



Aging Research from the End of Last Century: An Important Retrospective

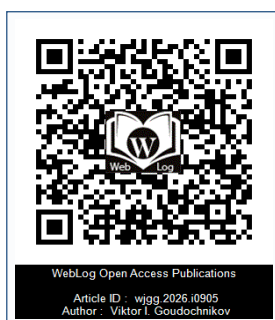
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Abstract

This mini-review is devoted to evaluation of gerontologic advances approximately till the onset of current century, making some prognostic considerations for the next decades. An attention is focused on the works of some Russian authors, together with our own studies related to stress hormones and proteins.

Keywords: Aging; Gerontology; Glucocorticoids; Stress



We live at present in the epoch of rapid scientific progress that can change the state of investigative minds even during several years (and not decades, as previously). Therefore, it is interesting to evaluate the situation in aging research about a quarter of century ago, the time of turning from the 2nd to 3rd millenium, in order to make some predictions, at least up to the half of current century. We shall focus our brief essay only on some topics that appear to be the most relevant for us.

Already at the end of 20th century and shortly thereafter the population aging was quite evident worldwide. In fact, the number of elderly persons was growing rapidly in many countries, approaching sometimes to one third of the whole population [1, 2] and representing a considerable burden to financial resources of even rich industrialized states of Europe and Northern America [3].

Therefore, already at that time there existed a great interest to advanced research on aging and age-related diseases, using both experimental studies on laboratory animals and epidemiological investigations. Partly this interest was a continuation of research efforts since the beginning of 20th century, when the discipline of gerontology emerged.

It is important that the term “gerontology” was used once in 1903 by Russian immunologist, Nobel prize laureate Elie I. Metchnikoff, but only after the later its use by Russian psychologist Nikolai A. Rybnikov in 1929 this term was accepted in a worldwide mode [4]. This occurred also due to promotion by Vladimir G. Korenchevsky, another scientist of Russian origin that participated actively in the first steps of International Association of Gerontology and Geriatrics during the decades of thirties and fourties of the last century.

A century after the foundation of gerontology in 1903 the most important discoveries were related to Caloric Restriction (CR) and its mechanisms. Indeed, till the present moment this dietary intervention is considered as the only confirmed manner of lifespan extension, at least in some animal species [5-7]. What for the mechanisms of CR, it appeared that they could involve hormonal alterations, especially related to Growth Hormone (GH) and Insulin-Like Growth Factor type I (IGF-I) [8-10].

We began to participate in parallel studies on hormonal regulation during the eighties and nineties of the last century, investigating functional activities of cultured liver and pituitary cells obtained from the rats of different age groups: perinatal, prepubertal and adults [11]. Only later it became clear to us that these studies were important for gerontology also, if to consider this discipline as the science of whole ontogeny [12], and not only of its senescent part. In fact, several researchers affirm that aging begins, at least, together with formation of zygote (see, e.g., ref. [13]) and perhaps even earlier, if to take into account also the alterations in gametes, i.e., in transgenerational mode.

However, for us the most important topic from the very beginning was the role of Glucocorticoids (GC) as principal candidates to mediators of the phenomena of programming / imprinting and embedding in the framework of the concept of Developmental Origins of Health and Disease - DOHaD [14], as well as in theoretical models of the onto- and phylopathogeny. In this regard, it is interesting that CR provokes the increase in GC levels, what contradicts to their participation in

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the etiopathogeny of several age-related diseases, as well as in aging itself [15, 16].

Therefore, our present attention became more focused on other mediators of stress, especially those associated with cellular stress, including heat shock proteins - HSP [17]. It is important that CR results in improved resistance to stress, probably because of higher HSP levels [18-20]. However, these levels appear to decrease with aging, what explains also age-related compensatory increase in GC levels (see discussion in ref. [16]).

Just recently our attention was attracted to exosomes, nanosized extracellular vesicles released from the cells by means of exocytosis [21, 22]. In fact, exosomes contain many “non-classical” bioregulators including HSP and non-coding RNAs and may actively participate in the intercellular communication [23, 24]. More importantly, together with “classical” hormones, exosomal bioregulators may be responsible for the mechanisms of aging [25, 26], according also to the evidence provided by heterochronic parabiosis [27].

In conclusion, the next quarter of current century will be related probably more to studies on combined mechanisms of aging, both hormonal and biochemical, especially GC and HSP, as well as exosomes. We can expect also exponentially growing use of artificial intelligence, in order to evaluate rapidly expanding volumes of scientific information in adequately short and acceptable periods of time.

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