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Overview of Aging and Life Expectancy

Reading Assignment

Textbook: Chapter 1 and Introduction.

Commentary

The aging process is described as a universal, progressive, irreversible impairment of physiological function that occurs over time. A quick examination of key concepts in this definition is warranted:

Universal: affects all members of a population
Progressive: a compounding process that shows a cumulative effect of changes
Irreversible: most changes appear to be permanent (no fountain of youth on the horizon)
Impairment: most changes appear to be deleterious to normal function

This definition implies that most age-related changes are detrimental. We use the term **senescence** to describe these detrimental changes and this implies that aging is essentially a collection of pathological changes throughout the body. Our current understanding indicates that aging affects the body at all levels of organization including:

Molecular
Cellular
Intracellular spaces
Tissues
Organs
Whole Organism

This means that no refuges exist in the body where aging does not occur and what we recognize as aging is actually an accumulation of changes across all levels of body organization.

Aging can be assessed in two principal ways. **Chronological Aging** asks specifically, how old is the individual being measured; in days, months, years, or some other standard time measurement? The other way to assess aging is biological aging. **Biological Aging** measures how well the physical structures function in the body, as time progresses. This can include assessment of physical appearance, but more likely uses routine measures of physiological function to assess the progression of the aging process. Such measurements might include skin elasticity, blood pressure, cardiac output, body temperature, and urine concentration. Measurements or tests that can be used to quantify the aging process are called **Biomarkers of aging**.

A key consideration in measuring changes in body function with age is **homeostasis**. This term was first described by the eminent physiologist Walter B. Cannon, and was defined as the maintenance of constancy or stability of the cellular, tissue, and organ environments. In simpler terms, homeostasis describes the body's ability to maintain and manage key set points for normal body function. For example, baseline homeostasis settings would include maintaining a body temperature of 98.6 degrees F, maintaining a normal blood pressure of 120/80 mm Hg, maintaining a normal resting heart rate of 72 beats per minute, or maintaining a normal cardiac output of 6 liters per minute. Our ability to maintain homeostasis is actually quite good as we age, providing baseline conditions apply. This means that most seventy year olds can maintain a normal body temperature when exposed to relatively normal temperatures ranging from 50-80 degrees F. However, expose an elderly person to hot temperatures in the nineties, or cold temperatures in the twenties, and their ability to maintain a normal body core temperature becomes compromised. For this reason, the elderly are more susceptible to homeostasis failures when exposed to extremes in ambient temperature, and more prone to dying in heat waves, than younger members of the population.

Mean Life Expectancy

Mean life expectancy is the average age of death predicted for a particular birth cohort, or the age where 50 percent of a population has died. **Median lifespan** is the most commonly reported age of death. For this reason, mean and median lifespan, although similar, are different.

All mammals age. They experience a progressive loss in the efficiency of organ system functioning until death. Interestingly, the *average* "life span" is related to body size, breathing rate, and heartbeat. Smaller animals with faster heart rates and metabolic rates have shorter life spans. Larger ones have longer life spans. Regardless of size, all mammals breathe about 200 million times and their hearts beat a total of 800 million

times during their life span. Man "appears" to be the one exception to this body size/life span ratio. In the United States, humans live three times longer than mammals of comparable size and have an average lifespan of 77 years (74 years for men, 80 years for women). But is man really an exception? Probably not. In ancient Egypt and Rome, it is estimated that the average age at death was around 20 to 30 years. At the start of this century, life expectancy was only 45–50 years and most died from common infectious diseases. The spectacular increase in the American life span from 47 years in 1900 to 77 years in 2006 is largely attributable to the advent of antibiotics and vaccines in the 1940s and the virtual elimination of life threatening diseases such as pneumonia, influenza, tuberculosis, and enteritis. These four diseases alone accounted for more than one-third of the mortality in 1900 and only 1 percent or less today. Additionally, we have seen improvements in public sanitation, water supplies, and sewage treatment. We also have a better understanding of healthy lifestyles and can recommend, with confidence, life extending regimes including exercise, diet modification, and the elimination of poor health choices such as smoking and heavy alcohol consumption.

Today, the leading causes of death are cardiovascular disease, cancer, and stroke. Other significant causes of death include obstructive lung disorders (including emphysema), accidents, diabetes, pneumonia and Alzheimer's Disease. It is noteworthy that the incidence of Alzheimer's Disease is increasing and it has climbed from the number 12 to number 8 leading cause of death in the past five years. Among people age 40 and under, accidents, suicide, and homicide claim the most victims, and HIV/AIDS ranks number 6 on this list.

At the present time, about 12 percent of people in the United States die before reaching age 50. Fifty percent survive to age 77, which is why we call this the ***average* life expectancy**. Even if we would eradicate all major killer diseases, it is unlikely that the average life expectancy would increase much past 85 since accidental deaths would still occur. In fact, actuarial tables used by life insurance companies are based in part on the finding that after age 35 the probability of death doubles every seven years. In all age groups, women have a life expectancy several years longer than men. Thus, among the consequences of postponing death by curing diseases is an increase in numbers of elderly and also an increase in the ratio of elderly women to men.

The World Health Organization (WHO) defines four age categories of older individuals: **the elderly (60–75), the old (76–90), the very old (90+)**, and a relatively new but expanding **centenarian (100+ population)**. Currently, the fastest growing segment of our society is the 85+ group. Unfortunately, this group experiences a high incidence of debilitating, long-term diseases of aging such as Alzheimer's, osteoporosis, congestive heart failure, and diabetes complications. Individuals with these diseases often require personal, long term care, resulting in health care costs for the elderly escalating at an alarming rate. At present, more than a quarter of all government spending for health care goes to the 12 percent of the population who are 65 or older.

Our elderly population is due for a dramatic increase over the next 40 years. A large birth cohort arose following World War II called "**the baby boomers**" (those born 1946–64) and will begin entering the elderly population in 2005 and reach Social Security age in 2010. Between now and the year 2040 it is projected that more than 60 percent of the federal budget will be needed for health care as the "baby boomers" grow old and result in a several-fold increase in the percentage of the 85+ segment of our population. It is this reality that worries those looking at the long-term funding prospects for government entitlement programs, including Social Security and Medicare.

Maximum Life Expectancy

The **maximal life span**, the age of the oldest surviving member of a population, is species-specific and presumed to have a genetic basis. For example, records from thoroughbred stables indicate that no horse has lived beyond age 40; zoological garden records indicate the maximal life span of the chimpanzee is 50 and that of the Asian elephant is 60. The oldest documented human is Jean Calumet from France, who lived to age 122, although there are now many people living over age 100 (call centenarians), and several who have reached age 115. It is estimated that there are over 100,000 people in the U.S. over 100 years old and worldwide, about 80 living "super centenarians," those over 110 years old. Mathematical projections suggest the maximum human life span is 130 years; this is also called **maximum longevity**. At present, maximum lifespan is thought to be fixed and the majority of interventional treatments for aging are thought to only be able to increase mean life expectancy, and not maximum life span.

Life Expectancy

Life expectancy is the average survival of individuals within a group all born on the same date. Conventionally, the age at which 50 percent of the initial population survives is designated as the average life expectancy. Insurance companies calculate life expectancy tables for different age groups (i.e., at birth, ages 20, 30, etc.) to determine the average life expectancies of young versus elderly. Having said this, I'd like you to consider whether the average life expectancy for a 65-year-old group is higher, lower, or the same as that of a 1-year-old group of individuals (which the United States Bureau of Census records indicate has an average life expectancy of 77 years)? If your answer was "higher," you were correct. A 65-year-old cohort has lived through the childhood diseases, accidents, the threat of heart attacks early in life, and 50 percent of 65-year olds will survive past age 77 despite the fact that all of the individuals exhibit varying degrees of age-related loss of organ system functioning.

Although the average life span has increased spectacularly from 47 years in 1900 to 77 in 2006, most Americans won't live much past their 85th birthday; they'll simply wear out or succumb to an accidental death. Since death is inevitable and aging undoubtedly has a genetic basis, the present goal of gerontology is not to increase the life span, but to

expand the number of years that one can lead a relatively normal, productive life. However, as we increase life expectancy, the incidence of intrinsic diseases and disabilities also increases. We are already in a health care crisis. Over the past five years, the cost of health care has risen 42 percent, much faster than the cost of housing, food, and transportation. Health insurance premiums continue to escalate and are pricing more and more people out of the market. It is estimated that between 30 and 40 million people have no health insurance because they can't afford it or because insurance companies refuse to sell them a policy at any price. This approximates 15 percent of the total population of the United States. Many believe that the only solution is to adopt some form of national health insurance program, perhaps using the Canadian system as a model. The insurance industry opposes this, since at stake is the $175 billion it collects in annual premiums. Many physicians and the A.M.A. traditionally oppose universal healthcare programs, since there would undoubtedly be caps on the fees charged for services, whereas at present doctors have the option of billing patients for considerably more than an insurance company's allowable charge.

In short, despite current advances in establishing the importance of exercise and proper diet (e.g., low cholesterol) in expanding the number of years elderly can remain active and healthy, it is unlikely that the inner city poor segment of our population, which lacks health care coverage, will benefit much from such advances.

Gerontology vs. Geriatrics

Gerontology is the scientific study of all aspects of the aging process: molecular, cellular, organ, organ system, and organism, as well as social aspects of the aging process involving community, psychological, and sociological aspects of aging. However, this course is limited to only investigating the biological aspects of aging.

Geriatrics is a specialty branch of medicine centered around the diagnosis, treatment, and care of elderly patients. While it might use discoveries gleaned from gerontology research to improve quality of life and healthcare, it is a branch of medicine, not a scientific study.

Methods of Investigating the Aging Process

There are two major methods for studying normal aging and age-associated disease. **Cross-sectional studies** are by far the most common and involve comparisons of physical, biochemical, behavioral, and functional traits among different age groups or cohorts, such as comparing 20-year-olds to 60, 70, and 80+ year-old individuals. Essentially, an investigator could go out tomorrow and recruit different age groups out of a local population and run these individuals through a battery of tests to examine aging. One problem with such studies is that each age group potentially has a different life history. For example, the 80+ cohort has a much different past history than a 20- or

even 40-year-old group since they suffered through the Depression, World War II, survived many infectious diseases, and were not as aware of the importance of exercise and diet when they were younger. Their exposure to hazardous elements at their workplace, especially in the case of miners and industrial workers, was also markedly different in the 1930s than in recent years. Thus, the elderly or old-old age cohorts represent select groups of "survivors." Such age-group differences, referred to as "**birth-cohort**" differences, can result in misleading interpretations that result from confusing intrinsic changes that are due to normal aging with those caused or accelerated by extrinsic environmental or socioeconomic factors. This can be addressed with a **time lag design**, measuring, for example, different groups of 65 year olds, over a 10 or 20 year time period, to include different birth cohorts.

Longitudinal studies overcome some of the limitations of cross-sectional studies by following and measuring the same group of individuals over an extended time period. However, these studies also have limitations. They are extremely costly in terms of money and time and, depending on the scope of the study, it can be difficult to locate the individuals for repeated measurements, as people in our society tend to move over time. Also, since they are conducted over the investigator's own life span, there is a potential for turnover of individuals conducting measurements, changes in instrumentation and measuring techniques, and often changes in decisions regarding which parameters should be measured.

As a consequence, longitudinal studies usually have a limited scope in that they focus on only a few variables and address specific critical questions over an extended age span. For example, ***The Framingham Study***, initiated by the United States Public Health Service in 1949 and later transferred to the National Heart Institute, focused on risk factors in the development of heart disease such as smoking, high blood pressure, blood cholesterol, and dietary intake of saturated versus unsaturated fats. Another study, the ***Duke Study***, initiated in 1955, focused on physical, mental, and socioeconomic processes in normal aging; a parallel study started somewhat later measured the effects of spousal death, serious illness, and menopause on aging processes. A third study, the ***Baltimore Longitudinal Study of Aging*** (BLSA) focused on the effects of extrinsic factors such as educational background, socioeconomic conditions, and disease and how these influence processes believed to represent normal intrinsic aging processes.

In addition to their limited focus, longitudinal studies have several important drawbacks. Not many people will agree to a long-term commitment with limited compensation. As a result, researchers often start with a highly select group: upper middle class, educated, and motivated, essentially a selection bias for the study participants. Over time, longitudinal studies often have a high drop out rate and have to be replaced by comparable individuals. There is also a progressive attrition in the older age groups, which are more prone to fatal disease, so sample size can dramatically decline in older age groups.

The Use of Animal Models:

Because of their long life spans, genetic variability, mobility, and compliance issues with study protocols, humans are less than ideal subjects for aging studies. For this reason, scientists routinely use animal models for gerontology research. Commonly used mammalian models include mice, rats, and rhesus monkeys.

Animal models offer the advantages of uniform genetic backgrounds (called **inbred strains**) and specific genotypes can even be ordered from biological supply firms for study use and comparison. For example, a short lived mouse strain called DBA/2 live their lifespan within 2 years; a longer lived C57 black mouse can live as long as 3 years. Additionally, unique, genetically engineered strains of animals can now be obtained. "**Knockout mice**" are mice that have particular gene segments removed from their genetic background. **Transgenetic mice** are modified while still at an embryo stage, to include new gene sequences. For example, there are now "Alzheimer's mice," which have insertions of actual human genes thought to control Alzheimer's disease.

Additionally, animals can be housed in controlled conditions that regulate important parameters including diet, temperature, exercise, and even disease contact. Disease free facilities called **barrier facilities** can filter air and essentially eliminate most common pathogens from the environment, ensuring that the researcher is looking at results due to aging, rather than disease. Also, the short lifespan of some animal models makes longitudinal studies more practical. Finally, it is possible to do interventional aging studies that examine the use of extreme diets, experimental drugs, surgical procedures, gene therapies, or even stem cell transplants that are not practical or ethical to perform using human subjects.

It should also be noted that scientists use a wide variety of invertebrate animal models for aging studies including **Drosophila**, a fruitfly, useful in genetic and mutational studies and **Caenorhabiditis elegans** (C. elegans), a nematode worm with an identified aging gene called AG1 that can be removed, resulting in worms with 1/3 longer lifespans. A single celled organism called **Saccharomyces cerevisiae**, commonly known as Baker's yeast, is used to investigate aspects of aging at the cellular level, including the cell cycle, which controls cell division.