EVER SINCE GOMPERTZ*

S. JAY OLSHANSKY AND BRUCE A. CARNES

In 1825 British actuary Benjamin Gompertz made a simple but important observation that a law of geometrical progression pervades large portions of different tables of mortality for humans. The simple formula he derived describing the exponential rise in death rates between sexual maturity and old age is commonly referred to as the Gompertz equation—a formula that remains a valuable tool in demography and in other scientific disciplines. Gompertz's observation of a mathematical regularity in the life table led him to believe in the presence of a law of mortality that explained why common age patterns of death exist. This law of mortality has captured the attention of scientists for the past 170 years because it was the first among what are now several reliable empirical tools for describing the dying-out process of many living organisms during a significant portion of their life spans. In this paper we review the literature on Gompertz's law of mortality and discuss the importance of his observations and insights in light of research on aging that has taken place since then.

> In these days of continuous change in mortality, with the necessity of forecasting in many of our operations, a paper concerned with the graduation of mortality statistics may appear to be academic, the more so if attention is restricted to the fitting of mathematical curves, with or without any attempt to advance that elusive and, as some think, delusive conception, the law of mortality.
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> Most of us retain, consciously or unconsciously, a feeling that, underlying all the roughness in our data referable to errors of observation and an ever-changing environment, there may be an inherent mathematical system of law and order, which if it could but be discovered would give such insight into the meaning of the unadjusted figures that a considerable advance would be made in the practical application of our science (Wilfred Perks 1932).

In 1825 British actuary Benjamin Gompertz (1825:514) made a simple but important observation: A "law of geometrical progression pervades, in an approximate degree, large portions of different tables of mortality." This observation was based largely on observed death and population records for people in England, Sweden, and France between ages 20 and 60 in the nineteenth century. The simple formula describing the exponential rise in death rates between sexual maturity and extreme old age, $[\gamma(t) = \exp(\gamma t)]$,[1] is now commonly referred to as the Gompertz equation. Gompertz (1825:519) further concluded that "I derive the same equation from various published tables of mortality during a long period of man's life, which experience therefore proves that the hypothesis approximates to the *law of mortality* [our emphasis] during the same portion of life..." Gompertz's law of mortality has captured the attention of scientists for the past 170 years because it was the first among what are now several reliable empirical tools for describing the dying-out process of many living organisms during a significant portion of their life spans.

In this paper we review the literature on Gompertz's law of mortality and discuss the importance of his observations and insights in light of research on aging that has taken place since then. The literature related to the Gompertz equation and his proposed law of mortality is extensive. We will focus on what we believe represent important conceptual and methodological developments that have occurred since Gompertz's initial observations over 170 years ago. In presenting the historical work we have attempted to retain as much of the original language as possible to preserve the intent of the authors as well as to entertain the readers. Although the language of Gompertz and his contemporaries is often cumbersome, we find it equally enlightening.

GOMPERTZ'S LAW OF MORTALITY

Gompertz was a practicing actuary who, like his contemporaries, was interested in the practical problem of estimating premiums for life annuities. What separated Gompertz from the other actuaries of his time was that he saw the life table as more than just a working tool. He endeavored to go beyond the simple mathematics of insurance tables in an effort to understand why there were consistent age patterns of death among people. His motivation is perhaps best exemplified in a statement he made near the end of his career: "The object of research is not only to give information of facts, but to draw beneficial and general views; and if generalisations lead to probable theories, they should be regarded as pleasing associates, to be entertained at the feast of knowledge..." (Gompertz 1872:330).

*S. Jay Olshansky, Department of Medicine, University of Chicago, 5841 S. Maryland Avenue, MC 6098, Chicago, IL 60637; e-mail: sjayo@cicero.spc.uchicago.edu. Bruce A. Carnes, Argonne National Laboratory. The authors thank Shiro Horiuchi and anonymous reviewers for comments on an earlier draft of this manuscript. Funding for this work was provided by the National Institute on Aging (Grant AG-00577-01), the Social Security Administration (Grant 10-P-98347-5-01), and the Office of Health and Environmental Research and Office of Epidemiology and Health Surveillance (Contract W-31-109-ENG-38). Portions of this manuscript were presented at the Michigan-RAND Summer Seminar on the Demography and Economics of Aging held in Santa Monica, California in August 1995 and at the annual meetings of the Gerontological Society of America, held in Los Angeles, California in November 1995.

1. This is the modern formulation of Gompertz's original formula.

In spite of the importance of his early work, Gompertz appears to have published only three articles. In the first published in 1820, he identified a consistent rate of increase in death rates for some nineteenth century European populations for a limited portion of the age range. He observed "the near agreement with a geometrical series for a short period of time, which must pervade the series which expresses the number of living at ages in arithmetical progression, proceeding by small intervals of time, what the law of mortality may be, provided the intervals be not greater than certain limits..." (Gompertz 1825:513).

In his second article, published in the *Transactions of the Royal Society*, Gompertz (1825) set forth what is now recognized as the law of mortality. Gompertz used equal intervals of longer periods of time than in his previous work, and noted that the differences between the common logarithm of the number of persons living in successive equal age intervals were almost identical during a significant portion of the life span. For example, Gompertz (1825:514–15) found that the differences in the natural logarithm between successive 10-year age intervals between ages 15 and 55 in a mortality table for Deparceaux, France were all nearly identical; he concluded that "consequently these being nearly equal (and considering that for small portions of time the geometrical progression takes place very nearly) we observe that in those tables the numbers of living in each yearly increase of age are from 25 to 45 nearly, in geometrical progression."

It is important to recognize that the time frames Gompertz used for his calculations encompassed the majority of the observed range of survival for humans at that time (for those who survived past sexual maturity) because survival beyond age 60 or 70 was uncommon.[2] After observing similar patterns of geometrical progression in other tables of mortality, Gompertz believed he had discovered a general law of mortality that linked arithmetic increases in age with geometric increases in death rates. From 1825 to 1862 Gompertz (1872:330) was "engaged on the subject of what is called Vital Statistics," and published a paper (Gompertz 1862) focused primarily on revising his original notation.

Recall, however, that Gompertz's primary reason for performing such calculations was for the purpose of estimating premiums for life annuities. He translated his finding about the law of geometrical progression into the conclusion that "if the law of mortality were *accurately* such that after a certain age the number of living corresponding to ages increasing in arithmetical progression, decreased in geometrical progression, it would follow that life annuities, for all ages beyond that period, were of equal value..." (Gompertz 1825:515). Makeham (1889:152) restated Gompertz's views on this issue perhaps more clearly: "Mr. Gompertz assumes that the power to oppose destruction loses equal proportions in equal times." This conclusion is based on the supposition that humans are endowed with a recuperative power—a force that Gompertz called "the power to oppose destruction," but which Makeham referred to as the "vital force" that becomes less efficient with the passage of time.

Gompertz presented a fourth article to the International Congress in 1860, but it was published after his death in the *Journal of the Institute of Actuaries* by his colleague, Dr. William Makeham (see Gompertz 1872). Here he elaborated on his earlier observations. Gompertz (1872:331) noted that in his primary equation for geometric progression the parameters of his equation "were supposed to represent constant quantities, or at least were shown to differ very little from constants, for a very long term of years, for instance, about 50 years... But in making the investigation, I did not pretend that [the parameters] were absolutely constant; they were determined by a random selection from three distant periods of age, from a statement of the number of persons who will be living at different ages, out of a certain number of persons stated to have been born. And therefore as $L_x = A \cdot \overline{B}^{qx}$ will not perfectly, during the whole term of life, express the facts..."

Gompertz (1872:333) not only observed that mortality progresses geometrically as age increases arithmetically, but endeavored to go beyond his empirical observation into a biological explanation for what he observed: "And contemplating on this law of mortality, I endeavored to enquire if there could be any physical cause for its existence." Gompertz's basic supposition was that "life requires certain powers of integration in the material of its necessary organization to be kept up," and that those powers could be divided into two portions: one a principal or fundamental part and the other an auxiliary part designed to maintain the principal power of integration. He further speculated on the presence of powers that destroy the auxiliary force. Gompertz multiplied this hypothetical force to destroy life by the population alive to estimate the number of deaths in the age interval.

Gompertz (1872:336) realized that if the force to destroy life operated equally on everyone born in a given year, then his theory implied that "all individuals of a birth in the same locality should have ultimately the same length of life..." —a condition he acknowledged was absurd and knew from observation could not be true.[3] To address this problem,

2. Gompertz, Makeham, and their contemporaries were influenced not only by the need to produce working tools for their fellow actuaries, but by the patterns of survival observed at that time which served as the basis for determining the portion of the lifespan most useful to evaluate. In this regard, Makeham (1860:304) stated why only a limited portion of the lifespan of humans would be useful to examine: "the data for the ages between 20 and 80 is by far the most important in comparison with the rest; first, because the observations on the ages not included between those limits are made upon numbers too small to give much weight to the deductions made from them; and, secondly, because the great mass of the calculations of an Assurance Office will be but slightly affected by errors in estimating the rate of mortality at the excluded ages. For these reasons, the following law of mortality has been deduced entirely from the observations on lives between the ages of 20 and 80, leaving the remaining portions of the table to be constructed on the assumption that the law so deduced may be taken to represent the true rate of mortality—say, from the age of 10 years upwards, to the extremity of human life."

3. Although we are speculating on this point, it appears to us that in his last published article Gompertz was responding to his critics. One critic argued for three separate laws of mortality, which Gompertz extended to

Gompertz (1825:517) emphasized the importance of chance in the timing with which death occurs: "it is possible that death may be the consequence of two generally co-existing causes; the one chance, without previous disposition to death or deterioration; the other, a deterioration, or an increased inability to withstand destruction."

Makeham (1889:153) attempted to clarify Gompertz's concept of chance: "Chance, then, in Gompertz's phraseology—rather than reduced vital force—is, properly speaking, the primary or essential element in the cause of death, and the effect of the diminution of vital force is merely to increase proportionately the chance of death in a given time." Makeham used, as an example, the death of the Duke of Wellington from an apparent attack of indigestion at an advanced age. The Duke's "inability to withstand destruction," a result of advancing age, led to his ultimate demise. Given that he had successfully overcome many previous bouts of indigestion,[4] however, the actual timing of his death must have involved an element of chance. According to Makeham (1889), the incorporation of chance into Gompertz's law of mortality explained why death occurred at different ages even though the "vital force" (and its age-specific rate of loss) was assumed to be a constant quantity for all individuals of the same age. Lacking the concept of genetic heterogeneity, Gompertz invoked chance to explain why members of a presumed homogeneous cohort die at different times.

Gompertz (1825:516) was somewhat vague on the issue of an age beyond which humans were incapable of living. At one point, he emphatically stated: "though the limit to the possible duration of life is a subject not likely ever to be determined, even should it exist, still it appears interesting to dwell on a consequence which would follow, should the mortality of old age be as described above. The non-appearance on the page of history of a single circumstance of a person having arrived at a certain limited age, would not be the least proof of a limit of the age of man; and further, that neither profane history nor modern experience could contradict the possibility of the great age of the patriarchs of the scripture." Later he qualified his position on a limit to life by stating: "Such a law of mortality would indeed make it appear that there was no positive limit to a person's age; but it would be easy, even in the case of the hypothesis, to show that a very limited age might be assumed to which it would be extremely improbable that any one should have been known to attain."[5]

To summarize, what Gompertz discovered was straightforward: For various human populations between ages 20 and 60[6] in the eighteenth and nineteenth centuries, arithmetic increases in age were consistently accompanied by geometric increases in mortality. He referred to this phenomenon as a law of mortality because of the consistency with which it occurred.

MAKEHAM'S THEORY OF PARTIAL FORCES OF MORTALITY

In a series of articles published in the latter half of the nineteenth century, Makeham (1860, 1867, 1872, 1889, 1890) set out to refine Gompertz's law of mortality. Makeham (1860) first noted that the logarithms of the probabilities of living from Gompertz's formula, instead of proceeding in uniform geometrical progression, increased at a faster pace at higher ages than at younger ages. He attempted to solve this problem by 1) adding a "constant" term, redefining the Gompertz law as "the probabilities of living, increased or diminished in a certain constant ratio, from a series whose logarithms are in geometrical progression," (p. 303); and 2) limiting the analysis to the age range 20–80 and assuming that the formula applied beyond age 80.

Makeham's (1867:332) most important modification of the Gompertz formula was his development of "a theory of partial forces of mortality." His argument, based on the supposition that some "diseases depending for their intensity solely upon the gradual diminution of the vital power" (1867:335), fit the Gompertz law far more closely than a mortality schedule based on all causes of death combined (i.e., total mortality). Makeham again was referring to his earlier observation of accelerated increases in the force of mortality at older relative to younger age groups. The diseases associated with the "diminution of the vital power" were linked to specific organ systems—the lungs, heart, kidneys, stomach and liver, and brain. Although Makeham (1867) acknowledged that medical science was not advanced sufficiently to permit a complete partitioning of total mortality into its constituent elements, the diseases he chose represented a significant portion of total mortality at that time and worked well in solving the problem of observed greater increased forces of mortality at older ages than at younger ages. Precisely how Makeham determined cause of death was never revealed.

four, and another may have claimed that the Gompertz equation required everyone to live to the same age.

4. Dr. John Bailar, III from The University of Chicago pointed out to us that the Duke of Wellington actually may not have died of a bout of indigestion; it may have been heart failure. Apparently the symptoms of the two conditions are remarkably close.

5. It is surprising that, with such a large body of literature involved in the search for a law of mortality, only a few of the researchers involved had anything to say directly about the implications of a law of mortality on the concept of a biological limit to life. Consistent with Gompertz's view, Weismann (1891:9) stated that "the duration of life is forced upon the organism by causes outside itself, just as the spring is fixed in its place by forces outside the machine, and not only fixed in its place, but chosen of a certain length so that it will run down after a certain time." Brownlee (1919:55) stated that, while comparing values of the life table, "it almost looks as if some kind of limit were being approached beyond which much greater improvement cannot readily be expected. It is not certain that the limit has been attained, but it is improbable that for persons over 10 years of age life will ever be much longer on the average than that exhibited in rural England at the present day." Perks (1932:29) stated that "it is not unlikely also that at the old ages there is an upper limit to the mean inability to withstand destruction."

6. In Gompertz's 1862 article he noted that elements of his formula applied to the age range 10–80, but in 1872 he made it clear that his primary formula applied to the age range 20–60. A reasonable argument could be made on the basis of the combined work of Gompertz and Makeham that the Gompertz equation was intended to apply to either the 20–60 or the 10–80 age range.

THE HISTORICAL SEARCH FOR A LAW OF MORTALITY

Early in the twentieth century, scientists began looking for biological explanations for Gompertz's law of mortality and for why increases in mortality among nonhuman species also conformed to Gompertz's law for a significant portion of their life span. Their goal was to expand upon Gompertz's effort to attribute biological significance to the life table and to extend his law of mortality to include all living things. Differences among species were assumed to be just a matter of scale—the time scale over which deaths occur being compressed for short-lived species.

One of the earliest efforts to develop a biological explanation for differences in the life spans of species was based on the research of Jacques Loeb and colleagues in the early part of the twentieth century. Loeb and Northrop (1916:456) asked the question "what is the cause of the fact that each species has a limited duration of life the magnitude of which is characteristic for the species?...If the duration of life depended upon the presence of certain substances which were used up during life; or if the duration of life were limited by the cumulative injurious effects of certain products of metabolism[7]... [then] it may be expected that there should be found a temperature coefficient for the duration of life of the order of magnitude of that of chemical reactions." These were particularly prophetic concepts given their obvious relationship to the modern view of vitality (Shock 1961) and to the free radical hypothesis of aging (Harmon 1992). Loeb and Northrop (1917a, 1917b) demonstrated for small populations of *Drosophila* living under "aseptic" conditions, that the temperature in which hatched flies were reared, as well as the availability of various kinds of food, had a significant influence on their longevity: For every 10° reduction in temperature the duration of life was approximately doubled.

Brownlee (1919) was one of the first scientists to attempt to link the basic biology of humans to major quantitative elements of the life table. He suggested that mortality attributable to senescent causes should be expressed first at about age 12, become the dominant force of total mortality by age 30, and advance at an exponential rate from ages 12 to 85. Brownlee recognized that if a law of mortality existed, it was likely to be obscured by nonsenescent mortality, and that a single Gompertz distribution did not apply to the entire life table. He further argued that the physical sciences, in particular "the theory of molecular motion of gases and the allied problems in physical chemistry" (p. 38), would yield insights into estimating the vitality of humans in terms of molecular energy.

Brownlee (p. 43) identified a formula that accurately described "the rate of decay of capacities or of substances subject to the action of organic ferments" (i.e., bacteria exposed to a disinfecting solution), which he believed produced a time dependent decay that is analogous to the loss of vital processes. He found that his formula corresponded to Makeham's adjustment of Gompertz's formula, and therefore concluded that "the substances or capacities on which life depends decay according to the law of the uni-molecular reaction, that is that the amounts present at the end of equal intervals of time can be represented by the terms of a geometrical progression" (p. 43). Brownlee found that his formula accurately portrayed the mortality experience of various human populations between ages 10 and 95, leading to his second set of conclusions: 1) "it thus becomes possible to look upon the continuance of life as dependent on the inherent energy of certain substances in the body, an energy which is gradually being destroyed throughout life" (p. 49); and 2) "that no particular life table can any longer be regarded as an isolated document referring to one time and place, but that the values of death-rates and expectations given in all life-tables must have some kind of definite relationship" (p. 47). Brownlee was one of the first scientists to bring experimental evidence to bear on the concept of biology in the life table that Gompertz originally proposed in 1825.

Brody (1924) attempted to discover a link between the duration of life and the time required to complete chemical reactions. He used Loeb and Northrop's (1917b) biochemical hypothesis to argue that chemical reactions either produced toxic substances in sufficient quantity to cause senescence and ultimately death, or led to the destruction of a substance needed to sustain life. In earlier research, Brody and colleagues demonstrated an exponential relationship between age and milk production in cows and the speed of egg production in domestic fowl—a relationship that could be characterized by the same formula used to measure the decline in the speed of a monomolecular chemical reaction with time. Brody (1924) suggested that "the course of decline of vitality with age due to the process of senescence, when not complicated by the process of growth, follows a simple exponential law; that is the degree of vitality or of senescence (defining vitality as the reciprocal of senescence) at any moment is, regardless of age, a constant percentage of the degree of vitality or senescence of the preceding moment (p. 257). It therefore appears that growth and senescence both follow the same exponential law—the law of monomolecular change in chemistry; and that the two processes are simultaneous and consecutive" (p. 248).

Another perspective on the "order of dying-out" in a population was presented by Greenwood (1928), who echoed Brownlee's (1919) view that a life table was likely to be a reflection of underlying biological processes. Greenwood (p. 271) recognized that "to an actuary, a life table is not a subject for curious speculation but a working tool, [that is] sufficient to explain why, in actuarial circles, interest in biological 'laws' of mortality is lukewarm." But Greenwood (p.268) believed it was possible to develop an "arithmetical form" (i.e., equation) that would enable researchers to understand the "biological grounds as to the intrinsic connection between age and mortality." After comparing the mortality experience of mice and human populations using a scaling method simi-

7. It is evident that this phrase was drawn directly from Gompertz's research published nearly 100 years before, but Loeb and his colleagues never mentioned Gompertz and his writings in any of their publications.

lar to Pearl's (1922) and Gompertz's formula for graduating a life table, Greenwood (1928) concluded that "we have no sound reason for thinking that the force of mortality of mice increases with age more nearly geometrically than the force of mortality in men" (p. 283), nor is there any "reason to think that any more complex formulation of a physiological law would describe the observed facts better than Gompertz's century-old simple formula" (p. 293).

Raymond Pearl was the first scientist to attempt to perform an interspecies comparison of mortality—in this case, the mortality schedules of *Drosophila* and humans. In his first paper on this topic Pearl (1921) plotted the survival curves of U.S. males in 1910 on a scale with those of the longwinged male *Drosophila,* with L_0 at 15 years for humans and 1 day for the flies. Although Pearl acknowledged the arbitrary nature of this comparison, particularly in the choice of the beginning age interval for both species, he nevertheless demonstrated a remarkable similarity in the curves. After noting that the survival curves were more favorable at older ages for humans than for the flies, Pearl (1921:502) speculated that "the *Drosophila* l_x curves represent more nearly the normal, fundamental, biological law of mortality, and that the human curve has been warped from this form as a result of those activities which may be comprised under the terms public health and sanitation." We also point out, because of its relevance to a subsequent discussion, that in this study Pearl (1921) was the first to manipulate experimentally the living conditions of his study populations to test the importance of accidental deaths on the survival curves.

In his second study Pearl (1922) refined his interspecies scaling approach by 1) identifying the beginning of the life span as the point of lowest mortality for both species (i.e., 1 day for *Drosophila* and 12 years for humans); 2) choosing the age at which there is 1 survivor out of 1,000 as the end of the life span; and 3) scaling mortality for both species by dividing the duration of time between the beginning and end of the life span into deciles. He found that approximately 97 days of a *Drosophila's* life is equivalent to 86 years in humans, and that 1 year of a human life is the same as 1.279 days of a *Drosophila's* life. Once again, Pearl found "the form of the l_x distributions is fundamentally the same...over the equivalent life spans [and] considering the extreme differences in habits of life, structure, physiology, and environmental stresses and strains in the two cases, this is a truly remarkable result" (p. 401). Unlike in his earlier study, however, in this second study he found that once life span was scaled, humans had a higher life expectancy at every age relative to the *Drosophila*—a finding he again tentatively attributed to humans' control over their environment. Pearl (1922) was so convinced from his first two interspecies comparisons of survival curves that he had discovered a fundamental biological law that he made the following statements: "the similarity [in the survival curves of humans and *Drosophila*] is even closer than was supposed from the rough comparison, and that in fact we are dealing here with qualitatively identical expressions of an obviously fundamental biological law" (p. 398); "...the factors which determine individual longevity, and differences in this character, are biologically deeply rooted, at least as fundamental, apparently, as the factors which determine the specificity in the morphogenesis of organisms, and perhaps even more so" (p. 401).

Pearl was convinced early on that his research would reveal a "fundamental biological law" of mortality for more than one species; but after two decades of research using his scaling approach on an expanded repertoire of species, Pearl and Minor (1935) emphatically declared that a universal law of mortality did not exist. They arrived at this conclusion because the death curves for the animals studied never overlapped perfectly, even after repeatedly adjusting for life span differences. In discussing their unanticipated failure, Pearl and Minor (1935) identified what Makeham (1867) had identified 68 years earlier as the main problem—the inability to partition total mortality into its intrinsic and extrinsic causes of death.[8] Whereas Makeham's development of the theory of partial forces of mortality was designed to show how Gompertz's law would apply consistently among different subgroups of the human population, Pearl and Minor declared that partitioning total mortality into its constituent elements would extend Gompertz's law to other species. Recall that Pearl attempted to eliminate the effects of external sources of mortality in his early *Drosophila* studies, but was unable to perform a similar partitioning of human mortality. The problem was that no one at the time had the data available for any species to partition confidently total mortality into its constituent elements.

The intensive search for a biological "law of mortality" as originally conceived by Gompertz essentially ended after Pearl and Miner's declaration. Since then, researchers have attempted instead to classify (Deevey 1947) or to develop alternative mathematical models (Beard 1959; Gavrilov and Gavrilova 1991; Heligman and Pollard 1980; Perks 1932; Pollard and Streatfield 1979; Pollard and Valkovics 1992; Sacher and Trucco 1962; Simms 1948; Weibull 1951) to describe better the temporal nature of the dying-out process. (For summaries of these mathematical models of mortality see Economos 1982; Gavrilov and Gavrilova 1991; Mildvan and Strehler 1960; Pollard and Streatfield 1979.)

8. Intrinsic mortality is defined as causes of death that result from 1) the expression of inherited lethal genes at any age in the lifespan; 2) the expression of disease processes arising from endogenously acquired genetic damage (e.g., metabolic free radicals); 3) traditional senescent-related diseases and disorders arising from the progressive deterioration of cells, tissues, organs, and organ systems (resulting from some combination of inherited and acquired damage); and 4) intrinsic causes of death that have been influenced—either positively or negatively—by lifestyle modification, living conditions, or medical technology. For a more detailed discussion of this issue see Carnes et al. (1996).

Intrinsic mortality differs from senescent mortality in that deaths are anticipated throughout the age structure. Under this partitioning of total mortality, intrinsic mortality is a subset of total mortality, and senescent mortality is a subset of intrinsic mortality. A more precise enumeration of intrinsic causes of death will also emerge as biomedical researchers improve their understanding of the genetic mechanisms that are either responsible for or closely linked to causes of death such as cancer and heart disease. This definition of intrinsic mortality acknowledges that humans have developed an ability to influence intrinsic disease processes.

BIODEMOGRAPHY

Biodemography represents an attempt to discover a biological pattern to the dying-out of individuals within a population (Carnes and Olshansky 1993). It is an explicit effort to answer the *when* question of intrinsic mortality; that is, it explains why death occurs when it does for individual members of a population. For example, why do deaths concentrate at about 1,000 days for most laboratory mice, at 5,000 days for most dogs, and at about 28,000 days for modern humans? Why do some individuals die shortly after birth whereas others live to ripe old ages? Why does the risk of death decline to its lowest point at sexual maturity for many species, and thereafter increase along a predictable path? Could Gompertz, Makeham, Loeb, Brody, Brownlee, Greenwood, and Pearl all have been correct in their belief in the existence of some sort of biological "law of mortality" that explains why species differ in longevity and cause of death?

The intellectual origins of biodemography date back to the pioneering work of scientists who dared to go beyond their empirical observations about patterns of mortality in order to attribute biological significance to the life table. In this sense Gompertz may be considered the father of biodemography. Most of the actuaries in Gompertz's time were content just to observe the rising risk of death following sexual maturity and to use that observation to calculate insurance annuities. After all, that was the primary function of the actuary. Gompertz had the insight to draw from this simple observation a more general concept of a "law of mortality" based on hypothesized physiological explanations for its occurrence. Makeham's explicit attempt to partition the mortality schedule into its biological and external elements was a critical development. It not only led to an improvement of Gompertz's original formula, but set the stage for an improved method of addressing the concept of a law of mortality.

In the early twentieth century, the biological significance of the life table became a central theme among researchers, many of whom were working at biological levels of organization focused on the biochemistry of senescence. Brownlee (1919), Greenwood (1928), and others (e.g., see Brody 1924; Loeb and Northrop 1917a) led the way in this effort. The interspecies comparison of patterns of mortality performed for the first time by Pearl and his colleagues (Pearl 1922; Pearl and Minor 1935) and later addressed by Deevey (1947) were more purely demographic, but represented perhaps some of the most critical early tests of the generalizability of Gompertz's law of mortality across species. Later Clark (1950:12–13) recognized the practical importance, as well as the risks, of linking the actuarial and biological sciences "that the path of co-ordinating the actuarial and medical approaches to mortality is beset with many snares cannot be denied and it is always necessary to beware that in scrutinizing the parts too closely we do not lose sight of the whole. Furthermore, absence of data may sometimes drive the investigator into realms of hypothesis. However, if such a method of approach should lead to any conclusions on ways and means in which medico-actuarial statistics might be developed so as to facilitate the forecasting of mortality, the effort will have been worth while."

As the search for natural laws governing duration of life began to wane in favor of more "practical" approaches to understanding patterns of mortality, an interesting form of biodemography emerged. Researchers attempted to evaluate the process of aging and the prospects for interspecies extrapolation of mortality risks by exploring what was thought to be a method of experimentally accelerating senescence—exposure to radiation. This was a physiologically based level of analysis representing a significant departure from the studies at lower levels of organization that preceded them. The physiologically based studies had a profound impact on the theoretical and methodological study of senescence. As might be expected, mortality data organized in life tables were used to quantify the effects of radiation exposure. Initially attempts were directed at estimating a "tolerance" or "permissible" dose in laboratory animals, principally mice (Lorenz 1950). The endpoint used for these studies was variously referred to as the mean expectation of life or the mean survival time.

As the biological effects of radiation exposure became better known, a need arose to develop a link between the actuarial measures of radiation injury and the biological consequences of radiation exposure. George Sacher (1950b:105), a pioneer in the field of gerontology and radiation biology, postulated that "radiation initiates in organisms a lethal process that is a function of the many forms of physiological injury produced." He developed an impulse injury function that, when combined with a presumed "lethal bound" of injury, led to a metric (i.e., the integral lethality function) that described a "generic mammalian radiation-injury process" (p. 105). Sacher assumed the effects of radiation to combine additively with the process of natural aging, "accelerating pathological tendencies but introducing no qualitatively new pathology" (p. 116). Under the assumption of independence, the Sacher model (1950a, 1950b) accounted for natural aging by the inclusion of a simple linear time-dependent term to the integral lethality function for radiation injury.

In a very brief passage Sacher (1950a) introduced a quantitative relationship that would reappear in the radiation literature for decades to come and that would eventually become dogma within the field of radiation biology. He began by observing that at low daily dose rates, the reciprocal difference in mean survival times for a control and for an exposed population was proportional to the intensity of exposure (measured in units of dose rate). With a little algebraic manipulation, the relationship of reciprocal survival times implies that the lethality function is an "always-increasing" function of time. Because Sacher accounted for natural aging in the model and entered the dimensions of time as only a ratio, he had provided researchers with an easily calculable statistic (later called the cumulant lethality function) to serve as "a purely empirical transformation in the investigation of the comparative lethality in different species, especially where these have widely different life expectations" (p. 40).

In 1952 Austin Brues and George Sacher formalized a linkage between the physiological processes and the actuarial response to radiation injury. They envisioned injury as a process that disrupts the normal physiological oscillations about a mean homeostatic state within an organism. They further reasoned that there must be limits (lethal boundaries) to departures from the mean homeostatic state that an organism could tolerate. Thus an animal would be expected to die when an insult was large enough to cause a pulse in the homeostatic state that crossed the lethal boundary. Brues and Sacher (1952:459) noted that this biological model of injury and failure lead directly to the "mathematicophysical formulation" Gompertz (1825) derived to describe his law of human mortality.[9]

For the remainder of the 1950s, the cumulant lethality function continued to play a dominant role in the comparative analyses of radiation lethality. Using mean survival times, Sacher estimated cumulant lethality functions to compare empirically the similarities and differences in species' responses to radiation injury within phases of the injury process (Sacher 1955, 1956a). In his formal derivation of the mathematical relationship between physiological injury and mortality (i.e., the Gompertz function), Sacher (1956b:256) felt that his model was still "far from adequate...making valid inferences about effects on man in terms of laboratory experience."

As Sacher noted (1956b:251), his procedure was the "first to account for mortality in terms of the statistical nature of physiological processes." Sacher and Trucco (1962: 989), however, also noted that "we have insufficient knowledge about the nature of the fluctuation process in real physiological systems." Poorly understood dynamics of the physiologic function include species-specific (host) factors such as distance to lethal bounds and the normal behavior of oscillations around the physiologic steady state (Sacher 1960). In addition, Sacher and Trucco (1962:989) noted that "the very fact of performing an observation introduces a disturbance that makes it impossible as a matter of principle to study the system's behavior with unlimited precision." As Sacher (1960:9) so aptly put it, "any living system, even the simplest, is a control system of a complexity and sophistication that surpasses our present ability to understand or describe."

Failla (1958) also recognized that mortality patterns conformed to the Gompertz distribution once "adulthood" was attained. He interpreted the similarity of mortality patterns adjusted for extrinsic (violent) causes of death across species (e.g., mouse, rat, and human) as evidence for a common aging process. Like Brody (1928) before him, Failla (1958:1127) defined "vitality" as the reciprocal of the age-specific mortality rate. After expressing the Gompertz function in terms of vitality, he suggested that the resulting equation described the loss of vitality from a "one hit" random process acting on the cell population of the body. The decline in the vitality curve by the end of the life span exceeded what could be attributed to a depletion in the number of cells. Failla concluded, therefore, that the vitality curve must describe a deterioration in the function of cells with age. He attributed the deterioration of function to somatic mutation, and interpreted the Gompertz aging parameter (derived from mortality data) as an estimate of the "spontaneous somatic gene mutation rate per cell per year." With some assumptions about "generation" length and the number of genes in diploid cells, Failla's (1960) calculations suggested that the mutation rate per generation was similar across species (e.g., mouse, rat, man, and *Drosophila*). If true, the somatic mutation rate per unit time must be higher in short-lived animals than in animals with longer life spans. Failla (1960:1132) concluded that "life span is determined by the inherent stability of the genetic system of a given species, which determines the spontaneous mutation rate, which in turn determines the increase in mortality rate with age (beyond middle age)."

Szilard (1959) also developed a theory on the nature of the aging process based on the concept that accumulated somatic damage interferes with the functional capability of cells. Inherited "faults" (mutations) in somatic genes whose function is critical late in the life span was viewed as the major explanation for why adults differ in length of life. While similar in concept to the Failla theory, Szilard's approach was far more extensive in transforming the theory into a quantitative form. Like Sacher's lethal bound, Szilard envisioned death occurring when the fraction of somatic cells unaffected by "hits" reached a critical threshold. Szilard developed numerical relationships that permitted the estimation of the surviving fraction of cells, the critical threshold, the number of somatic mutations, and the reduction in life expectancy per mutation. He suggested that the magnitude of life shortening following exposure to radiation should be inversely related to the square root of the number of chromosomes of a species. As such, mice and humans should experience a similar radiation-induced life shortening when expressed as a fraction of the life span.

The quantitative as well as the biological importance of the Gompertz distribution was further enhanced by the work of Bernard Strehler and Albert Mildvan. In a series of papers (Mildvan and Strehler 1960; Strehler 1959; Strehler 1960; Strehler and Mildvan 1960), these investigators presented a Gompertz-based theory of mortality and aging that, like the Sacher model, was based on disruptions of the homeostatic state of an organism. Their approach differed from that of Sacher in the functional form of the equations used to describe the disturbances of the "energetic environment" of an organism when challenged by a stress. This difference, they argued, was critical if derivative implications of the theory

9. It is useful to note that the Gompertz distribution is but one member of a larger family known as extreme value distributions (Gumbel 1954). The extreme value distributions have played an important role in reliability analysis within engineering as well as within the biomedical sciences (Lawless 1982). They typically are employed to describe the failure times of systems that cease to function whenever the weakest (and hence extreme) component of the system fails. In the context of the Brues and Sacher model, the organism dies whenever the homeostatic control of a critical physiological process fails because of an injury process initiated by a radiation insult.

concerning issues such as the predicted loss of physiologic function with time and the quantitative relationship between the two parameters of the Gompertz distribution, were to conform with "observation or natural law."

Strehler (1959) also made several important observations on the biological effects of radiation compared to the effects of aging. He noted that (1) aging effects are typically associated with post-mitotic cells whereas radiation primarily affects dividing cells; (2) radiation damage is primarily genetic whereas the effects of aging appear to be more broad spectrum; (3) some species (e.g., *Drosophila*) do not exhibit life shortening even after large doses of radiation; and 4) the dose required to double the mortality rate (i.e., Gompertz slope) produces a much larger increase in the mutation rate. Based on these observations, Strehler (1959:138) rejected the notion that radiation acts through "a general acceleration of the normal aging process."

Investigations of radiation effects continued to make extensive use of the Gompertz distribution throughout the 1960s (Berlin 1960; Sacher 1966; Sacher and Grahn 1964). Some of the popularity of the Gompertz distribution was due to computational convenience. Linearity of the hazard function on a logarithmic scale made least squares estimates of the Gompertz parameters easy to calculate. Like Greenwood (1928) before him, Grahn (1970) proposed using the ratio of Gompertz slopes to adjust for life span differences when making mortality comparisons between species. Grahn successfully used this scaling approach to predict reductions in human life expectancy following radiation exposure from dose response relationships observed in mice.

At first glance, there appears to be a discrepancy between Pearl's conclusion that a fundamental law of mortality does not exist and the reasonable success of interspecies extrapolation efforts within the field of radiation biology. The paradox is resolved when the environmental conditions of the animals being compared are considered. Pearl's studies and the work of the ecologists (e.g., Deevey 1947) who followed him were based on the comparison of species that experienced dramatically different levels of intercurrent (i.e., exogenous) mortality. The laboratory animals used in radiation studies, on the other hand, benefitted from husbandry practices that included highly controlled environments where predation was eliminated and the effects of infectious diseases were minimized. These environmental conditions are far more similar to the sheltered environment and medical attention received by humans than to that experienced by natural populations of animals.

Another element of biodemography emerged recently with the development of medical demography or population epidemiology (see Manton et al. 1985; Manton, Patrick, and Stallard 1980; Manton and Soldo 1985). Although this line of research has not focused on the two central historical themes of biodemography—the biology of the life table and the search for a law of mortality—it is a unique and valuable effort at attempting to understand the complex relationship between risk factor modification and population trends in death rates. These are useful concepts for biodemography because they contribute to an understanding of reasons why interspecies comparisons of senescent death rates are difficult to perform.

The modern development of biodemography originated with a series of articles published by Weiss and colleagues (e.g., see Connor, Weiss, and Weeks 1993; Weiss 1989; Weiss 1990; Weiss, Ferrell, and Hanis 1984). According to Weiss (1990:186) "a great deal has been learned in the past 20 years about genetically based heterogeneity in regard to the major determinants of survivorship in industrial nations. Yet demographers and geneticists seem to be relatively unaware of each other's work. Partly, this may be because even though causal genetic variants themselves can be identified, most work in genetic epidemiology has been concerned with the effects of such variants on overall susceptibility rather than on the hazard function itself." Weiss recognized that the field of genetic epidemiology could provide insights into the biological constraints influencing the shape of the hazard function in populations as well as to unobserved heterogeneity hypothesized by demographers (Manton, Stallard, and Vaupel 1981; Vaupel, Manton, and Stallard 1979). According to Weiss (1990:198) "if genes ultimately affect how variation in the hazard function is distributed in the population, human physiology and its genetic basis affect how pathology develops with age and hence the shape of the hazard function itself." Weiss's merging of the fields of demography and genetics and his subsequent elaboration using principles of evolutionary biology served as a launching point for the latest developments in the field of biodemography.

The latest work in this area brings the two basic questions of biodemography back into the central theme of research and makes more extensive use of theoretical developments from the field of evolutionary biology. Because details of these developments in biodemography may be found in the literature (Carnes and Olshansky 1993; Carnes, Olshansky, and Grahn 1996; Olshansky and Carnes 1994), a condensed summary of this line of reasoning follows.

Evolutionary biologists have been working for over a century on the question of why senescence occurs. The most basic question to ask is why organisms senesce: Why is immortality an unattainable goal for individuals? The answer begins with Weismann's (1891) observation that causes of death extrinsic to the basic biology of the organism are, and probably always have been, ubiquitous and unavoidable. For most species, even if senescence did not exist, survival beyond the age of reproduction is an extremely rare event with most deaths for a cohort occurring just after birth. At these ages the vast majority of deaths result from forces of mortality that are unrelated to senescence (e.g., hostile environments where predation or infectious and parasitic diseases prevail).

In hostile environments, where death almost invariably precedes senescence, early reproduction (relative to potential life span) has become an essential element in species' reproductive strategies (Stearns 1992). Consistent patterns of growth and development observed within species suggests

that the reproductive biology of organisms alive today represents a genetic legacy of responses to environmental conditions that prevailed during the early evolutionary history of each species.

The argument that selection alters the genetic composition of a population through the differential reproductive success of individuals is a basic tenet of modern evolutionary biology. According to Medawar (1952) and Williams (1957), opportunities for selection to alter gene frequencies should be greatest before individuals begin reproduction, diminish as the cumulative reproductive potential of individuals is achieved, and become weak or nonexistent once reproduction has ceased. This age-based gradient for the effectiveness of selection permits the potential life span of organisms to be partitioned into biologically meaningful time periods: the prereproductive, reproductive, and postreproductive periods.[10]

The modern evolutionary theory of senescence is based on the premise that selection is effective in altering gene frequencies until the time before the end of the reproductive period. When the normally high force of external mortality is controlled and survival beyond the end of the reproductive period becomes a common occurrence, senescence and senescent-related diseases and disorders have the opportunity to be expressed. The full array of potential senescent processes, their consequences, and the mortality schedule for intrinsic deaths (i.e., the intrinsic mortality signature) can be revealed only under the "unnatural" condition of survival beyond the age of sexual maturity (Medawar 1952) by a significant proportion of a birth cohort. This rarely happens for animals living in the wild because death almost always precedes senescence. For species living under controlled living conditions where extrinsic causes of death are dramatically reduced (e.g., humans, household pets, and zoo and laboratory animals), however, we have argued that a species' intrinsic mortality signature should become visible for the first time (Carnes et al. 1996). Because there are common forces (i.e., extrinsic mortality) responsible for molding species' reproductive strategies, a common pattern of intrinsic mortality—an evolutionary imprint—may become visible when species are compared on a biologically comparable time scale.

If gene expression, whether favorable or deleterious, in the postreproductive period is beyond the reach of natural selection, then a genetic basis for either immortality or senescence resulting from the direct action of selection should not be possible. Instead, senescent-related diseases and disorders observed in organisms not molded by selection for extended survival (beyond the genetically defined reproductive period) may be an inadvertent consequence of selection operating uniformly on reproduction (Hamilton 1966). As a consequence, investments in the biochemical machinery necessary to maintain the integrity of the organism should diminish as the reproductive potential of the individual is achieved.

We have argued that the logic used to link natural selection and reproduction, and reproduction and senescence for individuals, has a direct bearing on *when* intrinsic mortality should occur in a population (Carnes et al. 1996; Carnes and Olshansky 1993). Our logic is as follows: The timing of genetically determined processes such as growth and development are driven by a reproductive biology, molded by the necessity for early reproduction, which in turn is driven by the normally high external force of mortality. If individual senescence is an inadvertent consequence of these developmental processes as predicted from the evolutionary theory of senescence, then *age patterns of intrinsic mortality* in a population should also be calibrated to some element(s) of a species' reproductive biology. As previously indicated, several researchers (Makeham 1867; Medawar 1952; Pearl and Minor 1935; Weismann 1891) have already recognized the important role played by the force of external (i.e., nonsenescent) causes of death, but the problem has been partitioning total mortality into its constituent elements so that only intrinsic mortality could be observed. This has been the focus of our first empirical test of a prediction from the biodemographic paradigm of mortality (Carnes et al. 1996).

Thus the common age pattern of mortality first noticed for humans by Gompertz in 1825 and subsequently identified for other organisms throughout the twentieth century, makes logical sense when the evolutionary theory of senescence is extended from individuals to populations. Evolutionary biologists have not attempted to explain mortality patterns for populations because they have focused almost exclusively at the individual level. By the same token, researchers who tried to find empirical evidence for a law of mortality were operating without knowledge of the evolutionary theories of senescence that were being developed during the past 100 years, and did not have the data that would permit the partitioning of total mortality into its constituent elements. It is only when these two bodies of literature are brought together that it becomes possible to understand how the ideas and concepts from one discipline may be used to explain the common age patterns of mortality observed across species.

We have suggested (Carnes et al. 1996) that: 1) there are common age patterns of mortality across species as long as the causes of death considered are restricted to those having a biological origin (just as Pearl predicted in 1922); and 2) a plausible biological mechanism that would lead to common age patterns of intrinsic mortality across species becomes evident when the evolutionary theory of senescence is extended from individuals to populations. In short, we have provided empirical evidence supporting Gompertz's argument that a law of mortality exists, and that there is a biologically based explanation for its existence.[11] There are

10. For this discussion, the reproductive period includes the production and nurturing of offspring and, for some species, a grandparenting period during which parents contribute to the reproductive success of their offspring.

11. It should be emphasized that we did not attempt to quantify the law of mortality itself; we simply tested for its existence. Whether it is the Gompertz equation or some other empirical tool that mathematically de-

many more biodemographic questions, however, that demographers, actuaries, and mathematicians are particularly well equipped to answer (e.g., see hypotheses and predictions in Carnes et al. 1996; Carnes and Olshansky 1993; Olshansky and Carnes 1994).

NON-GOMPERTZIAN MORTALITY AT OLDER AGES

As previously noted, both Gompertz and Makeham recognized that the original Gompertz equation did not apply to the entire age range. In fact, Gompertz (1872) suggested in his last paper that there are four distinct periods in the life span between which separate laws of mortality apply: birth to 12 months, 12 months to 20 years, 20 years to 60 years, and 60 years to 100 years. The Gompertz equation was intended from its inception to apply only to a limited age range for humans—between the ages of 20 and 60 (Gompertz 1872). Even within this age range he recognized that his formula worked best "provided the intervals be not greater than certain limits" (Gompertz 1825:514).

The observation that the Gompertz equation does not apply to humans and other animals during later portions of the life span has been a persistent theme throughout the historical literature on senescence and the search for a law of mortality. For example, Makeham (1867:346) argued that even after he used his "partial forces of mortality" to characterize mortality schedules, the rapidity of the increase in the death rate decelerated beyond age 75. Similarly, Brownlee (1919:47) suggested that the Gompertz equation does not apply equally throughout the age range; "the graduation is made in two sections, one section from the age of 15 to the age of 50, the second beginning at the latter age and extending upwards to the end of life." Brownlee (1919:58) also asked "Is it possible that a kind of Indian summer occurs after the age of 85 years is passed, and that conditions improve as regards length of life on the grounds either of greater care being taken, or that the second childhood relieves nervous strain and thus permits some recuperative effect?"

In Perks' (1932) development of the logistic equation to improve the graduation of death rates at older ages, he recognized that "the ungraduated rates and the rates by adopted graduation show a curious peak in the rate of increase in q_x round about age 80...it is thought that the sharpness of this peak may be due in some way to an element of neglected selection which would naturally rapidly wear itself away at about age 80..." (p. 15). He further stated that "the graduated curve [of mortality] starts to decline in the neighborhood of age 84" (p. 30). In Beard's (1959) discussion of mathematical mortality models, he recognized that "what evidence is available tends to support the idea that the force of mortality does not continue to increase indefinitely with age" (p. 303). Strehler (1960:311) argued that one of the four distinct phases of the human mortality curve was "a period of departure from the Gompertzian relationship at great ages so that mortality rises more slowly than anticipated after age 85–90." He argued that this phenomenon would occur "when the vitality has decreased to the point where it is similar to the average energy of fluctuations" (p. 314) about a homeostatic mean. One of Mildvan and Strehler's (1960) "observations that any mathematical theory of mortality must incorporate into its postulatory structure, explain, or at least not violate" (p. 217) included the fact that "at extremely advanced age, the mortality rate curves of several species rise at a rate progressively lower than exponential" (p. 224).

The limited applicability of the Gompertz function to only a specified range within the life span and a deceleration in death rates at older ages (including possible explanations for this phenomenon) have been recognized by many other researchers (e.g., see Abernathy 1979; Brooks, Lithgow, and Johnson 1994; Doubal 1982; Economos 1980; Gavrilov and Gavrilova 1991; Horiuchi and Coale 1990; Horiuchi and Wilmoth 1996; Pakin and Hrisanov 1984; Riggs 1993; Weiss 1989; Witten 1988).

Based on lack of fit at older ages, there has been a repeated historical recognition (beginning with Gompertz himself) that a single Gompertz equation does not adequately describe mortality for humans or for other animals over the entire life span. It is particularly surprising, therefore, that some researchers reject the entire Gompertz paradigm after finding that it does not apply to older ages for some organisms. For example, Carey et al. (1992) found that death rates for older medflies leveled off; therefore they concluded that "another concept that is not consistent with our data is that the basic pattern of mortality at adult ages in nearly all species follows the same unitary pattern described by the Gompertz model (exponential increase). The finding that medfly age-specific mortality is not described by this model at old ages provides direct empirical evidence that Gompertz's law does not hold in all populations" (p. 460). Fukui, Xiu, and Curtsinger (1993) found a leveling off of old-age mortality among a large population of *Drosophila*, leading them to conclude that "contrary to the predictions of the Gompertz model, mortality rates tend to decelerate at the most advanced ages" (p. 585). In describing the results of the original fruit fly studies, Barinaga (1992:398) stated that "until now, most researchers have talked about mortality largely in terms of the 'Gompertz law,' proposed by British actuary Benjamin Gompertz in 1825, which holds that mortality rates increase exponentially with age. If it is true, the Gompertz law implies that for any species the death rate will climb dramatically in very old age, effectively capping the life span." Perls (1995) reached a similar misconception about the age range to which the Gompertz equation applies in his description of a sample of "healthy" centenarians.

With regard to the presence of non-Gompertzian mortality in certain regions of the life span, the facts are that: (1) Gompertz never predicted exponentially rising death rates at

scribes age patterns of mortality across species is of less interest to us. This question should be addressed by mathematical demographers and actuaries who are adept at fitting equations to observed distributions of death. In fact, it may very well be the case that some other formula characterizes the dying-out process and the law of mortality better than does the Gompertz equation. The law of mortality as we define it is a common pattern to the dying-out process for many species between sexual maturity and extreme old age, and a biological explanation for why these patterns exist.

older or younger ages for humans or any other species; (2) death rates for many species (including humans) rise exponentially with age for a significant portion of their life span (e.g., see Finch 1990; Finch, Pike, and Witten 1990), just as Gompertz and Pearl predicted; and (3) there are exceptions to exponentially rising death rates in the postmaturational phase of life for some species (Finch 1990).

CONCLUSION

Ever since Gompertz, scientists have had a heightened interest in explaining why death occurs, what biological forces might be involved, and why death occurs along a predictable path for many species between sexual maturity and old age. The Gompertz equation was developed exclusively for humans both as an empirical tool to describe the age pattern of death from all causes during a limited time frame (principally between ages 20 and 60), and as representing a law of mortality that arises from inherent biological processes. Gompertz never extended his ideas to other species, nor was he able to elaborate on the biological mechanisms he thought might be involved. Within 100 years of Gompertz's original article, his law of mortality had been refined by Makeham to a limited set of causes of death, extended by Pearl to other species, and examined by Loeb and Northrop and others with regard to its biological origins. Since the early twentieth century, numerous statistical distributions have been shown to characterize reliably the age pattern of the dying-out process (e.g., Gamma, Logistic, and Weibull). Nevertheless, a long history of empirical utility has made the Gompertz distribution one of the major quantitative tools used in the analysis of failure times for living organisms as well as for mechanical devices.

Although the mortality distribution of many species follow the Gompertz or Gompertz/Makeham distributions for a significant portion of their life spans, the mortality schedules of different species (based on total mortality) do not overlap when observed on a comparable time scale—a finding originally attributed to Pearl. In addition, biological explanations for the Gompertzian rise in death rates following sexual maturity were initially problematic, principally because it was difficult to explain how an exponential rise in death rates would follow from linear declines in physiological functioning. Various studies have addressed the experimental (Simms 1948) and theoretical (Economos 1982; Strehler 1960, 1977) aspects of this problem.

Evolutionary biologists (Charlesworth 1994; Kirkwood 1977; Medawar 1952; Weismann 1891; Williams 1957) have addressed the reason why aging or senescence occurs at all, but they have focused on gene selection and expression within individuals—not on age patterns of death within and across populations. A biodemographic approach represents an attempt to use biological arguments to investigate demographic phenomena: For example, why do death rates increase exponentially following sexual maturity, and why might common age patterns of death be expected among species? Biodemography offers an excellent opportunity for demographers involved in research on aging to test hypotheses about human mortality that are derived from theoretical and empirical research in the biological sciences (Carnes et al. 1996; Olshansky and Carnes 1994; Weiss 1990). Although the merging of the fields of demography and biology has been ongoing for years with regard to research on fertility, the application of biology to demographic models of human mortality has been limited.

Finally, it is interesting that Gompertz proposed his ideas at a time when religion was particularly influential—a factor that undoubtedly had an impact on his writing. For example, based on his belief in a biological force responsible for the patterns of death he observed, Gompertz concluded that it was highly improbable that humans could live much beyond the observed limits of his time (which was at or near 100 years of age). He then equivocated on this point, however, by suggesting that nothing could contradict the purported ages of patriarchs reported in the Bible. Thus it appears that Gompertz tried to appease the religious patriarchs while speculating on biological forces that were operating to limit the longevity of humans.

A similar kind of resistance prevails today regarding the concept of a law of mortality, probably because a law invokes images of bounds and limitations. Today, however, resistance follows from a public health paradigm predicated on the belief that human diseases have modifiable risk factors that, once modified, can lead to their total elimination. Resistance to the limitations implied by a law of mortality is easily understood. Humans have altered their environments and lifestyles to such an extent that extrinsic causes of death have been reduced dramatically. Almost everyone now has an opportunity to live to his or her biological potential—something that only humans and a few of the animals they manage (zoo animals, household pets, and animals raised under laboratory conditions) have achieved (Carnes et al. 1996). What is being revealed by human intervention is a more "pure" biologically influenced mortality schedule for these species (as Makeham had attempted with his partitioning of total mortality and as Pearl suggested would be the case).

In addition, a greater understanding of biological processes (knowledge unavailable to Gompertz) has permitted the expression of intrinsic diseases (i.e., age at death and/or morbidity) to be modified, thereby, altering the survival trajectories of individuals whose intrinsic diseases have already been expressed. The expression of intrinsic mortality has been influenced by: 1) lifestyle modifications such as diet and exercise; 2) the introduction of pharmaceuticals to postpone the onset of intrinsic disorders (e.g., medication for hypertension or the introduction of insulin for diabetics); and 3) medical interventions such as life extending technologies (e.g., dialysis, heart-lung machines), surgical procedures (e.g., coronary bypass surgery, organ transplants), and treatment protocols (e.g., chemotherapy and radiation therapy for cancers).

Successful modifications to the expression of intrinsic disease processes have led many to believe that continued progress can be made in improving life expectancy, particularly at older ages. When extended, this perspective suggests that there is no "biological" limit to life because there is no

limit in the development of new and effective life-extending technologies. On the other hand, the emergence of new strains of bacteria, viruses, and parasites and the reemergence of more virulent strains of infectious diseases such as tuberculosis and meningitis suggest that modern advances in public health can have both positive and negative effects on human longevity (e.g., see Lederberg, Shope, and Oaks 1992; Olshansky et al. forthcoming; Patz et al. 1996; Pinner et al. 1996; Wilson, Levins, and Spielman 1994). In any case, this public health paradigm has created an unprecedented new set of "biological" conditions such that the age- and cause-specific mortality schedules of modern humans bear little resemblance even to human populations of just 20–30 years ago.

We have suggested that there is a biologically based mortality schedule for a species—one that would be revealed under living conditions where external sources of mortality are greatly reduced and conditions (e.g., diet and exercise) are favorable for living to one's biological potential. From this perspective, the biological life span of a species, containing individuals of varying endowments for longevity, is one based on a mortality schedule that would prevail in the absence of medical intervention of any kind—a view consistent with that of Raymond Pearl. A life that is extended by having survival time "manufactured" by pharmaceuticals or medical technology does not permit survival only up to one's biological potential: In some cases it may permit individuals to survive beyond their life span. When enough members of a population benefit from these medical interventions, it is possible that the life span of the population will exceed its biologically based limits.

The reduction of extrinsic mortality in the twentieth century has revealed a more "pure" intrinsic mortality schedule for humans, a phenomenon comparable to that observed for a few other species protected by humans from external causes of death. It is interesting to note that some species that exist in the wild—including elephants, whales, and some species of birds and turtles (Finch 1990)—also have very low extrinsic sources of mortality. Species known to have low rates of extrinsic mortality also have longer life spans than do related species, and often have delayed and prolonged reproductive schedules. These findings are consistent with predictions from the modern perspective on biodemography (Carnes et al. 1996).

A biological basis for a common pattern of intrinsic mortality has been put forth within the conceptual framework of biodemography. The basic argument is as follows:

(1) Extrinsic mortality creates a need for early reproduction relative to potential life span.
(2) Age of sexual maturity determines genetically controlled patterns of growth and development.
(3) Differential survival and reproductive success occurs within the reproductive period (i.e., a gradient for the effectiveness of natural selection).
(4) The selection gradient provides a mechanism (i.e., gene expression) that influences why intrinsic mortality occurs when it does for individuals.
(5) Genetic differences between individuals lead to an age distribution for intrinsic mortality within a population (i.e., an intrinsic mortality signature).
(6) A common set of evolutionary forces (points 1–5) acting on species suggests that differences in their intrinsic mortality signatures may be simply a matter of time scale.

In 1825 Gompertz noticed that common age patterns of mortality existed among subgroups of the human population, and speculated that these patterns arise from an underlying biological force. Ever since Gompertz, scientists from a variety of disciplines have (1) suggested that species other than humans share common age patterns of death, (2) revealed biological mechanisms associated with senescence, and (3) developed a variety of quantitative tools for describing patterns of death. A biodemographic analysis of mortality suggests that Gompertz was right all along: There are biological reasons for why death occurs when it does, and a law of mortality may very well exist that applies to many species—not just to humans. Where the limits implied by a law of mortality are for humans and the degree to which these limits can be manipulated and controlled certainly will be a subject of great interest and debate in the coming years.

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