Editorial

“"The Rate of Aging”: A Counterproductively Undefinable Term"
Perfectly clear that they would not necessarily (nor even probably) be varied in unison. This is (unsurprisingly) best illustrated by examining extremes. A perfect achievement of the “one-hoss shay” trajectory of aging—the compression-of-morbidity ideal trumpeted by so many of my colleagues as the ultimate goal of biogerontology¹—would cause everyone to die as soon as their health begins to decline. Is this slowing aging? Not at all—it is quite clearly accelerating aging! It is only conceivably desirable if combined with a postponement of the onset of frailty, such that life expectancy is not diminished. Further, such an intervention would not make the Gompertz slope vertical, since the variation between individuals would remain: hence, it would not accelerate aging to an infinite rate by demographic measures, even though it would do so by biological measures. Conversely, extending the period of frailty at the end of life (which is what slowing aging would actually do—think about it, we spend a lot longer in a frail state than an aging mouse does) is generally considered undesirable. Yet, commentators frequently conflate these things, and use mortality and morbidity interchangeably when discussing modulation of “the rate of aging”: for example, asserting that the rectangularization of the survival curve seen in developed nations in the period 1900–1950 represents compression of morbidity.

Even this fiasco is trumped however—not least in terms of the money wasted over the years—by the concept of biomarkers of the rate of aging as pointers to the discovery of age-retarding therapies. A biomarker of aging is generally defined as a measureable physiological parameter that correlates well with mortality risk across a wide range of circumstances (e.g., species, interventions): the idea is that the rate of change of that parameter reflects the rate of aging. The absurdity of this concept is revealed when one considers interventions targeting that particular feature of aging. Its progression could be completely eliminated (or even reversed) with little or no effect on frailty or life-span, if (as is virtually inevitable) other, largely independent types of accumulating damage are also eventually fatal. Conversely, it could be obviated—its contribution to frailty and death eliminated—thereby allowing it to progress to levels exceeding those seen in present-day humans without any indication of attenuated frailty. This is the likely scenario for mitochondrial mutations, for example: the mitochondrial DNA may be made superfluous by inserting copies of its genes (with suitable modifications) into our nuclear genome, so that the proteins it encodes would be properly synthesized and localized, even if their mitochondrial template were mutated to oblivion.² A third scenario is a change that is harmless within a normal lifetime, such as (almost certainly) aspartate racemization in cartilage: here, interventions that postpone all pathogenic aspects of aging and thus extend healthspan and life-span will not necessarily alter the rate of change of the “marker.” In all three circumstances, what was a marker of the rate of progression of frailty prior to the intervention ceases to bear any relation to that rate.

I rest my case. The mission of this journal is the postponement of frailty and consequent death, but when you want to talk about the rate of progression of frailty, don’t call it the “rate of aging,” because that is one of the most misused terms in the field.

REFERENCES

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