

THE FORESEEABILITY OF REAL ANTI-AGING MEDICINE

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ABSTRACT

Anti-aging medicine does not yet exist, in the sense in which the term “medicine” is generally used. Effective medicine nearly or completely eliminates the risk of death from its target cause; antibiotics, for example, have cut American deaths from bacterial infections by a factor of 20 in the past century. All we have to combat aging, at this point, is interventions that modestly (if at all) delay the onset and progression of age-related frailty. In the past few years, however, it has become possible to enumerate a comprehensive panel of technically feasible interventions, which, jointly, would probably constitute real anti-aging medicine: that is, would probably reduce the risk of death from current age-related causes to a level similar to our present risk of death from bacterial infections. The timeframe for developing these interventions in laboratory mice has recently been authoritatively estimated to be around a decade from now. We don’t know how long it would take thereafter to translate them to humans, but it might only be a couple of decades. As the population aged while in possession of these medicines, new aspects of aging would doubtless emerge that would need progressively more sophisticated medicine, but these might well not be beyond us once aging’s aura of immutability has at last been swept aside.

The aim of this paper is to describe (a) the main components of this panel of interventions and the reasons why more and more biogerontologists feel that they will be so much more effective than anything we have today, and (b) the reasons why it is in the interest of anti-aging providers today to maintain a strong interest in this research and to communicate its progress to their patients so as to expedite that research’s success and to profit from it at that time.

KEYWORDS

Aging, rejuvenation therapies, SENS, escape velocity, real anti-aging medicine, longevity

INTRODUCTION

Anti-aging medicine does not yet exist, in the sense in which the term “medicine” is generally used. Effective medicine nearly or completely eliminates the risk of death from its target cause; antibiotics, for example, have cut American deaths from bacterial infections by a factor of 20 in the past century. All we have to combat aging, at this point, is interventions that modestly (if at all) delay the onset and progression of age-related frailty. In the past few years, however, it has become possible to enumerate a comprehensive panel of technically feasible interventions, which, jointly, would probably constitute real anti-aging medicine: that is, would probably reduce the risk of death from current age-related causes to a level similar to our present risk of death from bacterial infections. The timeframe for developing these interventions in laboratory mice has recently been authoritatively estimated to be around a decade from now. We don’t know how long it would take thereafter to translate them to humans, but it might only be a couple of decades. As the population aged while in possession of these medicines, new aspects of aging would doubtless emerge that would need progressively more sophisticated medicine, but these might well not be beyond us once aging’s aura of immutability has at last been swept aside.

The aim of this paper is to describe the main components of this panel of interventions and the reasons why more and more biogerontologists feel that they will be so much more effective than anything we have today. The reasons why it is in the interest of anti-aging providers today to maintain a strong interest in this research and to communicate its progress to their patients so as to expedite that research’s success and to profit from it at that time will also be discussed.

ANTI-AGING MEDICINE IS AN OXYMORON

There is a big running battle going on between the anti-aging industry and the biogerontological establishment in academia. One of the aims of this paper is to point out that a lot of the differences that exist between these groups are actually really more terminological than anything else. For example, the Gerontological Society of America (GSA), which is in many ways the emblem of the biogerontological establishment, tends to feel that their goal is “successful aging”, but that they can’t do it yet. They declare that anti-aging medicine is some sort of contradiction in terms. That was something that Leonard Hayflick wrote recently. However, “successful aging” is probably accurate for the A4M, and indeed the anti-aging industry in general, because successful aging is to some

extent already possible, and successful aging is therefore what the anti-aging industry provides. In the terminology of the A4M, anti-aging medicine is merely a synonym for therapies that promote successful aging.

In my opinion, however, the phrase “successful aging” is a contradiction in terms because aging is fundamentally a system failure. Thus, anti-aging medicine is something that really doesn’t exist yet in the sense that the term ought to be used. If we look back and think about what we have done to infectious diseases, for example, today we can treat most infectious diseases. However, if we look back at what people could do 150 years ago to prevent or delay, for example, tuberculosis then we are thinking of things like hygiene and fresh air. But we would not call those things anti-tuberculosis medicine now. We would call vaccines anti-tuberculosis medicine. Similarly, when we have really conquered aging to the extent that we have today conquered most of the major infectious diseases, we will look back and say that anti-aging practitioners did their best – they were providing generally worthwhile interventions – but those interventions were not really worthy of the name “anti-aging medicine”. Therefore, a better name for what we can provide at present may be anti-aging pre-medicine.

AGING IN A NUTSHELL

What is aging? Aging is fundamentally a side effect of being alive in the first place, or to put it another way, a side effect of metabolism. In other words, the whole network of things that our cells and organs do chemically and biologically all the time to keep ourselves alive causes pathology. Most biogerontologists take this completely uncontroversial statement as the reason why they feel that it is a completely hopeless situation – a reason why we are not going to be able to do anything serious about aging for a very, very long time. And the reason of course that they come to that conclusion is because both metabolism and pathology are incredibly complicated.

We know much more about metabolism than we did 40 years ago, but we have still hardly scratched the surface. There are enormous holes in our knowledge of how we work. And similarly, pathology is an incredibly messy and chaotic process. The only real major difference between these two processes is that metabolism is homeostatic, it works to enable us to recover from poor health when we have got rid of disease or an infection or other sorts of challenge. Whereas pathology is anti-homeostatic in the sense that when something goes wrong it makes other things more likely to go wrong, and therefore harder to recover from. But one could go even further than that. One could say that aging doesn’t really happen at a functional level until middle age. And this is an incredibly important feature. Even though it’s really obvious, it is something that we need to bear in mind.

Therefore we know that aging is a side effect of essential biochemical and cellular processes, but so long as a person does not get too overweight or things like that, then they will be more or less as functional when they are 40 as they were when they were 20. So not a lot has happened. Now this is actually pretty strange if we think about the fact that aging is a side effect of metabolism. Because of course metabolism is a process of interactions between bioactive molecules, molecules that are chemically reactive and that are relatively short-lived in the body. And therefore what we have to conclude is that there is a threshold effect. That being alive has immediate side effects but these effects must accumulate with time throughout life starting even from before we are born. And they must have some sort of threshold level of abundance below which they are completely harmless, but if they go beyond this threshold level they become pathogenic. Therefore we can say that metabolism causes this thing called damage. It is important to emphasize this because the word “damage” is going to be used in a very specific way in this paper. Damage can be defined as a thing that metabolism causes right throughout life as a side effect of what it does. And damage is a thing that accumulates progressively during time until it eventually causes pathology.

THE GERIATRICIAN, THE GERONTOLOGIST, AND THE ENGINEER

There are three real ways to go about doing something about aging, and only two of them are really popularly understood. Metabolism causes damage and that causes pathology. The business of the geriatrician and anti-aging physicians is prevention rather than cure. Thus, the geriatrician is interested in stopping damage from causing pathology as it normally would by inhibiting the rate at which this happens. Of course this is possible to some extent. It is possible to slow down or inhibit the functional decline that results from this accumulating damage. But obviously, it is like fighting a losing battle. As the damage carries on accumulating it gets harder and harder to prevent the pathology and to alleviate the pathology, and eventually frailty and consequently death will occur.

Gerontologists take the view that prevention is better than cure, but they take it a bit too far. They think that the way to go in general is to try to clean up metabolism. To try to inhibit the rate at which metabolism causes damage. This is fine in principle, but the problem with it in practice is that because metabolism is so complicated the chances are that you will have no effect at all to speak of on the rate of which damage accumulates. And if you

do have an effect then the chances are very good that you will also have serious side effects that outweigh the benefits. Which is all a bit of a shame.

Therefore, it seems that an engineering approach is likely to be more successful. And the engineering approach starts by saying let's stop worrying about the processes by which metabolism causes damage or damage causes pathology. Let's just look at what this intermediate actually is. What are the compositional differences between, let's say, 40 year olds and 20 year olds that contribute to giving the 40 year olds a shorter remaining lifespan. Once those things have been identified we can look at ways to actually reverse the accumulation of these things so as to make sure that they never get to the threshold level of abundance that causes pathology. If we can do that, if we can repair all the types of damage well enough to keep them below this threshold level then we are done. We have uncoupled metabolism from pathology and we have more or less cured aging. Furthermore, unlike the other two approaches, which are a long way off in terms of efficacy, the engineering approach is something that we may be able to implement pretty soon.

We know how to build houses and keep them intact and habitable more or less forever with a modest amount of maintenance. What happens to a house if it gets no maintenance? One of the things that will happen is that it will get storm damage to the roof and water will get in, and eventually there will be pathology. Ceilings will collapse, staircases will fall down and so on, and the house will become uninhabitable. Now, we could bring in a geriatrician and he could take a look at the pathology and try to stop it from causing the house to decline functionally. So, the geriatrician is fixing the ceilings and the staircases and so on and not actually worrying about the primary damage. And of course it's a losing battle and pretty soon the geriatrician is going to have to find somewhere else to live. Then we could bring in the gerontologist, now he is trying to be preemptive and is building tall trees around the house so that the storm damage doesn't happen in the first place. And of course he's forgetting that this is going to introduce the risk of large branches being blown off one of the trees and smacking into the roof and making a bigger hole than what was going to happen in the first place. So it's all a little bit hopeless. And then we have the engineer. The engineer is up on the roof and is doing the obvious thing of actually fixing the damage as and when it occurs. The geriatrician and the gerontologist are not being stupid here because they are using much more primitive technology than the engineer. The engineer would have needed scaffolding, for example, to get up onto the roof in the first place. Therefore until such time as the technology exists where the engineering approach can be implemented, the other two approaches are perfectly fine. However, we have now reached the point where the technology required to implement the engineering solution to aging is actually within our grasp.

COMBATting THE SEVEN DEADLY THINGS

<div> <div>METABOLISM</div> <div>— DAMAGE —</div> <div>PATHOLOGY</div> </div> <div>THE SEVEN DEADLY THINGS</div>		
Respiration (oxidation)	Cell loss / atrophy	Neurodegeneration
Carbohydrate metabolism (glycation)	Nuclear mutation and epimutations	Atherosclerosis
	mtDNA mutations	Cancer
	Senescent cells	Diabetes
Cell turnover (mutations, telomere shortening, dysregulation, stem cell depletion)	Protein crosslinks	Hormone decline
	Extracellular junk	Blindness
	Lysosomal junk	Immune decline
Etc, etc, etc	That's it!	Etc, etc, etc

Figure 1. Metabolic processes, the immediate damage they cause, and the resulting pathology.

In Figure 1, the column on the left shows some different types of metabolism, but the only thing that really matters is the entry at the bottom, which declares that this list is comically incomplete. This is a list of a few of the aspects of metabolism that tend to get a lot of the blame for causing aging. But really, of course, the point about metabolism is that it is a network. It is a massively complex network of interrelated processes. Therefore it is biologically naive to absolve any aspect of metabolism from being involved in aging. So this is a ridiculously incomplete list. Similarly, on the right there is a list of some of the major things that can wrong with people as they get older. But, again, this list could easily be greatly extended. So I'm pointing this out at the bottom that this is an extremely incomplete list. The key thing about Figure 1 is the central list; the list of types of damage. The figure is claiming that the central list is complete. It is an exhaustive list of all the major categories of damage that accumulate as an intrinsic result of metabolism and that may, or in most cases are clearly known to, be causative of some of these pathologies. Many of these things also contribute to many of these other things and *vice versa*.

So these seven things, cell loss, mutations in our chromosomes, mutations in the mitochondrial DNA, senescent cells (supernumerary cells that have become toxic but are not dying), cross links between proteins that cause things like hardening of the arteries, extracellular garbage such as that in Alzheimer's disease, and of course intracellular garbage, which accumulates principally in the lysosome of cells in many different tissues in different sorts of compounds, are the things that constitute damage by the definition mentioned earlier.

Theories of Damage, Who Proposed them, and the Date of Proposal	
DAMAGE RISING WITH AGE	PROPOSED AS CONTRIBUTING TO AGING BY:
Cell loss / atrophy	Brody (1955) – or earlier
Extracellular junk	Alzheimer (1907)
Extracellular crosslinks	Monnier and Cerami (1981)
Cell senescence	Hayflick (1965)
Mitochondrial mutations	Harman (1972)
Lysosomal junk	Strehler (1959) – or earlier
Nuclear [epi]mutations (only cancer matters)	Szilard (1959) and Cutler (1982)

Figure 2. Theories of damage, the scientist behind it, and the date in which the theory was first proposed.

How on earth can we claim that this list is exhaustive? Firstly, one can make fairly sophisticated biological arguments based on the fact that we know more or less what we are made of. We may not have a very complete idea of how it works, but we do know what the body is actually composed of. Secondly, there is actually a rather good circumstantial argument, which is that the list has not been extended now for 22 years. These are important papers introducing the ideas that each of the various things in the left-hand column in Figure 2 was a major contributor to determining the rate of aging. The most recent date in the list is 1982. In 20 years we've come a very long way in terms of our analytical techniques in biology. We know a great deal more than we did 20 years ago about how to find things out and yet nothing has been added to this list in that time. So that is pretty good news for our argument.

Methods of Fixing the Seven Causes of Damage (In Mice)	
<i>Damage rising with age</i>	<i>It or its effects reversible by:</i>
Cell loss / atrophy	Exercise, cell therapy, growth factors
Extracellular Junk	Phagocytosis by immune stimulation
Extracellular crosslinks	AGE-breaking molecules and enzymes
Cell senescence	Ablation of senescent cells
mtDNA mutations	Allotopic expression of 13 proteins
Lysosomal junk	Transgenic microbial hydrolases
Nuclear [epi]mutations (only cancer matters)	Telomerase / ALT gene deletion plus periodic stem cell reseed

Figure 3. Known methods of fixing the seven causes of damage in mice.

So the important question now is: How long is it going to take to actually develop ways to fix each of these seven things? In mice, we already know how to fix every single one of them in principle. Some of them we are a great deal closer than that. Figure 3 presents these methods in a rough order of difficulty. There are already treatments for the top three items – cell loss, extracellular junk, and extracellular crosslinking. These are not just treatments to slow down that process, but treatments that can actually repair the damage, treatments that are already in clinical trials. Of course exercise is something that only works for certain tissues in terms of any sort of reversal of decline. But cell therapy, or stem cell therapy, is something that is showing enormous promise in humans, not just in mice. There are vaccines being developed, and vaccines that have been involved in preliminary clinical trials, for removal of beta-amyloid in Alzheimer's disease. There are small-molecule drugs that are being used to restore the elasticity of the arteries by breaking AGE crosslinks caused by glycation. So these things are going really well.

The treatments for the other causes of damage are a little bit further away. Indeed, treatments for cell senescence, such as things like getting rid of visceral fat that causes insulin resistance is going very well in mice, but is not being tested in humans yet. The bottom three items are the hardest of all. They are the ones that will possibly take a decade to get working in mice, and then it could be at least another decade or two before they get working in humans, although it could be a little less.

WHAT DOES THIS MEAN FOR US?

What this means in terms of time scales for humans is quite important. Each of these various therapies will only be a partial solution to the problem that it addresses. And some might say, well that's a bit of a shame, we'll only get maybe 20 or 30 years extra lifespan out of it and that will be it. But actually it turns out that that's not true. We have the advantage, which is often thought of as a disadvantage, that we live a long time. If you're a fruit fly you live a few weeks. So if you figure out how to extend the lifespan of fruit flies by 30%, then that means that you have given them an extra week or so of life – maybe two weeks if they are long-lived fruit flies. Science does not advance very greatly in two weeks. But if you do the same to humans – if you extend their lifespan by 30% that equates to 20 years. And 20 years is an eternity in science. So we have an altogether rosier prognosis.

If you are already in your 80s, you are probably not going to benefit all that greatly from these therapies. But if you are 50 when they first come along, then you might just about have a very small chance of actually benefiting from these therapies and from the increasingly comprehensive, safe, cheap, and convenient therapies as fast as your frailty is increasing. So eventually your frailty will start to diminish. You will start to actually become more youthful again as a result of the increasingly sophisticated rejuvenation therapies that you are benefiting from. And if you are only 30 when these treatments become available, you won't even get anywhere near frailty.

THE WAR ON AGING

As mentioned earlier, it has been 20 odd years now since we figured out all the important components of human aging, or that is how it seems anyway. It has been at least a couple of years since we came up with feasible, foreseeable ways to fix each of those things well enough to work, and in particular to fix them well enough in mice. I have thrown down a bit of a gauntlet to my colleagues, which I like to call Robust Mouse Rejuvenation. The idea behind this is to take middle-aged mice, mice that are already about two-thirds of the way through their lifespan, and do a number of things to them that are sufficiently powerful enough to treble their remaining lifespan. Therefore, a typical long-lived strain of mice will live for about three years, however if intervention is started on its second birthday, the mouse should live to five years. That is something that we probably could, if we had the finances, actually develop within ten years from now. We are not talking about massive amounts of money here. However, it could take another 20 years, or it could take another decade on top of that if the funding remains sluggish.

Now the critical point about that is that it is going to unleash the real War On Aging. When you wake up one morning and you hear that mice have been developed whose healthy lifespan has been extended by that much starting in middle-age, you are going to know that real rejuvenation medicine, real anti-aging medicine is on its way. You won't know how long it is going to take, but you sure as hell will know that it might be in time for you. And that means you are going to make damn sure that the quest to translate that technology to humans gets done as soon as possible. That means, among other things, that it is going to be impossible to get elected except on a manifesto commitment to start a Manhattan Project to cure aging in humans. This may be in as little as five years from then if we are really lucky. However, we are more likely to see the first generation of human therapies, or Late-Onset Human Engineered Negligible Senescence (LOHENS), 15 years or so after it is achieved in mice. That is when the War On Aging is really going to be finished. And of course, universal dissemination of those therapies is going to take longer, and we don't know how long that will be.

Public Duty

What does this mean for us today? This means three things, and the first is public duty. What does it mean in terms of our responsibility to society? In 1776, Jefferson said that all people were created equal. I would like to add to that. Firstly, everyone stays equal. Old people are people too. Now in the current world where we can't cure aging, where we have no cure for aging, it is at least arguable, or defensible, to feel that it is more important to cure life-threatening diseases of young people than those of old people. If you give a 70-year old a heart transplant, then you won't give them the same number of subsequent years of healthy life that you would give a child if you cure them of leukemia. So one might argue that it is more important to cure the child of leukemia. Many elderly people tend to take that view. They tend to feel that younger people should be first in the queue. But of course, when we have a cure for aging, or even when we are in sight of a cure for aging, that whole logic disappears, it collapses, because however old you already are you can get the same amount of benefit from access to a cure for a life-threatening ailment. Thus, the curing of aging will enable medicine to help everybody equally. The critical thing is that we are already in sight of this. We already have sufficient detail about what we might be able to do to actually implement this cure, thus serendipity is no longer an excuse. We cannot say anymore that our delay in prevaricating today and not going on and developing these therapies is okay because in practice it won't really affect the date at which these therapies arrive because serendipity will dominate the timeframes. We can't say that anymore. We know too much. We can make a difference today.

Political Reality

The second thing is political reality. What does it mean socio-politically? "Eventually" is a very important word when gerontologists use it. It is a word that needs to be avoided. "Eventually" is not the sort of word that makes people agitate for proper anti-aging medicine to be developed soon. It makes people think about life extension and the elimination of aging in the same bracket that they think about teleportation. It is a wonderful idea and everything, but you don't vote for it. Therefore, gerontologists have a duty to talk about time scales. But they don't talk about time scales in general, and the reason they don't, of course, is because they talk about the research that they themselves are doing, which is research that they can get the money to do. And they get it from two sources – industry and government.

Industry, of course, is a dead loss because industry is interested in short-term profits. No company will ever pay good money for research that has a 50/50 probability of making money in 20 years, if they have the option of something with a 99% probability of making money in two years. Not even if the amount of money made in the short-term is a tiny fraction of the prospective of money to be made in the longer term. So industry is a dead loss.

One of jobs of the government is to fund research that does not have a commercial incentive. Unfortunately, what the government actually does is it uses peer review. And peer review is a fine system for evaluating the publishability of research results, but in the way it is currently implemented it is hopeless when it comes to actually allocating grant funds, because it is geared to be extremely conservative. People who sit on study sections and decide who gets money to do research are accountable. They are made accountable so that if they recommend funding for work that does not eventually lead to prominent publications then it does not look good for them. So they always fund research that is going to work, even if it's relatively un-ambitious compared to the high-risk, high-gain research that they might otherwise be tempted to fund. And of course gerontologists know this, and so they don't usually even submit the grant applications for this sort of research as they know that they are not going to get funded.

So then we have to ask why are government and industry like this? Why are they so unwilling to fund ambitious research? We know why industry feels this way; it is because shareholders and directors don't want to fund research that is not going to make money. With government, voters are the main problem. Voters think aging can't be cured. The majority of people out there think that aging is inevitable. So they are not keen to agitate the government to do anything about it. And the government knows perfectly well that if it is seen to be funding pipedream blue sky projects that have no chance of success, or rather that its electorate think have no chance of success, then it won't remain the government for very long. Therefore it is not really the government's fault that this work is not funded, it's the voters' fault. Except that it's not the voters' fault, because the voters have the misfortune to watch television on which they see gerontologists saying words like "eventually".

Philanthropic Funding

So this is the fundamental problem and it's a bit of tricky problem to deal with. But there is a way out. In fact, there are two ways out. The first way out is logic. The vast majority of the arguments that people use to say why curing aging might be very difficult or very undesirable are unintelligent. The alternative strategy to logic is

bribery. Namely, finding another source of funding. The fact is that scientists do like to do interesting work and if their funding for that work is secure and is sufficient they'll do it. So the philanthropic sector is the place where serious progress is going to come from, rather than the other two sources of funding discussed earlier.

The question then is: How do we make this happen? To make this happen there should be an institute, an Institute of Biomedical Gerontology, a physical body in place in which a lot of this targeted work gets done. The idea is to promote, co-ordinate, and fund the focused development of solidly science-based rejuvenation biotechnologies. To do this we would need about \$100 million a year, or \$1 billion spread over ten years, of purely philanthropic funding. This would enable us to create Robust Mouse Rejuvenation, and once we get to this point it will kick-start the real War On Aging. With that sort of funding and a timeframe of ten years or so we have a 90% chance of success.

Now you may think a billion dollars is a lot of money, but think about it again, how many billionaires are there in the world? And how many would be needed to fund this Institute of Biomedical Gerontology? Not a large number. This is not as much of a pipedream as it may seem.

The Methuselah Mouse Prize

Something of interest is the Methuselah Mouse Prize (<http://www.mprize.org>). The Methuselah Mouse Prize is not the same as the X Prize, for which once it was won that was it. It is a structured rolling prize that awards incremental progress. The Methuselah Mouse Prize awards people who have beaten the previous record. So the first prize that was awarded laid down a milestone, it was the inaugural prize. The inaugural prize laid down the bar that one has to exceed in order to win another prize. And the amount you win depends on how much there is in the prize fund, and it also depends on how much you beat the previous record by. The reason why the Methuselah Mouse Prize is really useful is that it provokes interest. And it carries with it an extra ingredient, which is of course fame, because it gets a lot of media attention. At this point there is more than \$1 million in the prize fund.

Market Opportunity

What is the commercial relevance of all of this? That might not be obvious because the War On Aging is not even going to begin for ten years, not until we get these mice. And it's not going to end for some time after that. Because it's not going to end until we actually get to the point where LOHENS has been achieved. In other words, when we have products that we can actually give people to actually reverse their aging and rejuvenate them. That's a long time away. Why should you care now? We have to bear in mind what the War On Aging will be like. This will not be just another War On Cancer. The War On Cancer is a complete misnomer, as everybody knows. It was a good thing to do; there is no question that it has been effective. It led to a doubling or more of funding for cancer research, and if it hadn't been for that then cancer would probably be the number one killer in the USA now. So there is no question that the War On Cancer has been a good thing. But calling it a war was a misnomer.

Calling the War On Aging a war will not be a misnomer. People will make sacrifices typical of wartime. They will be willing and indeed eager to have enormous increases in taxes, for example, just to make sure that the money is spent to train the medical personnel to deliver the results of this research once it succeeds. Because once people finally escape from the collectively-induced trance that society is in at the moment with regard to the idea of curing aging, once people finally wake up and realize that we're talking about lives here, then ending aging is going to be thing that matters most. People will want to survive in good health for long enough to benefit. They will want to make the cut, which is particularly true of course because these therapies are rejuvenation therapies that actually make people more useful. Actually reverse rather than simply retard aging. What that means in practice is that the market for traditional medical care, especially for the elderly, will grow even faster than it's grown before. The people who will thrive will be the people with an established reputation for providing high quality care. The market for breaking medical care in new products, products that are just coming along, especially for the elderly, will also grow faster than ever. That means that service providers or product providers with an established reputation for foresight will boom.

CONCLUSION

Anti-aging medicine does not yet exist. All we have to combat aging, at this point, are interventions that modestly (if at all) delay the onset and progression of age-related frailty. In the past few years, however, it has become possible to enumerate a comprehensive panel of technically feasible interventions, which, jointly, would probably constitute real anti-aging medicine: that is, interventions that would probably significantly reduce the risk of death from current age-related causes. The timeframe for developing these interventions in laboratory mice has

recently been authoritatively estimated to be around a decade from now. As soon as we reach this point, the real War On Aging will begin.

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