An Introduction to Evolutionary Biology

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Introduction to Aging

Hi, so in the last 2 to 3 weeks we have looked at the various processes of evolution, selection, mutation, migration, etc. And then we said that we were going to look at the outcomes of those processes. And the first outcome that we are going to look at is aging, also known as senescence in the technical literature. Now what exactly does one mean by aging? Now in common usage, aging essentially refers to the passage of time. So you know about the aging of wine, beer, cheese, and so on. However, when it comes to biology, particularly living systems, the term aging has a slightly different meaning.

Now, what is that? Now think about it: all multicellular organisms, when they are born, are born as a single cell, a zygote, right? And then that zygote divides, and you have the formation of an embryo; at some point, it becomes a fetus in the context of humans. And then at some point we come out of our mother's body, and at that point, you know we are roughly about this size. And then, you know, as time progresses, we become, say, something like this at some point in our lives. And, yeah, we become something like this, and then, as time progresses, you know, other changes happen in our body.

And somewhere, you know, towards the end of our lives, we end up like this. Now, is the entire thing called aging? And the answer for biological organisms is no. So the first part that I talked about when you go from a single cell all the way up to, you know, A baby that is born is typically called development. Then from the, you know, point when you

are born, you are about this big all the way up to, you know, this point. When you come up here, or maybe when you come up here, that is also not called aging; that is typically called growing up.

However, we know that at some point in our lives, things kind of start going bad. So, for example, you know at some point in our lives we start losing hair like this, and at some point in our lives. Other physiological functions start to decline, and typically it is this decline of the physiological functions. From the peak that it has attained, what is called aging or senescence is going down. Now, I am going to define it properly in a few minutes, but right now we will just talk about this going down.

The deterioration, so to speak. Now, what exactly happens during this deterioration? So, if you look at what is happening inside our body, I am taking a slightly human perspective right now. But as I am going to show you, most of this is actually true across almost all known organisms. So inside the human body, it has been shown that there are 12 major what are known as hallmarks of aging. Hallmarks mean distinguishing features, specific features.

So, this is a very famous paper; it came out in 2023. The predecessor of this paper actually came out in 2013, where it ended up talking about 9 hallmarks of aging and Then, after 10 more years, they revised that statement and added 3 more, and that is how today we have 12 hallmarks of aging. Now, what are these hallmarks? I will just show you a list. So, you know these are things like the genome getting all kinds of mutations, and therefore, Becoming unstable, you know there is a problem with what is known as the gut microbiota. The communities become, you know, the structure of the communities becomes altered with what is known as gut dysbiosis.

You have the stem cells in the body becoming exhausted; you have inflammation in all parts of the body. Chronic inflammation, and so on and so forth. Now, the first major point that you need to note here is that these hallmarks are not really independent of each other. Many of these feed into one another. So, for example, you know the genomic

instability that I have talked about here.

Some of it, at least, happens because of the second point, which is telomere attrition. We are going to talk about these things not in this discussion, but in the next one; however, some of this stuff we will get back to. Now, if this were not an evolutionary biology course, I would have gone into the details of each one of these hallmarks. But because our aim is slightly different, we do not really have either the time or the bandwidth. Therefore, I will guide you to this particular video by Science in Motion.

It is slightly long at 13.54 minutes, but it is actually excellently done. Now, remember I told you that in 2013 they gave 9 hallmarks and in 2023 they added 3 more. So, 9 became 12. So, this video predates 2023; that is why when you start, you will see that they are talking about 9 hallmarks.

However, I also told you that these hallmarks are not independent of one another. So, the way 9 became 12 was that in 2023 they said, "Look at three of the things that we had spoken about earlier." But we thought that they were not of sufficient importance. Hence, we had not placed them in the category of the major hallmarks. Now, we are putting them in the context of the major hallmarks.

That is how 9 became 12. These were not new discoveries; they were simply a shift in emphasis. And that is why, although this pre-2023 video talks about 9, In reality, it also covers those three other things, like gut dysbiosis, chronic inflammation, and so on. So, if you look at it, you will get all the information. And people who are slightly more advanced, who have taken, let us say, one or two courses in cell biology and biochemistry, I will strongly recommend that they look at the original paper itself.

Very nicely written, slightly dense; there is too much information, but if you know your cell biology, You will enormously benefit from reading the original paper. However, as far as this particular course is concerned, neither of these is a mandatory reading. Which basically means we are not going to put questions from any of them on your exams. So,

this is what happens inside the body. From our perspective, we are slightly more interested in looking at what happens outside and what exactly we can see.

And here you see a picture of a 95-year-old lady, and on her lap, you see a young boy. And if you try to compare the lady with the young boy, you can immediately see that there are certain things that are different. I mean these are stuff that all of us have seen, you know, looking at our parents or grandparents. As time progresses, you know, for example, their hearing gets affected, right? They particularly notice that their ability to hear high-frequency sounds goes down drastically in terms of what frequencies they can hear. Similarly, you have all kinds of wrinkles developing on the skin, which you can see over here very clearly.

The body mass declines in both fat and muscle mass as they decrease. Because of that, one of the major things that happens with old people is that their muscle strength goes down. They are not able to walk as much as they could during their younger years; they cannot lift things, and so on. Of course, one of the most well-known things that happen is that their vision declines. You know in terms of how far they can see and how accurately they can see.

Similarly, this is the most well-known feature: for most individuals, the hair turns gray. As you can clearly see in this picture as well, cognitive impairment sets in somewhere. They cannot remember new things, and many of the old things they tend to forget. Their ability to understand new and slightly complicated things often goes down, and so on. So, these are very major changes, and the most important thing that happens is that their probability of death goes up.

An older person typically has a higher probability of dying than a younger person; that is a given. Now, one thing I need you to understand is that there is a lot of individual-to-individual variation in all these declines. So, there are many 60-year-old people who, let us say, have more muscle strength than certain other 30-year-old or 40-year-old people. So, that variation is always there; that is always there for any

biological feature, but What I am telling you here is generally true; on average, this is correct. Now, with this understanding of what some of the outward manifestations of aging are, we are now in a position to define aging.

And we are going to define it from the perspective of two slightly different subjects: one is physiology, and the other is gerontology. And for a physiologist, aging is a progressive deterioration of physiological function, you know. Some of which we listed are accompanied by an increase in vulnerability and mortality with age, which basically means That at some point, your physiological functions will start going down, and your probability of death will go up. If you look at an evolutionary biologist, he or she is going to say pretty much the same thing. Except that they will put their emphasis elsewhere.

They will say that aging is characterized by increased mortality. Mortality means the chances of death and decreasing reproductive success with advancing adult age. So, after a point, your chances of death go up, your reproductive capacity goes down, and that is what aging is. So, if you look at the two definitions, there is no conflict between them. Both are talking about increased mortality and increased chances of death with age.

It is just a slight shift in focus. The physiologist is focusing primarily on the physiological functions that are declining. The evolutionary biologist is focusing on the reduction in reproductive success and the increase or reduction in mortality probability. Now, why these two people are doing things this slightly different way will become clear, not in this discussion. But in the next one and the one after that, we will look at the various theories of aging.

Now, up to this point, all the examples that I gave you were primarily in the context of humans. But as we all know, aging is almost a universal phenomenon. There are very few animals or plants that are thought not to age. But even in those cases, people have now started understanding that, probably, they are not immortal as the press says. It is just that for many of them, things happen at a much slower pace than the time scale in which we have studied them.

However, without getting into those exceptions, if we just look at the non-human animals around us, we can see them age all the time. I mean, anybody who has had a pet dog or a pet cat might have seen them age right in front of their own eyes. So, for example, here I am showing you a pet dog, a Neapolitan mastiff, and can you see the white hairs on its muzzle over here, right? And this should remind you of, you know, for example, You know, the white hairs on my face or the white hairs on my moustache are exactly analogous to that, right? So, the point I am trying to make is that aging is a universal thing and by no means is it only a human thing. And the other distinction that aging has is that it is one of the most well-studied phenomena in the whole of biology. So, just to give you one figure, between 2013 and 2023 alone, there were about 300,000 papers that were published on this topic.

And this is not to say that aging work started in 2013; no, aging work started long ago. In fact, as I am going to show you, even Aristotle was writing about aging. So, aging has been studied forever, and this figure that I am giving you is by no means an exceptional you know period of activity during that those 10 years. This is like the rate at which aging papers are published. Now, obviously one has to ask the question: why does one have such a massive interest in this particular topic? And it turns out that there are multiple reasons for it, again somewhat interconnected to some extent.

The first, and perhaps the biggest, reason is cultural. No one wishes to die; no one wishes to look old; no one wishes to feel old. And this is something that we know is cultural. I mean, take for example our own Mahabharata, right? You have the story of Yayati and Puru. So, Yayati was a king who, for some reason, was cursed by a sage that you know, you will become old, and he did not want to become old; he wanted to enjoy life. So, he actually goes and tells his sons, "Hey, will any of you exchange your youth for my old age?" so that I can enjoy my youth for some more time. You know, four of his five sons say, "Sorry, not happening." The fifth son, Puru, says, "Yes, okay, done," and they exchange their youth. and you know senescence and yayati enjoys young age for some more time And then at some point, he realizes that, you know, it is not really taking him

anywhere.

So, at that point, they basically exchange it back, and then Puru goes on to rule for many, many years. Yayati goes to heaven, and so on and so forth. The point I am trying to make is that this thing about enjoying youth and not getting old. This is mentioned in our epics, and by no means are we special. If you look at the Bible, for example, there is again this mention of a king called Methuselah who apparently lives for Some 900 plus years, and people have tried all kinds of ways to justify how that could have been possible.

So, this thing about not wanting to die, not wanting to be old, is one of the fundamental features of the human psyche. And of course, in modern times, we still have not figured out how to exchange youth, etcetera. So, in modern times, what we do is think in terms of cosmetics. For people who have a little bit more money, we think in terms of cosmetic procedures. Now, you know there was a time when people thought that cosmetic procedures were only for the rich and famous.

However, one thing that we have understood now, even in India and in many Western countries, is that people are. Even common people, those who are not in show business or other fields, are investing heavily in cosmetic procedures. And because of that, each one of these things that I am showing you is the cosmetic business itself. The cosmetic procedure business, each one of them, is like hundreds of billion-dollar businesses in their own right. So, obviously, both of these businesses, you know, depend in some sense on aging; that is their raw material.

And their whole procedure, or their whole reason for existence, is trying to figure out. How not to look old or how not to feel old, and so on. However, this is just cosmetic. There is something even more important that has happened over the last, let us say, 100 years or so. This has made aging a very, very important topic, and that is in the context of our life expectancy.

Now, what is life expectancy? Life expectancy is the average length of time a person is

expected to live from the moment of birth. Now you can have your life expectancy calculated at various ages. So what I told you is that life expectancy at birth, and one of the things that has happened over the last 100 years is That in almost every society on every continent, the life expectancy of humans at birth has been going up. So, for example, if you look at Asia, you know this is where we have Asia; somewhere in 1955, this was about 42 years of age. You know a baby born in Asia could expect to live for about 42 years; whereas, By 2025 or so, this is roughly speaking where we are; by this time, this has gone up to about 70, plus 72 or so, right? This has happened because of multiple factors.

First of all, you know there has been greater food security and greater food production all over the world. There has been access to clean water and hygienic living conditions. Medical science has made tremendous progress, which means that the impacts of infectious diseases have decreased. This is because of two things: both the availability of lots of antibiotics and the process of immunization, vaccination. And more importantly, the medical care that we are able to give to babies and mothers to old age people, the standard of medical care has gone up quite a bit. Now this is good; this is the kind of figure that we show everybody. To show that humanity has been progressing over the last 100 years or so. However, this has led to a social issue, and the social issue is that Because the life expectancy has gone up, the number of elderly in society has also increased. Now, because the number of elderly has gone up, it is not that they are living long and not suffering from all those problems.

They are suffering from all those problems, so society needs to take care of them, and this is just to give you some context. Figures in 2025 in India alone had 102 million people above the age of 65, which represents about 7 percent of the population. Now, at the same time, our fertility rate—how many babies are being produced on average per female—has gone down to 1.9, which is Less than what is known as the replacement rate, which basically means that our population in 2025 has already started going down. Now the effect of this will not be felt for some time, and our overall population number will increase for some time, but, By 2070 or so, our population is expected to go down quite a

bit.

And what is the impact of that? The impact of that is that we see the old people become dependent on the young people, right? And the ratio of dependent people to independent people is going up, right? And because of this, you know, people in the younger generation need to take care not only of their babies, They are now needed to take care of their elderly parents for a much longer time. And, of course, the other major thing that is happening is that the cost of health care Particularly for the elderly, the cost is also going up. Now, this again is not an India-specific problem. This particular issue is already real for many countries, the biggest example of which is China. So remember, China had a one-child policy for quite some time, because of which most parents have just one kid.

Let us say you have a male child, and then that male grows up, becomes an adult, marries a female, and both of them are only children. So now this particular couple has to take care of two sets of parents, right? So, 2 + 2 = 4; people become dependent on this one couple, and this particular issue has It has become extremely important for China, and they are doing all kinds of things to solve it. China, of course, is also facing the same problem of a shrinking population. This also explains why China is investing so heavily in AI and robotics.

Anyway, that is a different ballgame altogether. The main point here is that because of these issues, the number of elderly in society is increasing everywhere. The world, because of which there is an enormous emphasis on figuring out how to keep people healthy for as long as possible. Now, typically up to this date, we have been focusing on what is known as a lifespan: how long a person lives. However, of late, the focus has somewhat changed to what is known as health span. How long is a person able to live healthily in a way in which they are not dependent on other people? In a way that they are able to enjoy life, this span when they are able to live healthily is what is known as a health span.

A lot of emphasis in research these days is on how to enhance the health span of

individuals. Now, whatever I have talked to you about up to this point, these are the social reasons and the cultural reasons. But from a purely scientific perspective as well, I mean, aging is a huge enigma. Why is that? That is because we know we have seen that, all else being equal, natural selection is supposed to increase the fitness of organisms. And the fitness of organisms, of course, is defined in terms of how many babies they can produce.

How long they can live, and these are exactly the two things—reproduction and survivorship—that are being reduced by aging. That is why aging is definitely reducing the fitness of organisms. If that is the case, why has selection not been able to get rid of aging? And remember, you know we are not talking about aging being a recent phenomenon. Aging has been there forever, as I told you, right? Even in the time of the Mahabharata and Aristotle, people were writing about aging. So, if that is the case, aging has been there forever for millions of years.

So, why has such a powerful evolutionary force as natural selection not been able to get rid of aging after all these years? What prevents it? This question remains one of the major unanswered questions in biology. Now, as we are going to show you, it is not totally unanswered; we have some very good, you know, answers here and there. But we still have not been able to come up with an overarching theory of aging that kind of takes care of everything. Why has selection not been able to get rid of aging? Evolutionary biology has some answers, as I said. But it has not been able to integrate that answer with other kinds of molecular insights, as we are going to talk about.

So, as I was telling you, one of the earliest scientific treatises on aging was Aristotle's work on longevity and shortness of life was written in 350 BC. And people have been theorizing about why aging happens for a very, very long time, and in 1990, That is 35 years ago; one paper listed and reviewed over 300 theories of aging. I was telling you right that it is a very, very well-studied topic in biology; that is just one piece of evidence for that. Now, many of these theories we now know conclusively are wrong; they are just not correct.

And we obviously cannot look at even the subset that has some possibility. So, we are going to look at maybe a few of the more prominent ones, and we are also going to discuss. What are the pieces of evidence that we have to support, or you know, not support each one of those theories? However, that stuff is what we are going to discuss in the next discussion and the one after that. See you. Bye.