### Introduction

## Erectile Dysfunction and Comorbid Depression: Prevalence, Treatment Strategies, and Associated Medical Conditions

H. George Nurnberg, M.D., Guest Editor

E rectile dysfunction and depression are common medical conditions and frequently coexist. Fifty-two percent of men aged 40 to 70 years may be expected to have some degree of erectile dysfunction (mild, moderate, or complete), including 10% with complete erectile dysfunction (total absence of erections). Lifetime prevalence estimates of 16% for major depression and 10% for minor depression, determined from a nationally representative survey of persons aged 15 to 54 years living in the United States, suggest that depression is also highly prevalent.

Men who have depression have a nearly 2-fold greater likelihood of having erectile dysfunction compared with men with no depression.<sup>3</sup> Several studies have determined that major depressive disorder is associated with decreased libido, erectile dysfunction, and decreased sexual activity.<sup>4</sup> In addition, sexual dysfunction, including erectile dysfunction, is a well-described side effect in patients taking serotonin reuptake inhibitor (SRI) antidepressants.<sup>5</sup>

Occurrence of sexual dysfunction as well as other common adverse events associated with SRIs (e.g., weight gain and sleep disturbance) frequently result in compromise of patient adherence to treatment regimens. Therefore, although depression is readily treatable, with up to 90% of patients responding to their first or second antidepressant, typically less than 30% of patients complete the recommended 6 to 9 months of antidepressant therapy following an acute episode. Frequently, patients discontinue treatment because of side effects such as weight gain, sleep disturbances, and sexual problems, including erectile dysfunction. Such premature discontinuation of antidepressant therapy may result in recurrence or relapse, exposing the patient to increased morbidity or mortality.

From the Department of Psychiatry, Health Sciences Center, University of New Mexico School of Medicine, Albuquerque, N.M.

Support was provided by Pfizer Inc, New York, N.Y. Corresponding author and reprints: H. George Nurnberg, M.D., Department of Psychiatry, University of New Mexico School of Medicine, 2400 Tucker NE, Albuquerque, NM 87131-52886 (e-mail: geon@unm.edu). The articles in this supplement examine conventional and newer treatment strategies for antidepressant-associated sexual dysfunction and investigate further the interrelationships between erectile dysfunction and depression.

#### PREVALENCE AND MANAGEMENT

In the first article, Rosen and Marin present an overview of the available findings on the prevalence of sexual dysfunction, particularly erectile dysfunction, in untreated depression and secondary to antidepressant therapy compared with healthy populations. Possible mechanisms involved in SRI-associated erectile dysfunction are also examined.

Labbate, Croft, and Oleshansky evaluate the empirical evidence for the current strategies of pharmacotherapy commonly used in the management of antidepressantassociated sexual dysfunction. These strategies include avoidance of the problem by selecting an antidepressant that has little or no associated sexual dysfunction, switching to such an antidepressant, use of adjunctive antidote pharmacotherapy with an antagonist/agonist or non-SRI antidepressant that has little or no associated dysfunction, and adaptation. Few randomized placebo-controlled trials have been conducted to evaluate these treatment options even fewer have demonstrated clinically significant effectiveness-making evidence-based claims of efficacy difficult to substantiate. In addition, this lack of empirical data suggests that many patients are receiving random pharmacotherapy for this pernicious side effect.

Sildenafil citrate, a selective and competitive inhibitor of phosphodiesterase type 5, possesses many of the qualities that are considered ideal for an antidote therapy to treat antidepressant-associated erectile dysfunction. These include a peripheral site of action, a novel mechanism that is not competitive with the primary treatment, administration on an as-needed basis, significant efficacy, high tolerability, and a relatively short duration of action. The most common adverse events with sildenafil use are headache, flushing, dyspepsia, and visual effects. However, before treating erectile dysfunction, physicians should consider

the impact of resuming sexual activity and the mild and transient vasodilatory effects of sildenafil on blood pressure. Physicians should also carefully consider whether patients with underlying cardiovascular disease or other more unusual conditions could be adversely affected by vasodilatory effects, especially in combination with sexual activity. Sildenafil is contraindicated with the use of organic nitrates in any form.

In their article, Nurnberg and Hensley review findings from double-blind, placebo-controlled trials assessing the efficacy and tolerability of sildenafil in the treatment of erectile dysfunction in untreated depression and erectile dysfunction occurring secondary to antidepressant therapy. The broad evidence-based efficacy of sildenafil for treating erectile dysfunction of wide-ranging etiologies underscores the importance of the treating physician in establishing the cause of the erectile dysfunction (e.g., neurogenic, vasculogenic, endocrine, metabolic, immune, medication, other treatment, situational, idiopathic).

# ASSOCIATIONS WITH HORMONAL STATUS AND ISCHEMIC HEART DISEASE

Associations between depression and ischemic heart disease (IHD),<sup>7</sup> IHD and erectile dysfunction,<sup>1</sup> and erectile dysfunction and depression<sup>3</sup> have also been established. In his article, Roose discusses these complex and multifaceted relationships, presenting the current clinical and research findings that suggest a more substantial role for depression in the development of IHD and its treatment outcome and point to a growing list of risk factors shared by all 3 medical conditions.

The increasing prevalence of erectile dysfunction with age parallels age-related changes in androgen levels.

Consequently, age-related declines in testosterone have been suggested as a possible explanation for some symptoms (e.g., weakness, fatigue, reduced muscle and bone mass, sexual dysfunction, depression) experienced by elderly men, and testosterone replacement has been proposed as a potential therapy for some of these symptoms. Seidman reviews the relationships among androgens, sexual function, and depression in aging men and analyzes the evidence to date that supports potential uses of testosterone replacement therapy.

Together, these articles provide a comprehensive and updated look at the interrelationships among highly prevalent medical illnesses in the adult and aging male. These articles also offer insight into some of the current trends in optimizing the management of these conditions.

#### REFERENCES

- Feldman HA, Goldstein I, Hatzichristou DG, et al. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. J Urol 1994;151:54–61
- Kessler RC, Zhao S, Blazer DG, et al. Prevalence, correlates, and course of minor depression and major depression in the National Comorbidity Survey. J Affect Disord 1997;45:19–30
- Araujo AB, Durante R, Feldman HA, et al. The relationship between depressive symptoms and male erectile dysfunction: cross-sectional results from the Massachusetts Male Aging Study. Psychosom Med 1998;60:458–465
- Seidman SN, Roose SP. The relationship between depression and erectile dysfunction. Curr Psychiatry Rep 2000;2:201–205
- Nurnberg HG. Managing treatment-emergent sexual dysfunction associated with serotonergic antidepressants: before and after sildenafil. J Psychiatr Pract 2001;7:92–108
- Depression and Bipolar Support Alliance. Beyond Diagnosis: A Landmark Survey of Depression and Treatment. Available at: http://www.dbsalliance.org. Accessed April 24, 2003
- Musselman DL, Evans DL, Nemeroff CB. The relationship of depression to cardiovascular disease: epidemiology, biology, and treatment. Arch Gen Psychiatry 1998;55:580–592