Joan, a 55-year-old woman, presented to the gynecologic oncology clinic after her physician palpated an adnexal mass on the left ovary. She also reported mild abdominal bloating for the past four months but otherwise felt fine.

Her past medical history was remarkable for stage IIB unilateral breast cancer at age 40; she was treated with a left lumpectomy, chemotherapy, radiation, and tamoxifen for five years. Subsequently, she was without disease recurrence. Her obstetrical and gynecologic history included two full-term pregnancies; breast-feeding of both babies for six months; menstruation at age 12; and menopause induced by breast cancer chemotherapy treatment at age 41. Prior birth control methods included the diaphragm for 12 years. She also reported occasional talc use over the past 20 years.

Her physical examination was unremarkable except for a 7 cm mass palpated on the left ovary. Transvaginal ultrasound revealed a complex mass in the left adnexa measuring 8.2 cm x 2.7 cm (normal ovaries measure about 2 cm x 3 cm). Surrounding the ovary was a tubular cystic interface. The cyst borders appeared very irregular, and the power Doppler showed large tortuous vessels within the ovarian tissue. The right ovary measured 3.8 cm x 2.5 cm. The final ultrasound reading indicated, “malignancy cannot be excluded.”

Joan was taken to surgery the following week for exploratory laparotomy. At that time, she had a total abdominal hysterectomy, bilateral salpingo-oophorectomy, and lymph node biopsy. Pathology confirmed a diagnosis of stage IIC ovarian cancer, characterized by abdominal metastasis and positive lymph nodes.

Advances in surgery and treatment modalities have slightly improved five-year survival rates, but the prognosis for most women continues to be poor. Rectovaginal examination, ultrasound, and the CA-125 blood test are three modalities currently used to screen for ovarian cancer, although no universal ovarian cancer screening guidelines are recommended for the general population. Developments in the early detection of ovarian cancer are emerging and include blood tests that could lead to identifying asymptomatic, early-stage ovarian cancer. Nurses should be knowledgeable about these developments in ovarian cancer as they educate women about ovarian cancer risk, prevention, and early detection.

Key Words: ovarian neoplasms, CA-125 antigen, ultrasonography

Ovarian cancer is the leading cause of gynecologic cancer deaths and the fifth leading cause of cancer deaths among American women. Advances in surgery and treatment modalities have slightly improved five-year survival rates, but the prognosis for most women continues to be poor. Rectovaginal examination, ultrasound, and the CA-125 blood test are three modalities currently used to screen for ovarian cancer, although no universal ovarian cancer screening guidelines are recommended for the general population. Developments in the early detection of ovarian cancer are emerging and include blood tests that could lead to identifying asymptomatic, early-stage ovarian cancer. Nurses should be knowledgeable about these developments in ovarian cancer as they educate women about ovarian cancer risk, prevention, and early detection.

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**Epidemiology**

The majority of cases of ovarian cancer are diagnosed in an advanced stage because it presents with few, if any, distinctive symptoms. These subtle symptoms may include abdominal bloating and discomfort; dyspepsia; changes in bowel or bladder function, including constipation and urge urinary incontinence; and unexplained weight loss or gain. These symptoms are fairly vague and often are seen only after the extensive spread of ovarian cancer. Symptoms often are so subtle that they are dismissed or misdiagnosed by healthcare providers. Because of a lack of specific or early warning symptoms, the accurate detection of early-stage disease remains a challenge (Ozols, Robboy, Rubin, & Thomas, 1997). Figure 1 includes some epidemiologic facts about ovarian cancer.

**Risk Factors**

The first step in evaluating a woman’s risk for ovarian cancer is a thorough review of her personal and family health history. Women...
such as Joan illustrate why risk assessment is so important. Knowledge of the risk factors associated with ovarian cancer is essential for nurses to tailor patient care and teaching. Without an accurate and comprehensive risk assessment, selecting appropriate strategies for cancer prevention and early detection is impossible (Mahon, 1998, 2000).

**Age**

As with most cancers, increasing age is the most significant risk factor for the development of ovarian cancer. Women aged 75–79 have the highest incidence of ovarian cancer, with a rate of 60 cases per 100,000 women. The mean age for developing ovarian cancer in the United States is 58 years (National Cancer Institute, 2002). Incessant ovulation over time is one theory that may help to explain why age is a significant risk factor in ovarian cancer development (Ozols et al., 1997).

**Personal History of Cancer**

A personal history of breast or colon cancer increases the risk for developing ovarian cancer three to four times more than the general population’s risk. In women diagnosed with breast cancer before age 50, the risk of developing ovarian cancer increases as much as fourfold (Suris-Swartz, Schildkraut, Vine, & Hertz-Picciotto, 1996). The association between breast and ovarian cancer may be a function of shared risk factors and, in select cases, a common genetic basis including an inherited mutation for BRCA1 and BRCA2 (Costalas & Daly, 1999). Breast and ovarian cancer also share an increased incidence among women of higher socioeconomic status, suggesting a role for environmental or lifestyle factors. The precise nature of these risk factors is not understood clearly.

A personal history of colon cancer increases the risk of developing ovarian cancer, especially in women diagnosed with colon cancer before age 50 (Hall, Jamison, & Weir, 2001). The association between colon and ovarian cancer appears to be bidirectional (i.e., colon cancer risk increases after ovarian cancer, and ovarian cancer risk increases after colon cancer), although most women who develop ovarian cancer will not survive long enough for the risk of colon cancer to become a factor (Gold & Neugut, 1999). The risk of developing multiple primary cancers of the colon and ovary may be related to hormonal and nutritional interactions or their relationship with regard to hereditary nonpolyposis colorectal cancer (HNPCC) syndrome (Westhoff & Zimmerman, 1999). HNPCC syndrome is an inherited syndrome that may increase a person’s risk of developing colon, endometrial, and ovarian cancers.

**Family History of Cancer**

A family history of ovarian cancer can significantly increase a woman’s risk of developing ovarian cancer. Joan is worried that her daughters are at higher risk because of her history of ovarian and breast cancer. When a woman has one first-degree relative affected with ovarian cancer, her chance of developing ovarian cancer by age 70 increases from 1.8% to 4.7% (Stratton, Pharoah, Smith, Easton, & Ponder, 1998). Having two first-degree relatives affected with ovarian cancer increases the risk to 7%–10% (Kerlikowski, Brown, & Grady, 1992).

An inherited genetic mutation is the causative factor in 5%–10% of cases of epithelial ovarian cancer. A BRCA1 mutation may increase a woman’s risk of developing ovarian cancer by age 70 by 20%–44% (Ford, Easton, Bishop, Narod, & Goldgar, 1994). A BRCA2 mutation may increase the risk of developing ovarian cancer 10%–27% (Ford et al., 1998). HNPCC syndrome accounts for 2% of all ovarian cancers and may increase a woman’s risk of developing ovarian cancer as much as 12% (Aarnio et al., 1999).

Assessment of ethnic and religious background also is important. Ashkenazi Jews, Jewish women of Eastern European ancestry, have been found to carry the BRCA1 and BRCA2 mutations at a much higher rate than the general population (Mosleh et al., 2000). About 1 in 40 Ashkenazi Jews are carriers of the BRCA1 and BRCA2 mutations, which may increase their chances of developing breast and ovarian cancer (Mosleh et al.). Figure 2 summarizes the lifetime risk for developing ovarian cancer.

Oncology nurses must have an understanding of cancer genetics and be able to incorporate this knowledge into the care of their patients. Middelton, Dimond, Calzone, Davis, and Jenkins (2002) recently published a comprehensive guide to cancer genetics for nurses. Referring women to genetic counselors, gynecologic oncologists, or advanced practice nurses specializing in risk assessment is appropriate when a hereditary mutation is suspected and a need exists for more specific cancer prevention and detection recommendations. The interaction between personal and family history of cancer can be complicated and may require expert resources to interpret this complex information for patients.

**Undesired Infertility**

Endocrine factors such as nulliparity and infertility have been cited as contributing to the development of ovarian cancer. The increased risk may be related to uninterrupted ovulation or increased levels of hormones associated with ovulation (Ozols et al., 1997). Women who never have been pregnant have a slightly higher risk of developing ovarian cancer as compared to women who have had more than one child. Distinguishing between women who choose infertility versus women who have undesired infertility is important. Women who choose
infertility have lower rates of developing ovarian cancer. This probably is related to the use of oral contraceptives and, in some cases, tubal ligation (Narod et al., 2001). Women who begin mensturating early or start menopause late do not have an increased risk of developing ovarian cancer (Titus-Ernstoff et al., 2001).

Although fertility drugs once were thought to be associated with higher rates of ovarian cancer (Whittemore, Harris, & Imyre, 1992), recent studies have contradicted the idea. No association has been found between use of fertility drugs and epithelial ovarian cancer, although use of fertility drugs is associated with a slight increase in nonmalignant serous tumors (Ness et al., 2000; Titus-Ernstoff et al., 2001).

**Diet and Obesity**

Industrialized nations have the highest rates of ovarian cancer, suggesting that certain dietary factors may be associated with an increased risk of developing it. A diet high in fat may increase the risk, and a diet high in fiber may decrease the risk (Risch, Jain, Marrett, & Howe, 1994). In two studies (Kushi et al., 1999; Risch et al.), the increased risk and protective effect seen with certain dietary factors were minimal.

A recent study examining the relationship between obesity and ovarian cancer found a twofold increase in premenopausal ovarian cancer risk with a body mass index (BMI) of 25 kg/m² or higher versus women with a BMI less than 20 kg/m² (Fairfield et al., 2002). Researchers have theorized that endogenous levels of hormones, specifically estrogen, may affect the risk of developing ovarian cancer. In another study, an inverse relationship between increasing body weight and the risk for ovarian cancer was found. This effect may be related to an increased number of anovulatory cycles associated with higher BMI (Lukanova et al., 2002). More studies are needed to clarify the relationship between obesity and ovarian cancer risk.

**Talc**

Perineal talc exposure has been cited as a risk factor in the development of ovarian cancer because of its similarity to asbestos (Chang & Risch, 1997). The theory was refuted with study findings indicating that women who used talc daily for more than 20 years had no increased risk for the development of ovarian cancer (Gertig et al., 2000; Wong, Hempling, Piver, Natarajan, & Mettlin, 1999).

**Hormone Replacement Therapy**

The use of hormone replacement therapy (HRT) recently was linked to an increased risk of ovarian cancer. Women who used estrogen-only therapy, especially those who used estrogen replacement for more than 10 years, were at significantly increased risk for developing ovarian cancer (Lacey et al., 2002). Additional studies evaluating the relationship between HRT and ovarian cancer risk have not been consistent. In one study evaluating various HRT preparations, no significant links were found between ovarian cancer risk and any use of HRT (Sit, Modugno, Weissfeld, Berga, & Ness, 2002).

**Reducing the Risk of Ovarian Cancer**

Although healthcare providers do not know how to completely prevent the development of ovarian cancer, several strategies reduce the risk of developing the disease. Oral contraceptives, pregnancy, breast-feeding, and removal of the ovaries (i.e., oophorectomy) have been shown to lower the risk of developing ovarian cancer. Nurses should be familiar with factors that may reduce the risk of developing ovarian cancer and should develop nursing interventions and educational programs to help raise awareness of these means to reduce the risk.

**Oral Contraceptives**

The risk of developing ovarian cancer decreases 40%–60% with the use of oral contraceptives (Narod et al., 1998; Ness et al., 2000; Walker, Schlesselman, & Ness, 2002). A greater reduction in risk is seen as years of usage increase, and the risk does not differ among women who stop oral contraceptives even 10–30 years earlier (Ness et al.). The mechanism for the reduced risk has been attributed to inhibiting ovulation, suppressing gonadotropins, and inducing an apoptotic response (Schildkraut, Calingaert, Marchbanks, Moorman, & Rodriguez, 2002). In a recent study evaluating the impact of progesterin and estrogen potency on ovarian cancer risk, oral contraceptives with higher progesterin dosages were associated with a greater reduction in ovarian cancer risk independent of the estrogen dosage (Schildkraut et al.).

**Pregnancy and Breast-Feeding**

Pregnancy and breast-feeding also help to lower the risk of developing ovarian cancer, presumably in a similar manner to oral contraceptives. Parous women have lower risks of developing ovarian cancer, and the protective effect increases with more parity. Women with one child have a 40% reduced risk; women with five or more children have an 80% reduced risk. Breast-feeding for an average of three to six months is associated with a 30% reduction in risk as compared to women who never breast-fed (Titus-Ernstoff et al., 2001).

**Salpingo-Oophorectomy**

Removal of the ovaries and fallopian tubes, salpingo-oophorectomy, often is recommended to women with documented mutations in either the BRCA1 or BRCA2 gene. Recent retrospective and prospective data suggest a clear benefit for prophylactic oophorectomy in mutation carriers after a mutation is identified in a family. Removal of healthy ovarian tissue is thought to reduce the risk of ovarian cancer because the susceptible tissue is unavailable to become cancerous. Removal of ovarian tissue also reduces serum estradiol levels, which may further reduce the risk. Evidence also has suggested that prophylactic oophorectomy reduces the risk of breast cancer in mutation carriers (Kauff et al., 2002; Rebbeck et al., 2002).

Prophylactic oophorectomy usually is recommended for women with a known hereditary mutation who are older than 35 or when childbearing is complete (National Institutes of Heath [NIH] Consensus Development Panel on Ovarian Cancer, 1995). Women who undergo prophylactic bilateral salpingo-oophorectomy still are at risk for developing primary peritoneal cancer, which presents similarly to ovarian cancer, although primary peritoneal cancer is relatively rare (Kauff et al., 2002; Rebbeck et al., 2002).

Other risks associated with prophylactic oophorectomy include surgical complications and, more commonly, early menopause. Premature menopause places women at increased risk for osteoporosis and cardiovascular problems. Women with BRCA1 and BRCA2 mutations may not be candidates for HRT because of a personal history of breast cancer or their significantly elevated risk for developing breast cancer. Because the risks and benefits associated with oophorectomy are significant, women considering this procedure need extensive counseling and education so that they can make informed decisions. Genetic testing may enable women to avoid unnecessary surgery, if it can show that they do not carry the mutation associated with affected family members.
Current Screening for Ovarian Cancer

The potential benefit of a screening test for ovarian cancer is the ability to identify the disease in its early stages, when treatment is more likely to be effective. Such a test should have high sensitivity (i.e., a positive test in individuals with the disease) and high specificity (i.e., a negative test in individuals without the disease) with an acceptable positive predictive value (i.e., probability that a person who tests positive has the disease). At present, no such screening test exists for ovarian cancer.

According to NIH, insufficient evidence exists to recommend population-based screening for ovarian cancer because currently available methods have not been shown to be effective in reducing mortality and morbidity from the disease (NIH Consensus Development Panel on Ovarian Cancer, 1995). Recommendations for management of women with known hereditary mutations include participation in clinical screening trials, referral to a gynecologic oncologist, annual bimanual rectovaginal examinations, CA-125 determinations, and ultrasound. Most authorities do not advocate CA-125 and ultrasound for the detection of early-stage ovarian cancer in women at average risk.

A bimanual rectovaginal examination, ultrasound, and CA-125 blood test are three modalities used to screen for ovarian cancer, although their ability to detect early-stage ovarian cancer is poor. Nurses should be aware of the concerns regarding these methods and direct their patients toward the most appropriate management plan based on their personal risk of developing ovarian cancer.

Physical Examination

Ovarian cancer occasionally is detected during bimanual rectovaginal examination, although detection by this method usually reveals advanced disease (Smith & Oi, 1984). This primarily is because of the physical location of the ovaries deep within the abdominal cavity. Physical examination also can be complicated in obese women. Even though the sensitivity and specificity of rectovaginal examination are estimated to be low in the detection of early-stage ovarian cancer, rectovaginal examination is incorporated into most ovarian cancer screening programs as part of a multimodal approach. A Pap smear may detect malignant ovarian cells but is not considered a valuable screening test for ovarian cancer because its sensitivity is estimated to be 10%–30% (Smith & Oi).

CA-125

CA-125 is a glycoprotein that is shed from the cell surface of the fallopian tubes, endometrium, endocervix, peritoneum, pleura, pericardium, and bronchus. CA-125 is elevated (> 35 U/ml) in the blood of 80% of patients with advanced stage epithelial ovarian cancer (Bast et al., 1983). It detects early-stage, asymptomatic ovarian cancer less than 50% of the time (Berek & Bast, 1995). CA-125 is not specific for ovarian cancer.

Elevated levels have been found in women with nongynecologic cancers and with benign gynecologic conditions such as pregnancy, pelvic inflammatory disease, endometriosis, fibroids, and menstruation (Berek & Evans, 1997).

Ultrasound

Ultrasound has demonstrated value in detecting ovarian cancer in asymptomatic women, although the disease was advanced (Cohen & Fishman, 2002). The accuracy of ultrasound in detecting early-stage disease is poor, as demonstrated by results from two large, retrospective studies in high-risk women (Bell, Petticrew, & Sheldon, 1998; van Nagell et al., 2000). The sensitivity for detection of stage I epithelial ovarian cancer was 25% and 31%, respectively. Figure 3 illustrates the differences between benign and malignant masses.

Three-dimensional (3-D) power Doppler is useful in identifying abnormal blood flow and structural changes within ovaries. In a sample of high-risk women, the use of 3-D Doppler improved the ability to distinguish benign from malignant changes. The researchers were unable to determine whether 3-D imaging assisted in improving the identification of stage I ovarian cancer (Cohen, Escobar, Scharm, Glimco, & Fishman, 2001).

Multimodal Approach

The use of CA-125 as a primary screening method, followed by ultrasound if CA-125 is elevated, decreases the number of false positives seen with ultrasound screening alone. In a sample of postmenopausal women who had annual screening with CA-125 and subsequent ultrasound if CA-125 was greater than 30 U/ml, 29 operations were performed to detect six cancers (three at stage I and three at stage III), providing a positive predictive value of 21% (Jacobs et al., 1999).

Future Developments in Screening

New developments in the ability to detect ovarian cancer in an early and highly treatable stage are emerging. The ability to detect ovarian cancer by a simple blood test long has been a goal in medical screening, but another option, an ovarian Pap test, also may assist in identifying early-stage or premalignant disease. The hope is that the combination of an ovarian cancer-specific blood test(s), an ovarian Pap test, and improvements in diagnostic imaging will allow for the accurate identification of early-stage ovarian cancer. Nurses should have a thorough understanding of these screening developments.

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so that they can educate their patients and peers. Nurses can provide comprehensive education about new scientific developments and their clinical applications.

Blood Tests

Proteomic or protein patterns in the blood of women with ovarian cancer can distinguish malignant from benign tumors of the ovaries. Researchers found that a computer could look for patterns among proteins that are characteristic of ovarian cancer and map out a bar code, which could help distinguish cancer from noncancer. In the preliminary study, all samples from women with ovarian cancer were identified correctly, including all women with stage I cancer. In the noncancerous group, 63 of 66 samples were classified accurately. The results yielded 100% sensitivity and 95% specificity. The positive predictive value for the sample was 94% compared to 35% positive predictive value for CA-125 levels in the same sample (Petricoin et al., 2002).

Lysosphathic acid (LPA) normally is produced and released by activated platelets during coagulation. In a study comparing LPA blood levels and CA-125 levels, LPA levels were elevated in all women with stage II–IV ovarian cancer, in all women with recurrent ovarian cancer, and in 9 of 10 women with stage I disease. In contrast, CA-125 levels were elevated in 28 of 47 women with ovarian cancer, including 2 of 9 women with stage I disease. In preliminary studies, the sensitivity of the LPA test was 95% and the specificity was 89% (Xu et al., 1998).

Epidermal growth factor and the ErbB1 receptor are expressed in ovarian cancer. Levels of p110 ErbB1 in the blood were found to be significantly lower in women with stage I–IV epithelial ovarian cancer than in healthy controls or in women with benign pelvic disease (Maihle et al., 2002). The observation has led to the suggestion that p110 ErbB1 levels may provide important information for the management of patients with epithelial ovarian cancer.

Osteopontin is a protein that is overexpressed in ovarian cancer. In a study of blood and tissue from women with and without ovarian cancer, blood levels of osteopontin were significantly higher in women with ovarian cancer compared to healthy controls. The specificity of the samples was 80.4%, and the sensitivity was 80.4% in early-stage disease and 85.4% in later-stage disease (Kim et al., 2002).

Although the potential of the blood tests in this article is exciting, their clinical utility is limited. Many of the studies had small sample sizes, which limit their generalizability to larger groups. Larger clinical trials are needed to better understand whether the blood tests will be effective in detecting early-stage ovarian cancer. Nurses should be educated about these blood tests and be prepared to discuss these modalities with women and their families. Nurses also can help recruit for and explain the risks and benefits of clinical trials designed to evaluate the blood tests.

Ovarian Pap Test

The cervical Pap test can identify precancerous changes in the cervix and provide an effective means for the early detection of cervical cancer. The ability to identify premalignant changes of the ovaries could be of significant value in preventing the development of ovarian cancer. The ovarian Pap test collects cells from the surface of an ovary during a minimally invasive outpatient procedure. The ovarian Pap test is performed in an office setting and involves a short recovery time. The procedure has been likened to that of egg retrieval for in vitro fertilization. Using a small laparoscopic device (0.9 mm), physicians can visualize the ovaries and obtain cells for analysis (see Figure 4). In preliminary studies, tissue obtained in a similar manner to the ovarian Pap test correlated 100% with final pathology readings. This preliminary research indicates that the ovarian Pap test can discern between malignant and normal cells (Fishman & Bozorgi, 2002).

Implications for Practice

The case study of Joan illustrates the typical presentation of a woman with epithelial ovarian cancer. Examination and ultrasound revealed that Joan had a large ovarian mass, although she presented with few symptoms. She was diagnosed with advanced ovarian cancer, which already had spread to other abdominal organs and the lymph nodes. Her five-year survival rate likely is less than 30%. Her case highlights several issues of which nurses need to be conscious when counseling and educating women who may be at risk for ovarian cancer.

Figure 5 depicts Joan’s pedigree, or family tree. Several features of the pedigree suggest a hereditary cancer syndrome. Joan is of Ashkenazi Jewish descent and, therefore, has a higher probability of having an inherited genetic mutation. Members of several generations had breast or ovarian cancer; more importantly, they were diagnosed at ages much younger than the average ages of diagnoses. Assessment of risk is central to selecting appropriate screening recommendations for women and their families.

Joan may have benefited from intervention and education at the time of her breast cancer diagnosis. Interventions may have included a referral for genetic counseling and testing, as well as a referral to a gynecologic oncology team. Other possible interventions may have included participation in an ovarian cancer screening program or screening with ultrasound or physical examination. Prophylactic oophorectomy may have been recommended if Joan had tested positive for either the BRCA1 or BRCA2 mutation. Education should have focused on pertinent information about risk reduction, screening options, and the implications for Joan’s family.

A positive BRCA1 or BRCA2 result for Joan has implications for her daughters. Each daughter has a 50% chance of inheriting the mutation from Joan. Both daughters should receive education and support as they make their own decisions about genetic testing, prevention, and early detection of breast and ovarian cancer. Oncology nurses can provide such education and support.

Nurses can employ several methods to educate their patients and peers about ovarian cancer. They can develop educational brochures and posters, answer questions at health fairs and information tables, and provide education at support groups and other informational programs. Newly diagnosed patients with breast, ovarian, or colon cancer should have an assessment and interpretation of their risk for developing other cancers. The implications associated with a diagnosis of cancer should be discussed with patients and their families. Figure 6 provides...
This pedigree shows how ovarian cancer is transmitted across three generations. Note the ethnic background of the family, the early ages at diagnoses, and the presence of both breast and ovarian cancer.

**Figure 5. Joan’s Pedigree**

A list of helpful Web sites and organizations to share with patients and family members.

Nurses should become advocates for women and their families by disseminating information from health journals and research studies at a comprehensible level. Nurses also can encourage and support patients as they enroll and participate in clinical trials designed to determine better ways to detect ovarian cancer early, when it is most likely to be treatable. The National Cancer Institute’s Web site provides information about open clinical trials throughout the country.

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Bimanual rectovaginal examination, ultrasound, and CA-125 do not detect early-stage ovarian cancer accurately and are not recommended as screening methods in the general population.