

Gynaecomastia:

when and why to refer to specialist care

A COMMON COMPLAINT IN GENERAL PRACTICE

Gynaecomastia is the commonest male breast complaint. Most cases are benign but the condition may signify a serious underlying illness. The challenge in primary care is to identify which patients with gynaecomastia are at greatest risk of pathological aetiology, so that they may be offered prompt specialty-appropriate referral and treatment.

This article offers guidance on the assessment and management of patients with gynaecomastia, including when and why to refer to secondary care.

HOW DO PATIENTS WITH GYNAECOMASTIA PRESENT?

Gynaecomastia refers to the enlargement of male glandular breast tissue. The condition develops because of an imbalance in the male oestrogen:testosterone ratio from a relative oestrogen excess or testosterone deficiency. Pseudo-gynaecomastia is caused by an excess of adipose tissue and does not warrant investigation or treatment.

Gynaecomastia is frequently observed in general practice. Prevalence is between 35%–65% in males aged 50–69 years in the UK.¹ Patients typically describe a soft

swelling in one or usually both breasts. Tenderness, social embarrassment, or worry about cancer are typical reasons for presentation to primary care. Other men are asymptomatic and gynaecomastia may be noted incidentally on physical examination of the chest.

Physiological gynaecomastia is common in newborns, adolescence, and senility. Most do not require investigation or referral. Neonatal gynaecomastia arises from the placental transfer of oestrogen. Over half of all adolescent boys will experience transient gynaecomastia during puberty due to a lag in testosterone secretion, with median age of onset at 14 years.² Physiological gynaecomastia is common among males aged >50 years as testosterone levels fall with increasing age.

Adult gynaecomastia is most commonly idiopathic (Figure 1). Male breast enlargement may be indicative of an underlying systemic illness or malignancy.³ Gynaecomastia is associated with underlying health conditions (Box 1) including chronic renal failure, liver cirrhosis, thyrotoxicosis, malabsorptive states, and testicular infiltration. Drugs, environmental exposures, and genetic conditions (for example, Klinefelter's)

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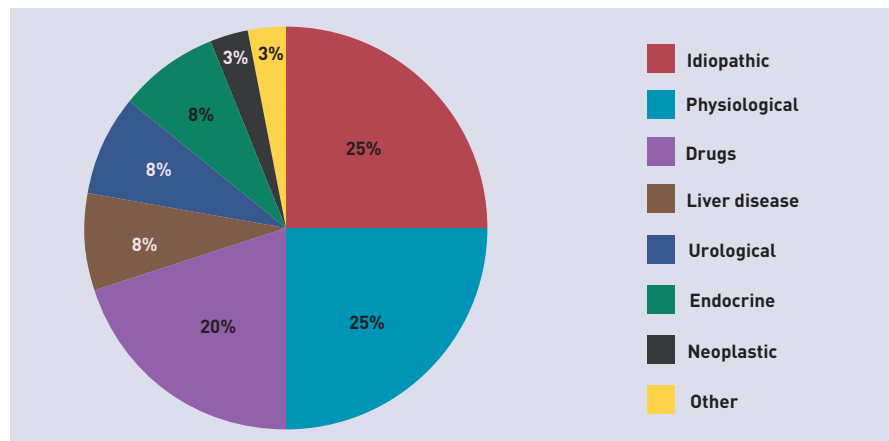
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Figure 1. Aetiology and prevalence of gynaecomastia in adults.



Box 1. Common causes of gynaecomastia

Cause	Underlying pathology
Physiological	Newborn, pubertal, senility
Benign	Idiopathic, familial, obesity
Endocrine	Hyperthyroidism, primary hypogonadism (Klinefelter's, Kallmann's), secondary hypogonadism, hyperprolactinaemia (hypothalamic/pituitary tumour)
Urological	Testicular tumour, trauma, viral orchitis, testicular infiltration, haemochromatosis, chronic renal insufficiency, renal dialysis
Liver	Chronic liver disease, cirrhosis, refeeding syndrome, malabsorption (cystic fibrosis, ulcerative colitis)
Drugs	Prescribed medication, illicit drug use, anabolic steroid misuse

Box 2. Red flags for urgent breast referral

Refer *urgently* to the rapid-access breast clinic if:

- male aged ≥ 50 years with a unilateral sub-areolar mass +/- nipple discharge +/- skin changes;
- bloody nipple discharge; or
- unilateral ulceration of the nipple.

further increase the risk of gynaecomastia.

Rapid breast enlargement should raise concerns about a hormone-secreting tumour. Adrenal or testicular tumours account for $<3\%$ of gynaecomastia. Primary breast cancer is an important differential diagnosis. Clinical suspicion of malignancy should be considered in the presence of unilateral eccentric breast enlargement or red-flag symptom (Box 2).

HOW TO ASSESS THE PATIENT WITH GYNAECOMASTIA IN GENERAL PRACTICE

A detailed history and clinical examination should be undertaken in all patients presenting with gynaecomastia. The duration and clinical course of symptoms and any history of sexual dysfunction or systemic illness should be ascertained. Nipple discharge, skin changes, masses, and systemic symptoms should raise concerns about a pathological cause.

A review should be undertaken of prescribed and recreational medications (Box 3), alcohol misuse, and anabolic

steroid misuse. Any specific symptoms of hypogonadism (for example, erectile dysfunction or loss of libido) or comorbid disease should be noted.

Examination of the chest should be performed with the patient supine. All four quadrants of each breast should be palpated, with the thumb and forefinger slowly brought together in a pincer-like movement along the chest wall, until a mound of firm breast tissue is located beneath the nipple-areolar complex. A palpable disc of sub-areolar breast tissue, which may or may not be tender, is consistent with gynaecomastia.⁴ In many cases, patients may complain of unilateral symptoms, but bilateral gynaecomastia may be noted on clinical examination and may be asymmetrical in size.

General physical examination should screen for any stigmata of chronic liver or kidney disease, hyperthyroidism, or hypogonadism. Nodal areas including the axillae and supraclavicular fossae should be examined for lymphadenopathy. Testicular examination should be offered if the history is suggestive of hypogonadism or a testicular mass.

WHAT INVESTIGATIONS ARE RECOMMENDED IN GENERAL PRACTICE?

Recent guidelines⁵ recommend that primary care physicians do *not* routinely investigate:

- newborns or adolescents with physiological gynaecomastia;
- older males with senile gynaecomastia;
- males with fatty pseudo-gynaecomastia;
- males with drug-related gynaecomastia (prescribed or illicit); and
- obvious breast cancer.

If the cause of gynaecomastia is not obvious then further investigation is necessary before referral to secondary care. GPs should investigate males with:

- rapid breast enlargement;
- recent gynaecomastia onset in lean males aged >20 years;
- persistent painful gynaecomastia;
- eccentric breast mass;
- massive gynaecomastia in adolescents; and
- persistent gynaecomastia in adolescents (>18 months).

Routine blood tests in primary care

Box 3. Drugs associated with gynaecomastia

Anti-androgen	5- α reductase inhibitors (finasteride)
Antihypertensive	Calcium channel blockers, spironolactone, angiotensin-converting enzyme (ACE) inhibitors
Antiretroviral	Protease inhibitors, nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs)
Antifungal/-microbial	Ketoconazole, metronidazole, isoniazid
Antipsychotic	Haloperidol, olanzapine, risperidone, ziprasidone, paliperidone, fluoxetine, gabapentin, pregabalin, venlafaxine, aripiprazole, diazepam, amisulpride, quetiapine
Antiparasite	Phenothrin
Analgesics	Opioids
Cardiovascular	Digoxin, amiodarone, statins, clonidine, clopidogrel, sildenafil
Chemotherapy drug	Methotrexate, alkylating agents, cisplatin, vincristine, bleomycin, dasatinib, imatinib
Exogenous hormones	Oestrogens, steroids, androgens
Gastrointestinal drug	Proton pump inhibitors, H ₂ histamine blockers, domperidone, misoprostol
Illicit and recreational	Amphetamines, cannabis, heroin, methadone, alcohol
Herbal supplements	Lavender, soy protein, tea tree oil, tribulus, common nettle
Other	Theophylline, penicillamine, ivacaftor, gonadotrophin-releasing agents

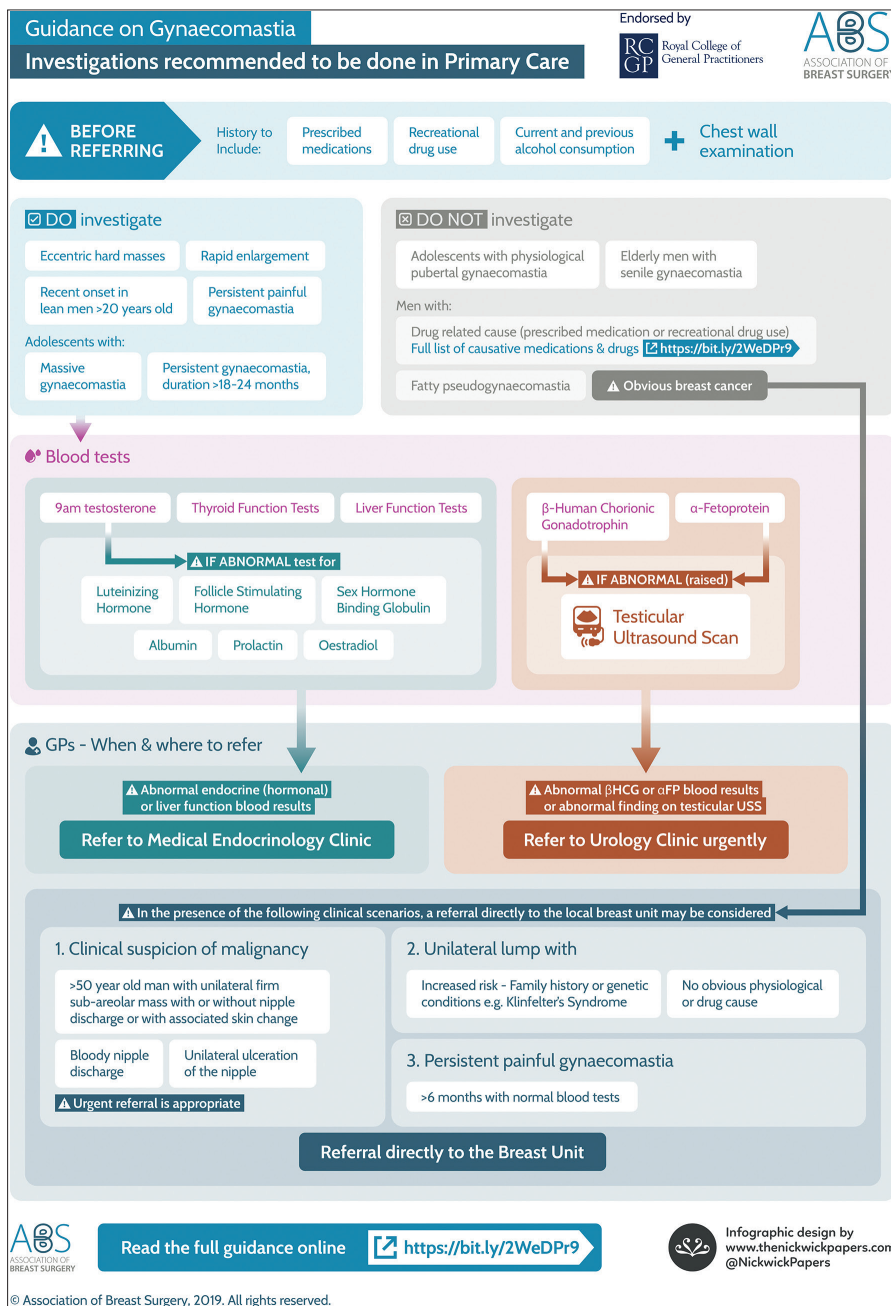


Figure 2. Infographic summarising the assessment of gynaecomastia in primary care.

Source: Association of Breast Surgery (ABS), <https://associationofbreastsurgery.org.uk/media/334385/breast-surgery-v7.pdf>.

should include measurement of 9 am testosterone, liver, renal, and thyroid function tests, α-fetoprotein (AFP) test, and β-human chorionic gonadotrophic (HCG) test.

If testosterone is abnormal then further hormone blood tests should be checked to facilitate appropriate specialty referral: luteinising hormone (LH), follicle-stimulating hormone (FSH), sex hormone-binding globulin, albumin, oestradiol, and prolactin.

Testicular ultrasonography should be requested with a raised AFP or β-HCG to examine for potential urological malignancy.

Referral for breast imaging must not be delayed if breast cancer is suspected, as these patients should be referred directly to the 2-week rapid-access breast clinic.

WHEN TO REFER TO SECONDARY CARE?

Most patients with gynaecomastia do not warrant further investigation or treatment. However, any red-flag symptoms should prompt urgent referral to the appropriate medical specialty for further investigation and treatment.

Referral to medical endocrinology is advised in the presence of abnormal endocrine (hormonal) blood results. An abnormal AFP or β-HCG, testicular ultrasound, or a testicular mass on clinical examination should prompt urgent referral to a urologist.

Referral directly to the rapid-access breast clinic is recommended if there is:

- any clinical suspicion of breast malignancy;
- persistent painful gynaecomastia (>6 months) with normal blood tests; and
- a unilateral lump with no obvious physiological/drug-induced cause, a family history of breast cancer, or genetic predisposition (Klinefelter's).

Patients with physiological gynaecomastia or pseudo-gynaecomastia may be safely reassured and given advice on maintaining a healthy body mass index. If breast enlargement has developed secondary to an underlying condition, then management should be directed toward the underlying illness, such as adequate thyroid, renal, or liver function.

Drug-induced gynaecomastia may be managed through stopping the causal precipitant or trying an alternative medication. GPs should discuss the trade-off between clinical benefits (for example, antiretroviral control in HIV) and side effects of the drug with patients, prior to stopping any medication. If breast tissue is fibrotic then stopping the causal drug may prevent further progression but will be unlikely to regress gynaecomastia substantially. In many cases, patients will accept gynaecomastia symptoms once a diagnostic explanation and link with their medication is provided.

Medical management may be trialled in patients with rapid-onset, non-pathological gynaecomastia. However, tamoxifen and anastrozole use is unlicensed in gynaecomastia and should only be prescribed under advice from secondary care. Males who develop gynaecomastia

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after anti-androgen therapy for prostate cancer respond well to medical treatment.

The impact of gynaecomastia on patients' social and personal wellbeing should not be underestimated. Understanding patients' concerns can help to direct communication and management. Surgery should be considered in select patients with significant pain or profound psychological distress, where gynaecomastia does not resolve spontaneously or respond to medical treatment. Most regions have stringent local guidelines limiting cosmetic procedures on the NHS.⁶ Funding is dependent on local clinical commissioning groups and applications can be sought from primary care.

SUMMARY

Gynaecomastia is the commonest male breast complaint encountered in primary care. Careful history and physical examination are warranted to

differentiate benign breast enlargement from serious underlying systemic disease or malignancy. Blood tests and imaging should be undertaken in primary care to facilitate optimal secondary care referral and management. An infographic produced by the Association of Breast Surgery and endorsed by the Royal College of General Practitioners provides a visual summary of this article (Figure 2).

Provenance

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Competing interests

The authors have declared no competing interests.

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