Purpose
These guidelines are for the assessment, referral, and investigation of men with breast symptoms consistent with gynaecomastia, and cover the process from primary care to the specialist clinics of the Breast Unit and Endocrinology. They take into account the Best Practice Diagnostic Guidelines for Patients Presenting with Breast Symptoms from 2010.

Background
Gynaecomastia is the enlargement of the male breast due to hyperplasia of the glandular tissue driven by alterations in male oestrogen:testosterone ratios. Pseudogynaecomastia is bilateral breast enlargement entirely due to adipose tissue. It does not require investigation or treatment.

Male breast cancer accounts for about 0.6% of all breast cancer: there almost 400 cases annually in the UK (c.f. 55,000 in women).
Benign gynaecomastia can be secondary to multiple medical and recreational drugs, as well as many chronic medical conditions.

- Physiological
  1. Neonatal: due to placental oestrogen transfer
  2. Pubertal: pubertal oestrogen production begins prior to testosterone production due to early maturation of aromatase (catalyzes conversion of androgens to oestrogens). Regression occurs in 90% of cases
  3. Senile: Age 70+. Up to 65% of men. Due to the reduction in testosterone relative to oestrogen

- Drug induced - 10-20% of gynaecomastia is due to prescribed drugs
  1. Oestrogen containing drugs eg. Bicalutamide, Buserelin, Goserelin
  2. Androgen receptor blocking drugs e.g. Cyproterone acetate, spironolactone, flutamide
  3. Androgen production inhibiting e.g. Finasteride, ketoconazole, dutasteride
  4. A list of medications that can cause gynaecomastia can be found in Appendix A

- Drug induced - recreational drugs such as marijuana, amphetamines, heroin, methadone

- Pathological
  1. Adrenal or testicular tumours <3% of gynaecomastia
     a. Oestrogen or androgen producing tumours
     b. Aromatase producing tumours
     c. hCG producing tumours
  2. Endocrine
     a. Primary hypogonadism [10% of gynaecomastia]
     b. Secondary hypogonadism
     c. Prolactinoma
d. Thyrotoxicosis  
e. Acromegaly  
f. Androgen insensitivity

3. Systemic illness  
a. Liver cirrhosis  
b. Renal failure  
c. Malnutrition  
d. Obesity  
e. HIV

**INVESTIGATIONS RECOMMENDED TO BE DONE IN PRIMARY CARE**

Before Referring  
1. History to include:  
   • Prescribed medications  
   • Recreational drug use  
   • Current and previous alcohol consumption

2. Chest wall examination – bilateral breasts

**Do Not Investigate**  
• Adolescents with physiological pubertal gynaecomastia  
• Elderly men with senile gynaecomastia  
• Men with a drug related cause (prescribed medication or recreational drug use)  
• Men with obvious breast cancer  
• Men with fatty pseudogynaecomastia

**Do Investigate**  
• Eccentric hard masses  
• Rapid enlargement  
• Recent onset in lean men >20 years  
• Persistent painful gynaecomastia  
• Massive gynaecomastia in adolescents  
• Persistent gynaecomastia in adolescents, duration > 18-24 months

**WHAT INVESTIGATIONS?**

**Blood tests**  
• 9am Testosterone, Thyroid Function Tests, Liver Function Tests, α-Fetoprotein, β-Human Chorionic Gonadotrophin  
• If Testosterone is abnormal: Luteinizing Hormone, Follicle Stimulating Hormone, Sex Hormone Binding Globulin, albumin, oestradiol, prolactin

• Testicular Ultrasound Scan if any of the following abnormal blood results are noted: raised βHCG, raised α-Fetoprotein

**GPs - WHEN AND WHERE TO REFER**

**Abnormal endocrine (hormonal) blood results**  
• Refer to Medical Endocrinology clinic

**Abnormal βHCG or αFP blood results or abnormal finding on testicular USS**  
• Refer to Urology Clinic urgently
Referral directly to the Breast Unit
In the presence of the following clinical scenarios, a referral directly to the local breast unit may be considered.
1. Clinical suspicion of malignancy
   • >50 year old man with unilateral firm sub-areolar mass with or without nipple discharge or with associated skin change
   • Bloody nipple discharge
   • Unilateral ulceration of the nipple
   • Urgent referral is appropriate
2. Unilateral lump with
   • No obvious physiological or drug cause
   • Increased risk - family history
   • Genetic conditions e.g. Klinfelter’s Syndrome
3. Persistent painful gynaecomastia (>6 months) with normal blood tests

GYNAECOMASTIA IN THE BREAST UNIT
Gynaecomastia does not require all aspects of triple assessment
1. History:
   • Drug history
   • Alcohol history
   • Recreational drug use
   • Steroid use
   • Family history
2. Clinical examination:
   • Chest, bilateral
   • Nodal areas: axillae and supraclavicular fossae
3. Imaging
   • Bilateral pseudogynaecomastia: No imaging
   • Bilateral gynaecomastia P2: No imaging
   • Unilateral lump <25 P2: No imaging
   • Unilateral lump <25 P3+: USS +/- mammogram
4. Pathology
   • Biopsy only if one or more of the following: P3+, M3+, U3+

HORMONAL TREATMENT
The patient must be informed that this treatment is off-licence. It is most effective for recent onset gynaecomastia, i.e. before gynaecomastia becomes fibrotic, and alleviates mastalgia, not always regression of the mass.
   • Tamoxifen 10mg PO OD: 3-9 months.
   • Anastrozole 1mg PO OD: 3 months.

SURGICAL REMOVAL
   • Dependent on local CCG guidelines

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Version: 1
SUMMARY STATEMENT:
MANAGEMENT OF GYNAECOMASTIA IN PRIMARY & SECONDARY CARE

APPENDIX 1

Simon classification for gynaecomastia

- Grade 1: Small enlargement, no skin excess
- Grade 2a: Moderate enlargement, no excess skin
- Grade 2b: Moderate enlargement, with extra skin
- Grade 3: Marked enlargement, with extra skin

REFERENCES

Best Practice Diagnostic Guidelines for Patients Presenting with Breast Symptoms. Department of Health 2010
Gloucestershire Clinical Commissioning Group Policy for Male Breast Reduction for Gynaecomastia. 2015
Wallis M et al. The diagnostic value of clinical examination and imaging used as part of an age-related protocol when diagnosing male breast disease: an audit of 1141 cases from a single centre. Breast 2013 Jun;22(3):268-72
Zonderland HM et al. Overuse of imaging the male breast -findings in 557 patients. Breast J 2015 May-Jun;21(3):219-23
### SUMMARY STATEMENT:
**MANAGEMENT OF GYNAECOMASTIA IN PRIMARY & SECONDARY CARE**


APPENDIX 2

<table>
<thead>
<tr>
<th>DRUGS KNOWN TO CAUSE GYNAECOMASTIA</th>
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<tbody>
<tr>
<td><strong>Antiandrogens</strong></td>
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<tr>
<td><strong>Antihypertensive</strong></td>
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<tr>
<td><strong>Antiretrovirals</strong></td>
</tr>
<tr>
<td><strong>Environmental exposures</strong></td>
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<tr>
<td><strong>Exogenous hormones</strong></td>
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<tr>
<td><strong>Gastrointestinal drugs</strong></td>
</tr>
<tr>
<td><strong>Analgesics</strong></td>
</tr>
<tr>
<td><strong>Antifungals</strong></td>
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<tr>
<td><strong>Antihypertensives</strong></td>
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<tr>
<td><strong>Antipsychotics (1st gen)</strong></td>
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<tr>
<td><strong>Antiretrovirals</strong></td>
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<tr>
<td><strong>Chemotherapy drugs</strong></td>
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<tr>
<td><strong>Exogenous hormones</strong></td>
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<tr>
<td><strong>Cardiovascular drugs</strong></td>
</tr>
<tr>
<td><strong>Recreational/illicit drugs</strong></td>
</tr>
<tr>
<td><strong>Herbals</strong></td>
</tr>
</tbody>
</table>

### DRUGS RARELY CAUSING GYNAECOMASTIA

Amiodarone (um)
Aripiprazole, atorvastatin (um)
Captopril (um), cetirizine, clonidine, cyproterone acetate (ishbg)
Dasatinib, diazepam (ishbg), digoxin (e), domperidone, entecavir, fenofibrate (um)
Fluoxetine (um)
Gabapentin (aa)
Imatinib (aa)
Lisinopril, loratadine (aa)
Metronidazole (aa), misoprostol (um)
Paroxetine (um), penicillamine (aa), phthalates (um), pravastatin (um), pregabalin (aa)
Ranitidine (aa), rosuvastatin (um)
Sulindac, sulpiride, sunitinib (um)
Theophylline (um)
Venlafaxine (um)
### SUMMARY STATEMENT:
MANAGEMENT OF GYNAECOMASTIA IN PRIMARY & SECONDARY CARE

<table>
<thead>
<tr>
<th>Codes</th>
<th>Definition</th>
</tr>
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<tbody>
<tr>
<td>AA</td>
<td>Antiandrogenic</td>
</tr>
<tr>
<td>RA</td>
<td>Reduced androgens</td>
</tr>
<tr>
<td>E</td>
<td>Oestrogenic</td>
</tr>
<tr>
<td>IAM</td>
<td>Increased androgen metabolism</td>
</tr>
<tr>
<td>ISHBG</td>
<td>Increased concentration of sex hormone binding globulin</td>
</tr>
<tr>
<td>IP</td>
<td>Increased prolactin</td>
</tr>
<tr>
<td>UM</td>
<td>Unknown mechanism</td>
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