Medical Education Systems, Inc.

Course 716

The Biology of Aging

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The Biology of Aging

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Learning Objectives

Upon successful completion of this course, you will be able to:

- Define and discuss the term "aging"
- Identify the "mechanisms/causes" of aging
- List and discuss the various "theories" of aging
- Discuss what is meant by "Lifespan and Life Expectancy"
- Identify and discuss at least 5 common characteristics of aging in mammals
- Discuss the Issues of Gender and Race regarding why people age differently

Abstract

In humans, aging is inexorable. The progressive decrease in physiological capacity and the reduced ability to respond to environmental stresses lead to increased susceptibility and vulnerability to disease. Consequently, mortality due to all causes increases exponentially with aging. Attempts at understanding the causes of aging are limited by the complexity of the problem. Aging changes are manifest from the molecular to the organismic level; environmental factors affect experimental observations; secondary effects complicate elucidation of primary mechanisms; and precisely defined, easily measurable "biomarkers" are lacking.

No one unifying theory may exist, since the mechanisms of aging could be quite distinct in different organisms, tissues, and cells. Evolutionary pressures have selected for successful reproduction, making it likely that the post-reproductive physiology of an organism (i.e., aging) is an epigenetic and pleiotropic manifestation of the optimization for early fitness. Indeed, antagonistic pleiotropy, wherein genes that enhance early survival and function but are disadvantageous later in life, may play an overriding role in aging. Theories of aging can be divided into two general categories: stochastic and developmental-genetic. These are not mutually exclusive, particularly when considering the free radical/mitochondrial DNA theory of aging. Increasing evidence suggests that cellular senescence and organismic aging are antagonistically pleiotropic manifestations of evolutionary pressures to prevent malignant transformation.

In other words, aging may be the price we pay to avoid cancer. The beneficial paradox may be that the maximum lifespan potential of humans may have been achieved, in part, due to our ability to grow old.

"Every day you get older — that's a law."

- Butch Cassidy and the Sundance Kid (1)

"There is no such thing as a free lunch."

- Anonymous (2)

"Aging seems to be the only available way to live a long life."

- Daniel Francois Esprit Auber (3)

DISCUSSIONS OF AGING invariably begin by establishing satisfactory definitions for the term "aging" and the related word "senescence." Although the term "aging" is commonly used to refer

to post-maturational processes that lead to diminished homeostasis and increased organismic vulnerability, the more correct term for this is “senescence.” “Aging” can refer to any time-related process. In this course, however, “senescence” and “aging” will be used interchangeably.

“Normal” aging involves inexorable and universal physiological changes, whereas “usual” aging includes age-related diseases. For example, menopause and the decline in renal function represent aspects of normal aging. In contrast, coronary artery disease is an example of usual aging and is not found in all older persons. This approach to aging can utilize a conceptual framework that identifies intrinsic (developmental-genetic) versus extrinsic (stochastic) causes. However, accumulation evidence increasingly stresses the importance of both. Indeed, the altered homeostasis in older organisms is likely the result of a genetic program that determines the response to exogenous influences and thereby increases the predisposition to illness and death.

Lifespan and Life Expectancy

The average/median lifespan (also known as life expectancy) is represented by the age at

which 50% of a given population survive, and maximum lifespan potential (MLSP) represents the longest-lived member(s) of the population or species. The average lifespan of humans has increased dramatically over time, yet the MLSP has remained approximately constant and is usually stated to be 90 – 100 years (Fig. 1) (4).

For 99% of our existence as a species, the average life expectancy for humans was very short compared to the present. Due to disease and accidents, people living 50,000 years ago rarely lived beyond the age of 40. Throughout most of recorded human history, socioeconomic status and nutritional status have been strongly associated with life expectancy and, along with disease, resulted in significant variations in the lifespan of individuals.

By 1900, improved sanitation helped to raise the average life expectancy at birth in the United States to 57 years, but infectious disease was still a major killer. In the latter half of the twentieth century, better diet, health care, and reduced infant mortality had resulted in an average life expectancy in the United States of about 80 years as of 1980 (5). The increase in the average life expectancy has resulted in a compression of morbidity (a squaring of the mortality curve) toward

the end of the lifespan (Fig. 1).

The unavoidable presence of trauma and accidents prevents 100% survivability. Of note, the longest lived human for whom documentation exists was Jeanne Calment, who died in France at the age of 122, in August 1997. The longest-lived male was Christian Mortensen, who died in San Francisco at the age of 115, in 1998. As causes of early mortality have been eliminated as a result of public health measures and improved medical care, more individuals have approached the maximum lifespan.

Between 1960 and 1994, the population of those aged 85 and older increased by 274%. During this interval, the less elderly population doubled while the entire U.S. population increased by 45% (6).

MLSP appears to be species specific, implying a significant genetic component to the rate of aging. For example, humans have an MLSP 25 – 30-fold higher than mice. Some biodemographic estimates predict that elimination of most of the major killers such as cancer, cardiovascular disease, and diabetes would add no more than 10 years to the average life expectancy, but would not affect MLSP (7, 8).

This implies an upper limit to the MLSP. Some models suggest that genes operate to raise or lower the relative risk of death, by making cancer, coronary disease, or Alzheimer's disease more likely, rather than by fixing the lifespan. One mathematical model predicts that if participants in the Framingham Heart Study had been able to maintain the levels of 11 different risk factors to be similar to those of a typical 30 year old, the men and women would have survived to an average age of 99.9 and 97.0 years, respectively (7).

There are three known regimens that can extend lifespan. The first two involve lowering ambient temperature and reducing activity, and are effective in poikilotherms (cold-blooded species). A decrease of 10%C or the elimination of a housefly's capacity to fly extends the maximum lifespan approximately 250% (9). Both of these manipulations decrease the metabolic rate and are accompanied by decreases in free radical generation and oxidative damage to protein and DNA.

Dietary restriction without malnutrition can increase both the average and maximum life spans of mice and rats by more than 50% (10, 11). Although calories are severely restricted (up to 40%), essential nutrients such as vitamins and minerals are maintained at levels equivalent to those found I *ad libitum* diets. The diet-restricted animals also exhibit a delay in the onset of physiological and pathological changes associated with aging (12). These include hormone and lipid levels, female reproduction, immune function, nephropathy, cardiomyopathy, osteodystrophy, and malignancies.

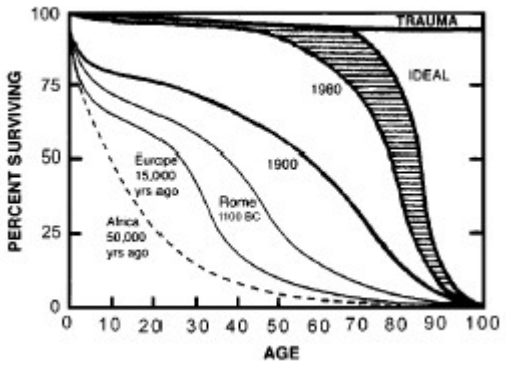

Fig. 1. Percent survival curve for humans at different times in history with varying environments, nutrition, and medical care. The 50% survival values have improved, but maximum lifespan potential has remained the same.

Size, weight, fat percentage and some organ weights are markedly less in calorically restricted animals (13). The specific metabolic rate, the amount of oxygen consumed per gram of tissue, decreased in rats subjected to caloric restriction (14, 15). However in one study, long-term food restriction did not alter the metabolic rate (16).

This finding suggests that the specific metabolic rate may not be a critical determinant of longevity. To date, the effect of dietary restriction on lifespan has been convincingly demonstrated only in rodents. Caloric restriction in rhesus monkeys leads to reductions in body temperature and energy expenditure, consistent with changes seen in rodent studies in which aging is retarded by dietary restriction (17, 18). Calorie restriction also increases high-density lipoprotein (19) and retards the post-maturational decline in serum dehydroepiandrosterone sulfate in the rhesus monkeys (20).

Characteristics of Aging

There is evidence supporting at least 5 common characteristics of aging in mammals

(Table 1):

TABLE 1

Characteristics of Aging

1. Increased mortality with age after maturation.
2. Changes in biochemical composition in tissues with

age.

3. Progressive decrease in physiological capacity with

age.

4. Reduced ability to respond adaptively to

environmental stimuli with age.

5. Increased susceptibility and vulnerability to disease.

1. Increased mortality with age after maturation.

In the early nineteenth century, Gompertz first described the exponential increase in mortality with aging due to various causes, a phenomenon that still pertains today (21). In 1995, the death rate for all causes for people in the U.S. between the ages of 25 – 44 was 189.5/100,000 and for those aged 65 and over was 5,069.0/100,000: a >25-fold increase (22). Indeed, the pattern of age-related survival is similar across species, including invertebrates and single cell organisms (Fig. 2) (23).

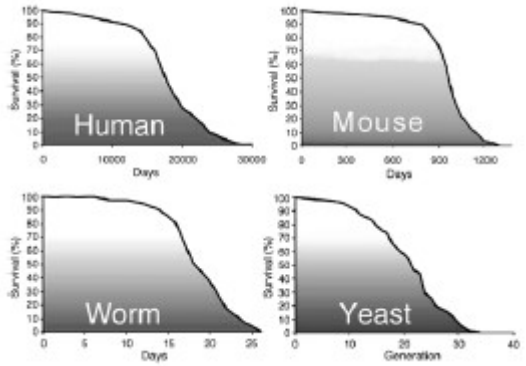

Fig. 2. Viability curves from different model organisms have a similar characteristic shape. Representative mortality data are shown for Homo sapiens, Mus musculus, Caenorhabditis elegans, and Saccharomyces cerevisiae.

2. Changes in biochemical composition in tissues with age.

There are notable age-related decreases in lean body mass and total bone mass in humans (24, 25). Although the amount of subcutaneous fat is either unchanged or decreases, total fat remains the same (24). Consequently, the percentage of a dipose tissue increases with age. At the cellular level, many markers of aging have been described in various tissues from different organisms (26). Two of the first to be described were increases in lipofuscin (age pigment) (27) and increased cross-linking in extracellular matrix molecules such as collagen (28, 29). Additional examples include age-related changes in both the rates of transcription of specific genes and the rate of protein synthesis and numerous age-related alterations in post-translational protein modifications, such as glycation and oxidation (30, 31).

3. Progressive decrease in physiological capacity with age.

Many physiologic changes have been documented in both cross-sectional and longitudinal studies. Examples include declines in glomerular filtration rate, maximal heart rate, and vital capacity (32). These decreases occur linearly from about the age of 30; however, the rate of physiological decline is quite heterogeneous from organ to organ and individual to individual (33, 34).

4. Reduced ability to respond adaptively to environmental stimuli with age.

A fundamental feature of senescence is the diminished ability to maintain homeostasis (35).This is manifest not primarily by changes in resting or basal parameters, but in the alteredresponse to an external stimulus such as exercise or fasting. The loss of "reserve" can result I blunted maximum responses as well as in delays in reaching peak levels and in returning to basal levels. For example,

the induction of hepatic tyrosine aminotransferase activity by fasting is both attenuated and delayed in old rodents (35).

5. Increased susceptibility and vulnerability to disease.

The incidence and mortality rates for many diseases increase with age and parallel the exponential increase in mortality with age (36). For the five leading causes of death for people over 65, the relative increase in death rates compared to the rates for people age 25 – 44 are: heart disease 92-fold, cancer 43-fold, stroke greater than 100-fold, chronic lung disease greater than 100-fold, and pneumonia and influenza 89-fold (22). The basis for these dramatic rises in mortality is incompletely understood, but presumably involves changes in the function of many types of cells, which lead to tissue/organ dysfunction and systemic illness. Interestingly, a retrospective study of centenarians demonstrated that they live 90 – 95% of their lives in very good health and with a high level of functional independence (37). The centenarians do suffer a 30 – 50% annual mortality at the end of their lives, but this represents a marked compression of morbidity toward the end of life and is close to the idealized survival curve in Fig. 1.

Mechanisms / Causes of Aging
Evolutionary

In an effort to adequately explain the phenotype of aged organisms, many theories about the cause(s) of aging have been proposed. However, what is supposedly "known" about the fundamental molecular mechanisms involved in aging remains controversial and largely unproven.

A major reason for this is the obvious complexity of the problem. Aging changes are manifest from the molecular to the organismic levels; environmental factors affect experimental observations; secondary effects complicate elucidation of primary mechanisms; and precisely defined, easily measurable "biomarkers" are lacking. No one unifying theory may be valid, since the mechanisms of aging could be quite distinct in different organisms, tissues, and cells.

A general framework for a plausible theory of aging begins with understanding the evolutionary basis of senescence. Evolutionary pressures select for a minimum successful life: this includes the ability to reach reproductive age, procreate, and then care for offspring until they are weaned (so that they, in turn, will achieve reproductive age and continue the cycle) (38, 39). Within this context, it is likely that the post-reproductive/parental physiology of an organism is an epigenetic and pleiotropic manifestation of the optimization for early fitness.

Kirkwood proposes that three categories of genes may be involved in senescence (40):

(a) those that regulate somatic maintenance and repair,

(b) negatively pleiotropic genes that enhance early survival but are disadvantageous later in life (antagonistic pleiotropy), and

(c) harmful late-acting mutations upon which little evolutionary selection is exerted. The presence of these genes may represent a spectrum from general to species specific (Fig. 3).

Genes involved in cell maintenance and repair are likely to be present in all (or most) organisms, since such essential processes are similar across species. Late-acting mutations are probably species specific, because they are likely to be individualistic and random. Non-maintenance pleiotropic genes could be

universally found within a population or species, but may not be shared between species. An example of antagonistic pleiotropy would be the high expression of testosterone in a male gorilla, which could lead to increased aggression and strength that would allow the male to become dominant and mate more frequently, but may eventually lead to a shortened lifespan due to increased atherosclerosis.

Recent studies at the molecular genetic level have suggested that cellular senescence may be antagonistically pleiotropic because it prevents tumorigenesis, but also contributes

to organismic aging (see below).

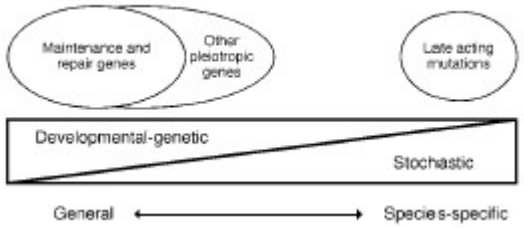

Fig. 3. Genes / events regulating longevity and senescence. Adapted with permission from Kirkwood TB.Human senescence. Bioessays 1996; 18:1009 – 1016 (reference

40). **Vol. 70 No. 1** BIOLOGY OF AGING—TROEN 7

Historically, theories of aging have been divided into two general categories: stochastic and developmental-genetic (Table 2). The term "developmental-genetic" implies a more active genetic control of senescence than likely exists. In addition, these categories are not mutually exclusive, particularly when considering the free radical/mitochondrial DNA theory of aging.

TABLE 2

Theories of Aging

	Stochastic
Somatic Mutation and DNA Repair	
Error-Catastrophe	
Protein Modification	
Free Radical (Oxidative Stress) / Mitochondrial DNA	

Developmental-Genetic

Longevity Genes

Accelerated Aging Syndromes

Neuroendocrine

Immunologic

Cellular Senescence

Cell Death

Indeed, there is probably a spectrum from birth to senescence that reflects a decreasing influence o active genetic influences and an increasing effect of stochastic events (Fig. 3). This would parallel the shift in importance from general to species-specific genes.

Stochastic Theories

Somatic Mutation and DNA Repair Stochastic theories propose that aging is caused by random damage to vital molecules. The damage eventually accumulates to a level sufficient to result in the physiological decline associated with aging. The most prominent example is the somatic mutation theory of aging, which states that genetic damage from background radiation produces mutations that lead to functional failure and, ultimately, death (41, 42). Exposure to ionizing radiation does shorten lifespan (43).

However, analysis of survival curves of radiation-treated rodent populations

reveals an increase in the initial mortality rate without an effect on the subsequent rate of aging (44).

The lifespan shortening is probably due to increased cancer and glomerulosclerosis rather than accelerated aging *per se* (45). The DNA repair theory is a more specific example of the somatic mutation theory.

The ability to repair ultraviolet-radiation-induced DNA damage in cell cultures derived from species with a variety of different life-spans correlates directly with the MLSP (46). Unfortunately, there is not enough experimental support to conclude that these differences between

species are a causative factor in aging.

The cumulative evidence indicates that overall DNA repair capacity does not appear to

change with age, although the site-specific repair of select regions of DNA appears to be important in several types of terminally differentiated cells (47). Future studies will need to focus upon repair rates of specific genes rather than indirect general measurements.

Error-Catastrophe

The error-catastrophe theory proposes that random errors in synthesis eventually occur in

proteins that synthesize DNA or other "template" molecules (48). Generally, errors occurring in proteins are lost by natural turnover and simply replaced with error-free molecules.

Error-containing molecules which are involved in the protein-synthesizing machinery, however, would introduce errors into the molecules that they produce. This could result in an amplification such that the subsequent rapid accumulation of error-containing molecules would result in an "error-catastrophe" that would be incompatible with normal function and life.

However, although there are numerous reports of altered proteins in aging, no direct evidence of age-dependent protein mis-synthesis has yet been reported. The altered proteins that do occur in aging cells and tissues are, instead, due to post-translational modifications such as oxidation and glycation (49, 50). The increases in altered proteins appear to be due to decreased clearance in older cells (51).

Protein Modification

In addition to age-related changes in the steady-state levels of proteins, qualitative alterations leading to changes in function occur. Aging is accompanied by decreased specific activity in many enzymes, altered heat stability, and increased carbonyl content of proteins (50).

These changes can be caused by direct oxidation of amino acid residues, metal-catalyzed oxidation, modification by lipid oxidation products, and glycation. Kohn (29) and Bjorksten (28) hypothesized that the accumulation of post-translationally altered proteins could impair cellular, and ultimately, organ function. Although collagen undergoes increased cross-linking with age (52), such alterations can lead to improved function at some sites and to impaired function at others (53).

The nonenzymatic reaction of carbohydrates with amino groups of proteins (glycation) can give rise to advanced glycosylation end-products (AGEs) (50). These AGEs increase with aging and are implicated in diabetes, eye disorders, and amyloid accumulation Many extracellular matrix proteins exhibit increased cross-linking with age.

Proper organ function depends upon a normal extracellular matrix for processes such as diffusion of essential molecules. In addition, the extracellular matrix plays an important role in the regulation of gene expression. The cross-linking of macromolecules such as collagen, elastin, osteocalcin, and the eye lens protein crystallin (which may be responsible for cataract formation in both the diabetic and aged lens) could alter both of these processes. These covalent protein-protein interactions probably play a role in the increased stiffness of vascular walls with aging. Protein carboxy methyltransferase

(PCMT) assists in the repair of spontaneously arising atypical protein isoaspartyl residues

(54).

Over-expression of PCMT at 29°C in flies extended lifespan, suggesting that under certain environmental conditions, protein repair could be important in longevity.

Free Radical (Oxidative Stress) /Mitochondrial DNA

Another potential cause of cross-linking — free radicals — forms the basis for a theory that has elements of both the stochastic and developmental- genetic classes. Harman initially proposed that most aging changes are due to molecular damage caused by free radicals (55, 56), which are atoms or molecules that contain an unpaired electron and are therefore highly reactive.

Aerobic metabolism generates the superoxide radical (O2•-), which is metabolized by superoxide dismutases to form hydrogen peroxide (H2O2) and oxygen (57). Hydrogen peroxide can go on to form the extremely reactive hydroxyl radical (OH•). These oxygen-derived species can react with macromolecules in a self-perpetuating manner; they create free radicals out of subsequently attacked molecules, which in turn create free radicals out of other molecules, thereby amplifying the effect of the initial free radical attack (9). Reactive oxygen species appear to play a role in regulating differential gene expression, cell replication, differentiation, and apoptotic cell death (in part by acting as secondary messengers in signal transduction pathways) (58, 59).

Production of free radicals in the heart, kidney, and liver of a group of mammals was found to be inversely proportional to the maximum lifespan, although the activities of individual anti-oxidative enzymes were not consistently related to maximum lifespan (60). Over-expression of either superoxide dismutase or catalase alone in transgenic flies does not extend lifespan (61), but some transgenic flies with increased expression of both Cu, Zn-superoxide dismutase and catalase, which act in tandem to remove O2•- and H2O2, respectively, exhibit up to a one-third extension of average and maximum lifespan (61). In addition, there was increased resistance to oxidative damage and an increase in the metabolic potential (total amount of oxygen consumed during adult life per unit body weight).

The mitochondrial DNA /oxidative stress hypothesis represents a synthesis of several theories and therefore comprises elements of both stochastic and developmental-genetic mechanisms of aging (see below). It is proposed that reactive oxygen species contribute significantly to the somatic accumulation of mitochondrial DNA mutations, leading to the gradual loss of bioenergetic capacity and eventually resulting in aging and cell death (Fig. 4) (62 – 64). Ozawa has dubbed this the "redox mechanism of mitochondrial aging" (65). Mitochondrial DNA (mtDNA) undergoes a progressive age-related increase in oxygen free radical damage in skeletal muscle (66 – 68), the diaphragm (69, 70), cardiac muscle (71 – 74), and the brain (75, 76). This exponential increase in damage correlates with the increase in both point and deletional somatic mtDNA mutations seen with age.

Interestingly, extrapolation of the curve to the point where 100% of cardiac mtDNA exhibits deletion mutations produces an age of 129 (65). A deleterious positive feedback results, wherein mtDNA damage leads to defective mitochondrial respiration, which in turn enhances oxygen free radical formation, leading to additional mtDNA damage. Mitochondrial DNA is maternally transmitted, continues to replicate throughout the lifespan of an organism in both proliferating and post-mitotic (non-proliferating) cells, and is subject to a much higher mutation rate than nuclear DNA. This is due, in large part, to inefficient repair mechanisms and its proximity to the mitochondrial membrane

Fig. 4. Mitochondrial DNA and free radical interaction.

where reactive-oxygen species are generated. Defects in mitochondrial respiration with age are found not only in normal tissues (77), but also in people with diseases that are increasingly manifest with age, such as Parkinson's disease (78, 79), Alzheimer's disease (80, 81), Huntington's chorea (82), and other movement disorders (83). Diseases for which mtDNA mutations have been found include Alzheimer's (84, 85) and Parkinson's diseases (75, 85 – 88), and a large number of skeletal and cardiac myopathies (69, 89 – 93). Apoptosis has also been associated with mtDNA fragmentation (94). Is the phenotype of aging in tissues actually due to mtDNA mutation? Specific mutations, while increasing with age, seldom account for more than several percent of the total mtDNA.

However, some studies suggest that the total percentage of mtDNA affected by mutations is much greater, as much as 85%, and increases with age (65). In addition, calor restriction in mice retards the age-associated accumulation of mtDNA mutations (95).

Inherited mitochondrial DNA variants are associated with aging and longevity (96). The J haplogroup was found in a significantly greater percentage of male centenarians in northern Italy than in younger subjects. Interestingly, this same mitochondrial haplotype is over-represented in a number of complex diseases (97), raising the possibility of an antagonistically pleiotropic gene or genes that exert deleterious effects in younger individuals, but lead to better health at later ages (successful aging). To complicate matters further, mitochondrial DNA polymorphisms are present in different frequencies in

various aged populations from Italy, Ireland, and Japan (98). Ongoing studies in Utah, utilizing extensive genealogical records of Mormons, are testing the hypothesis that longevity is maternally determined, given the inheritance of only maternal mtDNA.

Agents that bypass blocks in the respiratory chain, such as coenzyme Q10, tocopherol,

nicotinamide, and ascorbic acid, would be predicted to ameliorate some of the effects of mitochondrial disease and aging. Withdrawal of coenzyme Q from the diet of nematodes extends their lifespan by approximately 60% (99).

Caloric restriction, which can extend lifespan, reduces oxidative damage in primates (100). There are epidemiological studies that suggest roles for dietary antioxidants in the reduction of vascular dementia, cardiovascular disease, and cancer in humans (101). However, results to date in treatment of patients with myopathies have been variably or only anecdotally successful (65). This suggests that a complex interaction exists between pro-oxidant and antioxidant forces in the cell, and that regulation of the balance between the two may be the critical determinant in mitochondrial, and subsequently, cellular

and tissue integrity during aging.

Developmental-Genetic Theories

Developmental-genetic theories consider the process of aging to be part of the genetically

programmed and controlled continuum of development and maturation. Although this is an attractive notion, the diverse expression of aging effects is in sharp contrast to the tightly controlled and very precise processes of development.

Also, evolution selects for the optimization of reproduction; the effects of genes

expressed in later life probably do not play a large role in the evolution of a species. This

class of theories is supported by the observation that the maximum lifespan is highly species specific. As noted above, the maximum lifespan for humans is 30 times that of mice.

In addition, studies comparing the longevity of monozygotic and dizygotic twins and non-twin siblings have shown a remarkable similarity between

monozygotic twins that is not seen in the other two groups.

Longevity Genes

There is ample evidence in many species that MLSP is under genetic control, though the degree of heritability is likely to be less than 35% (102). Despite this apparently low figure, genetic mutations can significantly modify senescence. In yeast a number of genes affect both the average and maximum lifespan (103). The products of these genes act in diverse ways, including modulating stress response,

sensing nutritional status, increasing metabolic capacity, and silencing genes that promote aging. In the nematod (*Caenorhabditis elegans*), mutants with increased lifespan have revealed various genes that appear to play a relevant role (104): *age*-1 alters aging rate; *daf*-2 and *daf*-23 activate a delay in development; *spe*-26 reduces fertility; and *clk*-1 alters the biological clock.

These genes alter stress resistance (particularly in response to ultraviolet light), development, signal transduction, and metabolic activity. The recently isolated *daf*-2 gene appears to encode an insulin-receptor family member (105). Mutations in *daf*-2 can double the lifespan, but require the *daf*-16 gene (106). A mutation in the *daf*-16 gene suppresses the UV resistance and increases longevity of the other gene mutants, suggesting that it acts at a critical point downstream of the other genes (104). The *daf*-16

gene is a member of the hepatocyte nuclear factor- 3/forkhead family of transcriptional regulators, involved in a variety of signal transduction pathways, including insulin signaling (107).

A notable connection between single gene effects upon aging in yeast and higher eukaryotes was revealed by the finding that over-expression of the *SIR2* gene and its homolog extend lifespan in yeast and nematodes, respectively (23). Despite acting via different mechanisms, *SIR2* and its homolog may both exert their effects by linking the regulation of metabolic rate to aging.

A line of Drosophila melanogaster has been identified that exhibits an approximately 35% increase in average lifespan and enhanced resistance to various forms of stress, including starvation, high temperature, and dietary paraquat, a free-radical generato (108). The mutation responsible, dubbed "Methuselah," appears to reside within a single gene that is homologous to GTP-binding transmembrane domain receptors. Another single gene mutation leads to an almost doubling of the average adult *Drosophila* lifespan

without a decline in fertility or physical activity (109). This gene, named "Indy" (for "I'm

not dead yet"), is homologous to a mammalian sodium dicarboxylate cotransporter, which is a membrane protein that transports Krebs cycle intermediates.

The investigators speculate that the mutation in the Indy gene may create a metabolic

state that mimics caloric restriction. Previous studies have demonstrated that one group of

long-lived flies is more resistant to oxidative stress (110), whereas another group exhibits resistance to starvation and desiccation (111).

Genetic analysis of longevity in mammals has not been as revealing. However, immune

loci in mice and humans have been implicated in long-lived subjects (103) (see below). In addition, in the gene encoding the signaling molecule p66(shc), there is a mutation which significantly enhances the resistance to oxidative stress and increases the mean lifespan of mice by 30% (112). The Snell

dwarf mouse contains a single gene mutation that alters pituitary development and prevents the production of growth hormone thyrotropin, and prolactin (113). The dwarf mouse also exhibits an extended

lifespan of 25 – 50%, but is much smaller than normal mice. In contrast, the mice with the mutant p66 develop normally and are not significantly smaller than wild type mice.

As noted above, a number of mitochondrial DNA polymorphisms are associated with

longevity. In addition, the epsilon 4 allele of apolipoprotein E (ApoE), which is associated with increased coronary disease and Alzheimer's disease, is inversely correlated with longevity (114). In contrast, the epsilon 2 allele of ApoE and an angiotensin-converting enzyme (ACE) allele are found more frequently in French centenarians (114). Interestingly, the ApoE2 allele is associated with type III and IV

hyperlipidemia, and the ACE allele predisposes to coronary disease.

These findings further suggest that genes can exert pleiotropic age-dependent

effects upon longevity. Perls et al. note that support for a genetic contribution to human

longevity is further provided by data demonstrating that siblings and parents of centenarians live longer (115). Linkage analysis implicates the presence of a gene or genes on chromosome 4 that are associated with exceptional longevity (115). These authors report that a high percentage of centenarians have had children while in their 40s (well before assisted reproduction). They therefore postulate that an evolutionary force to prolong the period of child bearing would lead to the selection of longevity-enabling genes.

Collectively, these studies also raise the question as to whether some genes affect susceptibility to disease rather than alter intrinsic aging.

In contrast to studies that uncover alterations in the expression of single genes during aging, Weindruch and Prolla and their colleagues have begun investigating the broad spectrum of changes in gene expression that occur during aging and calorie restriction in mice and in monkeys (116 – 119).

A common theme is that aging induces a differential gene expression pattern in muscle and brain consistent with inflammatory and oxidative stress, and reduced expression of metabolic and biosynthetic genes. In muscle and brain from mice, caloric restriction either completely or partially prevented the age-related changes in gene expression. Interestingly, caloric restriction did not ameliorate the age-induced alteration in the program of gene expression seen in muscle from aging monkeys. So even though

the age-related changes in gene expression may be similar across species, the response to

caloric restriction may not be similar.

Accelerated Aging Syndromes

Although no genetic disease exists that is an exact phenocopy of normal aging, several

human genetic diseases, including Hutchinson- Gilford syndrome (the "classic" early-onset progeria seen in children), Werner's syndrome ("adult" progeria), and Down's syndrome (trisomy 21), display some features of accelerated aging (120). Werner's syndrome (WS) is an autosomally recessive inherited disease (121). Patients prematurely develop arteriosclerosis, glucose intolerance, osteoporosis, early graying, loss of hair, skin atrophy, and menopause. However, they do not typically suffer from Alzheimer's

disease or hypertension. WS patients have an increased incidence of sarcomatous tumors and develop cataracts on the posterior surface of the lens, not in the nucleus, as is usually seen in older people. In addition, they develop laryngeal atrophy and ulcerations on the arm and legs. Most patients die before the age of 50.

The gene responsible for WS has been localized to chromosome 8 (122) and appears to be a helicase (123), an enzyme involved in unwinding DNA. DNA helicases play a role in DNA replication and repair. Cells from WS patients display chromosomal instability, elevated rates of gene mutation, and nonhomologous recombination. However, there is no obvious defect in DNA repair mechanisms, as evidenced by a resistance to ultraviolet exposure or other DNA damaging agents, similar to normal cells.

Hutchinson-Gilford syndrome is an extremely rare, autosomal recessive disease in which aging characteristics begin to develop within several years of birth (121).

These include:

Wrinkled skin, stooped posture, and growth retardation. These patients suffer from advanced atherosclerosis, and usually die from myocardial infarction, by the age of 30. However, unlike WS patients, they do not typically suffer from cataracts, glucose intolerance, or skin ulcers.

People with Down's syndrome have trisomy or a translocation involving chromosome 21

(120, 121). They suffer from the early onset of vascular disease, glucose intolerance, hair loss, and degenerative bone and joint disease, as well as increased incidence of cancer. Their lifespan is apparently 50 – 70 years (not as short as previously believed, since earlier mortality may have represented neglect of these individuals).

Dementia occurs earlier and more often in patients with Down's syndrome than in the general population. Patients develop neuropathological changes similar to the changes seen in dementia of

Alzheimer's type, including amyloid deposition and neurofibrillary tangles. This may be related to the presence of the ß-amyloid gene on chromosome 21.

Kuro-o recently reviewed a number of mouse models which have been developed that

exhibit many of the aging phenotypes seen in humans (124).

Of these, the *klotho* mouse suffers from a defect in a single gene that codes for a membrane protein; it exhibits a plethora of marked age-related phenotypes that are also seen in humans. These include reduced lifespan, decreased activity, premature thymic involution, skin atrophy, arteriosclerosis, osteoporosis, emphysema, and lipodystrophy. There are a number of strains of senescence-accelerated mice (SAM) that exhibit variable aging phenotypes consistent with multigenic effects.

Targeted disruption of genes responsible for premature aging syndromes in humans results in incomplete or absent age-related phenotypes. Despite the fact that none of the mouse models displays all of the phenotypes associated with human aging, they are likely to be valuable tools in identifying some of the molecular mechanisms of aging.

Neuroendocrine Theory

The neuroendocrine theory proposes that functional decrements in neurons and their associated hormones are central to the aging process (125). An important version of this theory holds that the hypothalamic-pituitaryadrenal (HPA) axis is the master regulator of aging in an organism. Because the neuroendocrine system regulates early development,

Growth, puberty, control of the reproductive system, metabolism, and many other aspects of normal physiology, functional changes in this system could exert effects throughout the organism.

The decline in female reproductive capacity is an obvious neuroendocrine age-related

change. Mounting evidence suggests that both the ovary and the brain play key roles in

menopause (rather than the previously held view of ovarian exhaustion) (126). The neuroendocrine theory of aging is supported by experiments that show that hypophysectomy, followed by the replacement of known hormones, maintains (and may extend) lifespan in rodents (127). In addition, reductions in brain dopaminergic neurotransmission are more prominent in a shorter-lived rat strain (128). Levodopa, a dopaminergic drug, can prolong the mean lifespan in mice (129). Treatment of rats with deprenyl facilitates the activity of the nigrostriatal dopaminergic neurons and protects these neurons from their age-related decay (130), and deprenyl increases both the average and maximum lifespan (131, 132).

Many human studies demonstrate gradually decreasing levels of peripheralhormones accompanied by normal levels of trophic hormones (125). This suggests either

increased response to the peripheral hormones by the HPA axis or inappropriately low

expression of the stimulating hormone. However, many organisms with aging phenotypes

similar to those of higher vertebrates lack complex neuroendocrine systems. The changes that occur in the neuroendocrine system may be due to fundamental age-related changes in all cells and may therefore be secondary manifestations of the aging phenotype.

Immunologic Theory

The immunologic theory of aging is based upon two main observations: (a) the functional

capacity of the immune system declines with age, as evidenced by a decreased response of T cells to mitogens and reduced resistance to infectious disease; and (b) autoimmune phenomena increase with age, such as an increase in serum autoantibodies (133). There is a shift toward increasing proportions of memory T cells, accompanied by enhanced expression of the multidrug-resistance p-glycoprotein (134). Humoral (B-cell mediated) immunity also declines with age, as evidenced by decreased antibody production and a disproportionate loss in the ability to make high affinity IgG and IgA (immunoglobulin

G and A) antibodies. In addition, differences in the MLSP of different strains of mice have been related to specific alleles in the major histocompatibility gene complex (135).

The genes in this region also contribute to the regulation of mixed-function oxidases (P-450 system), DNA repair, and free-radical-scavenging enzymes.

Caruso et al. suggest that mouse and human histocompatibility genes may be associated with longevity via different mechanisms, in mice via susceptibility to lymphomas and in humans via infectious disease susceptibility (136). There is also evidence that cytokine

gene polymorphisms may interact with histo-compatibility genes to influence longevity

(136).

Although the immune system obviously plays a central role in health maintenance and

survival, similar criticism can be directed at the immunologic theory as has been directed at the neuroendocrine theory. Complex immune systems are not present in organisms that share aspects of aging with higher organisms. In addition, the inability to distinguish between fundamental changes occurring in many types of cells and tissues, not just those of the immune system, and the secondary effects mediated by the aging-altered immune system, make interpretation of this theory difficult. Proposed mechanistic studies of the immune theory include producing transgenic mice that carry the histocompatibility

complex from a longer-lived rodent species, to determine effects on disease incidence

and lifespan.

Cellular Senescence

The complexity of studying aging in organisms has led to the use of well-defined cell culture systems as models for cellular aging or senescence. Hayflick and Moorhead (137) pioneered the model of replicative senescence and identified normal human diploid fibroblasts in culture as a model for aging. They observed an initial period of rapid and vigorous proliferation, invariably followed by a decline in growth rate and proliferative activity, finally leading to a cessation of proliferation. This model proposed that aging is a cellular as well as an organismic phenomenon, and that the loss of functional capacity of the individual reflected the summation of the loss of critical functional capacities of individual cells.

It is important to note that populations of senescent cells do not necessarily die, and that they can be maintained in culture for years in a post-mitotic (non-proliferating) state, with regular changes of culture medium (138 – 140). The loss of proliferative capacity of human cells in culture is intrinsic to the cells and not dependent upon environmental

or culture conditions (137). In addition, senescence is inevitable unless the cells undergo

transformation and acquire a constellation of abnormal characteristics such as multiple chromosomal abnormalities, genetic mutations, and changes in morphology and growth rate.

The number of times the cells divide is also more important in determining proliferative lifespan than the actual time the cells spend in culture (141). Cells continuously passaged in culture until the end of their proliferative lifespan achieve approximately the same number of population doublings (PDLs) as cells that are held in a stationary phase for an extended period (months) and then recultured until senescence. The cells therefore seem to possess an intrinsic mechanism that "counts" the number of divisions and not the time that passes.

In addition to studies on fibroblasts, limited *in vitro* lifespan has been reported for glial cells (142), keratinocytes (143), vascular smooth muscle cells (144), lens cells (145), endothelial cells (146), and lymphocytes (147). *In vivo*, serial transplants of normal somatic tissues, such as skin and breast, from old donor mice to young genetically identical recipients show a decline in proliferative activity and eventual failure of the graft (148). Similarly, skin from old donors retained an increased susceptibility to carcinogens whether transplanted to young or old recipients (149). Do changes in cells in culture parallel changes in cells from aging organisms?

The replicative lifespan of fibroblasts in culture is inversely related to the maximum

lifespan of several diverse vertebrate species (150). Studies suggest that the replicative lifespan of cells in culture is inversely related to the age of the donor in both humans and rodents (151 – 153). This *in vivo-in vitro* relationship also holds for several different cell types, including hepatocytes (154), keratinocytes (155), and arterial smooth muscle cells (144). However, in these cross-sectional studies,

there is a great deal of variability, and the correlation coefficient, though statistically significant, is low.

Cells cultured from healthy individuals do not appear to exhibit a consistent age-related proliferative capacity (156). Cells from people with Werner's syndrome do senesce more rapidly I culture than age-matched controls; however, a consistently similar relationship does not hold for cells from people with Hutchinson-Gilford syndrome (121). Thus, under some circumstances, the proliferative characteristics of cells during aging *in vivo* are maintained in culture.

Unfortunately, convincing evidence that senescent cells accumulate with age *in vivo* is lacking to date. A potential biomarker for aging, ßgalactosidase, has been described; it initially seemed to distinguish between senescent cells and either pre-senescent or quiescent cells (157). However, subsequent data indicate that *in situ* expression of ß-galactosidase exists in confluent, quiescent, pre-senescent cells and is not necessarily specific for senescence (e.g., possibly lysosomal damage rather than senescence *per se*) (158).

Rubin proposes that the *in vitro* limit on replication is an artifact that reflects

the cells' traumatic response to establishment *in vitro* and that their subsequent maintenance in a foreign environment is starkly different from their *in vivo* milieu (159). He suggests that a decline in the rate of cellular proliferation more accurately correlates with aging in animals.

A major approach to studying the regulation of cessation of replication in senescent cells has been to examine pathways, at various levels, which likely play significant roles in regulating cell proliferation and adaptive responses. Senescent cells are often less responsive to mitogens but can exhibit variable changes in growth-factor and growth-factor receptor expression compared to young cells (160). Senescent-related alterations in signal transduction pathways and nuclear transcription factors have also been documented. These alterations indicate that senescent cells exist in a growth state

that is quite distinct from that of young cells and hint at the complex alteration in cellular

physiology during senescence.

The phenomenon of telomere shortening with aging represents a potential "clock" or

counting mechanism for senescent cells (161). Telomeres are structures at the end of chromosomes that prevent degradation and fusion with other chromosome ends (162). The average length of the terminal restriction fragment of chromosomes decreases with both *in vitro* and *in vivo* aging of fibroblasts and peripheral blood lymphocytes (161, 163 – 167). Indeed, telomere length in lymphocytes progressively declines as a function of donor age from newborn to great-grandparents in their eighties

(168). Immortalized and transformed cells and germline cells express telomerase, which prevents shortening of the telomeres (169, 170).

However, some immortal cells exist without detectable telomerase (171), and stem cells and some normal somatic cells which express telomerase, continue to experience telomeric shortening (172 – 174). These data suggest that the length of the telomeres *per se*, rather than the degree of telomerase activity, is the more important factor in cellular senescence. A recent study further demonstrates that the shortest telomere, not the average telomere length, determines cell viability and chromosomal stability

(175). Experimental nonenzymatic elongation of telomeres extends the lifespan of cells

(176).

Furthermore, reactivation of telomerase, via the introduction of the telomerase reverse

transcriptase unit into normal human cells, increases telomere length and extends the lifespan of both retinal epithelial cells and foreskin fibroblasts (177).

Cells that had exceeded their normal lifespan by 20 population doublings exhibited normal karyotype and morphology similar to their younger counterparts. Shortened telomeres also led to a form of premature aging *in vivo* (178).

Sixth generation telomerase-deficient mice with markedly shortened telomeres exhibited decreased weight and fecundity, graying and alopecia, increased ulcers and cancer, and shortened lifespan.

Products of the retinoblastoma (Rb) and p53 tumor-suppressor genes have also been implicated in replicative senescence (179, 180). Although similar levels of p53 are expressed in young and old cells *in vitro*, both DNA binding and transcriptional activity are increased in senescent cells (181). The Rb gene product is not phosphorylated in senescent cells (182).

Simian virus 40 large T antigen, which is bound by the p53 and Rb gene products, can facilitate escape from senescence (183). T-antigen deletion mutants that lack either Rb- or p53-binding domains are unable to mediate escape from senescence (184). Furthermore, treatment with antisense oligonucleotides to the Rb and p53 tumor-suppressor genes can extend the *in vitro* lifespan of human fibroblasts (185). The p21

(186 – 188) and p16 (189 – 191) inhibitors of cyclin kinases (and therefore cell cycle progression) are over-expressed in senescent cells. The p21 protein appears to act by forming complexes with members of the family of E2F transcription factors in senescent cells (Rb/CDK2 [cyclin-dependent kinase 2]/cyclin E or with the Rb-relate p107/CDK2/cyclin D), down-regulating transcriptional activity and thereby

inhibiting progression through the cell cycle (186).

Targeted disruption of the p21 gene delays the onset of senescence in fibroblasts derived

from human lung (192). However, adrenocortical cells express high levels of p21 throughout their *in vitro* lifespan up to and including senescence (193). Skin fibroblasts from patients with Li-Fraumeni syndrome are heterozygous for p53. In culture, these cells lose the remaining p53 allele and are subsequently unable to express p21, but still undergo *in vitro* aging (194), suggesting that p53 and p21 are not required for senescence.

In senescent cells, p16 complexes to and inhibits both the cyclindependent kinase 4 (CDK4) and CDK6 cell cycle kinases (189). The *ras* oncogene product can induce senescence that is accompanied by accumulation of p53 and p16 (195). This occurs

only in nonimmortalized cells and may reflect a homeostatic response of the cell to a transforming stimulus. Induction of expression of p16 by demethylation-dependent pathways or of p21 by demethylation-independent pathways can induce senescence in immortal fibroblasts that do not express p53 (196).

Of those genes whose expression is required for G1/S cell cycle progression, senescent fibroblasts express no CDK2 and cyclin A, and reduced amounts of the G1 cyclins, C, D1, and E, compared to

young cells (197). The expression of early G1 markers, but not late G1 markers, indicates that senescent cells may be blocked at a point in late G1.

The p53 gene plays an important role in a slew of critical cellular processes in addition to

senescence, including cell cycle control, apoptosis, DNA repair, and transcription (198). Cells from telomerase-deficient mice (see above) exhibited high levels of p53 (199). In addition, deletion of p53 in the mice initially mitigated the effects of the telomerase deficiency, but ultimately contributed to greater malignant transformation. The p53 and p21 stress response is diminished in the p66shc null mice (also see above) that exhibit an increased lifespan (200). p53 has also been implicated in the effects exerted

upon aging by radiation, oxidative stress, and the SIR2 gene (201).

Recently p53 has been thrust to center stage in helping to increase our knowledge of the underlying mechanism(s) responsible for *in vivo* aging. Since p53-deficient

mice die early due to marked increases in tumors, they do not represent a practical model to study aging. Therefore, Tyner et al. capitalized upon the serendipitous generation of a mouse that expresses a mutant p53 that enhances wild-type p53 activity (202). Not surprisingly, the mice are resistant to tumor development. However, the unexpected and fascinating finding is that the mice with augmented p53 activity also age prematurely and exhibit osteoporosis, generalized organ atrophy, diminished wound healing as well as stress tolerance, lymphoid atrophy, and reduced body weight. Consequently, it appears

that increasing p53 activity reduces the incidence of cancer, but concurrently increases the aging rate (Fig. 5). A fine equilibrium between the antineoplastic and pro-aging characteristics of p53 may lead to the optimal lifespan for an organism;

too little p53 results in death from cancer, whereas too much p53 leads to death by accelerated aging. Since p21 can be induced by p53-dependent mechanisms, it is possible that p21 is partly responsible for some of the observed aging phenotypes in these mice (203).

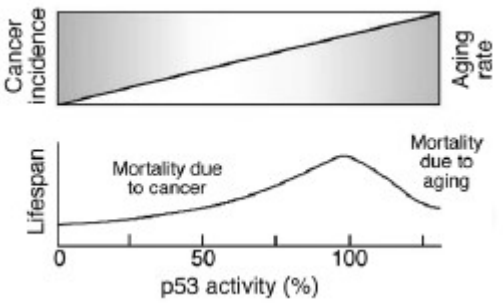

Fig. 5. Balancing cancer and aging. Adapted with permission from:Ferbeyre G, Lowe SW. The price of tumour suppression? Nature 2002; 415:26 – 27 (reference 201).

These observations emphasize the presence of complex and incompletely understood, overlapping networks regulating cell cycle progression and proliferation. Depending upon the balance of positive and negative influences, cell proliferation can continue or senescence may ensue. These data are consistent with the theory that cellular senescence evolved as a mechanism of tumor suppression and that aging is an antagonistically pleiotropic manifestation of evolutionary pressures to prevent malignant transformation, perhaps in large part via the actions of p53. The unavoidable conclusion is that cellular senescence is good for the organism; aging may be the price we pay to avoid, for the

most part, cancer. However, even this concept has been qualified by the demonstration that senescent cells can foster the growth of pre-malignant and malignant epithelial cells in culture and the tumorigenesis of these cells in mice (204). The stimulation was due to both soluble and insoluble factors secreted by senescent cells.

While these findings seem at odds with the beneficial effects of cellular senescence,

they are themselves another example of antagonistic pleiotropy wherein a process that has evolved to protect against cancer may in fact predispose to cancer later in life.

Cell Death

There are two distinct patterns of cell death: necrosis and apoptosis. Massive cell injury, often accompanied by inflammation, can lead to necrosis. Necrosis is essentially accidental and entails clumping of chromatin into ill-defined masses, swelling of organelles, and ultimately membrane and cell disintegration (205). In contrast, apoptosis is an active, gene-directed "suicide" in response to external or internal stimuli, usually in the absence of significant external injury (205).

In most circumstances, apoptosis is important, thereby permitting the organism to maintain homeostasis. Apoptosis initially involves compaction and segregation of chromatin adjacent to the nuclear membrane and condensation of the cytoplasm. This rapidly progresses to nuclear/cellular pedunculation and fragmentation. The membrane-bound apoptotic bodies are then phagocytosed by adjacent cells. Although "programmed cell death" and "apoptosis" are often used interchangeably, they are not actually synonymous terms. Lockshin and Zakeri (203) stress that programmed cell death is a developmental event, whereas apoptosis is a mode of cell death.

Programmed cell death often involves increases of lysosomal enzyme and rarely exhibits the laddering of DNA seen in apoptosis. It is likely that programmed cell death is a type of apoptotic (controlled) cell death. Understanding the genetic basis of apoptosis initially depended upon work conducted in the nematode *C. elegans*, which has been a useful model system because the developmental fate of every cell has been determined (206); of the 1,090 cells formed, 131 eventually die.

Three genes (*ced-3, ced-4,* and *ced-9*) play an important role in cell death in the nematode (207, 208). *Ced-3* is required for apoptosis in *C. elegans*; mammalian homologs include cysteine proteinases (ICE, CPP32, and ICH-1) (209). *Ced-9* blocks apoptosis; mammalian homologs include bcl-2 and bcl-XL (208). Bcl-2 was originally identified as an oncogene because of its over-expression in a form of B-cell lymphoma. Additional mammalian homologs of bcl-2, which promote apoptosis, include bax, bad, and bak (210). Bcl gene family members can form homodimers or heterodimers, permitting a fine degree of control of cell survival. Heterodimerization with either bcl-2 or bcl-XL prevents cell death.

Research is ongoing to elucidate the possible role of apoptosis in aging and diseases associated with aging. If cells are unable to repair DNA damage, apoptosis may ensue, followed by replacement via division of another cell. Senescent fibroblasts in culture are resistant to apoptotic signals, being unable to downregulate bcl-2 expression (211). This raises the possibility that damaged senescent cells may accumulate with increased organismal age, potentially compromising tissue function.

Induction of apoptosis in the livers of old rats by a genotoxic agent is significantly reduced, compared to the induction of apoptosis in the livers of young rats (212). Caloric restriction in rodents upregulates apoptosis in the liver via the removal of preneoplastic cells (213, 214). Warner et al. suggest that this may counteract the diminished apoptosis in aging and explain life extension induced by caloric restriction (215).

Apoptosis plays a critical role in the immune system, where as many as 95% of T lymphocytes undergo cell death (presumably because they recognize self-antigens) (216). Lymphocyte apoptosis is mediated by a cell-surface receptor, Fas. Mice lacking Fas exhibit increased autoimmune disease and are short lived. Caloric restriction

in such mice increases T-lymphocyte apoptosis and extends lifespan (217). Fas expression decreases in older mice, and transgenic over-expression maintains Fas-induced apoptosis (218).

Cell death is a characteristic in a number of neurodegenerative diseases common in aging

(219). Specific neuronal loss is seen in Alzheimer's disease (hippocampus and cortex), Parkinson's disease (substantia nigra), Huntington's disease (striatum), and amyotrophic lateral sclerosis (motor neurons). □-amyloid protein is cytotoxic to cultured neurona cells, which then undergo apoptosis.

Conclusions

Despite the near-universal phenomenon of aging in living organisms, there is an extraordinarily varied phenotype that accompanies aging in specific individuals. Furthermore, it appears that evolutionary pressures have led to the development of a remarkable homeostatic complexity to the underlying mechanisms that cause us to grow old. The three quotations at the beginning of this article aptly represent these processes. Butch Cassidy recognized the inexorable forces that cause us to age. The concept of antagonistic pleiotropy is reflected in the other two insights. It seems that we clearly pay

a price to maintain a high level of reproductive fitness — there is no free lunch. However, the ironic, yet ultimately satisfying, paradox may be that the only way that we can actually live as long as we do is, in fact, to grow old.

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Aging Differently: Issues of Gender and Race

Recognition of the diversity of health conditions and functional challenges that determine long-term care use has been central to the analysis of current and potential delivery systems. Yet elders plagued by chronic illness and disability are now also being increasingly recognized as diverse, from the perspectives of race and ethnicity. Persons of European descent still form a clear majority among elders, even more than they do among other age groups, but improved health care for the poor and more relaxed immigration policies have yielded a more rapidly expanding population of aged persons of color than of aged whites. Elders of color are currently found to be at greater risk of chronic illness and disability, to have shorter life spans, and to utilize more acute-care but fewer chronic care services than majority group elders.

Although observed differences in family support and health care expectations are often cited to explain lower rates of chronic care use, these hypothesized cause-and-effect relationships have not been demonstrated and may be merely a framework in which to blame the victims of inaccessible and inadequate services. Given current patterns of societal under-investment in communities of color and the resulting inequities in access to medical care and social services, these utilization and outcome differences can be expected to persist or grow larger. As the baby-boom generation ages toward long-term care, its complexion will be anything but monochromatic. The implications of these changes for policy, program design, and service delivery have received scant attention.

Life spans, and particularly the aging experience, differ not only by race and ethnic group, but also by gender. Long-term care has been dubbed a "women's issue" since men constitute the minority among care recipients and care providers. There is increasing evidence that, compared with men, women have lower age-adjusted mortality rates and higher morbidity and disability rates, as well as lower rates of acute-care use and higher rates of physician and long-term care utilization. Women are likely to spend both more years disabled and more years caring for the disabled than are men. New research suggests that providers respond less to the objective burdens women shoulder and more to the competing demands of life faced by men. It is unclear whether the historical/cultural preference for female caregivers can be maintained as generations more used to gender equality approach long-term care. Politically and economically feasible alternatives to chronic care policies that do not assume maximal reliance on women's informal care need more attention.

This course explores the question of how race and gender differences in long-term care use and outcomes should be considered in assessing current programs and proposals for reform. Understanding

the reasons for and consequences of these differences can illuminate basic issues in community care. The focus on gender and race highlights the intersection of clinical judgments and personal preferences in defining the need for care, as well as consumer and care-provider roles in shaping servicedelivery dynamics. Evidence is first presented for race and gender differences in disease prevalence, morbidity, mortality, and levels of disability. Group differences in care-giving and their consequences are also highlighted.

Examining the relationships between client diversity and use of services suggests the need for a broader model to explain what determines service use. The implications these differences may have for the design of delivery systems for both medical and long-term care are also explored.

WHO LIVES LONGER AND WHO STAYS HEALTHIER?

In order to better understand and identify ways to strengthen the community-based LTC system, we must first identify the intended care recipients, including what determines their service use and the duration of their need for service. To begin exploring policy and service-delivery implications of well-known racial and gender differences in longevity, health status, and levels of functional impairment, this section presents gender and racial comparisons along these dimensions. While elders have generally benefited from medical and technological breakthroughs, gender and racial differences in morbidity and mortality persist. White women live longer than white men, and white elders live longer than elders of color.

Research has identified several factors that contribute to these gender differences, such as a higher incidence among men of fatal diseases associated with the stress of male occupational and social roles and of less healthy life-styles that often include alcohol abuse, smoking, and high-risk and violence-related behavior (Verbrugge 1984, 1985; Hazzard 1986; Manton 1988; Waldron 1976, 1983; Wingard 1984; Hess 1990). Gender differences in the age of onset of fatal diseases contribute to the greater life expectancy of women. In 1980 a white woman aged sixty or older could expect to live nearly 30 percent longer than a white man of her age. White women have a longevity advantage over men, but this advantage is often coupled with chronic disease and riddled with increased risks of functional impairment. For example, analysis of the coexistence of multiple chronic conditions, or comorbidity, reveals that in each age group the proportion of women with two or more of nine chronic conditions-arthritis, hypertension, cataracts, heart disease, varicose veins, diabetes, cancer, osteoporosis, and stroke--is higher than the proportion of men with two or more conditions (Guralnick et al. 1989).

Although many of the same factors are found to be associated with higher mortality among white men and among elders of color, other factors, such as the impact of lifelong exposure to poverty and discrimination, and cultural norms that influence behavior have also been suggested as explanations for the racial/ethnic differentials in longevity. Higher rates of morbidity and mortality due to the leading causes of death are found among elders of color. For example, Native American, Latino, and African-American elders have a higher incidence than white elders of cardiovascular disease, diabetes, hypertension, asthma, and strokes (Cook 1989; Kramer, Polisar, and Hyde 1990; National Caucus and Center on Black Aged, Inc. 1988; U.S. Senate Special Committee on Aging 1986; MacDonald, Harlow, and Ludwin 1989; Cuellar 1990a, 1990b; MoriakeDouglas and Yeo 1990).

Racial differences in the incidence of fatal diseases result in racial differences in longevity that are as dramatic as those attributed to gender. In 1982, life expectancy for African-American men was sixty-

five years, as opposed to seventy-one years for white men. Gender differences between African-American elders parallel gender differences between older whites. Older African-American women have a longevity advantage over African-American men, but older African-American women have a shorter life expectancy than older white women (Manuel 1980).

In 1980, Pacific/Asian elders were shown to have had the lowest age-adjusted overall mortality rate of any group over the past twenty years (MoriakeDouglas and Yeo 1990).

Among Hispanics, Puerto Ricans have the highest mortality rates in all age groups except those aged seventy-five or older (Cuellar 1990a). Native American elders living on reservations have a higher life expectancy than Native American elders living in urban settings (Cuellar 1990b). These latter results suggest that environmental, behavioral, and service-utilization factors may be as important as genetic or biological factors in explaining morbidity and mortality differentials.

Directly related to the incidence of fatal diseases and the corresponding differences in longevity are the levels of functional impairment associated with advancing age. It is generally accepted that functional disability increases for both men and women with advancing age. Marked gender differences between white elders hold consistently across all definitions of functional status, with higher disability rates for white women in every age group (Leon and Lair 1990). Compared to all white elders, however, a significantly higher proportion of African-American, Latino, and Native American elders experience difficulties with activities of daily living (ADLs) and instrumental activities of daily living (IADLs) (Commonwealth Fund 1989; O'Donnell 1989; Weibel- Orlando 1989). (Comparable data are not readily available for Pacific/Asian elders.)

In sum, all of these comparisons indicate that white women, in general, enter old age with a longevity and health status advantage over white men and that, in general, white men and women have these advantages over elders of color. However, older white women and elders of color are generally more functionally impaired than older white men. There are several reasons why these gender and racial differences are important to consider in policy formulation.

First, community populations may require a different mixture of community-based LTC services (e.g., emphasizing skilled versus paraprofessional care) depending on their race and gender distribution. Older men, due to their briefer, more acute episodes of illness, may require more medically intensive types of care. On the other hand, older women, given their less often fatal, but chronic disorders, may require less medically intensive, but long-term, care. This distinction has implications for benefit design and care planning.

Second, gender and racial differences in longevity affect the duration of functional impairment and, consequently, the period of time over which services will be needed by individual elders. One can expect that older white women will use services the longest since they generally outlive white men and elders of color. These differences also imply that elders of color, given their greater vulnerability to fatal disease and their greater degree of functional impairment, can be expected to use a combination of medically oriented and unskilled care over a shorter period of time than white elders.

A third implication of these differences for community-oriented care has to do with the need to train care providers to be sensitive to gender and racial differences and responsive to diverse life histories. Because old men are in the minority in most LTC programs, and because men are also often the minority among staff, there are fewer accepted social roles for older men in LTC programs. Frequently, LTC programs are ill prepared to deal with the needs of older men. For example, our experience in evaluating adult day-care centers has been that many of the activities designed for

participants, such as sewing, knitting, or arts and crafts, are more in keeping with traditional female roles. Few activities, such as carpentry, reflect traditional male roles. Older men in these settings have been observed to struggle with being one of a few men surrounded by a majority of women. Similar struggles have been observed in the behavior of older men of color in adult day-care centers.

In their case, the additional complication of their historical relations with whites becomes another concern. Through a better understanding of gender and racial differences, care providers can begin to identify how conventional service approaches need to be modified or strengthened. While care must be planned and delivered to meet the needs of the individual, both professional and paraprofessional providers can be trained to take racial and gender differences into account in designing programs and activities.

PATTERNS OF SERVICE USE

In order to more fully understand how racial and gender differences in longevity, health status, and functional impairment affect service utilization rates, this section examines the literature on service use by women and elders of color. We will begin with the use of acute-care services, and then go on to address the use of long-term care services.

Physician and Hospital Services

There is clear evidence of gender differences in the use of physician and hospital services: women tend to make more physician visits per year than men, and the interval between visits is shorter for women (Soldo and Manton 1985); but for both physician and dentist visits, gender disparities are reduced with advancing age (Wan 1982; Wan and Arling 1983). While some research on health-care use has found no gender effects among the oldest sample members, gender differences in reporting illness persist throughout all the age groups studied; and the data suggest that the process leading elders to consult a physician, namely, help-seeking behavior, may differ by gender and race (Mutran and Ferraro 1988). They further suggest that the incidence of acute versus chronic conditions may also influence behavior differently. Men who assessed their health as poor were more likely to see a physician than were women who assessed their health as poor.

These gender disparities may be related to differences between men's and women's perceptions of symptoms and definitions of ill health, as well as to their different degrees of willingness to talk about illness. Verbrugge (1985) concludes that there is some evidence of women's tendency to utilize more extensive care for major medical episodes (i.e., to take more drugs or more kinds of actions) than men. In addition, women's episodes of illness are more protracted, involving more days spent in bed, for example.

Another explanation for observed gender differences in the use of physician services focuses on physician attitudes and behavior toward women. This view, as summarized by Wingard (1984), holds that women are diagnosed and treated differently from men. Women are viewed as hypochondriacs by physicians, who give women less thorough diagnostic assessments but more unnecessary treatment and follow-up care. The evidence for this explanation is inconclusive.

The literature on physician attitudes and behavior toward the poor and toward people of color, on the other hand, more clearly suggests their differential treatment by physicians. Hall, Rote, and Katz (1988) reviewed the literature on physician/patient behavior, which consistently shows that nonwhite patients and those with low incomes receive less information about their conditions, less positive feedback, or reassurance, and less communication overall from physicians than higher-income patients receive. Ventres and Gordon (1990) cite the results of an Ohio survey of family practice residents (Price et al. 1988), one-fourth of whom felt that people were poor because they were lazy and that most

poor people lived well on government assistance. Additionally, the majority of these residents believed that low-income patients were relatively less knowledgeable about illness, less likely to understand medical care directions, and less inclined to comply with medical regimens.

These findings suggest that, for many people of color or of low income, interactions with physicians and the acute-care system are qualitatively different than for (white) people with higher incomes. As gatekeepers of the acute-care system, physicians play a critical role in determining access to hospitals and other sources of medically skilled care.

Explanations for racial disparities in the use of medical services have focused primarily on access issues related to insurance coverage, funding sources, or income. For example, while 96 percent of all elders aged sixty-five or older are enrolled in Medicare, a lower proportion of Latino elders (83 percent) are covered. Among those who are, only 21 percent of Latinos, compared to 69 percent of all elders, purchase supplemental insurance policies (Commonwealth Fund 1989).

Byrd (1990) points to additional structural inequities and institutional racism in the delivery of health care as factors that influence the use of services by elders of color. Medicare requirements for deductibles and co-payments are examples of inequities resulting from the design of a program. For example, catastrophic out-of-pocket expenses were twice as likely to be incurred by elders with incomes below $10,000 as for those with incomes above $10,000, suggesting that Medicare's seemingly equal treatment of all elders in its benefit structure actually leaves low-income elders inadequately covered (Feder 1990). Another example of structural inequity is the exclusion from Medicaid of 40 percent of elders whose incomes fall below the official, government poverty line (Butler and Hyer 1990). This situation is partly due to state policies on Medicaid eligibility which purposely set income-eligibility cut-off points below the federal poverty level. For those elders with low incomes who cannot qualify for Medicaid, there is no access to nursing home care or other community-based long-term care services funded by Medicaid programs.

Institutional racism, consisting of such actions as discounting race/ ethnicity as a valid factor to consider in planning and delivering care, can lead to inequities of access to care. For example, research has shown that the number of multilingual ethnic staff and administrators is significantly correlated with access to services and minority-elder utilization (Holmes et al. 1979; Scannel 1989; Morrison 1982). Failure by an organization to respond to an articulated community need, such as a call for outpatient clinics to be staffed by bilingual personnel in order to facilitate diagnosis and treatment and to enhance physician/patient communication, perpetuates institutional racism by excluding all persons who cannot avail themselves of needed services because they do not speak the language or have access to a translator. As Wolinsky and colleagues (1990) indicate, sufficient research has demonstrated inequitable access to health care, so the development of new programs committed to eliminating ethnically based inequities is now warranted.

There are several implications for community care delivery in the data presented above. Given the prominent role that the acute-care health system plays in controlling access to long-term care, existing barriers to acute care only increase the barriers to LTC. Additionally, limited access to health care by elders of color means that their health problems will only become more complex as these problems go untreated. For the long-term care system, this means that once elders of color do gain access to LTC, they are likely to have more complex needs than their white counterparts. The repercussions of greater degrees of need for any service organization can be felt at most levels of that organization. A more complex caseload, for example, requires greater personal attention from staff, requiring, in essence, a higher staff/client ratio.

Finally, provider attitudes have a significant impact on how elders of color view and respond to the community care system.

A long history of exclusion from mainstream services, as personally experienced by an elder of color, can lead to lower expectations about what is reasonable and appropriate care. Not only will expectations be lower, but organizational features (e.g., lack of bicultural staff) may contribute to a client's sense that, even if a need is recognized, the organizational response is likely to be negative, so the need will not be met. To use a term from psychology, this client's behavior represents "learned helplessness." In such situations, all parties are deadlocked, unable to make any progress in addressing the issues. For the community care provider, that might mean failing to recognize some of the needs in a particular community. For the needy member of the community, however, it means that care is not provided.

Nursing Home Care

Predictors of nursing home placement have been analyzed extensively, and most analysts have identified the following predictors: being white, female, and elderly; not having an informal support network; preferring or having a family who prefers nursing home placement; having severe functional impairments, including cognitive deterioration (Greenberg and Ginn 1979; Cohen et al. 1986; Hing 1987). Three out of every four nursing home residents are women, and they are disproportionately white. In addition, women are more likely than men to be transferred to LTC facilities following discharge from a hospital (Hess 1990).

It has been well documented that African-American, Latino, and Pacific/Asian elders are less likely than white elders to use nursing homes (Hug 1989; McCoy and Edwards 1981; Macdonald, Harlow, and Ludwin 1989; Mindel and Wright 1986; Hing 1987; Palmore 1976; Simmons 1988). Some research on the use of Medicare-covered skilled nursing homes has shown that white Medicare enrollees, compared to those of all other races, have shorter stays per admission (Latta and Keene 1990). A major difficulty in interpreting cross-sectional data is their failure to distinguish between strictly post-acute admissions and those that mark the beginning of long-term placements. Nevertheless, two interpretations of these data are possible. First, white elders are prescribed short-term SNF care more often than elders of color are. All other factors being equal, it is quite possible that short-term SNF is seen as appropriate for white elders but not for elders of color, who may have linguistic and other culturally unique needs, or who may be seen as having more informal support in the community. A second (and possibly complementary) interpretation is that, by the time they are referred for SNF care, elders of color have greater health deficits and are in more critical condition than white elders.

Overall, it is not well understood why the under-representation of elders of color in nursing home populations persists. In contrast to the extensive research done on majority elders, no studies of minority groups have used sample sizes large enough to permit the determinants of their service use to be confidently identified. Using data from the National Channeling Demonstration Project to identify factors influencing nursing home use, Hernandez-Gallegos (in progress) found that predictors for service use among the total sample (5,470) and among a subsample comprised of white elders (4,017) were not significant predictors for service use by a subsample comprised of African-American elders (1,237). Testing the same multivariate model using Tobit Analysis on each subsample separately, Hernandez-Gallegos found, for both the total sample and the white subsample, the following factors to be significant predictors of nursing home use: cognitive deficits, more than three ADL impairments, living alone, lack of informal care, advanced age, the total amount spent over the previous six months on hospital and physician services, and Medicaid coverage. An extremely negative attitude toward

nursing homes was also found to be statistically significant for both samples, although negatively associated with nursing home use.

By contrast, only one factor among all of these was a significant predictor of nursing use for African-American elders, namely, an extremely negative attitude to nursing home placement, which was negatively associated with use.

These results suggest that traditional models for explaining nursing home use, which focus on health status, impairment levels, and such access factors as Medicaid coverage or income, fail to capture other dimensions that are relevant to African-American elders and their families in making decisions to use nursing home services. These dimensions may include agency prescriptive practices, familial and personal preferences, income/resources, and LTC-system features, such as Medicaid reimbursement rates. Usually lower than private payment rates, Medicaid reimbursement rates are known to cause providers to accept patients with private payment means over Medicaid patients. Two unintended consequences of those rates affect access. First, providers create waiting lists for Medicaid clients, so these elders must remain in the community while experiencing intense and complex LTC needs. Second, access to services by elders of color is further restricted because the longer a private payment patient remains institutionalized, the more likely he or she is to "spend-down" and be placed in a "Medicaid slot."

Another set of factors that is not encompassed by traditional models for explaining service use has to do with prescriptive practices by hospital discharge planners, who may rely on one form of rehabilitative treatment, such as skilled home care, for one group and on facility-based treatment for another group. Although no research has been done on this issue, concerns about differences in access to SNF care point to a need to examine features of the post-acute care system that act as barriers to care for elders of color as well as a need to develop mechanisms to enhance equitable treatment. For example, nursing home preadmission screening programs are designed to assess and determine the appropriateness of nursing home placement. Such a feature ensures equitable access to skilled nursing care and to a broader range of community-based alter- natives. Evaluating care plans at the time of hospital discharge and developing care-planning guidelines can also help to redress structural inequities of access to care.

Another deficiency of traditional explanatory models is their exclusion of personal/familial preferences as factors influencing nursing home use. As has been well established, service use is greatly enhanced when a facility's staff reflects community demographics. This reality has broad implications for community care policy and service delivery. First, in order to increase service use by elders of color, incentives need to be created to enhance work-force diversity at all levels. This will have repercussions not only on service use by elders of color, but also on the organization itself: for example, the capacity to provide culturally sensitive care will be increased as bicultural, bilingual staff are hired. Another implication for LTC policy is that provider accountability to consumers will become an explicit factor to consider in program design and delivery. Such organizational policies as visiting hours or acceptable roles for family members to assume within facilities are then redefined as legitimate aspects of service delivery that need to come under scrutiny. Examining these implications can lead to a review of infrastructure features that may ultimately improve the quality of LTC for all elders.

Community-Based Care

It has been estimated that for every disabled elder residing in a nursing home, two or more equally impaired elders live in the community (Brody 1985). Since we know that elders of color are relatively under-represented in nursing homes, it is reasonable to assume that, given their greater impairment and poorer health status, elders of color use comparable or higher levels of community-based long-term

care, relative to older white Americans. In order to understand how the needs of those community-residing impaired elders are met, this section and the next will examine the use of community-based services and informal support.

Research on how gender and race affect the use of community-care services by elders has been confounded by two major factors: different definitions of the services covered by community-care systems, and tremendous variation in the availability of community-based services among states and localities. Although the data base for community-care service use is smaller than for hospital or physician services, the utilization of community-based services has been found to be associated with significant degrees of functional and cognitive impairment, low income, unmarried status, weak informal support, and living alone (Soldo 1983; Stone 1986; Krout 1983). Recent research on community-based LTC suggests that gender and race effects persist even after accounting for these other variables (Coughlin et al. 1990; Capitman and Kron 1990; Manton and Hausner 1987; Hernandez-Gallegos, in progress).

Using the 1982 National Long-Term Care Survey, Manton and Hausner (1987) developed a classification system to generate a case-mix index for home care use based on dimensions that were clinically distinct, had significant differences in reimbursement that were consistent with the clinical category, and predicted both individual costs and individual visits over a long period of time. These dimensions concerned the needs of elders who had hip and other fractures, cancer, chronic medical problems, acute medical problems, multiple medical problems, and neurological impairment. The analyses revealed a gender effect, with older women having a higher probability than men of using home-care services.

In analyzing data from the Social Health Maintenance Organization (SHMO) demonstrations to compare the utilization and costs of Medical-recovered professional home-health aides versus other paraprofessional home-care providers, Capitman and Akron (1990) also found gender effects. Older women were found to have higher utilization rates for both types of services. Similarly, a study by Coughlin and colleagues (1990) on predictors and expected costs for home care use by disabled elders found that women were more likely than men to use home care services. In addition, they found that the expected number of visits was also higher for women than for men.

As with research on the use of community-based services by the general aged population, service use by elders of color has not been adequately studied. However, a growing body of literature on policy and program development for the aged raises the underutilization of community-based services by elders of color as a persistent problem needing attention (U.S. Commission on Civil Rights 1982; U.S. Senate Special Committee on Aging 1988).

Explanations for the lesser use of these services by elders of color extend beyond identifying the barriers to access common to all elders, which are due to unavailability of services, stringent eligibility requirements, inadequate transportation to and from service sites, lack of information on specific programs, as well as complex forms and other onerous paperwork. Elders of color appear to face additional barriers not normally encountered by the general aged population: a lack of sensitivity to the needs and feelings of nonmajority-race elders, including the cultural insensitivity of providers and the failure of programs to accommodate cultural preferences, different degrees of acculturation, or difficulties with English; a lack of provision for ethnic group members to participate in planning; a lack of adequate health insurance; and a lack of bilingual/ bicultural staff (Bell, Kasschau, and Zellman 1976; Trevino and Moss 1983; Eribes and Rawles 1978; Torres-Gil and Fielder 1986; Irrizary 1988; Espino et al. 1988; Holmes, Teresi, and Holmes 1983; Starret et al. 1988; Cubillos, Prieto, and Paz 1988; Kramer, Polisar, and Hyde 1990; Gallagher 1988; Kapke 1988; National Indian Council on Aging

1982; Lee 1987; Berkowitz 1989; Die and Seelbach 1988). From this perspective, which focuses on system features and the attitudinal dimensions associated with the delivery of care, it appears that organizational features play a crucial role in the decisions to consume services made by elders of color. The implications of the data presented above for LTC policy are numerous. First, it is clear that if the needs of elders of color are to be met, provider orientation to diversity must be reflected in staffing patterns, training, and ongoing program-management policies. This underscores the need to develop a policy framework that explicitly allows local variation to be considered in determining who is to be served and how services are to be delivered. Additionally, such a framework would open the door to the examination of systemic weaknesses that perpetuate existing barriers to service use, such as absence of coordination among local care providers or between LTC and medical care providers. Finally, a specific focus must also be placed on patterns of service authorization in order to identify any gender bias that may lead to inequitable provision of services.

Informal Caregivers: Shouldering the Care-Giving Responsibility

It has been universally accepted that the overwhelming majority of all long-term care needs of elders in this country are met in the community by means of informal support networks (Liu, Manton, and Liu 1985; Stone, Cafferata and Sangl 1986; Rivlin and Wiener 1988). Moreover, it is widely known that well over 60 percent of the costs of long-term care are shouldered by the families of elders who need such care (Comptroller General of the United States 1977; Doty 1986; Shanas 1979). In terms of how these care-giving burdens are distributed among the population, they are disproportionately borne by women and people of color. To begin exploring how race, gender, and care-giving are related to the use of formal, long-term care services, the next section will focus on the ability of white women and people of color to purchase and consume long-term care and to provide it to frail, disabled family members as "informal support." (The implications for long-term care policy will be considered in the last section of this course.)The relationship between the availability of informal support and the use of formal services is a growing area of research. In a review of the relevant literature, Horowitz (1985) has identified five general patterns of service use that are indicative of the relationship between formal and informal support systems.

1. **The availability of informal support reduces not only the probability of nursing home placement, but also the probability that community-based care will be used.**
2. **When formal services are used, family members continue to provide the majority of all care.**
3. **Formal care users tend to be those needing higher levels of family care.**
4. **Typically, the community-based services that are requested represent a supplement to and respite from what the caregiver continually provides.**
5. **When family caregivers approach the formal-care system, they tend to be selective and modest in their requests.**

Women, more often than men, are the caregivers to frail and disabled elders living in the community. A recent survey of informal caregivers providing assistance to elders residing in the community found that 72 percent of the caregivers were women, 64 percent of the care-giving spouses were wives, 77 percent of the care-giving children were daughters, and 74 percent of the other, non-family caregivers were also women (Stone, Cafferata, and Sangl 1986). Summarizing the recent literature, Montgomery and Borgatta (1989) conclude that, as caregivers, women are more likely than men to provide more hours of care, to provide hands-on care, and, when employed, to adjust their work schedules, but not to limit their care-giving responsibilities. Male caregivers, on the other hand, have been found to command more resources and to mobilize others more readily than female caregivers (Olesen 1989). While women have traditionally been expected to assume the care-giving role, they are also more apt to be expected to do so without formal support.

These data suggest that informal care-giving is inextricably bound up with gender roles in our society. A recent study of the relationship between caregiver gender and access to community-based long-term care services in the SHMO demonstration sites (Karon 1991) examined service authorizations over time. Three major findings underscore the role of gender in the process of service use and authorization. First, Karon found that, following the initial month of receiving community-based services, elders whose primary caregivers were female experienced a decrease in service authorizations over time, while those with male caregivers were nearly twice as likely to have service authorizations increased as decreased. Second, Karon's study confirmed the observation that care-giving tasks are defined by gender roles. For elders with male caregivers, service authorizations increased over time in response to the need for assistance with intimate ADLs, whereas service authorizations for patients with female caregivers increased in response to the caregiver's conflicting employment responsibilities. Third, Karon found different predictors of initial service prescription for men and for women, suggesting that even prior to their actual utilization of services, men and women are treated differently by the system.

While only a few studies of the care-giving and long-term care services provided to elders of color could be located, one of the most persistent explanations they offer for differences in service use by elders of color is that informal support networks function efficiently to meet the LTC needs of these elders. Some researchers indicate that the types of assistance available to elders supplement, rather than substitute for, formal services. Other research suggests regional differences (Gallagher 1988; Gratton and Wilson 1988; Mindel and Wright 1982; Taylor 1985). While the literature may indicate differences between white and African-American elders with respect to the structure of their extended informal support system, the availability and the nature of their informal care, or the attitudes toward care-giving of their families, there is no conclusive evidence for the claim that these differences explain African-American elders' lower rates of service use. A similar lack of evidence is associated with claims about family support among Latinos. One view endows Latino elders with extensive and strong familial support, while another cites the recent deterioration of the traditional Latino family structure, with erosion of its interdependence and reciprocity (Maldonado 1989; Sotomayor and Randolph 1988).

In summary, it is clear that we have not adequately addressed the impact of race and gender on community care. First, nowhere in the published literature are differences among ethnic groups in expectations of community care services discussed. Although differential utilization of formal services is evident, there has not been enough attention paid to whether or not people are receiving a fair deal, either by their own standards or by some comparable external ones. We simply lack a concept of "ethnic geriatrics." Second, what the few available studies also show is that when race and gender are included as variables, they have complex interactions with other variables among clients and service programs. These findings are consistent with the idea of people overcoming their prejudices and increasing their sensitivity to different preferences, needs, and styles, along race/ethnicity and gender lines.

Economic Issues and the Use of Community-Care Services

As the relationship between the availability of informal support and the use of formal care becomes clearer, other factors influencing service utilization assume greater prominence.

The apparent tendency among elders to use fewer formal services and more informal care may be related to their financial ability to purchase care beyond what may be available through Medicare, Medicaid, or other publicly funded programs. Research using large data bases, such as those generated

by the Channeling Demonstration Project or the National Long-Term Care Survey has shown that higher-income elders use more services than lower-income elders do, even in the Channeling sites where many services were covered. These differences have not been found, however, by researchers studying SHMO participants, for whom all care is capitated and for whom the cost of care is less of a factor in deciding to use a particular LTC service than it is for elders paying the full price in the fee-for-service system (Capitman and Karon 1990). Because a high proportion of older women and elders of color are at a financial disadvantage in purchasing LTC, the funding aspects of service-delivery systems are critical to their receiving care. One could conclude that low-income females and elders of color would fare better in comprehensive, capitated delivery systems than they do in the fee-for-service system.

Although economic conditions for the general aged population have improved over the last twenty years, older women are still highly at risk of being impoverished. Some of the factors contributing to their high-risk status include inadequate retirement benefits, Social Security policies that adversely affect widows, and the catastrophic costs of medical and long-term care for their spouses (Schulz 1988). Growing awareness of these factors has led to the coining of the term the "feminization of poverty." Poverty among older women is worse for those who are widowed and who live alone. While accounting for 63 percent of all elders, women comprise over 73 percent of those living in poverty (Gonyea 1990; Dressel 1988). Among elders of color, the poverty rates parallel and, for some subgroups, exceed those of older white women (Cook 1989; Kramer, Polisar, and Hyde 1990; Agree 1988; Kamikawa 1989).

These income disparities along race and gender lines suggest that very high proportions of older women and elders of color are at a disadvantage when faced with the need to purchase LTC services beyond those provided by Medicare, Medicaid, or other public programs, such as the home care services available through state Medicaid-waiver programs. Nearly three-quarters of all non-institutional paid care is privately financed by elders and their families (U.S. Bureau of the Census 1983; Liu, Manton, and Liu 1985). Using the 1982 National Long-Term Care Survey data, Coughlin and colleagues (1990) found that elders with incomes 300 percent above the poverty line were nearly two and half times more likely to use community services than were elders at or below the poverty line. It is not clear from the research why elders with greater resources use more services. On the face of it, higher-income elders can afford more services, which are also more likely to be available in their communities. Furthermore, it is plausible that higher income, being strongly correlated with more education, may define a population capable of articulating and asserting their needs more effectively, leading to their higher utilization rates. And while the greater use of services by elders who are better off may well be accounted for by their ability to purchase services, one consequence of poor elders' using fewer services is that the responsibility for care continues to be disproportionately shouldered by women, who represent the overwhelming majority of caregivers, and especially by women of color.

DIVERSITY: IMPLICATIONS FOR THE DELIVERY OF LONG-TERM CARE

In this section, gender and race disparities in health status, mortality, functional impairment, income, and utilization of informal and formal services have been examined in order to demonstrate that these differences must be considered in LTC policy development and implementation. To summarize the points made in the discussion above:

- **Older women use more services because their longevity entails longer periods of chronic disability and functional impairment. Men use fewer formal services, but this is partly due**

to their greater reliance on family members (primarily spouses and adult children) to care for them in old age.

- **The manner in which services are designed, implemented, and allocated supports (1) the established social norms of informal care-giving that relies heavily on women as caregivers, and (2) the organizational gender bias that favors male over female caregivers.**
- **More research is needed to clarify racial/ethnic disparities in the use of long-term care services; recent research suggests that service use is influenced by such provider practices as staffing and by such system features as financing.**
- **While the research does not clearly explain the greater use of LTC by high-income elders, the consequence is clearly that lower-income women, especially women of color, carry a relatively greater burden of informal care provision.**
- **Elders of color have been found to experience greater degrees of functional and chronic impairment than white elders, which implies that, given their poorer health status, greater functional impairment, and lower-income status, elders of color should use more LTC services than they do. Yet the research consistently finds lower rates of LTC use among elders of color.**
- **While underutilization of LTC services by elders of color has been documented, data on local-level use, relative to that of the community population, are not available.**

The evidence summarized indicates that the aging process differs for men and women and for people of color. The concluding section will discuss approaches for ensuring that race and gender differences are addressed in the design and delivery of long-term care.

Gender and race pose significant challenges to the planning, design, and delivery of long-term care services. The relationships of race and gender to public policy are complex, and perhaps no single approach to these challenges can ensure an equitable system. This is all the more reason to make race and gender primary considerations as alternative approaches are evaluated. Some features of these proposals and policy options affect women and people of color differently, depending on the methods proposed for financing, delivering, and allocating services. We believe that there are at least three policy dimensions from which, first, to interpret gender and racial differences and, second, to develop recommendations:

1. **Financing and access aspects of LTC;**
2. **equity and system incentives from the consumer's perspective; and**
3. **provider and organizational knowledge and behavior.**

The following sections discuss how these dimensions of various reform strategies may affect women and elders of color.

Financing and Access Aspects of Community Care

Proposals calling for system-wide reforms, such as major modifications to the Medicare and Medicaid programs, will not automatically redress the gender and racial biases of the current system that block access to care. First, most proposals relying on Medicare or analogous types of social insurance as the source of funding have required substantial cost-sharing in the form of deductibles and co-payments, such as the 20 percent co-payments for home care of the Pepper Commission proposal. As has been indicated above, the largest group of elders who could potentially benefit from the services of such a program, namely, older white women and elders of color, are predominantly low-income. A 20 percent co-payment, while substantially less than the full cost of services, would continue to pose significant financial barriers to access.

Medicaid as a funding source for expanded community care, while designed to meet the needs of persons living in poverty, would exclude many elders with low incomes who would not qualify in terms of state Medicaid income criteria. Nearly 40 percent of low-income elders are ineligible for

Medicaid, and, therefore, without changes in eligibility criteria, a large group of older white women and elders of color would continue to be denied access to community-based care. Inequities in the distribution of Medicaid benefits were first documented by Davis and Schoen (1978), when Medicaid payments for white recipients were 74 percent higher than those for African-American recipients. The literature suggests that this imbalance in the distribution of Medicaid benefits persists (Wolinsky et al. 1990).

There is currently no Medicaid oversight process to ensure equity by race and gender. Exclusive reliance on Medicaid as a funding source would require that gender and racial equity be an explicit policy consideration. A third approach to funding community care is through block grants with demographic adjustments. This financing method can explicitly take into account the relative proportions of people of color or of frail women who may be potential consumers of services. An example of this type of policy is the Administration on Aging's interstate funding system, which allocates funds to states based on several factors, particularly the percentage of people of color in the state population. While such a policy may be feasible for the aging network's delivery of community services, it could not be implemented in programs like Medicare (in principle, a universal program) or Medicaid (a welfare-based program).

Research on the SHMO suggests that capitated delivery systems improve access to community-care benefits for low-income elders by reducing the importance of personal income as a barrier to care. More research is needed on how the SHMO model can improve access for elders of color. Research on comprehensive, full-coverage, case-managed delivery systems, such as the Channeling Demonstration Project, suggests that once enrolled in these systems, elders of color use services at rates comparable to those of their white counterparts (Hernandez-Gallegos, in progress).

Equity and System Incentives from the Consumer's Perspective

Another way to redress gender and race inequities is to develop benefits that directly or indirectly compensate caregivers. This could take the form of dependent-care tax credits, state payments to caregivers, or the elimination of eligibility requirements based on the availability of informal caregivers, such as eliminating informal support as a factor in determining the types and levels of formal care to be authorized (Osterbusch et al. 1987). Doty (1986) review identified the difficulties with implementing some of these approaches to gender equity. First, federal dependent-care tax credits already exist, so changing current caps and conditions would require that tax laws be revised. Furthermore, increased dependent-care tax credits are likely to benefit primarily higher-income persons, who are already in a better position to pay for care. Second, payments to family caregivers have been initiated by some states, the most prominent being California. One of the problems with this approach is the difficulty of determining the market value of in-kind services. It is unclear whether that determination should be made on the basis of the minimum wage paid to professional home-care workers or even whether, indeed, that wage is an accurate measure of the caregiver's value and costs.

Third, multicultural and feminist perspectives bring other, more global societal issues to the forefront. Is it reasonable to expect the community care system alone to resolve growing concerns about race and gender equity? How can a single service system revise what until now have been normative gender roles or determine what level of care is acceptable from men versus women? It is important that community-care providers and policymakers join this debate and help to heighten awareness of how traditional norms are viewed. Central to this debate is our vision of equity and justice. Until such time as these broader issues are resolved, care managers, as the gatekeepers of the delivery system, can have some influence on equitable service allocation. For example, operating from the premise that all services are provided to address unmet needs, care managers can be sensitive to imbalances occurring in informal care arrangements that jeopardize the quality of life of the overburdened female or minority

caregiver. By focusing on how services are authorized, especially in relation to gender biases that favor men over women, and by correcting these biases, providers can play a role in fostering gender equity.

Provider and Organizational Knowledge and Behavior

Although attention to the financing and targeting practices of programs is important, it is also important to recognize that these practices are implemented through an infrastructure of provider organizations that actually deliver a range of long-term care services. Therefore, proposals must also focus on provider organizations as gatekeepers whose service delivery practices may create barriers to access. By adding this dimension to the evaluation of proposals, provider accountability to the consumer of services becomes an integral aspect of service delivery.

Research on the utilization of both health care and community LTC has demonstrated the influence that provider attitudes and organizational behavior exert over consumers of services. However, public policy proposals have not incorporated this knowledge in order to address gender and racial inequities. Donabedian (1973) influential model posits utilization as the result of a process in which the users and providers of services respond to a need and, in concert, create a service-use event. This framework, however, does not recognize the influence of organizational factors, such as staffing mix and provider orientation to diversity, on service use. Capitman and Hernandez (1990) expanded current conceptual approaches for explaining service use by adding a framework derived from private industry's response to diversity (Foster et al. 1988), particularly such organizational features as clarity of mission, personnel/ staffing practices, care coordination, services, and strategies for achieving cultural diversity.

The extent to which a commitment to diversity is explicitly made in concrete terms, such as mission statements, well-defined outreach objectives, and leadership strategies to ensure success in meeting objectives, influences the composition of the organization's work force, the extent of its outreach to different cultural communities, the characteristics of the services it provides, the quality of its client/staff relationships, and the utilization of its services by elders of color. On the basis of surveys and focus-group meetings, Capitman and Hernandez (1990) developed a typology of organizational approaches to cultural diversity and identified five types of elder-care service providers.

1. Monocultural organizations **. In monocultural organizations, cultural diversity in staffing, service development, and provision of care is not an articulated goal. These providers do not acknowledge either the differences among cultural groups, such as in the needs or preferences of personnel or elderly consumers, or the relationships among care coordination, service approaches, and service utilization.**
2. Nondiscriminatory organizations **. A commitment to the recognition of diversity in staffing and service provision is articulated by nondiscriminatory organizations, yet they focus on compliance with numerical measures of affirmative action and on creating settings that are not hostile to personnel or elderly clients of different racial/ethnic groups. Care coordination and service approaches are recognized as factors influencing utilization, but that recognition is not explicitly incorporated in coordination or delivery approaches.**
3. Multicultural organizations **. In multicultural organizations, the recognition and appreciation of cultural diversity in all aspects of personnel practices and service approaches are articulated as goals to be achieved through specific programs or activities. For example, staff retention efforts include career ladders and opportunities for promotion. Care coordination and service approaches include, for example, maintaining communication links with the media, churches, and racial/ethnic service providers, and flexible hours of operation to accommodate community needs. These organizations (which include many mainstream elder-service agencies) are proactive in minority recruiting, hiring, training, and retention at all organizational levels and in reaching out to elders of color through culture-specific, integrative program design and care provision.**
4. Sustained-focus organizations **. Focusing on specific racial/ethnic groups and seeking to**

provide services that are not available or accessible through mainstream providers, sustained-focus organizations concentrate on meeting the needs of a well-defined community through narrowly targeted staffing and service approaches.

5. Expanded-focus organizations **. While maintaining their focus on specific racial/ethnic groups, expanded-focus organizations also recognize the contribution that their unique service approaches can make to caring for a broader spectrum of elders. By reaching out to the larger community in both their personnel and care-provision practices, these providers combine a multicultural perspective with a strong commitment to meeting the needs and preferences of particular racial/ethnic groups.**

Organizational orientation toward diversity is shaped by the combined efforts of many individuals as well as by external policy features, such as program design and funding. This typology can be used to develop a process for generating assessments at the organizational level to determine how well an organization currently addresses the needs of women and elders of color. As movement toward a more multicultural service-delivery approach becomes an organizational goal, providers will need to focus on several domains: mission, governance and administration, personnel practices and staffing patterns, range of services and care-giving approaches, population targeting, and outreach, or marketing, strategies. Questions will need to be asked with respect to each of these organizational domains.

Mission . Is the commitment to serve elders from all racial/ethnic/cultural groups made explicit through a stated intent to reach out to all population groups? How is that commitment being communicated to staff at all organizational levels, as well as to the communities being served?

Governance and administration . Has the agency sought to achieve at least proportional representation of persons of color on the governing board or consumer advisory board? Is the governing board empowered to participate meaningfully in funding, personnel, program, and other policy decisions? Does the organization regularly schedule formal board and/or staff opportunities for self-assessment of multiculturalism?

Personnel practices and staffing patterns . Are there explicit outreach strategies for recruitment from communities of color? Does the agency recognize and have policies to address different needs among staff for leave, holidays, work schedules, and other types of employee benefits? Is there a career ladder?

What are the barriers that minority staff members may face if they seek promotion?

Range of services and care-giving approaches . Are services available, reasonable, and useful to all segments of the community? Are professional and paraprofessional staff members attuned to cultural factors that may come into play in caregiver/consumer interactions? Is the staff trained to empower clients by asking them how they wish to be addressed, how they want care to be provided, and how they feel about the care-giving situation?

Population targeting . What is known about ethnic/racial differences in the incidence of specific chronic diseases, poverty levels, or help-seeking behavior? Have known patterns been used to develop appropriate targeting goals? Does the agency collaborate with other service providers, particularly those focused on specific ethnic/racial groups, to address the unmet needs in a multicultural community?

Marketing, or outreach strategies . Do marketing/outreach efforts reflect an appreciation of differences in message and method? Are less traditional efforts, such as enlisting indigenous leaders, clergy, and providers, used to reach particular ethnic/racial communities?

This typology can be applied to organizational assessments of gender issues as well. In either case, the process can generate recommendations emphasizing sensitivity to cultural differences, including the cultural values and norms underlying preferences that affect service use--in short, an emphasis on consumer satisfaction and the staff/client relationship. Additionally, this approach facilitates a reexamination of other organizational features, such as the availability, location, scope, and mix of services, or, in terms of personnel practices, such features as staff turnover rates and the composition of an agency's work force. Finally, such an analysis of provider and organizational behavior also emphasizes how the coordination of care with other community agencies can be accomplished, so recommendations are generated for improving interagency referrals and agreements and for identifying system-wide weaknesses and strengths, thereby facilitating local infrastructure development in a culturally sensitive manner.

In summary, gender and racial differences are important factors to consider in the planning, design, and delivery of long-term care services. The central question raised by the data on women and elders of color is whether community-based long-term care is equitable, as it is currently defined. Do older women, their caregivers, and people of color indeed have fair access to needed community-based LTC? For the present, it is essential that this question be continually asked so that the necessary steps can be taken to eliminate existing barriers to care. For the future, it is critical that new proposals focus on how older women and elders of color will be affected in order to avoid perpetuating current structural inequities in the funding and design of benefits. It is crucial that infrastructures for the delivery of care be held to high standards of quality, as measured by outcomes that begin with equitable access to care for all elders who need it.

Glossary: Biology of Aging

The glossary is an alphabetical list of selected terms in aging and longevity medicine that are commonly employed in gerontology

Aging -- A gradual and relentless process by which sexually-reproducing organisms lose their youthful capacity for homeostasis. Aging doesn't normally begin until the completion of a characteristic interval of reproductive competence during which a species rears its progeny to independence. As a result of aging, older organisms are increasingly vulnerable to a wide variety of age-related diseases, ultimately culminating in their death. The tradeoff between aging and repair processes is extremely complex and observed to operate systematically within a hierarchy of at least seven different interacting levels: (1) *molecules*; (2) *organelles* (small membrane-bound cellular components with specialized functions); (3) *cells*; (4) *tissues* of various architectures; (5) *organs*; (6) *organ systems*; and ultimately (7) the entire *organism*. Aging occurs silently from within, in the same sense that termites, if unchecked, will ultimately destroy the structural integrity of a large wooden house.

Altricial - Newborns unable to take care of themselves at birth, often naked or blind, and thus dependent on parents for a much longer time for food and protection from predators. In ornithology, *precocial* newborns, on the contrary, rapidly become autonomous and leave the nest after less than two

days without supervision. *R-selected* (reproductive rate-limited) species have a high rate reproduction during a single pregnancy (per litter; parity), and generally have precocious young. On the other hand, *k-selected* (capacity limited) species generally have altricial young with singletons normal or twins or triplets only rarely.

Apoptosis **-- Programmed Cell Death (PCD). This process gets rid of unneeded cells and is particularly important for "sculpting" tissue and organ structure during development of the embryo (or larval metamorphosis in insects), but may occur at any time even in adult cells when a tissue needs to be remodeled. Signals to trigger apoptosis may come from within the cell or from outside, by stimulating suicide receptors in the cell's external membrane. Internal signals producing apoptosis depend on interactions of several proteins and may serve to protect the organism from cancer by killing cells that have pre-cancerous changes.**

Average Life Expectancy **-- The age at which 50 percent of the members of a population have died, when plotted on a standard survival curve. This statistic is normally calculated from birth, but may be recomputed in terms of expected years remaining at any age.**

Bases **– These are molecules with one or two nitrogen containing ring structures. The biologically important bases are the *purines* Adenine and Guanine and the *pyrimidines* Cytidine, Thymine, and Uracil. DNA and RNA are composed of linked sequences of nucleotides. In DNA, the purine nucleotides are Adenosine (A) and Guanosine (G); the pyrimidine nucleotides are Thymidine (T) and Cytosine (C). In RNA, the pyrimidine nucleotide Uridine (U) is substituted for Cytosine.**

Biomarker **-- A measurable parameter of physiological age that is a more useful predictor of remaining life expectancy than chronological age. The ability to measure biomarkers is extremely important in evaluating the efficacy of any potential life-extending intervention.**

Caloric Restriction (CR) **– A diet in which calorie intake is reduced, compared with *ad libitum* (eat as much as you like) diets, without any reduction in nutritional requirements (protein, water, vitamins, or minerals).**

CR is not the same as starvation or famine. CR is the only known intervention that systematically extends maximum lifespan. CR has been effective in all species in which it has been tried (although the jury is still out on humans).

Cancer **-- A clonal growth (cells all descended from one ancestral cell) that undergo continuing mitotic divisions and are not inhibited in their growth when they come in contact with neighboring cells (contact inhibition). Thus, cancers obliterate the normal architecture of the host tissue. Cancer cells often spread (or *metastasize*) throughout the body by way of the blood stream or lymphatic vessels to form tumors in new locations beyond the primary site of origin. Cells become cancerous by accumulating, stepwise, a series of several mutations that alter the function of genes important for cell growth.**

Chromosome **– The structures in the nucleus of the cell, consisting of DNA bound to histones and other proteins. The genes are made of DNA (although the majority of the DNA sequence is not part of any gene). Genes are arranged along the chromosomes in a continuous sequence. Chromosome protein structure allows for selective activation (genes are transcribed into protein) or silencing (genes are not expressed), and thus for differential expression of the genome in different cell types and expression of genes in appropriate sequences during development of the organism or under various metabolic conditions. Chromosomes exist in pairs, one inherited from the mother (*egg*) and the other from the father (*sperm*). Thus, normal *somatic* cells carry two, usually slightly different, versions of each gene (*alleles*) and are called *diploid*, while the *germ-line* cells are called *haploid.***

Cloning **-- The use of the chromosomes from an adult cell to create an identical twin (copy) of an organism by inserting the adult nucleus into an egg from which the nucleus has been removed, stimulating embryogenesis, and implanting the embryo into the uterus of a surrogate mother. Reproductive cloning of sheep, goats, cows, pigs, and mice have been widely accomplished. However, attempts at cloning of dogs, cats, and horses have not yet met with success. Laws banning human reproductive cloning have been proposed in many countries, including the US. Therapeutic cloning (without the intent to implant the embryo into a surrogate mother) but with the aim of creating a large collection of embryonic (totipotent/pluripotent) stem cells to treat the original donor is a potentially a significant medical intervention for the future.**

Diploid Cell **-- A cell with pairs of homologous chromosomes.**

DNA **-- An abbreviation for Desoxy Ribonucleic Acid. Double stranded DNA molecules consist of antiparallel (running in opposite directions) chains of nucleotides in which the sugar component is *desoxyribose*. The chains are arranged in a *double helix* with the two chains wrapped around each other and bound together so that each "A" is paired with a "T" (A:T pair) and each "G" is paired with a "C" (G:C pair). Thus, when the chains unwind and separate, new identical antiparallel sequences can be copied along their lengths. DNA is thus self-replicating.**

Disposable Soma **-- From an evolutionary point of view, the *prime directive* of any organism is to transform available energy from the environment into the maximum number of progeny. Part of the energy is consumed in the maintenance of the organism's somatic (body) tissues (for growth and repair of injury) and part is used to propagate the germ-line tissues. Natural selection favors genetic combinations that produce the most efficient trade-off between these two forms of energy utilization in such a fashion as to maximize evolutionary fitness (i.e., reproductive performance). As a consequence, less energy is directed to somatic maintenance than would be required for the indefinite survival of any individual.**

This results in the death of individuals, but the immortality of the germ line. The details of the trade-off are largely a function of the ecological niche in which the organism propagates, including predators, prey, parasites, and other environmental factors. According to this theory, the least energy would be devoted to somatic maintenance in a hazardous niche; conversely, more energy would be dedicated to somatic renewal in a relatively protected niche.

Egg **-- A female haploid germ cell.**

Entropy **-- A measure of the level of disorder or randomness in a closed system. It can be thought of either in the sense of thermodynamic/metabolic processes or the increasing molecular disorder in a structure. It can be thought of as the process by which erosion occurs when soil is exposed to the elements.**

Evidence-Based Medicine **-- The practice of medicine with treatment recommendations that have their origin in objective tests of efficacy published in the scientific literature rather than anecdotal observations.**

Fecundity **-- The ability to produce offspring. High fecundity means the ability to produce progeny rapidly and in large numbers. In the demography of human populations, fecundity is the physiological ability to reproduce, as opposed to fertility.**

Fertility **-- Reproductive Potential. In demography, the number of births per year divided by the number of women of childbearing age, expressed as a rate.**

Gene **-- a functional unit of heredity. It is a segment of DNA located at a specific site on a chromosome whose length is typically several thousand base pairs. A gene directs the formation of an enzyme or other protein by means of transcription and translation.**

Geriatrics **-- A branch of Internal Medicine concerned with the care and treatment of older persons and the treatment and amelioration of diseases of old age and frailty.**

Gerontology **-- A branch of biology focusing on the common mechanisms of aging across all multicellular species. Gerontologists, for example, are keen to understand species that appear to exhibit very gradual or negligible senescence over a long time interval. In this context, gerontologists may study yeast, worms, fruit flies, mice, rock fish, tortoises, bats, parrots, humans, and other creatures exhibiting exceptional longevity.**

Gene **– A sequence of DNA that can be activated and copied into messenger RNA or mRNA (by a process known as *transcription*). mRNA is processed and then translated by ribosomes into a sequence of amino acids, which are joined together by peptide bonds to form a protein at cell organelles called endoplasmic reticulum Each triplet of bases (or *codon*) in mRNA specifies a different amino acid (out of 20 possible choices). It's this sequence of amino acids that determines the identity of a protein (its *primary* structure). The folding pattern (*secondary, tertiary*, and *quartinary* structure) of the primary sequence determines its three-dimensional morphology and ultimately its function (e.g., a structural vs. an enzymic function).**

Genotype **-- The genetic makeup of a cell, organism or group of organisms, with respect to a single trait or group of traits; the sum total of genes transmitted from parents to their offspring.**

Genome **-- The complete collection of genes in the nucleus of each cell of our bodies. There are known to be about 35,000 genes in the human genome.**

Germ Cell **-- An egg or a sperm cell.**

Gerontome **-- The subset of the genome whose genes affect longevity, either significantly reducing or increasing the average lifespan of an organism.**

Gompertz Model **-- A class of statistical models first proposed by the nineteenth-century British actuary Benjamin Gompertz, in which the hazard rate for death rises geometrically with increasing age of the organism (at least after an initial period of high risk of mortality at birth and infancy and a much lower risk in late childhood and adolescence). Today, the *Wibel Model* is a successor to the Gompertz Model, as it more accurately explains the observed demographic data.**

Grandparenting Hypothesis **– This is the supposition that abruptly terminating reproduction at a particular age (menopause) and prolonged survival of human females after menopause may have been selected for because of better success in child-rearing (and hence survival of the gene pool) when older women focus their resources on the welfare of their grandchildren and thereby increase their likelihood of survival, rather than investing energy in producing more children of their own and potentially compromising the reproductive success of their adult progeny.**

Haplid Cell **-- A cell with half the normal compliment of chromosomes, typically a germ cell.**

Hayflick Limit **– The limit to the number of times a cell is can divide during serial cell culture. The value of this limit as a predictor of maximum lifespan of the organism is still unproven. In cultures of normal human fibroblasts, for example, the Hayflick Limit = 50 (± 10) cell doublings. Cancer cells grown in culture, however, exhibit no such limit and continue to divide**

indefinitely. Normal cells grown in culture that have been instructed to manufacture *telomerase* (to relengthen their chromosomal telomeres after each division) can achieve replicative immortality and do not obey the Hayflick Limit, but they do not appear to manifest other pathological characteristics of a cancer cells (like loss of contact inhibition).

***Homeostasis* -- The physiological capacity of an organism to regulate itself by rapidly restoring internal conditions following a sudden perturbation in the external environment.**

***Life History* -- The combination of age-specific survival probabilities and fertilities characteristic of a species; the time-table of individual development and aging for a representative organism (e.g., in humans, from fertilization, to embryogenesis, implantation/placentation; organogenesis/fetogenesis, birth, infancy, adolescence, puberty, adulthood, menopause, loss of vitality, frailty/morbidity, and ultimately, death).**

***Lifespan – The maximum lifespan* of a species is the characteristic observed age of death for its very oldest individual(s) (e.g., for humans 120 - 125 years). On the other hand, <u>average lifespan</u> is the age at which 50 percent of the members of a species or group has died. Over the last two centuries, average life expectancy has risen significantly, while maximum lifespan has hardly changed, if at all.**

***Longevity Genes* -- Genes that extend the maximum lifespan of a species.**

***Multipotent Cell* -- A stem cell that is limited capabilities for specialization, normally within a specific tissue type.**

***Mutation* -- Any change in DNA structure which alters the established order of the bases. This may cause a gene (or series of genes) to fail to be activated normally (either to be silenced or, the opposite, to be expressed inappropriately) or may cause a gene to express a protein with abnormal structure (and hence abnormal function). Most mutations that have any effect are deleterious. Rarely, mutations may produce some advantage for the organism carrying them. Alleles with advantageous mutations are selected for and tend to become more common in the species' genome. The opposite is true for deleterious mutations. Some mutations move the cell carrying them toward a malignant phenotype (cancer).**

***Necrosis* -- Cell death secondary to traumatic injury. Necrosis invariably induces a subsequent inflammatory reaction, as distinguished from <u>apoptosis</u> which does not.**

***Nucleotides* -- molecules which consist of a *purine* or *pyrimidine* base, a ribose or desoxyribose sugar, and a phosphate group.**

***Phenotype* -- The external manifestations of gene expression whether at the level of the cell (e.g., muscle cells are long and thin and contain contractile fibrils; nerve cells have exciteable membranes and communicating processes) or the organism (e.g., the giraffe has a long neck; a leopard, spots, and humans of Asian descent, black hair).**

***Pluripotent Cell* -- A cell capable of giving rise to most tissues of an organism.**

***Progeria* -- A human disease or syndrome in which some characteristics of senescence are accelerated so that relatively young individuals appear prematurely aged. Examples include *Hutchinson Guilford Syndrome*, *Rothmund's Syndrome*, *Cockayne's Syndrome*, *Bloom's Syndrome*, *Marfan's Syndrome*. *Down's Syndrome*, *Huntington's Disease*, and *Werner's Syndrome* (an enzymatic [helicase] defect in DNA repair).**

***Protein* -- A linear sequence of Amino Acids whose three-dimensional shape determines a particular function in the body.**

Proteome **-- The collection of all proteins in the body of an organism. For humans, it is estimated that there are 150,000 - 300,000 proteins, of which fewer than half have been catalogued thus far. Only about 10,000 proteins have been fully characterized to date, but systematic efforts to identify and characterize them all are now underway and could be completed before the end of this decade. Understanding their functions and interactions could take much longer.**

Reproductive Cloning **-- The creation of an embryo using SCNT with the aim of creating a new (identical twin) individual of that species.**

RNA **– Ribonucleic acid. RNA is a sequential chain of the nucleotides Adenosine, Guanosine, Thymidine, and Uridine. In RNA, the sugar molecules are *ribose*. RNA is typically single stranded. The sequence of most RNA molecules is copied from specific DNA sequences by enzymes in a process called *transcription*.**

Somatic Cell **-- A diploid cell of the body; a cell other than a germ cell (an egg or a sperm).**

Somatic Cell Nuclear Transfer (SCNT) **-- The transfer of a cell nucleus from a somatic cell into an enucleated egg (one from which the nucleus has been removed).**

Sperm **-- A male haploid germ cell.**

Stem Cell **-- A cell that has the ability to divide for indefinite periods in culture and may give rise to specialized cells.**

Survival Function **-- The probability that an individual will remain alive at a particular age. The percentage of an experimental cohort that remains alive over the course of the experiment.**

Telomere/Telomerase **– Repetitive DNA sequences at the four ends of the chromosome, which can be lengthened by an RNA-containing enzyme called *telomerase*. For mammals, this repeat sequence is "TTAGGG." Telomeres allow the entire functional sequence of the chromosome to be copied during cell division by providing "spare DNA" at the ends. Because the normal DNA replication process cannot be initiated at the very end of a chromosome without telomerase, chromosomes would get systematically shorter each time they were copied. Chromosomes in germ cells are passed on for unlimited numbers of generations, so that germ cells require telomerase to avoid destruction of their chromosomes and extinction of the species. Most somatic cells do not have an active telomerase, so their telomeres shorten at each cell division. When telomeres become critically shortened, the cells either die by apoptosis or cease dividing (see Hayflick Limit). Cancer cells typically develop an active telomerase enzyme as an essential ingredient of the process of becoming malignant. Therefore, a drug that blocked telomerase might function as an important anticancer therapy with very few side effects if such a drug could be identified.**

Therapeutic Cloning **-- The creation of a several day-old embryo using SCNT with the aim of harvesting the cells for subsequent tissue-culture amplification and injection into a host for therapeutic purposes (presumably without fear of *GVH* [Graft vs. Host] *Disease* or immunological rejection).**

Totipotent Cell **-- A cell having an unlimited capability to create a new organism. A totipotent cell has the capacity to specialize into an embryo, extraembryonic membranes and tissues, and all postembryonic tissues and organs.**

Translational Research **-- Clinical investigation with human subjects (patients or normal volunteers) in which knowledge obtained from basic research with genes, cells, or animals is**

translated into diagnostic or therapeutic interventions that can be applied to the treatment or prevention of disease or frailty.

More Terms

Antagonistic Pleiotropy -- Multiple gene effects in an organism, such that alleles which improve fitness early in life have detrimental effects later in life.

Ecdysone -- The juvenile insect hormone produced in caterpillars that induces molting and metamorphosis.

Emortality -- Indefinite life expectancy for individuals of a sexually reproducing species without death secondary to cellular senescence. However, an emortal individual may still die secondary to environmental trauma or an accident. **Etymology:** This term was first coined by Alvin Silverstein, Ph.D., Professor of Biology at College of Staten Island/CUNY (2800 Victory Blvd.; Staten Island, NY 10314; E-mail: silverstein@postbox.csi.cuny.edu or DrASilverstein@aol.com) to distinguish it from the more usual term of *immortality* and thereby avoid all of its religious connotation. He states, "I was using it among colleagues and friends back in the 1950's, although it did not appear "in print" until my book, *Conquest of Death: The Prospects for Emortality in Our Time* (Macmillan, NY; 1979). [Editor's Note: Although this book is now "out-of-print," there are 193 other books authored by Dr. Silverstein that can be found on Amazon.com.]

Gerontogene -- a gene affecting longevity, either significantly reducing or increasing average lifespan of the organism.

Hormesis The stimulating effect of a subinhibitory concentration of any toxic substance on an organism. In other words, some members of a population, after a period of illness, may actually benefit from a "poison" that normally shortens the life span of other members of the group, as in an LD50 dose of a poison that is lethal to half the members of a population of mice but then strengthens those mice who manage to survive the injury.

Iteroparity -- The state in an individual organism of reproducing repeatedly or more than once in a lifetime.

Life Expectancy -- The Mean Life Span of a standard survival curve of a population.

Maximum Life Span -- Age at death for the oldest observed individual in a species after many generations.

Mortality Trajectory -- Plot of death rate against age group over time.

Neoteny -- A prolongation of the larval state, as in certain salamanders or axolotls or in certain insects, as bees, wasps, ants, or termites, where a young female is maintained in the larval stage as a future replacement for the queen of the hive. Note that queens tend to live [10 - 30] times longer than workers in the same hive. If the genomes are the same and the external environment is essentially the same, what in genotypic expression can explain this dramatic phenotypic difference? Unanswered question: It can't just be eating royal jelly (ambrosia) that confers this advantage on a young female insect by switching on a hidden cassette of genes, can it?

Pleiotropy -- Multiple phenotypic effects of a single gene.

Semelparity -- A life-history pattern that is characterized by an orgasmic burst of reproduction followed by rapid senescence.

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* To be distinguished from *Geriatrics* [that branch of internal medicine concerned with the clinical care and treatment of older persons in our society], while *gerontology* is that branch of biology concerned with the common mechanisms of aging and senescence as manifested in all species.

Accidental nonverbal communication

Refers to the interpretation of an act or line of action by others when it was not intended by the actor.

Acculturation
The processes by which people acquire culture, starting at their birth and ending at their death.

Action language
Refers to how body behaviors, or lines of action, are interpreted, simulating language.

Additive model of aging
An approach to the aging process that suggests that people can maintain or increase their general abilities as they age.

Adaptors
Body behaviors, such as scratching or itching, that people use unconsciously, considered to be evolutionary adaptations to the biological environment.

Affiliation
Refers to identification with, or relationship to, one person with another.

Ageism
The stereotyping of the aging process, often expressed by the media or by people who are uninformed by the scientific intricacies of aging.

Agentry
Refers to the ways that people, on their own be
half, enact behaviors creatively in response to perceived expectations in a situation.

Agonistic
Refers to difficult behaviors that tend to be aggressive, associated with early growth, especially among males.

Androgyny
The process whereby males and females are able to manifest behaviors associated with either gender. Males can become more empathic and females can become more assertive, for example.

Anosmia
Refers to the impairment of the human sense of smell.

Anthropomorphism
The process of labeling animal behavior using terms that apply to human behavior.

Archetypes
In Jungian psychology, an inherited and unconscious mode of thought that is derived from the prior experience of the human race, but found in the modern individual.

Assimilation
Referring to the process by which people become absorbed into a group.

Automatic pilot

Refers to the fact that human behavior is often ritualized such that little or no thought is necessary to perform an action.

Autonomic nervous system

The hunan nervous system that governs involuntary actions.

Artifacts

Products, articles and goods that humans create and used, often serving to help interpret their behaviors, values or beliefs.

Aurality

Refers to the sense and process of hearing.

Back-channeling

The ways that people respond to others in conversations, usually nonverbally, to affirm or deny what others are saying; for example, by nodding their heads, indicating agreement.

Bi-culturalism

Refers to people who share more than one culture in a society.

Body identity

Refers to the symbolic representation of one's physical body.

Body language

The suggestion that bodily actions can be organized into patterns resembling patterns found in spoken language.

Body shine

Erving Goffman's phrase suggesting that the body gives off cues to others in human interaction, although the cues may not be known to the body's owner.

Body signature

Refers to the characteristic ways that people use their bodies.

Broca's area

The area of the brain in which many scientists think that language is encoded.

Channels

Many scholars in nonverbal communication refer to the use of the various senses as channels; nonverbal communication is multi-channeled compared to verbal communication, employing many channels at once.

Chronemics

Refers to time as a nonverbal background factor influencing human communication.

Chronobiology

The interaction of time and biology in the regulation of human behavior.

Circadian rhythm

Daily biological changes that influence human behaviors. For example, sleep and waking are daily events.

Co-construction

The process of jointly creating meaning in interaction with single or multiple others.

Communicative technologies

All technologies affect and effect communication, the principle ones being television and the computer, the internet in modern society.

Contact hypothesis

Refers to the patterns of behavior associated with first contacts among groups of humans, whether hostile or friendly, for example.

Co-cultures

The emphasis upon equality among ethnic cultures.

Codes

Refers to the often hidden set of rules or symbols, physical or social, which when interpreted give meaning to an event, body behavior or activity.

Cognition

The process of perceiving and knowing, becoming aware of phenomena.

Collective behavior

Group or mass behaviors that are often patterned and interpretable.

Communal

Refers to the emphasis upon groupness among various cultures, as opposed to the emphasis upon invidualism.

Construal

The creative process of translating the meaning of experiences throughout life.

Contingency

Referring to the enactment of lines of nonverbal action, one act dependent upon another in an ongoing sequence of interactions.

Cosmologies

The ways that members of cultures collectively organize their beliefs about the meaning of life and the universe.

Craniometry

The study of the shape of the human head to determine how races compare, one with the other.

Culture

The distinctive customs, religious beliefs, habits, languages and technologies that are shared commonly by people in various parts of the world.

Deficit model of aging

An approach to aging that suggests that people lose their general abilities as they age, suffering a decline in mental and physical abilities.

Digital divide

Refers to the general lack of access to computers and the internet which affects women, various ethnic groups and older citizens.

Discourse styles

The distinctive ways that various groups communicate verbally and nonverbally.

Disinhibition

The freedom to act out behaviors on the internet that would normally be suppressed in face-to-face communication.

Display rules

Cultural and social expectations that influence people to act appropriately; guides to dress and other behavioral actions.

Dramaturgy

Use of a theatrical model to do research and to explain human actions.

Dyads

Two person units involved in human interaction.

Dysfunctional

Refers to behaviors that are considered impaired or abnormal.

Ectomorphs

In Sheldon's research, refers to a slight body build, a somatype.

Egalitarianism

The belief that people are equal or that barriers to social, economic and political inequality should be removed.

Emoticons

Symbols and icons used on the internet to substitute for emotional expressions.

Endomorphs

In Sheldon's research, refers to the short, heavy, often fat person, as a somatype.

Emblem

A nonverbal cue or act that can take the place of words.

Engagement-disengagement

Words used to describe how people are said to behave, either by interactive withdrawal or increased involvement.

Enclave

A culturally distinct region of a city or country; for example, Chinatown.

Enculturation

The processes by which people learn the ways of their culture.

Ethnicity

Refers to the characteristics, traits and behaviors of groups whose members share a common identity, often minorities in a society.

Ethnographic

A type of research that uses the methods of field study to focus on the behaviors of specific group members, often ethnic.

Ethology

The scientific study of animal behaviors, especially higher order primates.

Evolution

The general theory that existing living things have their origins in pre-existing types and that modifications have occurred over time.

Face

In interaction, the symbolic front that people display to other people.

Facial primacy

The emphasis upon the face as the primary expressor of emotions, compared to other parts of the human body.

Filtered reality

Refers to mediated communication in which television, for example, alters daily reality. Refers as well to perceptual processes which act as selective lenses.

Folkculture

A type of culture that is transmitted orally, containing stories and myths associated with that culture.

Gaze aversion

Refers to the avoidance of eye contact with others.

Gender

Male and female identities, constructed in social interaction.

Genderlect

The spoken language of a male or female speech community.

Genetics

A branch of biology that deals with the heredtiy and variation of living things.

Genome Project

A scientific project devoted to the task of unlocking the secrets of the genetic code.

Gentling

The process of providing tactile nurturance to newborns, whether human or other animals.

Gestalt

Refers to the process of perceiving objects, physical and social, as whole units, not separable into parts.

Gesture

In Meadian philosophy and psychology, it was a body act, simple or complex, by which meaning is established in interaction.

Glass ceiling

A see-through boundary in organizations and businesses that stopped females and people of color from gaining access to higher level positions although they could see the positions usually filled by white males.

Global Village

The construction of a universal village ied together by modern media forms that crossed international boundaries, as discussed by Marshall McLuhan.

Gustatory

Refers to the taste sense.

Habituation

The ability to perform acts, or lines of actions, without requiring active or prior thought by the actor.

Haptics

The study of the ways that humans and other animals use touch or grasping behaviors.

Hardwired

The imaginative idea that human behavior is the direct result of instinctive or biologically driven mechanisms.

Hierarchy

A graded or ranked system that locates different species on different levels of importance.

High and low contexts

Refers to Hall's analysis of the place of implicit or explicit communicative patterns of behavior; high contexts are implicit and low are explicit.

Historiography

A scientific approach to the study of history to uncover, or discover, patterns of behaviors that may help to understand present day behaviors.

Hormonal cycles

Male and female body secretions that effect changes in the body over a period of a day, month or year, thereby affecting behavior.

Hyper-reality

The creation or simulation of everyday behaviors by computerized methods.

Hysterical personalities

The old belief that women were negatively affected by traumas or disturbances of the womb.

Icon

A pictograph used on the computer. An image of a person, place or object to which people attach devotion or adulation.

Identity

The distinguishing character of the personality or behaviors of an individual.

Imbeddedness

The process in which social dynamics are an inherent part of everyday activities and behaviors.

Immediacy

The attractive behaviors of an individual or people that increase their likability and reduce physical distance between people, as suggested by Mehrabian.

Impression management

The process of monitoring and managing oneself in the presence of others.

Information technologies

All technologies yield information, but reference in this case is to the computer and computer related technologies.

Intentional nonverbal communication

Acts, or lines of action, that are pre-planned by the actor or actors.

Interaction analysis

The study of interactive behaviors by the use of scientifically valid instruments and methods.

Interethnic adaptability

The ability of members of ethnic groups to relate to members of other ethnic groups in positive and flexible ways.

Intersubjectivity

The mutual sharing of meanings, behaviors, activities and events by actors in interactive situations.

Jim Crow Laws

Laws that were enacted to prevent Negroes from having the same rights as Whites despite the emancipation of the Negro.

Joint interactions

The working together of participants in dyads or groups to accomplish goals or share activities.

Kinesics

The study of body movements and actions in human nonverbal communication.

Knowbots

A robot that can perform tasks in libraries and other places that require specialized knowledge.

Labeling process

The naming of people, objects or social events for identification purposes.

Leakage Hypothesis

The scientific statement that suggests that human bodies give off information to observors without the body owner's knowledge that it is occurring.

Lifeworld

Refers to all of the events, meanings and activities that constitute a person's sense of the meaning of life.

Logic-in-use

The pragmatic schemas and thoughts that guide individuals as they enact behaviors in daily life.

Looking glass self

Cooley's theory that in social interaction, people 'see' themselves reflected in the appraisals of others.

Manifest destiny

The American White man's belief that it was inevitable that he would expand to the Pacific. It was his destiny, regardless of the consequences.

Man principle

Reference is to the fact that, for centuries, men were in charge of social, political and economic events. The power of men to control human interactions.

Marginalization

The forcing of minorities and women out of the mainstream of political, economic or social life.

Matriarchal society

A social system in which the woman is head of the family, tribe or nation in which descent of future generations is from the female line.

Media ecology

The study of the influence of the media, especially television, film, radio and the internet upon the quality and character of a given society or milieau.

Meta-analysis

The systematic study of numerous research outcomes to determine the patterns that are common to them, not apparent when one focuses on a few studies.

Metaphor

Figurative language that is used to describe a person, an object or an event. For example, people say that a computer 'thinks'.

Methusaleh factor

The focus on very old age as noted in the Bible in reference to Methusaleh, allegedly the oldest man who ever lived.

Microcosm

A unit that is a smaller version of something larger; in Meadian philosophy, child play was a microcosm of later adult behaviors.

Micro-meso-macro processes

The idea that human behavior may be studied in the context of small, mid-sized, or large, society-wide processes.

Mindlessness

The inattentiveness of humans to events that when mindfully attended to can provide meanings that are otherwise not known, as discussed by S. Langer.

Minimal universality

The thesis that some human behaviors are universal, at least in a minimal way. Ekman and others described body movements that they thought revealed this phenomenon.

Modeling

The direct and indirect following of the behaviors of another person by a young child or other person.

Monolithic ethnic group

The false assumption that members of an ethnic group are all alike.

Moore's Law

The knowledge that changes in technologies are increasing in their doubling time.

Motor skill

Skills that arise from the physiological development of the human body, such as the ability to walk.

Multi-culturalism

The study of the interplay of groups from many different ethnic backgrounds.

Native

Members of oral cultures, as studied by early anthropologists; however, the word is used sometimes to describe people who live in modern societies as well.

Negotiation

In symbolic interactionism, the act of mutually creating meaning with others in interaction, resulting in an interpretation of the interaction or event by each actor.

Networking

Patterned ways that people interact with others in play or work and in interpersonal and group relationships.

Nonconsciousness

Personal unawareness of events that are occurring. Inattentiveness.

Neurological system

The neural-chemical brain system in humans and other species.

Olfaction

The smell system in the human body and in other species.

Oculesics

The study of eye movements, including pupillometry, or action of the pupils.

Oral tradition

The passing on to new generations the culture of the older generation through storytelling, singing, chanting or other rituals, not by the use of modern technologies.

Paradigm

An organized model or pattern used by researchers.

Paralanguage

Vocalized patterns, tones and emphases associated with spoken words that can convey special meanings separate from the meaning of the words in use.

Parapsychology

A field of study that is associated with the study of telepathy, clairvoyance or psychokinesis; the popular study of the sixth sense.

Patriarchal society

A society that is controlled by men in which the descendants of males continue the practice.

Perception

The ability of humans to make symbolic sense of information derived from the senses, from intuition or from imagination.

Pheromones

In many, perhaps most species, including humans, the smells that are produced by the skin or other organ to attract others of the same species.

Phrenology

The study of the structure of the skull in the belief that it is indicative mental abilities or character.

Physiognomy

The attempt to establish character or other thoughts about people by examining their outward appearance.

Place

Used in this text to indicate that people create personal and collective meanings for the areas where they have been raised or presently occupy.

Polysemia

The idea that words, events, people and objects can be interpreted in many different ways by individuals or by groups.

Post-modernism

The view held by many scholars that new patterns of authority and organization brought about essentially by the computer in an information age, are replacing those of the prior industrialized structure of society, thereby altering human relationships and ways of interpreting human behavior.

Pragmatism

Part of the symbolic interactionist view, which suggests that meaning lies essentially in how people act or behave. James and Peirce believed that the function of thought is to guide human action.

Primates

Mammalian species that include humans, higher order animals, such as chimpanzees and other species.

Proxemics

The study of the human uses of space; patterns of use in various cultures.

Pupilommetry

The study of the movements of the pupil in the eye, which are under the control of the autonomic nervous system, as initiated by Hess in his studies of cats.

Qualitative methods

The multiple ways that researchers use to try to understand the meaning of events and activities as understood by the subjects themselves, often referred to as participatory or the living subjects research.

Quantitative methods

The multiple ways that researchers use when they study subjects usually in the laboratory, in which, often, they represent subjects numerically.

Race

The older classification of humans according to physical characteristics, such as shape of head, color of skin, hair patterns, body structure and so on. Now considered scientifically ineffective.

Racism

The stereotypical characterization, usually negative, of members of ethnic groups by the members of other ethnic groups.

Racial profiling

The deliberate act of targeting members of ethnic minorities, usually Black, by White police officers and others, in an attempt to solve crimes or effect other policies, usually established by Whites.

Reductionism

The practice of some researchers to reduce complex behaviors to simple terms, often simplistic, thereby creating error in their interpretations of the behaviors.

Reflexivity

Perhaps better stated as reflectivity, it is the process of self-thought, of thinking about the meaning of events, of interactive situations, of the behavior of self and others in an effort to make sense of the circumstances.

REM studies

The study of the rapid eye movement associated with dreaming.

Reptilian stare

It has been suggested that some schizophrenic people use the fixed stare interactively, sometimes due to the effects of medical treatment.

Rituals

Customized, repeated acts found in events and in interpersonal situations, such as in marriages, funerals and festivities. It can refer to ritualized behaviors by individuals as well.

Role playing

In symbolic interactionism it is the ability of an individual to observe and take the role of another that is key to identity. One learns how to play roles, such as playing the role of a student.

Saturated self

Gergen's idea that the creation of personal identity is made difficult, complex and very uncertain in an age saturated by television and other media.

Scripts

In symbolic interactionism, it is the observation that humans act as though they were following a script; they are influenced by past events and experiences and act accordingly in ways that make sense to them.

Segregation

In this context, it is the idea that young boys and young girls gradually segregate themselves by genders, as noted by Maccoby, only to return to cross-gendered relationships later in life.

Semantics

Essentially the study of meanings that humans create in interaction with others.

Self-presentation

In symbolic interactionism, the idea that humans present themselves to others as though they were on the stage of life. From the work of Erving Goffman.

Self-talk

The process of holding a conversation the self in an attempt to create meaning for the actions of self or of others.

Semiosis

The study of how objects, events and behaviors mean something to people, as signs and symbols.

Sensemaking

The interpretation of the meaning of behaviors in interaction. The ability to construct meaning from events, from self and others.

Sensory

Of or relating to the senses and how the information from them is used.

Signification

The human act of giving meaning to a sign or symbol.

Situated self

The human being is located in a milieau or context which influences her or his behaviors.

Sixth sense

Intuition, esp, clairvoyance or precognition are sometimes thought to comprise a sixth sense.

Socialization

The various and complex social processes that influence the growth of a human from birth to death.

Socio-drama

In symbolic interactionism, using a dramaturgical metaphor, human acts in interaction are referred to as socio-dramas. Television programs are sociodramatic forms.

Sociometry

The scientific measurement of the uses of space by humans.

Somatypes

As in Sheldon's studies, the placing of body shapes and sizes into categories.

Standpoint theory

The idea that all humans are born into and occupy a location in society that influences their behaviors.

Stereotypes

The labeling of people and events by using poor or little information, leading to false conclusions.

Stigmas

The creation of negative stereotypes for people that tend to limit their social success, such as acting toward 'fat' people pejoratively.

Strategy

In symbolic interactionism, the deliberate use of a line of action to accomplish an interactive goal, whether it is to build a good relationship or to deceive others.

Style

Refers to the ways that people present themselves, often in patterned ways; style is sometimes interpreted in opposition to substance, suiggesting that style is transitory.

Symbols, signs and signals

Taken together, these terms refer to the metaphorical ways that humans assign meaning to objects, people and events.

Symbolic interactionism

The scientific investigation of the ways that human create meaning for their lives in interaction.

Synchronicity

Things that occur together; Jung's theory that the collective unconscious of humans acts to create events that occur together.

Taboo

A behavior or act that is risky to perform, unacceptable to society.

Tactility

Similar to haptics, it refers to the use of the hands or limbs to grasp or touch objects or humans.

Techno-language, techno-speak

Specialized language that is derived from modern technologies, such as emoticon or web-site, words that are part of the new lexicon.

Technology

Any tool that is created by humans to be used by them; all tools have a communicative potential.

Telepresence

The saturation of society by the media, especially television, creates a new form of human presence, a mediated presence.

Testosterone

The hormone found in humans, mostly in males, that can lead to aggressive behavior.

Threshold

The idea that each human sense operates within a range of capabilities, beyond which it cannot function.

Tie-signs

Focuses on the importance of relational ties with others that humans create over a life-span.

Time, monochronic and polychronic
The breakdown of types of time associated with various cultures. The United States is said to operate on a monochronic scale.

Transactionalism
A scientific approach to the study of human relationships that focuses on how people give and take information.

Triangulation
In symbolic interactionist research, the use of various scientific methodologies to focus on a research topic in order to provide accuracy.

Victimology
The study of how groups of people have been victimized by other groups and how some groups perceived themselves as victims.

Virtual reality
The simulated reality that can be created by using computers programs.

Vocal signatures
The suggestion that humans have unique, identifying vocal features, one individual in comparison to another.

Voice set
The concept that vocal patterns seem inflexible, especially when one listens to older people speak.

White man's burden
The alleged duty of the White man to manage the affairs of less developed nations or peoples, as described in Kipling's poem, 1899.

Worldview
The concept that every individual, under the influence of culture, possesses a way of viewing the world.

Weltanschauung
A German word to describe the concept of a worldview.

Xenophobia
Essentially the fear of foreigners, arising from background influences or prior relationships.

Yellow Peril
The term used to describe the presence of Chinese in America, who, in theory, under economically difficult times, took jobs away from Whites.

Zoomorphic gods
Mythological gods in the form of animals often worshipped in ritual or feared, who could control the fate of humans, such as the dragon in Chinese society or the coyote, a trickster in Navajo beliefs.

Anti-Aging Glossary

amino acids
Organic compounds that generally contain an amino (-nh2) and a carboxyl (-cooh) group. Twenty alpha-amino acids are the subunits which are polymerised to form proteins.

amino group
An -NH2 group. Organic compounds which have this group are called amines.

bovine growth hormone
A hormone secreted by the bovine pituitary gland. It is used to increase milk production by improving the feed efficiency in dairy cattle.

growth factor
A complex family of polypeptide hormones or biological factors that are produced by the body to control growth, division and maturation of blood cells by the bone marrow. They regulate the division and proliferation of cells and influence the growth rate of some cancers. These factors occur naturally but some can be synthesised using molecular biology techniques and are used clinically to stimulate normal white cell production following chemotherapy or bone marrow transplantation.

Examples include epidermal growth factor, platelet-derived growth factor, fibroblast growth factor. Insulin and somatomedin are also growth factors, the status of nerve growth factor is more uncertain. Perturbation of growth factor production or of the response to growth factor is important in neoplastic transformation.

growth hormone
Polypeptide (191 amino acids) produced by anterior pituitary that stimulates liver to produce somatomedins 1 and 2.

growth hormone regulating hormone
Hypothalamic hormones that induce (somatoliberin) or inhibit (somatostatin) the release of growth hormone (somatotropin).

Growth Hormone-Releasing Hormone (GHRH)
Hormone produced in the hypothalamus that promotes production of Human Growth Hormone. [See Human Growth Hormone]

Prime Vitality LLC

hormone
A naturally occuring substance secreted by specialised cells that affects the metabolism or behaviour of other cells possessing functional receptors for the hormone. Hormones may be hydrophilic, like insulin, in which case the receptors are on the cell surface or lipophilic, like the steroids, where the receptor can be intracellular.

Human growth hormone
A protein produced in the pituitary gland that stimulates the liver to produce somatomedins, which stimulate growth of bone and muscle.

Also called Somatotropin, HGH is a protein-like hormone that many researchers believe has greater capacity to prevent and reverse aging than any other substance. Under a physician's care, HGH replacement therapy is administered with daily injections. Alternatively or in addition, HGH releasers are widely available without prescription, including arginine, ornithine, and other amino acids taken orally as supplements.

Prime Vitality LLC

IGF - Insulin like Growth Factor
Insulin like growth factors I and II are polypeptides with considerable sequence similarity to insulin.

They are capable of eliciting the same biological responses, including mitogenesis in cell culture. On the cell surface, there are two types of insulin like growth factor receptor, one of which closely resembles the insulin receptor (which is also present).

Insulin like growth factor I = somatomedin A = somatomedin C

Insulin like growth factor II = MSA (Multiplication stimulating activity).

Insulin like growth factor 1 is released from the liver in response to growth hormone.

Acronym: IGF

peptide
A compound of two or more amino acids where the alpha carboxyl group of one is bound to the alpha amino group of another.

Link between two amino acids; peptide also refers to the resulting chain of two or more amino acids.

Prime Vitality LLC

precursor
Something that precedes.

1. In biological processes, a substance from which another, usually more active or mature substance is formed.

2. In clinical medicine, a sign or symptom that heralds another.

Origin: L. praecursor = a forerunner

pituitary
An endocrine gland located at the base of the brain, in the small recess of a bone - certain sections of the pituitary each secretes important hormones including growth hormone (GH) and antidiuretic hormone (ADH).

polypeptide
A peptide which on hydrolysis yields more than two amino acids, called tripeptides, tetrapeptides, etc. According to the number of amino acids contained.

somatotropin-releasing hormone
hypothalamic peptide that regulates the synthesis and secretion of somatotropin in the anterior pituitary gland.

Chemical name: Somatoliberin

secretagogue
Substance that induces secretion from cells, originally applied to peptides inducing gastric and pancreatic secretion.

somatomedins
Insulin-like polypeptides made by the liver and some fibroblasts and released into the blood when

stimulated by somatotropin. They cause sulfate incorporation into collagen, RNA, and DNA synthesis, which are prerequisites to cell division and growth of the organism.

somatostatin
Gastrointestinal and hypothalmic peptide hormone (two forms: 14 and 28 residues), found in gastric mucosa, pancreatic islets, nerves of the gastrointestinal tract, in posterior pituitary and in the central nervous system. Inhibits gastric secretion and motility: in hypothalamus/pituitary inhibits somatotropin release.

somatotrophin
growth hormone, somatotropin.

somatotropin
Hormone (191 amino acids) released by anterior pituitary that stimulates release of somatomedin, thereby causing growth.

An amino-acid based substance secreted by the pituitary gland that promotes cell growth and maintenance, stimulates the immune system, etc. [See Human Growth Hormone]

Prime Vitality LLC

somatropin
synthetic or naturally occuring growth hormone from the human pituitary gland. It is given to children with open epiphyses for the treatment of pituitary dwarfism. Chemical name: Somatotropin (human)

Examination

Select the best answer to each of the following items. Mark your responses on the Answer form.

1. Aging involves the progressive decrease in physiological capacity and the reduced ability to respond to environmental stresses which lead to increased susceptibility and vulnerability to disease.

a. True
b. False

2. Theories of aging can be divided into two general categories: stochastic and developmental-genetic. These are mutually exclusive, particularly when considering the free radical/mitochondrial DNA theory of aging.

a. True

b. False

3. Although the term “aging” is commonly used to refer to post-maturational processes that lead to diminished homeostasis and increased organismic vulnerability, the more correct term for this is “_____.”

a. stochastic
b. maximum lifespan potential
c. senescence
d. None of the above

4. “Normal” aging involves inexorable and universal physiological changes, whereas “_____” aging includes age-related diseases.

a. abnormal
b. usual
c. stochastic
d. None of the above

5. The average/median lifespan (also known as life expectancy) is represented by the age at which 50% of a given population survive, and maximum lifespan potential (MLSP) represents the longest-lived member(s) of the population or species. The average lifespan of humans has increased dramatically over time, yet the MLSP has remained approximately constant and is usually stated to be _____ years.

a. 70-80
b. 80-90
c. 90-100
d. None of the above

6. A fundamental feature of senescence is the diminished ability to maintain homeostasis.

a. True
b. False

7. Somatic Mutation and DNA Repair Stochastic theories propose that aging is caused by random damage to vital molecules.

a. True
b. False

8. The error-catastrophe theory proposes that random errors in synthesis eventually occur in proteins that synthesize DNA or other “template” molecules.

a. True
b. False

9. A complex interaction exists between pro-oxidant and antioxidant forces in the cell, and that regulation of the balance between the two may be the critical determinant in mitochondrial, and subsequently, cellular and tissue integrity during aging.

a. True
b. False

10. A common theme is that aging induces a differential gene expression pattern in muscle and brain consistent with inflammatory and oxidative stress, and reduced expression of metabolic and biosynthetic genes.

a. True
b. False

11. The longest-lived human for whom documentation exists was Jeanne Calment, who died in France at the age of _____, in August 1997.

a. 107
b. 115
c. 122
d. 130

12. The mitochondrial DNA /oxidative stress hypothesis represents a synthesis of several theories and therefore comprises elements of both stochastic and developmental-genetic mechanisms of aging

a. True
b. False

13. Agents that bypass blocks in the respiratory chain, such as _____, would be predicted to ameliorate some of the effects of mitochondrial disease and aging.

a. coenzyme Q10
b. tocopherol,
c. nicotinamide
d. All of the above

14. Caloric restriction, which can extend lifespan, reduces oxidative damage in primates.

a. True
b. False

15. Developmental-genetic theories consider the process of aging to be part of the genetically programmed and controlled continuum of development and maturation. Although this is an attractive notion, the diverse expression of aging effects is in sharp contrast to the tightly controlled and very precise processes of development.

a. True
b. False

16. Unfortunately, convincing evidence that senescent cells accumulate with age in vivo is lacking to date. A potential biomarker for aging, ßgalactosidase, has been described; it initially seemed to distinguish between senescent cells and either pre-senescent or quiescent cells.

a. True
b. False

17. The phenomenon of telomere shortening with aging represents a potential “clock” or counting mechanism for senescent cells. Telomeres are structures at the end of chromosomes that prevent degradation and fusion with other chromosome ends

a. True
b. False

18. There are two distinct patterns of cell death: necrosis and apoptosis.

a. True
b. False

19. Although “programmed cell death” and “apoptosis” are often used interchangeably, they are not actually synonymous terms. Researchers Lockshin and Zakeri stress that programmed cell death is a developmental event, whereas apoptosis is a mode of cell death.

a. True
b. False

20. Cell death is a characteristic in a number of neurodegenerative diseases common in aging.

a. True
b. False

21. Apoptosis is an active, gene-directed “suicide” in response to external or internal stimuli, usually in the absence of significant external injury.

a. True
b. False

22. Recognition of the diversity of health conditions and functional challenges that determine long-term care use has been central to the analysis of current and potential delivery systems. Yet elders plagued by chronic illness and disability are now also being increasingly recognized as diverse, from the perspectives of race and ethnicity.

a. True
b. False

23. Elders of color are currently found to be at greater risk of chronic illness and disability, to have shorter life spans, and to utilize more acute-care but fewer chronic care services than majority group elders.

a. True
b. False

24. Although many of the same factors are found to be associated with higher mortality among white men and among elders of color, other factors, such as the impact of lifelong exposure to poverty and discrimination, and cultural norms that influence behavior have also been suggested as explanations for the racial/ethnic differentials in longevity.

a. True
b. False

25. Older African-American women have a longevity advantage over African-American men, but older African-American women have a shorter life expectancy than older white women.

a. True
b. False

26. Directly related to the incidence of fatal diseases and the corresponding differences in longevity are the levels of functional impairment associated with advancing age. It is generally accepted that functional disability increases for both men and women with advancing age.

a. True
b. False

27. Predictors of nursing home placement have been analyzed extensively, and most analysts have identified the following predictors: being white, female, and elderly; not having an informal support network; preferring or having a family who prefers nursing home placement; having severe functional impairments, including cognitive deterioration.

a. True
b. False

28. A Biomarker is a measurable parameter of physiological age that is a more useful predictor of remaining life expectancy than chronological age. The ability to measure biomarkers is extremely important in evaluating the efficacy of any potential life-extending intervention.

a. True
b. False

29. A Gene is a sequence of DNA that can be activated and copied into messenger RNA or mRNA (by a process known as transcription).

a. True
b. False

30. Despite the near-universal phenomenon of aging in living organisms, there is an extraordinarily varied phenotype that accompanies aging in specific individuals. Furthermore, it appears that evolutionary pressures have led to the development of a remarkable homeostatic complexity to the underlying mechanisms that cause us to grow old.

a. True
b. False

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