

Chapter 13 Questions and Answers

As I have presented this material in lectures and discussions, there are some questions that routinely arise.

Do you believe that solving the problem of aging is a good thing?

Reducing aging will have both positive and negative aspects. I am neither promoting it, nor condemning it. Instead, I view it as inevitable, and want all to be aware of the negative, as well as positive, aspects. Since a partial solution to the problem of senescence seems to be just around the corner, it may help if we are more prepared. Perhaps the greatest good to come from slowing aging would be a delay in most age related diseases. Perhaps the greatest harm would result from the resulting growth in size of the human population. Already we are taxing the environment, and, at least in the short run, advances in combating aging will only increase the problem.

Many have proposed solutions to aging in the past, and none was right. Why should we believe you?

First, I'm not selling any elixir or treatment. Second, I am proposing that we are close to a partial solution because of recent advances in science, which I have documented in the book. So, you should only accept what I say if you accept my evidence as strong enough to support my conclusions. Advances in the biology of aging have allowed us to gain a much better idea of why and how we age. Understanding why we age points to the importance of repair and maintenance processes. Cellular and molecular biologists are developing the detailed knowledge of genetic regulatory mechanisms that allow other organisms to gain significantly in lifespan, and we soon will be able to find the right control pathways to impact on expression of the repair and maintenance genes in humans.

Won't people who extend their lives start to have a number of disorders?

Not necessarily, but we really won't know until someone tests the proposed solution. Preliminary tests in rodents may give us some idea, but all who jump at the chance for extended life expectancy will be taking risks because no one will know for sure how their lives will be impacted and what kind of quality of life they will have after age 100, or so. It may be that the reduction of aging will allow us to remain healthy for 120, or 140 years, or more. It might also be that, with a "first draft," the reduction of aging will be uneven, with some aspects of aging not being affected adequately, or at all, by the treatment. Such problems might be solved later, but the first group of individuals could exhibit some of the signs of aging and be stuck with certain late-onset disorders. The worst case probably would be if individuals experienced extended periods of decline, with rising morbidity. That is a fear that most of us already have today, even without life-span extension, and no one wishes to prolong periods of serious disability, but the risk would be there.

We may get some idea of what to expect from the "first draft" solutions by testing the proposed treatment on shorter-lived mammals, such as mice, to see how they are doing in years 3-5 of their extended life. Assuming they look healthy, we can test the

treatment on longer-lived primates to see if there is uniform delay of many of the features of aging by examining biomarkers. Given positive results, there may be increased confidence that the prolongation will not bring prolonged morbidity, but the first group of humans to try it still will be guinea pigs. This uncertainty will make for a difficult decision for some who wish extended life. The uncertainty will discourage some, but present day consumption of untested and unconfirmed remedies and elixirs suggests that there will be no shortage of volunteers among us, even with risks.

Even if you slow the rate of senescence, won't such age-related diseases as heart disease and cancer still bring about disability and death?

While I cannot rule out the possibility that there are some age-related diseases that might continue, what is hopeful is that most age-related diseases, that is, diseases whose frequency increases dramatically with age, are being generated at least partly as a result of aging processes. The fundamental processes of senescence underlie most age-related diseases, and our knowledge of the causes of such diseases point to this linkage. Earlier, I gave the story of cancer and how its development is related to the senescence-related changes to our genetic material and gene regulation.

What if the cost is high for the treatments, or the treatments are only available for a few? Doesn't this raise moral issues? Could such concerns block the use of the treatment?

If the cost of the treatment is high, or for some other reason only available to a few, obvious moral issues would arise. I'd like to think that moral issues would be primary and cause a delay in use until any treatment is more universally available, but the current experience in the United States suggests otherwise. We proceed with expensive cures or treatments for a variety of age-related disorders for those with health insurance or other means to pay at a time when we continue to have millions without health coverage for even minor problems. We seem even less concerned about the lack of adequate health care and sicknesses in the rest of the world, outside of our own country. We actively discourage individuals from other nations coming here for treatment unless they can pay. We spend little of our government's biomedical research dollars on illnesses common in other parts of the world, but uncommon here, such as malaria. It already is established that lower economic status contributes to earlier death, at least in part because of lack of adequate health care. The U.S. and its elected representatives have not been concerned enough to correct the current problems within our own nation. There is little doubt that we are condemning the poor in our country to shorter life expectancy than they otherwise would have. I think that fixing this inequity should be a priority, but it is one thing to raise moral issues and another for the moral issues to prevent the "haves" from doing what they wish. Given such facts, I don't expect there to be any blocking of new anti-aging treatments on such moral grounds, at least not in the U.S.

I've heard about "insulin pathways" as being important for reducing aging in other animals, but you have said little about this. How does it fit with what you have said?

One of the primary examples of "insulin pathways" being involved in longevity comes from the nematode mutants that were discussed in Chapter 10. Those mutants, and the insulin-like growth factor pathway, involve repair and maintenance processes.

So, it actually is at the heart of the proposed solution—up-regulation of such pathways leads to increased life expectancy. However, it might not be the insulin/IGF-1 pathway that will be used if another is found that does a better job in humans of up-regulating all of the necessary repair and maintenance processes. Only more studies will give us the answer.

Why should there be just a few processes that need to be impacted to reduce aging? Why aren't there a large number of separate processes, each with its own genetic control? We'd then be a long way from having all of the necessary pieces.

As indicated earlier, when we examine the causes of aging at the cellular and molecular level, we find what appears to be a relatively small number of causes underlying most of the aging processes that we witness at the level of organs and organisms. Were we to be mistaken about this, finding a solution would be much more difficult. If there were many unrelated things going on, we would not soon find a solution. However, there is every indication that the number is limited. Let me add a bit more detail so that what I am saying is clear. For one example, we can look at DNA damage and mutations. There are a large number of different ways that DNA can be damaged. Among the agents that can cause such damage are gamma rays, toxic chemicals that we ingest or inhale, oxidative agents that are by-products of normal metabolism, mistakes during DNA replication, and ultraviolet light exposure on the skin. There also are a number of different kinds of repair processes that deal with this damage and attempt to repair it before it becomes irreversible. While these processes are numerous, they appear to be under linked genetic control, as indicated below, and, the more abundant such repair enzymes and systems are, in general, the more likely that they will detect and repair damage before it becomes permanent.

Concerning genetic, regulatory linkage of repair pathways, as I have indicated in the book, there is strong evidence for linked pathways for repair and maintenance. These come from studies of individual organisms as well as evolving populations. We have seen that the rate of senescence is adjustable in some individual organisms under certain environmental conditions, suggesting such a linkage exists, and also we see selection for longer life spans during evolution over relatively few generations. This strongly suggests a linkage among the repair and maintenance processes, since such increases would appear to be necessary for any substantial increase in longevity, and, were their expression not linked, changes would be much slower during evolution, and virtually impossible for individuals.

Would you be among those who take the “cure?”

The possibility of a longer, healthier life is very tempting, but there are significant risks for individuals as well as for the environment. I don't think that I, personally, will have to make the decision because I am likely to be either quite old or dead before a partial solution is found.

Were it available today, I would look very hard at all the data and evidence before making a decision. Does the treatment “fit” with what is known about why and how we age? What happens to animals that have had the treatment? Do they show significant increases in morbidity late in their extended lives? Are they at higher risk of infection.

Do some of them die quite young, while most live much longer? What do the early results show in humans who have had the treatment for shorter periods of time?

For the first generation or two that tries it, the risks will be great and the evidence would need to be pretty convincing before I would be willing to try it. Living organisms are complex, and what may be beneficial in the short run can be detrimental in the long run. Look at how long it has taken us to sort out the benefits and hazards of hormone replacement therapy in women. Before deciding what to do, I also would determine whether those I love the most were planning to take the treatment. Their answer could well influence mine, as it would determine who would likely be around to share a longer life with me.

Beyond longevity extension, life's bigger picture should be kept in mind. Adding life to the years can be more important than adding years to life. We are here for a finite time and should make the most of it. Do something you enjoy; do something you are good at; and do something that benefits others. There are careers that allow one to satisfy all three, but whatever stage of life you are in, if you can do all three you will likely have a happy and fulfilling life.