Debates

Response to Dr. Hayflick

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Len Hayflick’s first sentence clearly indicates that we are in substantial agreement. He then goes on to discuss some differences in our respective viewpoints. In this response, I will attempt to explain why these differences are minor, and relate more to the use of particular words or phrases, rather than any fundamental biological issues. In my article, I should have made it clear that I was discussing only intrinsic pathologies or diseases, not extrinsic ones caused by an infection, such as pneumonia.

Len Hayflick states throughout that advancing age increases vulnerability to age-associated diseases, with which I agree. However, I would argue that increased vulnerability is simply that a given amount of damage or disorder has accumulated throughout adult life, and therefore an additional increment may precipitate disease late in life. I provide here two examples. It is well known that the cross-linking of collagen increases linearly throughout life. This may have no deleterious effect at all for several decades, but at a certain point it may become important. It may lead to the loss of elasticity of the walls of the major arteries, and subsequently contribute to multiple effects, including hypertension, malfunction of kidneys, and cardiovascular and cerebrovascular disease. The second example is tumor progression. It is widely agreed that malignancies (carcinomas) arise only after several prior events have occurred. These are not themselves harmful, but as we get older, the chance of the final steps in tumor progression become greater.

Len Hayflick discusses “one cause” of aging. In effect, this is the overall loss of “molecular fidelity” by the innumerable stochastic events that eventually give rise to the aging phenotype. The only difference between us is that I would say that the causes of the cross-linking of collagen, the deposition of amyloid plaques in the brain, the accumulation of AGEs (advanced glycation end products), the increase in defects in mitochondrial DNA or chromosomal DNA, the decline in the immune system, and so on, are distinct, and are also studied by different research scientists using different techniques. I would say that there are many causes that give rise to all these and other defects, not just one leading to a loss of “molecular fidelity.” He also writes that I should distinguish between longevity determinants and the aging process. Again, I think that this relates more to the use of language, rather than real biology. I assume “longevity determinants” to be the genetically determined stability, or instability, of molecules, cells, and tissues, and that the efficiency of maintenance mechanisms play a vital role in setting that stability. However, maintenance eventually breaks down, and then “the aging process” begins. This aging process comprises a number of different molecular and cellular events, so I would prefer to believe there are several concomitant processes of aging, which together contribute to senility and death.

A few years ago, I wrote an article on the urgency of research on aging (1). It included the following passages: “What are the aims of research on age-associated diseases? There are three: 1) a better understanding of the aetiology, or cause, of the disease in question; 2) the development of procedures to prevent or delay the onset of the disease, and 3) better treatment of each disease as it arises . . . Of these three aims of biomedical research, the first two are certainly within the province of gerontology, the scientific study of the processes of aging. Thus, if we want to know the aetiology of an age-related disease, we need to study aging itself. We need to study the cellular and molecular changes which precede the overt onset of any particular deleterious disease. Thus, the study of gerontology must have a central position in biomedical research.” Len Hayflick points out that physicians understand that the greatest risk factor for age-associated disease is the aging process itself, and writes “why then is support for the study of the greatest risk factor microscopic compared to the support available for geriatric medicine.” I think here we are in complete agreement. Although biomedical research scientists studying each particular disease may well be interested in the three aims listed above, they are also specialists, and by and large they are not interested in other diseases, and most important, the processes of aging itself. This does indeed receive very minor support compared to all the research on age-associated diseases. I further agree that research on better treatment of each disease as it arises (that is, aim three above) may tell us very little, if anything, about aging itself.

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