Introduction

Depressive Disorders: Advances in Clinical Management

James W. Jefferson, M.D.

In 1999, the Annual Meeting of the American Psychiatric Association will have as its theme, "The Clinician." While the symposium upon which this supplement is based actually took place at the 1998 Annual Meeting, its contents clearly anticipate next year's theme. Our goal was to address the continual diagnostic and therapeutic challenges presented by depressive disorders in ways they would be of practical value to clinicians. Both the symposium and the supplement were made possible by a grant from Organon Inc., whose commitment to fair balance is greatly appreciated.

"One size fits all" could not be farther from the truth when it comes to managing depression. Despite current lore, one does not simply load a magic antidepressant bullet into a therapeutic weapon, fire away at a patient, and come back 6 weeks later to be greeted by the smile of full remission. On the contrary, the successful use of antidepressants depends on many factors, including the type of depressive illness, response to previous treatment, patient preferences and idiosyncracies, and how well the drug will be tolerated.

Dr. Paula J. Clayton tackles the issue of diagnostic subtyping of clinical depressions and the treatment implications that follow. Does your depressed patient have major depressive disorder or bipolar disorder? Could the major depressive episode be superimposed upon a dysthymic disorder? Should atypical or psychotic features modify your treatment choice? What special problems are presented postpartum? Are anxious depressions in a class all their own? What about seasonal affective disorder and its response to light and antidepressants? These are but some of the questions ably addressed by Dr. Clayton.

In the best of all worlds, there would be ideal antidepressants and, as a result, there would be no treatment-resistant depression. Until that day arrives, however, we must continue to contend with the 50% of patients who fail to respond to or tolerate the first antidepressant used (this figure may actually be higher in psychiatric practices because of treatment failures referred from primary care practices). Strategies for overcoming treatment resistance are capably and comprehensively discussed by Dr. J. Craig Nelson, who expertly leads us through the advantages and disadvantages of augmenting and switching. If one chooses to augment, what are the choices? Beyond that, what are the data to support the choices? Lithium, thyroid, stimulants, buspirone, pindolol, tryptophan (if you can get it), and other antidepressants are among the augmentation possibilities laid out and ordered by Dr. Nelson. If one antidepressant fails, some clinicians would choose to switch to a different drug—but how different should that drug be? Is switching within a class (e.g., one selective serotonin reuptake inhibi-

---

From the Madison Institute of Medicine, Madison, Wis.

Presented at the symposium "Depressive Disorders: Advances in Clinical Management," which was held May 31, 1998, in Toronto, Canada, in conjunction with the 151st Annual Meeting of the American Psychiatric Association and supported by an unrestricted educational grant from Organon Inc.

Reprint requests to: James W. Jefferson, M.D., Madison Institute of Medicine, 7617 Mineral Point Road, Madison, WI 53717.

tor [SSRI] to another) any more or less effective than switching across classes (e.g., SSRI to bupropion)? How should one make a transition from one antidepressant to another? Is switching because of ineffectiveness different from switching because of intolerance? You will find Dr. Nelson's answers to these and related questions most gratifying.

There are nonpharmacologic approaches to treating depression that can be quite effective as stand-alone or complementary therapies. Both cognitive and interpersonal psychotherapy have fared well in clinical trials of mild to moderately severe depression. Dr. John H. Greist takes a giant step beyond the more traditional approaches to psychotherapy and explores the assessment and treatment of depression by computer. Innovative programs that use interactive voice response (IVR) allow depression to be diagnosed, monitored, and even treated by computer programs administered via Touch-Tone telephones. As Dr. Greist is careful to explain, these programs are not designed to replace clinicians but rather to "complement, supplement, and reinforce the services" that clinicians provide.

For almost 20 years, Dr. Edmund C. Settle has been in the trenches, a private practitioner specializing in the treatment of mood disorders. He would be among the first to acknowledge that all drugs have side effects and that how these side effects are managed can make or break a treatment. At the same time, he quite appropriately recognizes that failure to treat depression is far more deadly than the risks imposed by antidepressant medications. Nonetheless, antidepressants can have "disturbing and potentially dangerous side effects" that are best avoided and at next best recognized and managed appropriately. As you will see, Dr. Settle has grappled successfully with the management of cardiovascular side effects, apathy and extrapyramidal symptoms, the serotonin syndrome, the syndrome of inappropriate antidiuretic hormone (SIADH), bleeding and bruising, seizures, sexual dysfunction, and disturbed sleep.

Life should be so simple that all our patients would take but a single medication and avoid the possibility of adverse drug interactions (and refrain from eating to avoid drug/food interactions). Since quite the opposite is true in today's world, clinicians must be attuned to the possibility of interactions that can cause either toxicity or loss of efficacy. While the cytochrome P450 system is not the only drug-metabolizing system in the body, it is clearly head and shoulders above the others. To conclude the supplement, I discuss drug interactions with a focus on the P450 system and a more specific focus on how antidepressants alter and are altered by these enzymes. There are marked differences among antidepressants in this regard, and an awareness of these differences will help ensure the safe management of patients.

I wish you good reading.