Life Span in the Light of Avian Life Histories

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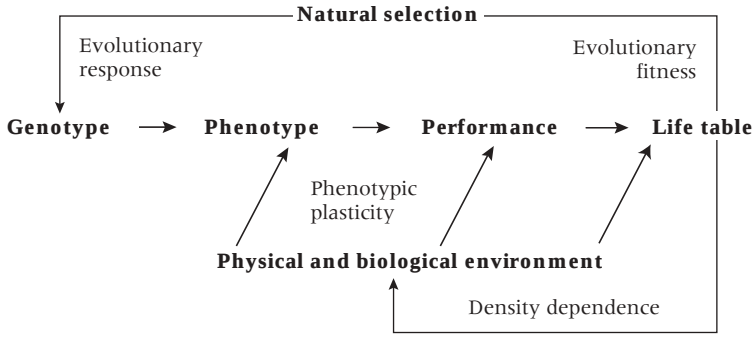
Our purpose is to consider the comparative study of aging in natural and captive populations as a potential source of insight into the future of human aging. In conducting this assessment in the context of life-history comparisons, we consider only birds and mammals to restrict our analyses to organisms whose physiology is similar to that of humans. We show that the basic evolutionary theory of aging is well supported, and we explore variation in aging among species to characterize its relationship to factors in the environment and to other aspects of the life histories of organisms. Finally, we draw some inferences from comparative studies about possibilities for changes in human aging in the future.

The life history of an individual consists of a set of optimized tradeoffs related to its allocation of time, energy, materials, and body components to different functions (Roff 1992, 2002; Stearns 1992). Individuals have limited resources at their disposal, and resources devoted to one function cannot be used for another. The allocation of resources among functions can be mapped onto evolutionary fitness (Figure 1). This mapping occurs through the interaction of the genotype with the environment to determine survival and reproductive success at each age, which are summarized in a life table. Fitness can be defined retrospectively for an individual as the number of descendants it leaves in future generations. Fitness can be estimated prospectively from the life table entries, as we see below. Evolutionary fitness ties particular genotypes to variation in reproductive success. Variation in evolutionary fitness within a population is the basis for evolutionary response to the environment. We presume that the pattern of aging of an individual is in part genetically controlled and influences individual fitness, and that allocation of resources to extend potential life span reduces other aspects of the individual's performance and thus also affects its fitness. These relationships represent a tradeoff that defines the range of possible form and function of individuals—the phe-

FIGURE 1 The connection between the genotype and the life table involves several steps with progressively increasing environmental influence; variation in the reproductive success of different genotypes shapes the gene pool of the population through natural selection and evolutionary response, thereby closing the circle of adaptation; the life table expression of the genotype may also be influenced by density-dependent feedbacks on the conditions and resources of the environment

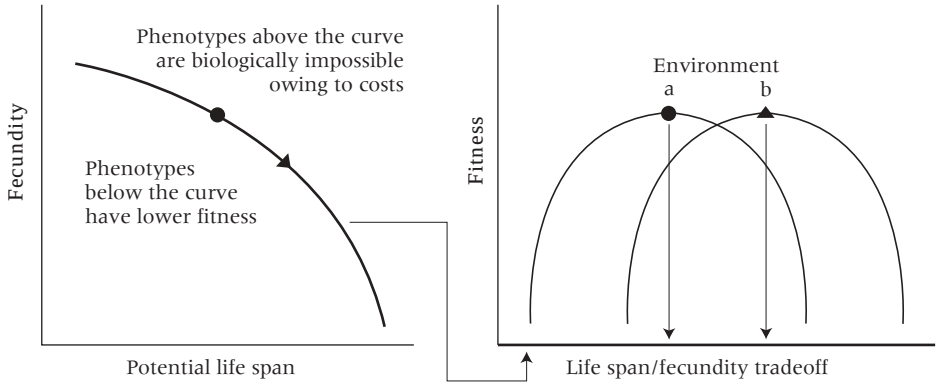


SOURCE: After Arnold (1983); Ricklefs (1991, 2000a).

notype. Every point along this tradeoff continuum may be represented by a fitness value (Figure 2).

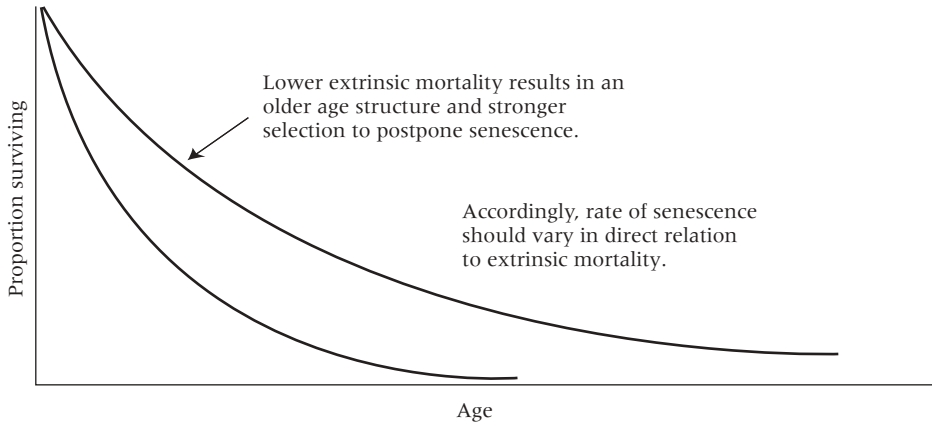
We presume that evolution maximizes fitness and that any particular value of a tradeoff is selected according to its contribution to evolutionary fitness, as shown in Figure 2. A population's demography, as defined by the life table, may influence the optimum value of a tradeoff between fecundity and survival at different ages. With respect to aging, the fitness contribution of a life-history trait that extends life depends on the proportion of the population that lives long enough to experience the trait, as well as its reproductive success after that point (Abrams 1991, 1993). Thus, where individuals survive at a high rate through most of their lives, many achieve old age and the fitness value of extending life further is relatively high. Of course, this applies only when older individuals produce offspring or contribute post-reproductively to the survival and reproductive success of their own offspring (individual fitness: Hawkes et al. 1998; Alvarez 2000) or those of close relatives (inclusive fitness: Alexander 1974). Where individuals rarely survive through young adulthood, few reach old age and the fitness value of extended life span is small (Figure 3). Thus, selection to extend life span is strong in populations with high survival. Accordingly, the central prediction of evolutionary theory is that the rate of aging should be directly related to the mortality rate of adults from causes unrelated to aging (Edney and Gill 1968; Hamilton 1966; Medawar 1952; Williams 1957). As we see below, this prediction is supported by comparisons of the rate of increase in

FIGURE 2 The constrained relationship, for example between fecundity and potential life span (left), is optimized by maximizing fitness; each point along the constraint curve is a potential phenotype; the fitness value of phenotypes may vary between environments, leading to different optimized points



aging-related mortality in natural populations. If senescence could be postponed without cost, potential life span would evolve to be infinite because fitness increases with increasing life span, all else being equal. That life span is finite shows that the evolutionary modification of life span is constrained.

FIGURE 3 Lower extrinsic mortality results in more individuals surviving to old age and therefore potentially greater strength of selection on traits that influence fitness through contributions to fecundity or further survival at old age



Mechanisms and tradeoffs in aging

The mechanisms of senescence are thought to include (1) wear and tear induced by the environment and by life activity itself, (2) accumulation of deleterious mutations with delayed onset of expression, or at least delayed onset of their influence on survival and reproductive success, and (3) pleiotropic genes that have beneficial effects early in life and deleterious effects at older ages. The means that organisms employ to postpone senescence are not well understood, but certainly include mechanisms that prevent and repair damage (Finkel and Holbrook 2000; Perez-Campo et al. 1998; Promislow 1994). These mechanisms may impose energetic or other costs, which would lead to tradeoffs between modification of senescence and other life-history traits that affect fitness in opposite ways.

Constrained relationships, such as the one shown in Figure 2, may embody mechanisms controlling the rate of senescence. As yet, we have little insight into the nature of such constrained relationships. George Williams (1957) introduced a general term, "antagonistic pleiotropy," to describe constrained relationships, and this has been elaborated by Michael Rose (1991) and others. Antagonistic pleiotropy implies a genetic link between two functions or aspects of performance having contrasting effects on evolutionary fitness (e.g., Weinstein and Ciszek 2002). Originally, antagonistic pleiotropy was thought to result from genes whose expression extended life span but also reduced early reproductive success. Relatively few such genes have been identified (Caruso et al. 2000; Ricklefs and Finch 1995; Rose 1991; Silbermann and Tatar 2000; Stearns and Partridge 2000), but antagonistic pleiotropy also can arise by way of functional rather than genetic connections (Ricklefs 2000a). For example, if aging resulted from wear and tear, mechanisms that prevented or repaired damage might prolong life span at a cost of resources allocated to reproduction, even though the deterioration associated with aging itself did not have a direct genetic cause (Kirkwood 1990; Kirkwood and Holliday 1979). This idea, known as the disposable soma theory, implies that the body (soma) is maintained only for the purpose of propagating the germ line.

One of the ways in which biologists have searched for insights into tradeoffs between life-history traits is to look for correlations between variables among species (e.g., Sacher 1959). This approach presupposes that the relationships between life-history variables observed among species in some way reflect the constrained relationships that pertain to tradeoffs within a species. Because the purpose of comparative analyses is to gain insight into the ways that aging mechanisms might be modified to prolong life span, it is important to tie comparisons to particular explanations by making predictions that are unique to each hypothesis. For example, any explanation relating prolonged life span to mechanisms that also extend development

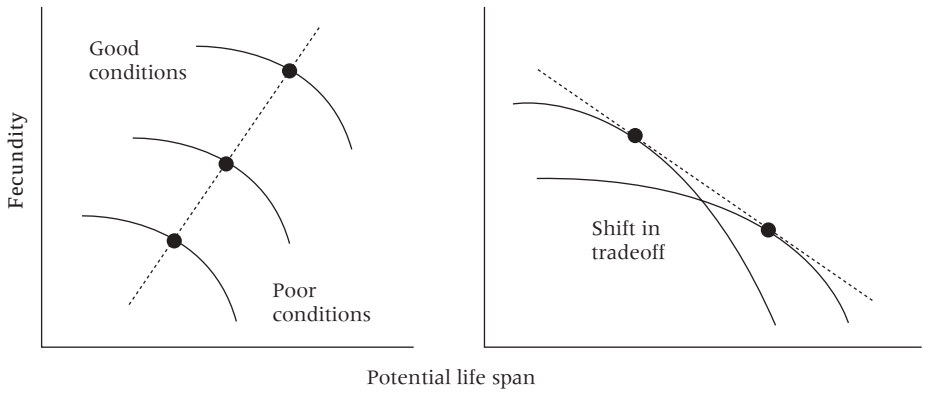
could be rejected by failing to find a relationship between life span and development periods. Unfortunately, this approach has several difficulties.

First, correlations may arise fortuitously among interrelated variables. The life history encompasses many fundamental tradeoffs that are interconnected in some way through functional relationships within the organism or through various environmental feedbacks in the population, such as density dependence (Figure 1; Ricklefs 2000a). Thus, correlations between variables do not necessarily imply causal or evolved relationships.

Second, variation among species need not parallel variation within populations (i.e., tradeoffs expressed among alternative phenotypes). The reason for this is that the tradeoff relationship, such as shown in Figure 2, may vary among populations owing to differences in body plan or life style or to differences in environmental influences on life-history traits. Thus, for example, one may observe a positive correlation between life span and fecundity among species over a gradient of habitat productivity from generally stressful to generally favorable conditions, whereas the tradeoff between these traits within a population (thus holding environment constant) might be negative (Figure 4).

Finally, a particular theory might make multiple predictions and therefore be consistent with a wide range of observations or experimental results. For example, in a population with senescence, selection favors increased reproductive investment toward the end of life. The argument is that if an individual has a low probability of surviving to reproduce in the future, it may as

FIGURE 4 The relationship between optimized traits among populations may not parallel variation among phenotypes within populations; at left, under better conditions, both constrained traits have higher values; at right, the optimized traits are consistent with constraint but in fact represent shifts in the constraint functions rather than different optimization points on the same constraint function



well increase investment in the present in spite of increasing its risk of death. As a result, reproductive success toward the end of life might actually increase owing to a response to selection rather than decrease as a result of physiological deterioration. Thus, a simple correlation between reproductive success and longevity might be uninformative or even misleading.

As we search for insights among patterns of correlation between life-history traits, we must be aware of several potential limitations of the approach and, in particular, we must not view correlations as confirming a functional relationship at the organismic level. In general, comparative studies are most useful when a hypothesis based on functional relationships predicts a pattern of correlation that we can either confirm or reject.

Comparative studies

The most general prediction of life-history theory concerning aging is that the "rate" of senescence should vary in direct relation to the age-independent risk of mortality (Charlesworth 1994; Edney and Gill 1968). This prediction arises because the strength of selection on factors that prolong life span varies in direct relation to the proportion of individuals who survive to old age. Theories of aging involving the optimization of tradeoffs also predict an inverse relationship between life span and reproductive success or survival rate. This points up a difficulty with comparative approaches. We have already seen that life span should be positively correlated with survival of young adults, but a tradeoff between early and late survival would predict the opposite relationship. The inconsistency arises because extrinsic factors, for example predation and accidental death, contribute to variation in survival rate independently of mechanisms that influence the rate of aging.

Empirical patterns among species suggest pervasive relationships between maximum life span, reproductive rate, body size or a particular aspect of body size, and development rate (Austad 1997; Calder 1983, 1984). These relationships may reflect allometric physiological connections, perhaps mediated through growth and metabolism, or they may reflect shifts in optimization related to the different demographic environments experienced by large and small species (Ricklefs 2000a). When body size is removed from such analyses by considering residuals from regressions against body size, life histories of organisms still appear to be organized on a single fast–slow continuum interrelating variation in life span, development period, metabolism, and reproductive rate (Bennett and Harvey 1985, 1987; Calder 1984; Promislow and Harvey 1990; Ricklefs 2000a; Sæther 1988).

Tests of the fundamental evolutionary prediction of aging models, that the rate of aging should be positively related to the rate of mortality of young adults, have met with varying success. Austad (1993) demonstrated a correlation between both physiological and demographic indexes of rate of aging and extrinsic mortality in insular and continental populations of the

opossum *Didelphis virginianus*. Other studies have found that the rate of aging is lower where individuals are protected from external mortality factors (e.g., Dudycha 2001; Keller and Genoud 1997). These studies suggest the possibility that life span may evolve in response to variation in the environment, and that life span and the rate of aging might be phenotypically flexible as well. In general, short life span is associated with high mortality rates of young adults, as predicted. For example, under protected conditions in captivity, mice and ungulates, which suffer severe mortality in nature, never achieve the longevity of primates or, for that matter, most birds. Promislow (1991) attempted to place this observation on a quantitative footing by estimating the rate of aging by the rate parameter γ of the Gompertz aging model. However, he failed to find a relationship between γ and the minimum rate of mortality among adults. Ricklefs (1998) characterized the rate of aging by an index ω derived from the age-dependent mortality term of the Weibull aging model and found a positive relationship between ω and the estimated mortality rate of young adults among many species of birds and mammals. In this case, different ways of quantifying the rate of aging produced contradictory results. Therefore, it is clear that we need to consider how aging is measured demographically and how to interpret these measures in light of the questions that we have posed.

Methodological considerations

Quantifying aging

Our first task is to define what we mean by the rate of aging. We restrict ourselves to demographic measures of aging, sometimes referred to as actuarial senescence (Holmes and Austad 1995b). We assume that there is a general correlation between actuarial senescence and physiological decline in function. Most models of aging-related death relate increased vulnerability to disease, accidental death, and other causes to deteriorating physiological condition (e.g., Strehler and Mildvan 1960).

The most commonly used measure of the rate of aging is the maximum reported life span. This measure has the potential disadvantage of being determined to some degree by the age-independent rate of mortality and the number of individuals sampled. When the mortality rate does not increase with age and individuals potentially are immortal, a sample of individual ages at death will nonetheless have a maximum value, which would be the maximum reported life span. Moreover, errors in reporting introduce considerable variation in estimated life span (Carey and Judge 2000). However, when aging does occur and the mortality rate rises rapidly with increasing age, maximum reported life span may reasonably parallel the rate of aging in an underlying model of the increase in mortality with age (Finch 1990; Scheuerlein and Ricklefs unpubl.).

Botkin and Miller (1974) used maximum reported life span to infer that birds actually expressed the effects of aging in natural populations. Previously, it was thought that natural (extrinsic) mortality of birds was so high that few individuals reached "old age" (Lack 1954; Medawar 1952). This was supported by the observation from band return studies of natural populations that the adult mortality rate did not decline with increasing age. Botkin and Miller showed that a non-aging model of reported life span, assuming a constant exponential decline in survivorship with age, substantially overestimated maximum longevity. From this discrepancy, Botkin and Miller inferred that an increasing mortality rate with age must be responsible for the difference (see also Curio 1989).[1] Nevertheless, the misconception remains that natural populations lack aging individuals (Hayflick 2000; Kirkwood and Austad 2000).

A more informative index to the rate of aging than maximum reported life span can be obtained by fitting a model that incorporates the rate of increase in mortality with age to data on ages at death within a sample of individuals. Two types of models have been used for the most part (Gavrilov and Gavrilova 1991; Wilson 1994). The first, typified by the Gompertz model, represents the rate of aging by the exponential rate of increase γ of an initial mortality m_0. Thus, the mortality rate at age x is

$$m_x = m_0 e^{\gamma x}.$$

The rate of aging may also be expressed as the mortality rate doubling time, which is calculated as $\log_e 2/\gamma$ (Finch, Pike, and Witten 1990; Sacher 1977). In the second type of model, the aging component of mortality adds to an initial, or baseline, rate. Thus, according to the Weibull aging function,

$$m_x = m_0 + \alpha x^{\beta}.$$

In this equation, β describes the shape of the aging-related mortality curve and α is a scaling factor that describes its magnitude.[2]

Ricklefs (1998) devised an index from the parameters α and β of the Weibull function that has units of 1/time:

$$\omega_W = \alpha^{1/(\beta+1)}.$$

Thus, ω is a rate.[3] Although the Gompertz γ also has units of 1/time, the rate of mortality at any given age is also a function of the initial mortality rate, m_0. For comparison with the Weibull rate of aging (ω_W), Ricklefs and Scheuerlein (2001) devised an ad hoc index including both m_0 and γ, which has units of 1/time:

$$\omega_G = \sqrt{m_0 \gamma}.$$

In general, simulated data for actuarial aging show that maximum recorded life span and the parameters of Gompertz and Weibull functions are highly correlated with each other and therefore provide adequate descriptions of the rate of aging in most cases (Ricklefs and Scheuerlein 2002).

Aging models and the biology of life span

Regardless of their similar abilities to describe empirical data, the Gompertz and Weibull equations imply different mechanisms for the increase in mortality with age. In the case of the Gompertz model, the mortality rate of young adults (m_0) is multiplied by a factor that increases exponentially with age to obtain the mortality rate at age x. Thus, the model suggests that older individuals become progressively more vulnerable to causes of death that also afflict young adults. Presumably, these causes are for the most part extrinsic and comprise primarily death by predation and accident, including effects of inclement weather. Increasing vulnerability to extrinsic causes of death results from deterioration of physiological function with age. Strehler and Mildvan (1960) explained the exponential rise in the mortality rate of the Gompertz model in terms of a linear increase in vulnerability to aging factors combined with a sensitivity threshold that was exponentially distributed among individuals in a population.

In the Weibull model, aging-related mortality is added to the baseline (extrinsic) level, implying that different mechanisms cause the increasing rate of death in old age. Thus, the Weibull model would be consistent with catastrophic causes of death from acute illness or system failure (cardiovascular disease, carcinoma) in older individuals. These are intrinsic causes of death that would likely kill regardless of extrinsic mortality factors, even though the immediate cause of death may nonetheless be extrinsic. That is, a terminally ill individual almost certainly would have an elevated risk of death from predation, inclement weather, social strife, and other external causes. Several mathematical derivations have developed the idea, which may serve as a model of intrinsic mortality, that a sequence of randomly occurring events (e.g., mutations, radiation damage) is required to initiate a fatal cancerous growth or other failure. This theory shows that a series of $\beta + 1$ such events produces a Weibull mortality function with shape parameter β (Armitage and Doll 1954, 1961).

With increasing age, humans suffer higher mortality rates from both extrinsic and intrinsic causes of death, although the aging-related rate of increase is lower for accidental death than it is for spontaneous intrinsic causes, such as cancer and cardiovascular disease (e.g., Horiuchi and Wilmoth 1997). The few data available for nonhuman populations, such as rhesus macaques, show a similar rapid increase in geriatric disease with advancing age (Uno 1997). Although few studies address changes in the rate of death

from extrinsic causes, comparative analyses of natural and captive populations shed some light on the relative balance of extrinsic and intrinsic mortality factors in aging-related mortality.

The proportion of aging-related deaths

Another insight that can be gained from fitting aging functions to data concerns the proportion of deaths that can be attributed to aging-related causes (P_S). This can be calculated from the parameters of the Weibull model by the expression

$$P_S = \int_{x=0}^{\infty} \alpha x^{\beta} l_x dx,$$

where l_x is the proportion of individuals who survive to age x. This expression integrates over age the proportion of deaths that occur in excess of the fraction expected from constant mortality at rate m_0. This index is proportional to the potential strength of selection on factors that delay senescence. Ricklefs (1998) used Weibull functions fitted to empirical data to show that the proportion of senescent deaths in wild populations is high—up to 50 percent—when m_0 is low and a large proportion of the population attains old age. Because a large proportion dies at old age, reducing α should result in a large increase in fitness. Failure to reduce aging-related mortality, as observed in populations with long life spans, implies that there is limited genetic variation for mechanisms to delay aging at old age or that the associated cost of these mechanisms is too high.

Aging and evolutionary fitness

In order to place senescence in an evolutionary context, it is necessary to determine how changes in the rate of actuarial senescence influence fitness (Abrams 1991, 1993). We have already seen that the strength of selection on life span depends on the proportion of the population reaching a certain age, more specifically on the future reproductive potential of a cohort upon reaching that age. Any gain in fitness caused by an increase in life span must be sufficient to balance the cost of the mechanisms that extend life. The effect on fitness (λ) of changes in survival and reproduction at a particular age can be evaluated by the Euler–Lotka equation, also referred to as the "characteristic equation" of a population, which relates fitness to the life table variables of age-specific survival (l_x) and age-specific fertility (b_x)—

$$1 = \sum_{x=a}^{z} \lambda^{-x} l_x b_x$$

—where a and z are the ages at the onset and termination of reproduction, and age-specific survival is the product of annual survival probabilities s_x up to age $x - 1$. Each term of the sum is the realized production of offspring at a given age (x) discounted by the rate of population growth (λ).[4] To illustrate the use of the equation to evaluate changes in fitness resulting from changes in life span in as simple a manner as possible, we use a life table in which fertility (B) and adult survival rate (S) are constant, and we express senescence as a truncation of the life table at life span z (Figure 5). The age at maturity is a, and survival to maturity is S_a. Accordingly, the Euler–Lotka equation becomes

$$1 = \sum_{x=a}^{z} \lambda^{-x} S_a S^{x-a} B,$$

which may be solved for

$$\lambda = S + S_a B \lambda^{1-a} - S_a B S^{z-a+1} \lambda^{-z}.$$

This equation can then be differentiated to determine the effect of changes in life span (z) or adult mortality rate ($1 - S$) on evolutionary fitness (λ).[5]

The differential forms of this equation show how changes in life table entries influence fitness. These are illustrated in Figure 6 for changes in life span (z) and adult mortality rate ($1 - S$) as a function of the maximum life span. First, we see that a change in life span influences fitness most when life span is short, that is, when a large proportion of individuals are still alive toward the end of the truncated life span and thus will benefit from

FIGURE 5 Diagram of a simplified life table in which fertility (B) and mortality rate (M) are constant after the age at maturity (a), to which proportion S_a survive, and the life span is truncated at age z.

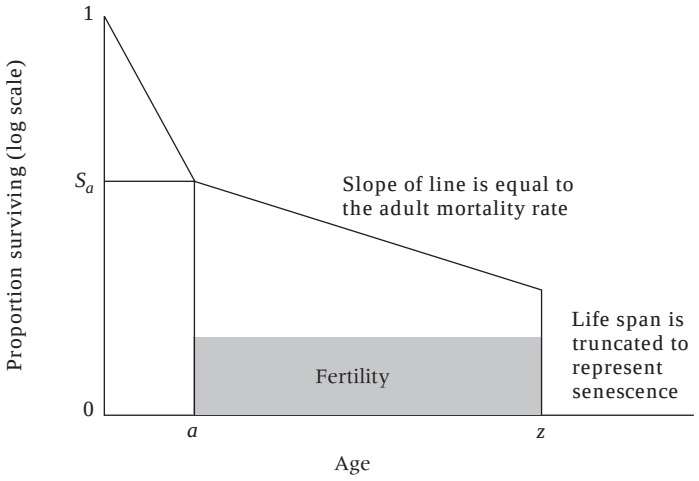
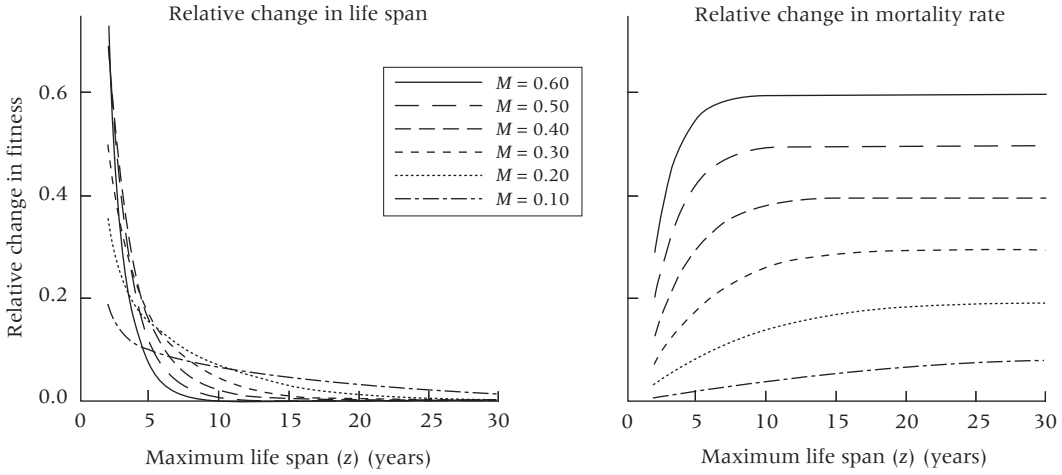


FIGURE 6 Relative (percentage) change in fitness (□) resulting from changes in life span and mortality rate, plotted for different values of adult mortality rate (*M*) as a function of the maximum life span (*z*)



the extension. For the same reason, the benefits of prolonging life at older ages are greater for populations with lower adult mortality rates. A decreasing mortality rate benefits populations with high adult mortality rates more than it does those with low adult mortality rates, as one would expect. For this discussion, the telling point is that variation in the mortality rate has a much greater influence on fitness than does variation in life span, especially beyond a modest maximum life span (for birds) of about ten years. This means that selection on patterns of aging is more likely to modify aging-related mortality at all ages, for example by changing the α parameter of the Weibull function, than it is to extend life span alone. Increasing z in this simple model would be equivalent to simultaneously increasing β and decreasing a. In comparative studies, we find that β is independent of initial mortality m_0 and ω, and that variation in the pattern of aging among species involves solely changes in α (Ricklefs and Scheuerlein 2001).[6]

How does one analyze and interpret life-history variation?

Correlations between the rate of aging and other life-history traits may provide insights into the mechanisms of extending life. Comparative analyses are fraught with problems, however. The most important of these are spurious correlations arising from third variables and lack of evolutionary in-

dependence of the data. The first problem may be addressed using analytical techniques that account for the correlations among independent variables: multiple regression, path analysis, and multivariate analysis. These analytical tools seek unique correlations between two variables that are independent of correlations with other variables, or they combine independent variables into derived axes that incorporate their intercorrelations. The problem of evolutionary independence has been addressed by a number of techniques based on phylogenetic relationships among taxa that isolate independent aspects of their evolutionary history. In most cases, however, it may be reasonable to proceed with correlations based on terminal taxa in a phylogeny, that is, with raw species values.[7]

Another issue in evolutionary analysis that is not addressed by analyzing either contrasts or terminal taxa is the evolutionary lability versus conservatism of life-history traits. Some traits vary substantially among closely related species and presumably are responsive to variation in selection. Other traits are much more conservative, with a large part of their variation concentrated in comparisons among higher taxonomic categories. This situation may reflect rapid evolution of life-history patterns in conjunction with the early expansion of a group followed by a subsequent period of relative stasis to the present (Nealen and Ricklefs 2001; Ricklefs and Nealen 1998). The distribution of variation in traits and covariation between traits with respect to evolutionary history can be approached by hierarchical nested analysis of variance. This procedure partitions variation into components associated with a hierarchy of taxonomic categories (Bell 1989; Derrickson and Ricklefs 1988; Stearns 1983), such as families within orders and species within genera.[8] We apply this analytical technique below.

Can one apply experimental approaches to life-history variation?

Most experimental work on the evolution of aging has been carried out with laboratory organisms, most notably *Drosophila melanogaster* (Partridge and Barton 1993; Rose and Graves 1990). The general approach is to select on variation in life table traits and to observe correlated evolutionary responses. Laboratory populations tend to respond rapidly to selection on life span or on fertility during early or late portions of the life span. In such experiments, increased life span is typically associated with increased ability to tolerate stress (Harshman et al. 1999) but also with reduced fertility early in life (Rose 1984). In many laboratory populations, individual genes with striking effects on life span have been identified. One must be careful, however, in placing such cases in the context of life span in natural populations. One should ask, for example, whether the extension of

life span in laboratory populations exceeds that of individuals in nature or remains within the biological potential of natural populations (Linnen, Tatar, and Promislow 2001; Sgrò and Partridge 2000). Most domesticated and laboratory populations have been selected for rapid maturation and high early fertility, which would under most circumstances reduce potential life span. In this case, variation in laboratory populations and, particularly, large effects of individual genes, as well as the response of laboratory populations to selection on life span, may have limited application to understanding limits to life span in natural populations (Clark 1987; Promislow and Tatar 1998).

Natural experiments

In some cases, it may be possible to observe closely related natural populations under different environmental conditions to detect the evolutionary response of life span to variation in environmental conditions. Such natural experiments may offer reasonable control over the intrinsic biological characteristics of the organism (such control is more difficult to achieve in broader comparative studies); however, environmental variables may be more difficult to control. Such natural experiments nonetheless provide insights into the evolutionary flexibility of the life span and, presumably, the aging process. In one case already mentioned, Austad and Fischer (1991) compared populations of opossums separated over several thousand years in mainland and island environments and found that the rate of actuarial senescence was lower on the island, where predators were absent and individuals suffered lower mortality from extrinsic factors. Austad also found that a physiological index of aging—the cross-linking of collagen fibers—occurred more slowly among island opossums.

Comparison of survival curves in populations of the water flea *Daphnia pulex* in lakes and ponds that differ in the intensity of predation showed parallel variation in longevity consistent with a response of aging to selective factors in the environment (Dudycha 2001). Several authors have emphasized the disparity in life span between workers and reproductive castes of social insects as indicative of environmental controls over the rate of aging; but because the genotypes of queens and workers do not differ, these differences clearly do not reflect evolutionary responses (Keller and Genoud 1997). Nonetheless, they indicate the strong direct environmental influence on aging, presumably mediated through rate of activity or differences in hormonal and physiological state.

Another type of experiment that can elucidate mechanisms responsible for aging is the establishment of captive populations, whereby extrinsic mortality factors are reduced considerably compared to natural populations. We discuss the results of such comparisons below.

Patterns of life-history variation involving life span

Until recently, most empirical studies of variation in longevity were based on maximum reported life span. When organisms exhibit an increase in mortality rate with age and a natural population is sampled for a sufficient period to cover the maximum natural life span, simulated data show that the maximum reported life span is highly correlated with aging parameters of Gompertz and Weibull models of aging (Ricklefs and Scheuerlein 2002; Scheuerlein and Ricklefs unpubl.). Problems arise primarily when studies are too brief. For example, among the maximum reported life spans in Carey and Judge's (2000) thorough compilation, those for red-legged kittiwakes (4 years) and Townsend's shearwater (5.1 years) are barely long enough for these seabirds to attain maturity.[9] Although the data must be viewed cautiously, life span analyses nevertheless reveal general patterns in the rate of aging among animals.

Body mass

Biologists have recognized for many years that maximum potential life span in birds and mammals is closely related to body size (Comfort 1979; Finch 1990). Large animals live longer (Austad and Fischer 1991; Calder 1983, 1984, 1985; Sacher 1959). This has been attributed to several causes. First, many physiological parameters, such as metabolism, development rate, and fecundity, vary with body size. Large animals have a slow rate of living, and long life may express this general property. Reduced metabolism may also result in reduced concentrations of reactive forms of oxygen, thereby slowing the aging process (e.g., Barja and Herrero 2000). Another consequence of large body size is a lower extrinsic mortality rate. Larger animals are better able to avoid encounters with predators, and their bodies are also better buffered against vagaries in the environment.

Second, it is well understood that greater survival in the face of extrinsic factors increases the strength of selection on life span, leading to a demographic or life-history connection between body size and rate of aging. Several authors have examined this demographic connection directly by relating aging parameters of Gompertz or Weibull functions to the estimated extrinsic mortality rate. As mentioned previously, Promislow (1991) compared the aging parameter γ of the Gompertz equation to an estimate of the minimum mortality rate of young adults but found no relationship between them. In contrast, Ricklefs (1998) found a strong relationship between the derived aging parameter ω and the fitted initial mortality rate (m_0) of the Weibull equation. This discrepancy raises a fundamental issue concerning the proper definition of the rate of aging. Using the Gompertz γ,

one defines aging as the exponential rate of increase in mortality with age. Using ω derived from either the Gompertz or Weibull equation, one defines aging according to the magnitude of the mortality rate at a particular age. In the case of the Gompertz function, the magnitude of the mortality rate depends on both m_0 and γ, hence it is difficult to separate their effects.

Multiple regression shows that the Weibull ω varies with the initial mortality rate independently of the relationship of both to body size, thereby making the demographic connection between extrinsic mortality and rate of aging more plausible and the direct allometric physiological connection between size and m_x less plausible. This is further substantiated by comparisons between birds and mammals. For individuals of a given body size, birds have longer life spans than mammals, perhaps by an average factor of 2–3 times (Calder 1983; Holmes and Austad 1995a). When birds and mammals are analyzed together, the rate of aging ω is related to the initial mortality rate m_0 independently of body size or of differences between birds and mammals (Ricklefs 1998). Accordingly, the difference in longevity between birds and mammals of the same body size is statistically associated with the greater ability of birds to escape mortality factors, as shown by their lower values of m_0. This observation strengthens the idea that the rate of aging is evolutionarily flexible rather than being tied closely to other aspects of physiology, such as the rate of metabolism (Holmes and Austad 1995a, b).

Brain mass

Life span has been related to other attributes besides body mass. Brain mass, in particular, has captured the attention of comparative biologists, perhaps because the brain is considered the pacemaker of life in general and is the organ that most resists aging-related change. Sacher (1959, 1978) found a good correlation between life span and brain mass for mammals, and Allman et al. (1993) have explored this relationship in more detail for primates. However, the brain–life span relationship was questioned by Economos (1980a, b), who pointed out that brain mass is not uniquely highly correlated with longevity, given the strong intercorrelations, for example, between brain mass and body mass. Why mass itself should exercise a dominant influence over life span is also not clear. Ricklefs and Scheuerlein (2001), comparing the Weibull parameter ω to both body mass and brain mass in birds in a multiple regression, found that only brain mass was uniquely related to rate of aging. Clearly, however, in comparisons involving both birds and mammals, brain mass does not explain as much of the variation in life span or rate of aging as extrinsic mortality. Thus, it is likely that the correlation observed within either class between brain mass and life span reflects some aspect of the ecology of species that is expressed independently in both brain mass and extrinsic mortality.

Genome size

Another attribute that has been linked to longevity is the size of the genome. Although the two do not appear to be related in mammals (see Finch 1990), Monaghan and Metcalfe (2000) have recently made such a claim for birds based on independent contrasts calculated from phylogenetic relationships among avian families (Sibley and Ahlquist 1990). Ricklefs and Scheuerlein (2001) and Morand and Ricklefs (2001) failed to find a relationship between the Weibull aging parameter ω and genome size in a correlation among terminal taxa at the species level. However, a hierarchical analysis of covariance based on Monaghan and Metcalfe's data reveals a strong correlation between life span and genome size at the level of families within orders but no correlation at the level of species within genera (Table 1). Even though the family-level correlation is significant, the amount of the total variance that resides at this taxonomic level is relatively small, hence it is hard to attach a biological meaning to the correlation. Indeed, when the data were partitioned into equal halves, only one of the two data sets retained a significant correlation between life span and genome size at the family level. This suggests that the significant correlation may have resulted from a chance association of data rather than an underlying mechanistic connection between the two.

A broader life-history perspective

Ricklefs and Scheuerlein (2001) investigated life-history correlations of the rate of aging (ω) in birds and mammals separately. The rate of aging was generally inversely related to body size, brain size (tested only for birds), and rate of postnatal development (significant only for mammals), and was directly related to the lengths of incubation (birds) or gestation periods (mammals). When the independent variables were treated together in a multiple regression, only brain mass (birds) and postnatal growth rate (mam-

TABLE 1 Distribution of variance components in life span, genome size, and their correlation among birds over nested taxonomic levels

Taxonomic level	Life span	Genome size	Correlation
Order	0	0	0.00
Family	26	6	1.59
Genus	74	94	0.02
Total	100	100	—

NOTE: Life span is the maximum recorded value and is subject to considerable error; correlations exceeding 1.0 are possible because variance components are estimates.
SOURCE: Data are from Monaghan and Metcalfe (2000) as analyzed by Morand and Ricklefs (2001); based on 67 species.

TABLE 2 Distribution of variance components in life-history traits and aging parameters of birds over nested taxonomic levels

Taxonomic level	Mass	Brain	Incubation period	Growth rate	Initial mortality (m_0)	Rate of aging (ω)
Order	42	20	47	80	10	25
Family	1	0	41	0	21	0
Genus	52	76	9	20	49	61
Species	5	4	4	0	21	14
Total	100	100	100	100	100	100

NOTE: Variance components are estimates based on the hierarchical structure of mean squares in a nested analysis of variance. When the data are poorly balanced, as in analyses of this type, mean squares may decrease from one level to the next higher level, resulting in a negative variance component, which is arbitrarily set to zero.
SOURCE: Data from Ricklefs and Scheuerlein (2001), based on 53 species.

mals) were uniquely related to rate of aging. Hierarchical analysis of variance for life-history and aging traits of birds reveals differences in the distribution of variation related to the evolutionary responsiveness of each of the traits (Table 2). In particular, about 80 percent of the variance in embryonic and postnatal growth rates resides at the level of orders and families, reflecting body size differences between large taxonomic groups and differences in mode of development (i.e., altricial versus precocial) that influence growth rate (Starck and Ricklefs 1998). Variance in mass itself is about equally distributed between higher and lower taxonomic levels, whereas the variance in initial mortality and rate of aging is more heavily weighted toward the taxonomic level of genus. For the smaller number of species for which brain masses are available, variance in brain mass is concentrated at the level of genus, as is the variance in rate of aging.

Variance component correlations relating the rate of aging ω to other life-history traits show consistent significant correlations between rate of aging and extrinsic mortality at the level of orders and genera within families, but correlations with body mass and incubation period are weaker (Table 3).

TABLE 3 Variance component correlations for the rate of aging (ω) and initial mortality rate (m_0), mass, and incubation period in birds

Taxonomic level	ω versus mass	ω versus m_0	Mass versus m_0	ω versus incubation period
Order	–0.41	1.10	0.59	–0.67
Family	0.00	0.00	–0.80	0.00
Genus	–0.84	0.76	–0.92	–0.56
Species	–0.19	0.33	–0.51	–0.31

SOURCE: Data from Ricklefs and Scheuerlein (2001).

Comparisons between wild and captive populations

When individuals are brought into captivity, the rate of extrinsic mortality is reduced considerably, except perhaps for the incidence of stress-related and contagious disease. If the increase in mortality with age resulted from increasing vulnerability to extrinsic mortality factors, then one would expect animals in captivity to exhibit lower mortality rates at older ages than they do in the wild. If aging-related mortality were caused by intrinsic factors that kill independently of external causes (even though the latter may hasten intrinsically caused death), then aging-related mortality would not differ between captive and wild populations. Comparing wild and captive populations is complicated by the fact that ages at death are often estimated by different methods, and mortality rates of young adults in captivity may have additional causes related to stress and contagion that are not prominent in the wild. Thus, such comparisons must be made with caution.

Using phylogenetically controlled comparisons, Ricklefs (2000b) showed that captive populations of birds had lower initial mortality (m_0) but comparable rates of aging (ω) vis-à-vis wild populations. This suggested that the Weibull model of aging, which separates extrinsic and intrinsic causes of death in additive terms, provides a reasonable demographic description of the aging process. A similar comparison of taxonomically matched wild and captive populations of mammals suggested in contrast that the Weibull rate of aging decreases in captivity by an amount expected of the multiplicative Gompertz model (Ricklefs and Scheuerlein 2001). This result was particularly striking for mammals of open savanna habitats, for which survival rate must be closely tied to speed and endurance. For such species, physiological decline would seemingly lead to higher vulnerability to extrinsic mortality factors, particularly predation. Predators themselves should be similarly afflicted by physiological decline, and it is perhaps relevant that the lion *Panthera leo* shows a pattern of reduced aging-related mortality in captivity, as do several ungulates that are potentially its prey.[10]

Discussion

Comparative analyses of the rate of aging in the context of life histories have provided insights into the aging process while leaving many issues unresolved. In the case of birds, which are long lived compared to mammals of the same size, comparisons between wild and zoo populations suggest that the Weibull model provides a better description of the aging process than the Gompertz model. Causes of aging-related deaths are apparently unrelated to extrinsic mortality factors; accordingly, an additive model of extrinsic and intrinsic mortality, such as the Weibull function, is appropri-

ate. Comparison of rates of aging with body size and the extrinsic (initial) mortality rate indicates that the rate of aging responds to selection based on the demography of a population rather than on physiological characteristics of individuals. Thus, for the most part, evolutionary theories of aging are supported by comparative studies. Moreover, comparisons between natural and captive populations indicate that birds in the wild do not die because of increasing vulnerability to extrinsic causes. This suggests that individual birds maintain high fitness late into life and that the increase in mortality with age is due to the increasing probability of catastrophic causes of death, such as cancer and stroke. The increasing proportion of aging-related deaths in populations with a large proportion of old individuals further suggests that there are inherent biological limitations on the control of intrinsic aging-related mortality.

Correlations of the rate of aging with life-history attributes other than extrinsic mortality are not particularly informative because of the strong correlations among independent variables. By considering mammals and birds together, however, one can break this pattern of intercorrelation because the different life styles of birds and mammals result in contrasting patterns of extrinsic mortality. Thus, although the rate of aging is related to body size and other correlated life-history attributes within both birds and mammals, analyses involving both groups clearly tie the rate of aging to extrinsic mortality. Accordingly, the rate of aging appears to be responsive to selection on traits that extend life span or modify the rate of increase in mortality. Because the rate of aging varies in response to the demographic environment of a population, we may infer that postponing aging imposes a fitness cost, although the mechanisms involved are not understood. Because the proportion of aging-related mortality increases with maximum potential life span, this cost evidently increases as senescence is delayed further. Moreover, the difference in the rate of aging between birds and mammals of the same body size is not due to some fundamental biological difference between the two groups of organisms. Rather, it is related to the fitness benefits of delayed aging, which are lower for mammals owing to their higher extrinsic mortality rates.

The nature of the fitness cost of postponing aging (Abrams 1991) is not evident in comparative analyses. In general, increasing body size is associated with a reduced rate of aging, reduced extrinsic mortality, lower fecundity resulting from smaller brood size and longer development, and a higher prereproductive survival rate. If postponing senescence imposes a cost in terms of early fecundity or survival, this might be obscured either by contrasting or supplementing contributions to fertility and survival from other factors. For example, there are many reasons, related to lower metabolic intensity and slower life processes, why larger organisms might have lower fecundity than smaller organisms besides the costs of delayed senescence.

Comparative analyses of life histories might provide more information concerning mechanisms of delayed senescence if they were applied in conjunction with mechanistic models of control of the aging process (Abrams and Ludwig 1995). For example, Ricklefs (1992, 1993) suggested that variation in the development period among birds of the same body size might involve mechanisms to prolong life through production of a better immune system or a larger, more complex nervous system. In this case, one could search for a direct correlation between the rate of aging and the development rate, where the latter was sufficiently uncoupled from body size to permit separation of the two effects statistically. To the extent that such analyses have been performed for birds and mammals, they are consistent in that a longer development period is associated with lower extrinsic mortality and longer life span independently of body size (Ricklefs 1993). Clearly, slow development reduces fitness because it extends the period of exposure of highly vulnerable offspring to extrinsic mortality factors. The size of this fitness impact can be estimated from mortality rates of parents and offspring during the development period. If prolongation of life span were achieved by reducing fertility, one might be able to use comparative analyses to identify associated adaptations of organisms that secondarily decrease the reproductive rate.

What the comparative analysis of aging requires most at this point is an unambiguous quantitative definition of the rate of aging; mechanistic models of aging to inform comparative analyses; and comparative data specifically related to aging and its causes. General insights have been gained by comparative life-history analyses of aging; however, at present these lack the specificity to help characterize mechanisms of aging by their effects on life-history traits. More-focused gathering of data and application of comparative methods should help considerably in this regard.

We conclude with four general observations about life span—its nature, evolution, theoretical study, and future prospects.

(1) What are the nature and fundamental properties of life span? Comparative studies of life tables do not address physiological processes directly. What they can say is that senescence leads to a continuous increase in the mortality rate with age and that differences between populations reflect primarily the magnitude rather than the pattern of this increase. Although a species may have a maximum potential life span, it is clear that few individuals reach this age. From the standpoint of the evolution of the aging pattern, factors that influence adult mortality throughout life determine the overall pattern of aging-related mortality. An important issue is whether the demographic expression of aging results from increasing vulnerability to extrinsic causes of death due to reduced physiological capacity, or from increasing frequency of catastrophic intrinsic mortality factors, such as carcinomas and cardiovascular disease. In birds, the relative constancy of the

aging-related component of mortality when extrinsic mortality varies between captive and natural populations weighs in favor of intrinsic causes. The data for mammals are less conclusive and may reflect a basic difference in the way mammals age.

(2) How does life span evolve in the context of the life history? Comparative studies make quite clear that the primary selective factor is the level of extrinsic mortality. The role of other factors, such as parental care and sociality (Allman et al. 1998; Carey and Judge 2001), over and above extrinsic mortality, has not been evaluated quantitatively in a comparative context. Because most of the variance in the rate of aging resides at the level of genera within families, this observation suggests that the rate of aging is relatively flexible from an evolutionary standpoint, but also that most of the variance in extrinsic mortality rates is expressed at this level.

(3) Why is there no theory of life span per se, notwithstanding the dominant focus on aging? From an evolutionary standpoint, one answer is that the fitness effect of variation in life span is much smaller than the effect of changes in mortality throughout adult life (Figure 6). This is because so few individuals in natural populations reach the maximum potential life span. This does not mean that life span per se is not responsive to selection; the evolutionary response also depends on genetic variation for a trait within a population. Comparative studies provide no evidence, however, that maximum potential life span varies independently of changes in aging-related mortality throughout adult life.

(4) What is the future of the human life span? The increasing proportion of aging-related mortality in populations with older age structures suggests that natural populations have approached biological constraints limiting the potential length of life. Average human life span clearly has increased greatly in recent years, with many of the gains coming from reduced mortality rates in the oldest age classes (Robine et al. 1997). It is clear that these changes have resulted from manipulation of the environment rather than changes in the genetic makeup of the human population. Thousands of generations of selection on natural populations of long-lived animals, such as elephants and albatrosses, have failed to reduce aging-related mortality to low levels. Thus, it is likely that future progress in extending average human life span will require either further improvement in the conditions of life conducive to survival at old age or manipulations of the human genome that exceed the genetic repertoire of natural populations. A more important lesson from the study of aging in natural populations of birds is that individuals can maintain high personal fitness to an advanced age as part of the normal progress of aging. This lesson suggests that it may be more fruitful to focus our attention on realizing and enhancing for humans the potential natural quality of life of elderly individuals rather than trying to extend life per se.

Notes

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1 The failure of banding studies to detect aging-related mortality can be attributed to several factors. First, most banding studies with large sample sizes were restricted to small species with short life spans and high adult mortality rates, such as tits (*Parus*) and flycatchers (*Ficedula*). As shown by Ricklefs (1998), only a small proportion of the mortality in populations of this type is associated with the expression of aging. Second, techniques for analyzing demographic data in early studies of band returns were not well developed and may have had little power to detect age dependency of the survival rate. Recent development of maximum likelihood models has made demographic analysis much more sensitive (Lebreton et al. 1992). Third, recovery of ages at death from natural populations, unlike cohort analysis, is not well suited to analysis of age-specific changes in the survival rate. This is because, in populations that are sampled through recoveries of dead individuals, the declining sizes of successively older age classes are balanced by an increasing mortality rate with age. Thus, the changes in age structure associated with aging are partly or completely compensated by change in the mortality rate, often resulting in a distribution of ages at death sampled from a natural population that resembles a constant exponential (that is, nonsenescing) decline.

2 Additional models incorporate additional additive and multiplicative terms (e.g., the Gompertz–Makeham function) or a leveling off at high age (e.g., logistic function) to match observations on humans and on laboratory populations of flies (Carey et al. 1992; Fukui et al. 1993; Horiuchi and Wilmoth 1998; Vaupel et al. 1998). We have not used functions with an upper asymptote because too few data are available for natural populations of birds and mammals to reveal aging plateaus, and we wished to keep the number of aging parameters small to facilitate comparisons among taxa. Note also that the Gompertz–Makeham function,

$$m_x = m_0 + A_0 e^{\gamma t},$$

incorporates an additive term for initial mortality rate, but, as in the Gompertz equation, the aging-related mortality term remains an exponential increase in a portion (A_0) of the initial mortality. Thus, it does not provide the independence between initial and aging-related mortality that the Weibull function does.

3 Specifically, ω is the value of the aging-dependent mortality term αx^{β} obtained when $x = 1/\omega$. From the logarithmic form of the expression, $\log\omega = \log\alpha/(\beta + 1)$, one can see that for a given value of β, the value of $\log\omega$ is directly proportional to $\log\alpha$. Empirically, β averages about 3 in bird and mammal populations.

4 Application of this equation involves many assumptions, most notably that the life table of the population is constant over time and that males and females are demographically indistinguishable. When survival and fertility vary stochastically over time, selection generally favors longer life (lower adult mortality) over reproduction (Hastings and Caswell 1979; Schaffer 1974). For a constant life table, the change in fitness resulting from a change in any life table entry, i.e., fertility or survival rate at a particular age, can be obtained by differentiating the equation to find $d\lambda/ds_x$ or $d\lambda/db_x$ (Hamilton 1966). However, as Abrams (1991, 1993) has pointed out, genetic changes influencing the aging process typically have an age at onset and affect life table values at all subsequent ages. These considerations complicate the application of the Euler–Lotka equation to the evolution of aging. Nevertheless, it has heuristic value for exploring the effects of changes in life table variables on evolutionary fitness, which can be illustrated by the simple approach taken here.

5 Because populations are maintained in an approximate equilibrium by density-dependent factors, this equation can be simplified by assuming $\lambda = 1$, at which point recruitment of young individuals into the breeding population ($S_a B$) can be replaced by

$$S_a B = \frac{1 - S}{1 - S^{z-a+1}}.$$

6 The estimated fitness value of extending average life span also shows how much

mechanisms for extending life cost in terms of life table values. In the simple model presented above, costs may be expressed as an increase in age at maturity (a), decrease in prereproductive mortality (increase in S_a), decrease in fertility (B), or any combination of these. For example, suppose life span were extended by some mechanism that lengthened the development period. This would incur a cost in terms of the reduced survival (expressed as lower B or S_a) resulting from a longer period of exposure of the more vulnerable offspring to extrinsic mortality factors. In tropical birds, for example, daily rates of nest predation commonly exceed 5 percent, hence extending development even for a few days, as so many tropical species do, can be very costly.

7 The technique of independent contrasts used to correct for phylogenetic relationship (Garland et al. 1992; Harvey and Pagel 1991) requires estimation of the character values or states of ancestral nodes and thus shifts the problem of independence to a problem of estimation. Restricting comparisons to terminal pairs of species (sister-taxon comparisons) eliminates the problem of independence and does not rely on estimation of ancestral states, but results in a considerable reduction of sample size. For example, in a sample of 20 taxa, the number of independent contrasts is 19, while the maximum number of sister-taxon comparisons is 10 or fewer. However, results based on independent contrasts and results based on terminal taxa rarely differ qualitatively and generally are similar quantitatively (Price 1997; Ricklefs and Starck 1996).

8 One assumption of this approach is that taxonomic ranks are homogeneous throughout a phylogeny. In the case of birds, Sibley and Ahlquist (1990) have defined taxonomic categories on the basis of genetic divergence estimated by DNA hybridization. Genetic differences are expressed as difference in the melting point temperatures of homoduplexed and heteroduplexed DNA ($\Delta T_H 50$, °C). Thus, for example, families include taxa descending from a single ancestral node at a depth of 9–11 °C.

9 Most data on maximum life span for natural populations of animals come from birds, which have been the subjects of banding programs for many years. When birds are fitted with an individually numbered leg band as chicks or in the first year of life, when age can be assessed by plumage, age at death can be determined. Ages at death in mammal populations are based primarily on patterns of growth or tooth wear and are therefore less accurate than those for birds. In some cases, long-term studies of individually recognizable mammals have provided more accurate demographic information in natural populations (Gaillard et al. 1994).

10 One nagging feature of captive populations is the relatively high "extrinsic" mortality rate in the absence of most extrinsic mortality factors. We suggest that relatively high values of m_0 are related to the stress of the zoo environment, which may impair immune system function and render zoo animals more vulnerable to infection and other stress-related causes of mortality in young adults. The higher rate of initial mortality may also result in a lower apparent rate of aging as an artifact. This result might be particularly pronounced if the high initial mortality rate of captive populations actually decreased with age. We have tested the idea that stress might be related to high initial mortality in captive populations by comparing captive populations of wild species with those of domesticated species, which presumably have been selected for reduced stress response to the conditions of captivity (Scheuerlein and Ricklefs, unpubl.). Preliminary results show that initial mortality of domesticated populations is very low, but that the rate of aging (ω) differs little from that of comparable wild or captive populations. Thus, it seems plausible that captivity and domestication have reduced extrinsic mortality considerably, but that the pattern of actuarial senescence has changed little. This result is contrary to Austad's (1993) observation that an insular population of opossums isolated from the mainland for about 4,000 years (i.e., similar to the period of domestication of dogs and livestock) exhibited both reduced extrinsic mortality and slower aging-related increase in mortality. The result with domesticated mammals also reinforces the idea that the additive terms of the Weibull function portray the underlying causes of actuarial senescence more realistically than the multiplicative terms of the Gompertz equation.

References

Abrams, P. A. 1991. "The fitness costs of senescence: The evolutionary importance of events in early adult life," *Evolutionary Ecology* 5: 343–360.

———. 1993. "Does increased mortality favor the evolution of more rapid senescence?" *Evolution* 47: 877–887.

Abrams, P. A., and D. Ludwig. 1995. "Optimality theory, Gompertz' law, and the disposable soma theory of senescence," *Evolution* 49: 1055–1066.

Alexander, R. D. 1974. "The evolution of social behavior," *Annual Review of Ecology and Systematics* 5: 325–383.

Allman, J., T. McLaughlin, and A. Hakeem. 1993. "Brain weight and life-span in primate species," *Proceedings of the National Academy of Sciences USA* 90: 118–122.

Allman, J., A. Rosin, R. Kumar, and A. Hasenstaub. 1998. "Parenting and survival in anthropoid primates: Caretakers live longer," *Proceedings of the National Academy of Sciences USA* 95: 6866–6869.

Alvarez, H. P. 2000. "Grandmother hypothesis and primate life histories," *American Journal of Physical Anthropology* 113: 435–450.

Armitage, P. and R. Doll. 1954. "The age distribution of cancer and a multi-stage theory of carcinogenesis," *British Journal of Cancer* 8: 1–12.

———. 1961. "Stochastic models for carcinogenesis," *Proceedings of the Fourth Berkeley Symposium on Mathematical Statistics and Probability* 4: 19–38.

Arnold, S. J. 1983. "Morphology, performance and fitness," *American Zoologist* 23: 347–361.

Austad, S. N. 1993. "The comparative perspective and choice of animal models in aging research," *Aging-Clinical and Experimental Research* 5: 259–267.

———. 1997. "Comparative aging and life histories in mammals," *Experimental Gerontology* 32: 23–38.

Austad, S. N. and K. E. Fischer. 1991. "Mammalian aging, metabolism, and ecology: Evidence from the bats and marsupials," *Journal of Gerontology: Biological Sciences* 46: B47–B53.

Barja, G. and A. Herrero. 2000. "Oxidative damage to mitochondrial DNA is inversely related to maximum life span in the heart and brain of mammals," *FASEB Journal* 14: 312–318.

Bell, G. 1989. "A comparative method," *American Naturalist* 133: 553–571.

Bennett, P. M. and P. H. Harvey. 1985. "Brain size, development and metabolism in birds and mammals," *Journal of Zoology* 207: 491–509.

———. 1987. "Active and resting metabolism in birds: Allometry, phylogeny and ecology," *Journal of Zoology* 213: 327–363.

Botkin, D. B. and R. S. Miller. 1974. "Mortality rates and survival of birds," *American Naturalist* 108: 181–192.

Calder, W. A., III. 1983. "Body size, mortality, and longevity," *Journal of Theoretical Biology* 102: 135–144.

———. 1984. *Size, Function, and Life History*. Cambridge, MA.: Harvard University Press.

———. 1985. "The comparative biology of longevity and lifetime energetics," *Experimental Gerontology* 20: 161–170.

Carey, J. R. and D. S. Judge. 2000. *Longevity Records: Life Spans of Mammals, Birds, Amphibians, Reptiles, and Fish*. Odense, Denmark: Odense University Press.

———. 2001. "Principles of biodemography with special reference to human longevity," *Population: An English Selection* 13: 9–40.

Carey, J. R., P. Liedo, D. Orozco, and J. W. Vaupel. 1992. "Slowing of mortality rates at older ages in large medfly cohorts," *Science* 258: 457–461.

Caruso, C. et al. 2000. "HLA, aging, and longevity: A critical reappraisal," *Human Immunology* 61: 942–949.

Charlesworth, B. 1994. *Evolution in Age-structured Populations*, 2nd edition. Cambridge: Cambridge University Press.

Clark, A. G. 1987. "Senescence and the genetic correlation hang-up," *American Naturalist* 129: 932–940.

Comfort, A. 1979. *The Biology of Senescence*, 3rd ed. Edinburgh and London: Churchill Livingstone.

Curio, E. 1989. "Is avian mortality preprogrammed?" *Trends in Ecology and Evolution* 4: 81–82.

Derrickson, E. M. and R. E. Ricklefs. 1988. "Taxon-dependent diversification of life histories and the perception of phylogenetic constraints," *Functional Ecology* 2: 417–423.

Dudycha, J. L. 2001. "The senescence of *Daphnia* from risky and safe habitats," *Ecology Letters* 4: 102–105.

Economos, A. C. 1980a. "Brain-life span conjecture: A re-evaluation of the evidence," *Gerontology* 26: 82–89.

———. 1980b. "Taxonomic differences in the mammalian life span-body weight relationship and the problem of brain weight," *Gerontology* 26: 90–98.

Edney, E. B. and R. W. Gill. 1968. "Evolution of senescence and specific longevity," *Nature* 220: 281–282.

Finch, C. E. 1990. *Longevity, Senescence, and the Genome*. Chicago: University of Chicago Press.

Finch, C.E., M.C. Pike, and M. Witten. 1990. "Slow mortality rate accelerations during aging in some animals approximate that of humans," *Science* 249: 902–905.

Finkel, T. and N. J. Holbrook. 2000. "Oxidants, oxidative stress and the biology of ageing," *Nature* 408: 239–247.

Fukui, H. H., L. Xiu, and J. W. Curtsinger. 1993. "Slowing of age-specific mortality rates in *Drosophila melanogaster*," *Experimental Gerontology* 28: 585–599.

Gaillard, J. M., D. Allaine, D. Pontier, N. G. Yoccoz, and D. E. L. Promislow. 1994. "Senescence in natural populations of mammals: A reanalysis," *Evolution* 48: 509–516.

Garland, T., Jr., P. H. Harvey, and A. R. Ives. 1992. "Procedures for the analysis of comparative data using phylogenetically independent contrasts," *Systematic Biology* 41: 18–32.

Gavrilov, L. A. and N. S. Gavrilova. 1991. *The Biology of Life Span: A Quantitative Approach*. New York: Harwood Academic Publishers.

Hamilton, W. D. 1966. "The moulding of senescence by natural selection," *Journal of Theoretical Biology* 12: 12–45.

Harshman, L. G., K. M. Moore, M. A. Sty, and M. M. Magwire. 1999. "Stress resistance and longevity in selected lines of *Drosophila melanogaster*," *Neurobiology of Aging* 20: 521–529.

Harvey, P. H. and M. S. Pagel. 1991. *The Comparative Method in Evolutionary Biology*. Cambridge: Cambridge University Press.

Hastings, A. and H. Caswell. 1979. "Role of environmental variability in the evolution of life history strategies," *Proceedings of the National Academy of Sciences USA* 76: 4700–4703.

Hawkes, K., J. F. O'Connell, N. G. B. Jones, H. Alvarez, and E. L. Charnov. 1998. "Grandmothering, menopause, and the evolution of human life histories," *Proceedings of the National Academy of Sciences USA* 95: 1336–1339.

Hayflick, L. 2000. "New approaches to old age," *Nature* 403: 365.

Holmes, D. J. and S. N. Austad. 1995a. "Birds as animal models for the comparative biology of aging: A prospectus," *Journal of Gerontology: Biological Sciences* 50A: B59–B66.

———. 1995b. "The evolution of avian senescence patterns: Implications for understanding primary aging processes," *American Zoologist* 35: 307–317.

Horiuchi, S. and J. R. Wilmoth. 1997. "Age patterns of the life table aging rate for major causes of death in Japan, 1951–1990," *Journals of Gerontology Series A—Biological Sciences and Medical Sciences* 52: B 67–B 77.

———. 1998. "Deceleration in the age pattern of mortality at older ages," *Demography* 35: 391–412.

Keller, L. and M. Genoud. 1997. "Extraordinary lifespans in ants: A test of evolutionary theories of ageing," *Nature* 389: 958–960.

Kirkwood, T. B. L. 1990. "The disposable soma theory of aging," in D. E. Harrison (ed.), *Genetic Effects on Aging*. Caldwell, NJ: Telford Press, pp. 9–19.

Kirkwood, T. B. L. and S. N. Austad. 2000. "Why do we age?" *Nature* 408: 233–238.

Kirkwood, T. B. L. and R. Holliday. 1979. "The evolution of ageing and longevity," *Proceedings of the Royal Society of London—Series B: Biological Sciences* 205: 531–546.

Lack, D. 1954. *The Natural Regulation of Animal Numbers*. Oxford: Clarendon Press.

Lebreton, J. D., K. P. Burnham, J. Clobert, and D. R. Anderson. 1992. "Modeling survival and testing biological hypotheses using marked animals: A unified approach with case studies," *Ecological Monographs* 62: 67–118.

Linnen, C., M. Tatar, and D. Promislow. 2001. "Cultural artifacts: A comparison of senescence in natural, laboratory-adapted and artificially selected lines of *Drosophila melanogaster*," *Evolutionary Ecology Research* 3: 877–888.

Medawar, P. B. 1952. *An Unsolved Problem in Biology*. London: H. K Lewis.

Monaghan, P. and N. B. Metcalfe. 2000. "Genome size and longevity," *Trends in Genetics* 16: 331–332.

Morand, S. and R. E. Ricklefs. 2001. "Genome size, longevity, and development time in birds," *Trends in Genetics* 17: 567–568.

Nealen, P. M. and R. E. Ricklefs. 2001. "Early diversification of the avian brain:body relationship," *Journal of Zoology, London* 253: 391–404.

Partridge, L. and N. H. Barton. 1993. "Evolution of aging: Testing the theory using *Drosophila*," *Genetica* 91: 89–98.

Perez-Campo, R., M. Lopez-Torres, S. Cadenas, C. Rojas, and G. Barja. 1998. "The rate of free radical production as a determinant of the rate of aging: Evidence from the comparative approach," *Journal of Comparative Physiology—B, Biochemical, Systemic, & Environmental Physiology* 168: 149–158.

Price, T. 1997. "Correlated evolution and independent contrasts," *Philosophical Transactions of the Royal Society of London—Series B: Biological Sciences* 352: 519–529.

Promislow, D. E. L. 1991. "Senescence in natural populations of mammals: A comparative study," *Evolution* 45: 1869–1887.

———. 1994. "DNA repair and the evolution of longevity: A critical analysis," *Journal of Theoretical Biology* 170: 291–300.

Promislow, D. E. L. and P. H. Harvey. 1990. "Living fast and dying young: A comparative analysis of life-history variation among mammals," *Journal of Zoology* 220: 417–437.

Promislow, D. E. L. and M. Tatar. 1998. "Mutation and senescence: Where genetics and demography meet," *Genetica* 103: 299–314.

Ricklefs, R. E. 1991. "Structures and transformations of life histories," *Functional Ecology* 5: 174–183.

———. 1992. "Embryonic development period and the prevalence of avian blood parasites," *Proceedings of the National Academy of Sciences USA* 89: 4722–4725.

———. 1993. "Sibling competition, hatching asynchrony, incubation period, and lifespan in altricial birds," *Current Ornithology* 11: 199–276.

———. 1998. "Evolutionary theories of aging: Confirmation of a fundamental prediction, with implications for the genetic basis and evolution of life span," *American Naturalist* 152: 24–44.

———. 2000a. "Density dependence, evolutionary optimization, and the diversification of avian life histories," *Condor* 102: 9–22.

———. 2000b. "Intrinsic aging-related mortality in birds," *Journal of Avian Biology* 31: 103–111.

Ricklefs, R. E. and C. E. Finch. 1995. *Aging: A Natural History*. New York: Scientific American Library.

Ricklefs, R. E. and P. M. Nealen. 1998. "Lineage-dependent rates of evolutionary diversification: Analysis of bivariate ellipses," *Functional Ecology* 12: 871–885.

Ricklefs, R. E. and A. Scheuerlein. 2001. "Comparison of age-related mortality among birds and mammals," *Experimental Gerontology* 36: 845–857.

———. 2002. "Biological implications of the Weibull and Gompertz models of aging," *Journals of Gerontology Series A—Biological Sciences and Medical Sciences* 57: B69–B76.

Ricklefs, R. E. and J. M. Starck. 1996. "Applications of phylogenetically independent contrasts: A mixed progress report," *Oikos* 77: 167–172.

Robine, J.-M., J. W. Vaupel, B. Jeune, and M. Allard. 1997. *Longevity: To the Limits and Beyond*. Berlin: Springer.

Roff, D. A. 1992. *The Evolution of Life Histories*. New York: Chapman and Hall.

———. 2002. *Life History Evolution*. Sunderland, MA: Sinauer Associates.

Rose, M. R. 1984. "Laboratory evolution of postponed senescence in *Drosophila melanogaster*," *Evolution* 38: 1004–1010.

———. 1991. *Evolutionary Biology of Aging*. New York: Oxford University Press.

Rose, M. R. and J. L. Graves, Jr. 1990. "Evolution of aging," *Review of Biological Research in Aging* 4: 3–14.

Sacher, G. A. 1959. "Relation of lifespan to brain weight and body weight in mammals," in G. E. W. Wolstenholme and M. O. Connor (eds.), *CIBA Foundation Colloquia on Aging*. Boston: Little, Brown, pp. 115–141.

———. 1977. "Life table modification and life prolongation," in C. E. Finch and L. Hayflick (eds.). *Handbook of the Biology of Aging*. New York: Van Nostrand, pp. 582–638.

———. 1978. "Evolution of longevity and survival characteristics in mammals," in E. L. Scheider (ed.), *The Genetics of Aging*. New York: Plenum, pp. 151–168.

Sæther, B.-E. 1988. "Pattern of covariation between life-history traits of European birds," *Nature* 331: 616–617.

Schaffer, W. M. 1974. "Optimal reproductive effort in fluctuating environments," *American Naturalist* 108: 783–790.

Sgrò, C. M. and L. Partridge. 2000. "Evolutionary responses of the life history of wild-caught *Drosophila melanogaster* to two standard methods of laboratory culture," *American Naturalist* 156: 341–353.

Sibley, C. G. and J. E. Ahlquist. 1990. *Phylogeny and the Classification of Birds*. New Haven, CT: Yale University Press.

Silbermann, R., and M. Tatar. 2000. "Reproductive costs of heat shock protein in transgenic *Drosophila melanogaster*," *Evolution* 54: 2038–2045.

Starck, J. M. and R. E. Ricklefs. 1998. "Variation, constraint, and phylogeny: Comparative analysis of variation in growth," in J. M. Starck and R. E. Ricklefs (eds.), *Avian Growth and Development: Evolution within the Altricial-Precocial Spectrum*. New York: Oxford University Press, pp. 247–265.

Stearns, S. C. 1983. "The impact of size and phylogeny on patterns of covariation in the life history traits of mammals," *Oikos* 41: 173–187.

———. 1992. *The Evolution of Life Histories*. New York: Oxford University Press.

Stearns, S. C. and L. Partridge. 2000. "The genetics of aging in *Drosophila*," in E. Masoro and S. Austad (eds.), *Handbook of Aging*, 5th ed. San Diego: Academic Press, pp. 345–360.

Strehler, B. L. and A. S. Mildvan. 1960. "General theory of mortality and aging," *Science* 132: 14–21.

Uno, H. 1997. "Age-related pathology and biosenescent markers in captive rhesus macaques," *Age* 20: 1–13.

Vaupel, J. W. et al. 1998. "Biodemographic trajectories of longevity," *Science* 280: 855–860.

Weinstein, B. S. and D. Ciszek. 2002. "The reserve-capacity hypothesis: Evolutionary origins and modern implications of the tradeoff between tumor-suppression and tissue-repair," *Experimental Gerontology* 37: 615–627.

Williams, G. C. 1957. "Pleiotropy, natural selection and the evolution of senescence," *Evolution* 11: 398–411.

Wilson, D. L. 1994. "The analysis of survival (mortality) data: Fitting Gompertz, Weibull, and logistic functions," *Mechanisms of Ageing and Development* 74: 15–33.