespan extension" interventions you'd be willing to try?

Genetic Approach

Many lines of evidence point toward the central role of genetics in fixing the longevity of each species, although for any individual, length of life is the result of both genetic and environmental factors. We often think of genetic inheritance as the element that is fixed and unalterable, but some genetic studies have shown a dramatic ability to improve maximum life span over generations.

For example, studies have been conducted on bread mold, fruit flies, mice, and nematode worms. In all these species, genetic manipulation has been shown to modify maximum life span. Some mutated forms of nematode worms have exhibited substantial increases. Among mice, large differences in average life expectancy and maximum life span exist among different strains because of hereditary differences. In the fruit fly, scientists have achieved an increase in average as well as maximum life span by using artificial selection as a breeding technique.

Some recent genetic experiments have produced astonishing gains in longevity. For example, Michael Rose, a population geneticist, used artificial selection to produce fruit flies with a life span of 50 days (double the normal average of 25 days); the equivalent would be a human being living to 240 years of age. Rose, in effect, has in the laboratory mimicked an increase in the evolutionary rate of

change. As a result, successive generations of fruit flies passed along genes favoring prolonged youth and longevity (Rose, 2005).

Thomas Johnson, a behavioral geneticist, went further and altered a single gene (known as Clock-1) out of the roundworm's 10,000 genes. He also achieved a doubling of the worm's 3-week life span (Johnson, 1990). Still other studies suggest that in some fruit fly populations, the risk of mortality may decrease with advancing age, a finding that challenges previous assumptions about maximum life span (Barinaga, 1992). These dramatic successes, through breeding or direct genetic manipulation, point to the way that genetic change may have come about rapidly through natural selection.

Whether any of these findings can be applied to humans is, again, unknown, but we can draw some conclusions about the genetics of aging. For instance, in at least several of the animal studies cited here, the genes involved governed antioxidant enzymes and mechanisms for repair of damage to DNA, which have been at the center of several theories about the biology of aging. Second, in the species benefiting from genetic change, a small number of genes have been involved in determining longevity. Thus, these results could possibly be applied to higher animal species.

New horizons for genetic application are already visible. Scientists have found a way to double the life of skin cells by switching off the gene that regulates production of a specific protein responsible for manifestations of aging. A similar method of genetic engineering has been used with tomatoes, permitting them to be stored and shipped without decay. The key here is the so-called mortality genes, which determine the number of times that cells divide. Thus, this intervention addresses the Hayflick limit, which remains central to aging at the cellular level. Even without affecting maximum life span, this sort of gene therapy could have major applications in the future, perhaps leading to a cure for age-related diseases such as Parkinson's, Alzheimer's, and cancer.

The recent Human Genome Project has produced a comprehensive map of the entire sequence of genes on the human chromosome. Genetic engineering could draw on that knowledge in ways that might dramatically change what we have thought of as the process of aging and even our assumptions about the maximum human life span. Such speculations, however, belong to the future.

Global Perspective

Blue Zones for Longer Life

When we think of Italy, we often think of pizza or the ancient city of Rome. But if you're thinking about longevity, think instead about the Italian

island of Sardinia. Demographers have identified its mountain slopes as a distinctive *Blue Zone*, a region of high longevity. In fact, the proportion of



A Japanese grandmother carries her young grandson.

centenarians in Sardinia is more than twice as high as in the rest of Italy. That prompts a question: Why do people there live so long? Both lifestyle and genetics may play a part, but in what proportion? The isolated, mountain-dwelling Sardinians tend to be descendants of settlers dating back to

Source: Buettner (2005).

the Bronze Age. Sardinians have also been known for eating a *Mediterranean diet* and for maintaining a traditional, family-oriented way of life. So, gerontologists wonder, what makes Sardinia such a standout as a Blue Zone for extreme longevity?

Some answers can be found on the opposite side of the globe, in Okinawa, an island in Japan, the country with the greatest longevity. Okinawans have an average life expectancy of more than 82 years and also enjoy an old age largely free of disabilities. Rates of heart disease, cancer, and dementia are lower than among Americans. Again, we wonder, what's the reason? Some observers point to the Japanese word *ikigai*, which means "purpose for living." A traditional Okinawan diet of vegetables, tofu, and a small amount of fish is also part of the picture. Finally, Okinawans have strong social ties among family, friends, and neighbors. Gerontologists have confirmed that the powerful effect of such social networks on longevity is comparable to giving up smoking a pack of cigarettes a day.

Blue Zones around the world are natural laboratories for the study of longevity. Lessons learned from these regions can help give guidance for a healthier and happier old age closer to home.

Compression or Prolongation of Morbidity?

Biology has not yet succeeded in unraveling the mystery of aging, so it is not surprising that medical science has produced no technology or method for raising the maximum life span of human beings. Caloric reduction and genetic methods have worked with lower organisms, but human beings are more complex organisms, and the research studying humans has yet to provide conclusive evidence on this point. To extend life expectancy and promote healthy aging, we may need to identify genes responsible for harmful mutations, whether expressed early or late in life. A parallel approach would be to identify those environmental agents

(e.g., diet, sunshine, smoking) that have a cumulative impact on sickness and survival. Health promotion might then succeed in postponing chronic illness, thereby making the idea of the one-horse shay more possible.

Progress in these directions depends on answering the question of why we age. In the reading titled “Why Do We Live as Long as We Do?” Leonard Hayflick highlights some basic facts about the biology of aging that are relevant to our hopes for compressing or extending our longevity.

In the other readings that follow, we hear different voices in the compression-of-morbidity debate. On one side, James F. Fries and Lawrence Crapo take the optimistic position that improving life expectancy will also lead to compressed morbidity: People will live longer and not be sick until the very end of their natural life span. Fries and Crapo believe that successful aging involves optimizing life expectancy while reducing physical, psychological, and social morbidity. Their “sunny” view of aging is paradoxical, in a way, because it presumes that the maximum life span remains fixed, a limitation other biologists might reject. In support of their view, we can note that some postponement of morbidity has already occurred: Declining death rates from heart disease and stroke reflect improvements in health due to lifestyle, diet, hypertension detection, and so on.

But not everyone is persuaded by Fries and Crapo’s interpretation of the evidence on morbidity and death rates. Researchers and demographers disagree about whether compression of morbidity is occurring and whether maximum human life span is really finite, as Fries believes. Vincent Mor notes that, although it seems that morbidity rates and functional decline have decreased in the industrialized world, because of population aging, there will be more older people than ever before suffering from chronic and disabling health conditions. Still other conditions, such as depression and sensory losses, are not linked to causes of improved life expectancy at all, so we remain haunted by the fear that longer life might mean only prolongation of morbidity (Olshansky, Carnes, & Cassel, 1990; Verbrugge, Lepkowski, & Imanaka, 1989).

Finally, as we look further into the 21st century, we might consider possibilities beyond the range of current science and medicine. In visionary terms, biologist Aubrey de Grey believes, contrary to most gerontologists, that aging is a disease, a condition to be “cured.” Some scientists argue that if we began to accept the idea that aging is a disease, it could dramatically alter the way we think about getting old (Adam, 2019; Sinclair, 2019). Some technologists active in Silicon Valley take the view that now is the time to prepare for living indefinitely (Regalado, 2019).

S. Jay Olshansky, by contrast, reminds us that a “cure for aging” is a fantasy that has deluded seekers for biological immortality down through the ages. Olshansky favors research on the biology of aging, but he distrusts any claim that raising the maximum life span is right around the corner.

The debate over why we grow old shows that scientific “facts” are rarely as simple as we imagine. The meaning of the facts depends on our theories and interpretations, and our own hopes about the aging experience, and it is therefore subject to debate and construction in different ways. Different views of the facts

about illness and survival in old age today are leading us to new ways of thinking about mortality and morbidity among older adults. Indeed, the debate about compression of morbidity is rooted in biology, but it has implications for health care economics in an aging society as well as how individuals experience later life. What can we expect in the future if medical technology succeeds in prolonging life still more? How much emphasis should we give to health promotion as opposed to curing diseases in old age? Whatever our view, the compression-of-morbidity theory stands out as an important reminder of how critical biological research will be for the future of an aging society.

Focus on Practice

Health Promotion

Can we take steps now to control our own longevity? The consumer market for “antiaging” products is growing. Magazines on the subject can be found on every newsstand. But most claims for life-extending products are not proved by science. For example, melatonin, antioxidants, human growth hormone, and DHEA have all been hailed as antiaging breakthroughs, but proof has not lived up to the promise (Weintraub, 2010). There are no diets, hormone injections, or vitamin or mineral supplements that have so far been proven to slow down the process of aging (Butler et al., 2002). However, it is possible that a breakthrough in our knowledge of the biology of aging could give us ways to slow down aging in the 21st century.

When we think about the prospect of slowing the process of aging or dramatically extending maximum life span, many questions present themselves. Would people really want to triple their life spans? Would they want to hold the same job or be married to the same person for 150 years? What would society be like if people lived for centuries instead of decades (Post & Binstock, 2004)?

These questions are still in the realm of science fiction, but many interventions already have been

shown to promote health and longevity in ways that can benefit people today (Haber, 2016). For example, the death rate from cardiovascular disease has been cut in half in the past two decades chiefly because of a reduction in high-risk behaviors such as smoking. Changes in diet or exercise patterns could provide further gains in adult life expectancy.

The secrets to keeping the effects of aging at bay are actually well known (Brody, 2001). Most of the causes of lost years of life today are related to lifestyle choices: alcohol, tobacco, exercise, and diet (Arking, 1991). Herbert de Vries, a highly regarded exercise physiologist from the University of Southern California, has estimated that regular exercise could give a huge boost to the life expectancy of most people. Millions of Americans have already started eating a low-fat, high-fiber diet, just as they have given up smoking. Others go even further and seek to minimize free radical damage to cells by including more antioxidant carotenes in their diets (Walford, 1986).

The topic of health promotion and aging engenders a familiar argument between optimists and pessimists. On the one hand, Hayflick argues that calorie-restricted, long-living mice are merely living out their fixed natural life spans. In the end, our

(Continued)

(Continued)

genetic program prevails, and environmental interventions, such as diet, can accomplish only a limited amount. If Hayflick is right, then Walford (1986), like Juan Ponce de León, has embarked on a vain search for the fountain of youth.

But the optimists hold a different view. According to one scenario for the future, as a result of prudent nutrition and more exercise, the average life span could well rise from 76 to beyond 80 years during the 21st century. Then, early in the next century, through hormone replacement and genetic engineering, the maximum life span could push well beyond the current limit of 120 years. Optimists believe that lifestyle enhancement and new technologies could combine to delay or even reverse aging, thus extending youthfulness and pushing the limits of the life span itself (Hall, 2003).

Steps to improve longevity are already becoming part of popular culture. Changes in diet and exercise, reductions in smoking, and health-promotion activities of many kinds are now far more common than they were two decades ago.

In thinking about these scenarios for the future, we should retain a measure of skepticism. We

should also focus on practical steps that are proven and feasible right now. Health promotion has to be based on science, not on conjecture, fear of frailty and mortality, or hopes for the future.

Health promotion seems clearly to be a desirable trend, but it also raises some difficult questions about personal and social responsibility (Centers for Disease Control and Prevention, 2003). What should we do about groups in our society who cannot or will not change their unhealthy behaviors? Are harmful behaviors ultimately a matter of free choice, or do environmental and social factors also shape behavior? The cost of Medicare depends a great deal on the cost of chronic illnesses. If we embrace an ethic of personal responsibility for health care, might we be less willing to support public funding for medical care? Should health promotion take into account inequality in income, education, and access to health care? How do we motivate people in favor of health promotion when the results of “bad choices”—such as smoking, poor diet, lack of exercise, or use of alcohol—don’t show up until decades later? These questions will remain both personal and societal issues for years to come.

Urban Legends of Aging

“Drinking red wine will make you live longer.”

A lot of people believe this one based on a TV story on *60 Minutes*. There is a substance called resveratrol that is found in red wine and grapes and has been shown by some laboratory studies to promote longevity in mice (Bauer, 2006). But you would have to drink

amounts of wine far beyond what is humanly possible in order to have any of the hypothetical effects. Studies of resveratrol on human longevity continue, but in the meantime, wine lovers will need to find a different excuse for drinking more wine.

Reading 5: Why Do We Live as Long as We Do?

Leonard Hayflick

The premise upon which the following ideas rest is that the survival of a species depends upon a sufficient number of its members reaching sexual maturation and producing enough progeny that reach independence to guarantee the continuation of the species. Natural selection, guided by beneficial mutations, has molded the biology and the survival strategies of all living things to achieve this fundamental goal. As previously indicated, the best strategy to guarantee that an animal or human will survive long enough to mature sexually is to provide it with more than the minimum required capacity in its vital organs. In this way, if damage or pathology occurs in an essential system before sexual maturation, there is a greater likelihood that the animal will still survive to reproduce and pass on to its progeny its superior physiological capacity. This general strategy, essential for the survival of all species, has evolved in different ways for various life forms. Energy and purpose are concentrated to achieve reproductive success, which assures the immortality of the genes. The continuation of the germ line is the driving force of natural selection. Longevity of individual animals is of secondary importance.

Animals are selected through evolution for having physiological reserves greater than the minimum necessary to reach sexual maturation and rear progeny to independence, but once this critical goal has been attained, they have sufficient excess reserve capacity to “coast” for a period of time, the remainder of which we call their life span. This time period, then, is *indirectly* determined genetically. During the coasting period the animal functions on its excess capacity. This physiological reserve

of energy and functional capacity does not renew at the same rate that it incurs losses, so molecular disorder—entropy—increases. Random changes or errors appear in previously well-ordered molecules, resulting in the normal physiological losses that we call age changes. These changes increase the vulnerability of the animal or human to predation, accidents, or disease (Holiday, 2004).

What happens after reproductive success and raising progeny to independence is not important for the survival of a species. What happens next, of course, is aging and, ultimately, death. Wild animals, because they rarely live long enough, do not experience aging. The entire scenario is analogous to the ticking on of a cheap watch after the guarantee period has ended. The watch’s guarantee period corresponds to the time spent by animals to reach sexual maturation and to finish rearing progeny. After the warranty period ends, the watch does not simply “die” because it would be prohibitively expensive to put a mechanism in a cheap watch that would cause it to self-destruct on the day after the guarantee expires. Likewise, it would cost too much of energy to make a system in an animal that would cause it to die precisely on the day that its progeny become independent. What happens after the guarantee period expires in watches and after the reproductive period in animals is aging, which inexorably leads to failure in watches and death in animals.

In this way of thinking, survival to sexual maturation is accomplished by postponing until after reproductive maturity the effects of genes that perform well in youth but become mischief-makers later. When these once good, now harmful genes

Source: “Why Do We Live as Long as We Do?” from *How and Why We Age* by Leonard Hayflick, PhD. Copyright ©1994 by Cell Associates, Inc. Foreword copyright © 1994 by Robert N. Butler, MD. Reprinted by permission of Leonard Hayflick, PhD.

eventually do switch on, they provide the blueprint for age changes. . . .

Until now we have almost always thought about aging by asking, “Why do we age?” And biogerontologists have designed their experiments to attempt to answer this question. The results have not been impressive. With the exception of the discovery that age changes occur within individual cells, we do not know much more today about the fundamental cause of aging than we did a century ago. Most of what we have learned is descriptive: we know much more about *what* happens than we did before but very little about *why* it happens. Biogerontologists have described changes that occur as we age from the molecular level up to the level of the whole animal. However, these descriptive observations add little to our understanding of the basic process.

It is for this reason that George Sacher proposed that we have been asking the wrong question. Instead of asking “Why do we age?” we should ask “Why do we live as long as we do?” By asking that question we might reorder our thinking and be able to design experiments to obtain more fundamental information. I think this is a useful new approach and I hope that more biogerontologists will come to appreciate the subtle but important reason for asking this better question.

Implicit in the question “Why do we live as long as we do?” is the idea that our longevity has increased and may be capable of increasing further. That appears to be true, since the human life span is known to have increased since prehistoric times. If our life span has

increased, then it is likely that the start of the aging process has changed within the new time frame. Based on this reasoning, we may conclude that the aging process is malleable, that we can understand how it occurs, and that perhaps we can tamper with it. . . .

I do not believe that we have a sufficient understanding of either the aging process or the determinants of life span to expect to significantly manipulate either during our lifetime. A more important issue, however, is whether it would be desirable to manipulate either process. The capacity to halt or slow the aging process, or to extend longevity, would have consequences unlike most other biomedical breakthroughs. Virtually all other biomedical goals have an indisputably positive value. It is not at all clear whether or not the ability to tamper with the processes that age us or determine our life span would be an unmixed blessing. As pointed out earlier, resolution of all disease and other causes of death would result in a life expectation of about one hundred years. I am apprehensive about extending average life expectation beyond age one hundred once the leading killers are resolved because the result would be disease-free but nonetheless functionally weaker, still inexorably aging people. . . .

Virtually all biomedical research has the implicit goal of eliminating disease in all of its forms. It is logical to ask what will happen if we are successful. The answer seems to be that if we are successful, our life expectation will be increased but we will eventually die from the basic aging processes that lead to failure in some vital system.

Reading 6: Vitality and Aging

Implications of the Rectangular Curve

James F. Fries and Lawrence Crapo

Why do we age? Why do we die? How can we live longer? How can we preserve our youth? Questions about life, aging, and death are fundamental to human thought, and human beings have speculated

about the answers to these questions for centuries. Our own age values the methods of science—the methods of gathering evidence, of observation, of experiment—above the musings of philosophy.

Yet, philosophical speculation and scientific theory may interact and enhance each other. The scientific theories of Copernicus and the conception of a sun-centered solar system, of Newton and an orderly universe, of Einstein and the relationship between matter, energy, and spacetime, of Darwin and the evolution of species have influenced our notions of who we are, where we are, how we came to be here, and the meaning of life itself. Similarly, the study of health and aging may contribute a new philosophical perspective to these age-old questions about life and death.

The implications of new scientific discoveries are often not widely appreciated for many years. Scientific knowledge develops by small increments within a relatively cloistered scientific community, whose members are sometimes more interested in the basic ideas than in their social implications. . . .

So it is with the study of human aging. The ancient philosophical questions have largely fallen to those who search for the biological mechanisms that affect our vitality and that cause our death. The study of aging as a separate scientific discipline is relatively new and is not yet the province of any single science. Independent observations have been made in medicine, in psychology, in molecular biology, in sociology, in anthropology, in actuarial science, and in other fields. There are remarkable parallels in the ideas that have emerged from these independent fields of research. It is our intention to review these parallel developments and to present a synthesis of scientific ideas about human aging that will offer insights into the fundamental questions about the nature and meaning of the life process, aging, and death.

The Incomplete Paradigm

The growth of scientific knowledge historically has been impeded by thought systems (paradigms) that

worked well for a time but that increasingly failed to explain new observations. For the study of aging, the contemporary paradigm is often called the medical model. The medical model defines health as the absence of disease and seeks to improve health by understanding and eradicating disease. This model of life and health, while useful, has obscured a larger perspective. There are four prevalent beliefs in the medical model that have proved to be limiting (see box). Certainly, few present scholars hold these beliefs literally, but these ideas nonetheless have largely defined contemporary opinion about the aging process.

The Limiting Premises

1. The human life span is increasing.
2. Death is the result of disease.
3. Disease is best treated by medication.
4. Aging is controlled by the brain and the genes.

These four premises seem to imply the following conclusions. If the human life span is increasing, then our scientific goal can be the achievement of immortality. If death results from disease, our objective must be the elimination of disease. If disease is best treated with medication, our strategy is to seek the perfect drug or surgical procedure. With regard to aging, the medical model suggests that we should perform basic research to understand the genetic, neurologic, or hormonal mechanisms that control the process, and then learn to modify them.

Historically, these premises, objectives, and strategies have been useful. They are still worthy and deserving of study and hope. But they are certainly incomplete, and, taken literally, they are misleading. The human life span is not increasing; it has

Source: Vitality and Aging: Implications of the Rectangular Curve by James F. Fries and Lawrence Crapo. New York: W. H. Freeman, 1981. Reprinted by permission of the authors.

been fixed for a period of at least 100,000 years. The popular misconception of an increasing life span has arisen because the average *life expectancy* has increased; the *life span* appears to be a fixed biological constant. Three terms must be understood. The maximum life potential (MLP) is the age at death of the longest-lived member of the species—for human beings, 115 years. The life span is the age at which the average individual would die if there were no disease or accidents for human beings, about 85 years and constant for centuries. The life expectancy is the expected age at death of the average individual, granting current mortality rates from disease and accident. In the United States, this age is 78 years and rising.

Death does not require disease or accident. If all disease and all trauma were eliminated, death would still occur, at an average age not much older than at present. If premature death were eliminated, and it may be in large part, we would still face the prospect of a natural death.

Medical treatment is not the best way to approach current national health problems. The major chronic diseases (atherosclerosis, cancer, emphysema, diabetes, osteoarthritis, and cirrhosis) represent the major present health threats. They are deserving of continued medical research, and further advances are to be expected. But abundant evidence points to personal health habits as the major risk factors for these diseases. Preventive approaches now hold far more promise than do therapeutic approaches for improving human health.

Aging does not appear to be under direct control of the central nervous system or the genes. Rather, the aging process occurs in cells and in organs. The aging process is most likely an essential characteristic of biological mechanisms. The process of aging, or *senescence*, is an accumulation in cells and organs of deteriorating functions that begins early in adult life. Aging may result from error-prone biological processes similar to those that have led to the evolution of species.

So the prevailing ideas about aging are incomplete. An increasing body of new scientific information requires revision and extension of these ideas.

The time for a new synthesis has arrived, heralded by a number of new discoveries that do not fit well into the old paradigm but that as yet lack a coherent paradigm of their own.

Competing Themes

Changes in our ideas about health and aging are now being reflected in our social institutions and lifestyles. Change in a prevalent system of thought is often turbulent, and such turbulence is now manifest in health by a set of new movements. Within the medical community, there has been increasing recognition of the importance of preventive medical approaches. Such technical strategies as mass screening have been promoted. New departments of preventive medicine have been developed within medical schools; previously, such efforts were largely carried out within schools of public health. These developments are not entirely successful (screening efforts have proved disappointing, and some departments of preventive medicine have not thrived), but their very creation acknowledges the ferment of new approaches to health care.

The public has asked for more active involvement in consumer choices and for more accurate information on which to base such choices. In response, a self-care movement in health has developed, which now represents a considerable social force. At its best, this movement encourages critical consumption of medical services and increased autonomy from professional dominance. At its worst, the self-care movement takes an adversary stance and would replace professional medical treatment with idiosyncratic folk remedies. Still, the growth of these movements indicates discontent with the prevailing medical orthodoxy.

Recent changes in personal lifestyles have been even more significant. Joggers organize footraces in which tens of thousands compete, and cocktail party conversations concern the number of miles run per week. The number of militant antismokers has grown, and the nonbelievers are being packed into smaller and smaller spaces in the back of the airplane. Such

spontaneous social changes are very likely to have constructive effects on health, and we applaud them, but the point is that the phenomenon itself represents a profound changing of the public consciousness.

Within professional medicine, new themes are evident. There is an increased interest in long-term patient outcome as a goal and less interest in correcting the trivial laboratory abnormality that does not materially affect the patient. Benefit-cost studies are sometimes advocated as a solution to the astronomical increases in the cost of medical care. Many observers have pointed out that orthodox medical approaches have reached the area of diminishing returns. The quality of life, rather than its duration, has received increasing emphasis.

Both psychologists and physicians have recently described strong relationships between psychological factors and health, and theories explaining such relationships have been developed that emphasize life crises, helplessness, loss of personal autonomy, depression, and other psychological factors. Correction of some psychological problems, it is implied, will improve health, and indeed the circumstantial evidence that this may be true is quite convincing. Again these approaches are outside the orthodoxy of the medical model.

Two new research areas have recently been emphasized—chronic disease and human aging. Increasingly, researchers recognize the central roles that aging and chronic disease play in our current health problems. The study of aging and chronic disease is oriented toward long-term outcomes, is interdisciplinary, requires preventive strategies, seeks to demonstrate the relevance of psychological factors, and uses lifestyle modification as a major tactic. The student of aging and the student of the diseases of the aged now have a unique opportunity to harmonize the incomplete old orthodoxy and the emerging new themes.

A New Syllogism

Using new knowledge of human aging and of chronic disease, we attempt here to provide a model that

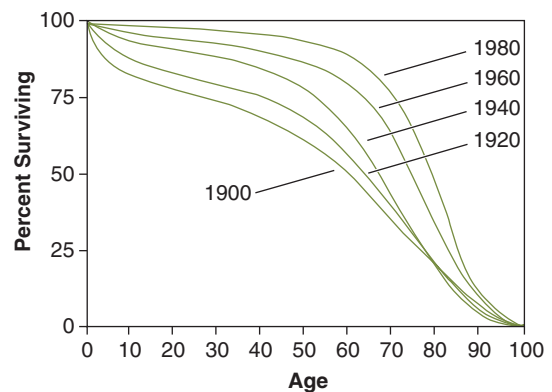
harmonizes these competing and chaotic themes, one that points toward new strategies of research and of health attainment. Our theoretical structure allows predictions to be made, and the predictions are strikingly different from those traditionally expected.

These curves are correct. They converge at the same maximum age, thereby demonstrating that the maximum age of survival has been fixed over this period of observation.

Figure 1 shows the actual data. Quite . . . startling conclusions follow from these data. The number of extremely old persons will not increase. The percentage of a typical life spent in dependency will decrease. The period of adult vigor will be prolonged. The need for intensive medical care will decrease. The cost of medical care will decrease, and the quality of life, in a near disease-free society, will be much improved.

Adult life may be conveniently divided into two periods, although the dividing line is indistinct. First, there is a period of independence and vigor. Second, for those not dying suddenly or prematurely, there is a period of dependence, diminished capacity, and often lingering disease. This period of infirmity is the problem; it is feared, by many, more

Figure 1 Human Survival Curves for 1900, 1920, 1940, 1960, and 1980



Source: U.S. Bureau of Health Statistics.

than death itself. The new syllogism does not offer hope for the indefinite prolongation of life expectancy, but it does point to a prolongation of vitality and a decrease in the period of diminished capacity.

There are two premises to the syllogism; if they are accepted, then it follows that there will be a reversal of the present trend toward increasing infirmity of our population and increased costs of support of dependency. . . . The first premise is almost certain; the second is very probable. If, after careful evaluation of the supporting data, one accepts the premises of this syllogism, then one must accept the conclusion and the implications of the conclusion.

Some Questions of Semantics

Nuances of meaning may mask the substance of a subject, and slight changes in emphasis may allow a new perspective to be better appreciated. There are problems with several of the terms often used to describe health, medical care, and aging. Among these are *cure*, *prevention*, *chronic*, *premature death*, and *natural death*. We will use these terms in slightly different senses than is usual.

Cure is a term with application to few disease processes other than infections. The major diseases of our time are not likely to be cured, and we have tried to avoid this term. *Prevention* is better but is unfortunately vague; this term, as we shall see, is sometimes misleading. We prefer the term *postponement* with regard to the chronic diseases of human aging, since prevention in the literal sense is difficult or impossible. *Chronic* is a term usually used to denote illnesses that last for a long period of time. It serves as a general but imprecise way of distinguishing the diseases that may be susceptible to cure (such as smallpox) from those better approached by postponement (as with emphysema). Regrettably, this important distinction cannot be based solely on the duration of the illness, since some diseases that last a long time both are not chronic conditions and might eventually be treatable for cure (such as rheumatoid arthritis and ulcerative colitis). We limit our use of the term *chronic* to those conditions that are

nearly universal processes, that begin early in adult life, that represent insidious loss of organ function, and that are irreversible. Such diseases (atherosclerosis, emphysema, cancer, diabetes, osteoarthritis, cirrhosis) now dominate human illness in developed countries. We have defined *premature death* simply as death that occurs before it must, and we have used *natural death* to describe those deaths that occur at the end of the natural life span of the individual. . . .

A New Syllogism

1. The human life span is fixed.
2. The age at first infirmity will increase.
3. Therefore the duration of infirmity will decrease.

The Rectangular Curve

Survival curves for animals show a similar pattern of rectangularization with domestication or better care. Old age in wild animals is very rare, as it probably was for prehistoric man living in a dangerous environment. In uncivilized environments, accidental deaths and violent deaths account for a greater proportion of deaths than the biologically determined life-span limit. For the great majority of wild animal species, there is a very high neonatal mortality, followed by an adult mortality rate that is almost as high and is nearly independent of age. In such environments, death occurs mostly as a result of accidents and attacks by predators. One day is about as dangerous as the next.

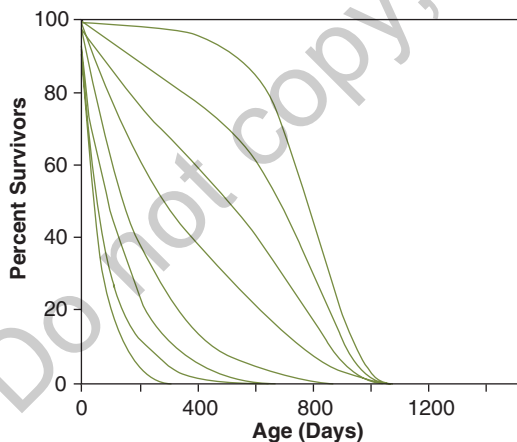
By contrast, animals in captivity begin to show survival curves much more rectangular in shape. Such animals are removed from most threats by accident or predator, and for them the second term of the equation, that of the species' life span, begins to dominate. Figure 2 shows theoretical calculations of this phenomenon after Sacher (1977). Such rectangularization has been documented for many

animals, including dogs, horses, birds, voles, rats, and flies. . . .

Figure 3 is drawn from the data Shock developed in 1960, and it is modified only slightly from what has been called “the most frequently shown data in the field of gerontology.” The data show that many important physiological functions decline with age, and the decline is quite close to being a straight line. It is important to emphasize that these data were obtained from healthy human subjects in whom no disease could be identified that was related to the function being measured. Thus, the observed decline does not depend on disease.

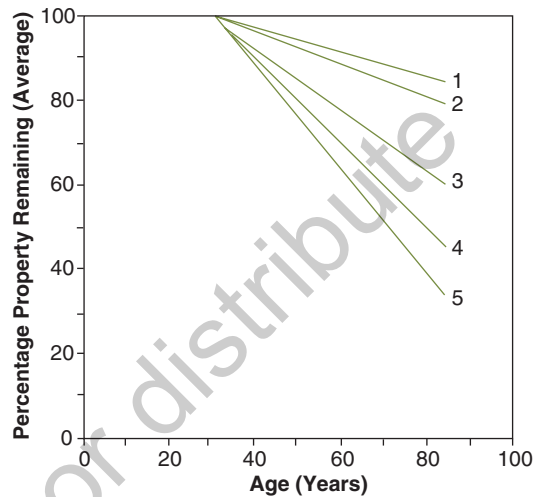
Figure 3 is a major oversimplification of complex data. . . . The lines are not actually as straight as portrayed, and some of the data have been contested. The point is that a considerable body of research supports a gradual, nearly linear decrease in organ function with age.

Figure 2 Theoretical Survival Curves for an Animal Become Progressively More Rectangular as the Environment Progresses From Wild to Domestic



Source: Redrawn from G. A. Sacher, “Life Table Modification and Life Prolongation,” in C. E. Finch and L. Hayflick, eds., *Handbook of Aging*, Van Nostrand Reinhold, 1977.

Figure 3 The Linear Decline of Organ Function With Age



Source: U.S. Bureau of Health Statistics. Redrawn from N. Shock, “Discussion on Mortality and Measurement of Aging,” in B. L. Strehler, S. D. Ebert, H. B. Glass, and N. W. Shock, eds., *The Biology of Aging: A Symposium*. Copyright © 1960, American Institute of Biological Sciences.

Normal, healthy organisms maintain an excess organ reserve beyond immediate functional needs. We have four to ten times as much reserve function as we need in the resting state. The heart during exercise can increase its output sixfold or more. The kidneys can still excrete waste products adequately if five-sixths of the functional units, the nephrons, are destroyed. Surgeons can remove one entire lung, and sometimes part of the second, and still have an operative success. Three-fourths of the liver can be removed, under some circumstances, and life is still maintained.

However, the mean level of reserve in many of our organs declines as we grow older. We seldom notice this gradual loss of our organ reserve. Only in the circumstances of exceptional stress do we need all that excess function anyway. Shock and others suggest that the decline may be plotted as a straight line.

Homeostasis and Organ Reserve

The human body may be viewed as a remarkable assembly of components functioning at various levels of organization. Systems of molecules, cells, and organs are all marvelously integrated to preserve life. The eminent nineteenth-century physiologist Claude Bernard emphasized that these integrated components act to maintain a constant internal environment despite variable external conditions. Bernard saw life as a conflict between external threats and the ability of the organism to maintain the internal milieu.

These fundamental observations have stood well the test of time. Indeed, the human organism cannot survive if the body temperature is more than a few degrees from normal, if acid-base balance is disturbed by a single pH unit, or if more than 20% of the body water is lost. Body chemicals are regulated closely, often to within 2% or 3% of an average value. A change in one direction in body constituent is often followed by a complicated set of responses that act to restore equilibrium.

Bernard also noted that living beings change from a period of development to a period of senescence or decline. He stated that “this characteristic of a determined development, of a beginning and an end, of continuous progress in one direction within a fixed term, belongs inherently to living beings.”

The regulation of bodily functions within precise limits was termed *homeostasis* by Cannon (1932). Living organisms under threat from an extraordinary array of destructive sources maintain their internal milieu despite the perturbations, using what Cannon called the “wisdom of the body.” Dubos (1965) has pointed out that this “wisdom” is not infallible. Homeostasis is only an ideal concept; regulatory mechanisms do not always return bodily functions to their original state, and they can sometimes be misdirected. Dubos sees disease as a “manifestation of such inadequate responses.” Health corresponds to the situation in which the organism responds adaptively and restores its original integrity.

The ability of the body to maintain homeostasis declines inevitably with decreasing organ reserve. Figure 3 shows the decline for lungs, kidneys, heart, and nerves. The decline is not the same for all individuals, nor is the decline the same for all organs. For example, nerve conduction declines more slowly than does maximal breathing capacity. And some organs, such as the liver, intestinal lining cells, and bone marrow red cells, seem to show even less decline with age.

The important point, however, is that with age there is a decline in the ability to respond to perturbations. With the decline in organ reserve, the protective envelope within which a disturbance may be restored becomes smaller. A young person might survive a major injury or a bacterial pneumonia; an older person may succumb to a fractured hip or to influenza. If homeostasis cannot be maintained, life is over. The declining straight lines of Figure 3 clearly mandate a finite life span; death must inevitably result when organ function declines below the level necessary to sustain life. . . .

Implications of the Rectangular Curve

The rectangular curve is a critical concept, and its implications affect each of our lives. The rectangular curve is not a rectangle in the absolute sense, nor will it ever be. The changing shape of the curve results from both biological and environmental factors. Many biological phenomena describe what is often called a normal distribution. This is the familiar bell-shaped or Gaussian curve. If one studies the ages at death in a well-cared-for and relatively disease-free animal population, one finds that their ages at death are distributed on both sides of the average age of death, with the number of individuals becoming less frequent in both directions as one moves farther from the average age at death. A theoretical distribution of ages at death taking the shape of such a curve in humans is shown in Figure 4. This simple bell-shaped curve, with a mean of 85 years and a standard deviation of 4 years, might exemplify the age at death of an ideal disease-free,

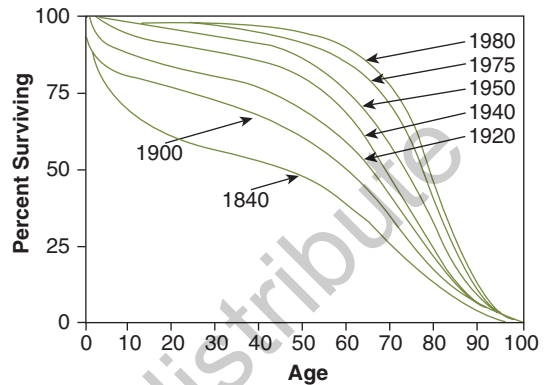
violence-free human society. The sharp downslope of the bell-shaped survival curve is analogous to the sharp downslope of the rectangular curve. In Figure 5, the first part of the curve becomes ever flatter, reflecting lower rates of infant mortality. Several factors prevent the total elimination of infant mortality and thus prevent the curve from becoming perfectly horizontal. These premature deaths are the result of birth of defective babies, premature disease, and violent death. Improvements in medicine can lower but never eliminate the birth of defective babies and premature disease. It seems likely that the ever dominant proportion of violent deaths during early life will prove recalcitrant to change and will form an ever larger fraction of total premature deaths.

So, the rectangular curve has an initial brief, steep downturn because of deaths shortly after birth, a very slow rate of decline through the middle years, a relatively abrupt turn to a very steep downslope as one nears the age of death of the ideal Gaussian curve, and a final flattening of the curve as the normal biological distribution of deaths results in a tail after the age of 90. . . .

Thus, two profound characteristics of the mortality of man, the elimination of premature disease and the development of the sharp downslope representing natural death, have remained far from the public consciousness. These data have been available for many years. The first solid comments about rectangularization of the human survival curve can be found in prophetic statements in the 1920s. Many statisticians and actuaries working with national health data since that time have noted the increasingly rectangular shape of the curve, and many have speculated that it represents a natural species life limit. Entire theories of the aging process . . . have been built around the observed fact of a natural life span in man and animals. Yet, the public has remained largely ignorant of these developments.

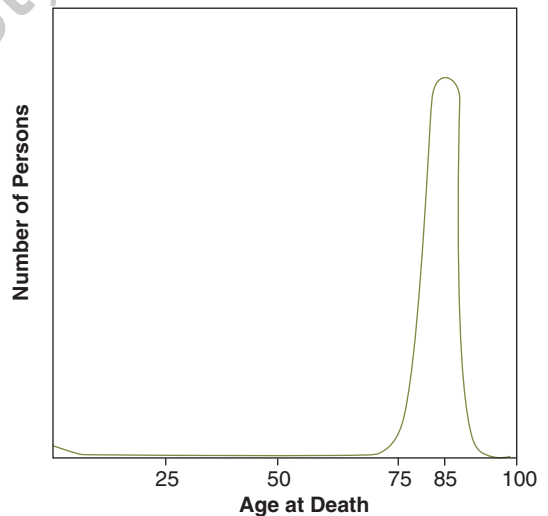
A society in which life expectancy is believed to increase at every age and in which one becomes increasingly feeble as one grows older is a society heading for trouble. A society moving according to

Figure 4 Sequential Survival Curves in the United States



Source: U.S. Bureau of Health Statistics.

Figure 5 Ideal Mortality Curve in the Absence of Premature Death



Source: U.S. Bureau of Health Statistics.

the curves of Figure 5, as our society is, is a society moving toward a world in which there is little or no disease, and individuals live out their natural

life span fully and vigorously, with a brief terminal period of infirmity. . . . Dramatic changes in mortality patterns result in equally dramatic social changes.

References

Cannon, W. B., *The Wisdom of the Body*, New York: Norton, 1932.

Dubos, R., *Man Adapting*, New Haven, CT: Yale University Press, 1965.

Sacher, G. A., "Life Table Modification and Life Prolongation," in J. Birren and C. Finch, eds., *Handbook of the Biology of Aging*, New York: Van Nostrand Reinhold, 1977, pp. 582–638.

Reading 7: The Compression of Morbidity Hypothesis

A Review of Research and Prospects for the Future

Vincent Mor

Cross-national evidence for the validity of the compression of morbidity hypothesis originally proposed by Fries is generally accepted. Generational improvements in education and the increased availability of adaptive technologies and even medical treatments that enhance quality of life have facilitated continued independence of older persons in the industrialized world. Whether this trend continues may depend upon the effect of the obesity epidemic on the next generation of older people.

For more than 2 decades, gerontologists have been debating the implications of the progressive reductions in old-age mortality and increasing survival of the very old, with some noting that lengthening life necessarily extends the duration of functional dependency in an aging population. It has been hypothesized that increasing survival does not necessarily mean that the added years of life accruing to older individuals would be spent sick and disabled.¹ This compression of morbidity hypothesis stated that better health care, an active lifestyle, and greater preventive health behavior

would preserve health even in the face of increasing survival. Shortly thereafter,² other researchers were able to quantify "active life expectancy," setting the stage for the application of sophisticated demographic techniques to test the hypothesis that the duration of morbidity and disability would not increase or might even be reduced in the population, even as mortality was decreasing. . . .

There are several important clarifications that should be made to better understand the dispute surrounding the compression of morbidity hypothesis. First, using morbidity and disability interchangeably ignores the evidence that the presence of different diseases may have quite different effects on mortality, hospitalization (a health services use-based marker of real morbidity), disability, and functional impairment.⁹ For example, although cardiovascular disease mortality declined, partially because of improved treatment, outreach efforts also led to earlier identification of more individuals with early-stage disease. Earlier detection of disease (morbidity) is one reason why increases in the prevalence

Source: "The Compression of Morbidity Hypothesis: A Review of Research and Prospects for the Future" by Vincent Mor, PhD, in *Journal of the American Geriatrics Society*, 53(9), pp. 308–309. Copyright © 2005 by the American Geriatrics Society.

of chronic illness have not translated into increases in disability and impaired function.^{10,11} . . .

Efforts to understand what has caused the reduced rate of functional decline in the aged population have focused on the improved education of the newer cohorts of elderly, improvements in the built environment (e.g., barrier-free housing, elevators) and material amenities, and improvements in function-enhancing medical interventions.¹⁴ First, the average 75-year-old in developed countries of the 1990s is less likely to be constrained by stairs and more likely to have an automobile and to live in housing that is architecturally barrier free. Second, that same older person has his/her Social Security check directly deposited, meals warmed in a microwave, and groceries ordered over the telephone. Third, the disability of cataracts has been virtually eliminated with new surgical techniques, disabling arthritic hips and knees are routinely replaced, and improvements in the medical management of heart disease, for example, clearly facilitate retained functioning and independence. The relative contributions of each of these major classes of technological innovations to improvements in population functioning is not known, but it is likely that these, as well as other significant shifts in the lives of older persons in the industrialized world, have improved their quality of life and functional independence.^{6,15} Indeed, it may be that the education advantage observed in most studies that find reduced functional decline is partially achieved by older persons being able to manipulate the environment without exertion.¹¹

Nevertheless, before we celebrate and ignore the pending explosion of the aged population in all industrialized countries in the world, it is critical to understand that, even if the rate of functional decline has dropped several percentage points over the last decades, the sheer numerical increase in the size of the aged population over the next 30 years will mean that the number of older persons who are dependent, disabled, and suffering the functional consequences of multiple chronic conditions will be larger than it has ever been, far larger than most countries are prepared to manage. Healthy life

expectancy (another expression of “active life expectancy”) is increased via reductions in mortality and morbidity, but disease prevalence is increasing, so functional independence must be maintained in the face of advancing age and comorbidity.¹¹

The emerging epidemic of obesity among the middle-aged population, particularly in the United States, is another factor that may temper the optimism some have expressed about being able to compress the duration of functional morbidity.^{6,15,16} Recent evidence of the rising prevalence of obesity in the middle aged and the consequences of obesity for independence and for the ability to function and fill social roles suggests that we may be in for a reversal of the hard-fought gains of functional decline.^{12,17–19} Indeed, these findings reinforce the importance of an active lifestyle and low-risk health habits such as avoiding obesity in maintaining functional independence into the advanced years. Although technology, the built environment, and medical care advances may have yielded benefits in function and quality of life for the “greatest” generation, unless the health habits of the baby boomers change dramatically, future researchers may be trying to explain the cohort effect that found a short-lived reduction in the duration of age-related functional impairment.

Notes

1. Fries J. Aging, natural death and the compression of morbidity. *N Engl J Med* 1980; 303: 130–133.
2. Katz S, Branch LG, Branson MU, et al. Active life expectancy. *N Engl J Med* 1983; 309: 1218–1224.
6. Cutler D. Declining disability among the elderly. *Health Aff* 2001;20:11–27.
9. Verbrugge LM, Patrick DL. Seven chronic conditions: Their impact on US adults' activity levels and use of medical services. *Am J Public Health* 1995; 85: 173–182.
10. Freedman VA, Martin LG. Contribution of chronic conditions to aggregate change in old-age functioning. *Am J Public Health* 2000; 90: 1755–1760.

11. Crimmins EM, Saito Y. Trends in healthy life expectancy in the United States, 1970–1990: Gender, racial, and educational differences. *Soc Sci Med* 2001; 52: 1629–1641.
12. Crimmins EM, Saito Y. Change in the prevalence of diseases among older Americans: 1984–1994. *J Dem Rsrch*.
14. Cutler DM. The reduction in disability among the elderly. *Proc Natl Acad Sci USA* 2003; 98: 6546–6547.
15. Freedman VA, Martin MG, Schoeni RF. Recent trends in disability and functioning among older adults in the United States. *JAMA* 2002; 288: 3137–3146.
16. Fries J. Measuring and monitoring success in compressing morbidity. *Ann Intern Med* 2003; 139: 455–459.
17. Lakdawalla DV, Bhattacharya J, Goldman DP. Are the young becoming more disabled? *Health Aff* 2004; 23: 168–176.
18. Peeters A, Barendregt JJ, Willekens P, et al. Obesity in adulthood and its consequences for life expectancy: A life-table analysis. *Ann Intern Med* 2003; 138: 24–32.
19. Sturm R, Ringel J, Andreyeva T. Increasing obesity rates and disability trends. *Health Aff* 2004; 23: 199–205.

Reading 8: We Will Be Able to Live to 1,000

Aubrey de Grey

Aging is a physical phenomenon happening to our bodies, so at some point in the future, as medicine becomes more and more powerful, we will inevitably be able to address aging just as effectively as we address many diseases today.

I claim that we are close to that point because of the SENS (Strategies for Engineered Negligible Senescence) project to prevent and cure aging.

It is not just an idea: it's a very detailed plan to repair all the types of molecular and cellular damage that happen to us over time.

And each method to do this is either already working in a preliminary form (in clinical trials) or is based on technologies that already exist and just need to be combined.

This means that all parts of the project should be fully working in mice within just 10 years and we might take only another 10 years to get them all working in humans.

When we get these therapies, we will no longer all get frail and decrepit and dependent as we get older, and eventually succumb to the innumerable ghastly progressive diseases of old age.

We will still die, of course—from crossing the road carelessly, being bitten by snakes, catching a new flu variant, etcetera—but not in the drawn-out way in which most of us die at present.

So, will this happen in time for some people alive today? Probably. Since these therapies repair accumulated damage, they are applicable to people in middle age or older who have a fair amount of that damage.

It is very complicated, because aging is. There are seven major types of molecular and cellular damage that eventually become bad for us—including cells being lost without replacement and mutations in our chromosomes.

Source: “We Will Be Able to Live to 1,000” by Dr. Aubrey de Grey is reprinted with permission from BBC News at <http://www.bbcnews.co.uk>.

Each of these things is potentially fixable by technology that either already exists or is in active development.

The Alternative View

Nothing in gerontology even comes close to fulfilling the promise of dramatically extended lifespan.

—S. Jay Olshansky

“Youthful Not Frail”

The length of life will be much more variable than now, when most people die at a narrow range of ages (65 to 90 or so), because people won't be getting frailer as time passes.

The average age will be in the region of a few thousand years. These numbers are guesses, of course, but they're guided by the rate at which the young die these days.

If you are a reasonably risk-aware teenager today in an affluent, non-violent neighbourhood, you have a risk of dying in the next year of well under one in 1,000, which means that if you stayed that way forever you would have a 50/50 chance of living to over 1,000.

And remember, none of that time would be lived in frailty and debility and dependence—you would be youthful, both physically and mentally, right up to the day you mis-time the speed of that oncoming lorry.

Should We Cure Aging?

Curing aging will change society in innumerable ways. Some people are so scared of this that they think we should accept aging as it is.

I think that is diabolical—it says we should deny people the right to life.

The right to choose to live or to die is the most fundamental right there is; conversely, the duty to give others that opportunity to the best of our ability is the most fundamental duty there is.

There is no difference between saving lives and extending lives, because in both cases we are giving people the chance of more life. To say that we shouldn't cure aging is ageism, saying that old people are unworthy of medical care.

The Alternative View

There is no difference between saving lives and extending lives, because in both cases we are giving people the chance of more life.

—Aubrey de Grey

Playing God?

People also say we will get terribly bored but I say we will have the resources to improve everyone's ability to get the most out of life.

People with a good education and the time to use it never get bored today and can't imagine ever running out of new things they'd like to do.

And finally some people are worried that it would mean playing God and going against nature. But it's unnatural for us to accept the world as we find it.

Ever since we invented fire and the wheel, we've been demonstrating both our ability and our inherent desire to fix things that we don't like about ourselves and our environment.

We would be going against that most fundamental aspect of what it is to be human if we decided that something so horrible as everyone getting frail and decrepit and dependent was something we should live with forever.

If changing our world is playing God, it is just one more way in which God made us in His image.

Reading 9: Don't Fall for the Cult of Immortality

S. Jay Olshansky

Some 1,700 years ago the famous Chinese alchemist, Ko Hung, became the prophet of his day by resurrecting an even more ancient but always popular cult, Hsien, devoted to the idea that physical immortality is within our grasp.

Ko Hung believed that animals could be changed from one species to another (the origin of evolutionary thought), that lead could be transformed into gold (the origin of alchemy), and that mortal humans can achieve physical immortality by adopting dietary practices not far different from today's ever-popular life-extending practice of caloric restriction.

He found arrogant and dogmatic the prevailing attitude that death was inevitable and immortality impossible.

Ko Hung died at the age of 60 in 343 AD, which was a ripe old age for his time, but Hsien apparently didn't work well for him.

The famous 13th Century English philosopher and scientist, Roger Bacon, also believed there was no fixed limit to life and that physical immortality could be achieved by adopting the "Secret Arts of The Past." Let's refer to Bacon's theory as SATP.

According to Bacon, declines in the human lifespan occurred since the time of the ancient patriarchs because of the acquisition of increasingly more decadent and unhealthy lifestyles.

All that was needed to reacquire physical immortality, or at least much longer lives, was to adopt SATP—which at the time was a lifestyle based on moderation and the ingestion of substances such as gold, pearl, and coral—all thought to replenish the innate moisture or vital

substance alleged to be associated with aging and death.

Bacon died in 1292 in Oxford at the age of 78, which was a ripe old age for his time, but SATP apparently didn't work well for him either.

Physical immortality is seductive. The ancient Hindus sought it, the Greek physician Galen from the 2nd Century AD and the Arabic philosopher/physician Avicenna from the 11th Century AD believed in it.

Alexander the Great roamed the world searching for it, Ponce de Leon discovered Florida in his quest for the fountain of youth, and countless stories of immortality have permeated the literature, including the image of Shangri-La portrayed in James Hilton's book *Lost Horizon*, or in the quest for the holy grail in the movie *Indiana Jones and the Last Crusade*.

What do the ancient purveyors of physical immortality all have in common? They are all dead.

The Alternative View

I think the first person to live to 1,000 might be 60 already.

—Aubrey de Grey

What do the ancient purveyors of physical immortality all have in common? They are all dead.

—S. Jay Olshansky

Source: "Don't Fall for the Cult of Immortality" by Dr. S. Jay Olshansky is reprinted with permission from BBC News at <http://www.bbcnews.co.uk>.

Prophets of Immortality

I was doing a BBC radio interview in 2001 following a scientific session I had organised on the question of how long humans can live, and sitting next to me was a young scientist, with obviously no sense of history, who was asked the question: “how long will it be before we find the cure for aging?”

Without hesitation he said that with enough effort and financial resources, the first major breakthrough will occur in the next 5–10 years.

My guess is that when all of the prophets of immortality have been asked this question throughout history, the answer is always the same.

The modern notion of physical immortality once again being dangled before us is based on a premise of “scientific” bridges to the future that I read in a recently published book entitled *Fantastic Voyage* by the techno-guru Ray Kurzweil and physician Terry Grossman.

They claim unabashedly that the science of radical life extension is already here, and that all we have to do is “live long enough to live forever.”

What Kurzweil and others are now doing is weaving once again the seductive web of immortality, tantalising us with the tale that we all so desperately want to hear, and have heard for thousands of years—live life without frailty and debility and

dependence and be forever youthful, both physically and mentally.

The seduction will no doubt last longer than its proponents.

“False Promises”

To be fair, the science of aging has progressed by leaps and bounds in recent decades, and I have little doubt that gerontologists will eventually find a way to avoid, or more likely delay, the unpleasant-ries of extended life that some say are about to disappear, but which as anyone with their eyes open realises is occurring with increasing frequency.

There is no need to exaggerate or overstate the case by promising that we are all about to live hundreds or even thousands of years.

The fact is that nothing in gerontology even comes close to fulfilling the promise of dramatically extended lifespan, in spite of bold claims to the contrary that by now should sound familiar.

What is needed now is not exaggeration or false promises, but rather, a scientific pathway to improved physical health and mental functioning.

If we happen to live longer as a result, then we should consider that a bonus.

Focus on the Future

“I Dated a Cyborg!”

Dateline: 2030. As Tony walked back to the college dormitory, his feelings were confused. He needed to talk to his roommate.

“You know, I really like her,” Tony began. “I mean, I really fell for her. And now . . . I just don’t know . . .” Tony’s voice trailed off.

“What’s the problem?” Tony’s roommate asked.

Odating—Cynthia? It turns out she’s a lot older than I thought she was.”

“So. How much older?” asked his roommate.

(Continued)

(Continued)

“Hey, she remembers the assassination of President Kennedy, which happened when she was 10. That makes Cynthia 77 years old. She’s 55 years older than I am! Can you believe that?”

Tony’s roommate was aghast. He’d seen Cynthia. He figured she was around 30, not much more. Tony was pleased about going out with an “older” woman. But neither Tony nor his roommate had guessed just how much older she really was.

“I don’t believe it! I mean, how could she be so old?” stammered Tony’s roommate.

“Well, I found out she’s had skin grafts and plastic surgery on her face; that’s why there are no wrinkles. And of course her hair is dyed, so there’s no gray at all. But it’s the rest of her that’s . . . I don’t know how to say it . . . that’s all been replaced. It’s weird. It’s like Cynthia’s body is artificial, the way it is with a cyborg.

“To begin with, she’s got silicone breast implants. OK, not so unusual. But inside she’s artificial, too: all plastic valves in her heart, a liver transplant, hip replacements, and a lot of artificial bones. She’s been on estrogen replacement for years and on other antiaging hormones, too. That’s why she looks so young.

“Cynthia never talked much about things that happened before the turn of the century, and now I see why. I never suspected that she was born in the early 1950s. She admitted it to me last night. I came home and suddenly realized I’ve been dating a cyborg!”

Science fiction stories have had titles such as “I Married a Martian,” and a Star Trek film, *First Contact*, featured a female “Borg” (for cyborg) as a leading character. Star Trek fans remember that the alien species known as the Borg are creatures that are part human and part machine. Like Tony, Captain Picard found himself in a relationship with a Borg and faced perplexing questions. Is the experience of Tony or Captain Picard a glimpse of things to come?

Cyborgs are not outside the realm of possibility (Clark, 2004). In fact, the era of modern bioethics may be said to have started in 1967, when Christiaan Barnard performed the first successful heart transplant on Louis Washkansky. Tissue transplants have long since become a standard part of modern medicine. Some tissues, such as cartilage and the cornea of an eye, are transplanted easily. With proper safeguards, blood can be safely transfused. Modern medicine has also shown success in transplanting skin, bone, kidneys, and, more recently, lungs, livers, and hearts. The development of monoclonal antibodies, which help suppress rejection of transplanted tissues, has opened up a vast field of surgery to replace organs diseased or worn out with age.

At the same time, biomedical scientists are developing artificial tissues and organs that have been successfully inserted into the human body. Bioengineering has already made possible a variety of “replacement parts”:

- *Skin:* Skin tissue has been successfully grown in the laboratory, and biotechnology companies are now producing it in quantity for use with burn victims.
- *Cartilage:* One of the most common effects of aging is the wear and tear on cartilage. Surgeons can now use cartilage grown in the lab to treat joint injuries.

- *Bone:* Hip replacements have long been a staple of geriatric medicine—even Elizabeth Taylor had one. Today, biotechnology companies are selling bone substitutes manufactured from artificial substances. Companies are working on grafts that would enable the body to replace living tissue with artificial bone.

More exciting innovations are on the horizon with the expanding field of regenerative biology and medicine (Stocum, 2012):

- *Breast tissue regeneration:* Breast implants made of silicone have long been in use, but the results have been controversial. Tissue engineers are working on new techniques to stimulate women's bodies to grow new breast tissue. Already, plastic surgery has become enormously popular. Tissue engineering and “body sculpting” are likely to become even more important in years to come.
- *Artificial vision:* In *Star Trek: The Next Generation*, the character Geordi (played by LeVar Burton) is able to see by using a “VISOR”—an artificial vision device worn over the eyes. Today, older adults are the age group most likely to be afflicted with impaired vision or total blindness. But in the future, electronic devices may replace lost visual capacity.
- *Heart valves:* Cardiovascular disease is the biggest cause of death among older Americans. Researchers have long been at work on a totally implantable artificial heart. Today, heart valves from pigs have been transplanted into humans. Researchers have discovered how to grow valves from blood vessel cells in the laboratory, and these lab-grown valves work well in lambs. In the future, thousands of people could benefit from artificially grown heart valves.
- *Bladder:* Urinary incontinence is one of the most troubling afflictions for older adults, and it is a factor in nursing home placement. But scientists are working on producing molded lab-grown cartilage that could function as a valve to keep urine flowing in the proper direction.
- *Pancreas:* Late-life diabetes is one of the most serious diseases of old age, entailing complications such as blindness, amputation, and heart failure. Diabetes results from basic organ failure. The pancreas doesn't produce enough insulin to metabolize sugar properly. Bioengineers are now working on implants made of pig islet cells, which could produce insulin without injections for people who develop diabetes.
- *Brain:* No one expects medical science to produce anything like *Donovan's Brain*, a tissue-culture brain that was the centerpiece of a 1950s science fiction movie. But drugs to stimulate nerve growth are under investigation today, and techniques may soon be available to implant cells or introduce growth factors that would reverse damage to the central nervous system.

So far, cyborgs, like those in *Star Trek*, are just science fiction. But bioengineering work on transplants and artificial organs is not fictional. Moreover, other scenarios are possible. For instance, Bruce Sterling's novel *Holy Fire* (1996) has as its heroine a wealthy 94-year-old woman who gets total cellular rejuvenation

(Continued)

(Continued)

based on new genetic material added to chromosomes in her body. The result is an organism constructed from “designer genes,” which is different from Cynthia and her replacement

parts. Stay tuned as the 21st century progresses and biomedical technology reshapes our vision of what human aging is all about.

QUESTIONS FOR WRITING, REFLECTION, AND DEBATE

1. What are the arguments for and against the view that aging in and of itself is actually a disease? Pick one side of this issue and then try listing the points that can rebut the opposing point of view.
2. What do James F. Fries and Lawrence Crapo mean by natural death? What is the relationship between natural death and the natural life span? Should we consider the natural life span to be identical to the maximum life span?
3. Swedish data have turned up the surprising fact that death rates for the oldest-old (85+) have actually been going down. Some scientific studies suggest an ever-increasing life expectancy is quite possible. These findings sound like good news. Do we have any reasons to believe that these findings are not good news? What would be Fries and Crapo’s response to these claims?
4. The Human Genome Project has now produced a complete map of all human chromosomes. Considering the different theories of aging, what are some of the ways in which new genetic knowledge might change how we think about the causes of biological aging? What are the social and ethical implications of that knowledge?
5. Write a science fiction or imaginary scenario of how the United States might look in the year 2030 if dramatic breakthroughs in the genetics of aging occur. In developing this scenario, be sure to state the year you expect the key discoveries or inventions to occur, and describe the likely social consequences of those discoveries or inventions.
6. What is the best scientific evidence in favor of, or against, the compression-of-morbidity thesis? Conduct an online search of current journal articles to consider how various researchers are consider this topic, including changes in rates of disability over time. What questions are left open by this research—for example, what exactly is “disability” as measured across different subgroups? What are the most effective ways to intervene to “compress” morbidity?

SUGGESTED READINGS

Austad, S. N., *Why We Age: What Science Is Discovering About the Body's Journey Through Life*, New York: Wiley, 1999.

Kirkwood, T., *Time of Our Lives: The Science of Human Aging*, Oxford, UK: Oxford University Press, 2001.

McDonald, R. B., *Biology of Aging*, New York: Garland Science, 2013.

Scientific American Editors, *Forever Young: The Science of Aging*, New York: Scientific American, 2013.

Silvertown, J., *The Long and the Short of It: The Science of Life Span and Aging*, Chicago: University of Chicago Press, 2013.

Do not copy, post, or distribute