

Microbiome and Nanobiota of the Lungs, Gut and Other Sources as Important Contributors to the Concepts of Phylo- and Ontogenetic Bioregulation

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Abstract

The overview is presented of our own studies showing the importance of including the endotoxins and other components of microbiome and nanobiota of the lungs and airways, gut and other sources to the concepts of phylo- and ontogenetic bioregulation.

Keywords: Microbiome; Ontogeny; Lipopolysaccharide; Endotoxins

Introduction

This story began at the onset of last century when a Russian researcher, Alexandre M. Besredka worked together with Elie I. Metchnikoff, a Nobel prize laureate, in the Institute of Louis Pasteur in Paris. In fact, Dr. Besredka had a courage to insist that bacteria, even dead, could kill humans and animals by means of endotoxins, the components of bacterial wall, whereas specific antibodies could neutralize this threat. At present one of these components, lipopolysaccharide (LPS) is well known as exogenous pyrogen that causes endotoxic shock via interleukins, endogenous pyrogens, i.e. substances provoking fever.

We became connected to this topic at the end of last century, during the work as Visiting Professor in the Laboratory for Biological Research of Drugs (Head – Prof. Dr. Sergio L. Dalmora) in the South of Brazil. Really, during our activities as advisor of several dissertations of Master of Science, we realized finally that biological properties of LPS and other endotoxins are much broader than only pyrogenic and include also, especially in low doses, the symptoms of seakness syndrome: a decrease in motor activity, somnolence and a tendency to social isolation, i.e. the parameters related even to psychology and mental health [1].

Finally, in 2024 we were in touch with another Russian researcher, Prof. Dr. Mikhail Yu. Yakovlev who had a courage to insist that LPS (and perhaps, other endotoxins also) may be highly involved in the mechanisms of humans and animal aging. As a result of these circumstances, we have supported a broader idea of the involvement of LPS, together with glucocorticoids (GC), in the mechanisms of programming/imprinting and embedding phenomena, beginning from perinatal stage of development [2,3], that are included in the concept of ontogenetic bioregulation [4] on the crossroad of amplified versions of endocrinology and gerontology [5,6].

However, LPS is only one representative of microbiome, an integral population of many microorganisms in human and animal bodies. Therefore, our logical next step was to expand the research from LPS to microbiome.

Microbiomes of the gut, lungs and other sources

Today the incredible greatness of microbiome is already well known. As a matter of fact, human body, composed of approximately 10 trillion (10^{13}) its own cells, is a symbiont, together with 100 trillion (10^{14}) microorganisms. How is it possible? Indeed, the size of bacteria ($\sim 1 \mu\text{m}$) is a one tenth part of cellular size ($\sim 10 \mu\text{m}$). It means that in its size human symbiotic organism as a half is composed of bacteria and other microbes [7].

Historically, since the studies of Elie I. Metchnikoff, the main attention was attracted to the gut microbiome concentrated in the colon, and only just recently it became clear that microbiomes of other parts of human body that are in direct (or semidirect) contact with external environment, i.e. oral cavity, airways and lungs, skin and reproductive organs, especially in women, are equally important.

Moreover, the studies of several last years clearly show that microbiomes of the oral cavity, gut and lungs may be interconnected, thus being the components of integrated oral - gut - lung axis. In addition, bacterial LPS was already considered as exohormone, i.e. exogenous compound that nevertheless is deeply involved in the complex loops of neuroimmunoendocrine regulation (See discussion in ref.7).

Here we are approximating to another important discussion related to ontopathogenic model.

The role of microbiomes in development and aging

It appears that human fetus is relatively devoid of microbes, although this theme is poorly understood till the present time. However, it is already quite clear that in the immediate neonatal period, i.e. shortly after birth, human infant is a target of numerous external microorganisms [7,8].

Therefore, it can be easily previewed that at least GC, well known anti-inflammatory and immunosuppressive drugs, can largely interfere with neonatal adaptation of human infants to external microflora that performs the vast colonization of several parts of human body: first of all, the gut, respiratory system and the skin. In fact, previously we have demonstrated that neonatal administration of GC in rats results in long-term thymus suppression, at least till the prepubertal period [9].

Here we must remember that at present synthetic GC (betamethasone and dexamethasone) are widely used worldwide, in order to boost the lung maturation in premature newborns [10]. Therefore, from our point of view, it is very important to study in near future the interactions of GC with LPS and other components of microbiome in early human life. It is essential to mention here that although growth-inhibitory GC action is already well known [11], the same activity of LPS was not well studied, especially in combination with GC (See discussion in ref.7).

Since GC are widely used in geriatrics including pulmonary and respiratory medicine, it is also critically important to study the interactions of GC with LPS and other components of microbiome during senescent phase of human ontogeny [12].

Final Remarks

Already in the title of this short essay we have introduced two novel terms: nanobiota and phylogenetic bioregulation. We had the courage to do this for the following reasons. In the first place, not only the majority of microorganisms (bacteria etc.), but also viruses and prions, i.e. nanosized pathogens can probably interact with GC in ontogenetic bioregulation. Moreover, ontopathogenic model is a particular case of phylopathogenic one, and it is already quite clear that there exists co-evolution of animals and microorganisms, with mutual co-adaptation and perhaps, co-regulation.

In this case we only continue the introduction to pulmonary and respiratory medicine of more general aspects (non-respiratory pulmonary functions, tissue streaming, gap junctions, exosomes) [13-16] that from our point of view, represent important endeavors

of associative thinking easily crossing the artificial barriers between disciplines, concepts and paradigms. But increasing interest to respiratory microbiome in the last several years allows to preview that such theoretical approach may be highly promising already in near future.

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