

The Link Between Healthcare, Sexuality, And Successful Aging

Richard Allen Williams, Clinical Professor of Medicine, UCLA School of Medicine

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"If I knew I was going to live this long, I would have taken better care of myself."

Legendary ragtime piano player Eubie Blake, on his 100th birthday

Abstract

The general topic is Successful Aging, an issue that has intrigued, puzzled, and challenged some of the best minds on planet Earth for millennia. I feel humbled to be among so many of the world's experts today to present my views which are based upon research largely carried on by others; nonetheless, I will try to incorporate my research, which most recently has been in the area of human sexuality and the connection between erectile dysfunction and cardiovascular disease, into the general body of data that I will present on the triumvirate of healthcare, sexuality, and successful aging, and I will attempt to show some interrelationship of these subjects. That is a daunting task to accomplish in a limited time frame, but I will give it my best effort. I will conclude with some recommendations about how the information I am providing should be viewed.

Introduction

A very striking development in the aging of the American population is occurring and is predicted to intensify: the numbers of older individuals is increasing at an alarming rate. For instance, at the present time, 79 million "baby boomers" have moved into the senior sector, and as they become older, they threaten to break the bank of Medicare and Social Security. Interestingly, increased longevity has been the goal of health planners for decades, and now that this is coming about, it could wreak havoc on the economy of the United States.

Indeed, there has been a dramatic change in longevity. At the beginning of the 20th century, in 1900, the average length of life was 47 years and the principal causes of death were respiratory diseases such as pneumonia, influenza, and tuberculosis. One hundred years later, the average life span has increased to 75 years of age, and the main causes of death are now cardiovascular disease, cancer, stroke, chronic obstructive pulmonary disease, and diabetes. The change in longevity is attributable to the excellent healthcare system which has emerged over the past two centuries that has also decreased the amount

of disability suffered by the elderly. This has cost huge amounts of money; a scenario has developed in which extending life through improving health has become more expensive rather than less, and it will continue. For example, the 79,000 centenarians now living will increase to over 1 million by 2050, and healthcare costs will have become the largest part of the nation's gross domestic product.

Objectives

With such obviously dire portents at hand, we have decided to go back to the drawing board, as it were, and to carry on further investigations into the genetic makeup of man in order to determine how to control aging in such a way that increased longevity may be achieved in a more cost-effective manner, e.g., with less associated morbidity and more wellness. Along with that objective is a wish to maintain and sustain a greater quality of life, such as through continued sexual functioning. It must be made clear that in this presentation we are not investigating how to achieve life everlasting, but rather, how to age in a fashion associated with health, fitness, and wellness.

Definitions

Aging: The time-related deterioration of the physiological, biochemical, and genetic functions necessary for survival, fertility, and reproduction. It is a continuous and inevitable process which begins at conception and ends with death.

Senescence: The period of decline that is experienced by all species.

Maximum Lifespan: The maximum number of years a member of that species has been known to survive. Jeanne Calment (1875-1997) lived to the age of 122 and is the oldest person whose age has been documented by modern means. Her age defines the human lifespan (unless you consider Methuselah of the Bible, who was said to have lived 969 years). The oldest known living organism is the Methuselah Tree, a 4,700-year-old bristlecone pine in the White Mountains of Northern California. Harriet, a Galapagos tortoise dating back to Charles Darwin's time, was 175 when she died recently. She was the oldest known living animal.

Life Expectancy: The amount of time a member of a species can expect to live. It refers to populations and may be given as the median, mean, or maximum age of survival. Life expectancy varies by population and by time period. For example, the life expectancy of a baby born in Massachusetts in 1780 was 28 years; today, it is about 80 years, especially if female and Caucasian. In some areas of the world (Togo, Cambodia, Afghanistan), it is less than 40 years.

Longevity: Long life or the length of a person's life (life expectancy).

Basic Scientific Observations

Much of the research into aging, longevity, and lifespan has been initiated with work on lower forms of life such as mice, yeast, roundworms, and fruit flies. Research done at Harvard by Sinclair and Ruvkun (1) and at Berkeley by Kenyon (2) has revealed much: a billion years ago, life forms evolved genetic mechanisms designed to protect them against environmental stress by stabilizing DNA and essentially preventing

oxidation by free radicals. All complex forms of life contain these mechanisms which influence metabolic rate and stability; genes and proteins that literally prevent organisms from becoming worn out through breakdown and fragmentation of DNA have now been identified in yeast and other life forms; these include *sir2*, found in yeast. Likewise, removal of certain genes such as *daf-2* from roundworms increases lifespan by 50 percent, and the beneficial effect on aging is even more pronounced in elderly worms. Another gene called *age-1* also has age-related functions. Clancy et al (3) reported recently in the journal *Science* that median lifespan of the fruit fly is extended by up to 48 percent when the *chico* gene is mutated. Thus, loss of this gene, which is a *Drosophila melanogaster* insulin receptor substrate protein, causes dramatic extension of lifespan in this insect.

All of this suggests that a small set of genes controls lifespan, and that they may be manipulated to decided advantage such as increasing longevity perhaps without all of the negative aspects associated with the aging process. This might be defined as successful aging, and if successfully accomplished, it could revolutionize the way in which we view getting old. It would also diminish those dramatically increasing healthcare costs which I mentioned earlier by decreasing the incidence of conditions such as cardiovascular disease, which at present is the most common disease entity affecting industrialized nations and is responsible for more than 40 percent of the annual death toll.

Sinclair (4) and others have boldly suggested that these findings in lower life forms such as rodents may be applicable to humans, which would truly be a story of mice and men, so to speak. A further step would be the development of substances which could be fed to the organism that could influence these gene systems related to aging, or sirtuins.

These sirtuin-activating compounds, or STACs, increase longevity when fed to yeast, the roundworm *C. elegans* and the fruit fly *Drosophila melanogaster*. One might speculate on future development of STACs for humans.

What might the link be between aging and physiological function such as in reproduction, and even sexuality? We find, for instance, that there has been a shift over the past several decades such that female and male fertility seem to last appreciably longer than before, and women are commonly having children when they are in their middle ages.

There is actually a connection between caloric restriction or CR and longevity which is believed to be mediated through the sirtuin pathway. It is widely acknowledged that the only intervention that can increase longevity at the present time is programmed sustained caloric restriction, and this phenomenon has been repeatedly documented in laboratory rats.

Commercialization Of Anti-Aging Science

An anti-aging, pro-longevity pharmacopoeia is emerging that includes growth hormone (somatostatin), which has become widely available as a synthetically-derived product developed through the use of cloning techniques. Pfizer Pharmaceuticals has also created a growth hormone stimulator that “turns on” the natural substance which is secreted by the anterior lobe of the pituitary gland. The new drug, called capromorelin, not yet approved by the Federal Food and Drug Administration (FDA), has been used in a placebo-controlled study (5) by Dr. George Merriam, a professor of medicine at the University of Washington. The study was conducted in 395 women and men aged 65 to 84 and was found to be associated with better balance, an increase in lean muscle mass,

and improved ability to climb stairs. Possible improvement in cognitive function was not investigated. Although investigational, this drug has great financial and commercial potential through the anti-aging market, despite the general perception among scientists in the field that they are doubtful about the benefits of growth hormone itself. In fact, the principal evidence that underlies the tremendous interest in this area and which led to a huge proliferation of anti-aging clinics using growth hormone was an article by Rudman et al (6) in the New England Journal of Medicine in 1990. This small study of only 12 elderly men given growth hormone purported to show an increase in lean body mass associated with a decrease in adipose tissue. However, the study was not double-blind, was too small, was not placebo controlled, and made no measurement of parameters such as muscle strength, exercise endurance, or quality of life. Other studies performed more recently and more properly by other researchers including Papadakis (7) have not shown any benefit of growth hormone; body composition may change but physical function such as improvement of maximal oxygen uptake during exercise and increased muscle strength is not enhanced. In an editorial response to the Rudman article and in reaction to the upswing in interest about anti-aging propensity of growth hormone, Dr. Mary Lee Vance of the University of Virginia has stated, "Antiaging therapy with growth hormone has not proved effective according to objective outcome criteria"(8). Indeed, Dr. Jeffrey Drazen, Editor-In-Chief of the New England Journal of Medicine, wrote an editorial of his own in which he decried the inappropriate advertising of dietary supplements, including growth hormone, and he specifically criticized the Rudman article and its after-effects (9).

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All of this raises the question as to what causes aging and if we should even attempt to halt it or prevent its progression. Dr. Andrew Weil, (10) probably the most recognized guru of complementary and alternative medicine in the United States, feels that to fight aging and to deny it are counterproductive; he advises that we should accept the inevitability of aging and concentrate on aging healthfully and successfully. This, he believes, will maximize happiness and health. He advises against using artificial means to prevent aging and instead recommends allowing nature to take its course while keeping our minds and bodies as healthy as possible and aging gracefully. That, he feels, is the definition of successful aging, rather than attempting to become younger or to extend longevity ad infinitum. And in focusing on longevity, we must be careful to pay attention to aging. Otherwise, we may end up like Tithonios, who was depicted in Greek mythology as a miserable wretch because he asked for and was granted eternal life by the gods, but not eternal youth.

Theories Of Aging

There is no uniform consensus about whether we should battle the aging process or give into the consequences of senescence. In 350 B.C., Aristotle pondered the question in his treatise “On Longevity and Shortness of Life”, and he wondered why some plants and animals have long lives while others have markedly shorter ones. Since his time, many theories of aging have been proposed.

The first theory on aging was proposed in the late 19th century by Weismann (11), who postulated that there was direct evolutionary control of life span which involved “programmed death” of individuals via inborn genetic mechanisms so that parents were

removed from the environment and thus were not available to compete with their offspring for resources. This theory has not gained much support.

Peter Medawar (12) has offered his alternative theory of aging which he contends results from an accumulation of deleterious mutations which ultimately cause death. These mutations, he states, cannot be suppressed by natural or evolutionary selection, rendering aging and eventually death inevitable in every individual.

About 50 years ago, George Williams (13) published what has been called the antagonistic pleiotropy theory which hypothesizes that a gene that may have a positive impact on several traits (pleiotropy) may actually lead to detrimental effects by affecting fitness in a negative manner (antagonistic) at a later stage in life. An example might be that a gene responsible for calcium deposition in bone early in life may later lead to atherosclerosis or hardening of the arteries, a change which is associated with senescence.

Beyond the theories mentioned above, there are other proposed causes of aging which are biochemically based, with include mechanisms operating at the cellular level. One of the most prominent theories posits that normal metabolic processes in the animal cause the development of reactive oxygen species (ROS) as a byproduct of mitochondrial metabolism (14). The ROS include powerful free radicals such as superoxide, hydrogen peroxide, and hydroxyl ions; these can damage cell membranes, nucleic acids such as desoxyribose nucleic acid (DNA), and proteins, leading to senescence. This theory is a cause of the upswing in interest in genetic and biochemical manipulation to control aging and extend longevity. In fact, it has been observed that fruit flies (*Drosophila melanogaster*) that are genetically programmed to overexpress enzymes which destroy ROS live 30-40 percent longer than controls. Concern about damage to cells by oxidizing

from ROS has spurred the use of anti-oxidants in clinical medicine to prevent and treat disease such as the utilization of vitamins E and C in heart disease, as well as the application of medicines such as BiDil

(a vasodilating drug which is believed to increase the nitric oxide content in the endothelium of blood vessels) in heart failure. Coronary heart disease and arteriosclerosis result from oxidative “rust” of the endothelial cells which line our blood vessels.

The general “wear-and-tear” theory of aging suggests that constant damage to mitochondrial DNA over a period of time without sufficient genetically-controlled repair mechanisms simply wears the individual out. Premature aging in humans as in the progeria syndrome where affected individuals appear as elderly people while in childhood, has been attributed to lack of adequate DNA repair systems. Victims of progeria usually die by the age of 15 years.

Another popular theory of the cause of aging considers telomere shortening (15). Telomeres, which are repeated sequences of DNA at the ends of chromosomes, need the enzyme telomerase to prevent chromosomal shortening at each cell division; in fact, this enzyme adds the telomere to the chromosome when cells divide. (Telomerase inhibition involves the use of molecules that block expression of telomerase, which is an enzyme that allows cancer cells unlimited replication.) If shortening does occur, the cell is unable to divide any further, which is thought to result in aging. However, a correlation between life span and telomere length has not been found in animals; mice, which have much longer telomeres than humans, have a much shorter life span than we do. Thus, the notion of the telomere being an “aging clock”, as proposed by Salk and Harley, seems to be unfounded. However, it is intriguing to speculate on whether a treatment could be

invented which would artificially lengthen telomeres and arrest or reverse aging in the process.

The Reliability Theory of Aging and Longevity has been advanced by the team of Gavrilov and Gavrilova (16) at the University of Chicago. It focuses on systems failure and uses mathematical formulas to predict the age-related failure kinetics for a system of given architectural structure and given reliability of its components.

Human Sexuality

In this section, we discuss the decline of human sexual function as a by-product of aging, and consider what can be done to maintain it. We will not cover reproduction or discuss reproductive capacity.

This is an extremely large and complex topic which is impossible to discuss in its entirety. I will focus on how sexual function is impacted by chronic diseases in the elderly, how sexual dysfunction may be treated, and how sexuality can be maintained despite aging.

Sexual dysfunction may occur in both males and females for different reasons. In the male, as aging progresses, there is a falloff of sexual prowess which is usually caused by a decline in erectile function (ED). It is believed to be due primarily to endothelial dysfunction, although there are certainly other causes. It is estimated that about 30 million men in the United States have ED and are unable to persistently achieve or sustain a penile erection sufficient for satisfactory sexual performance, i.e., intercourse. This is the earliest and most common symptom of ED. The Massachusetts Male Aging Study (MMAS) investigated 1,290 mostly Caucasian men between ages 40 and 70 and

discovered that ED was present in 52 percent (17). There also seem to be some racial and ethnic overtones to ED; the National Health and Social Life Survey (NHSLs) found that African Americans are 20 percent more likely than Caucasians to have ED (18).

The pathogenesis of ED is multifactorial. It may be caused by arterial, hormonal, neurogenic, psychogenic, cavernosal, and iatrogenic factors, and it is widely accepted that the most common cause is vascular, i.e., atherosclerosis. Since atherosclerosis is a regular companion to aging, ED is mostly seen in older men, but it does occur with fairly high frequency in younger men. It is often associated with comorbid conditions such as hypertension, dyslipidemia, obesity, diabetes mellitus, cigarette smoking, and physical inactivity. From a pathophysiological standpoint, ED is part of a spectrum of body-wide disorders which have endothelial dysfunction as their basis. This includes hypertension, dyslipidemia, renal disease, coronary heart disease, cerebrovascular disease, peripheral vascular disease, and many other disorders. These are all linked through an impairment of endothelial function caused by a deficiency of nitric oxide, which is a nonadrenergic, noncholinergic vasodilatory neurotransmitter principally responsible for regulation of vascular wall function. Oxidative stress caused by reactive oxygen species or free radicals leads to damage of the endothelium and results in increased adhesion and aggregation of platelets and neutrophils, causing the release of vasoconstrictor substances. ED results when these factors impinge upon the penis and its rich vascular network.

The original epidemiological research performed by my group which was published in 2005 in the *Journal of Sexual Medicine* showed that ED is a marker for cardiovascular disease and demonstrated that endothelial dysfunction is the etiologic factor linking the

two disorders (19). We emphasized the importance of considering all patients who present with ED as candidates for occult cardiovascular disease, and we urged that they be worked up for the latter.

The treatment of ED depends on the etiologic factor or factors involved. The emergence of phosphodiesterase (PDE5) inhibitors, beginning with sildenafil (Viagra) in 1998 (20) was a pivotal point in the treatment of ED, and it has been highly successful, with positive response rates of up to 70 percent. This has led to a virtual revolution in sexuality, and PDE5 inhibition therefore must be regarded as a genuine and authentic approach to managing the occurrence of ED as males go through the aging process. Although there are other approaches to the problem of ED including psychological counseling, PDE5 inhibition has been by far the most successful intervention. It must be stressed, however, that the pathophysiological mechanisms underlying ED such as cardiovascular disease must be addressed rather than limiting the interventions to the use of temporary therapies.

Consideration of sexual dysfunction in the female is a much more complex problem. Unlike men, women do not appear to develop sexual dissatisfaction due to vascular disease (21). Estrogen is the major sex hormone in women and a decline in its availability occurs with aging and the development of menopause. In many but not all women, vaginal dryness results from decreased lubrication, which can lead to dyspareunia, or painful intercourse. Vaginal atrophy may also cause dyspareunia. Androgen deficiency also occurs in the aging female, but large population studies have not shown a strong correlation between low testosterone levels in women and sexual dysfunction (22).

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Possessing too little sexual desire has been called the most common sexual issue among women and has been found in 10 to 51 percent of surveys of women in various countries (23). In addition, the Study of Women's Health Across the Nation (SWAN) revealed that this is a widespread phenomenon, with 40 percent of 2400 multiethnic women reporting an absence or infrequent occurrence of sexual desire (24). This is usually associated with low levels of arousal, sexual excitement, dissatisfaction, and infrequent orgasms. In addition to hormonal changes, many other factors may be responsible for this phenomenon such as psychological and mental changes, neural damage, chemical alterations involving nitric oxide, dopamine, and acetylcholine, and drugs including anti-hypertensive agents, alcohol, selective serotonin reuptake inhibitors (SSRIs), beta-blockers, changes in neurotransmitter levels, environment, and sedatives. In addition, the general health of the aging female is important to consider, because the presence of disorders such as obesity, cigarette smoking, hypertension, insomnia, diabetes, and arthritis may initiate or aggravate the problem of reduced female libido. To counteract this decline and to enhance libido, an effort should be made to eliminate these risk factors and to increase the level of physical fitness. Other basic, non-drug approaches include psychological counseling, yoga, adding fish oils to the diet, increased rest and sleep, biofeedback, meditation, and stretching and relaxation techniques. There are also many herbal remedies which are advocated. To correct androgen deficiency, dihydroepiandrosterone (DHEA) may be acquired over the counter, but its effectiveness is variable. Medically prescribed drugs may include the testosterone patch; however, this is not approved by the FDA for treatment of sexual dysfunction in women. The off-label use of a number of drugs for this purpose is sometimes practiced, including yohimbe,

bupropion (an agonist of norepinephrine and dopamine), ephedrine, and sildenafil (Viagra, Pfizer). Treatment is best left in the hands of experts.

What Is The Burden Placed On Society By Aging?

Aging has important implications for society as well as for the individual. The elderly have many chronic diseases which place a burden on society which is ever-increasing, and if expenditures for health care of the elderly are not decreased, they may lead to bankruptcy. The 1973 film, *Soylent Green*, was a fictional depiction of a futuristic country where aged people were turned into food for human consumption, so that the old and feeble not only were eradicated and were no longer a strain on resources, they actually became a food resource. While fictional, this motion picture pointed up the fact that our capacity is strained and solutions need to be found for this condition.

According to the Data Warehouse on Trends and Aging (25), between 1981 and 2002 the population of the United States increased by 59 million people, an increase of 26 percent. During that same time period the elderly population 65 and older increased by 9.4 million people, or a rise of 36 percent. Most of this increase in the aged is occurring in the two oldest groups, 75-84 and 85 and older (sometimes called “the oldest old”). It is also recognized that the “baby boomer” cohort which is the huge generation of people born within two decades after the conclusion of World War II in the time period 1945-1964 is perilously close to “coming of age”. It has been growing faster than the older age groups. The baby boomers are starting to have a dramatic impact on the nation from every perspective as they age. In 2010, the leading edge of the baby boomers will reach 65 years of age, which will cause the relative size of the population to increase in even

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more dramatic fashion. By 2030, 20 percent of the population will be in the elderly ranks, or about double the current percentage.

There have been some very striking racial developments in the time period that we selected, 1981-2002. First, whites have the highest percentage of people over 65, making Caucasians the oldest in the U.S. population, although that is changing as Asian Americans continue to have the largest percentage increase in elderly (a 306 percent increase since 1981, more than 10 times the increase for the general population). Significantly, in 2002, all racial groups *except blacks* had an increase in percentage of individuals over 65 compared to 1981 (26); therefore, the component of black elderly is shrinking rather markedly. These differential demographic factors are caused by many things including the continued persistence of healthcare disparities which lead to a constant attrition of the black population and a loss of black elderly, who are not being replaced proportionately by younger blacks due to a relatively low fertility rate and a higher death rate, as well as a continued gap in longevity between whites and blacks. The government, organizations dealing with economic, political, legal, social, public policy, and health-related issues, and agencies concerned with geriatric factors should place more emphasis on these statistics which also relate to strategies involved with planning for changes in Social Security and Medicare. It should be very clear that since fewer blacks than whites live beyond 65 years of age, when they would be eligible for Social Security and Medicare which blacks have paid into since the inception of the programs, blacks are essentially cheated of the opportunity to reap the benefits of their work. The current consideration by the Federal government to change the age of eligibility for these programs from 65 to 70 would appear to worsen matters. Although blacks are considered

by some to be a health burden to society because of higher health costs for more chronic diseases, this is untrue. In actual fact, their reduced life expectancy almost completely offsets the increase in annual healthcare spending for them. In other words, the contraction of the elderly black population over time is a phenomenon that is cost-saving.

This introduces my final subject, which I call the longevity paradox. A study by Joyce et al (27) suggests that reducing chronic illness such as heart disease, diabetes, and stroke in the future elderly will have only a modest effect on stabilizing Medicare, basically because healthier people live longer and therefore use more Medicare resources over time. For example, Lubitz (28) noted that a 70-year-old person in good health lives longer but incurs about the same medical costs over his or her remaining lifetime to those of a 70-year-old in poor health.

We can conclude that although reduction of chronic disease in the elderly is an admirable goal and should be an objective of successful aging, the benefits that may be reaped in terms of reduced healthcare spending may be greatly exaggerated. It would be better to think of aging successfully as an attainable goal which we should strive for in order to improve life in other ways. As we become elderly, we can take steps, as I have shown, to be healthier, to maintain our sexuality, and to be happier. Quality rather than quantity of life should be our focus. We have the power to change the image of the senescent person created by Shakespeare in *As You Like It*, who was doomed to leave the world “sans teeth, sans eyes, sans taste, sans everything”. Although we cannot identify a “magic bullet” to halt aging---will it be stem cells, or some type of gene-altering pill?---nor do we need to, I hope this presentation will inspire others to delve further into the

phenomenon of aging, which, to paraphrase Sir Winston Churchill, is like a riddle wrapped in a dilemma surrounded by mystery. Thank you.

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