Chapter 9
Hypoactive Sexual Desire Disorder

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Diagnosis

Hypoactive Sexual Desire Disorder (HSDD) is diagnosed when an individual indicates persistent or recurrent blunted levels of sexual desire and/or a lack of sexual fantasies that cause marked distress and/or interpersonal difficulties [1]. This diagnosis is intended to include only individuals who experience dissatisfaction with their low levels of sexual desire. Women with this condition will often report that they "want to want" more sex, while women with low levels of sexual desire that do not meet HSDD criteria will indicate no bother or concerns with the frequency of their sexual desire. The subjective experience of distress caused by low desire is a critical component of the diagnosis of HSDD because many individuals are not alarmed by low levels of sexual desire. Indeed, an epidemiological study conducted in Australia demonstrated that 32% of women who are 20–70 years old report low sexual desire, but only 16% report distress caused by the low sexual desire [2].

Few studies have empirically evaluated variations in levels of sexual desire in women. A recent study on frequency of sexual fantasies, which is an aspect of sexual desire, reported that, on average, women experience sexual fantasies between once-twice per month to once a week [3], although an older study on the frequency of sexual fantasies reported that, on average, women experience two sexual fantasies per day and the majority of these fantasies are activated by outside cues [4]. Because of this great variance between women, the DSM-IV-TR [1] diagnosis relies on reports of distress caused by the low desire. Nevertheless, it is possible that individuals who desire sex once a year and are content with their levels of sexual desire and sexual activity may not be diagnosed with HSDD. Conversely, individuals who desire sex 3 times a week, but are distressed by this frequency may be diagnosed with HSDD. To add to the confusion, the DSM-IV-TR [1] indicates that a diagnosis can be made when the low levels of sexual desire cause interpersonal difficulties. Because of this criterion, if a woman is in a relationship with a partner with a much greater level of sexual desire than hers and the discrepancy in desire is causing relational distress, she would nevertheless receive a diagnosis for HSDD. However, if the same woman were in a relationship with a partner whose desire was more similar to hers, she would not meet criteria for HSDD. These caveats seriously question the theoretical assumption that "abnormal" levels of sexual desire can be identified and reliably assessed.

Theoretically, sexual desire has been conceptualized as the motivating mechanism behind sexual activities. This impetus is central to the survival of the species. The chronic and distressing experience of inhibited sexual desire can

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adversely affect quality of life, lead to high levels of personal distress, and cause relational difficulties [5]. Women who experience a loss of sexual desire might be faced with the choice of engaging in sex without feeling desire, but capitulate because they fear losing their partners, or experience guilt for withholding an important part of a satisfying relationship and harbor feelings of inadequacy and poor self-esteem – all of which could impair mental health. Because of the guilt often associated with inhibited sexual desire, women report they no longer express affection or touch their partners. For example, they often report withholding a hug, kiss, or casual touch, such as holding hands, because they are afraid this would mislead their partners to think they want to engage in sexual activities. The guilt of "starting what they cannot finish" prevents them from exchanging innocent forms of affection and this leads to greater distance in the relationship.

It has been well documented in the literature that inhibited sexual desire has relational consequences beyond the sexual realm. For example, studies have shown that couples reporting low frequencies of physical intimacy score lower on relationship adjustment and relationship satisfaction as compared to couples with higher frequencies of physical intimacy [3, 6]. However, the directionality of this relationship remains debated [7]. It is important to note that the frequency of sexual activities per se may not be the problem and that a decrease in frequency of sexual activities may cause greater distress in couples whose sexual lives are dramatically affected by HSDD as compared to couples who are satisfied with a low frequency of sexual activities. When couples experience different levels of sexual desire, there is often resentment on the part of the partner who has high levels of desire, while the partner with little or no sexual desire feels guilt and shame. Couples are often left to grapple with a cyclical and nonproductive conversation to make a change, each not knowing how to move out of their preferred sexual stance. In the long term, this cycle, with or without professional intervention, is likely to erode the relationship.

To prevent this dysfunctional cycle where HSDD fosters resentment and greater sexual dysfunction, information regarding potential changes and shifts in sexual desire over a lifetime can be incorporated in a preventive health education or sexual education program. Healthcare providers may be instrumental in reducing sexual dysfunction by simply educating their patients about sexual desire changes that may be the result of an illness, medication, surgery, or psychiatric condition, or even changes that result from life changes such as pregnancy or menopause. Having realistic expectations for changes in sexual health is an important aspect of health care that can help prevent sexual desire problems and can also help managing treatment and medication doses. Indeed, treatment-induced inhibition of sexual desire is one of the most commonly cited reasons for treatment discontinuation even for conditions that cause high levels of emotional distress, such as depression, and for drugs that provide an important function in women's lives, such as hormonal contraceptives. Indeed, research on antidepressants showed that 42% of men and 15% of women discontinue the medication over perceived beliefs of sexual adverse effects [8].

In summary, severe personal and relational distress caused by changes in sexual desire can be addressed by healthcare providers through simple education of how treatment, surgery, and illnesses can affect sexual desire. By providing accurate information to the patients, the healthcare provider can have a significant impact on the prevention of dysfunctional patterns in the relationship that can lead to chronic sexual dysfunctions. Moreover, accurate information about changes in sexual desire associated with a treatment can help prevent treatment discontinuation and promote overall quality of life not only for the patient, but also for her partner.

Theoretical Models of Sexual Desire

The HSDD diagnosis is based on the early models of the sexual cycle. Masters and Johnson [9] were the first to conceptualize the model of the sexual cycle to begin with sexual arousal and continue with plateau, orgasm, and resolution.

Kaplan [10] revised Masters and Johnson's original theoretical model by adding sexual desire in the beginning of the cycle (i.e., prior to sexual arousal). To date, Kaplan's model is considered controversial. The debate is centered on whether desire and sexual arousal are distinct experiences, with desire always *preceding* sexual arousal.

A more recently proposed model of female sexual response posits that desire is experienced after sexual arousal [11]. In this model (often called the Circular Model), it is proposed that the woman experiences sexual arousal after her partner approached her with sexual cues and stimulation. The sensation of sexual arousal leads to positive associations with sexual behavior and these associations motivate desire for further sexual stimulation. Once the sexual activity has led to satisfying emotional and physical sexual experiences, the woman internalizes the desire for future sexual activities that, she anticipates, will lead to similar sexual rewards. The emotional and physical rewards resulting from sexual activity are the sources of spontaneous motivation for later sexual activities. Therefore, sexual activities that fail to provide satisfying physical and emotional rewards may diminish sexual desire in women [11]. According to this model, the treatment of sexual desire is contingent to the experience of satisfying sexual activities.

A third model, proposed by Levine [12], emphasizes that variations in individuals' experiences of sexual desire provide more clinically relevant information than just frequency of sexual thoughts or fantasies. According to Levine's theory, an overall frequency of sexual thoughts or fantasies is less relevant than information changes in the cues that activate sexual desire. For example, according to this model, a clinician would benefit from assessing whether a woman who used to experience sexual desire after a romantic dinner is no longer feeling sexual desire after similar activities. Thus, an assessment of how a woman used to respond to a sexual cue (e.g., a specific scent, romantic experiences, erotic material, seeing a partner acting competently) is more important than the assessment of overall frequency of sexual thoughts. This model, originally developed through extensive clinical experience, has found support in a recent empirical study [13]. A group of 50 women identified 125 different cues of sexual desire that were analytically grouped into four cue types based on the responses of a second group of 874 women of 17–72 years old (Table 9.1; 13). The four analytically derived types of sexual cues are reminiscent of the 11 sexual cues that Levine identified based on his clinical observations. Later, a study on premenopausal and menopausal women showed that individuals with HSDD endorsed significantly fewer cues than women without HSDD [14]. The combination of clinical and empirical evidence for this model provides unique support for the validity of perceived sexual cues as meaningful contributing factors of HSDD. The next step will be to establish whether increasing the variety of sexual cues and modulating the sensitivity to sexual cues (e.g., lowering the threshold of desire activation in the presence of a sexual cue) could alleviate HSDD symptoms.

Today, desire continues to be understood as a motivating force to engage in activities that can lead to sexual satisfaction [14]. From a behavioral perspective, motivation is the driving force behind the initiation and maintenance of goal-oriented behavior [16]. However, sexual desire does not always directly precede the behavior it motivates, and sexual behaviors may occur in the absence of desire. There are a number of reasons women may not act on their sexual desire, for example, social norms or fear of pregnancy. On the other hand, sexual desire aside, women may engage in sexual activities, for instance, to ensure the fidelity of a mate, to spite someone, or to succumb to peer pressure [17]. The distinction between sexual desire and frequency of sexual behaviors connected to desire [3] makes the assessment of desire more complicated than it may initially appear.

As noted above, the theoretical model for sexual desire proposed by Basson argues that spontaneous sexual desire is not the norm in women, but rather it is the product of sexual arousal. An empirical study that asked women whether they identified more strongly with the model proposed by Kaplan (the model proposing that desire always precedes sexual arousal) or the model

Table 9.1 Type of cues of sexual desire

Type of cues	Examples of cues
Emotional bonding	Feeling a sense of love with a partner
	Feeling a sense of security in your relationship
	Your partner is supportive of you
	Your partner does "special" or "loving" things for you
	Feeling a sense of commitment from a partner
	Your partner expresses interest in hearing about you
	Talking about the future with your partner
	Feeling protected by a partner
	Experiencing emotional closeness with a partner
	Feeling protective of a partner
Explicit/erotic	Watching an erotic movie
	Reading about sexual activity (e.g., pornographic magazine)
	Watching or listening to other people engaged in sexual behavior/activity
	Talking about sexual activity or "talking dirty"
	Watching a strip tease
	Sensing your own or your partner's wetness, lubrication, or erection
	Asking for or anticipating sexual activity
	Hearing your partner tell you that he or she fantasized about you
	Having a sexual fantasy (e.g., having a sexual dream, daydreaming)
	You experience genital sensations (e.g., increased blood flow to genitals)
Visual/proximity	Seeing someone who is well dressed or "has class"
	Seeing/talking with someone powerful
	Being in close proximity with attractive people
	Seeing/talking with someone famous
	Seeing a well-toned body
	Seeing/talking with someone wealthy
	Watching someone engage in physical activities (e.g., sports)
	Seeing someone act confidently
	Seeing/talking with someone intelligent
	Flirting with someone or having someone flirt with you
Romantic/implicit	Whispering into your partner's ear/having your partner whisper into your ear
	Dancing closely
	Watching a sunset
	Having a romantic dinner with a partner
	Watching a romantic movie
	Being in a hot tub
	Touching your partner's hair or face
	Giving or receiving a massage
	Laughing with a romantic partner
	Smelling pleasant scents (e.g., perfume/cologne, shampoo, aftershave)

From McCall and Meston [13].

proposed by Basson found that women with a sexual dysfunction identified more with the latter and women with no sexual dysfunction identified more with the former [18]. Future studies are needed to assess whether (1) the tendency to identify with a specific model can be a factor in developing sexual dysfunction and (2) whether women's perceptions of their sexual response cycle can change as their sexual functioning develops and changes over time. Both models are currently utilized in clinical settings. A useful tool for clinicians may be to present both models to a patient and ask her to identify the model that reflects her personal experience. Presenting the patient with this option opens the opportunity for education on different perspectives of sexuality and provides a

theoretical framework to conceptualize sexual symptoms, goals, and expectations of treatment.

In sum, the debate on whether desire precedes or follows arousal is implicitly a discussion on the nature of sexual desire. The perspective that some women experience sexual desire before sexual activities implies that a woman may experience spontaneous sexual desire, suggesting that desire can be activated by internal forces and may not necessarily be based on outside cues. Examples of spontaneous sexual desire are sexual fantasies that emerge during the day, or the night, and are not activated by any external stimulation. Conversely, the circular model, proposing that sexual desire occurs after sexual arousal, supports the idea that women's sexual desire is naturally derived from outside cues or is reactive in nature. In other words, this model questions the importance of spontaneous sexual thoughts or fantasies. Establishing the definition of normal sexual desire as internally vs. externally derived determines what is perceived as "abnormal" and thus directs the focus of treatment. Although an in-depth explanation of this pressing discourse is beyond the scope of this chapter, an understanding of these two conflicting positions can be useful for understanding the utility of different treatment modalities and the aspects of desire to include in a preliminary HSDD assessment.

Assessment of HSDD (Table 9.2)

A number of instruments developed for the assessment of HSDD are available to the public. Clinics not specialized in the treatment of sexual dysfunction can utilize a brief screener of HSDD to identify women who are more likely to experience problems with sexual desire. There are two such screeners currently available: the Hypoactive Sexual Desire Screener [19] and the Decreased Sexual Desire Screener [20]. Both screeners exhibit good sensitivity and specificity, meaning that the instruments are able to correctly identify people with the disorder. Individuals scoring positive on the screener, and indicating interest in greater support in this area, can complete aimed questionnaires that measure severity of sexual symptoms. According to a recent review of 28 questionnaires for female sexual functioning [21], the Female Sexual Functioning Index [22] and the Sexual Function Questionnaire [23] were recommended for both clinical and research use for women who may have sexual dysfunctions [21]. Although these questionnaires cannot be a substitute for a thorough interview covering the sexual, psychological, and medical history of each patient, they are adequate measures of severity of the sexual problem and provide the clinician with population-based norms on levels of distress associated with low desire. Clinical cutoffs based on population norms allow clinicians to quickly assess the severity of the symptoms in relation to the larger population.

Questionnaires assessing distress and satisfaction can be utilized to provide a measure of the impact of the problem on the patient's daily life. Measures of distress/satisfaction can also be useful to set goals for treatment and to track treatment-related improvements. Among the available published measures for sexual satisfaction, the Sexual Satisfaction Scale for Women [24] is one that captures both satisfaction and distress with sexual functioning. Although norms for women with and without HSDD are available, currently the scale lacks cutoffs for clinical levels, therefore it is best used to monitor treatment-related improvements.

A more comprehensive sexual health history can uncover important diagnostic information not fully captured by brief questionnaires. For example, potential etiological factors of low sexual desire can emerge from an interview that includes questions about the relationship dynamic. A personal interview also provides an opportunity to assess whether the low levels of desire are lifelong, the product of a slow decline, or whether a reduction followed a specific triggering event. For instance, a crisis caused by infidelity, a lifelong issue, or perhaps a slow decline since menopause can be important factors in the assessment and treatment of HSDD. If the change was sudden, other issues can be

Table 9.2 Topics addressed during a complete assessment of hypoactive sexual desire disorder

Topics to target during HSDD assessment
1) Ensure patient understands the definition of desire. Desire is both spontaneous desire for sexual activities and the tendency to respond when a partner initiates sexual activities
2) Assess whether levels of sexual desire are lower than wished by the patient (not necessarily her partner)
3) Assess whether the low level of sexual desire causes distress or bother in the patient (not necessarily her partner)
4) Investigate whether the levels of desire have always been low (lifelong) or if they were higher at some point (e.g., in pervious relationship or earlier in current relationship, before menopause, before pregnancy, or before a specific event)
a) Investigate the circumstances of the event
b) Explore the pattern of change (sudden or gradual change)
c) Establish the amount of change noticed by the patient
5) Assess the attribution for the low sexual desire by the patient
6) Assess relationship satisfaction, ability of the couple to communicate emotional material, points of disagreement, and power distribution within the couple
7) Determine the major points of life stressors in the patient and her coping style
8) Inquire about relevant past sexual experiences including a history of sexual abuse and childhood trauma including emotional and physical abuse
9) Assess emotional responses to sex that could affect sexual desire, including beliefs that could lead to guilt, shame, and anxiety

explored during an interview, for example, whether the patient experienced a recent illness, a change in medication, or whether problems emerged within the romantic relationship, with alcohol or substance use, or as aftermath of a sexually abusive experience. Other clinically meaningful information that can be explored during an interview include whether the low desire causes personal or interpersonal distress (or both), and whether partner's sexual health is playing a role in the low desire of the patient. Moreover, interviews aid in identifying other coexisting sexual dysfunction, including whether desire was an antecedent or consequence of the accompanying sexual dysfunction. As we will discuss later, it is common for women with sexual arousal dysfunction to experience concurrent low sexual desire. In such cases, determining whether the sexual arousal dysfunction occurred prior to, in concurrence with, or after the decline in sexual desire may help identifying important etiological factors to target during treatment.

In addition to clinical interviews, laboratory tests can provide useful information for treatment of HSDD. The most commonly used laboratory tests include an assessment of abnormally low androgens levels. Usually, laboratory exams include an assessment of free testosterone, DHEA-S, and DHEA. Patients' androgens levels can be compared to population-based norms; however, information on intrapersonal drops in androgen has been identified as more accurate information. An assessment of medical conditions associated with estrogen and androgens abnormalities can also be useful. For examples, conditions resulting in amenorrhea, oligomenorrhea, polycystic ovarian syndrome, and diabetes have been linked to impaired levels of sexual desire and it would be appropriate to treat these conditions before attempting the direct treatment of sexual desire, since the low desire may be a symptom of a larger problem rather than a circumscribed and independent condition.

Differential Diagnosis

Low sexual desire is often observed in people experiencing other psychiatric conditions such as depression, anxiety disorders, and eating disorders [25–28]. In addition, low levels of sexual desire are commonly reported by women who also experience other types of sexual dysfunction, including female orgasmic disorder, female sexual arousal disorder, and sexual pain disorders.

Identifying whether HSDD is part of a more complex sexual or psychological cluster of symptoms or whether it is a symptom independent of other pathology is a requisite part of a complete HSDD diagnosis.

The high coexistence of HSDD and other types of sexual dysfunction [22] can be best understood if we look at desire as a motivating force to pursue or engage in gratifying sexual experiences [15]. If desire is the motivation to engage in behaviors that lead to sexual rewards, any obstacle to the rewarding aspect of the sexual experience, or with motivating mechanisms in general, can potentially have an adverse effect on sexual desire. For example, a woman who experiences difficulties becoming sexually aroused or reaching an orgasm is not likely to experience the physiological pleasure associated with sexual activities and this could lead to a reduction in motivation for sexual activities. It is also possible for the inverse to be true and problems with desire could eventually lead to low arousal or problems with orgasm and sexual pain. From a treatment point of view, factors that maintain HSDD may be equally (or more) important than initiation factors. Therefore, understanding the factors that perpetuate the dysfunction in the present moment is central to the assessment. For example, levels of sexual desire may have dropped after a series of sexual experiences that failed to lead to orgasm. After numerous unsuccessful and frustrating sexual experiences, the woman may feel a loss of desire along with the difficulty in reaching orgasm. In such a case, the orgasm is the primary dysfunction that subsequently caused the development of HSDD; therefore, treating the desire problem alone may not be sufficient. At the same time, treating the orgasm without addressing the low desire caused by feelings of anxiety, sadness, inadequacy, and disappointment may overlook an important aspect of her sexual health. Thus, a clear understanding of what started the sexual problems needs to be addressed along with the exploration of potential maintaining factors.

Female sexual arousal disorder and HSDD are particularly difficult to distinguish because women often do not intuitively differentiate arousal from desire. However, women are not the only ones confused about the desire-arousal distinction. As we have discussed above, experts are still debating whether desire and arousal should be considered two distinct experiences [29]. Currently, desire is defined as the experience of longing or wanting to engage in sexual activities, whereas subjective sexual arousal comprises the sensations that women experience during sexual stimulation. Questions to distinguish between problems with arousal, orgasm, and desire are listed in Table 9.3. Although these questions have not been empirically validated, they are commonly used in clinical practice and they can be quite informative.

It should be noted that despite the importance to ascertain the temporal precedence between HSDD and the other types of sexual dysfunction, to date, very little is known about the coexistence of desire and other diagnoses and even less is known about the importance of treating desire in relation to other sexual difficulties. Indeed, it is unclear if it is possible to maintain normal sexual desire in the presence of chronic sexual arousal or orgasm problems.

Problems of sexual desire are highly prevalent in women experiencing clinical depression. Indeed, the diagnostic criteria for depression include loss of sexual desire as part of the vegetative symptoms of this condition. Individuals with major depression lose interest in many pleasurable experiences, including sexual activities. According to the DSM-IV-TR [1], the occurrence of reduced sexual desire as part of a depressive episode precludes the diagnosis of HSDD because the change in desire is conceptualized as part of a more generalized loss of motivation and interest. Nevertheless, the relationship between loss of desire and depression is poorly researched and quite complex. For example, young college students experiencing depressive symptoms within the clinical levels for major depression reported a strong interest and desire to masturbate, yet, interestingly, they also reported reduced interest in engaging in sexual activities with a partner [30, 31]. These findings suggest that individuals experiencing major depression do not completely lose interest

Table 9.3 Questions to differentiate between HSDD and other sexual dysfunction

If I had a pill that increased your level of sexual arousal (how much your body gets turned on during sexual activities) do you think your desire would increase as well?
If I had a pill to increase the frequency and/or the intensity of your orgasms, would your sexual desire increase as well?
Was there a time when it was easier to become sexually aroused than now? If so, what was your sexual desire then, and what was the relationship like during that time?
Was there a time when your orgasms were more intense and more frequent than now? If yes, what was your sexual desire then?
[If the individual indicated that she is also experiencing sexual arousal or orgasm problems] What started first, the problems with sexual desire or the problems with sexual arousal/orgasm?

for activities that lead to sexual reward. The loss of sexual desire for these women may be specific to a subset of sexual activities that include partners (potentially as an extension of social isolation often experienced with depression).

To complicate the relationship between HSDD and depression, the literature has shown robust evidence for a relationship between antidepressant medication use and decreased sexual desire, with women on antidepressants being 2.2–2.5 times at greater risk for sexual dysfunction [32, 33]. The standard critique of studies correlating antidepressant use with blunted desire is that sexual disturbances are part of the diagnostic criteria for depression and this redundancy complicates our ability to accurately measure prevalence of sexual dysfunction in this population. This sound critique is overshadowed by stringent exclusion criteria in most studies that limit the extrapolation of findings from a specific sample (e.g., no comorbid medical or psychiatric conditions, no concurrent use of other psychotropic medications, and restricted duration of antidepressant use). Years of research have targeted selective serotonin reuptake inhibitors (SSRIs) as primary culprits for antidepressant-induced reductions in desire based on the astoundingly high prevalence of impaired sexual desire associated with these medications, yet some serotonin-norepinephrine reuptake inhibitors (SNRIs) show equally dismal rates of reduced desire (see [33] for review). Data on newer antidepressants with highly specific mechanisms of action (i.e., flibanserin, a 5-HT1A agonist, 5-HT2A antagonist, and a D4 partial agonist) indicate that future antidepressants may not adversely impact sexual desire, but may indeed facilitate levels of desire [34].

It is also possible that when the depression abates due to psychotherapy (individual and/or couple therapy), and the use of SSRIs, then partnered sexual relationships improve. For example, Mary was 54-year-old married woman who had been postmenopausal for several years before she sought help. Her primary complaint was that after her surgery for uterine cancer, she had no sexual desire. She was in a satisfying marriage of 26 years with a husband who was very supportive and not demanding of sexual contact. They both were affectionate with one another and shared kisses, hugs, and touching one another in nonintercourse encounters. However, during an initial attempt at vaginal intercourse, she experienced a great deal of pain. They were both very anxious that they might never be able to have intercourse again. During Mary's diagnosis and treatment for cancer, she and her husband had not been given any information about how the treatments and surgery might affect their sexual relationship.

Mary had depressive episodes prior to her diagnosis of uterine cancer and had not been treated. After a thorough evaluation, it was decided that couple therapy would be the best modality for treatment as the issue was both relational as well as personal. Mary brought up the idea of trying antidepressants as she had a mother who was depressed most of her life. Mary knew a great deal about the current family of medications that were available and wished her mother had been able to take advantage of them. She felt confident that without being

depressed, she would be more willing to engage in sexual contact with her husband even if she did not feel much desire. Prior to the surgery, she had always been orgasmic and willing to engage in intercourse. She felt she would enjoy sex once she and her husband were engaged even if she felt no desire going into the encounter. A pelvic physical therapist was suggested for dealing with vaginal pain, pelvic floor strengthening, and building confidence for vaginal containment. Couple therapy enhanced their ability to communicate about sexual issues and to develop a broader repertoire for sexual expression. While their relationship was stable, therapy enhanced their ability to communicate about expectations regarding sex and allowed them to become a more "intimate team" working together to meet the challenge of "good enough sex" after cancer [35].

HSDD Prevalence in Epidemiological Studies

Population-based studies indicate that 29–39% of women report low or no sexual desire in the previous month [2, 36, 37], and between 15 and 34% report that the low desire causes distress [2, 38, 39]. These rates elucidating that low sexual desire is not experienced as distressful by all women. Rates of low sexual desire are independent of age up until age 50. After age 50, the rates of low sexual desire and distress caused by desire increase noticeably. A study of Swedish women found that rates are double in the 50–60-year-old cohort compared to younger women. The age trend found in Sweden is comparable to what has been reported in population-based studies in Iceland and Morocco [40].

The only incidence studies available to date were conducted in Finland and Sweden in the early 1990s. These studies found between 40 and 45% of women report a decrease in sexual desire within the prior 5 years [41]. Due to the lack of information on levels of distress, it is not possible to deduce the actual incidence of HSDD from this study, although we would expect reduced reports of distress in these incidence rates, based on prior studies of desire frequency and distress [39].

Factors Implicated with Sexual Desire

The complexity of HSDD is reflected in the myriad of mechanisms that the literature has linked to sexual desire. Although we attempt here to highlight the independent effect of biological, psychological, and relational factors, it is important to note that, in the patient, these three domains do not manifest independently from each other, and at times, may not be distinguishable from one another. The impact of each separate variable on low sexual desire is difficult to isolate. We have discussed, for example, how in Mary's case, a lifelong struggle with depression provided an impairment in her serotonergic system. Cancer provided additional psychological and physiological problems. In this case, the depression and cancer worked together to provide low sexual desire, physiological impairments to intercourse, and relational issues.

Biological Factors

From a biological perspective, it is undeniable that sex hormones play an important role in sexual desire [30]. However, the relationship between desire, androgens, and estrogens is poorly understood. Even with this lack of clarity, there is persuasive data on the impact of sex steroid hormones on desire. Most of this information comes from studies on sexual desire during the menopausal transition. Developmental fluctuations in estrogens and androgens observed during menopause are associated with a decrease in sexual desire (for a review see 30). A few studies have found that for women with particularly low levels of androgens, an androgen patch [42] and injections [43] can be effective at increasing sexual desire. However, the safety of these treatments is under investigation and the

positive effects of such treatments are modest [44]. This evidence provides an indirect indication that abnormal decreases in androgen levels can negatively impact desire. However, increasing androgen levels in women not experiencing androgen deprivation is unlikely to lead to an increase in sexual desire [45]. Thus, androgens are better conceptualized as hormones that facilitate the normal fluctuations and peaks in sexual desire, rather than hormones that directly modulate desire.

Estrogens levels are also associated with sexual desire. In animal studies, sexual behavior is tightly connected to the estrous cycle and deprivation of estrogen (via ovariectomy or the use of estrogen antagonists) leads to the complete cessation of receptive behavior in the female rat [15]. In women, however, estrogen does not have such a clear effect on sexual desire. Normal fluctuations in estrogens during the menstrual cycle have been linked with fluctuations with desire in some studies, but not others [30]. Characteristics of estrogen receptors are also key in understanding the modulation of circulating estrogen. The regulation of estrogen receptors is modulated by progesterone and androgens. Therefore, it is often the combination of low estrogen and testosterone, rather than low estrogen per se, that has been associated with low sexual desire [46].

Given that sexual desire is comprised of essential motivating mechanisms to engage in specific behavior, other neurotransmitters implicated with the general motivation system are likely to affect sexual desire. Dopamine and endogenous opioids are some of the most studied neurotransmitters in the modulation of sexual desire [47]. Animal studies have found that opioid antagonists prevent female rats from learning that specific stimuli can lead to sexual satiation, indicating that when sexual activities are not paired with opioid release, sexual rewards are not perceived. As a result, learned sexual preferences and desire for access to sexually intact males will not be expressed [15]. Dopamine antagonists also impair the expression of sexual desire by altering the salience of sexual cues and the behavioral response to rewarding stimuli. Female rats given dopamine antagonists will not express sexual preferences for specific cues that they have previously learned to pair with sexual rewards [15]. Recent studies on humans have found that a compound that acts on both the dopaminergic and serotinergic systems, flibanserin (a 5-HT1A agonist, 5-HT2A antagonist, and a D4 partial agonist), increases levels of sexual desire in premenopausal women, providing further evidence for the role of dopamine in the modulation of sexual desire. Indeed, antipsychotics (most of which antagonize D2 receptors) are notorious for reducing the appreciation of pleasure [48].

Psychological Factors

Psychological well-being is highly correlated with sexual desire, and conversely, a lack of sexual desire can signal a problem in the area of psychological adjustment. In a study of 126 women seeking sex therapy, 50% were diagnosed with a coexisting psychiatric diagnosis [49]. An organism functions according to a hierarchy of needs, as first proposed by Maslow [50], and psychological maladjustment can adversely impact multiple levels of needs. From an evolutionary perspective, the suppression of sexual desire during states when the individual is fighting for survival ensures that reproduction occurs when energy and resources are available. It is therefore practical for people perceiving threat to their well-being to focus on self preservation over any other activity. In states where the individual is struggling with a threat to safety, physiological needs, such as procreation, are disrupted. Similarly, individuals who tend to be overly sensitive to stressors in their environment and may show an exaggerated response to stressors (i.e., individuals with mood or anxiety disorders) may show a reduction in sexual function that is not warranted.

Individuals suffering from depression, a disorder that disrupts primary physiological needs including sleep and eating, also report lower

levels of sexual desire compared to people with no depressive symptoms [51]. Women with HSDD are indeed more likely to have a history of major depression compared to women with no HSDD [52]. In addition to mood and anxiety disorders, other psychopathologies often accompanied by inhibition of sexual desire include schizophrenia and anorexia nervosa. The relationship between schizophrenia and sexual desire is poorly understood. From a theoretical point of view, it is feasible that impairment in the mesocortical pathway, a pathway associated with emotional processes and motivation, may be also responsible for the low level of sexual desire in patients with schizophrenia. However, the lack of empirical studies on this topic and the complexity of both schizophrenia and sexual desire prevent a clear acceptance or rejection of such hypothesis, at this point. Alternatively, the antipsychotics used to treat schizophrenia may depress appreciation of sexual reward, thereby blunting sexual desire.

The association between anorexia nervosa and desire may be implicated with the impairment in the hypothalamus-pituitary-adrenal (HPA) axis, a system closely connected with stress that is responsible for facilitating the release of resources to key organs involved in the fight and flight response. States of food deprivation affect this system and send signals that the organism is in a state of potential starvation. Resources are released in the body, which enters a survival state. It is plausible that during this state, the motivation system for functions not necessarily linked to immediate survival is shut down. This hypothesis is largely speculatory at this point given the lack of information available on sexual function in women with eating disorders.

Relationship

When sexual desire occurs within the context of a relationship, a woman's desire to engage in sexual activities may be affected by her sense of closeness and intimacy with her partner and her overall relationship satisfaction [7]. Quality of the relationship is also important for treatment outcome. A review of clinical outcome studies for desire [53] found that overall quality of the couple's nonsexual relationship and degree of physical attraction between partners were the first and third most commonly reported factors associated with positive treatment outcome, respectively.

In addition to the quality of the relationship, the sexual dysfunction and the health of the partner can affect a woman's sexuality. Data from longitudinal and cross-sectional studies found that poor health in the male partners of heterosexual women was associated with lower sexual desire functioning and greater overall sexual dysfunction in women [54, 55].

Cancer

The majority of the studies that investigated sexual function in cancer survivors focused on gynecological or breast cancer. In our review of Medline, PsychInfo, and PubMed databases for articles published in the past 50 years on cancer and sexual desire, only a handful of articles focused on nongynecological cancers (including lung, pituitary, and rectal cancers). Therefore, the majority of the information currently available on cancer and sexual desire must be understood as limited to these specific types of cancer populations as it is unclear whether these results would apply to other forms of cancer.

While the initial studies on breast cancer were mostly focused on the potential effect of mastectomy on women's body image and therefore on her sexuality, later studies [56, 57] painted a different picture and provided evidence that side effects of treatment (and especially radiotherapy) on sexual desire are more debilitating than the psychological effects caused by mastectomy. Because of the multifaceted nature of desire, and the multitude of systems affected by cancer and cancer treatment, we will discuss the effects of cancer and its treatment on the three components

of sexual desire preciously identified in our review of desire: biological, relational, and psychological.

Prevalence of Low Desire and HSDD in Cancer Patients

The prevalence of desire problems in cancer populations is elevated compared to national averages. In a sample of 20 women treated for gynecological cancer, 56% reported low levels of sexual desire and 35% of the 20 women had both depression and sexual dysfunction [58]. For patients with breast cancer, the rates of women reporting interferences with sexual desire (31%) are comparable to patients with gynecological cancer [59].

In a sample of 96 patients treated for ovarian, cervical, endometrial, vaginal, vulvar, and sarcoma cancer, 43% complained of HSDD and asked for clinical recommendations [60]. After 6 months, of all patients requesting clinical consultation, 70% reported improvement after complying with treatment recommendations, indicating that women were both interested in receiving support for the side effects on sexuality and demonstrated the motivation to follow through with such suggestions.

Direct Effects of Cancer on HSDD: Biological, Psychological, and Relational

Based on data from 817 women who had undergone breast cancer treatment, including chemotherapy, researchers found that the best predictors of sexual function and satisfaction postbreast cancer are: absence of vaginal dryness, emotional well-being, body image, quality of the relationship, and partner's sexual problems. These variables accounted for 33% of variance in sexual satisfaction in breast cancer survivors [61]. We will now look individually at main factors impacting sexual desire with the understanding that these factors often act in orchestration and not independently.

Biological

The only data available on the direct biological effects of cancer on sexual desire come from studies on cancer affecting the HPA axis. According to a study on 53 women with pituitary tumors, levels of sexual desire were inhibited or desire was lacking in approximately 80% of patients [62]. Levels of sexual desire were neither correlated with hyperprolactinemia nor with serum testosterone (although no data was presented on free testosterone, a measure of androgen that is more closely associated with levels of sexual desire), but age and presence of intrasellar tumors were positively associated with loss of sexual desire [62].

Psychological Factors

Depression is a common consequence of a life-threatening condition like cancer. Indeed, between 15 and 40% of individuals with cancer will experience depression or anxiety during the course of their illness [63]. Symptoms of depression are difficult to tease apart from physiological and treatment-related effects of cancer treatment (e.g., fatigue, changes in appetite and weight). Both clinical depression and treatment-related depressive symptoms may impair sexual desire. Sexual desire may be diminished following chronic depression, which is associated with altered HPA axis function and persistent immune activation [64], which, in turn, may compound the broad immune, endocrine, and metabolic changes associated with cancer and its treatment. Prominent psychological issues that arise in individuals suffering from cancer include feelings of grief and loss, existential anxiety related to death, adoption of poor coping strategies, problematic social support, and tolerance of prolonged treatment and cancer

recurrence. The combination of the stress caused by this life-threatening condition and cognitive vulnerabilities that may lead to depression can affect sexual desire.

Receiving a life-threatening cancer diagnosis can motivate a number of fears that directly, or indirectly, inhibit sexual desire. More often than not, a cancer diagnosis has a profound impact on not just the patient, but their spouse/partner as well, and it is likely to create ripples in the entire family system. Assessing a patient's sexual history and her baseline sexual functioning (i.e., before the surgery) and establishing a rapport with the patient and her spouse/partner are important steps for the healthcare provider interested in preventing or containing HSDD symptoms associated with treatment. In the case of gynecological cancer, fears specific to sexual activities may be particularly relevant for understanding sexual dysfunction. Schultz and van de Wiel [65] listed common feelings evoked by gynecological cancer that affect sexual desire: guilt, fear that the disease will reoccur, the wish to reject physical contact, the fear of damaging one's body, contaminating others, or losing the ability to procreate.

Fear and guilt are among the most commonly reported types of negative affect and are frequently addressed in the literature. Fears associated with cancer can have a direct effect on sexual function since it can activate avoidance of sexual activities. Guilt is more commonly experienced among women with cervical cancer because this form of cancer is linked to genital herpes, and thus a promiscuous sexual history may be likely among individuals with this type of cancer and this may lead to the feeling that she caused (and deserves) the disease. Negative affect caused by fear and guilt acts as a motivator to avoid sexual activities or any form of intimacy. This avoidance can counterintuitively lead to the strengthening of these negative emotions.

The psychological effects of cancer on the sexual desire of a woman are moderated by her view of herself as a sexual being, prior to the diagnosis [67]. The perception a person has of her self (self-schemas) provides a blueprint on how the individual perceives and responds to events. Schemas emerge from past experiences and the meaning that the individual gives to these experiences. At their basic level, schemas provide a framework on which the individual forms a sense of self that is coherent across time and situations. Studies have indeed found that a woman's sexual self-schema affects how the woman faces cancer and how her sexuality changes during treatment [66]. Although schemas are stable features of our identity, they are of particular interest for treatment since they can be modified through psychotherapy. In a series of studies on sexual self-schemas, Andersen and coworkers [66–68] found that endorsing adjectives that describe the self as embarrassed and sexually conservative, and not endorsing adjectives such as passionate, loving, romantic, open, and direct, predicted a decrease in sexual function at 4 and 8 months postcancer diagnosis [66]. A quick assessment of sexual self-schemas conducted at the time of diagnosis can aid in identifying individuals who are at higher risk for later sexual problems, who may therefore be good candidates for therapy.

Relational Factors

A life-threatening diagnosis can change a romantic relationship in a variety of ways. For example, if a partner or spouse is supportive and caring, the diagnosis will likely increase the sense of intimacy and commitment between the partners. These relationships can have a positive effect on both the individual and the prognosis of treatment. Indeed, supportive relationships are associated with better health outcomes for cancer survivors.

Alternatively, it is possible that the sexual dysfunction secondary to cancer treatment may upset the relationship, leaving the patient to deal with her medical condition and the relationship problems [69]. Patients who feel compelled to please their partners by trying to maintain their prediagnostic sexual life may engage in sexual activities despite a lack of sexual desire. Such behavior can lead to physically and psychologically painful sexual experiences, which eventually lead to resentment, thereby causing even

greater inhibition of sexual desire. For example, when Joan was diagnosed with leukemia, she had been married to David for 10 years. She was a high power attorney and came from a very wealthy and well-connected family. During those years, David had pressured Joan for sexual intercourse every day. At the time of diagnosis, the marriage was suffering from polarization around sexual frequency. Severe sexual desire incompatibility is associated with pair-bond dysfunction, a common issue in men who have compulsive sexual behaviors [70]. At this time, Joan also found out that David had an affair. Since Joan was already well practiced at "keeping David happy," she was determined not to risk a divorce by denying his sexual "needs." In this instance, cancer played a positive role when David, threatened by the loss of Joan to cancer, agreed to counseling. His pressure for sex also hid a needy, dependent man with well-hidden poor self-esteem who wanted sex to prove he was loved. The cancer diagnosis made him afraid Joan would die leaving him alone in the world. In spite of his affair, he needed the connection to Joan and the wealth and prestige she represented. During the diagnostic stage of the cancer, David's doctor suggested they talk with a mental health professional on the medical team. It was then that David and Joan started discussing and preparing for the sexual side effects that they were likely to encounter during treatment.

Effect of Cancer Treatment on HSDD

Not only can cancer directly affect sexual desire, but as mentioned above the interventions utilized to treat the cancer are likely to have adverse effects as well. Chemotherapy and radiation therapy in the treatment of gynecological cancer are the two most commonly documented interventions that impair sexual desire function.

Chemotherapy

Chemotherapy is accompanied by fatigue, nausea, and vomiting. These somatic symptoms can strongly inhibit sexual desire. For 50% of women, the sexual dysfunctions experienced during the active phase of treatment persist even after treatment [71, 72].

Radiation Therapy

Radiation for gynecological cancer is associated with higher sexual dysfunction than levels found in healthy controls, and sexual dysfunction increases after radiotherapy [73, 74]. This research hypothesized that the increase in sexual dysfunction following radiotherapy is partially explained by stenotic changes to the blood vessels in the vagina, vaginal shortening, necrosis, and vaginal adhesion or agglutination, where the elastic vaginal tissue is substituted by fibrous tissue present in 78–96% of women receiving radiotherapy [75, 76]. These changes in the vagina lead to lack of lubrication and problematic and painful intercourse, which then reduces sexual pleasure and therefore the incentive to further engage in sexual activities. Thus, even physiological changes associated with treatment can disturb normal motivation (i.e., desire) for sexual activities.

Moreover, radiation artificially induces menopause, thus reducing the production of testosterone [30]. It is important to note that studies have not always found an association between sexual desire and radiotherapy-induced changes in the vagina, when women were tested posttreatment. However, studies that tested desire 1 year posttreatment did report a reduction in desire [76, 77]. This posttreatment shift in desire suggests that the changes caused by radiotherapy may be delayed and therefore patients may benefit from consultation for sexual functioning *after* the termination of treatment. A qualitative study suggested that during treatment patients are mostly focused on their condition and dealing with the shock of receiving a life-threatening diagnosis than they are about their sexual functioning. During the later phases of treatment, quality of life becomes more important and survival is less of a pressing concern and it follows that women report a greater interest in information regarding their sexual function [78].

Breast Conservation

Breast conservation has been found to be consistently better for body image following a cancer diagnosis, but results are mixed for its effects on sexual desire. Initially it was believed that one of the major reasons for women to experience a loss in sexual desire, after breast removal, was due to the effect of mastectomy on body image. Recent studies have identified menopausal symptoms as a much stronger risk factor for HSDD in breast cancer survivors (c.f., 81). Two studies utilizing random assignment to mastectomy vs. breast conservation have reported fewer problems in sexual desire among women who underwent breast conservation therapy [80, 81]. However, six studies did not find greater sexual desire in women receiving breast conservation therapy compared to mastectomy.

Researchers have hypothesized that the benefit gained from a less severe loss in body image may be overshadowed by the fear that the cancer may return. For a study of breast cancer conservation with radiotherapy, a sample of 86 patients was recruited from an Italian general hospital. Forty-three percent reported they experienced a decrease in desire that they attributed to the treatment and 41% reported a decrease in sexual desire attributed to the disease [59]. Some women opt for breast reconstruction, and although some evidence points to greater body image satisfaction among them, it is not clear whether breast reconstruction can help a woman to increase her levels of desire since there is a lack of controlled studies. Another limitation of the available data is that women not interested in breast reconstructions usually do not participate in these studies. It is feasible that only women who experience greater body dysmorphia after the mastectomy choose breast reconstruction and therefore we cannot assume that all women would show a similar improvement in their sexual function after breast reconstruction.

Among breast cancer survivors, antiestrogenic medication could potentially have a negative effect on sexual desire [79]. A paucity of data exists on the sexual side effects of tamoxifen, which is the most common antiestrogen utilized for menopausal women with breast cancer. Two studies compared women currently taking tamoxefin to healthy women, in a trial for chemoprevention [59, 82]. These studies did not find a significant difference in sexual desire between groups, but they utilized a very crude measure of sexual desire. In these studies, the researchers asked participants to indicate whether they desired sex more or less than once per month. As indicated in our review of the definition of sexual desire, this information is not meaningful if not accompanied by subjective measures of distress. Given that there is no set frequency of sexual thoughts, the interpretation of this item is highly problematic. The arbitrary frequency of sexual desire selected for these studies (more or less than once per month) may cause a ceiling effect since many women with low sexual desire are likely to desire sex more than once per month. A third study utilizing a more sophisticated measure of sexual desire and comparing sexual function in women taking low vs. high levels of tamoxifen found that sexual desire increased more when the tamoxifen treatment was discontinued as compared to women who continued a low tamoxifen dose [83]. Separating the effects of tamoxifen from the effects of menopause is not easy and thus, at this point, we should interpret these results carefully, since we cannot exactly identify the effects of tamoxifen independently from the effects of menopause.

Overall, the studies on breast cancer treatment seem to indicate that body image is less salient for the sexual function of cancer survivors and that treatments that affect the production of steroids may have a stronger impact on sexual desire. Interestingly, little is known on the psychological vulnerabilities of individuals with breast cancer. Given that sexual dysfunction can be affected by biological, psychological, and relational factors, more studies are needed to explore potential vulnerabilities that may be specific to women going through breast cancer.

Oophorectomy

In addition to breast cancer, which is a prevalent type of cancer for women, oophorectomy, the surgical removal of ovaries, is the procedure that

is most commonly identified with a decrease in sexual desire. Removal of the ovaries, to all intents and purposes, induces surgical menopause. It is important to note that the literature consistently points to menopausal symptoms in response to the surgical removal of the ovaries as causing greater HSDD symptoms than natural menopause [84, 85]. This difference has been attributable to the fact that, during natural menopause, the production of testosterone continues, although at a much reduced rate, while surgical menopause causes a dramatic and definite cessation of androgen production. During surgical menopause, androgen levels drop to less than 50% of the normal production of testosterone in naturally menopausal women (for a review, see [86]). However, the changes in the sexual cycle caused by oophorectomy are quite pervasive and have been found to affect all aspects of sexual function, including sexual arousal, orgasm, and pain [84], and therefore it is difficult to identify whether the low desire is exclusively the product of the changes that affected the entire cycle or if there is a direct effect on desire per se.

Oophorectomy may affect sexual desire through the reduction in vaginal lubrication and thus a greater likelihood for damage to the vaginal epithelium during intercourse which leads to sexual pain. As we noted above, painful intercourse is, of course, a reason to be avoidant of sexual activities and can provide a lessening of sexual desire. Therefore, it is essential that preemptively, patients and their partners be advised about this outcome and be provided with information about pelvic physical therapy and lubricants which can mitigate painful vaginal issues.

Estrogen administered to women who have received oophorectomy can also have a negative effect on desire because estrogen increases levels of sex hormone-binding globuline (SHBG) levels, which cause the already low levels of testosterone to bind and not be physiologically active, therefore reducing the amount of testosterone available to bind with receptor sites involved with sexual desire. Indeed, in a perspective study on estrogen replacement therapy [87], individuals who underwent salpingo-oophorectomy or abdominal hysterectomy did not show any improvement in their postoperative sexual function after receiving estrogen replacement therapy.

Conclusions

In conclusion, the literature on HSDD in women with a history of cancer is in its infancy. Nevertheless, we can clearly see patterns emerging that point at essential impairments caused by the side effects of cancer treatments. While addressing sexual dysfunction in the early acute phase of a cancer diagnosis may be relevant only for a limited number of women, sexual dysfunction become more relevant for women after a year of treatment.

Sexual dysfunctions, and particularly hypoactive sexual desire, are complex phenomena regulated by biological, psychological, and relational aspects of the woman's life and, for this reason, the referral to a specialist in sexual medicine may be the best approach for an oncologist. Lately, we are seeing emergence of the inclusion of sex specialists on treatment teams. For example, since 2008, the University of Chicago has had a Program for Integrative Sexual Medicine Clinic for Women and Girls with Cancer. This is a program supported by the Department of Obstetrics /Gynecology, Section of Gynecology Oncology and the Cancer Research Center. Mental health professionals are also part of the oncological program at the University of Vermont Medical center. These are multidisciplinary programs which include an advance-practice nurse, a gynecologist, a psychologist and/or clinical sexologist, and a pelvic physical therapist with expertise in addressing pelvic floor issues and sexual problems in women with cancer. The focus is on generating new knowledge about sexuality and treatment of sexual problems in the context of cancer treatment and survivorship. For the oncologist who has limited time and resources, often just introducing the topic about sexual desire and providing a referral or titles of books (see Appendix) can help the patients and their partners gaining a perspective on their sexual health.

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