Journal of Pigmentary Disorders

Iotti and Perra, Pigmentary Disorders 2014, 1:5
DOI: 10.4172/JPD.1000e101

Editorial Open Access

Bases and Principles of Low Dose Medicine and P.N.E.I. Foundations of Low Dose Pharmacology

Torello Lotti[1] and Alessandro Perra[2*]

[1]Professor & Chair of Dermatology, University of Rome, Italy
[2]President, GUNA Foundations, Italy

Low Dose Medicine (LDM) arises from Molecular Biology, Psycho-Neuro-Endocrine-immunology and Quantum Physics and originates, for what concerns the use of low doses of the active ingredients of its drugs from historical tradition of Homeopathy.

Low Dose Medicine is an expression of the most innovative person-centered medicine, and its founding principles are:

- to treat the Man and not just the disease;
- to act on the causes and not just the symptoms;
- to consider Man as a whole mind-body and as an individual.

The cornerstone of Low Dose Medicine is P.N.E.I. (Psycho-Neuro-Endocrine-Immunology).

The P.N.E.I. system (Figure 1) is a complex physiological control network in which the 3 major homeostatic control systems (CNS and ANS, Endocrine and Immune System) are interconnected in order to drive the physiological functions.

They contribute in an integrated way (through signaling molecules such as neuropeptides, hormones, cytokines and growth factors and through the control mechanisms of negative and positive feedback) to the continuous monitoring and adjustment of vital parameters, providing a fundamental adaptive action between a living organism and the external environment.

The P.N.E.I. system may be considered as the "big brother" that controls the homeostatic mechanisms and, ultimately, the physiological structure (Figure 2).

Any alteration of the physiology is defined as an alteration of the entire P.N.E.I. axis.

Although localized in a specific organ or tissue, every disease is to be considered as the expression of a general imbalance of the whole P.N.E.I. axis.

The importance of P.N.E.I. axis emerges clearly observing diseases such as gastric ulcer, in which mucosal injury is only the epiphenomenon of general alteration of physiology involving all 3 systems, or considering the oncological pathology in which the immune dysregulation of the patient is consequently also of a hyper-activation of the stress axis or, still, in pathologies such as depression, IBDs, and autism.

To act on the PNEI axis, and more precisely on the alterations induced on it by endogenous or exogenous stressors, means to deeply act primarily on the intimate pathogenesis of the disease and then restore the body to its original physiological conditions.

Low Dose Medicine takes origin from a revolutionary idea in the medical field: to return a sick organism to the starting physiological conditions (homeostasis) through the use of biological molecules normally present in the body, which control and drive homeostatic functions in healthy conditions.

A great number of molecules, known and studied by Molecular Biology, (defined messenger molecules or signaling molecules) are able to direct different cells to the "right directions" for their proper operation. These molecules are neuropeptides (messengers of the nervous system), hormones (messengers of the endocrine system), cytokines (messengers of the immune system).

These molecules are flanked by growth factors, fundamental regulatory molecules for tissues stimuli.

These substances are recognized to play a decisive role in determining the health or disease state and it is now established that each disease is an expression of the changes in concentrations (in excess or deficiency) of these substances; world-wide research in the medical field is moving toward the study of messenger molecules, which determine the destiny in a positive way (healing) or negative (disease) of many pathological conditions, to evaluate the possibility for therapeutic usage.

In conditions of homeostatic balance (healthy state) the concentration of these molecules at the extra-cellular matrix level is comprised in a specific range (between 10^{-6} and 10^{-12}); the initiation and the development of a pathological process determines the variation, (in excess or in defect) of this concentration. We can affirm that every disease is the expression and the consequence of varied concentrations of signaling molecules (Figure 3).

Only by restoring the physiological concentration of neuropeptides, hormones and cytokines are we able to recover the homeostatic equilibrium and to restore the physiology of the sick organism. Being able to correct, for example, alterations of the immune system with the use of cytokines or endocrine disorders with the use of hormones is one of the most fascinating research areas of Molecular Biology applied to medicine. Unfortunately the clinical application of this knowledge has the limiting factor in the side effects shown by these substances when administered at the high doses, normally recommended to date.

Thanks to the pharmaceutical technology called SKA (Sequential Kinetic Activation), discovered, codified and standardized by GUNA Laboratories, it is now possible to use lower doses of hormones, neuropeptides, cytokines and growth factors with therapeutic results comparable to those induced by high concentrations but without side effects.

SKA technology is a sophisticated drug delivery system, which allows the nano-concentrations to be active even below the actually considered minimum effective dose.

***Corresponding author:** Alessandro Perra, President, GUNA Foundations, Italy, Tel: 06891420157; E-mail: a.pizzoccaro@guna.it

Received September 25, 2014; **Accepted** September 27, 2014; **Published** September 29, 2014

Citation: Lotti T, Perra A (2014) Bases and Principles of Low Dose Medicine and P.N.E.I. Foundations of Low Dose Pharmacology. Pigmentary Disorders 1:e101. doi:10.4172/JPD.1000e101

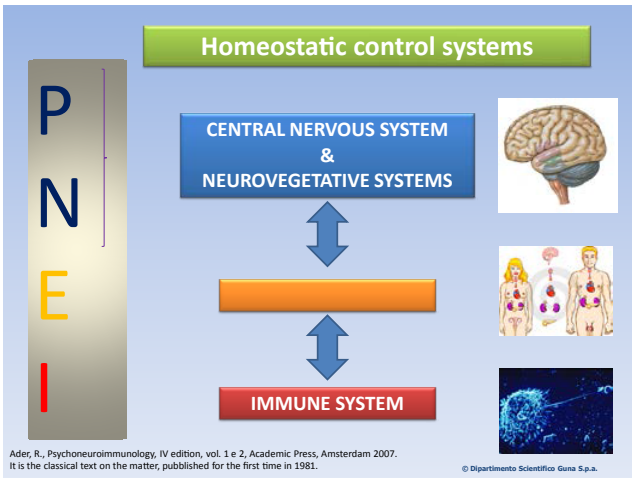

Figure 1: Schematic representation of the P.N.E.I. axis: the 3 homeostatic regulation systems are interconnected in order to drive the physiological processes by a downward route (psycho-somatic) and an ascending route (somato-psychic) both mediated by messenger molecules (neuropeptides, hormones, cytokines)

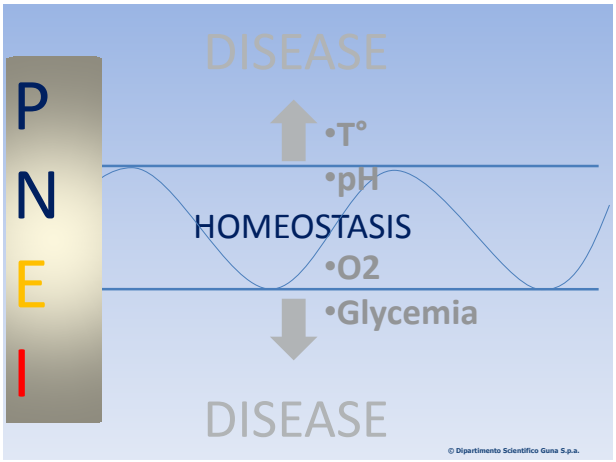

Figure 2: Schematic representation of the relationship between P.N.E.I. axis, vital parameters, homeostasis and disease states

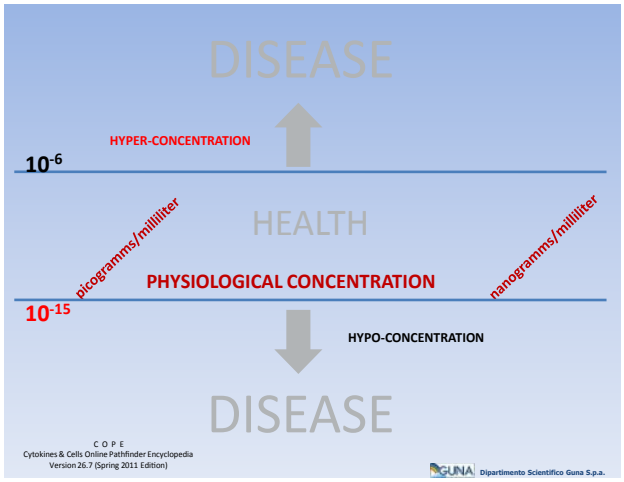

Figure 3: Signaling molecules

The GUNA SKA method inaugurates a new era in the possibility of clinical use of messenger molecules and realizes the "scientific dream" of being able to use biological molecules such as cytokines or hormones or neuropeptides at low doses (the only ones possible to have no side effects), thanks to the particular procedure used by GUNA pharmaceutical in the production of these molecules.

The action mechanism of SKA low dose cytokines, hormones, neuropeptides and growth factors consists in sensitization or activation of some units of cellular or plasmatic receptors (thanks to their low concentration, that is the same in which these substances work physiologically, and precisely between **10^{-6} (microgram), and 10^{-12} (picogram)**. This receptor sensitization allows the trigger of chain reactions (complex systems) and a restart of the biological function of the whole neuro-immune-endocrine network.

SKA Low dose cytokines and hormones work by bringing to the system information able

to activate autoregulation mechanisms.

By a clinical point of view, there are 2 therapeutic uses:

1) using the same cytokine, hormone, neuropeptide or growth factor in order to enhance the physiological activity of the same messenger molecule

2) according to the principle of opposing cytokine (or hormone): since different cytokines or hormones can have different effects on the same cell, i.e. a cytokine can antagonize the effect of another one (for e. IL4/INF gamma) and a hormone can antagonize the effect of another one (for e. progesteron/estrogens), both targeted at the same cell, in Low Dose Medicine antagonistic cytokines or hormones are utilized in order to brake a biological effect.

Scientific research has validated the thesis of Low Dose Medicine: in November 2009, in fact, was published the first paper on the effects of SKA activated low-dose cytokine in the treatment of allergic asthma [Gariboldi et al. Low dose oral administration of cytokines for treatment of allergic asthma. *Pulmonary Pharmacology & Therapeutics* 22 (2009) 497-510]. In this work was clearly shown that low doses used in the study induced the same effects of high doses in modifying a number of clinical and laboratory parameters that identify the allergic state.

Since 2009, new publications followed the paper published on *Pulmonary Pharmacology & Therapeutics*.

Some of the major works in the field of Low Dose Medicine are listed below

1. D'Amico L, Ruffini E, Ferraccini R, Roato I. Low Dose of IL-12 stimulates T Cell response in cultures of PBMCs derived from Non Small Cell Lung Cancer Patients. Journal of Cancer Therapy. 2012; 3: 337-342.
2. Cardani D, Dusio GF, Luchini P, Sciarabba M, Solimene U, Rumio C. Oral Administration of Interleukin-10 and Anti-IL-1 Antibody Ameliorates Experimental Intestinal Inflammation. Gastroenterology Research . 2013; 6(4): 124-133.
3. Radice E, Miranda V, Bellone G. Low-doses of sequential-kinetic-activated interferon-gamma enhance the ex vivo cytotoxicity of peripheral blood natural killer cells from patients with early-stage colorectal cancer. A preliminary study. Intern. Immunopharm. 2014; 19: 66-73.
4. Roberti ML, Ricottini L, Capponi A, et al. Immunomodulating treatment with low dose Interleukin-4, Interleukin-10 and Interleukin-11 in psoriasis vulgaris. J Biol Regul Homeost Agents. 2014; 28(1): 133-139.