

Think Again: Integrating Psychological and Physiological Factors in Diagnostic Medicine

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When considering illnesses that have dramatically altered our understanding of human health, the severity of symptoms associated with HIV and smallpox makes them obvious candidates. In contrast, a less intuitive example is that of peptic ulcers, which are characterized by nausea and stomach pain. However, the way in which the origin of these ulcers was finally discovered is indeed indicative of a pervasive trend in medicine. Namely, it illustrates the historically skewed consideration of the balance between physiology and psychology when investigating the causes of illness.

In the early 1980s, peptic ulcers had long been ascribed to bad relationships, hateful jobs, rich food, or general stress. Dr Barry Marshall, who thought that this may be an overly simplistic dismissal of any causes linked to microorganisms or systemic biology ('pathogenic causes'),

the cases that were once treated with bland foods and counseling can be cured with antibiotics (3). In terms of physical maladies, ulcers are relatively benign, but the story of this discovery represents a frame of mind that even today may be hindering our understanding of human health and physiology. The tendency to attribute illnesses to causes inherent to the individual—such as personality or neurochemical imbalances—may blind researchers to external, pathogenic contributors.

Past examples of doctors being misled by this tendency include the belief that diabetes is mainly caused by "excessive sexual intercourse, and... copious evacuation of the bowels..." to the conviction that most women are susceptible to endless varieties of hysteria (4). Clearly, we have been able to overcome these beliefs, and we now know that diabetes is caused by a hormonal imbalance.

However, there may be less trivial examples of misattributed medical conditions that are more engrained in the medical establishment.

Although certain neurodegenerative diseases, such as Alzheimer's disease or syphilis, have been historically regarded as psychological illnesses due to limited scientific knowledge, problems also arise when researchers focus on simple explanations for complex disorders. For example, a popular and scientific focus on a psychoanalytic theory of autism had significant social effects (5). Autism, while still not fully understood, is now generally accepted to be caused by both genetic and environmental factors (6). However, until the 1960s, the prevailing theory of autism placed the blame solely on the affected individual's troubled relationship with his or her mother. Bruno Bettelheim, noting a resemblance in the behavior of autistic children to that of concentration camp survivors, hypothesized that the antisocial tendencies of the autistic individual were a defense mechanism (5). Autistic children were shielding themselves from the quiet abuse of unloving 'refrigerator mothers', who subconsciously wished for escape from their children, hoping secretly for their death. For decades, guilt-ridden parents and a judgmental public labored under this misconception. It must be noted that such an example, though provocative, should not be taken as a refutation of the role of psychological factors in illness; indeed, in the case of autism, many of the hallmark

characteristics are thought to be escape mechanisms from the sensory overload that sufferers are thought to experience on a near-constant basis. However, it does serve as a reminder of the necessity of simultaneously considering many potential causes for an illness. By focusing on psychology alone, we are in danger of overlooking important contributing physiological factors.

Much has changed since the era of Bettelheim's



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was prompted to drink a culture of the bacterium that he suspected was responsible (1). Only when he developed ulcers, and the same bacteria was isolated from his stomach lining, were the previously dismissive researchers willing to consider his theory (2). In 1994, the National Institutes of Health Consensus Development Conference announced that there was a strong correlation between the bacteria and stomach ulceration; it is now accepted that 75% of

theories; then so-called mental conditions are now no longer thought to mirror the character of the family or the patient. As our knowledge of psychological disorders grows, more and more mental illnesses are found to be attributable to neurotransmitter imbalance or structural abnormalities in the

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brain, which may themselves be susceptible to environmental triggers. However, as the example of peptic ulcers illustrates, there may still be danger in blaming all aspects of an illness on internal factors. Even mental illnesses whose causes appear well-defined may be greatly influenced by seemingly unrelated pathogens.

For example, a number of studies have shown that cognitive deficits in individuals with bipolar disorder are strongly associated with the virus that causes some forms of herpes (HSV-1). Compared to bipolar individuals who had not been exposed to the virus, those who tested positive for the herpes antibodies were more likely to show reduced cognitive function (such as problem solving skills or reading comprehension) as assessed by the Repeatable Battery for the Assessment of Neuropsychological Status (7, 8). Care was taken to ensure that other factors potentially responsible for impaired cognitive function were controlled, including levels of education and medication status. It is worth noting that the same type of cognitive impairment, particularly a decline in verbal reasoning skills, is often seen in acute encephalitis, an infection of the brain in the areas necessary for proper functioning. The herpes virus is usually responsible for the most severe cases of this type of encephalitis (9). While citing the herpes virus as a causative or even influential factor in the onset of bipolar disorder is certainly premature, future studies investigating the potentially far-reaching ramifications of the body's inflammatory response to infection appears warranted.

A less commonly seen, but nonetheless widespread, pathogen is a parasite called *Toxoplasma gondii*, which can be spread through accidental consumption of the parasite's eggs and through contact with feline feces. In general, infection generally displays no symptoms for most healthy individuals and treatment is unnecessary (10). However, a widening body of evidence has suggested that this parasite may play a significant role in the development and appearance of schizophrenia (11, 12).

The causes of schizophrenia are not well characterized; while genetic factors play a role, ambient factors such as *Toxoplasma* infection may also exert a considerable influence. In a study of 600 schizophrenia patients in China, nearly 17% were found to have been infected with *Toxoplasma*; these patients also tended to have a slightly different clinical expression of schizophrenic symptoms. Such a result may indicate the necessity of developing and refining subcategories of mental illness, as our inability to do so may confuse diagnoses. While the researchers acknowledged certain limitations, including a small sample size and difficulty in proving that infection occurred before

the onset of schizophrenic symptoms, their results lend credence to a link between *Toxoplasma* parasites and schizophrenia. In a related study, researchers discovered that schizophrenic medications (haloperidol and valproic acid) were as successful at treating the behavioral symptoms of infection of the central nervous system by *Toxoplasma* as traditional anti-*Toxoplasma* treatments (13). This startling finding suggests noteworthy similarities between the two disorders—similarities that may be elucidated with further research.

When considering the sources of such ill-defined medical conditions as bipolar disorder and schizophrenia, it can be easy to adopt a polarized stance. Both diseases seem to have strong genetic components, and other, more elusive environmental factors. While pathogens appear to exert a major influence over the development and expression of symptoms, a causative role has not yet

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been proven. Even in disorders where pathogens play a well-defined role, other factors may be at work. Despite the now-accepted influence of bacteria, 25% of peptic ulcer cases cannot be attributed to an infection. Nevertheless, the discovery of new connections between outside infection and mental illness appears to suggest that other poorly-understood disorders may be significantly influenced by pathogens. A revision of the perceptions of psychological disorders and an acceptance of the not-fully-understood role of infectious agents may lead to important discoveries and the development of new treatment options.

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References:

1. Marshall, B.J. et al. *Med. J. Aust.* **1985**, *142*, 436-439.
2. Marshall BJ et al. *Lancet* **1984**, *1*, 1311-1315.
3. Centers for Diseases Control and Prevention, *Helicobacter pylori and Peptic Ulcer Disease*, 2006 www.cdc.gov/ulcer/history.htm
4. Weingarten, G. *The Hypochondriac's Guide to Life. And Death*. New York: Simon and Schuster, New York, NY, 2001.
5. Roazen, P. *Psychohist. Rev.* **1992**, *30*, 221-250.
6. NIMH, *Autism Spectrum Disorders (Pervasive Developmental Disorders)*, 2007 www.nimh.nih.gov/publicat/autism.cfm
7. Dickerson, F.B. et al. *Biol. Psychiat.* **2004**, *55*, 588-593
8. Dickerson, F.B. et al. *Bipolar Disord.* **2006**, *2*, 124-132.
9. Hokkanen, L. et al. *Neuropsychol. Rev.* **2000**, *10*, 151-167.
10. CDC, *Parasites and Health: Toxoplasmosis*, 2004 www.dpd.cdc.gov/dpdx/HTML/Toxoplasmosis.htm
11. Alvarado-Esquivel, C. et al. *BMC Infect. Dis.* **2006**, *6*, 178.
12. Wang, H.L. *Acta Psychiat. Scand.* **2006**, *114*, 40-48.
13. Webster, J.P. et al. *Proc. Roy. Soc. B.* **2006**, *73*, 1023-1030.