

# Introduction

## Beyond SSRIs

A. John Rush, M.D.

© **T**his supplement (1) reviews new developments in our understanding of the mechanisms of action, therapeutic efficacy, and safety of antidepressants (especially bupropion), (2) provides an update on antidepressant interactions, (3) presents new data on bupropion for smoking cessation and attention-deficit/hyperactivity disorder (ADHD), and (4) evaluates proposed medication management plans (e.g., algorithms) for the treatment of depressed phase bipolar disorder.

These multiple objectives are exceptionally well addressed by an outstanding faculty of highly experienced investigators and clinicians. Stephen M. Stahl, M.D., Ph.D., reviews the basic pharmacology of today's antidepressants, noting a wide range of diverse compounds that differ both in their presumed mechanisms of action as well as in their tolerability and side effect profiles. Dr. Stahl also describes the use of exogenous hormone therapy as an adjunct to treatment with antidepressants. The therapeutic efficacy of the new sustained-release (SR) form of bupropion is reviewed by Jonathan R. T. Davidson, M.D., and Kathryn M. Connor, M.D., while Edmund C. Settle, Jr., M.D., summarizes side effect data on this new formulation. As expected, the SR formulation makes t.i.d. dosing unnecessary and appears to further improve upon an already favorable side effect profile. James W. Jefferson, M.D., provides a thorough review of drug-drug interactions and makes practical clinical suggestions regarding the relationship of these interactions to treatment with antidepressants. This knowledge is of substantial clinical relevance—especially given the ever evolving nature of this topic.

Robert Taylor Segraves, M.D., Ph.D., provides a more selective focus and useful clinical tips on the side effect of sexual dysfunction, a problem not infrequently encountered with the serotonin selective reuptake inhibitors (SSRIs), but which can be largely avoided with either bupropion or nefazodone.

Data on new clinical conditions for which bupropion appears useful are presented by Michael G. Goldstein, M.D. (smoking cessation), and Dennis P. Cantwell, M.D.† (ADHD).

Michael E. Thase, M.D., provides a cogent, up-to-date review of sleep abnormalities found in depression and new data on the effects of antidepressant medication on sleep architecture. Sidney Zisook, M.D., and Nancy S. Downs, M.D., review the medication choices and management methods for depression in later life, cogently weighing critical issues of concurrent general medical conditions, tolerability, and drug interactions. Allen J. Frances, M.D., and colleagues summarize the issues of medication choice for those patients in the depressed phase of bipolar illness based on the Expert Consensus Guidelines developed for bipolar disorder.

Taken together, these papers constitute an extremely clinically relevant set of review articles based on scientific data that are weighed and interpreted by highly experienced practitioners. All of us who treat depressed patients realize that no one medication (or class of medications) is a panacea. We now find ourselves confronted with a

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plethora of new antidepressive agents—all with greater safety, equal efficacy, and better tolerability than the older tricyclic agents.

The opportunities and challenges now are to move beyond the aim of simple response, to attain for as many patients as possible full symptomatic remission (and the associated functional restoration). We need to aim at this higher outcome threshold (i.e., not just response but remission) as those patients who do attain a clinical remission—as contrasted with those who respond but do not remit—return to a better level of day-to-day functioning and generally have a better prognosis.<sup>1</sup> This objective has now become more realistic as the SSRIs have ushered in an era of greater safety and tolerability of antidepressant drug treatment. Now, with additional new, safe, effective, and more tolerable agents, early detection and fully effective treatments are feasible for an even larger proportion of depressed patients.

#### REFERENCE

1. Rush AJ, Trivedi MH. Treating depression to remission. *Psychiatr Ann* 1995;25:704–705, 709

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