Session 11

Clinical Assessment of Drug-Induced Impairment of Sexual Function in Men

Stanley G. Korenman, M.D.*

Although there is an increasing awareness of the importance of induced sexual dysfunction in understanding noncompliance in hypertensive men, the fundamental nature of the dysfunctions produced, the ability to predict outcome before therapy, the selection of drugs, and the basal level of sexual function have not been thoroughly assessed in relation to psychosocial, neurologic, vascular, and endocrine parameters, particularly in men as they age. Treatment of hypertension with drugs into advanced age will be associated with a substantial incidence of impotence. The exact role of the agent must be elucidated. It is the responsibility of the therapist and the drug manufacturer to identify the incidence of untoward effects, their physiologic basis, and modes of prevention and of reversibility. Investigation of sexual dysfunction has been adversely affected because physicians are not well trained in pursuing the question of sexual performance. There also prevails the feeling that open discussion of sexual matters may induce a dysfunctional state. This no longer seems to be a tenable proposition, considering the strength of the sexual drive and the openness with which sexual matters are now discussed in our society.

The need to treat hypertension creates an excellent experimental setting for investigation of the physiology of erection. A better understanding of the mechanisms may make it possible to reduce the risk of sexual dysfunction, improve compliance, and avoid more completely the complications of elevated blood pressure.

Physiology of Sexual Function

Human sexual behavior is derived from two forces: libido or sexual desire, which is influenced by the reproductive hormones, the emotional and physical health of the individual, and the availability, interest, and attractiveness of a stimulus. In the presence of strong libidinous urges, sexual gratification will be pursued at all costs. However, with a lower degree of sexual desire, the intensity of the stimulus, the absence of distractions, and other factors play an important role in determining the frequency of attempted sexual satisfaction.

Potency depends, in addition to the above, on the intactness of the complex mechanisms responsible for penile erection and ejaculation involving neural, vascular, and endocrine factors. Neural input is derived from psychogenic and sensory stimuli, which, after integration, are transmitted via the spinal cord to two erectile centers. Parasympathetic effectors are the principal regulators of penile tumsescence. Sympathetic terminals are responsible for the mechanisms of ejaculation, including contraction of smooth muscles of the testis, seminal vesicle, prostate and ureterovesicular junc-

*Professor of Medicine, University of California School of Medicine, Los Angeles.

Erection is due to increased flow through the helical branches of the profunda arteries of the penis pouring blood into the lateral and ventral corpora cavernosa through AV fistulas as a consequence of the action of the nervi erigentes. There is no evidence of impairment of venous return. Since erection requires a substantial arterial blood flow through the penis, the presence of major hypogastric or pudendal artery obstruction due to atherosclerosis may influence potency. The incidence of diminished penile pressure as a cause of impotence is really not known, but it is found not infrequently in men with disordered nocturnal penile tumescence.

Sex hormones play a significant role in both libido and potency. Testosterone is responsible for the development and maintenance of the secondary sexual organs. Testosterone also stimulates sexual desire. There is some evidence that dihydrotestosterone, which is not aromatizable to estrogens, is ineffective in stimulating libido, leading, with other evidence, to the suggestion that local estrogens in the brain may regulate libido in both sexes. The role of estrogens on libido and potency in men is not clear, except for evidence that exogenous estrogens produce gonadotropin suppression and diminished testosterone production, both as a result of reduced gonadotropic stimulation and as the result of a direct inhibition of Leydig's cell function.

In addition to physiologic changes associated with illness and aging, administration of various chemical substances may influence sexual function.

The major categories are tranquilizers and hypnotics, antihypertensives, alcohol and other recreational drugs, as well as a scattering of other agents. In only a few cases have their effects been characterized. Clearly a systematic approach to assessment of sexual function is necessary prior to and after initiation of therapy with drugs.

Assessment

The approach to assessment of men whose sexual functional status is presumed normal and who must be examined repeatedly and at little cost involves examination of current sexual functioning, emotional, vascular, neurologic, and endocrine systems.

1. The sexual function questionnaire. This form, which the subject fills out in private with the availability of a knowledgeable member of the research team, explores elements of sexual history, including maximum activity, current sexual functioning, specific questions about dysfunctional elements, the sexual partner, and satisfaction and previous history of sexual dysfunction. There must also be an assessment of general health and drug and alcohol intake.

In the presence of significant sexual dysfunction, a more intimate inventory of mood, attitudes, information, and fantasies should be used.

2. The vascular assessment possible under control conditions includes, in addition to a standard history and examination of peripheral pulses, assessment of penile blood pressure in the supine and standing positions. A penile pressure, assessed by Doppler examination, of less than 80 percent of
the brachial pressure is suggestive of a vascular problem, which, if associated with erectile dysfunction, requires more extensive assessment.

3. Neurologic assessment should include evaluation of the cremasteric and bulbocavernous reflexes and of sacral sensation, including penile vibratory sense. In those complaining of sexual dysfunction, assessment of the bulbocavernous reflex latency has been proposed as a good measure of neurologic integrity, but studies have failed to indicate their specific relation to impotence, although latencies are increased in impotent diabetic patients. This test, which requires a perineal needle and electric stimulation, is inappropriate for screening. Of course, evidence of neurogenic bladder or a peripheral neuropathy may contribute to the belief that neurogenic impotence may be present.

4. The endocrine evaluation of impotence has usually consisted of a random serum testosterone or prolactin measurement. In only a few cases have gross abnormalities been noted. There are major problems in assessing the intactness of the reproductive endocrine system in men. Not only are testosterone levels variable, but also the influence of endogenous estrogens is unknown. The role of androgens and estrogens on the behavioral vascular and neurologic systems is difficult to define. There is a wide variety of influences on testosterone secretion, including stress and ethanol. There is binding of androgens to sex hormone binding globulin (SHBG) and effects of androgens, estrogens, and obesity on the concentration of SHBG binding sites. Gonadotropin assays are not very helpful. Although hyperprolactinemic patients have a problem with sexual function, hyperprolactinemia is a rare cause of sexual impairment in men who do not have a pituitary tumor.

The routine endocrine workup should include AM fasting total and free serum testosterone, estrone, estradiol, prolactin, FSH, and LH levels, as well as a glucose. Indicators of deficient androgen action in the physical examination includes loss of androgen-dependent hair and vertical wrinkling around the mouth. Estrogen excess may be manifested by spider angiomas, loss of hair, and palmar erythema. A careful assessment must be made of testicular volume and consistency as well as the presence of a varicocele.

**FOLLOW-UP**

Regular inquiries regarding sexual function should be made of all men undergoing therapy. Should sexual dysfunction accompany therapy, it is of great value to repeat the questionnaire and proceed to carry out a more extensive examination, including the endocrine consequences of the therapy through reassessment of baseline hormone values and evaluation of responsiveness to luteinizing hormone-releasing hormone and to human chorionic gonadotropin. If possible, inhibition of estrogen effect should be attempted while continuing therapy and then after cessation for two weeks. Reassessment of neurologic and vascular function should be done as well as assessment of the consequences of changing medications.

What should be done regarding patients complaining of sexual dysfunction prior to antihypertensive therapy? Therapy is essential, so it cannot be withheld indefinitely, but assessment of the basis for the dysfunction should be evaluated thoroughly as noted and the consequences of therapy further assessed. It may indeed be possible to show that appropriately managed cases will experience an improvement in sexual function with antihypertensive therapy.

The incidence of preexisting sexual dysfunction in hypertensive patients has been reported to be as high as 35 percent, although a lower value seems more appropriate. The reported consequences of therapy have been so fragmentary and so unrelated to prior condition, other medications, alcoholic intake, endocrine status, or condition or partner that conclusions are difficult to draw. A good study will clear the air, define the problem, and permit appropriate therapy to be undertaken wherever possible.

**Management of Hypertension in the Asthmatic Patient**

Irwin Ziment, M.D., F.C.C.P.*

The management of the hypertensive asthmatic can be doubly jeopardized by pharmacotherapy, and it is therefore important to maximize prophylactic measures and non-drug therapy and to use specific antihypertensive and antiasthmatic drugs minimally and carefully. The general measures employed in hypertension management are usually appropriate for the asthmatic patient, *i.e.*, low-salt diet, maintenance of optimal weight, management of stress, and appropriate use of exercise and relaxation. The asthmatic patient should avoid smoking, air pollution, and specific allergens, and should take reasonable precautions to avoid respiratory infections; this general advice is appropriate for the hypertensive patient who is predisposed to bronchospasm.

**Pharmacotherapy for Asthma**

Most of the drugs used in the management of asthma can have effects on blood pressure.

**Sympathomimetics**

The effects of bronchodilator adrenoceptor agonist drugs in hypertension have not been adequately studied, and a survey of the extensive literature on catecholamine cardiovascular effects reveals considerable variations in the findings of individual investigators. Numerous factors can affect the response. Drug factors include: the preparation used, the route of delivery, the rate of administration, the total dosage, and prior exposure to the same or to similar drugs. Patient factors include: individual susceptibility, the relative physiologic responsiveness of the heart and blood vessels, variables such as patient anxiety, and prior or concomitant exposure to other cardiovascular therapies. These variables may account for the contrasting findings that are often recorded in bronchodilator studies on asthmatic patients.

Table 1 shows an attempt to summarize the more frequently reported changes in blood pressure that may follow the administration of the various bronchodilators to normotensive patients. Hypertensive patients may demonstrate