CHAPTER 1

Symptoms, Assessment and Guidelines for Referral

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OVERVIEW

- Breast conditions account for approximately 25% of all surgical referrals
- Guidelines for referral exist to ensure that patients with breast cancer do not suffer delays in referral
- Cancer can present as localised nodularity, particularly in young women
- All discrete masses and the majority of localised asymmetric nodularities require triple assessment
- Delay in diagnosis of breast cancer is the single largest cause for medicolegal complaints

One woman in four is referred to a breast clinic at some time in her life. A breast lump, which may be painful, and breast pain constitute over 80% of the breast problems referred to hospital and breast problems constitute up to a quarter of all female surgical referrals (Table 1.1).

When a patient presents with a breast problem the question for the general practitioner is: 'Is there a chance that cancer is present and, if not, can I manage these symptoms myself?' (Figure 1.1; Tables 1.2 and 1.3).

For patients presenting with a breast lump, the general practitioner should determine whether the lump is discrete or there is nodularity, as well as whether any nodularity is asymmetrical or is part of generalised nodularity (Figure 1.2). A discrete lump stands out from the adjoining breast tissue, has definable borders and is measurable. Localised nodularity is more ill defined, is often bilateral and tends to fluctuate with the menstrual cycle. About

Table 1.1 Prevalence of presenting symptoms in patients attending a breast clinic.

Breast lump	**36%**	**Strong family history of breast cancer**	**3%**
Painful lump or lumpiness	33%	Breast distortion	1%
Pain alone	17.5%	Swelling or inflammation	1%
Nipple discharge	5%	Scaling nipple (eczema)	0.5%
Nipple retraction	3%		

ABC of Breast Diseases, Fourth edition. Edited by J Michael Dixon.

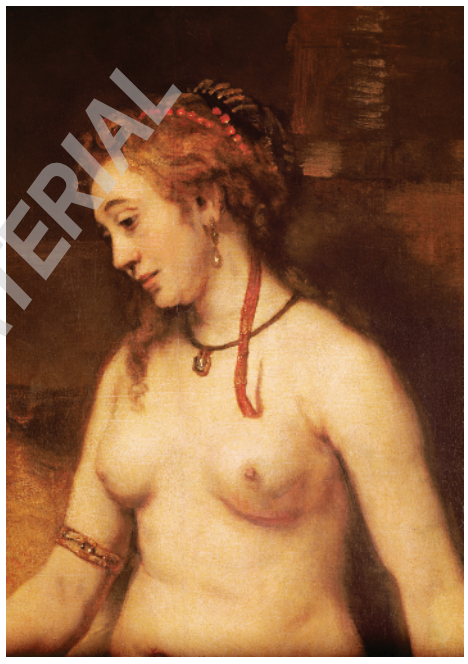


Figure 1.1 Bathsheba by Rembrandt. Much discussion surrounds the shadowing and possible distortion of the left breast and whether this represents an underlying malignancy. Such findings would be an indication for hospital referral. With permission of the Bridgeman Art Library.

10% of all breast cancers present as asymmetrical nodularity rather than a discrete mass. When the patient is sure that there is a localised lump or lumpiness, a single normal clinical examination by a general practitioner is not enough to exclude underlying disease (Tables 1.2 and 1.3). Reassessment after menstruation or hospital referral is indicated in such women.

Assessment of symptoms

Patient's history

Details of risk factors, including family history and current medication, should be obtained and recorded. Knowing the duration of a symptom can be helpful, as cancers usually grow slowly but cysts may appear overnight.

Inspection should take place in a good light with the patient's arms by her side, above her head, then pressing on her hips

Table 1.2 Conditions that require hospital referral.

Lump
- Any new discrete lump
- New lump in pre-existing nodularity
- Asymmetrical nodularity in a woman over the age of 35
- Asymmetric nodularity in a younger woman that persists at review after menstruation
- Abscess or breast inflammation that does not settle rapidly after one course of antibiotics
- Palpable axillary mass including an enlarged axillary lymph node

Pain
- If associated with a lump
- Intractable pain that interferes with a patient's lifestyle or sleep and that has failed to respond to reassurance, simple measures such as wearing a well-supporting bra or anti-inflammatory drugs
- Unilateral persistent pain in postmenopausal women that is in the breast rather than in the chest wall (see Chapter 3)

Nipple discharge
- All women aged >50
- Women aged ≤50 with either
  - bloodstained discharge
  - spontaneous single duct discharge
  - bilateral discharge sufficient to stain clothes

Nipple retraction or distortion
Nipple eczema
Change in skin contour
Family history
Request for assessment of a woman with a strong family history of breast cancer should be to a family cancer genetics clinic.

Table 1.3 Patients who can be managed, at least initially, by their GP.

- Women with bilateral tender, nodular breasts provided that they have no localised abnormality on examination
- Young women (≤35 years) with asymmetrical localised nodularity; these women require assessment after their next menstrual cycle, and if nodularity persists hospital referral is then indicated
- Women with minor and moderate degrees of breast pain who do not have a discrete palpable lesion
- Women aged <50 who have nipple discharge that is small in amount **and** is from more than one duct and is intermittent (occurs less than twice per week) and is not bloodstained. These patients should be reviewed in 2–3 weeks and if symptom persists hospital referral is indicated

(Figure 1.3). Skin dimpling or a change in contour is present in up to a quarter of symptomatic patients with breast cancer (Figure 1.4). Although usually associated with an underlying malignancy, skin dimpling can follow surgery or trauma, and can be associated with benign conditions or occur as part of breast involution (Figures 1.5–1.7).

Breast palpation

Breast palpation is performed with the patient lying flat with her arms above her head (Figure 1.8), and all the breast tissue is examined using the most sensitive part of the hand, the fingertips. It is important for the woman to have her hands under her head to spread the breast out over the chest wall, because it reduces the depth of breast tissue between your hands

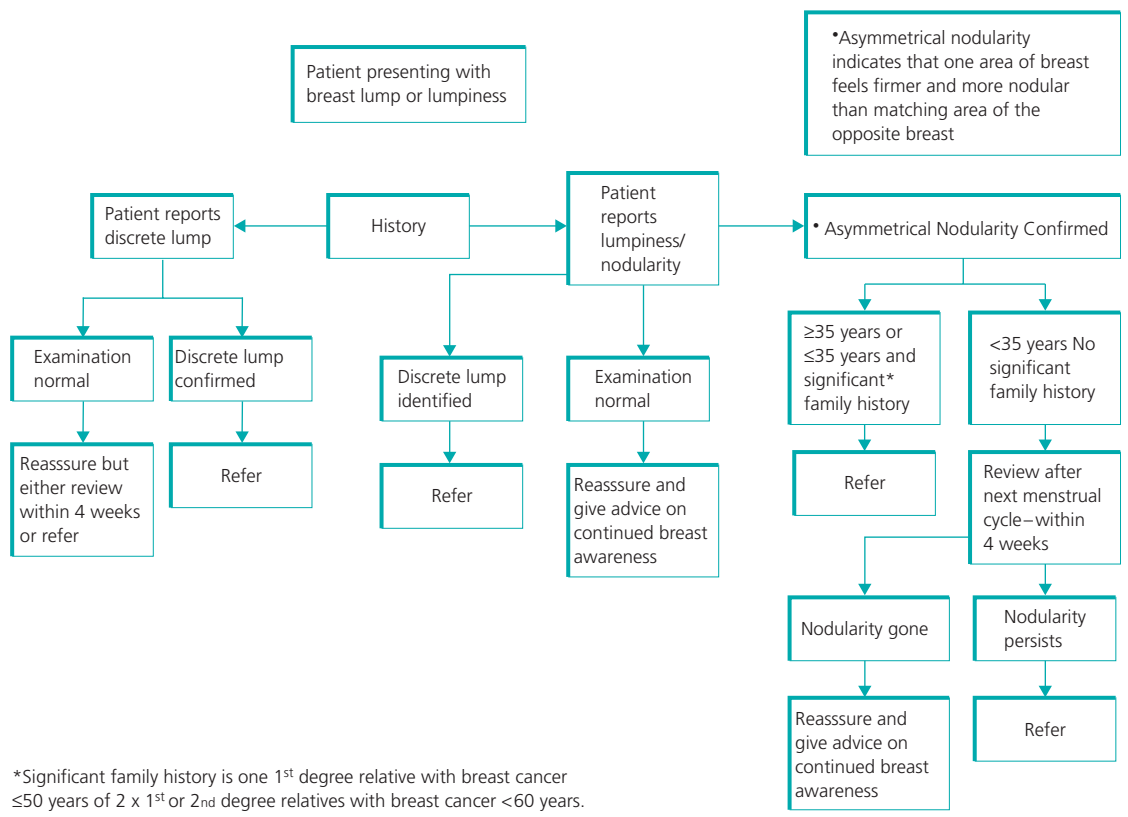


Figure 1.2 Management of patient presenting in primary care with a breast lump or localised lumpy area or nodularity.

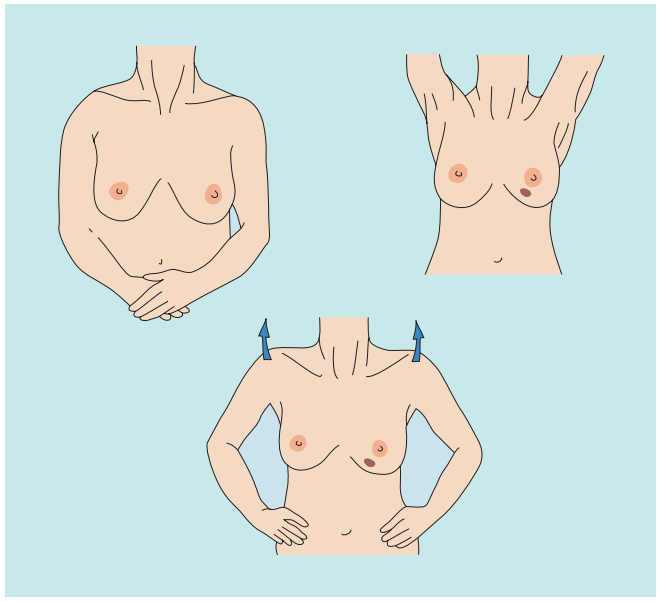


Figure 1.3 Position for breast inspection. Skin dimpling in lower part of breast evident only when arms are elevated or pectoral muscles contracted.

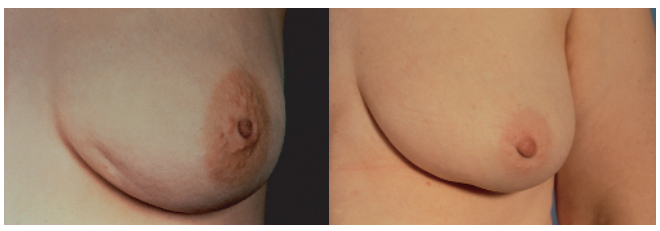


Figure 1.4 Skin dimpling (left) and change in breast contour (right) associated with underlying breast carcinoma.

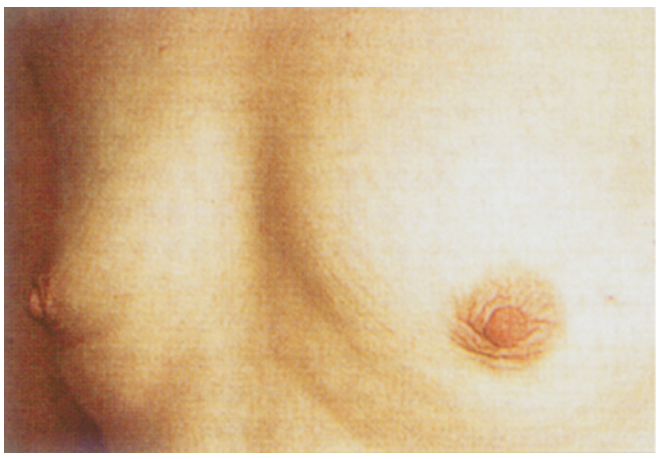


Figure 1.5 Skin dimpling visible in both breasts due to breast involution.

and the chest wall and makes abnormal areas much easier to detect and define. If an abnormality is identified, it should then be assessed for contour and texture. The presence of deep fixation is checked by tensing the pectoralis major, which is accomplished by asking the patient to press her hands on her hips. All palpable lesions should be measured with calipers. A clear

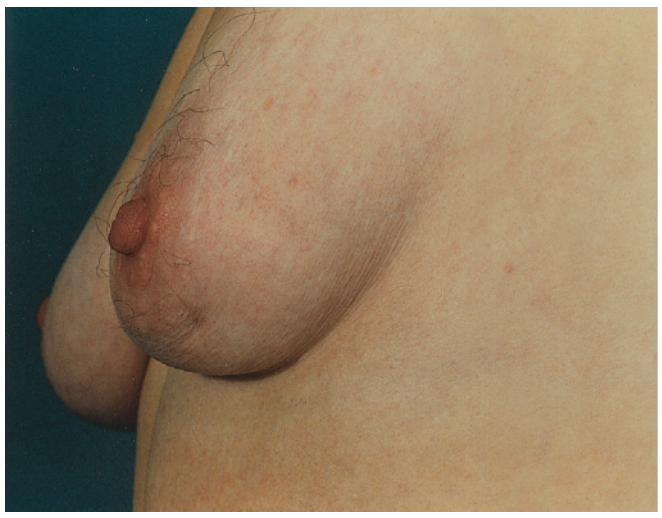


Figure 1.6 Skin dimpling after previous breast surgery.

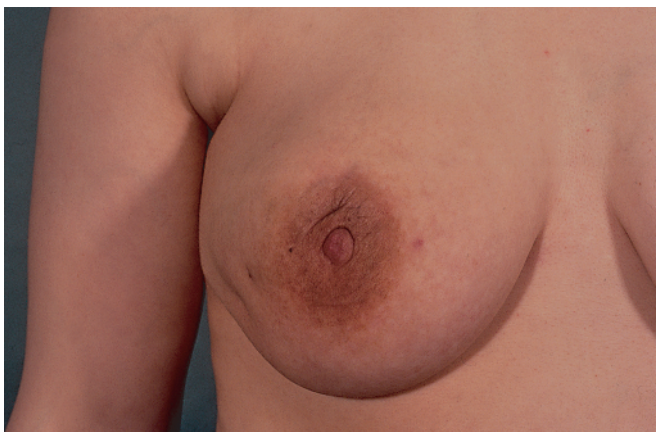


Figure 1.7 Skin dimpling associated with breast infection.

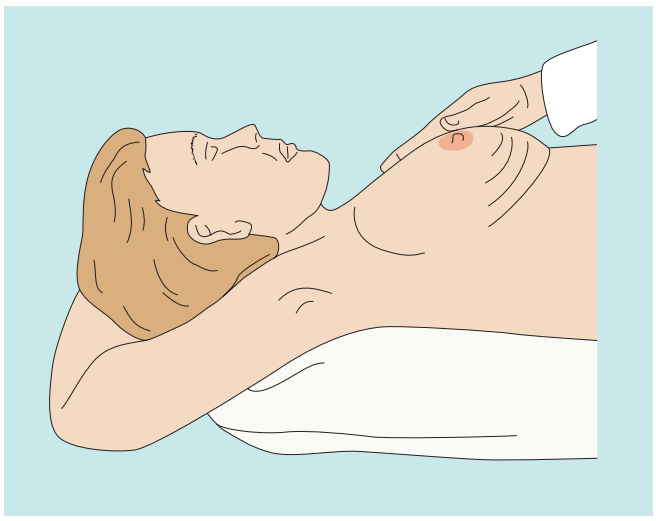


Figure 1.8 Breast palpation.

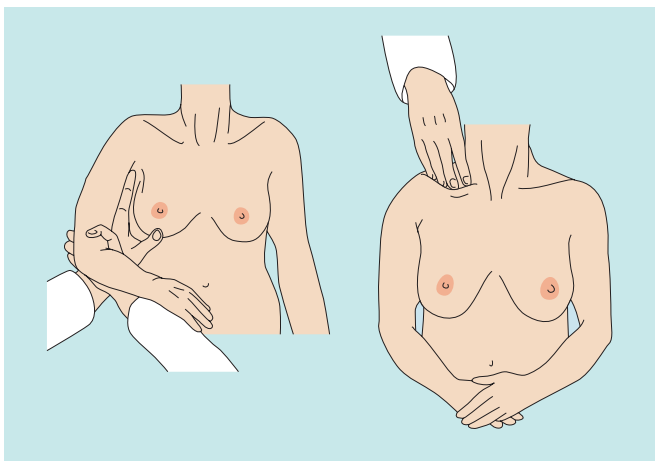


Figure 1.9 Assessment of regional nodes.

diagram of any breast abnormalities, including dimensions and the exact position, should be recorded in the medical notes.

Patients with breast pain should also be examined, the underlying chest wall being palpated for areas of tenderness while the woman lies on each side (see Chapter 3). Much so-called breast pain in fact emanates from the underlying chest wall.

Assessment of axillary nodes

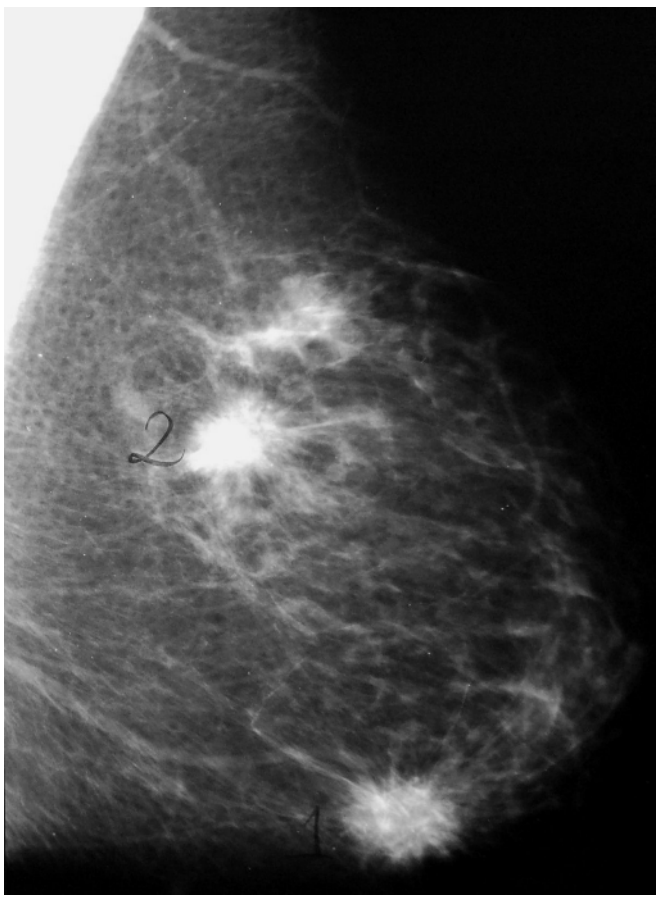
Once both breasts have been palpated, the nodal areas in the axillary and supraclavicular regions are checked (Figure 1.9). Clinical assessment of axillary nodes can be inaccurate: palpable nodes can be identified in up to 30% of patients with no clinically significant breast or other disease, and up to a third of patients with breast cancer who have clinically normal axillary nodes have axillary nodal metastases.

Mammography

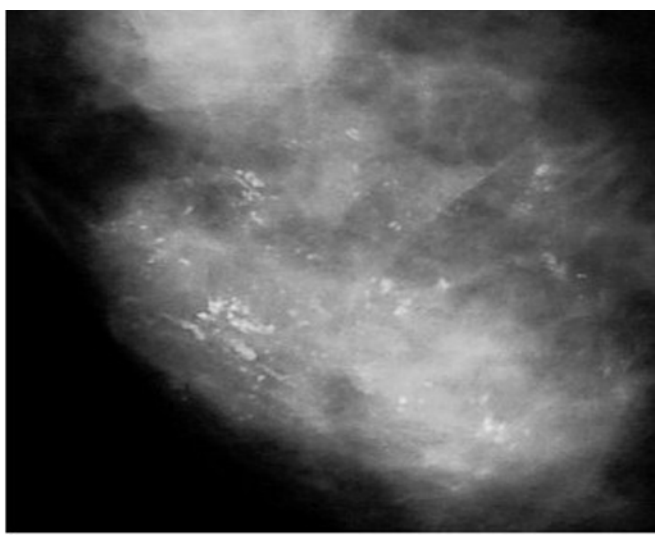
Mammography requires compression of the breast between two plates and is uncomfortable. Two views – oblique and craniocaudal – are usually obtained. With modern equipment a dose of less than 1.5 mGy is standard. Mammography allows detection of mass lesions (Figure 1.10), areas of parenchymal distortion and microcalcifications. Breasts are relatively radiodense, so in younger women aged under 35 mammography is of more limited value and should not be performed unless on clinical examination, cytology or core biopsy there is a suspicion that the patient has a cancer (Figure 1.10). Digital mammography, which is now being used in most units, has a greater sensitivity for cancer detection in young women than standard film mammography. All patients with breast cancer, regardless of age, should have mammography before surgery to help with assessment of the extent of disease.

Ultrasonography

In ultrasonography high-frequency sound waves are beamed through the breast and reflections are detected and turned into images. Cysts show up as transparent objects; other benign lesions tend to have well-demarcated edges (Figure 1.11(a)), whereas cancers usually have indistinct outlines (Figure 1.11(b)). Blood



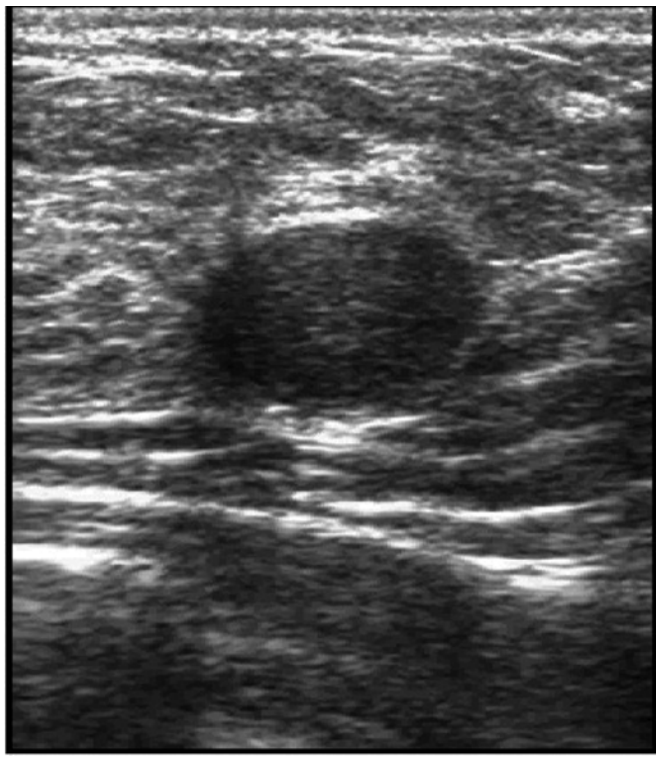
(a)



(b)

Figure 1.10 (a) Oblique mammogram showing two spiculated mass lesions characteristic of breast cancers in left breast. (b) Malignant calcification characteristic of high-grade DCIS.

flow to lesions can be imaged with colour flow Doppler ultrasound. Malignant lesions tend to have a greater blood flow than benign lesions, but the sensitivity and specificity of colour Doppler are insufficient to differentiate benign from malignant lesions



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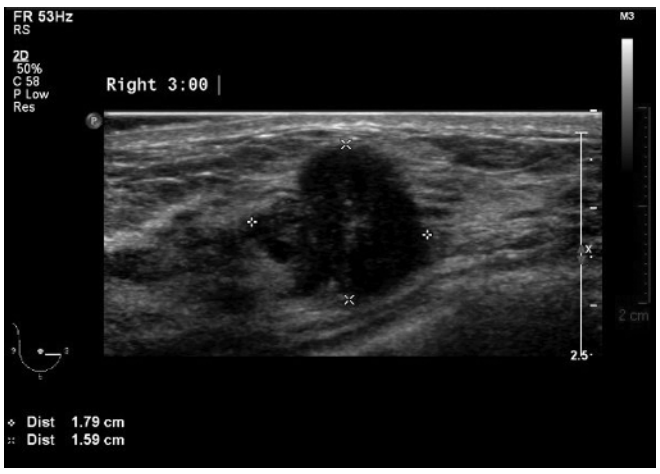


(b)

Figure 1.11 (a) Ultrasound of a fibroadenoma. (b) Ultrasound showing a solid irregular mass lesion characteristic of a cancer.

accurately. All patients with a diagnosis of breast cancer should have both a whole breast and an axillary ultrasound. If other evidence of disease is identified or abnormal nodes are seen, they should be biopsied under ultrasound guidance. Ultrasound contrast agents are available and continue to be investigated, but they are of no proven value in the routine assessment of breast masses or axillary nodes.

Magnetic resonance imaging (MRI)

Magnetic resonance imaging is an accurate way of imaging the breast (Figure 1.12). It has a high sensitivity for breast cancer

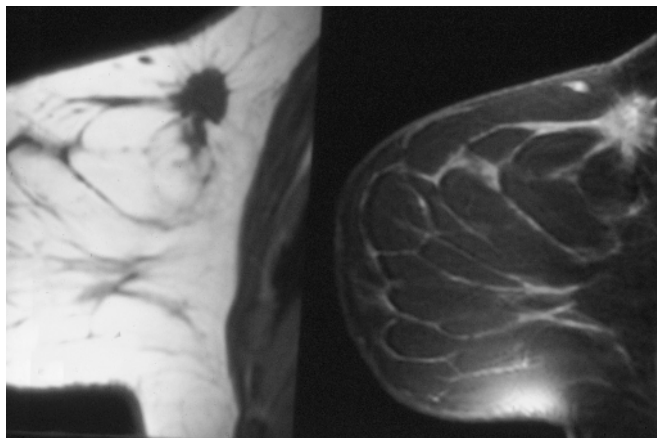


Figure 1.12 MRI scan showing cancer.

and may be valuable in demonstrating the extent of both invasive and non-invasive disease. The problem with MRI is a relatively low specificity and a positive predictive value of only two-thirds. It appears to be particularly valuable in assessing the extent of invasive lobular cancers, which are sometimes not well seen on mammography and ultrasound. It is also of value in assessing early response to neoadjuvant therapy in women with established breast cancer. MRI is useful in the treated, conserved breast to determine whether a mammographic lesion at the site of previous surgery is due to scar or recurrence. It has been shown to be a valuable screening tool for high-risk women between the ages of 35 and 50. MRI is the optimum method for imaging breast implants.

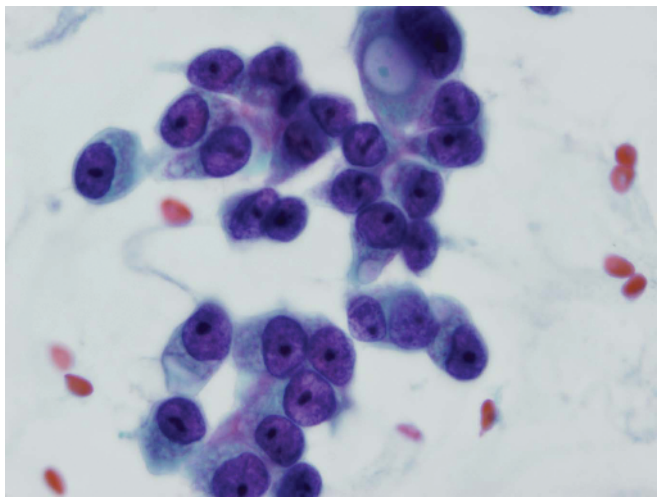
Fine needle aspiration cytology (FNAC)

FNAC is no longer commonly used to assess breast masses, but is valuable in assessing enlarged axillary or supraclavicular nodes visualised on ultrasound. Needle aspiration can differentiate between solid and cystic lesions. Aspiration of solid lesions requires skill to obtain enough cells for cytological analysis, as well as to interpret the smears. Image guidance increases accuracy, particularly in small lesions. A 21- or 23-gauge needle attached to a syringe is introduced into the lesion and suction is applied by withdrawing the plunger; multiple passes are made through the lesion. The plunger is then released and the material is spread onto microscope slides. These are then either air dried or sprayed with a fixative, depending on the cytologist's preference, and are stained (Figure 1.13). In some units a report is available within 30 minutes. The disadvantage of FNA in the breast is that it cannot differentiate invasive from in situ cancer.

Touch prep cytology of core biopsy samples and sentinel lymph nodes is possible and allows immediate reporting. If the biopsy sample contains a significant amount of tumour this technique is very accurate. Sensitivity of touch prep cytology of lymph nodes approaches 90%, which is better than the sensitivity of frozen section.

Core biopsy

Local anaesthetic containing adrenaline solution is infiltrated into the overlying skin and breast tissue surrounding the area to be



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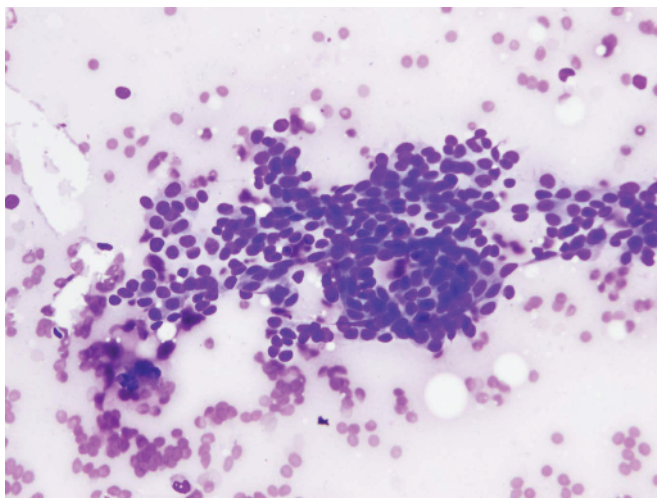


(b)

Figure 1.13 Smear from fine needle aspirate showing (a) malignant cells that are poorly cohesive and have large polymorphic nuclei, (b) a benign lesion, a fibroadenoma.

biopsied. After a minimum of 7–8 minutes, through a single small skin incision, multiple cores of tissue are removed from the clinical mass or the area of mammographic or ultrasound abnormality by means of a cutting needle technique (Figure 1.14). A 14-gauge needle combined with a mechanical gun produces satisfactory samples and allows the procedure to be performed single-handed. Unless the lesion is large, core biopsy should be performed with image guidance. For calcification at least three cores need to contain the target calcification or five calcifications need to be visible in the cores to ensure adequate sampling. For mass lesions the number of cores required is less clear, but with adequate local anaesthesia the procedure is painless, so multiple cores (three or more) are recommended to ensure adequate sampling of all parts of the lesion.

Large-bore vacuum-assisted biopsy

Performed under local anaesthesia, an 11- or 8-gauge needle attached to a vacuum device provides much larger specimens than

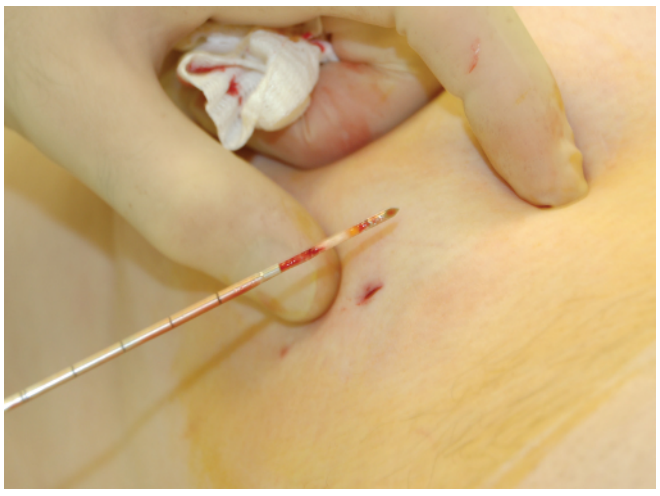


Figure 1.14 Core biopsy; central white portion of core represents the small cancer evident clinically.

a standard 14-gauge core biopsy. Such a device is particularly useful in areas of microcalcification because more tissue is obtained and there is a greater likelihood of the lesion being sampled adequately. These large-bore needles can be used to remove benign lesions such as fibroadenomas and small papillomas completely.

> Vacuum assisted core biopsy devices are now available that allow 11- or 8-gauge cores of tissue to be obtained, enabling more extensive sampling without the need to withdraw the needle from the breast. They are more accurate than 14-gauge core biopsy in sampling microcalcifications.

Open biopsy (Table 1.4)

Open biopsy is rarely required to establish a histopathological diagnosis except in the screening setting. All women undergoing open biopsy should have been assessed by imaging and at least one attempt at core biopsy. Women who are told that core biopsy has shown their lesion to be benign do not often request excision.

Breast biopsy is not without morbidity. A fifth of patients develop either a further lump under the scar or pain specifically related to the biopsy site over the ensuing decade.

Frozen section

Frozen section should no longer be used to diagnose breast cancer. The only exception would be its use in a patient with a cytological

Table 1.4 Indications for excision of a breast lesion.

- Diagnosis of malignancy on cytology not confirmed by subsequent core biopsy when a mastectomy or axillary clearance is planned
- Certain benign lesions, e.g. benign phyllodes tumours
- Diagnosis of atypical hyperplasia on core biopsy
- Radial scar: diagnosed by imaging and core biopsy
- Indeterminate papillary lesion on core biopsy
- Suspicion of malignancy on one or more investigations with indeterminate or inadequate core biopsy, usually in patients with screen-detected microcalcification
- Large lesions such as large or giant fibroadenomas
- Request by patient for excision

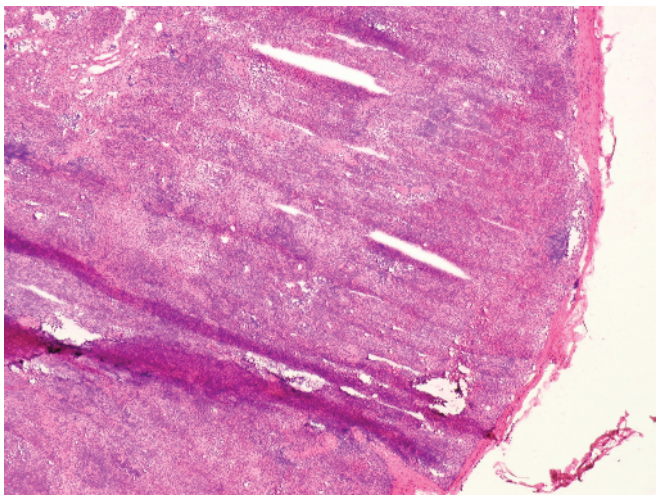


Figure 1.15 Frozen section of an axillary lymph node. It was reported as showing no evidence of metastases and this was confirmed on the subsequent paraffin section.

and imaging diagnosis of breast cancer when core biopsy has failed to establish cancer and a one-stage surgical procedure is planned. Before proceeding to definitive surgery the patient should have been told that her lesion is considered to be malignant and have been appropriately counselled, and should have had time to consider treatment options.

The use of frozen section has been reported in the assessment of excision margins after a wide local excision to ensure the complete excision and assessment of axillary lymph nodes, particularly sentinel nodes, during an operation to identify patients who are node positive who can proceed to axillary dissection (Figure 1.15). In both assessing excision margins and axillary nodes reported sensitivity varies between 66% and 90%. Use of immunohistochemistry and multiple frozen sections improves the sensitivity of axillary node assessment, but considerably increases costs and the length of time require to obtain a definitive result. Imprint cytology of sentinel nodes has a higher sensitivity and seems a better alternative to frozen section. Imprint cytology of surgical margins is an alternative to frozen section if intraoperative assessment is considered necessary.

> The routine use of frozen section to diagnose breast cancer is not acceptable.

Accuracy of investigations

False positive results occur with all diagnostic techniques (Table 1.5). It is not acceptable to plan treatment solely on the basis of malignant cytology, even if supported by a diagnosis of malignancy on clinical examination and imaging. Cytology has a false positive rate of 0.2–0.5%; the lesions most likely to be misinterpreted are fibroadenomas, papillary lesions and areas of breast that have been irradiated. For this reason a histological diagnosis is necessary to proceed with mastectomy. Cytology also has a false negative rate of 4–5%. Core biopsy has the advantage

Table 1.5 Symptoms, assessment, and guidelines for referral.

	Sensitivity for cancers*	Specificity for benign disease†	PPV for cancers‡
Clinical examination	86%	90%	95%
Mammography	86%	90%	95%
Ultrasonography	90%	92%	95%
MRI	98%	75%	66%
Fine needle aspiration cytology	95%	95%	99.8%
Core biopsy	98%	95%	100%§

*% of invasive cancers detected by test as malignant or probably malignant (that is, complete sensitivity).
†% of benign disease detected by test as benign.
‡% of lesions diagnosed as malignant that are cancers (that is, absolute PPV – positive predictive value).
§Sensitivity if core biopsy is image guided.

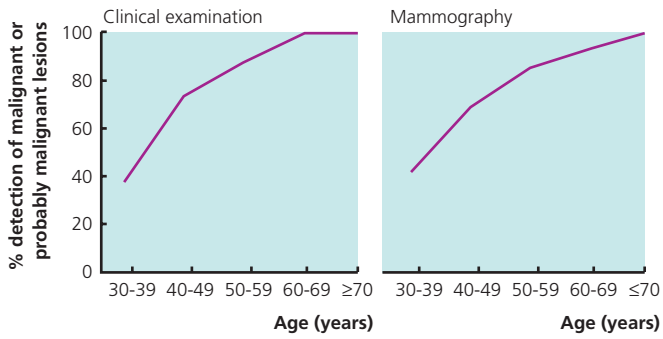


Figure 1.16 Sensitivity of clinical examination and mammography by age in patients presenting with a breast mass.

of providing a histological diagnosis and can differentiate between invasive and in situ carcinoma. Errors with core biopsy occur mainly because of geographical misses and inadequate sampling. Image guidance, taking images to show that the needle has sampled the lesion and taking multiple cores are recommended to maximise sensitivity.

The sensitivity of clinical examination and mammography varies with age; only two-thirds of cancers in women aged 50 are deemed to be highly suspicious or definitely malignant on clinical examination or mammography (Figure 1.16). Breast cancer in women aged under 40 is a particular problem, as it often presents with asymmetric nodularity rather than a discrete lump. General practitioners need to be aware of this.

Triple assessment

This is the combination of clinical examination, imaging (mammography with or without ultrasonography for women aged ≥35 and ultrasonography alone for women aged <35) and core biopsy, fine needle aspiration cytology or both (Table 1.6; Figure 1.17). Each component of the assessment is graded and for clinical examination (E), mammography (R) and ultrasound (U) the system used is 1: normal; 2: benign; 3: probably benign; 4: probably malignant; and 5: malignant. Cytology has a slightly different annotation as C1 is acellular not normal. Core biopsy likewise considers B1 as normal and therefore maybe unrepresentative if there is considered to be

Table 1.6 Advantages and disadvantages of techniques for assessment of breast masses.

Technique	Advantages	Disadvantages
Clinical examination	Easy to perform	Low sensitivity in women ≤50 Operator dependent*
Mammography	Useful for screening women aged ≥50	Requires dedicated equipment and experienced personnel Low sensitivity in women ≤50 Unpleasant (causes discomfort or actual pain)
Ultrasonography	Same sensitivity in all ages Useful in assessing impalpable lesions and the axilla Painless Useful to target core biopsy or FNA	Operator dependent* Slightly more sensitive than mammography; not useful for screening
MRI	High sensitivity in all ages Better at assessing size of cancer than other imaging techniques**	Costly and time consuming Claustrophobic Low specificity and low positive predictive value
Core biopsy	Easy to perform Less painful than FNA High sensitivity, particularly if image guided Provides a definitive histological diagnosis Almost zero false-positive rate	Operator dependent Cannot easily be reported immediately Uncomfortable but less painful than FNA Bruising and swelling
Fine needle aspiration cytology	Cheap High sensitivity Provides differential diagnosis in most instances Low incidence of false positives Can be reported immediately	Operator dependent Needs experienced cytopathologist Painful Cannot differentiate invasive from in situ cancer Some false positives

*Sensitivity varies in relation to expertise of individual.
**MRI did not appear to be valuable in increasing the rate of complete excision of patients undergoing breast-conserving surgery in a randomised study, but it did correlate better with the pathology size than either mammography or ultrasound.

a definite lesion, B2 as benign, B3 as atypical, B4 as suspicious indeterminate, B5a as in situ carcinoma and B5b as invasive cancer.

Delay in diagnosis

Delay in diagnosis of breast cancer is a common reason for patients taking legal action against medical practitioners.

Currently between 1.5% and 4% of patients with breast cancer experience a diagnostic delay of eight weeks or longer. Diagnostic delay is a particular problem in younger women, because cancers in such women often manifest as localised nodularity rather than a discrete lump. For this reason all women who have discrete lumps or localised areas of asymmetric nodularity should have full assessment by experienced clinicians. The doctor who orders the investigations

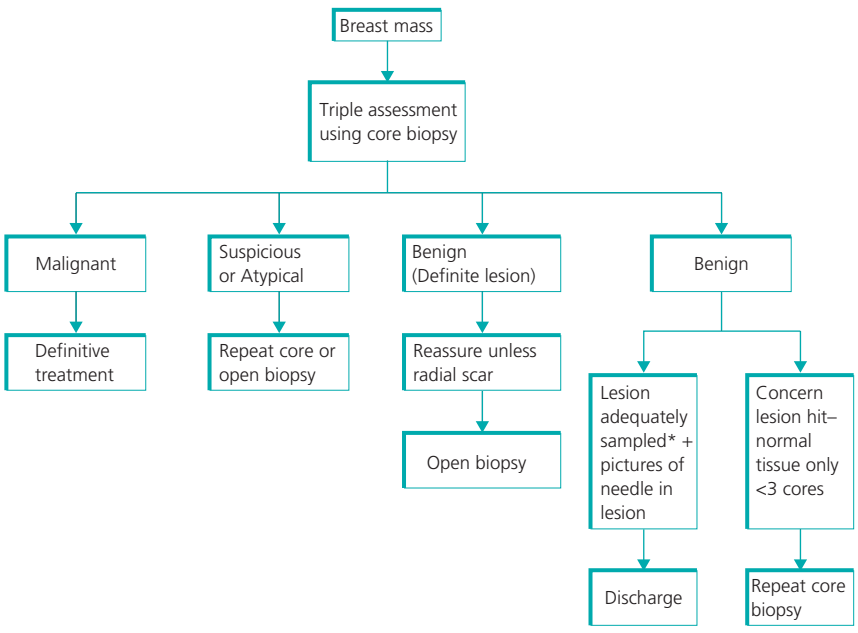


Figure 1.17 Investigation of a breast mass or localised area of nodularity with core biopsy.
*Minimum of 2–3 cores required to be certain that lesion is adequately sampled.

should check and sign all results of these investigations, which should then be filed in the patient's notes. Details of any clinical findings from clinic visits must be recorded legibly and include a diagram marking all areas of abnormality as well as a doctor's signature.

One-stop clinics

In a patient with a discrete breast mass or a localised area of nodularity, some treatment centres offer immediate reporting of imaging and cytology from a fine needle aspirate or touch preparation from a core biopsy sample. Although one-stop clinics with cytology have potential advantages, with modern imaging few lesions are truly indeterminate. With the increasing use of core biopsy and the limited numbers of experienced cytologists, few one-stop clinics remain.

Investigation of breast symptoms

Breast mass and localised nodularity

All patients should have a clinical and imaging assessment with biopsy of any indeterminate or discrete lesion. It is not necessary to excise all solid breast masses, and a selective policy is recommended on the basis of the results of triple assessment. Core biopsy, preferably image guided, has replaced cytology and is the diagnostic investigation of choice to achieve a definitive histological diagnosis in a solid lesion.

Nipple discharge

Treatment depends on whether the discharge is spontaneous and whether it is from one or several ducts (Figure 1.18). Single-duct discharge should be checked for the presence of haemoglobin. Only moderate or large amounts of blood are significant. About 5–10% of patients with bloodstained discharge will be found to have an underlying malignancy. Most bloodstained discharges are due to papillomas or other benign conditions. All patients with spontaneous discharge should have a clinical examination. All patients aged 35 or over with spontaneous discharge and younger patients with bloodstained or haemoserous discharge should have mammography. Ductography and ductoscopy can localise lesions and may have a role in young women to direct and limit any excision in an effort to maintain the ability to breastfeed. Physiological nipple discharge is common and is not usually spontaneous: two-thirds of premenopausal women can be made to produce nipple secretion by cleansing the nipple and applying suction (Figure 1.19). This physiological discharge varies in colour from white to yellow to green to blue-black.

Surgery is indicated in cases of spontaneous discharge from a single duct that is confirmed on clinical examination and has one of the following characteristics:

- Is bloodstained or contains moderate or large amounts of blood on testing.
- Is persistent (occurs on at least two occasions per week).
- Is a new development in a woman older than 50 years of age but is not thick or cheesy.

Discharge from multiple ducts requires surgery only when it causes distressing symptoms such as persistent staining of clothes.

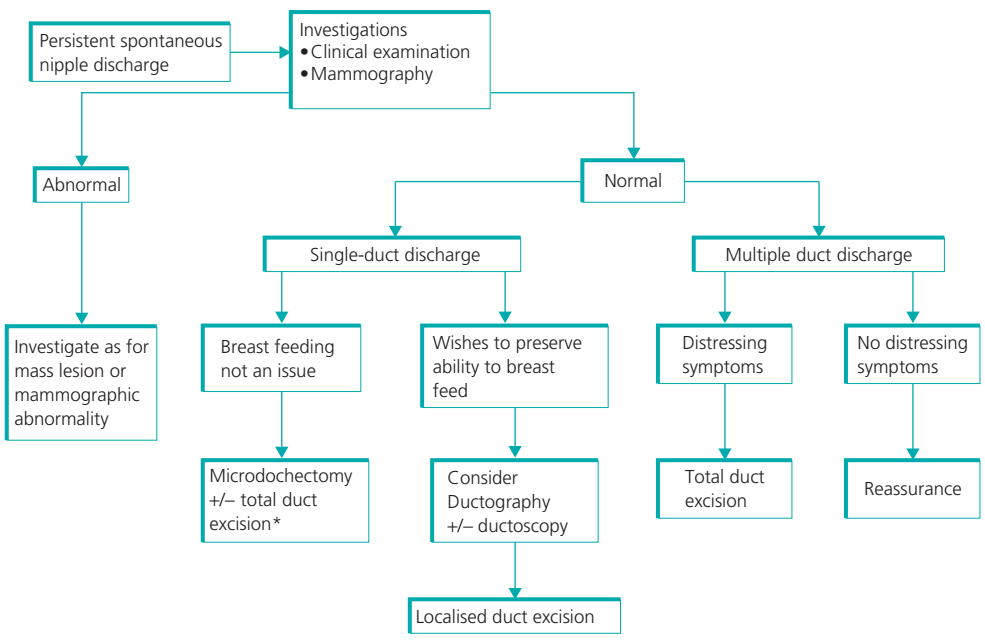
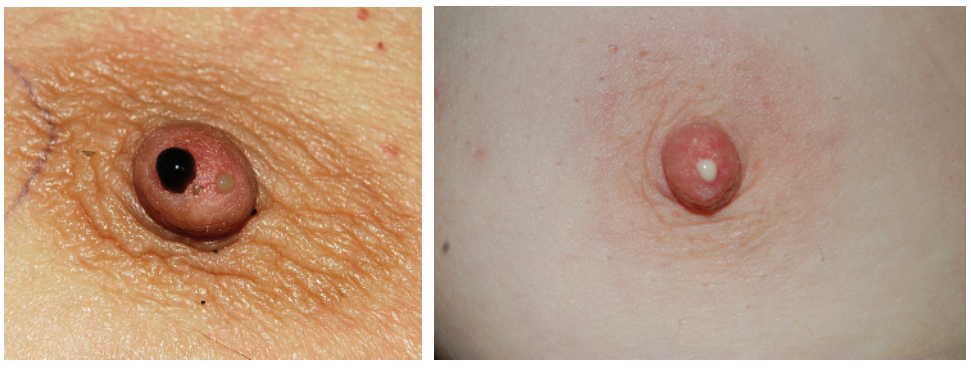


Figure 1.18 Investigation of nipple discharge.
*Some surgeons prefer total duct excision in women aged >45 to reduce incidence of discharge from other ducts.
†If lesion on mammogram is incidental and unlikely to be related to nipple discharge, combine with investigation of single- or multiple-duct discharge as appropriate.



(a) (b)

Figure 1.19 (a) Multiple physiological discharge. Note the range of colours characteristic of physiological discharge. (b) Physiological multiple duct coloured. Note the colours are lighter than those in Figure 1.19a; there is a whole range of colours from white to yellow to green to blue black.

Galactorrhoea

Galactorrhoea is copious bilateral milky discharge not associated with pregnancy or breastfeeding (Figure 1.20). Prolactin levels are usually but not always raised. A careful drug history should be taken, as various drugs, particularly psychotropic agents, can cause hyperprolactinaemia. In the absence of relevant drugs, a search for a pituitary tumour should be instituted in a patient with a raised prolactin greater than 1000 IU/l.

Nipple retraction

Slit-like retraction of the nipple is characteristic of benign disease (Figure 1.21), whereas nipple inversion, when the whole nipple is pulled in, occurs in association with both breast cancer and inflammatory breast conditions. For patients with congenital nipple retraction and acquired nipple retraction, which is unsightly and does not respond to conservative measures such as suction devices or nipple shields, surgery including duct division or excision can be successful at everting the nipple. Women need to be informed that duct excision can result in loss of ability to breastfeed and loss or reduction of nipple sensation or sometimes nipple hypersensitivity.

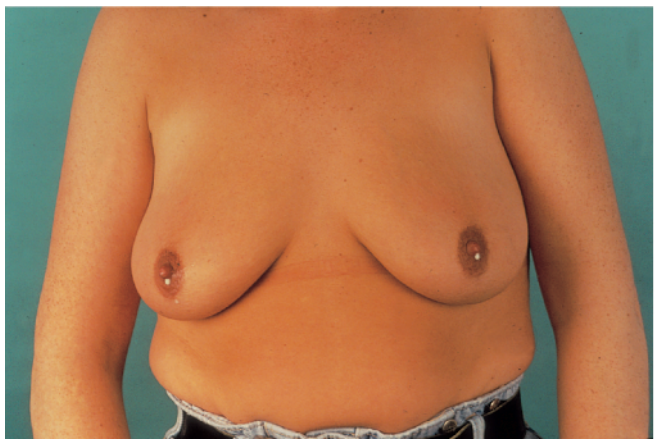
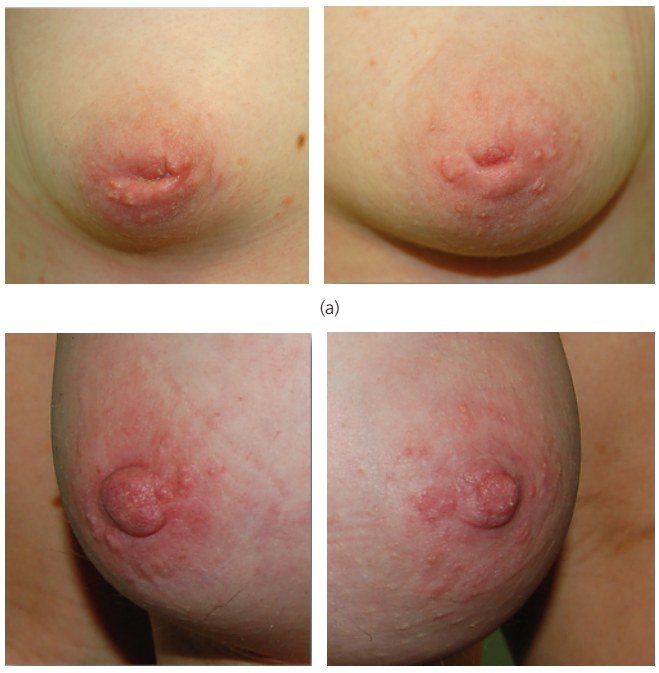


Figure 1.20 Galactorrhoea.



(a)

(b)

Figure 1.21 (a) Bilateral benign congenital nipple inversion prior to surgery. (b) After nipple eversion.

Breast pain

Breast pain should be assessed by means of a careful history and clinical examination. Mammography or ultrasonography, or both, is indicated in patients with unilateral persistent mastalgia or a localised area of painful nodularity. The management of breast pain is covered in Chapter 3.

Further reading

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