Pregnancy-associated breast cancer (PABC) is defined as breast cancer diagnosed during pregnancy and up to one year postpartum (Eedarapalli & Jain, 2006). About 75% of PABC tumors are estrogen receptor– and progesterone receptor–negative, exhibit HER2/neu overexpression, and are biopsy-proven to be poorly differentiated (Aebi & Loibl, 2008). Breast cancer is the second most frequent malignancy occurring during gestation after cervical cancer (Singh, 2009), with an estimated incidence of one in 3,000 and an average age range of 32–38 years at diagnosis (Logue, 2009). In the United States, about 3,500 women are diagnosed with PABC on a yearly basis, and an estimated 30,000 cases are diagnosed per year worldwide (Fajdic, Gotovac, Hrgovic, & Fassbender, 2008). Because increasing age is a known risk factor for the diagnosis of breast cancer, the incidence of concurrent breast cancer and pregnancy has the distinct possibility of increasing as women delay child bearing well into their 30s and 40s (National Cancer Institute [NCI], 2010; Theriault & Hahn, 2007).

Because PABC is relatively rare, no large prospective clinical trials exist from which to gather information; therefore, current knowledge is based primarily on a few retrospective case-controlled studies or review of case series (Rovera et al., 2010). The clinical challenge in managing PABC lies in controlling the cancer while maximizing the survival outcome for the expectant mother without compromising the health and safety of the developing fetus (Morris, King, & Kennedy, 2009). Although other cancers do occur during pregnancy, the focus of this article will be on PABC, presenting a general overview of the diagnostic modalities available, the multidisciplinary approach to care and treatment for the mother and fetus, and the oncology nursing role specific to this patient population.

### Presentation

Breast cancer most often presents as a painless mass or density (Logue, 2009). In addition, dimpling of the breast, nipple retraction, or axillary lymphadenopathy may occur (Eedarapalli & Jain, 2006). During pregnancy, breasts undergo significant changes, including edema, hypervascularization, and lobular and glandular hyperplasia, all of which can make tumor detection extremely difficult (Fajdic et al., 2008). Therefore, a comprehensive baseline breast examination is imperative during the early stages of pregnancy, before physiologic variances become evident (Guidroz, Scott-Conner, & Weigel, 2011; Logue, 2009). Because of the increased weight, glandularity, and density of the breast tissue, lumps and bumps may be attributed to benign conditions; therefore, breast self-examination should be instilled in women with PABC as an important component of their care.
proliferative changes (Litton & Theriault, 2010). Consequently, delays in diagnosis can occur, often by several months. A delay of just one to two months may significantly increase the chance of metastasis to the axillary lymph nodes (Guidroz et al., 2011). The diagnosis of PABC presents a unique clinical challenge requiring collaboration between the patient, her family, and the multidisciplinary team. The multidisciplinary team—typically consisting of the oncologist, obstetrician, surgeon, nurse, radiation oncologist, pediatrician, and maternal fetal medicine physician—must work together to provide a cohesive front for the patient and her family, as the decisions being made directly affect both the woman and her unborn child (Halaska et al., 2009; Keleher et al., 2002).

**Diagnostic Imaging**

**Mammography:** Current practice recommendations state that the amount of radiation exposure from a diagnostic mammogram to the fetus is negligible with the use of abdominal shielding (Garcia-Manero et al., 2009; Litton & Theriault, 2010). However, although these images can provide important information regarding suspicious microcalcifications, masses, or multicentric disease, they also can be associated with high false-negative findings within this patient population, often adding to the delay in diagnosis (Eedarapalli & Jain, 2006; Keleher et al., 2002).

**Ultrasound:** Ultrasonography provides a rapid and accurate method of differentiating between cystic and solid masses and can be performed safely during pregnancy (Eedarapalli & Jain, 2006; Litton & Theriault, 2010).

**Other imaging techniques:** Magnetic resonance imaging is contraindicated because of its heating and cavitation effects and potential risk to the fetus of gadolinium toxicity (Litton & Theriault, 2010; Navrozoglou et al., 2008). Gadolinium has been shown to cross the placenta and cause malformations in rats (Molckovsky & Madarnas, 2008; Navrozoglou et al., 2008).

Routine computed tomography scans of the abdomen and bone scans are also contraindicated during pregnancy because of the dangerous levels of ionizing radiation to the fetus (Sasidharan & Harvey, 2010). Chest x-rays are considered safe with appropriate abdominal shielding (Singh, 2009).

**Fine needle aspiration and core biopsy:** A fine needle aspiration (FNA) or a core biopsy may be performed as part of the initial evaluation. FNA is the preferred method but requires a pathologist who is not only experienced in interpreting breast pathology but also the hyperproliferative changes consistent with pregnancy and lactation (Eedarapalli & Jain, 2006; Theriault & Hahn, 2007).

Core biopsy is an effective means of diagnosing breast cancer and is reserved for masses when an FNA is not diagnostic (Eedarapalli & Jain, 2006). If diagnosis via FNA or core biopsy is not successful, an incisional or excisional biopsy may be performed (Guidroz et al., 2011).

**Treatment**

Treatment for patients with PABC is targeted toward pregnancy preservation, giving careful consideration of the potential risks to the developing fetus while determining an appropriate individualized treatment plan for the patient based on the stage of her disease (Loibl et al., 2005). Treatment modalities typically consist of surgery, chemotherapy, and radiation therapy (Galimberti et al., 2009; Ring, 2007) (see Table 1).

### Surgery

Surgery can be performed during pregnancy with low risk (1%-2%) of spontaneous abortion during the first trimester and low relative risk of premature birth in subsequent trimesters (Ring, 2007). The primary objective is to provide safe surgical treatment and anesthesia to the mother while minimizing risk of fetal demise or preterm labor (Rimes, Gano, Hahn, Ramirez, & Milbourne, 2006). With careful monitoring, general anesthesia can be safely administered to these patient population with minimal increased risk to the mother or fetus (Jones, 2006; Ring, 2007).

Radical modified mastectomy and breast-conserving surgery with axillary lymph node dissection are the surgical options of choice in the treatment of local disease. However, mastectomy is performed more often in this patient population because the cancer, at diagnosis, has a higher probability of being locally advanced because of the physiologic changes occurring within the breast, which may make early diagnosis difficult (Fajdic et al., 2008; Navrozoglou et al., 2008).

### Sentinel Node and Lymphatic Mapping

Axillary lymph node status is determined either by an axillary dissection or a sentinel lymph node biopsy. About half of patients with PABC are diagnosed with node-negative disease and may find the minimally invasive technique of lymphatic mapping and sentinel lymph node biopsy beneficial, as it may eliminate the need for a complete axillary lymph node dissection (Khera et al., 2008). Sentinel lymph node biopsy can be performed safely in pregnant women using Tc-99m sulfur-colloid localization.

<table>
<thead>
<tr>
<th>TABLE 1. Diagnostic Imaging and Treatment Options for Patients With Breast Cancer During Pregnancy</th>
</tr>
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<tbody>
<tr>
<td><strong>Modality</strong></td>
</tr>
<tr>
<td><strong>Diagnostic Imaging</strong></td>
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<tr>
<td>Magnetic resonance imaging</td>
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<tr>
<td>Mammogram</td>
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<tr>
<td>Ultrasound</td>
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<tr>
<td><strong>Treatment</strong></td>
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<tr>
<td>Chemotherapy</td>
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<tr>
<td>Radiation</td>
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<tr>
<td>Surgery</td>
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</tbody>
</table>
The Tc-99m dose is extremely low and well below the threshold absorbed dose associated with adverse fetal effects, presenting a low risk of harm to the fetus (Jones, 2006).

**Radiation**

External beam radiotherapy usually involves the breast, thoracic wall, and axilla. Fetal exposure to ionizing radiation is not considered a safe therapeutic option, largely because of internal radiation scatter (Loibl et al., 2005; Navrozoglou et al., 2008). Microcephaly, urinary system defects, eye abnormalities, and skeletal deformities have been noted during early organogenesis from the high level of radiation sensitivity (Galimberti et al., 2009).

To date, no evidence exists to support any novel mode of adjuvant radiation therapy, including partial breast irradiation (MammoSite®). The use of partial breast irradiation currently is contraindicated in this patient population, largely because of the limited breast volume that is irradiated (Navrozoglou et al., 2008).

**Chemotherapy**

Adjuvant chemotherapy is recommended in an effort to decrease the chance of disease recurrence and to prolong progression-free survival. However, certain patient-specific criteria must be considered prior to the administration of chemotherapy, including the natural physiologic changes that occur within the pregnant woman, the gestational age of the fetus, and the chemotherapy agents to be administered (Torgersen & Curran, 2006). Chemotherapy during pregnancy definitely requires a multidisciplinary approach (Rimes et al., 2006).

During pregnancy, hemodynamic changes occur in blood volume, cardiac output, and blood flow distribution (Rimes et al., 2006; Torgersen & Curran, 2006). As the plasma volume increases, peak drug concentration decreases (Rugo, 2003). The decrease in active drug concentration can significantly affect drug clearance; therefore, adjusted chemotherapy dose calculations may be needed for patients with PABC (Navrozoglou et al., 2008; Pereg & Lishner, 2008).

Chemotherapy is not recommended during the first trimester of pregnancy because of the significant risk for spontaneous abortion, teratogenesis, and fetal malformation, but chemotherapy can be less toxic to the fetus when administered during the second and third trimesters of pregnancy because organ formation is complete (Navrozoglou et al., 2008) (see Table 2). As most chemotherapy agents can cross the blood/placenta barrier, teratogenicity is related directly to gestational age at exposure, total dose administered, and placental transfer (Azim, Del Mastro, Scarfone, & Peccatori, 2011).

Fetal evaluation is essential prior to initiation of chemotherapy. In an effort to protect the fetus, close monitoring with ultrasounds to evaluate fetal growth, amniotic fluid, and placental function should be done at regular intervals during chemotherapy (Azim et al., 2011; Litton & Theriault, 2010). According to Logue (2009), about 50% of fetuses in patients with PABC exposed to chemotherapy in the second and third trimesters exhibit intrauterine growth restriction, preterm labor, or low birth weight. Despite those potential risks, appropriate treatment should not be delayed because of pregnancy (Litton & Theriault, 2010). Doxorubicin, epirubicin, 5-fluorouracil, and cyclophosphamide are chemotherapy agents that are relatively safe to administer to patients with PABC during the second and third trimesters (Jones, 2006; Loibl et al., 2005) (see Table 3).

**Anthracyclines**: Two studies have validated the safe use of anthracycline chemotherapy agents in patients with PABC. The Royal Marsden Hospital in London, England, conducted a retrospective series (Ring et al., 2005), whereas investigators at MD Anderson Cancer Center in Houston, TX, conducted a prospective case study (Ring et al., 2005). Results showed that the combination of doxorubicin and cyclophosphamide in a

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**TABLE 2. Fetal Development Timetable**

<table>
<thead>
<tr>
<th>Trimester</th>
<th>Weeks of Gestation</th>
<th>Fetal Development</th>
</tr>
</thead>
</table>
| First     | 0–5               | • Brain, spinal cord, heart, and gastrointestinal tract are developing.  
|           |                   | • Eye and ear structures are forming.  
|           |                   | • Heart starts to pump regularly around five weeks. |
| Second    | 6–8               | • Lung formation begins.  
|           |                   | • All other vital organs begin to form.  
|           |                   | • Fingers and toes are noticeable, hair follicles and nipples form, and facial features continue to develop. |
| Third     | 9–12              | • Eyelids close (reopen around 28 weeks).  
|           |                   | • Face formation is complete.  
|           |                   | • Genitalia are well formed. |
|           | 20–24             | • Eyebrows, lashes, and nails appear.  
|           |                   | • Muscle development increases.  
|           |                   | • Bone marrow begins to make blood cells.  
|           |                   | • Lower airways of the lungs are developing but are not producing surfactant.  
|           |                   | • Fat storage begins. |
|           | 25–32             | • Rapid brain development occurs.  
|           |                   | • Nervous system is intact.  
|           |                   | • Respiratory system has developed sufficiently enough to enable gas exchange.  
|           |                   | • Rhythmic breathing movements occur.  
|           |                   | • Bones are fully developed and fetus begins storing essential nutrients. |
|           | 33–40             | • Significant increase in body fat  
|           |                   | • Fingernails reach end of fingers.  
|           |                   | • Hair is now coarse and thicker. |

Surgical Treatment

Subsequent Therapy

Adjuvant Treatment

5-fluorouracil is used in combination with

E186 October 2012  •  Volume 16, Number 5  •  Clinical Journal of Oncology Nursing

12-week regimen was far superior in efficacy to six months of cyclophosphamide, methotrexate, and fluorouracil (Aebi & Loibl, 2008; Ring et al., 2005; Sukumvanich, 2011). Weekly administration of anthracycline-based regimens leads to lower peak blood level concentrations with lower maternal myelotoxicity and lower placental transfer of drug, limiting potential drug toxicities (Peccatori et al., 2009; Pereg & Lishner, 2008).

**Cyclophosphamide:** Cyclophosphamide is one of the most commonly used chemotherapy agents in breast cancer (Pereg & Lishner, 2008). Fetal malformations have been reported when administered during the first trimester; however, cyclophosphamide can be safely administered in the second and third trimesters with no detectable increase in fetal malformations or fetal loss (Psyrri & Burtness, 2005).

**5-Fluorouracil:** 5-fluorouracil is used in combination with doxorubicin and cyclophosphamide and has been proven to be safe and efficacious when used in the treatment of PABC (Pereg & Lishner, 2008). First trimester administration is associated with fetal malformations, but treatment in the second and third trimesters has shown good maternal and fetal outcomes (Psyrri & Burtness, 2005).

**Taxanes:** Limited information is available regarding the safety of taxane use during pregnancy, but in the third trimester, increased drug metabolism does lead to a shorter drug half-life (Sukumvanich, 2011). Therefore, the resulting decrease in peak concentration levels may not be efficacious during pregnancy (Litton & Theriault, 2010).

**Trastuzumab**

Trastuzumab is a monoclonal antibody that blocks the HER2/neu protein. With HER2 overexpression, cell growth and proliferation are increased, resulting in a more aggressive breast cancer (Shrim, Garcia-Bournissen, Maxwell, Farine, & Koren, 2008). Anhydramnios and reversible fetal renal failure have been reported with trastuzumab and paclitaxel use during the second trimester of pregnancy (Bader, Schlembach, Tamussino, Pristauz, & Petru, 2007). Those toxicities appear to be transient, but if trastuzumab is to be used during pregnancy, renal development and amniotic fluid volume must be monitored closely (Bader et al., 2007).

**Hormonal Therapy**

Tamoxifen is a selective estrogen receptor modulator used to treat patients who have estrogen- or progesterone-positive cancer and is contraindicat-ed during pregnancy. Tamoxifen use during pregnancy is associated with spontaneous abortions and fetal malformations (Sasidharan & Harvey, 2010; Sukumvanich, 2011).

**Supportive Care**

Chemotherapy, by its nature, is associated with side effects that need to be addressed. Nausea and vomiting, as well as cytopenias, are the most common. Cytopenias, including neutropenia, have the potential to increase susceptibility to infection, which can have an adverse effect on the developing fetus. Supportive care with antiemetics and growth factors is essential in maintaining the health of the mother and fetus (Pereg & Lishner, 2008).

**Maternal and Fetal Monitoring**

**Frequency of Ultrasound**

Prior to initiating chemotherapy, an ultrasound of the fetus must be performed to confirm gestational age and fetal development (Loibl et al., 2005; Rimes et al., 2006). In addition, an ultrasound to evaluate fetal growth and chemotherapy tolerance should be performed prior to each cycle of chemotherapy (Hahn et al., 2006; Rimes et al., 2006). Amniocentesis may be recommended if any abnormalities are observed by ultrasound and should be followed up by Doppler ultrasound of the cord vessels (Azim et al., 2011).

**Pregnancy Termination**

Termination of pregnancy is no longer recommended; however, patients may elect to terminate pregnancy in the first trimester if immediate treatment with chemotherapy becomes necessary for survival (Fajdic et al., 2008). If breast cancer is diagnosed later in pregnancy (i.e., third trimester), chemotherapy or radiation therapy can be delayed until after delivery (Loibl et al., 2005).

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**TABLE 3. PABC Treatment Modalities Based on Gestational Age at Diagnosis**

<table>
<thead>
<tr>
<th>Time of Diagnosis</th>
<th>Surgical Treatment</th>
<th>Adjuvant Treatment</th>
<th>Subsequent Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>First trimester</td>
<td>MRM; lumpectomy and ALND</td>
<td>Second trimester adjuvant chemotherapy</td>
<td>± Radiotherapy ± Endocrine therapy</td>
</tr>
<tr>
<td>Second trimester and early third trimester</td>
<td>MRM; lumpectomy and ALND</td>
<td>± Adjuvant chemotherapy</td>
<td>± Radiotherapy ± Endocrine therapy</td>
</tr>
<tr>
<td>Second trimester and early third trimester</td>
<td>MRM; lumpectomy and ALND</td>
<td>± Adjuvant chemotherapy</td>
<td>± Adjuvant chemotherapy ± Radiotherapy ± Endocrine therapy</td>
</tr>
<tr>
<td>Late third trimester</td>
<td>MRM; lumpectomy and ALND</td>
<td>Adjuvant chemotherapy</td>
<td>± Radiotherapy ± Endocrine therapy</td>
</tr>
<tr>
<td>Late third trimester</td>
<td>MRM; lumpectomy and ALND</td>
<td>± Adjuvant chemotherapy</td>
<td>± Radiotherapy ± Endocrine therapy</td>
</tr>
</tbody>
</table>

±— and/or; ALND—axillary lymph node dissection; MRM—modified radical mastectomy; PABC—pregnancy-associated breast cancer

Note. Subsequent therapy occurs after delivery.

Delivery

Timing of delivery is based on gestational age and fetal development (Logue, 2009). Delivery should be delayed until at least gestational weeks 35–37 and three to four weeks after the last dose of chemotherapy to minimize the effects of maternal myelosuppression and to allow for fetal drug excretion via the placenta (Azim et al., 2011; Jones, 2006). Neutropenia, anemia, and alopecia are some of the short-term and reversible side effects experienced by the fetus on delivery (Logue, 2009).

Breast Feeding After Delivery

If treatment continues postpartum, breast feeding is contraindicated, as chemotherapy agents are expressed in the milk (Rimes et al., 2006). Breast surgery and radiation therapy also can hinder effective nursing because of lobular atrophy, periductal fibrosis, and stenosis of the galactophoric ducts (Lawrenz et al., 2011; Molckovsky & Madarnas, 2008).

Long-Term Effects of Chemotherapy Exposure on the Infant

Current data—less than 20 years’ worth—suggest that most children exposed to chemotherapy in utero exhibit no significant congenital, neurologic, cognitive, developmental, or social aberrations, but of concern are the long-term effects of compromised physical and mental development, heart function, secondary malignancies, and infertility (Aebi & Loibl, 2008; Theriault & Hahn, 2007). Therefore, a definite need exists for prolonged follow-up with a large cohort study to properly assess the long-term status of children exposed to chemotherapy in utero (Pereg & Lishner, 2008).

Nursing Implications

Nurses caring for patients with PABC must serve as the liaison and primary contact between the patient, oncologist, and obstetrician. Effective communication among all modalities must be promoted, ensuring continuity of care for this patient population.

Education

Nurses who provide care for pregnant women must educate their patients about the signs and symptoms of breast cancer and encourage them to report any unusual masses or nipple discharge (Dean, 2008). Patient education and constant reinforcement regarding chemotherapy treatment options and potential side effects is essential. Nurses function not only as patient advocates by keeping the multidisciplinary team members informed of any patient concerns, but also as dedicated and constant resources for the patient, providing appropriate support and referrals for the management and treatment of any identified issues (Logue, 2009).

Psychosocial Issues

Nursing responsibilities span across the continuum of care as the patient makes life-and-death decisions about herself and her unborn child (Visco, Meyer, Xi, & Brown, 2009). Pregnant patients experience a wide range of emotions on learning they have breast cancer, and maternal/fetal conflict is a huge emoti-
menses after cytotoxic chemotherapy when GnRHa analogs were administered (Recchia et al., 2006). Nursing implications would include appropriate counseling with a fertility specialist.

Pregnancy After Breast Cancer

Discussing pregnancy after breast cancer should be based on each woman’s disease prognosis and conversations should include not only fertility assessments but also address the possibility of disease recurrence. The current medical recommendation for any patient desiring pregnancy after chemotherapy is to wait two years before attempting conception. Waiting at least two years helps discern which women have a better chance of long-term survival versus those with aggressive disease (Eedarapalli & Jain, 2006). Nurses should be cognizant of the fact that pregnancy in itself is an emotional stressor and when fear of disease recurrence is added to the equation, patients may become totally overwhelmed. Emotional support is absolutely vital to this patient population (Keleher, Wendt, Delpassand, Stachowiak, & Kuerer, 2004; Navrozoglou et al., 2008).

Conclusion

As the number of pregnant women diagnosed with breast cancer increases, so, too, does the need for more evidence-based guidelines. Efforts to control the cancer and maximize the expectant mother’s survival outcomes must not compromise the health and safety of her unborn child.

Collaboration and communication between multidisciplinary team members is crucial when treating this patient population. Education is key in providing a general overview of the diagnostic modalities available, the multidisciplinary approach to care and treatment for the mother and fetus, and the oncology nursing role for patients with PABC. Patients need to be kept informed of all aspects of care so that they can participate actively in the decision-making process, as they are not only concerned for their own well-being but also for the safety of their unborn child. Anxiety levels often are high, and steady, open communication offers a modicum of control to this already stressed patient population. Using a multidisciplinary approach to treatment allows the best possible outcome for the mother and the fetus.

References


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