Ageing Research Reviews 12 (2013) 214–225

Contents lists available at SciVerse ScienceDirect

Ageing Research Reviews

journal homepage: www.elsevier.com/locate/arr

Review

Senescence in natural populations of animals: Widespread evidence and its implications for bio-gerontology

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ARTICLE INFO

Article history:
Received 15 May 2012
Received in revised form 24 July 2012
Accepted 30 July 2012
Available online 4 August 2012

Keywords:
Antagonistic pleiotropy
Disposable soma
Ecology
Evolution
Free-living populations
Wild animals

ABSTRACT

That senescence is rarely, if ever, observed in natural populations is an oft-quoted fallacy within bio-gerontology. We identify the roots of this fallacy in the otherwise seminal works of Medawar and Comfort, and explain that under antagonistic pleiotropy or disposable soma explanations for the evolution of senescence there is no reason why senescence cannot evolve to be manifest within the life expectancies of wild organisms. The recent emergence of long-term field studies presents irrefutable evidence that senescence is commonly detected in nature. We found such evidence in 175 different animal species from 340 separate studies. Although the bulk of this evidence comes from birds and mammals, we also found evidence for senescence in other vertebrates and insects. We describe how high-quality longitudinal field data allow us to test evolutionary explanations for differences in senescence between the sexes and among traits and individuals. Recent studies indicate that genes, prior environment and investment in growth and reproduction influence aging rates in the wild. We argue that – with the fallacy that wild animals do not senesce finally dead and buried – collaborations between bio-gerontologists and field biologists can begin to test the ecological generality of purportedly 'public' mechanisms regulating aging in laboratory models.

1. Introduction: Wild animals fail to senesce – a brief history of the fallacy

1.1. Medawar and the origins of the fallacy

The notion that animals in nature do not senesce – that environmental challenges whether they be predators, floods, famine or something else kill all wild animals before aging can take a measurable toll – can be traced at least as far back as Peter Medawar's first full theoretical treatment of the evolution of senescence (Medawar, 1952). This idea is clearly fallacious as we will show, undercut by both subsequent theoretical work and copious empirical data from a wide range of animals, yet it was crucial to the development of Medawar's central hypothesis about the genetic mechanism by which senescence could evolve.

Medawar's paradigm-shifting contribution to the evolutionary understanding of aging was his insight that due to the inevitability of death from environmentally driven causes, the ability of natural selection to favour or disfavour genetically-based traits depended on the age at which those traits appeared. As he phrased it, "the force of natural selection weakens with increasing age". This specific insight forms the basis of all subsequent analyses of the evolution of senescence. Based on this idea, Medawar proposed a particular genetic mechanism – that senescence evolves by the accumulation in the genome of harmful alleles, such as those predisposing to cancer, dementia, or heart disease, whose effects appear sufficiently late in life that "the force of natural selection will be too attenuated to oppose their establishment and spread." In other words, such deleterious alleles could spread only when the probability that they could have a measurable effect on reproductive success was very low. Consequently observable senescence should only occur at ages "which the great majority of the population do not reach" (all quotes from Medawar, 1952). Only under conditions in which animals are protected from natural hazards, he theorized, such that they commonly survive to ages they would very seldom or never achieve in the wild, would senescence be manifest. He was quite specific about this latter point, repeating it four times in the same monograph. To cite one of these,

> "Whether animals *can*, or cannot, reveal an innate deterioration is almost literally a domestic problem; the *fact* is that under the

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http://dx.doi.org/10.1016/j.arr.2012.07.004

exactions of natural life they do not do so. They simply do not live that long."
– Medawar, 1952 (italics in original)

As evidence for this claim, Medawar cites a personal communication from field mammalogist Dennis Chitty, in which Chitty states that "wild mammals of any perceptible degree of senility" seldom turned up in his traps, and if they did he assumed that some cause other than senescence (e.g. infection, injury) was responsible for their condition (Medawar, 1952). For wild birds, Medawar's source was David Lack, the pioneering field ornithologist. Lack had noted in several papers in the 1940's, that the probability of death seemed to be independent of age in birds in nature, implying that senescence, at least in its actuarial sense, did not occur (Lack, 1943a,b). Medawar's claim was repeated in the first comprehensive consideration of senescence as a general biological phenomenon – Alex Comfort's classic tome, *The Biology of Senescence* (Comfort, 1956). Since then, the idea that senescence fails to occur in nature has been often repeated within bio-gerontology (e.g. Hayflick, 2000; Kirkwood and Austad, 2000; Rose, 1991).

In Medawar and Comfort's time there was in fact scant evidence for senescence in the wild because few detailed long-term studies of natural populations existed. Those that were available tended to be short-term, cross-sectional and often did not know the exact age of adults in the population. It has since become apparent that long-term studies that monitor marked individuals from birth to death are required to reliably detect and investigate senescence in the wild. In an earlier monograph on aging and death published in 1946, Medawar seems to acknowledge this, highlighting the importance of studies of exactly this kind:

"No-one has yet made a systematic study of whether even mammals *in their natural habitat* do indeed live long enough to reach a moderate though certifiable degree of senility. . . The difficulties of constructing life tables in the wild are technically formidable, but they must be solved."
– Medawar, 1946 (italics in original)

As we will demonstrate, despite Medawar and Comfort's subsequent assertions to the contrary, there was never any theoretical reason to adduce the absence of senescence in the wild (Williams, 1957), and there has been an avalanche of recent data from wild populations clearly demonstrating the senescence does indeed occur commonly in natural populations (Bennett and Owens, 2002; Brunet-Rossinni and Austad, 2006; Nussey et al., 2008a).

1.2. Unravelling the fallacy

Quite probably, Medawar's belief that animals in nature failed to senesce allowed him to dismiss one clear implication of his insight. Whilst he focused nearly exclusively on the accumulation of late-acting deleterious alleles, he mentioned in passing – even giving an example – that because of the gradual weakening strength of natural selection with age, "a relative small advantage conferred early [in life]. . .may outweigh a catastrophic disadvantage withheld until later" (Medawar, 1952). This, of course, is a succinct description of an idea George Williams later developed: antagonistic pleiotropy, in which alleles with beneficial effects on survival or reproduction early in life can be actively favoured by natural selection despite negative effects on health and fitness later in life (Williams, 1957). So although Medawar described antagonistic pleiotropy, he failed to appreciate its significance. In summarizing the implications of his theory at the end of his 1952 paper, he never mentioned it, focusing instead on the accumulation of late-acting alleles and on hypothetical modifier alleles that might postpone the effects of deleterious alleles to ages at which they would be effectively neutral (Medawar, 1952). However, if antagonistic pleiotropy is a common mechanism of senescence, then there is no necessary expectation that wild animals will fail to display progressive deterioration of health in later life or that such deterioration need be subtle. Williams' clearly appreciated this, referring to Comfort's argument that senescence was 'outside the developmental program that concerns natural selection', as follows:

"I believe that this theory is incorrect. Its fallacy lies in the confusion of the process of senescence with the state of senility, and in an inaccurate conception of the relationship of age to selection processes."
– Williams, 1957

By way of example, Williams noted that an examination of athletic records reveals 'rampant' senescence in humans as early as their 30's, a period which no-one could disagree humans commonly reached even in a state of nature (Williams, 1957). Williams highlighted two crucial points that alter the way we think about senescence in natural populations. First, in an evolutionary sense, senescence is the progressive physiological process of deterioration leading to a decline in fitness with age, which is not synonymous with infirmity and frailty associated with extreme old age in humans and captive animals. Classical evolutionary theory does not refer to or consider a state of senility in very late adulthood, rather it predicts that senescence should begin at the age of sexual maturity and progress from that point as the force of natural selection weakens (Hamilton, 1966; Williams, 1957). Second, under antagonistic pleiotropy, natural selection is expected to favour the evolution of life histories in which senescence has a detectable fitness cost within the natural life expectancies of organisms, as long as the genes associated with this deterioration confer a sufficient fitness benefit in earlier life.

Kirkwood's (1977) disposable soma theory of senescence is also compatible with the manifestation of senescence in the wild. Developed from a different theoretical framework – optimization theory as opposed to population genetics theory – the disposable soma theory makes largely similar predictions to antagonistic pleiotropy. Briefly, it hypothesizes that because critical resources such as energy are limited, natural selection will adjust the allocation of cellular and physiological resources between the fundamental processes of somatic maintenance and reproduction appropriately for an organism's ecological context (Kirkwood, 1977; Kirkwood and Rose, 1991). Since natural selection is expected to weaken with age, selection will tend to favour investment in early reproduction over long-term somatic maintenance, and senescence will result (Kirkwood and Rose, 1991). Antagonistic pleiotropy and disposable soma theories, often referred to together as 'life history' theories of aging (Partridge and Barton, 1996), now form the basis of the majority of theoretical work on the evolution of aging. This emerging body of evolutionary theory now clearly demonstrates that selection can favour senescence occurring within a species' natural life expectancy, and that the pattern of senescence can vary depending on the specifics of organism's life history, ecology and the interplay between "intrinsic" and "extrinsic" factors influencing mortality (e.g. Abrams and Ludwig, 1995; Baudisch, 2008; Cichon, 2001; Mangel, 2008; McNamara et al., 2009; Williams and Day, 2003).

Current empirical support from model laboratory organisms for disposable soma theory and antagonistic pleiotropy as mechanisms of senescence is dramatically stronger than for mutation accumulation. For instance, many single gene mutations known to extend life in model laboratory organisms have detrimental effects on early components of Darwinian fitness (Table 1). To pick one illuminating example, a partial loss of function mutation in *daf-2*, the *Caenorhabditis elegans* ortholog of the vertebrate insulin/IGF receptor, doubles the longevity of worms in the laboratory, yet its depressive effects on early reproduction (Chen et al., 2007) cause it to be quickly