

# Investigation of breast symptoms meeting the challenge

Determining whether or not a particular breast symptom is likely to be due to cancer can be difficult. Judicious use of the 'triple test' – thorough history and clinical examination, imaging, and nonexcision biopsy – provides the most effective means of detecting breast cancer.

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Breast cancer is the greatest cause of cancer-related death in Australian women and, despite much research into causes and risk factors, we have no means of preventing it. Early detection is critical for reducing mortality from this disease. Over recent years, despite increasing incidence, the mortality rates from breast cancer have decreased by about 2% per year.<sup>1</sup> This is likely to be the result of a number of factors, including the introduction of a population-based mammographic screening program (BreastScreen Australia),

better diagnostic techniques and improved treatments. Five-year relative survival rates for women with breast cancer in Australia have improved from 72% in 1982–1986 to 84% in 1992–1997.<sup>2</sup>

Even with a fully implemented mammographic breast cancer screening program, however, more than half of all breast cancers will be found as a result of a change in the breast detected by women or their doctors. The GP is the first port of call for women who notice a

**IN SUMMARY**

- Based on the best available evidence, the triple test – thorough history and clinical examination, diagnostic imaging, and nonexcisional biopsy – provides the most effective means of diagnosing breast cancer in women with breast symptoms.
- The assessment of breast symptoms using the triple test requires a multidisciplinary approach, and is preferably managed by a single clinician who takes responsibility for co-ordinating the entire investigative pathway.
- A positive result on any component of the triple test (indeterminate/equivocal/atypical, suspicious or malignant) means that the woman should be referred for specialist surgical assessment and/or requires further investigation, irrespective of any other normal test results. This implies that not all three components of the triple test need to be performed to reach the conclusion that appropriate referral is needed.
- A negative result (normal, benign or no significant abnormality detected) on all three components of the triple test provides good reassurance that the symptom is not due to breast cancer.
- All test results must be correlated with symptoms. If results are inconsistent or if they are benign but do not account for symptoms then further investigation is warranted.

change in their breast. The challenge for GPs is to investigate these symptoms effectively and determine which may be due to cancer.

In 1997 the National Breast Cancer Centre (NBCC) produced the first evidence-based resource for GPs in Australia that detailed the recommended steps to be taken when investigating breast symptoms.<sup>3,4</sup> *The investigation of a new breast symptom: a guide for general practitioners* (the Guide) has proved to be an often used resource that has been shown to improve practice in a number of significant areas.<sup>5</sup>

In the eight years since the Guide was released, new studies have been conducted in the areas of breast diagnosis and delivery of care within a multi-disciplinary team setting. In 2005 the NBCC convened a working group representing professional organisations, specialist clinicians, GPs and consumers to evaluate the current evidence relevant to decision making when investigating women who present with breast or nipple symptoms. Members of the working group are listed in the adjacent box. Specifically, the evidence in relation to the following diagnostic areas was examined using well established systematic review methodology:<sup>7</sup>

- the accuracy of the triple test
- the value of ultrasound in addition to, or in place of, mammography in different age groups
- the value of core biopsy compared with fine needle aspiration cytology, and
- the significant features of nipple discharge

## NBCC 'The investigation of a new breast symptom' updated

*The investigation of a new breast symptom: a guide for general practitioners*<sup>6</sup> was updated in 2006 and is endorsed by the Royal Australian and New Zealand College of Radiologists, Royal Australian College of General Practitioners, Royal Australasian College of Surgeons, and Breast Cancer Network Australia.

All practising GPs will be sent a copy of the updated Guide. Additional copies can be downloaded or ordered from the NBCC website ([www.nbcc.org.au](http://www.nbcc.org.au)).



### Working group

Dr Jane Armes, pathologist representing the Royal College of Pathologists of Australasia

Dr Kathleen Burns, GP representing the Australian Divisions of General Practice

Dr Bronwyn Kennedy, breast physician representing the Royal Australian College of General Practitioners

Dr Marjorie Kossoff, radiologist representing the Royal Australian and New Zealand College of Radiologists

Ms Ros Lawson, consumer representing the Breast Cancer Network Australia

Dr Warwick Lee, radiologist with expertise in breast imaging

Mr David Oliver, surgeon representing the Royal Australasian College of Surgeons

Dr Wendy Raymond, pathologist representing the Royal College of Pathologists of Australasia

Dr Julie Thompson, GP with expertise in rural general practice

and cytology of discharge.

In this paper, we present the major findings and recommendations of the working group for practice.



Figure 1. Performing a thorough clinical examination with particular attention to the area of clinical interest.

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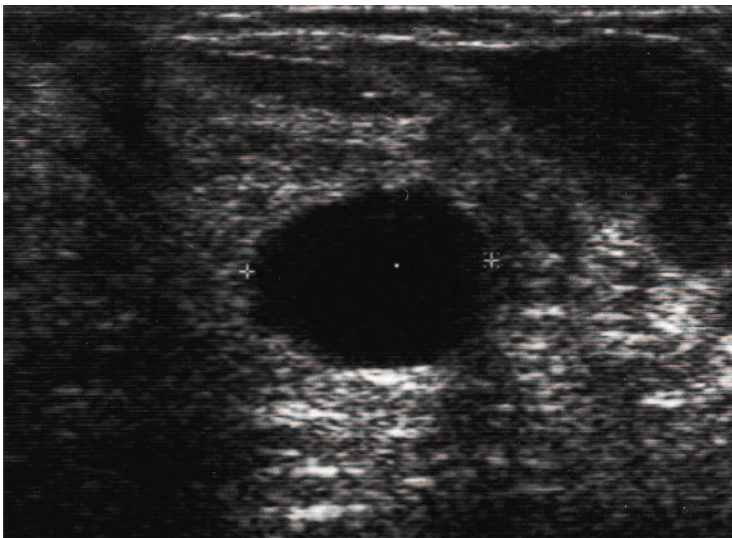


Figure 2 (above). Targeted ultrasound imaging of a clinical lump has identified a normal cyst.



Figure 3 (left). A dense mammogram. No abnormality is seen. However, if there is a clinical abnormality, further imaging and investigation are required.

The triple test

The triple test approach to diagnosis provides the most effective means of detecting breast cancer without the need for excisional biopsy. It refers to:

- medical history and clinical breast examination, see Figure 1
- diagnostic breast imaging (breast ultrasound, mammography or both), see Figures 2 and 3
- nonexcisional biopsy (fine needle aspiration cytology, core biopsy, or both).

The triple test is positive if any of its

components returns a result that is indeterminate/equivocal/atypical, suspicious or malignant; it is negative if all components return a result of normal or benign. The sensitivity of the triple test for detecting breast cancer approaches 100%, and is greater than any of its individual components (Table 1). Its specificity is at least 60%. A negative triple test provides good reassurance that the symptom is not due to breast cancer, with fewer than 1% women being falsely reassured that they do not have cancer. In the event of a positive triple test, surgical referral is recommended, preferably to a specialist with expertise in breast disease.

The effectiveness of each component of the triple test for an individual woman will depend on a number of factors, including her age and past medical and family histories, and the characteristics of her breast tissue and of the breast lesion, if present. For the GP charged with assessing the presenting symptom, it is important to pursue a systematic approach to investigation that minimises the risk of missing breast cancer. The correct sequence of tests is important, but it is not always necessary to conduct all three diagnostic components. It may be possible to reassure a patient after taking a history and performing a clinical examination only, such as for a woman with bilateral breast pain occurring cyclically before her menstrual period and no clinical abnormality on examination.

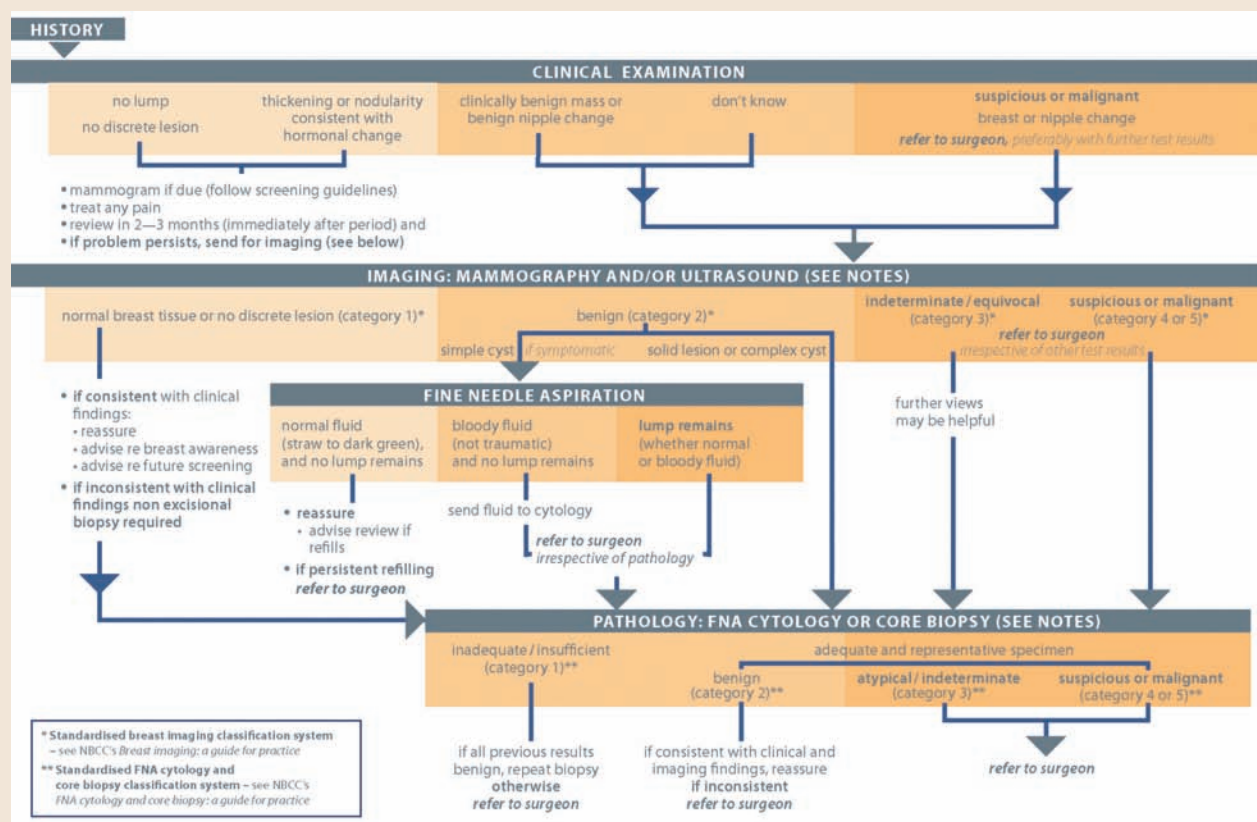
The recommended pathway for investigating a new breast symptom such as a lump or pain (any symptom other than nipple discharge), which requires a multi-disciplinary approach, is shown in the

Table 1. Accuracy of the triple test and each of its components<sup>7</sup>

	Triple test	Detailed history and clinical examination	Imaging (mammography and ultrasound)	Nonexcision biopsy (fine needle aspiration cytology and core biopsy)
Sensitivity	>99.6%	85%	95%	90%
Specificity	>62%	90%	92%	99.5%



## The investigation of a new breast symptom (other than nipple discharge)



Source: NBCC. *The investigation of a new breast symptom: a guide for general practitioners*, 2006.<sup>6</sup>

flowchart above. Based on the triple test, it provides the most effective means of detecting breast cancer. The implications for clinical practice are summarised in the box below. The investigative approach integrates diagnostic categories in imaging and pathology as described in detail in the NBCC booklets *Breast imaging: a guide for practice* and *Breast fine needle aspiration cytology and core biopsy: a guide for practice*.

### Breast imaging

Breast imaging is a key component of the triple test. Both mammography and ultrasound are used, often in conjunction to give complementary information. Referring doctors may consult with their radiologist about the most appropriate test for individual cases.

Patient age is a major determinant of the accuracy of diagnostic imaging studies, with the sensitivity of mammography for detecting breast cancer increasing with

age. The sensitivity is improved by the addition of ultrasound for patients of all ages, although the size of the benefit is greater in women younger than 50 years.

In women under the age of 35 years, ultrasound is recommended as the initial imaging modality. In the absence of strong evidence, no absolute age recommendation can be provided in relation to

the use of mammography or ultrasound as the initial modality for symptomatic women between the ages of 35 and 50; expert consensus opinion suggests that mammography and ultrasound be used as complementary modalities in this age group. In women over the age of 50 years, mammography is recommended as the first imaging modality. In pregnant or

### The triple test: implications for practice

The triple test is the recommended approach to maximise diagnostic accuracy in the investigation of breast changes.

- A triple test positive (indeterminate, suspicious or malignant) is found in 99.6% of breast cancers. Women with any positive result require specialist referral and further investigation, with the likelihood of cancer increasing if more than one component of the test is positive.
- A triple test negative on all components provides good evidence that cancer is unlikely (less than 1%) and further investigation can be avoided (if there are no other high risk factors).
- Where symptoms persist or there are high risk factors, such as a strong family history or previous personal history of breast cancer, or the woman remains concerned, a specialist opinion may be warranted.

**Table 2. Probability of cancer by age and nature of nipple discharge<sup>8</sup>**

	Patient age <60 years	Patient age ≥60 years
Bloody	3%	9%
Serous	<1%	3%
Other	<1%	Very few cases available to allow precise estimation

lactating women, ultrasound is the most useful initial modality; mammography is used if the clinical or ultrasound findings are indeterminate, suspicious or malignant, or if there is inconsistency between test results.

### Nonexcisional biopsy

Both fine needle aspiration cytology and core biopsy are highly sensitive and specific for breast cancer. They are complementary, although one may be more appropriate in achieving a definitive diagnosis in some cases. For example, if imaging shows microcalcification at the site of a clinical abnormality, core biopsy can often demonstrate invasive disease whereas fine needle aspiration cannot differentiate between *in situ* and invasive

cancer. Fine needle aspiration is important in the evaluation of cystic lesions. General guidance is provided in the NBCC booklet *Breast fine needle aspiration cytology and core biopsy: a guide for practice*.

### Nipple discharge

Discharge from the nipple most commonly presents with serous or milky characteristics in women younger than 60 years. In 86% of cancers presenting with nipple discharge, the discharge is either bloody or serous. The likelihood of cancer is a function of both the discharge characteristic and the age of the patient (Table 2).

Guaiac-based stick tests may be used to detect blood in nipple discharge; surgical referral is recommended if blood is present. Further investigations, such as surgi-

### Nipple discharge: implications for practice

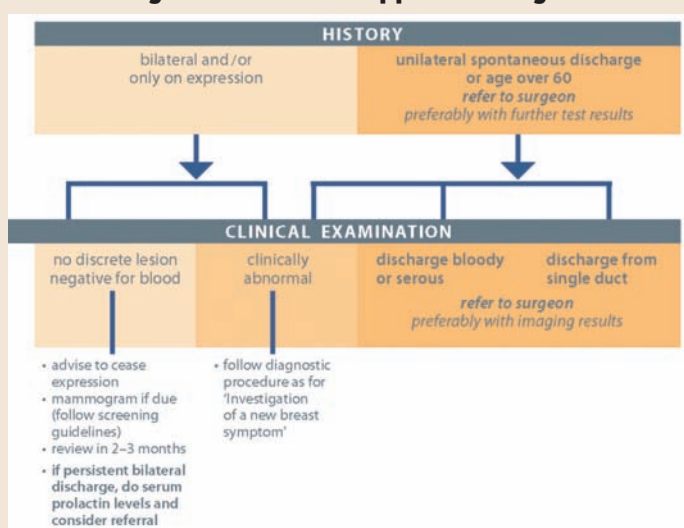
- Spontaneous, unilateral, bloody or serous discharge from a single duct raises the possibility of cancer, especially if it occurs in older women.
- A positive discharge cytology result is indicative of cancer, but a negative result cannot be used to rule out the disease.
- The use of galactography should be based on the availability of expertise, preferably after consultation with a surgeon.

cal microductectomy, may be warranted to reach a definitive diagnosis.

The cytology of discharge smears has a sensitivity of between 40 and 50% and a specificity of over 99% for breast cancer. A positive result is indicative of cancer, but a negative result cannot be used to rule out the disease.

The recommended pathway for investigating a new nipple discharge is shown on this page. The implications for clinical practice are summarised in the box above.

### The investigation of a new nipple discharge



Source: NBCC. *The investigation of a new breast symptom: a guide for general practitioners*, 2006.<sup>9</sup>

### Review and referral

A key aspect of the investigation of a new breast symptom is the review of all test results and correlation with the presenting symptom. It is recommended that GPs refer the patient to a surgeon with expertise in breast disease when:

- any component of the triple test is positive
- the aspiration of a cyst is incomplete, or results in a bloody aspirate (not traumatic), or a lump remains after aspiration
- there is unilateral, spontaneous discharge from a single duct, especially in a woman aged 60 years or over
- any test result is inconsistent and additional investigation is required.

Surgeons who are members of the RACS Breast Section are listed on the

College's website ([www.surgeons.org](http://www.surgeons.org)).

If the results are benign but do not account for the woman's symptom or are not consistent then further investigation is warranted. When the triple test is negative, although the likelihood of cancer is exceedingly low, specialist opinion may be warranted if there is a high pretest probability of cancer, such as in women who have high risk factors (e.g. a strong family history of breast cancer or previous personal history of the disease). In addition, specialist referral should be considered if the woman remains concerned or if her symptoms persist beyond a 12 to 16 week review.

## Discussion

As the incidence of breast cancer increases and women heed messages about the

importance of seeking prompt consultation with their doctors when recognising changes in the look and feel of their breasts, GPs need to meet the challenge of providing accurate and timely diagnosis of breast cancer in women who present with breast symptoms. Although most of these symptoms will not be due to cancer, investigation is vital. Delays in the diagnosis of breast cancer remain a significant cause of litigation for GPs.

*The investigation of a new breast symptom: a guide for general practitioners*<sup>6</sup> focuses on judicious use of the triple test and prompt specialist referral as providing the most effective means of detecting breast cancer in women with a breast symptom, such as a lump, thickening, nipple changes or nipple discharge. Each component of the triple test plays a part in revealing the likelihood of breast cancer or other diagnosis, but it is in the collective interpretation and correlation of findings that the true advantage of the triple test emerges. When used in an astute and judicious manner, the triple test has a sensitivity that approaches 100% in the detection of breast cancer. The implications of this statistic are useful to emphasise. When the triple test is used to guide the investigation, a woman with a breast symptom has a chance of less than a 1% of a false negative result. A negative triple test provides good evidence that cancer is unlikely and further investigation can be avoided.

On the other hand, no guide is to be used in a rigid and prescriptive manner, especially in the context of complex health decisions about critical diagnoses such as breast cancer. The NBCC recommends use of the updated Guide as a means of maximising the effectiveness of clinical investigations in women seeking advice about breast symptoms, but the woman's specific circumstance and the GP's medical judgement may influence the investigative process in any particular situation. Additional NBCC resources may be of assistance (see the box on this page).

The triple test relies on a multidisciplinary approach to the assessment of breast symptoms. In this setting, it is preferable that a single managing clinician takes responsibility for co-ordinating the investigative pathway, including the correlation of cytological or histological results with clinical and diagnostic imaging findings. It is important to emphasise that it is not expected that a single clinician perform all steps enumerated in the Guide. Rather, it is preferable that unified co-ordination of diagnostic activities and results be established. In addition, discussions about the explicit management considerations arising from the diagnostic findings require an equally co-ordinated approach. The GP is ideally placed to provide co-ordination and continuity of care.

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## Additional NBCC resources

To access these guides and other information on breast and ovarian cancer, visit [www.nbcc.org.au](http://www.nbcc.org.au) (clinicians) and [www.breasthealth.com.au](http://www.breasthealth.com.au) (consumers).

### For clinicians

- *Advice about familial aspects of breast cancer and epithelial ovarian cancer: a guide for health professionals* (card)
- *Breast imaging: a guide for practice* (booklet)
- *Breast fine needle aspiration cytology and core biopsy: a guide for practice* (booklet)
- *Clinical practice guidelines for the management of women with early breast cancer* (booklet)

### For women\*

- *Do you have a breast change?* (tear off sheet)
- *Do you have breast cancer in your family?* (tear off sheet)
- *A guide for women with early breast cancer* (booklet)

\* These resources for women are also available in five key languages.

## References

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