

Common Breast Problems

Breast Care Guideline Team

Team leader

Amy F Saunders, MD, MPH
General Medicine

Team members

Amy B Locke, MD
Family Medicine

R Van Harrison, PhD
Medical Education

Lisa A Newman, MD, MPH
General Surgery

Mark D Pearlman, MD
Obstetrics & Gynecology

Mark A Helvie, MD, MS
Radiology/Breast Imaging

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UMHS Guidelines Oversight Team

Connie J Standiford, MD
William E Chavey, MD
R Van Harrison, PhD

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734-936-9771

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These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

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

Objectives: Identify appropriate evaluation and management strategies for women who present with four common breast problems. Identify appropriate indications for referral to a breast specialist.

Assumptions

- Appropriate mammographic screening per NCI, ACS, and UMHS Cancer screening guidelines. Generally mammogram is not indicated for women age <30 because sensitivity and specificity are low.
- “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 asymmetry (Figure 1)

- Discrete solid masses have a medium to high index of suspicion because physical exam cannot be a reliable tool to rule out malignancy.
 - Breast imaging is the best diagnostic approach.
 - Fine needle aspiration (FNA) by a qualified practitioner is an acceptable diagnostic tool, though if it precedes imaging it may disrupt tissue and affect mammography sensitivity. If aspiration reveals cyst, send fluid for cytology if it is bloody, if mass does not resolve completely with aspiration, or if cyst is recurrent in same location. A definitive report of fibroadenoma by FNA requires no further workup. Masses not reported as definitive fibroadenomas or cysts should be evaluated by a breast specialist.

Follow up physical exam after imaging or FNA is important. Cysts that recur are more likely to be malignant, and any nondiagnosed mass that persists should be evaluated by a specialist whether imaging has detected it or not.

- A non-discrete possible mass or thickening has a lower index of suspicion and should be reexamined in 1-2 months, preferably the week after menses in premenopausal woman. If a localized area remains abnormal on repeat exam then workup for possible malignancy is indicated, with diagnostic imaging and referral to a breast specialist. Persistent asymmetry, especially in postmenopausal women, is more suspicious than asymmetry that varies with the menstrual cycle [D*].
- Referral to breast care specialist is recommended for: (a) any suspicious mass, (b) any mass that is undiagnosed after diagnostic imaging, or (c) any woman at very high risk for breast cancer [D*].

Breast Pain - Negative Exam (Figure 2)

- If physical exam and appropriate breast imaging are negative, the likely diagnosis is benign cyclic or noncyclic mastalgia: reassure patient. Trial of evening primrose oil (1000 mg bid for 3-6 months (or its active ingredient, gamma linoleic acid 160 mg bid) is reasonable [A*]. Topical diclofenac gel is also promising for mastalgia [A*]. Recommendation for a well-fitted bra is often helpful [C*].
- If persistent or localized pain not responsive after 2-3 months of conservative treatment, refer to breast specialist [C*].

Nipple Discharge without abnormal exam findings (Figure 3)

- If discharge is serous or sanguinous, or if other risk factors are present (spontaneous discharge, single duct discharge), refer to breast specialist [C*].
- If discharge is not suspicious. If clearly galactorrhea, pursue medical workup and do not refer to breast specialist [D*]. 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.

Assessment and Management of Women at High Risk for Breast Cancer

Primary care providers (PCPs) should identify and counsel women regarding breast cancer risk. Breast cancer screening frequency for high risk women is in Table 4. Women at high risk (5 year risk >1.7%) according to the NCI Breast Cancer Risk Assessment Tool (<http://www.cancer.gov/bcrisktool/>) should be:

- offered referral to breast specialist, if available.
- considered for risk reduction therapy if appropriate candidate and with appropriate follow up.

* **Levels of evidence for the most significant recommendations:**

A = randomized controlled trials; B = controlled trials, no randomization; C = observational trials; D = opinion of expert panel

Figure 1. Palpable Breast Mass or Asymmetry: Diagnosis and Treatment

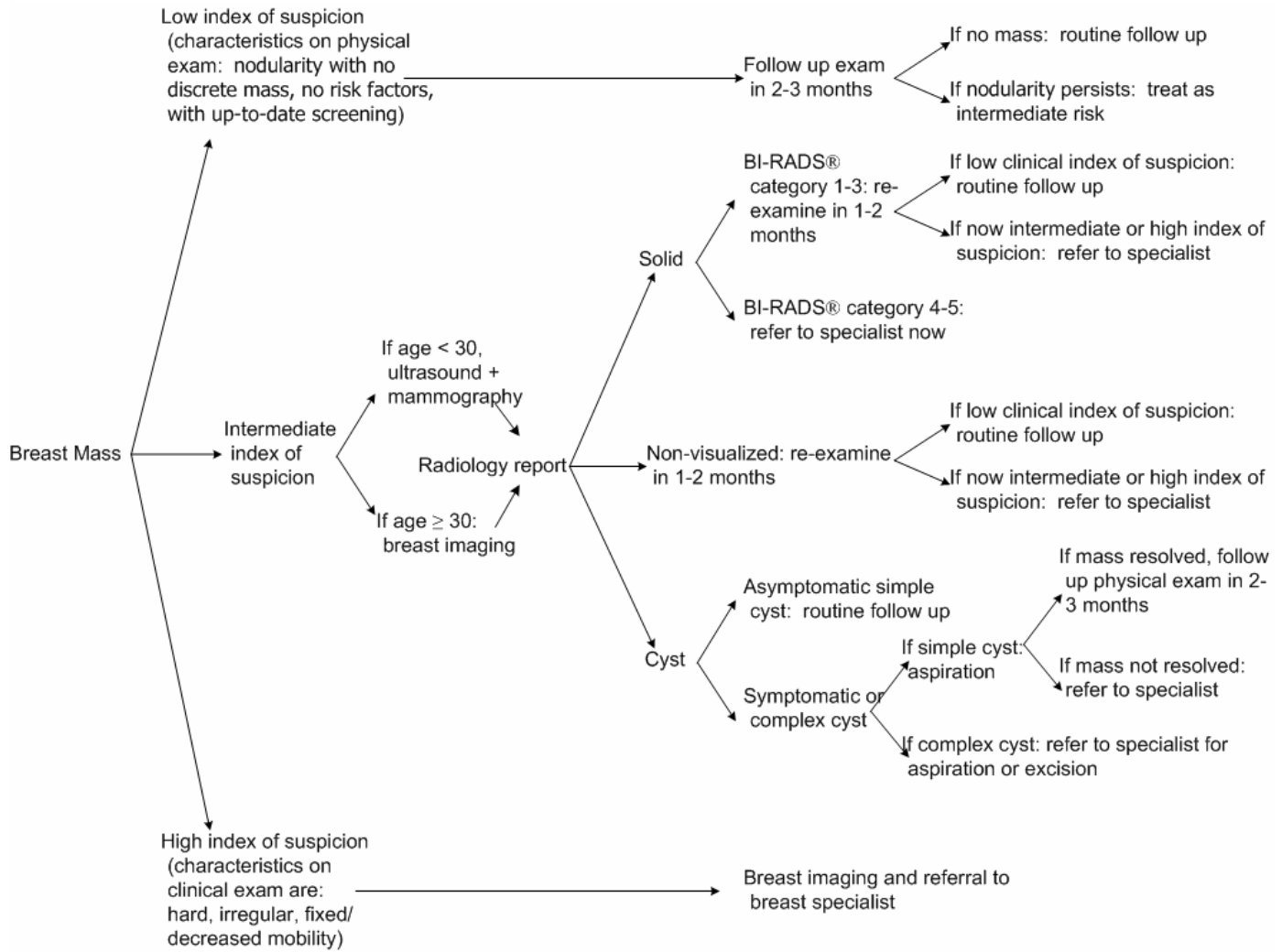


Table 1. Terminology of Mammography Report (BI-RADS®)*

Category 1: Negative	Category 2: Benign Finding	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	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.

Figure 2. Breast Pain Diagnosis and Treatment

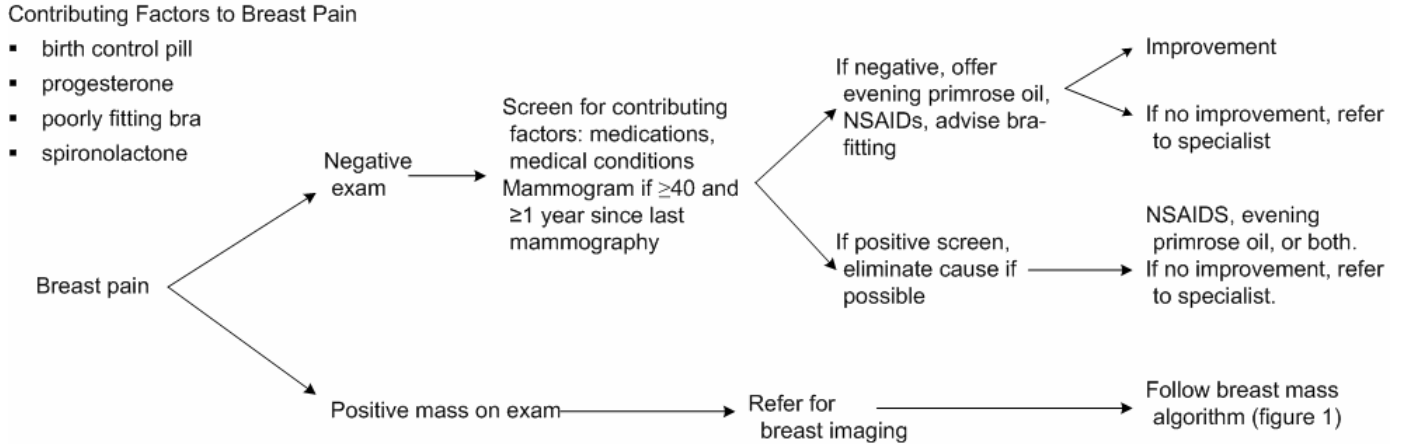


Figure 3. Nipple Discharge Diagnosis and Treatment (no mass) If mass present, follow algorithm for palpable lesion (figure 1)

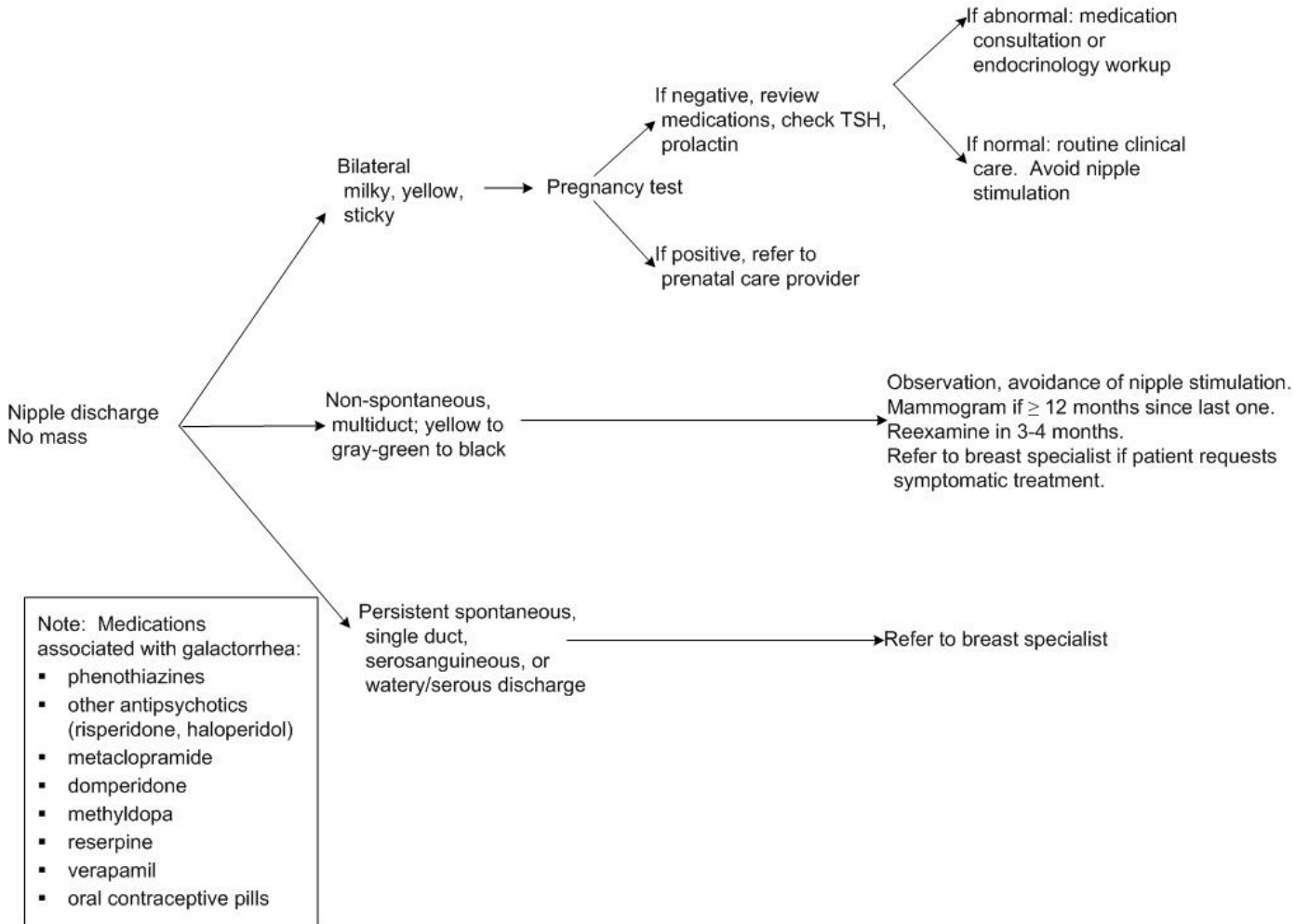


Table 2. Typical Characteristics* of Breast Lumps on Physical Exam

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
Inframammary 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].

Table 3. Risk Factors used in the NCI Breast Cancer Risk Assessment Tool (“Gail Model”)

Risk factors included in the assessment tool	
<ul style="list-style-type: none"> • Current age • Age at menarche • Age at first live birth or nulliparity • Number of first-degree relatives with breast cancer 	<ul style="list-style-type: none"> • Number of previous benign breast biopsies • Atypical hyperplasia in a previous breast biopsy • Race ¹
For a calculation of individual’s risk using the NCI Breast Cancer Risk Assessment Tool, see bcra.nci.nih.gov/brc/	

Note: The tool is for patients without a previous history of breast cancer. The risk projections assume that the woman is receiving regular clinical breast exams and screening mammography. The tool does not take into account specific genetic predisposition such as mutations in BRCA1 or BRCA2 (breast cancer susceptibility genes).

¹ Projections of breast cancer risk are less certain for non-Caucasian women. However, race does not influence breast cancer risk as much as other factors.

Table 4. Screening Recommendations for High Risk Women*

High Risk Category	Age to Begin Screening	Screening Procedures
5 year risk of invasive cancer $\geq 1.7\%$ based on NCI Breast Cancer Risk Assessment Tool (see Table 3)	Age 35	Annual mammogram + clinical breast exam (CBE) every 6–12 months, periodic breast self exam encouraged
LCIS/atypical hyperplasia	After diagnosis of LCIS/hyperplasia	As above
Prior thoracic radiation therapy	8-10 years after thoracic radiation therapy or age 40, whichever is earlier	As above, with MRI controversial**
Strong family history or genetic predisposition	5-10 years prior to age of diagnosis of earliest index case	Annual mammogram + clinical breast exam (CBE) every 6–12 months, periodic breast self exam encouraged. Consider annual MRI for women with 20%–25% or greater lifetime risk.
Known or suspected hereditary breast and ovarian cancer	Age 25	As above.

* From: National Comprehensive Cancer Network Breast Cancer Screening and Diagnosis Guidelines, 2007 (<http://nccn.org>) and American Cancer Society Guidelines for breast screening with MRI as an adjunct to mammography, 2007.

** For prior thoracic radiation therapy, ACS guidelines include MRI and NCCN guidelines do not..

Clinical Background

Clinical Problem and Current Dilemma

Incidence. Breast cancer is the most common malignant neoplasm besides skin cancer in women in the United States. It is exceeded only by lung cancer as a cause of cancer death in women. Based on current incident rates, the lifetime probability that a woman at average risk will develop breast cancer is 11.3%.

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 (family history or personal history of breast cancer, older age, early age at menarche, nulliparity or age of first childbirth >30, age of onset of menopause >55, postmenopausal hormone therapy – see also Table 3), the predictive value of risk factors 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 four major categories:

- Evaluation / Imaging Techniques
- Specific Breast Signs and Symptoms
- Assessment and Management of High Risk Women
- The Anxious Patient.

Evaluation / Imaging Techniques

The techniques discussed include: inspection and palpation, diagnostic breast imaging and fine needle aspirate. Typically, diagnostic breast imaging includes mammogram and ultrasound directed at the area of concern, with approach determined at the discretion of the radiologists.

Inspection and palpation. 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 presenting complaint of palpable mass, CBE performs a different function: characterizing the features of the breast exam in the area of the patient's concern. For the primary care provider, the clinical breast exam is important because it determines the index of suspicion for malignancy (pretest probability).

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.

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.

In evaluation of breast complaint, mammography is not a perfect diagnostic tool. False negatives are not uncommon, especially in younger women. 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.

For evaluation of a palpable lesion, diagnostic mammography 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 Category 4 (suspicious) and Category 5 (highly suggestive of malignancy) assessments. Category 3 (probably benign) 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

Ultrasound. Ultrasound is used to characterize a palpable or mammographic mass as a simple cyst or potentially solid mass. Masses that meet all the diagnostic criteria for simple cysts do not require aspiration unless painful or possibly infected. Ultrasound can assist in differentiating benign and malignant solid masses. 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. The American Cancer Society has recently released guidelines to assist in determining appropriate candidates for routine screening MRI breast imaging in addition to annual mammography (see Table 4). While MRI increases sensitivity compared to mammography alone in women at highest risk for breast cancer, it does so at the cost of decreased specificity and an increased need for invasive diagnostic procedures. Moreover, the cost of the procedure and its lack of demonstrated efficacy (improved early breast cancer diagnosis with reductions in mortality rate) obviates the routine use of this modality for screening in all but the highest risk women. At this time an assessment of very high risk and decision to screen with MRI is likely to be better made by a breast specialist and/or genetic counselor. Even with MRI screening, a significant minority of high risk women will already have axillary metastatic disease at time of detection.

No guidelines have been established for the use of MRI as a diagnostic tool for evaluation of a palpable breast mass. MRI should not be used routinely as a diagnostic tool, although it may have a limited role when specifically requested by a radiologist or breast specialist.

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 with biopsy for definitive diagnosis.

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 first step in the evaluation of a palpable abnormality is to determine index of suspicion for benign versus malignant disease (the pretest probability of disease).

Low level of suspicion encompasses prominent nodularity, asymmetric thickening, and non-discrete possible mass. This can be followed with repeat exam in 1-2 months. Breast imaging is also recommended if no screening mammogram has been done within the last 12 months in women over age 40. If the abnormality persists or progresses on repeat examination, further diagnostic testing is indicated. If diagnostic breast imaging is negative or indicates benign lesion, then exam should be repeated in 2-3 months. If exam confirms stability or regression, return to routine follow up. If there is clinical suspicion of possible false negative imaging or progression of mass, the woman should be referred to a breast specialist.

Distinct mass should be interpreted as being intermediate or high index of suspicion. This should be evaluated with diagnostic testing. Both needle aspiration (FNA) and urgent diagnostic imaging (within 2 weeks) are acceptable methods for evaluation, but there are several reasons to begin with diagnostic imaging. FNA sensitivity is variable, depending on the experience of the physician. The procedure is associated with risks of tissue disruption or hematoma that may reduce mammographic sensitivity.

FNA should not be done for persistent asymmetric thickening, as FNA has very low sensitivity in that setting. Mammographic sensitivity is better, but also variable, in evaluating asymmetric thickening. If the mammographic reading indicates anything other than “normal” or “probably benign abnormality” then the patient should be referred to a breast care specialist for evaluation.

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 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 mammogram 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 evaluation 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 PCP must reassess the clinical index of suspicion independent of the initial index of suspicion or the mammogram results. One of the most common mistakes, and the cause of the largest number of malpractice suits regarding breast cancer diagnosis, is for a PCP to fail to reexamine and follow through with referral for a woman who has a malignant mass but had a false negative mammogram. If the PCP 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.

Other breast abnormalities on physical exam. A fluctuant painful mass suggests probable abscess and the patient should be urgently referred to a breast specialists for surgical intervention.

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 insure resolution. 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. 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 two groups. Cyclic mastalgia, common in younger women occurs prior to the menses, increasing in severity until onset of menstrual bleeding. It is usually 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. Important historical factors include timing and features of pain, 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, but 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. If an abnormality is found, referral for diagnostic breast imaging is appropriate. Other indications for imaging include age over 30, high 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.

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 also can be used for general pain relief. Topical NSAIDs have been shown in randomized trials to be effective in reducing mastalgia.

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 progesterone, Danazol, and Bromocriptine, however, side effects tend to limit their tolerability.

Galactorrhea. Nipple discharge is not uncommon in premenopausal women. 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.
- Prolactinoma or other conditions that reduce dopamine inhibition of prolactin secretion in the hypothalamic-pituitary pathway can be screened with prolactin level.
- Medication effect is the most common etiology. The list of medications in Figure 3 contains those commonly associated with galactorrhea. Discuss the pros and cons of continuing the medication with the patient.
- Hypothyroidism and renal failure are medical conditions associated with galactorrhea.
- If no physiologic cause of elevated prolactin is found, MRI imaging of the hypothalamus/pituitary and referral to an endocrine specialist is appropriate.

Otherwise, 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.

Other nipple discharge. If the patient is more than 30 years of age, diagnostic breast imaging should be performed for any new nipple discharge. Green, gray, milky or black discharge are all consistent with fibrocystic breast disease or ductal ectasia and are benign characteristics. However, 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. Watery or serous discharge is also very suspicious for malignancy.

The benefit of cytology testing of suspicious nipple discharge is not clear. Several studies have failed to find increase in diagnostic sensitivity from routine cytologic evaluation of discharge. However, while most studies of nipple discharge show low sensitivity, the specificity of cytologic testing is high. A large Japanese study found that a small number of breast cancers were diagnosed by cytology when all other tests were negative. If one does cytologic testing, a negative result is not definitive, but a positive result is very significant.

Women with High Risk of Breast Cancer

The primary care provider will encounter both women who are at high risk for breast cancer who are unaware of their

risk as well as women who are concerned that their risk is high but whose risk is not substantially higher than the average. It is important for the health care provider to be a source of information and guidance for both groups. Easily accessible websites can be used in the clinic setting to help determine an individual woman's risk and to help guide screening, evaluation, and prophylactic therapy decisions.

Risk assessment. The NCI's Breast Cancer Risk Assessment Tool (see Table 3) is based on the Gail model and can be used to calculate an individual's risk for cancer in her lifetime and within the next 5 years. The website is bcra.nci.nih.gov/brc (also accessible through cancer.gov/bcrisktool/ or via the U of M clinical home page under clinical references: clinical calculators, or by calling 1-800-4 cancer). The criteria used are listed in Table 3. Assistance with risk assessment can be arranged through referral to genetic counseling.

Screening high risk women. Unfortunately the NCI model is not applicable to very high risk women who have known or suspected genetic mutations (BRCA1, BRCA2, p53, PTEN or others) or a very strong family history of breast cancer, as this tool can underestimate their risk. A personal history of thoracic radiation or prior lobular carcinoma in situ also substantially increases a woman's risk for breast cancer; these risk factors should be considered in addition to those conditions included in the NCI's Breast Cancer Assessment Tool. At this time an assessment of very high risk and decision to screen is likely to be better made by a breast specialist and/or genetic counselor.

Table 4 outlines the National Comprehensive Cancer Network's (NCCN) screening recommendations (age to screen and screening procedure) for categories of high risk women.

Risk Reduction therapy. A woman is considered to be at high risk if she is >35 yrs old and her calculated 5 year risk of breast cancer is > 1.7 %. According to the study by the National Surgical Adjuvant Breast and Bowel Project, use of Tamoxifen for 5 years in high risk women decreased the incidence of breast cancer by 49%. Risks and adverse side effects of Tamoxifen include increased incidence of endometrial cancer, deep venous thrombosis, potential increase in cataract formation, and increased liver enzymes. In perimenopausal women, hot flashes generally occur and there is a potential for adverse effect on bone density.

Raloxifene, another selective estrogen receptor modulator (SERM), has been compared to Tamoxifen in the STAR trial. The results indicate that raloxifene was as effective as tamoxifen in reducing breast cancer incidence, with less increased risk of endometrial cancer. The risk of lower extremity DVT was increased with both Raloxifene and Tamosifen; stroke risk was equal. The risk of adverse events with both interventions increases with a woman's age. Because the SERM therapy works only on ER positive cancers, the patient with a strong family history of

ER negative breast cancer, as with BRCA 1 and 2, is less likely to respond.

Hormone therapy in high risk women is controversial. Benefits and risks need to be considered in the individual patient's circumstances. In complicated or unclear cases, referral to a specialist in hormone therapy or breast disease may be appropriate.

The primary care provider plays an important role in counseling regarding risk and risk reduction. The US Preventive Services Task Force recommends that they assess risk in their primary care patients at risk for breast cancer and discuss pros and cons of risk reduction therapy. The components of counseling include discussion of:

- 1) Overall health status and risk of breast cancer
- 2) Genetic risk, with an offer to refer to genetic counseling/high risk clinic for women with strong family history
- 3) Risks and benefits of Tamoxifen or Raloxifene therapy, as well as absolute contraindications (history of deep venous thrombosis or pulmonary embolism, thrombotic stroke, TIA's, or pregnancy/pregnancy potential).

Women at high risk for breast cancer can be referred to a breast care specialist. The specialist can advise women at most high risk (suspected BRCA1 and BRCA2 or others) about genetic testing as well as surgical options such as prophylactic mastectomy or oophorectome or participation in risk reduction research trial. SERM's are not indicated for BRCA1 patients as the vast majority are ER negative.

When specialist referral is unavailable or patient declines referral but desires prophylaxis, a primary care provider may prescribe Tamoxifen 20 mg/day for 5 years or Raloxifene 60 mg daily. It is essential to maintain close follow up. Annual pelvic exam and screening for liver enzyme abnormalities and symptoms of cataracts are required, as well as inquiring about vaginal bleeding or symptoms of venous or cerebrovascular thrombosis. Vaginal spotting requires prompt referral for endometrial biopsy. Evidence of thrombosis requires prompt discontinuation of either SERM as well as diagnostic workup.

The NCCN Guidelines for Breast Cancer Risk Reduction (www.nccn.gov) include further discussion and algorithms for issues regarding women at high risk.

The Anxious Patient

While the risk for breast cancer is meaningful for all women, in the current media atmosphere of hypersensitivity to risk for disease, more women overestimate their risk for breast cancer than underestimate it. Many women are reassured by the primary care provider quantify the individual's risk (see Table 3) and outlining a plan for screening. For those who remain very anxious regarding their risk, referral to a breast specialist may be appropriate.

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 2000. For this update the Breast Cancer Screening and Diagnosis Guidelines of the National Comprehensive Cancer Network (2004,

www.nccn.org/professionals/physician_gls/PDF/breast-screening.pdf) and its supporting literature through early 2004 were used to address the topics of nipple discharge, palpable mass, and screening of high risk women. The topics of breast pain and galactorrhea were used as major key words in separate MEDLINE searches of literature published from 1/1/99 through 5/31/05 in English for adult women with additional key words of guidelines and controlled trials.

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 clinical 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.

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.)

Acknowledgments

The following individuals are acknowledged for their contributions to the 2000 version of this guideline: Helen Pass, MD, Surgical Oncology, and Mack Ruffin, MD, Family Medicine.

Annotated References

National Comprehensive Cancer Network. Breast Cancer Screening and Diagnosis Guidelines. Jenkintown, Pennsylvania: National Comprehensive Cancer Network, 2007. (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.

Colak T, Ipek T, et al. Efficacy of Topical Nonsteroidal Antiinflammatory Drugs in Mastalgia Treatment. *J Am Coll Surg* 2003;196:525-530.

Randomized Controlled Trial of diclofenac diethylammonium topically resulted in very substantial improvement in mastalgia both in patients with cyclic and noncyclic mastalgia when compared to patients receiving placebo.

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