Introduction

Gynaecomastia is defined as the benign enlargement of male breast tissue, resulting from a proliferation of the glandular component of the breast. Firm subareolar gland and ductal tissue will be palpable on examination, as opposed to breast enlargement caused by excess adipose tissue, which is referred to as pseudogynaecomastia.

Gynaecomastia is common, with an incidence of more than 30%. It can occur at any age and may be physiological or pathological. It results from relative oestrogen excess or relative testosterone deficiency resulting in a high oestrogen-to-testosterone ratio.

Physiological gynaecomastia occurs in the newborn period, during puberty, and with ageing and obesity. Gynaecomastia is more common in men aged over 50, owing to the general decline in testosterone levels and a tendency towards weight gain in later life. In overweight men, breast tissue is stimulated by excess oestrogen resulting from the conversion of testosterone to oestradiol by the enzyme aromatase found in adipose tissue.

Many drugs, environmental exposures, illnesses, and some genetic conditions increase the risk for gynaecomastia.

Pathological gynaecomastia

Any condition or medication associated with low levels of testosterone (whether true reduction or due to high SHBG levels), significant conversion of testosterone to oestrogen, or raised oestrogen levels can result in gynaecomastia.

Symptoms and signs

Being aware of the causes of gynaecomastia will assist with appropriate history-taking and examination. It is important to ascertain the duration and course of symptoms, and note any history of sexual dysfunction as well as medications and any recreational drugs, especially alcohol (as a risk factor for cirrhosis) and anabolic steroids.

Gynaecomastia is often asymptomatic, but can present with tenderness or nipple irritation. Ideally, breast examination should be carried out with the patient at 45 degrees. The breast disc sits behind the areola. It can be palpated using the flat of the fingers.

A general physical examination should also be undertaken to look for signs of hyperthyroidism, chronic liver disease and hypogonadism, and include measurement of BMI. Testicular examination should be done to assess size, because small testicles suggest hypogonadism, and to check for masses or abnormal consistency, suggestive of testicular cancer.

Gynaecomastia is usually bilateral and although about 10% of cases can involve just one breast, always consider the possibility of breast cancer in a unilateral presentation.

If an unusual mass, distorted nipple or areola, skin abnormality or axillary lymphadenopathy are found, the patient should be referred urgently to the breast cancer clinic.
Medicines Associated with Causing Gynaecomastia

<table>
<thead>
<tr>
<th>Medicines frequently causing gynaecomastia</th>
<th>Medicines possibly causing gynaecomastia</th>
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<tbody>
<tr>
<td><strong>Antiandrogens</strong></td>
<td>Bicalutamide, flutamide, finasteride, dutasteride</td>
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<tr>
<td><strong>Antihypertensive</strong></td>
<td>Spironolactone</td>
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<tr>
<td><strong>Antiretroviral</strong></td>
<td>Protease inhibitors (saquinavir, indinavir, nelfinavir, ritonavir, lopinavir), reverse transcriptase inhibitors (stavudine, zidovudine, lamivudine)</td>
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<tr>
<td><strong>Environmental exposure</strong></td>
<td>Phenothrin (antiparasitical)</td>
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<tr>
<td><strong>Exogenous hormones</strong></td>
<td>Oestrogens, prednisone (male teenagers)</td>
</tr>
<tr>
<td><strong>Gastrointestinal drugs</strong></td>
<td>H2 histamine receptor blockers (cimetidine)</td>
</tr>
<tr>
<td><strong>Antipsychotic (first generation)</strong></td>
<td>Haloperidol, olanzapine, paliperidone (high doses), risperidone (high doses), ziprasidone</td>
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In drug-induced gynaecomastia, the offending agent should be withdrawn. Where an underlying disorder has been identified, treating the condition should result in resolution of the gynaecomastia, especially if onset is recent.

**Investigations**

Further investigation will depend on history and examination findings. Blood tests are not necessary in pubertal boys or in men on medications associated with gynaecomastia.

If the underlying cause is not obvious, appropriate baseline blood tests would include liver function, thyroid function and renal function. If these are normal, consider a hormone blood screen, which might include testosterone, luteinising hormone (LH), follicle stimulating hormone (FSH), oestradiol, sex hormone binding globulin (SHBG) (to allow estimation of free testosterone levels), and prolactin. **Referral to endocrinology is recommended in the event of any abnormality.**

If the history or examination is suggestive of testicular malignancy, check levels of β human chorionic gonadotrophin (β-hCG), α-fetoprotein, and lactate dehydrogenase.

<table>
<thead>
<tr>
<th>Hormone test result</th>
<th>Possible diagnoses</th>
</tr>
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<tbody>
<tr>
<td>All normal</td>
<td>Idiopathic gynaecomastia</td>
</tr>
<tr>
<td>Low testosterone with elevated LH</td>
<td>Primary hypogonadism; Klinefelter’s syndrome</td>
</tr>
<tr>
<td>Low testosterone with normal LH</td>
<td>Pituitary/hypothalamic disease</td>
</tr>
<tr>
<td>Elevated testosterone with elevated oestradiol</td>
<td>Androgen exposure; testicular tumour</td>
</tr>
<tr>
<td>Elevated oestradiol with elevated SHBG</td>
<td>Oestrogen exposure; testicular/adrenal tumour</td>
</tr>
<tr>
<td>Elevated DHEA</td>
<td>Adrenal tumour</td>
</tr>
<tr>
<td>Elevated β-hCG</td>
<td>Testicular/ectopic tumour</td>
</tr>
<tr>
<td>Elevated prolactin</td>
<td>Pituitary tumour; drug-related cause</td>
</tr>
</tbody>
</table>

If there is testicular pain or a mass, testicular ultrasound is indicated and chest X-ray should be performed if lung cancer is suspected.

Approved: September 2016 (minor amendment May 2018), Review: September 2019
Management

If an unusual mass, distorted nipple or areola, skin abnormality or axillary lymphadenopathy are found, the patient should be referred urgently to the breast cancer clinic.

Men with pathological gynaecomastia should be considered for referral to the appropriate specialist.

The clinical course of gynaecomastia is proliferation of glandular tissue followed by fibrosis (thickening of tissue). If clinically the breast tissue feels fibrotic then treating the cause or stopping the implicated drug may stop progression but is unlikely to reduce the excess breast tissue. It is not often possible to predict in which patients gynaecomastia will resolve and who will experience progression to the fibrotic stage.

If the underlying cause is still unclear after primary care investigations, the GP may wish to consider referring the patient to the breast clinic. A quarter of cases turn out to be idiopathic.

Drug Treatment of Gynaecomastia

In patients with physiological gynaecomastia, especially adolescent boys, reassurance can be given that most cases are transitory, with more than 90% resolving within three years.

Medical management is associated with a high success rate and avoids surgical intervention, but once fibrosis occurs it is largely ineffective. Tamoxifen (an oestrogen-receptor antagonist), although widely used for the treatment of gynaecomastia, is not licensed for this indication. However good response rates have been seen and it is therefore recommended by local clinicians.

**Tamoxifen 20mg od for 3 months** is recommended. Treatment should be stopped after 3 months whether a response is seen or not. It is important to inform patients that it is being used ‘off-label’. The use of tamoxifen for this indication is classified as Amber 3.

Monitoring of Drug Treatment

There are no suggested monitoring parameters specific to these medicines for this indication in male patients. The short term nature of usage (3 months) would suggest that monitoring for any possible effects on bone density would be unnecessary.

When to Refer

Referral for male gynaecomastia falls under the 2 week wait process. Referral to the Breast Clinic for further assessment is indicated in those with:

- a clinical suspicion of malignancy
- no obvious physiological or drug-related cause
- a unilateral lump
- persistent pain and swelling
- increased risk such as family history; Klinefelter’s syndrome; androgen deficiency or oestrogen excess

If endocrinological abnormalities are suspected then they should be referred to the Nottingham Endocrine Service at Nottingham Treatment Centre.
**Surgery**

The East Midlands Commissioning Policy for Cosmetic Procedures has strict criteria for access to surgery for gynaecomastia. CCGs will only commission male breast reduction surgery when ALL the following criteria are met:

1. Sexual maturation has been reached.
2. In cases of idiopathic gynaecomastia in men under the age of 25 then a period of at least 2 years has been allowed for natural resolution
3. Screening has been undertaken, prior to referral, for endocrinological and drug related causes.
4. Non-surgical treatments have been tried and have been unsuccessful
5. BMI as measured by the NHS is between 18 and 25 and has been within this range for 1 year as measured and recorded by the NHS
6. Confirmed non-smoker and/or documented abstinence prior to procedure
7. Photographic evidence

Within the policy it states that non-surgical treatments (ie weight loss and medication) have been tried.

Surgical removal may involve liposuction or subcutaneous mastectomy. The risks of surgery include haematoma, infection, scarring, sensory changes, breast asymmetry and a poor cosmetic result.

**Reference**