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October 2013

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**Literature Search Results**

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**Enquiry Details**

What evidence exists for the use of a 2 year watchful waiting period in cases of idiopathic gynaecomastia in men aged under 25.
Male Breast Reduction for Gynaecomastia Surgery to correct gynaecomastia is allowable if the patient is:

Post pubertal and of normal BMI (≤ 25 Kg/m²)

There should be a pathway established to ensure that appropriate screening for endocrinological and drug related causes and/or psychological distress occurs prior to consultation with a plastic surgeon.

Liposuction may form part of the treatment plan for this condition.

Rationale
Commonly gynaecomastia is seen during puberty and may correct once the post-pubertal fat distribution is complete if the patient has a normal BMI. It may be unilateral or bilateral. Rarely it may be caused by an underlying endocrine abnormality or a drug related cause including the abuse of anabolic steroids. It is important that male breast cancer is not mistaken for gynaecomastia and, if there is any doubt, an urgent consultation with an appropriate specialist should be obtained.

www.bapras.org.uk/downloaddoc.asp?id=425
The Basics - GP management of gynaecomastia
By Dr Kamilla Porter, 29 February 2012

Physiological gynaecomastia
Prominent breast tissue in newborn males is extremely common, resulting from transfer of maternal estrogens, and can last several weeks.

About 60% of boys up to the age of 14 years have gynaecomastia which may affect one breast more than the other; by age 20, prevalence is 19%.1


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.

Consider the latter cause in a young man whose family report changes in behaviour and character. A rapid enlargement of breast tissue with no causative drugs would raise the suspicion of a hormone-secreting tumour.

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

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.

For those who remain distressed by their symptoms despite reassurance, tamoxifen 10mg daily for six months could be of benefit. However, it is important to inform patients that this is an unlicensed use.

The impact of gynaecomastia on a patient's social and personal life should not be underestimated. Most regions now have stringent local guidelines limiting cosmetic procedures on the NHS, but where a patient experiences significant pain or profound psychological distress, surgical removal of breast tissue may be undertaken.

References
Best Practice: gynaecomastia. www.bestpractice.bmj.com; last updated September 2011.
Gynecomastia Treatment – Up-to-Date

The best treatment for gynecomastia depends upon its cause, duration, and severity, and whether it causes pain or discomfort.

**Adolescents** — Because pubertal gynecomastia usually goes away on its own, treatment is not usually recommended initially. Instead, the provider will keep close tabs on the condition for several months. In most cases, pubertal gynecomastia resolves during that time.

For boys with severe gynecomastia that is causing substantial tenderness or embarrassment, a short course of a drug called tamoxifen (Nolvadex) or raloxifene (Evista) may be recommended. These drugs block the effects of estrogen in the body and can reduce the size of the breasts somewhat. However, neither of these drugs is approved in the United States for the treatment of gynecomastia. Drugs may be prescribed without FDA approval, although the risks and benefits have not been studied completely.

**Adult men** — Treatment is also usually delayed in adult men whose gynecomastia is likely to be caused by an underlying health problem or by drugs. In these men, treating the underlying condition or suspending the problematic drug usually allows the gynecomastia to resolve.

For men with **idiopathic gynecomastia** that causes discomfort and lasts more than three months, a short course of tamoxifen or raloxifene may be recommended.

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Research

Gynecomastia is defined as benign proliferation of glandular breast tissue in men. Physiologic gynecomastia is common in newborns, adolescents, and older men. It is self-limited, but can be treated to minimize emotional distress and physical discomfort.

Treatment
- Few patients with gynecomastia need treatment for cosmesis or analgesia. 37
- In a study on treatment for gynecomastia, about one-half of men were not significantly bothered by symptoms. 38
- Pain is more common in patients with gynecomastia that is rapidly progressive or of recent onset.
- For patients with nonphysiologic gynecomastia, treatment is directed toward improving the underlying illness or discontinuing use of the contributing.
- Watchful waiting with biannual follow-up is appropriate for those with physiologic gynecomastia who are untroubled by symptoms and who have no features that suggest underlying disease or malignancy.
- Early treatment will maximize benefit in men with significant physical symptoms or emotional distress.
- Medications are more effective if used as early as possible after symptoms are first noted, whereas surgery can be performed at any time with similar results.

www.aafp.org/afp/2012/0401/p716.html

Gynecomastia: When is treatment indicated?
Vol 61, No 12 I December 2012 | The Journal of Family Practice
An algorithmic approach to simplify clinical evaluation and help you decide whether intervention or watchful waiting is appropriate.

Management of gynecomastia
Gynecomastia often results from transient hormonal imbalance and regresses spontaneously. Therefore, no specific treatment is necessary for neonatal, pubertal, or drug induced gynecomastia. In other situations, prompt diagnosis and treatment are important important to maximize the likelihood of successful medical therapy. It has been shown that fibrosis develops 6 to 12 months after the onset of gynecomastia, making it unlikely that medical treatments beyond that stage will result in significant regression of the breast enlargement.” In such long-standing cases, surgical intervention with subcutaneous mastectomy or liposuction can be considered for patients who have significant psychological problems or esthetic issues. Indications for surgery also include continued growth and tenderness of breast tissue or malignancy.

REQUEST FROM LKRS

The aim of this review is to discuss the pathophysiology, etiology, evaluation and therapy of GM. A hormonal imbalance between estrogens and androgens is the key hallmark of GM generation. The etiology of GM is attributable to physiological factors, endocrine tumors or dysfunctions, non-endocrine diseases, drug use or idiopathic causes. Clinical evaluation must address diagnostic confirmation, search for an etiological factor and classify GM into severity grades to guide the treatment. A proposal for tailored therapy is presented. Weight loss, reassurance, pharmacotherapy with tamoxifen and surgical correction are the therapeutic options. For long-standing GM, the best results are generally achieved through surgery, combining liposuction and mammary adenectomy.

Pubertal GM Mild degrees of pubertal GM generally appear at 13 or 14 years of age, last for 6-12 months and then spontaneously regress in 95% of the cases.13 The glandular enlargement may be asymmetric and tender. The hypertrophy may reach severe proportions, leading to an effeminate appearance in boys. Such occurrences may alter self-perceptions, especially in the sexual sphere.34 Relative excess of serum levels of estrogens compared with androgens is implicated in the pathogenesis, due to estradiol production rising sooner than testosterone production. Some other factors may also interact, and usually there is concomitant elevation in serum IGF-1 concentrations. Interestingly, a family history has been elicited in more than half of the patients with persistent pubertal GM.17,34

Idiopathic GM So far, at least 20 clinical conditions and 30 medications have been implicated in relation to causing GM. However, the etiology of GM is still only understood to a limited extent, and up to 50% of the cases may have no obvious cause.33 Given the high frequency of idiopathic GM, we hypothesize that multiple environmental endocrine disruptors are likely to be involved in excessive breast development in men.

TREATMENT General measures
If the GM is slight, without noteworthy psychological repercussion and the appropriate work-up does not reveal any underlying disease and only shows weight loss, reassurance and periodic follow-up visits (every 3-6 months) are recommended. Reassurance is widely regarded as the safest and most reasonable form of treatment, given that the condition is usually self-limiting and asymptomatic.58

For mild enlargements in pubertal boys, the simplest therapeutic approach is verbal explanation and reassurance regarding the signs and symptoms. Reassurance should be based on full and authoritative explanations about the common transient hormonal imbalance at this age, the natural involution of the condition and the absence of later sexual and fertility effects.3-13

Although fibroglandular overgrowth may also be present, this is typically overwhelmed in obese boys by the surrounding fat accumulation. For this reason and, equally as important, for other developmental and psychological reasons, a weight loss program (diet and physical exercises) should be the first-line treatment.

If possible, any causative medications or anabolic agents should be immediately withdrawn. Ceasing to use the offending agent may result in regression of GM. If GM either persists or becomes more severe and is associated with pain, psychological distress or embarrassment caused by avoidance of activities in which the chest is exposed, pharmacological and surgical therapeutic options should be considered, especially when the patient wishes to pursue treatment.17

REQUEST FROM LKRS
Department of Breast & Reconstructive Surgery, The Leeds Teaching Hospitals Trust, Great George Street, Leeds, United Kingdom. rahmanisamir@hotmail.com
Gynecomastia is a benign enlargement of male breast glandular tissue. At least a third of males are affected at some time during their lifetime. Idiopathic causes exceed other etiologies and relate to an imbalance in the ratio of estrogen to androgen tissue levels or end-organ responsiveness to these hormones. Assessment must include a thorough history and clinical examination, specific blood investigations and usually tissue sampling and/or breast imaging. Management consists of a combination of measures that may include simple reassurance, pharmacological manipulation, medical treatment or surgery. Hormone therapy may help to abort the acute proliferative phase of gynecomastia with a 30% response rate but should not be considered in chronic established cases. Surgical treatment may comprise simple liposuction for a predominant fatty component or direct excision when glandular tissue is predominant. The main aim is to control the patient's symptoms and to exclude other etiological factors.

MEDICAL TREATMENT OF GYNAECOMASTIA
The first principle of treatment for suspected iatrogenic gynecomastia is the withdrawal of any nonessential drug therapy (or change to an alternative) in cases of ongoing pharmacologic-induced gynecomastia. Reassurance alone is all that is needed for most cases of physiologic gynecomastia as they are often transient. In adolescents, with normal hematological screening tests, active monitoring for a period of 12–24 months will suffice for most, and intervention reserved for those that fail to regress spontaneously after 2-years. Because gynecomastia is usually caused by an imbalance of androgenic and estrogenic effects on the breast, medical therapies have traditionally involved anti-estrogens, androgens, or Aromatase Inhibitors to block or lower the estrogen level. Tamoxifen is an estrogen antagonist. It is a treatment associated with a good safety profile which is relatively nontoxic and well tolerated (32). It rapidly relieves associated tenderness (33). It should be considered as a first line treatment for cases of acute gynecomastia that fail to resolve spontaneously and are symptomatic. The typical dose of Tamoxifen that has been used in men in various trials range from (10– 20 mg /po /od) for 2–4 months (34). It is less effective in established or chronic gynecomastia.

REQUEST FROM LKRS

Approach to the patient with gynecomastia. Carlson HE. Journal of Clinical Endocrinology & Metabolism, 2011, vol./is. 96/1(15-21)
Gynecomastia is a common and sometimes distressing condition that may occur in males of all ages. Although most cases have benign causes and many are self-limited, male breast enlargement may also be a sign of underlying systemic disease or drug toxicity. Although rare, male breast cancer must also be considered in the differential diagnosis. A careful diagnostic evaluation should be pursued, tailored to the individual patient's circumstances. Treatment may include reassurance, medication, or surgery. Teenage boys with pubertal gynecomastia can usually be observed, with the expectation that the gynecomastia will spontaneously resolve over 1–2 yr in most cases (26).


REQUEST FROM LKRS
Gynecomastia: pathophysiology, evaluation, and management.
Mayo Clinic Proceedings, 2009, vol./is. 84/11(1010-5). Johnson RE, Murad MH
Gynecomastia, defined as benign proliferation of male breast glandular tissue, is usually caused by increased estrogen activity, decreased testosterone activity, or the use of numerous medications. Although a fairly common presentation in the primary care setting and mostly of benign etiology, it can cause patients considerable anxiety. The initial step is to rule out pseudogynecomastia by careful history taking and physical examination. A stepwise approach that includes imaging and laboratory testing to exclude neoplasms and endocrinopathies may facilitate cost-effective diagnosis. If results of all studies are normal, idiopathic gynecomastia is diagnosed. The evidence in this area is mainly of observational nature and lower quality.

REQUEST FROM LKRS

Catherine B Niewoehner, Anna E Schorer BMJ 2008;336:709-13
When is gynaecomastia physiological? 
Overall, 65-90% of neonates have breast tissue, which results from the transfer of maternal and placental oestrogen and progesterone and persists up to several months.
By age 14 up to 60% of boys have gynaecomastia. This usually resolves within one or two years (table 1). At puberty, surges of luteinising hormone and follicle stimulating hormone in conjunction with growth hormone and insulin-like growth factor-1 stimulate testosterone production in Leydig cells. Oestrogen concentrations increase threefold, peaking earlier than testosterone concentrations that eventually increase up to 30-fold. Whether gynaecomastia results from the relative delay in full testosterone production, a temporary increase in aromatase activity, varying sensitivity to oestrogen, or all of these is uncertain.
Gynaecomastia increases with age as free testosterone levels decline and obesity becomes more common.1


In an unselected group of men admitted to hospital, the prevalence and diameter of breast enlargement was highly correlated with increasing body mass index.2 Autopsy studies have found gynaecomastia in 40-55% of unselected cases.3

When and how should gynaecomastia be treated? 
Physiological gynaecomastia requires no treatment unless accompanied by pain or significant embarrassment. Withdrawing an offending drug or treating an underlying disorder may be sufficient, especially if gynaecomastia is relatively recent.

REQUEST FROM LKRS
Gynecomastia in adolescents.
Nordt CA, DiVasta AD

PURPOSE OF REVIEW: Gynecomastia is a common finding in adolescent men. The primary care provider should feel equipped to thoroughly evaluate this condition and to differentiate physiologic from pathologic breast enlargement. The present review focuses on the epidemiology, pathogenesis, evaluation, and treatment of gynecomastia during adolescence.

RECENT FINDINGS: While gynecomastia has long been attributed to an imbalance between estrogen and androgen concentrations, recent literature has begun to illuminate other potential mechanisms for breast development in adolescent men. Increased leptin levels, as well as human chorionic gonadotropin and luteinizing hormone receptors on male breast tissue, may play a role. Newer treatment strategies, such as the antiestrogen raloxifene, have shown promising results; however, further studies are needed to determine long-term efficacy. As a result of the limited pharmaceutical treatment options, many more adolescents are seeking surgical intervention.

SUMMARY: Gynecomastia is frequently encountered in the primary care setting. During adolescence, male breast enlargement is most often benign and rarely represents a pathologic mechanism. Careful attention should be paid to both the breast and testicular examination. A detailed history should include an inquiry regarding the use of illicit substances, anabolic-androgenic steroids, herbal products, and medications. The impact of gynecomastia on the adolescent's mental health should be assessed. A workup for pathologic causes is rarely required. Reassurance remains the standard of care for physiologic gynecomastia.

Clinical practice. Gynecomastia.
Braunstein GD, New England Journal Of Medicine, 2007; 357, Issue 12

Conclusions and Recommendations
Asymptomatic gynecomastia is a relatively common finding on physical examination, and a careful history taking and physical examination are usually sufficient to identify pubertal gynecomastia, drug-induced causes, or an underlying pathologic process, with the possible exception of mild hypogonadism.

Pubertal gynecomastia resolves with time in the majority of adolescent boys, and reassurance and follow-up physical examination usually suffice.

In adults who present with the acute onset of painful gynecomastia without an obvious cause, hormonal evaluation, including measurements of serum hCG, testosterone, luteinizing hormone, and estradiol levels, should be performed in order to rule out serious and treatable causes, although serious disease is unlikely in this setting. During the acute florid stage of gynecomastia, a trial of tamoxifen, at a dose of 20 mg per day for up to 3 months, may be attempted.
Gynecomastia: Its features, and when and how to treat it
Cleveland Clinic Journal of Medicine Volume 71 • Number 6 June 2004
Gynecomastia is common, being present in 30% to 50% of healthy men. A general medical history and careful physical examination with particular attention to features suggestive of breast cancer often suffice for evaluation in patients without symptoms or those with incidentally discovered breast enlargement. Men with recent-onset gynecomastia or mastodynia need a more detailed evaluation, including selected laboratory tests to search for an underlying cause. Treatment depends on the cause and may include observation, withdrawal of an offending drug, therapy of an underlying disease, giving androgen or antiestrogen drugs, or plastic surgery.

Puberty.
Gynecomastia may occur in 48% to 64% of boys at puberty. It may first appear as early as 10 years of age, with a peak onset between ages 13 and 14, followed by a decline in late teenage years.
There are periods during puberty when the balance of sex hormone secretion favors estrogen, despite an increase in androgen production. This ratio returns to more normal adult values as puberty advances. The condition is usually asymptomatic and self-limited and regresses spontaneously after about 2 years.

REQUEST FROM LKRS

BACKGROUND: The purpose of the present paper was to review the management of men referred to a breast clinic with presumed gynaecomastia.
METHODS: A retrospective analysis was carried out of 175 men over the age of 16 years who presented with breast enlargement and/or 'lumps', during a 7-year period to a single-surgeon. All patients had complete biochemical assessment (liver function tests, gamma-glutamyl transferase, prolactin, alpha-fetoprotein, beta-human chorionic gonadotropin), and mammography and/or ultrasound with fine-needle biopsy if indicated.
RESULTS: One hundred and seventy-five men, median age 44 years (range: 18-89 years), were assessed. Thirty-nine had bilateral true gynaecomastia and 88 had unilateral gynaecomastia (53% left). Carcinoma of the breast was diagnosed in eight, pseudo-gynaecomastia in 18, 13 had physiological pubertal changes only and nine had other diagnoses. Adverse drug reactions were possibly implicated in the aetiology of 47 patients, alcohol in seven patients, cannabis in one patient, testicular malignancy in four patients and hepatocellular carcinoma in one patient. Five patients were found to have hyperprolactinaemia. Twenty-four per cent of patients were reassured without intervention; 18% failed to attend follow up. Sixteen per cent were treated with danazol, 15% underwent surgery and 28 were referred for management of their cause. Danazol was effective in 81%, and three patients required surgery when danazol was ineffective. One further patient developed testicular cancer 9 months after presentation.
CONCLUSION: Men presenting to a breast clinic require clinical assessment to exclude diagnoses other than gynaecomastia. True gynaecomastia can be managed with exclusion of causative factors by non-invasive investigation and examination. Many patients can be reassured as to the idiopathic nature of the condition and many will fail to attend follow up. Danazol is successful in some patients and surgery should be reserved for resistant cases.
**Pubertal gynecomastia.** Journal of Pediatric Endocrinology, 2002, vol./is. 15/5(553-60)
Lazala C, Saenger P

Gynecomastia is a benign condition in males, characterized by proliferation of glandular elements resulting in concentric enlargement of one or both breasts. During puberty, there is often a transient relative imbalance between estrogen and testosterone, leading to gynecomastia. This condition usually resolves by age 18 years when adult androgen/estrogen ratios are achieved. Laboratory evaluation should include testosterone, estradiol, and gonadotropins; karyotype should be obtained in pubertal patients with testes volumes less than 6 ml. The mainstay in treatment of pubertal gynecomastia is still sympathetic reassurance considering the benign nature of the condition. Surgical removal of the breast glandular tissue should be considered in boys who have had persistent pubertal gynecomastia and have completed or nearly completed puberty.
Examples of localised commissioning documents

North West London Commissioning Support Unit - Gynaecomastia

North West London Commissioning Support Unit on behalf of eight Clinical Commissioning Groups in North West London (Brent CCG, Central London CCG, Ealing CCG, Hammersmith and Fulham CCG, Harrow CCG, Hillingdon CCG, Hounslow CCG and West London CCG).

NHS NWL CCGs will not routinely fund gynaecomastia surgery because it is considered as a cosmetic procedure.

Gynaecomastia is a benign condition of the male breast. In most cases a thorough history and physical examination, along with laboratory investigations, should help to exclude breast malignancy and any serious underlying endocrine or systemic disease, as well as to identify pseudogynaecomastia. Careful clinical observation may then be all that is necessary, because gynaecomastia often resolves spontaneously, especially in the case of adolescence, with regard to pubertal gynaecomastia.

There is a lack of consensus as to the non-surgical management of gynaecomastia. Because gynaecomastia is usually caused by an imbalance of androgenic and estrogenic effects on the breast, medical therapy may include anti-oestrogens, such as tamoxifen (unlicensed indication), androgens or aromatase inhibitors. However, although idiopathic gynaecomastia is highly prevalent, there is no proven medical therapy for this condition and the quality of the medical research for pharmaceutical agents is very poor.

Psychological support may be important in relation to reassurance, especially in view of the social pressure on young men around body image and so-called “man boobs”.

Gynaecomastia may have an extrinsic cause in up to 39% of cases. Of the suspected idiopathic cases, some will be found to have an important aetiology, such as testicular carcinoma. Selected endocrinological investigation is therefore important to address such aetiology.

There are at least 69 drugs that are known to be associated with gynaecomastia. Patients who are on medication that may cause gynaecomastia may not always be able to have that medication stopped, for example: anti-androgens as a monotherapy for prostate cancer. Furthermore, withdrawal of the medication may not always be associated with resolution of the gynaecomastia.

REQUEST FROM LKRS
NHS Hull Commissioning Statement - Gynaecomastia

Where the request for male breast reduction is deemed cosmetic, with no clear evidence that glandular breast tissue is present, as with other cosmetic procedures to improve appearance, such requests will NOT be routinely funded.

(Liposuction may be involved in the surgical treatment of gynaecomastia along with excision of breast tissue, but a request solely for liposuction of fatty tissue in the breast will be deemed cosmetic and will not be routinely approved.)

Surgery for Gynaecomastia

Surgical correction of unilateral or bilateral gynaecomastia is only considered in exceptional individual (non-cosmetic) cases in post-pubertal adolescents and men where ALL of the following apply:

- if there are red flag symptoms for suspecting possible underlying breast malignancy, evidence that this has been excluded (breast cancer is only detected in 1% of cases of male breast enlargement)
- AND true gynaecomastia has been diagnosed (ie. true breast tissue is present not just adipose tissue - pseudogynaecomastia)
- AND evidence that treating the underlying cause, where known, has not resolved the problem
- AND there is clear evidence of clinical need (such as significant pain - unresolved by analgesia
- OR significant psychological distress supported by documented evidence of a valid psychological assessment and interventions, together with a clear statement from a relevant healthcare professional that they support and recommend the requested treatment

Patients should be made aware that surgery can be associated with nipple inversion, nipple necrosis, painful scar tissue and possible sensory changes.

General

Assuming the patient meets the criteria outlined above, the referring clinician should complete the standard pro-forma, ensuring all information required is included. Additional supporting information that would help the decision making process is as follows:

- if aged < 20, a clinical view of whether full body maturity has been reached (because enlarged breasts in young men may resolve once post pubertal fat distribution is completed)
- details of any screening for an endocrine or drug related cause of the gynaecomastia (it is acknowledged however that an underlying cause is found in less than 50% of patients).
- current BMI and stability of body weight (plus previous weight loss if linked to obesity)
- details of associated functional and / or medical problems and treatment to date
- details of psychological problems (with supporting evidence) and treatment to date

Refs:

http://www.patient.co.uk/doctor/Gynaecomastia.htm

Information for Commissioners of Plastic Surgery Services - Referrals and Guidelines in Plastic Surgery (NHS Modernisation Agency)

REQUEST FROM LKRS