HIRSUTISM: AN OVERVIEW

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Abstract:

Hirsutism is defined as the excessive growth of terminal hair on the face and body of a female in a typical male pattern distribution. Hirsutism is a common clinical problem in women and the treatment depends on the cause of hirsutism. Untreated hirsutism can be associated with considerable loss of self-esteem and psychological morbidity. Hyperandrogenemia is the key trigger for excess hair growth. Polycystic ovary syndrome and idiopathic hirsutism are the most common cause of hirsutism. As with all medical problems, investigation begins with a careful history, examination and then investigation directed at the possible cause. A raised serum testosterone level of > 150 mg/dl (5.2 nmol/l) should prompt further investigations to exclude an underlying androgen-secreting tumour. The treatment of hirsutism is most effective using combination therapy, including lifestyle therapies, androgen suppression, peripheral androgen blockage and cosmetic treatments. Women should be warned not to expect improvement or at least 3–6 months after therapy is begun and lifelong therapy may be needed to prevent recurrence. The current review discusses definition, pathogenesis, differential diagnosis, diagnostic strategies, management, guidelines and the authors' recommendations about hirsutism.

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Definition:

The individual woman's definition of hirsutism may differ depending upon her ethnic background and upon her interpretation of normal. Hair growth varies widely among women, and distinguishing normal variations of hair growth from hirsutism is important[1,2]. Most Asian and Native American women have little body hair, while Mediterranean women on average have moderately heavy body hair[3]. Hirsutism is the development of androgen-dependent terminal body hair in a woman in places in which terminal hair is normally not found. Terminal body hairs are normally seen in men on the face, chest, abdomen and back, and which are not normal in women[1,4]. Hirsutism is a common disorder and usually of benign a etiology affecting between 5% and 10% of women of reproductive age in the general population. The presence of hirsutism is extremely distressing to patients, with a significant negative impact on their psychosocial development; 70–80% of hirsute patients have hyperandrogenism conditions such as polycystic ovary syndrome and androgen-secreting tumours rather than an isolated disorder[5-7].

Pathogenesis:

Before puberty, hair is vellus (small, straight, fair and non-pigmented), and the sebaceous glands in androgen- sensitive follicles are small. Sex steroids and a number of local and systemic factors can act directly and indirectly on the dermal papilla to regulate hair growth. In response to the increased levels of androgens at puberty, vellus follicles in specific areas develop into terminal hairs (larger, curlier and darker, hence more visible)[4,6]. Androgens increase hair follicle size, hair fibre diameter, the proportion of time terminal hairs spend in the anagen (growth) phase and sebum secretion. Therefore, not only do androgens alter the type of hair present, they will increase the oiliness of skin and hair[6,8]. Androgen excess in women leads to increased hair growth in most androgen- sensitive sites, but will manifest with loss of hair in the scalp region, in part by reducing the time scalp hairs spend in anagen phase[9]. In other areas (e.g. the forehead and cheeks), the increased androgen levels dramatically increase the size of the sebaceous glands, but the hair remains vellus. Hirsutism is a sign of increased androgen action on hair follicles, from increased circulating levels of androgens (endogenous or exogenous) or increased sensitivity of hair follicles to normal levels of circulating androgens. The severity of the hirsutism does not correlate well with the level of androgen, because the response of the androgen-dependent follicle to androgen excess varies considerably within and among persons[2,4]. The term idiopathic hirsutism has been used to describe the circumstance in which hirsutism is present with circulating androgen levels within the normal

range[6]. Nearly all hirsute women have an increased in androgens, usually testosterone, but the increase may not be sufficient to raise the serum total testosterone concentration above the normal range because the carrier protein for testosterone, sex hormone-binding globulin, is suppressed when androgen production is increased. In the remaining women, the hirsutism may be due to increased conversion of testosterone to dihydrotestosterone by the enzyme 5a-reductase in peripheral tissue, including hair follicles which this metabolite is the more potent of testosterone[10-15]. Thus, elevated 5a-reductase activity has been demonstrated in the hair follicles of women with idiopathic hirsutism, and excess hair growth is likely to be due to an exaggerated response of the hair follicle to normal androgen levels[5]. Nearly all circulating testosterone is bound to sex hormonebinding globulin and albumin, with free testosterone being the most biologically active form[2]. Several different androgens may be secreted in excess. Testosterone excess is usually of ovarian origin while dehydroepiandrosterone sulphate excess is of adrenal origin and androstenedione excess can be of either adrenal or ovarian origin. Although, dehydroepiandrosterone and dehydroepiandrosterone sulphate are general markers of adrenal androgen production, they have little if any intrinsic androgenic activity. Small amounts are converted to androstenedione and then to testosterone in both the adrenal glands and peripheral tissues, including hair follicles and external genitalia[16].

Strategies and Evidence

Differential diagnosis: Hirsutism must be distinguished from hypertrichosisgeneralised excessive growth of androgen-independent hair which is vellus, prominent in non-sexual areas. Hypertrichosis is most commonly familial or caused by systemic disorders (hypothyroidism, anorexia nervosa, malnutrition, porphyria, epidermolysis bullosa, dermatomyositis and as a paraneoplastic syndrome in some patients with cancer) or the use of medications such as glucocorticoids, phenytoin, penicillamine, diazoxide, minoxidil, levothyroxine or cyclosporine. It also may occur after severe head injury, be present at sites of skin trauma[1,2,4,7,17,18]. The most common causes of hirsutism are the polycystic ovary syndrome and idiopathic hirsutism[19,20]. Between 50% and 70% of all hirsute women demonstrate regular menses, suggestive of idiopathic hirsutism. Although, a history of regular menses should not be used to exclude the presence of ovulatory dysfunction or hyperandrogenemia and cannot be used to determine idiopathic hirsutism[6]. Polycysticovary syndrome affects approximately 6% of women of reproductive age. It is the most common endocrine and metabolic disorder of reproductiveaged women that presents with varied symptoms such as hyperinsuli-

naemia, anovulatory dysfunction, infertility, obesity and elevated incidence of cardiac problems[2,21-25]. Because of this clinical heterogeneity, it is sometimes challenging to diagnose polycystic ovary syndrome, as most cases will not have all the primary features. As an example, half of the cases are non-classic, that is, patients present with hyperandrogenism without evidence of anovulation or ovarian dysfunction (i.e. polycystic ovaries). Polycystic ovaries need not be present to make a diagnosis of the polycystic ovary syndrome, and conversely, their presence alone does not establish the diagnosis[26,27]. This diagnosis is made when there is otherwise unexplained chronic hyperandrogenism and oligo-ovulation or anovulation[4]. The androgen excess in women with the polycystic ovary syndrome usually becomes evident about the time of puberty or soon thereafter, because androgen production is increased by both puberty (increased ovarian steroid production) and adrenarche (increased adrenal androgen production). Over the past decade, several serious metabolic complications have been associated with polycystic ovary syndrome including type 2 diabetes mellitus, metabolic syndrome, sleep apnoea, and possibly cardiovascular disease and non-alcoholic fatty liver disease[27-28]. The prevalence of the metabolic syndrome (including central obesity, hypertension, glucose abnormalities and dyslipidaemia) appears to be very high in women with polycystic ovary syndrome[4,27]. In addition, anovulatory women with polycystic ovary syndrome may be at increased risk for endometrial hyperplasia, and possibly endometrial carcinoma[29]. Other causes of androgen excess occur infrequently. Late onset or non-classic congenital adrenal hyperplasia is present in only 1.5–2.5% of women with hyperandrogenism[4,5]. Affected women present peripubertally with hirsutism and sometimes menstrual irregularity or primary amenorrhoea. It is nearly always because of 21-hydroxylase deficiency[30-33]. Androgen-secreting tumours are present in about 0.2% of women with hyperandrogenism; more than half of such tumours are malignant[4]. Androgen- secreting tumours constitute only 5% of all ovarian tumours; histologically they are Sertoli- Leydig cell tumours, granulosa-theca cell tumours and hilus cell tumours. Adrenal tumours are a rare cause of androgen excess. A few are adrenal adenomas that secrete mostly testosterone, but most are carcinomas that often secrete not only androgen mostly dehydroepiandrosterone and dehydroepiandrosterone sulphate[34-36]. Cushing's syndrome, hyperprolactinaemia, acromegaly, thyroid dysfunction and insulin resistance syndromes must be considered as causes androgen excess[4,18,37]. Androgen therapy (testosterone), danazol and the androgenic progestins present in some oral contraceptives such as levonorgestrel, norethindrone and norgestrel can cause hirsutism[2,18,38]. The causes of hirsutism are summarised in Table 1.

Diagnostic strategies:

As Table 2 shows, the medical history and physical examination should address risk factors associated with virilising disorders, polycystic ovary syndrome or other endocrinopathies, and the use of androgenic medications include danazol and oral contraceptives that contain androgenic progestins such as levonorgestrel. The history should review the onset and progression of the hirsutism. Its presence from puberty with slow progression is more consistent with polycystic ovary disease or late-onset congenital adrenal hyperplasia. Given that most women with hirsutism have polycystic ovary syndrome or idiopathic hirsutism, the problem is how best to identify thesmall number of women who have other causes for their hirsutism. The basic approach to the differential diagnosis should be: documentation of the degree of androgen excess and exclusion of the serious but rare causes of hirsutism such as androgen-secreting tumours. Several clinical findings that suggest one of the rare and more serious causes of hirsutism include: abrupt onset, rapid pace of development or progression of hirsutism or evidence of virilisation (such as clitorimegaly, deepening of the voice, breast atrophy, increased muscle bulk and increased libido). In young women the possibility of an androgen-secreting tumour should be considered with the following: onset in the third decade of life or later, rather than near puberty, moderately elevated (or higher) serum androgen concentrations, e.g. serum testosterone values above 150 mg/dl (5.2 nmol/l); serum-free testosterone values above 2 mg/dl (0.07 nmol/l); and serum dehydroepiandrosterone sulphate values above 700 lg per dl (19 lmol/l)[2,4,15,35,39,40]. The diagnosis of idiopathic hirsutism is given to women with normal serum androgen concentrations, no menstrual irregularity and no identifiable cause of their hirsutism[6,41,42]. The high frequency of polycystic ovary syndrome as a cause of hirsutism warrants attention to evidence of anovulation (such as menstrual irregularity), obesity, the metabolic syndrome or insulin resistance (such as the presence of acanthosis nigricans, skin tags or a family history of type 2 diabetes mellitus)[4,27,28]. A history of galactorrhoea or symptoms of thyroid dysfunction should be investigated because hyperprolactinaemia can be accompanied by increased adrenal androgens[7,15]. Acromegaly is suggested by the coarsening of facial features or by hand enlargement[4]. Acne, seborrhoea, temporal balding and acanthosis nigricans should be sought. Moon face, muscle atrophy, striae, thin skin or bruising suggest the possible presence of Cushing's syndrome. Abnormal body fat distribution characterised by truncal obesity, buffalo hump and supraclavicular fat are also consistent with this diagnosis[18,37,43]. The presence of any breast discharge, spontaneous

or expressible, is suggestive of hyperprolactinaemia and warrants measurement of serum prolactin even if the woman's menstrual cycles are regular. Clinical evaluation should include: an assessment of the amount, distribution and severity of hirsutism[4,5]. Height, weight and a calculation of body mass index (BMI) should be obtained because many women with polycystic ovary syndrome are obese (BMI ‡ 30 kg/m2)[43]. Abdominal and pelvic examinations may reveal mass lesions that could indicate the presence of an androgen-secreting tumour[4]. Laboratory findings in polycystic ovary patients include high serum luteinising hormone levels with normal or low follicle-stimulating hormone concentrations on day 3 of the cycle resulting in elevated luteinising hormone–follicle-stimulating hormone ratios (the ratio is generally above two). In addition, testosterone, androstenedione and dehydroepiandrosterone all may be mildly elevated. Classically, testosterone concentrations in polycystic ovary patients usually are not > 200 mg/dl[15,18]. Diagnosis rests on the finding of polycystic ovaries on pelvic ultrasound, which are reported in 60–97% of women presenting with hirsutism. In congenital adrenal hyperplasia, significantly elevated 17a-hydroxyprogesterone levels before and in response to a single dose of adrenocorticotropin hormone are diagnostic[5]. It has been suggested that ovarian androgen-secreting tumours are associated with serum total testosterone concentrations > 200 mg/dl. In those patients with elevated testosterone, the ovaries often can be imaged satisfactorily by transvaginal ultrasonography and the adrenal glands, with computed tomography or magnetic resonance imaging[15]. A normal serum dehydroepiandrosterone sulphate level essentially excludes the adrenal as a source of hyperandrogenism. When dehydroepiandrosterone sulphate levels exceed 700 lg/dl, with or without testosterone elevation, the presence of an androgen-producing adrenal tumour is strongly suggested[44]. In Cushing's syndrome, an appropriate screening test is a 24 h urine analysis for freecortisol or an overnight dexamethasone-suppression test[15]. A normal screening test excludes the diagnosis of Cushing's syndrome. Patients with an abnormal screening test should be referred to an endocrinologist[37]. Figure 2 presents a practical approach.

Management:

Hirsutism can be a mild cosmetic problem that requires reassurance and cosmetic therapy or it can have considerable psychological or medical impact. Before initiating any therapy, a careful objective examination should be made so that the response to therapy can be assessed and the clinician be familiar with a scoring system for the severity of hirsutism. Hirsutism can be reduced with the

use of cosmetic and hormonal therapy for as long as treatment is given[4,14]. Lifestyle therapies are first-line treatment in women with polycystic ovary syndrome, particularly if they are overweight[28]. It has been shown that obese women with polycystic ovary syndrome who manage to lose more than 5% of their initial body weight have a significant improvement in their biochemical profile, including a reduction of testosterone, an increase in sex hormone-binding globulin. Women should be warned not to expect improvement or at least 3–6 months after therapy is begun, because hair follicles have a half-life of up to 6 months and lifelong therapy may be needed to prevent recurrence. The treatment response can be assessed by improvement in hirsutism scores, and follow-up hormonal testing is not required[5,45].

Hormonal treatments

Most therapies fall into two major categories. One group of drugs acts by suppressing androgen-production from either the ovaries or the adrenal glands. The other group acts peripherally to reduce the effect of androgens on the skin. The selection of a pharmacological agent depends on the severity of the hirsutism, patient preference and the need to treat associated conditions such as hypertension or oligomenorrhoea[15]. Table 3 reviews medications used for treatment of hirsutism.

Oestrogen–progestin oral contraceptives: Combination oestrogen–progestin oral contraceptives slow hair growth in approximately 60–100% of hyperandrogenic women and are considered first-line therapy. The mechanisms by which oral contraceptives reduce hirsutism include: inhibition of luteinizing hormone secretion and therefore luteinizing hormone-dependent ovarian androgen production, stimulation of sex hormone-binding globulin production by the liver because of the oestrogenic effects of the contraceptive, so that the serum concentrations of free testosterone and other sex hormonebinding globulin-bound androgens decrease and the inhibition of adrenal androgen secretion. Therapy should be begun with a formulation that contains a low dose of oestrogen and a non-androgenic progestin such as desogestrel and norgestimate[46-50]. A past history of venous thrombosis constitutes an absolute contraindication to the oral contraceptive[15].

Anti-androgens

Anti-androgens are an effective treatment for hirsutism. Combined therapy with an oral contraceptive and anti-androgen is more likely to be effective in women with severe hirsutism than either

alone. Spironolactone inhibits testosterone binding to its receptors, thereby inhibiting the action of testosterone. It also decreases the ovarian production and the clearance of testosterone. Cyproterone acetate is a progestin with anti-androgenic activity that is effective for the treatment of hirsutism, either alone or with an oral contraceptive. Cyproterone acetate is probably best used in combination with an oestrogen to avoid bone loss. This drug is not available in the United States, but is available in Europe and Canada as a combination oral contraceptive (Diane) containing ethinyl oestradiol and cyproterone acetate[51-55]. In mild-to-moderate hirsutism, a dose of 2 mg taken in combination with 21 days of ethinyl oestradiol 35 lg (Diane) has been shown to improve symptoms in over 50% of cases. In more severe hirsutism, cyproterone acetate is prescribed at a dose of 25–100 mg combined with either Diane or 30 lg ethinyl oestradiol taken for a 21-day cycle[5]. Flutamide, which also inhibits testosterone binding to its receptors, has proven to be effective in women with hirsutism and may be more potent than spironolactone. However, flutamide is expensive and can be hepatotoxic at the doses typically used, and has been associated with deaths. It is not approved by the Food and Drug Administration for use in women with hirsutism. Finasteride inhibits type2 5-alphareductase. Compared with spironolactone, finasteride is as or less effective in women with hirsutism. Finasteride lowers hirsutism scores better when given in combination with an oral contraceptive[56-61].

Other hormonal therapies

Glucocorticoid treatment can lower adrenal androgen production. These drugs are indicated in the treatment of hirsutism secondary to all forms of congenital and late-onset adrenal hyperplasia[15]. In women with hirsutism, administration of a gonadotropin- releasing hormone agonist such as leuprolide inhibits gonadotropin and therefore ovarian androgen secretion, resulting in slowing of hair growth but also in oestrogen deficiency. The combination of a gonadotropin-releasing hormone agonist with either low-dose oestrogen and progesterone or an oral contraceptive eliminates the adverse effects of oestrogen deficiency without diminishing the benefits of the gonadotropin-releasing hormone agonist. However, the combination of an agonist and an oral contraceptive is less effective than either flutamide or cyproterone plus an oral contraceptive[2,62]. Metformin and rosiglitazone increased insulin sensitivity in both obese and lean patients (BMI < 25 kg/m2) with polycystic ovary syndrome. These drugs may also reduce androgen production and restore normal menstrual cyclicity[63.]

Cosmetic and physical measures

Cosmetic measures play an important role in the management of hirsutism. Physical methods of removing hair or making it less visible can be effective, and their use should be encouraged either alone or as a supplement to drug therapy. Bleaching removes the hair pigment. The active ingredient in most preparations is hydrogen peroxide, ideally in a 6% solution. This often is combined with ammonia[15,64]. Shaving is safe and effective, but is often unacceptable to patients[2,22,64]. Shaving is a good short-term solution for facial hair. Chemical depilatories break down and dissolve hair by hydrolyzing disulphide bonds[5,15]. They produce results similar to shaving[2]. Plucking is used for areas where little hair is present such as the eyebrows and nipples. Electrolysis is safe and effective but expensive. Electrolysis is a form of permanent hair removal. Treatment involves inserting a needle into the hair follicle, using current to destroy the follicle, removing the needle, and using a forceps to remove the hair. Hair regrowth rates are variable and range from 15% to 50%. The need for rapid methods of hair for hirsutism. It is most effective in women with lightly pigmented skin and dark terminal hairs and also can often result in permanent reduction in hair growth[2, 15, 22,64]. Eflornithine hydrochloride cream 13.9% (Vaniqa) is a topical drug that has been approved by the US Food and Drug Administration for the treatment of unwanted facial hair in women and also useful in treating hair that is unresponsive to laser therapy, such as white or vellus hairs. It is an inhibitor of hair growth by irreversible inhibition of the enzyme ornithine decarboxylase. Topical eflornithine is applied twice daily to affected areas of the face. This drug is classified as a pregnancy category C agent, so risk to the fetus cannot be ruled out[5,22,27,65]. Table 4 illustrates advantages and disadvantages of hair removal techniques. **Areas of uncertainty:** There is currently no agreement concerning a standard evaluation programme for hirsutism. As a result, patients are examined depending on current interests or traditions in departments of endocrinology, gynaecology, dermatology or fertility. In patients with hirsutism of peripubertal onset and slow development, regular menses with normal physical examination, and no virilisation, the possibility of an underlying neoplasm is small. Whether laboratory investigation in these patients is warranted is controversial. Table 5 presents our recommended blood tests based on history and physical examination.

Guidelines: The 2006 guidelines of the Alberta Medical Association recommend the majority of cases of mild hirsutism require no laboratory investigation. In severe or rapidly developing hirsutism, appropriate medical consultation is recommended. Tests that may be useful in the investi-

gation of hirsutism include: total testosterone, dehydroepiandrosterone sulphate and androstenedione (drawn after 10 am). Luteinising hormone, follicle-stimulating hormone, oestradiol, progesterone, dehydroepiandrosterone and prolactin measurements may be of use in the evaluation of accompanying menstrual disturbance or diagnosis of polycystic ovarian disease. If the complaint is limited to hirsutism and menses are normal, these tests are not indicated. Other assessments of hyperandrogenism, including free testosterone and sex hormonebinding globulin levels, have also been utilised. While these may provide an increased detection rate in mild cases of hirsutism, the values associated with mild hirsutism overlap with the normal range and have not been shown to be of additional advantage in the diagnosis of more serious conditions[66]. The 2002 guidelines of Reproductive Endocrinology Infertility Committee of Canada recommend the patients should be educated regarding associated health problems or long-term medical consequences of hyperandrogenism, including obesity, irregular menses, anovulation, infertility, pregnancy-induced hypertension, diabetes, hyperlipidaemia, hypertension and heart disease[67].

Conclusion :

The treatment of hirsutism is most effective using combination therapy, including androgen suppression, peripheral androgen blockage and mechanical or cosmetic treatments. Hirsutism can be effectively treated in many women by combining a non-pharmacological method of hair removal and an oral contraceptive, assuming that they do not wish to become pregnant. It is important to counsel the woman that it may take 3–4 months for a decrease in hair growth to become evident. If there is no improvement in 6 months, we would recommend spironolactone, which would be added to the oral contraceptive. However, some clinicians prefer to initiate hormone therapy with a combination of herapy in combina women with mode drogen therapy ha ause it can reduce

Table 1: Causes of hirsutism

- Polycystic ovary syndrome
- Idiopathic
- Late-onset or non-classic congenital adrenal hyperplasia
- Androgen-secreting tumours
- Ovarian tumours
- Adrenal tumours
- Cushing's syndrome
- Hyperprolactinaemia
- Acromegaly
- Thyroid dysfunction
- Insulin resistance syndromes
- Iatrogenic
- Androgen therapy (testosterone)
- Danazol
- Androgenic progestins (levonorgestrel, norethindrone
- and norgestrel)

Table 2 History and physical examination in the evaluation of hirsutism

1. **History**

- Medication history
- Onset and progression of the hirsutism
- Anovulation (such as menstrual irregularity) and
- reproductive history
- Family history
- Galactorrhoea
- Symptoms of virilisation
- Symptoms of thyroid dysfunction
- Weight gain

2. **Physical Examination**

- Assessment of the amount, distribution and severity of hirsutism
- Signs of virilisation
- Skin changes (i.e. acne, seborrhoea, temporal balding, striae, acanthosis nigricans)
- Signs of Cushing's syndrome(i.e. moon face, muscle atrophy, truncal obesity)
- Breast discharge (spontaneous or expressible)
- Height, weight and a calculation of body mass index
- Abdominal and pelvic examinations

Table 3 Medications used in the treatment of hirsutism[2,4]
GI, gastrointestinal; NSAIDs, non-steroidal anti-inflammatory drugs; ACE, angiotensin-converting enzyme; Gn-RH, gonadotropin-releasing hormone).

Class of drug	Drug	Indication	Dosage	Side effects	Comments
Oral contraceptives	Ethinyl oestradiol with norgestimate, desogestrel, norethindrone, ethynodiol diacetate	Generalised hirsutism	One tablet per day for 21 days, followed by 7-day pill-free interval	GI distress, breast tenderness, headache, weight gain, emotional lability, intolerance to contact lenses	Pregnancy category X. Least androgenic progestin component preferred
	Ethinyl oestradiol with drospirenone			Hyperkalaemia may occur. Contraindicated with hepatic dysfunction, renal insufficiency, adrenal disease	Monitor serum potassium during first cycle with concurrent use of NSAIDs, ACE inhibitors, angiotensin-II receptor blockers, heparin, potassium supplements, potassium sparing diuretics
Anti-androgens	Spironolactone (Aldactone)	Moderate or severe hirsutism	50–200 mg/day	Hyperkalaemia (rare), male pseudohermaphroditism in fetus, gynaecomastia, decreased libido, gastrointestinal discomfort, irregular menstrual bleeding, hypotension, liver dysfunction	Pregnancy category D, monitor electrolytes
	Cyproterone acetate	Moderate or severe hirsutism	Induction: 50–100 mg by mouth at bedtime, days: 5–15.	Male pseudohermaphroditism in fetus, irregular menstrual	Contraception is mandatory when taking cyproterone

			Maintenance: 5 mg by mouth at bedtime, days: 5–15	bleeding, decreased libido, nausea, depression, fatigue, mood changes and weight gain	acetate and is recommended for at least 3 months after stopping treatment. Liver function should be checked regularly during long-term use
	Flutamide (Eulexin)	Severe hirsutism	125–250 mg, two to three times daily	Male pseudohermaphroditism in fetus, hepatotoxicity	Combine with other method of contraception. Pregnancy category D. Monitor liver function
	Finasteride (Proscar)	Hirsutism	5 mg daily	Minimal gastrointestinal disturbances, headaches, dry skin and decreased libido	Pregnancy category X. Monitor liver function
Glucocorticoids	Dexamethasone prednisone	Congenital adrenal hyperplasia, may be combined with oral contraceptives or Gn-RH agonists for severe hirsutism	Dexamethasone 0.5 mg nightly, prednisone 5–7.5 mg by mouth at bedtime	Weight gain, hypokalaemia, impaired glucose tolerance, adrenal suppression, de-creased bone density, im-mune suppression, changes typical of Cushing's syndrome	Pregnancy category C
Gn-RH agonist	Leuprolide acetate (Lupron)	Alternative to oral contraceptive	7/5 mg monthly intramuscularly, with 25–50 lg transdermal oestradiol	Hot flushes, decreased bone mineral density, atrophic vaginitis	Pregnancy category X. Use with caution for short periods because of hypoestrogenic effect
Insulin-sensitising Agents	Metformin (Glucophage	Hirsutism, polycystic ovary syndrome	850 mg twice a day or 500 mg three times daily (maximal dosage 2.0–2.5 g/day)	GI distress, lactic acidosis (rare with mortality nearly 50%), numerous drug Interactions	Pregnancy category B. Resumption of ovulation may occur. Monitor liver function, confirm normal renal function before

					starting, and monitor

Table 4 Advantages and disadvantages of hair removal techniques[65]

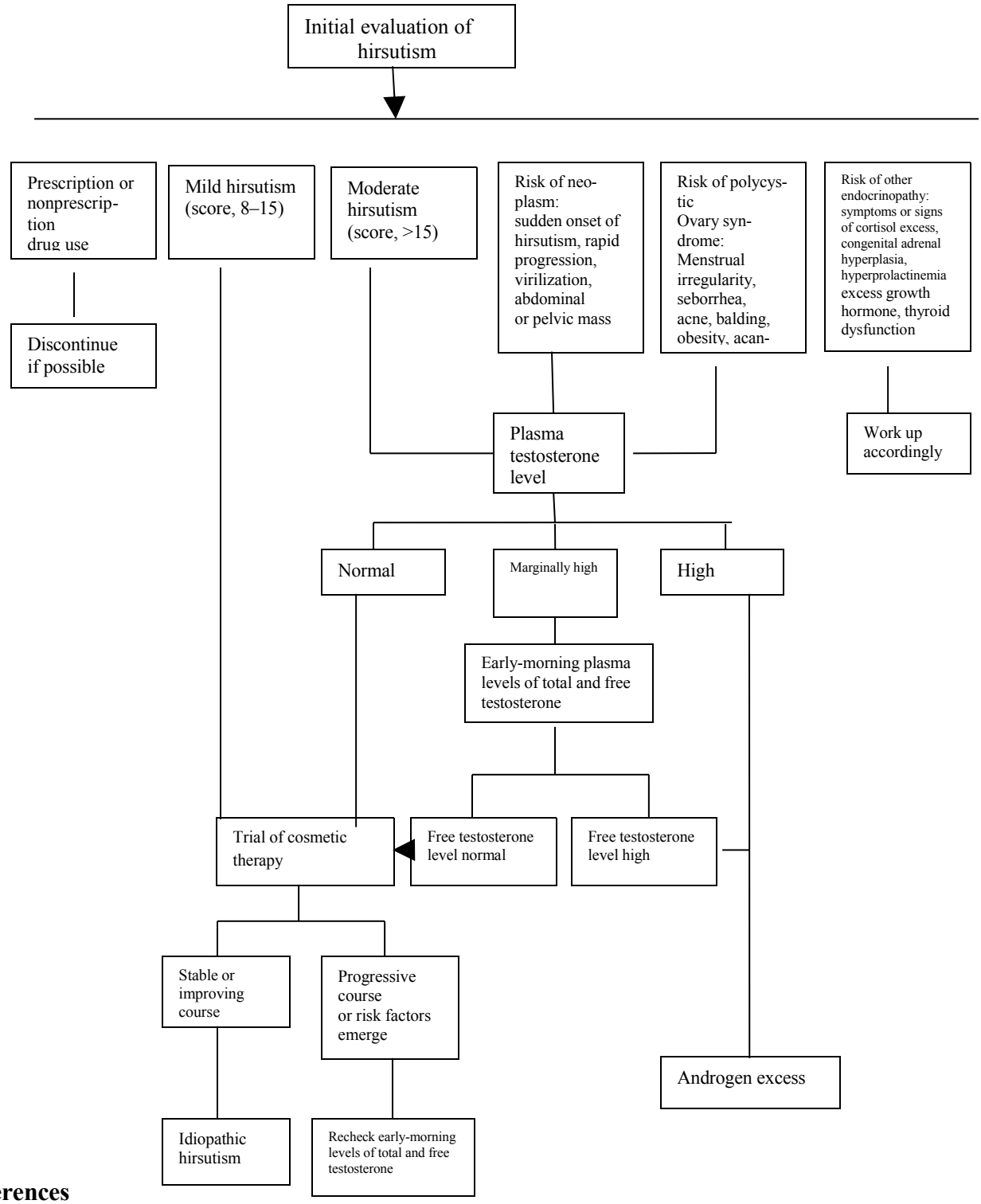
Technique	Body area	Advantages	Disadvantages
Bleaching	Face, Arms	The hydrogen peroxide will soften the hair, Inexpensive	Skin irritation, Hair discolouration, Lack of effectiveness
Shaving	All areas	Easy, Inexpensive, Effective	Quick regrowth, Risk of folliculitis Time consuming, Beard stubble
Depilatories	Extremities, Groin Face	Quick, Inexpensive, Effective	Can be irritating, Regrowth in days
Plucking	Face, Eyebrows Nipples, Bikini area	Inexpensive Regrowth can take weeks	Painful, Slow Skin irritation Post inflammatory pigmentation, Folliculitis, Ingrown hairs Scarring
Waxing	Face, Eyebrows Groin, Trunk, Extremities	Regrowth can take weeks	Painful, Slow, Expense, Irritation Risk of folliculitis, Possible thermal burn from applying the ax when too hot
Electrolysis	All areas, but usually the face	May give permanent removal	Painful, Repeat treatments needed Very time consuming, Expensive Risk of scarring and skin pigment changes
Laser and intense pulsed light	All areas	May give permanent hair reduction, Efficient	Painful, Repeat treatments needed Dark hair required, Expensive Risk of scarring and skin pigment changes, Rare reports of paradoxical hypertrichosis
Eflornithine 13.9% cream	Face, Neck	On stopping, regrowth can take 2 months, Minimal adverse effects Can be used in conjunction with other treatments such as lasers and intense pulsed light	Must be continued indefinitely to prevent regrowth, Skin-related side effects such as stinging, burning and tingling are seen occasionally

Table 5 Recommended blood tests based on history and physical examination

History and physical findings	Diagnosis	Blood tests
Hirsutism, regular menses	Idiopathic hirsutism	Blood tests
Hirsutism, anovulatory dysfunction (such as menstrual irregularity),acne, seborrhoea, temporal balding, infertility, obesity, insulin resistance (such as acanthosis nigricans), metabolic complications (type 2 diabetes mellitus, metabolic syndrome, sleep apnoea)	Polycystic ovary syndrome	Total testosterone, luteinising hormone, follicle-stimulating hormone
Hirsutism, menstrual irregularity or primary amenorrhoea	Late-onset or non-classic congenital adrenal hyperplasia	17a-hydroxyprogesterone, ACTH stimulation may be necessary to make diagnosis
Abrupt onset, rapid pace of development or progression of hirsutism,evidence of virilisation, mass lesions in abdominal and pelvic examinations	Androgen-secreting tumours	Total testosterone, dehydroepiandrosterone Sulphate
Hirsutism, moon face, muscle atrophy, striae, thin skin, bruising, truncal obesity, buffalo hump and supraclavicular fat	Cushing's syndrome	Urine analysis for free cortisol or an overnight dexamethasone-suppression test
Hirsutism, history of galactorrhoea, presence of any breast discharge (spontaneous or expressible)	Hyperprolactinaemia	Prolactin
Hirsutism, coarsening of facial features or hand enlargement	Acromegaly	IGF-I level

ACTH, adrenocorticotropic hormone; IGF, insulin-like growth factor.

Figure 1 Algorithm for the initial evaluation of hirsutism[4]



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