the need to interpret statistical analyses of therapeutic effects, and translating these in a way that is understandable for the individual patient.

When the adage in neurology is still (as quoted on page 168 of this book) ‘If you believe you have discovered something new, first look it up in Gowers’, then certainly, if we consider ourselves to have unearthed something new regarding historical aspects of multiple sclerosis or have questions related to these details, we will do well to look it up in Murray; or, as Confucius said: ‘he who puts in front of his eyes the old again in order to understand the new—he may be a teacher to others’. Jock Murray, with this monumental book, has proved himself to be a teacher of the history of multiple sclerosis that sets a new standard and is unlikely to be surpassed, on this scale, for some time. Even in his darker moods, Friedrich Schiller would undoubtedly not have contemplated ascribing the misdemeanours of the professional scholar to Jock Murray: rather he would surely have elevated his work to the upper house of the true philosophical mind—where the passions are the questions, even if the soothing answers to the difficult problem of multiple sclerosis remain stubbornly enigmatic.

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On the way to Curing MS: an insider’s view
Everyone needs help with interpretation in an age when information is in the ascendant, and items that claim the imprimatur of fact so often suffer the eventual fate of reclassification as fiction. To be useful, the narrator must synthesize and explain the details, and in language that is sympathetic to the educational and cultural background of the listener. Patients with multiple sclerosis are extremely well informed. They often know a great deal about the mechanisms of their disease and have views on current treatments. They draw their knowledge not only from the lay press, but also commonly by following scientific digests offered by self-help organizations, and some even immerse themselves directly in the scientific literature.

Indeed, there is no shortage of disease-related writing by professional medical authors. But would it not be interesting to hear from a real insider about how scientific insights into the disease originate, the uncertain pathway to drug development offering new therapies, and the people and personalities who make the science? Such literature is rare—for a simple reason. Most scientists, brilliant as they may be in their particular fields, are not particularly gifted writers. Howard Weiner, Professor of Neurology at Harvard Medical School, is one of the rare exceptions. Not only is he an internationally leading figure in multiple sclerosis research, but he is also a literary talent. Now, over more than 300 pages, he fills this gap in the literature with a book that leads the reader through the intricate field of multiple sclerosis.

During his guided tour, cicerone Weiner touches upon virtually all aspects of multiple sclerosis and related research, covering the general principles as well as specific details. Dr Weiner addresses the history of multiple sclerosis, its various clinical manifestations, the pathogenesis, role of animal models, the complexity of therapeutic trial designs, the role of the Food and Drug Administration in approving new therapies, drug marketing, research funding, scientific reasoning, publications and authorship, dealings with the media, and many other interesting issues. All these various stops on the tour are intertwined with Professor Weiner’s personal experiences as a physician caring for people with multiple sclerosis and his distinguished contributions to original research. In addition, there are many touching encounters with real, individually (pen-)named patients. Overall, the book conveys a compelling picture of the many facets and faces of the disease, making it an exciting read for patients, relatives, doctors, nurses and researchers.

CURING MS: How science is solving the mysteries of multiple sclerosis
By Howard L. Weiner
Price $24.95
ISBN 0-609-60900-9
The many faces of multiple sclerosis

The book begins and ends with a meeting between doctor and patient. ‘Norm’ has typical secondary progressive multiple sclerosis, and is confined to a wheelchair. Norm, a schoolmate of Howard Weiner, takes his old friend on a tour through his home—an assisted living facility—and asks frustrating questions, such as ‘You promised me thirty years ago you would cure multiple sclerosis, and you still haven’t done it—why?’. We have all met patients who ask this uneasy type of question. Weiner’s apt answer invokes a simple comparison: ‘trying to understand and treat multiple sclerosis is like trying to fix a car without being able to look under the hood . . . the problem with the car were that the tyres were flat, then we could fix it easily . . . the problem with multiple sclerosis is under the hood, and checking under the hood is a long and laborious process. After thirty years, we still do not know enough of the parts’. During the course of the book many other patients enter the scene. They have different types of multiple sclerosis, various hopes and fears: they are asking many questions, some of which can and others cannot be answered. Soon, we become aware that, in a Socratic fashion, these questions can themselves teach us about the disease. In one chapter, the reader is invited to spend a day with Howard Weiner in the outpatient clinic of the modern Multiple Sclerosis Center at the Brigham and Women’s and Massachusetts General Hospitals. This part, with the dramatic title ‘Taming the Monster’, contains very instructive and lively case vignettes that serve as an excellent introduction to the clinical features of multiple sclerosis.

Struggling for new therapies

One major theme of the book is how to find a ‘cure’ for multiple sclerosis. Currently the condition is considered to be treatable but not curable. Howard Weiner cites from an editorial by the late Dale McFarlin (McFarlin, 1983): ‘Therapeutic claims in multiple sclerosis are drenched in cynicism even to this day’, and McFarlin listed six reasons why therapeutic claims have fostered controversy: the cause (of multiple sclerosis) is unknown; there is no good laboratory marker for the disease; multiple sclerosis varies between patients; symptoms are exacerbated by fever, activity, and emotional components; and the disease is variable but does not shorten life in most patients, so that treatments associated with major side effects are not given early in the course, and at a time when they might be most effective. Remarkably, these statements remain no less true today than when they were first made more than 20 years ago.

The book tells an exciting story of how the immunomodulatory agents β-interferons, copaxone (glatiramer acetate) and mitoxantrone were approved. Weiner gives a dramatic account of the FDA hearings that led to the approval of these agents. By citing directly from the protocols and by deftly capturing the atmosphere of the hearings, he recreates the excitement of these decisive sessions—important moments in the history of multiple sclerosis and its social history. These episodes help us to understand the disparate roles of the different players and opponents at such meetings—the FDA, the pharmaceutical industry, patients, and the expert panelists.

As thrilling as these FDA hearings are, the actual clinical trials that form the basis for drug approval are even more important. Weiner describes the strengths and weaknesses of these pivotal clinical trials, and openly addresses the dark side of therapeutic progress: enormous financial pressures and interests, which always drive and accompany the development of new drugs. After approval, the competing companies often fight nasty battles to expand their market shares. Prescribing physicians are the main targets of these rivalries. Taking a daunting Big Brother perspective, Weiner envisions a secret video camera with ‘representatives of each of the drug companies watching to hear what I would recommend to my patients. In a world in which drugs licensed for use in multiple sclerosis cost over $10 000 per year per patient, companies want doctors to prescribe their medicine. Even without the video cameras, drug companies can gain access to the prescribing pattern of every doctor in the country that uses their drug, and doctors who tend to prefer the drug marketed by one company are often invited on medical educational junkets set up by that company.’

Apart from the currently approved agents, Weiner also discusses more experimental treatments. For example, in the chapter entitled ‘Plasma, placebos, and clinical trials’ he recalls his own early experiences with clinical trials, notably those involving plasma exchange. He frankly acknowledges having made common mistakes during these early trials: ‘there was no way we could be sure that we had truly done something significant, as there was no comparison or control group, and even if the improvement was real, we had no idea what actually caused it . . . Doctors like to believe they are helping patients and patients like to believe they are being helped, but both can be fooled’. In the same chapter, Weiner gives a brief but lucid account of the striking progress that has since been made in trial design, partly owing to developments in MRI.

In search of the cause (or causes?) of multiple sclerosis

Reflections on scientific discovery in multiple sclerosis are the core and essence of the book, as indicated in the subtitle ‘How science is solving the mysteries of multiple sclerosis’. Weiner muses on the beginnings of his own lifelong attraction to research in this most difficult of diseases. He first saw patients with multiple sclerosis in 1971, when he was a first-year neurology resident: ‘it was a time when there was no MRI scan by which to diagnose and follow treatment effects . . . it was a time when there was no internet, no fax machines, and not even a Xerox machine’. The reader cannot help but sympathize with young Howard, his enthusiasm and youthful optimism and naivety: ‘I had done some research as a medical student, and now I began to think about doing research on multiple sclerosis. This was such a mysterious disease, but also one for which we had a major clue (evidence of inflammatory cells and antibodies in the cerebrospinal fluid). I wondered
whether with a little more research, that mystery about whether an infection or some kind of problem with the immune system was the culprit could be solved’. Today, more than 30 years (and 25,000 scientific articles) later, the weight of evidence points to an autoimmune pathogenesis in at least some forms of the disease, but the possible role of infection(s) is still far from clear.

Howard Weiner is a typical physician–scientist, regarded by some as increasingly an endangered species. He divides his time between the clinic and laboratory, drawing inspiration from seeing and treating patients at the bedside, pursuing research at the bench, and—ideally—taking the results of research back to the clinic. Like so many others, Howard Weiner started his research career with experiments in models of multiple sclerosis (in particular experimental autoimmune encephalomyelitis, EAE). He gives a brief overview of EAE and its history, which, incidentally, nicely complements another elegant, highly recommended essay on the same topic (Steinman, 2003).

Over the years, Howard Weiner made several major discoveries in EAE, most notably by establishing the concepts of oral tolerance and bystander suppression (Weiner, 2000). These are very clearly explained in the book, so that lay people can easily follow. Bystander suppression is a core principle of selective immunotherapy, and forms the conceptual basis for various therapeutic approaches that are currently being explored (Hohlfeld and Wekerle, 2004). Other treatments discussed in the book include T-cell vaccination, anti-T4 and anti-T11 monoclonal antibodies, and anti-α4 integrin monoclonal antibody (formerly known as Antegren and recently approved as Tysabri—but with a more recent glitch in establishing its role as front runner in the register of effective and safe medicines available for people with multiple sclerosis).

It becomes obvious to the reader that many if not all of our present concepts of the immunopathogenesis of multiple sclerosis are based on parallels and comparisons with EAE. Weiner courageously distils the major ideas into 21 points (courageously, because there is always the risk that some of the more hypothetical bullets will eventually prove wrong). A whole chapter is devoted to these ‘21 points of Weiner’, which can serve as didactic guidelines and as signposts for any discussion on the pathogenesis and treatment of multiple sclerosis.

Apart from specific scientific findings, Weiner also has included many reflections on the general process of scientific reasoning, which are both refreshing and amusing to read. For example, the reader is treated to the funeral joke, which highlights the concept of statistical significance. And the parable of the marathon runner nicely illustrates that ‘a crucial part of making discoveries is knowing how to ask the right question, a question that will uncover differences and result in a positive experiment and a statistically significant P value’.

Incidentally, Howard is also a marathon runner, in science and in normal life. Indeed, this book is one of the major landmarks along this course. And it is selling well, Amazon.com rating Curing MS somewhere between Naipaul’s House for Mr Biswas and Proust’s Swann’s Way! The book is quite simply a must—for people with multiple sclerosis, for the amateur interested in medicine and the medical research business, and for the professional working in this specific area of clinical neuroscience. Stories need characters—on stage and in the wings—in order to enliven the account and make more real the narrative. For those of us who aspire to be part of living history, it may prove entertaining (and rewarding) to scan the index of a book, covering a subject where we claim special knowledge, for mention of our own names. Many who are part of the contemporary story of multiple sclerosis, and have contributed to the sum of knowledge that will surely end with a solution for Norm and others who suffer the reality of what it is to have multiple sclerosis, will not be disappointed.

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