

Endocrinology and gerontology: Disciplines that Need the Broadening and Expansion

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Abstract

The evidence is presented for the necessity of expansion of endocrinology and gerontology by inclusion of various types of bioregulators and different phases of ontogeny respectively. The main focus is made on contribution of Russian researchers and on our own works during, at least, the last 30 years.

Keywords: endocrinology; gerontology; hormonal regulation; ontogeny

Introduction

Both endocrinology and gerontology are disciplines that at present are well established. There exist institutes and university departments, clinics and laboratories that are highly engaged in their continuous studies. However, not always the situation was the same. So, the first our task will be to review briefly conceptual histories of these disciplines, from their onset and up to the present moment, in order to understand, what are the main problems that result in the necessity of their expansion.

The History of Concepts in Endocrinology

It is curious that at first the term “hormone” was applied to gastrointestinal secretin, nevertheless adrenaline (epinephrine) was discovered somewhat earlier [1, 2]. The problem is that similar compound, noradrenaline (norepinephrine) is considered as neurotransmitter and not hormone, although adrenal medulla is secreting both adrenaline and noradrenaline. On the other hand, serotonin (5-

hydroxytryptamine) is not only the neurotransmitter in central nervous system, but also widely spread bioregulator in gastrointestinal tract, being produced by enterochromaffin cells of so called diffuse neuroendocrine system. It is important that earlier such cells were called APUD according to abbreviation of the phrase “Amine Precursor Uptake and Decarboxylation” [3], but for some reasons this earlier term was later completely abandoned. Today “classical” endocrinology describes, first of all, four regulatory axes (see table 1). It is supposed that PRL is under predominant inhibitory control of dopamine that in this case can be considered as hormone-like neurotransmitter.

Besides these axes, there are at least three regulatory loops:

- 1) Insulin / glucagon-for regulation of glucose
- 2) Parathyroid hormone (PTH) / calcitonin-for the control of Ca^{2+}
- 3) Renin-angiotensin-aldosterone.

Table 1: Principal Regulatory Axes in Endocrinology.

Hypothalamus	Pituitary	Peripheral glands
GHRH	GH	IGF-I
TRH	TSH	Thyroid hormones
CRH	ACTH	Corticosteroids
GnRH	LH / FSH	Sex steroid hormones

Abbreviations: 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

However, the progress in immunology was able to describe many interleukins (IL) that are characterized as cytokines, together with numerous growth factors.

And here we have the following problems: on one hand, insulin-like growth factor type I (IGF-I) is considered as both hormone and growth factor, but

other growth factors are not discussed by “classical” endocrinology. On the other hand, IL-1 appears to participate in the regulatory hypothalamic-pituitary-adrenal (HPA) axis and therefore, it can be described as hormone-like substance (see discussion in [4]). The

main advances in biomedicine have confirmed that many internal organs are not only targets for “classical” hormones of peripheral glands, but also are producing hormone-like compounds or participate in hormonal regulation, as demonstrated in table 2 [5-7].

Table 2: Participation of various organs and tissues in hormonal regulation.

System or organ / tissue	Hormone-like products
Heart	ANP
Vascular endothelium	Endothelin, NO
Kidneys	Erythropoietin, renin
Lung	Non-respiratory function (hormone metabolism)
Gastro-intestinal tract	Gastrin, cholecystokinin, secretin and many others
Liver	CBG / transcortin, SHBG and others
Adipose	Leptin
Thymus	Thymosin and others

Abbreviations: ANP - atrial natriuretic peptide, CBG - corticosteroid-binding globulin, NO - nitric oxide, SHBG - sex hormone-binding globulin.

Therefore, at present endocrinology needs the expansion to a science of bioregulation that should include, besides “classical” hormones, also some neurotransmitters, eicosanoids and cytokines. Let’s discuss now some aspects of gerontology.

History of Concepts in Gerontology

It is interesting that from the very beginning, this science was directly linked to several Russian researchers. In fact, Elie Metchnikoff, Nobel prize laureate, is considered as a pioneer in gerontology, although it appears that he almost never used this term. Really, Russian psychologist Nikolai A. Rybnikov was one of the first to use the term “gerontology” in 1929 (see discussions in [8, 9]). Just recently we have offered own interpretation of this term. On our opinion, we should consider gerontology as a science of the whole ontogeny that includes not only senescence, but also postnatal development and intermediate age categories in the sense that N.A.Rybnikov, one of the creators of the term “gerontology” used to elaborate biographical method. In fact, nobody can describe the behavior of any old person without complete knowledge of his biography, from infancy, childhood and adolescence to adult state, middle age and senescence. Here we should remember the concept of Developmental Origins of Health and Disease (DOHaD) that describes long-term consequences of events in pre- and postnatal development till adult state, middle age and senescence [10-12]. On the basis of this concept, we have offered two new terms: “ontopathogeny” and “phylopathogeny” [4, 12-14], in order to describe

etiopathogeny that proceeds through the whole ontogeny (or at least, its main part) and also in multi-, inter- or transgenerational mode. In conclusion, the expansion of gerontology should occur by inclusion of all the phases of ontogeny and perhaps, even across the generations.

Possible Interrelations Between the Variants of Endocrinology and Gerontology In Expansion

Usually, endocrinology begins to discuss hormonal regulation from fetal stages with already well-developed endocrine glands. However, recent advances clearly show that many hormones, neurotransmitters and cytokines are active from the very beginning of human and animal life. Here another Russian researcher Gennady A. Buznikov was the first to show the effects of several neurotransmitters on embryogenesis [15]. On the other hand, although chorionic gonadotropin and placental lactogen are well known placental hormones, we cannot forget that trophoblast has embryonic origin and therefore, we should consider endocrine regulation already shortly after the formation of early embryo. Moreover, the progress in embryonic stem cells research has clearly demonstrated the effects of numerous cytokines and morphogens like LIF (leukemia-inhibitory factor), BMP (bone morphogenetic protein) and many growth factors [16, 17]. Of course, we cannot exclude the possibility of hormonal regulation (in broad sense, including cytokines and neurotransmitters) of so-called adult stem cells, therefore there is a necessity of

discipline in expansion, including endocrinology of stem cells in general.

Final Comments

The aspects discussed in this, rather short communication is not comprehensive, since bioregulation is quite a complex phenomenon. Earlier Russian researchers have studied the role of gap junctions in the mechanisms of acupuncture [18]. We participated briefly in these investigative efforts, suggesting the contribution of diffuse neuroendocrine system to internal parts of acupuncture meridians [19]. On the other hand, earlier we classified all the bioregulators to two groups, with the majority of subgroups with low molecular weight (< 800 dalton), being able to penetrate through gap-junctional channels and therefore, serving as intercrine substances [20]. It means that the levels of bioregulators not only in biological fluids (blood plasma or serum, interstitial fluid etc.), but also inside the tissues should be considered, thus amplifying the whole concept of internal secretion by means of adding one more class (intercrine) to already well characterized endocrine, paracrine, intracrine and autocrine regulators. What for our studies in a new variant of gerontology in expansion, since 1997 we have shown already the existence of ontogenetic transitions (infantile, juvenile and pubertal) on the basis of linearization of somatic growth curves by means of mono- and bilogarithmic plots [21, 22]. We have suggested especially that juvenile transition may serve as event of metamorphosis for transformation from development to aging [23], with the subsequent onset of increases in morbidity and mortality in human populations. These our studies have allowed to propose that programming / imprinting and embedding phenomena can occur before and after infantile transition respectively [24].

Conclusion

In conclusion, short communication presented here is destined to show that our own works are already deeply involved in the new broadening variants of endocrinology and gerontology, as well as in their interactions.

Declarations

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Conflict of interest

The author affirms that conflict of interest does not exist.

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