QUALITY AND QUANTITY IN MEDICAL EDUCATION
CONFERENCE IN MILAN, ITALY: 24-25 MAY 2005

EPISTEMOLOGY AND MEDICAL SCIENCE
CHANGE OF THE PARADIGM

Giuseppe R. Brera[1]

Epistemology is the mother of science and vice versa. Medical science, from Claude Bernard, entrusted theories' corroborations to experimental laboratory and clinical investigations. This approach lead to the "Evidence Based Medicine" theory (EBM) which links clinical reasoning to scientific results of clinical trials and underrates the traditional Medicine DNA: empirical - qualitative observations of clinical nature. EBM calls for standardized applications of therapeutic protocols which physicians are invited to execute and is functional to finance-centred health systems. EBM is the triumph of an applying mechanistic determinism in clinical research founded on a linear causality between stimulus (S) and biological reaction (R) (S-R Paradigm), without any consideration of the interaction paradigm posed by the epistemological evidence of a psycho-neuro-endocrine-immunological network. EBM maintains the Cartesian dualistic paradigm and consequently it is epistemologically unreal. At human level, according to the interaction research model, biological reactions to a stimulus belong to individuals and depict a S-P-R paradigm (P= Person) overcoming the S-R mechanistic model because of animals' immunological reactions which appear to be relative to possibilities to escape or not the experimental stress. "Possibility" is an undeterminable concept closer to philosophy than to science. The Selye paradigm is fallen under the psychoneuroimmunological research results. Like physics in thirties, medical science presents a non-deterministic shift with an epistemological crisis, and it is possible to demarcate two main models: a mechanistic "genoma –centred" and a person-centred medicine founded on human nature interaction and teleonomia, according to the Hippocratic tradition founded on ethics (person's well) and science (the truth). Following the Karl Popper's critical empiricism, in nineties a relativistic theory of medical science was constituted: the "Relativity of Biological Reactions to Possibilities and Quality of Coping" (RBR) which postulated a biological relativity subjected to human and only human possibilities and qualities, with a demarcation between animals and humans and the introduction of new epistemological concepts like "biological reactions" distinguished by "biological constants" interacting with "possibility and quality" of coping. This paradigm originated from experimental, probabilistic theories and was corroborated by experimental confirmations at experimental and clinical level. Biological reactions (e.g., gene expression) are result of interactions between biological constants and subjective, relational, social and environmental variables which could be protective or risk factors. A new non-deterministic concept of health was born. In humans this model depicted the "*Indeterminate theory of human coping"* (EquationB), the *"General Determinate Relativity*" *referred to animals* (Equation C) and the "*Quality Indeterminate Relativity of Biological Reactions"* (Equation D*),* referred only to humans.

The RBR model introduces medical science to the concept of "protective factors", "resilience" and "vulnerability". These concepts are the fundamentals of "Person-Centred Medicine" and "Person centred clinical method" which take in consideration empathic phenomena, strength points and resources before problems. Interaction, Teleonomy, Protection, Resilience and Vulnerability are new epistemological concepts to be studied and integrated with new meanings in traditional investigation and clinical methods usually centred only on patients' problems and risk factors. Medical education curricula and post graduate medical courses must be re-formulated on Person-centred clinical method and an interaction-teleological medical science epistemology.

[1] Giuseppe R. Brera, MD – Rector of Università Ambrosiana and Dean of Milan Medical School, Università Ambrosiana, Milano, Italy E-mail: gbrera@unambro.it

PHYSIOPATHOLOGY OF A SUPERSYSTEM: EMERGING EVIDENCE OF THE INTERACTION BETWEEN THE BRAIN AND THE IMMUNE SYSTEM

Georges Jean Marie Maestroni[2]

The two major adaptive systems of the body, the brain and the immune system, operates by a continuous cross-talk to maintain homeostasis. The autonomic nervous system (ANS) links the brain and the immune system either via a direct neural influence, or neuroendocrine mechanisms mainly as the hypothalamic-pituitary -adrenal axis and the pineal gland. Glucocorticoids that are the end product of the hypothalamic-pituitary -adrenal axis provide one of the best and widely known examples of the powerful influence of the ANS on immunity. More recent evidence indicates, however, that a major component of the ANS, the sympathetic nervous system (SNS) also plays an important role in the fine tuning of the immune response. The sympathetic (noradrenergic) system which innervates all parts of the body, constitutes the largest and most versatile component of the ANS. The sympathetic neurotransmitter norepinephrine (NE) has been historically associated with the "fight or flight" response and also contribute to the regulation of autonomic activity such as cardiovascular function. In addition, the SNS may regulate immunity by acting on various phases of the immune response. Of special interest, seems the NE effect on dendritic cells (DCs) functions that play a major role in the innate phase of the response. In particular, NE may regulate DCs migration and antigen-presenting ability by acting on alpha- and beta-adrenoceptors. The effect of NE seems to be aimed at shaping the immune response which is more appropriate to clear the invading pathogen. Alterations in SNS activity and/or adrenoceptors expression and function might thus play a pathogenetic role in a variety of diseases. More recently, we also found that the role of the skin adrenergic system seems to be functional in limiting the Th1 response to pathogens that are recognized by Toll-like receptors expressed in epidermal keratinocytes. This mechanism might have evolved to shape the appropriate immune response to gram-positive bacteria or viruses that may hit the skin more frequently. Disorders of the adrenergic regulation of the skin immune response may thus results in excessive Th1 priming and have pathological consequences. Excessive Th1-priming has been associated to an augmented risk for organ-specific autoimmune diseases. Current pathogenesis concepts consider, in fact, skin disorders such as psoriasis vulgaris as a T cell mediated autoimmune disease. A better understanding, of the SNS–immune system connection may thus provide novel therapeutic approaches in a variety of diseases.

[2] George J. M. Maestroni, PhD - Center for Experimental Pathology. Istituto Cantonale di Patologia, 6601 Locarno, Switzerland. E-mail: georges.maestroni@ti.ch

TEACHING CLINICAL PSYCHONEUROIMMUNOLOGY: A BRAVE NEW WORLD?

Paolo Lissoni[3]

The Clinical Psychoneuroendocrinoimmunology (PNEI) is the reinterpretation of the human pathologies as a consequence of an altered psychoneuroendocrine regulation of the immune responses. The episthemology of PNEI is founded on the scientific basis of the existence of physiological interactions between psychoneuroendocrine and immune systems. Then, the application of PNEI knowledgments to the clinical approach to the human diseases requires new laboratory examinations, new therapeutic strategies and a real personal relationship with the patients. The PNEI may explain the mechanisms responsible for the influence of functionless, which plays a fundamental role in the pathogenesis of several neuroendocrine system influences the immunity by modulating T helper-1 lymphocytes (TH1) and dendritic cells, which are the most important cells in the activation of the immune reactions. The opioid system trough the mu-opioid receptor and the catecholaminergic system trough the beta-adrenergic receptor play an inhibitory effect on both TH1 and dendritic cell activities, with a consequent diminished production of IL-2 and IL-12, respectively. At the other side, the pineal gland stimulates IL-2 production by TH1 lymphocytes and that of IL-12 by dendritic cells, whose activation is amplified by the endogenous cannabinergic agonist, anandemide. Then, pineal gland and brain cannabinergic system play a natural anticancer activity. Stress, anxiety, chronic pain and depression are characterized by hyperactivity of brain opioid system, whereas both pleasure and spiritual expansion of consciousness are associated with activation of pineal gland and brain cannabinergic ssystem. Then, the clinical investigations of the future Medicine will have to routinarely include the analysis of the psychoneuroimmune status of patients. Moreover, from a therapeutic point of view, the neuroimmune alterations to restablish the psychoneuroimmune biochemistry of the status of health. The Clinical PNEI is not an empiristic medical Science, since the elaboration of new therapeutic strategies has been elaborated on the basis of physiopathological evidence, consisting of the characterization of the neuroimmune alterations occurring in several chronic human diseases, namely cancer.

[3] Paolo Lissoni, MD, Magister ad Honorem Milan Medical School, Università Ambrosiana – San Gerardo Hospital, Monza, Italy