LIVING TO 100 SYMPOSIUM*

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General Session 3: Theories on Aging Q&A

Presenters: Steven C. Goss, Discussant
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MIKE COWELL: Steve, I'm going to suggest maybe a practical limit to upper age. In my paper I gave sort of tentative analysis of the probability that Jeanne Louise Calment would have lived from 1875 to 1997 on an apriori basis and I came up with something in the order of magnitude between 10^{-13} and 10^{-12}**.** If you accept current levels of probability of survival from age 0 to 100, and then let's say for argument's sake, that q_x from 100 is around .5, in order to get from age 0 to 125, you'd have to have a population of 10 to the 10th power—ten billion people which is larger than the current population of the earth—to get one survivor to age 125. So I submit that while there may not be an absolute limit, it is highly unlikely that any of us will live in this generation of the earth's population to see anybody meet or substantially exceed Jeanne Louise Calment's age of 122 and 1/2. We may see one, but the population has got to be many orders of magnitude larger or, the rate of survival beyond 100 has got to go from .5 to .9 to see one such person.

STEPHEN C. GOSS: Well just a quick reaction, obviously outliers happen and extremely improbable events occasionally occur. If they didn't occur, we wouldn't observe them and they wouldn't be remarkable. Which is why I guess I'm just suggesting as sort of a practical omega concept of you know, 1 in a 100,000 or maybe 1 in a million if you like? You know, just pick a number. But one in 10 to the 10th is low.

GENE HELD: This is not really a question so much as it is a comment building on the points that Dr. Hayflick made and also points that were made in the health expectancy panel discussion this morning by Jay and also by Michael. And that is, that again, if you look at the funding of the National Institute of Aging and discover that less than 5 percent of it is going to aging research per se, as opposed to geriatric medicine, and if you buy into it and believe the fact that the diseases of old age are caused by the aging process, and you begin looking at the cost of all of these old age diseases and everything, you have to believe that the right thing to do is exactly what Jay is doing and that is, let's go to Congress and see if we can get those funds shifted around to where they should be going. And the point that I'm trying to make with all this is perhaps it's time for the

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Society to make it self felt in that area. And again, I recognize this is an Academy point as much as anything else. But it seems to me like it's time for us as a nation to begin addressing the aging process itself if, for no other reason, than simply to avoid the tremendous healthcare costs that we're looking at for the future. Thank you.

STEPHEN C. GOSS: Could I just react to that and pose the question to Len and others, and that is that's wonderful but unless and until we can put forth what will the result of this research be, by way of understanding the aging process, and showing what actions can be taken as a result of it, to actually what extends the aging process, diminish the effects of aging, not diminish diseases, but diminish the effects of aging, how can we hope to really get real action on this?

LEONARD HAYFLICK: Well because it's our belief and the belief of others, that the aging process increases vulnerability to pathology, the next leap of understanding is that if you know what's occurring at the molecular level or higher levels of order, in older cells that increases that vulnerability you will then discover the underlying cause not only of cancer, but cardiovascular disease, stroke and many other abnormalities. The aging process simply creates a soil in which these pathologies can more easily spring. It's not necessarily the goal to perturb the aging process itself. There are perhaps two different processes. It's reasonable to assume that the beginning accumulation of molecular damage is what makes the soil, prepares the soil for subsequent pathology and then there are second order changes, that initiate these age associated diseases, and I think that that is as you correctly point out, not understandable by policy makers, but I think it can be made understandable. It's not a terrible complex notion.

JAY OLSHANSKY: Jay Olshansky from Chicago. Actually, I really want to respond to Steve's comment because it's an important one. I don't believe that we need to know in advance either the mechanisms that we should be pursuing to go after aging itself, or the consequences of succeeding, in order to make the decision that it's the right approach to take. For the same reason, that when we made the decision to go after cancer, years ago, we didn't exactly know how we were going to do it, but it was a reasonable goal to set. By the same token, today I think as Len has made the argument as well, there is every reason to go after aging itself, because we know if we succeed even modestly, the benefits would be huge in terms of its implications for health and longevity.

STEPHEN GOSS: Succeed at doing what Jay?

JAY OLSHANSKY: In slowing and going after aging.

STEPHEN GOSS: In slowing aging.

JAY OLSHANSKY: Yes.

JEAN-MARIE ROBINE: Yes, I think there is a misunderstanding about the term of aging. And it will be extremely difficult to go up against that. And I think we are all following you. By the way, I'm talking about blueprint for development. I'm adding

development, but the blueprint for maintenance and repair. We totally follow you, but it's really difficult for us, to attach this to this term of concept of aging and I don't know maybe it's just impossible now to forget this word and create a new word. But you know, in the past, if we go back to Bacon for example, he was talking about the vital spirit. So why not talk about studying vitality? And understanding vitality and this will be a combination of what we put beyond the word of longevity and aging? What do you think about that?

LEONARD HAYFLICK: Well, if I understand you correctly, you're suggesting that we study something called vitality. I need a definition for that word.

STEPHEN GOSS: What if we called it soil?

LEONARD HAYFLICK: No, we can't call it soil, and we can't call it spirit. I use the term soil because I was responding to a question that addressed how we can convince essentially lay people to understand this phenomenon. But I don't think any biologist could work on a problem whose goal was to effect vitality without a strict definition in biological terms of what it is in order to have it addressed properly. I think in ordinary lay terms, we understand what we think we understand to be vitality, but you can't address a problem like vitality or aging without defining it with great precision.

STEPHEN GOSS: If I can just pick up momentarily on Len's mention of the idea of soil that I think Jay was starting to address. I would guess that medical researchers, who were looking after cancer, would suggest that they are looking at the soil. They are looking at the current condition at the time people start to become cancerous and they think they understand that to some degree. I guess what I'm getting at is, if for going after the fundamental understanding of the soil or of the aging process, if there is a way of saying you know what? We can find a way to put some fertilizer in that soil so that cancer won't have as much of a shot. Now I don't know whether the medical researchers claim that's what they're thinking they're doing, whether that's health, diet and exercise, but I would just suggest that those are the kinds of things that if you can put those forth, then the idea of looking at fundamental aging as opposed to just the diseases, you might have a better argument. I don't know if fertilizer is the best analogy but since you mentioned soil I thought I'd give it a shot.

JAY SIEGEL: As a political matter, so far as getting increased funds for biogerontology, I would suggest that incrementalism may be the word; that is, you're not going to get anywhere by taking an all or none approach to this problem. You should say, well here is another way of getting at the health issue in the United States or wherever—that an increase in funds in basis research would serve this purpose--and at the same time, you can proceed with the effort to reduce the mortality rates from specific causes because you have of course so many interest groups backing each of these causes of death. On another matter, I want to commend Siu Lan and Jean-Marie for extending the methods of trying to measure the compression of mortality, even though I think we've come to the point where the compression of morbidity is the key issue at interest. Their preferred method or the method presented, however, I think misses the issue that Steve is

raising, i.e., the symmetry or rather the combination of the shape of the curve on the left and right. I've already talked about the more common measures that have been used for this purpose, namely the coefficient of variation and the relative interquartile range. These answer the question of the effect of the two sides of the curve. Another point that could seemingly get overlooked at this meeting, because we don't have the other side of this issue represented here very strongly, is, the evidence, however you look at history, of the possibility that what we generally think of as the maximum observed lifespan is going up; that is to say, the evidence that the maximum age at death recorded in several countries of the west, on a curve, of course, allowing for fluctuations, has been going up for a few hundreds years and more rapidly in more recent decades than in earlier years. And therefore, that the point on the right, that point where the curve hits the horizontal axis, may be pushing out in real fact or could do so. It's true that--and I presented this yesterday--there is no indication of that fact or insufficient indication I mean, that life expectancy is rising enough at age 100 for the compression of mortality not to continue out to the year 2100, as reflected in the Social Security projections of mortality.