Breast Disorders in Pregnant and Lactating Women

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After completing this article, the reader should be able to:

- Identify breast changes associated with pregnancy and lactation.
- Describe the advantages and limitations of breast imaging techniques used during pregnancy and lactation.
- Discuss some benign breast conditions that occur in this patient population, including diagnostic challenges and treatment options.
- Compare and contrast pregnancy-associated breast cancer with breast cancer in other patients.
- Outline the treatment of breast cancer in pregnant patients.
- Summarize recent research findings on the prognosis for pregnancy-associated breast cancer.

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Pregnancy and lactation are known to slightly reduce a woman's lifetime chance of developing breast cancer, as well as some other types of cancer. Yet the breasts remain susceptible throughout pregnancy and lactation to all the disorders that affect the breasts of nonpregnant, nonlactating women, as well as some breast conditions unique to this phase of the lifecycle. In addition, changes in the breasts of pregnant and lactating women can make diagnosing breast conditions particularly challenging. As a result, imaging and treating breast conditions that occur during pregnancy and lactation require specialized knowledge.

Breast Anatomy and Changes During Pregnancy and Lactation

Situated between the second and sixth ribs, and between the edge of the sternum and the midaxillary line, the breast lies anterior to the pectoralis major muscle and is supported by ligaments attached to the sternum. Each breast comprises 15 to 20 lobes arranged in a circle and covered by subcutaneous fat. The lobes are made up of 20 to 40 lobules that end in saclike glands called acini where milk is produced. Ducts connect the acini, lobules, and lobes, leading to openings in the nipple. The nipple is surrounded by the areola, a darker area with large sebaceous glands. Each breast has a complex network of lymphatic vessels. Most of the lymph from the breast drains to the axillary lymph nodes, which number between 20 and 30 (see Figure 1).

Beginning in the middle of the first trimester of pregnancy, a number of changes take place in a woman's breasts under the influence of hormones. Rising levels of estrogen cause vascular proliferation and increased blood flow to the breasts. In addition, new ducts begin to form and...
During the second and third trimesters, progesterone induces lobular hyperplasia and involution of the breast's fibrofatty tissue. Progesterone and estrogen also inhibit the production of milk at this stage. Late in pregnancy, colostrum (a yellowish or clear sticky fluid, the earliest form of breast milk) is produced by the alveolar cells. Within hours after delivery, progesterone and estrogen levels decrease sharply, becoming almost undetectable. Another hormone, prolactin, increases during the 2 weeks after delivery and is responsible for milk production. Breastfeeding further stimulates the release of prolactin. The lobules and ducts dilate because of the accumulation of milk and other secretions. Figure 2 shows the ductal system of a lactating breast. Approximately 3 months after breastfeeding ends, the breasts return to their prepregnant state as the lobules atrophy significantly.

**Breast Imaging Techniques for Pregnant and Lactating Women**

Most breast masses detected during pregnancy or lactation are benign; nevertheless, it is important to evaluate any breast mass promptly and accurately to rule out cancer. Because of the dramatic increase in breast density associated with pregnancy and lactation, diagnosis of breast masses can be challenging. In general, ultrasonography is the preferred modality for imaging breast masses in pregnant and lactating women, although mammography and magnetic resonance (MR) imaging also are used, and biopsies often are necessary to confirm or clarify imaging findings.

In pregnant patients, the breast usually appears hypoechoic on sonograms because of the increase in fibro glandular tissue. In lactating patients, the breast appears diffusely echogenic or hyperechogenic with hypervascularity and prominent ducts. Ultrasonography’s reported sensitivity for breast masses in pregnant and lactating women ranges from 86.7% to 100%. Color Doppler sonography can be helpful in assessing the vascularity of a mass. In addition, ultrasonography is useful for assessing the axillary lymph nodes. The sonographic appearances of some breast disorders that affect lactating women are described in Box 1.
Mammography is less useful in pregnant and lactating patients because their breasts typically show a diffuse increase in glandular density that can obscure lesions on mammograms (see Figure 3). It is worth noting, however, that in a study by Robbins et al, mammography accurately identified the 4 cases of breast cancer in a group of 155 women with breast lesions who were pregnant, lactating, or up to 12 months postpartum and not lactating, despite comparatively dense breast tissue in most of the patients.9

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**Box 1**

**Ultrasonographic Characteristics of Some Common Pathologies of the Lactating Breast**

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyst</td>
<td>Well-circumscribed margins with thin smooth walls, centrally anechoic, posterior enhancement, edge shadowing, no internal vascularity</td>
</tr>
<tr>
<td>Fibroadenoma</td>
<td>Well-defined or occasionally ill-defined margins, homogeneous to heterogeneous echogenicity, no posterior enhancement unless internal calcification is present, internal vascularity</td>
</tr>
<tr>
<td>Lactating Adenoma</td>
<td>Well-circumscribed to ill-defined margins, hypo- hyper-, or isoechoic echogenicity, homogeneous or heterogeneous, posterior enhancement or acoustic shadowing, +/- internal vascularity</td>
</tr>
<tr>
<td>Abscess</td>
<td>Wide, indistinct, hypoechoic margins, predominantly echo-free to heterogeneous echogenicity, posterior enhancement, no internal vascularity</td>
</tr>
<tr>
<td>Malignancy</td>
<td>Irregular and ill-defined margins, heterogeneous echogenicity, stellate appearance, +/- posterior shadowing, internal vascularity</td>
</tr>
<tr>
<td>Galactocele</td>
<td>Acute – anechoic and simple or mainly anechoic with some diffuse echoes and multiloculated, subacute – contain echoes of mild to moderate intensity, chronic – diffuse echogenicity ranging from moderate to highly echogenic, can be simple, multilocular, and heterogeneous, possible fat-fluid level, movement of the contents can be demonstrated by compression with the transducer, galactoceles are centrally devoid of blood vessels. However, flow might be demonstrated in the walls; use of color Doppler can confirm this.</td>
</tr>
<tr>
<td>Blocked Duct</td>
<td>Focal – similar appearances to an acute galactocele, noncompressible, diffuse – often an area of increased echogenicity associated with a palpable solid region. Occasionally, a hypoechoic rim surrounds a more echogenic central region.</td>
</tr>
<tr>
<td>Engorgement</td>
<td>Increased echogenicity of the glandular tissue due to the large volume of milk in the breast, severe engorgement might exhibit ultrasonographic signs similar to mastitis.</td>
</tr>
<tr>
<td>Mastitis</td>
<td>Early/acute phase – might be no discernable ultrasonographic changes in echogenicity of breast tissues, skin thickens and becomes more hyperechoic; skin thickening is prominent in advanced stages, Cooper ligaments and stromal fibrous tissue decrease in echogenicity, areas of inflammation frequently have increased blood flow, distinction between different breast tissues disappears, breast thickness increases.</td>
</tr>
</tbody>
</table>

In addition, mammography is useful for visualizing malignant microcalcifications\(^6\) and for determining whether a breast cancer is multicentric or bilateral.\(^8\)

Mammography is considered safe during pregnancy when clinically indicated.\(^6\) Organ malformation in developing fetuses is thought to occur at radiation doses many times higher than the dose delivered during standard 2-projection mammography. During the first trimester, when the fetus is most vulnerable, exposure to more than 0.05 Gy of radiation is associated with fetal malformations. Craniocaudal and mediolateral oblique projections of both breasts with abdominal shielding deliver a dose of 0.004 Gy to the fetus.\(^7,11\) There are no special concerns regarding radiation dose from mammographic examinations in women who are lactating.\(^12\)

MR is rarely used to image the breasts of pregnant or lactating patients because normal changes can make it difficult to distinguish pathology.\(^6\) The American College of Radiology recommended that MR imaging be reserved for cases in which benefits outweigh possible risks and that gadolinium-containing contrast agents not be used in pregnant patients. Gadolinium crosses the placenta and has been shown to retard fetal growth in animal studies when administered in high doses.\(^7,11\) The U.S. Food and Drug Administration (FDA) and the International Commission on Non-Ionizing Radiation Protection also advised against using gadolinium contrast in pregnant patients.\(^7\) In lieu of gadolinium contrast, gadobenate dimeglumine is approved by the FDA for use in pregnant women.\(^10\)
Lactating women can have gadolinium contrast, and it is safe for them to continue breastfeeding after gadolinium is administered, according to the American College of Radiology.

In lactating women, breast tissue enhances rapidly following the administration of a contrast agent, followed by an early plateau. This might be due to the increased vascularity of the lactating breast. In contrast, nonlactating breast tissue tends to enhance more slowly.

**Benign Breast Conditions in Pregnant and Postpartum Women**

Among breast masses detected in pregnant and postpartum women, more than 80% are benign. Hosny et al, for example, reported on a series of 48 pregnant or lactating patients with palpable breast masses. All of the women were examined with ultrasonography; those found to have suspicious masses also underwent mammography (12 patients), breast MR (4 patients), biopsy (20 patients), ultrasound-guided aspiration (3 patients), or a combination of these. The final diagnoses were as follows: 14 simple cysts, 14 fibroadenomas, 11 galactoceles, 1 case of bilateral gigantomastia, 2 lactating adenomas, 2 cases of mastitis, 1 abscess, and 3 ductal carcinomas including an advanced case and 2 earlier-stage cancers.

Some of the benign breast conditions that occur in pregnant and lactating women include several conditions that occur exclusively in these patients (see Table 1 for an overview).

**Cysts**

Breast cysts are fluid-filled sacs described as having the consistency of a grape or a water balloon, although they can be firmer. Some cysts are too small to be felt while others measure up to 2 inches. Cysts occur in women of all ages but are more common in premenopausal women aged 35 to 50 years. A cyst usually can be diagnosed confidently using ultrasonography. On sonograms, cysts appear anechoic, well circumscribed, and have thin walls and no internal vasculature.

The cause of breast cysts is unknown, although they might be due to high levels of estrogen. If cysts are painful or uncomfortable, they can be drained with a needle. Some women with cystic breasts report that reducing caffeine or sodium intake seems to improve symptoms. Over-the-counter pain medications also can be helpful. Generally, however, no treatment or intervention is necessary for breast cysts, and they often disappear after menopause.

**Fibroadenomas**

Fibroadenomas are the most common benign breast tumors in women who are pregnant or lactating. Generally, they are firm or rubbery masses that are mobile and painless. Although they might be first detected during pregnancy, they often were present before pregnancy but grow rapidly because of increased estrogen levels associated with pregnancy and lactation. Often, fibroadenomas are detected by the woman or during a clinical examination when they measure 1 cm to 2 cm. “Giant” fibroadenomas are sometimes classified as those measuring more than 5 cm. Fibroadenomas often shrink when lactation ends and during menopause.

Fibroadenomas develop in the terminal ductal lobes and contain both glandular and connective cells. Ultrasonographically, they typically appear as hypoechoic oval masses, with circumscribed margins and sometimes with lobulations. They can affect both breasts and sometimes appear in multiples. When a fibroadenoma becomes infarcted, internal cysts might be detectable on ultrasound examination, and the fibroadenoma’s borders might become less regular. Infarcted fibroadenomas also can appear more heterogeneous.

Excessive estrogen and hypersensitivity to estrogen have been suggested as possible causes for fibroadenomas; however, treatment with antiestrogen medications has not proven effective. For many women, the treatment of choice for fibroadenomas is surgical excision. For younger women with fibroadenomas (usually those aged younger than 35 years), conservative management is considered acceptable when there is a biopsy-proven diagnosis. If allowed to remain in place, fibroadenomas should be reassessed regularly for any changes.

To gain a clearer picture of fibroadenomas in the clinical setting, one group of researchers prospectively studied patients who presented with breast pain or a breast lump during a 6-year period between 2003 and
After analyzing 210 fibroadenoma cases, they confirmed that fibroadenoma was the most commonly diagnosed breast lesion. In this study, the fibroadenoma patients’ mean age at presentation was 27 years, and two-thirds were aged 16 to 30 years. Most of these patients...
(80%) reported having had symptoms for less than a year. In slightly more than half of the cases studied (51.9%), the fibroadenomas measured 3 cm to 5 cm. The upper lateral breast quadrant was the most common site for fibroadenomas, with the right and left breasts approximately equally affected. In this study, multiple fibroadenomas and bilateral fibroadenomas were relatively uncommon (4.9% and 5.4% of cases, respectively).17

Fine-needle aspiration cytology was used to diagnose approximately two-thirds of these cases, whereas one-third of the cases were diagnosed via excisional biopsy. Surgical excision was the most common treatment (n = 164), and no surgical complications were reported. Forty-six patients were managed conservatively. Many of the patients were lost to follow-up; however, among the 40% who were reassessed a year later, none had recurrent fibroadenomas.17

Very rarely, breast cancer arises within or adjacent to a fibroadenoma.18 The incidence of co-occurring fibroadenoma and breast cancer in a screened population in one study was 0.1% to 0.3%, with a peak from ages 42 to 44 years. Approximately two-thirds of these cancers were lobular, whereas one-third were ductal or mixed lobular-ductal. Fibroadenoma-associated breast cancer behaves similarly to other breast cancers.18

Lactating Adenomas

Like fibroadenomas, lactating adenomas are common benign tumors during pregnancy and lactation and often shrink or resolve when a woman stops lactating.6 Also like fibroadenomas, these tumors tend to be painless and mobile, and they might be multiple or bilateral.16 Ultrasonographically, fibroadenomas and lactating adenomas tend to be similar as well: Both appear as ovoid masses with circumscribed borders (see Figure 4).16 Unlike fibroadenomas, however, lactating adenomas tend to be soft and are sometimes compressible with an ultrasound probe.16

Lactating adenomas are more common late in pregnancy and postpartum but sometimes arise during the first and second trimesters.16,17 They are known to recur during subsequent pregnancies and are made up of connective tissue and secretory lobules.17 Bromocriptine can help shrink lactating adenomas.19

Galactoceles

Galactoceles are cystlike dilated ducts caused by ductal obstruction. They often are surrounded by a fibrous capsule and contain milklike material, including proteins, fats, and lactose.6,20 The term galactoceles is derived from 2 Greek words: galatea, meaning milky white, and cele, or pouch.20 The material in a galactoceles can be either thick and viscous or thinner, depending on how old it is.20

Galactoceles rarely occur in women who are not lactating but are the leading type of benign lesions in younger women who are lactating or recently stopped lactating.6,20 Galactoceles typically are painless lumps. They can be single or multiple, occur in one or both breasts, and develop over a period of weeks or months.6,20 The area under the areola is a common site for galactoceles.20

On ultrasonography, galactoceles can have a benign, well-defined, cystic appearance, or they can appear malignant: solid, irregular in shape, and with ill-defined

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margins. One study reported that about half of galactoceles appeared cystic on ultrasonography, approximately 37% had a mixed cystic and solid appearance, and 13% appeared solid.

On mammography, the appearance of galactoceles depends on their contents. When a galactocele is primarily fat-filled, it appears radiolucent. This type of galactocele is termed a pseudolipoma. Conversely, a lipoma containing mostly milk appears heterogeneous. These are also known as pseudohamartomas. The appearance of a fat-fluid line on a mammogram is considered diagnostic for galactocele.

Usually, galactoceles resolve without intervention. However, infection is possible because the milk inside galactoceles provides nutrients for bacteria. An infected galactocele might present as breast inflammation. The usual treatment in these cases is needle aspiration with ultrasonographic guidance.

**Gigantomastia**

Gigantomastia is a rare condition in which the breasts rapidly become extremely enlarged during pregnancy. It is believed to be the result of excessive hormonal stimulation of breast tissue, and a possible association with autoimmune disease has been suggested. However, in some cases, no specific cause can be determined.

Because the breasts grow so rapidly, blood supply might become inadequate and serious complications can result, including necrosis, ulceration, and bleeding. In the most severe instances, patients with gigantomastia might have trouble breathing and walking. The first-line treatment for gigantomastia is bromocriptine, a drug that decreases prolactin levels. Mammoplasty or mastectomy also might be necessary and generally are performed after delivery.

Antevski et al reported on an extreme case of gigantomastia in a 24-year-old woman who was in her second pregnancy. She presented at 28 weeks’ gestation with breasts weighing 33 kg (72.8 lb). The enlargement had begun at 21 weeks’ gestation and progressed quickly. She reported pain, dyspnea, and difficulty standing and walking. Venous engorgement, skin atrophy, and necrotic ulcerations measuring up to 6 cm were noted. Infection with *Klebsiella aerogenes* was confirmed and antibiotic therapy prescribed.

A life-saving double mastectomy was performed at 29 weeks’ gestation. Analysis of the breast tissue showed lobular hyperplasia, interstitial edema, and lymphoplasmacytes, with areas of increased fat and connective tissue. The patient was discharged from the hospital a week postsurgery without complications. She later spontaneously delivered a healthy, full-term infant.

**Milk Duct Fistula**

A fistula or pathway can occur between a milk duct and the skin of a lactating woman, resulting in milk leakage that can be bothersome. Generally, milk duct fistulas happen as a result of a medical intervention, such as a breast biopsy. The risk of developing a fistula increases with larger-gauge needles, more passes of the needle, and biopsy of lesions that are deep within the breast or centrally located, as opposed to peripheral or superficial lesions. Despite the possibility of this complication, necessary biopsies should not be avoided in lactating women.

Stopping lactation is the usual treatment for milk duct fistulas, although fistulas sometimes heal while lactation continues. Lactation generally stops about a week after breastfeeding ends. Breast engorgement associated with weaning is sometimes painful, and women might be prescribed bromocriptine to speed the process and relieve discomfort.

**Granulomatous Mastitis**

Granulomatous mastitis is a rare inflammatory condition that primarily affects women of child-bearing age and often is associated with pregnancy or lactation, although girls and older women also sometimes develop the disease. Inflammatory granulomas are noncaseating (ie, not cheeselike) and centered in the breast’s lobules. Generally, the disease is unilateral, but it occasionally occurs in both breasts.

Granulomatous mastitis was first described in 1972, and no cause has yet been established. However, it might be associated with autoimmune disease or an infectious organism. Another hypothesis is that long-term breastfeeding might cause distention of the breast’s ducts and acini, leading to rupture and consequent granulomatosis.
The most common sign of granulomatous mastitis is a firm breast mass. Other, less common signs and symptoms are pain, erythema, and inflammation, with possible skin ulceration and abscess.\textsuperscript{24,26}

Both clinically and on imaging examinations, this disease can mimic breast cancer.\textsuperscript{25} Mammographically, it tends to appear as an ill-defined, asymmetric density (see Figure 5). Ultrasonographically, it often appears as an irregular hypoechoic mass.\textsuperscript{6,26} Skin thickening and axillary adenopathy also might be detected.\textsuperscript{26} However, the imaging appearance of granulomatous mastitis can vary.\textsuperscript{6} On MR images, for example, granulomatous mastitis can appear as a heterogeneous lesion with either circumscribed or spiculated borders, or as a heterogeneous increase in signal intensity in breast parenchyma.\textsuperscript{25}

Core biopsy or fine-needle aspiration of the mass and histopathological analysis is diagnostic for the disease.\textsuperscript{26} It is critical to rule out a variety of other conditions that might have a similar appearance, including malignancy, certain infections, and autoimmune diseases.\textsuperscript{24} For example, granulomatous mastitis might be confused with tuberculosis or sarcoidosis.\textsuperscript{24}

When granulomatous mastitis is caused by an infection, antibiotics are prescribed.\textsuperscript{6} For noninfectious cases, treatment is less clear-cut. Prior to 1980, surgical excision of the mass was routine; although surgery still is used to treat the disease, a more conservative approach now is favored.\textsuperscript{24} Treatment with corticosteroids is often prescribed, either alone or following surgery.\textsuperscript{6,26} However, in one study, half of patients with granulomatous mastitis who were treated with corticosteroids had a relapse.\textsuperscript{24} Immunosuppressant drugs also are used.\textsuperscript{24} Observation might be the preferred treatment for patients with only mild symptoms,\textsuperscript{26} and some researchers suggest that granulomatous mastitis is a self-limiting condition, typically resolving on its own in 2 to 24 months.\textsuperscript{24}

In 2009, Ocal et al reported on a retrospective review of 16 cases of granulomatous mastitis.\textsuperscript{25} These patients were aged 24 to 51 years; all had been pregnant at least once and had breastfed their infants. Most of the women had breastfed for 12 months or longer. Surgery was the treatment of choice for these patients, and evaluation of the excised tissue confirmed the diagnosis of granulomatous mastitis in all 16 patients. Some patients also received an 8-week course of steroid treatment.

The rate of recurrent disease in this study was 31\% (5 of 16 patients).\textsuperscript{25}

**Puerperal Mastitis**

This infection usually occurs in lactating women and is believed to be transmitted from an infant’s mouth or nose to the mother via a crack or abrasion on the nipple or breast skin.\textsuperscript{6} About 10\% of breastfeeding women develop puerperal mastitis, and it is most common 2 to 3 weeks after childbirth.\textsuperscript{27} Patients generally present with tenderness in one area of the breast, as well as fever, malaise, achiness, and fatigue.\textsuperscript{27}

Two primary types of infectious organisms have been identified as common causes of puerperal

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mastitis: *Staphylococcus aureus* and *Streptococcus*. *Staphylococcus* -caused mastitis is more common and tends to be more focal. *Streptococcus* -caused mastitis is less common and more diffuse. Other organisms such as *Candida albicans*, *Escherichia coli*, and *Mycobacterium tuberculosis* rarely cause mastitis. Mastitis typically is diagnosed clinically, without imaging of the breast.

A 10- to 14-day course of antibiotics is the recommended treatment for most patients with puerperal mastitis. Some commonly prescribed antibiotics include amoxicillin, cephalaxin, ciprofloxacin, and clindamycin. It is not generally necessary for a patient with mastitis to stop breastfeeding; the breast milk usually is not harmful to babies. In addition to completing a course of antibiotics, rest, hydration, and warm compresses are helpful for treating mastitis, and a breastfeeding woman with puerperal mastitis should empty her breasts of milk frequently and completely.

Sometimes incorrect breastfeeding technique or an abnormality in an infant’s mouth can cause nipple irritation that leads to mastitis. For example, the infant might incorrectly latch on to the breast, or have a cleft palate or very short frenulum. The frenulum is the membrane that connects the tongue to the bottom of the mouth. Thus, it might be helpful for patients with mastitis to meet with a lactation specialist to check for possible breastfeeding problems.

Abscesses are a possible complication of puerperal mastitis. They can be detected with ultrasonography and drained with needle aspiration. Repeated drainings are sometimes necessary. The aspirated fluid should be cultured and antibiotics prescribed accordingly.

Puerperal mastitis and inflammatory breast cancer share a similar appearance, and inflammatory breast cancer should be considered as a differential diagnosis if a patient does not respond to treatment for presumed puerperal mastitis.

Mastitis caused by methicillin-resistant *Staphylococcus aureus* (MRSA) is termed epidemic mastitis and can be life threatening for the infant of an infected woman who is breastfeeding. For example, Gastellum et al reported the death of a newborn, one of a set of quadruplets, in a neonatal intensive care unit as a result of MRSA sepsis. MRSA was identified in expressed breast milk fed to the newborn, and the siblings also were colonized with MRSA. Premature and seriously ill newborns are particularly susceptible to MRSA infection.

**Breast Cancer in Pregnant and Postpartum Women**

Overall, cancer is diagnosed in about 1 in 1000 pregnant women in developed nations. These cancers include lymphoma, melanoma, cervical cancer, breast cancer, colon cancer, ovarian cancer, and leukemia.

Breast cancer in pregnant and lactating women is rare. Only about 1 in 3000 pregnancies is affected, and pregnant or lactating women make up only 1% to 3% of all breast cancer cases. Among women aged younger than 40 years who have newly diagnosed breast cancer, between 7% and 14% are pregnant, recently were pregnant, or are lactating. However, as more women in developed countries opt to delay childbearing until later in life, the incidence of breast cancer in pregnant and postpartum women probably will rise because breast cancer is positively associated with aging.

Pregnancy-associated breast cancer (PABC) refers to cancer that occurs during pregnancy, within a year after delivery, or at any time a woman is lactating. Approximately two-thirds of PABC cases are diagnosed after the patient has given birth, often within 6 months of delivery.

In about 90% of cases, PABC is discovered by the patient and manifests as a painless mass (see Box 2). Other, less common signs of PABC are erythema, swelling, and breast enlargement. These signs tend to be associated with more advanced cancer. In a study by Middleton et al of 39 patients with PABC, for example, 32 patients presented with a breast mass they discovered themselves. In addition, one patient had bloody nipple discharge, and one had diffuse erythema of the breast skin.

Any new breast mass in a pregnant patient that does not resolve within 2 weeks should be investigated. Unfortunately, diagnosis of breast cancer often is delayed in pregnant and postpartum women. Some studies report an average delay of 5 to 7 months, with occasional delays of up to 18 months. In comparison, breast cancer in nonpregnant, nonlactating women...
usually is diagnosed within a month of detecting a mass.11,34 Based on their review of 15 PABC studies, Ulery et al suggested that the delay might be due to a lower index of suspicion among physicians and patients.31 In other words, breast cancer is not an expected finding in pregnant and postpartum women, and so it is discounted as a differential diagnosis. Instead, breast masses in pregnant and lactating women tend to be seen as normal variants.31

To minimize delays in PABC diagnosis, Ulery et al recommended that health care professionals take the following steps31:

- At each prenatal office visit, ask patients about any changes in their breasts.
- Include PABC among differential diagnoses for breast masses in pregnant and postpartum women.
- Use mammography, ultrasonography, and biopsy to make a prompt and definitive diagnosis.

In addition, pregnant and postpartum patients should be encouraged to perform monthly breast self-examinations and to have their breasts examined clinically at the first prenatal visit and as indicated thereafter.31

Perhaps because of diagnostic delays, PABCs are on average larger, at a more advanced stage, and more likely to be associated with metastasis than breast cancers not associated with pregnancy.10 In pregnant women, the average size of a breast tumor at diagnosis is 3.5 cm, compared with 2 cm among nonpregnant women. Pregnant breast cancer patients also are much more likely to have lymph node involvement (56-89%) than are nonpregnant patients with breast cancer (38-54%).34 Compared with nonpregnant women, pregnant women are less likely to receive a diagnosis of stage 1 breast cancer and 2.5 times more likely to receive a higher-stage breast cancer diagnosis.10 Consequently, PABCs also carry a poorer prognosis than non-PABCs as a whole.4

It is not clear, however, whether pregnancy per se contributes to the poorer prognosis for patients with breast cancer or merely delays diagnosis because of normal breast changes that can mask breast cancer, including engorgement, hypertrophy, and nipple discharge.10 For example, some suggested hypotheses are that PABC might be accelerated because of breast hypervascularity during pregnancy and lactation, increased exposure of breast cancer cells to hormones during pregnancy, or immune suppression associated with pregnancy.16

Histologically, the most common type of PABC by far is invasive ductal carcinoma,10,32 which accounts for 75% to 90% of PABCs.11 Invasive lobular carcinoma is the next most commonly occurring histologic type. Figure 6 illustrates ductal carcinoma in situ and lobular carcinoma in situ, the precursors of invasive carcinoma. Inflammatory carcinoma is comparatively rare among PABC cases, accounting for no more than 4% of the total.11

In the study by Middleton et al of 39 patients with PABC, 32 were found to have invasive ductal...
carcinoma, 6 had some other histologic type, and one patient’s tumor type was unknown. In addition, 61% of the patients in this series had lymphovascular invasion at the time of diagnosis. In terms of metastatic disease, 2 of the 39 patients in this study presented initially with metastasis, and 7 additional patients developed metastatic disease subsequently. The liver was the most common site of metastasis, followed by the brain, bones, and nonaxillary lymph nodes.

BRCA1 and BRCA2 genetic mutations are more common in women with PABC than in patients with non-PABC tumors. This is an expected finding because BRCA-mutation–associated cancers tend to occur more frequently in younger women. In addition, between 28% and 58% of PABC tumors express ERBB2 (formerly HER2 or HER2/neu), a rate higher than for breast cancers in younger women who are not pregnant or lactating. Most women with invasive breast cancer should be tested for ERBB2 because their status can affect treatment decisions. Breast cancers that test positive for ERBB2 tend to be more aggressive and might not respond well to hormone treatments, although other therapies are available.

Finally, PABC tumors are both estrogen-receptor negative and progesterone-receptor negative in about 70% of cases. Such tumors are less likely to respond to endocrine therapy than estrogen-receptor positive or progesterone-receptor positive tumors.

**Diagnosing and Staging PABC**

As with any breast mass detected during pregnancy, ultrasonography...
is the first-choice imaging examination for suspected breast cancer because of its high sensitivity and lack of radiation.\textsuperscript{10,12} On sonograms, breast cancers often show an irregular shape, microlobulations or spiculated margins, a heterogeneous internal echo texture, posterior shadowing, and a nonparallel orientation.\textsuperscript{12,39,40} However, among patients with PABC, parallel orientation is seen on ultrasonographic examination in 58% of cases, according to one report.\textsuperscript{12}

Following ultrasonographic examination, mammography might be performed to rule out bilateral or multicentric disease. The mammographic appearance of breast cancer is the same in PABC and non-PABC. Possible indicators of breast cancer on mammograms include masses, microcalcifications, asymmetrical densities, skin thickening, and architectural distortion.\textsuperscript{12} The reported sensitivity of mammography for PABC ranges from 78% to 90%.\textsuperscript{12,13} This limitation might be because of the increased glandularity and water content of the breasts in women who are pregnant or lactating.\textsuperscript{13}

MR imaging should be reserved for instances when ultrasonography is inadequate or MR images will affect treatment decisions.\textsuperscript{10} The appearance of PABC on MR imaging has not been widely reported in the literature. However, one small study indicated that in lactating women, breast cancer appears similar to non-PABC on MR images. Specifically, breast cancers can be either homogeneously or heterogeneously enhancing on MR, or they might appear as a mass with an enhanced rim or as diffuse enhancement.\textsuperscript{12}

When a suspicious mass is identified, image-guided biopsy should be performed promptly.\textsuperscript{11} For histological analysis, core-needle biopsy is the preferred technique, with a reported sensitivity of approximately 90%.\textsuperscript{10} However, core biopsy carries several risks including infection, bleeding, and development of milk fistulas.\textsuperscript{11,12} To help reduce these risks, lactation should be stopped before performing a core-needle biopsy, and the biopsy team should be especially careful about controlling bleeding and maintaining an aseptic field.\textsuperscript{12} Antibiotics also might be administered.\textsuperscript{11} Fine-needle aspiration cytology is not recommended because pregnancy-related changes in the breast tissue are more likely to cause both false-negative and false-positive findings with this technique.\textsuperscript{10,12}

Sentinel lymph node staging using technetium-99m-labelled sulphur colloid can be performed on pregnant patients. Fetal absorbed radiation doses are below threshold levels. However, blue dye should not be used for lymph node staging in pregnant women with breast cancer because of the possibility that the patient might have an anaphylactic reaction to the dye, which could stress her fetus.\textsuperscript{10} In addition, the dye has been shown to cause malformations in fetal rats.\textsuperscript{34} Because the sensitivity of sentinel lymph node staging is reduced without the use of blue dye, axillary lymph node dissection is preferable for pregnant patients.\textsuperscript{34} To evaluate possible metastatic disease, PABC patients should undergo chest radiography, liver ultrasonography, and skeletal MR imaging without a contrast agent.\textsuperscript{18}

The most widely recognized system for staging breast cancer is the tumor, nodes, metastasis (TNM) system, developed by the American Joint Committee on Cancer. Using the TNM system, breast cancers are classified according to:

- The size of the primary tumor.
- Whether the cancer has spread to nearby lymph nodes, and if so, how many nodes are affected.
- Whether the cancer has metastasized to distant organs such as the lung, liver, or bones.

The various stages are classified into 4 prognostic groups or grades.\textsuperscript{41,42} Grade I cancers are early stage and carry a better prognosis; grade IV cancers are later stage and carry a poorer prognosis. Most PABCs are grade II or III.\textsuperscript{11}

**Terminating Pregnancy Because of Breast Cancer**

Medical professionals once believed that a breast cancer patient’s prognosis might be worsened by pregnancy, so termination might have been medically advised in some cases. However, it is now known that terminating pregnancy does not improve a breast cancer patient’s prognosis. Prognosis is based on factors other than pregnancy status,\textsuperscript{43} and some studies have suggested that women with PABC who opt to terminate their pregnancy might actually have decreased
survival. Nevertheless, the guidelines developed by the National Comprehensive Cancer Network, a consortium of leading U.S. cancer organizations, for breast cancer treatment during pregnancy suggest discussing this option with patients in the first trimester of pregnancy. Ultimately, the decision is personal and should be made by a well-informed patient.

**Treating PABC**

As with any breast cancer patient, the goals of treatment for women with PABC are local control and prevention of metastatic disease. However, with pregnant patients, the well-being of the fetus is an additional consideration in treatment planning. Chemotherapy can be safely administered after the first trimester of pregnancy, but radiation therapy and endocrine treatment generally are reserved until after delivery. Treatment decisions are guided by the fetus’ gestational age when the cancer is diagnosed, the cancer’s stage, and the woman’s condition. Box 3 provides an overview of treatment recommendations for pregnant patients by trimester.

To illustrate how the timing of diagnosis, cancer type, and stage affect treatment decisions, Bodner-Adler et al reported on a series of 5 patients who received breast cancer diagnoses during pregnancy. The patients’ mean age was 37 years (range: 33-40 years). Three of the 5 patients began cancer treatment before delivery; treatment was delayed until after delivery in 2 cases. Although each cancer and each treatment was different, all 5 patients were living cancer-free at the time of the report. In addition, all 5 had normal pregnancies with normal fetal development, and all of the infants had normal Apgar scores after delivery. The Apgar score is a brief assessment of newborn well-being. Some specifics of these cases are summarized in Table 2.

**Surgery**

Until the middle of the 20th century, many physicians believed that breast cancer during pregnancy was particularly aggressive and that surgery was therefore pointless. That thinking has since changed completely. Generally speaking, the surgical recommendations for pregnant and postpartum women with breast cancer are the same as those for other patients with breast cancer.

Mastectomy and axillary lymph node dissection can be performed at any time during pregnancy; most surgical anesthetics are not harmful to fetuses. Breast-conserving surgery can be performed for women during the second and third trimesters of pregnancy but is not advised during the first trimester. This is not because breast-conserving surgery is risky in early pregnancy, but because adjuvant radiation therapy must be delayed until after delivery, a lag of 6 months or more. Delaying adjuvant radiation therapy increases the risk that breast cancer might metastasize.

If possible, the fetal heart rate should be monitored throughout surgery. In addition, special care should be taken during surgery to avoid maternal hypoxia, hypotension, hypoglycemia, and certain other conditions because the fetus’s development might be affected. It also is important that surgical pain be well controlled because pain can trigger premature labor. Pregnancy is associated with a higher risk for blood clots, so pregnant surgical patients should be treated with heparin to control clotting. Breast reconstruction should be delayed until after delivery.

**Chemotherapy**

Although surgery is the first-line treatment for PABC, adjuvant chemotherapy benefits patients.
with certain high-risk factors such as a higher tumor grade, or estrogen and progesterone receptor-negative tumors.\textsuperscript{13} Chemotherapy can be administered during the second or third trimester of pregnancy but is not advised during the first trimester, when fetal organs are still forming.\textsuperscript{10} The estimated risk of fetal malformation or spontaneous abortion due to chemotherapy during the first trimester is up to 17\%.\textsuperscript{11} This risk drops to 1.5\% or less during the second and third trimesters.\textsuperscript{11} The FDA classifies most chemotherapy drugs as pregnancy category D, meaning that despite evidence of some risk to the fetus, their use is acceptable in certain situations, such as life-threatening disease (see Table 3).\textsuperscript{33,47}

The guidelines developed by the National Comprehensive Cancer Network indicate that most women with PABC have been treated safely with combinations of doxorubicin, cyclophosphamide, and fluorouracil.\textsuperscript{46} At the MD Anderson Cancer Center in Houston, Texas, for example, the standard treatment protocol for pregnant women with breast cancer is 500 mg/m\textsuperscript{2} of 5-fluorouracil administered intravenously on days 1 and 4, 50 mg/m\textsuperscript{2} doxorubicin or adriamycin infused continuously over 72 hours, and 500 mg/m\textsuperscript{2} cyclophosphamide given intravenously on day 1.\textsuperscript{33} Although the National Comprehensive Cancer Network guidelines do not mention the taxanes (eg, paclitaxel and docetaxel), some studies suggest these drugs also might be safe for use in pregnant breast cancer patients during the second and third trimesters.\textsuperscript{46} However, methotrexate, another chemotherapeutical sometimes used to treat breast cancer, is specifically contraindicated in pregnant women because of possible harm to the fetus.\textsuperscript{13} Methotrexate is known to cause various types of fetal malformations and fetal death.\textsuperscript{13}

Antiemetic drugs used to control nausea during chemotherapy are classified as FDA pregnancy category B, meaning well-controlled studies have not shown a risk to fetuses, and antiemetics should be included in the treatment protocol.\textsuperscript{33}

Chemotherapy might be less effective in pregnant women because of pregnancy-related physiological changes such as a higher volume of plasma and an increased rate of glomerular filtration. However, in one small study of women with inflammatory breast cancer, pregnant patients showed similar chemosensitivity when compared with nonpregnant patients.\textsuperscript{10}

The placenta is a fairly effective filter, but chemotherapeutics are known to cross the placenta. Studies of this phenomenon in humans are limited, but a study involving pregnant baboons that received common chemotherapy agents showed much lower concentrations of the drugs in fetal plasma than in maternal plasma.

Table 2

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Maternal Age (Years); Gestational Age (Weeks) at Diagnosis</th>
<th>Cancer Type; Stage</th>
<th>Treatment Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>33; 26</td>
<td>Bilateral inflammatory and invasive lobular; T4b, N4a</td>
<td>Before delivery: neoadjuvant FEC and ET chemotherapy; after delivery: bilateral mastectomy and lymph node removal, adjuvant Taxol and Herceptin chemotherapy, radiation therapy</td>
</tr>
<tr>
<td>2</td>
<td>40; 16</td>
<td>Invasive ductal; T2, N0</td>
<td>Before delivery: neoadjuvant FEC chemotherapy, lumpectomy, and sentinel lymph node dissection; after delivery: locoregional radiation therapy</td>
</tr>
<tr>
<td>3</td>
<td>40; 22</td>
<td>Invasive lobular; T3, N0</td>
<td>Before delivery: neoadjuvant FEC chemotherapy; after delivery: additional neoadjuvant FEC chemotherapy, mastectomy, hormonal therapy</td>
</tr>
<tr>
<td>4</td>
<td>40; 32</td>
<td>Invasive ductal; T1c, NOS</td>
<td>After delivery: lumpectomy and sentinel lymph node dissection, adjuvant hormonal therapy, locoregional radiation therapy</td>
</tr>
<tr>
<td>5</td>
<td>37; 34</td>
<td>Mucinous; T2, N0</td>
<td>After delivery: neoadjuvant ET chemotherapy, lumpectomy and lymph node dissection, radiation therapy, hormonal therapy</td>
</tr>
</tbody>
</table>

Abbreviations: ET, etoposide; FEC, 5-fluorouracil, epirubicin, and cyclophosphamide; NOS, not otherwise specified.
For example, the average fetal concentration of doxorubicin was only 7.5% of the maternal concentration. For epirubicin, the average fetal concentration was only 4% of the maternal concentration.\(^10\)

Several studies have suggested that developmental abnormalities do not appear to be more common in children whose mothers received chemotherapy during pregnancy than in children not subjected to chemotherapy in utero.\(^10\) For example, a study of 84 children whose mothers received chemotherapy during pregnancy for hematological cancers did not reveal any congenital, neurologic, or psychological abnormalities.\(^14\) The median follow-up period in this study was 18.7 years.\(^14\)

Nevertheless, premature delivery and lower birth weights are more commonly associated with prenatal chemotherapy. Therefore, care should be taken to avoid preterm delivery in patients undergoing treatment for PABC.\(^10\)

Patients with PABC who decline chemotherapy while pregnant are advised to have labor induced between 32 and 34 weeks' gestation. This minimizes the delay between diagnosis and commencement of chemotherapy.\(^14\)

It is generally recommended that no chemotherapy be administered after the 35th week of pregnancy as it has a greater association with leukopenia in both the patient and her fetus, which could make them more vulnerable to delivery-related infection, such as one following a cesarean delivery.\(^10,13\)

Chemotherapy can resume, and radiation therapy can begin, immediately after a normal vaginal delivery; however, a one-week delay is advised for women who have a cesarean delivery without complications. Women who are currently undergoing chemotherapy should not breastfeed because the drugs have been detected in breast milk.\(^11,13,34\) Because of insufficient data on the safety of breastfeeding after chemotherapy, women are discouraged from breastfeeding for 4 weeks postchemotherapy.\(^10\) To ensure continued milk production, the woman can pump and discard her breast milk during this waiting period, and breastfeeding can resume thereafter; however, surgical scar tissue and reduced milk production associated with chemotherapy might make breastfeeding after PABC treatment difficult.\(^13\) In one study, for example, only 55% of women were able to breastfeed successfully after receiving chemotherapy during pregnancy.\(^33\)

Endocrine Therapy

Endocrine therapies used to treat breast cancers, such as the estrogen receptor modulator tamoxifen, should be avoided during pregnancy and lactation. These treatments are associated with up to a 20% possibility of fetal abnormalities.\(^11\) Specifically, tamoxifen is associated

<p>| Table 3 |</p>
<table>
<thead>
<tr>
<th>U.S. Food and Drug Administration Pregnancy Categories for Drugs</th>
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<tr>
<td><strong>Category</strong></td>
</tr>
<tr>
<td>A</td>
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<tr>
<td>B</td>
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<tr>
<td>C</td>
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<tr>
<td>D</td>
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<tr>
<td>X</td>
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</tbody>
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with genital tract anomalies, growth restriction, preterm labor, and spontaneous abortion. However, endocrine therapies can be used after delivery.

**Biological Agents**

For breast cancers that overexpress ERBB2, trastuzumab is standard treatment. Trastuzumab is a monoclonal antibody, a manmade version of a protein that seeks out ERBB2, which can be present on tumor cells in breast cancer patients. When trastuzumab locks onto the ERBB2 protein, it induces cytotoxicity and the tumor cells die. However, trastuzumab should not be used in pregnant patients because it can reduce the amount of amniotic fluid, a condition known as oligohydramnios that is associated with birth defects. Trastuzumab also is associated with fetal renal dysfunction.

**Radiation Therapy**

Radiation therapy to treat breast cancer during pregnancy should be avoided because it is not considered safe for the developing fetus, although the exact fetal dose would depend on gestational age and the shielding methods and treatment technique used. Late in pregnancy, as the uterus expands toward the woman’s thorax, the fetal radiation dose might reach 2 Gy, a dangerous level. As mentioned previously, radiation therapy often can begin soon after delivery, but milk from the irradiated breast should not be fed to the baby.

Although not widely accepted, the use of radiation therapy during pregnancy for patients with breast cancer has been reported. In one case, for example, a pregnant woman with advanced breast cancer received both chemotherapy and radiation therapy beginning in the 25th gestational week. She was treated with 20 cGy at the T7-8 level with abdominal shielding. The patient delivered spontaneously at 33 weeks’ gestation and died one year postpartum. Her child was reportedly developing normally at 2 years of age, despite complications at birth.

**Fetal Surveillance and PABC**

Because of the possible hazards of chemotherapy during pregnancy, such as lower birth weight and preterm delivery, fetal development should be monitored closely in women with PABC. One group of authors recommended ultrasonographic assessment of fetal growth every 4 weeks, or more often if growth restriction is detected. Other tests of fetal well-being, such as evaluation of the amniotic fluid, also should be ordered if a fetus’ growth is shown to be restricted.

Breast cancer does not metastasize to the fetuses of women with PABC, but metastatic disease occasionally is detected in the placenta. Therefore, the placentas of women with PABC should be evaluated by a pathologist after delivery.

**Psychosocial Issues and PABC**

Many women with breast cancer share common concerns, such as the possibility of a future recurrence or an altered body image because of breast surgery. In addition, some breast cancer patients worry about socioeconomic issues such as job loss or job discrimination because of their health status. Women with PABC might have additional, unique anxieties. They might, for instance, worry about whether their fetus is developing normally or will be born prematurely. Some PABC patients also are concerned about whether they will survive to parent their child or children. Family members and health care professionals both play a role in supporting PABC patients and promoting their emotional health.

**Survival Rates for Patients With PABC**

Studies of survivorship among patients with PABC have yielded mixed findings, perhaps because PABC is relatively rare and small numbers of patients were included in some of the studies. Some studies suggest that survival rates for women with PABC are similar to survival rates for women who are not pregnant or recently delivered a baby and who have comparable breast cancers; other studies have concluded that PABC is independently associated with worse outcomes. It seems that medical science still is clarifying exactly how pregnancy factors into the breast cancer survival equation.

In 2013, Amant et al found that survival rates were similar for women who received a breast cancer diagnosis while pregnant compared with nonpregnant breast cancer patients who had the same type and stage of disease. This study, which the authors believed to be the largest of its kind to date, examined long-term overall survival and disease-free survival in 311 pregnant breast cancer patients, median age 33 years, and...
Breast Disorders in Pregnant and Lactating Women

865 nonpregnant breast cancer patients, median age 41 years. After adjusting for a variety of prognostic factors, including patient age, disease stage and grade, hormone receptor status, histologic type, and type of treatment, the researchers found “a modest, if any” effect of pregnancy on disease-free survival and overall survival. At a median follow-up period of slightly more than 5 years, 14% of the women who had been pregnant at the time of diagnosis had died vs 12% of the nonpregnant patients.

Conversely, Azim et al performed a meta-analysis in 2012 of 30 studies comparing survival in PABC and non-PABC patients. Based on these varied studies, some dating back decades, they determined that PABC was independently associated with poorer survival. This was especially true among women whose breast cancer was diagnosed postpartum, rather than during pregnancy, as in the Amant study. In addition, PABC was more often associated with local disease recurrence.

Finally, Litton et al reported in 2013 on a study of overall survival and disease-free survival in 75 patients with breast cancer who received chemotherapy while pregnant. Each of these patients was matched with 2 nonpregnant patients of similar age and breast cancer stage. The researchers concluded that survival rates for the pregnant patients were comparable to, if not better than, survival rates for the nonpregnant control cases. For example, the 5-year overall survival rate was 77% among the pregnant patients vs 71% for the control cases. However, the comparatively small size of the study population might have been a limitation of this study.

Subsequent Pregnancy After PABC

Breast cancer treatment can affect fertility. Each course of chemotherapy reduces a woman’s ovarian reserve, thereby causing menopause to occur earlier than it would have otherwise. The specific chemotherapy agents administered and the woman’s age at the time of treatment both affect the extent to which her fertility is reduced. Women with PABC who will receive chemotherapy and might want to become pregnant again should be informed about reproductive options such as egg or embryo freezing that could enable a future pregnancy.

If breast cancer recurs, it usually presents within 2 years after the original diagnosis. Consequently, some experts recommend waiting 2 years to conceive again after PABC, and the suggested waiting period might be longer for patients with advanced-stage PABC. It is not known whether or how a subsequent pregnancy affects the likelihood of breast cancer recurrence in women who had PABC. Most women with PABC (about 90%) do not become pregnant again after treatment.

Conclusion

During pregnancy and lactation, a woman’s breasts undergo marked changes triggered by fluctuating hormone levels. Throughout this process, the breasts continue to be susceptible to the same disorders that affect the breasts of women who are not pregnant or lactating, as well as some conditions unique to pregnancy and lactation. Many of these are benign and might not require treatment; others are treated surgically or with drugs.

Although rare, breast cancer does occur in pregnant and postpartum women and often is discovered at more advanced stages than breast cancer in women who are not pregnant or were recently pregnant. This is probably due, at least in part, to pregnancy-related changes in the breast tissues that can obscure cancer and delay diagnosis. The incidence of PABC is expected to rise as women in developed countries increasingly choose to delay childbearing until later in life. Pregnant women with breast cancer can safely undergo surgery at any time and chemotherapy after the first trimester, but radiation therapy and endocrine therapy should be delayed until after delivery.

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References


Breast Disorders in Pregnant and Lactating Women

1. Which hormone induces involution of fibrofatty breast tissue during the second and third trimesters of pregnancy?
   a. estrogen
   b. prolactin
   c. progesterone
   d. oxytocin

2. What happens to the levels of estrogen and progesterone within hours after a woman gives birth?
   a. They decline gradually to prepregnancy levels.
   b. They rise steadily until the milk supply is well established, then level off.
   c. They begin to rise and fall, synchronizing with the breastfeeding cycle.
   d. They decrease sharply, becoming almost undetectable.

3. Which imaging technique is the preferred modality for pregnant and lactating women's breasts?
   a. mammography
   b. magnetic resonance mammography
   c. ultrasonography
   d. Imaging should be delayed until after delivery and cessation of breastfeeding.

4. Malignancy typically appears on ultrasonography as:
   1. irregular, ill-defined margins.
   2. internal vascularity.
   3. heterogeneous echogenicity.
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3
5. Organ malformation in first-trimester fetuses is thought to occur at radiation doses of ______ , while the dose delivered to the fetus during standard 2-projection mammography with abdominal shielding is ______ .
   a. more than 0.05 Gy; 0.004 Gy
   b. less than 0.05 Gy; more than 0.004 Gy
   c. 0.10 Gy; 0.014 Gy
   d. 0.15 Gy; more than 0.14 Gy

6. In the study by Hosny et al of 48 pregnant or lactating women with palpable breast masses, what were the 2 most common diagnoses?
   a. ductal carcinomas and lactating adenomas
   b. simple cysts and puerperal mastitis
   c. fibroadenomas and lobular carcinomas
   d. simple cysts and fibroadenomas

7. ______ typically appear(s) as oval masses with circumscribed margins on ultrasonography.
   a. Fibroadenomas
   b. Granulomatous mastitis
   c. Simple cysts
   d. Puerperal mastitis

8. Lactating adenomas share several characteristics in common with fibroadenomas. One difference is that lactating adenomas tend to be:
   a. painless.
   b. mobile.
   c. soft.
   d. multiple.

9. A fat-fluid line seen on a mammogram is considered diagnostic for a:
   a. cyst.
   b. milk duct fistula.
   c. galactocele.
   d. lactating adenoma.

10. A(n) ______ commonly causes milk duct fistulas.
    a. medical procedure, such as a biopsy
    b. abrupt stop to breastfeeding
    c. infectious organism
    d. underlying cancerous tumor

11. Which benign breast condition can mimic breast cancer, in that it can appear as ill-defined, asymmetric densities, with skin thickening and axillary adenopathy?
    a. galactocele
    b. granulomatous mastitis
    c. fibroadenoma
    d. gigantomastia

12. Antibiotics, rest, hydration, and warm compresses are recommended for treating puerperal mastitis. In addition, the patient should:
    a. stop breastfeeding immediately.
    b. alternate breastfeeding with bottle feeding until the infection clears.
    c. empty her breasts of milk frequently and completely.
    d. pump and discard milk from the infected breast.

13. Which of the following benign breast conditions can appear similar to inflammatory breast cancer?
    a. fibroadenomas
    b. galactoceles
    c. milk duct fistulas
    d. puerperal mastitis

continued on next page
14. According to the article, the incidence of breast cancer in pregnant and postpartum women probably will rise in developed countries because:
   a. screening recommendations were revised to include all women aged 25 to 35 years.
   b. women are increasingly opting to delay pregnancy until later in life.
   c. ultrasonography of the breasts has become a routine part of prenatal care.
   d. more women are choosing to breastfeed and for longer periods.

15. Approximately two-thirds of pregnancy-associated breast cancer (PABC) cases are diagnosed:
   a. in the first trimester.
   b. in the second or third trimester.
   c. after the patient has given birth, often within 6 months of delivery.
   d. when the patient stops breastfeeding.

16. In about 90% of cases, PABC initially manifests with the presence of:
   a. a painless mass.
   b. erythema.
   c. swelling.
   d. enlargement of the breast.

17. Histologically, the most common type of PABC is:
   a. invasive ductal carcinoma.
   b. invasive lobular carcinoma.
   c. inflammatory breast cancer.
   d. mucinous carcinoma.

18. All of the following imaging examinations should be performed to evaluate possible metastatic disease associated with breast cancer in a pregnant patient except:
   a. liver ultrasonography.
   b. chest radiography.
   c. skeletal magnetic resonance imaging without a contrast agent.
   d. computed tomography without a contrast agent.

19. At one time, medical professionals believed that a breast cancer patient’s prognosis might be ______ because of pregnancy. However, it is now known that terminating a pregnancy ______ the prognosis.
   a. improved; improves
   b. worsened; does not improve
   c. improved; has little effect on
   d. worsened; markedly improves

20. Which of the following precautions should be observed when pregnant patients undergo breast cancer surgery?
   1. The fetal heart rate should be monitored during surgery, if possible.
   2. Maternal hypoxia and hypotension should be avoided.
   3. The patient should be treated with heparin to control blood clotting.
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2, and 3

21. If the risk of using a particular drug in a pregnant patient clearly outweighs any possible benefit, the drug is considered pregnancy category ______ by the U.S. Food and Drug Administration.
   a. A
   b. B
   c. C
   d. X

22. All of the following are contraindicated for treating breast cancer during pregnancy except:
   a. methotrexate.
   b. trastuzumab.
   c. tamoxifen.
   d. cyclophosphamide.
23. ______ for breast cancer treatment should be delayed until after delivery.
   a. Chemotherapy and surgery
   b. Radiation therapy and endocrine therapy
   c. Endocrine therapy and chemotherapy
   d. Surgery and radiation therapy

24. Breast cancer does not metastasize to the fetuses of women with PABC, but metastatic disease occasionally is detected in the placenta.
   a. true
   b. false

25. When breast cancer recurs, it usually presents within ______ year(s) after the original diagnosis.
   a. 1
   b. 2
   c. 3
   d. 4