Gerontology & Geriatrics: Research

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Austin Publishing Group

Editorial

Toward Treating Aging and Extending Life

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Received: December 03, 2015; **Accepted:** December 09, 2015; **Published:** December 11, 2015

Editorial

Treating and preventing aging is the ultimate goal of medicine and the ultimate goal of human emancipation. Any kind of political power a person can achieve is limited by her/his own degradation. In George Orwell's "1984", a political prisoner points to the limit of the immense power a leader in a dictatorship can reach: the decay of his body he can't do anything against. Defeating aging would transform humans into a kind of gods, immortal in the Ancient vision.

And Ancient people were more optimistic in this regard. The epic of Gilgamesh (c. 2150-1400 BCE) depicts the human dream of immortality. The Christian Bible states that "humans will learn to live forever". This message looks very promising. Closer to our times, one of the predictions Nostradamus made for 2015 was that humans will live over 200 years old thanks to the remarkable advances in medicine.

Life-extension - Just evolutionarily predictable

But what does tell biology about life extension? A wider view on human evolution may suggest that extending life, treating and preventing aging may be just the next phase in human cultural and biological evolution. Throughout their history, humans have gained more and more autonomy from their environment. This is culture's role; it offers autonomy from resource availability and makes the interaction with the environment less energetically demanding. Culture is a behavioral tool which have reached an incredible level in humans, but it is present in other related (but not only) species. But culture itself is the normal consequence of animal evolution. Because they can move, animals tend toward more autonomy. They chose their environment, to the extent that they can. Culture is just an elongation of animal behavior. And animals actively seek safety, i.e. the maintenance and integrity of their organisms.

Intelligence, the complexity of the nervous system, directly correlates with a longer life expectancy throughout animal evolution. Birds and mammals are considered the animals with the most complex nervous system and behavior. Is there a biological relationship between the evolution of a complex brain and a resilient organism able to confer longevity or does a complex brain lead to a complex behavior that helps preserve the life of the organism for longer?

First of all, we have to differentiate between short and long term organism maintenance. A complex, fine-tuned behavior offers higher chances for survival at every moment. Intelligent animals may fail to die because of the dangerous environment (predators, accidents, starvation) oftener than animals with less complex brains and behaviors. The environment becomes safer and safer as animals become more intelligent. In fact, intelligent species tend to live longer and have fewer offspring. Looking at the animal kingdom, one can notice that there is an inverse relationship between intelligence and fitness, i.e. the capacity of having viable off spring [1]. They live longer, reproduce less and later in life, their development is slower. In this respect, *Homo sapiens* are a champion in a clade (Mammalia), an order (Primata), of species with long and slow lives and reduced fitness.

Like any physical and chemical system, living beings tend to an energetic minimum, in this case, the energetic minimum of the interaction of the organism with the environment. Adaptation is the result of this interaction. Related to the channels of interaction with the environment, various reactions may appear, leading to increasing complexity in some organs and tissue. Epigenetic changes follow the chemical changes in cells, in fact the syntheses in the cytoplasm. Then epigenetic changes lead to mutations and other changes of the genetic material (DNA). Epigenetic changes influence subsequent syntheses for long time, but at the beginning they may be the consequences of metabolic changes. Reaction change, cells change, genes may change. Organisms change. Evolution may be led by energetically favorable reactions, not fitness and spreading genes. And sometimes in chemistry, complex syntheses are energetically favorable. The same principle may underlie the occurrence of complex traits, like intelligence, but not only.

Complexity makes interaction with the environment more specific and energetically cheaper. This vision may explain the evolutionary appearance of complexity, constantly associated, at least in animals, with a decrease in fitness. Is there any kind of genes more frequent in nature, more successful, than bacterial ones? Is there any complex organism fitter than a bacterium? So, following the logic of the selfish gene, complex organisms should not exist. They are the failure of evolution. The pinnacle of failure is the species with the lowest fertility, *Homo sapiens*.

Fitness is a reaction product. If there is no fitness, there is no life, and nothing to talk about. But fitness can't be a life's goal. Chemistry doesn't make plans, chemistry doesn't have goals and strategies. Chemistry works with reactions, their conditions and their products.

The correct question about complex organisms is why these organisms still exist, despite their low fitness. They appeared and still exist because they have a short term survival rate higher than other organisms.

Bacteria are virtually immortal. The signs of aging in bacteria are weak and controversial, related with chemical gradients [2]. Bacteria can live forever, if they don't die because of environmental factors complex organisms hardly feel like stressors. For example, at least some bacteria and other microorganisms are very sensitive to weak ionized radiation (which questions the theory of free radicals in aging). This is a trait disinfection is based upon.

Citation: Diaconeasa AG. Toward Treating Aging and Extending Life. Gerontol & Geriatr Res. 2015; 1(1): 1001.

Is there any program for aging?

Although intelligent organisms have long lives, they are not among the species with negligible senescence. Birds and mammals suffer clear degeneration during aging. Organisms with negligible senescence, with no noticeable rise in mortality and decrease in fertility with age [3], are coelenterates (*Hydra*), arthropods or mollusks [4].

The champions of longevity and regeneration among Chordata are not mammals or birds, but fish and reptiles. Why? Is there any genetic program for aging, a new and valuable acquisition of evolution in the complex organism? What is aging in the first place?

For a long time, putative mutations accumulating with age were considered the cause of aging. But there is a problem with such mutations: they were not discovered or they are not as widely spread as proposed [2]. Now, it's certain that there are epigenetic changes with aging, variable in amount in different tissues. But, as mentioned above, epigenetic changes follow chemical changes in the cytoplasm; they follow chemical changes in cells. Life is chemistry, cells and organs consist of chemical reactions. In chemistry, any reaction is virtually reversible. But the equilibrium of these reactions may change. For example, some reaction products are gases or they precipitate and the elimination of a reaction product will alter the equilibrium of the reaction. Aging may result from this alteration of equilibrium. What initiates it? If one thinks about the initial phase of tissue formation, and then after the tissue has been functioning for a long time, it sends and receives different signals, it functions at different rate. Various reactions have different levels. Aging may be the loss of cellular specificity and differentiation. Although homeostasis saves an organisms life for short term, sometimes it can accelerate the chemical alterations responsible for aging. There is no surprise that the champions of longevity or/and regeneration are recruited from poikilothermic species. They simply initiate long chains of reactions with a high degree of conservation. Homeostasis involving hormones may have similar effects, forcing cells to proliferate and differentiate.

According to our biochemical hypothesis of aging [2], this process may result from an organism's functioning. Aging and its rate depends on the capacity of an organism to maintain its specific reactions. Genetics is important in aging only because genes determinate aging in a species, because genes determinate the limits of biochemical functioning.

In chemistry, reactions and their conditions are what matters, not the source of the reactants. So, it is not necessary for a reaction to appear only because it has been taking place for millions years. Longevity may disappear and appear again during evolution. The importance of environmental factors in aging is suggested by the effect of caloric restriction, which increases the lifespan by almost half in various species, from worms and insects to mammals. There is a life span gap between the flying birds and non flying birds with similar body mass. Flying mammals, like bats, have a lifespan similar to flying birds with similar body mass, although in general there is a considerable life span gap between birds and mammals [2].

Toward extending life and immortality in humans

If aging is loss of reaction specificity, stimulating those reactions, restoring their previous level may be the key for preventing, delaying and even curing aging. In this respect, new perspectives on aging are needed, new hypotheses, able to find new biomarkers of aging and treatments based on the predictions of such hypotheses.

We hope this new magazine will provide a new approach to aging, aging prevention and life extension. We also hope it will be a host of nonconformist debates, new ideas concerning aging, able to support a rapid progress.

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