

Sexual Dysfunction in Multiple Myeloma: Survivorship Care Plan of the International Myeloma Foundation Nurse Leadership Board

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The World Health Organization describes sexuality as a “central aspect of being human throughout life and encompasses sex, gender identities and roles, sexual orientation, eroticism, pleasure, intimacy, and reproduction. Sexuality is influenced by the interaction of biological, psychological, social, economic, political, cultural, ethical, legal, historical, religious, and spiritual factors.” Currently, no research has been conducted regarding sexual dysfunction in patients with multiple myeloma; therefore, information related to the assessment and evaluation of sexual dysfunction is gleaned from other malignancies and diseases. In this article, members of the International Myeloma Foundation’s Nurse Leadership Board discuss the definition, presentation, and causes of sexual dysfunction; provide recommendations for sexual assessment practices; and promote discussion among patients with multiple myeloma, their healthcare providers, and their partners.

Sexual dysfunction is characterized by physiologic or psychological changes that have a negative impact on sexuality, leading to distress within relationships (Shabsigh & Rowland, 2007). Sexual dysfunction occurs when the “sexual response cycle—including desire, arousal, orgasm, and resolution—is disrupted” (Tierney, Facione, Padilla, Blume, & Dodd, 2007, p. 299). In one study among older adult patients, the most commonly reported sexual dysfunction among women was decreased sexual desire and vaginal dryness, whereas men commonly reported erectile dysfunction (Kagan, Holland, & Chalian, 2008). Sexual dysfunction has been reported to affect 43% of women and 31% of men in the United States (Ganz & Greendale, 2007). A review of the literature regarding sexual function in patients with cancer is limited primarily to patients diagnosed with prostate, breast, or gynecologic cancers. One study focused on women with hematologic malignancies prior to hematopoietic

At a Glance

- ◆ Sexual dysfunction is caused by multiple factors and affects men and women physically and psychologically, altering their relationships with their partners.
- ◆ Open and honest communication between patients and nurses, as well as patients and partners, is fundamental in identifying and treating the underlying issues.
- ◆ Evidence-based practice recommendations have been developed for promoting dialogue and assessment, education, and management practices among patients with multiple myeloma and their healthcare providers and partners.

cell transplantation and found that 73% of patients reported decreased libido and 48% were dissatisfied with their overall sex life (Tierney et al., 2007).

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Digital Object Identifier: 10.1188/11.CJON.S1.53-65

Sexual dysfunction occurs as a result of physical illness or psychological factors rather than part of the normal aging process (Clayton & Ramamurthy, 2008). Physical and emotional illnesses affect sexual function through a variety of mechanisms such as disease, therapeutic interventions, depression, physical or emotional trauma, or anatomic changes. Sexual dysfunction may be the presenting symptom in patients with a physical illness (e.g., cardiac disease) (Clayton & Ramamurthy, 2008).

To gain an understanding of sexual dysfunction, the normal sexual response cycle must first be understood. Historically, the sexual response cycle was described by Masters and Johnson (1960) to be a linear, four-stage model consisting of the excitement phase (arousal), plateau phase (full arousal, but orgasm not achieved), orgasm, and resolution phase (after orgasm). However, Basson (2001) developed a nonlinear approach to female sexual response that incorporates intimacy, interpersonal relationships, and stimuli (see Figure 1).

Sexual Dysfunction

According to the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (American Psychiatric Association, 2000), sexual dysfunction can be described as one of four main categories: sexual desire disorder (decreased libido), sexual arousal disorder, orgasm disorder, and sexual pain disorder (see Table 1). The hallmark feature of sexual dysfunction is that it causes the individual distress or relationship difficulties (Shabsigh & Rowland, 2007).

The etiology of sexual dysfunction has been described as primary, secondary, or tertiary. Sexual dysfunction that occurs from a direct illness is considered primary. Secondary dysfunction occurs as a result of a symptom of an illness, such as fatigue, incontinence, weakness, or overactive bladder. Sexual dysfunction from emotional and psychological factors (e.g., depression, fears, body image), is considered tertiary (Clayton & Ramamurthy, 2008).

Primary Causes

Physical illnesses—including endocrine abnormalities, cardiovascular disease, pelvic disease, cancer, renal insufficiency, and treatment-related side effects (pain, medications, chemotherapy, or radiation)—may affect sexual functioning. In addition, treatment of these illnesses or their associated complications, particularly pharmacologic interventions, may worsen symptoms (Clayton & Ramamurthy, 2008).

The median age of patients with myeloma is about age 70, which may further increase the likelihood of sexual dysfunction because of the presence of other comorbidities and hormonal changes. In addition, patients undergoing treatment for myeloma may experience an exacerbation of preexisting comorbidities (diabetes, hypertension, or anemia) or develop them as a consequence of treatment (steroid-induced diabetes or hypertension, stem cell transplantation, or associated endocrine disorders) (Faiman, Bilotti, Mangan, Rogers, & the International Myeloma Foundation [IMF] Nurse Leadership Board [NLB], 2008; Miceli, Colson, Gavino, Lilleby, & the IMF NLB, 2008; Tariman, Love, McCullagh, Sandifer, & the IMF NLB, 2008; Tauchmanová et al., 2005).

Comorbidities

Sexual dysfunction may result from endocrine abnormalities such as diabetes, androgen deficiency, thyroid disorders, or estrogen deficiency (Clayton & Ramamurthy, 2008; Faiman et al., 2008). These conditions may arise from a variety of factors, including disease complications and treatment-related toxicities. In particular, therapy for myeloma places individuals at increased risk for endocrine changes because of treatment with steroids (androgen deficiency and diabetes), thalidomide (thyroid disorders), lenalidomide (thyroid disorders), or stem cell transplantation (estrogen and androgen deficiency) (Faiman et al., 2008). Sexual function also may be affected by other comorbidities such as cardiovascular disease and renal disease.

Diabetes

Some form of sexual dysfunction related to diabetes has been reported in about 75% of men and about 61% of women (Bhasin, Enzlin, Coviello, & Basson, 2007). Factors affecting diabetic sexual dysfunction include suboptimal glycemic control, fatigue, altered body image, and end organ damage. Erectile dysfunction from diabetes occurs as a result of dysfunction of the endothelial and smooth muscle (reduced nitric oxide synthase), as well as autonomic neuropathy (pelvic neuropathy) (Clayton & Ramamurthy, 2008). Interestingly, men suffering from erectile dysfunction and diabetes are more susceptible to developing other diabetic complications such as retinopathy, hypertension, and microalbuminuria

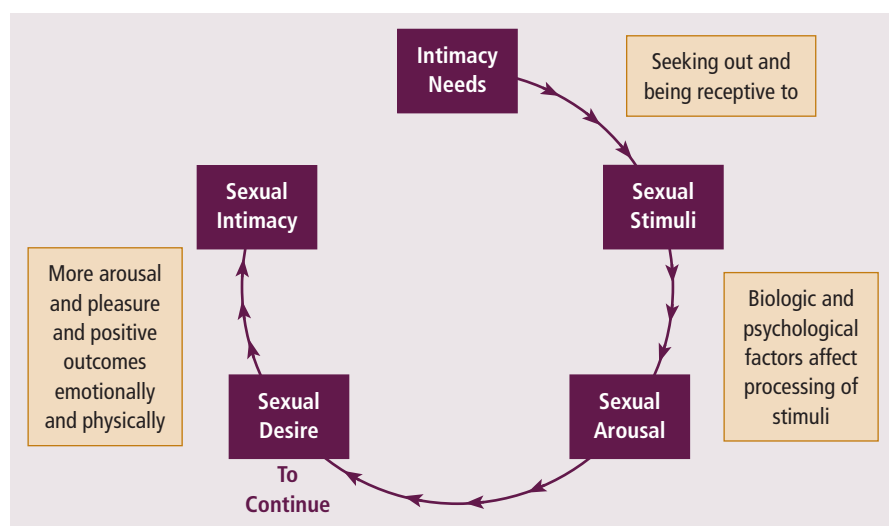


Figure 1. Basson's Nonlinear Approach to Female Sexual Response

Note. From "Using a Different Model for Female Sexual Response to Address Women's Problematic Low Sexual Desire," by R. Basson, 2001, *Journal of Sex and Marital Therapy*, 27, p. 396. Copyright 2001 by Taylor and Francis Group. Reprinted with permission.

Table 1. Sexual Dysfunction Definitions

DYSFUNCTION AND CLASSIFICATION	DEFINITION
Sexual desire disorder	
Hypoactive sexual desire disorder	Absence of sexual fantasies or thoughts, desire, or receptivity to sexual activity. Depression, weakness, pain, or low body image may impact arousal.
Sexual aversion disorder	Avoidance of sexual contact with a partner. Individuals may go to great lengths to avoid sexual encounters, including self-neglect, travel, or going to bed early.
Sexual arousal disorder	
Arousal disorders (women)	Inability to attain or maintain adequate lubrication or swelling response during sexual activity.
Male erectile disorder	Episodic or continuous inability to obtain and/or maintain an erection during sexual activity. Erectile dysfunction includes inability to obtain from onset, during penetration, or before or during thrusting.
Orgasm disorder	Episodic, continuous, or complete absence of orgasm following excitement phase. Body image, self-esteem, and relationship satisfaction may affect the ability to obtain orgasm in women.
Sexual pain disorder	
Dyspareunia	Recurrent genital pain that occurs during penetration or penile thrusting.
Vaginismus	Involuntary painful perineal muscle contraction that occurs with vaginal penetrations. Infertility, sexual abuse, or trauma may be associated with this condition.

Note. Based on information from American Psychiatric Association, 2000.

(Bhasin et al., 2007). Research regarding sexual dysfunction among women with diabetes is limited, but women report difficulties with desire, arousal, orgasm, lubrication, and dyspareunia (Bhasin et al., 2007; Clayton & Ramamurthy, 2008).

Hormonal

The exact mechanism of testosterone regulation in sexual dysfunction is not clearly understood in either gender. However, reduced sexual activity and decreased libido is found in both women and men. Androgen deficiency results as testosterone levels decrease in men by 1%–2% annually (Clayton & Ramamurthy, 2008). The most common causes of androgen deficiency are categorized into primary testicular failure (radiation, chemotherapy, surgery, or trauma) or secondary gonadal failure (excess drug and alcohol use, systemic illness, glucocorticoid therapy, or deficiency of luteinizing hormone [LH], follicle-stimulating hormone [FSH], or gonadotropin-releasing hormone). In women, testosterone levels fall progressively from their 20s until they plateau in their mid-40s. Currently, women do not have standard normal ranges because they vary with the menstrual cycle. Risk factors for developing low testosterone levels in women include bilateral oophorectomy, chronic obstructive pulmonary disease (COPD),

panhypopituitarism, and oral contraceptives (Clayton & Ramamurthy, 2008; Davis & Tran, 2001). In both men and women, autologous stem cell transplantation may decrease testosterone levels and induce menopause in women (Chatterjee et al., 2000; Tauchmanová et al., 2005; Tierney et al., 2007).

Estrogen deficiency may occur as a result of natural menopause, premature ovarian failure, or bilateral oophorectomy (Nappi & Lachowsky, 2009; Tierney et al., 2007). Decreased estrogen levels may lead to decreased libido, decreased vaginal lubrication, and dyspareunia (Nappi & Lachowsky, 2009).

Thyroid

Hypothyroidism or hyperthyroidism may affect sexual function in men and women in a variety of mechanisms, including decreased desire, erectile dysfunction, menstrual irregularities, and in some cases, infertility (Bhasin et al., 2007). In addition, men and women with hypothyroidism may develop fatigue or depression, leading to sexual dysfunction (Bhasin et al., 2007). Patients with multiple myeloma who develop hypothyroidism while undergoing treatment with thalidomide or lenalidomide have been reported in the literature (de Savary, Lee, & Vaidya, 2004; Menon, Habermann, & Witzig, 2007). Therefore, patients receiving these drugs who develop sexual dysfunction alone or in combination with other symptoms of hypothyroidism such as dry skin, hair loss, fatigue, and weight gain should be evaluated for this disorder (Bhasin et al., 2007).

Cardiovascular Disease

Cardiovascular disease, including hypertension, atherosclerosis, vascular disease, or a cerebral vascular event, have systemic effects that include sexual dysfunction (Reffellmann & Kloner, 2006). In particular, men with erectile dysfunction have an increased incidence of cardiovascular events (Reffellmann & Kloner, 2006). The risk of cardiovascular events among women who have cardiovascular disease is unknown. One study conducted among postmenopausal women showed a greater incidence of decreased sexual satisfaction among women with peripheral vascular disease; however, an increased risk of cardiovascular events was not noted (Lane & Thayer, 2008; McCall-Hosenfeld et al., 2008).

The prevalence of self-reported sexual dysfunction among patients with hypertension ranges from 14%–35% (Manolis & Doumas, 2008). In comparison, self-reported sexual dysfunction in nonhypertensive men ranges from 15%–74%, possibly reflecting differences in the study populations and data collection methods (Manolis & Doumas, 2008). Although no large studies have been conducted among women, one study did report that 42% of hypertensive women versus 19% ($p < 0.001$) of nonhypertensive women reported sexual dysfunction (Doumas et al., 2006). Factors correlating with sexual dysfunction include increased systolic blood pressure, increasing age, and beta blockers (Doumas et al., 2006).

Although patients with hypertension should receive anti-hypertensives, clinicians should be aware that beta blockers and thiazide diuretics may worsen erectile dysfunction and decrease libido, whereas angiotensin receptor blockers may reduce the incidence of erectile dysfunction. Calcium channel blockers and ACE inhibitors are thought to have little effect on erectile dysfunction; however, additional studies are needed to evaluate their effect on sexual dysfunction (Manolis &

Clinician Tear-Out Tool Long-Term Survivor Sexual Function

This communication tool is designed to help healthcare providers assess sexual function in patients with multiple myeloma or other cancers. The tool specifically demonstrates when, during either the review of symptoms or physical examination, to engage in conversation regarding sexuality, as well as examples of questions to facilitate discussion.

Discussion regarding sexual function:

- Time points: key moments to discuss sexual dysfunction
- Symptoms of myeloma
 - Review of systems: how symptoms of myeloma may affect sexual function (e.g., anemia, bone disease, pain)
- Toxicity effects
 - Effects of treatment on sexual function (e.g., neutropenia, thrombocytopenia, peripheral neuropathy)
- Physical examination
 - Inquire if patients are having difficulty with sexual function
- Fatigue management

Questions to ask your patient regarding sexual dysfunction:

These questions facilitate opening the dialogue between patients and healthcare providers and providing information necessary in assessing for sexual dysfunction.

1. Do you have any questions about sexuality or sexual function?
2. Are you satisfied with your sexual response?
3. Is your level of sexual activity normal for you?
4. How has your myeloma diagnosis or treatment affected your view of yourself?
5. Have you talked to your sexual partner about your feelings?
6. Are there any additional questions or concerns related to your sexual function you would like to discuss?

Important points

- Include the above questions and physical examination in your patient assessment.
- No norm exists for sexual function, and one does not have to engage in sexual activity to be classified as normal.
- Remember it is only a dysfunction if it causes the patient distress.

Note: This clinician education tool may be reproduced for noncommercial use.

Doumas, 2008). Patients with myeloma receiving treatment with either dexamethasone or prednisone are at increased risk of developing hypertension and require close monitoring of their blood pressure during treatment (Faiman et al., 2008). Patients should be encouraged to make lifestyle changes (e.g., exercise, low-sodium diet, weight loss) to reduce the need for treatment with antihypertensives and, thereby, improve overall sexual function (Faiman et al., 2008).

Renal Disease

Women with end-stage renal disease may develop alterations in hormone levels (FSH and LH) that lead to ovarian dysfunction, particularly in patients receiving dialysis (Anantharaman & Schmidt, 2007). Men with renal disease develop decreased levels of testosterone, both free and total, because of alterations in LH, FSH, and elevated estrogen levels. In men and women, increased levels of prolactin from decreased creatinine clearance have been noted (Anantharaman & Schmidt, 2007).

Women with chronic kidney disease tend to report difficulties with decreased libido, inability to achieve orgasm, vaginal dryness, and dyspareunia (Anantharaman & Schmidt, 2007). Men with kidney disease report diminished libido, erectile dysfunction,

infertility, and oligospermia related to low levels of testosterone. In addition, renal insufficiency decreases production of erythropoietin leading to anemia, which decreases oxygenation to tissues and may hinder sexual function. In men and women, erythropoietin has been shown to increase sexual function through normalization of FSH, LH, prolactin, and testosterone levels (Anantharaman & Schmidt, 2007).

The primary effects of disease on sexual dysfunction vary in the degree and the type of dysfunction in both sexes. Nurses play a critical role in understanding how diseases and treatments affect sexuality and sexual function. In patients with myeloma, treatments may precipitate diseases such as diabetes, hypertension, and anemia. In addition, myeloma may impact renal function, mobility, and pain related to bone disease or neuropathy. Identifying these factors is an important step in the identification and treatment of sexual dysfunction.

Secondary Effects

Patients receiving treatment may experience disruptions in the sexual response as a result of fatigue, weakness, pain, and alterations in body image (Clayton & Ramamurthy, 2008). Many treatment regimens include steroids, which may cause fatigue, proximal muscle weakness, weight gain, fluid retention, and decreased concentration (Faiman et al., 2008). Sixty-three percent of patients newly diagnosed with multiple myeloma present with compression fractures, resulting in pain and diminished mobility, which may inhibit sexual function (Kyle & Rajkumar, 2009).

As previously mentioned, multiple myeloma generally occurs in later stages of life. Lower urinary tract symptoms occur in about 63% of men and 67% of women; these include urinary incontinence, overactive bladder, frequency, and nocturia (Coyne et al., 2008). Lower urinary tract symptoms affect sexual health and quality of life. Urinary incontinence may impact an individual's sexual function because of concerns of urine leakage, odor, or embarrassment. Younger women with an overactive bladder have diminished self-esteem compared with older women (Bruner & Calvano, 2007). Individuals with overactive bladder plus voiding symptoms (e.g., weak, slow, or intermittent stream, hesitancy, straining, dribble) have reported higher rates of decreased sexual satisfaction than those with overactive bladder alone or urinary incontinence alone. In addition, lower urinary tract symptoms correlated with higher rates of depression that may further exacerbate sexual dysfunction (Coyne et al., 2008).

Men with multiple myeloma also are at risk of developing prostate cancer during their treatment course because of their age. Men who develop prostate cancer may develop erectile dysfunction as a consequence of the diagnostic procedures and treatment for prostate cancer. The risk of retrograde ejaculation is as high as 20%–50% in men undergoing transurethral resection of the prostate (Bruner & Calvano, 2007). Men who undergo surgical resection of the prostate may experience erectile dysfunction with rates of 50%–80% (Bruner & Calvano, 2007). Erectile dysfunction is not the only sexual dysfunction associated with prostatectomy. Weakening of the orgasmic sensation (50%) and involuntary loss of urine at orgasm (64%) have been reported, which may cause avoidance of sexual encounters. Hormone therapy for prostate cancer lowers testosterone levels, resulting

in decreased semen production, erectile dysfunction, low sexual desire, and less pleasurable orgasm (80% risk). In addition, radiation therapy decreases the ability to have voluntary erections in 40%–60% of men (Bruner & Calvano, 2007; Hughes, 2008).

Women with a diagnosis of multiple myeloma may develop difficulties with sexual function if they receive radiation to the pelvis. Radiation may cause delayed arousal and orgasm through damage of the pelvic vascularity and nerves. Women also may develop vaginal dryness, stenosis, and fibrosis leading to dyspareunia and painful pelvic examinations (Hughes, 2008).

Pain

According to Gevirtz (2008), “Many patients with chronic pain consider their pain symptoms to be the major obstacle to enjoying sex with their partner” (p. 17). Treatment of chronic pain improves libido and sexual function. Patients with chronic pain often adapt to pain and make lifestyle adjustments (Gevirtz, 2008; Kwan, Roberts, & Swalm, 2005); however, spouses may fear inflicting pain or causing fractures in their partner, and this needs to be taken into consideration when discussing sexual function (Kwan et al., 2005). Nurses play an integral role in counseling patients on interventions to overcome obstacles related to the disease or its treatment. Patients with myeloma may have chronic pain that requires long-term opiate use; this also affects erectile function, hormone levels, and libido.

Oral Contraceptives

Oral contraceptives may cause decreased libido in a number of women; they also affect sexual function by inhibiting androgen production and increasing the amount of sex hormone-binding globulin, which decreases testosterone levels (Clayton

& Ramamurthy, 2008). However, the effect that oral contraceptives have on decreased libido is unclear, with the literature reporting mixed results. Prior to initiating therapy, particularly with thalidomide or lenalidomide, patients’ beliefs regarding contraception use should be addressed.

Tertiary Causes

The impact of body image, depression, concerns about the future, abandonment issues, and history of abuse may negatively affect sexual function (Clayton & Ramamurthy, 2008; Frank, Mistretta, & Will, 2008). Discussions with patients regarding potential psychological etiologies of sexual dysfunction are important. In addition, exploring a patient’s cultural and religious beliefs regarding sexuality is necessary to determine what affect these areas may have on sexual function.

Body Image

In a study of body image among patients with cancer, body image-related side effects were reported as the most severe chemotherapy side effect (DeFrank, Mehta, Stein, & Baker, 2007). The impact of multiple myeloma and its treatments (e.g., steroids) produce temporary and permanent changes in patients’ height, weight, or mood, as well as loss of hair; these may affect an individual’s body image, thereby influencing sexuality (Faiman et al., 2008). Although no studies have focused exclusively on patients with multiple myeloma, the effects of cancer treatment on other patient populations have revealed diminished sense of well-being, thus impacting body image (DeFrank et al., 2007).

Intimate Partner Violence

The prevalence of intimate partner violence (IPV) among women receiving healthcare services is estimated to be 15% for those currently experiencing IPV and 44% for lifetime prevalence (Coker, 2007). The consequences of IPV on sexual health includes increased risk of sexually transmitted infections, pain during intercourse, reduction in sexual pleasure or desire, and increased depression rates (Coker, 2007).

Cultural Impact

Culture is the shared beliefs, social norms, and material traits of individuals within the same racial, religious, or social group (Fourcroy, 2006). Cultural practices and beliefs may affect sexuality in a variety of ways, including female genital mutilation, variations of sexual function, and lack of adequate social support (Fourcroy, 2006).

When discussing sexuality, nurses should be aware of the norms that exist across different cultures (Shell, 2007). Among African Americans, discussion regarding sexuality must occur one on one; however, a spouse or partner may be present. The nature of the sexual dysfunction may not be provided if discussed in front of other family members. One study among African Americans found that participants rarely discussed the impact treatment had on sexuality, even to close friends. In addition, nurses may encounter “insider/outsider” dilemma; therefore, establishing and maintaining trust is essential (Shell, 2007).

Patient Tear-Out Tool Long-Term Survivor Sexuality

Sexuality is an important part of your overall well-being and should be discussed with your healthcare provider. Do not be concerned about bringing up the topic of sexuality to your healthcare provider. Listed here are topics for you to discuss with your healthcare provider as well as questions you may want to discuss.

Questions to discuss with your healthcare provider:

1. How can myeloma or the side effects of treatment affect my sexual activity?
2. Describe any changes in your sexual function.
3. What could be causing the change in my sexual ability?
4. Are there any precautions I need to take while on treatment?
5. Is oral sex okay while on therapy? Are there any specific precautions my partner and I need to take when performing oral sex?

Topics to discuss with your healthcare provider:

- Decreased sexual drive: not wanting sex
- Dryness with intercourse: vaginal dryness
- Fear of sexual contact: scared to be touched
- Lack of erection: unable to obtain or maintain penis fullness during sex
- Lack of orgasm: lack of complete satisfaction
- Pain with intercourse: pain that occurs during sexual activity

Note. This patient education tool may be reproduced for noncommercial use.

Among Asian Americans, discussions regarding sexuality are commonly considered taboo, particularly among older adults. A review of the literature on the impact of culture on sexual function found Pap smear screening rates are lower among Asian American women, secondary to fear and/or embarrassment (Shell, 2007). In addition, among Asian women, acculturation was found to be associated with more liberal attitudes and increased sexual desire (Shell, 2007). One study found that, among this group, obtaining information via the mail rather than in group encounters was a preferred method of receiving information (Shell, 2007). Therefore, discussions on sexuality should include assessment of culture and occur as a one-on-one encounter with the patient (Shell, 2007).

Within Hispanic culture, family involvement has been reported as a positive factor in medical care and treatment (Shell, 2007). Healthcare decisions often are made by more than one family member; therefore, discussion regarding sexuality may be avoided. Because of patients' reluctance to discuss sexuality, nurses may need to be more assertive with this population (Shell, 2007).

Impact of Myeloma Treatment

Depression and Body Image Disturbance

Depression can lead to sexual dysfunction as well as body image disturbance (Hughes, 2008), which may not only be a symptom of depression but also a cause leading to sexual dysfunction. Depression can be associated with pain, functional decline, and decline in cognition. In addition, dependency on caregivers may impact psychological well-being, particularly if patients require assistance that minimizes their privacy (Hughes, 2008; Kagan et al., 2008). Although depression may be treated successfully with pharmacologic intervention, sexual side effects of antidepressant medications are common (Kagan et al., 2008; Zemishlany & Weizman, 2008). Managing depression and body image disturbance in patients receiving treatment for myeloma may be difficult and prompt referral to a psychologist or psychiatrist is necessary.

Estrogen deficiency occurring after ovarian failure results in depression and changes in appearance (Tierney et al., 2007). The declining estrogen levels from cancer treatments may alter sexual functioning through the loss of adequate lubrication as well as changes in appearance, which may diminish self-image and self-esteem (Tierney et al., 2007). Patients with erectile dysfunction may feel a sense of inadequacy, leading to depression and body

image disturbance, which then can lead to sexual dysfunction. The partners of patients with erectile dysfunction may feel pressured to have sexual encounters or feel a lack of control because of patients' use of phosphodiesterase type 5 inhibitor medications (Kagan et al., 2008) (see Table 2). In addition, younger patients with myeloma still in their childbearing years may develop a sense of loss because of the infertility that occurs as a result of treatment.

Myeloma Treatment

Disruption of patients' normal sexual function has been documented in patients with cancer receiving traditional

Table 2. Pharmacologic and Nonpharmacologic Interventions for Erectile Dysfunction

INTERVENTION	INDICATION AND DESCRIPTION	PRECAUTIONS
Pharmacologic Interventions		
Intercavernous vasoactive agents	Erectile dysfunction: improves penile rigidity	Bleeding, infection, priapism, penile ache, and penile fibrosis
Phosphodiesterase type 5 inhibitors (sildenafil, vardenafil, tadalafil)	Erectile dysfunction: inhibits phosphodiesterase type 5 and increases blood flow to the corpus cavernosum	Abnormal vision, nonarteritic anterior ischemic neuropathy; phosphodiesterase in patients on nitrates is an absolute contraindication. Use cautiously in men with cardiovascular disease (refer to cardiologist).
Testosterone replacement	Erectile dysfunction and decreased libido: increases testosterone levels	Lower urinary tract symptoms, sleep apnea, gynecomastia, decreased HDL; requires lipid panel, digital rectal examinations, and monitoring of PSA
Nonpharmacologic Agents		
Acupuncture ^a	Erectile dysfunction: traditional Chinese acupuncture	Infection, peripheral nerve injury, bleeding, hematoma, central nervous system injury, syncope, dermatitis, and needle breakage
L-arginine	Erectile dysfunction: smooth muscle relaxation	—
Penile prosthesis ^a (implant)	Erectile dysfunction: creates a negative pressure, which increases blood flow into the corpus cavernosum	Penile bruising and ischemia
Penile prosthesis ^a (semi-rigid, fully inflatable, and semi-inflatable)	Erectile dysfunction: silicone rods placed into the corpora cavernosa	Permanent erection and rod breakage
Vacuum constriction devices ^a	Erectile dysfunction: negative pressure pump designed to fill corpora cavernosa	Penile bruising and ischemia may occur.
Yohimbine	Erectile dysfunction: penile vasodilation	Increased blood pressure and heart rate

^a All invasive or minimally invasive procedures should be discussed with the patient's physician in case of cytopenias.

HDL—high-density lipoprotein; PSA—prostate-specific antigen

Note. Based on information from Aung et al., 2004; Bruner & Calvano, 2007; White et al., 2001.

Resources on Sexuality and Cancer

Sexuality for women and their partners: http://nccu.cancer.org/docroot/MIT/MIT_7_1x_SexualityforWomenandTheirPartners.asp

Sexuality for men and their partners: http://nccu.cancer.org/docroot/MIT/MIT_7_1x_SexualityforMenandTheirPartners.asp

Supportive care patient information: <http://health.msn.com/health-topics/articlepage.aspx?cp-documentid=100227628>

Sexuality and reproductive issues: www.cancer.gov/cancertopics/pdq/supportivecare/sexuality/HealthProfessional

Talking with your spouse or partner about cancer: www.cancer.net/patient/Coping/Relationships+and+Cancer/Talking+About+Cancer/Talking+With+Your+Spouse+or+Partner

chemotherapy agents such as alkylating agents, vinca alkaloids, and platinum-containing regimens (King et al., 2008). Traditionally, cyclophosphamide and melphalan have both been used in low and high doses, leading to infertility in men and women. High-dose therapy with melphalan followed by autologous stem cell transplantation precipitate a chemically induced menopause in younger women (Lee et al., 2006). These changes can result in emotional and psychological sequelae, leading to decreased quality of life. Vincristine and cisplatin temporarily or permanently damage parts of the central nervous system, leading to erectile dysfunction and ejaculation difficulties (Lee et al., 2006).

Disruption of estrogen, androgen, and testosterone production secondary to steroids (dexamethasone or prednisone) in patients with myeloma may decrease sexual desire, result in dyspareunia from vaginal wall thinning, and trigger impotence (Contreras et al., 1996; Kalantaridou & Calis, 2006). In addition, steroid side effects include increased glucose levels, electrolyte imbalances, and mood alterations (Faiman et al., 2008). Patients may experience body image changes such as weight gain, hair loss, or cushingoid appearance, which can interfere with sexual arousal (Contreras et al., 1996; Faiman et al., 2008).

Erectile dysfunction and loss of libido have not been reported in patients treated with bortezomib in clinical trials; however, erectile dysfunction and loss of libido have been reported in patients with multiple myeloma receiving lenalidomide therapy in clinical trials (Celgene Corp., 2010a). Impotence has been reported in patients with erythema nodosum leprosum being treated with thalidomide in clinical trials, but not in patients with multiple myeloma in clinical trials (Celgene Corp., 2010b). Whether these side effects are dose dependent is unknown. Although as yet undocumented in any formal studies, members of the NLB have observed that sexual dysfunction is a common occurrence with many of the novel therapies now being used in the treatment of multiple myeloma. Reports of erectile dysfunction and decreased libido in patients receiving bortezomib and lenalidomide are becoming a common experience for NLB members treating patients with multiple myeloma. The causality of erectile dysfunction with

thalidomide has not been determined (Isoardo et al., 2004; Laaksonen, Remes, Koskela, Voipio-Pulkki, & Falck, 2005; Murphy & O'Donnell, 2007). Some have proposed that it may be related to neurogenic effects, diminished blood flow, or visceral neuropathy. Although anecdotal reports exist of erectile dysfunction without loss of libido, no formal studies have been conducted (Isoardo et al., 2004; Laaksonen et al., 2005; Murphy & O'Donnell, 2007).

The use of both thalidomide and lenalidomide are restricted because thalidomide causes severe birth defects in humans and lenalidomide causes similar birth defects in monkeys (Celgene Corp., 2010a, 2010b). Formal studies have not been performed to determine if compliance with birth control regimens and the personal surveys as required by the STEPS® (System for Thalidomide Education and Prescribing Safety) program for thalidomide use and the RevAssist® program for lenalidomide use have psychological effects and inhibit patients' sexuality or create fears that interfere with sexual desire. However, members of the NLB feel that these reactions are possible and that they should be considered. In addition, some patients may not enjoy intercourse with the use of barrier methods that may be required in the STEPS® and RevAssist® programs (Celgene, 2010a, 2010b; Zeldis, Williams, Thomas, & Elsayed, 1999). Studies to assess sexuality and desire in these settings are needed.

Assessment of Sexual Function

A literature review conducted by Srivastava, Thakar, and Sultan (2008) found that 30%–50% of women describe difficulties in sexual problems as a result of distress and interpersonal difficulty; 54% of women report one sexual problem lasting at least one month. The most common sexual problems affecting women are lack of interest, inability to achieve orgasm, and dyspareunia. Of those who reported sexual dysfunction, only 21% sought intervention (Srivastava et al., 2008). The most common sexual problems affecting men include erectile dysfunction (problems achieving or maintaining an erection), decreased or absent sexual desire, disorders of ejaculation or orgasm, and failure of detumescence (sustained erection) (Kandeel, Koussa, & Swerdloff, 2001).

An international survey of 27,500 men and women ages 40–80 was conducted by Kingsberg (2004) to evaluate attitudes, beliefs, and health between intimate partners. A subanalysis of participants from the United States revealed that only 14% reported that a physician had inquired about sexual function within the preceding three years (Kingsberg, 2004). Reluctance on the part of healthcare providers and patients to discuss sexuality

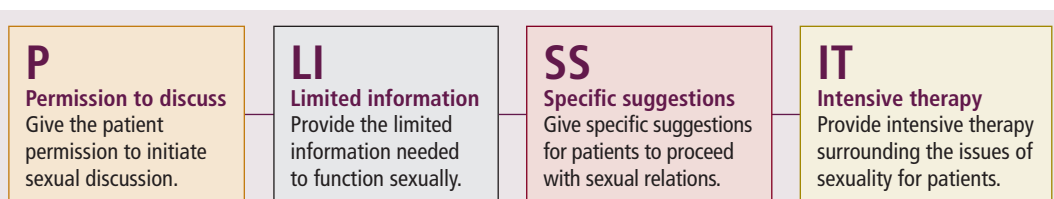


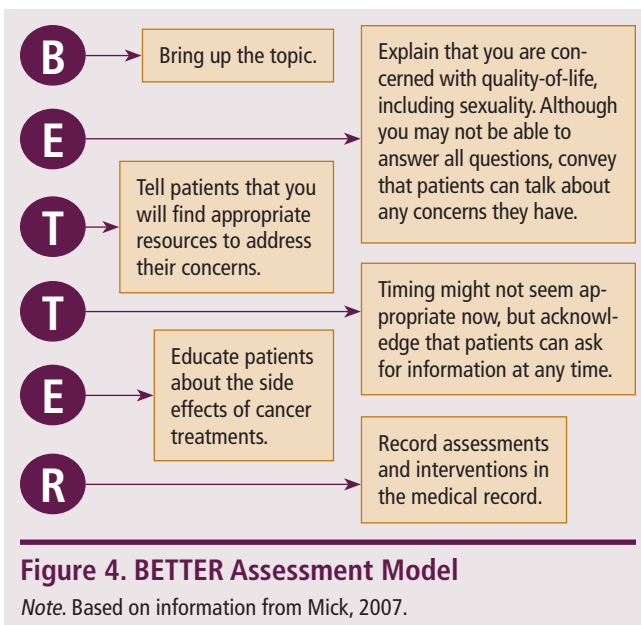
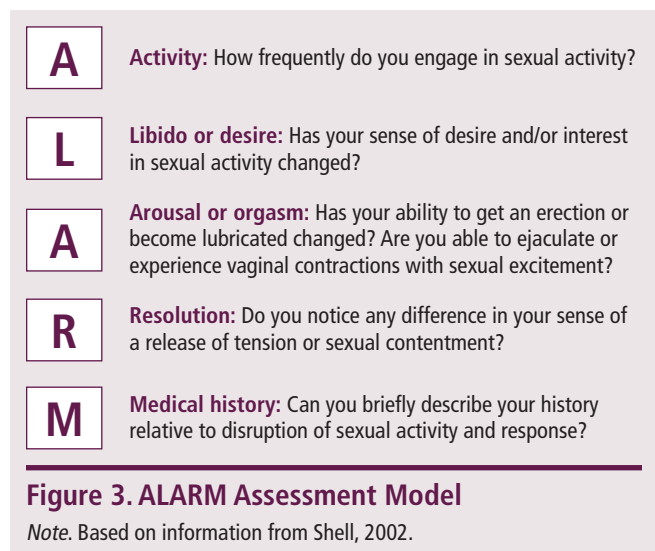
Figure 2. PLISSIT Assessment Model

Note. Based on information from Mick, 2007; Taylor & Davis, 2006.

has been well documented in all disease states (Harsh, McGarvey, & Clayton, 2008). Studies suggest that oncology nurses and physicians are reluctant to discuss sexual health with their patients (Harsh et al., 2008). In addition, patients are hesitant to disclose sexual dysfunction or seek medical treatment for sexual function (Harsh et al., 2008). A need exists for more open and improved communication between doctors, nurses, and their patients about sexuality issues.

According to Srivastava et al. (2008), healthcare providers need to provide an environment that promotes discussion of sexual dysfunction. Patients may feel uncomfortable or embarrassed discussing sexual function; therefore, healthcare providers need to engage in effective communication and develop interpersonal skills. In addition, a nonjudgmental attitude, frank discussions, and emphasizing that sexual health is an integral part of their overall health may reduce the stigma associated with sexual dysfunction. Engaging in effective communication and interpersonal skills provides patients with an environment in which they feel comfortable and less embarrassed. Bridge statements facilitate the flow from less comfortable to comfortable discussions. For example, “Has anyone talked to you about how your illness and treatments affect your ability to have sex?” or “Do you have any sexual concerns that you would like to talk about?” Questions should be asked in a professional nature and direct eye contact should be used (Bruner & Berk, 2004; Srivastava et al., 2008; Zator Estes, 2002). Maintaining a relaxed, open, and nonjudgmental appearance is important as well when discussions regarding sexuality occur (Tomlinson, 1998). Models such as PLISSIT, ALARM, and BETTER have shown to be effective in the assessment of sexual function (Hughes, 2008) (see Figures 2, 3, and 4).

To assess sexual dysfunction, a thorough medical history, including sexual and psychological history, should be conducted at the initial visit (McVary, 2007; Srivastava et al., 2008). Current medications should be reviewed to determine their role in decreased sexual functioning (see Table 3). Discussions surrounding sexual function at the initial visit enable patients to bring up concerns as they arise during their course of treatment. Assessment of the patient and their partner’s sexual behavior, attitudes, and expectations may be beneficial in determining



how treatment may affect their relationship (McVary, 2007; Srivastava et al., 2008).

Physical Examination

The physical examination of all patients, regardless of gender, should include both a vascular and neurologic assessment. Evaluation of blood pressure, peripheral pulses, skin integrity, and general appearance may reveal evidence of peripheral vascular disease, secondary sex characteristics, and cardiovascular disease (McVary, 2007; Srivastava et al., 2008). Women with sexual dysfunction should, in addition to this workup, receive a genital examination to evaluate for estrogen deficiency, sexually transmitted disease, vaginal trauma, and bladder, vaginal, or rectal prolapse (Srivastava et al., 2008). Men with sexual dysfunction should undergo a penile assessment, examining for scrotal swelling or tenderness and areas of discoloration, masses, or trauma (McVary, 2007). If the oncology practitioner cannot perform the physical assessment, the patient should be referred to a specialist (gynecologist or urologist) for interdisciplinary consultation.

Laboratory Testing

Laboratory studies that may be beneficial include lipid profiles, thyroid function (thyroid stimulating hormone, T₃, T₄), hormone levels (estrogen, luteinizing hormone, sex hormone binding globulin, and free testosterone) (see Table 4), and prostate-specific antigen (McVary, 2007; Srivastava et al., 2008). An important consideration when evaluating for testosterone level in both men and women is that it is “secreted by the adrenal glands and testes in men and by the adrenal glands and ovaries in women. Testosterone exists as both unbound (free) fractions and bound fractions: sex hormone-binding globulin and testosterone-binding globulin” (Hansen, 2003, p. 400). Unbound (free) testosterone is the active portion (Margo & Winn, 2006; National Menopause Society, 2005). The role of androgens in women has gained recognition; however, normal

values have yet to be fully determined and vary with age. Androgen deficiency in women has not been clearly defined (Davis & Tran, 2001). Many women have reported improved libido, increased energy, and a sense of well-being with testosterone replacement (Shifren, 2004). Testosterone therapy, however, is unsuitable for women suffering from postmenopausal symptoms, having a history of breast or uterine cancer, or having cardiovascular or liver disease (National Menopause Society, 2005).

Radiographic Findings

The use of Doppler flow and ultrasound imaging may be of assistance in detecting erectile dysfunction, ejaculatory problems, or vascular flow impairments (Sáenz de Tejada et al., 2005). In addition, sleep studies may help to diagnose sleep apnea, which may affect male erections (Basson & Schultz, 2007). Evaluating for neurogenic issues with an electromagnetic vibrating device may be useful, although not definitive. In women, vaginal temperature and vibratory sensory testing may assist in diagnosing sensory loss (Srivastava et al., 2008). Measuring vaginal blood flow and oxygen tension within the vagina, clitoris, and labia may be beneficial (Mayer et al., 2007). Patients with myeloma require a bone survey to determine if a current or impending fracture is contributing to pain or causing risk during sexual activity.

Treating Sexual Dysfunction in Men

Pharmacologic and nonpharmacologic interventions are available to patients and may restore erectile function. Phosphodiesterase type 5 inhibitors have been shown to improve erectile dysfunction; side effects may include short duration of action, flushing, headaches, changes in visions, tachycardia, and the potential for prolonged erection (Bruner & Calvano, 2007; McVary, 2007). For patients currently receiving nitrate therapy, the use of phosphodiesterase type 5 inhibitors is an absolute contraindication because it may result in hypotension (McVary, 2007). Other interventions for the treatment of erectile dysfunction include intracavernous or transurethral injections, testosterone replacement, vacuum erection devices, surgical interventions, and/or psychotherapy (Bruner & Calvano, 2007; McVary, 2007). The use of intracavernous or transurethral injections is an absolute contraindication in patients with multiple myeloma, thrombocytopenia, sickle cell disease or trait, or history of priapism because of increased risk of priapism with the injections (McVary, 2007).

Table 3. Impact of Multiple Myeloma Medications on Sexual Function

MEDICATION	EFFECT ON SEXUAL FUNCTION
Antidepressants (MAO inhibitors, SSRIs, tricyclic antidepressants)	Orgasm disorder; less frequent with duloxetine, paroxetine, nefazodone, and trazodone because of less frequent anticholinergic and anti-adrenergic effects; more frequent with bupropion, sertraline, and citalopram (Krychman et al., 2004; Taylor et al., 2005; Zemishlany & Weizman, 2008)
Antihypertensives (diuretics, calcium channel blockers, ACE inhibitors, and antiadrenergics)	Reduced libido and orgasm disorder; less incidence with ACE inhibitors than with others (10% versus 30%) (Brock & Lue, 1993; Carvajal et al., 1995; Smith & Talbert, 1986; Zemishlany & Weizman, 2008)
Antipsychotics, benzodiazepines, narcotics	Decreased arousal (libido), orgasm disorder, and delayed ejaculation (Basson & Schultz, 2007; Hitiris et al., 2006; Zemishlany & Weizman, 2008)
Antiseizure medication (clonazepam, diazepam, phenytoin, carbamazepine, phenobarbital, gabapentin, pregabalin)	Orgasm disorder, decreased arousal (libido), and decreased testosterone (Basson & Schultz, 2007)
Anti-ulcer agents	Decreased arousal (libido) (less with ranitidine), erectile dysfunction, and gynecomastia; less effects on sexual function with proton pump inhibitors (Bonfils et al., 1981; Lardinois & Mazzaferrri, 1985; Pierce, 1983; Santucci et al., 1991)
Cardiac agents	Decreased arousal (digoxin), increased estrogen levels, and decreased testosterone and luteinizing hormone levels (Basson & Schultz, 2007; Zemishlany & Weizman, 2008)
Chemotherapeutics (platinums, alkylating agents, stem cell transplantation)	Erectile dysfunction, sterility (amenorrhea and spermatogenesis), difficulty with ejaculation, dyspareunia from vaginal dryness (pegylated doxorubicin), decreased arousal, and orgasm disorder (Chatterjee et al., 2000; Krychman et al., 2004)
Herbs	Decreased arousal (St. Johns Wort) (Hypericum Depression Trial Study Group, 2002)
Illicit drugs (e.g., cocaine, marijuana)	Impotence (Brock & Lue, 1993)
Immunomodulatory agents	Erectile dysfunction, decreased libido, polyneuropathy, and decreased thyroid function (Celgene Corp., 2010a, 2010b; Isoardo et al., 2004; Laaksonen et al., 2005; Murphy & O'Donnell, 2007)
Interferon	Thyroid function changes (Fentiman et al., 1985; Micromedex, 2010; Quesada et al., 1986), changes in menses, increased fatigue and depression, and decreased arousal (libido)
Lipid-lowering agents	Erectile dysfunction (Do et al., 2009)
Proteasome inhibitors (e.g., bortezomib)	Erectile dysfunction and decreased libido, testicular swelling and pain, and peripheral neuropathy (Millennium: The Takeda Oncology Company, 2010)
Steroids and hormonal agents	Incontinence, erectile dysfunction, and decreased arousal (Contreras et al., 1996)

ACE—angiotensin-converting enzyme; MAO—monoamine oxidase; SSRI—selective serotonin reuptake inhibitor

Table 4. Normal Hormone Values for Men and Women

HORMONE	MEN	PREMENOPAUSAL WOMEN	POSTMENOPAUSAL WOMEN
Follicle-stimulating hormone	1.6–18.6 mIU/ml	2.8–17.2 mIU/ml	24–170 mIU/ml
Luteinizing hormone	3.9–22.6 mIU/ml	3.6–28.4 mIU/ml	35–129 mIU/ml
Prolactin	0–5 ng/ml	0–17 ng/ml	0–17 ng/ml
Testosterone	270–1,070 ng/dl	6–86 ng/dl	One-half of normal
Urine estradiol	1–11 mcg per day	13–54 mcg per day	0–11 mcg per day

Note. Based on information from Fischbach, 2000.

Fertility Preservation

Although the median age of patients diagnosed with myeloma is 66 years, some patients are diagnosed in their 20s and 30s (King et al., 2008). Therefore, nurses need to be aware of the implications that chemotherapy and radiation may have on fertility in younger patients. The effects of chemotherapy and radiation may lead to infertility in 30%–75% of male patients aged 18–45 years (King et al., 2008). In women, the

effects of chemotherapy and radiation may lead to premature menopause, thereby leading to a loss of fertility. In a study conducted by Schover et al. (1999), only 50% of cancer survivors diagnosed prior to age 35 recalled receiving information regarding the risks cancer treatment may have on their fertility (King et al., 2008).

Nurses have the opportunity to discuss risks of infertility to patients and also to discuss options regarding fertility preservation (King et al., 2008). Currently, the American Society of Clinical Oncology recommends sperm cryopreservation for men and embryo cryopreservation for women. Other available options offered at specialty centers include testicular sperm extraction and testicular freezing for men, and oocyte freezing or ovarian tissue freezing for women (Lee et al., 2006).

Treating Sexual Dysfunction in Women

Sexual dysfunction in women may occur at all stages of life and involves loss of interest or desire, decreased arousal, difficulty achieving orgasm, or dyspareunia. The most common sexual disorder in women is low sexual desire (22%) (Fourcroy, 2003). Researchers have reported these effects with androgens such as testosterone replacement for treatment of decreased libido (Fourcroy, 2003).

Side Effects of Testosterone

The potential side effects of testosterone and other androgen therapies include acne, lowering of high-density lipoprotein, changes in liver function, increased hair growth, voice deepening, or clitoral engorgement (Davis et al., 2008; Margo & Winn, 2006). In one study of women who were randomized to either placebo or two different testosterone dose levels, three women were diagnosed with breast cancer and 13 women developed vaginal bleeding (Davis et al., 2008). Of those women with vaginal bleeding, two women had proliferative endometrium.

Referrals

If the cause of sexual dysfunction is related to psychological factors, a referral to a clinical psychologist, certified sex therapist, or marriage and family therapist is appropriate. These specialists may be certified by the American Association

The oncologist and healthcare team should build a referral network of specialists for the treatment of sexual dysfunction. The type of referral will depend on the problem that the patient presents with.

A comprehensive referral network should include

- A mental health professional who provides sex therapy and sexual counseling
- A gynecologist who has expertise in assessing and treating pain with sexual activity or one who can help women make decisions about hormone replacement therapy after cancer
- An urologist who has specialized knowledge and skill regarding problems of the male and female urinary tract and the male reproductive organs; who also provides medical treatment for loss of sexual desire and erectile dysfunction
- An endocrinologist who treats the deficiency or excess production of hormones causing such diseases as diabetes, thyroid diseases, and menopause
- A sperm bank that can store semen samples for men about to begin cancer treatment that could potentially damage fertility
- An infertility clinic offering in vitro fertilization and donor gamete programs that has a good success rate and staff who are familiar with cancer-related infertility in men and women
- A genetics clinic that can counsel cancer survivors regarding their concerns about birth defects or cancer risks in their offspring.

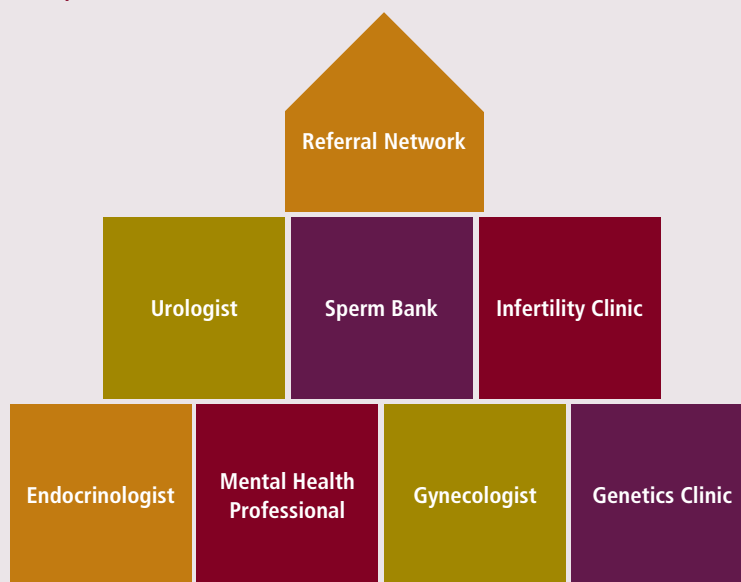


Figure 5. Building Blocks of a Successful Referral Network

Organizations With Information on Sexuality

CancerCare: www.cancer.org

Cancer Survivors Gathering Place: www.cancersurvivorsplace.org

Fertile Hope: www.fertilehope.org

LIVESTRONG: www.livestrong.org

National Cancer Institute: <http://dccps.nci.nih.gov/ocs>

National Coalition for Cancer Survivorship: www.canceradvocacy.org/toolbox/multiple-myeloma

Oncolink: www.oncolink.org/oncolife

of Sex Educators or hold a diploma from the American Board of Sexology. If the dysfunction is physiologic, referral to the appropriate specialist (e.g., gynecologist, endocrinologist) is indicated. Because sexual dysfunction may be multifactorial, multiple referrals may be necessary. Building a referral network of specialists to optimize treatment of sexual dysfunction is imperative (see Figure 5).

Summary

Sexual dysfunction is caused by multiple physical and psychological factors, including comorbidities, medical treatments, lack of psychological well-being, altered body image, and cultural and societal influences. Both men and women are affected by sexual dysfunction, altering their relationships with their partners. Encouraging open communication between patients and healthcare providers, as well as between patient and partner, is essential in treating the underlying cause of the problem. Identifying sexual dysfunction and providing the necessary education and specific interventions is imperative. Resources to manage sexual side effects and to address reproductive issues and birth control are needed. Patients deserve to have any sexual difficulty carefully assessed and appropriately managed.

The authors gratefully acknowledge Brian G.M. Durie, MD, and Robert A. Kyle, MD, for critical review of the manuscript; Lynne Lederman, PhD, medical writer for the International Myeloma Foundation, for preparation of the manuscript; and Lakshmi Kamath, PhD, at ScienceFirst, LLC, for assistance in preparation of the manuscript.

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