Problems with Non-Adaptive Aging Theories

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This paper summarizes the important non-adaptive aging theories and provides analysis of the logical difficulties and other problems with these theories. This material is excerpted from the book *The Evolution of Aging* ISBN 0978870905.

Most present-day biologists, and many medical researchers, physicians, and health scientists believe in one or more of the following "traditional" theories of aging. If you take a college level biology course, you will probably be taught that one or more of these traditional theories is "generally accepted."

Evolutionary theories of aging are those based on evolutionary mechanics theory. As described elsewhere, it was obvious to biologists and others familiar with many species that life span was extremely unique to individual species. Efforts to find some generic, species-independent explanation for aging had failed. Clearly, life span had to either be a part of the design of each individual species or somehow very closely related to and dependent on the specific design of the species. Since theories of evolutionary mechanics specify what sorts of design characteristics can or cannot evolve, and how organism designs result from an evolutionary process, it was reasonable and necessary to invoke evolutionary mechanics theory in searching for an explanation.

Let us review the circumstances surrounding aging theory in 1950:

Weismann's adaptive theory had failed because of major undefended incompatibility with Darwin's evolutionary mechanics. By 1950 both Darwin's theory of species origin and the orthodox theory of evolutionary mechanics had nearly universal acceptance in the scientific community. It was apparent that many, possibly most, biologists would summarily reject "out of hand" any theory of aging that conflicted with Darwin's mechanics. (This situation continues to a lesser extent today)

The generic accumulation of damage theories had failed because of incompatibility with observed characteristics, notably the inter-species life span variations.

Therefore, in 1950, the scientific situation was that the fundamental nature of aging was a total mystery, "an unsolved problem of biology."

The popular situation was much less confused. Anybody with "half a brain" could see that people wore out in virtually exactly the same way as the family Ford or Aunt Hattie's sewing machine.

Because of these circumstances, it is fair to say that new scientific theories of mammal aging needed to meet the following criteria, in order of decreasing importance:

1. Maintain compatibility with orthodox evolutionary mechanics. As a minimum, plausibly claim compatibility with orthodox theory.
2. Explain the inter-species life span variations, at least in mammals. Compatibility with other organisms was less important. Obscure, bizarre, life

span observations could be ignored. Specifically, ignore instances of biological suicide.

All the traditional theories meet these criteria.

These theories are often called "evolutionary", "non-adaptive", theories of aging because they, in effect, combine natural selection with "accumulation of damage." Natural selection explains why animals live long enough to reproduce and "accumulation of damage" explains why they age after reproducing when aging apparently has little effect on fitness.

A major difference between the accumulation of damage theories and the traditional theories is that in the traditional theories, the factors that cause aging are genetically transmitted but not "genetically programmed." (The term "genetically programmed" is used to mean an "adaptive" function such as Weismann's theory.) Because aging traits are genetically transmitted, inheritance of aging traits can be explained by the traditional theories.

Medawar's Mutation Accumulation Theory

Sir Peter Medawar (1915 – 1987) was a noted British professor of zoology and anatomy at the University of London who won the Nobel Prize in medicine (1960) for his work on acquired immunological tolerances. In Medawar's 1952 paper[i], *An Unsolved Problem of Biology,* (originally presented as a lecture at University College London) he presented an ingenious theory, which, in effect, combines the properties of the accumulation of damage theories with Weismann's evolved characteristic theory.

Medawar suggested that the force of natural selection decreases once an organism reaches an age where it has had some opportunity to reproduce. If, for example, some trait of an animal tended to be fatal prior to puberty, that trait would be very strongly selected against because most animals having that trait would die before having any progeny and would therefore not pass their adverse trait to descendents.

If, on the other hand, an animal had a trait which caused a fatal effect only after the animal had reached sexual maturity, survived to least one mating season, mated, had progeny, and nurtured and protected those progeny long enough for them to become self sufficient (assuming it is an animal that nurtures and protects young), the effect of that trait on fitness would be relatively insignificant. The negative trait would only affect the animal's ability to survive yet longer and have subsequent descendents. Such a trait would apparently only weakly affect fitness. Aging seemed to fit this description.

Medawar proposed that even if an animal did not age, that is, did not have an increased probability of death as a function of age, the numbers of adult animals of any given age would decrease exponentially because of deaths due to other causes such as predators, environmental conditions, etc. Some constant percentage of the animals of any given age would be killed in any given time period. As a metaphor, he used the random breaking and replacing of test tubes. If, in a lab with hundreds of test tubes, when a test tube is broken it is replaced with a new (age = 0) test tube, then after a while the number of test tubes of a given age in the test tube population will decline exponentially with age. Figure 4 shows the kind of survivor's curve (number as a function of age) that would be expected for the test tubes (or ageless animals) as presented in Medawar's paper. This behavior is known as an *exponential decline* and is characterized as having a *half-life*. If

half of the animals die in four years (as shown here), then half of the remaining half will die in another four years, and so forth. Very old animals would be very rare even in a non-aging species.

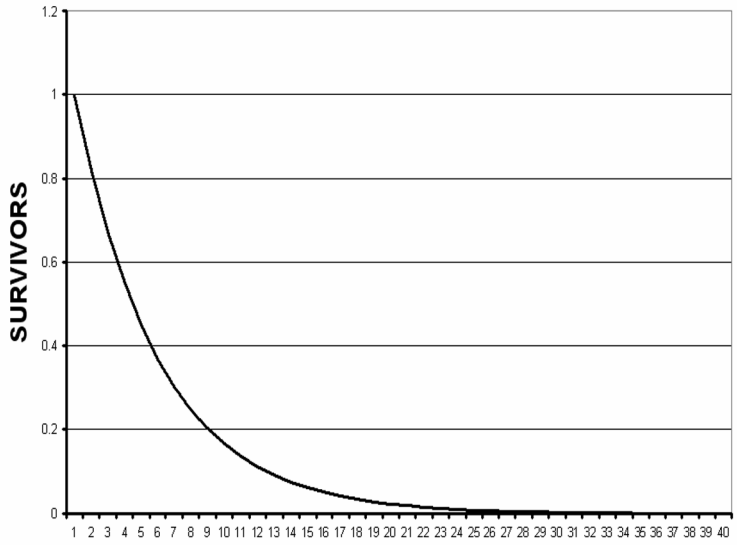

Figure 4

The number of progeny any given non-aging animal would produce was assumed by Medawar to increase linearly with age. An ageless animal would tend statistically to have the same number of progeny every year from puberty to death. The total number of progeny (on average) produced by animals, as a function of their age, would therefore look like Figure 5 in which total descendents produced by an animal are zero until puberty and then increase with age. Puberty is shown here as occurring at age 6. It is assumed that reproductive vigor in an ageless animal would not change with age. (We could have assumed that general reproductive effectiveness and aging were different, independent phenomena. However, an evolved characteristic that causes a decline in reproductive effectiveness has the same problems with Darwin's mechanics as aging and the same arguments, pro and con, apply.)

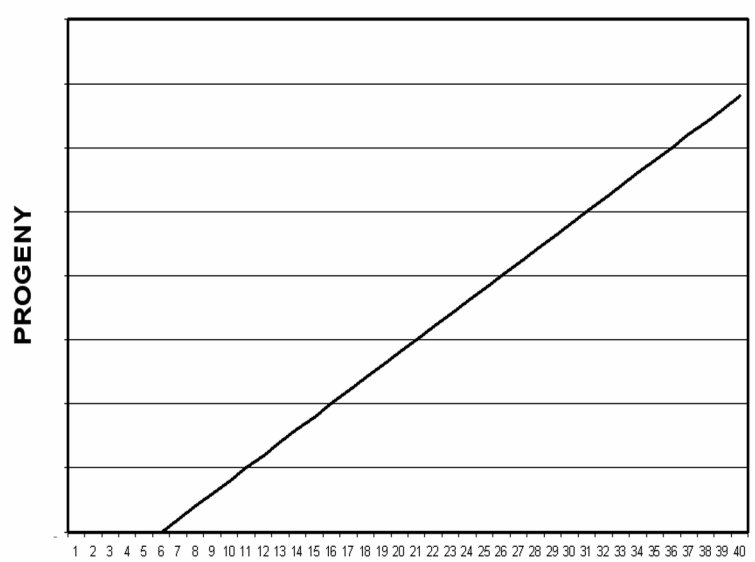

Figure 5

If we multiply the number of progeny produced by animals of a given age by the number of animals at that age we can determine the *reproductive effect* contributed by each age group or *cohort*. Since the number of animals is exponentially decreasing with age and the number of progeny is only linearly increasing with age, the reproductive effect of older animals (and therefore their apparent evolutionary impact) declines. Graphically, this would look like Figure 6 in which reproductive effect rises from zero at puberty to a maximum and then declines.

Figure 6

These curves, Figures 4-6, represent the *traditional model* of a non-aging species. Medawar's paper was almost entirely devoted to the development of this model.

You will note that there are no numbers specified on the vertical axes of Figures 5 and 6. Some species, subject to high death rates due to predators or other cause would need a correspondingly high birth rate to survive. Other species would need a lower birth rate.

Medawar proposed that aging was caused by random mutations causing adverse aging characteristics. In effect, aging was caused by an assortment of genetic diseases, each of which has adverse symptoms only at advanced ages. Medawar discussed in this connection human genetic diseases such as Huntington's chorea, which does have increasing symptoms with age. While Huntington's and other genetic diseases each individually only affect part of the population, it is easy to imagine that other adverse genetic conditions could have spread to encompass essentially the entire population and thus be considered a "natural" part of aging.

Medawar's theory was written in response to, and as an alternative for, Weismann's earlier programmed death theory, and neatly reverses the main disadvantages of Weismann's theory turning them into advantages. Most importantly, Medawar's theory does not require a violation of Darwin's natural selection theory. By 1952 (and still to a lesser extent today) many biologists considered the natural selection theory to be essentially infallible, "a given." Second, if you reject Weismann because most wild animals do not live long enough to die of old age, and that therefore programmed death cannot be an evolved characteristic, then you should accept Medawar's idea that mutations can accumulate causing death of old age. These two ideas are opposite sides of the same coin.

By combining evolution (to explain early longevity) and accumulation of damaging mutations (to explain lack of later longevity), Medawar neatly sidestepped Darwin's dilemma, while still explaining some of the inter-species differences in aging. Since Medawar's theory tied aging to sexual maturity and reproduction, it provided a much better fit to observed characteristics of animals.

Medawar's theory is still respected today.

It is important to note that, unlike the earlier wear out or entropy theories, the mutation accumulation theory does not suppose any fundamental, inescapable, cause of aging. Aging is the result of adverse mutations. If these mutations could be removed or contravened, longevity could be extended, perhaps indefinitely.

Furthermore, aging affects only what might be described as "maintenance" functions, namely, those activities needed merely to maintain the condition of an already developed, fully functional, adult, organism. The scope and difficulty of maintenance would appear to be relatively minor, even trivial when compared to the activities involved in the growth, development, and normal day-to-day functioning of an organism.

Many of the activities involved in maintenance, such as cell division and replacement, would appear to largely duplicate those involved in the original growth and development. Therefore, it is reasonable to believe that a relatively small number of genes are exclusively associated with the maintenance function, such as genes that control initiation of cell division only in a maintenance context. It is only these genes that are affected by the adverse mutations.

Finally, in relatively longer-lived animals, only those few maintenance functions involved in relatively long-term maintenance are adversely mutated since the shorter-

term functions are already fully operational. Even the shortest-lived mammal would have needs for maintenance. Wounds heal. Hair and claws grow. Short-lived cells are replaced.

Medawar's theory therefore suggested that medical intervention that contravened the relatively small number of adversely mutated functions was at least a possibility.

We know from modern genetics (See Genetics.) that related organisms such as mammals have a very high degree of similarity in their genes, which leads to the conclusion that they share very similar logical processes or "genetic programs." The differences between different mammals are directed by relatively minor genetic differences that in turn cause differences mainly in degree or magnitude rather than in the logic. In other words, mice and men probably have the same "maintenance program." It is just that the program in mice is less aggressive and effective than the program in humans so lab mice live perhaps 14 months after reaching maturity and humans live about 60 years after maturity.

The idea that mutations could occur that would cause adverse effects has been verified by substantial work that has been done in an effort to understand human genetic diseases. (See Genetics.) Many human diseases have been traced to errors that have occurred in genetic code. Symptoms of some genetic diseases are even age-related and tend to increase with age.

However, there are problems with the idea that such mutations cause aging as put forth in the mutation accumulation theory:

The mutation accumulation theory only works if the fitness effect of aging is negligible. Mutation accumulation says that "absence-of-aging" does not evolve because the beneficial effect of absence-of-aging is small enough that mutations that contravene absence-of-aging can accumulate and not be selected out. This would *also* apply to *any other trait* that had the same or less beneficial effect. If "slightly longer claws" is very mildly beneficial then "slightly shorter claws" is only very mildly adverse. Evolution is still able to evolve slightly longer claws. Darwin's theory of tiny incremental steps requires that very small beneficial characteristics can evolve. Medawar's hypothesis depends on the idea that aging can exist solely because of the declining fitness effect of adverse events with age and therefore depends on the idea that aging has a negligible fitness impact.

Although "death of old age" probably only occurs frequently in species that have few predators, aging in mammals obviously has effects other than death that would affect fitness and therefore death rate. Aging in mammals affects strength, speed, agility, and other factors that affect fitness even in relatively young animals. It therefore does not appear plausible that aging has a negligible effect on fitness.

If we assume a Medawar scenario in which a species (e.g. mouse) lives in a brutally vicious world where virtually no animals survive long enough to die of old age, then even a very minor difference in a survival trait (speed, strength, etc.) would presumably influence the probability of survival. Such minor differences due to aging could plausibly be expected to appear at very young ages.

If we assume a species (e.g. elephant) that has relatively few predators and therefore lives a relatively peaceful existence in the wild, then presumably death of old age is a

fitness factor. These issues led to the subsequent development of the antagonistic pleiotropy theory described in the next section.

Another problem is that a number of diverse non-mammal organisms (salmon, octopus, and bamboo – see chapter 6) display instances of death closely following an act of sexual reproduction. Death in these species appears to be *controlled* by the reproductive function or controlled by whatever triggers reproduction as opposed to calendar age. Aging in mammals, as a gradual, diffuse, and multi-tissue degradation loosely tied to sexual maturity, could plausibly result from random mutations variably degrading a family of beneficial maintenance characteristics. However, this scenario does not appear to work for bamboo and salmon, which exhibit what appears to be programmed death tied directly to reproduction and clearly not associated with a generalized maintenance function. How could suicidal behavior result from the random mutation degradation of a beneficial characteristic? What beneficial characteristic was degraded to result in biological suicide?

The basic problem is that mutation accumulation is too simple a mechanism to explain the detail in the observed aging processes of different species. As we will see in later sections of this book, the traditional model of non-aging species also grossly understates the negative fitness effects of aging in actual animals.

Some gerontologists think of Medawar as a major prophet, essentially the father of modern gerontology. Some of us think that eventually Medawar will be found to have had a major negative effect on medicine by pointing many generations of researchers in the wrong direction. Time will tell.

Williams' Antagonistic Pleiotropy Theory

George Williams, then a professor at the Michigan State University, published a paper[ii] in 1957 titled *Pleiotropy, Natural Selection, and the Evolution of Senescence*. *Pleiotropy* is defined as a situation in which a single *allele* or form of a gene (see Genetics) may affect more than one trait. In human genetic diseases, a defect in a single gene typically can affect a number of traits and have simultaneous diverse symptoms such as nerve and vision problems, bone deficiencies, and skin changes. In general, a single gene can be activated in more than one tissue and therefore a defect in a gene can affect more than one tissue.

Williams specifically criticized Medawar's assumption that the fitness effect of aging was negligible:

> "No one would consider a man in his thirties senile, yet, according to athletic records and life tables, senescence is rampant during this decade. Surely this part of the human life-cycle concerns natural selection. … It is inconceivable in modern evolutionary theory that senescence, such as operates in man between the ages of thirty and forty is selectively irrelevant."

Williams proposed that aging was caused by the combined effect of many pleiotropic genes that each had a beneficial effect in an animal's youth but had an adverse side effect in older age.

Williams' concept was similar to Medawar's in that it built on the idea that adverse effects have a progressively smaller impact on fitness as an animal gets older. A gene

resulting from natural selection could have a rather catastrophic negative effect on an older animal if the negative effect was balanced by an even relatively minor beneficial effect on younger animals.

Williams' theory, like Medawar's, provided a better fit to the observed inter-species variations in aging than the accumulation of damage theories while simultaneously avoiding Darwin's dilemma and did not depend on accumulation of adverse mutations in equilibrium with out-selection. Williams' theory avoided the apparent difficulty in the mutation accumulation theory that required the negative fitness effect of aging to be negligible because the assumed beneficial effect of the pleiotropic genes balanced the negative (aging) effect. Williams predicted that species with younger age of sexual maturity and more vigorous reproduction traits would tend to have shorter life spans.

One consequence of Williams' theory was that prospects for any significant treatment of the fundamental causes of aging were considered negligible because of the assumed large number of antagonistic genes and the assumption that the harmful aging genes had beneficial and probably essential functions in youth. Hopes that only a relatively small number of factors causing aging would be eventually found and successfully treated as suggested by the mutation accumulation theory were therefore, according to Williams, misplaced. Williams said it this way:

> "Any such small number of primary physiological factors is a logical *impossibility* if the assumptions made in the present study are valid. This conclusion banishes the "*fountain of youth*" to the limbo of *scientific impossibilities* where other human aspirations, like the perpetual motion machine and Laplace's 'superman' have already been placed by other theoretical considerations." [*Emphasis* added.]

Clearly, believers in Williams' theory, which is still popular, also believe that anti-aging research is a fundamentally foolish endeavor, a chase after the fountain of youth.

The antagonistic pleiotropy theory has a number of difficulties.

One problem with the antagonistic pleiotropy theory is that the force of natural selection, although apparently progressively smaller in older individuals is not zero, even according to the traditional model. (This was the genesis of the antagonistic pleiotropy theory.) Evolution would therefore presumably be trying to find ways of accomplishing the beneficial effects *without* the adverse (aging) side effects. Why would it not succeed? One obvious answer is that *there is no way* to accomplish the presumably essential beneficial effect without the side effect, (a conclusion that is very pessimistic regarding successful treatment of aging).

It seems implausible that this "unavoidable side effect" difficulty would only affect maintenance of the condition of an adult organism when the tasks that have to be performed in the development and growth of an organism are apparently so much more complex and difficult.

Another difficulty with the antagonistic pleiotropy theory is the very great variation in observed aging characteristics between otherwise similar animals such as similar birds and fish. If aging is a side effect of genes that have a beneficial effect in youth, then why would the adverse side effects of such presumably similar genes be so different? If the side effect is an unavoidable consequence of the beneficial effect, then why would a very similar animal need a different gene and display a different side effect?

The antagonistic pleiotropy theory also appears to have a fundamental conflict with modern genetics (See Genetics.) as follows. The "antagonistic" aspect of the theory works. Essentially any feature of an organism has tradeoffs. Faster is antagonistic to stronger.

"Pleiotropy" works. Genes are known to affect multiple tissues. The problem is that this theory proposes a sort of *time-sequential* antagonistic pleiotropy in which the *same* gene has beneficial net value at one stage in an animal's life and adverse net consequences at another stage.

The difficulty with this is that we now know that genes are activated and deactivated in accordance with a very complex genetically controlled system of logic or program. Essentially any gene would have adverse consequences if activated in the wrong tissue, or under the wrong circumstances, or at the wrong stage in an organism's life just as failure to activate the gene at the proper times in the proper tissues has adverse consequences. Cancer is an illustration of one of the consequences of activating genes at the wrong place or time. Many genetic diseases result from failure to activate a gene at the proper time.

The genetic program is apparently capable of coordinating the vastly different activities that must take place in the various developmental stages of an organism. Grossly different combinations of genes must be activated during, say, embryonic development than in late childhood because of the grossly different growth activities that must be performed. There does not appear to be any plausible reason to believe that the activation program would fail to deactivate a gene that would cause a problem in later adulthood if it worked so well in programming the differences between all the other stages in an animal's life, especially when the differences between other stages are so much greater than between "adult" and "older adult." Why wouldn't time-sequential antagonistic pleiotropy generally be more of a problem in early development where there is a greater need for age sequential changes?

In many ways, Williams' theory is a restatement of Darwin's circular "explanation": There must be some individual benefit compensating for the individual disadvantage of aging merely and entirely because orthodox theory says so.

Despite the major difficulties, the antagonistic pleiotropy theory is respected among some current scientists. This has a serious negative impact on anti-aging research since, according to Williams, anti-aging medicine is impossible.

Disposable Soma Theory

In 1977, a statistician named Thomas Kirkwood (now a biologist and professor of medicine at the University of Newcastle) published his *disposable soma theory*[iii] of aging. Kirkwood's idea was that organisms only have a limited amount of energy that has to be divided between reproductive activities and the maintenance of the non-reproductive aspects of the organism (soma). Aging is the result of natural degrading processes that result in accumulation of damage but the damage can be repaired by the organism at the expense of reproductive effort. Because of the declining evolutionary impact of adverse events on older animals (Medawar's hypothesis), a tradeoff exists in which it does not make sense for an organism to invest effort in maintenance (at the

expense of reproductive activity) to result in living much beyond the initial breeding years.

This theory also, in effect, combines the apparent declining force of natural selection after breeding age is reached with accumulation of damage, and additionally explains a relationship between reproduction and life span while avoiding conflict with Darwin's mechanics.

The disposable soma theory seems to make sense on a philosophical level but has many severe problems if one looks at it in any detail. One obvious issue is that it has not been demonstrated that "maintenance and repair" actually takes a significant amount of effort or resources when compared to the energy and resources required by the day-to-day existence of an organism much less the initial growth of the organism. Why would replacing a few cells take more effort or resources than producing trillions of cells in the first place or providing for their routine operation?

Another problem with the disposable soma theory is that it is not obvious why effort or energy spent in reproduction in an animal's early years would necessarily decrease the energy available in later years for "repair." One would think a post-menopausal woman would cease aging or even become stronger as a result of the absence of the resource drain caused by reproductive effort. Instead, damage appears to increase exponentially.

Another obvious problem is that by essentially any method of accounting females use more resources and energy in reproduction than males. Why don't males therefore live longer than females? A fan of the disposable soma theory once suggested to me that males, by amazing coincidence, spend as much extra energy and resources protecting their mates and young as females spend in reproduction and therefore have approximately the same life span. If you believe this, I have some stock in the Brooklyn Bridge I would like to sell to you!

A fundamental difficulty is that animals obtain the resources and energy they need from eating. A pregnant animal needs more resources and therefore eats more. An animal that is growing needs more resources and therefore eats more. If indeed an animal needed significant resources to perform maintenance and repair functions why would it not simply eat more to provide those resources?

One way out of this problem is to assume that some unknown property that increases reproductive effectiveness somehow, for unknown reasons, decreases life span by causing deterioration in later years. This is very similar to the antagonistic pleiotropy theory. Aging must be a hidden unavoidable side effect of reproduction. Of course this amounts to a restatement of Darwin's "explanation": There must be some hidden individual benefit to offset the individual disadvantage of aging. In fact, some traditional biologists such as Leonid Gavrilov, of the Center on Aging at the University of Chicago, consider the disposable soma theory to be a "version of" the antagonistic pleiotropy theory and a "widowed concept."

Common Problems with Traditional Evolutionary Theories

All of the traditional theories depend on the idea that the evolutionary importance of individuals in a non-aging population declines with calendar age and that therefore natural selection allows the existence of progressively more negative traits with age, up to

and including "death of old age." This idea, the traditional model, is based on a very important assumption, namely, that the evolutionary contribution of each individual animal can be accurately described by "reproductive effect" as described graphically in figure 6.

You will recall that figure 6 reflects the combined effect of the reproductive contribution we could expect from individual animals (figure 5) and the rate at which we could expect the non-aging animals to die off (figure 4). Because the population of older animals declines more rapidly with calendar age than the reproductive contribution of older individuals increases with calendar age, the net effect (figure 6) is that evolutionary importance declines with calendar age beyond some point that varies with age of puberty. This traditional model of a non-aging species is over-simplified and ignores a number of important characteristics of actual animals, all of which tend to increase the evolutionary importance of *older* animals.

First, the characteristics of Medawar's test tubes (and non-aging animals) were presumed to be constant and did not change with the age of the test tube. However, the characteristics of actual non-aging animals would change greatly with calendar age, at least between puberty and "maturity."

Suppose we had a group of prehistoric 15-year-old humans and another group of 20-year-olds. According to the reproductive effect concept, these two populations are equivalent and have the same evolutionary importance. In actuality, the 20-year-olds are superior with regard to essentially any survival characteristic. They are stronger, faster, and smarter. They would win in any competitive situation. It is obvious that a 20-year-old has a greater chance for survival than a 15-year-old, everything else being equal. Therefore, death rates would nominally tend to decline with calendar age in the interval between 15 and 20 as opposed to remaining constant as proposed by the traditional model. (In actual animals, still additional complexity such as protection-of-young might affect this.)

There is a more profound difficulty. The curve of figure 6 assumes that ten young individuals each producing one descendent have the same evolutionary importance as one older individual producing ten descendents. Because they are more mature, the 20-year-olds more fully exhibit *adult* survival characteristics. A case could therefore be made that a single 20-year-old has more evolutionary importance than any number of 15-year-olds. The reproductive effect concept does not take into account this "maturity factor."

This is the same argument made against Weismann's theory. Natural selection can not operate relative to a characteristic that is not expressed. Adult characteristics are not fully expressed in juveniles. Therefore, adults are required in order to evolve adult characteristics. Evolutionary importance is not the same as reproductive effect.

Second, the individuals in the population of Medawar's test tubes were presumed to be identical and have identical characteristics. The characteristics of actual animals *vary*. More specifically their characteristics regarding capacity for survival vary. Therefore, their probability of survival varies.

The traditional model as shown in figure 4 assumes that the probability of death for an ageless animal is a constant, independent of calendar age. That is, older animals are just as likely to die in any given time period as younger animals. While true for test tubes,

this idea is incompatible with the theory of natural selection. According to Darwin, animals that are more fit are less likely to die than animals that are less fit. Therefore, in any given time period, more of the less fit animals in a population would die. At the end of the period, the surviving animals would therefore, on average, be *more fit* than at the beginning of the period. In other words, average fitness of a non-aging population cohort *increases* with calendar age. Because older animals are more fit, they are also less likely to die relative to younger animals. The probability of death therefore *decreases* with calendar age in a non-aging population. Figure 4 therefore *does not* accurately represent the relative prevalence of older individuals in a population of actual non-aging animals.

Third, more complex animals have other characteristics that tend to increase the evolutionary importance of older animals. Mating rituals and other societal behavior traits such as those that result in "pecking order" tend to reduce the relative chance that younger animals will reproduce and in some cases also reduce the relative probability of death for older individuals. The old king is far less likely to die in the war than the young foot soldier, especially if the old king does not age.

Animals learn from experience. Older non-aging animals are therefore less likely to die than genetically identical younger animals having less experience.

Finally, the increase in fitness with calendar age has a multiplying effect. Not only did the older individuals survive longer and have more descendants because they are more fit, but their descendents are also likely to be more fit and therefore survive longer, and their descendents descendents are likely to survive longer. This multiplication factor would appear to cause the *evolutionary importance of individuals to increase exponentially with age*.

If we attempted to modify figure 6 to develop an "evolutionary importance" curve based on these factors would it still decline with calendar age? Would the increasing evolutionary importance of older individuals compensate for their decreasing numbers?

It should be clear from the above discussion that the traditional model grossly underestimates the evolutionary impact of older non-aging individuals, especially in more complex organisms such as mammals. Further, the actual shape of an evolutionary importance curve is dependent on complex interactions that vary from species to species and probably even vary depending on the species' situation regarding predators and other factors that affect life span. In effect, the traditional evolutionary theories of aging embrace the convenient aspects of Darwin's mechanics while ignoring the inconvenient aspects.

Could it be that nature *needs* aging or other life span control mechanism to prevent a relatively few older individuals from dominating the evolutionary process?

These concepts are further developed in the section on evolvability theory.

Experimental attempts to confirm the traditional theories have been generally unsuccessful. For example, investigators have been unable to find a rigid, fixed connection between reproduction and lifespan as would be expected by the disposable soma theory.

So where do the traditional theories leave us? What collective wisdom does biology have for the rest of the world regarding the main questions listed earlier? We can summarize this as follows:

- Regarding the nature of aging: We don't really know. There are a number of different theories that attack each other. The theories all have logical flaws. Efforts at experimental confirmation have been generally unsuccessful. Aging is *still* "an unsolved problem of biology."
- Regarding the practical aspects: The general consensus seems to be that treatable common factors are either very unlikely or possibly even "impossible." Of course, the credibility of this finding is degraded by the inability to definitively determine even the basic nature of aging.

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[i] Medawar, P.B, *An Unsolved Problem of Biology*., 1952. H.K. Lewis & Co., London.

[ii] Williams, G *Pleiotropy, natural selection and the evolution of senescence,*. 1957. *Evolution* 11, 398-411

[iii] Kirkwood T.B.L. & F.R.S. Holliday, *The evolution of ageing and longevity*, 1979. *Proceedings of the Royal Society of London B* 205: 531-546