CONTENTS

Preface
Robert M. Bennett xiii

The Rational Management of Fibromyalgia Patients
Robert M. Bennett 181

The exponential increase in pain research over the last 10 years has established fibromyalgia (FM) as a common chronic pain syndrome with similar neurophysiologic aberrations to other chronic pain states. As such, the pathogenesis is considered to involve an interaction of augmented sensory processing (central sensitization) and peripheral pain generators. The notion, that FM symptomatology results from an amplification of incoming sensory impulses, has revolutionized the contemporary understanding of this enigmatic problem and provided a more rational approach to treatment. To date, the management of FM has been mainly palliative, with the aims of reducing pain, improving sleep, maintaining function, treating psychologic distress and diminishing the impact of associated syndromes. The rapidly evolving neurophysiologic, psychophysiologic and molecular biologic basis for chronic pain states has already opened up new avenues for management which should be applicable to this difficult group of patients. Indeed, it is now possible to think about a “rational” approach to managing FM patients that was unthinkable just a few years ago.

A Comprehensive Medical Evaluation of Patients with Fibromyalgia Syndrome
Muhammad B. Yunus 201

Fibromyalgia syndrome (FMS) is a common and distressful condition. It is imperative that all physicians do their best to help these suffering patients with understanding and respect, since the primary responsibility of a physician is to ameliorate suffering of a patient, irrespective of the type of the disease or the illness. (The authors use the terms “disease” and “illness” synonymously, since any distinction between these two terms are really pointless because the word “disease” means lack of ease or presence of...
suffering.) It is clear that a physician cannot optimize management of a patient with FMS without a thorough medical and psychologic evaluation. A good evaluation helps to make a proper diagnosis, assess severity, recognize aggravating and relieving factors of symptoms, appraise psychologic factors, evaluate relevant associated or concomitant conditions, document individualized problems in a given patient, and subsequently formulate proper and individualized management. This article focuses on the major elements of a comprehensive medical evaluation, with some reference to psychologic aspects—are covered in detail in the article by Turk et al in this issue.

Psychological Evaluation of Patients Diagnosed with Fibromyalgia Syndrome: A Comprehensive Approach
Dennis C. Turk, Elena S. Monarch, and Arthur D. Williams

The conventional way of thinking about pain assumes that it always results from the presence of underlying organic pathology. In the absence of objective pathology, reports of pain and other unexplained symptoms may be ascribed to psychological causes. However, pain is a complex perceptual phenomenon and is always determined by organic, behavioral, and psychosocial factors. Somatogenic and psychogenic factors alone are insufficient to explain individual differences in the experience of pain. Consequently, assessment of pain symptoms requires an integrated rather than dualistic approach. In addition to obtaining information about patients' pain difficulties through physicals, history, and laboratory and imaging tests, all patients with fibromyalgia should routinely receive a psychological screening by the healthcare provider. An integrated assessment allows health professionals to identify, and treat, the various factors in a patient's life that contribute to their unique experience of pain. This article provides recommendations about what information to obtain in routine psychological screenings through a patient's self-report and the healthcare provider's observations of the patient's behaviors. Based on information gathered from the screening, a subset of patients may be referred for comprehensive psychological assessments. This article describes the essential components of a comprehensive psychological assessment for patients with fibromyalgia, including the content of a psychological interview and illustrative self-report measures. Finally, an example of how information gathered from comprehensive evaluation can contribute to treatment planning is presented.

The Neuropharmacology of Centrally-acting Analgesic Medications in Fibromyalgia
Srinivas G. Rao

Chronic widespread pain is the sine qua non of the fibromyalgia syndrome, differentiating this disorder from other related conditions such as chronic fatigue syndrome. Several lines of experimental data suggest that aspects of the pain of fibromyalgia (FM) are the result of changes in pain processing at the level of the
central nervous system. In this article, an overview of the pharmacology of the central nervous system pain pathways is presented, focusing on both ascending and descending systems from the periphery to the level of the midbrain. The central sites of analgesic action of medications commonly used to treat the pain of FM are then reviewed.

Rational and Targeted Pharmacologic Treatment of Fibromyalgia
André Barkhuizen

Despite disappointing results when subjected to randomized clinical trials, pharmacologic agents remain an important component of fibromyalgia (FM) management. Addressing the main symptoms of pain, disturbed sleep, mood disturbances, fatigue and associated conditions are essential to improve patient functioning and enhanced quality of life. However, much work remains to design clinical trials that address the complexity of FM, while satisfying evidence-based medicine paradigms.

Nonpharmacologic Management Strategies in Fibromyalgia
Carol S. Burckhardt

Clinicians using the results of the extant research base can take an optimistic view of the role of nonpharmacologic treatment strategies for fibromyalgia. There were no negative outcomes in any of the reviewed studies, although in a few studies the experimental treatment did not prove to be more effective than the attention control. Rather than viewing this negatively, one could look more closely at the attention control groups and attempt to better understand what they contained that worked as an active treatment. A number of trials included a follow-up component and all but one of them found maintenance of at least one outcome change. Maintenance of changes is more likely to occur when the patient continues to participate in the experimental activity long-term. Patients especially need strategies that help them continue in exercise regimens. Unlike cognitive skills strategies that once learned are likely to become part of a person’s coping repertoire, both exercise and behavioral strategies, like progressive muscle relaxation, need to be performed on a consistent basis in order to have their effect. The goals of increased self-efficacy, symptom reduction, increased functional status and quality of life along with decreased inappropriate use of health care resources are realistic when patients persevere in their use of strategy combinations and receive support from their providers.

Management of Peripheral Pain Generators in Fibromyalgia
Joanne Borg-Stein

Fibromyalgia (FM) is a widespread chronic pain disorder that is characterized in part by central sensitization and increased pain response to peripheral nociceptive and non-nociceptive stimuli.
Part of the comprehensive pain management of patients with FM should include a thoughtful evaluation and search for peripheral pain generators that either are associated with FM or are coincidentally present. The identification and treatment of these pain generators lessens the total pain burden, facilitates rehabilitation and decreases the stimuli for ongoing central sensitization.

**Current Experience with 5-HT\textsubscript{3} Receptor Antagonists in Fibromyalgia**

Michael Späth

Serotonin (5-HT) and its receptors play a crucial role for pain perception, pain transmission, pain processing and pain modulation. Despite partly contradictory study results concerning nociceptive and antinociceptive properties of 5-HT\textsubscript{3} receptor antagonists, their antinociceptive effect was investigated in fibromyalgia (FM) patients. The data from the preliminary studies indicate a benefit in a subgroup of FM patients.

**The Promise of Substance P Inhibitors in Fibromyalgia**

I. Jon Russell

The fibromyalgia syndrome (FMS) is a chronic pain disorder that exhibits elevated levels of cerebrospinal fluid (CSF) substance P (SP). Because SP is known to influence the normal process of pain perception, there is reason to address its role in the pain of FMS. The discovery and characterization of the SP receptor (neurokinin-1 receptor, NK1r) for the action of SP have disclosed new opportunities to understand a wide variety of conditions that are mediated, at least in part, by SP. Knowledge about the receptor prompted an aggressive search for agonists and antagonists that might be useful in mimicking (modeling) or in treating the relevant conditions. This article will draw heavily from the descriptions of the pioneers in the field, as they have summarized their years of careful study; it will then briefly summarize the results of a study designed to examine the response of FMS patients to an NK1 antagonist; and finally, it will attempt to forecast some ways in which this technology may be used in the future to more effectively manage FMS.

**The Promise of N-methyl-d-aspartate Receptor Antagonists in Fibromyalgia**

Karl G. Henriksson and Jan Sörensen

In fibromyalgia an NMDA-receptor antagonist (ketamine) has been used for diagnosis of central sensitization of the nociceptive central nervous system in patients with fibromyalgia. The combination of another NMDA-receptor antagonist (dextromethorphan) and a weak opioid (tramadol) has been studied with respect to pain relief. A subset of patients may benefit from this treatment.
Management of Sleep Disorders in Fibromyalgia
Harvey Moldofsky

The studies of sleep physiology show that nonrestorative sleep is important in the pathogenesis of fibromyalgia (FM). More than 90% of patients with FM describe disturbed sleep. The sleep is usually perceived to be light and unrefreshing, irrespective of its duration. On the rare occasion that there is a night of restful sleep, the patient often finds that pain and fatigue are substantially improved on the following day. Some patients may be aware of restlessness with kicking and involuntary leg movements, which may delay or disrupt sleep. Sometimes the bed partner may complain that the loud snoring is disturbing his sleep. There may be pauses in the snoring with the appearance of interruptions to breathing during sleep, or the patient may awaken with choking, gasping or a sense of suffocation. Some patients complain of difficulty keeping awake and have uncontrollable sleepiness during the day that is interfering with their social life, work, and their ability to drive safely. This article describes the methods for assessing these various sleep disorders and how they might be managed as part of the comprehensive approach in treating FM patients.

Treatment of Fatigue in Fibromyalgia
Emma K. Guymer and Daniel J. Clauw

Fatigue is a major problem for sufferers of fibromyalgia (FM), and it contributes significantly to disability and impairment of the syndrome. The fatigue needs to be evaluated carefully for reversible causes, remembering especially that some medications used to treat FM can contribute to this symptom. The treatment of fatigue is best managed by a multimodal approach. This includes patient education, nonpharmacologic therapies such as aerobic exercise and cognitive behavioral therapy, and adjunctive medications such as some antidepressants and CNS stimulants.

Management of Dysautonomia in Fibromyalgia
Manuel Martinez-Lavin

Recent evidence coming from different groups of investigators suggests that sympathetic nervous system dysfunction is frequent in patients with fibromyalgia (FM). This new knowledge has led to the proposal that FM is a sympathetically maintained pain syndrome. Dysautonomia may cause its remaining multisystem manifestations. This article discusses evidence of autonomic dysfunction in FM as well as theoretical nonpharmacologic approaches (avoidance of sympathomimetic products, aerobic exercises, biofeedback, fitted stockings, mineral water) and pharmacologic therapies (benzodiazepines, adrenergic blocking agents, serotonin receptor antagonists, and antineuropathic compounds) that could improve FM symptoms through autonomic nervous system manipulation.
Evaluation and Management of Endocrine Dysfunction in Fibromyalgia
Ririe Geenen, Johannes W.G. Jacobs, and Johannes W.J. Bijlsma

Fibromyalgia-like symptoms such as muscle pain and tenderness, exhaustion, reduced exercise capacity, and cold intolerance, resemble symptoms associated with endocrine dysfunction like hypothyroidism, and adrenal or growth hormone insufficiency. To investigate the potential of management of endocrine abnormalities for relief of symptoms of patients with fibromyalgia (FM), we reviewed experimental and clinical studies of endocrine functioning and endocrine treatment. Serum GH, androgen, and 24-hour urinary cortisol levels of patients with FM tend to be in the lower part of the normal range, while serum levels of thyroid hormone, female sex hormones, prolactin, and melatonin are normal. With exception of GH, these conclusions are based on studies in small samples. With respect to dynamic responsiveness of the hypothalamic-pituitary-adrenal (HPA) axis, the dexamethasone suppression test and stimulation with ACTH show normal results, while patients show marked ACTH hypersecretion in response to severe acute stressors, perhaps indicative of chronic CRH hyposecretion. This finding and slightly altered responsiveness of growth hormone, thyroid hormone, and prolactin in pharmacologic stimulation tests suggest a central rather than peripheral origin of endocrine deviations. Because hormone level deviations were not severe, occurred in subgroups of patients only, and few controlled clinical trials were performed, there is—unless future research shows otherwise—little support for hormone supplementation as a general therapy in the common patient with FM. In patients with clinically overt hormone deficiency, hormonal supplementation is an option. In patients with hormone levels that are in the lower part of the normal range, interventions aimed at pain, fatigue, sleep or mood disturbance, and physical deconditioning may indirectly improve endocrine functioning.

The Management of Fibromyalgia-Associated Syndromes
David S. Silver and Daniel J. Wallace

Ten independently recognized syndromes are statistically more prevalent in fibromyalgia (FM) patients than in healthy individuals. Linked by a common feature of central sensitization abnormalities in chronic pain perception, only some result in chronic neuromuscular pain. This article reviews these associated syndromes and presents a rational template for managing them in individuals who also have FM.

Individualizing the Exercise Prescription for Persons with Fibromyalgia
Kim Dupree Jones and Sharon R. Clark

"Exercise is good for you; you must exercise, and just do it" are common admonitions to fibromyalgia (FM) patients by health professionals. "I can't exercise; I hurt too much to exercise; and, I don't
have enough energy to exercise” are equally common responses from patients with FM. Such exchanges can lead to frustration for both patient and provider. The factor that neither participant in the dialogue is addressing is that exercise carries both risks and benefits for persons with FM. Although for decades exercise has been acknowledged to be a key component of the treatment of FM, the majority of FM patients remain aerobically unfit, with poor muscle strength and limited flexibility. Unfit muscle is theoretically more prone to muscle microtrauma, which causes localized pain and may trigger widespread pain through disordered central processing. The purpose of this article is to provide practicing health care providers with guidelines for prescribing exercise to FM patients that take into account the risk/benefit ratio. A sample exercise prescription is included.

Office Management of Fibromyalgia
Don L. Goldenberg

The office management of fibromyalgia (FM) is best determined by two variables: (1) the severity and complexity of each patient’s symptoms, and (2) the specialization and interest of the treating physician. Because there are 6 to 10 million Americans with FM, most patient visits will be to the primary care physician. Rheumatologists, physiatrists, and other musculoskeletal specialists must work with primary care physicians to foster the early diagnosis and appropriate treatment of FM. Primary care physicians are faced with enormous challenges in caring for patients with chronic pain disorders like FM. Our managed health care system insists that patient encounters be brief. Specialty referrals are often discouraged. There is little if any reimbursement for patient education. FM treatment is labor-intensive. Therefore, optimal planning and use of precious office time and resources are most important. Rheumatologists should train our primary care colleagues to recognize FM. Many patients still go months or years before this common syndrome is diagnosed. Rheumatologists should also spearhead teaching primary care physicians the basic treatment principles of FM. If the diagnosis is made early, patients with FM in community practice do very well with simple management techniques. As consultants, rheumatologists should confirm the diagnosis of FM and suggest basic FM management. Some primary care providers or other specialists will be fully capable of bypassing this consultation, especially if the patient responds to simple management suggestions. Manpower surveys have not studied the cost-effectiveness of specialty care in FM. Rheumatologists should also assume the responsibility for the management of FM patients who have not responded to basic FM management. Additionally, some rheumatologists may wish to subspecialize in FM, a major career commitment to this perplexing disorder. These situations constitute advanced FM management.