

Non-Respiratory Pulmonary Functions: Focusing on Bioregulation in a Broader Sense

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Abstract

The evidence on the role of neuroendocrine cells and neuroepithelial bodies, as essential pulmonary parts of diffuse neuroendocrine system is briefly discussed in relation to non-respiratory functions of the lungs, outlining also some our own, earlier and recent hypotheses.

Keywords: *Glucocorticoids; Neuroendocrine Cells; Neuroepithelial Bodies*

Abbreviations

APUD: Amine Precursor Uptake and Decarboxylation; DNES: Diffuse Neuroendocrine System; GC: Glucocorticoids; NEC: Neuroendocrine Cells; NEB: Neuroepithelial Bodies

At first glance, it is somewhat strange to publish this short commentary in the journal dedicated to *Pulmonary and Respiratory Medicine*. As a matter of fact, for a long time external respiration had the priority in research as essential, vital function. However, already 50 years ago the topic “non-respiratory functions of the lung” had attracted some attention [1], and this situation continued till the relatively recent time [2].

Just recently we have proposed to expand the area of endocrinology to the science of bioregulation by including many “non-classical” bioregulators, such as cytokines (growth factors and interleukins), neuropeptides, neurotransmitters, eicosanoids, etc. [3], especially in relation to progenitor and stem cells [4]. In one of those articles [3] we mentioned the lungs as organs essential for metabolism of hormones. And indeed, some (albeit non strictly proved) data suggest very significant role of the lungs in this regard [5,6].

It is already well established also that the lungs are important targets for “classical” hormones including glucocorticoids (GC). In a series of our articles published in *E-Cronicon Pulmonary and Respiratory Medicine* [7-9] and in another journal [10,11] we tried to call for attention to GC considered also to be the mediators of programming/imprinting phenomena [12]. In fact, these agents are used for accelerating the lung maturation in perinatal period [7], as well as for anti-inflammatory and immunosuppressive action in pediatric pulmonology [8-11], in spite of serious adverse effects, first of all somatic growth inhibition [13].

However, there exists one more non-respiratory function of the lungs, being executed by two types of their structures: neuroendocrine cells (NEC) and neuroepithelial bodies (NEB) [14]. They take part of diffuse neuroendocrine system (DNES), present in many other organs

and much earlier designated as apudocytes, i.e. the cells that perform amine precursor uptake and decarboxylation (APUD). Although at present the last two terms are not widely used, nevertheless at least some authors continue to employ them in recent publications [15,16].

Much earlier we have made two suggestions: 1) about the passage of inner parts of acupuncture channels through DNES, obviously including NEC and NEB of the lungs [17]; 2) on the possible existence of endocrine-disrupting substances that can interfere with bioregulators produced by DNES [18].

It is interesting that NEC and NEB of the lungs secrete a number of neuropeptides, besides serotonin and perhaps, some other neurotransmitters [14]. It is important also that in principle, at least some of them, possessing $M_r < 800$ dalton, are able to penetrate through gap junction channels and therefore, they may be considered as intracrine regulators [19].

Finally, NEC possess dense core granules, probably containing chromogranins and secretogranins that can really function as pro-hormones, liberating a number of bioactive peptides during their physiological proteolysis. Just recently we have suggested an important role of at least one of these neuroendocrine proteins in anterior pituitary gland also [20].

In conclusion, non-respiratory pulmonary functions should be studied in much more detail, in particular NEC and NEB of the lungs as parts of DNES. In this regard, present-day literature describes mainly hyper- and neoplasias of these structures, whereas some scarce data suggest their important functions in normal respiratory physiology, as well as in the inflammatory pulmonary disorders including pneumonia [15]. Especially interesting are the data about different numbers of NEC and NEB in early life [16] and their probable participation in the niches for progenitor and stem cells [14]. It means that the utilization of GC in perinatal medicine and pediatric pulmonology should be re-evaluated also, as referred to their probable actions on these pulmonary DNES structures.

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