

## Gynaecomastia

Gynaecomastia is enlargement of the male breast tissue. *Gynae* means 'woman' and *mastos* means 'breast' in Greek. It can be defined as the presence of >2 cm of palpable, firm, subareolar gland and ductal breast tissue<sup>[1]</sup>.

It may occur at any time and there are a number of causes, some physiological and others pathological. Pathological causes involve an imbalance between the activity of androgens and oestrogens - the former is decreased compared with the latter.

## Epidemiology

- Gynaecomastia is common and is thought to be present in at least a third of men in the course of their lifetime<sup>[2]</sup>.
- Prevalence of asymptomatic gynaecomastia is reported as 60–90% of neonates, 50–60% of adolescents, and 70% in men aged 50–69<sup>[3]</sup>.
- Breast cancer is only detected in 1% of cases of male breast enlargement<sup>[4]</sup>.

## Pathophysiology<sup>[5]</sup>

Oestrogen stimulates breast tissue growth whilst androgens inhibit it. The important factor is the ratio of active androgens to oestrogens. The ratio can be altered as a result of reduced testosterone production/action or enhanced oestrogen production/action or both. Therefore, it may be caused by :

- Conditions which cause raised oestrogen levels.
- Conditions which cause low testosterone levels.
- Conditions which affect levels of sex hormone-binding globulin (SHBG), as it affects the free testosterone:oestrogen balance.

- Conditions which cause androgen resistance.
- Conditions which cause an increased conversion of androgens to oestrogens. Aromatase is one of the cytochrome P450 enzymes and is involved in the aromatisation of androgens to oestrogens - eg, changing androstenedione to estrone and testosterone to estradiol. This enzyme is found in many tissues - eg, brain, adipose tissue, blood vessels and the gonads. Enhanced adipose tissue, as in obesity, provides increased levels of the enzyme and, hence, increased production of oestrogens leading to gynaecomastia.

Once this ratio falls, breast tissue is stimulated to grow. This leads to proliferation of breast ducts and fibroblastic stroma. If the stimulus to proliferation continues then the ducts and fibroblastic stroma are replaced by fibrosis and gynaecomastia becomes well established and irreversible.

## Causes of gynaecomastia<sup>[1]</sup> <sup>[6]</sup>

### Physiological

- Newborn. This is the result of maternal oestrogens, and the gynaecomastia resolves after a few weeks.
- Adolescence. This is common around the age of 14, may be unilateral and may be tender. It resolves spontaneously within one to two years. It may be due to the relatively delayed testosterone surge with relation to oestrogen at puberty, or due to a temporary increase in aromatase activity.
- Increasing age - associated with low testosterone levels.

### Pathological

- **Lack of testosterone:**
  - Congenital absence of testes. There are absent levels of testosterone with normal estradiol levels and patients experience severe gynaecomastia
  - Androgen resistance.
  - [Klinefelter's syndrome](#) (XXY syndrome). Associated with gynaecomastia in 80% of cases. Men with Klinefelter's syndrome have an increased risk of breast cancer and this needs to be considered (risk is increased up to 20 times that of other patients with gynaecomastia).
  - Viral orchitis.
  - Trauma.
  - Castration.
  - Renal disease and dialysis.

- **Increased oestrogen levels:**
  - **Testicular tumours** (eg, Leydig's cell tumour) which secrete estradiol.
  - Hermaphroditism.
  - Neoplasms producing human chorionic gonadotrophin (hCG) – eg, **lung**: hCG stimulates Leydig's cells to excrete estradiol. Also, **gastric carcinomas**, **renal cell carcinomas** and **hepatomas**.
  - Adrenal tumours: these can release oestrogens.
  - **Congenital adrenal hyperplasia** (high androgens and oestrogens).
  - Liver disease or **cirrhosis**. In liver disease there is an increased production of androstenedione by the adrenal glands, increased aromatisation of androstenedione to oestrogen, loss of clearance of adrenal androgens by the liver and a rise in SHBG, resulting in gynaecomastia.
  - Malnourishment and re-feeding syndrome.
  - **Hyperthyroidism**.
  - Obesity.
  - Extreme stress.
  - Aromatase excess syndrome. Mutation of the aromatase gene causes excess oestrogen levels, prepubertal gynaecomastia and premature epiphyseal fusion<sup>[7]</sup>.

- **Medication:**

Medication accounts for up to 25% of all cases in adult men:

- Oestrogens or oestrogenic action: diethylstilbestrol, herbal remedies with phytoestrogens, creams and cosmetics containing oestrogen, and possibly tea tree oil and lavender oil products, phenytoin, clomifene.
- Digoxin. (By virtue of an oestrogen-like effect. The effect is enhanced if liver derangement is co-existent.)
- Inhibitors of testosterone synthesis: eg, metronidazole, ketoconazole, spironolactone, chemotherapy, gonadotrophin-releasing hormone (GNRH) agonists such as leuprolide and goserelin.
- Inhibitors of testosterone action: eg, cyproterone, flutamide, bicalutamide, finasteride, dutasteride, H2 receptor antagonists, proton pump inhibitors (PPIs), marijuana.
- Androgens causing high oestrogen levels: anabolic steroids, excessive testosterone replacement therapy.
- Medications which increase prolactin levels: eg, antipsychotics, tricyclic antidepressants, metoclopramide, verapamil.
- Antiretrovirals. The exact mechanism by which antiretrovirals cause gynaecomastia is unknown. It often presents as unilateral and tender gynaecomastia. Efavirenz has been implicated and stopping it results in resolution of gynaecomastia. However, there can be more sinister causes for the gynaecomastia which should not be missed - eg, lymphoma.
- Others - eg, amiodarone, isoniazid, methyldopa, diazepam, calcium-channel blockers, angiotensin-converting enzyme (ACE) inhibitors, alcohol, amfetamines, growth hormone, isoniazid, theophylline, heroin.

- **Other causes:**
  - Long-term [type 1 diabetes mellitus](#).
  - Chronic illness.
  - Spinal cord injury.
- **Idiopathic.**

## Approach to a patient presenting with gynaecomastia

### Thorough history

- Commonly, gynaecomastia is asymptomatic.
- Onset and duration of breast enlargement.
- Tenderness.
- Presence of sexual dysfunction.
- Medication history.
- Any use of drugs of abuse – eg, anabolic steroids, alcohol, heroin and marijuana.
- Past medical history, family history.

### Examination

- Is it true enlargement of breast tissue? Enlargement of breast tissue may represent adipose tissue (pseudogynaecomastia) or true proliferation of breast tissue. This can be examined by pinching breast tissue between the thumb and forefinger – true proliferation can be felt as a distinct disc of tissue under the skin. If there is any doubt ultrasonography or mammography may help.
- Size and asymmetry.
- Any evidence of liver disease or renal impairment – eg, [palmar erythema](#), bruising, [spider naevi](#), [hepatomegaly](#).

- Evidence to suggest lack of testosterone – eg, hairless, shiny skin, testicular size, testicular masses, tenor of voice.
- Presence or absence of sexual characteristics.
- Signs of [hyperthyroidism](#) or [Cushing's syndrome](#).

## Investigations<sup>[4]</sup>

These should be performed on a clinical basis, ie according to the history and examination. For example, if the patient is on gynaecomastia-inducing medication then these tests may not be necessary.

### Blood tests

Blood tests are not indicated in those with fatty breast enlargement, physiological pubertal or senile changes, an identified drug cause, or a clinically apparent cancer.

- Renal function.
- LFTs.
- TFTs.
- Hormone profile:
  - Estradiol.
  - Testosterone.
  - Prolactin.
  - Beta-hCG level.
  - Alpha-fetoprotein (AFP).
  - Luteinising hormone (LH):
    - LH high and testosterone low – indicates testicular failure.
    - LH and testosterone both low – indicates increase in oestrogens.
    - LH and testosterone both high – androgen resistance or neoplasm secreting gonadotrophins.
- Chromosomal karyotyping may need to be considered.

## Imaging

- Ultrasonography or mammography of breasts in all cases of suspicious or unilateral breast enlargement. Also if there is clinical doubt about whether there is gynaecomastia or fatty enlargement.
- Ultrasonography of testes if there is any abnormality on examination, or if there is a raised beta-hCG or AFP.
- CXR if a lung lesion is suspected.

## Biopsy

- Needle core biopsy for those with suspicious clinical or radiological findings.
- Biopsy will provide a definitive diagnosis – eg, proliferation of ductules and loose connective tissue confirms gynaecomastia.

If no underlying cause is found, it is said to be idiopathic.

## Gynaecomastia and male breast cancer<sup>[1]</sup>

See the separate [Male Breast Cancer](#) article.

- Male breast cancer is uncommon. It accounts for less than 1% of all breast cancer, around 400 cases per year in the UK compared to 55,000 in women<sup>[8]</sup>. Breast cancer is only diagnosed in around 1% of cases of male breast enlargement<sup>[4]</sup>.
- Mean age of male breast cancer is 65 years – but it can occur at any age.
- There is increased risk in Klinefelter's syndrome (58-fold higher risk) and treatment with oestrogens, such as in gender change.
- Levels are also increased with a positive family history and breast cancer risk genes – eg, BRCA1 and BRCA2.
- A history of ionising radiation increases risk.



- **Red flags which increase suspicion of breast cancer in men:**
  - Unilateral enlargement.
  - Hard or irregular breast tissue.
  - Rapidly enlarging.
  - Recent onset.
  - Fixed mass.
  - Nipple or skin abnormalities.
  - Painful.
  - >5 cm.
  - Axillary lymphadenopathy.

In these cases, imaging and needle core biopsy will usually be required<sup>[4]</sup>. Refer to a local 'one-stop' breast clinic if there is any doubt or suspicion of a sinister cause.

## Management

- Refer any man with red flag symptoms, as mentioned under 'Gynaecomastia and male breast cancer', above. Also refer if the underlying cause is unclear and/or gynaecomastia is causing significant distress to the patient.
- Intervention choice will depend on the aim, be it alleviation of tenderness, cosmetic appearance, anxiety regarding cause, or treatment of underlying disease<sup>[6]</sup>. Early phases are more amenable to treatment; once fibrosis has occurred, surgery may be the only option.
- Treat the underlying cause if found - eg, removal of the offending medication, or androgen replacement in testicular failure. Gynaecomastia associated with obesity may respond to weight loss although breast tissue usually remains.
- Reassurance may be sufficient if gynaecomastia is asymptomatic and no sinister cause has been discovered.

- Of the medical treatments used, tamoxifen is the most effective, particularly for pain in acute gynaecomastia. It is effective because of its anti-oestrogen effect. It may be used if physiological or medication-induced gynaecomastia is painful<sup>[1]</sup>. Other medications which have been used, with limited evidence of benefit, are danazol, raloxifene and clomifene.
- If no underlying cause is discovered or gynaecomastia is long-standing with development of fibrosis then surgical removal of breast tissue is the only effective therapy. Surgery involves subcutaneous mastectomy or liposuction-associated mastectomy. Surgery can be associated with nipple inversion, nipple necrosis, painful scar tissue and possible sensory changes. It is considered an option only where medical treatment has failed or side-effects are unacceptable, there is malignancy, if gynaecomastia is long-standing, where symptoms are severe or if the condition is causing considerable distress, irrespective of size. Surgical complications can be minimised by the use of minimally invasive surgery and cosmetic techniques<sup>[9]</sup>.
- In prostatic carcinoma the development of gynaecomastia is a common reason for poor treatment adherence<sup>[10]</sup> <sup>[11]</sup>. Prophylactic breast irradiation prior to starting treatment with androgen deprivation therapy has been used with good results. However, tamoxifen has been shown to be more effective both for prophylaxis and treatment<sup>[12]</sup>.

## Prognosis

- Gynaecomastia is mostly a benign condition.
- Complete resolution can occur if the underlying cause is identified and treatment initiated before fibrosis of breast tissue occurs.
- Gynaecomastia can be physically embarrassing and psychologically distressing for patients and this should not be underestimated.

---

## Further reading

- [Aslan O, Bayraktaroglu S, Cinkooglu A, et al](#); Prevalence of Incidental Gynecomastia by Chest Computed Tomography in Patients with a Prediagnosis of COVID-19 Pneumonia. *Eur J Breast Health*. 2021 Mar 31;17(2):173-179. doi: 10.4274/ejbh.galenos.2021.6251. eCollection 2021 Apr.
- [Acharya SV](#); Clinical features, presentation and hormonal parameters in patients with pubertal gynecomastia. *J Family Med Prim Care*. 2021 Feb;10(2):648-651. doi: 10.4103/jfmpc.jfmpc\_1987\_20. Epub 2021 Feb 27.

**Disclaimer:** This article is for information only and should not be used for the diagnosis or treatment of medical conditions. Egton Medical Information Systems Limited has used all reasonable care in compiling the information but makes no warranty as to its accuracy. Consult a doctor or other healthcare professional for diagnosis and treatment of medical conditions. For details see our [conditions](#).

Authored by:	Peer Reviewed by: Dr Hayley Willacy, FRCGP	
Originally Published: 20/11/2023	Next review date: 21/07/2021	Document ID: doc_1301

View this article online at: [patient.info/doctor/gynaecomastia](http://patient.info/doctor/gynaecomastia)

Discuss Gynaecomastia and find more trusted resources at [Patient](#).



To find out more visit [www.patientaccess.com](http://www.patientaccess.com)  
or download the app



Follow us

