

Low dose medicine

**Healing without side effects using low dose cytokines,
interleukins, hormones, and neurotrophines**

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Max Corradi

Jaborandi Publishing

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Contact: kristinajr.cristina@gmail.com

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Other books by the author:

Heal Yourself

Practical methods on how to heal yourself from any disease using
the power of the subconscious mind and natural medicine.

Ayni Books/John Hunt Publishing

The seven Laws of Reality and Being

A practical manual explaining how to make use of the seven
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This book is dedicated to all the great healers that work
for the benefit of beings.

Important Disclaimer:

**The informational knowledge presented in this book is intended to complement medical treatment and not to replace conventional medicine or the advice of your doctor.
Always seek professional help.**

**NOTHING CONTAINED IN THIS BOOK IS INTENDED TO BE
NOR CAN IT BE TAKEN FOR MEDICAL DIAGNOSIS OR
TREATMENT**

Introduction

In my book 'Heal yourself' I have introduced the concept of healing without side effects using the power of the subconscious mind and natural medicine.

In part two of that book I have described the Biotherapy system and the homeopathic and herbal remedies which can be employed in order to heal oneself without any side effects.

Moreover, in that book I have also introduced and explained, somewhat succinctly, the concept of using low dose cytokines, interleukins, hormones and growth factors in order to re-program and regulate deranged biochemical pathways.

This book covers in much more details how to use this new form of therapy called 'low dose medicine' or 'physiological regulating medicine', and in particular, how to heal oneself using low dose cytokines, interleukins, neurotransmitters, neurotrophines, hormones and growth factors.

The aim of this book is to be at the same time a manual and also a compendium to my first book 'Heal yourself' in describing possible different ways to cure oneself without side effects.

Part 1

Low dose medicine, cytokines, hormones, and neurotrophines

Chapter 1

What is low dose medicine?

Low dose medicine is a new therapeutic approach which aims at restoring physiology through communicating or signaling molecules such as cytokines, interleukins, growth factors, neuropeptides, neurotransmitters and hormones prepared in low dose-active dilutions (through the homeopathic method of dilution and succussion) and therefore without side effects. (For more information about classic homeopathy and the 'homeopathic processing' of dilution and dynamization see my book 'Heal yourself').

Since these molecules have the same physiological concentration (nanograms to picograms) as the molecules present in our organism which control and regulate organic functions under healthy conditions, one could define low dose medicine as 'physiological regulating medicine' but also as 'preventive medicine' since low dose active preparations have virtually no side effects.

Low dose medicine is also in many cases a resolutive therapy because it works on the whole organism directly by using molecules which work at the cellular level in order to re-direct biochemical pathways when these are deranged or inhibited.

By using low dose medicine one can act directly on the PNEI (psycho-neuro-endocrine-immunitary) system with the aim of regulating cell's activity, when this is inhibited or disturbed by endogenous or exogenous stressors. At this level one is able to restore the capacities for cellular self-regulation which are indispensable for maintaining homeostasis (*for more information on the PNEI system see related section in this book and my book 'Heal yourself'*).

Recent findings have shown that cytokines, interleukins, hormones, growth factors and neuropeptides correctly diluted and dynamized become active, through a mechanism of sensitization and activation of cellular receptors.

As we will see in the therapeutic strategy, one of the best way to correct a deficiency is to provide low (activated) doses of the same substance to stimulate its metabolism and **physiologic** production, and the result of the action of these low dose active molecules is a physiological modulation and regulation of the biochemical pathways when these are deranged or inhibited.

In a nutshell, low dose medicine can be defined as an up-to-date integration of homeopathy, Psycho-Neuro-Endocrine-Immunology (PNEI) and molecular biology.

The therapeutic strategy

In general low dose medicine should be used according to the following decisional process:

- If the pathological condition is the expression of a down-regulation (deficiency) of a certain molecule (cytokine, interleukin, hormone, neuropeptide, neurotransmitter, growth factor), the same low dose molecule will be **used in order to stimulate (up-regulate) its physiological production.**
- If the pathological condition is the expression of an up-regulation (excess) of a certain molecule (cytokine, interleukin, hormone, neuropeptide, neurotransmitter) **the 'opposing low dose molecule' will be used in order to down- regulate its physiological production.**
- According to a more 'symptoms oriented decisional processes' where the low dose molecules are **prescribed to suit and to manage the particular symptoms of the disease.**
- In combination with classic homeopathic single and/or complex remedies in order to achieve a faster remission (*for*

more information on single and complex homeopathic remedies consult the chapter about treatments in my book 'Heal yourself').

- **In addition to conventional medications with the aim of counteracting their side effects or in order to reduce the dosage and frequency of the conventional medication.**

General dosage: the daily dose is 15 to 20 drops in little mineral water to be taken twice a day, and kept under the tongue for deep absorption before swallowing, for periods ranging from 3 to 6 weeks or longer, and according to the particular condition and individual reaction.

Chapter 2

What are cytokines?

Cytokines can be described as small messenger and signaling molecules released by cells that have a specific effect on the interactions between cells, on the communication between cells and on the behavior of cells.

The term 'cytokine' encompasses a large and diverse family of messenger and signaling molecules produced throughout the body by cells of diverse embryological origin. There is no general agreement as to which molecules should be termed cytokine, and part of this difficulty in distinguishing cytokines from other molecules, is that some of the immunomodulating effects of cytokines are systemic, meaning that they act on the whole body system rather than on a localized system or organ.

Cytokines were officially recognized in 1979 and this discovery created a revolution in immunology and medicine in general. Since then, an enormous amount of research has been devoted to cytokines.

Cytokines are critical to the development and functioning of both the innate and adaptive immune response, they are often secreted by immune cells that have encountered a pathogen, thereby activating and recruiting further immune cells to increase the system's response to the pathogen.

Although pivotal in triggering and regulating the immune response, they are not limited to the immune system alone, in fact many cytokines are now known to be produced by cells other than immune cells and they can have effects on non-immune cells as well.

Cytokines are also involved in several developmental processes during embryo genesis. **The complex network of cytokines balances pro-inflammatory and anti-inflammatory effects, and an imbalance between pro- and anti-inflammatory**

cytokines or the uncontrolled production of cytokines can result in chronic inflammatory disease, allergies or auto-immune disease.

Broadly speaking, cytokines can include different types of molecules like 'monokines' produced by mononuclear phagocytic cells, 'chemokines' produced by many kinds of leukocytes and other cell types, 'lymphokines' produced by activated lymphocytes (especially T helper cells), 'interleukins' that act as mediators between leukocytes, 'peptides' (cell signaling molecules), 'growth factors' which promote cell growth and 'interferons' (INF) which respond to infected cells and cancer cells.

We could also divide cytokines according to their biological role such as growth factors which promote cell growth proliferation and differentiation, interleukins and lymphokines which are capable of creating a communicating network within the immune system, and chemokines and lymphokines which are mainly involved in inflammation.

Unfortunately cytokines used by immunologists and other medical specialists in conventional medicine are in pharmacological doses and have very strong and sometimes lethal side-effects.

In low dose medicine, on the other hand, cytokines are used in low 'activated' doses without any side effects and with the therapeutic concept of modulating and regulating cell activity and cell communication and restoring natural physiology.

Low dose cytokines have the same physiological concentration (nanograms to picograms) as the molecules present in our **organism and work through a mechanism of sensitization and activation of cellular receptors.**

The result of the action of these low dose cytokines is a physiological modulation of the system cell's activity and restoration of the capacity for cellular self-regulation.

Cytokine storm

A common mistake people usually make is to try to 'boost' one's immune system through the use of herbal or nutraceutical remedies and molecules with the idea of fighting off an infection, but in fact **an over reacting immune system can sometimes be the cause of an over-secretion of cytokines which can trigger a dangerous syndrome known as a 'cytokine storm'.**

Cytokine storms have the potential to do significant damage to body tissues and organs. If a cytokine storm occurs in the lungs, for example, fluids and immune cells such as macrophages may accumulate and eventually block off the airways, potentially resulting in death.

Cytokine storms were the main cause of death in the 1918 'Spanish Flu' pandemic, the 2003 SARS (caused by coronavirus) and the Avian Flu (A/H5N1) virus in 2008. Deaths were weighted more heavily towards people with healthy immune systems, due to its ability to produce stronger immune responses, with increasing cytokine levels.

By using low dose cytokines, on the other hand, one can up-regulate or down-regulate, if needed, the immune system responses without any side-effects according to each individual case, resulting in a perfect modulation of all immune processes during an infection outbreak.

Recombinant cytokines

The cytokines used in low dose medicine are called 'recombinant cytokines' and are the same as the ones used by specialists and immunologists in conventional medicine, with the enormous difference that in low dose medicine these recombinant cytokines are then properly diluted and activated through a process called 'succussion' to avoid any side-effects (*for the homeopathic method of dilution and succussion see my book 'Heal yourself'*).

Recombinant cytokines are mostly produced by expression from suitable cloning vectors containing the desired cytokine gene, including 'Escherichia coli', 'Pichia pastoris', 'Baculovirus' and 'Poxvirus' systems which can be expressed in yeast, mammalian (human) cells or insect cell systems.

Expression in each system results in a protein that differs, to a varying extent, from the native molecules. The expression system can influence the pharmacokinetic properties, biologic activity, and clinical toxicity of recombinant proteins.

The 'Pichia pastoris' expression system seem to be particularly well suited for the production of recombinant cytokines because the yeast cells are not a source of endogenous toxins, as for example is the case with E. coli.

Recombinant human cytokines (produced from human cells) are more authentic in terms of both physical properties and biochemical functions, however, the current process of human cell expression requires a large quantity of DNA and medium supplemented with bovine serum with increasing costs.

Another emerging technology for the production of recombinant cytokines is the 'plant-based processing'. Recent development of DNA recombination and plant transformation techniques resulted in creating the novel protein production platforms based on either whole plants or plant cells. The process of using plant-based systems as highly effective production platforms is named 'molecular farming', while the pharmaceutical products obtained in the plant-based systems are often called plant-made pharmaceuticals (PMPs).

Whatever the source of the recombinant cytokine is, in low dose medicine the signaling molecule undergoes a process of dilution and activation and is therefore rendered highly active and, at the same time, harmless in terms of side-effects, not to mention the incredible reduction of costs for the end user.

Pro and anti - inflammatory cytokines

Cytokines are commonly classified into pro and anti - inflammatory, **although recent studies have proven that this distinction is far too simplistic as there are numerous examples illustrating that a given cytokine may behave as a pro- as well as anti-inflammatory** depending on the cytokine amount released, the nature of the target cell, the nature of the activating signal and even on the temporal sequence of several cytokines acting on the same cell.

Recent findings from a wide range of cytokine investigations indicate that the net effect of the inflammatory response is determined by a delicate balance between pro-and anti-inflammatory cytokines acting in concert to coordinate the immune response initiated upon an external signal, and that any perturbation in this equilibrium can drive the host immune response either towards chronic inflammation or towards healing.

Despite what has just been said, we can generally list some of the cytokines which behave as pro or anti-inflammatory.

Among the **inflammatory cytokines** according to the severity of the inflammatory response we can list:

Interleukin 1 alpha and beta (IL-1 α and IL-1 β)

Interleukin 6 (IL- 6)

Tumor necrosis factor α (TNF- α)

Interleukin 8 (IL- 8)

Interleukin 12 (IL- 12)

Interleukin 17 (IL -17)

Interleukin 18 (IL -18)

Interleukin 23 (IL -23)

Granulocyte-macrophage colony stimulating factor (GM-CSF)

Interferon gamma- (IFN- γ)

Ciliary Neurotrophic Factor (CNTF)

Anti-inflammatory or immunoregulatory cytokines that counteract various aspects of the inflammatory response include

the following in order of importance of inhibition of pro-inflammatory cytokines:

Anti- interleukin 1 (Anti-IL1)

Interleukin 10 (IL- 10)

Interleukin 4 (IL- 4)

Transforming growth factor-beta (TGF-beta)

Interleukin 11 (IL- 11)

Interleukin 13 (IL- 13)

Interleukin 35 (IL- 35)

Interaction between cytokines and innate and adaptive immunity

In humans two main types of immunity are recognized: the innate (non-specific) and the adaptive (also known as acquired) immunity. Both innate and adaptive immunity depend on the ability of the immune system to distinguish between self and non-self molecules (pathogens).

If a pathogen such as a bacteria or virus manages to breach the layered defenses such as the physical barriers of the skin, the innate immune system provides an immediate, but non-specific response. If the pathogen then successfully evades the innate response, vertebrates possess a second layer of protection called the adaptive immune system, which is activated by the innate response.

The innate immune system is the dominant system of defense in most organisms and it is found in all plants and animals.

The innate immune system is non-specific, its response comes into play immediately or within hours of an antigen's appearance in the body in a very effective way but does not confer long lasting immunity against such a pathogen since it lacks an immunological memory.

Cells of the innate immune system include phagocytes cells (white blood cells that engulf and absorb waste material, harmful

micro organisms or other foreign bodies) **such as monocytes and macrophages, and also natural killer (NK) cells, basophils, mast cells, eosinophils and dendritic cells.**

Cytokines released from innate immune cells play a key role in the regulation of the immune response.

Cytokines secreted by different innate immune cells includes tumor necrosis factor (TNF), interleukins IL-1, IL-6, IL-10, IL-12, IL-15, and IL-18, interferons such as IFN- α , IFN- β and IFN- γ .

The adaptive (acquired) immune system, on the other hand, allows for a stronger immune response as well as an immunological memory which is maintained by 'memory cells'.

This highly effective specificity allows for the generation of responses that are tailored to specific pathogens or pathogen-infected cells.

Cells that make up the adaptive immune system include the B and T lymphocytes which are derived from hematopoietic stem cells in the bone marrow.

B lymphocytes are involved in the humoral immune response whose primary function is the production of antibodies, whereas T lymphocytes differentiate into different subtypes like the T cytotoxic (T_c) cells, T helper (T_h) cells, natural killer T cells (NKT cells).

Cytokines that play a role in the adaptive immune system include interleukins IL-2, IL-4, IL-5, IL-10, IL-12, TGF- β and IFN- γ .

Interaction between cytokines and T lymphocytes

As we have seen, T lymphocytes are a type of white blood cell that plays a central role in adaptive immunity which, once activated, divide rapidly and secrete cytokines which regulate and assist all immune responses.

They are distinguished from other lymphocytes, such as B cells and natural killer cells (NK cells) by the presence of a T-cell

receptor (TCR) on their surface and **they are called T cells because they mature in the thymus** (whereas B cells migrate to mature in secondary lymphoid tissues such as the spleen, lymph nodes, Peyer's patches, etc).

Within the T lymphocyte group we can distinguish various subgroups of cells like T helper cells (Th₁, Th₂, Th₃ and Th₁₇), T cytotoxic (Tc) cells, regulatory cells (T reg cells) and Natural Killer T (NKT) cells (not be confused with Natural Killer or NK cells of the innate immune system) which bridge the adaptive immune system with the innate immune system.

Among these different T lymphocyte subgroups, of particular importance are the T helper (Th) lymphocytes also known as CD₄⁺ T cells (because they express the CD₄ glycoprotein on their surface) **and also the T cytotoxic (Tc) lymphocytes** also known as CD₈⁺ T cells (since they express the CD₈ glycoprotein at their surface).

Moreover, as we will see in the next chapter, T helper (Th) cells are categorized into several subtypes including Th₁, Th₂, Th₃ and Th₁₇.

Interaction between cytokines and T helper (Th) lymphocytes

In general, T helper (Th) cells are important because they assist all other white blood cells immunological processes, including maturation of B cells into plasma cells and memory B cells, and activation of T cytotoxic (Tc) cells and macrophages.

T helper 1 cells (Th₁) are the immunity effectors against intracellular pathogens (viruses and bacteria inside host cells) by promoting a cellular immune response.

They are triggered by interleukin IL-2, IL-12, interferon gamma (IFN- γ) and they activate macrophages as well as T cytotoxic cells, Natural Killer (NK) cells and interferon gamma (IFN- γ) to kill intracellular organisms.

Low dose cytokines which up-regulate Th1 lymphocytes include interleukins IL2, IL12, IFN γ , and the hormone melatonin. There are also many mushrooms which stimulate Th1 cell mediated immunity (see my book 'Heal yourself').

Low dose cytokines which down regulate Th1 cells are mainly interleukin IL 4 and IL10 and the hormones cortisol and ACTH.

Th 2 cells (Th2) are the immunity effectors against parasitic infection and toxins and promote a humoral immune response.

They are triggered by interleukin 4 (IL-4) and their effector cytokines are IL-4, IL-5, and IL-13. Their main effector cells are eosinophils, basophils, and mast cells and they also help B cells to secrete protective antibodies.

Th2 cells over activation stimulate mast cells to release histamine and are the cause of IgE mediated allergic reactions and hypersensitivity including allergic rhinitis, atopic dermatitis, and asthma.

Low dose cytokines which up-regulate Th2 lymphocytes include interleukins IL4, IL5, IL10, IL13 and the hormones cortisol and ACTH.

Low dose cytokines which down regulate Th2 cells are mainly interleukin IL2, IL12, IFN γ and the hormone melatonin.

Th17 cells (Th17) are a subset of T helper cells which mediate immunity against extracellular bacteria and fungi. They are considered developmentally distinct from Th1 and Th2 cells and an excessive amount of Th 17 cells are thought to play a key role in autoimmune diseases such as multiple sclerosis (MS), psoriasis, autoimmune uveitis, diabetes type 1, rheumatoid arthritis (RA), and Crohn's disease.

IL1, IL-6 and IL 23 are thought to drive differentiation into Th17 cells and the effector cytokines associated with Th 17 are IL-17, IL1, IL-21, IL-22 and TNF alpha.

Low dose cytokines which up-regulate Th17 lymphocytes include interleukins IL-6, IL 17, IL 21, IL 23 and also TGF- β .

Low dose cytokines which down regulate Th17 cells are mainly interleukin IL4 and IFN γ .

Th3 cells have suppressive/regulatory properties which control auto-aggressive immune responses, they assist mucosal immunity and are involved in protecting mucosal surfaces in the gut from nonpathogenic antigens. They mediate and regulate anti-inflammatory environment by secreting TGF-beta, IL-4 and IL-10. Th3 cells inhibit Th1 and Th2 cells.

Low dose cytokines which up-regulate Th3 are interleukin IL10 and TGF-β.

Interaction between cytokines and T regulatory (Treg) lymphocytes

Regulatory T cells (T reg), formerly known as suppressor T cells, are a subpopulation of T cells which modulate the immune system, maintain tolerance to self-antigens, and abrogate autoimmune disease.

T reg cells do not prevent initial T cell activation but rather inhibit a sustained response preventing chronic and potentially damaging pathological responses like self-reactivity, autoimmunity .T reg cells suppress both Th1 and Th2 responses.

Low dose cytokines which up-regulate T reg cells are interleukin IL10 and TGF-β.

The Th1/Th2 driven immune response in relations to common ailments

A healthy immune system is both balanced and dynamic switching back and forth between the Th1 and Th2 driven immune responses as needed, and this allows for a quick eradication of any threat and a return to balance before responding to the next threat.

The inability to respond adequately with a Th1 response and therefore an overactive Th2 response can result in chronic viral

infections, AIDS, chronic fatigue syndrome, candida yeast infections, multiple allergies, asthma, multiple chemical sensitivities (MCS), atopic dermatitis, scleroderma, viral hepatitis and other related illnesses and cancer.

Factors which contribute to induce a Th2 switch and suppress cell-mediated immunity are: vaccinations, heated vegetable oils high in trans-fatty acids, glucose (white sugar), asbestos, lead, mercury and other heavy metals, pesticides, air and water pollutants, morphine, tobacco, the hormone cortisol (due to prolonged stress), HIV, candida yeast infections, HCV, E-coli, UV-B light, alcohol, sedentary lifestyle, negative mind attitudes, low body temperature, chronic insomnia, weight lifting, and steroids (for muscle gain).

An overactive Th1 response, on the other hand, can worsen already activated (Th17 driven) auto immune diseases like rheumatoid arthritis, multiple sclerosis, diabetes type 1, psoriasis, Chron 's disease, alopecia, vitiligo and most autoimmune endocrine pathologies.

Interaction between cytokines and T cytotoxic (Tc) lymphocytes

Cytotoxic T cells (also known as CD8+ T cells or killer T cell) are cells specialized in killing cancer cells, virus, bacteria and protozoan infected cells or cells that are damaged in other ways.

Low dose cytokines which up-regulate cytotoxic T cells are interleukin IL2, IL12, IFN- α , IFN- γ , and TNF α .

Low dose cytokines which down regulate cytotoxic T cells are mainly interleukin IL10 and TGF- β .

Interaction between cytokines and Natural killer (NK) cells and lymphokine-activated killer (LAK) cells

Natural killer cells (also known as NK cells) are a type of lymphocyte which evolves from lymphoid stem cells and are a major component of the innate immune system.

Their main role is to contain viral infections while the adaptive immune response is generating antigen-specific cytotoxic T cells that can clear the infection, and they also play a major role in the host defense and destruction of both cancer cells and all kinds of mutated cells. They differentiate and mature in the bone marrow, lymph node, spleen, tonsils and thymus from where they enter into the blood stream.

NK cells are activated in response to interferons or macrophage-derived cytokines.

Low dose cytokines which up-regulate NK cells are interleukin IL 2, IL7, IL 12, IL 15, IL 18, IFN- α and IFN γ and the hormone melatonin (there are also many mushrooms which stimulate NK cells-see my book 'Heal yourself').

Lymphokine-activated killer cells (or LAK cells) are a type of white blood cell that has been stimulated to kill tumor cells.

Lymphocytes exposed to IL 2, are capable of destroying cancer cells, both primary and metastatic. The mechanism of LAK cells is distinctive from that of natural killer (NK) cells because they can destroy cells that NK cells cannot, moreover, LAK cells are specific to tumor cells and do not display activity against normal cells.

Low dose cytokines which up-regulate LAK cells are interleukin IL 2 and IL7.

Hormones and cytokines cross regulation

Hormones can influence cytokines levels and create a connection between the endocrine system and the immune system.

Female sexual hormones inhibit the Th₂ reaction and stimulate Th₁ cytokines whereas **cortisol (the stress hormone) inhibits Th₁ reaction and in particular IL-2 with detrimental effects on cell mediated immune responses.**

Some pro-inflammatory interleukins like IL-1, IL-6 and TNF- α stimulate ACTH secretion and also cortisol secretion with the same detrimental effect on the organism immune system responses.

IL-1, TNF- α , IFN- γ and IL-6 play a role in the thyroid function as they inhibit the iodide uptake and the release of thyroid hormones, by hindering thyrocytes growth and thyroglobulin synthesis.

IL-1- β and tumor necrosis factor (TNF) - α inhibit thyrotropin-releasing hormone (TRH) by stimulating the secretion of somatostatine. Tumor necrosis factor (TNF) also inhibits insulin like growth factor 1 (IGF-1).

Melatonin increases the effect of interleukin IL₂, IL₁₂ and interferon (IFN) gamma, inhibits cortisol (the stress hormone) and stimulates Th₁ cellular immune responses.

Hematopoietic cytokines

Haematopoietic (blood producing) stem cells reside in the bone marrow and have the unique ability to give rise to all of the different mature blood cell types and tissues. All blood cells types are divided into three lineages:

- **Erythroid cells** which are the 'oxygen carrying' red blood cells.
- **Lymphocytes (white blood cells)** derived from common lymphoid progenitors cells pertaining to the adaptive immune system.
- **Myelocytes** include granulocytes, megakaryocytes and macrophages derived from common myeloid progenitor cells, and they are involved in both innate and adaptive immunity and blood clotting.

The production of hematopoietic cells is under the tight control of a group of hematopoietic cytokines like interleukins IL 3, IL 7, IL 9, IL 11, granulocyte colony-stimulating factor (GCSF), and granulocyte-macrophage colony-stimulating factor (GM-CSF).

IL-3 stimulates hematopoietic stem cells into myeloid progenitor cells. IL 7 stimulates hematopoietic stem cells into lymphoid progenitor cells. IL 9 acts as a regulator for a variety of hematopoietic cells. IL 11 stimulates platelet development in the bone marrow. GCSF and GM-CSF stimulate stem cells to produce granulocytes (neutrophils, eosinophils, and basophils) and monocytes.

Low dose cytokines which up regulate the production of hematopoietic cells are mainly interleukin IL 3, IL 7, granulocyte colony-stimulating factor (GCSF) and to a lesser degree also IL 9 and IL 11.

Low dose medicine and PNEI

Psycho-neuro-endocrine-immunology (PNEI) is the study of how psychological and neurological factors on one hand and, endocrine and immune responses, on the other hand, influence each other interdependently.

The comprehension of the constant contact, communication and interdependence of these four systems, is the key for the identification of physiopatological mechanisms which lie at the heart of many if not all illnesses.

Factors like psychological-behavioural patterns, and, above all, sustained stress can change and alter the hormonal and immunological answer.

Psychological factors are the most common trigger of PNEI imbalance. Stressful states with sustain high cortisol and adrenalin levels disturb the hypothalamic-pituitary-adrenal (HPA) axis, resulting in thyroid problems and impaired immune responses.

In the PNEI vision, the neuroendocrine and immunitary systems act, respectively, as sense organs in the management of cognitive and non-cognitive stressors. Exposure to repeated cognitive, non-cognitive, physical or environmental psycho-emotional stress of sufficient intensity can cause or exacerbate an imbalance (up or down –regulation) in the formation and metabolism of cerebral chemicals like dopamine, serotonin, noradrenaline which are involved in mood regulation, attention, appetite control, reward, addiction and chronic inflammation .

As we have seen, in low dose medicine one can use various cytokines, growth factors, hormones and neurotransmitters with the intention to up-regulate or down-regulate each and every branch of the PNEI system without any side effects, and, most important, without altering the physiological biorhythm of the individual.

Relevant terminology:

- **Cytokine:** general name for small messenger and signaling molecule (protein, glycoprotein, and peptide) released by cells which has a specific effect on the interactions between cells.
- **Interleukin:** name for a specific signaling molecule (cytokine) expressed by white blood cells and pertaining to the immune system.
- **Interferon:** cytokine or chemical substance (protein) made and released by host cells in response to the presence of pathogens such as viruses, bacteria, parasites or tumor cells, which trigger s the protective defenses of the immune system to eradicate such pathogens or tumors.
- **Lymphocyte:** a type of white blood cell that plays a central role in the adaptive or acquired immune system.
- **Protein:** name for large biological molecule consisting of one or more chains of amino acids performing a vast array of functions within living organisms, including catalyzing

metabolic reactions, replicating DNA, responding to stimuli, and transporting molecules from one location to another.

- **Peptide:** name for a smaller protein-like chemical compound that is composed of a chain of two or maximum 50 amino acids and is distinguished from a protein on the basis of the smaller size. Many hormones and antibiotics are peptides.
- **Neuropeptide:** general name for a peptide (small protein) signaling molecule used by neurons to communicate with each other.
- **Neurotransmitter:** chemical substance (amino acid, peptide, or monoamine) which transmits signals between neurons and target cells of the nervous system (synapses).
- **Growth factor:** chemical substance, usually a protein or a steroid hormone, which acts as a signaling molecule, capable of stimulating cellular growth, proliferation and cellular differentiation. Growth factors play an important role in promoting cellular differentiation and cell division.
- **Neurotrophin or Neurotrophic factor:** a family of proteins that are responsible for the growth and survival of developing neurons and the maintenance of mature neurons.
- **Hormone:** a general name for a chemical messenger molecule that transports a signal from one cell to another. In humans, endocrine hormones are usually residing within a particular endocrine gland and directly released into the bloodstream.

Important note

In the following chapters under the name of some but not all specific cytokine, growth factor or hormone I have attempted to give the 'general flavour' of the molecule, but this should not confuse the reader in thinking as that as the only function of the molecule; **one should read well each complete description and**