Breast Care Guideline Team

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Common Breast Problems

Patient population: Adults age 18 and older (non-pregnant).

Objectives: Identify appropriate evaluation and management strategies for common breast problems. Identify appropriate indications for referral to a breast specialist.

Assumptions

Appropriate mammographic screening per NCCN, ACS, USPSTF and UMHS screening guidelines. Generally mammogram is not indicated for women age <30 because of low sensitivity and specificity.

"Diagnostic breast imaging" refers to diagnostic mammogram and/or ultrasound. At most ages the combination of both imaging techniques yields the most accurate results and is recommended based on patient age and the radiologist's judgment.

Key Aspects and Recommendations

Palpable Mass or Asymmetric Thickening/Nodularity on Physical Exam (Figure 1)

Discrete masses elevate the index of suspicion. Physical exam cannot reliably rule out malignancy.

- Breast imaging is the next diagnostic approach to aid in diagnosis *[I C*]*.
- Initial imaging evaluation: if age ≥ 30 years then mammogram followed by breast ultrasound; if age < 30 years then breast ultrasound *[I C*]*. Follow-up depends on results (see Figure 1).

Asymmetrical thickening / nodularity has a lower index of suspicion, but should be assessed with breast imaging based on age as for patients with a discrete mass. If imaging is:

- Suspicious or highly suggestive (BIRADS category 4 or 5) or if the area is assessed on clinical exam as suspicious, then biopsy after imaging *[I C*]*. Referral to a breast care specialist may be useful.
- Probably benign (BI-RADS 3): if clinically benign, observe every 3–6 months and image every 6-12 months for 2 years to assess stability *[I C*]*; if clinically suspicious, biopsy tissue *[I C*]*.
- Negative or benign (BI-RADS 1 or 2): if clinically benign, then follow-up physical exam in 3 months *[I C*]*, if clinically suspicious, biopsy tissue *[I C*]*. Simple cysts (Benign finding, BI-RADS 2) need aspiration only if symptomatic. *[I C*]*.

Referral to breast care specialist is also recommended for: (a) any suspicious mass or (b) any woman at very high risk for breast cancer *[I D*]*.

Inflammation and Other Skin Changes

If cellulitic breast skin changes:

- Do not completely resolve after a course of antibiotics, refer to a breast specialist for consideration of breast biopsy to rule out inflammatory breast cancer *[I C*]*.
- Are associated with a fluctuant, painful mass, refer to a breast specialist or emergency department for management of a possible breast abscess *[I C*]*.

If eczematoid changes of the nipple-areolar skin persist > 1-2 weeks or do not respond to topical treatment, refer to a breast specialist for possible biopsy to rule out Paget's disease of the nipple *[I C*]*.

Breast Pain with Negative Physical Exam (Figure 2)

- If physical exam and appropriate breast imaging are negative, the likely diagnosis is benign mastalgia: reassure patient. A trial of topical agents is reasonable (see text) *[II A*]*. Recommendation for a well-fitted bra is often helpful *[II C*]*.
- If persistent or localized pain not responsive after 2-3 months of conservative treatment, refer to breast specialist *[I C*]*.

Nipple Discharge Without Abnormal Exam Findings (Figure 3)

- If discharge is spontaneous or watery/serous or if other risk factors are present (persistent, serosanguinous, single duct), refer to a breast specialist and consider diagnostic imaging *[I C*]*.
- If discharge is non-spontaneous, if clearly galactorrhea, pursue medical workup and do not refer to breast specialist *[I C*]*. If discharge is from multiple ducts and gray to green in color, do not refer to a breast specialist unless patient requests referral for symptomatic relief *[I C*]*.

Special Populations

Pregnant women. If concerning indications, imaging is relatively safe and should be done *[I C*]*.

Men. Diagnose and treat enlargement or pain *[I C*]*. Breast mass is rare, but suspicious for cancer *[I C*]*.

Augmented breasts. Evaluation/management of above conditions is similar, but imaging issues *[I C*]*.

* **Strength of recommendation:**
I = generally should be performed; II = may be reasonable to perform; III = generally should not be performed.
Levels of evidence reflect the best available literature in support of an intervention or test:
A=randomized controlled trials; B=controlled trials, no randomization; C=observational trials; D=opinion of expert panel.

Figure 1. Palpable Breast Mass or Asymmetric Thickening / Nodularity: Diagnosis and Treatment

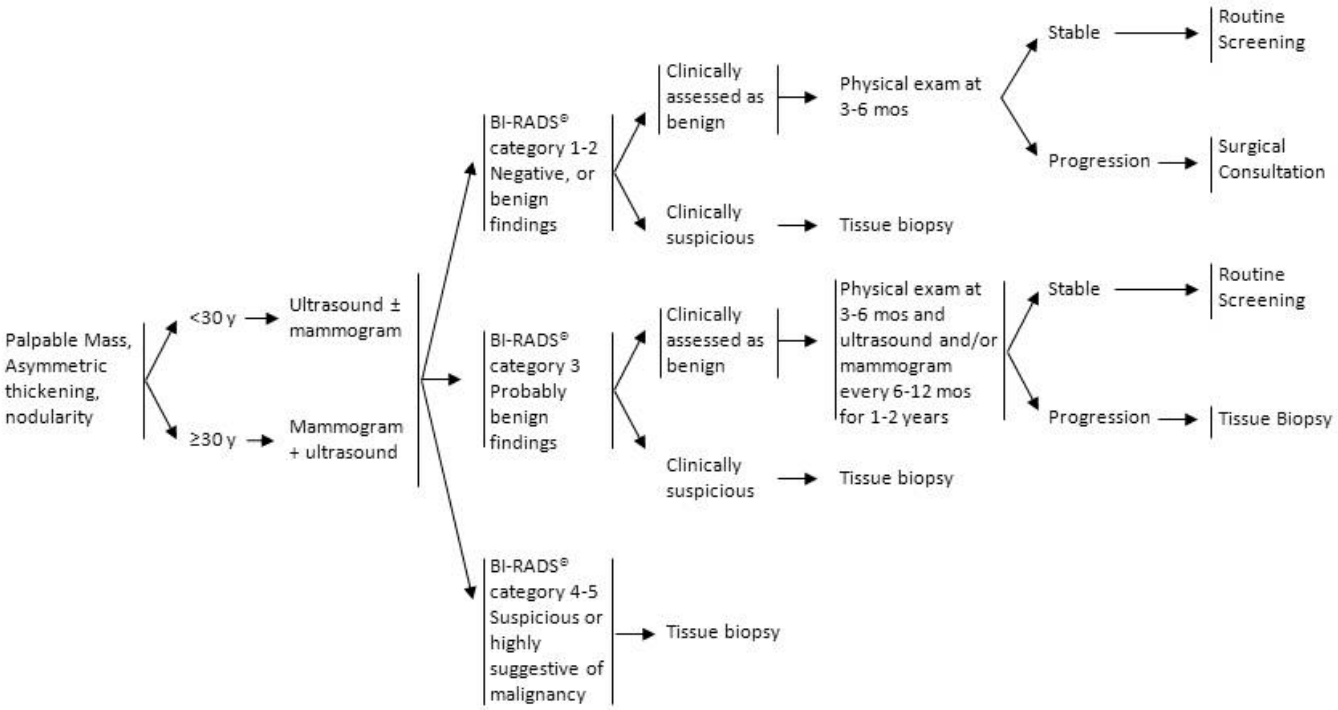

Table 1. Terminology of Mammography Report (BI-RADS®)*

Category 1: Negative	Category 2: Benign Findings	Category 3: Probably Benign Finding	Category 4: Suspicious Abnormality	Category 5: Highly Suggestive of Malignancy
Nothing to comment on	This is also a negative mammogram, but the interpreter may wish to describe a finding while still concluding that there is no mammographic evidence of malignancy	**Initial short interval follow up is recommended.** A finding placed in this category must have a very high likelihood of being benign. It is not expected to change over the follow up interval, but the radiologist would prefer to establish its stability.	**Biopsy should be considered.** These are lesions that do not have the characteristic morphologies of breast cancer but have a definite probability of being malignant.	**Appropriate action should be taken.** These lesions have a high probability of being cancer.

* Breast Imaging Reporting and Data System ® (BI-RADS®) Atlas, 4th edition, Reston, VA: American College of Radiology, 2003. *Reprinted as modified and approved with permission of the American College of Radiology. No other representation of this material is authorized without expressed, written permission from the American College of Radiology.*

Figure 2. Breast Pain Diagnosis and Treatment
(If mass present, follow Figure 1)

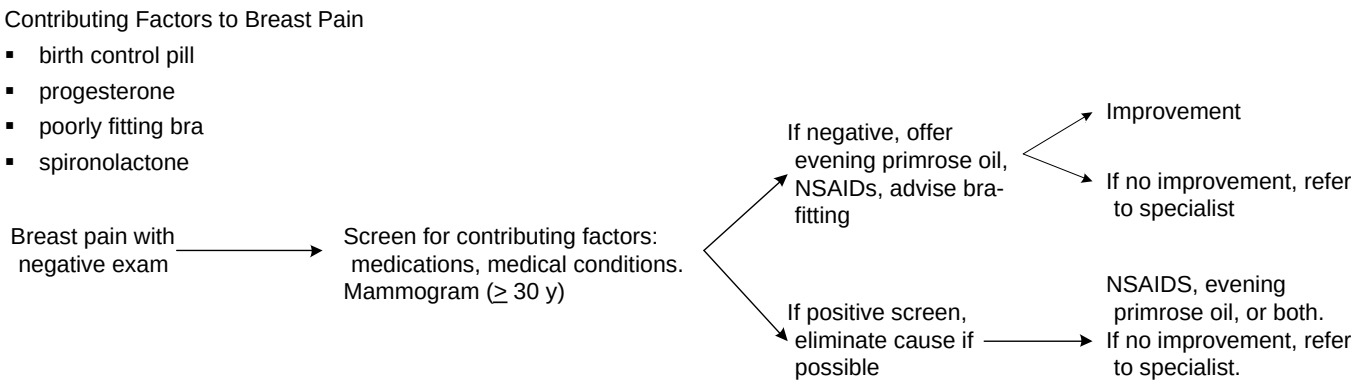

Figure 3. Nipple Discharge Diagnosis and Treatment (no mass)
(If mass present, follow Figure 1)

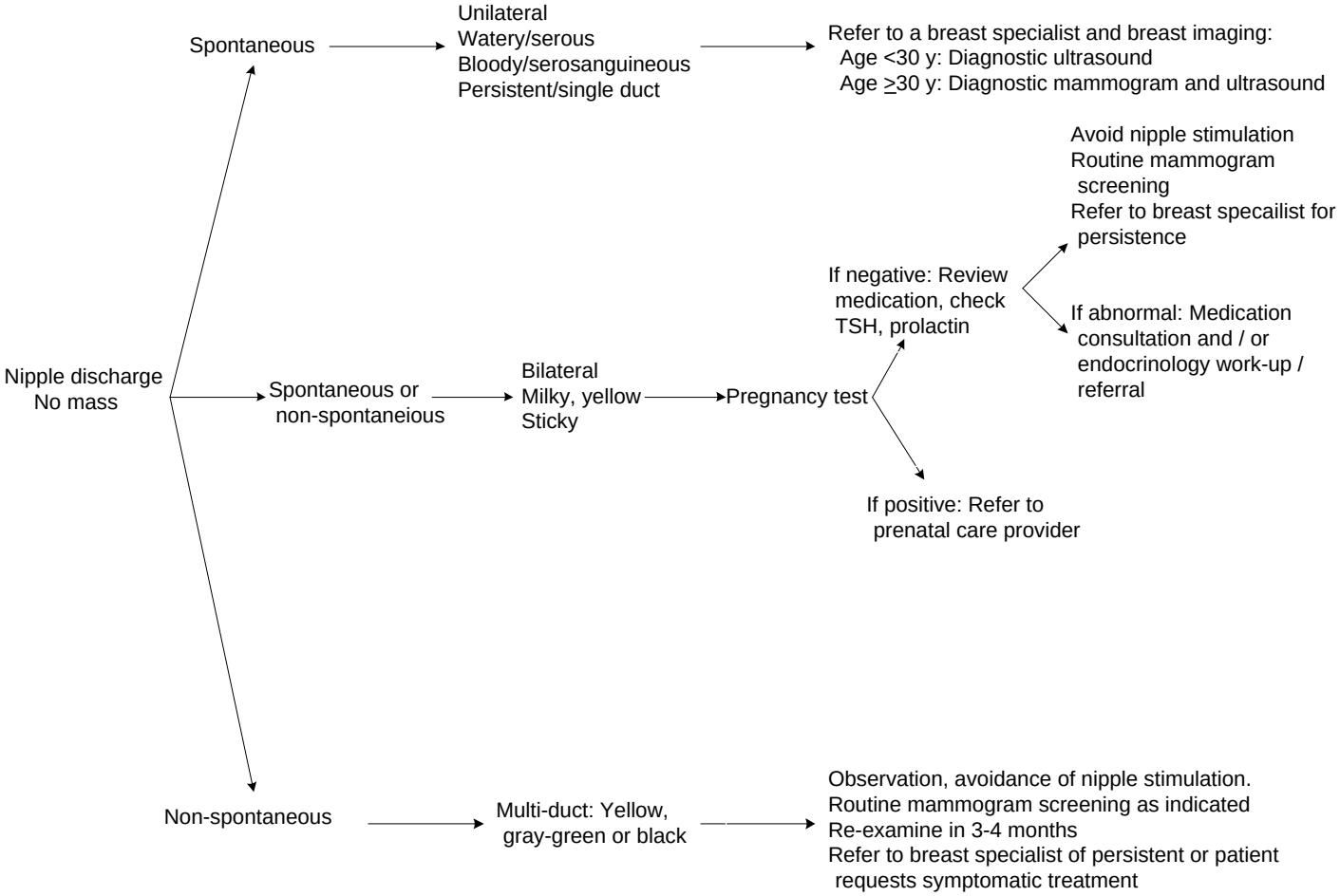

Table 2. Typical Characteristics* of Breast Lumps on Physical Exam

Type of Lesion	Consistency of Lesion	Surface Characteristics	Mobility
Fibroadenoma	Rubbery	Smooth / lobular	Very mobile
Cyst	Variable: soft, tense or hard	Variable – often smooth	Fairly mobile
Normal nodularity	Glandular – like normal breast tissue: prominent nodularity or moderate asymmetry without discrete mass or tissue changes suggestive for malignancy	Indistinct	Indistinct
Fat lobule	Soft breast tissue	Smooth; often found along inferior margin	Indistinct
Intramammary lymph node	Usually impalpable	Smooth ovoid mass in axillary tail; often found along edge of previous biopsy	Indistinct
Malignant tumor	Hard	Irregular (not smooth)	Fixed/decreased mobility

From: Hughes L, Webster D. Benign Disorders of the Breast: Concepts and Clinical Management, Ch 5. Bailliere Tindall, 2000.

* Typical characteristics of breast lumps are not sufficiently reliable to make a final diagnosis when a breast mass is detected. Further imaging and/or tissue diagnosis may be necessary [see text].

Clinical Background

Clinical Problem and Current Dilemma

Incidence. Breast cancer is the most common non-cutaneous malignant neoplasm in women in the United States. It is exceeded only by lung cancer as a cause of cancer death in women. About 1 in 8 women will develop invasive breast cancer over the course of her lifetime.

Although breast cancer is the most common malignancy of women in the United States, the majority of breast disorders are benign. In a population-based study of HMO patients in a primary care setting found over a 10 year period of time, 16% of female patients over 40 presented with a breast symptom. The most common complaint was pain, followed by palpable mass. Overall, the incidence of breast cancer found during evaluation was 6.2%. Other studies estimate a higher rate of malignancy, 10 to 20%, but are based on data from a referral population.

Risk factors for breast cancer. While it is important to be aware of risk factors for breast cancer in the general population, their predictive value differs in a symptomatic population. For example, while age is an important risk factor in asymptomatic women, a study of women presenting to their doctors with breast complaints found little difference in rates of cancer diagnosis in women of different ages between age 40 and 70. Symptoms in women at any age, with or without risk factors, need to be considered as potentially serious. Also, some risk factors (e.g., genetic predisposition) place a small percentage of women at particularly high risk of developing breast cancer.

Management. Little scientific information is available on evaluation and management of women who present to their primary care providers with breast problems. However, guidelines such as the NCI's National Comprehensive Cancer Network's Breast Cancer Screening and Diagnosis Guidelines provide a consensus among nationally recognized experts in the field and can serve as the standard of care. Their website, NCCN.org, provides more in-depth algorithms and explanatory, research-based text supporting the guidelines.

Rationale for Recommendations

The rationale for recommendations is presented in three major categories:

- Evaluation / Imaging Techniques
- Specific Breast Signs and Symptoms
- Special populations: pregnancy, men, augmented breasts

Examination / Imaging / Diagnostic Procedures

The techniques discussed include: clinical breast exam, diagnostic imaging and diagnostic procedures. Typically, diagnostic breast imaging includes mammogram and ultrasound directed at the area of concern, with approach determined at the discretion of the radiologists.

Clinical breast examination. Few data are available on the positive predictive value, sensitivity, or specificity of clinician breast exam (CBE). As a screening test, CBE sensitivity has been measured at 63% in the Canadian NBSS. What constitutes a good clinician breast exam is still open to debate. No clear-cut guidelines are available, though the American Cancer Society recommends examining in the upright as well as the supine position. Time is the only variable found to correlate with accuracy of exam – at least 3-5 minutes on the exam is recommended.

For evaluation of a palpable mass, CBE performs a different function: characterizing the features of the breast exam in the area of concern. For the primary care provider, the clinical breast exam is important because it determines the index of suspicion for malignancy, i.e. the pretest probability. Physical characteristics and the likely type of lesion are described in Table 2.

CBE is only moderately accurate in this diagnostic mode, with estimated sensitivity in a study of 201 palpable solid masses of 88% and specificity of 71%. Sensitivity and specificity are improved significantly with the addition of mammography. One UCSF study of the combination found that when the physical exam and mammography were in agreement, positive predictive value was 96.4% and negative predictive value was 96.3%.

Repeating the CBE can be a useful diagnostic tool when breast asymmetry is detected, as asymmetry is commonly transient. Persistence of an abnormality increases pretest probability of disease.

Diagnostic imaging. Breast Imaging is the starting point for assessment of breast findings. Mammography and ultrasound form the basis of most imaging. MRI is used infrequently for diagnostic assessment of common clinical problems.

Mammography. In these guidelines we recommend ordering a *diagnostic* mammogram for those women who visit their health care provider for a breast problem, who have not had a mammogram recently, and are at least thirty years old. This minimum age recommendation is based on the expected density in the breasts in women under 30, which significantly limits diagnostic sensitivity and specificity of mammography and the infrequency of malignancy. A *screening* mammogram is reserved for women with no current problems and should not be ordered for women with current clinical breast problems.

Ultrasound is performed for most women with palpable masses or asymmetrical thickening/nodularity and can be performed at same visit as the mammogram. In evaluation of breast complaint, mammography is not a perfect diagnostic tool. False negatives are not uncommon, especially in younger women or women with radiographically dense breast tissue. Overall, 10% of diagnostic mammograms are false negatives, with approximately twice that rate for younger women and half that rate for women over age 65. However, when diagnostic mammography is combined with ultrasound, the false negative rate is much lower, typically 1-3%.

For evaluation of a palpable mass, diagnostic mammogram alone has been shown to have a sensitivity of 82 to 94%, and a specificity of 55 to 84%. It is used as an adjunct in the diagnostic workup. A negative mammogram should not end the workup unless clinical suspicion has become lower through other diagnostic modalities as well. An additional benefit of mammography in this setting is to look for other suspicious areas in either breast that may not be palpable, as multiple foci of primary breast carcinoma can occur concurrently. It can also be used as a guide for invasive diagnostic procedures.

The Food and Drug Administration now requires all mammographic reports to include one of the five final assessment categories (Table 1). Tissue sampling is recommended for Suspicious Findings (BI-RADS Category 4) and highly suggestive of malignancy (BI-RADS Category 5) assessments. Probably benign (BI-RADS Category 3) assessments carry a 0.5-2.0% risk of malignancy and are generally recommended for periodic short-term mammographic follow-up at 4-6 months if the clinical suspicion is benign.

Ultrasound. Ultrasound is used as the initial imaging method of symptomatic women younger than 30 years and combined with mammography for women older than 30. Ultrasound is used to characterize a palpable or mammographic mass or thickening as a cystic or potentially solid mass. Masses that meet all the diagnostic criteria for "simple" cysts do not require aspiration unless painful or possibly infected. Non-simple cysts include "complicated cysts" (Probably benign, BIRADS 3) and "complex" cystic masses (Suspicious, BI RADS 4). While the former may be followed with imaging surveillance or aspiration, biopsy is recommended for the latter due to the much higher probability for malignancy. Ultrasound can assist in differentiating benign and malignant solid masses, but is not tissue specific. Some solid masses having probably benign sonographic findings (BIRADS 3) and benign clinical assessment may be followed with imaging if less than 2 cm. Ultrasound can be used to guide image-directed procedures.

Magnetic resonance imaging (MRI). MRI, as an adjunct to other breast imaging modalities, has emerged as a useful technology with increased sensitivity in certain high-risk groups. MRI is used primarily as an adjunct screening method for high-risk women. MRI has limited utility for routine use for symptomatic women. Mammography and ultrasound should be performed first. MRI may be indicated for women with significant nipple discharge when diagnosis remains unclear after mammography, ultrasound and breast specialist evaluation. MRI is not routinely recommended for evaluation of women with breast masses. MRI is the most accurate imaging test to assess silicone breast implants for potential intracapsular or extracapsular rupture.

Diagnostic procedures. Definitive diagnosis of breast cancer can be established by any procedure that yields cells or tissue from the breast that can be analyzed microscopically by a pathologist or cytologist. A diagnostic technique should be selected for:

- any clinical or breast imaging finding that is suspicious for cancer
- any breast problem where the work-up and evaluation are not conclusive for a benign etiology.

The selection of diagnostic procedure or biopsy is based upon level of suspicion and type of abnormality. In cases that are highly suspicious for breast cancer, the diagnostic histopathology specimen should be one that provides adequate tissue for determination of an in situ versus an invasive cancer, as well as for histopathologic evaluation and molecular marker characterization (e.g. estrogen receptor, progesterone receptor, and HER2/neu).

Fine needle aspirate. Fine needle aspiration (FNA) is an appropriate diagnostic procedure when a practitioner is familiar with the technique and its limitations. It can be helpful for a discrete mass, but is not helpful in evaluating vague nodularity. FNA is diagnostic for a benign cyst when the aspirated fluid is nonbloody and the mass disappears with aspiration. For evaluation of solid masses, or nonpalpable masses detected by mammography, the sensitivity is variable, primarily dependent on the skill of the aspirator. Estimates of false negatives range from 1% to 35% for palpable lesions and up to 68% for nonpalpable lesions. It is important to note that negative or nonspecific cytology (anything other than diagnosis of fibroadenoma) needs to be followed up by an alternative biopsy strategy (core or open surgical) for definitive diagnosis.

Core biopsy. A core needle biopsy also requires specialized training and experience by the practitioner. A core biopsy is usually performed with a local anesthetic. It involves percutaneous insertion of a specially-designed device (usually 16 gauge or larger) into a breast abnormality for extraction of tissue fragments. These devices are often spring-loaded, and penetration through the skin generally requires prior piercing of the skin with an 11 blade scalpel tip. The practitioner usually performs several passes of the device in order to extract several fragments of tissue, which are then placed in formalin for transfer to the pathology department. Clinicians perform some core needle biopsies "freehand" and others guided by image (ultrasound or mammographic). Core needle biopsies performed with image guidance have higher diagnostic accuracy.

Punch biopsy. A punch biopsy device employs circular scalpel and is frequently utilized for office- or clinic-based biopsies of abnormal-appearing skin lesions. The punch biopsy devices are available in several sizes ranging from 2 mm to 8 mm circumferences. Punch biopsy can easily be performed under local anesthesia, larger circumference blades often require sutures to close the biopsied skin. Punch biopsies are often performed on the areolar skin to diagnose Paget's disease of the nipple.

Open (surgical) biopsy. An open biopsy is an operative procedure performed by a surgeon to remove a portion or wedge of breast tissue after making an incision on the breast skin. Open biopsies are usually performed as ambulatory/outpatient procedures in an operating room. An excisional biopsy implies that entire breast mass or lesion is being resected. An incisional biopsy implies that only a portion of a mass is being sampled or resected. Some open/surgical biopsy procedures are performed with guidance provided by the breast imaging staff. For example, a suspicious but non-palpable breast abnormality identified on mammogram (or by breast ultrasound) may need to be biopsied surgically. The radiologist would insert a wire preoperatively to demonstrate the location of the abnormality for the operating surgeon. These image-guided open biopsies are called wire-localization surgical biopsies.

Order of diagnostic testing. The order of diagnostic testing is important. Both ultrasound and mammography accuracy can be adversely affected if fine needle aspirate (FNA) is performed prior to imaging studies. Therefore, ultrasound and mammography are generally recommended prior to FNA.

If a cyst is suspected on mammogram, the radiologist may recommend either:

- ultrasound and aspirate for relief of pain and/or diagnosis
- clinical follow-up without intervention if the cysts are small and asymptomatic

Specific Breast Signs and Symptoms

The signs and symptoms discussed include: palpable mass, breast pain and negative exam, and nipple discharge.

Palpable mass, nodularity or asymmetry. The evaluation of a palpable mass on CBE is nearly always begins with breast imaging. For women < 30 years old, initial imaging is with ultrasound. (Mammography might be used at the discretion of the radiologist if findings are inconclusive or suspicious.) For women ≥ 30 years old, mammography followed by ultrasound should be performed. The results of the imaging will dictate further management (see Figure 1).

- Benign finding (BI-RADS 2, e.g., simple cyst) that is geographically consistent (Mass and imaging finding are the same) requires no additional evaluation. Aspiration of a simple cyst can be performed if it is symptomatic.
- Probably Benign finding (BI-RADS 3) associated with a suspicious palpable finding should be referred to a breast specialist.
- Suspicious or Highly suggestive finding (BI-RADS 4 or 5) should undergo a tissue diagnosis (most commonly core needle biopsy performed with image guidance).

Suspicious findings on clinical examination should be referred to a breast care specialist even if imaging is negative, benign, or probably benign.

In women with frequent cyst development, clinical judgment should be used when multiple breast masses (presumed to be cysts) are present on clinical examination. Ideally, definitive identification of these masses should be confirmed, either by aspiration and resolution of the cysts or by breast imaging with ultrasound. Any complex cystic mass or non-resolving, cyst warrants referral to a breast specialist

For distinct masses, if the provider performs a FNA, any aspirated fluid should be visualized and the character of the lesion on physical exam should be evaluated. If the fluid is nonbloody and the mass disappears, the fluid can be discarded. If the fluid is bloody or there is residual mass on breast exam, the fluid should be sent for cytology and the patient referred for diagnostic breast imaging and to a breast specialist for further evaluation. If no fluid is obtained, the cells should be sent to cytology in an appropriate medium (e.g., Cytolyte™, not formalin). If cytology indicates clear diagnosis of fibroadenoma, no further diagnostic testing is needed. If cytology is nondiagnostic or negative then the patient should be referred to a breast specialist.

It is very important to follow through with repeat clinical exam after negative diagnostic imaging. The clinician must re-assess the clinical index of suspicion independent of the initial index of suspicion or the breast imaging results. If the clinician is uncertain about index of suspicion then the patient should be referred to a breast care specialist to avoid the risk of losing the patient to follow up. One of the most common mistakes, and the cause of the largest number of malpractice suits regarding breast cancer diagnosis, results when a falsely negative mammogram and a clinician fails to reexamine after negative diagnostic imaging. If the follow up exam is clinically suspicious, referral should occur.

Inflammation and other skin changes. Signs of breast inflammation include erythematous and/or edematous or thickened skin, with or without associated symptoms such as pain or fever. The skin changes may be localized to a small area of skin, diffuse involvement of the entire breast, or limited to the nipple-areolar skin. Inflammatory changes may develop acutely (within a few days) or they may be of a chronic nature (several weeks). While acute onset is suggestive of an infectious process, inflammatory breast cancer can develop quite suddenly as well.

Patients may also develop benign rashes on the breast. However, if what is thought to be eczema, contact dermatitis or cellulitis is confined to the breast, is unilateral and does not respond as expected to a short trial of appropriate treatment, patient should be referred to breast specialist to evaluate for malignancy.

Inflammatory skin changes associated with pain and a fluctuant or pointing mass can be indicative of a breast abscess. A breast abscess requires operative incision and drainage, and concern regarding the presence of an abscess warrants referral to a breast specialist or the emergency department the same day for possible surgical treatment.

Erythematous changes in the breast raise the consideration of mastitis or inflammatory breast cancer. If there is no mass, a short (10-14 day) course of antibiotic therapy for presumed mastitis is indicated. Close follow-up is important to ensure resolution. (Puerperal mastitis is more common than non-puerperal mastitis – see discussion in section on pregnancy.) Persistent inflammation warrants immediate referral to a breast specialist.

Nipple symptoms such as burning or itching in association with abnormalities on physical exam are concerning for Paget's disease of the breast. Exam findings may include persistent scaling or ulcer with serous fluid drainage or bleeding. Whereas the majority of cases of Paget's occur in association with mammographically detectable breast cancer, up to 40% may have negative mammogram. All suspicious nipple changes should be referred to a breast specialist.

Breast pain and negative exam. Breast pain or mastalgia is a common patient complaint and can be divided into three categories: cyclic mastalgia, noncyclical mastalgia and nonmammary pain.

- Cyclic mastalgia is common in younger women, occurs prior to the menses, and usually increases in severity until onset of menstrual bleeding. It is typically bilateral and may be felt as a heaviness or soreness and be poorly localized with radiation to axilla.
- Noncyclic mastalgia occurs in older women (most common in 40's and 50's) and may be constant or intermittent. It is often unilateral, more focal, and may be felt as a sharp or burning pain.
- Nonmammary pain perceived in the breast may be caused by costochondritis, by pectoral or intercostal muscle strain, or radicular thoracic back pain. Important historical factors include timing and features of pain, history of trauma, emotional stress, medications and family history.

Many women present to their provider's office because of fears that their pain is a sign of breast cancer. Fortunately breast cancer is rarely associated with breast pain in the absence of mass or physical exam changes. If pain is focal and persistent, however, referral to a breast specialist is indicated.

A thorough breast exam is essential in the evaluation of breast pain. If an abnormality is found, referral for diagnostic breast imaging is appropriate. Other indications for imaging include age over 30, elevated personal risk of breast cancer or family history of breast cancer at a young age. Isolated focal pain in any age woman requires appropriate diagnostic imaging

In cases where no focal pain is present and no abnormality is found on exam, reassurance is sufficient. Women can be reassured that as many as 60-80% of cases resolve spontaneously. A large portion of patients are satisfied with reassurance alone and require no further intervention.

Nonpharmacologic interventions should be reviewed and include instruction for a well fitting bra. Relaxation techniques, warm compresses or cold packs, gentle massage and a diet low in fat may decrease pain. Dietary changes such as restriction of methylxanthines/caffeine, fat and salt intake, and intermittent diuretic use are commonly used,

though none have been conclusively demonstrated to be more effective than placebo.

A large number of medications have been implicated in breast pain, including hormonal medications such as contraceptives and post menopausal hormone replacement, antidepressants and several cardiac/antihypertensive medications including spironolactone and digoxin. If these medications are related temporally, a change in dose or medication may be helpful.

If pharmacologic treatment is desired, a trial of evening primrose oil 1000 mg bid (or its active ingredient gamma linoleic acid 160 mg bid) for 3-6 months is indicated. Research has shown varied success in treatment, but it is a low cost, low risk intervention. Oral or topical NSAIDs (e.g., diclofenac gel) also can be used for general pain relief. Topical NSAIDS have been shown in randomized trials to be effective in reducing mastalgia. Avoid long term NSAID treatment as this increases the risk of GI bleeding and renal insufficiency. NSAID use in patients with heart disease or its risk factors increases overall risk of heart attack or stroke.

If these are not successful and patient continues to have significant pain requiring intervention, referral to a breast care specialist is indicated. Available therapies at that point primarily include hormonally active medicines, including tamoxifen, danazol, GnRH analogs medications, and bromocriptine. However, side effects and cost tend to limit their use to the most severe cases.

Galactorrhea and other nipple discharge. Nipple discharge is common, ranking third in prevalence amongst presenting breast complaints, with an incidence of 4-8%. Though most nipple discharge is secondary to a benign breast process, breast cancer rates are 5%-21% in women with this presentation.

Initial evaluation of a patient with nipple discharge begins with a thorough history to identify the characteristics of the discharge and a complete physical exam including CBE. Usual characteristics of benign and pathologic discharges are:

- Benign – Non-spontaneous, bilateral, milky, green-yellow or black and multi-ductal, occurs only with expressing or manipulation.
- Pathologic –Spontaneous, persistent, unilateral, clear, bloody, serous or serosanguinous or arising from a single duct. These require evaluation by a breast specialist.

Given the low sensitivity, guaiac and/or cytology is not recommended in the evaluation of nipple discharge, as a negative result should not preclude further evaluation.

Galactorrhea. Galactorrhea is the most common type of discharge and is usually bilateral, expressible from multiple ducts, sticky and milky to yellowish in color. Primary care providers can generally evaluate and manage this condition without further imaging or referral.

- Pregnancy needs to be ruled out.
- Medication effect is the most common etiology. Figure 3 lists medications commonly associated with galactorrhea. Discuss the pros and cons of continuing the medication with the patient and consider alternatives.
- Prolactinoma or other conditions that reduce dopamine inhibition of prolactin secretion in the hypothalamic-pituitary pathway can be screened with prolactin level.
- Hypothyroidism and renal failure are medical conditions associated with galactorrhea.
- Elevated prolactin levels with no identified cause warrant MRI imaging of the hypothalamus/pituitary and referral to an endocrine specialist.
- Routine mammogram screening should be recommended in age-appropriate patients.

If the above evaluation is negative, women with this complaint may be reassured and counseled that nipple stimulation (sexual activity, jogging, poorly fitted bras, repeated attempts to express discharge) may induce galactorrhea and should be avoided. For persistent or bothersome galactorrhea a referral to a breast specialist should be considered for further evaluation and treatment.

Other benign nipple discharge. Green, gray, milky or black discharge is often seen with fibrocystic breast disease or ductal ectasia and are benign characteristics. If the discharge occurs only with expressing and is multi-ductal, observation is appropriate. Patients should be counseled against nipple stimulation similarly to patients with galactorrhea. Development of spontaneous discharge indicates the need for further evaluation, as the color of nipple discharge cannot reliably exclude pathologic processes.

Pathologic discharge. Spontaneous discharge (without nipple manipulation), presence of a suspicious mass, or discharge from a single duct or in a postmenopausal woman are of concern and should lead to referral. Bloody, watery or serous discharge is also suspicious for malignancy. Diagnostic mammogram is the initial imaging test of choice in women age 30 and older. Ultrasound can be used in addition and as the initial imaging test of choice in women under age 30.

Special Populations and Circumstances

Pregnant Women

Breast problems in pregnancy and lactation can be a challenge to evaluate given the hormonal changes that occur in the tissue. Despite this, breast disorders in pregnant and lactating women are similar to their non-pregnant counterparts.

Breast mass. Approximately 1-3% of all breast cancers are diagnosed during pregnancy, including the post-partum year. Any palpable breast mass found in pregnancy should be evaluated with CBE and imaging as physical exam alone is not sufficient. Ultrasound is recommended as the initial screening modality given the increased density of the breast in pregnancy. Ultrasound does not carry any risk of radiation and therefore can be done at any gestational age. Abnormal ultrasound findings should be further evaluated with diagnostic mammogram and referral to a breast specialist. For women over age 30, could also consider initial evaluation with both diagnostic ultrasound and mammography in accordance with guidelines for evaluation of a palpable mass.

Mammogram screening with abdominal shielding is safe, providing less than 0.03 microGy (0.003 mrad) of radiation to the fetus and can be safely performed in pregnancy, though is not recommended in the first trimester during organogenesis.

Inflammatory changes. Puerperal mastitis is an inflammatory condition of the breast seen in lactating women. Mastitis usually presents as a localized, tender, engorged, erythematous area of the breast often accompanied with systemic symptoms including fever and malaise. This distinguishes it from a plugged duct or galactocele, which may also cause an engorged, tender breast – but typically does not produce systemic symptoms. Initial treatment consists of oral antibiotics and supportive care measures. Antibiotics with activity again S. aureus and Group A streptococcus (dicloxacillin, clindamycin, trimethoprim-sulfamethoxazole) are first-line agents; clindamycin and trimethoprim-sulfamethoxazole offer some coverage for MRSA. This is important as MRSA has been isolated in women with puerperal mastitis and in recent studies MRSA was the predominant organism isolated. In addition to antibiotics, supportive measures include NSAIDs for pain management and ice packs. Patients should be encouraged to continue with breastfeeding or pumping as breast emptying is necessary for resolution. Patients should have close follow-up to monitor for response to therapy which should occur with 48 hours. Failure of initial therapy may be due to resistant bacteria (e.g., MRSA) or breast abscess.

Breast abscess is a serious complication that can occur in the setting of mastitis. This often presents as a firm, fluctuant mass within an inflamed breast. Breast abscess should also be considered in any patient with mastitis that does not respond appropriately to treatment. Urgent referral to a breast specialist is required as breast abscesses often require surgical intervention. Changes of inflammatory breast cancer can also mimic mastitis and should be considered in patients that do not respond to treatment and/or have persistent skin changes.

Breast pain. Breast pain or mastalgia, is a common symptom of pregnancy. In the absence of abnormal physical exam findings most breast pain can be treated conservatively. A supportive, well-fitting bra can often relieve breast pain, especially since breast cup size usually changes during pregnancy. Other recommendations as listed previously in the guideline can also be utilized. Persistent breast pain requires further evaluation (see breast pain).

Nipple discharge. Nipple discharge is another common symptom in pregnancy and is often related to hormonal changes in preparation for lactation. Galactorrhea is the most common form of nipple discharge in pregnancy and can be managed conservatively. Galactorrhea that persists longer than 6-12 months following completion of pregnancy/lactation requires investigation for other common causes (Fig. 3). Pathologic nipple discharge as described above should prompt referral to a breast specialist (see galactorrhea and other nipple discharge).

Breast Concerns in Men

Breast cancer is rare in men – fewer than 1% of all breast cancers. However, men do present to primary care clinics with breast concerns. Two common breast complaints in men are breast enlargement and breast pain or tenderness. These can be evaluated primarily by physical examination. Palpable masses are very rare and suspicious for cancer.

Enlargement or tenderness can be caused by gynecomastia or pseudogynecomastia. Pseudogynecomastia is a painless increased fat deposition in the breast area in obese men. Gynecomastia is benign ductal proliferation in the male breast caused by hormonal imbalances. It is often tender, usually bilateral, but can be unilateral or asymmetric. In examining the male breast in a patient with gynecomastia a firm disk-like area of tissue is found concentric to the nipple areolar complex. This retroareolar tissue disk is absent in men with pseudogynecomastia.

Gynecomastia can develop as a result of many conditions that disrupt the estrogen/androgen balance:

- Hormonal changes: puberty (transient), obesity, aging, hormone-secreting testicular or adrenal tumor, primary or secondary hypogonadism, renal failure, hyperthyroidism, cirrhosis
- Estrogen administrated therapeutically for prostate cancer or unintentional (e.g., anti-balding lotions or in food additives)
- Medications: spironolactone, cimetidine, flutamide, calcium channel blockers, tricyclic antidepressants, SSRI's, amiodarone, human growth hormone, amphetamines, diazepam, and marijuana

History and examination should be aimed at evaluating or eliminating these conditions as a cause of the gynecomastia.

Breast tenderness. Breast tenderness in men is usually due to many of the same processes as result in gynecomastia, and usually some degree of gynecomastia is present on exam. Physical irritation or trauma (i.e., chafing) of the nipple can also cause tenderness. Evaluation of this

complaint should begin with physical examination for gynecomastia or mass, and if absent, history or lab evaluation may be revealing. Imaging is rarely needed when exam finds a reasonable explanation for the pain.

Other palpable mass. Since fibroadenomas and cysts are very rare in men, any palpable breast mass in a male is suspicious. Masses should be evaluated with the same algorithm that applies to evaluation of a palpable mass in women, including physical examination, diagnostic imaging (mammography) and biopsy if suspicious (Figure 1).

The Augmented Breast

Breast augmentation and reconstruction surgery are common cosmetic procedures seen in the typical primary care practice. Most breast augmentation techniques in the United States involve placing a saline or silicone-filled implant behind the breast tissue or pectoral muscle. A fibrous capsule forms around the implant.

On mammography implants appear as dense oval masses. Mammography on augmented breasts is performed using a technique that displaces the implant and draws the breast tissue forward to be compressed for imaging (implant displacement technique). Augmented breasts can develop any of the problems addressed earlier in this guideline: palpable mass, inflammatory changes, cyclical or noncyclical pain, and nipple discharge, and the evaluation of these problems remains generally the same.

A few conditions are unique to augmented breasts:

- Peri-implant fluid collection. This may result from a local immune response to the implant. It usually presents as unilateral swelling or distortion of one breast.
- Capsular contraction and fibrosis. The contraction is a complication of augmentation in which thick scar tissue encapsulates the implant. This causes distortion of the implant shape (and contour of the breast), often accompanied by pain. This condition is usually apparent on clinical exam. Not many changes appear on imaging other than change in the shape of the implant.
- Implant rupture. Saline implants generally deflate after rupture, with the saline leaking into and being absorbed by the surrounding tissue. Silicone implants after rupture may or may not leak silicone into surrounding tissues, depending on the integrity of the fibrous capsule. Ruptures of silicone implants are classified as intracapsular or extracapsular, depending on whether the silicone material remains within the fibrous capsule or leaks outside of the capsule. Extracapsular rupture is detectable by ultrasound or mammogram due to the presence of free silicone in the surrounding tissue, intracapsular rupture may not be seen due to the relative radiographic density of the capsule itself. If rupture is suspected on history, examination, or due to imaging findings, MRI is the imaging modality of choice, for its heightened sensitivity and image detail in evaluating the implant.

Strategy for Literature Search

The literature searches for this update began with the results of the literature searches performed for the earlier version of this guideline through June 2005. For this update the Breast Cancer Screening and Diagnosis Guidelines of the National Comprehensive Cancer Network (2012) and its supporting literature through early 2012 was used to address the topics of: palpable mass, asymmetric thickening/nodularity, inflammation and other skin changes, breast pain. To supplement that literature, searches in MEDLINE were performed. For the major keywords of adult women; since 6/1/2005; English language; and guidelines, controlled trials (including meta-analyses), and cohort studies; specific searches were performed for breast pain, galactorrhea and other nipple discharge, and breast mass in pregnancy. For the major keywords of adult men; since 6/1/2005; English language; and guidelines, controlled trials (including meta-analyses), and cohort studies; specific searches were performed for breast mass or pain.

The searches were supplemented with recent clinical trials known to expert members of the panel. The search was single cycle. Conclusions were based on prospective randomized controlled trials if available, to the exclusion of other data. If RTC were not available, observational studies were admitted to consideration. If no such data were available, expert opinion was used to estimate effect size.

Related National Guidelines

The UMHHC Clinical Guideline on Breast Problems is consistent with the following national guideline. (See References for full citations.)

NCCN Guidelines: Breast Cancer Screening and Diagnosis, 2012.

Measures of Clinical Performance

At this time no major national programs have clinical performance measures specifically for the diagnosis and treatment of breast problems.

Disclosures

The University of Michigan Health System endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Disclosure of a relationship is not intended to suggest bias in the information presented, but is

made to provide readers with information that might be of potential importance to their evaluation of the information.

None of the members of the Breast Problems Guideline Team have relationships with commercial companies whose products are discussed in this guideline. (The members of these teams are listed on the front page of this guideline.)

Review and Endorsement

Drafts of this guideline were reviewed in clinical conferences and by distribution for comment within departments and divisions of the University of Michigan Medical School to which the content is most relevant: Family Medicine, General Medicine, General Obstetrics & Gynecology, Radiology/Breast Imaging, and Surgical Oncology. The Executive Committee for Clinical Affairs of the University of Michigan Hospitals and Health Centers endorsed the final version.

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2000: Amy F. Saunders, MD, General Medicine, Helen A. Pass, MD, Surgical Oncology, Mark A. Helvie, MD, Radiology/Breast imaging, Mark D. Pearlman, MD, Obstetrics & Gynecology, Mack T. Ruffin, MD, Family Medicine.

2005: Amy Saunders, MD, General Medicine, Amy B. Locke, MD, Family Medicine, R. Van Harrison, PhD, Medical Education, Lisa A. Newman, MD, MPH, Surgical Oncology, Mark D. Pearlman, MD, Obstetrics & Gynecology, Mark A. Helvie, MD, Radiology/Breast Imaging.

Annotated References

National Comprehensive Cancer Network. Breast Cancer Screening and Diagnosis Guidelines. Fort Washington, Pennsylvania: National Comprehensive Cancer Network, 20012. (available at www.nccn.org/professionals/physician_gls/pdf/breast-screening.pdf)

These guidelines recommend sequences of screening, diagnostic, and follow-up activities for negative physical findings, symptomatic or positive physical findings (mass, nipple discharge, asymmetric thicken/nodularity, skin changes) and mammographic evaluation related to breast cancer.

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