Comparison between two paradigms about aging

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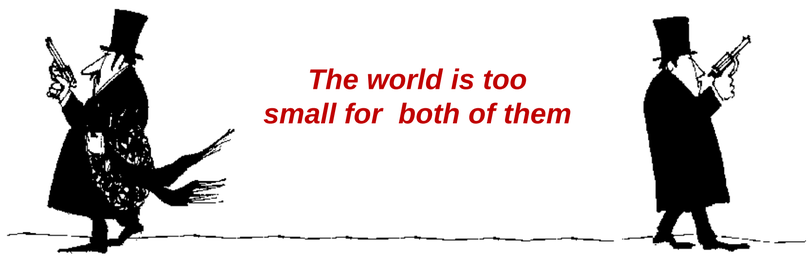
Definitions:
IMICAW = Increasing Mortality with Increasing Chronological Age in the Wild [1], alias "actuarial senescence in the wild" [2]
IMICAC = Increasing Mortality with Increasing Chronological Age in Captivity [1]
"aging" or "senescence" = imprecise term that includes both IMICAW and IMICAC [1,3]
"state of senility" = the deteriorated state of individuals in artificially protected conditions with low mortality (captivity, civilization, etc.) at ages rarely or never observable in the wild, namely the state of individuals with age-related reduced fitness to wild conditions smaller than an arbitrarily established value [4,5]
m_e = extrinsic mortality (= mortality due to environmental factors) [6]
m_i = intrinsic mortality (= mortality due to intrinsic factor, i.e. senescence) [6]
P_s = proportion of deaths due to intrinsic mortality [6]
t-gene = a harmful gene that acts only from age t [1]
MAH = Mutation Accumulation Hypothesis [7-11]
AP H = Antagonistic Pleiotropy Hypothesis [4,12]
DSH = Disposable Soma Hypothesis [13,14]
} **+ Wear and tear hypotheses, Stochastic hypothesis, etc. (1st paradigm)**
AAH = Adaptive Aging (or, more precisely, IMICAW) Hypothesis [1,5,15-18] (2nd paradigm)



	First paradigm (Aging is not adaptive) [4,7-14,19]	Second paradigm (IMICAW / aging is adaptive) [1,5,15-18]
I	The evident alterations of "aging" or "senescence", in the meaning of "state of senility" [4], are totally or almost incompatible with the survival in the wild.	In the study of evolutionary mechanisms it is illogical to have as principal object an artificial condition, the "state of senility", totally or almost absent in the wild and, hence, not or little influenced by natural selection.
II	So, "senescence", in the meaning of the "state of senility", being nearly absent in the wild, is not object of efficacious selection.	IMICAW, a documented reality [6,20] (Fig. 1), is influenced by natural selection and is, consequently, a proper object for the analysis of evolutionary mechanisms.
III	Moreover, "any hypothetical 'accelerating aging gene' would be disadvantageous to the individual. It is therefore difficult to see how genes for accelerated aging could be maintained in stable equilibrium, as individuals in whom the genes were inactivated by mutation would enjoy a selection advantage." [19]	An IMICAW-causing gene reduces the individual fitness but this does not mean inevitably that the inclusive fitness of the same gene is negative. Only when a gene has no effect on the fitness of other individuals where the gene is present, the evaluation of its inclusive fitness may be disregarded. In the particular case of an IMICAW-causing gene it has been shown that such a gene may, in certain conditions, have a positive inclusive fitness [1,5].
IV	Therefore, "senescence" is the outcome of insufficient selection (against harmful genes for MAH, antagonistic pleiotropic genes for APH, physiological, biochemical or environmental constraints for DSH, etc.) .	Therefore, IMICAW is not the result of insufficient selection but of a balance between positive and negative selecting factors .
V	From this, it can be deduced that the less efficacious is the remaining selection, in particular when m_e is greater, the more rapid must be the onset of the "senescence". With m_e at its greatest values, P_s should be at the highest. But, this prediction is falsified by data from natural observation [6] (Fig. 2) with no sound justification for this contradiction.	From this, it can be deduced that in the case of a weaker favorable selection, e.g. as when m_e is high, an IMICAW-causing gene is less selectively favored and, therefore, P_s is reduced. With m_e at its greatest values, P_s should be zero [1,5]. These apparently paradoxical predictions, contrary to those of the first paradigm, are confirmed by data from natural observation [6] (Fig. 2).
VI	There is no explanation for the existence of non-IMICAW species and, indeed, they should not exist for MAH, APH, DSH, etc. (except when there is no separation between soma and germ line [22]).	The existence of non-IMICAW species is predicted in well-defined and common conditions [1,5].
VII	In short, "senescence", in the meaning of "state of senility", is the result of insufficient selection pro a greater longevity and against noxious agents.	"Age changes" in their initial expression coincide with the greatest IMICAW alterations observable in the wild, while in their advanced manifestation are the artificial (by reduction of m_e) utmost and unnatural amplification of IMICAW alterations [5]. The "state of senility" is the "age changes" plus the effects of t-genes insufficiently eliminated by natural selection in the wild because of the tardiness of their manifestation ("age-associated diseases") plus damages by wrong lifestyles [5] (category 2 in Masoro's classification [23]).
VIII	So, to contrast "senescence", identifying the damaging factors (harmful genes, pleiotropic genes, physiological alterations such as oxidant factors, etc.) is an indispensable prerequisite.	Since IMICAW is determined by genes that are in part favored by natural selection, it is necessary to investigate the physiological mechanisms that reduce the fitness in the wild and that cause the "age changes" in conditions of low mortality. The existence of these mechanisms is the main prediction of AAH. For the "age-associated diseases", plainly interpreted as the outcome of t-genes effects, it is appropriate to act as for other diseases caused by genetic alterations [1,5].
IX	The life limiting mechanisms caused by the limits in cell duplication capacities determined by telomere-telomerase system are not predicted by the first paradigm and are hardly compatible with it [24].	Life limiting mechanisms as the limits in cell duplication capacities determined by telomere-telomerase system are entirely compatible with the second paradigm and essential for its validity [24].
X	The concept of IMICAC is absent and so there is no distinction between IMICAW and IMICAC and no specific care in experimental data evaluation.	The concept of IMICAC is well defined, with a clear distinction between IMICAW and IMICAC, and the necessity of considering this distinction in experimental data evaluation is strongly underlined [1,5].
	Aging is only a common term for many age-related different diseases: aging as a distinct entity does not exist and, in principle, cannot be mastered	**All manifestations of IMICAW, usually defined aging in their more advanced expressions, have common mechanisms: aging is a distinct entity and, in principle, can be mastered**

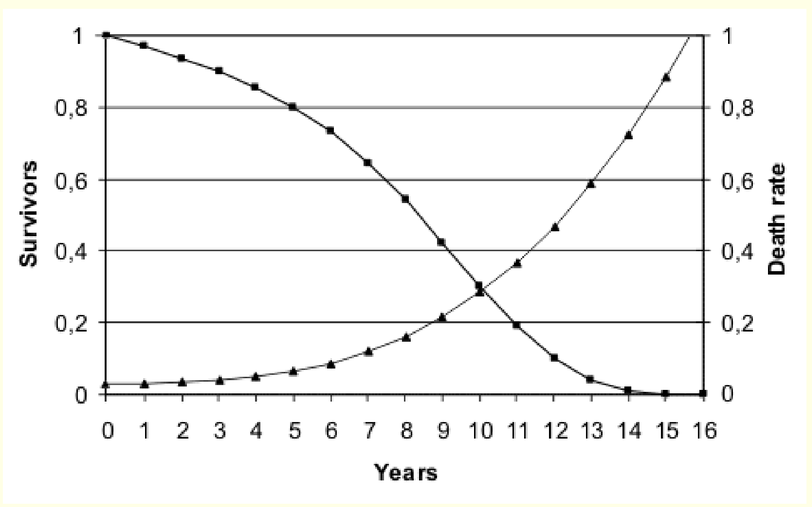


Fig. 1 – Life table of *Panthera leo* in natural conditions (Data from [6]). Fitness decline is well documented in the wild for many species [6,20].

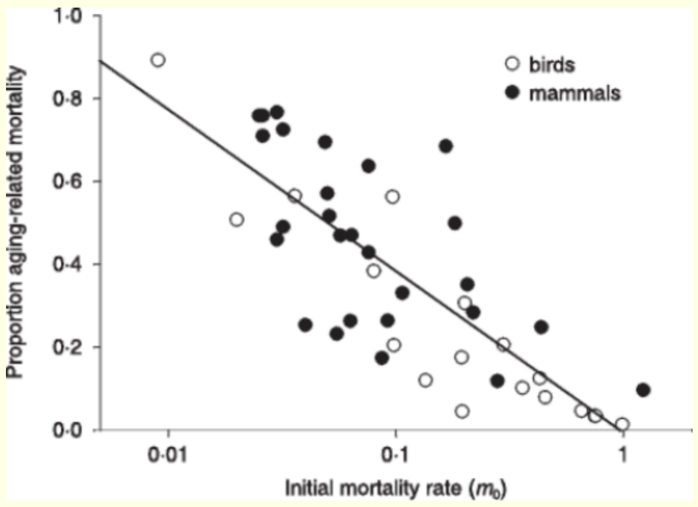


Fig. 2 – Inverse relation between extrinsic mortality and the proportion of deaths due to intrinsic mortality (Figure from [21]).

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