Living to 100 and Beyond: Survival at Advanced Ages

Session 1: Theory of Aging Session

Discussant: Jay S. Olshansky, PhD

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The Roles of Aging, Longevity Determination and Pathology on Human Life Span and Life Expectation

Leonard Hayflick, PhD

Plastic Omega

Gene Held, FSA, MAAA

Underlying and Multiple Cause Mortality at Advanced Ages: United States 1980-1998

Eric Stallard, ASA, MAAA

First of all, I would like to thank the organizers for inviting me to participate in this well organized workshop on Living to 100 and Beyond. It is a topic that is of interest to us all, and I am fortunate to have been given the opportunity to serve as the discussant for three excellent papers in this first session on Theories of Aging.

I will discuss the papers in the order in which they were presented.

The first paper, by Len Hayflick, is an overview of aging, with an emphasis on ensuring the reader gets beaten over the head with the longevity determination 2 by 4. It is a worthy task, and one that Len has undertaken for decades, but for some reason both scientists and the lay public want to believe in the worst way that aging and death are programmed, and that by making progress against major fatal diseases, we are somehow forestalling the aging process.

As I'm sure you all know, Len is a pioneer in this field, having made important contributions to our understanding of fundamental aging processes for several decades. I used to use some of Len's articles for teaching purposes when I was a young professor at the University of Utah in the mid-1980s, but it has only been in the past five years that I have really come to appreciate his ideas, and the fact that they occurred decades before many came to appreciate them. Several years ago I was working on a book with my colleague Bruce Carnes when Len and I attended the same scientific meeting. I introduced myself, sought his counsel on several issues, and we quickly became engaged in a conversation on the very topic of this conference. Bruce and I have worked together for some time now, and we've spent a considerable amount of time talking and writing about the forces that influence length of life. As I spoke about some of these ideas with Len, he mentioned a term that I had not heard of before, although I was intimately familiar with the underlying premise of the idea. The phrase was "longevity determination", not to be confused with aging program, or longevity genes, or a myriad of other names given to the forces that many people still believe influence the length of life of different species. As Len, Bruce and I have been working together for the past year on a manuscript, I have come to appreciate now more than ever the importance of this concept, and which few people (including many scientists) still seem unable to comprehend. This paper is yet another valiant effort to get across the point of "longevity determination", in addition to a general discussion of prospects for increasing human longevity in the future.

I'm going to do something in this case that I do not usually do as a discussant – provide a graphic of my own. I'm doing this for a reason, although I'm not certain it'll work. Len has not seen this graphic before, but Bruce and I have taken the liberty of trying to communicate the concept of Longevity Determination using one of the best mediums of communication – visual imagery. As it turns out, this is an image that Bruce and I created, with the help of a professional artist, back in

1996 as part of an article we eventually published in the American Scientist. This image never made it to print because it was far too complicated to explain in the limited space available. Although we did not use the term "longevity determination" to describe this image, as it turns out, it is exactly the same concept that Len has been trying to get across to scientists and the lay public for decades. Let's see if this helps at all – Len, you can tell me what you think after the conference.

DISCUSS THE IMAGE

The second paper, entitled Plastic Omega, is a survey of aging research by actuary Gene Held. It is not easy drafting a survey of the various fields that inform the study of aging, if for no other reason then the fact that so many disparate disciplines have to be covered. Given the difficulty, I have to commend Gene for undertaking such a difficult task and doing it so well. I assume an effort such as this is intended to inform those in the insurance industry what the current state of knowledge is about human aging, and what might be expected in the way of breakthroughs that could influence the industry in the coming decades.

Let me start out by commending Gene for his work. The summary provided at the beginning of the manuscript is extremely well done, and I would agree with Gene that a balanced perspective requires more detailed reading. He touched on most of the important hot buttons in the field, including not just why we age, but how aging might be altered in the future. Here is where I would urge caution. There is a tendency among some scientists in the field to exaggerate their findings in order to get attention. Others simply fail to appreciate the importance of the concept of "longevity determination" coined by Len Hayflick – a concept I like to refer to as "the shadow of senescence" – which places a more realistic spin on anticipated advances in the field. Some of these exaggerated concepts crept into Gene's essay through no fault of his own, for they appear repeatedly throughout the scientific and lay literature. To illustrate the importance of this, I will focus on a single issue raised in this manuscript – Aging Programs and Death Genes.

I'll begin with the conclusion – **there is no aging program with a suite of associated genes intended to bring forth everything we recognize as aging, and as such, there are no death or aging genes – period.** When scientists refer to aging genes, what they really mean is that they're trying to identify genes that are associated with one or more biological processes related to aging, but which have as their primary function, some other biological purpose. This is not a subtle play on words – it is a critically important distinction to make that has a direct bearing on what might be expected in the coming years with regard to the effects of genetic engineering, and other interventions, on length of life. To assist me in this effort to explain aging programs and death genes, I will borrow from an essay published recently by Richard Miller from the University of Michigan in Science Magazine's online aging site known as SAGE KE.

Miller identifies 6 categories of so-called "longevity genes." Although not everyone will agree with this classification system, I believe it is a useful way to begin thinking about how it might be possible, or nearly impossible, to alter the rate of aging by manipulating genes.

The third paper, by Eric Stallard, is on the topic of underlying and multiple cause mortality among people dying at advanced ages, principally beyond age 65 in the United States in 1980, 1990, and 1998. Examining multiple cause mortality in humans is a valuable exercise because it permits the development of logical linkages between disease states – particularly the fatal and non-fatal ones. Stallard's analysis reveals an underlying dynamic about mortality in the United States that could be revealed by no other means. Particularly interesting is the reversal in mortality from cancer in the decade of the 1990s, and the established, but already well known linkage between diabetes and hypertension. There is an underlying biology to be gleaned from the information on death certificates, and no one does it better then Stallard and his colleagues from Duke – this manuscript is a perfect example.

Three other observations in this paper caught my attention. One is the recognition that extrinsic mortality exists. For those of you unfamiliar with the term, extrinsic mortality has been around as a concept for centuries – it is generally thought of as a cause of death that is unrelated to aging or its consequences. It has been recognized by pathologists as so obvious that to think it doesn't exist is to deny the existence of the obverse underlying biology that drives intrinsic mortality. The first to formalize the concept of extrinsic and intrinsic mortality was William Makeham in the late 19th century. The second observation was the trend in life expectancy, which not surprising to some, had decelerated in the last decade of the 20th century. However, the most important observation I can make about this paper is the absence of a single word – AGING. Think about it for a second. There were nearly 40 million deaths in the United States from 1980 to 1998, all documented in excruciating detail by the National Center for Health Statistics, and not one of them is listed as having died of aging. Why? Because aging is not an acceptable underlying or contributing cause of death to place on a death certificate because aging it currently unmeasurable. And yet, can anyone deny that the processes that contribute to aging lead to an age dependent increase in the risk of chronic degenerative diseases. This problem is at the very heart of the distinction between aging and disease that Len Hayflick has emphasized for decades. By examining only those causes of death on death certificates, and drawing conclusions about human longevity by manipulating those causes of death, we completely miss the most important biological force of them all. This is not a criticism of Eric's analysis – it is a classic illustration of the importance of Len's point that attacking disease is not the same as attacking aging. With the focus of modern scientific research on diseases, we are not anywhere close to producing large increases in life expectancy like those observed during the 20th century.

In closing, while it is interesting to focus on centenarians as the topic of this conference, the vast majority of the human population has little or no chance of living that long. And even if we continue to push out the envelope of survival to later and later ages, doing so without influencing aging itself is, in my opinion, a dangerous undertaking. I too remain hopeful that stem cell technology, gene therapy, and the development of new pharmaceuticals will help us forestall the consequences of aging. I'd be much more impressed by definitive empirical evidence that aging itself can be modified