Psychiatrists are called upon to manage the behavioral and emotional manifestations of a range of neuropsychiatric conditions characterized by immune-inflammatory mechanisms. We might refer to this newly emerging field as “immunopsychiatry.”

These conditions include rheumatologic disorders with central nervous system (CNS) manifestations such as: systemic lupus erythematosus (lupus) and fibromyalgia; infectious disorders such as Lyme disease, and pediatric neuropsychiatric disorders associated with streptococcal infection (PANDAS); or psychiatric conditions such as depression or autism in which inflammatory mechanisms play a critical role in the onset and/or maintenance of the condition.

Some of these diagnoses, such as fibromyalgia, have been considered controversial and have been viewed either as psychiatric manifestations of physical illness or physical manifestations of psychiatric illness. In some cases, our conceptualization of illnesses such as syphilis and peptic ulcer has progressed from somatic to infectious (ie, *Helicobacter pylori*).¹

In contrast, a hygiene hypothesis states that a lack of early childhood exposure to favorable gut parasites increases immune activation and susceptibility to immune-inflammatory disorders (including CNS disorders),² which has led to the development of helminthic therapies for various conditions.³ In the age of the microbiome, we may even be seen as superorganisms made up of thousands of different species.⁴

Our psychiatric diagnostic process, including the *Diagnostic and Statistical Manual IV* text revision, characterizes conditions based on observable behavioral criteria, rather than underlying mechanisms. This has allowed psychiatry to progress beyond earlier conceptualizations that rested on underlying mechanisms such as psychodynamic processes.

In turn, clinicians and researchers are afforded more reliability in what they call a psychiatric diagnosis. However, a diagnostic process based on observable behavioral criteria inadvertently may have contributed to our current state in which there is a serious paucity of new treatment developments for CNS disorders.

Psychiatric conditions that have heterogeneous causes or underlying mechanisms are likely to have a much less robust “signal” in phase 3 placebo-controlled trials, in contrast to conditions that have a homogeneous cause or mechanism. Further, in our current diagnostic classification system, if a condition is determined to have an identified underlying mechanism (ie, Rett’s syndrome), it may no longer be classified as a psychiatric condition.

Also, if a condition occurs in the path.
setting of ‘medical’ illness, then it is classified as being secondary to a medical illness (ie, PANDAS may be thought of as obsessive-compulsive disorder, secondary to medical illness).

A further understanding of the role of immune-inflammatory mechanisms in psychiatric illness may lead to practical benefits such as a refined history and assessment, and the development of new treatments. For example, an assessment of biomarker measures of inflammation in selected patients may include tests of inflammatory cytokines, acute phase proteins, and anti-brain antibodies. A careful history of inflammatory stimuli in selected patients may reveal past use of interferon associated with the development of depression, or history of maternal immune activation associated with the development of autism in offspring.

A better understanding of inflammatory molecular signaling pathways may ultimately lead to the development of personalized treatments in genetically stratified or biologically homogeneous subgroups of patients with immune-inflammatory illness.

If you would like to comment, email Eric Hollander at ehollander@montefiore.org.

ACKNOWLEDGMENT
Casara Jean Ferretti, MS, of Albert Einstein College of Medicine and Montefiore Medical Center; and Stefano Pallanti, MD, PhD, of the University of Florence, contributed to the writing of this editorial.

doi: 10.3928/00485713-20120906-03

REFERENCES

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