Libido as Part of Sexuality in Female Cancer Survivors

Debra Barton, RN, PhD, AOCN®, MaryBeth Wilwerding, RN, MS, Lisa Carpenter, RN, BSN, and Charles Loprinzi, MD

Purpose/Objectives: To present the state of knowledge and a suggested program of research related to one part of sexual functioning in female cancer survivors: libido.

Data Sources: Journal articles, monographs, and book chapters.

Data Synthesis: Sexuality is a broadly defined term with many components. Libido is a component of sexuality and is reviewed with respect to definition, physiology, and measurement. Evidence-based interventions also are discussed.

Conclusions: Most of the evidence related to enhancing libido involves testosterone, but this has not been tested in cancer survivors. Several clinical questions are yet to be answered regarding physiology as well as nonpharmacologic and pharmacologic interventions for enhancing libido.

Implications for Nursing: Nurse researchers could add much to the evidence base on interventions for improving libido and, subsequently, sexual health. Implementing behavioral interventions to enhance libido would be an appropriate nursing function.

Key Points . . .

- ➤ Sexuality is a broad concept with many possible etiologies that may be difficult to study.
- ➤ Libido is a subcomponent of sexuality and may be an easier concept to affect through intervention research.
- ➤ Measurement is an important issue to consider in libido research.
- ➤ Many potentially effective interventions, pharmacologic and nonpharmacologic, can be studied to enhance libido in female cancer survivors.

Goal for CE Enrollees:

To enhance nurses' knowledge related to changes in libido in female cancer survivors.

Objectives for CE Enrollees:

On completion of this CE, the participant will be able to

1. Define libido within the context of sexual health.
2. Describe factors that can affect libido in female cancer survivors.
3. Discuss potential pharmacologic and nonpharmacologic interventions for decreased libido.

Problems with sexual functioning are a prevalent issue with regard to the quality of life of female cancer survivors. In a survey study reporting the prevalence of sexual dysfunction in the United States, 1,749 women aged 18–59 were questioned about their interest in sex, ability to achieve orgasm, and experience of pain during sex. Overall, authors concluded that some form of sexual dysfunction was present in 43% of women (Laumann, Paik, & Rosen, 1999). Andersen (1985) reported that, in female cancer survivors, the rate of morbidity related to sexual functioning can be as high as 90%. A long-term study about the quality of life of breast cancer survivors surveyed women who were 5–10 years postdiagnosis. Results indicated that women reported a statistically significant decrease in sexual activity since diagnosis (Ganz et al., 2002). Sixty-five percent were sexually active at baseline, a figure commensurate with the prevalence of sexual activity in the United States, reported at 70% (Greendale, Lee, & Arriola, 1999). However, at follow-up 5–10 years later, survey data indicated that only 55% of the breast cancer survivors were sexually active (Ganz et al., 2002).

Debra Barton, RN, PhD, AOCN®, is a nurse scientific coordinator, North Central Cancer Treatment Group (NCCTG), at the Mayo Clinic Cancer Center in Rochester, MN; MaryBeth Wilwerding, RN, MS, is executive director at the Missouri Valley Cancer Consortium in Omaha, NE; and Lisa Carpenter, RN, BSN, is a research nurse and Charles Loprinzi, MD, is scientific coordinator of cancer control, NCCTG, both at the Mayo Clinic Cancer Center. *(Submitted September 2003. Accepted for publication October 29, 2003.)*

Digital Object Identifier: 10.1188/04.ONF.599-609

Several studies have attributed changes in sexuality to chemotherapy. A study by Young-McCaughan (1996) reported that women who had been treated with chemotherapy were three times more likely than those receiving endocrine therapy to report decreased libido, seven times more likely to report trouble reaching orgasm, and six times more likely to report pain with intercourse and vaginal dryness. Although not statistically significant, findings by McPhail and Smith (2000) indicated that women who received chemotherapy for breast cancer more often reported a loss of interest in sex than did a control group of women without breast cancer. Fifty patients with breast cancer contacted through a radiation oncology department reported a decrease in sexual desire, more pain during intercourse, and vaginal dryness (Barni & Mondin, 1997). Although the subjects were contacted through radiation oncology, the authors attributed changes in sexuality mainly to chemotherapy.

Any woman treated for cancer with surgery that results in a change in body image may experience a change in sexual function. Changes in sexual functioning have been reported in descriptive studies using many different populations and people who had received various treatments (e.g., radiation, hormones, surgery, immunotherapy, chemotherapy) (Andersen & Elliot, 1993; Shell, 2002; Wilmoth & Botchway, 1999). Most descriptive studies have indicated that systemic chemotherapy and radical pelvic surgery may have the greatest impact on sexual functioning (Cartwright-Alcarese, 1995; Ganz, Rowland, Desmond, Meyerowitz, & Wyatt, 1998; Thors, Broeckel, & Jacobsen, 2001). Pelvic radiation may affect sexuality through physiologic changes (e.g., vaginal stenosis, scar tissue) or initiation of menopause (e.g., ovarian ablation) (Anderson & Lutgendorf, 1997; Burke, 1996; Ezzell, 1999).

Despite the prevalence of problems with sexuality, healthcare practitioners often do not assess such issues, nor are evidence-based interventions routinely offered to women. More research is needed to describe the problem and develop interventions to improve functioning. This article presents the state of knowledge related to one part of sexuality: libido.

Differentiating Sexuality and Sexual Functioning

Sexuality often is referred to as sexual functioning. For the purposes of this article, however, sexual functioning will be differentiated from sexuality and defined in terms of the phases of the sexual response cycle. This differentiation allows the concept of sexuality to be broken down into smaller components. The rationale for concentrating on one component of the sexuality puzzle is to provide a stronger foundation on which to build a program of research. Working with a concept that is precisely defined makes measuring, assessing, and effecting change easier.

Sexuality is a broad term that includes social as well as emotional and physical components. Etiologies for changes in sexuality as a result of a cancer diagnosis include alterations in self-image, fears related to cancer treatment and recurrence, and physical changes such as vaginal dryness, fatigue, and anatomic changes from surgery. One factor involved in sexuality and sexual functioning encompasses partner issues. These include, but are not limited to, the couple's sexual history (separately and together), the partner's ability to function sexually, communication problems, and marital stresses.

Sexual health can be regarded much like sexuality, and the terms may be used interchangeably. Sexual health is defined by the World Health Organization (2003) 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 experienced and expressed in thoughts, fantasies, desires, beliefs, attitudes, values, behaviors, practices, roles, and relationships." That definition reflects the tremendous breadth of the concept of sexuality.

One way to study sexual health is to break down the concept and focus on one facet: sexual functioning. Components of sexual functioning are described as the sexual response cycle and comprise four phases: libido, arousal, orgasm, and resolution (Auchincloss, 1991; Beckham & Godding, 1990; Hughes, 2000). Libido can be defined as the urge for, or interest in, sexual activity. Arousal refers to the intensification of sexual tension and includes the physiologic response to sexual activity. Aspects of this phase are vasocongestion, myotonia, and lubrication. The ability to experience arousal not only is a physiologic or anatomic phenomenon but also has psychosocial aspects. Orgasm is the peak and release of sexual tension. In resolution, both partners experience relaxation; for men, this includes a refractory period when erection is not possible. Resolution is the return to a physiologic, homeostatic state, as well as an emotional evaluation of the sexual experience (Graziottin, 2001).

Sexual response cycle is not necessarily linear or sequential. For example, desire not does have to precede arousal, but arousal may lead to desire (Meston & Frohlich, 2000). Although together these four phases of the response cycle comprise some part of sexuality or sexual health, they do not totally define sexuality but are more limited in scope. This provides the opportunity for a more focused program of research.

Figure 1 outlines a schematic of the various subconcepts involved in the definition of sexuality and sexual functioning. The bolded concept is the one with which this article is concerned.

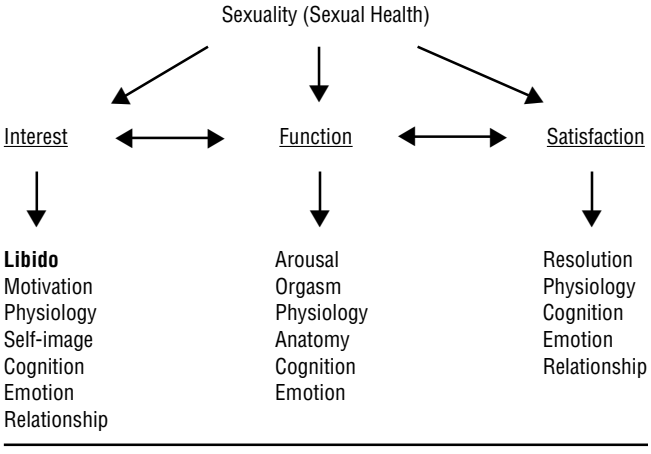

Figure 1. Schematic Drawing of Concepts Involved in Sexuality and Sexual Functioning

Problems with one of the phases of the sexual response cycle, libido (or low sexual desire), has been defined by an international consensus panel as "the persistent or recurrent deficiency (or absence) of sexual fantasies/thoughts, and/or desire for or receptivity to sexual activity, which causes personal distress" (Basson et al., 2000, p. 890). Based on this definition, a person with decreased libido experiences fewer thoughts about sex and a decreased desire to engage in sexual activity and is unhappy with this change. The etiology for this particular deficiency could be in any or all of three areas: biologic (hormones), motivational-affective, or cognitive (Graziottin, 2001). Sex hormones, such as testosterone, are considered necessary for libido but may not be entirely sufficient in and of themselves. Energy level and emotions contribute to the motivational-affective dimension of libido. Furthermore, self-image, self-esteem, and whether a person believes that a partner finds him or her attractive and desirable are factors involved in the cognitive domain (Graziottin). Each of these areas has been the object of interventions to improve libido (Ganz, Desmond, Belin, Meyerowitz, & Rowland, 1999; Thors et al., 2001).

In a qualitative study of 18 Caucasian women with breast cancer, Wilmoth (2001) described four components of losses related to an altered sexual self as discussed by participants. These four components included missing parts (results of surgery), loss of bleeding and becoming old (the menopause experience), loss of sexual sensations (including libido, arousal, and orgasm), and loss of womanhood (self-image alterations resulting from the cancer experience). Hence, loss of libido is one of four major themes to emerge from this research.

Andersen, Anderson, and deProsse (1989) reported results of a descriptive study of 47 women with early-stage gynecologic cancer. Their levels of sexual desire were compared with those of 57 healthy women and 18 women with benign gynecologic disease. Although group differences between women with cancer and those with benign disease were not statistically significant, differences between the group with cancer and the healthy sample were significant. Fifty-eight percent of women with gynecologic cancer experienced and reported inhibited sexual desire compared to 11% of the healthy women. This difference did not change over time, persisting over 12 months of follow-up.

Sexual health or sexuality, then, is a phenomenon that may be altered by cancer diagnosis and treatment. Changes in sexual functioning, specifically libido, is one element that may contribute to changes in sexual health. Libido has multiple components with which a person may intervene for enhancement.

Physiology of Libido

Phases of the sexual response cycle, in a broad sense, are physiologically affected by elements of the endocrine, neurotransmitter, and central nervous systems. Sorting out precisely what mechanisms are involved in each separate phase of the sexual response (e.g., libido versus arousal) is difficult because they are unequivocally interrelated. However, some data describe the physiology of libido or sexual desire. Although numerous medications (e.g., psychotropics) can adversely affect libido through negative side effects (Gitlin, 1994), these effects on sex drive can be ameliorated by discovering the cause and discontinuing medications, if possible. Some substances have the potential to exert an enhancing effect on libido. This is quite a different concept than simply taking away something that has a negative effect.

Hormones

Testosterone: Most of the evidence to date correlates sexual desire or libido with the presence of androgens or, more specifically, bioavailable testosterone (Kaplan, 1992; Meston & Frohlich, 2000). The activation of sex centers in the limbic system of the brain is thought to be dependent on testosterone levels (Kaplan, 1992). However, evidence is established more firmly with respect to men than women (DeCherney, 2000; Meston & Frohlich). Only indirect data have suggested a relationship between testosterone and libido in women. Some evidence came from intervention studies where androgen replacement was given to women who had undergone an oophorectomy and subsequently experienced improved libido-related outcomes. Other indirect evidence came from the treatment of transsexuals with androgen (Meston & Frohlich). The studies that looked at correlations between testosterone and sexual desire or libido have not been conclusive, and no definitive research has been completed in women who are living with a diagnosis of cancer.

In one study of 61 postmenopausal women who had been diagnosed with breast cancer, variables that significantly predicted sexual interest included the perception of health and body image and bioavailable testosterone (Greendale, Petersen, Zibecchi, & Ganz, 2001). Another study investigating the relationship between plasma testosterone and sexual activity in couples reported that higher baseline testosterone levels in women were correlated with higher sexual self-rated gratification scores and good interpersonal relationship scores (Persky, Lief, Strauss, Miller, & O'Brien, 1978). Not clear, however, is whether total testosterone or some measure of bioavailable testosterone was evaluated. A subsequent study by some of the same authors found that at least one androgen level was significantly related to every stage of the sexual response cycle. The study examined sexual behaviors and androgen levels between two age groups of healthy, married women: 11 women with a mean age of 24 and 19 women with a mean age of 54 (Persky et al., 1982). One study that failed to find differences in libido related to testosterone levels, however, did not take into account bioavailable testosterone or sex hormone binding globulin levels (Stuart, Hammond, & Pett, 1987).

Two reasons exist why definitive data about testosterone and sexual desire are not available. The first is the theory that testosterone levels necessary for adequate libido in men can be lower than their normal level of testosterone (Meston & Frohlich, 2000). Therefore, studies with large numbers of women would need to be performed to correlate and pinpoint a specific range of testosterone levels at which libido is negatively affected. Furthermore, this correlation may be unique for individuals. The second reason is that researchers use various outcomes when measuring sexual desire or libido and may not be measuring the same thing (McCoy, 1998).

Estrogen: Researchers generally accept that estrogen levels do not have a direct role in libido or sexual desire. Estrogen has been associated more directly with the arousal phase of the sexual response cycle, affecting vaginal lubrication and preventing dyspareunia (Sarrel, 2000). However, estrogen may

affect libido indirectly. For instance, hot flashes that interrupt sleep every hour may result in exhaustion and, therefore, curtail energy for sexual desire. This type of influence probably is not one that would lead to testing the use of estrogen for sexual desire.

Prolactin: A body of literature reports a link between increased prolactin levels and decreased sexual desire or libido, particularly in men (Dornan & Malsbury, 1989; Franks, Jacobs, Martin, & Nabarro, 1978; Schwartz, Bauman, & Masters, 1982). Descriptive studies have revealed that high prolactin levels are accompanied by low testosterone levels. Decreasing prolactin levels restored libido in men (Schwartz et al.). Studies have used bromocriptine to decrease prolactin to normal levels and have found subsequent improvement in libido in women (Bancroft, O'Carroll, McNeilly, & Shaw, 1984). Other mediating variables have not been well controlled in this research, and one speculation is that the improvement in libido with bromocriptine has nothing to do with prolactin but rather the effect it has on the neurotransmitter dopamine. This is a ripe area for further study.

Cortisol: Cushing syndrome is a disease in which cortisol and corticotropin levels are abnormally high. In this illness, decreased libido is reported (Meston & Frohlich, 2000). However, other symptoms are associated with this syndrome, such as insomnia and depression. Both lack of sleep and mood disorders can affect libido negatively. Therefore, whether the libido changes are a direct result of the cortisol levels (physiologic) or whether they are indirectly resulting from other symptoms (motivational-affective) is not clear. A direct relationship between cortisol and libido has not been studied.

Neurotransmitters

Serotonin: Considerable literature claims that antidepressants, specifically serotonin reuptake inhibitors, decrease sexual functioning. These drugs block the reuptake of serotonin, thus increasing serotonin levels. For women, most of the documented sexual changes are related to difficulties with orgasm, the third phase of the sexual response cycle. However, decreased libido also has been reported. Serotonin receptors are located both centrally and peripherally, with most of the receptors being in the periphery. These receptors are believed to be responsible for vasodilation and vasoconstriction, enhancing sexual function physiologically (Frohlich & Meston, 2000). Serotonin may be responsible for the functioning of sexual organs in the arousal and orgasm phases. Centrally, serotonin may be responsible for desire. Researchers have suggested that activating serotonin$_2$ receptors makes sexual functioning worse but that activating serotonin$_{1A}$ receptors may make sexual functioning better (Frohlich & Meston). The literature does not specify how these receptors relate to desire, arousal, or orgasm.

Dopamine: Drugs that stimulate dopamine have been shown to increase sexual desire (Meston & Frohlich, 2000). A comprehensive review article by Melis and Argiolas (1995) described evidence that substances eliciting catecholamines from dopaminergic centers increased arousal and orgasm phase behaviors in male rats. In fact, in male rats, such behaviors could be stimulated by affecting dopamine receptors independent of low testosterone levels. Similarly, drugs that antagonize D_1 or D_2 receptors in male rats decreased sex-seeking behaviors. Studies in female rats have been less conclusive, with dopamine agonists and antagonists appearing to have both positive and negative effects on sex-seeking behaviors. Thus, although the effects of dopamine in enhancing sexual desire in male rats are fairly well established, in females this relationship still needs to be studied (Melis & Argiolas).

Opioids: The use of opioids is linked to decreases in sexual desire (Meston & Frohlich, 2000; Paice, Penn, & Ryan, 1994). How opioids actually cause this is not known, but researchers speculate that it may occur indirectly through decreasing levels of luteinizing hormone and testosterone (Meston & Frohlich). Paice et al. measured testosterone levels of six patients receiving interspinal opioids. Five of the six men had testosterone levels below normal. The mean age of the patients was 40. Four of the patients sought testosterone replacement, and three of the four experienced improvements in libido and sexual functioning.

Central Nervous System

The central nervous system is thought to have more of a role in the arousal and orgasm phases of the sexual response cycle. However, one part of the brain, the medial amygdala, is thought to be responsible for sexual desire in men and has been looked at with regard to sexual behavior in women. This part of the brain is thought to interact with dopamine and other neuropeptides that are influenced by testosterone (Dornan & Malsbury, 1989; Everitt, Cador, & Robbins, 1989).

Measurement of Libido

Various outcome measures are used to examine libido. Some of these include sexual aspects such as sexual interest, sexual desire, frequency of intercourse, frequency of masturbation, or sexual thoughts and fantasies (McCoy, 1998). Unlike arousal, desire is more of a subjective measure. Referring back to the definition of libido, interest in or desire for sexual activity, sexual thoughts and fantasies, and reception of sexual activity (which could include frequency of engagement in such activity) are all components and should be considered part of a comprehensive measure assessing libido.

Several instruments measure various aspects of sexual functioning. Most are self-report and use numerical analog scales. Table 1 lists some of the most commonly used validated instruments containing subscales to measure libido. Some of the measures are quite short and, therefore, are easily adapted to a clinical setting. An article evaluating a short scale to assess female sexual functioning described study findings demonstrating a single question on sexual frequency and a single question on sexual libido were each sensitive enough to pick up changes after an intervention of sexual group therapy (Dennerstein, Anderson-Hunt, & Dudley, 2002). Similar validity has been shown with a one-item question related to quality of life (Sloan et al., 1998; Sloan, Aaronson, Cappelleri, Fairclough, & Varricchio, 2002). Therefore, to measure libido, measurement instruments do not have to be laboriously long or complicated.

Table 1. Libido Measurement Tools

Instrument	Items and Scoring	Validity	Reliability Coefficient	Populations Studied
Brief Index of Sexual Functioning for Women (Mazer et al., 2000; Taylor et al., 1994)	22 items. Seven-point numeric analog scale. Recently expanded to seven subscales: thoughts/desire, arousal, frequency of activity, receptivity/initiation, pleasure/orgasm, relationship satisfaction, and problems with function	Concurrent validity established with the Brief Sexual Function Questionnaire (men) and Derogatis Sexual Function Inventory	Sexual activity –0.83 Satisfaction –0.74 Desire/interest –0.39	Surgically menopausal women with reported problems of sexual functioning
Cancer Rehabilitation Evaluation System–Short Form (Schag et al., 1991)	Three items: sexual interest (two items) and sexual dysfunction (one item). Categorical scale	Validated with longer version of scale, correlated 0.73. Also correlated with Functional Living Index–Cancer –0.74 (7 months after diagnosis) and –0.70 (13 months after diagnosis.)	Alpha coefficient for sexual subscale was 0.88.	Patients with lung, prostate, and colorectal cancer; more than 500 other heterogeneous patients with cancer; newly diagnosed women with breast cancer; and patients in rehabilitation
Changes in Sexual Functioning Questionnaire (Clayton et al., 1997)	Female version contains 35 items, including five domains: frequency, desire/interest, pleasure, arousal, and orgasm/completion. Five-point numeric analog scale	Face validity established with the Diagnostic and Statistical Manual–IV criteria. Concurrent validity was with the Derogatis Interview for Sexual Functioning-Self Report.	Frequency 0.72 Desire/interest 0.75 Pleasure (one item) N/A Arousal 0.64 Orgasm 0.80	Depressed men and women, psychiatric residents, nonpsychiatric outpatients, and medical students
Derogatis Interview for Sexual Functioning–Self Report (Derogatis, 1997)	25 questions with five domains: sexual cognition and fantasy, sexual arousal, sexual behavior and experience, orgasm, and sex drive and relationship. Numeric analog scales of varying lengths	Demonstrated discriminant validity with community women versus women who reported sexual dysfunction	Sexual cognition/fantasy 0.79 Arousal 0.76 Behavior/experience 0.77 Orgasm 0.80 Sex drive and relationships 0.74	Men with prostate cancer, community women, and women with diagnosed sexual dysfunction
Female Sexual Function Index (Rosen et al., 2000)	19 items broken down into six factors: desire, subjective arousal, lubrication, orgasm, satisfaction, and pain. Six-point numeric analog scale	Developed and tested with data from five distinct centers in various geographic locations. Discriminate validity shown	Desire 0.83 Arousal 0.85 Lubrication 0.86 Orgasm 0.80 Satisfaction 0.83 Pain 0.79	Women with sexual arousal disorder
McCoy Female Sexuality Questionnaire (McCoy & Matyas, 1998)	19 items on a seven-point adjectival scale. Five subscales: sexual interest, satisfaction, vaginal lubrication, orgasm, and sex partner	Discriminate validity shown in a longitudinal study with postmenopausal women. Convergent validity with Women's Health Questionnaire sex life subscale	Established with 364 university women aged 18–26. Overall internal consistency alpha of 0.77	Postmenopausal women, university women on oral contraception, women on estrogen replacement therapy versus placebo
Short Personal Experiences Questionnaire (Dennerstein et al., 2002)	Nine items representing six areas: feelings for partner, sexual responsivity , sexual frequency (one item), libido (one item), dyspareunia (one item), and partner problems (one item)	Distinguished between sex therapy group and family-planning group. Concurrent validity with Derogatis Interview for Sexual Function, r = 0.74 for libido	Test-retest reliability was 0.71–0.95. Cronbach alpha was not reported.	Family planning, psychiatric group, and sex therapy group
WATTS Sexual Function Questionnaire (Daker-White, 2002)	17 items on a five-point adjectival scale. Four subscales: sexual desire, arousal, orgasm, and satisfaction	Limited published data on validity; not known	Limited data published; not known	Breast cancer survivors

Interventions for Libido

Nonpharmacologic

Many nonpharmacologic interventions address the cognitive etiology of libido. Counseling can be useful to evaluate and enhance an individual's perception of body image, self-image, and view of self as an attractive, sexual person (Andersen, 1996; Feldman, 1989; Gallo-Silver, 2000; Schover, Evans, & von Eschenbach, 1987). The psychotherapist's role is to help create a nonthreatening environment in which a patient and significant other can understand changes and current responses to various sexual stimuli. In this way, loss of desire created by fear of the unknown can be reversed. Randomized clinical trials regarding this type of counseling intervention are not common. However, one study randomized 80 women with gynecologic cancer to receive standard counseling (usual interactions between patient and healthcare team), eight sessions of individual prespecified topical counseling, or eight sessions of group prespecified topical counseling (Cain, Kohorn, Quinlan, Latimer, & Schwartz, 1986). Topics of the counseling sessions included general aspects of cancer; causes of cancer; impact of treatment; behavioral coping strategies such as relaxation, diet, and exercise; talking with family and friends; setting goals; and relating to caregivers. Sexual functioning outcomes were operationalized using the sexual relationships subscale of the Psychosocial Adjustment to Illness Scale. In both thematic counseling groups, sexual relationships were significantly better than in the standard counseling group. An earlier nonrandomized study compared individual inpatient counseling with a control group and reported increases in frequency of intercourse among those receiving counseling (Capone, Good, Westie, & Jacobson, 1980).

Annon (1976) developed a model for discussion of sexual problems called PLISSIT, which stands for four steps of intervention: permission, limited information, specific suggestions, and intensive therapy. The first level of intervention involves giving permission to patients to explore their sexual needs and to normalize their experiences and feelings. Including sexual concerns in the same way that other symptoms are assessed makes them seem more natural, perhaps making them easier to discuss. The second level is to provide education (limited information) regarding how cancer and its treatment may affect libido or desire. The third level, specific suggestions, includes providing interventions to help patients and their partners meet their goals. Finally, for some, intensive therapy with a psychiatrist, psychologist, or sex therapist may be necessary, and referral should be provided. Whether this model of counseling has been tested in cancer survivors is not known.

Behavioral techniques can be part of the therapy repertoire. Sensate focus is one behavioral technique intended to decrease fear, anxiety, and self-doubt related to sexual activity (Gallo-Silver, 2000; Kaplan, 1974). Sensate focus is a technique of massage that partners perform with each other that does not initially involve any genital stimulation. The goal is to simply experience a sense of pleasure and relaxation, as well as an increased sensitivity to each other's enjoyment (Kaplan, 1974). To the authors' knowledge, sensate focus has not been tested in a clinical trial to improve libido in women surviving cancer.

In women with cancer, emotional distress about diagnosis and treatment and feelings of loss related to surgical changes in the body must be addressed (Andersen, 1996; Gallo-Silver, 2000). Education about expected changes and effects of treatment are essential components of any intervention for people experiencing cancer (Andersen, 1996; Cain et al., 1986). In addition, relaxation, imagery, and coping strategies can be explored with patients and partners.

To optimize sexual desire, symptoms resulting from disease and treatment must be well managed (Shell, 2002). One randomized, controlled clinical trial used a comprehensive menopausal assessment (CMA) intervention program to look at various outcomes in 76 women who were postmenopausal and diagnosed with breast cancer (Ganz et al., 2000; Zibecchi, Greendale, & Ganz, 2003). Sexual functioning was measured with the Cancer Rehabilitation Evaluation System (CARES) sexual functioning scale. The intervention included symptom management (hot flashes, vaginal dryness, and urinary symptoms), as well as education and counseling. Thirty-seven women received the intervention, and 39 were randomized to standard care. In the women receiving the intervention, all eight items in the CARES sexual summary improved significantly, including interest in sex for self and partner and frequency of sex. Because the CMA was truly multifaceted, what specifically contributed to the increase in interest and frequency of sex is unclear. However, as a comprehensive intervention, this clinical trial provides an insightful model.

Pharmacologic

Testosterone: The hormonal intervention most discussed and studied in the literature with regard to libido or sexual desire is testosterone. The literature includes case study reports, as well as retrospective and prospective studies. Some of them are randomized, placebo-controlled clinical trials; some are not. None of the studies has been done in women with cancer. Almost all of the studies showed increased libido, sexual motivation, and fantasy over placebo or estrogen alone (Sarrel, 2000; Warnock, Bundren, & Morris, 1999).

One retrospective study was conducted with 44 women postoophorectomy who had been on estrogen with androgens, estrogen alone, or no hormone replacement. The studied outcome was sexual functioning (Sherwin & Gelfand, 1987). Women treated with androgens reported more sexual desire, arousal, and fantasies. The study did not mention tolerance to treatment or reported side effects. Testosterone doses were 150 mg intramuscularly monthly. The Daily Menopausal Rating Scale, developed by the investigators in a previous study (Sherwin, Gelfand, & Brender, 1985), was used to measure three behaviors related to sexual functioning: desire, arousal, and fantasies (a subset of the five areas covered in the instrument). The instrument is a one-item-per-behavior scale.

A prospective crossover study with 53 women who had undergone oophorectomy used a combination of estrogen and androgen versus estrogen alone versus androgen alone versus a placebo and looked at sexual functioning (Sherwin et al., 1985). The study also included a control group of women who had had a hysterectomy but not an oophorectomy. The study consisted of a one-month baseline period before surgery. After surgery was a three-month hormone/placebo phase followed by a one-month placebo phase. All

participants then were crossed over to another three-month phase of hormone/placebo. The combined estrogen/androgen arm consisted of 12 women receiving doses of testosterone of 150 mg monthly. The androgen-only arm contained 10 women, and the dose consisted of testosterone 200 mg monthly. The estrogen-only arm had 11 women and consisted of 10 mg of estrogen. The placebo arm had 10 women and used a formulation of sesame seed oil, and the control group had 10 women. The study measured five dimensions of sexual functioning (desire, fantasy, level of arousal, frequency of intercourse, and orgasm) using the Daily Menopausal Rating Scale. Both androgen groups reported higher levels of sexual desire and more fantasies (Sherwin et al.).

A prospective study by Shifren et al. (2000) involved 75 women who had undergone a bilateral oophorectomy and received one of two doses of transdermal testosterone, 150 mg or 300 mg, or a placebo. Women on the higher dose of testosterone reported more sexual fantasies, increased masturbation, and increased intercourse frequency. Another study of 40 women who experienced natural menopause and did not report any problems with sexual functioning used estrogen, an estrogen/progesterone combination, an estrogen/testosterone combination, or a placebo for 10 weeks. The estrogen/testosterone group reported more pleasure from masturbation, but no other differences among groups were found with regard to sexual functioning (Myers, Dixon, Morrissette, Carmichael, & Davidson, 1990). The findings are not surprising given that the participants did not report any sexual difficulties at baseline.

Newer studies from Sweden (Jarkander-Rolff, Nathorst-Boos, Carlstrom, & von Schoultz, 2001) and Australia (Goldstat, Briganti, Tran, Wolfe, & Davis, 2003) have shown that treatment with testosterone gel at 10 mg or transdermal 1% testosterone cream improved libido in women diagnosed with sexual arousal disorder as well as those reporting general low libido. The study by Goldstat et al. involved 34 women aged 32–45 years who had concerns about decreased libido and low total testosterone levels. The women were randomized to receive a placebo or 1% testosterone cream (10 mg) daily. The study was a crossover design, with each treatment phase consisting of a 12-week period with a 4-week washout, a period when participants used no cream between 12-week phases. Statistically significant improvement on the Sabbatsberg Sexual Self-Rating Scale occurred with testosterone cream over placebo. Total testosterone levels improved to the high normal range, but estradiol remained unchanged. No significant differences in adverse events were found between the groups.

Bromocriptine: Bromocriptine is a medication used to lower prolactin in patients who have higher than normal levels. High levels of prolactin, as mentioned earlier, are associated with depressed sexual desire or libido. Therefore, treatment with bromocriptine could improve libido. In a case study of a 44-year-old man who came to his physician because of a loss of sexual interest and erectile dysfunction, a trial of bromocriptine/placebo was performed. Sexual activity was assessed during a two-week baseline period. The man was given a placebo and assessed, followed by six weeks of bromocriptine 7.5 mg daily with assessment. The patient was unaware of when he was receiving placebo and when he was receiving active drug. Published results indicate that sexual interest was significantly higher while the man was on bromocriptine, although frequency of intercourse did not change (Bancroft et al., 1984).

Antidepressants: Altered mood states, such as depression, can affect the ability and desire to engage in sexual activity. Treating etiologies such as depression with antidepressant medication may help sex drive. This approach, however, is complicated by the fact that many medications used to counter depression affect serotonin, and such drugs also can adversely affect sexual functioning. However, this often is dose dependent, and, in some cases, decreasing the dose of antidepressants can reverse any negative effects on sexual functioning (Gitlin, 1994; Woodrum & Brown, 1998). For instance, in a placebo-controlled study of venlafaxine as treatment for hot flashes (Loprinzi et al., 2000), interest in sexual activity improved over the four weeks of the study with all doses of venlafaxine, as well as in the placebo recipients. However, all of the venlafaxine arms (the highest dose being 150 mg per day) showed a larger improvement in interest in sexual activity over the placebo arm. This could be related to mood effects or replenished energy obtained by achieving control of hot flashes.

Directions for the Future

Critical clinical questions are yet to be answered. With respect to the first phase of the sexual response cycle, libido, the most logical question to investigate appears to be, "What is the role of testosterone in female sex drive/libido?" Areas to investigate regarding this question include whether a correlation exists between below-normal testosterone levels and a women's experience of decreased sex drive, to what physiologic levels must testosterone be replaced to enhance or improve libido, and, finally, what product and dose of testosterone is best for use in women with regard to safety and efficacy.

Behavioral studies looking at cognitive therapies to improve self-esteem and help people cope with changing body image, mood, and energy would have a potential impact on libido through cognitive and psychological means. Findings also could complement pharmacologic interventions.

Conclusion

Within the realm of sexuality research, work on libido is admittedly a small piece of a large puzzle. Pharmacologic and nonpharmacologic studies could be done on each of the remaining three phases of the sexual response cycle: arousal, orgasm, and resolution. In addition, multidisciplinary intervention studies are needed to address social, cognitive, and psychological factors that contribute to sexual health as a whole.

A comprehensive program of research on sexuality could begin with physiologic studies examining the specific roles of various biomarkers in libido for women surviving cancer. Once knowledge about predictive and correlative biomarkers in women is determined with respect to what women define as a sufficient sex drive, then studies can focus on assessment and, subsequently, interventions.

Author Contact: Debra Barton, RN, PhD, AOCN®, can be reached at Barton.Debra@mayo.edu, with copy to editor at rose_mary@earthlink.net.

References

Andersen, B., & Elliot, M.L. (1993). Sexuality for women with cancer: Assessment, theory, and treatment. *Sexuality and Disability, 11,* 7–37.

Andersen, B.L. (1985). Sexual functioning morbidity among cancer survivors. Current status and future research directions. *Cancer, 55,* 1835–1842.

Andersen, B.L. (1996). Predicting and treating the sexual difficulties of gynecologic cancer survivors. *Cancer Control, 3,* 113–119.

Andersen, B.L., Anderson, B., & deProsse, C. (1989). Controlled prospective longitudinal study of women with cancer: I. Sexual functioning outcomes. *Journal of Consulting and Clinical Psychology, 57,* 683–691.

Anderson, B., & Lutgendorf, S. (1997). Quality of life in gynecologic cancer survivors. *CA: A Cancer Journal for Clinicians, 47,* 218–225.

Annon, J. (1976). The PLISSIT model: A proposed conceptual scheme for the behavioral treatment of sexual problems. *Journal of Sex Education and Therapy, 2*(2), 1–15.

Auchincloss, S. (1991). Sexual dysfunction after cancer treatment. *Journal of Psychosocial Oncology, 9*(2), 23–43.

Bancroft, J., O'Carroll, R., McNeilly, A., & Shaw, R.W. (1984). The effects of bromocriptine on the sexual behavior of hyperprolactinaemic man: A controlled case study. *Clinical Endocrinology, 21,* 131–137.

Barni, S., & Mondin, R. (1997). Sexual dysfunction in treated breast cancer patients. *Annals of Oncology, 8,* 149–153.

Basson, R., Berman, J., Burnett, A., Derogatis, L., Ferguson, D., Fourcroy, J., et al. (2000). Report of the international consensus development conference on female sexual dysfunction: Definitions and classifications. *Journal of Urology, 163,* 888–893.

Beckham, J., & Godding, P. (1990). Sexual dysfunction in cancer patients. *Journal of Psychosocial Oncology, 8*(1), 1–16.

Burke, L.M. (1996). Sexual dysfunction following radiotherapy for cervical cancer. *British Journal of Nursing, 5,* 239–244.

Cain, E.N., Kohorn, E.I., Quinlan, D.M., Latimer, K., & Schwartz, P.E. (1986). Psychosocial benefits of a cancer support group. *Cancer, 57,* 183–189.

Capone, M.A., Good, R.S., Westie, K.S., & Jacobson, A.F. (1980). Psychosocial rehabilitation of gynecologic oncology patients. *Archives of Physical Medicine and Rehabilitation, 61,* 128–132.

Cartwright-Alcarese, F. (1995). Addressing sexual dysfunction following radiation therapy for a gynecologic malignancy. *Oncology Nursing Forum, 22,* 1227–1232.

Clayton, A.H., McGarvey, E.L., & Clavet, G.J. (1997). The Changes in Sexual Functioning Questionnaire (CSFQ): Development, reliability, and validity. *Psychopharmacology Bulletin, 33,* 731–745.

Daker-White, G. (2002). Reliable and valid self-report outcome measures in sexual (dys)function: A systematic review. *Archives of Sexual Behavior, 31,* 197–209.

DeCherney, A.H. (2000). Hormone receptors and sexuality in the human female. *Journal of Women's Health and Gender-Based Medicine*, *9*(Suppl. 1), S9–S13.

Dennerstein, L., Anderson-Hunt, M., & Dudley, E. (2002). Evaluation of a short scale to assess female sexual functioning. *Journal of Sex and Marital Therapy, 28,* 389–397.

Derogatis, L.R. (1997). The Derogatis Interview for Sexual Functioning (DISF/DISF–SR): An introductory report. *Journal of Sex and Marital Therapy, 23,* 291–304.

Dornan, W.A., & Malsbury, C.W. (1989). Neuropeptides and male sexual behavior. *Neuroscience and Biobehavioral Reviews, 13*(1), 1–15.

Everitt, B.J., Cador, M., & Robbins, T.W. (1989). Interactions between the amygdala and ventral striatum in stimulus-reward associations: Studies using a second-order schedule of sexual reinforcement. *Neuroscience, 30*(1), 63–75.

Ezzell, P. (1999). Managing the effects of gynecologic cancer treatment on quality of life and sexuality. *Society of Gynecologic Nurse Oncologists, 8*, 23–26.

Feldman, J.E. (1989). Ovarian failure and cancer treatment: Incidence and interventions for premenopausal women. *Oncology Nursing Forum, 16,* 651–657.

Franks, S., Jacobs, H.S., Martin, N., & Nabarro, J.D. (1978). Hyperprolactinaemia and impotence. *Clinical Endocrinology, 8,* 277–287.

Frohlich, P.F., & Meston, C.M. (2000). Evidence that serotonin affects female sexual functioning via peripheral mechanisms. *Physiology and Behavior, 71,* 383–393.

Gallo-Silver, L. (2000). The sexual rehabilitation of persons with cancer. *Cancer Practice, 8,* 10–15.

Ganz, P.A., Desmond, K.A., Belin, T.R., Meyerowitz, B.E., & Rowland, J.H. (1999). Predictors of sexual health in women after a breast cancer diagnosis. *Journal of Clinical Oncology, 17,* 2371–2380.

Ganz, P.A., Desmond, K.A., Leedham, B., Rowland, J.H., Meyerowitz, B.E., & Belin, T.R. (2002). Quality of life in long-term, disease-free survivors of breast cancer: A follow-up study. *Journal of the National Cancer Institute, 94,* 39–49.

Ganz, P.A., Greendale, G.A., Petersen, L., Zibecchi, L., Kahn, B., & Belin, T.R. (2000). Managing menopausal symptoms in breast cancer survivors: Results of a randomized controlled trial. *Journal of the National Cancer Institute, 92,* 1054–1064.

Ganz, P.A., Rowland, J.H., Desmond, K., Meyerowitz, B.E., & Wyatt, G.E. (1998). Life after breast cancer: Understanding women's health-related quality of life and sexual functioning. *Journal of Clinical Oncology, 16,* 501–514.

Gitlin, M.J. (1994). Psychotropic medications and their effects on sexual function: Diagnosis, biology, and treatment approaches. *Journal of Clinical Psychiatry, 55,* 406–413.

Goldstat, R., Briganti, E., Tran, J., Wolfe, R., & Davis, S. (2003). Transdermal testosterone therapy improves well-being, mood, and sexual function in premenopausal women. *Menopause, 10*(5), 390–398.

Graziottin, A. (2001). Sexuality after breast cancer. *Menopausal Medicine, 9*(3), 1–4.

Greendale, G.A., Lee, N.P., & Arriola, E.R. (1999). The menopause. *Lancet, 353,* 571–580.

Greendale, G.A., Petersen, L., Zibecchi, L., & Ganz, P.A. (2001). Factors related to sexual function in postmenopausal women with a history of breast cancer. *Menopause, 8,* 111–119.

Hughes, M.K. (2000). Sexuality and the cancer survivor: A silent coexistence. *Cancer Nursing, 23,* 477–482.

Jarkander-Rolff, M., Nathorst-Boos, J., Carlstrom, K., & von Schoultz, B. (2001). Treatment with percutaneous testosterone gel in women with sexual arousal disorder [Abstract]. *Proceedings of the North American Menopause Society Conference, IV,* 88.

Kaplan, H.S. (1974). Basic principles of sex therapy. In *The new sex therapy: Active treatment of sexual dysfunctions* (pp. 187–220). New York: Random House.

Kaplan, H.S. (1992). A neglected issue: The sexual side effects of current treatments for breast cancer. *Journal of Sex and Marital Therapy, 18*(1), 3–19.

Laumann, E.O., Paik, A., & Rosen, R.C. (1999). Sexual dysfunction in the United States: Prevalence and predictors. *JAMA, 281,* 537–544.

Loprinzi, C.L., Kugler, J.W., Sloan, J.A., Mailliard, J.A., LaVasseur, B.I., Barton, D.L., et al. (2000). Venlafaxine in management of hot flashes in survivors of breast cancer: A randomised controlled trial. *Lancet, 356,* 2059–2063.

Mazer, N.A., Leiblum, S.R., & Rosen, R.C. (2000). The Brief Index of Sexual Functioning for Women (BISF-W): A new scoring algorithm and comparison of normative and surgically menopausal populations. *Menopause, 7,* 350–363.

McCoy, N., & Matyas, J. (1998). McCoy Female Sexuality Questionnaire. In C.M. Davis, W.L. Yarber, R. Bauserman, G. Schreer, & S.L. Davis (Eds.), *Handbook of sexuality-related measures* (pp. 249–251). Thousand Oaks, CA: Sage.

McCoy, N.L. (1998). Methodological problems in the study of sexuality and the menopause. *Maturitas, 29*(1), 51–60.

McPhail, G., & Smith, L.N. (2000). Acute menopause symptoms during adjuvant systemic treatment for breast cancer: A case-control study. *Cancer Nursing, 23,* 430–443.

Melis, M.R., & Argiolas, A. (1995). Dopamine and sexual behavior. *Neuro-*

science and Biobehavioral Reviews, 19(1), 19–38.
Meston, C., & Frohlich, P. (2000). The neurobiology of sexual function. *Archives of General Psychiatry, 57,* 1012–1030.
Myers, L.S., Dixon, J., Morrissette, D., Carmichael, M., & Davidson, J.M. (1990). Effects of estrogen, androgen, and progestin on sexual psychophysiology and behavior in postmenopausal women. *Journal of Clinical Endocrinology and Metabolism, 70,* 1124–1131.
Paice, J.A., Penn, R.D., & Ryan, W.G. (1994). Altered sexual function and decreased testosterone in patients receiving intraspinal opioids. *Journal of Pain and Symptom Management, 9,* 126–131.
Persky, H., Dreisbach, L., Miller, W.R., O'Brien, C.P., Khan, M.A., Lief, H.I., et al. (1982). The relation of plasma androgen levels to sexual behaviors and attitudes of women. *Psychosomatic Medicine, 44,* 305–319.
Persky, H., Lief, H.I., Strauss, D., Miller, W.R., & O'Brien, C.P. (1978). Plasma testosterone level and sexual behavior of couples. *Archives of Sexual Behavior, 7,* 157–173.
Rosen, R., Brown, C., Heiman, J., Leiblum, S., Meston, C., Shabsigh, R., et al. (2000). The Female Sexual Function Index (FSFI): A multidimensional self-report instrument for the assessment of female sexual function. *Journal of Sex and Marital Therapy, 26,* 191–208.
Sarrel, P.M. (2000). Effects of hormone replacement therapy on sexual psychophysiology and behavior in postmenopause. *Journal of Women's Health and Gender-Based Medicine, 9*(Suppl. 1), S25–S32.
Schag, C.A., Ganz, P.A., & Heinrich, R.L. (1991). Cancer Rehabilitation Evaluation System–Short Form CARES–SF: A cancer specific rehabilitation and quality of life instrument. *Cancer, 68,* 1406–1413.
Schover, L.R., Evans, R.B., & von Eschenbach, A.C. (1987). Sexual rehabilitation in a cancer center: Diagnosis and outcome in 384 consultations. *Archives of Sexual Behavior, 16,* 445–461.
Schwartz, M.F., Bauman, J.E., & Masters, W.H. (1982). Hyperprolactinemia and sexual disorders in men. *Biological Psychiatry, 17,* 861–876.
Shell, J.A. (2002). Evidence-based practice for symptom management in adults with cancer: Sexual dysfunction. *Oncology Nursing Forum, 29,* 53–66.
Sherwin, B.B., & Gelfand, M.M. (1987). The role of androgen in the maintenance of sexual functioning in oophorectomized women. *Psychosomatic Medicine, 49,* 397–409.
Sherwin, B.B., Gelfand, M.M., & Brender, W. (1985). Androgen enhances sexual motivation in females: A prospective, crossover study of sex steroid administration in the surgical menopause. *Psychosomatic Medicine, 47,* 339–351.
Shifren, J.L., Braunstein, G.D., Simon, J.A., Casson, P.R., Buster, J.E., Redmond, G.P., et al. (2000). Transdermal testosterone treatment in women with impaired sexual function after oophorectomy. *New England Journal of Medicine, 343,* 682–688.
Sloan, J.A., Aaronson, N., Cappelleri, J.C., Fairclough, D.L., & Varricchio, C. (2002). Assessing the clinical significance of single items relative to summated scores. *Mayo Clinic Proceedings, 77,* 479–487.
Sloan, J.A., Loprinzi, C.L., Kuross, S.A., Miser, A.W., O'Fallon, J.R., Mahoney, M.R., et al. (1998). Randomized comparison of four tools measuring overall quality of life in patients with advanced cancer. *Journal of Clinical Oncology, 16,* 3662–3673.
Stuart, F.M., Hammond, D.C., & Pett, M.A. (1987). Inhibited sexual desire in women. *Archives of Sexual Behavior, 16,* 91–106.
Taylor, J.F., Rosen, R.C., & Leiblum, S.R. (1994). Self-report assessment of female sexual function: Psychometric evaluation of the Brief Index of Sexual Functioning for Women. *Archives of Sexual Behavior, 23,* 627–643.
Thors, C.L., Broeckel, J.A., & Jacobsen, P.B. (2001). Sexual functioning in breast cancer survivors. *Cancer Control, 8,* 442–448.
Warnock, J.K., Bundren, J.C., & Morris, D.W. (1999). Female hypoactive sexual disorder: Case studies of physiologic androgen replacement. *Journal of Sex and Marital Therapy, 25,* 175–182.
Wilmoth, M.C. (2001). The aftermath of breast cancer: An altered sexual self. *Cancer Nursing, 24,* 278–286.
Wilmoth, M.C., & Botchway, P. (1999). Psychosexual implications of breast and gynecologic cancer. *Cancer Investigation, 17,* 631–636.
Woodrum, S.T., & Brown, C.S. (1998). Management of SSRI-induced sexual dysfunction. *Annals of Pharmacotherapy, 32,* 1209–1215.
World Health Organization. (2003). Sexual health: Working definitions. Retrieved October 27, 2003, from http://www.who.int/reproductive-health/gender/sexual_health.html
Young-McCaughan, S. (1996). Sexual functioning in women with breast cancer after treatment with adjuvant therapy. *Cancer Nursing, 19,* 308–319.
Zibecchi, L., Greendale, G.A., & Ganz, P.A. (2003). Comprehensive menopausal assessment: An approach to managing vasomotor and urogenital symptoms in breast cancer survivors. *Oncology Nursing Forum, 30,* 393–407.

The continuing education examination and test form for the preceding article appear on the following pages.