**Book Reviews**

**THE CASE OF THE FROZEN ADDICTS: HOW THE SOLUTION OF AN EXTRAORDINARY MEDICAL MYSTERY SPAWNY A REVOLUTION IN THE UNDERSTANDING AND TREATMENT OF PARKINSON'S DISEASE**

By J. William Langston and Jon Palfreman. 309 pp. New York, Pantheon, 1996. $25.

**Book Review**

This book dramatically recounts the discovery of the cause of a local outbreak of sudden, severe parkinsonism in a group of young adults in northern California and how this discovery led to greater insight into Parkinson's disease. Langston is the Bay Area neurologist who reported the event and led a team of investigators to pinpoint the toxicant responsible for the acute loss of dopamine-containing neurons in the substantia nigra, causing the parkinsonism in these patients. The story unfolds and builds suspense as Langston and his colleagues determine that the toxicant is 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). MPTP was the unwanted product resulting from a short step in the planned synthesis of an illicit type of synthetic heroin that was sold on the streets to addicts. The book describes how Langston, beginning with this discovery, went from being a general clinical neurologist to becoming a well-respected and widely known clinical and scientific investigator of Parkinson's disease.

Medical writer and coauthor Palfreman helps weave a highly readable and spellbinding medical detective tale. The book opens with the unfortunate victims becoming immobile (“frozen”), unblinking, and mute only hours after injecting the street drug. As can be imagined, Langston and colleagues at Santa Clara Valley Medical Center were perplexed by the strange state of the first patient they encountered. On examining the patient’s girlfriend and finding her in a similar frozen state, Langston and his neurology colleague, Phil Ballard, realized there must be a connection.

As luck would have it, Ballard attended a party given by a neurologist friend. The two chatted about interesting medical problems; the other neurologist, James Tetrud, had also just encountered two young people in the same physical state. All four affected persons were heroin addicts. After Langston went on television to alert the community about bad “heroin” being sold on the street, a viewer told him of two additional patients. Langston then consulted with Ian Irwin, a chemist at Stanford University, who determined that of the different meperidine analogues reported by the NIH scientists, only one fit the mass spectroscopic analysis carried out on the powder injected by Langston’s patients — namely, MPTP. After Langston phoned Markey and told him about his patients, the NIH scientists renewed their interest and began to pursue the scientific investigation of MPTP. One NIH scientist had two of Langston’s patients come to the NIH for studies, and it was shown that MPTP induced permanent parkinsonism in monkeys. Langston, meanwhile, worked with his colleagues to confirm this animal model and to provide tissue specimens to his collaborating neuropathologist, Lysio Forno, who described the animal pathology.

The race was on to achieve scientific prominence, reminding one of the competition described in James D. Watson’s *The Double Helix: A Personal Account of the Discovery of the Structure of DNA* (New York: Atheneum, 1968). Langston reported the discovery of his six patients in a February 1983 issue of *Science* just as the NIH team’s discovery of the primate model was accepted by the *Proceedings of the National Academy of Science*. Langston’s article brought him instant fame, and the scientific community bought out the stock of MPTP from its chemical supplier. The discovery of MPTP-induced parkinsonism stimulated many new investigations and prompted new investigators to work in Parkinson’s disease research. This heightened activity led eventually to the knowledge that MPTP had to be oxidized by the enzyme monoamine oxidase to yield the actual toxin, the positively charged metabolite MPP⁺. Subsequently, the mechanism of action of MPP⁺ as a mitochondrial toxin (which interferes with complex I) led to the finding that in Parkinson’s disease itself there is decreased complex I activity in the substantia nigra.

Unfortunately, the patients with MPTP-induced parkinsonism had severe complications from levodopa, much as had Oliver Sacks’s postencephalitic patients, as described in his book *Awakenings* (Harmondsworth, United Kingdom: Penguin Books, 1976). Langston’s patients had uncontrollable dyskinesias, deep “off” states of parkinsonism (in which levodopa is temporarily and frequently not effective), and drug-induced personality changes and psychosis. The book tells how some of these patients underwent transplantation of fetal dopamine neurons and have shown improvement, as subsequently reported in the *Journal* (1992;327:1556-63).

In addition to the story of scientific pursuit and discovery, the book describes the personalities of a number of scientists who had a role in the story, the advances in understanding Parkinson’s disease, the use of the MPTP primate model to test new drugs and surgical treatments, and sudden, severe parkinsonism. National Institutes of Health (NIH) biochemist Sanford Markey had identified several meperidine analogues, including MPTP, in the youth’s chemical flasks. But MPTP failed to induce parkinsonism in rats, and NIH scientists were not certain which of the analogues, if any, was responsible for the youth’s impairment. Levodopa treatment was effective in this case, but the youth died 18 months later of an overdose of cocaine. The brain showed a selective destruction of the dopamine neurons in the substantia nigra.

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the politics of transplantation of fetal dopamine neurons in patients with Parkinson’s disease.

The book should be enjoyed by physicians and scientists as well as the public. It is as absorbing as a good mystery, as entertaining as an exciting novel, and as enlightening as a good biography.

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DRUGS AND THE BRAIN
By Solomon H. Snyder. 228 pp., illustrated. New York, Scientific American Books, 1996. $19.95.
ISBN 0-7167-6017-7.

MANY people say we have learned more about the brain in the past 20 years than in all of recorded history. Much of this explosive growth in knowledge emanates from the technological advances that are revolutionizing all of biomedical research. These include the new tools of cellular and molecular biology and the advanced imaging techniques that are allowing our first look at the structure and function of the brains of living, awake, and functioning people. In Drugs and the Brain, Solomon Snyder does an outstanding job of explaining what the research community has learned. He meticulously chronicles the unusual history of one of the most compelling questions of neuroscience: how exogenous chemical substances, psychoactive drugs, modify moods and other experiences. Not only have advances in neuroscience transformed our understanding of how drugs affect behavior, but the reverse has also been dramatically true. As Snyder’s own work on endogenous opiate receptors and their natural ligands, the endorphins and enkephalins, illustrates, advances in drug research have stimulated a thorough reconsideration of many aspects of neurotransmission.

This book approaches the study of drugs and the brain from many directions. Snyder carefully chronicles the interesting trends in societal attitudes about drugs that can be abused and “medicinal” drugs. The book is also filled with beautifully told stories of discovery. For example, his description of the discovery of antipsychotic agents and antidepressants as involving “large doses of serendipity coupled with occasional flashes of brilliant scientific insights” illustrates how science actually moves forward.

Drugs and the Brain also provides many interesting and informative clinical observations and insights. A particularly interesting discussion centers on whether antipsychotic medications work on the “core” or essence of psychosis or whether they deal with more superficial symptoms. Snyder gives the reader excellent, detailed clinical descriptions of depression and mania.

If I have any complaint about this book, it is that in some instances issues that would have benefited from expanded discussion are only touched on. One example is the complexity of addiction. The book speaks about tolerance, dependence, and withdrawal but focuses too little on the clinical features of addiction — compulsive, uncontrolable drug use — the aspect of addiction that for most people matters the most. This may be because the understanding of the neuroscience of addiction is quite thin. But it is a lost opportunity to move the debate from whether specific drugs produce physical dependence, which clinically is not very important, to their potential to produce unrelenting drug-seeking in the face of serious negative consequences and their capacity to overpower other motivations.

Another minor flaw occurs in the last chapter, on hallucinogens, which devotes too much time to anecdotal experiences and too little to the science of how these drugs might work. These minor imperfections aside, this book represents an outstanding education for readers at many levels. It is about much of what we know about the brain and the mind — a most complex and intriguing relation that has drawn so many to study the brain in the first place. It well reflects the author’s broad understanding of both basic science and clinical issues.

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THE SPECTRUM OF FACTITIOUS DISORDERS
(Clinical Practice Series, No. 40.)
Edited by Marc D. Feldman and Stuart J. Eisendrath.
229 pp. Washington, D.C., American Psychiatric Press, 1996. $36.
ISBN 0-88048-909-X.

FROM 1783 to 1785, a woman named Kate Hudson plagued England’s Nottingham General Hospital with visits prompted by the mysterious appearance of needles, nails, and pieces of bone beneath her skin. Her medical record, which may be the first recorded account of factitious disorder, reveals evidence of drug-seeking (laundering), care-eliciting, and an array of surreptitious self-injuring behaviors (William Granger, Wonderful Museum, vol. 4. London: Alex. Hogg, 1803). Over the years, other factitious disorders were periodically described in the medical literature, but there was no broad interest in the phenomenon until 1951, when Richard Asher, in a flash of whimsy, connected it with the fabled liar Baron Munchausen.

To date, most information on factitious disorders has emerged from single case studies or letters to the editor, leaving the impression that they are uncommon or trivial. However, in the pages of the Journal James Jackson and I recently described 810 patients (“Habitually Wandering Patients,” 1994;331:1752-5) who accumulated 6266 hospital admissions in a single year, at a cost of $25 million. Although some of these admissions were necessary, we were able to show that the costs attributable to duplicity by patients were exceedingly high.

Now Feldman and Eisendrath have captured, in 11 brief chapters, the true dimensions of the problem of factitious disorders. In the opening chapter, Theodore Nadelson defines patients with such disorders as those who feign or produce their own disease, are aware of their role in the deception, and keep that role secret. He then sets the tone...
of the book by presenting a humane view of such patients that does not minimize their responsibility to society and the law. In the ensuing chapters, although multiple authorship produces some overlapping information and even some duplication of examples, the reader is rewarded with clear discussions of clinical, administrative, and ethical–legal problems.

Four especially useful chapters are devoted to factitious disorder by proxy, typically a form of child abuse in which a mother produces an illness, or the appearance of an illness, in her child. This diagnosis is currently confined to the speculative section of the diagnostic manual because its features have not been clearly established, and in a recent issue of Archives of Diseases in Childhood there has been a call to abandon the diagnosis in favor of describing exactly what has happened to the child. However, these four chapters will give the clinician sufficient tools for the task, because they discuss controversial and ethical issues with unusual wisdom. Anyone with a complex case will be inadequately prepared without this book, especially in a legal setting.

Another compelling chapter illustrates how patients may transfer their factitious disease to the legal arena. Legal professionals and law-enforcement officers, accustomed to the fabricated alibis of criminals and the exaggerated distress of plaintiffs, may be unprepared for the irrational deceptions that patients with factitious disorders introduce into their world. In case after case, this book demonstrates the seriousness of factitious disorders and their impact on family, friends, and practitioners in every medical specialty. This surprisingly comprehensive book is the first clinical guide to factitious disorders, and it is likely to remain for years the authoritative source in its field.

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DO THEY GROW OUT OF IT? LONG-TERM OUTCOMES OF CHILDHOOD DISORDERS
Edited by Lily Hechtman. 287 pp. Washington, D.C., American Psychiatric Press, 1996. $40.
ISBN 0-88048-703-8.

FOR many years, mental health professionals who work with children have been asked by parents, “Will my child grow out of it?” Those of us who have been careful to base our responses on the literature have had to reply in a way that undoubtedly seemed ambiguous to parents, often sounding as though we really didn’t know. Now, in this book, we have the data, at least as they exist today. Clearly, as the number of investigations in this area grows, we will have answers that allow better prediction. However, we can now say that a large proportion of children with emotional or behavioral problems do not grow out of them. The actual proportions of complete cure or remission vary with the disorder, being lowest in the more severe disorders, such as the pervasive developmental disorders, and highest in the more traditionally “neurotic” disorders. However, even in the case of anxiety disorders, the evidence suggests that many children and adolescents continue to have difficulties. We have known for several years that children with severe behavioral problems are likely to continue having difficulties in adolescence and adulthood, but it is helpful to have this information pulled together and analyzed with regard to the factors that may contribute to such poor outcomes.

The authors of the various sections of the book are clear in pointing out the limitations of the literature. These include the methodologic problems of the earlier studies, changing diagnostic criteria, the drawing of conclusions from clinical samples, and the problem of attrition in follow-up studies. Some of these issues are being addressed in recent and ongoing studies that will result in clearer answers. The question of treatment and its effects is also addressed, although in this area the literature remains limited and points to the critical need for more studies.

Coexisting conditions emerge as a confounder in many studies, but also as a very important variable that usually affects outcome in a negative direction. We have been aware for a number of years that in adults coexisting personality disorders affect the outcome of affective disorders. In this book coexisting conduct disorder and substance abuse in young people appear to have a similar negative effect.

The editor has wisely chosen to include not only disorders defined in the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, but also important behavioral problems, such as suicide, which is a concern for the families affected and also for society, given the dramatic increase in suicide among youths over the past three decades. The follow-up studies indicate that a substantial number of children and adolescents are continuing to struggle with suicidal ideation. The author of this chapter also highlights some of the factors related to successful suicide attempts, such as male sex, having or having had a depressive disorder, and past suicidal behavior, especially serious attempts at suicide. The lack of effectiveness of most efforts at prevention presents important challenges for the specialists in the field.

A related area is that of speech and language disorders in children. Again, the evidence is that children with more severe disorders are less likely to grow out of them. The connection with psychiatric disorders and learning disabilities is reviewed, because both of these are related to or affected by a history of speech and language disorders.

In this review I am focusing on the most striking findings. What this book provides, however, is a wealth of detail about the various studies in each area, with attention to factors that may affect outcome. The authors of each chapter are acknowledged experts in their areas, having all contributed to follow-up studies of children and adolescents with emotional and behavioral disorders.

Although the book will be of greatest interest to mental health professionals, it may also be useful to primary care physicians who counsel families with affected children. It is a must read for all child and adolescent mental health professionals.

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