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The chapters in this book provide comprehensive reviews of what is known about the epidemiology (Chapters 2.1–2.4), psychology (Chapters 3.1–3.4, 11.1–11.5, 17.2, and 17.3), biology (Chapters 6.1–6.5, 13.1–13.3, 14.1, and 14.2), and complex pathophysiologies (Chapters 7.1–7.7 and 16.1–16.9) of female sexual function. However, a recurrent theme is that our understanding of these dimensions of female sexual health remains limited.

It is only in recent years that acceptance of the high prevalence of female sexual dysfunction has broadened. A contributing factor was the publication of *The Social Organization of Sexuality* by Laumann et al. in 1994,[1] which presented the results of the National Health and Social Life Survey of 1410 men and 1749 women aged 18–59 years. Results from comprehensive interviews on sexuality brought to public attention that 43% of women aged 18–59 in the USA experience sexual concerns.[2] This report was criticized for labeling what was defined as sexual problems in the survey interviews as sexual dysfunctions in the results, the concern being that the high prevalence statistic would contribute to the over-medicalization of women's sexuality and consequent over-prescribing of drugs to treat psychologic problems.[3,4] Notwithstanding these valid concerns for women who are not clinically sexually dysfunctional, the National Health and Social Life Survey proved beneficial in spreading the word about women's sexual concerns for the significant number of women who meet the clinical diagnosis for sexual dysfunction. Starkly lacking, however, is comparable detailed information for women 60 years and older, since, clearly, sexual health is not limited to women of younger years.

The increased discourse and awareness of the extent of women's sexual dysfunctions has subsequently helped many women with sexual problems feel more comfortable in talking about their sexual concerns and justified in seeking help. Clinicians in the field of sexuality are now, more than ever, faced with the challenge of effectively diagnosing the many women who present with sexual dysfunction and offering them the best available treatment options.

In addition, the National Health and Social Life Survey brought to our attention the need for further exploration of a number of psychologically relevant variables affecting sexuality. Substantial differences in gender, age, marital status, race, and, less often, education were noted for a number of sexuality variables.[1] It is now incumbent upon future researchers to explore why these differences exist and the degree to which factors such as learning, sexual schemas and scripts, choices and opportunities, and network ties moderate these group differences.

Other events that have significantly influenced the assessment and management of female sexual dysfunction and research directions are the conferences devoted to the definition and classification of female sexual dysfunction. One of the first of these was a gathering of clinicians, researchers, government regulating agency representatives and pharmaceutical company representatives in Cape Cod in 1997[5] (see Chapter 1.2). This was followed by the first international consensus development conference of thought leaders in Boston in October 1988;[6] and, more recently, by a second series of multidisciplinary international consensus meetings in 2002 and 2003.[7] These were held during a time in which there has been increased advocacy from diverse groups for women's sexual rights internationally. The outcome has been the realization that the definitions of female sexual dysfunction listed by the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition, text revised (DSM-IV-TR), and the *International Statistical Classification of Diseases and Related Health Problems* (ICD) are unsatisfactory. As noted in the second conference publication,[6] this stems in part from the problematic conceptualization of women's sexual response cycle underlying those definitions. That is, the traditional models of women's sexual response[8,9] are based on a model more characteristic of men than of women, with the assumed linearity and sequential stages of desire, arousal, and orgasm. The most recent panel challenged six fundamental assumptions underlying the definitions of women's sexual dysfunctions listed by the DSM-IV-TR and ICD, and provided a revised classification system[7] (see Chapter 9.1). The most notable changes include a division of sexual arousal disorder into genital and subjective subtypes and the recognition of persistent sexual arousal. The panel also recommended that all diagnoses be accompanied by descriptors relating to associated contextual factors and degree of distress. These revised definitions and

descriptors, although a significant improvement, still do not adequately take into account the global sociocultural diversity in female sexual health. Future research needs to include the influences of culture and age on female sexual dysfunction as well as provide a more in-depth examination of individual differences in order to provide better insight into a number of key psychologic contributors to women's sexual health.

It is important to acknowledge that our understanding of women's sexual function from the physiologic and biochemical point of view is far from complete.

The physiology of genital arousal is highly dependent on the structural and functional integrity of the tissue, involving complex neurovascular processes modulated by numerous local neurotransmitters, vasoactive agents, sex steroid hormones, and growth factors. The vascular nature of genital tissue lends itself to many parallel comparisons from the already established field of cardiovascular biology. However, it is also well known that different vascular beds can yield diverse responses to the same disease state. Thus, there are probably mechanisms unique to the genital tissues and their vasculature. For example, delta-5-androstenediol, a steroid hormone possessing both androgenic and estrogenic activity, binds to a unique nuclear receptor that may be preferentially expressed in the vagina (see Chapter 5.5). In addition, the alpha-adrenergic, nitric oxide and purinergic signaling systems, the neurotransmitter vasoactive intestinal polypeptide, and the enzyme arginase have all been shown to regulate the genital arousal response in animal models (see Chapters 5.3–5.6). Whether any of these mediate genital arousal dysfunction remains to be seen. Additional understanding of the cellular and molecular mechanisms of normal physiology, as well as of pathogenesis, will help to identify potential points of intervention for the treatment of female genital arousal dysfunction. Much of this work will be facilitated by recently established tissue culture and female animal models.

The physiology of sex steroid hormones, the consequences of the depletion of these hormones, and their potential use in the management of female sexual dysfunction are yet to be established. With respect to the last, studies involving large numbers of women of adequate duration, and providing extensive safety data, are required before any therapy can be recommended for use. Furthermore, it is critical to understand the impact of imbalances in sex steroid hormone levels on the synthesis and function of growth factors and neurotransmitters, which play a key role in regulating genital tissue structure and the genital arousal response. These studies must first delineate the effects of sex steroid hormones on the expression of steroid receptors.

The basic premise of biologic management of women with sexual health concerns is that physiologic processes can be altered by pathologic states. Biologic pathophysiologies that adversely affect genital tissue structure and function now include genital tissue infections, genital tissue inflammatory conditions, mechanical compartment syndromes of the prepuce and labia, blunt or penetrating traumatic injuries to the perineum or vulva, pelvic support tissue weakness states with genitourinary organ prolapse, genital tissue alterations in immunologic defense capabilities, systemic alterations in hormonal milieu, peripheral and central nervous alterations, alterations in iliopudenal arterial blood inflow integrity, genital and nongenital tissue tumors and/or malignancies, and the adverse effects of cardiovascular, hormonal, and/or chemotherapeutic pharmacologic agents. The recorded number of biologic pathophysiologies keeps increasing as researchers expand biologic investigations.

The problem of how specific medical conditions modulate female sexual health urgently requires consideration and investigation. For example, the effects of diabetes on the physiology of sexual function in women have been poorly investigated, and the available information is limited and inconsistent. Similarly, all the other medical conditions that affect vascular function and endothelial integrity, and that are common in women, such as cardiovascular disease, rheumatoid arthritis, and systemic lupus, need to be included in female sexual dysfunction research (see Chapter 7.3).

From the perspective of the biologically focused clinician, the essential principle guiding medical decision making is identification of the underlying pathophysiology of the sexual dysfunction. If the biologic basis of the dysfunction can be diagnosed, management outcome may be successfully directed to the source pathophysiology.

Despite the research done so far, the paucity of proven medical interventions to help women with various forms of female sexual dysfunction is of concern. In the contemporary clinical armamentarium to treat female sexual dysfunction, the following medications and treatments are available with at least some level of evidence supporting safety and efficacy (see Chapters 14.1 and 14.2). Oral fluconazole is used to treat genital tissues (vagina, clitoris, and labia) infected with *Candida*. Oral acyclovir can treat genital tissues (vagina, clitoris, and labia) infected with genital herpes. Imiquimod, cryotherapy, electrotherapy, and silver nitrate are used to treat genital tissues (vagina, clitoris, and labia) affected by genital warts. Topical clobetasol can be used to treat genital tissues (vagina, clitoris, and labia) involved with lichen sclerosus or lichen planus. Topical lidocaine on the vestibule can lower genital sexual pain. Amitriptyline and gabapentin can lower genital sexual pain. Systemic testosterone may help manage low libido and sexual function. The therapeutic effects of dehydroepiandrosterone are yet to be determined in quality randomized, placebo-control trials. Systemic and local estrogen can improve diminished arousal, decreased lubrication, symptoms of atrophic vaginitis, and sexual function. Systemic progesterone can lower the opportunity for uterine epithelial hypertrophy in a woman with an intact uterus receiving systemic estrogen therapy. Systemic agents that are dopamine agonists, such as bupropion, can improve low libido, orgasmic function, and sexual function.

Oral phosphodiesterase inhibitors may improve arousal, genital sensation, orgasm, and sexual function in some women with sexual dysfunction, primarily those with normal hormonal profiles. However, two findings that emerged from the many

clinical trials of the phosphodiesterase inhibitors for women warrant mention. First is the finding of a substantial placebo effect of up to about 40% in women with sexual concerns, and second is the finding that often these drugs increased physiologic sexual arousal (e.g., vaginal pulse amplitude) in women without showing a congruent increase in subjective or mental sexual arousal.[10] The first finding points to the powerful influence of nonspecific drug effects on women's sexuality. That is, factors such as expectancies of improvement, simply enrolling in a study about sexuality, talking to a professional about one's sexual difficulties, and/or monitoring one's sexual responses may alone have enhanced women's sexual experience. Research is now needed to analyze the potential contribution of each of these factors to improved sexual well-being, and explore how best these beneficial elements might be applied in therapeutic settings.

The lack of a clinically meaningful drug influence on mental sexual arousal in women, despite evidence of an increase in genital engorgement, also highlights the limitations of applying a male template to study women's sexual concerns. That is, there may be substantial gender differences in the degree to which individuals focus on genital cues to estimate their degree of sexual arousal. As best described by Basson[11] in her model of the female sexual response, there are myriad factors that contribute to women's sexual desire and psychologic arousal, only one of which may be genital vasocongestion. Clinicians and theorists have noted endless contextual factors, past negative experiences, self-image, mood, and intimacy and relationship issues (e.g., commitment, sharing, tenderness, communication) that affect women's desire and ability to become sexually aroused and/or satisfied. The field could now benefit from an empirical examination of how and to what degree these factors affect a woman's sexual functioning, and how this may change across the life span. Research is also needed to clarify the relation between mental and physiologic sexual arousal in women. The degree to which these responses change in synchrony with sexual stimuli does not seem to be predicted by a woman's sexual functioning status.[12] Knowledge of what does affect the synchrony between responses would help to inform us of what subgroup of women might benefit from drugs that act primarily on physiologic mechanisms.

As a consequence of limited clinical and basic science research, the requisite knowledge underlying contemporary clinical decision making is quite rudimentary. This will change in the future as basic science investigations probe the physiologic principles of women's sexual activity. We also expect evidence-based management to be derived from double-blind, placebo-controlled, multi-institutional, and multicultural clinical trials (see Chapter 16.1).

Finally, effective care of women with female sexual dysfunction will depend on the education of health professionals and the community (see Chapters 18.1 and 18.2). Health professional education should not be limited to those with a special interest in this field, but rather, all health professionals must be cognizant of the importance, high prevalence, and potential consequences of women's sexual health problems and how they may adversely affect quality of life every day.

At present, in 2005, women's sexual health is hardly on the radar screen of afflicted patients or health-care professionals. Most women who have a sexual health concern do not even know they can seek help for their problem. Most do not know that any medical therapies are available to improve their function. There has not been universal acceptance of the biologic component of women's sexual disorders as a valid medical condition. Government granting agencies have not encouraged basic science research in this area. Government regulatory agencies have not yet approved pharmaceutic therapies to treat women's sexual health concerns safely and effectively. Sexual medicine practitioners in medical schools are not given the academic respect or teaching time enjoyed by other medical specialties. This situation must change.

As in any other area of medicine, primary care physicians, general psychologists, allied health-care professionals, physical therapists, and others should ask their female patients basic sexual health questions upon evaluation of any physical and/or mental health concern. Such primary care health-care professionals need to be knowledgeable regarding the broad management paradigms in women's sexual health. When health-care providers are uncomfortable with the subject, they are unable to manage effectively the sexual health problem; and when the issues exceed the realm of knowledge of the health-care clinician, patients must be referred to appropriate psychologic and biologic specialists in sexual medicine or women's sexual health.

The lack of academic representation of male and female sexual medicine in the core curricula of medical schools needs to be globally addressed. This will be substantially aided by the establishment of departments, divisions, or sections of sexual medicine in medical schools and teaching hospitals. To achieve these aims, we need a process by which sexual medicine specialists with expertise in the study, diagnosis, and treatment of sexual dysfunction can be "certified", such that this discipline achieves equal status with other specialties. Ideally, this will involve the development of a residency program to allow medical graduates the opportunity to choose a career in sexual medicine.

In summary, the contemporary ideal clinical management of women with sexual health concerns and sexual dysfunction is by multidisciplinary teams whose essential members include both psychologically focused and biologically focused health-care professionals.

We look forward to the future when the biologically focused health-care clinician has more pharmaceutical agents available with high levels of robust evidence supporting their safe and effective use in women with sexual health problems.

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