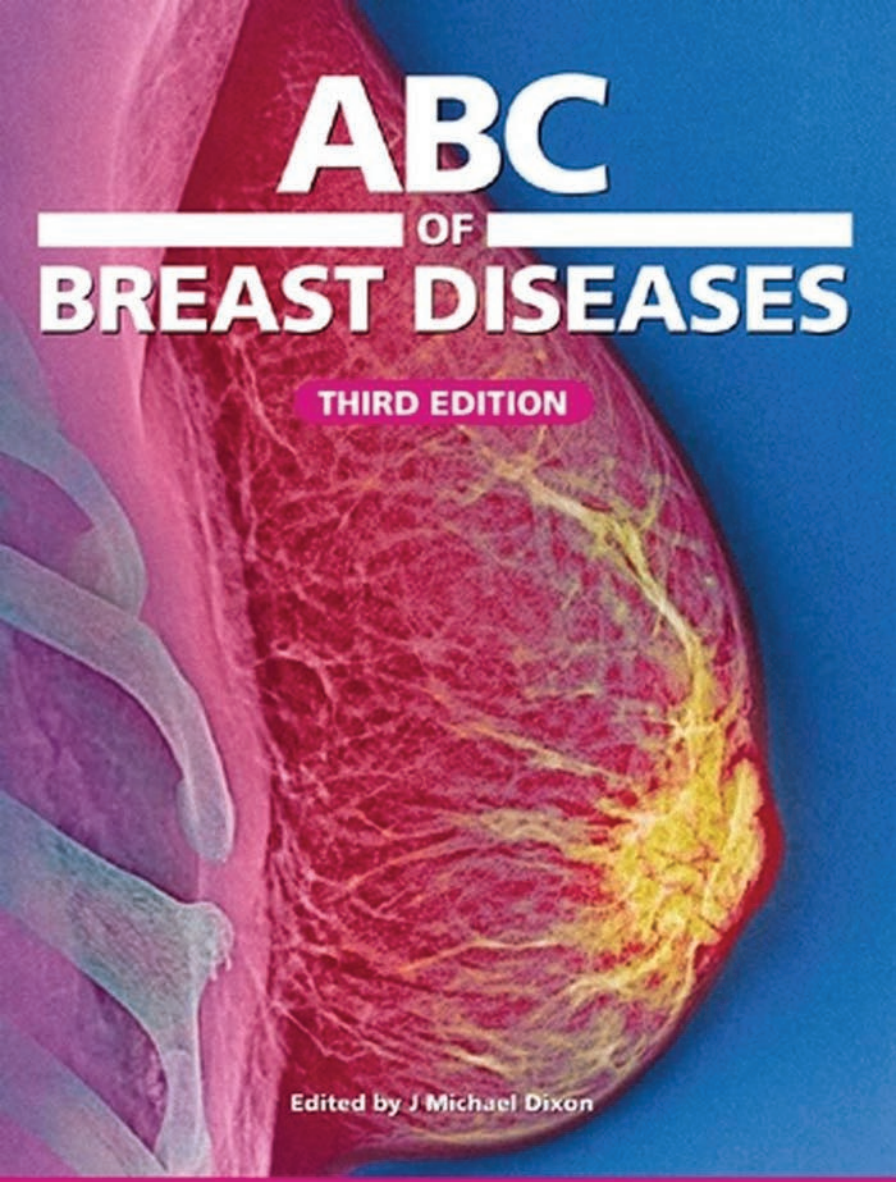
# ABC OF BREAST DISEASES

THIRD EDITION



Edited by J Michael Dixon

Blackwell Publishing BMJ

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Third Edition

Edited by

J MICHAEL DIXON

*Consultant surgeon and senior lecturer in surgery, Edinburgh Breast Unit, Western General Hospital, Edinburgh*

BMJ Books

Blackwell Publishing

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Blackwell Publishing, Inc., 350 Main Street, Malden, Massachusetts 02148-5020, USA
Blackwell Publishing Ltd, 9600 Garsington Road, Oxford OX4 2DQ, UK
Blackwell Publishing Asia Pty Ltd, 550 Swanston Street, Carlton, Victoria 3053, Australia



First published 1995
Second edition 2000
Third edition 2006

Library of Congress Cataloging-in-Publication Data
ABC of breast diseases/edited by J. Michael Dixon.—3rd ed.
p. ; cm.
Includes bibliographical references and index.
ISBN-13: 978-0-7279-1828-4
ISBN-10: 0-7279-1828-1
1. Breast—Diseases—Treatment. 2. Breast—Cancer—Treatment. I. Dixon, J. M. (J. Michael)
[DNLM: 1. Breast Diseases. 2. Breast Neoplasms. WP 840 A134 2006]
RG491A232 2006
616.99′449—dc22

2005020705

ISBN-13: 978 0 7279 1828 4
ISBN-10: 0 7279 1828 1

A catalogue record for this title is available from the British Library

The cover shows a coloured mammogram of an abscess of the areola of a woman's breast seen from the side. With permission from CRNI/Science Photo Library

Set in 9/11 pt New Baskerville by Newgen Imaging Systems (P) Ltd, Chennai, India
Printed and bound in India by Replika Press Pvt. Ltd, Harayana

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# Preface

The aim of the third edition of the *ABC of Breast Diseases* is to provide an up to date, concise, well illustrated, and evidence based text that will meet the dual challenges of managing the increasing numbers of women who attend breast clinics and the increasing numbers of women who are diagnosed with breast cancer. This edition contains many new illustrations and diagrams. The chapters on screening, adjuvant therapy, clinical trials, and prognostic factors have been completely rewritten, and all other chapters have been extensively revised. The topics of adjuvant therapy and metastatic breast cancer have been extended to cover the explosion of results gained from the many multinational breast cancer trials which have reported since the last edition of this ABC was published. New authors have added their work to that of those who have already contributed to the success of the book. Thanks to Jan Mauritzen my PA who has coordinated the many revisions, to Eleanor Lines. Commissioning Editor, ABC series, to Sally Carter, Development Editor, BMJ editorial and Nick Morgan, Senior Development Editor at Blackwell Publishing who converted the authors' words and pictures into the book that is before you. Such a comprehensive review has been time consuming. I continue to be grateful for the support of my colleagues in the Edinburgh Breast Unit, and to my family Pam, Oliver, and Jonathan. I also thank the many patients who agreed to be photographed for this book, but more importantly, for the inspiration they provide in how they cope, not only with their disease but with all that we do to them.

The care provided for patients with breast cancer is better coordinated and more truly multidisciplinary than that for any other cancer. This is a testimony to those multidisciplinary teams that treat breast cancer, and to the many groups and individual women who have demanded access to good quality care for all. As a clinician I hope that the knowledge and understanding gained through research will continue to result in improved treatments. Many challenges remain in the field of breast diseases, and there is much we do not know. This book is our effort to inform you of everything that we think we know and understand about breast diseases and its management.

J Michael Dixon
*Edinburgh*
*2005*

# 1 Symptoms, assessment, and guidelines for referral

JM Dixon, J Thomas

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 that require hospital referral, and breast problems constitute up to a quarter of all women in the general surgical workload.

**When a patient presents with a breast problem the basic question for the general practitioner is, "Is there a chance that cancer is present, and, if not, can I manage these symptoms myself?"**

For patients presenting with a breast lump, the general practitioner should determine whether the lump is discrete or if there is nodularity whether this is asymmetrical or is part of generalised nodularity. A discrete lump stands out from the adjoining breast tissue, has definable borders, and is measurable. Localised nodularity is more ill defined, often bilateral, and tends to fluctuate with the menstrual cycle. About 10% of all breast cancers present as asymmetrical nodularity rather than a discrete mass. When the patient is sure there is a localised lump or lumpiness, a single normal clinical examination by a general practitioner is not enough to exclude underlying disease. Reassessment after menstruation or hospital referral should be considered in all such women.

Bathsheba bathing by Rembrandt. Much discussion surrounds the shadowing on her left breast and if this represents an underlying malignancy (with permission of the Bridgeman Art Library)

### Prevalence (%) of presenting symptoms in patients attending a breast clinic

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

### Conditions that require hospital referral

#### Lump

- Any new discrete lump
- New lump in pre-existing nodularity
- Asymmetrical nodularity in a postmenopausal woman
- Asymmetric nodularity in a premenopausal woman that persists at review after menstruation
- Abscess or breast inflammation that does not settle after one course of antibiotics
- Cyst persistently refilling or recurrent cyst (if the patient has recurrent multiple cysts and the GP has the necessary skills, then aspiration is acceptable)
- Palpable or enlarged axillary mass including an enlarged axillary lymph node

#### Pain

- If pain is 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, and common drugs
- Unilateral persistent pain in postmenopausal women

#### Nipple discharge

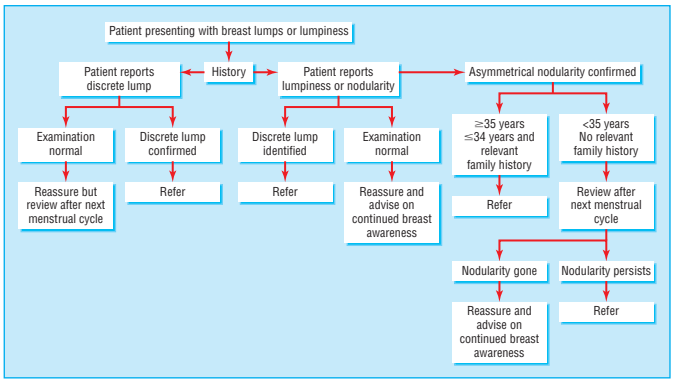
- All women aged ≥50
- Women aged <50 with:
  Bloodstained discharge
  Spontaneous single duct discharge
  Bilateral discharge sufficient to stain clothes

#### 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 (refer to a family cancer genetics clinic where possible)




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

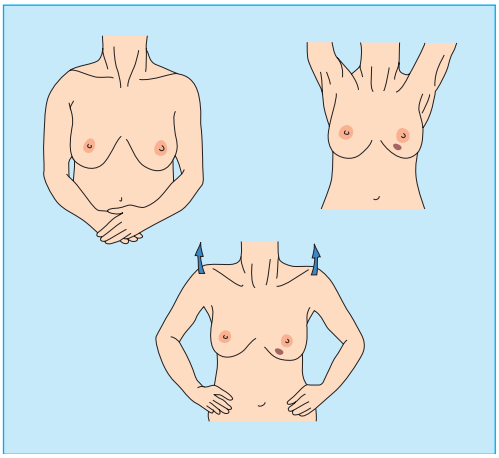
### Patients who can be managed, at least initially, by their GP include

- Young women with tender, nodular breasts or older women with symmetrical nodularity, provided that they have no localised abnormality
- Young women with asymmetrical localised nodularity; these women require assessment after their next menstrual cycle, 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

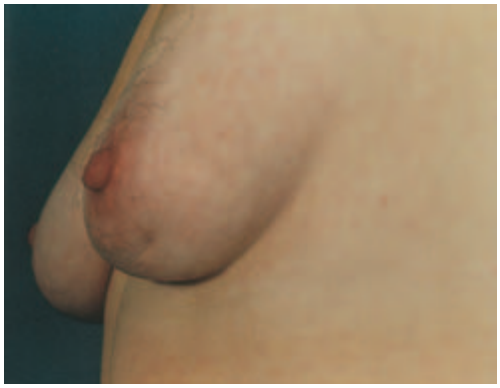
# Assessment of symptoms

**Patient's history**
Details of risk factors, including family history and current medication, should be obtained and recorded. Duration of a symptom can be helpful as cancers usually grow slowly but cysts may appear overnight.

**Clinical examination**
Inspection should take place in a good light with the patient's arms by her side, above her head, then pressing on her hips. Skin dimpling or a change in contour is present in up to a quarter of symptomatic patients with breast cancer. Although usually associated with an underlying malignancy, skin dimpling can follow surgery or trauma, be associated with benign conditions, or occur as part of breast involution.

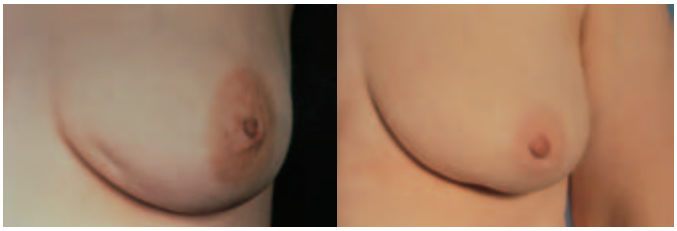


Positions for breast inspection. Skin dimpling in lower part of breast evident only when arms are elevated or pectoral muscles contracted

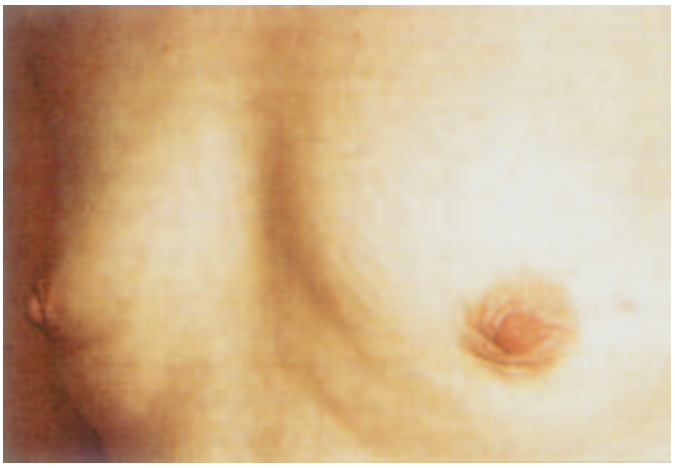


Skin dimpling after previous breast surgery

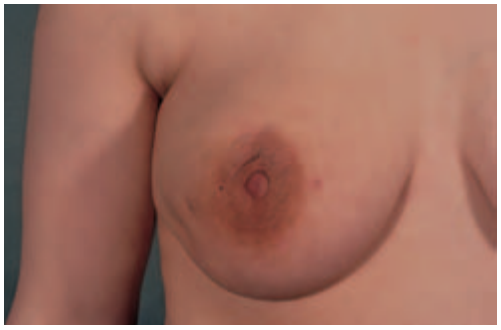
Breast palpation is performed with the patient lying flat with her arms above her head, and all the breast tissue is examined using the most sensitive part of the hand, the fingertips. It is essential for the woman to have her hands under her head to spread the breast out over the chest wall because it reduces the depth of breast tissue between your hands 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, texture, and any deep fixation 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 diagram of any breast abnormalities, including dimensions and the exact position, should be recorded in the medical notes.



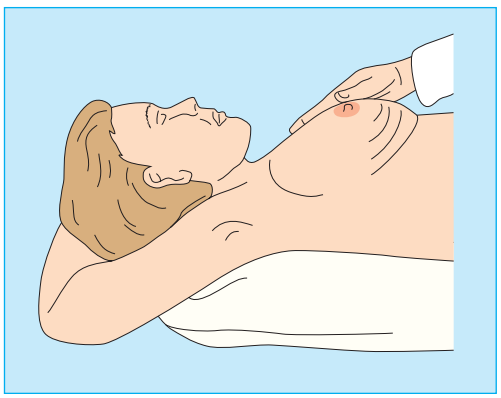
Skin dimpling (left) and change in breast contour (right) associated with underlying breast carcinoma



Skin dimpling visible in both breasts due to breast involution



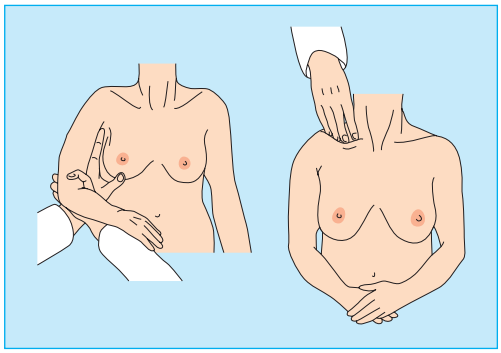
Skin dimpling associated with breast infection



Breast palpation

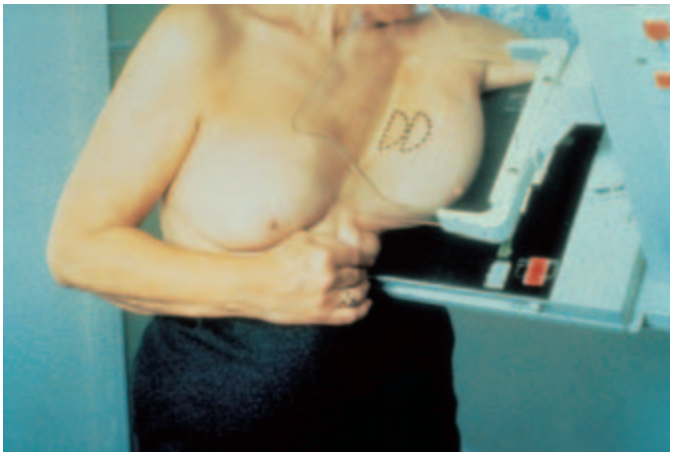
Patients with breast pain should also be examined with the woman lying on each side and the underlying chest wall palpated for areas of tenderness. Much of so called breast pain emanates from the underlying chest wall.

**Assessment of axillary nodes**
Once both breasts have been palpated the nodal areas in the axillary and supraclavicular regions are checked. Clinical assessment of axillary nodes is often inaccurate: palpable nodes can be identified in up to 30% of patients with no clinically significant breast or other disease, and up to 40% of patients with breast cancer who have clinically normal axillary nodes actually have axillary nodal metastases.

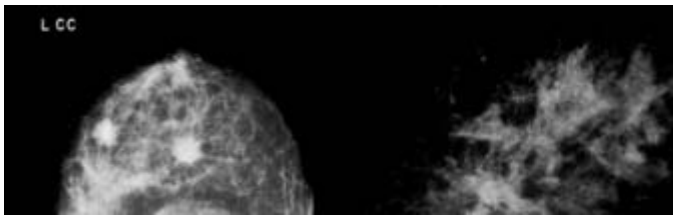


Assessment of regional nodes

**Mammography**
Mammography requires compression of the breast between two plates and is uncomfortable. Two views—oblique and craniocaudal—are usually obtained. With modern film screens a dose of less than 1.5 mGy is standard. Mammography allows detection of mass lesions, areas of parenchymal distortion, and microcalcifications. Breasts are relatively radiodense, so in younger women aged <35, mammography is of more limited value and should not be performed in younger women unless there is suspicion on clinical examination or on cytology or core biopsy that the patient has a cancer. All patients with breast cancer proved by cytology or biopsy, regardless of age, should undergo mammography before surgery for assessment of the extent of disease.

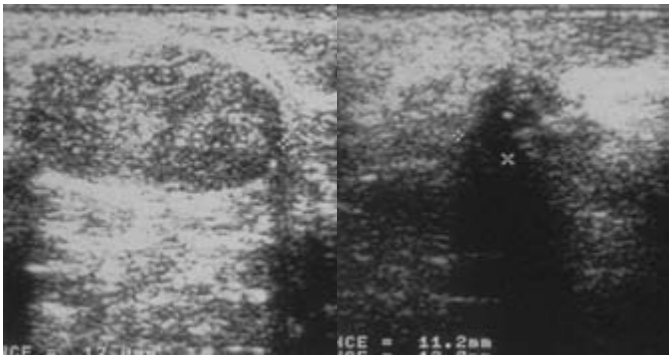


Mammography



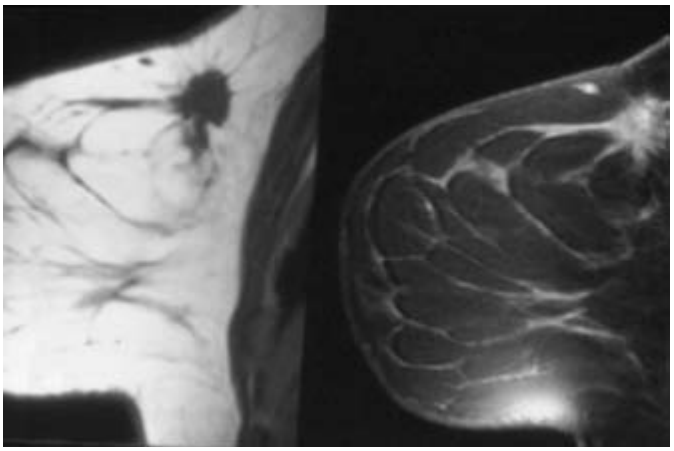

Mammograms showing (left) two mass lesions in left breast, irregular in outline with characteristics of carcinomas, and (right) mass lesion with extensive branching, impalpable microcalcification characteristic of carcinoma in situ

**Ultrasonography**
High frequency sound waves are beamed through the breast, and reflections are detected and turned into images. Cysts show up as transparent objects, and other benign lesions tend to have well demarcated edges whereas cancers usually have indistinct outlines. Blood 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 is insufficient to accurately differentiate benign from malignant lesions. Ultrasound contrast agents are available, but they are of doubtful value and not often used.



Ultrasound scans showing clear edges of fibroadenoma (left) and indistinct outline of carcinoma (right)

**Magnetic resonance imaging (MRI)**
Magnetic resonance imaging is an accurate way of imaging the breast. It has a high sensitivity for breast cancer and is valuable in demonstrating the extent of invasive and non-invasive disease. Ongoing studies are evaluating its role in improving the rate of successful breast conserving procedures. It is useful in the treated, conserved breast to determine whether a mammographic lesion at the site of 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. It is also of value in assessing early response to neoadjuvant therapy in women with established breast cancer.

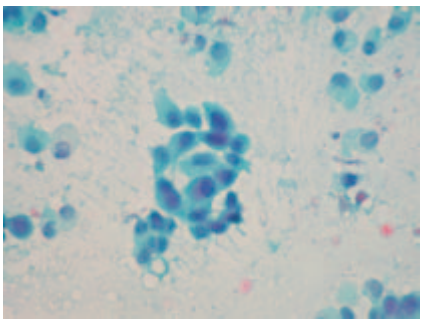


MRI scan showing cancer

**Fine needle aspiration (FNA) cytology**

Needle aspiration can differentiate between solid and cystic lesions. Aspiration of solid lesions requires skill to obtain enough cells for cytological analysis, and skill is needed 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. In some units a report is available within 30 minutes.

Touch prep cytology of core biopsy samples and sentinel lymph nodes is possible and allows immediate reporting. If the biopsy sample contains 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.



Smear from fine needle aspirate showing malignant cells that are poorly cohesive and have large polymorphic nuclei

**Core biopsy**

Local anaesthetic containing adrenaline solution is infiltrated into the overlying skin and surrounding breast tissue. After a minimum of 7–8 minutes, through a single small skin incision, cores of tissue are removed from the clinical mass or the area of mammographic or ultrasound abnormality by means of a cutting needle technique. A 14 gauge needle combined with a mechanical gun produces satisfactory samples and allows the procedure to be performed single handed. 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 usually taken to ensure adequate sampling of all parts of the lesion.

Core biopsy gun (left) and core needle with specimen (right)

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

**Open biopsy**

Open biopsy is now rarely required to establish a histopathological diagnosis except in the screening setting. All women undergoing open biopsy should have been assessed by imaging and fine needle aspiration cytology or core biopsy, or both. Women who are told that investigations have shown their lesion to be benign do not often request excision.

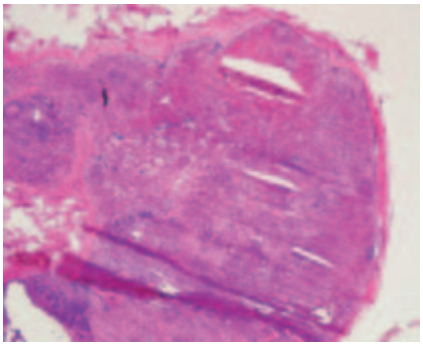
Breast biopsy is not without morbidity. A fifth of patients develop either a further lump under the scar or pain specifically related to the biopsy site.

**Frozen section**

Frozen section should be rarely, if ever, used to diagnose breast cancer and then should only be used to confirm a cytological diagnosis of breast cancer in a patient with clear evidence of cancer in whom core biopsy has failed to establish cancer and when 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 have had time to consider treatment options.

Its use has also been reported in assessment of excision margins after a wide local excision to ensure complete excision and assessment of axillary lymph nodes, particularly sentinel nodes, during operation to identify patients who are node positive and who may require only axillary dissection.

In both these instances reported sensitivity varies between 66 and 90%. Use of immunohistochemistry and multiple frozen sections improves sensitivity but considerably increases both



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

**The routine use of frozen section to diagnose breast cancer is no longer acceptable**

costs and the length of time to get a definitive result. Imprint cytology of sentinel nodes has a higher sensitivity and seems a better alternative to frozen section.

## Accuracy of investigations

False positive results occur with all diagnostic techniques. It is acceptable to plan treatment on the basis of malignant cytology 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 now considered necessary to proceed with mastectomy or axillary clearance, or both. Cytology also has a false negative rate of 4–5%. Core biopsy has the advantage of providing a histological diagnosis and can differentiate between invasive and in situ carcinoma. Errors with core biopsy occur with geographical misses and inadequate sampling. Image guidance, taking images to show the needle in the lesion, and taking multiple cores is 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 suspicious or definitely malignant on clinical examination or mammography. Breast cancer in women <40 is a particular problem as it often presents with asymmetric nodularity rather than a discrete lump.

**Accuracy of investigations in diagnosis of symptomatic breast disease in specialist breast clinics**

| | 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% | 80% |
| Fine needle aspiration cytology | 95% | 95% | 99.8% |
| Core biopsy | 85–98%§ | 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 increase if core biopsy is image guarded

**Advantages and disadvantages of techniques for assessment of breast masses**

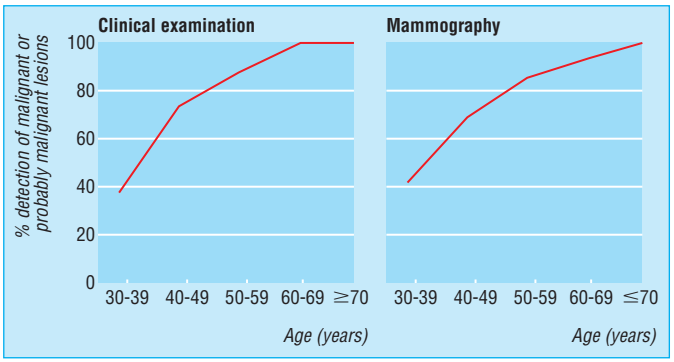
| Technique | Advantages | Disadvantages |
|---|---|---|
| Clinical examination | Easy to perform | Low sensitivity in women ≤50 |
| Mammography | Useful for screening women aged ≥50 | Requires dedicated equipment and experienced personnel<br>Low sensitivity in women ≤50<br>Unpleasant (causes discomfort or actual pain) |
| Ultrasonography | Same sensitivity in all ages<br>Useful in assessing impalpable lesions<br>Painless | Operator dependent<br>No more sensitive than mammography |
| MRI | High sensitivity in all ages<br>Accurately assesses size of cancer | Costly—time consuming<br>Claustrophobic—low specificity |
| Fine needle aspiration cytology | Cheap<br>High sensitivity<br>Provides differential diagnosis in most instances<br>Low incidence of false positives<br>Can be reported immediately | Operator dependent<br>Needs experienced cytopathologist<br>Painful<br>Cannot differentiate invasive from in situ cancer |
| Core biopsy | Easy to perform<br>Less painful than FNA<br>High sensitivity, particularly if image guided<br>Provides a definitive histological diagnosis<br>Almost zero false positive rate | Operator dependent<br>Cannot easily be reported immediately<br>Uncomfortable but less painful than FNA<br>Bruising and swelling |

### Triple assessment

This is the combination of clinical examination, imaging (usually mammography with or without ultrasonography for women aged ≥35 and ultrasonography alone for women aged <35), and fine needle aspiration cytology or core biopsy, or both.

### Delay in diagnosis

Delay in the diagnosis of breast cancer is a common reason for patients taking legal action against medical practitioners. Currently 1.5–4 % 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 these younger women often manifest as localised nodularity rather




Sensitivity of clinical examination and mammography by age in patients presenting with a breast mass. Adapted from Dixon JM et al. *Br J Surg* 1984; 71:593–6

than a discrete lump. For this reason all women who have either discrete lumps or localised areas of asymmetric nodularity should have triple assessment. The doctor who ordered the investigations should check all the reports, which should be filed in the patient's notes. Details of clinical findings must be recorded legibly in the patient's records and include a diagram marking all areas of abnormality and a doctor's signature.

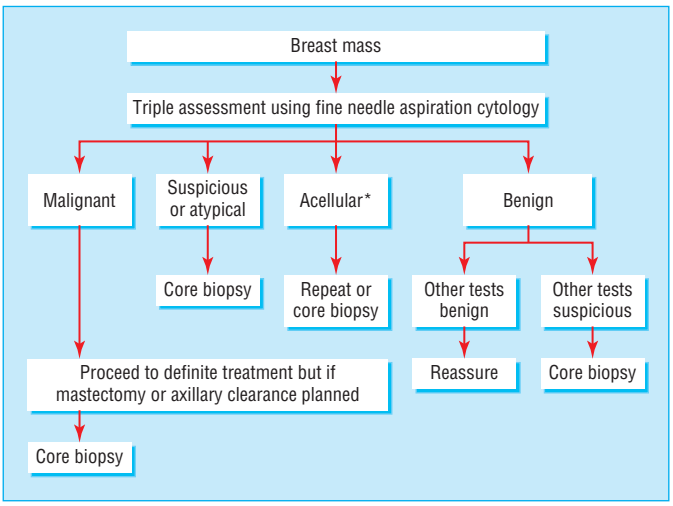
**One stop clinics**

In a patient with a discrete breast mass or a localised area of nodularity some centres offer immediate reporting of imaging and cytology from a fine needle aspirate or touch preparation from a core biopsy sample. One stop clinics have advantages for women with benign lumps, who can be reassured and discharged after a single visit; they are only cost effective in centres that see many patients.

# Investigation of breast symptoms

**Breast mass and localised nodularity**

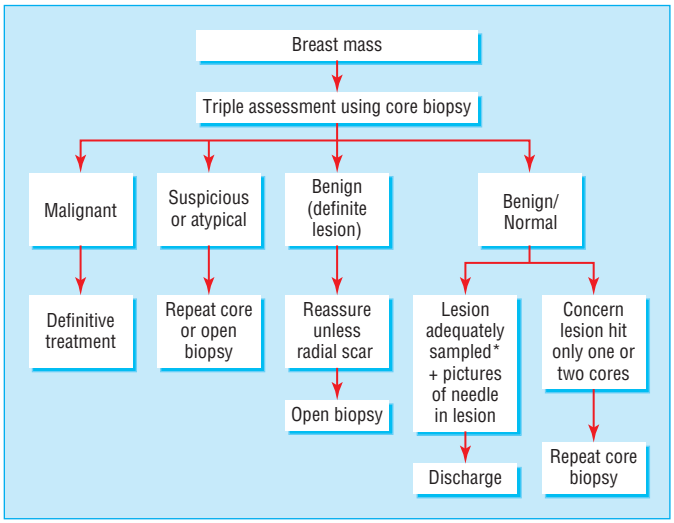
All patients should be assessed by triple assessment. It is not necessary to excise all solid breast masses, and a selective policy is recommended on the basis of the results of triple assessment. Core biopsy, preferably image guided, has replaced cytology as the most commonly used diagnostic investigation. Combining FNA and core biopsy increases sensitivity obtained with each investigation alone. Combining FNA and core biopsy or using core biopsy alone with touch preparation or roll cytology allows both immediate reporting and a histological diagnosis.



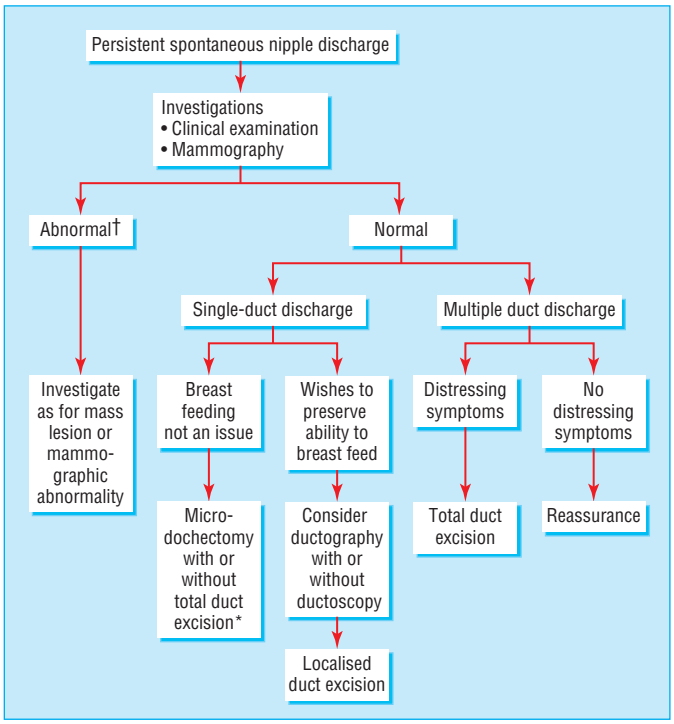

Investigation of a breast mass using fine needle aspiration as initial investigation (*acellular aspirates are not always inadequate specimens and in the presence of lucent breasts may be enough to exclude malignancy)

**Nipple discharge**

Treatment depends on whether the discharge is spontaneous and whether it is from one or several ducts. Single duct discharge should be checked by testing for 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 simple papillomas or other benign conditions. All patients with spontaneous discharge should have clinical examination and, if aged >35, mammography. Ductography and ductoscopy can localise lesions and may have a role in

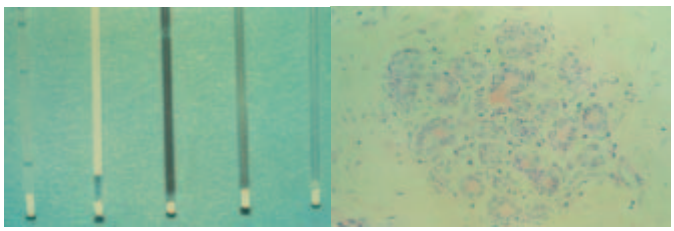



Investigation of a breast mass or localised area of nodularity with core biopsy (*minimum of three cores are required, preferably image guided, to be certain that lesion is adequately sampled)




Investigation of nipple discharge (*some surgeons prefer total duct excision in women aged >45 to reduce incidence of discharge from other ducts)

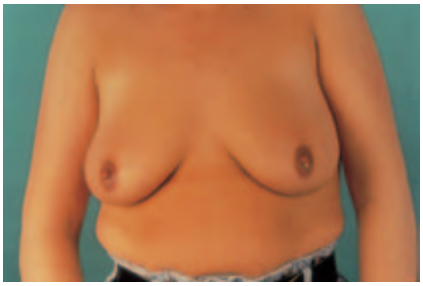
†If lesion on mammograms is incidental and unlikely to be related to nipple discharge combine with investigation of single or multiple duct discharge as appropriate



Physiological breast secretions collected from non-pregnant women (left). Note range of colours from white to blue-black. Physiological secretions visible in a normal breast lobule (right)

young women to direct and limit any excision in an effort to maintain the ability to breast feed. Physiological nipple discharge is common: two thirds of premenopausal women can be made to produce nipple secretion by cleansing the nipple and applying suction. This physiological discharge varies in colour from white to yellow to green to blue-black.

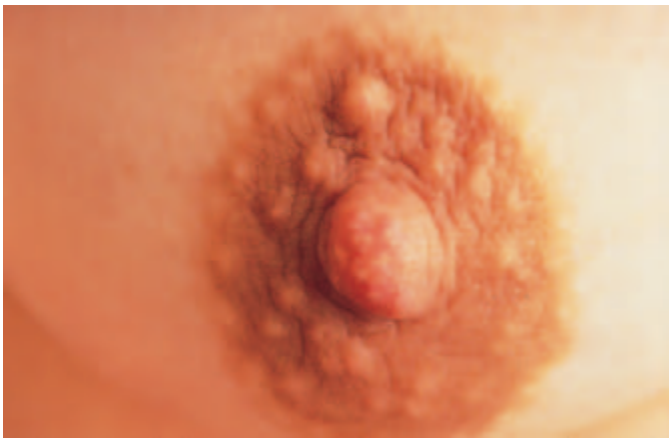
Galactorrhoea is copious bilateral milky discharge not associated with pregnancy or breastfeeding. Prolactin levels are usually but not always raised in women with galactorrhoea. A careful drug history should be taken as various drugs, particularly psychotropic agents, can cause hyperprolactinaemia.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



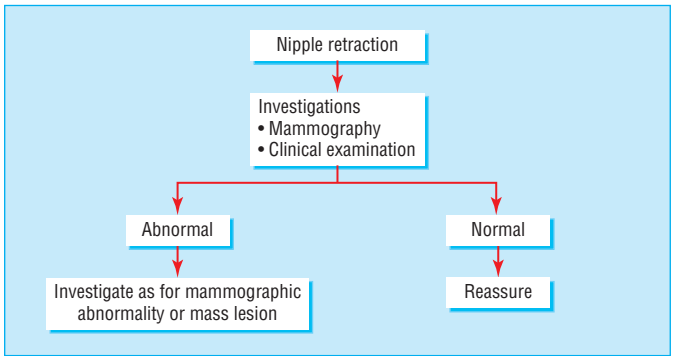
Galactorrhoea

### Blocked Montgomery's tubercle

Montgomery's tubercles are blind-ending ducts in the areola. Secretions from the lining cells may become inspissated and present as a periareolar lump that can be locally excised if troublesome. They can become infected.



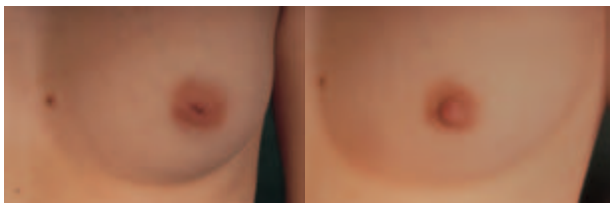
Blocked Montgomery's tubercle




Investigation of nipple retraction

### Nipple retraction

Slit-like retraction of the nipple is characteristic of benign disease, 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 duct excision can result in loss of ability to breast feed and loss or reduction of nipple sensation or sometimes nipple hypersensitivity.



Before and after surgery for nipple eversion

### Breast pain

Cyclical breast pain should be differentiated from non-cyclical pain, and its severity 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. Focal lesions should be investigated with fine needle aspiration cytology or core biopsy, or both.

### 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
- Diagnosis of atypical hyperplasia on core biopsy
- Radial scar: diagnosed by imaging and core biopsy
- Indeterminate papillary lesions
- Suspicion of malignancy on one or more investigations with indeterminate or inadequate core biopsy
- Request by patient for excision

### Further reading


- Dixon JM. Indications and techniques of breast biopsy. *Curr Prac Surg* 1993;5:142–8.
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- Helvie MA. Mammography in diseases of the breast. In: Harris JR, Lippman ME, Morrow M, Osborne CK, eds. *Imaging analysis*. Philadelphia: Lippincott Williams and Wilkins, 2004:131–48.
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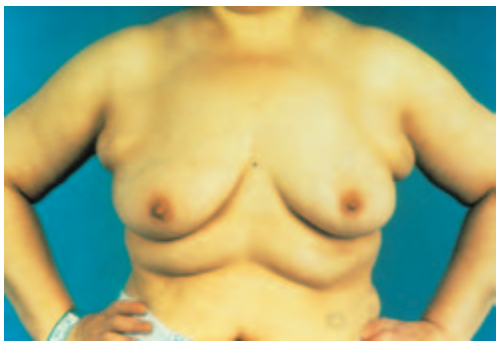
# 2 Congenital problems and aberrations of normal development and involution

JM Dixon, J Thomas

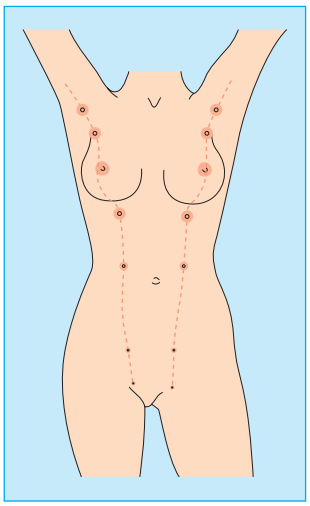
## Congenital abnormalities

**Extra nipples and breasts**

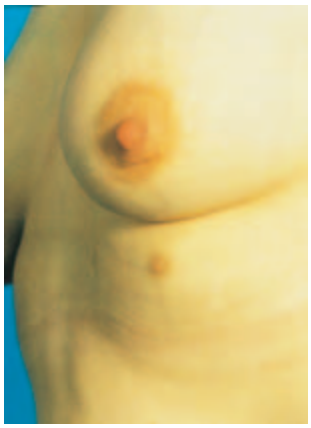
Between 1% and 5% of men and women have supernumerary or accessory nipples or, less commonly, supernumerary or accessory breasts. These usually develop along the milk line: the most common site for accessory nipples is just below the normal breast, and the most common site for accessory breast tissue is the lower axilla. Accessory breasts below the umbilicus are extremely rare. Extra breasts or nipples rarely require treatment unless they are unsightly, although they are subject to the same diseases as normal breasts and nipples.



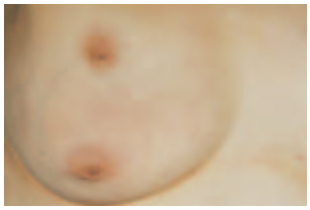
Patient with bilateral accessory breasts



Usual sites of accessory nipples and breast along milk lines



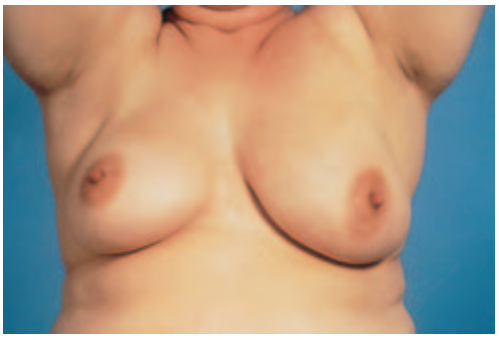
Patient with accessory nipple



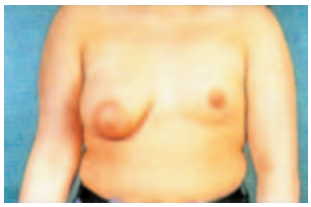
Patient with two nipples in one breast: One normal, and the other accessory

**Absence or hypoplasia of the breast**

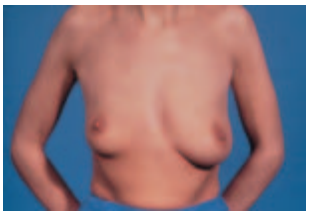
One breast can be absent or hypoplastic, usually in association with defects in one or both pectoral muscles. Some degree of breast asymmetry is usual, and the left breast is more commonly larger than the right. True breast asymmetry can be treated by augmentation of the smaller breast, reduction or elevation of the larger breast, or a combination of procedures.



Absence of left pectoralis major muscle but normal right breast



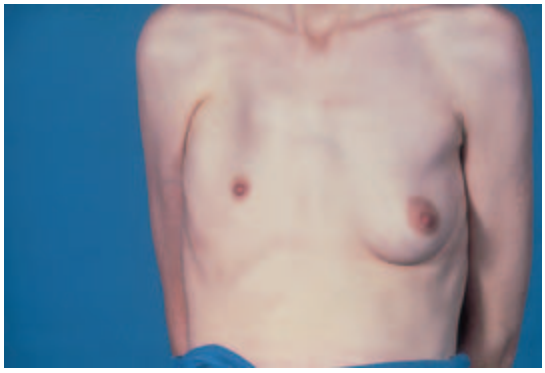
Left breast hypoplasia



Breast asymmetry

**Chest wall abnormalities**

About 90% of patients with true unilateral absence of a breast have either absence or hypoplasia of the pectoral muscles. In contrast, 90% of patients with pectoral muscle defects have normal breasts. Some patients have abnormalities of the pectoral muscles and absence or hypoplasia of the breast associated with a characteristic deformity of the upper limb. This cluster of anomalies is called Poland's syndrome. Abnormalities of the chest wall, such as pectus excavatum, and deformities of the thoracic spine, such as scoliosis, can also result in normal symmetrical breasts seeming asymmetrical.

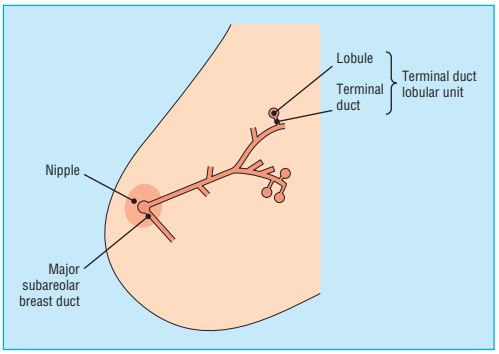


Poland's syndrome with hypoplasia of right breast and absent chest wall muscles (patient also had typical hand abnormality)

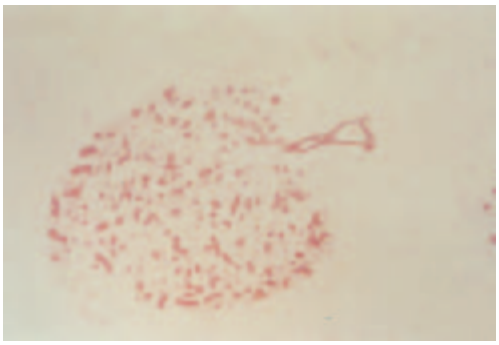
# Breast development and involution

The breast is identical in boys and girls until puberty. Growth begins at about the age of 10 and may initially be asymmetrical: a unilateral breast lump in a 9–10 year old girl is invariably a developing breast, and biopsy specimens should not be taken from girls of this age as this can damage the breast bud. The functional unit of the breast is the terminal duct lobular unit or lobule, which drains via a branching duct system to the nipple. The duct system does not run in a truly radial manner, and the breast is not separated into easily defined segments. The lobules and ducts—the glandular tissue—are supported by fibrous tissue—the stroma. Most benign breast conditions and almost all breast cancers arise within the terminal duct lobular unit.

After the breast has developed, it undergoes regular changes related to the menstrual cycle. Pregnancy results in a doubling of the breast weight at term, and the breast involutes after pregnancy. In nulliparous women breast involution begins at some time after the age of 30. During involution the breast stroma is replaced by fat so that the breast becomes less radiodense, softer, and ptotic (droopy). Changes in the glandular tissue include the development of areas of fibrosis, the formation of small cysts (microcysts), and an increase in the number of glandular elements (adenosis). The life cycle of the breast consists of three main periods: development (and early reproductive life), mature reproductive life, and involution. Most benign breast conditions occur during one specific period and are so common that they are best considered as aberrations rather than disease.




Anatomy of breast showing terminal duct lobular units and branching system of ducts



Terminal duct lobular unit

# Aberrations of breast development

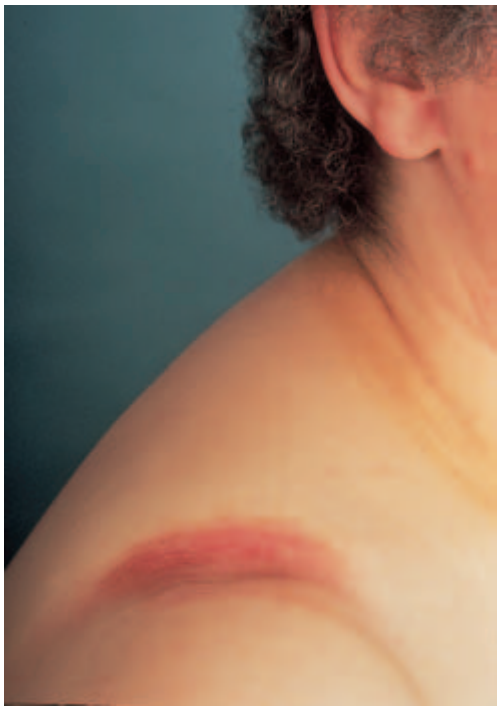
**Juvenile or virginal hypertrophy**

Prepubertal breast enlargement is common and requires investigation only if it is associated with other signs of sexual maturation. Uncontrolled overgrowth of breast tissue can occur in adolescent girls whose breasts develop normally during puberty but then continue to grow, often quite rapidly. No endocrine abnormality can be detected in these girls.

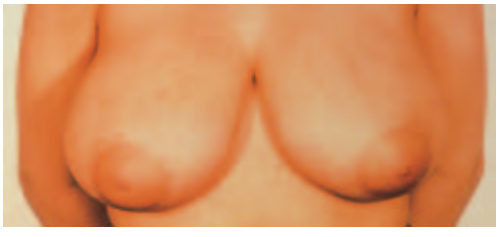
Patients present with social embarrassment, pain, discomfort, and inability to perform regular daily tasks. Reduction mammoplasty considerably improves their quality of life and should be more widely available.

**Aberrations of normal breast development and involution**

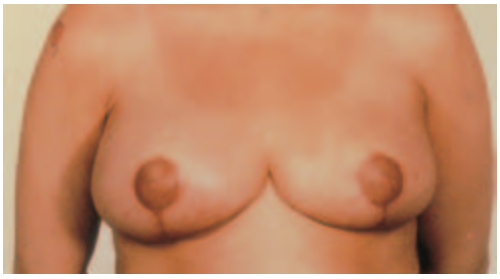
| Age (years) | Normal process | Aberration |
|---|---|---|
| <25 | Breast development: | |
| | • Stromal | Juvenile hypertrophy |
| | • Lobular | Fibroadenoma |
| 25–40 | Cyclical activity | Cyclical mastalgia; cyclical nodularity (diffuse or focal) |
| 35–55 | Involution: | |
| | • Lobular | Macrocysts |
| | • Stromal | Sclerosing lesions |
| | • Ductal | Duct ectasia |



Shoulder indentation resulting from bra strap in juvenile hypertrophy



Patient with juvenile hypertrophy before surgery



Patient with juvenile hypertrophy after surgery

**Fibroadenoma**

Although classified in most textbooks as benign neoplasms, fibroadenomas are best considered as aberrations of normal development: they develop from a whole lobule and not from a single cell, they are common, and they are under the same hormonal control as the rest of the breast tissue. Fibroadenomas account for about 13% of all palpable symptomatic breast masses, but in women aged ≤20 they account for almost 60% of such masses. There are three separate types of fibroadenoma: common fibroadenoma, giant fibroadenoma, and juvenile fibroadenoma. There is no universally accepted definition of what constitutes a giant fibroadenoma, but most consider that it should measure over 5 cm in diameter. Juvenile fibroadenomas occur in adolescent girls and sometimes undergo rapid growth but are managed in the same way as the common fibroadenoma.

Phyllodes tumours are distinct pathological entities. They are usually larger than fibroadenomas, occur in an older age group, have malignant potential, and cannot always be differentiated clinically from fibroadenomas. Phyllodes tumours focally have an infiltrative margin and form a spectrum from benign (80%) to malignant (20%). About 20% of benign phyllodes tumours recur after excision.

Fibroadenomas have characteristic mammographic features in older patients when they calcify. A few patients have multiple fibroadenomas. Over a two year period less than 10% of common fibroadenomas increase in size, about one third get smaller or completely disappear, and the remainder stay the same size. Fibroadenomas usually increase in size during pregnancy, sometimes dramatically. The appearance on ultrasonography also changes with fluid (milk) filled spaces, which should not be confused with the spaces seen sometimes in phyllodes tumours.

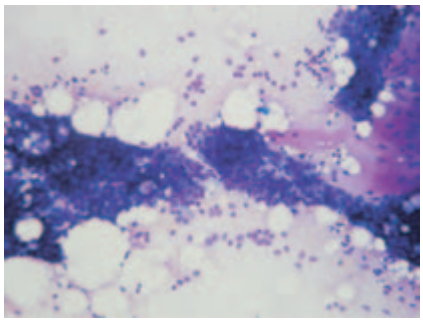
**Final diagnosis in patients with palpable breast mass**

| Diagnosis (%) | | Diagnosis (%) | |
|---|---|---|---|
| Localised benign* | 38 | Periductal mastitis | 1 |
| Cysts | 15 | Duct ectasia | 1 |
| Carcinoma | 26 | Abscess | 1 |
| Fibroadenoma | 13 | Others | 5 |

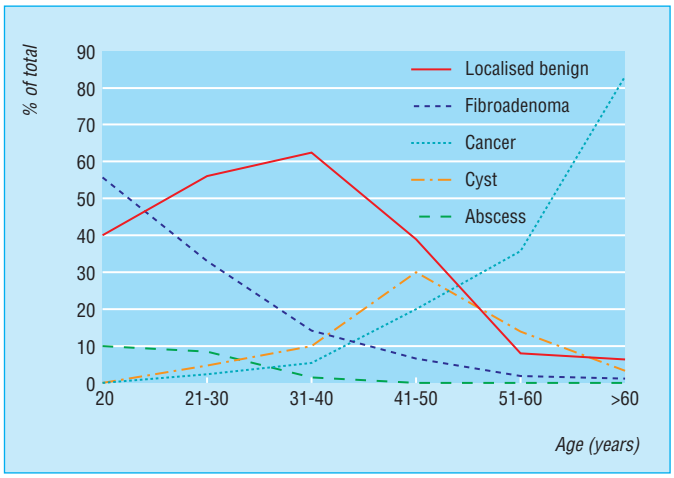
*Localised areas of nodularity that histologically show no clinically significant abnormality or aberrations of normal involution

*Management*

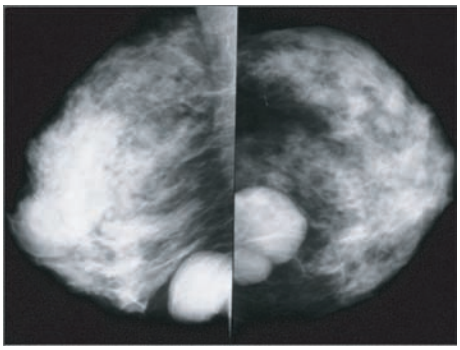
A diagnosis based on cytology is acceptable providing the patient is young (<30) and the lesion is small (<3 cm) and has characteristic clinical and imaging features. Otherwise a histological diagnosis should be established by core biopsy. In patients with multiple fibroadenomas, two or more lesions should be sampled and the rest should be imaged and monitored.



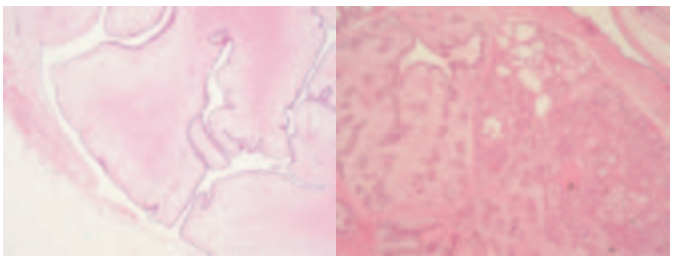
Fine needle aspirate of a fibroadenoma showing benign cells in a background of bare nuclei



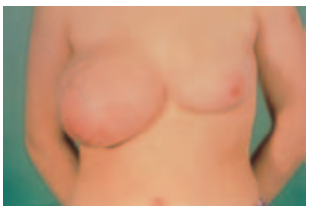

Changing frequencies of different discrete breast lumps with age



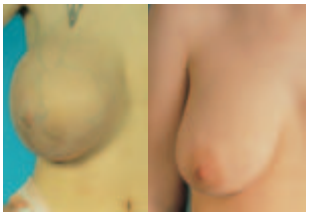
Mammogram of a benign phyllodes tumour



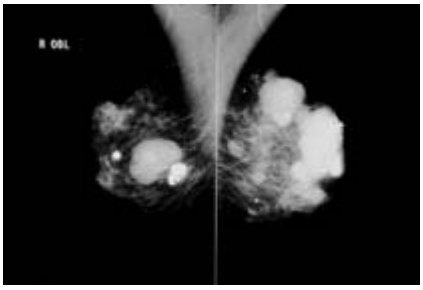
Histology of common fibroadenoma (left) and benign phyllodes tumour (right)



Juvenile fibroadenoma of right breast

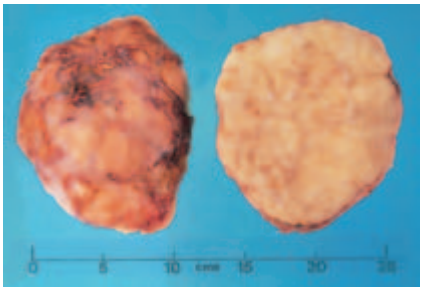


Juvenile (giant) fibroadenoma before and after surgery



Mammograms of multiple calcified fibroadenoma

Fibroadenomas over 4 cm require full assessment by core biopsy. Multiple passes are required to ensure that the lesion is not a phyllodes tumour. Cytology alone is not recommended in these larger lesions as it is not possible on cytology to distinguish with confidence fibroadenomas from phyllodes tumours. These larger lesions should be excised with a 1 cm margin if a phyllodes tumour is suspected on core biopsy. Large juvenile fibroadenomas can be excised through inferior or inferolateral incisions, which give good cosmetic results. Common fibroadenomas diagnosed in women aged <30 by clinical examination, ultrasonography, and fine needle aspiration cytology and in older women by core biopsy require excision only if it is requested by the patient. Excision of small fibroadenomas is possible with the new vacuum assisted larger core biopsy devices, such as the 8 gauge mammotome.

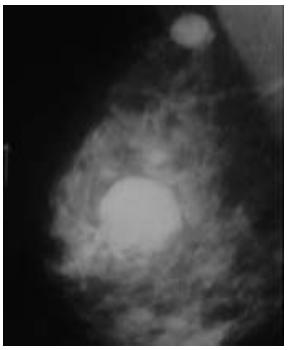


Cross section of giant fibroadenoma

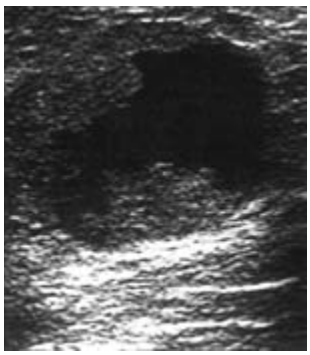
## Aberrations in the early reproductive period

**Pain and nodularity**

Cyclical pain and nodularity are so common that they can be regarded as physiological and not pathological. Severe or prolonged pain is regarded as an aberration. Focal breast nodularity is the most common cause of a breast lump and is seen in women of all ages. When excised, most of these areas of nodularity show either no pathological abnormality or aberrations of the normal involutional process such as focal areas of fibrosis or sclerosis. The preferred pathological term is benign breast change, and terms such as fibroadenosis, fibrocystic disease, and mastitis should no longer be used by clinicians or pathologists.



Mammogram of patient with cyst and cancer



Ultrasound picture of intracystic cancer

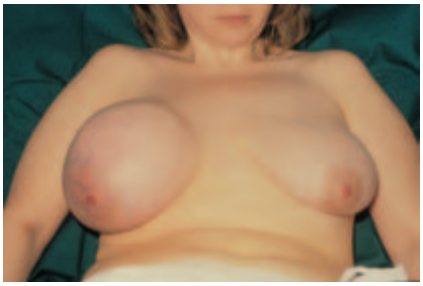
## Aberrations of involution

**Palpable breast cysts**

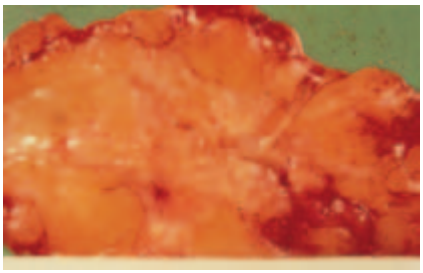
About 7% of women in Western countries will present at some time in their life with a palpable breast cyst. Palpable cysts constitute 15% of all discrete breast masses. Cysts are distended and involuted lobules and are most common in perimenopausal women. Most present as a smooth discrete breast lump that can be painful and is sometimes visible.

Cysts have characteristic halos on mammography and are readily diagnosed by ultrasonography. The diagnosis can also be established by needle aspiration, and providing the fluid is not bloodstained it should not be sent for cytology. After aspiration the breast should be re-examined to check that the palpable mass has disappeared. Any residual mass requires full assessment, including mammography. About 1–3% of patients presenting with cysts have carcinomas; most of these are not associated with the cyst but are incidental findings on ultrasonography or mammography.

Patients with cysts have a slightly increased risk of developing breast cancer (twice to three times the risk), but the magnitude of this risk is not clinically significant.



Patient with intracystic cancer of the right breast



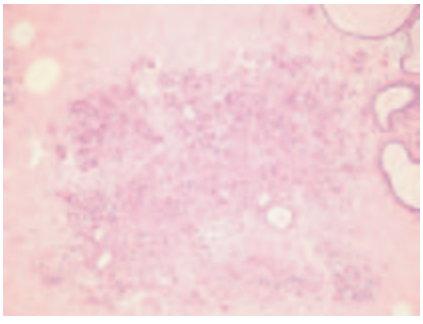
Excision specimen sliced to show area of sclerosis (histologically confirmed)

**The mammographic appearance of sclerosing lesions mimics that of cancer, causing diagnostic problems during breast screening**

**Sclerosis**

Aberrations of stromal involution include the development of localised areas of excessive fibrosis or sclerosis. Pathologically, these lesions can be separated into three groups: sclerosing adenosis, radial scars, and complex sclerosing lesions (this term incorporates lesions previously called sclerosing papillomatosis and includes infiltrating epitheliosis).

They are clinically important because of the diagnostic problems they cause during breast screening. Excision biopsy is often required to make a definitive diagnosis.



Histology of sclerosing adenosis, note the crowding of the acinar units

**Duct ectasia**

The major subareolar ducts dilate and shorten during involution, and, by the age of 70, 40% of women have substantial duct dilatation or duct ectasia. Some women with excessive dilatation and shortening present with nipple discharge, nipple retraction, or a palpable mass that may be hard or doughy. The discharge is usually cheesy, and the nipple retraction is classically slit-like. Surgery is indicated only if the discharge is troublesome or the patient wants the nipple to be everted.

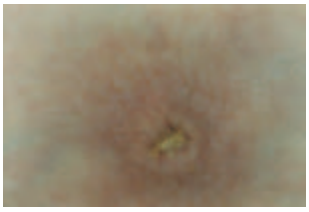
Slit-like nipple retraction due to duct ectasia (left) and nipple retraction due to breast cancer (right)

# Gynaecomastia

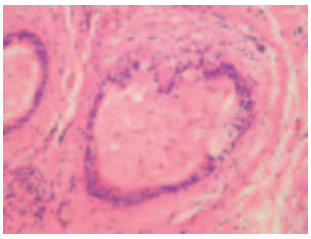
Gynaecomastia (the growth of breast tissue in males to any extent in all ages) is entirely benign and usually reversible. It commonly occurs in puberty and old age. It is seen in 30–60% of boys aged 10–16 years and usually requires no treatment as 80% resolve spontaneously within two years. Embarrassment or persistent enlargement are indications for surgical referral.

**Causes of gynaecomastia**

| Cause (%) | | Cause (%) | |
|---|---|---|---|
| Puberty | 25 | Testicular tumours | 3 |
| Idiopathic (senescent) | 25 | Secondary hypogonadism | 2 |
| Drugs (including cimetidine, digoxin, spironolactone, androgens, or antioestrogens) | 10–20 | Hyperthyroidism | 1.5 |
| Cirrhosis or malnutrition | 8 | Renal disease | 1 |
| Primary hypogonadism | 8 | | |



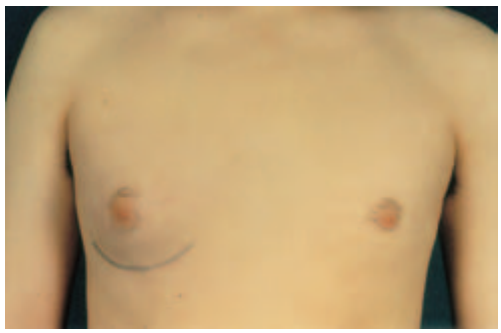
Patient with dried secretion in an inverted nipple characteristic of duct ectasia



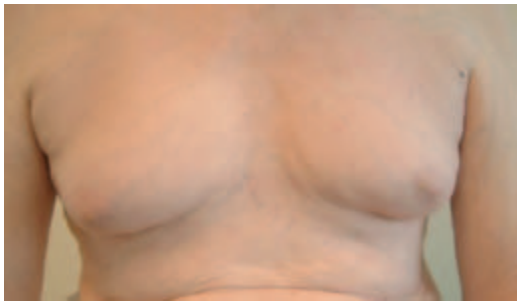
Duct ectasia showing dilated ducts but little active periductal inflammation

Senescent gynaecomastia commonly affects men aged between 50 and 80, and in most it does not seem to be associated with any endocrine abnormality. A careful history and examination will often reveal the cause. A history of recent progressive breast enlargement without pain or tenderness and without an easily identifiable cause is an indication for investigation. Mammography can differentiate between breast enlargement due to fat or gynaecomastia and is valuable if malignancy is suspected. Fine needle aspiration cytology and/or core biopsy should be performed if there is clinical or mammographic suspicion of breast cancer. Only if no clear cause is apparent should blood hormone concentrations be measured.

In drug related gynaecomastia withdrawal of the drug or change to an alternative treatment should be considered. Gynaecomastia is seen in body builders who take anabolic steroids; some have learnt that by taking tamoxifen they can combat this. Both tamoxifen and danazol improve symptoms in patients with gynaecomastia but recurrence after stopping drugs can be a problem. Surgery for gynaecomastia is not easy, should follow recognised protocols, and should be performed by experienced breast or plastic surgeons.



Adolescent left sided gynaecomastia. Black line indicates lower limit of dissection



Bilateral senescent gynaecomastia

# Benign neoplasms and proliferations

**Epithelial hyperplasia**

Epithelial hyperplasia is an increase in the number of cells lining the terminal duct lobular unit. This was previously called epitheliosis or papillomatosis, but these terms are now obsolete. The degree of hyperplasia can be graded as mild, moderate, or florid (severe).

If the hyperplastic cells also show cellular atypia the condition is called atypical hyperplasia. The absolute risk of breast cancer in a woman with atypical hyperplasia who does

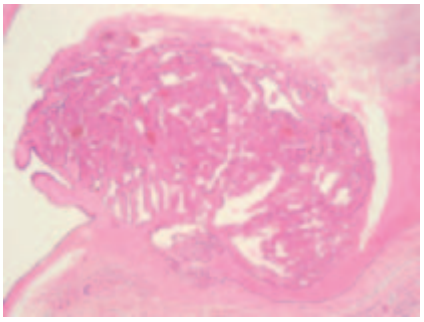
**Atypical hyperplasia is the only benign breast condition associated with a significantly increased risk of subsequent breast cancer**

not have a first degree relative with breast cancer is 8% at 10 years; for a woman with a first degree relative with breast cancer, the risk is 20–25% at 15 years.

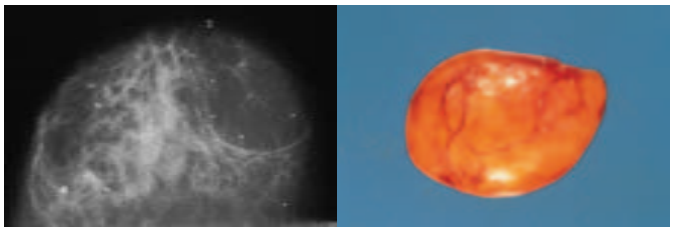
**Duct papillomas**
These can be single or multiple. They are common and should probably be considered as aberrations rather than true benign neoplasms as they show minimal malignant potential. The most common symptom is nipple discharge, which is often bloodstained.

Bloodstained nipple discharge

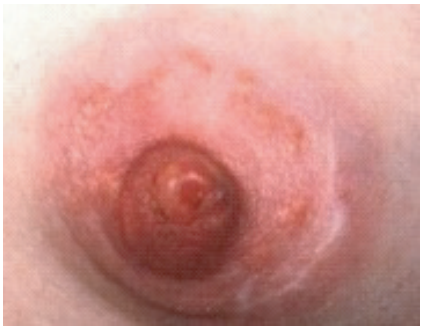
**Lipomas**
These soft lobulated radiolucent lesions are common in the breast. Interest in these lesions lies in the confusion with pseudolipoma, a soft mass that can be felt around a breast cancer and that is caused by indrawing of the surrounding fat by a spiculated carcinoma.



Histology of a duct papilloma that measures 5 mm



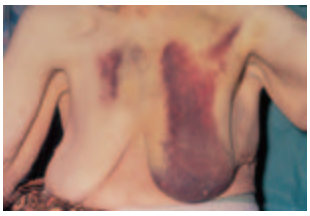
Mammogram (left) showing a large radiolucent lipoma present anteriorly and medially in breast (white mark represents lateral aspect of mammogram) and (right) the excised tumour



Adenoma of the nipple. There is a small nodule and a visible area of ulceration on the surface of the nipple. This patient had undergone a recent microdochectomy but the nipple adenoma had been missed and nipple discharge persisted

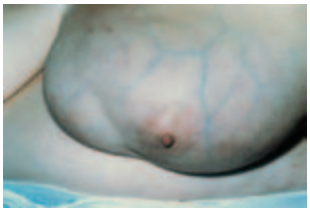
**Nipple adenoma**
This is an ulcerating lesion on the nipple that presents as a lump in the nipple or as nipple discharge. Treatment is wide excision. It is usually possible to save the nipple.

**Haematomas**
These most commonly follow trauma such as a road traffic incident or after fine needle aspiration, core biopsy, or open biopsy. In extremely unusual circumstances a breast carcinoma may present with a spontaneous haematoma. Breast haematoma can also occur spontaneously in patients on anticoagulant therapy.

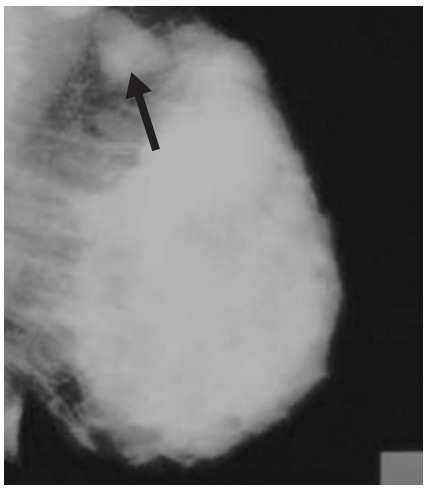


Breast haematoma

**Fat necrosis**
Fat necrosis of the breast is often called "traumatic fat necrosis," though a history of trauma is present in only about 40% of patients. It is most commonly seen after road traffic incidents as a result of seat belt trauma to the breast.



Fat necrosis of the breast after trauma caused by seat belt



Sarcoidosis of the breast

**Sarcoidosis**
Patients with sarcoid can present with single or multiple masses within the breast. A breast mass can occur either as the first