

Sexual Dysfunction, Part I: Classification, Etiology, And Pathogenesis

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Abstract: Background: The sexual dysfunctions are extremely common but are rarely recognized by primary care physicians. They represent inhibitions in the appetitive or psychophysiologic changes that characterize the complete adult sexual response and are classified into four major categories: (1) sexual desire disorders (hypoactive sexual desire, sexual aversion disorder), (2) sexual arousal disorders (female sexual arousal disorder, male erectile dysfunction), (3) orgasmic disorders (inhibited male or female orgasm, premature ejaculation), and (4) sexual pain disorders (dyspareunia, vaginismus).

Methods: Articles about the sexual dysfunctions were obtained from a search of MEDLINE files from 1966 to the present using the categories as key words, along with the general key word "sexual dysfunction." Additional articles came from the reference lists of dysfunction-specific reviews.

Results and Conclusions: Cause and pathogenesis span a continuum from organic to psychogenic and most often include a mosaic of factors. Organic factors include chronic illness, pregnancy, pharmacologic agents, endocrine alterations, and a host of other medical, surgical, and traumatic factors. Psychogenic factors include an array of individual factors (e.g., depression, anxiety, fear, frustration, guilt, hypochondria, intrapsychic conflict), interpersonal and relationship factors (e.g., poor communication, relationship conflict, diminished trust, fear of intimacy, poor relationship models, family system conflict), psychosexual factors (e.g., negative learning and attitudes, performance anxiety, prior sexual trauma, restrictive religiosity, intellectual defenses), and sexual enactment factors (e.g., skill and knowledge deficits, unrealistic performance expectations).

Understanding the cause and pathophysiology of sexual disorders will help primary care physicians diagnose these problems accurately and manage them effectively. (*J Am Board Fam Pract* 1992; 5:51-61.)

Sexual dysfunctions are exceptionally common but infrequently recognized. The classic "Content of Family Practice" study from the Department of Family Practice, Medical College of Virginia¹ recorded sexual dysfunctions rarely. Other investigators, however, have reported that sexual problems can occur in 50 percent of all marriages² and that they are present in 75 percent of couples who seek marital therapy.^{3,4} Moore and Goldstein⁵ found that 56 percent of patients in a family practice reported one or more sexual problems, but these problems were recorded in only 22 percent of the cases. In one of the most cited prevalence studies, Frank and colleagues⁶ surveyed well-adjusted couples with high marital

satisfaction and found that 63 percent of the women and 40 percent of the men experienced a specific sexual dysfunction, and an even higher percentage (77 percent of the women and 50 percent of the men) reported general "sexual difficulties."

Because many sexual problems are hidden, primary care physicians need to help discover them. Once discovered, to manage these disorders effectively, physicians must understand their cause and pathogenesis; evaluate them thoroughly by history, physical examination, and laboratory testing; initiate management; and refer to other appropriate professionals when necessary.

Classification of Sexual Dysfunctions

Inhibitions in the appetitive or psychophysiologic changes that characterize the complete adult sexual response are at the heart of the sexual dysfunctions. They are not usually diagnosed, however, if they occur exclusively during the course of an-

Submitted, revised, 9 August 1991.

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other psychiatric disorder, such as a major depression or an obsessive compulsive disorder

The complete sexual response cycle consists of four phases: appetitive, excitement (arousal), orgasmic, and resolution. The appetitive phase involves sexual fantasies and a desire for sexual activity. During the excitement phase, in addition to a subjective sense of sexual pleasure, men experience penile tumescence and erection, and secretions appear from the bulbourethral glands. Women experience pelvic vasocongestion, vaginal lubrication, swelling of the external genitalia, narrowing of the outer third of the vagina by increased pubococcygeal muscle tension and vasocongestion, vasocongestion of the labia minora, breast tumescence, and lengthening and widening of the inner two-thirds of the vagina. Sexual pleasure peaks during the orgasmic phase and is accompanied by the release of sexual tension and rhythmic contraction of the perineal and pelvic reproductive organs. In men, a sensation of ejaculatory inevitability precedes the contractions in the prostate, seminal vesicles, and urethra that results in seminal emission. In women, contractions occur in the outer third of the vaginal wall. During resolution, both men and women feel relaxed and free from muscular tension. Men are temporarily refractory to further erection and orgasm, but women can respond almost immediately to additional stimulation.

Inhibitions in the sexual response cycle can occur at one or more of these phases, although only the first three are of primary clinical significance. The major dysfunctions are classified and defined as follows⁷:

Sexual desire disorders include (1) hypoactive sexual desire disorder, characterized by deficient or absent sexual fantasies and desire for sexual activity; and (2) sexual aversion disorder, defined as extreme aversion to and avoidance of genital contact with a sexual partner.

Sexual arousal disorders include (1) female sexual arousal disorder, characterized by failure to attain or maintain the lubrication-swelling response of sexual excitement until completion of the sexual activity or by lack of a subjective sense of sexual excitement and pleasure during sexual activity; and (2) male erectile disorder, marked by failure to attain or maintain erection until completion of sexual activity or by lack of a subjective

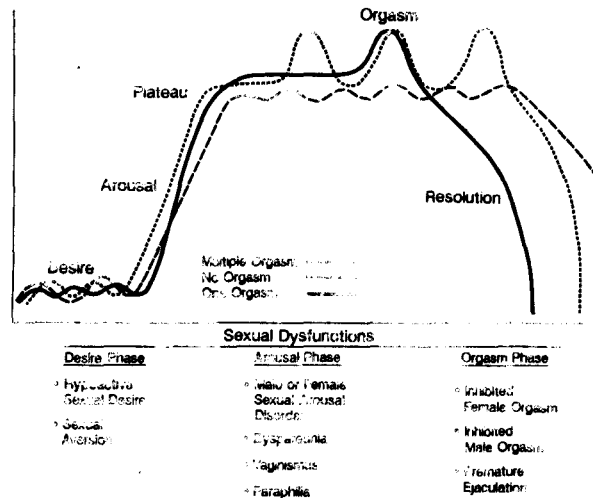


Figure 1. The sexual response cycle, with several normal patterns and the common dysfunctions classified by the phase that they affect.

sense of sexual excitement and pleasure during sexual activity.

Orgasm disorders include (1) inhibited male and female orgasm, characterized by delayed or absent orgasm following a normal sexual excitement phase that is adequate in focus, intensity, and duration; and (2) premature ejaculation, defined as ejaculation with minimal sexual stimulation or before, upon, or shortly after penetration and before the man wishes it.

Sexual pain disorders include (1) dyspareunia, characterized by genital pain in either sex before, during, or after sexual intercourse that is not caused exclusively by lack of lubrication or vaginismus; and (2) vaginismus, defined as involuntary spasm of the musculature of the outer third of the vagina that interferes with coitus.

Figure 1 summarizes these sexual dysfunctions according to the phase of the sexual response cycle that they affect. It also depicts several normal response patterns.

Cause and Pathophysiology

The sexual dysfunctions have both organic and psychogenic causes. A specific dysfunction can be mostly psychogenic, mostly organic, or mixed. Dysfunctions can be lifelong (primary) or acquired (secondary), generalized (occurring in any situation or with any partner) or situational (limited to certain situations or partners), and complete or partial in severity.

General Causative Factors

Organic Factors

Organic problems affect all phases of the sexual response cycle. According to current estimates, the cause of at least 50 percent of erectile dysfunction cases is primarily organic,⁸ with some estimates ranging as high as 75 to 85 percent.⁹ Thirty percent of surgical procedures on the female genital tract result in temporary dyspareunia, and 30 to 40 percent of the women seen in sex therapy clinics for dyspareunia have pathologic pelvic conditions.^{9,10} The common general organic factors that affect sexual function include chronic illness, pregnancy, pharmacologic agents, endocrine alterations, and chemical abuse. A variety of other medical, surgical, and traumatic factors can be implicated in specific dysfunctions.

The degree to which chronic illness interferes with sexual function depends on the type of chronic illness, the age of onset with regard to sexual maturation, and whether the illness was recognized before the current relationship.¹¹ Congenital illnesses and illnesses that begin before or during puberty have a greater impact on the course of sexual development. The more visible the problem, the more it will interfere with sexual development. Relationships that begin before the onset of a chronic illness are more affected by the illness because they require a greater number of difficult adjustments.¹¹

Pregnancy affects sexual desire in different ways.^{12,13} In the first trimester, nausea, fatigue, and the fear of miscarriage interfere with sexual desire. In the last trimester, increasing size and a perception of decreasing attractiveness, along with a focus on the well-being of the infant and on enduring labor and delivery, decrease sexual desire. During the middle trimester, increasing pelvic vasocongestion and an overall feeling of well-being facilitate sexual responsiveness.

Pharmacologic agents interfere with sexual functioning through several mechanisms.¹⁴ Some cause adrenergic inhibition.^{15,16} Drugs that alter the neurotransmitter norepinephrine by blocking α -adrenergic receptors, by depleting norepinephrine stores, or by blocking norepinephrine release can cause sexual dysfunction by altering emission or ejaculation. Adrenergic antagonists include such drugs as guanethidine, reserpine, methyl dopa, clonidine, prazosin, and phenoxybenzamine.

Drugs that sedate and depress the central nervous system adversely affect sexual functioning by decreasing libido and altering potency, perhaps by increasing brain serotonin and decreasing dopamine levels.^{15,17-19} Depressants include alcohol, cannabis, barbiturates, and benzodiazepines, as well as antihypertensive and anticonvulsant medications that have sedating properties.

Increased prolactin levels reduce the responsiveness of the male gonads to leutinizing hormone, thereby inhibiting testosterone production.^{15,19-23} Some drugs can cause increased prolactin release through dopaminergic antagonism (e.g., phenothiazines, thioxanthenes, butyrophenones). Other drugs, such as cimetidine and narcotics, increase prolactin levels through mechanisms that are incompletely defined. Some drugs have antiandrogen effects.^{15,24-26} The aldosterone antagonist spironolactone causes estrogenlike side effects with decreased libido, impotence, and gynecomastia in men and painful breast enlargement and menstrual irregularity in women. It likely causes these effects by inhibiting dihydrotestosterone binding to its cytosol protein receptor. Alcohol also decreases testosterone levels, perhaps by peripheral suppression of testosterone production in the testes. Oral contraceptives can decrease libido in women by decreasing estrogen levels. Progesterone is thought to suppress sexual activity in some women because of an antiandrogen effect.

Anticholinergic agents, or drugs with atropinelike actions, can cause sexual problems (chiefly arousal difficulties) secondary to their parasympatholytic activity.^{15,27-29} These agents include antiparkinsonian drugs, tricyclic antidepressants, many antipsychotic agents, antihistamines, antiemetics, antivertigo drugs, and the antiarrhythmic disopyramide.

Various mechanisms are proposed to explain the sexual dysfunction associated with drugs that do not appear to fit the other categories.^{15,19,30-38} Examples include decreasing receptor sensitivity to dopamine or a decrease in its intraneuronal turnover (lithium) and peripheral vasoconstriction or sympathetic blockade (propranolol).

The specific drugs that are associated with sexual dysfunction and the dysfunctions associated with each are listed in Table 1. The particular effect of any drug on a patient will vary depending on such factors as age, absorption, body

Table 1. Pharmacologic Agents Associated with Sexual Dysfunction.*

Drug	Phase of Sexual Response Cycle Affected (+) or Not Affected (-)		
	Desire	Arousal	Orgasm
		(erection)	(ejaculation)
<i>Anti-anxiety</i>			
Alprazolam	-	-	+
Clorazepate	+	-	+
Chlordiazepoxide	+	-	+
Diazepam	+	-	+
<i>Anticholinergic</i>			
Atropine	-	+	-
Benztropine	-	+	-
Glycopyrrolate	-	+	-
Mepenzolate	-	+	-
Methantheline	-	+	-
Propantheline	-	+	-
Scopolamine	-	+	-
Trihexyphenidyl	-	+	-
<i>Anticonvulsant</i>			
Carbamazepine	-	+	-
Phenytoin	+	+	-
Primidone	+	+	-
<i>Antidepressant</i>			
<i>Heterocyclic</i>			
Amitriptyline	+	+	+
Amoxapine	+	+	+
Clomipramine	+	+	+
Desmethylimipramine	+	+	+
Doxepin	+	+	+
Imipramine	+	+	-
Maprotiline	+	+	+
Nortriptyline	+	+	+
Protriptyline	+	+	+
Trazodone	-	-	-
<i>Monoamine oxidase inhibitor</i>			
Carboxazid	-	+	+
Fluoxetine	-	+	+
Pargyline	-	+	+
Phenelzine	-	+	+
Tranylcypromine	-	+	+
<i>Antihistamine</i>			
Cyproheptadine	+	+	-
Diphenhydramine	+	+	-
Hydroxyzine	+	+	-
<i>Antihypertensive</i>			
<i>Diuretic</i>			
Amiloride	+	+	-
Furosemide	-	+	-
Indapamide	+	+	-
Spiroglactone	+	+	-
Thiazide	+,-	+	+,-
<i>Centrally acting sympatholytic</i>			
Alpha-methyl dopa	+	+	+
Clonidine	+	+	+
Guanfacine	+	+	+
Reserpine	+	+	+
<i>α-Adrenergic blocker</i>			
Guanabenz	-	+	-
Guanadrel	+	+	+
Phenoxybenzamine	-	+,-	+
Phentolamine	-	+,-	+
<i>β-Adrenergic blocker</i>			
Labetalol	+	+	+
Metoprolol	-	+,-	-
Pindolol	-	+	-
Propranolol	+	+	-
Timolol	+	+	-
<i>Ganglionic blocker</i>			
Mecamylamine	-	+	+
Trimethaphan	-	+	+
<i>Sympathetic neuroeffector agent</i>			
Guanethidine	+,-	+	+
<i>Nonadrenergic vasodilator</i>			
Hydralazine	+,-	+	-
Prazosin	+,-	+,-	-

Continued

Table 1. Continued.

Drug	Phase of Sexual Response Cycle Affected (+) or Not Affected (-)		
	Desire	Arousal	Orgasm
		(erection)	(ejaculation)
<i>Angiotensin converting enzyme inhibitor</i>			
Captopril	-	+	-
Enalapril	-	+	-
Lisinopril	+	+	-
<i>Calcium channel blocker</i>			
Diltiazem	-	+	-
Nifedipine	-	+	-
Verapamil	-	+	-
<i>Antimicrobial</i>			
Ethionamide	-	+	-
Ketoconazole	-	+	-
<i>Antipsychotic</i>			
Chlorpromazine	+	+	+
Chlorprothixene	-	-	+
Fluphenazine	+	+	-
Haloperidol	+,-	+	+
Mesoridazine	-	-	+
Perphenazine	-	-	+
Pimozide	+	+	+
Thioridazine	+	+	+
Thiothixene	-	+	+
Trifluoperazine	-	-	+
<i>H₂-receptor antagonist</i>			
Cimetidine	+	+	-
Famotidine	+	-	-
Ranitidine	+	+	-
<i>Hormone</i>			
Danazol	+	-	-
Hydroxyprogesterone	-	+	-
Norethindrone	+	+	-
Oral contraceptives	+	-	-
Progesterone	+	+	-
<i>Narcotic</i>			
Codeine	+	+	+
Heroin	+	+	+
Meperidine	+	+	+
Metadone	+	+	+
Morphine	+	+	+,-
Propoxyphene	+	+	+
<i>Sedative-hypnotic</i>			
Alcohol	+,-	+	+
Barbiturates	+,-	+	+
Chloral hydrate	+	+	+
Ethchlorvynol	+	+	+
Methaqualone	+	+	+
<i>Other agents</i>			
Acetazolamide	+	+	-
Aminocaproic acid	-	-	+
Amiodarone	+	-	-
Amphetamines	-	+	+
Baclofen	+	+	-
Cannabis	+	+	-
Cocaine	-	+	+
Clofibrate	+	+	-
Digitalis	+,-	+	-
Disopyramide	-	+	-
Disulfiram	-	+	+
Fenfluramine	+	+	-
Interferon	+	+	-
Levodopa	-	-	+
Lithium	-	+	-
Mazindol	-	+	+
Methandrostenolone	+	-	-
Methazolamide	+	+	-
Metoclopramide	+	+	-
Metyrosine	-	+	+
Mexiletine	+	+	-
Naltrexone	-	+	+
Naproxen	-	+	+
L-Tryptophan	+	+	-

weight, dosage, duration of use, rates of metabolism and excretion, presence of other drugs, underlying disorders, patient compliance, and suggestibility.

Based on current research, it is unlikely that hormonal fluctuations during the menstrual cycle play a significant role in sexual dysfunction.^{11,39} The combination of somatic and emotional symptoms that some women experience during menses, however, can result in sexual disinterest and arousal difficulty. Furthermore, menstruation can affect sexual function because of religious teachings, taboos, sexual ignorance, fears of displeasing one's sexual partner, or simple esthetics rather than because of physiologic factors.¹¹

A number of commonly abused chemical agents also cause sexual dysfunction. Alcohol is associated with decreased libido and erectile difficulty.^{14,15,40} Marijuana also can decrease libido and cause erectile difficulty.^{14,15} Phencyclidine hydrochloride (PCP) can cause erectile and ejaculatory failure.^{14,41} Cocaine is associated with sexual indifference, dysphoria, aggressiveness, situational impotency, and anorgasmia.^{14,42} Heroin users also experience reduced sexual desire, erectile dysfunction, and anorgasmia.^{14,43} Methadone and amphetamines reportedly decrease sexual performance.^{14,44,45} Tobacco abuse results in sexual dysfunction primarily through its adverse effects on the vascular system.¹⁴

Androgens play an important role in the libido of both men and women. Androgen deficiency can result from panhypopituitarism,⁴⁶ combined bilateral adrenalectomy and ovariectomy in women, or castration in men. Hyperprolactinemia caused by a prolactin-secreting pituitary tumor has been associated with sexual dysfunction.⁴⁷ The mechanism responsible is not clearly defined but may relate to hypogonadism secondary to prolactin-induced hypogonadotropism. Both hypothyroidism and hyperthyroidism can also cause sexual dysfunction.^{8,48}

Psychosexual Factors

Sexual dysfunctions are invariably multidetermined; a single cause is rare.^{49,50} Even when an organic factor is present, it is essential to treat the principal psychological factors that can complicate the organic problem or that could have resulted from it. Three areas of psychological focus are important: individual psychological deter-

minants, relationship issues, and psychosexual factors.

Empirical studies have linked many individual psychological factors with sexual dysfunction.⁵¹ Depression⁵² and anxiety^{2,53,54} are most common. Diminished self-esteem,⁵⁵ frustration, guilt, hypochondria, sexual fear, hostility or anger,^{54,56} unrealistic expectations or perfectionism,⁵⁷ intrapsychic conflicts (such as grief, unresolved sex orientation, concerns about paraphilic arousal patterns⁵⁴), and serious psychopathologic disorders also contribute. Depression and anxiety are considered generic causes of sexual dysfunction, but they also commonly occur as consequences of sexual dysfunction⁵⁸; therefore, determining causality can be challenging. As a general rule, severe depression or anxiety is more likely causative; mild forms more commonly represent the impact of sexual failure.

Sexual and relationship factors can interact in several ways.⁵⁹ Relationship problems can cause sexual dysfunction, organic sexual dysfunction can precipitate relationship distress, or the two factors can exist independently. Recognizing that sometimes there is no clear relation between sex and marital problems is important. Some couples with serious marital dysfunction appear to have a satisfactory sexual relationship. The reverse is also true. The most common relationship factor that causes sexual dysfunction, however, remains marital dissatisfaction⁶⁰ involving relationship problems that generate stress, fatigue, or dysphoria. Dissatisfaction can focus on poor communication,^{53,54} unrealistic marital expectations,⁶¹ failure to resolve relationship conflict,^{53,61,62} diminished trust,⁵⁴ fears of intimacy or romantic success,^{54,63} a history of poor relationship modeling that is transferred to the marriage, family system distress (such as caring for an elderly relative or preschool and school-age children), sex role conflicts, divergent sexual preferences or sex values, career problems, and legal troubles.

The most common psychosexual factors causing sexual dysfunction are prior sexual failure (often at first intercourse), chronic sexual performance inconsistency, negative learning and attitudes about sex,^{2,64} and prior sexual trauma.^{2,54} Other identified factors include sexual guilt and shame,^{65,66} unrealistic expectations about sexual performance,⁶⁷ restrictive religiosity,² sexual performance anxiety generated by fears of failure or

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