Gerontology and endocrinology: The disciplines that need expansion

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ABSTRACT
Evidence is presented in favor of the expansion of gerontology and endocrinology by the inclusion of different phases of ontogeny and various types of bioregulators, respectively. The focus is on the contribution of researchers from Russia and on their own work, carried out for at least the last 30 years.

Keywords: Gerontology, Endocrinology, Ontogeny, Hormonal regulation.

1 INTRODUCTION

Both gerontology and endocrinology are disciplines that are now well established. There are university institutes and departments, clinics, and laboratories that are well involved in their ongoing studies. However, the situation was not always the same. Therefore, our first task would be to make a brief review of the conceptual histories of these disciplines, from their beginning to the present moment, in order to understand what are the problems that result in the need for their expansion.

2 THE HISTORY OF CONCEPTS IN GERONTOLOGY

It is interesting that since its inception, this discipline has been linked directly with some researchers from Russia. Indeed, Elie Metchnikoff, the Nobel laureate, is regarded as a pioneer of gerontology, although he almost never used this term. In fact, the Russian psychologist Nikolai A. Rybnikov was one of the first to use the term "gerontology" in the year 1929 (see discussion in: OLIVER et al., 1980; SCHAFER, 2005).

Very recently, we have suggested our own interpretation of this term. In our view, we should consider gerontology as the science of the whole ontogeny that includes not only old age, but also pre- and postnatal development and intermediate ranges, in the sense that N.A. Rybnikov, one of the originators of the term "gerontology" used to elaborate the method of biographies. Indeed, no one can describe the behavior of an elderly person without complete knowledge of his or her biography, from childhood, through the age of child and adolescence and to adulthood, intermediate age and old age.

At this point, we must remember the concept of Developmental Origins of Health and Disease (DOHaD), which describes the long-term consequences of events in pre- and postnatal development up to adulthood, intermediate age, and old age (GOUDOCHNIKOV, 2015, 2019; GOUDOCHNIKOV, PROKHOROV, 2016). On the basis of this concept, we suggest two new terms: "ontopathogenesis" and "phylopathogenesis", in order to describe etiopathogenesis throughout all ontogeny (or, at least, most of it),

as well as through generations respectively (GOUDOCHNIKOV, 2017, 2020, 2023; GOUDOCHNIKOV, PROKHOROV, 2016).

In conclusion, the expansion of gerontology should occur by including all phases of ontogeny and in a multi-, inter- and trans-generational way.

3 THE HISTORY OF CONCEPTS IN ENDOCRINOLOGY

It is curious that for the first time the term "hormone" was applied to gastro-intestinal secretin, but adrenaline (epinephrine) was discovered some time before that (TATA, 2005; WILSON, 2005). The problem is that the similar substance, noradrenaline (norepinephrine) is considered a neurotransmitter and not a hormone, even though the adrenal medulla secretes both adrenaline and noradrenaline.

On the other hand, serotonin (5-hydroxy-tryptamine) is not only a neurotransmitter in the central nervous system, but also a bioregulator widely disseminated in the gastrointestinal tract, being produced by enterochromaphynic cells of the so-called diffuse neuroendocrine system. It is important that previously such cells were called APUD, according to the abbreviation of the English phrase "Capture and Decarboxylation of Amine Precursors" (DAY, SALZET, 2002), but for some reasons, this term was later abandoned altogether.

Currently, "classical" endocrinology first describes the 4 regulatory axes (see table 1). It is suggested that prolactin is controlled predominantly in an inhibitory manner by dopamine, which in this case can be considered as a hormone-like neurotransmitter.

In addition to these 4 axes, there are at least 3 regulatory handles:

1) insulin/glucagon - for glucose regulation;
2) parathyroid gland hormone – PTH/calcitonin – to control $Ca2^{+}$;
3) Mother – English – Aldosterona.

However, progress in immunology has been able to describe many interleukins (IL) that are characterized as cytokines, along with numerous growth factors. And at this point we have the following problems: on the one hand, insulin-like growth factor type I (IGF-I) is considered as a hormone and growth factor, but other growth factors are not discussed by "classical" endocrinology. On the other hand, it seems that IL-1 participates in the regulatory axis of the hypothalamus – pituitary gland – adrenal glands (HPA) and therefore it can be described as a hormone-like substance (see discussion in: GOUDOCHNIKOV, 2017).

Major advances in biomedicine have confirmed that many internal organs are not only targets for "classical" peripheral gland hormones, but also produce hormone-like substances or participate in hormone regulation, as shown in Table 2 (BERN, 1990; AMEEN, 1996; BOUILLON, 2001).

Therefore, endocrinology currently needs to expand to the science of bioregulation, which should include, in addition to "classical" hormones, also some neurotransmitters, eicosanoids and cytokines.

4 POSSIBLE RELATIONSHIPS BETWEEN GERONTOLOGY AND ENDOCRINOLOGY IN EXPANSION

Endocrinology usually begins to discuss hormonal regulation, starting from fetal stages with well-developed endocrine glands. However, recent advances clearly show that many hormones, neurotransmitters and cytokines are very active, from the beginning of human and animal life. In this case another Russian researcher, Gennady A. Buznikov was the first to show the effects of various neurotransmitters on embryogenesis (BUZNIKOV, SHMUKLER, 1981). On the other hand, although chorionic gonadotropin (CG) and placental lactogen (PL) are well-known placental hormones, we must not forget that the trophoblast has an embryonic origin and therefore we must consider endocrine regulation soon after the formation of the embryo.

Moreover, progress in embryonic stem cell studies has clearly shown the effects of various morphogens and cytokines (HANLEY, 2008; ATWOOD, MEETHAL, 2011). Of course, we cannot exclude the possibility of hormonal regulation (in the broad sense, including cytokines and neurotransmitters) of so-called "adult" stem cells, so there is a need for the expanding discipline, including stem cell endocrinology in general.

5 FINAL THOUGHTS

The aspects discussed in this very short work cannot be comprehensive since bioregulation is a very complex phenomenon. Previously, Russian researchers studied the role of gap junctions in acupuncture mechanisms (LI et al., 1989). We participate in these research efforts briefly, suggesting the contribution of the diffuse neuroendocrine system in the inner parts of the acupuncture meridians (CHERNILEVSKY et al., 1992).

On the other hand, we previously classified all bioregulators into two groups, with most subgroups with low molecular weight (<800 dalton) being able to penetrate through slit channels and thus being able to serve as entercrine substances (Gudoshnikov, Fedotov, 1990). This means that the levels of bioregulators not only in biological fluids (plasma or blood serum, interstitial fluid, etc.), but also within tissues must be considered, thus expanding the entire concept of internal secretion by adding one more class (intracrine) to the already well-characterized endocrine, paracrine, intracrine, and autocrine regulators.

Regarding our studies in expanding gerontology, since 1997 we have already shown the existence of ontogenic transitions (infantile, juvenile, and pubescent) on the basis of the linearization of somatic growth curves through the use of mono- and bilogarithmic graphs (GOUDOCHNIKOV, PROKHOROV,

1998, 2020 a). We especially suggest that the juvenile transition can serve as a metamorphosis event for transformation from development to aging (GOUDOCHNIKOV, 2005), with a later onset of increased morbidity and mortality in human populations. These studies themselves have allowed us to suggest that the phenomena of imprinting/programming and embedding may occur before and after infant transition respectively (GOUDOCHNIKOV, PROKHOROV, 2020b).

In conclusion, the work presented is intended to show that our own studies are already deeply involved in the expanding gerontology and endocrinology, as well as their interactions.

Table 1. The main regulatory axes in endocrinology.

Hypothalamus	Pituitary gland	Peripheral hormones
Somatoliberina (GHRH)	Growth hormone (GH)	IGF-I
Thyroliberine (TRH)	Tireotropina (TSH)	Thyroid gland hormones
Corticoliberin (CRH/CRF)	Adrenocorticotropin (ACTH)	Corticosteroids
Gonadoliberina (GnRH)	Luteinizing hormone (LH) and follicle-stimulating hormone (FSH)	Sex Steroid Hormones

Abbreviations (in English): ACTH – adrenocorticotropic hormone, CRH – corticotropin-releasing hormone, GH – growth hormone, GHRH – growth hormone-releasing hormone, GnRH – gonadotropin-releasing hormone, FSH – follicle-stimulating hormone, IGF-I – insulin-like growth factor type I, LH – luteinizing hormone, TRH – thyrotropin-releasing hormone, TSH – thyroid-stimulating hormone.

Table 2. The Participation of Various Organs and Tissues in Hormonal Regulation

System or organ/tissue	Hormone-like products
Heart	ANP
Vascular endothelium	Endothelin, NO
Kidneys	I think of it, mother.
Lungs	Hormone metabolism
O gastro-interstinal tract	Gastrin, CCK, secretin and many others
Liver	CBG/transcurtain, SHBG and others
Adipose tissue	Leptin, adiponectin etc.
Timo	Thymosin and others

Abbreviations (in English): ANP – atrial natriuretic peptide, CBG – corticosteroid-binding globulin, CCK – cholecystokinin, NO – nitric oxide, SHBG – sex hormone-binding globulin.

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