

On first moving to Charleston, South Carolina we were invited to an Independence Day party at a country house on a tidal creek. After a blazing hot day, a dip into the salt water seemed a perfect ending. The setting was dark water and deep green marsh grass, and I thought I knew what I was getting into. On jumping in, however, I found myself in water that was too warm, and I was covered in fine muddy silt that didn't slide off when I climbed back on the dock. And, there were also the annoying sand gnats and mosquitoes swarming at my ankles. The initial scene fooled me; it was more complicated and less idyllic than I thought.

Similarly, when I read this book, I found that my expectations as a practicing clinician were unmet, though there was considerable interesting complexity and a glimmer that there were molecular findings that may someday be relevant for clinical practice. The book title suggested that the book was meant for the clinician, that this volume would somehow affect clinical practice. Although the book is clearly a primer on molecular neurobiology related to mental disorders, it offers little for the practicing clinician to advance his current treatment.

For the clinician uninitiated to neuroscience, however, this small paperback in the larger series of *Review of Psychiatry*, published by the publishing company of the American Psychiatric Association, provides a foretaste of how molecular biologists are attempting to understand the mechanisms of disease, genetic abnormalities, and neuropharmacology of psychiatric disorders. The book moves past nosology and shows the reader the state of molecular biology knowledge in mental disorders. The research is stymied by the complexity of the brain. The biology of mental disorders remains elusive. There are also, unfortunately, many limitations to gain this knowledge, including 1) rodent model approximations of mental illness 2) the limits of diagnostic certainty 3) the heterogeneity of mental illnesses and 4) the range of cellular or transmission defects that may lead to the common expression of any particular illness. That is, although researchers would like to unravel the genetics or intracellular second messenger changes in common mental illness such as depression, there are undoubtedly several forms of the illness, several genes related to the development of the illness, and the responsible genes may be widely found in the population. For the clinician looking for a summary biological understanding, there are many equations to solve at once.

The book is divided into five chapters, each written by research experts in their specialty, addressing the molecular biology related to clinical disorders: 1) Childhood disorders; 2) Genetics and diagnosis; 3) Schizophrenia; 4) Drug addiction; 5) Mood and anxiety disorders. None of the chapters suggest that the underpinnings of these mental illnesses are simple and make note that Mendelian, one-gene, one-illness solutions are unlikely. More likely, the authors suggest, it will be that a number of genetic variants interacting with a number of environmental events will lead to the expression of mental illnesses.

The chapters on drug addiction and schizophrenia are more focused than the other chapters and perhaps more digestible,

though still take some focused effort. The chapter on drug addiction informs the reader about how two intracellular proteins, CREB (cAMP responsive element binding protein) and DeltaFosB, may affect gene function and potentiate addiction. These two proteins are transcription factors which attach to and alter gene function. It has been found that both proteins are found in increased concentration in the nucleus accumbens, a sub-cortical nucleus associated with pleasurable activities, and these proteins may in turn affect behavior and lead to further drug seeking. These findings and hypotheses are supported by findings in normal and genetically altered mice. The rodent findings sustain the theory that increased concentration of CREB or DeltaFosB in the nucleus may represent molecular changes that may increase the likelihood of using drugs that stimulate pleasure. This understanding, however, lends no current benefit for addiction treatment. The hope remains that these findings may eventually translate into focused pharmacological treatments.

The chapter on schizophrenia presents an overview of the biological findings in schizophrenia and reports on topics more familiar to most psychiatrists, namely the range of neurotransmitters and receptors thought important in the pathophysiology of schizophrenia. The authors elaborate on the findings that certain genes affecting neurotransmission that may be implicated in schizophrenia. There are brief discussions on how variations in genes responsible for catechol-O-methyltransferase, G-proteins, nicotinic receptors or dysbindin may help explain the pathology in schizophrenia. There are also several dense pages discussing how variations in glutamate or GABA neurotransmission may underlie the abnormalities of schizophrenia.

The book is well referenced, but is often slow going. The authors honestly point out the directions and the limits of the current findings, but the current findings are hampered by how little is currently known about the molecular or even cellular abnormalities in the brains of patients with mental illness. The book is not light reading, and while it may inform the clinician about where the field is going, it does not aid current practice. For those interested in just getting their feet wet in biological psychiatry, a dip in a clinical psychopharmacology pool might be better than forging into the tidal creek of molecular neurobiology.

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Blindsided Lifting a Life Above Illness: A Reluctant Memoir.
By Richard M. Cohen; Harper Collins Publishers; 2004; ISBN 0060014105; \$23.95, pp 236.

This is a wonderful brief memoir. The television journalist turned autobiographer writes about living through intergenerational multiple sclerosis. His account is inspiring; not because

of his miraculous recovery, but because of the way he copes with a draining illness that strikes him when he is in his twenties. Cohen tells his story of illness and gives his philosophy of coping. He is determined to live despite his blindness, despite his limitations. He is Sisyphus, though he is unaware why he is damned.

This story is more about personal resilience than about suffering. Richard Cohen, unlike so many patients we see in clinical practice, decides to move forward rather than focus on loss. He uses denial in a healthy way. He tells that although many describe denial negatively, he sees it otherwise: "Denial encourages anyone to test perceived limits and, as a consequence, to postpone concessions." The less he focuses on his illness, the more he can live. He works on coping, no matter what the obstacles, and he is convinced that people can overcome difficult obstacles. Overcoming obstacles, however, is not easy, but is the work of life: "The strength to get by, I realized, is understated and powerful. We all do what we must as we try to make our lives work. Work it is. Coping is quiet. There is no fanfare, no confetti." This theme recurs throughout the book, and it is a good mantra for him, for he must not only cope with multiple sclerosis, but also, later, with rectal cancer surgery.

Cohen realizes how illness forces persons to focus on themselves, but he forces himself to think beyond himself to cope with his work and family. And he wonderfully points out the differences, how illness is not safe in the work place, and how family will accept illness if he conducts himself as father or husband. Cohen comes to terms with his limitations at work and sees that at some point a "career becomes a job," but that his role as father for his children remains as important as ever. He also recognizes that his children do not care that he cannot

run or see well enough to play sports with them. He comes to appreciate the importance of his family more than his vocation. These struggles are not easily resolved, but he describes how he comes to recognize these truths in his life. And what makes his account so inspiring, is that he perseveres through the struggles and shows his vulnerabilities, finally coming to a conclusion "We all need to appreciate ourselves for what we are and stop whining about what we are not. I grow weary of wishing so desperately for something else."

The book is not only a fine personal account of a man's struggle with illness, but also poignantly describes a man's life with debilitating multiple sclerosis. He describes the visual, motor and sensory changes and some of the emotional changes, though it is unclear if he is aware that some of his emotional swings may be the result of the demyelinating disease and not just frustration from it. He is also often frustrated with physicians, and sometimes refers to them as robots. These are patient perspectives worth reading for any clinician.

His writing is terse. Many sentences are just a few words. I read the book in two days, a rare feat in my highly distracted life of academics and family life. The story captured me because he juggles the two important balls of work and family like many of us, but also a third ball, a severe disease, and he does it with humor and determination. He is more fortunate than many of our patients, but he may end up being an inspiration for physicians and our patients through this memoir. This book is a rare one for the psychiatrist and the patient.

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