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Physiology and pathophysiology of female sexual function and dysfunction

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Abstract Female sexual dysfunction is age-related, progressive, and highly prevalent, affecting 30%–50% of American women. While there are emotional and relational elements to female sexual function and response, female sexual dysfunction can occur secondary to medical problems and have an organic basis. This paper addresses the anatomy and physiology of normal female sexual function as well as the pathophysiology of female sexual dysfunction. Although the female sexual response is inherently difficult to evaluate in the clinical setting, a variety of instruments have been developed to assess subjective measures of sexual arousal and function. Objective measurements, used in conjunction with the subjective assessment, help diagnose potential physiologic/organic abnormalities. Therapeutic options for the treatment of female sexual dysfunction, including hormonal, and pharmacological, are also addressed.

Keywords Female sexual dysfunction · Anatomy · Physiology · Pathophysiology · Evaluation · Treatment

Sexual dysfunction in women is age-related, progressive, and highly prevalent, affecting 30%–50% of American women [19, 40]. In the National Health and Social Life Survey (NHSLS) that included 1749 women, 43% of adult women had complaints of sexual dysfunction [19]. While this study had a large sample size, minority representation, and used modern probability sampling, it was limited by its cross-sectional design. In addition, the NHSLS did not include women over the age of 60, nor did it make any adjustment for menopausal status or medical risk factors.

While several groups have reported the prevalence of female sexual dysfunction, no study has adequately correlated sexual function domains with medical risk factors. Since the same disease processes and risk factors that are associated with erectile dysfunction in men, such as aging, hypertension, cigarette smoking, and hypercholesterolemia, can also be associated with sexual dysfunction in women [16, 31], these studies will be important.

Physiology of the female sexual response cycle

Masters and Johnson first characterized the female sexual response as consisting of four successive phases: excitement, plateau, orgasm, and resolution [21]. During sexual arousal, the clitoris and the labia minora become engorged with blood, and vaginal and clitoral length and diameter increase. Masters and Johnson observed that the labia minora increase in diameter by two to three times during sexual excitement and, consequently, become everted, exposing their inner surface.

In 1979, Kaplan proposed the aspect of “desire,” and the three-phase model, consisting of desire, arousal, and orgasm. In this model, the desire is the factor that incites the overall response cycle [18]. This three-phase model is the basis for the DSM-IV definitions of female sexual dysfunction, and the recent re-classification system proposed by the American Foundation of Urologic Disease (AFUD) Consensus Panel in October 1998 [4]. Others have recently suggested that sexual function should be viewed as a circuit, with four main domains: libido, arousal, orgasm, and satisfaction. Each of these four domains may overlap and feed back negatively or positively upon the other three domains [11].

Pathophysiology of female sexual disorders

Vasculogenic

High blood pressure, high cholesterol levels, smoking, and heart disease are associated with impotence in men
and sexual dysfunction in women. The recently named clitoral and vaginal vascular insufficiency syndromes are directly related to diminished genital blood flow secondary to atherosclerosis of the iliohypogastric/pudendal arterial bed [12]. Although a variety of psychological and medical disorders may result in decreased vaginal and clitoral engorgement, vascular insufficiency is an important cause of and should be considered in evaluating women with sexual arousal disorder. Diminished pelvic blood flow due to aortoiliac disease leads to vaginal wall and clitoral smooth muscle fibrosis, resulting in symptoms of vaginal dryness and dyspareunia [4, 12].

Histomorphometric evaluation of clitoral erectile tissue from atherosclerotic animals demonstrates clitoral cavernosal artery wall thickening, loss of corporal smooth muscle, and an increase in collagen deposition [12]. In human clitoral tissue, there is a similar loss of corporal smooth muscle with replacement by fibrous connective tissue in association with atherosclerosis of clitoral cavernosal arteries [41]. It is possible that the atherosclerotic changes that occur in clitoral vascular and trabecular smooth muscle may interfere with normal relaxation and dilation responses to sexual simulation.

Alterations in circulating estrogen levels associated with menopause contribute to the age-associated changes in clitoral and vaginal smooth muscle. In addition, traumatic injury to the iliohypogastric/pudendal arterial bed from pelvic fractures, blunt trauma, surgical disruption, or chronic perineal pressure from bicycle riding can result in diminished vaginal and clitoral blood flow and sexual dysfunction.

Neurogenic

The same neurogenic disorders that cause erectile dysfunction in men can also cause sexual dysfunction in women. These include spinal cord injury (SCI), diseases of the central or peripheral nervous system, including diabetes, and complete upper motor neuron injuries affecting sacral spinal segments. Women with incomplete injuries retain that capacity for psychogenic arousal and vaginal lubrication [38]. Women with spinal cord injuries have significantly more difficulty in achieving orgasm than normal controls. The effects of specific spinal cord injuries on female sexual response, as well as the role for vasoactive pharmacotherapy in this population, are being investigated. One study of women with spinal cord injuries demonstrated that sildenafil improved sexual function complaints commonly associated with SCI. Consistent with previous findings in men, the sexual effects of the drug were most evident under conditions of optimal stimulation. Further large-scale studies of sildenafil’s effects in women with neurogenic sexual dysfunction are indicated [37].

Hormonal

Dysfunction of the hypothalamic/pituitary axis, surgical or medical castration, premature ovarian failure, old age, and chronic birth control use are common causes of hormonally based female sexual dysfunction. The most common complaints associated with decreased estrogen and/or testosterone levels are decreased libido, vaginal dryness, and lack of sexual arousal. In addition, women may report increased emotional lability, sleep disturbances, and memory changes due to estrogen and androgen deficiencies. Estrogen improves the integrity of vaginal mucosal tissue and has beneficial effects on vaginal sensation, vasocongestion, and secretions, which lead to enhanced arousal. Estrogen deprivation causes a significant decrease in the clitoral intracavernosal, vaginal, and urethral blood flow. Histologically, diffuse clitoral fibrosis, thinned vaginal epithelial layers and decreased vaginal submucosal vasculature. Thus, a decline in circulating estrogen levels can produce significant adverse effects on structure and function of the vaginal and clitoral tissues, ultimately affecting sexual function. Serum testosterone concentrations in women decline with advancing age and are lower in older women than in younger women. However, in contrast to serum estradiol levels, serum testosterone levels do not decrease abruptly at menopause, but rather decline steadily with age [1, 3].

This is a consequence of the age-related decline in adrenal androgen production and the loss of the midcycle increase in ovarian testosterone in the late reproductive years.

In addition to the central effects of testosterone in women, there also may be peripheral effects in the vagina. Previous studies have described estrogen and androgen receptors in human female genital skin in an attempt to identify the potential target cells for each hormone [15]. In animal models, labium majora, labia minora, and vagina stain positive for the androgen receptor, and vaginal epithelium responds to testosterone replacement in a similar manner to estrogen replacement even in the absence of estrogen [13]. Androgens may play a role in regulating vaginal smooth muscle relaxation and blood flow, as testosterone receptors were identified in the nucleus of vascular endothelial, smooth muscle cells, and stroma in vaginal submucosa (Berman, et al., unpublished observations). Diminished androgen receptor expression was noted in vaginal sub-epithelium of women on estrogen replacement. This may result from estrogenic stimulation of sex hormone binding globulin (SHBG), leading to less free testosterone and less production of androgen receptors. Persistent symptoms of vaginal atrophy and dryness in menopausal women receiving estrogen replacement therapy may in part be related to impaired androgen responsiveness, derived from decreased vaginal androgen receptors, and/or reduced levels of circulating or vaginal testosterone.