Gynaecomastia is the abnormal development of mammary glandular tissue in men resulting in breast enlargement (Figure 1). It is the most common breast problem afflicting men – occurring in up to one third of men at some stage in life. It can be the source of significant social embarrassment, which is the reason some seek medical advice. The condition is often transient and self-limiting or reversible, and most cases can be diagnosed and managed within primary care. A minority of cases will, however, flag a serious underlying cause. Specialist referral is required if there is any doubt about the differential diagnosis of breast carcinoma or where surgical management is contemplated.

Gynaecomastia is characterised histologically by hyperplasia of stromal and ductal tissue, as opposed to pseudogynaecomastia, which is caused by excess adipose tissue, without ductal proliferation.

The underlying pathophysiology relates to an altered oestrogen:androgen ratio or an insensitivity to the effects of androgens. Oestrogen production in males arises mainly from the peripheral conversion of androgens to oestradiol and oestrone by the aromatase enzyme. Small amounts of oestrogens are secreted directly by the testes. Oestrogen imbalance results in ductal epithelial hyperplasia, ductal elongation and branching, proliferation of periductal fibroblasts and increased vascularity.

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AETIOLOGY
Causes of gynaecomastia may be classified as physiological, pathological, drug induced or idiopathic.

Physiological causes
These have a classic trimodal age distribution – neonatal, pubertal and senescent. Usually these are self-limiting and require only explanation and reassurance.

Pathological causes
These may be considered as conditions causing reduced androgen activity (either reduced production or resistance) or increased oestrogens, either by increased secretion or increased peripheral aromatisation of androgens to oestradiol and oestrone (Box 1).

Drug-induced gynaecomastia
A wide range of prescribed and illicit drugs are commonly implicated, and identification of the offending drug enables withdrawal (if possible) and resolution (Box 2).

Idiopathic gynaecomastia
Approximately 10 per cent of cases arise with no underlying cause identifiable.

DIAGNOSIS
Diagnosis of the cause of gynaecomastia relies on careful history taking, clinical examination and simple special investigations in selected cases. History taking should establish the onset of symptoms and include an assessment of self-consciousness and should evaluate the effect the condition has on lifestyle (for example, avoidance of tight clothing or undressing in public areas such as swimming baths) and associated pain or tenderness. A detailed social history, past medical history and drug history are essential.

Physical examination
A general examination should be conducted with consideration of chromosomal abnormalities (such as Klinefelter's syndrome; see Figure 1) and in particular examining for clinical signs of liver disease, thyrotoxicosis or hypothyroidism.

The typical clinical features are of a rubbery or firm disc-like mass extending concentrically from the nipples. The most important aim of breast examination is to differentiate gynaecomastia, which is very common, from male breast carcinoma, which is rare. Unilaterality, the presence of a hard or irregular lump, skin distortion or skin changes, nipple inversion or the presence of palpable axillary nodes should alert the examiner to the latter. A high index of suspicion for carcinoma should be maintained in a breast swelling arising over the age of 35 (particularly if no underlying

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**BOX 1. Pathological causes of gynaecomastia**

### DECREASED PRODUCTION OR ACTION OF TESTOSTERONE
- Chromosomal abnormalities, eg Klinefelter's syndrome (see Figure 1)
- Bilateral undescended testes
- Hyperprolactinaemia (causing suppression of the hypothalamus and resulting hypogonadism)
- Bilateral testicular torsion
- Viral orchitis
- Renal failure
- Testicular feminisation (androgen resistance/insensitivity)
- Congenital absence of testes or surgical castration

### INCREASED PRODUCTION OR ACTION OF OESTROGEN
- Testicular tumours, eg Leydig cell tumours, which secrete oestrogen
- Carcinoma of lung
- Liver disease (decreased conjugation and excretion of oestrogens)
- Adrenal disease
- Thyrotoxicosis

**BOX 2. Drugs causing gynaecomastia**

### OESTROGEN OR DRUGS WITH OESTROGEN–LIKE ACTIVITY
- Androgens, anabolic steroids, oestrogens, growth hormones

### DRUGS THAT ENHANCE OESTROGEN SYNTHESIS
- Gonadotrophins such as human chorionic gonadotrophin, following withdrawal of clomiphene

### DRUGS THAT INHIBIT TESTOSTERONE PRODUCTION OR ACTION
- Cyproterone acetate, flutamide, finasteride, dutasteride, ketoconazole, spironolactone, metronidazole, tricyclic antidepressants, chemotherapeutic drugs, H₂ blockers, proton pump inhibitors, cannabis

### DRUGS THAT ACT VIA UNKNOWN MECHANISM
- Tricyclic antidepressants, ACE inhibitors, heroin, amiodarone, methyl-dopa, calcium antagonists, antiretroviral therapy, isoniazid, theophylline, heparin, digoxin
cause for gynaecomastia is found), and any suspicion should prompt urgent referral to a breast clinic for further assessment. It should be noted that longstanding gynaecomastia is a risk factor for male breast carcinoma.5

Breast examination allows differentiation of gynaecomastia from pseudogynaecomastia. In true gynaecomastia, thickened buds of abnormal breast tissue will be palpated, whereas pseudogynaecomastia consists simply of diffuse fat hypertrophy. The severity of gynaecomastia can be graded from 1 to 3 (Box 3).6

Abdominal examination should include palpation for hepatomegaly and testicular examination, which may reveal undescended testes, hypogonadism or, rarely, testicular tumours.

INVESTIGATION
Biochemical assessment may be indicated for florid gynaecomastia and should include renal function, liver function, prolactin, beta human chorionic gonadotrophin and serum testosterone, but these tests are not undertaken in the majority of patients. Routine imaging of all suspected gynaecomastia is not required. Imaging by ultrasound initially and/or mammography may be used to differentiate gynaecomastia from carcinoma.7 Pathological assessment should preferably be performed by core biopsy, as fine needle biopsy frequently results in inadequate (C1) and indeterminate (C3) reports.8 The sensitivity of core biopsy is enhanced by performing this under ultrasound guidance.

MANAGEMENT
Management is determined by the aetiology and severity of gynaecomastia, the patient’s concerns and the detrimental effect on lifestyle or body image.

Physiological pubertal gynaecomastia usually simply requires reassurance that the condition will be transient in the majority of cases.9 Review after three to six months helps identify the persistent and more severe cases (Figure 2), which may require referral for specialist assessment.

Any underlying causes should be addressed. Medicines are the most common precipitating cause and the offending drug or drugs are stopped if appropriate, or switched to alternatives. Clearly, if the causative medication needs to continue unchanged (for instance a patient with prostate cancer on anti-androgen therapy), the gynaecomastia will need to be accepted as an inevitable but benign side-effect.

It is important to ask specifically about non-prescription drugs – including cannabis and anabolic steroids. Underlying medical conditions such as hepatic or renal dysfunction will require specialist medical management.

 Pharmacological treatment
Pharmacological management of gynaecomastia may be attempted in selected patients. While widely used, neither tamoxifen nor aromatase inhibitors (such as anastrazole) are licensed for use in gynaecomastia and any benefit is likely to be temporary. Tamoxifen acts by blocking the oestrogen receptor and is typically prescribed at a dose of 10mg daily (half the standard dose for treatment of breast cancer) for up to three months as a therapeutic trial. Tamoxifen increases the risk of thromboembolic events and previous thromboembolic disease would be a contraindication. It is prudent to discuss this heightened risk with patients before prescription.

Anastrazole acts by blocking the peripheral production of oestrogen by aromatisation within fat. There is no clear evidence of enhanced efficacy when compared to tamoxifen, but it does not carry the same thromboembolic risks.

Surgery
Surgical management of gynaecomastia should be reserved for severe and refractory cases. Patients should be carefully counselled preoperatively about the resultant scars, the potential for perioperative complications (in particular a relatively high risk of haematoma postoperatively), postoperative asymmetry, hypertrophic or keloid scarring, and recurrence of the gynaecomastia requiring possible further revisional surgery. Self-consciousness can continue as a result of the scars or an imperfect result.
from surgery. Patient dissatisfaction is surprisingly common postoperatively and gynaecomastia surgery has a high rate of associated litigation.

The most common operation performed is a subcutaneous or subareolar mastectomy (Figure 3) – but with preservation of an adequate disc of retroareolar tissue to avoid a disfiguring ‘saucer’ deformity, which can be very difficult to correct. Liposuction can be successfully used to reduce gynaecomastia, particularly when it is of a predominantly fatty type, and avoids the larger scars of subareolar mastectomy. Scarring around the areola is, however, inevitable when reduction of the skin envelope is required (Figure 4). Mammtomte excision is being investigated as a minimally invasive alternative to surgery, but inevitably will be suitable only for the least severe cases.

**CONCLUSIONS**

Gynaecomastia is a common condition, which can usually be managed within primary care. It should be differentiated from male breast carcinoma. Most cases simply require identification of and addressing the underlying cause and reassurance. Drug treatment and surgical treatment are reserved for the most severe cases. Patients undergoing surgery should be carefully selected and have realistic expectations as to what surgery can achieve.

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**REFERENCES**