

## **Podcast Episode 1: Aging and death**

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In this short episode I will talk about what the life-extension industry promises to solve for us: the problems of aging and death. I will touch on how people usually handle death, quickly followed by a few takes on the life-extension industry. Then I'll dive more deeply into aging – or rather what do scientists know about aging at cellular level, and what are the evolutionary reasons for aging. Last I will mention the mythological quest for immortality and the question if immortality is biologically possible at all.

The amount of suffering caused by aging and death is unimaginable. Or rather, we have chosen to see aging and death as natural or god-given and to ignore this cruel predicament of the human condition during most of the time. A few writers or thinking schools have looked into this, such as existentialism. But reading existentialist literature makes the reader feel despaired and takes away the pleasure of living. We know that those authors are right, and nevertheless choose to range their depressive books somewhere on our book shelves to never open them again. Why do people get out of bed in the morning, although they know that the suffering associated to aging and death is waiting for them and that there is no way out? We can hardly confront the thought that with death our individual consciousness will disappear. Most people suppress the idea that in the light of our own approaching death everything will be ultimately meaningless. Actually, this is classic repression of course, as described by Sigmund Freud. People repress the painful certitude of aging and death of themselves and others. They choose instead the bliss of not-knowing or imagine for themselves some reasons for hope. Engaging with death is only possible for most people within a religious framework. Buddhism describes in much detail the process of dying. Most religions promise a sort of paradise, projecting utopian versions of their respective societies and cultures into an imagined afterlife. Emile Durkheim is an excellent starting point to understand the meaning of religion for societies. Therefore, it is probably true for most people, independently of historical or cultural context, that they can bear to think of death only when they are directly and inescapably confronted by it: often they respond with utter grief and despair. Throughout known human history spiritual beliefs have helped to alleviate the pain or heal the scars left after the passing of loved ones. Belief has often provided hope, even if there was nothing to hope for.

We are now seeing a new industry, also called the longevity industry, promising radical life extension. The numbers they offer usually range from 120 to 300 years as life span, in a first phase. Some in this industry do not even shy away from claiming that immortality might be possible. Now, what shall we make of this? Well, we will probably react as humans always do: most will not take it too seriously, will perhaps feel entertained, then forget it and move on in their normal life. Others will conceptualize it as part of normal medical progress, although the new life extension industry is not part of mainstream medical industry or public health system yet, as many of their activities and claims still appear rather bizarre to the public. A few will become believers, finding their new religion. Especially those of course, who think that eternal life could become a reality through modern science.

The most important idea, on which the longevity industry is based, is that aging itself is a disease. This is new stuff, a radical but rational change in perspective, which cannot simply be dismissed as crazy or immoral. This claim makes us pause. By habit, humans have mostly assumed that aging is something

god-given, or natural. But this new perspective towards aging – aging as disease – lets us see immediately that something is fundamentally wrong with the traditional view to see aging as an intentional decision by nature. We can clearly see that the process of aging can be influenced by human behavior, environment, nutrition, society, etc. Also aging happens differently for different species. And there exist now sufficient examples to show very clearly that aging is not a linear downward process in all conditions. Certainly, in societies with a low level of violence and a good health care system aging is the most frequent cause of death. We thought that aging was the logical consequence of thermodynamic laws or entropy for basically the entirety of biological life, but there are strong reasons to believe that this is not so.

We know that maximum lifespan is species-specific and genetically controlled. There are individuals in the past who have reached a similar age as today's humans in the developed world, simply because they did not die of external factors like most everyone else in their time and place. In the absence of external mortality factors such as accident, being eaten by animals, infection, or malnutrition, all species are getting older on average, but are still limited by an intrinsic lifespan process.

Actually we die as the result of cellular aging. Organ failure is just a consequence of the aging of cells. We already have a rough idea about the root causes of cellular aging. They include problems in DNA repair, telomere shortening, epigenetic alterations, loss of proteostasis, deregulated nutrient-sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intercellular communication. They are not mutually exclusive and can all contribute to aging in parallel, or are connected in some ways. These root causes, also called hallmarks of aging, are encoded in genetic pathways and expressed as biochemical processes. They lead to functional breakdowns of organisms, cause diseases, and ultimately death. Scientists have only started to understand all those processes and interconnections.

But why did natural selection not eliminate aging? George Williams, an important evolutionary biologist, asked why evolution should be able to create highly complex life forms, but not to perform the much easier task to preserve what has been already created. There are actually a few evolution theories providing answers. When I was in highschool, we were taught a theory called group selection theory, which says that aging and death of individuals was evolutionarily necessary to preserve the species. This theory, in the meantime, has been disproven. According to contemporary evolution theories aging occurs because evolution did not select against harmful traits with effects late in life. This is mainly due to high mortality rates in former more dangerous environments. Humans and other animals in the wild just did not live long enough that the suppression of some negative trait would make a difference.

J.B.S. Haldane, a geneticist, found that natural selection did not suppress Huntington's disease, because it occurred only after the age of 40, when typical reproduction time has passed. Medawar, another biologist, expanded on Haldane's work and stipulated that harmful mutations in the germline are able to accumulate if they are expressed late in life. Therefore, the power of natural selection declines with age. Another evolution theory is called antagonistic pleiotropy. The same gene can be responsible for a beneficial process in young age, and a harmful process in old age. For example, it is the same gene, which influences male reproduction in young age and causes prostate cancer in old age. Because human population had much higher mortality rates and lower average life expectancies in the past, prostate cancer was rare and natural selection would not favor a genetic mutation to delete prostate cancer.

All of these new insights into aging and death are gradually supporting the idea that aging itself, based on our ever-improving understanding of underlying genetic pathways and biochemical processes, could be slowed down, stopped, or even reversed. Treating aging as a disease and not as natural provides the conceptual base to radically prolong lifespans. Some even hope for immortality.

But how realistic is it to heal aging and to radically extend lifespan? According to what we know, there is some clear evidence of immortality occurring in biological life. For example, stem cells and cancer cells don't age at all. The same seems to be true with the famous hydra. A few other life forms like the naked mole rat and the bristlecone pine tree show almost no signs of aging just until a very late death – which is termed negligible senescence. Life without aging and even immortality do therefore exist in the biological world. These observations nurture hopes and expectations that further advances of modern science will enable us to engineer genetic pathways and biochemical processes to extend live spans. Even rejuvenation is a theoretical possibility. People in the longevity industry say that rejuvenation will be a huge business, perhaps the biggest business ever, because every person will be a customer, and that rejuvenation might be financed one day through the public health system.

The idea of immortality has been explored by most, if not all human cultures in the frame of art, mythological tales, religion, and magical technologies, incl alchemy. The quest for immortality through modern science is the continuation of that same age-old human desire to imagine eternal life. In the past, concepts of immortality expressed themselves through individual fantasies, and were at the same time based on a collective need to imagine a perfect counter-world, just to make the present more bearable. It also served the interests of certain individuals or power groups. No matter what the longevity industry will offer us in the future, magical pills or the real thing – we should always consider this in the context of that age-old mythological quest. Such a perspective will keep us mentally healthy, while not hindering us to take advantage of opportunities in the future, should they arise.

### Bibliography

Molecular & Cellular Biology of Aging