BOOKS: BIOMEDICINE

# Mind and Medicine

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Jamie Tosney's flu began innocently after basketball and a swim on a steamy day in July 1950. But in a blur of frightening days, he complained of muscle aches, a stiff neck, and a 101.2°F fever. His mother grew terrified as he experienced left-leg weakness and difficulty swallowing. In the hospital, shortness of breath necessitated the dreaded iron lung. The latest model, however, could not replace Jamie's dying spinal respiratory neurons, and on 21 August, his eight years ended. Within a decade, the polio vaccine consigned the disease and the iron lung to dim memory.

Seemingly every week, the media report biomedical revolutions destined, we are assured, to transform our lives. The human genome project, stem cell biology, informatics, cell therapy, and gene therapy, to name a few, eclipse the triumphs of yesteryear: asepsis, antibiotics, anesthesia, and society's mastery of sanitation. In *The Balance Within*, Esther Sternberg eschews hyperbole, opting for admirable simplicity and clarity while introducing neuroimmunology as a potential foundation of psychosomatic medicine. Yet that very simplicity slips, at times, into ambiguity in an otherwise delicately crafted, informative narrative.

Sternberg, a researcher at the National Institute of Mental Health, is at her best describing biologic mechanisms in a jargon-free, common sense fashion devoid of the elliptical qualifications that obscure much current scientific writing. She draws on Leeuwenhoek, Priestley, Pasteur, and Lister to provide perspective on the concept of inflammation, a central integrating theme of her book. In the context of the subjective experience of inflammation—with its pain, swelling, and redness—Sternberg outlines clearly the temporal profile of the cellular immune response. She delineates the roles of the white blood cell neutrophils, B and T lymphocytes, macrophages, and fibroblasts. Focusing on interleukin-1 (IL-1), she discusses the function of cytokines (which signal among white blood cells) in orchestrating the multistep inflammatory process. Sternberg offers clear descriptions of proliferative, migratory, phagocytic, and apoptotic (cell death) responses. As importantly, she uses inflammation to examine disease as the interaction of inciting agent(s) and the all-important host response. Her account outlines autoimmune (host) disorders (including rheumatoid arthritis and lupus), the potential roles of stress, and the nervous system in general.

**The Balance Within**
**The Science Connecting Health and Emotions**
***by Esther M. Sternberg***
**Freeman, New York, 2000. 270 pp. $24.95. ISBN 0-7167-3479-6.**

IL-1, for Sternberg the prototypical immune effector, is a key to reciprocal interactions between the immune and nervous systems. Circulating IL-1 stimulates the hypothalamus and pituitary directly and elicits the fight-or-flight stress response. The hypothalamus secretes corticotropin releasing hormone (CRH) and the pituitary releases adrenocorticotropic hormone; these steroids increase adrenal glucocorticoid release. (CRH also evokes a repertoire of behavioral responses to stress.) Glucocorticoids, in turn, inhibit inflammation and prevent runaway immune responses. But they can also antagonize the normally protective inflammatory response. One level of the balance is thereby clearly delineated.

This account is satisfying in its economy and simplicity, but Sternberg does not address a number of critical questions. Although, from their sites of initial discovery and their actions, cytokines such as IL-1 could be classified as "immune" molecules, they are also endogenous neural growth factors. Cytokines affect neural proliferation, differentiation, and survival. Moreover, IL-1 is present in brain neuron systems and in support cells (glia) such as astrocytes and microglia. How do endogenous brain cytokines relate to immune function? Are the effects of IL-1 on the brain due to a circulating factor, to intrinsic neural systems, to support cells, or to all of the above? How would answers to these questions alter Sternberg's argument? Substantive discussion of these issues would have helped elucidate the IL-1, immune-neural connection. More generally, regulation of diverse cells and systems by a single molecule illustrates the emerging unity in biology. This central principle, well recognized by the author and implicit throughout *The Balance Within*, might have been explicitly explored.

Sternberg's intuitive approach helps maintain orientation and avoids obscurantism as she guides us through the labyrinth of stress, sensations, emotions, learning, and memory. Grounding these mind functions in brain anatomy, Sternberg avoids arcane arguments concerning their nature, while she describes pathways through which, directly or indirectly, experience, inflammation, and IL-1 itself may influence the nucleus accumbens (the "pleasure center") or the amygdala (the "fear center"). Along the way, Sternberg defines stress in a skillful, every-day fashion and presents a garden of delights of stressful situations, antecedents, manifestations, components, and consequences.

Difficulties are encountered, however, as Sternberg's account becomes more expansive and she focuses on personal relationships, beliefs, and mood. Citing interpersonal relationships as stress reducing, the author describes the archetypal maternal-infant interaction in a speculative, nearly casual manner. She presents disparate elements of ethology, ecology, sociology, and sociobiology in a distracting fashion. We are subjected to various assertions on such topics as the links between social connections and entertainment industries, electronic communications and loneliness, and social isolation and our mobile lifestyle. (For example, "the whole of our popular culture strives toward sealing or healing such connections.") Although this social commentary may be insightful and ultimately valid, Sternberg's speculations distract from her lucid central thesis.

The author's enthusiastic application of the strategy of simplifying presentation encounters turbulence in her descriptions of several neurologic disorders. Discussing the dementia of Alzheimer's disease and AIDS, she tells us that "[t]hose illnesses characterized by dementia and nerve-cell death are connected because the final bullets that kill these cells are cytokines." In the case of Alzheimer's, this statement ignores the vast literatures on the potential pathogenetic roles of amyloid plaques, neurofibrillary tangles, presenilin mutations, excitotoxicity, and trophic factor deprivation. Similarly, in describing cytokine functions in the nervous system, Sternberg asserts that "[i]n fact, in the adult nervous system that has been damaged by stroke or trauma—such as spinal cord injury—nerve cells regenerate just as they do early in life." This optimistic reading would be disputed by thousands of paralyzed victims restricted to bed and wheelchair.

Yet the errors of enthusiasm should not obscure the virtue of an all-too-rare lucidity, which *The Balance Within* exhibits. Sternberg's clear descriptions and demystification of neuroendocrine immunology provide a valuable contribution. We may all hope that an appreciation of the emerging unity of biology—based on the commonality of mechanisms governing multiple systems and on multisystem integration—will lead to a more compassionate medical approach to the whole patient.

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