Breast lumps and cancer

B reast lumps are a common presenting symptom in general practice. As a GP it is important to know how to manage them. Breast lumps can be a sign of breast cancer but 85% have innocent explanations. However, women presenting with a breast lump often assume that they have breast cancer and this can cause a great deal of anxiety. This article aims to overview the common causes of breast lumps, their assessment and management.

The GP Curriculum and breast lumps

Statement 10.1 of the GP Curriculum (Women's Health) requires GPs to demonstrate knowledge of women's health problems, conditions and diseases. Management of breast lumps and nipple discharge is specifically mentioned in the required knowledge base. In particular GPs should have a low threshold for referral of breast lumps.

Breast development

At puberty, the female breast develops under the influence of the sex hormones oestrogen, progesterone and others including growth hormone, cortisol and insulin. This complex process typically begins between ages 8 and 14 and spans about 4–6 years.

The breast contains mostly fatty tissue thus is related to body fat, and also connective tissue and glands that following pregnancy, will produce milk. The milk is collected in the ducts and transported to 15–25 openings through the nipple. Asymmetrical breast growth during adolescence is the rule rather than the exception. Reassurance is given that the asymmetry usually evens out by the time of full maturation. Mammary hypertrophy can be a distressing symptom, but because growth and development continues for a long time, surgical intervention, if contemplated, should be delayed until the breasts are fully mature.

During the menstrual cycle, the breast is smallest on days 4– 7, and then begins to enlarge, under the influence of estrogen and later progesterone and prolactin. Maximum breast size occurs just prior to the onset of menses. The breast is not round, but has a 'tail' of breast tissue extending up into the axilla. This is clinically significant because abnormalities can arise there just as they can in other areas of the breast. During breast examinations, this area should be palpated.

The breast is divided into quadrants to describe and compare clinical findings more easily. The upper outer quadrant is the

area of greatest mass of breast tissue. It is also the area in which about half of all breast cancers will develop.

Imaging

Mammography is most often used as a screening technique for breast cancer. Breast examinations detect most cancer, but will miss some, particularly the very early cancers that are too small to feel.

Mammograms are good at detecting some of these early cancers, but will miss others. This means that breast examinations and mammograms are complementary, each detecting problems the other might miss. Mammography looks for radio-opaque densities, microcalcifications and disruption of the normal breast architecture (parenchymal asymmetry). For women without strong risk factors for breast cancer, screening mammography is performed every 3 years between ages 50 and 70. In 2009, extension of the NHSBSP to start from age 47 and continue to 73 will begin. Those women over 73 can request mammography via their GP every 3 years.

Ultrasound

While mammography is very good at detecting radio-opaque changes, such as calcifications or architectural distortion from a mass effect, ultrasound, in contrast, is very good at distinguishing cystic from solid masses (Fig. 1). This is probably most useful following mammographic findings of a benign-appearing, non-palpable density, although it can also be used with palpable masses.

Pregnancy changes

During pregnancy, a number of changes occur over time which prepare the breast for lactation. Early in the first trimester, the breasts and nipples become tender. The tenderness persists until the end of the first trimester, at which time the tenderness disappears. By the end of the first trimester, enlargement of

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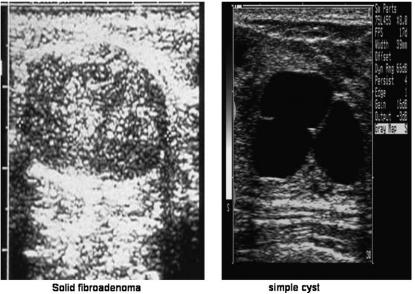


Figure 1. Ultrasound.

simple cyst

the breast and nipple is noticeable. By the third trimester, the breast and nipple have experienced further enlargement and the Montgomery's glands around the periphery of the areola become more pronounced. The nipples gradually darken, becoming dark brown or black by full term.

Puerperal mastitis

During lactation, breast infections (mastitis) are common. They are usually caused by common skin bacteria (particularly staphylococcus) being introduced into the ductal system through cracked nipples and the inoculation by the newborn suckling. Clinically, these patients present with a rapid onset of unilateral breast tenderness, redness, fever and sometimes a thickening of mass (Fig. 2). Breast infections can be very aggressive with high fevers developing quickly. Immediate treatment is important to keep an otherwise simple mastitis from developing an abscess, requiring surgical drainage.

Standard treatments include Co-fluampicillin 500 mg p.o. q.d.s. for seven days or Co-amoxiclav 375 mg t.d.s. for seven days. If allergic to penicillin, then erythromycin 500 mg p.o. q.d.s for one week. Continue to breast feed from the affected breast as drainage is important. Recurrent infections are common.

If there are signs of systemic infection, for example tachycardia, high fever, lethargy, etc., then intravenous antibiotics may be required. Most patients, however, manage with oral treatment.

Nipple discharge

This is a common finding in most women who have given birth. The only worrying discharge is that which contains bright red blood or single-duct serous discharge.



Figure 2. Mastitis. Post-partum mastitis: the breast is warm, tender and oedematous.

White, yellow, green and brown discharge can be seen in many benign conditions such as duct ectasia and is usually physiological.

Blood stained nipple discharge or single duct serous discharge may represent serious breast disease and needs urgent referral. However, the commonest cause of blood stained discharge is a benign papilloma, but breast cancer needs to be excluded.

Lumps of the breast

The likely cause of a breast lump varies according to the age of a woman (Fig. 3). A simple way to classify breast lumps is the ABC of lumps

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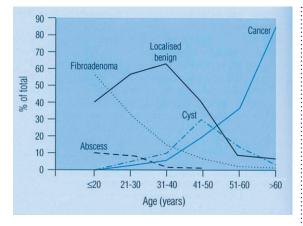


Figure 3. Age related incidence of a lump in the breast. ABC of Breast Disease 2nd edition. Edited by Mike Dixon. BMJ books. Reproduced with permission from Blackwell Publishing.

- A: Abscess and fibroAdenoma
- B: Benign fibrocystic change (sclerosis and adenosis)
- C: Cysts and Cancer

Abscess

The first stage in the development of an abscess is inflammation of the breast (mastitis) and has the following symptoms:

- painful localized swelling of the affected breast, localized redness
- tenderness and the breast feels very hot. Another sign of infection is flu-like symptoms, including aches and pains, headache and a raised temperature. The infection occurs in the parenchymal (fatty) tissue of the breast, causing swelling just outside the milk ducts. This swelling presses on the milk ducts and the result is pain and swelling of the infected breast (Fig. 4).

Management: 'If there is pus, let it out'. Topical anaesthesia such as EMLA cream can be applied, and needle aspiration (19G) or mini incision and drainage, with antibiotics is the treatment of choice. If there is a large amount of necrotic skin, then excision under anaesthesia is required. Most patients should be able to avoid hospitalization.

Fibroadenoma

These common, benign, solid, round or oval breast lumps are most common among women aged 15–35. They are rubbery in consistency, mobile and non-tender. They rarely grow larger than 2–3 cm.

The diagnosis is usually suspected on physical examination and confirmed with ultrasound and fine needle aspiration or core biopsy. When found in teenagers, they are often simply watched, but may be removed if it starts to enlarge. If they are over 4 cm in size or newly diagnosed in the over 40s, then excision is usually recommended to exclude malignancy.



Figure 4. Drainage of a superficial breast abscess under local anaesthetic.

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Benign fibrocystic change

Fibroadenosis or fibrocystic disease is the most common cause of breast lumps in women of reproductive age. It should be regarded as normal rather than a disease.

The peak incidence is between 35 and 50 years of age. It is rare before 25 years. The term embraces a spectrum of histologic changes and may encompass many patients who have cystic lesions detected clinically or sclerotic breast lesions detected on mammography as discussed elsewhere. Histologically, it is characterized by overgrowth of both fibrous stroma and epithelial elements, that is ducts and lobules, in differing proportions. These changes may be considered as aberrations of normal breast development and involution and not part of a disease process. The condition may be due to a disordered or imbalanced response to endogenous sex hormones. Typically, patients present with one or more lumps in the breast which may be painful and, frequently, bilateral. The size and pain usually vary with the menstrual cycle. One or more of these elements may be absent.

Patients with diffuse, bilateral nodularity can be reassured and managed symptomatically. Solitary asymmetric nodularity should be triple assessed with imaging and biopsy.

Breast cyst

Breast cysts present as smooth, well-defined masses which occasionally are tender if tense. They will often disappear over the course of the menstrual cycle, but those that persist will need further evaluation. They tender to occur in the perimenopausal women aged 45–55. Ultrasound confirms the diagnosis and cyst aspiration is attempted, using a small green needle and syringe. After aspiration of the cyst, most physicians discard the cyst fluid unless it is bloody as cyst fluid cytologic examination is felt to be of little value. Recurrent cysts in the same location may need to be excised, as below.

Breast cancer

Breast cancer is one of the most common cancers in the UK with more than 44000 people diagnosed each year. Breast cancer represents about 30% of all cancers in women. In broad terms, treatment is successful in 75–80% of patients, controlling or eliminating the disease. In about one of four, the cancer proves fatal.

The risk of developing breast cancer increases steadily with increasing age. It is rare among women under age 25 but affects nearly one in nine of those women reaching age 90. Although women are predominantly affected by the disease, it is estimated that more than 300 men per year are diagnosed with breast cancer. Breast cancer rates have shown a rising trend over recent years. The increase in the reported incidence of the disease may be the result of increased detection through the NHS screening programme, increasing body mass index, earlier menarche, late menopause, the tendency for women to delay having children, the use of hormone replacement therapy and other lifestyle factors such as alcohol consumption and reduced exercise.

However, more effective treatments and earlier detection have caused a fall in breast cancer mortality rates, with 10-year survival statistics for people diagnosed with breast cancer estimated at 80%, compared to 52% for women diagnosed between 1971 and 1975. Of the risk factors for breast cancer, approximately 5–10% of breast cancers are thought to be traced to a family history of breast disease and the most common implicated genes are BRCA1 (**BR**east **CA**ncer 1), BRCA2 and P53. Female sex and old age are the most significant risk factors. More than 80% of breast cancers occur in women over the age of 50 and the risk steadily increases with age. Earlier breast screening is available for high-risk patients.

Risk factors

E High risks

- Female gender, old age, BRCA1, 2 genes (family history)
- Previous exposure to radiation. (Hodgkin's lymphoma, etc.)
- A history of benign breast conditions with atypia, for example ADH and lobular carcinoma in situ (LCIS)

Moderate

- Obesity, high alcohol intake
- Hormone replacement therapy after the age of 50 years for more than 5 years

Low risk

- Nulliparity, early menarche or late menopause
- Use of the oral contraceptive

NICE has published referral guidelines for women with suspected breast cancer (Fig. 5). The gold standard for diagnosing breast cancer is 'triple assessment' consisting of 'clinical breast examination, breast imaging and needle biopsy'.

Needle biopsy can be carried out using fine needle aspiration to obtain a sample of cells or core biopsy to obtain a tissue sample. Core biopsy will reveal more about the nature of the tissue and, in most cases, means that women can avoid the need for an open surgical biopsy. The results of a core biopsy will usually take 3–5 working days and will demonstrate the type of cancer, the grade of the cancer and hormone receptor expression.

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Figure 5. NICE guidelines for urgent referral.

National Institute for Health and Clinical Excellence (2005) CG027 Referral guidelines for suspected cancer. London: NICE. Available from www.nice.org.uk/CG027. Reproduced with permission.

Histologic tumour grade (sometimes called the 'Bloom-Richardson grade') is based on the arrangement of the cells in relation to each other: whether they form tubules, how closely they resemble normal breast cells (nuclear grade) and how many cancer cells are in the process of dividing (mitotic count). This system of grading is used for invasive cancers but not for *in situ* cancers.

Grade 1 (well-differentiated) cancers have relatively normallooking cells that do not appear to be growing rapidly and are arranged in small tubules.

Grade 2 (moderately differentiated) cancers have features between grades 1 and 3.

Grade 3 (poorly differentiated) cancers, the highest grade, lack normal features and tend to grow and spread more aggressively.

Common types of breast cancer

The most common types of breast cancer originate in either the ducts (ductal carcinoma) or lobules (lobular carcinoma). The point of origin is determined by the microscopic appearance of the cancer cells from a biopsy.

In situ breast cancer

In situ breast cancer refers to a type of cancer in which the breast cancer cells have remained contained within their place of origin—they have not invaded breast tissue around the duct or lobule.

Ductal carcinoma in situ

Ductal carcinoma *in situ* (DCIS) refers to abnormal cells in the lining of a duct that have not invaded the surrounding breast tissue. This is early-stage breast cancer. Some experts consider DCIS a 'precancerous' condition. Almost all women with DCIS can be successfully treated, and no evidence suggests that DCIS affects a woman's lifespan. However, if left untreated, DCIS may eventually develop into invasive breast cancer.

Lobular carcinoma in situ

LCIS means that abnormal cells are contained within a lobule of your breast, but they have not invaded the surrounding breast tissue. Whether LCIS is an early form of breast cancer or is just a marker for the future development of cancer remains a point of controversy in the medical community. However, experts do agree that if you have LCIS, you are at an increased risk of developing breast cancer in either breast in the future. In the breast that had the LCIS, you are more likely to develop invasive lobular breast cancer. If cancer develops in the other breast, it is equally likely that it could be invasive lobular or invasive ductal carcinoma (IDC).

Invasive breast cancer

Invasive (infiltrating) breast cancers are those that break free of where they originate, invading the surrounding

tissues that support the ducts and lobules of your breast. The cancer cells can travel to other parts of your body, such as the lymph nodes.

Invasive ductal carcinoma

Invasive ductal carcinoma (IDC) accounts for the majority of invasive breast cancers (80%). If you have IDC, cancer cells form in the lining of your milk duct, break free of the ductal wall and invade surrounding breast tissue. The cancer cells may remain localized—staying near the site of origin—or they can metastasize, carried by the lymphatic system.

Invasive lobular carcinoma

Although less common than IDC, invasive lobular carcinoma (ILC) accounts for 5-10% of breast cancer, and acts in a similar manner. Invasive lobular carcinoma (ILC) starts in the milk-producing lobule and invades the surrounding breast tissue. It can also spread to more distant parts. With ILC you may perceive only a general thickening—or a sensation that the breast tissue feels different. ILC can be harder to detect by touch, and it is also less likely to appear on a mammogram.

Less common types of breast cancer

Not all types of breast cancer originate in a duct or lobule. Less common types of breast cancer include:

Inflammatory breast cancer

This is a rare but aggressive type of breast cancer. The skin on the breast becomes red and swollen and may take on a thickened, pitted appearance—similar to an orange peel. This results from cancer cells blocking lymph vessels in the skin of the breast.

Medullary carcinoma

This is a specific type of invasive breast cancer in which the tumour's borders are clearly defined, the cancer cells are large, and immune system cells are present around the border of the tumour.

Mucinous (colloid) carcinoma

With this type of invasive breast cancer, the cancer cells produce mucus and grow into a jelly-like tumour. The prognosis for mucinous carcinoma is better than for other, more common types of invasive breast cancer.

Paget's disease of the breast

This rare type of breast cancer affects the nipple and occasionally the areola. It starts in the duct, as either an *in situ* or invasive cancer. If associated with carcinoma *in situ*, the prognosis is very good.

Tubular carcinoma

This rare type of breast cancer gets its name from the appearance of the cancer cells under a microscope. Though it is an invasive breast cancer, the outlook is more favorable than it is for IDC or ILC.

Phyllodes tumour

A large, bulky tumour may be an indication of a phyllodes tumour. Phyllodes tumours develop in the connective tissue of the breast rather than in a duct or lobule. The outlook for a phyllodes tumour is variable, most are benign, but can reoccur locally.

Metaplastic carcinoma

Metaplastic carcinoma represents less than 1% of all newly diagnosed breast cancers. This lesion tends to remain localized and contains several different types of cells that are not typically seen in other forms of breast cancer. Prognosis and treatment is the same as for IDC.

Surgery

Surgery is the mainstay of breast cancer treatment and takes the form of either a wide local excision removing just the tumour and a rim of healthy normal tissue or a full mastectomy. Indications for mastectomy include tumours over 4 cm or a small breast, multicentric or multifocal tumours and patient choice. Patients requiring mastectomy should be offered reconstruction either immediate or delayed.

Any patient having a wide local excision will go on to have breast radiotherapy. Radiotherapy is not usually required after mastectomy, except in patients with large tumours associated with lymphovascular invasion and lymph node involvement.

Axillary staging

Axillary staging is performed in all patients with invasive disease. This is the best prognostic indicator of survival and often dictates adjuvant treatment.

Sentinel node biopsy removing only the nearest one or two lymph nodes is now the standard of care, with axillary clearance being reserved for those with pathological node involvement on ultrasound of the axilla or whose sentinel nodes showed disease involvement.

Adjuvant therapy

After surgery, all patients are discussed at the multidisciplinary team meeting and adjuvant treatments planned.

Chemotherapy

Chemotherapy is given to most patients who have involved lymph nodes or grade three tumours. Hormone receptor status is assessed on the tumour and if oestrogen receptor negative, again chemotherapy will be recommended.

Hormone therapy

Oestrogen receptor-positive patients will be offered adjuvant hormone therapy with tamoxifen or an aromatase inhibitor (AI) such as anastrozole, letrozole or exemestane.

Tamoxifen is the only effective drug in premenopausal women, whose oestrogen comes from the ovary. In postmenopausal women, oestrogen is manufactured in the muscle, liver and breast via the aromatase enzyme. Als block

this enzyme and are therefore effective only in postmenopausal women.

Five years of hormone therapy is given as standard. This may be 5 years of tamoxifen or 5 years of an AI. Alternatively, a switching strategy may be used where after 2–3 years of tamoxifen, 5 years of an aromatase inhibitor can be given in postmenopausal women. This lengthens the duration of treatment which may have an advantage over 5 years of tamoxifen. The ideal hormone treatment regime is still subject to trials and debate but should include an aromatase inhibitor in the postmenopausal women. The author's preference is 5 years of an aromatase inhibitor.

Side effects of hormone treatment include hot flushes, arthralgia, occasional pv bleeding and rarely stroke or deep vein thrombosis. Tamoxifen is associated with more vaginal (PV) bleeding and stroke, whereas aromatase inhibitors cause more joint pains and bone loss. A DEXA scan is recommended before starting aromatase inhibitors.

Herceptin

The HER2 receptor is another growth factor receptor overexpressed in about 25% of breast cancers. It is associated with a poorer prognosis. Patients undergoing chemotherapy who are HER2 positive will be offered a year's treatment of monthly intravenous herceptin which greatly improves outcome and survival in this group.

Follow up after treatment

All patients should receive annual mammographic follow-up for 10 years and then return to the national breast screening programme.

Breast cancer and pregnancy

The treatment of women who are pregnant at the time of diagnosis is similar to the non-pregnant women. Mammography is safe as it is of low radiation. Chemotherapy can be given during the second trimester but radiotherapy can only be used after delivery. There is no evidence to suggest that outcome is improved by termination of the pregnancy and this should not be encouraged.

Key points

- Most nipple discharge is physiological except blood stained
- Most lumps are benign
- Unilateral asymmetric lumps need triple assessment
- Cancer usually presents as a painless lump in the aged
- Surgery is the mainstay of treatment
- After breast-preserving surgery, radiotherapy is given
- Chemotherapy for node-positive disease
- Hormone therapy for oestrogen receptor-positive disease

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