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# **Urogenital Atrophy in Breast Cancer Survivors**

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bout 3.5 million women in the United States are living with breast cancer, 89% of whom reach their five-year survival mark after diagnosis (Jemal et al., 2009). Breast cancer mortality rates continue to improve with an accompanying increase in length of disease-free survival. This trend is the result of improvements in early detection and advances in treatment, allowing the vast majority of women to survive their breast cancer experience with a near-normal life expectancy or extended years of life before recurrence (Jemal et al.). Despite this improved quantity of life, side effects from breast cancer treatment can decrease quality of life (QOL). Unpleasant symptoms often are experienced secondary to consequences of diagnosis and the life-extending treatments of chemotherapy, hormonal therapy, hormone agonists, and ovarian ablation (Santoro, 2005; Woods & Mitchell, 2005). The purpose of this article is to discuss urogenital atrophy in breast cancer survivors, including the full range of symptoms of urologic, genital, and sexual symptoms. The Theory of Unpleasant Symptoms will be used to illustrate the effect(s) of influencing factors on symptoms and performance outcomes.

# **Urogenital Atrophy**

Urogenital atrophy is defined by the presence of subjective and objective urologic, genital, and sexual symptoms. Urologic symptoms include patient-reported symptoms describing urgency, urge incontinence, stress incontinence, dysuria or burning, pressure and frequency, recurrent urinary tract infections, and dryness. Genital symptoms include vaginal bleeding, burning, discharge or vaginitis, itching, irritation, soreness or tenderness, and dryness. Sexual symptoms include dyspareunia, decreased sexual satisfaction, difficulty in sexual arousal, loss of interest in sexual activity or decreased libido, vaginal discharge, decreased closeness with partner, and dryness (Barton, Wilwerding, Carpenter, & Loprinzi, 2004; Ganz, Desmond, Belin, Meyerow**Purpose/Objectives:** To review the symptoms of urogenital atrophy in breast cancer survivors, influencing factors, and their effects on performance.

**Data Sources:** Review of qualitative and quantitative research data that describe pain, function, satisfaction, and quality of life related to urologic, genital, and sexual function.

**Data Synthesis:** Breast cancer treatment can induce or exacerbate symptoms related to urogenital atrophy. The lower urinary and genital tracts are affected by physiologic alterations, the potential abrupt onset of menopause, and treatment side effects. Symptoms of urogenital atrophy often are more prevalent and severe in women treated for breast cancer than in age-matched women without breast cancer.

**Conclusions:** Symptoms related to urogenital atrophy are common in breast cancer survivors and can be affected by physiologic, situational, and psychological influences with negative effects on performance. Research is essential to the understanding of how transient or permanent hormonal alterations affect the urogenital system and the role of these symptoms on quality of life.

**Implications for Nursing:** Nurses must listen with sensitivity to breast cancer survivors and their descriptions of these significant and life-altering symptoms. Personalized discussion enables the nurse to explore issues, assess symptoms, recommend interventions, and evaluate at follow-up visits. Nurses are integral to the provision of survivorship care planning that can address the short- and long-term effects of a cancer diagnosis and related treatments.

itz, & Rowland, 1999; Gupta et al., 2006; Santoro, 2005). The subjective complaint of vaginal dryness is the most common symptom related to urogenital atrophy (Vega, 2007). A general decrease in QOL also is commonly reported (Morali et al., 2006).

Urogenital atrophy symptoms often are underreported by women and underaddressed by clinicians in clinical practice (Johnston & Farrell, 2004; Kelley, 2007). Women may be reluctant to discuss concerns related to urogenital atrophy because of embarrassment, cultural taboos, fear of lack of treatment, and concern about reactions to such intimate matters. Clinicians may be reluctant to ask because of a lack of expertise in assessment and treatment, lack of time, and uncertainty about treatment options (Krychman, 2007). Unfortunately, many women do not seek care even when moderate-to-severe symptoms are present (van Geelen, Van De Weijer, & Arnolds, 2000). Therefore, unpleasant symptoms may go unidentified and untreated, leading to increased pain and discomfort, urinary tract infections, and impaired sexual QOL caused by dryness, thinning tissues, and a decreased vaginal pH (Avis, Crawford, & Manuel, 2005; Henson, 2002; McKenna, Whalley, Renck-Hooper, Carlin, & Doward, 1999; Woods & Mitchell, 2005; Zibecchi, Greendale, & Ganz, 2003).

Urogenital atrophy is related to hormonal changes of the perimenopausal and menopausal periods in the life cycle of women. Originally thought to be a period of gradual, dwindling hormone production, the menopausal transition can be marked by adverse symptoms and fluctuating hormone levels that cause changes in the urogenital tract (Kelley, 2007). The onset of urogenital atrophy often is insidious and the prevalence and severity of symptoms is variable, although not all women experience these symptoms. Even so, at least one urogenital symptom is reported by 40% of postmenopausal women (Barlow, Samsioe, & van Geelen, 1997). Urogenital symptoms may occur after other menopausal hallmarks, such as vasomotor symptoms, have abated.

#### Pathophysiology

The pathophysiology of urogenital atrophy is related to estrogen receptors found in the structures of the lower urinary and genital tracts, including pelvic floor muscles, urethra, bladder, uterus, ovaries, vaginal walls, and external genitalia, including the mons pubis, labia majora and minora, clitoris, vestibule, Skene and Bartholin glands, and urethral meatus. These structures respond similarly to the estrogen loss that occurs as a result of menopause, postpartum changes, lactation, and hypothalamic amenorrhea. Degeneration of tissues occurs with decreases in size and blood flow, vaginal secretions, loss of elasticity, thinning of tissues, increase in pH, and overall structure atrophy (Kelley, 2007; Morali et al., 2006). This atrophic and dry vaginal epithelium, thinned endometrium, and increased pH predispose the woman to infection and mechanical weakness, with symptoms of vaginal dryness, loss of pelvic support, decreased tissue elasticity, dyspareunia, voiding changes, and overall urogenital discomfort. Additive influences on these structures include concomitant illness(s) or the use of pharmacologic agents that can hasten or aggravate the menopausal transition (Goodwin, Ennis, Pritchard, Trudeau, & Hood, 1999; Gupta et al., 2006).

#### Assessment

Visualization of the external genitalia may indicate atrophy and loss of connective tissue, with atrophy of the labia majora, absence of the labia minora, and narrowing of the vaginal introitus. Internal vaginal visualization may demonstrate atrophy of the vaginal canal and epithelium, with loss of vaginal rugae. The tissue may appear pale and dry, yet friable with submucosal petechiae. Physical examination may reveal decreased elasticity and pliability, minimal lubrication, and pelvic organ prolapse. The vaginal pH is typically greater than 5, with a vaginal wall maturation index indicative of a shift toward basal cellularity (Krychman, 2007). However, the absence of such anatomic changes does not necessarily mean the absence of subjective symptoms related to urogenital atrophy (Ballagh, 2005; Willhite & O'Connell, 2001).

Subjective symptoms of urogenital atrophy are not easily quantifiable and may be difficult to correlate with physical findings. Differences exist between selfreported and observed clinical symptoms, indicating potential assessment bias that could interfere with beneficial interventions (Ballagh, 2005; Willhite & O'Connell, 2001). Healthcare providers may neglect appropriate assessment in women who take systemic hormone replacement therapy by erroneously assuming that symptoms are absent.

# Urogenital Atrophy in Breast Cancer Survivors

A breast cancer diagnosis often coincides with menopause, with treatment modalities that either induce or exacerbate menopausal symptoms that are often more severe than in women without breast cancer (Ganz et al., 2000; Zibecchi et al., 2003). A constellation of unpleasant menopausal symptoms, including those related to urogenital atrophy, may occur. Life-extending treatments for breast cancer can diminish or eradicate ovarian function and cause acute or chronic urogenital atrophy.

Ovarian toxicity from chemotherapy, specifically alkylating agents, can induce symptoms of menopause such as alterations in menstrual cycles, dyspareunia, and vaginal dryness. The use of multiple agents in adjuvant therapy increases the risk of premature menopause, which has been reported in the range of 53%–89% (Del Mastro, Venturini, Sertoli, & Rosso, 1997). The effects of drugs on ovaries are measured by follicular destruction—the number of follicles a woman has at the onset of chemotherapy is related to her age and influences outcomes, including amenorrhea. The permanence of amenorrhea, the proxy measurement of ovarian function after chemotherapy, is directly related to a woman's age, type of chemotherapy, and its duration and cumulative dosage (Boekhout, Beijnen, & Schellens, 2006; Knobf, 1998).

Women younger than age 40 are less likely to have permanent amenorrhea than women aged 40 years or older. Even so, younger women may experience longterm menstrual irregularities as a result of chemotherapy and have a greater risk of experiencing menopause at an early age (Ganz, Greendale, Petersen, Kahn, & Bower, 2003; Knobf, 1998). This premature menopause increases the likelihood of symptoms, such as vaginal dryness and atrophy, with resulting decrease in QOL and sexual function. Hormonal treatments and ovarian ablation contribute to vaginal atrophy because of reduced circulating estradiol levels (Stricker, 2007). Women who previously experienced surgical menopause with bilateral oophorectomy or experience it after a breast cancer diagnosis may experience even more pronounced symptoms of estrogen deficiency (Gupta et al., 2006).

#### Prevalence

Research on the full range of symptoms related to urogenital atrophy has not been conducted in breast cancer survivors; however, studies demonstrate the prevalence of various symptoms of urogenital atrophy. Glaus et al. (2006) evaluated 373 women with breast cancer who completed a self-assessment tool measuring 13 side effects associated with hormonal treatment, specifically tamoxifen. Women with early (n = 301) and advanced disease (n = 72) reported symptoms of vaginal dryness (34%), decreased sexual interest (29%), vaginal discharge (12%), and vaginal bleeding (2%). Analysis of data demonstrated a cluster of menopausal symptoms, including hot flashes, weight gain, tiredness, reduced sexual interest, and vaginal dryness.

Gupta et al. (2006) studied the prevalence and severity of menopausal symptoms in women (aged 29–65 years) treated for breast cancer (N = 202) and their perceived effects on QOL. Sexual issues were reported by 60% of women, urinary issues by 55%, and vaginal dryness by 55%. Highly significant correlations were noted between vaginal dryness, urinary and sexual issues, and QOL. Gupta et al. concluded that menopausal symptoms, including symptoms related to urogenital atrophy, significantly affect a woman's and her partner's QOL.

Sexuality following breast cancer was examined in breast cancer survivors (N = 863) who had been previously studied for health-related QOL and sexuality related to their diagnosis (Meyerowitz, Desmond, Rowland, Wyatt, & Ganz, 1999). Participants had completed surgical and adjuvant treatment for breast cancer, although some women remained on tamoxifen during the study period. Vaginal dryness was noted in 52% of breast cancer survivors, with a resulting significant negative effect (p = 0.0005) on their sex lives. Sexually active women (38%) reported very little or no lubrication when excited, compared to 14% prior to their diagnosis. Significant (p < 0.0001) genital pain was experienced by 26% of women compared to 7% before diagnosis, and this pain interfered with sexual pleasure.

The physiologic health effects of breast cancer treatment and their relationship to menopausal symptoms and QOL in breast cancer survivors were studied by Schultz, Klein, Beck, Stava, and Sellin (2005). Breast cancer survivors (N = 291) were queried about QOL issues including self-reported health effects of cancer treatment and effects of their cancer experience on family and partners. Painful intercourse was reported by 63% of the responders, and was more frequently reported by younger women (p = 0.02). The authors concluded that the relationship among menopausal symptoms, QOL, and cancer treatment effects is complex and must be studied in breast cancer survivors (Schultz et al.).

#### Urogenital Atrophy in Breast Cancer Recurrence

Little documentation exists about the multiple and cumulative effects of treatment drugs on symptoms related to urogenital atrophy with breast cancer recurrence (Lee et al., 2007; Oh et al., 2004). Andersen, Carpenter, Yang, and Shapiro (2007) studied sexual well-being among partnered breast cancer survivors with recurrent disease by comparing women free of disease (n = 120) to women experiencing a breast cancer recurrence (n = 73). While the groups rated their sexual lives as somewhat inadequate, the only statistically significant (p = 0.03) difference between the groups was frequency of intercourse. Younger women (aged 29–51 years) as compared to older women (aged 52-81 years) with breast cancer recurrence were more likely to report this decline in their view of sexual life (p = 0.1). Based on the findings, the researchers inferred that women with recurrent breast cancer rated their level of sexual satisfaction, albeit less frequent intercourse, the same as their age-matched counterparts without recurrent breast cancer, and identified sexual activity as a measure of QOL.

# Urogenital Atrophy and the Theory of Unpleasant Symptoms

The exploration of self-reported symptoms of urogenital atrophy using the Theory of Unpleasant Symptoms (Lenz & Pugh, 2003) (see Figure 1) can improve understanding of the complex urogenital symptom experience. A symptom domain can occur by itself, in combination with another, or in an overlapping pattern that includes all domains. The symptoms of urogenital atrophy can be individual, multiplicative, additive, catalytic, related, or unrelated, but all are individually multidimensional with dimensions of distress, timing, intensity, and



#### Figure 1. Symptoms of Urogenital Atrophy

Note. From "The Middle-Range Theory of Unpleasant Symptoms: An Update," by E.R. Lenz, L.C. Pugh, R.A. Milligan, A. Gift, & F. Suppe, 1997, Advances in Nursing Science, 19(3), p. 17. Copyright 1997 by Lippincott Williams and Wilkins. Adapted with permission.

quality. Categorization of symptoms within the theoretical framework provide useful information to examine individual, concurrent, and concomitant symptoms, as well as performance and feedback with reciprocal influences on factor(s) or symptom groups.

The Theory of Unpleasant Symptoms focuses on subjective symptoms perceived by the woman, not objective symptoms observed by the clinician. This requirement commands the clinician to be more involved with the patient's perception of the symptom and prevents clinical decision making based on objective measurement only. The model allows for dynamic change with chronic, persistent symptom profiles or acute changes.

The multidimensional symptom experience of urogenital atrophy in breast cancer survivors can be influenced by related and interacting physiologic, psychological, and situational factors that affect functional outcomes (see Figure 2). Influences unique to women with breast cancer can include chemotherapy and hormonal therapies, estrogen deficiency states, and alterations in hormone conversion. The uncertainty of the cancer diagnosis, coupled with bodily image changes, can create distress and depression. The integrity of intimate relationships can be challenged by menopausal changes, fatigue, birth control, and fertility issues. These factors create a dynamic balance of influences that potentially affect the woman.

Performance is based on direct or indirect consequences of the presence (or absence) of symptoms and related influences. Alterations in performance are specific to each individual; what might be inadequate performance for one woman may be quite acceptable for another.

### Discussion

The prevalence of symptoms related to urogenital atrophy is apparent in women with and without breast cancer. Many influencing factors are beyond the control of breast cancer survivors and women at increased risk for breast cancer development, as well as others who are unable to take hormonal products for relief. Medications that save lives also can negatively alter lifestyle in a manner that is unacceptable. Women deserve unprecedented attention to their potential life-long alterations in sexual function, relationships, and other body functions. These symptoms often are unidentified and untreated, potentially impairing QOL (Avis et al., 2005; McKenna et al., 1999; Schover, 2008).

The study of unpleasant symptoms, specifically urogenital atrophy, as related to influences of estrogen deficiency and drugs used in breast cancer treatment, are important in breast cancer survivorship (Ganz, 2005; Knobf, 2006). Effects of cancer and related treatments on QOL and long-term survivorship issues remain priority research areas. The Oncology Nursing Society ([ONS], 2008) outlined their research goals in the ONS Research Agenda with attention to six major research areas. The goals referent to urogenital atrophy include research in cancer symptoms and side effects, with a focus on symptom clusters and associated outcomes; individual and family-focused psychological and behavioral research; late effects of treatment and long-term survivorship, with a focus on premature menopause, decreased sexual function, and stress incontinence; and nurse-sensitive patient outcomes. Research outcome goals also include the development of valid instruments to index late effects of survivorship.

A model or theory specific to cancer symptoms is not evident in the literature despite an increase in nursing research related to symptom identification, symptom clusters, and symptom management in patients with cancer. The Theory of Unpleasant Symptoms is a versatile model to study symptoms related to urogenital atrophy in all women, including breast cancer survivors. It enables the nurse and researcher to apply a theoretical framework to assess self-reported symptoms of urogenital atrophy with attention to symptom characteristics; physiologic, situational, and psychologic influences of

#### **Physiologic Influences**

- · Pharmacologics (prescribed and over the counter)
  - Chemotherapy
  - Hormonal therapies
  - Nicotine
- Estrogen deficiency states
  - Diminished ovarian function
  - Lack of exogenous estrogen
  - Altered endogenous supply
- · Alterations in hormone conversion or receptors
- · Changes of lower urologic tract
- Changes of lower genital tract

#### Psychological Influences

- Uncertainty of cancer
  - Diagnosis or recurrence
- Depression
- Distress
- Body image
- Knowledge deficits related to urogenital changes

#### Situational Influences

- Menopausal status
- Fatigue
- Relationship integrity
- Communication with healthcare team
- Fertility, birth control, and childbearing issues
- Figure 2. Influences on Symptoms of Urogenital Atrophy

breast cancer and treatment on the symptoms; and the resulting effects on performance. Objective signs can be correlated with subjective symptoms to explore alterations, accurately diagnose issues, and adequately treat with maximal satisfaction and outcomes. Most importantly, each woman can be treated as an individual with personalized care.

The notion of symptom clusters is of interest in cancerrelated symptoms and may be applicable to symptoms related to urogenital atrophy. Barsevick (2007) provided a summary of models of symptoms and symptom clusters and reinforced that the true operational definition of symptom clusters remains unclear. Whether the clustering of symptoms is efficacious in research, or if crossover treatments reliably affect more than one symptom, is unknown. Fatigue, insomnia, pain, and depression have been defined as a cancer symptom cluster (Carpenter et al., 2004), although oncology clinicians continue to identify other combinations of related symptoms. The components of urogenital atrophy create a cluster of related symptoms in breast cancer survivors, particularly when considering urinary, genital, and sexual symptoms. Perhaps this collection of symptoms is a cluster unique to women with breast cancer.

#### Summary

Urogenital atrophy occurs on a continuum and can become more severe as estrogen levels continue to drop, underlining the importance of identification of symptoms to decrease the experience of unpleasant symptoms and potential sexual dysfunction (Henson, 2002). Assessment of urogenital symptoms in the clinical setting may be hierarchically averted as a result of attention to multiple other issues involved in the cancer trajectory.

Research is needed to explore these symptoms, their influencing factors, and resulting effects on performance. Lack of comfort by the patient or the oncology healthcare team in readily discussing these issues may further decrease prioritization with perceived feelings by the patient of lack of attention to her significant issues. Oncology nurses must listen with sensitivity to breast cancer survivors and their descriptions of these significant and life-altering symptom, and continue the search for safe and effective interventions.

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