

The Biology of Human Longevity, Aging and Age-Associated Diseases

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Abstract

In order to better understand the finitude of life it must be divided into its four components: aging, longevity determination, age-associated disease and death.

Age changes result from the increasing rate of biomolecular disorder that, after reproductive maturation, exceeds repair and turnover capacity. These are stochastic or chance events governed by entropy or the tendency for concentrated energy to disperse when unhindered. The hindrance is the relative strength of chemical bonds. The maintenance of chemical bonds until reproductive maturation is absolutely necessary for species survival.

Genes do not cause aging but genes do indirectly govern longevity by determining the energy status of biomolecules before age changes occur, or to reproductive maturation. Longevity is indirectly governed by genes because the strategy of producing excess physiological capacity to better ensure survival to reproductive maturation allows life to continue beyond that crucial point.

Through natural selection biomolecules must retain structure and function until reproductive success or the species will vanish. Selection for the maintenance of molecular fidelity beyond reproductive success is unnecessary for species survival. Thus, the aging process begins.

The failure to distinguish age changes from disease or pathology is a fundamental problem that has not only blurred efforts to understand the biology of aging and the determination of longevity but it has profound political and economic consequences.

Aging is not a disease because, unlike any disease, age changes

(1) occur in every animal that reaches a fixed size in adulthood.

(2) cross virtually every species barrier.

(3) occur in all animals that reach a fixed size in adulthood and only after sexual maturation.

(4) occur in animals removed from the wild and protected by humans even when that species has not been known to experience aging for thousands or millions of years.

(5) increase vulnerability to death in 100 percent of the animals in which they occur.

(6) occur in both animate and inanimate objects.

Of the four aspects of the finitude of life, the only aspect that humans have manipulated is disease or pathology and that has a significant limit. If all causes of death currently written on death certificates were to be resolved, average human life expectancy at birth could not exceed about 93 years. The only way that this number can be exceeded is if we could intervene in the fundamental aging process itself or in the determinants of longevity. These possibilities are presently remote if for no other reason than the research investment in this effort is orders of magnitude less than what is available for research on age-associated diseases. The widespread belief that the resolution of age-associated diseases will increase our understanding of the fundamental aging process is spurious.

Aging is a process that is only experienced by humans and the animals that we choose to protect like zoo and domestic animals. We, and those animals, now survive well beyond young adulthood. That did not occur for the majority of time that we have been a species and it is, in fact, an aberration of civilization attributable to our discovery of how to eliminate many causes of death.

Immortality does not exist in biology because cells and their constituent molecules turn over or are replaced. The only long-lasting biological property on an evolutionary time scale is the information coded in the DNA of the genome and mitochondria, but even that information is subject to mutation or change.

There is an almost universal belief by geriatricians and others that the greatest risk factor for all of the leading causes of death is aging.

Why then are we not devoting significantly greater resources to understand more about the greatest risk factor for every age-associated pathology by attempting to answer this fundamental question:

"What changes occur in biomolecules that lead to the manifestations of aging at higher orders of complexity and then increase vulnerability to all age-associated pathology?"