
Breast Surgery

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Introduction

Management of breast disease has become increasingly specialised. A multidisciplinary and integrated approach is used, involving surgeons, radiologists, pathologists, oncologists and breast counsellors. A substantial component of the workload includes differentiation of benign breast disease from a breast cancer and allaying the patient's anxiety about breast cancer.

Anatomy of the adult breast

The breast is invested with the superficial fascia that divides into two layers. The anterior layer separates the relatively small subcutaneous fat lobules and the larger lobules of mammary fat. The posterior layer of superficial fascia abuts against the deep fascia derived from the pectoralis major and serratus anterior. Between the two layers of superficial fascia, there are condensations of fibrous tissue (suspensory ligaments of Cooper) that divide the breast into lobes.

The main blood supply is via the second perforating branch of the internal mammary and lateral thoracic branches of the axillary artery. Lesser supply is via the thoracoacromial and subscapular arteries. A rich subareolar venous plexus drains via the intercostal, internal mammary and axillary veins.

The distribution of major lymphatics follows the blood supply. About 75% of the lymphatic vessels drain to the lymph nodes in front of and below the axillary vein. These axillary nodes are divided into three groups according to their relationship to the pectoralis minor muscle (Fig. 32.1): level 1, nodes lying below the pectoralis minor; level 2, nodes lying behind the pectoralis minor; level 3, nodes lying above the pectoralis minor. Most lymph drains from nodes at level 1 sequentially

to those at levels 2 and 3, and a small amount drains in retrograde fashion to the subscapular and interpectoral groups of nodes. The latter becomes significant when there is extensive nodal metastasis in the axilla. A small amount of lymph drains from the superior aspect of the breast directly to the apical nodes in level 3, bypassing nodes in levels 1 and 2. About 25% of lymph (mainly from the medial half of the breast) drains to the internal mammary nodes in the second, third and fourth intercostal spaces.

Benign breast disease

Many so-called diseases of the breast are aberrations of the processes of development, cyclical change and involution (ANDI). Benign breast disease refers to more severe disorders. In general, there is a poor correlation between clinical, pathological and radiological features.

The symptoms of benign breast disease are summarised in Box 32.1.

Mastalgia

Mastalgia is a common breast symptom; however, mastalgia does not imply any specific pathological process and the condition is not well understood. Mastalgia can be cyclical, varying with the menstrual cycle, or non-cyclical where there is no such relationship.

Cyclical mastalgia

Cyclical mastalgia is the most common type of breast pain affecting premenopausal women. The median age of presentation is 35 years. The breast discomfort lasts for a varying period prior to menstruation and relief of the pain comes with menstruation. The pain is

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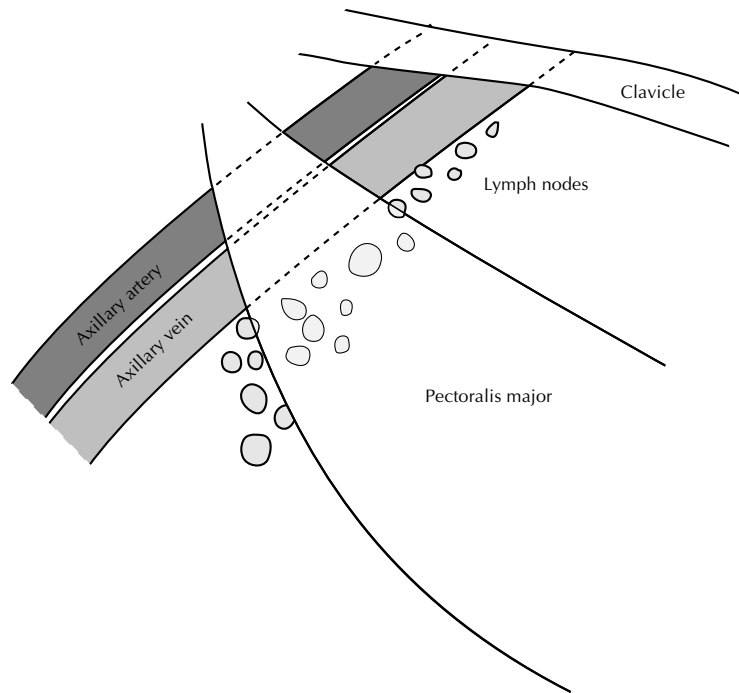


Fig. 32.1 Right axilla.

commonly in the upper outer quadrant of both breasts and radiates into the axilla and the medial aspect of the arm.

Box 32.1 Symptoms of benign breast disease

Mastalgia

- Cyclical
- Non-cyclical

Breast lumps

- Nodularity
- Cysts
- Fibroadenoma
- Mammary duct ectasia
- Sclerosing adenosis
- Fat necrosis
- Lipoma

Disorders of the peri-areolar region

- Discharge
- Retraction

Mastitis

- Lactational
- Non-lactational

Aetiology

As symptoms of cyclical mastalgia vary with menstrual cycle, there is probably a hormonal basis in the aetiology. The precise pathogenesis is, however, poorly understood. Possible factors may include abnormal prolactin secretion, fluid retention, excessive caffeine ingestion, inadequate essential fatty acid intake and psychoneurosis.

Treatment

More than 80% of women require no treatment other than reassurance that there is no cancer.

Drug treatments are described in Table 32.1. These drugs have a potential for side effects. The initial treatment is usually with evening primrose oil and a reduction of caffeine intake including tea, coffee, chocolate and cola drinks. Natural or treatment-induced remissions are common, but recurrence of mastalgia does occur.

Second-line treatment with low-dose tamoxifen, danazol or bromocriptine is reserved for severe refractory symptoms. The use of these drugs is limited by their side effects. Second-line treatment has a lower response rate.

Table 32.1 Drug treatments for cyclical mastalgia

Drug	Action	Response rate (%)
Evening primrose oil (6 capsules/day)	Essential fatty acid replacement	50
Oral contraceptives	Correct luteal insufficiency	50
Tamoxifen (10 mg/day)	Anti-oestrogen	80
Norethisterone (5 mg/day)	Progestogen	60
Danazol (200 mg/day)	Suppress FSH, LH	70
Bromocriptine (2.5 mg b.d.)	Dopamine agonist, correct hyperprolactinaemia	50

FSH, follicle-stimulating hormone; LH, luteinising hormone.

Non-cyclical mastalgia

The breast pain has no relationship to the menstrual cycle. It tends to be unilateral, more chronic and sometimes has a well localised ‘trigger spot’. It affects both pre- and postmenopausal women and the median age at presentation is 45 years.

Management

Any primary pathology of the breast and of adjacent structures should be excluded by a careful

clinical evaluation and appropriate imaging (see the following section). Treatment involves reassurance that there is no underlying pathology but drug treatment is generally unrewarding. Treatment principles similar to those for cyclical mastalgia are used. However, the response rate is worse and averages about 50%. The use of evening primrose oil is particularly disappointing in this subgroup. Occasionally, surgical excision of the painful trigger spot may alleviate the symptoms.

Benign breast lumps

More than half the women attending a breast clinic have a benign breast lump. Clinical history includes the nature and duration of the lump and its relationship to the menstrual cycle. Any changes in the lump and a similar past history are important. Risk factors for breast cancer are sought, including age, family history, use of hormone replacement therapy or oral contraceptives. The age at first pregnancy and the number of children are also of interest.

A careful examination is performed to determine whether the lump is truly present or whether it is within the spectrum of normality or an area of nodularity (thickening). The lump, if present, should be carefully examined to note for features of malignancy. Diagnosis now follows a structured algorithm (Fig. 32.2), following the development of diagnostic aids such as mammography (Fig. 32.3), ultrasonography and fine-needle aspiration cytology (FNAC).

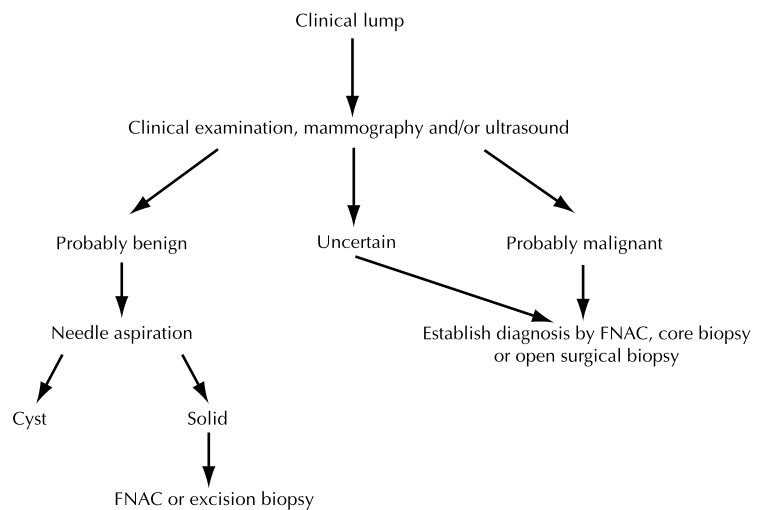


Fig. 32.2 Management of palpable breast lumps. FNAC, fine-needle aspiration cytology.

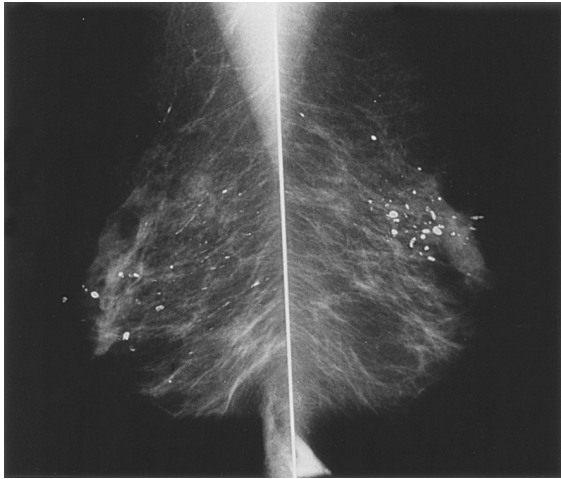
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Fig. 32.3 Bilateral mammography showing coarse calcifications consistent with benign breast disease.

If FNAC is inconclusive or if any doubt of a malignancy remains, then surgical biopsy is indicated. A discrete solid breast lump in women over the age of 30 years is best removed, especially in the presence of a strong family history of breast cancer and other risk factors.

Fibroadenoma

Pathology

Fibroadenoma is a benign breast tumour in young women between 15 and 25 years. It consists of a fibrous connective tissue stroma and epithelial proliferation, usually with low cellularity. It is very occasionally seen in association with lobular carcinoma. The incidence falls markedly after menopause, when the breast lobules undergo involution.

The fibrous stroma of a fibroadenoma may surround a duct circumferentially (pericanalicular pattern) or compress adjacent ducts to become slit-like structures (intracanalicular pattern). With a benign fibroadenoma, the fibrous stroma has low cellularity. Epithelial hyperplasia may be present but has no prognostic importance. Coarse calcification may also occur.

A locally invasive variant (phyllodes tumour) also occurs (see later).

Clinical features

Fibroadenoma is smooth and very mobile (breast mouse). It measures about 2 or 3 cm in diameter. Some patients have multiple fibroadenomas at presentation. Others have multiple recurrent fibroadenomas.

Investigations

A clinical examination is usually adequate in young women up to 25 years old. In women older than this, an ultrasound with either fine-needle aspiration cytology, core biopsy or excisional biopsy, confirming a benign fibroadenoma is required. Mammography has little place.

Management

Fibroadenomas have a tendency to slowly increase in size. Most of the growth phase is within the first 12 months. Following that period, fibroadenomas remain the same size or may, occasionally, gradually reduce in size.

In women under 25 years, the lump may be left alone unless the patient wants it removed. In older women, pathological confirmation with FNAC or core biopsy or removal of the lump is recommended.

Giant fibroadenoma

Giant fibroadenoma occurs in the very young (about 16 years old) or in the perimenopausal age group (about 50 years old). It is characterised by its rapid growth to a large size, and treatment is by surgical enucleation. This is a benign tumour.

Phyllodes tumour

Pathology

Phyllodes tumour has a wide spectrum of activity, ranging from almost benign to locally invasive. Histologically, the fibrous stroma is hypercellular with cellular atypia and mitoses.

Clinical features

Phyllodes tumours occur in premenopausal women and clinically resemble a fibroadenoma, but they grow quite rapidly. They rarely spread to the axilla.

Treatment

This entails a wide local excision with a clear margin of normal breast tissue. Local recurrence is common (25% at 10 years) and if the tumour is aggressive, then total mastectomy may be required.

Breast cysts

Pathology and incidence

Breast cysts are very common, with up to 10% of women developing a clinical breast cyst during their lifetime. Many women have subclinical breast cysts measuring 2–3 mm identified on ultrasound and most occur in the peri-menopausal age group, but they may occur at any age. Breast cysts are often multiple. The pathogenesis of breast cysts is not clear. The breast cyst may be lined by an apocrine or a simple cuboidal epithelium. There may be multiple cysts in a breast.

Clinical features

Breast cysts often appear suddenly and can be quite large. This is because the subclinical flaccid cyst accumulates a small amount of fluid and becomes tense and painful menstruation.

On clinical examination, the cyst is smooth and firm but not as mobile as a fibroadenoma. It is situated deep in the breast, and it may feel quite nodular.

The diagnosis of a breast cyst is confirmed by cyst aspiration, and cytological examination of the cyst fluid is generally unhelpful unless the fluid is blood stained. A breast cyst is usually well shown on ultrasound (Fig. 32.4), and imaging, mammography or ultrasound are only performed to exclude underlying breast cancer.

Treatment

Palpable breast cysts are treated by simple aspiration, in the consulting room, without any anaesthesia. If a mass persists, further investigations are required to define the cause of the mass.

Surgical excision is indicated if a non-traumatic aspirate is blood stained (because of the risk for intracystic cancer) or if the cyst continually recurs. A significant number of women develop further cysts which require repeat aspiration. Detection of breast cancer in this

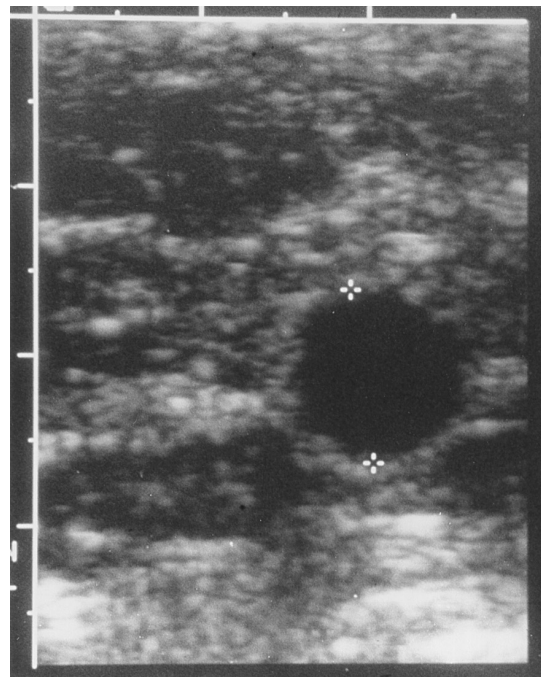


Fig. 32.4 A breast ultrasound showing a well-defined breast cyst.

group is slightly more difficult, and they require regular surveillance mammograms.

Mammary duct ectasia and periductal mastitis

Clinical features

Mammary duct ectasia and periductal mastitis have a diverse clinical spectrum. The aetiology is unclear but involves the accumulation of secretions in the duct and inflammation of the surrounding tissues leading to inflammation, sometimes secondary infection, a thick nipple discharge and nipple retraction. Secondary infections can sometimes follow and inflammatory masses in the peri-areola region can form abscesses and mammary fistulae between the ducts and the skin at the areola margin.

Treatment

The inflammatory phase is treated with antibiotics, for example metranidazole or surgery of the major ducts, including local incision and drainage of abscess or major duct excisions for more chronic cases.

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Box 32.2 Causes of nipple discharge

- Physiological (pregnancy, lactation)
- Duct ectasia
- Galactorrhoea
- Duct papillomas
- Fibrocystic disease
- Carcinoma
- Idiopathic

Nipple discharge**Clinical features and investigation**

Nipple discharge is a common problem and the causes are outlined in Box 32.2. Investigations include mammography and ultrasound with cytology of the discharge, ductography and ductoscopy. These investigations are often disappointing and may be confusing.

Galactorrhoea

Galactorrhoea may be a primary physiological process, occurring during menarche, menopause or secondary to drugs that stimulate dopamine activity.

Duct papillomas

The discharge may be serous but is often blood stained and arises from a single duct. The solitary papillomas are benign and do not have malignant potential. The risk for malignancy is slightly raised in the unusual circumstance of multiple papillomas affecting several ducts.

Management of nipple discharge

Clinical history should include use of drugs (haloperidol, metoclopramide), menstrual history and risk factors for breast cancer. Examination should determine the presence of lumps and imaging with ultrasound or mammogram if over 35 years old.

If a breast lump is present, management is directed to the lump itself. If a lump is not present, management depends on the nature of the discharge and the results of breast imaging by ultrasound and mammography.

Box 32.3 Relationship between benign and malignant breast disease**Moderately increased risk (4–5×)**

- Atypical ductal hyperplasia
- Atypical lobular hyperplasia
- Radial scar

Slightly increased risk (1.5–2.0×)

- Moderate or florid hyperplasia
- Multiple papilloma

No increased risk

- Cysts
- Fibroadenoma
- Duct ectasia
- Mild hyperplasia
- Sclerosing adenosis
- Apocrine change

Relationship of benign breast disease to breast cancer

Benign breast disease is a risk for cancer (Box 32.3), although the literature is confusing.

Gynaecomastia in males

About one-third of adult males and more than half of normal pubescent boys have some degree of gynaecomastia (Box 32.4, Fig. 32.5). Physiological gynaecomastia occurs in the neonate because of circulating

Box 32.4 Causes of gynaecomastia in males**Physiological****Pathological**

- Drug-induced (e.g. hormone supplements, alcohol, cimetidine, digoxin, phenothiazines, tricyclic antidepressants, some antihypertensive agents)
- Increased oestrogen production (e.g. hepatoma, testicular and adrenal tumours or paraneoplastic syndrome)
- Reduced production of testosterone (e.g. Klinefelter's syndrome, mumps orchitis)
- Testicular feminisation syndrome



Fig. 32.5 Bilateral gynecomastia in a man.

maternal sex hormones, at puberty because of a high serum oestradiol to testosterone ratio, and in the elderly because of reduced testosterone production. With significant gynecomastia causing social embarrassment, surgical excision of the breast plaque is recommended. This is done through an incision at the margin of the areola to minimise the cosmetic effect.

Breast cancer

Introduction

Breast cancer is a heterogeneous disease with a varying propensity for spread. The disease tends to be slow growing, with pre-invasive phases that may extend over a number of years. Breast cancer may recur many years after surgery, indicating the need for prolonged monitoring.

Incidence

Breast cancer is common and the incidence is increasing. The lifetime risk for breast cancer in an Australian woman is 1 in 13, but is lower in Asian countries. About 1 in 25 women die of breast cancer. The incidence of breast cancer rises with age, and the disease is more common in women of higher socioeconomic class.

Risk factors

Several interrelated factors are associated with an increased risk for developing breast cancer (Box 32.5).

Box 32.5 Factors associated with an increased risk for developing breast cancer

- Sex. Breast cancer is 100 times more common in women than in men.
- Increasing age. Breast cancer is uncommon in women under 30 years. The mean age at diagnosis is 60 years.
- Past history of breast cancer. The development of a second cancer may be part of the multifocal origin of the first cancer or an entirely new cancer.
- First-degree relatives (mother, sister or daughter) with breast cancer, especially if they were under 50 years of age when the cancer developed.
- Previous history of benign proliferative disease with cellular atypia, multiple papillomatosis, atypical ductal and lobular hyperplasia or lobular carcinoma *in situ*.
- Other factors (e.g. nulliparity at 40 years, previous breast irradiation, younger age of menarche). The data on the cancer risk with hormone replacement therapy is conflicting, but short duration (<5 years) appears safe. The oral contraceptive pill does not seem to be associated with any increased risk.

Spread of breast cancer

The rate and extent of spread varies between individuals because of the heterogeneous nature of the cancer. In some patients, regional nodal and distant metastases occur rapidly, even if the primary breast cancer is small, while in others the tumour remains largely localised in the breast.

Local invasion

This occurs by direct infiltration of the breast parenchyma, overlying skin or underlying fascia, giving rise to the characteristic stellate appearance of breast cancer. Invasion along the ducts may also occur (Pagetoid spread). Local lymphovascular spread indicates a worse prognosis.

Regional spread

The axillary lymph nodes are the most important and most common site of regional spread. Clinical assessment of axillary nodes is unreliable and the false positive and false negative rates are about 30%. Axillary nodal metastases are more common with larger tumours and are the most important prognostic factor.

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The incidence of axillary nodal metastases is less than 20% in tumours smaller than 2 cm but rises to more than 50% in tumours larger than 5 cm. A high number (>4) of nodes involved is associated with a particularly bad prognosis. Internal mammary lymph nodes lie in the anterior intercostal spaces adjacent to the internal mammary vessels and spread to the internal mammary nodes is usually associated with axillary node metastasis and carries a poor prognosis. Supraclavicular nodal metastases are also associated with a poor prognosis.

Distant metastases

The most common sites of disease are the bone, liver and lung. Other sites include the brain, skin and peritoneum. Micrometastases in the bone marrow may occur in up to one-third of patients who have breast cancer apparently confined to the breast.

Staging of breast cancer

Staging is an attempt to classify breast cancer according to the extent of the disease and thus stratify the prognosis. However, this is somewhat simplistic because of the large number of prognostic variables and the heterogeneity of the disease. The Manchester system is a simple clinical staging system, while the TNM classification provides a more accurate assessment and is useful in clinical trials (Table 32.2).

History

A thorough clinical history should be taken, including menstrual, obstetric, family and medication history, and the interview will establish a sound professional association with the patient.

Common symptoms include:

- a lump that may be firm or hard with a varying degree of fixity to surrounding tissues, overlying skin and underlying pectoral muscles. While pain is an uncommon symptom, the cancerous lump may have increasing discomfort, especially prior to menstruation. In neglected cases, a foul-smelling malignant ulcer may arise in the breast
- changes to the breast that include distortion, puckering of skin and nipple retraction
- a blood-stained nipple discharge may arise from an intraductal cancer and is typically unifocal

- rarely, regional or distant metastases may be the cause of symptoms such as a lump in the axilla or neck and bone pain or dyspnoea.

Table 32.2 Staging systems for breast cancer

Manchester system	
Stage I	Tumour confined to the breast with skin involvement less than the size of the tumour
Stage II	Tumour confined to the breast with palpable mobile axillary lymph nodes
Stage III	Locally advanced breast cancer with skin fixation larger than the tumour. Cutaneous ulcers or fixity to pectoralis fascia may be present. Peau d'orange or satellite chest wall nodules. Fixed axillary nodes, supraclavicular nodal involvement
Stage IV	Distant metastases
TNM classification	
Tumour categories	
T _x	Primary tumour cannot be assessed
T _{is}	Carcinoma <i>in situ</i>
T ₁	Tumour size <2 cm
T ₂	Tumour size 2–5 cm
T ₃	Tumour size >5 cm
T ₄	Any tumour size with fixation to chest wall or skin
Nodal categories	
N _x	Regional lymph nodes cannot be assessed
N ₀	Axillary lymph nodes not involved
N ₁	Ipsilateral axillary nodal metastases (mobile)
N ₂	Ipsilateral axillary nodal metastases (fixed)
N ₃	Ipsilateral supraclavicular or internal mammary nodal metastases
Metastasis categories	
M _x	Presence of distant metastases cannot be assessed
M ₀	No distant metastases
M ₁	Distant metastases

Clinical examination

Clinical examination can be normal, especially in screen-detected cancers, or in patients with small (<1 cm) lumps. Larger lumps may be firm to hard, irregular and have skin attachment or distort the breast shape. More advanced cancers can have Peau d'orange or even skin inflammation. If the tumour ulcerates, it becomes foul smelling.

Paget's disease of the nipple presents with an eczema of the nipple itself and is associated with underlying intraductal carcinoma, often with an invasive component.

Both breasts, axillae and supraclavicular fossae are examined for signs of local spread of the breast cancer. Clinical assessment of the axilla is inaccurate and lymph node metastases can only be determined by histological examination.

Systemic examination looking for metastatic disease should be carried out.

Investigations

Most cancers can be accurately diagnosed with a combination of mammography, ultrasound, fine-needle aspiration and core biopsy. It should be remembered however that negative imaging does not completely rule out breast cancer particularly and invasive lobular cancer.

Mammography

Mammography has a higher level of accuracy in detecting breast cancer, and its specificity increases with the age of the patient. Classic mammographic features include a mass, tissue asymmetry and microcalcification (Fig. 32.6). Mammography detects impalpable cancers and, in clinically palpable cancers, helps assess the extent of the disease and so helps planning of treatment.

Breast ultrasound

This is most useful to evaluate:

- a dense breast parenchyma (as in younger women) where mammography may fail to demonstrate the tumour clearly
- an equivocal mammographic abnormality
- a palpable lump (solid vs. cystic), especially in pregnant or lactating breast
- and guide a needle or core biopsy.

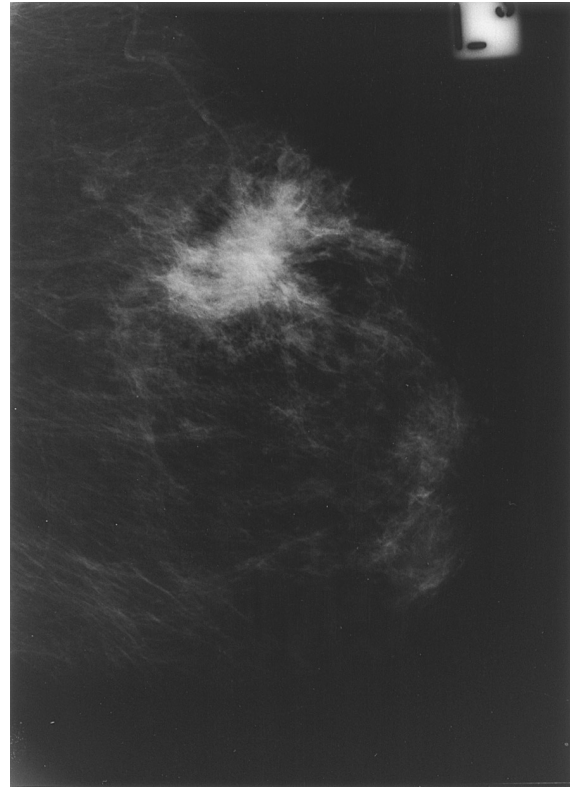


Fig. 32.6 Mammogram showing a stellate mass with irregular margins, consistent with a breast cancer.

Fine-needle aspiration cytology

Fine-needle aspiration cytology (FNAC) guided by either ultrasound, mammography, manually or palpation yields cells which are diagnostic of cancer. It is not possible to distinguish *in situ* from invasive cancer. False negatives arise from sampling errors or a cellular cancer; false positives also occur but are most unusual. Core biopsy, which provides histology and differentiates *in situ* from invasive, is progressively replacing FNAC. Diagnostic biopsy followed by definite surgery; for example Mastectomy with axillary clearance is now avoided.

Core biopsy

This is performed using a 14- or 16-gauge wide-bore needle under local anaesthesia and is replacing FNAC as it has a higher sensitivity and specificity.

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Open surgical biopsy

This is performed as a day procedure under general anaesthesia in the following cases:

- if FNAC or core biopsy is inconclusive and has not been helpful and there is a clinical suspicion of malignancy
- the patient is anxious
- there is a discrete lump which is increasing in size (e.g. fibroadenoma).

Impalpable lesions require pre-operative localisation with a needle or carbon or radio isotope and the lesion is carefully oriented for the pathologist.

Frozen section histology

This may be used to confirm a pre-operative cytological diagnosis of malignancy or to provide an immediate diagnostic report when the open biopsy is performed as an independent procedure.

Frozen section histology should not proceed to immediate mastectomy unless there has been discussion with the patient and agreement about the procedure to be followed, which will depend on the outcome of the frozen section. Frozen section has a false positive rate of 1%, because of confusion with sclerosing adenosis, nipple adenoma and mastitis.

Selective tests

Specific staging tests for breast cancer include:

- full blood examination, urea and electrolytes, liver function tests, bone scan, liver ultrasound and chest and abdominal CT scan.

These tests are usually performed after surgery when the nodal status for the patient has been established, that is node positive patients. Sometimes these tests are performed to reassure the patient; however, they have significant false positive rates and often cause considerable confusion.

Pathology features

Pathological examination is essential in confirming the diagnosis and complete excision of the lesion. It also provides useful prognostic information (Box 32.6). Breast cancer may be invasive or non-invasive (*in situ*) and may arise from the duct or the lobule. Most tumours arise from the terminal ductules, with mixed features of ductal and lobular components.

Box 32.6 Major prognostic determinants of breast cancer

- Axillary nodal status
- Tumour size
- Histological grade
- Hormone receptor status
- Others (e.g. vascular invasion, menopausal status, HER2 overexpression)

Ductal carcinoma *in situ* (DCIS)

This is a pre-invasive breast cancer and is characterised by proliferation of malignant breast epithelium that is confined to the duct system and has not yet invaded through the basement membrane. The entity is associated with microcalcification on mammography. Since the introduction of screening, ductal carcinoma *in situ* has risen from 2% of breast cancers to now around 20 to 25%. This condition is pre-malignant and often multicentric in the breast. A less severe form, atypical ductal hyperplasia, exists which has a four times increased risk for developing breast cancer.

Lobular carcinoma *in situ*

Lobular carcinoma *in situ* (LCIS) is asymptomatic and mammographically occult. It is often multifocal and bilateral and is an increased risk factor for breast cancer (relative risk $\times 10$) but it is not pre-malignant in itself. This is in contrast to DCIS. LCIS does not require radical excision but careful follow-up of the patient.

Less severe changes, called atypical lobular hyperplasia, carry a four times higher risk for developing breast cancer.

Invasive ductal carcinoma

'Invasive' ductal carcinoma refers to cancer which has invaded the basement membrane of the duct and invaded the surrounding tissue. The majority of these have no histological characteristic and are classified according to their differentiation as low-, intermediate- or high-grade.

Special types exist, including medullary, tubular, mucoid and inflammatory cancer, which are recognised as special behavioural types.

INFLAMMATORY CARCINOMA

This tumour has a very poor prognosis and is associated with tumour emboli in the dermal lymphatics and increased vascularity, producing a reddening of the skin.

Invasive lobular carcinoma

Classical lobular carcinoma has the histological feature of single files of malignant cells (Indian files). All the cells are similar and it is difficult to grade. It is often multifocal, meaning ductal carcinoma, and has a better prognosis.

Screen-detected breast cancer

Early detection of breast cancer by mammographic screening has been shown to improve survival. Whether this is truly cost-effective for the community is yet to be determined.

Early trials of breast cancer screening in Sweden, Holland, United States and Canada have confirmed the value of screening in early detection of tumours and, in particular, in increasing the rate of breast preservation. Screening has also detected an increased number of ductal carcinomas *in situ*, and this has improved the overall survival rate of breast cancer by including more favourable tumours in the treated group.

National Breast Screening programs have been established in many countries around the world, including Australia. In Australia, women aged 40 to 70 are screened at 2-year intervals. Patients have a two-view mammogram performed and if an abnormality is identified, they are recalled to an assessment clinic. The majority of abnormalities, greater than 90%, detected in the screening are benign and the patient is discharged. These assessment clinics are staffed by a multi-disciplinary team consisting of a surgeon, radiologist, radiographer, pathologist, breast care nurse and counsellor. To be effective, screening requires high participation rates and high-quality mammography and reporting.

Treatment of breast cancer

There has been a major change in the philosophy of the treatment of breast cancer because of an understanding of the systemic nature and heterogeneity of the disease. Surgery is now less radical and adjuvant therapy is now used more often.

The management of breast cancer involves a coordinated and multidisciplinary approach involving surgeons, radiologists, radiation oncologists, medical oncologists, pathologists and breast care nurses. Patient education, counselling and informed consent play an increasing role in the overall management.

Breast surgery

The principle of surgery in early breast cancer is to remove the tumour and have a clear margin of tissue around it. In many cases, particularly in screen-detected cancers, surgery will be curative.

Total mastectomy

This involves complete excision of the breast and nipple with preservation of the underlying pectoral muscles. Pectoralis fascia is usually removed as well. This is usually combined with excision of axillary lymph nodes. This used to be the standard therapy for all breast cancers but is now reserved for:

- a cancer that is large relative to the size of the breast
 - cancer that involves the nipple or overlying skin (breast conservation surgery might still be possible in selected cases)
 - multifocal disease or extensive intraductal carcinoma involving the surgical margins
 - prior breast irradiation
 - women who choose not to have breast conservation.
- Breast reconstruction is offered to most women after a total mastectomy.

Breast conservation surgery

This involves complete local excision of the primary breast tumour with a rim of macroscopically normal breast tissue on all sides. The overlying skin may be included, if necessary. The incision must be carefully planned and the specimen oriented.

Breast conservation surgery is routinely followed by radiotherapy. This reduced the local recurrence rate to between 1 and 2% per year compared with 0.5% per year following a total mastectomy. Breast conservation and radiotherapy has now become the standard procedure for patients with breast cancer and is performed on greater than 70% of all patients. Many trials have now confirmed that breast conservation is as safe as total mastectomy with regard to overall survival, and the cosmetic and psychological result is far superior. Breast

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conservation is however time-consuming and expensive, and radiotherapy is not easily available for all patients.

INDICATIONS

The indications for breast conservation surgery have gradually broadened. Now as long as you can achieve a reasonable cosmetic result and obtain clear margins on the tumour, breast conservation should be offered.

The patient does require counselling about the decision for breast conservation and the need for radiotherapy as well as the long-term swelling and discomfort which occurs in the breast.

CONTRAINDICATIONS

Relative contraindications include multicentric disease, a second breast cancer in the same breast or multifocal disease. Pregnant patients pose a particular problem, as do patients with connective tissue diseases, where radiotherapy may be contraindicated.

Axillary dissection

Axillary dissection aims to:

- remove metastatic disease within the axillary lymph nodes
- assess nodal status for prognosis
- assess nodal status to determine adjuvant systemic therapy.

Traditionally axillary surgery involves removal of all 3 levels of axillary nodes. More recently the lower axilla, in particular level 1 and level 2, nodes have been removed. More recently a new procedure called a sentinel node biopsy has been introduced where the specific lymph node draining the tumour is removed after being labelled as a radio isotope and marked with a blue dye.

This reduction in axillary surgery has been made possible because patients presenting with smaller tumours are less likely to metastasise in axillary lymph nodes. Whilst large tumours 50 mm or greater have a 60% node-positive rate, small tumours 10 mm or less have only an 8% lymph-node-positive rate.

In the future, it is likely that the sentinel node only will be removed and the axillary dissection will only be performed if the sentinel node is positive or if the axilla is clinically involved with tumour. If any axillary node is involved, then axillary dissection is required.

Box 32.7 Main risks for breast surgery

Mastectomy

- Breast haematoma
- Wound infection
- Seroma of the skin flap
- Psychological effects on body image and self esteem

Axillary dissection

- Seroma of axilla
- Pain and numbness of the upper medial aspect of the arm and the chest wall below the axilla as a result of division of the intercosto-brachial nerve
- Limitation of shoulder movement (especially abduction and elevation)
- Lymphoedema of the arm. The risk is about 5% but is increased substantially if radiation therapy is also given to a surgically dissected axilla

Currently the sentinel node procedure is being evaluated in a number of clinical trials around the world and its eventual role is being determined.

Complications of surgery

Breast surgery has few complications (Box 32.7). Lymphoedema of the arm requires special care because of a high risk for infection. Trauma to the arm should be avoided.

Breast reconstruction

Breast reconstruction can be performed both with patients having total mastectomy and breast preservation surgery.

In general, breast reconstruction is carried out either using the patient's own tissue and taking muscle flaps from the back or lower abdomen or by using prostheses made from a cohesive silicone gel. Currently, only about 10% of Australian women have breast reconstruction following mastectomy, but this incidence is slowly rising.

Radiotherapy

After breast conservation surgery

Breast irradiation is indicated following breast-conserving surgery after complete excision of the tumour and clear margins have been obtained.

A subgroup of women in whom breast irradiation can be omitted. There is no doubt that while breast irradiation reduces the risk of recurrence, it can probably be omitted in a subgroup of women, especially if they are elderly (older than 70), where the tumour is small (less than 10 mm), has low histologic grade and has abundant hormone receptors. Radiotherapy is not really available in a number of rural areas of Australia. This influences some women from rural areas to opt for a mastectomy, where breast conservation would have been a reasonable treatment.

After mastectomy

There is an increasing role for adjuvant radiotherapy following total mastectomy. In selected patients, particularly those with large tumours, large numbers of axillary lymph nodes are involved, the risk of local recurrence is significantly reduced. The value of radiotherapy in reducing overall survival however is more contentious, and further studies are awaited.

Complications

The complications following radiotherapy vary with the total dose, the number of fractions and the arrangement of the radiation fields. Recent improvements in delivery techniques have significantly reduced the complications.

Local effects which occur in the first 2 to 6 weeks include redness, soreness and ulceration of the skin. Discomfort and swelling of the breast occur early and often persist for a number of years and continue to improve over several years. It is not possible to breast feed from the radiated breast.

Cardiac damage particularly in patients with left sided tumours is reported however modern techniques should reduce this. Lymphoedema of the arm occurs in a small but significant number of patients following surgery and radiotherapy.

Adjuvant systemic therapy

The aim of this therapy is to eradicate micrometastases in order to ultimately improve survival. There is no evidence that adjuvant systemic therapy will maintain local control in women with a high risk of loco-regional relapse. Adjuvant systemic therapy with tamoxifen, with combination cytotoxic chemotherapy or, in premenopausal women, ovarian ablation, reduces the risk of recurrence and death after treatment for node-positive and node-negative breast cancer.

Combinations of various adjuvant systemic treatments may confer additional benefits and are currently being evaluated in clinical trials.

With systemic therapy, the risk for recurrence within 10 years of surgery with node-positive breast cancer will be reduced from 60 to 42%, and with node-negative breast cancer reduced from 25 to 15%.

Thus adjuvant systemic therapy is recommended for all women with involved axillary lymph nodes. Use of adjuvant systemic therapy in node-negative breast cancer is controversial and is considered if there are poor prognostic features, such as tumour size more than 2 cm, oestrogen and progesterone receptor negativity, poor differentiation or lymphovascular invasion. In contrast, a small screen-detected tubular cancer has such a good prognosis that adjuvant systemic therapy is unnecessary. The choice of the type of systemic therapy varies with the nature of the tumour, and the age, general health and preferences of the woman (Table 32.3). Hormonal manipulation with tamoxifen

Table 32.3 Schema for systemic adjuvant therapy

Menopausal status	Adjuvant therapy
Node-positive	
Premenopausal	Combination chemotherapy with doxorubicin and cyclophosphamide (CMF) (4 cycles). In receptor-positive women, ovarian ablation may be an alternative
Postmenopausal	Receptor-positive: tamoxifen for 5 years. In fit women with poor prognostic features, chemotherapy before tamoxifen may have additional benefit Receptor-negative: combination chemotherapy
Node-negative	
Premenopausal	Combination cytotoxic chemotherapy if there are poor prognostic features
Postmenopausal	Receptor-positive: tamoxifen for 5 years Receptor-negative: tamoxifen for 5 years. Note risk of endometrial cancer. If poor prognostic features are present, consider combination chemotherapy in younger patients

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or ovarian ablation is less valuable in women with oestrogen receptor (ER)-negative cancers.

Cytotoxic chemotherapy

Adjuvant cytotoxic chemotherapy gives a survival advantage for all node positive women 70 years old or younger. The value of the chemotherapy increases with decreasing age and increasing nodal involvement. In those negative women, adjuvant cytotoxic chemotherapy also conveys a survival advantage but of lesser proportions and is reserved for poor prognosis tumours, such as large high-grade tumours which lack estrogen receptor.

Commonly used regimens include adreomycin and cyclophosphamide, methotrexate and 5-fluorouracil and other combinations of these drugs for a period of approximately 6 months. The toxicities of cytotoxic chemotherapy, which include nausea, vomiting, lethargy, alopecia and early menopause, have been significantly reduced in recent years, by carefully planned drug regimens.

Adjuvant cytotoxic chemotherapy has become much more commonly accepted in early breast cancer.

Tamoxifen

Adjuvant tamoxifen is associated with an improvement of 6% at 10 years in both disease-free survival and overall survival. It is effective at all ages but most effective in women with ER-positive tumours. The value of tamoxifen adjuvant therapy in truly ER-negative tumours is uncertain but is probably minimal. Tamoxifen may also reduce the risk of cancer in the contralateral breast.

The optimal duration of treatment is 5 years, at a dose of 20 mg/day.

Side effects of tamoxifen include hot flushes, vaginal discharge and an increased incidence of endometrial cancer in postmenopausal women. This endometrial cancer risk is about 1 in 1000 women per year and is far outweighed by its beneficial effect. Annual gynaecological review is sometimes recommended, and abnormal vaginal bleeding should be promptly investigated.

Ovarian ablation

Ovarian ablation in premenopausal women is associated with an improvement of 10% at 15 years in both recurrence-free and overall survival. The beneficial

results are greater in women with positive oestrogen receptors and may confer additional effectiveness even in the presence of cytotoxic chemotherapy. Ovarian ablation is not indicated after menopause.

Ovarian ablation is achieved by surgical oophorectomy, ovarian irradiation or by using luteinising hormone-releasing hormone (LHRH) analogues such as goserelin. The LHRH agonists produce a medical oophorectomy that is usually reversible on cessation of therapy. Their use and efficacy in breast cancer is currently being studied. The safety of oestrogen replacement therapy in women who have had treatment for breast cancer is still not clear.

Counselling

The manner in which the diagnosis of breast cancer is communicated may have an important impact on the woman's ability to cope with the diagnosis and treatment. There are individual differences in women's views about and needs for information, options and support.

Women with breast cancer and their families will need further counselling to allow assimilation of information and should be given repeated opportunities to ask questions. Women with good emotional support from family and friends tend to adjust better to having breast cancer. Doctors, nurses, breast cancer support services and other allied health professionals are all important sources of support. Many specialist breast centres have a dedicated, well-trained breast counsellor to help coordinate the care with the doctor (the team approach).

Breast cancer support services are available in all states in Australia. They are staffed by trained volunteers who have had breast cancer or who have a broad perspective of the disease. Appropriate counselling has the potential to improve the quality of life.

Follow-up

With the multidisciplinary approach in the care for breast cancer, it is important that follow-up is coordinated so that patients are not subjected to an excessive number of visits. The rationale of follow-up is outlined in the following sections.

Detection of local recurrence

The local recurrence rate after breast conservation surgery and radiotherapy is 10–15% and less after mastectomy. Most recur within the first 3 years. Clinical examination of the skin flap, axilla and neck is performed after mastectomy, supplemented by mammography after breast conservation surgery.

Detection of distant recurrence

Intensive follow-up confers no survival benefit over a minimal follow-up regimen, because distant metastases are not curable.

Screening for a new breast primary

The risk of a new contralateral breast primary cancer is 1% per year. Annual mammography is recommended.

Management of treatment-associated toxicities

These include problems after axillary dissection (shoulder stiffness or lymphoedema), or with adjuvant chemotherapy (e.g. premature menopause) or anthracyclines (e.g. delayed cardiac toxicity). Gynaecological symptoms should be sought in women taking tamoxifen because of a relative risk of 2–5 times of endometrial cancer.

Psychosocial support

Anxiety and depression are common following diagnosis and treatment. Often there are difficulties with sexual image and adjustment.

Pregnancy and breast cancer

Women should be advised not to get pregnant during treatment for breast cancer because of the effect of the toxicities of treatment on the foetus and the additional physical demand of pregnancy on the women. The changing hormone levels with pregnancy may also induce progression of breast cancer. However, there is no evidence that pregnancy is harmful after completion of treatment.

Treatment of breast cancer in a pregnant woman is complex. The prognosis may be impaired because of

hormonal and immunological changes. Surgery is best performed during the second or third trimester. Radiotherapy and chemotherapy should, whenever possible, be avoided and deferred until the second trimester.

Metastatic breast cancer

Breast cancer tends to be slow growing and has a tendency to recur many years after apparently successful treatment. However, once metastasis has become evident it is associated with a poor outcome, with a median survival of 16 months. The most important prognostic factor in metastatic disease is disease-free interval after diagnosis of the primary breast cancer. Where recurrence is within 1 year, there is a much worse outcome than in those with recurrence more than 5 years after initial diagnosis.

Loco-regional (Fig. 32.7) or bony metastases also tend to have a better outcome than liver or cerebral metastases. The tumour burden, in terms of the extent of metastases, is also an important prognostic indicator.

Examination and investigation

A full clinical assessment and investigative staging are performed to determine the full extent of metastatic spread. This includes chest radiography, computed tomography (CT) scan of the chest and abdomen, and bone scan. A CT scan of the brain is performed only if there are relevant symptoms. A full assessment helps to determine prognosis and to plan appropriate therapy.



Fig. 32.7 A fungating local recurrence after mastectomy.

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The main aim of therapy is to palliate symptoms and demands a multidisciplinary approach. Counselling is particularly important. None of the plethora of new therapeutic options has reliably improved survival. Patients with tumours positive for oestrogen and progesterone receptors are more likely to respond to endocrine manipulation, so receptor status should be determined.

Treatment of metastases

Systemic therapy with endocrine manipulation or cytotoxic chemotherapy is the basis for treatment.

Endocrine therapy

The response to endocrine therapy is of the order of 50% in patients positive for oestrogen receptors.

Tamoxifen

The anti-oestrogen tamoxifen is the agent of choice in postmenopausal women and has side effects. Younger patients are more prone to hot flushes and weight gain with such treatment. Failure to respond is an indication to abandon endocrine therapy and to pursue treatment with cytotoxic chemotherapy.

Relapse after an initial response to tamoxifen can be treated with LHRH progestogens. In premenopausal women, such relapses may be treated with LHRH agonists such as Zoladex administered subcutaneously monthly.

Oophorectomy

An alternative is surgical oophorectomy, which may be performed by laparoscopic techniques with few complications or, if perimenopausal, by radiotherapy.

Progestogens

Progestogens are as active as tamoxifen as a first-line treatment but because of their side effects, particularly weight gain, fluid retention and nausea, they are more commonly used as the second-line treatment after failure of response to tamoxifen. However, the response rate to such second-line treatment is only half that seen with first-line treatment.

Non-steroidal aromatase inhibitors

Letrozole (Femara) or anastrozole (Arimidex) can markedly inhibit oestrogen synthesis within the breast cancer and is now used as second- or third-line treatment for advanced breast cancer after initial response to endocrine treatment. The treatment is fairly non-toxic.

Chemotherapy

The response rate to chemotherapy in previously untreated metastatic breast cancer is about 60%, but few obtain complete resolution of disease. The median duration of response is 1 year. Chemotherapy is the treatment of choice for visceral metastases, such as those in the liver and lung.

Combination therapy with cyclophosphamide, methotrexate and 5-fluorouracil is the most popular regimen. Replacement of methotrexate with adriamycin is associated with an increased response rate but with more side effects. Newer agents such as taxanes are evolving and are constantly being tested in clinical trials.

Radiotherapy

External beam radiotherapy has particular application for cerebral or painful bony metastases. Systemic agents often fail to cross the blood-brain barrier to treat cerebral metastases effectively, and radiotherapy is the treatment of choice. Rapid pain relief is usual after treatment with radiotherapy.

Surgery

Surgery has a limited role and is reserved for the treatment of troublesome metastases, such as excision of a symptomatic local recurrent skin nodule or full surgical clearance of an axillary relapse where no previous surgery has been undertaken, surgical fixation of pathological fractures, and pleurodesis for treatment of persistent pleural effusion. Surgery has a small role in the treatment of acute spinal cord compression.

Supportive treatment

Hypercalcaemia may complicate bony metastases and requires treatment with rehydration, forced diuresis with frusemide and, sometimes, use of steroids to

enhance excretion of calcium in the urine. Resistant cases require treatment with the diphosphonates or mithramycin.

Adjuvant pain control with adequate analgesia, and sometimes support braces, can be used for a painful bony metastasis.

Patients with metastatic breast cancer often are anaemic, malnourished and suffer from complications of therapy. These co-morbid factors must be corrected.

Prevention of breast cancer

Genetic factors account for breast cancer in less than 10% of cases. Most other breast cancers are sporadic. Until the causation of breast cancer is understood, attempts at its prevention are somewhat ineffective.

Chemoprevention with tamoxifen for 'high-risk' subjects is currently on trial. However, there are concerns about the risk of endometrial cancer following long-term use of tamoxifen.

Prophylactic mastectomy with or without breast reconstruction is occasionally performed for very-high-risk individuals who demand it.

MCQs

Select the single correct answer to each question.

- 1 A 48-year-old woman presents with thick greenish nipple discharge from both breasts. There is no palpable breast lump, although both nipples are slightly retracted. The patient does not take any medication. Mammogram and ultrasound do not show any evidence of cancer. The most likely diagnosis is:
 - a galactorrhoea
 - b duct papilloma
 - c mammary duct ectasia
 - d fibroadenoma
 - e lobular carcinoma *in situ*
- 2 A 42-year-old woman presents with a 2-cm breast lump, detected 2 weeks ago. The lump is discrete but soft. There is no past history of breast disease. The initial management includes:
 - a repeat clinical examination in 4 weeks' time to detect any changes
 - b bilateral mammogram with or without breast ultrasound
 - c fine needle aspiration cytology of the lump as breast imaging is unnecessary in this age group
 - d excision biopsy
 - e unilateral mammogram and ultrasound of the breast with the lump
- 3 Mammography screening programmes:
 - a reduce mortality of breast cancer, especially in women aged between 40 and 50 years
 - b detect smaller cancers with a lower incidence of axillary nodal metastases than in the unscreened population
 - c show a higher incidence of lobular but not ductal carcinoma *in situ*
 - d include quality assurance targets of attendance rates higher than 50% and recall rates lower than 50%
 - e involve radiologists as the primary personnel responsible for diagnosis and management
- 4 A 39-year-old woman has a 5-cm, grade III breast cancer. Twelve of 16 lymph nodes contain metastases. The oestrogen receptor is negative, although the progesterone receptor is positive. There is no evidence of systemic metastases on chest X-ray and bone scan. Following a total mastectomy and axillary clearance, the MOST likely follow-up management would be:
 - a regular review, with reservation of chemotherapy for recurrent disease
 - b adjuvant tamoxifen
 - c adjuvant chemotherapy
 - d adjuvant radiotherapy
 - e oophorectomy
- 5 Correct statement concerning ductal carcinoma *in situ* (DCIS):
 - a it is associated with microcalcification on mammography
 - b DCIS is less commonly found in women undergoing routine mammographic screening
 - c comedo subtype is rarely multicentric
 - d there is a high risk for lymph node metastasis with the papillary subtype
 - e the risk for progression to invasive cancer is smaller than with lobular carcinoma *in situ*

