1
Introduction to Sexual Medicine

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Introduction

Kolodny, Masters, and Johnson coined the term sexual medicine in their well-known *Textbook of Sexual Medicine* [1]. Sexual medicine is the branch of medicine that focuses on the evaluation and treatment of sexual disorders, which have a high prevalence rate. Approximately 43% of women and 31% of men are affected by these disorders [2]. Today the field of sexual medicine continues to evolve. There have been recent changes in classification of disorders, advancements in pharmaceutical management, and improvement in behavioral therapies. This introductory chapter provides a concise review of relevant topics to sexual medicine including recent classification changes in the International Classification of Diseases, 10th edition (ICD-10) and Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5).

Milestones in Sexual Medicine

The ancient Egyptians illustrated sexual scenes in tomb carvings/painting, papyrus, and sculptures (Figure 1.1). The Turin Erotic Papyrus dating back to 1105BC depicted at least 12 sex positions (Figure 1.2).

One of the first sex manuals in history is the Kama Sutra, written in India, in second century BC. Techniques of sexual pleasure enhancement including positions are fully explained including the spiritual aspects. Some of the positions were carved inside the Mukteswar Temple in Bhubaneswar, India (Figure 1.3).

In 1896, Havelock Ellis, an English physician (Figure 1.4), published "Studies in the Psychology of Sex," discussing normal and abnormal sexuality. Around the same time, in 1898, Richard von Krafft-Ebing, a German psychiatrist (Figure 1.5), published in Latin a book called "Psychopathia Sexualis" (Figure 1.6), which is the first modern text on sexual disorders including the paraphilias. By 1918, Sigmund Freud (Figure 1.7), the founder of psychoanalysis, considered sexuality central to his psychoanalytic theory.

Early in the twentieth century, German physician Magnus Hirschfeld (Figure 1.8) founded the first sex-research institute in Germany. He conducted the first large-scale sex survey, collecting data from 10,000 men and women. He also initiated the first journal for publishing the results of sex studies. The Nazis destroyed most of his materials during World War II. In the early 1930s, American anthropologist Margaret Mead and British anthropologist Bronislav Malinowsky began studying sexual behavior in different cultures [3].

In the USA, Alfred Kinsey (Figure 1.9) published a survey of 18,000 subjects regarding sexual behaviors in 1947. William Masters and Virginia Johnson followed this survey with rigorous lab study of sexual encounters. Masters and Johnson developed key concepts in sexual medicine such the sexual response cycle, and developed an effective treatment technique for sexual dysfunction named sex therapy. Helen Singer Kaplan followed with a major expansion on training sex therapists, including desire in the sexual response cycle, and examining premature ejaculation from psychological as well as behavioral angles.

In 1981, Ronald Virag (Figure 1.10) discovered during a surgical procedure on the penis that papaverine caused an erection when injected into the penis. In 1983, Giles Brindley (Figure 1.11) gave his notorious AUA Lecture in Las Vegas when he had previously injected himself with a vasodilator, identified as phentolamine in some accounts and papaverine in others. The self-injection became later one of the most reliable interventions to produce an erection.

The National Health and Social Life Survey (NHSLS), also known as the Chicago Study or Chicago Survey, is a landmark epidemiological study of sexual function and dysfunction examining randomly selected 3432 subjects who underwent face-to-face surveys. This well-designed survey revealed that about 43% of women and 31% of men suffer from sexual dysfunction.

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Figure 1-1. Small sculpture of a sexual scene [Reprinted from: https://commons.wikimedia.org/wiki/Category:Ancient_Egyptian_erotic_art#/media/File:Egypt-sex.jpg with permission from Creative Commons].

The most significant breakthrough was the identification of nitric oxide as the principal neurotransmitter responsible for the relaxation of the corpus cavernosum smooth muscle, by Louis Ignarro, Ph.D. in 1997, as a result of 2 decades of research. This discovery enabled the development of oral pharmacological agents for the treatment of erectile dysfunction. Dr. Ignarro (Figure 1.12) was awarded the Nobel Prize for this momentous discovery in 1998 [4].

The late 1990s brought more focus on women's sexual health, largely due to the efforts of Jennifer and Laura Berman, who were originally mentored by Irwin Goldstein at Boston University [5]. Rosemary Basson introduced the circular model of the sexual response cycle in women where arousal could overlap with desire. The current state of the field is an exciting one, with a plethora of biochemical and physical interventions, in addition to well-tested and effective psychosocial ones.

Classifications of Sexual Dysfunctions

There are several major classification systems of both male and female sexual dysfunction. One of the most common classifications is in the ICD-10: The International Classification of Diseases, 10th edition, which was published by the World Health Organization in 1992. The ICD-11 is expected to be published in 2017. The ICD codes disorders as either organic (physiologic) or non-organic (psychosomatic). Non-organic disorders may be intermittent and occur on a case-by-case basis. For example, a male who complains of erectile dysfunction (ED) but has a normal morning erection has a non-organic rather than organic cause of ED since there is no physiologic dysfunction. Non-organic disorders are those such as sexual aversion, sexual desire disorder, non-organic vaginismus, non-organic dyspareunia, and excessive sexual drive. Organic disorders have a physiological/somatic basis and include ED, vaginismus, and dyspareunia.

Another widely known system of classification for sexual dysfunction is the DSM-5: The Diagnostic and Statistical Manual of Mental Disorders (5th edition). The DSM has been widely used by the American Psychiatric Association to classify sexual disorders as well as other types of psychological conditions. The most recent edition has been published in May 2013 and contains several important changes including the criterion that nearly all sexual dysfunction diagnoses now require a minimum duration of 6 months as well as a frequency of 75–100% of the time. Additionally, many disorders are now listed as gender specific, and several of the female disorders are consolidated into single diagnoses. Additionally, a new group of criteria called "associated features" is introduced, dividing potential contributing factors of sexual dysfunction into five categories: (1) partner factors, (2) relationship factors, (3) individual vulnerability factors, (4) cultural factors, and (5) medical factors. Several disorders are deleted from the DSM such as male dyspareunia or sexual aversion disorder. Duration and frequency requirements are implemented to increase the validity and clinical usefulness of the manual to the psychiatric community [6].

Women and Sexual Medicine

In women, the most common cause of sexual dysfunction is vaginal dryness or failure of lubrication. Approximately 8–28% of sexually active women report lubrication difficulties, which can be attributed to pathologic/organic causes, psychogenic/non-organic causes, or estrogen deficiency [8].

Women's sexual function is a complex neuromuscular process. Along with hormonal changes, arousal is marked by blood volume and pressure changes in the clitoris and labia (Figures. 1.13 and 1.14). Irregularities in various psychological, hormonal, physiological, and environmental factors can account for female sexual dysfunction in a number of ways. Female sexual dysfunction can be characterized by sexual pain disorders, desire/arousal disorders, and orgasmic disorders [9].

The DSM-5 has eliminated and condensed the diagnoses of female sexual dysfunction from five disorders of desire, arousal, orgasm, vaginismus, and dyspareunia to three disorders [10]. Female hypoactive desire disorder is combined with arousal disorder to form female sexual interest/arousal disorder. This diagnosis is even less contingent upon physical stimuli and is characterized by persistent deficiency of sexual thoughts or desire for sexual activity [6]. Orgasmic disorder has remained unchanged. Vaginismus and dyspareunia are merged into genito-pelvic pain/penetration

FIGURE 1-2. Turin erotic papyrus (damaged) [Reprinted from: https://commons.wikimedia.org/wiki/File:Turin_Erotic_Papyrus.jpg].

FIGURE 1-3. Kama Sutra [Reprinted from: https://commons.wikimedia.org/wiki/File:Mukteswar_temple.jpg with permission from Creative Commons].

disorder, as it has been decided that the two disorders could not be reliably differentiated due to the lack of empirical evidence of vaginal muscle spasm and the overlap of fear of penetration [6].

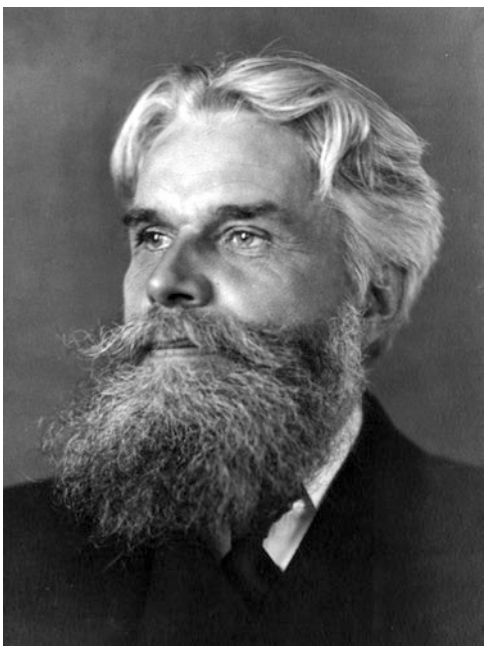


FIGURE 1-4. Havelock Ellis [Reprinted from: https://commons.wikimedia.org/wiki/File:Havelock_Ellis_cph.3b08675.jpg].

There is epidemiological data indicating that 40–45% of women have at least one form of sexual dysfunction. The prevalence of women expressing low levels of sexual interest increases with age, with about 10% of women up to age 49, 22% of those ages 50–65, and 74% of 66–74-year-olds expressing low levels of desire [11].

Such dysfunctions may be a lifelong problem or acquired later in life. Risk factors for decreased lubricative function,

FIGURE 1-5. Richard von Krafft-Ebing [Reprinted from: https://en.wikipedia.org/wiki/Richard_von_Krafft-Ebing#/media/File:Richard_v._Krafft-Ebing.jpg].

anorgasmia, and other sexual disorders include but are not limited to age, sociocultural factors, alcohol use, prescription and non-prescription drug usage. Other factors that increase the risk of sexual dysfunction include medical conditions such as hypertension, certain hormone imbalances, urinary incontinence, cardiovascular disease, diabetes mellitus, and depression [11].

Female sexual interest/arousal disorder is described as significantly reduced interest in sexual activity, reduced or absent erotic thoughts, or reduced initiation or receptivity to sexual activity. As many as 75–100% of these women may experience diminished pleasure during sexual encounters, absent/reduced sexual arousal in response to internal or external cues, and reduced genital sensations during 75–100% of sexual encounters. Different cases have reported various duration of symptoms. Older women generally report less distress about low sexual desire than younger women, as sexual desire also decreases with age [11].

Female orgasmic disorder constitutes a marked delay, infrequency, or absence of orgasm, or it can be defined as a reduced intensity of orgasmic sensations. Orgasmic disorder must be accompanied by clinically significant distress and cannot be justified by significant interpersonal or contextual factors. Approximately 10% of women do not experience orgasm throughout their lifetime. Reported prevalence rates for female orgasmic disorder range widely from 10 to 42%, though only a small proportion of women also report associated distress [10].

Genito-pelvic pain/penetration disorder is defined as at least 6 months of persistent or recurrent difficulties with vaginal penetration; vulvovaginal or pelvic pain during intercourse attempts; fear or anxiety about vulvovaginal or pain before, during, or after vaginal penetration; or marked tensing of the pelvic floor muscles during attempted vaginal penetration. The disorder can range from complete inability to experience vaginal penetration to situational inability to experience penetration. Inadequate sexual education and/or religious rigidity have been common predisposing factors of genito-pelvic pain/penetration disorder. Many women with this diagnosis are also diagnosed with a comorbid condition such as endometriosis, pelvic inflammatory disease, lichen sclerosis, or vulvovaginal atrophy. There are no tools or diagnostic methods that can determine if the penetration disorder is primary or secondary [10]. However, comorbidity with other diagnoses is high, as well as with relationship distress. Often amending factors within the relationship such as increasing foreplay or addressing sexual dysfunction of a male partner may ameliorate a women's fear of and pain during penetration [10].

Men and Sexual Medicine

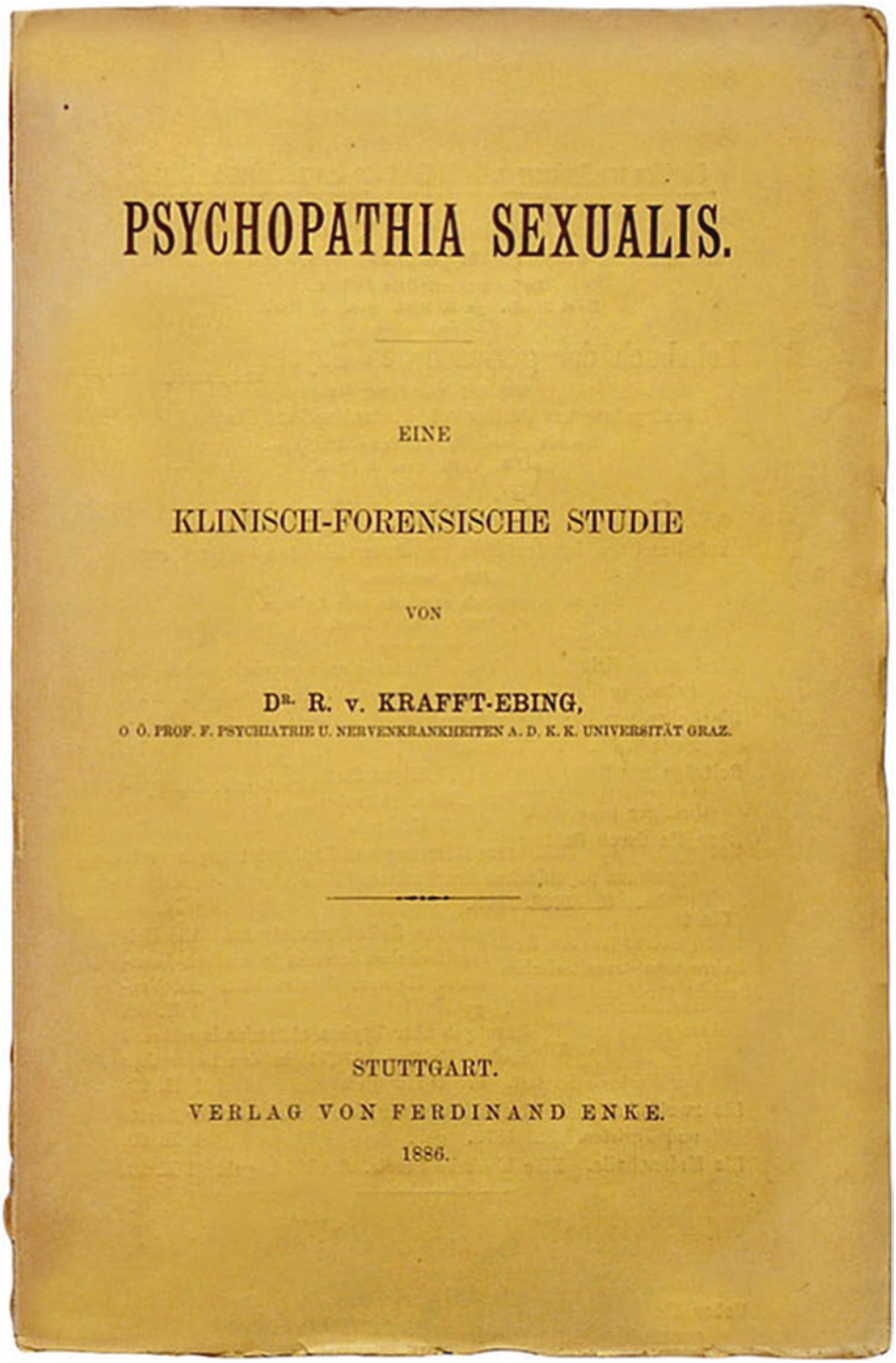
The penis, the primary organ responsible for male sexual function and reproduction, is composed of two functional compartments: the corpus cavernosum and the corpus spongiosum (Figures 1.15 and 1.16).

It is innervated by somatic and autonomic nerve fibers that provide the penis with sensory fibers and supply the perineal skeletal muscles with motor fibers. This autonomic innervation is both parasympathetic and sympathetic.

Norepinephrine is responsible for the regulation of the corpus cavernosum smooth muscle tone via the alpha-1 and alpha-2 adrenergic receptors. Other substances involved with the smooth muscle tone of the corpus cavernosum include endothelin-1, PGF-2a, thromboxane A-2, angiotensin II, and calcium [12]. The penis functions as part of the peripheral nervous system and is constantly modulated by sex steroid hormones as well as gonadal, adrenal, and neuroactive steroids that regulate the epithelium and vasculature.

Nitric oxide is believed to be the main vasoactive non-noradrenergic, non-cholinergic (NANC) neurotransmitter of erectile action. Penile nitric oxide synthase is fundamental to the cellular signaling of vascular tone in the corpus cavernosum, which is necessary to obtain an erection. NOS protein content showed a 55% decrease in castrated animals, proving its vital role in the physiological response to male sexual arousal and function [13].

Louis Ignarro's identification in 1997 of nitric oxide as the principal neurotransmitter responsible for the action of the smooth muscles of the corpus cavernosum enabled the development of oral pharmacological agents for erectile


PSYCHOPATHIA SEXUALIS.

EINE

KLINISCH-FORENSISCHE STUDIE

VON

Dr. R. v. KRAFFT-EBING,

O. Ö. PROF. F. PSYCHIATRIE U. NERVENKRANKHEITEN A. D. K. K. UNIVERSITÄT GRAZ.

STUTTGART.

VERLAG VON FERDINAND ENKE.

1886.

FIGURE 1-6. Krafft-Ebing's book [Reprinted from: https://en.wikipedia.org/wiki/Richard_von_Krafft-Ebing#/media/File:Krafft-Ebing_Psychopathia_sexualis_1886.jpg with permission from © Foto H.-P. Haack (H.-P. Haack)].

dysfunction [14]. Sildenafil (Viagra) was the accidental result of an experiment to find a treatment that would lower blood pressure in patients with angina in 1996. In 2008, sales of sildenafil had reached 1.5 billion dollars annually, with nine pills being dispensed every second. The further development of new drugs for both male and female sexual dysfunction is currently underway.

For men, sexual dysfunction includes male hypoactive sexual desire disorder, erectile disorder, premature ejaculation, and delayed ejaculation. Epidemiological data from the

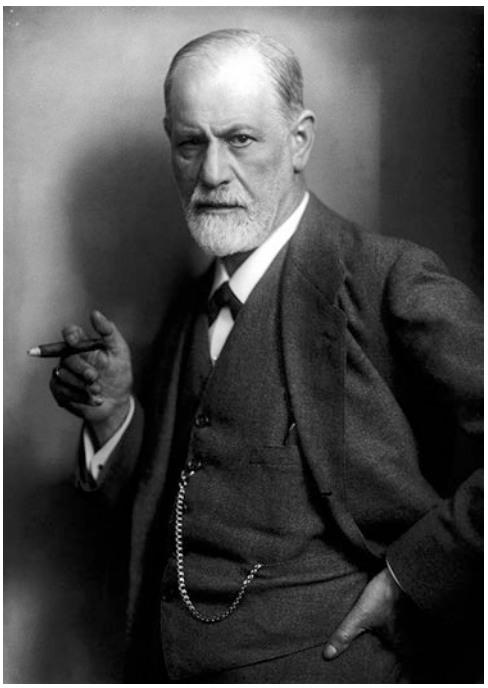


FIGURE 1-7. Sigmund Freud [Reprinted from: https://commons.wikimedia.org/wiki/File:Sigmund_Freud_LIFE.jpg].

FIGURE 1-8. Magnus Hirschfeld [Reprinted from: https://wellcomeimages.org/indexplus/email/299273.html with permission from Creative Commons].

National Health and Social Life Survey indicate that 15% of all men experience low sexual desire, 31% of men between the ages of 18 and 59 years have significant sexual concerns or problems, and that one-third of men struggle with premature ejaculation [15]. According to the Florey Adelaide Male Ageing Study in Australia, 31.7% of men between the ages of 35 and 80 who were normal at baseline developed ED at a 5-year follow-up [16].

FIGURE 1-9. Alfred Kinsey [Reprinted from: https://commons.wikimedia.org/wiki/File:Alfred_Kinsey_1955.jpg].

Potential risk factors for male sexual dysfunction, primarily erectile disorder (ED), include age, obesity, metabolic syndrome, insulin-dependent diabetes mellitus, cardiovascular disease, hypertension, tobacco use, hyperprolactinemia, abnormal dehydroepiandrosterone sulfate levels, urinary tract diseases, surgery, trauma, spinal cord injury, endothelial dysfunction, other chronic diseases, as well as psychological and psychiatric factors [15].

The DSM-5 describes male hypoactive sexual desire disorder (HSDD) as persistently or recurrently deficient (or absent) sexual/erotic thoughts or fantasies and desire for sexual activity. The clinician should also take outside factors into account when diagnosing HSDD such as age, relationship status, medical record, and other sociocultural contexts of the patient's life. HSDD may be lifelong, acquired, generalized, situational, mild, moderate, or severe. Some associated features supporting the diagnosis of HSDD are erectile and/or ejaculatory concerns, as persistent difficulties with erection may cause a loss of interest in sexual activity for many men. Relationship-specific preferences should also be taken into account. For example, men are generally more likely to initiate sexual activity, though many men prefer their partner to initiate. In this case, their diagnosis would be dependent upon their lack of receptivity rather than their hesitance or failure to initiate sexual acts. Relationship status should also be taken into account in accordance with one's emotional and psychosocial attitude towards new sexual partners. The development and course of this disorder is contingent on the mere fact that the potency of sexual cues is known to decrease with age. Endocrine disorders such as

FIGURE 1-10. Ronald Virag [Reprinted from: https://commons.wikimedia.org/wiki/File:Dr._Ronald_Virag,_working.jpg with permission from Creative Commons].

FIGURE 1-11. Giles Brindley [Reprinted from Goldstein, I.R.W.I.N., The Hour Lecture That Changed Sexual Medicine—The Giles Brindley Injection Story. Journal of Sexual Medicine 2012; 9(2): 337-342. with permission from Elsevier].

hyperprolactinemia (elevated levels of the protein prolactin) have been found to act as a significant risk factor for low levels of desire in males. Studies have also found higher prevalence of HSDD in hypogonadal men as well as a speculated critical threshold below which testosterone will affect sexual desire in men.

Erectile disorder can be defined as difficulty obtaining or maintaining an erection during sexual activity or a marked decrease in erectile rigidity. Symptoms must persist for a minimum of 6 months and, like most other disorders in the DSM, must cause clinically significant distress and not be explained by any other medical condition or substance. Many men with ED also suffer from low self-esteem and self-confidence, depressed affect, and a decreased sense of masculinity. As mentioned earlier, etiology, diagnosis, and potential treatments are dependent on the following five factors: (1) partner, (2) relationship, (3) individual vulnerability, (4) culture/religion, and (5) medical factors relevant to prognosis or treatment [10].

The DSM-5 classifies premature or early ejaculation as a persistent or recurrent pattern of ejaculation occurring during partnered sexual activity within approximately 1 min following vaginal penetration and before the individual wishes it on 75–100% of events of partnered activity. Symptoms must be present for at least 6 months and must cause clinically significant distress in the individual. The level of severity is established using the duration from vaginal penetration to ejaculation (severe = within 15 s, moderate = 15–30 s, and mild = 30–60 s).

The DSM-5 classifies delayed ejaculation as marked delay or infrequency/absence in ejaculation on 75–100% of events of partnered activity. Symptoms must be present for at

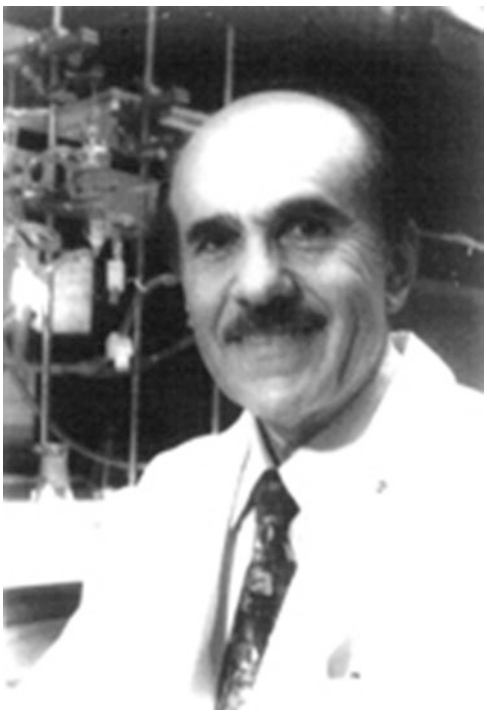


Figure 1-12. Louis Ignarro, Ph.D. [Reprinted from: https://sv.wikipedia.org/wiki/Fil:Louis_J._Ignarro_portrait.jpg].

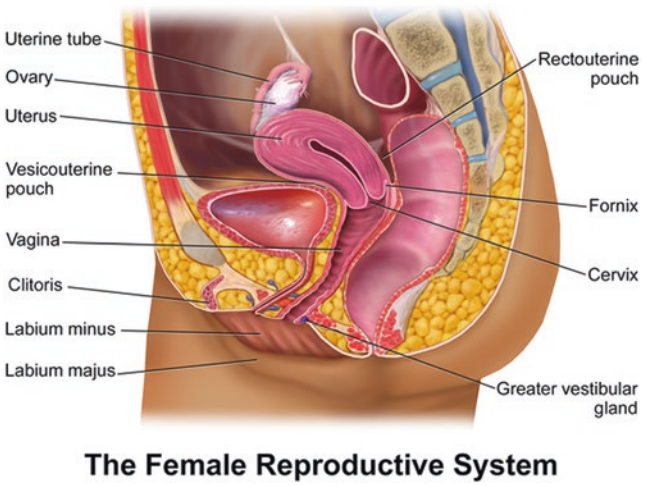


Figure 1-13. Female sexual and reproductive organs [Reprinted from https://commons.wikimedia.org/wiki/File:Blausen_0400_FemaleReproSystem_02.png with permission from Creative Commons].

least 6 months and must cause clinically significant distress in the individual. It is essential that the sexual dysfunction cannot be the result of a nonsexual mental disorder or other stressor or substance. Delayed ejaculation is specified as lifelong or acquired, generalized or situational, and mild or severe.

Treatments in Sexual Medicine

Treatment for sexual dysfunction may vary depending on the nature of the dysfunction, the patient, the desired outcome, and the physician. Some of the most commonly used pharmaceutical treatments are phosphodiesterase type 5 (PDE5) inhibitors. PDE5 inhibitors are primarily used to treat erectile disorder. They function by blocking the degradation of cyclic GMP in the smooth muscle cells of the blood vessels of the corpus cavernosum by cGMP-specific PDE5. Examples of common PDE5 inhibitor drugs are sildenafil (Viagra), tadalafil (Cialis), and vardenafil (Levitra).

Addressing biopsychosocial factors in behavioral therapy can also be a means of treating sexual dysfunction. Althof and Needle showed that "medical treatments are directed narrowly at a specific sexual dysfunction and fail to address the larger biopsychosocial issues" [17].

Sex therapy is a common strategy in treating sexual dysfunction. This consists of a form of psychotherapy administered by social workers, therapists, or physicians certified by the American Association of Sex Educators, Counselors and Therapists (AASECT). It is important to take into account the impact that mood disorders such as anxiety and depression can have on sexual functioning. In fact, mood and sexual disorders are often comorbid and share many of the same causes. Sex therapy has, in recent years, become an increasingly large part of treatment programs targeting sexual dysfunction. One form of treatment is an adaptation of the Masters and Johnson behavior modification style of therapy. It incorporates a masturbation desensitization program developed by LoPiccolo and Lobitz [11]. Many sex therapists suggest the use of sex toys, especially by women, in cases of sexual dysfunction in relationships. It is vital to focus mainly on the couple to improve sexual functioning and subsequent quality of life [14].

The Permission, Limited Information, Specific Suggestions, and Intensive Therapy (PLISSIT) model of sex therapy was introduced by American Psychologist Jack Annon in 1976. It provides a framework for therapists to intervene and treat patients for sexual dysfunction. Often times sexual problems are caused or worsened by guilt or anxiety about one's actions. This first step of the model merely gives the patient professional permission to do what he/she is doing (e.g., masturbation) in order to alleviate this unnecessary anguish. LI stands for limited information and means ensuring patients have sufficient anatomical and physiological information and expectations of themselves. The next step is SS, or specific suggestions, and includes many of the exercises of mutual pleasuring recommended by Masters and Johnson such as sensate focus and stop start. IT is the last step and is intensive therapy. It requires a long-term intervention to address complex underlying issues on an individual as well as partner level. [18]

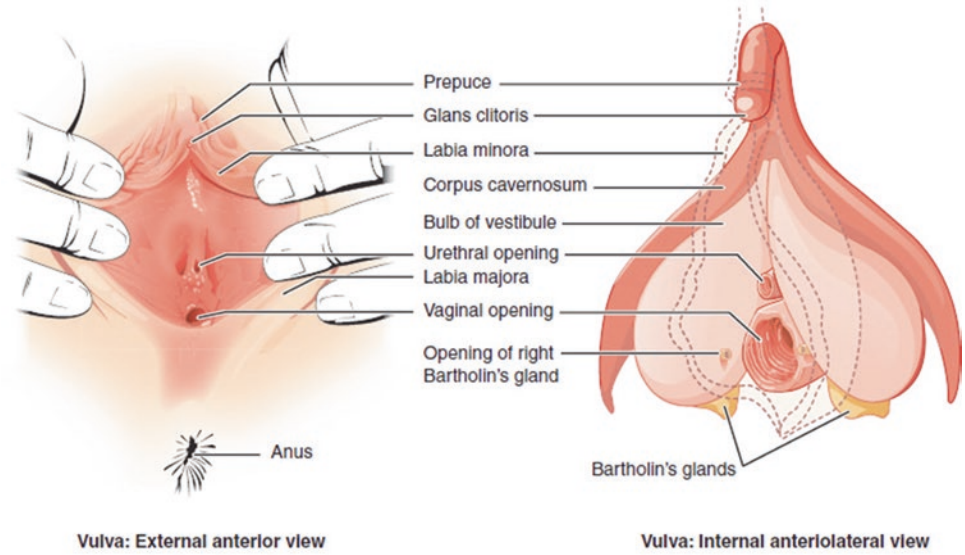


FIGURE 1-14. External female sexual organs [Reprinted from: https://commons.wikimedia.org/wiki/File:Figure_28_02_02.jpg with permission from Creative Commons].

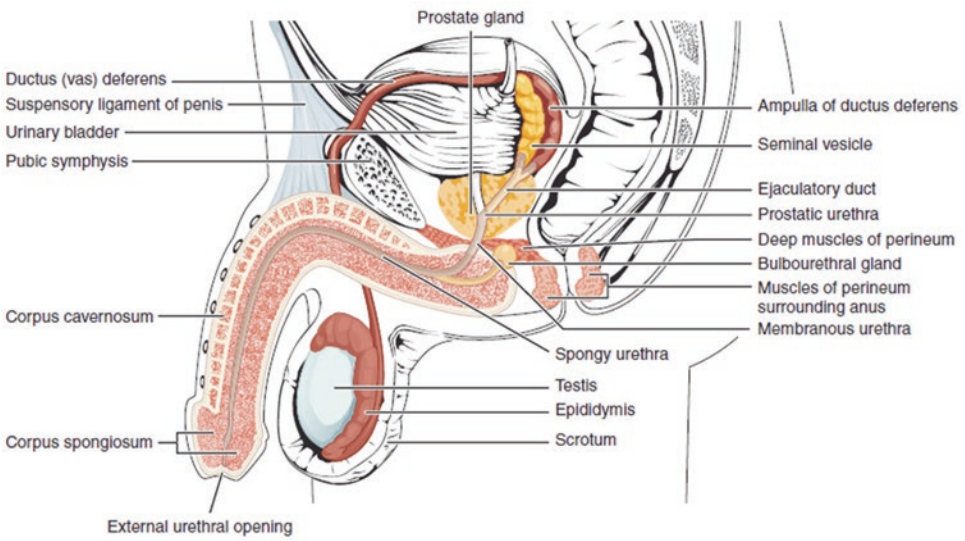


FIGURE 1-15. Male sexual and reproductive organs [Reprinted from: https://commons.wikimedia.org/wiki/File:Penis_lateral_cross_section.jpg with permission from Creative Commons].

The question remains unanswered as to what constitutes success for sex therapy as it is a lengthy process and outcomes vary on a case-by-case basis. Treatment can be extensive and must take into account the needs, flaws, and limitations of a sexual partner. A key step in treatment is the realization of "good-enough sex," or sex that realistically acknowledges that performance is variable and is vulnerable to both one's own and partner's current emotional and physical state [19]. Sex therapy is not focused on the frequency of sexual contact or changes in ejaculatory latency or coital orgasms, but rather emphasizes the patient's own report of enhanced sexual confidence, pleasure, or intimacy [19]. It is impossible to separate mind from body and it is paramount to recognize in treating sexual dysfunctions that these problems are most often a combination of physical and psychological factors. Therefore we must acknowledge that treatment should integrate a fusion of psychological, interpersonal, and pharmacological interventions [20].

Treatment specifically geared towards female sexual dysfunction has included hormone therapies, such as estrogen therapy, androgen therapy, flibanserin (Addyi), and oxytocin. Potential treatments that are currently being investigated are a synthetic steroid called Tibolone, phosphodiesterase inhibitors, and sildenafil (Viagra) [21]. It is important to note that flibanserin aims to treat a problem that exists on a continuum, therefore making it difficult to establish a clear-cut diagnosis. For many people who consider themselves asexual, absence of or diminished desire is considered a sexual orientation rather than a dysfunction. In addition, female sexual dysfunction is much less inconspicuous than male dysfunction, where the absence of arousal or orgasm is physically observable. The female sexual response

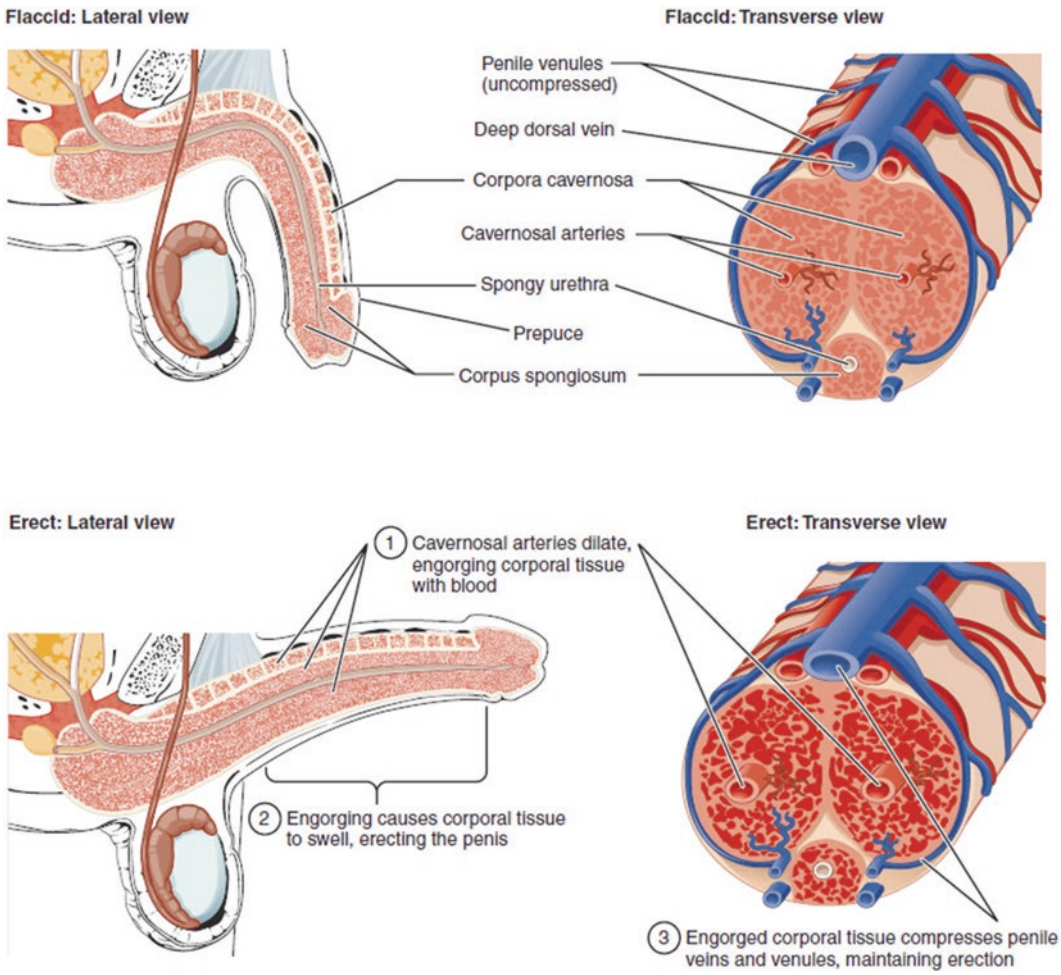


FIGURE 1-16. Penis, lateral view and cross section before and during erection [Reprinted from: https://pl.wikipedia.org/wiki/Zaburzenia_erekcji#/media/File:Figure_28_01_06.jpg. With permission from Creative Commons].

is not only more hidden but also more elusive and even taboo [22].

Estrogen and androgen hormonal therapy were both observed to have benefits on sexual function in females. One-fourth of menopausal women reported vulvovaginal atrophy and dyspareunia, symptoms which often lead to pain and decreased sexual interest, arousal, response. This then frequently leads to avoidance of sexual encounters [22]. The synthesis of estrogen within extragonadal compartments takes place during one's reproductive life as well as after menopause. Androgens are fundamental precursors in the biosynthesis of estrogens. Estrone sulfate is the most abundant estrogen in circulation in postmenopausal women at 10–24 times higher levels than estrone or estradiol. Estrone and estradiol are partly bound to sex hormone-binding globulin (SHBG) in their non-sulfate forms. Transdermal and oral estrogens increase sex hormone-binding globulin (SHBG) levels, and oral estrogen can lead to a clinically significant decrease in non-SHBG-bound sex steroids. Estradiol is most concentrated in the female brain in the hypothalamus and preoptic regions [23].

Topical estrogen therapy was reported by Santoro et al. to improve sexual function significantly in postmenopausal women with what was referred to by the DSM-IV as vulvovaginal atrophy (VVA) and dyspareunia. The topical treatment comes in various forms including creams, tablets, and rings. Vaginal topical estrogen treatment has been shown to improve vaginal lubrication and decrease dyspareunia [23].

Testosterone has also been demonstrated to have a role in treating sexual dysfunction in women. A testosterone patch has become a common treatment of hypoactive sexual desire disorder in surgically menopausal women with the intent to enhance female sexual motivation [23].

Oxytocin has been found in a large number of studies to have a positive impact on both the female and male sexual experience. Oxytocin is secreted by the pituitary gland during intimate physical contact, orgasm, and childbirth. It has been found to foster trust, cooperation, and openness, both in romantic relationships as well as in friendship and business. Oxytocin levels generally increase during arousal and peak during orgasm for both men and women. After an initial report of successful use of oxytocin in male anorgasmia, a 2014 study reported that oxytocin increased the intensity of orgasm and contentment after sexual intercourse [24]. The study administered intranasal oxytocin to 29 healthy heterosexual couples. Researchers then studied the acute effects on their sexual drive, arousal, orgasm, and refractory aspects of sexual behavior along with partner interactions. Biomarkers such as cortisol, alpha-amylase, and heart rate were monitored. Findings showed that while these effects were more pronounced in men, women also benefited from intranasal oxytocin doses. Women in the study reported feeling more relaxed in the context of their sexual experiences as well as an improved ability to share sexual desires or empathize with their partners. Intranasal oxytocin did not alter classical patterns of sexual function, but it did improve orgasmic and post-orgasmic sensation as well as partner interaction [25].

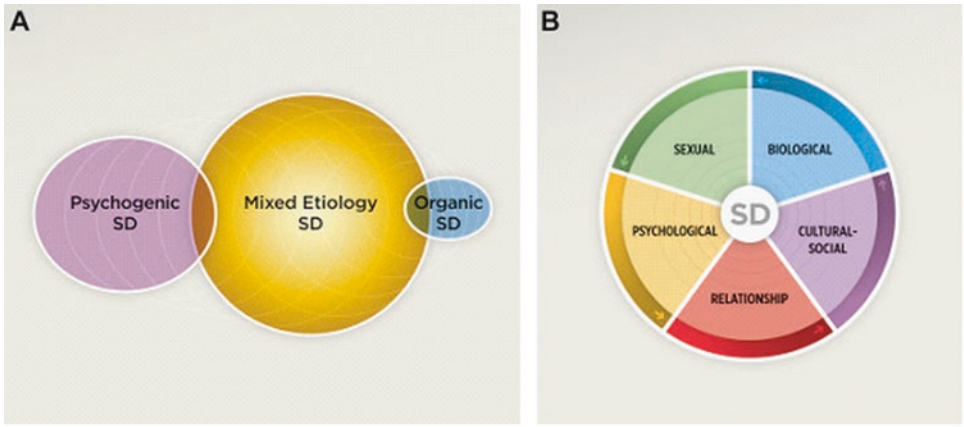
Several studies reveal that erection and orgasm in male rats are controlled by oxytocin as well as dopamine. For example, a study by Succu et al. shows that stimulation of dopamine receptors in the paraventricular nucleus of the hypothalamus of male rats induces penile erection and increases extracellular dopamine in the nucleus accumbens. More research is needed on effects of oxytocin and dopamine on female sexual function [26].

The FDA approved flibanserin (Addyi) in August 2015 to treat low sexual desire in premenopausal women. Flibanserin, colloquially known as the "female Viagra," is designed to treat female hypoactive sexual desire disorder. However, the two medications do not share a mechanism of action. While Viagra (sildenafil) acts by dilating blood vessels to increase blood flow, flibanserin raises levels of dopamine and norepinephrine while lowering levels of serotonin. This mechanism is thought to work because dopamine and norepinephrine are neurotransmitters involved with sexual excitement, but serotonin may contribute to sexual inhibition if these chemicals are out of balance. Flibanserin is generally prescribed to be taken once daily and the cost ranges anywhere from $400 to $800 per month [27].

Tibolone is a synthetic steroid used in Europe and Australia for treatment of postmenopausal osteoporosis. It mimics the activity of female sex hormones estrogen and progesterone and prevents dryness and soreness of the vaginal tissue. It has therefore been used to treat hypoactive sexual desire in menopausal women in other countries, but it is not approved by the FDA for use in the USA due to concerns of increased breast cancer risk [28].

Phosphodiesterase inhibitors are generally used to treat erectile disorder. These medications function by blocking the breakdown of cyclic guanosine monophosphate (cGMP) which results in vasodilation and prolongation of the mediators of blood flow such as nitric oxide. This means increased dilation of the veins, which allows for increased blood flow to the penis to obtain an erection. Phosphodiesterase inhibitors have been shown to elicit minor improvements in women with sexual dysfunction, though evidence is not strong enough to make generalized statements. PDE (phosphodiesterase) isoenzymes 4 (cAMP-PDE) and 5 (cGMP-PDE) were found in the human vagina. In addition, signals related to PDE10 and PDE11 were found in the epithelium and glandular-like structures [29]. Results indicated that PDE inhibitors could relax human vaginal tissue of the labia minora and increase levels of cGMP. This means that the pharmacological concept of PDE inhibition could be applicable to the treatment of symptoms of female sexual arousal disorder. PDE inhibitors have been used to treat erectile disorder since 1989, but the presence of cAMP-PDE type 4 and cGMP-PDE type 5 in vascular and nonvascular smooth muscle of the vaginal wall supports the hypothesis that the use of iso-enzyme-selective PDE inhibitors can lead to vaginal smooth muscle relaxation, thus improving hypoarousal. These findings also suggest a connection between the NO-cGMP pathway and control of the vaginal smooth muscle tone [30]. Ultimately this means that in addition to treating male erectile disorder, urinary incontinence, and lower urinary tract pathology, PDE-5 inhibitors may be a pharmacological treatment option for female arousal and orgasm disorders [27].

Sexual medicine is evolving, expanding, and advancing with recent strides in pharmacology, psychology, and relationship counseling. Recent changes in classification are changing the way we conceptualize and define sexual dysfunction. Combined with pharmaceutical advances, the available options for the management and treatment of sexual dysfunction continue to increase for both men and women. Evaluation of sexual dysfunction, however, begins with the understanding that the causes may be multifactorial (Figure 1.17). The biopsychosocial model ensures a comprehensive assessment of multiple factors (psychosocial, medical, and the effect of substances) (Figure 1.18) that can affect sexual functioning, so that the individual and/or the couple can benefit from different types of interventions, whether they are biological, psychosocial, or both [31].



Panel A shows the previously held, traditional view of SD as psychogenic, organic, or mixed. Panel B shows the alternative, current view of SD as a multifactorial problem, with interacting contributing factors. Arrows around the periphery are intended to illustrate the dynamic, interactive potential among the different factors shown. SD=sexual dysfunction.

FIGURE 1-17. Traditional and alternative views of the factors contributing to sexual dysfunction [Reprinted from Hatzichristou D, Kirana PS, Banner L, Althof SE, Lonnee-Hoffmann RA, Dennerstein L, Rosen RC. Diagnosing Sexual Dysfunction in Men and Women: Sexual History Taking and the Role of Symptom Scales and Questionnaires. J Sex Med. 2016;13(8):1166–82 with permission from Elsevier].

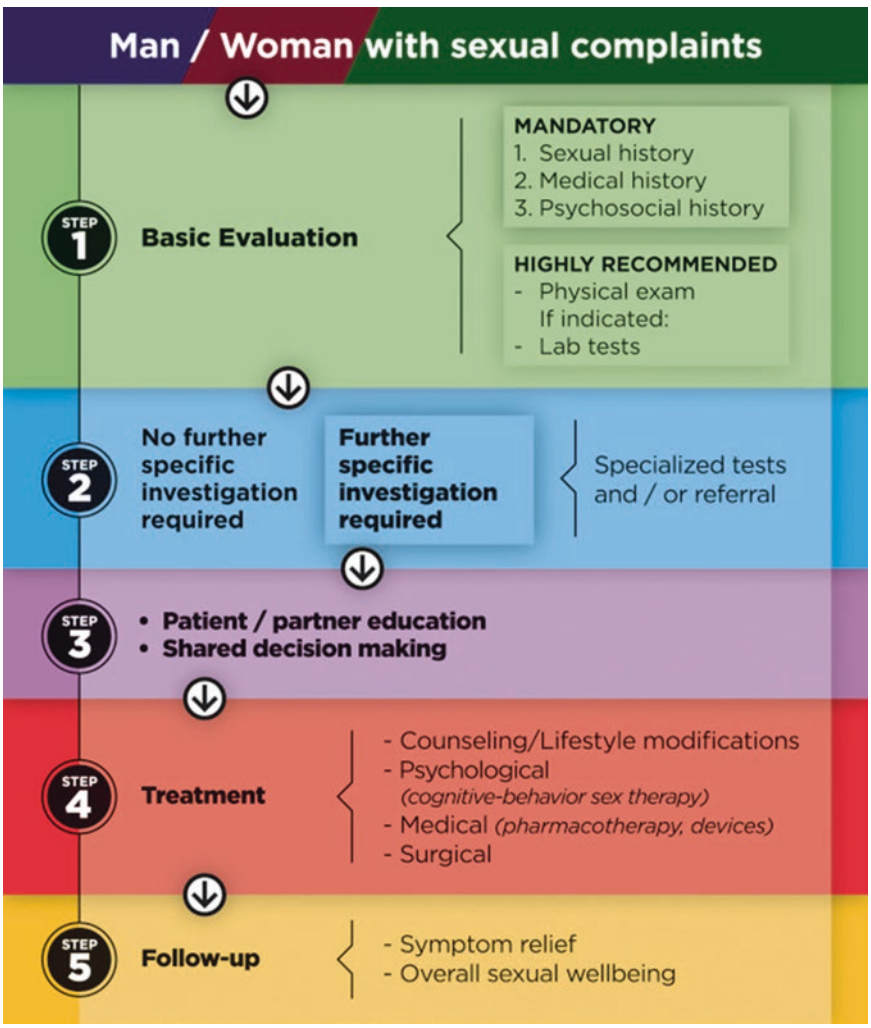


FIGURE 1-18. The revised international consultation on sexual medicine five-step algorithm for the management of sexual dysfunctions in men and women [Reprinted from Hatzichristou D, Kirana PS, Banner L, Althof SE, Lonnee-Hoffmann RA, Dennerstein L, Rosen RC. Diagnosing Sexual Dysfunction in Men and Women: Sexual History Taking and the Role of Symptom Scales and Questionnaires. J Sex Med. 2016;13(8):1166–82 with permission from Elsevier].

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