ABSTRACT

Broadly speaking, hirsutism is excessive hairiness. It is a terminology used to describe women with a terminal hair growth that is in a pattern that resembles a male's. The underlying cause of this excessive hair growth implicates abnormal blood hormonal levels and could be only the tip of the iceberg which is to say that there could be a serious medical problem. Regardless of the etiology, hirsutism can be the cause of significant mental trauma. Where so much importance is given to physical appearances, hirsutism even in its mildest form may be viewed by the patient as a presumptive loss of femininity. On the other hand, severe hirsutism may pose a serious cosmetic problem. Women falling under this disease spectrum fail to conform with societal norms for outer appearance. They feel stigmatized in the sense of a loss of "feminine identity." In addition to somatic impairment, mood disturbances such as depression and limitations in emotional well-being, quality of life, and life satisfaction, not to mention the negative impact that it has on one's sexual self-worth and sexual satisfaction. This disease spectrum can threaten a woman's well-being by taking a toll on her cardiovascular system, significantly upping her chances of developing type 2 diabetes and exposing her to the risk of endometrial cancer. In the article below we make an attempt to weave together several such concepts governing the cause of hirsutism, also highlighting its manifestations and relevant clinical investigations. Hirsutism as a simple cosmetic issue to a disorder of androgen excess, with all its causes and treatment approaches are discussed.

INTRODUCTION

The understanding of the clinical condition of 'hirsutism' has followed a typical pattern of evolution in the Medical folklore. From the initial stages of just case reports and case series, we have come a long way. The strong guidelines and recommendations which are a part of many medical journals today, throw more light on the implications of this disease spectrum. The prevalence of hirsutism amongst women ranges anywhere from 17-83% worldwide. Hirsutism is in part ethnically determined, being more prevalent in the dark-skinned communities and thus quite commonly seen in the Asian Indian population. Many clinical studies bear evidence to that fact. In fact some north Indian communities like sindhis and punjabis are hairy and may not have any underlying androgen disorder at all.

ETHNIC ORIGIN AND AGE OF ONSET

Ethnic origin significantly affects terminal hair growth in healthy women. The difference in the racial patterns of normal terminal hair growth may be related to genetic differences of 5-alpha-reductase activity in the skin. Northern, fair-skinned Europeans have the least amount of terminal hair, whereas southern European and dark-skinned Mediterranean women have the greatest amount of terminal hair. Wijeyaratne et al. studied ethnic differences in the clinical and biochemical characteristics of South Asian versus Caucasian women with PCOS (47 South Asians, 40 Caucasians) and their ethnically age-matched controls (11 South Asians and 22 Caucasians) in a case-control, cross-sectional observational study. They reported a significantly higher prevalence of hirsutism (Ferriman-Gallwey score 18 vs. 7.5, \( p = 0.0001 \)), acne, acanthosis nigricans, and secondary infertility in South Asians with PCOS. Insulin resistance (IR) is central to the pathogenesis of PCOS and has been associated with endothelial dysfunction, which is considered the initial step in the process of atherosclerosis. The association between increased IR and PCOS is a consistent finding in all ethnic groups. The strikingly high prevalence of abdominal obesity, diabetes, coronary artery disease (CAD), and metabolic syndrome in Asian Indians underscores this association and is making a lot of Indian physicians see red. Undoubtedly hirsutism predominates in women. Although hirsutism can occur in men, it is more difficult to recognize because of the wide variability of healthy male terminal hair growth. Amongst the Asian Indian communities, some studies of a late onset congenital adrenal hyperplasia exist in north Indian communities. North Indian Punjabi and Sindhi orgins communities tend to have excess hair compared to other counterparts.

Age - The age of onset of hirsutism depends on the etiology. Most forms of nonneoplastic hirsutism manifest around puberty. This includes polycystic ovary syndrome (PCOS), congenital adrenal hyperplasia (CAH), and idiopathic hirsutism. Hirsutism may also develop after weight gain and cessation of the use of oral contraceptives (OCs) in young women. Normally, terminal hair growth becomes apparent after adrenarche and accelerates after puberty. Terminal hair continues to develop gradually in healthy women until menopause. Rapidly worsening hirsutism,
The most widely accepted definition of PCOS is that of hyperandrogenism and anovulation with other specific causes such as late-onset 21-hydroxylase deficiency specifically excluded. PCOS is the most common cause of hirsutism and the most common endocrinopathy in reproductive aged women. PCOS is a complex and heterogeneous disorder. It is has a genetic predisposition with certain environmental factors. There is no single gene mutation that is both necessary and sufficient to cause PCOS. Genes most strongly linked to PCOS include CYP11 which encodes the cholesterol side-chain cleavage enzyme and a region two megabases centromeric from the insulin receptor gene.

The pathogenesis of PCOS, an intrinsic abnormality of theca cell steroidogenesis resulting in ovarian hyperandrogenism is likely to be the central event in most cases. There is a documented increase in the activity of ovarian thecal cell steroid production which is intrinsic to the thecal cell. The genetic basis of this hyperactivity strongly suggests that a primary thecal cell defect can initiate PCOS. This genetic abnormality of steroidogenesis could affect the adrenal as well as the ovary thus explaining the increased 17-ketosteroid response to ACTH which often occurs in PCOS.

At least three other factors have been identified and may contribute to the insulin resistance of PCOS. The first is hyperandrogenemia which may favor visceral fat distribution and in turn increase free fatty acid levels and lead to resistance to the metabolic effects of insulin especially in muscle tissue. Secondly an intrinsic resistance to insulin may also contribute to lipolysis in the adipocyte and increased free fatty acid levels. The third factor is restricted fetal growth, which may result in postmenarcheal insulin resistance. The hyperinsulinemia may synergize with both LH and ACTH to further increase both ovarian and adrenal hyperandrogenism. Increased intraovarian androgen levels increase the cohort of recruitable follicles resulting in polycystic ovaries. Anovulation is a result of the increased follicle cohort and increased sensitivity of the granulosa cell to FSH stimulation resulting in tonic estradiol and inhibin production. The increased sensitivity of the granulosa cell to FSH may be a result both of increased intraovarian androgen production and hyperinsulinemia. The elevated LH levels of PCOS are an epiphenomenon and result from lack of periodic progesterone production and androgen inhibition of the negative feedback effect of progesterone. It has been reported that 75% of women with clinical evidence of PCOS have an elevated LH level and 94% have an increased L/H ratio. Increased LH stimulation alone is unlikely to induce the ovarian stromal hyperplasia and hyperandrogenism characteristic of PCOS.

**Manifestations of Polycystic Ovary Syndrome**

The majority of women with PCOS have ovarian hyper-
androgenism as determined by elevated levels of total or free testosterone, which do not suppress normally with dexamethasone, or by abnormal 17-hydroxyprogesterone responses to pituitary-ovarian stimulation with a GnRH agonist. About one half of PCOS subjects have increased adrenal androgen production as defined by increased 17-ke-tosteroid response to ACTH, with the adrenal being the primary source of androgen excess in about one half of those with adrenal hyperandrogenism. Women with PCOS are hyperinsulinemic and insulin resistant compared to age and weight-matched controls. Insulin-stimulated glucose utilization is decreased 35-40% in women with PCOS, in-dependently of obesity, a decrease similar to that seen in type 2 diabetes. Pancreatic cell dysfunction also occurs and is more prominent in PCOS women with first degree relatives with type 2 diabetes. Consequently about one-third of obese women with PCOS have impaired glucose tolerance and about 10% have type 2 diabetes. Women with PCOS appear to be at risk not only for insulin resistance and type 2 diabetes but for the other metabolic abnormalities characteristic of syndrome X or the metabolic syndrome including obesity, dyslipidemia, and hypertension. About 50% of PCOS women are obese, and obese PCOS have increased abdominal and visceral fat compared to weight-matched controls. Both increasing BMI and increasing waist to hip ratio have been associated with increased risk of death from cardiovascular disease and overall risk of death in large, prospective studies. These also have lower HDL and higher LDL-cholesterol, triglyceride, VLDL levels. Fibrinolytic capacity is decreased in PCOS compared to age and weight-matched normal women. There is conflicting evidence for vascular endothelial dysfunction, (responsible for atherosclerotic plaque formation) in women with PCOS. Along with higher risk of cardiovascular disease there is an increased risk of endometrial cancer and cerebrovascular disease in the PCOS subjects.

**Hirsutism:** A rare variant of PCOS is ovarian hyperandrogenism. Unlike PCOS, hyperandrogenism presents in both pre- and postmenopausal women. Women with hyperandrogenism often have virilization and have higher testosterone levels (often > 200 ng/dl) and lower LH levels than classic PCOS. They are obese and usually have evidence of extreme insulin resistance. Ovarian ultrasound demonstrates a decreased number of follicles and markedly increased stroma. On histopathology there are abundant islands of luteinized theca cells throughout the stroma. Women with hyperandrogenism are resistance to clomiphene citrate and ovarian wedge resection for ovulation induction. Treatment with gonadotropin-releasing hormone agonist (GnRHa) improves hirsutism and may improve ovarian response to exogenous gonadotropins for ovulation induction. Metformin treatment may also increase the likelihood of ovulation in women with hyperandrogenism.

2. **Idiopathic Hirsutism**

Idiopathic hirsutism is excess terminal hair production in androgen dependent areas in the presence of regular ovulation and normal androgen levels. It is the second most common cause of hirsutism after PCOS and occurs in about 15% of hirsute women. It is thought to be secondary to increased 5 alpha-reductase activity in the skin or its appendages, or due to other alterations in androgen metabolism or to increased sensitivity of the androgen receptor. Hirsutism often begins at puberty and the disorder may be familial. It may or may not be associated with obesity and insulin resistance. Some patients with idiopathic hirsutism have normal plasma androgen levels. Dihydrotestosterone levels may be elevated in presence of normal total of free testosterone levels signifying a increased 5 alpha reductase activity and may partially respond to finasteride.

3. **Adrenal and Ovarian Steroidogenic Enzyme Deficiencies**

Adrenal or ovarian steroidogenic enzyme deficiencies are the most common cause of hyperandrogenism in postmenarcheal women after PCOS and idiopathic hirsutism. Nevertheless these conditions are uncommon to very rare. Late-onset 21-hydroxylase deficiency occurs in 1-5% of hirsute women, with the greatest prevalence in women of Ashkenazi Jewish descent. A 17-hydroxyprogesterone level greater than 1000 ng/dl one hour after 250 mcg of synthetic ACTH given intravenously establishes the diagnosis of 21-hydroxylase deficiency. Although adrenal and ovarian 3-hydroxy steroid dehydrogenase deficiency has been reported to occur in as many as 10-40% of hirsute women based on modest elevations in 15-steroids in response to ACTH these have been found to be very rare. In North India some communities may have late onset peripeubertal CAH as well. So are the other enzyme deficiencies mentioned in the table above.

4. **Ovarian and Adrenal Tumors**

Both adrenal adenoma and carcinoma may present with virilization and hyperandrogenemia. Androgen secreting ovarian tumors include Sertoli-Leydig cell tumors, Leydig cell tumors, lipid or lipid cell tumors and granulose-theca cell tumors. These also happen to be rare causes of hyperandrogenism. Typically women with androgen secreting tumors have abrupt onset of symptoms distinct from menarche and a more rapid progressions of symptoms compared to PCOS. Signs of virilization such as clitoromegaly, frontal balding and deepening of the voice are also more common. Testosterone levels are usually greater than 200 ng/dl or 2 1/2 times the upper limit of normal, but there is clearly an overlap between testosterone levels found in tumors and those seen in severe cases of PCOS or hyperandrogenism, and the majority of women with high testosterone levels will not have tumors. If a tumor is suspected, both
ovarian ultrasound and adrenal CT scan should be done to localize it. A dehydroepiandrosterone sulfate (DHAS) level less than 700-800 mg/dl does not rule out an adrenal tumor. New MRI with Chemical Shift Imaging can diagnose salient adrenal adenomas as well.

5. Other Endocrine Disorders

Endocrine disorders other than PCOS or late-onset 21-hydroxylase deficiency are rare causes of hyperandrogenism. Hirsutism may be present in hyperprolactinemia with or without pituitary adenoma. Cushing syndrome and acromegaly. However it is usually not the primary complaint in these disorders. Prolactin should be determined in all patients with anovulation. Cushing syndrome can be ruled out by a normal 24 hour urinary cortisol or normal overnight dexamethasone suppression test. If there is any suspicion of acromegaly, a somatomedin-C level (IGF-I) and/or growth hormone suppression test should be done.

EVALUATION OF PATIENTS

A critical part of evaluation of hirsutism is the history and physical. An accurate history of the patient's onset of hirsutism and developmental milestones can be helpful in the etiologic diagnosis.

Age of onset- Idiopathic hirsutism and the other less-serious causes of hirsutism usually begin at puberty. Conversely, hirsutism that occurs in middle-aged or older women should suggest an adrenal or ovarian tumor.

Family history- A patient with a family history of hirsutism is consistent with congenital adrenal hyperplasia (CAH); however, idiopathic hirsutism and polycystic ovary syndrome (PCOS) can also be familial.

Hirsutism severity and rate of progression- The history of a benign form of hirsutism is usually characterized by pubertal onset with slow progression over many years. This is often true of hirsutism with PCOS. When a history of rapid severe hirsutism or other signs of virilization are obtained, an androgen-secreting tumor is a possibility.

Adrenarche and puberty—Because the development of pubic hair depends on adrenal androgens, early development points toward CAH. In contrast, ovarian hyperandrogenism is associated with normal adrenarche and delayed menarche or irregular menses. The most widely accepted method of quantitation is the Ferriman and Gallwey scale. In this approach, hair growth is judged in each of 11 androgen-sensitive areas. The grade for each area ranges from 0 (no terminal hair) to 4 (frankly virile). The body areas used to grade hirsutism are (1) the upper lip, (2) chin, (3) chest, (4) leg, (5) thigh, (6) upper arm, (7) forearm, (8) upper back, (9) lower back, (10) upper abdomen, and (11) lower abdomen. Areas such as the axilla and pubis are not included because terminal hair grows in these places at normal androgen levels in women.

- The total score correlates roughly with the elevation of androgen levels. A woman with a score of 8 or higher is considered to have hirsutism. Most women who seek medical attention for the disorder have scores of 15 or higher.
- In women with moderate-to-severe hirsutism (score >15), seek additional signs of hyperandrogenism, including (1) temporal hair recession, (2) oily skin, (3) masculine voice, (4) well-developed musculature, (5) enlargement of the clitoris (>35 mm² in surface area), (6) irregular menses, and (7) psychological changes (eg, heightened libido, aggressiveness) are observed.
- The degree to which these clinical factors are present suggests the level of androgen overproduction and, thus, helps to determine the degree of concern for the presence of an underlying disease.
- A thorough abdominal and pelvic examination is important in patients with hirsutism because more than half of androgen-secreting adrenal and ovarian tumors are palpable.
- Examine the skin for acanthosis nigricans, a manifestation of insulin resistance.
- Women with hirsutism are usually obese, with increased waist-hip ratios, and are thought to be at an increased risk for atherosclerosis and coronary heart disease. They also have increased bone mineral density scores at the hip and spine. These increases correlate with higher levels of serum free testosterone and estrogen.

INVESTIGATIONS: Laboratory studies in hirsutism serve both to confirm the clinical impression of hyperandrogenism and to identify the source of excess androgens, either adrenal or ovarian. The workup described in the flowchart recommends 2 visits. A baseline evaluation followed by a 2-week dexamethasone treatment period. Specific discussion of the testing is below. (Fig I Protocol of work up of a case of hyperandrogenism)

Testosterone: The most important assay is the level of serum testosterone, the major circulating androgen. If the total serum testosterone level is normal, measure the free serum level because hyperandrogenism (and insulin resistance, if present) decreases the sex steroid-binding globulin, such that the unbound, biologically active testosterone moiety may be elevated even if the total level is unremarkable. Extremely high testosterone levels are likely to be associated with adrenal or ovarian tumors, whereas idiopathic and benign etiologies result in very mild elevations. Indeed, in idiopathic hirsutism, the results from testing androgen levels are often normal.

Dehydroepiandrosterone sulfate (DHEAS): Because testosterone can originate in either the adrenal cortex or the ovary, an elevated testosterone level does not indicate the gland of origin. Accordingly, measurement of elevated plasma levels of DHEAS, an androgen synthesized almost exclusively by the adrenal cortex, can indicate excess adrenal function. Elevations in both testosterone and DHEAS suggest an adrenal origin, whereas an isolated testosterone elevation indicates an ovarian source.
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IMAGING STUDIES

If indicated based on the findings from the clinical evaluation and laboratory testing, an ovarian ultrasonography and adrenal computed tomography scanning or magnetic resonance imaging to evaluate for either ovarian or adrenal sources of androgen production may be required. The PCOS ovary has a thickened tunica and about twice the cross sectional area of normal ovaries. The increased area is a result of both an increased stromal area and increased numbers of follicles of all stages past the primordial follicle. Polycystic ovaries, as defined on ultrasound by 10 or more 2-8 mm follicles and an increased, echodense stromal area, occur in 70-80% of women who meet the standard diagnosis of anovulation and hyperandrogenism.

DIAGNOSTIC CRITERIA

PCOS is diagnosed according to the Rott-PCOS criteria (Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004) if at least two of the following criteria were present: oligo/amenorrhea, clinical or biochemical hyperandrogenism and PCO on ultrasonography.

Clinical hyperandrogenism is defined as the presence of hirsutism (Ferriman–Galwey score >8) and/or acne. Biochemical hyperandrogenism is present if the calculated free androgen index [FAI = (testosterone/sex hormone-binding globulin (SHBG) × 100] was >4.5 (Vermeulen et al., 1999). PCO is defined as the presence of at least one ovary >10 cm³ in volume and/or at least one ovary with 12 or more follicles measuring 2–9 mm in diameter (Balen et al., 2003; Broekmans and Fauser, 2006). Insulin Resistance is assessed using the homeostatic model assessment (HOMA-IR: (fasting insulin × fasting glucose)/22.5) (Legro et al., 2004). A HOMA-IR value >3.8 probably reflects severe IR, considering the HOMA-IR threshold of 3.8 based on insulin concentrations above the upper limit of normal after a 100 g oral glucose tolerance test as standard test.

QUALITY OF LIFE AND HIRSUTISM (QoL)

QoL research in PCOS uses certain parameters like hirsutism, acne, irregular menses, infertility, and recently obesity. As PCOS often manifests at an age when finding a partner, sexual activity, marriage, and raising a family are important, its cosmetic and psychosexual implications are thought to cause profound emotional distress. 18 The three most bothersome symptoms commonly reported by affected women are hirsutism, irregular periods, and infertility. Appropriately, PCOS has thus been called “the thief of feminine identity.” Almost all women associate negative emotions of frustration, anxiety, and, to a lesser extent, sadness with PCOS. 20 PCOS cases have heightened likelihood of depression.

MANAGEMENT

Hirsutism is a part of a disease spectrum and thus mandates a multi-pronged approach. It is not just the medical condition that requires treatment but also the repercussions of its manifestations that need to be dealt with efficiently.

Medical Management of PCOS: A reasonable approach to medical therapy for women with hirsutism is to combine the oral contraceptive pills with an antiandrogen. Spironolactone is the first choice in the cheapest and has minimal side effects.
If satisfactory results are not obtained with this therapy in six to nine months, one could consider adding a GnRH agonist for more complete suppression of ovarian androgen production or substituting finasteride for spironolactone or adding finasteride to spironolactone. OCPs have commonly been used to treat patients with hirsutism and other signs of androgen excess. The progesterational component of the OCP inhibits pituitary secretion of LH, which in turn decreases ovarian androgen production. In addition, the estrogen component of oral contraceptive pills increases production of SHBG thus decreasing the amount of free testosterone available. Because the profound hypoestrogenism caused by GnRH agonists limits the length of treatment time and because hirsutism rapidly reappears after stopping therapy, the addition of an OCP may have some advantages. It will prevent bone loss and the vasomotor symptoms associated with hypoestrogenism, while still maintaining the advantage of rapid androgen reduction associated with GnRH use. In addition, the continued use of OCP after GnRH therapy has been discontinued may prevent the rapid recurrence of hirsutism. Given the cost of GnRHs, they are better reserved for patients who fail first line therapy with an oral contraceptive and antiandrogen. Eflornithine may be most appropriate for women with relatively mild facial hirsutism, or it may be a reasonable additional therapy in women with inadequate response to the oral contraceptive pill and spironolactone. This compound irreversibly blocks the enzyme ornithine decarboxylase (ODC) which is concentrated in the matrix of growing hair follicles this impairs cell differentiation and division, decreasing hair growth and converting new growth to finer hair. The idea of treatment with eflornithine is to decrease the frequency of and improve results of mechanical means of hair removal. Flutamide should be reserved for recalcitrant cases given the rare complication of hepatitis. Flutamide is a nonsteroidal antiandrogen that appears to work only at the androgen receptor. Flutamide 250 mg/d for six months is effective in treating hirsutism. Patients with more severe hyperandrogenism or alopecia, may respond better to flutamide than to spironolactone. Flutamide has the potential for a rare but severe drug-induced hepatitis which limits the usefulness of this medication and should be utilized after other therapies have failed. One should also monitor liver transaminases appropriately.

**Treatment of Insulin Resistance and Other Metabolic Abnormalities**

**Weight Loss**

Treatment of the metabolic abnormalities of PCOS has the potential to reduce the risk of developing type 2 diabetes and cardiovascular disease. The best method to increase insulin sensitivity is weight loss. Weight loss is more effective than metformin in reducing the rate of progression to diabetes in subjects at high risk for diabetes. Several studies have documented the salutary effect of modest loss of 5 to 10% of body weight in obese PCOS. An improvement in menstrual function has been reported in as many as 80-90% of patients. Fasting insulin and/or insulin response to glucose tolerance testing decrease significantly and insulin sensitivity as determined by euglycemic insulin clamp improves significantly after weight loss. Total cholesterol, LDL-cholesterol and triglycerides decrease by about 10%. Weight loss also has a consistent effect on hyperandrogenism with significant decreases to normal or near normal levels of total and free testosterone and a significant increase in sex hormone-binding globulin.

**Insulin-Sensitizing Agents**

Metformin is the insulin-sensitizing agent of choice in PCOS. Metformin therapy is begun at 500 mg/day with dinner and is increased by 500 mg increments every 1-2 weeks as gastrointestinal symptoms abate. Most studies in PCOS have used doses of 1500-1700 mg/day given in 2-3 doses. Metformin treatment usually results in modest weight loss, which may be due in part to its suppression of appetite. The most common side effects of metformin are gastrointestinal and include diarrhea, flatulence, nausea and abdominal discomfort. These symptoms usually can be minimized by slowly increasing the dose. However about 5% of patients cannot tolerate metformin because of gastrointestinal side effects. The most serious complication of metformin is lactic acidosis which occurs at a rate of about 3 cases per 100,000 patient years of use. About 90% of metformin-related cases of lactic acidosis had a predisposing condition such as congestive heart failure, renal insufficiency, chronic lung disease with hypoxia or age older than 80 years. Women with PCOS lose significantly more weight when treated with metformin and weight loss diet than with placebo and weight loss diet.

**Thiazolidinediones**

These are another class of insulin-sensitizing agents that have been studied in PCOS. Both Pioglitazone and Rosiglitazone have been studied and are especially useful in Metformin failure or resistant or refractory case who fail both metformin and clomiphene citrate.

**Treatment of anovulation**

Anovulation is the primary cause of infertility in about 20% of couples, and PCOS is estimated to be the cause of 70% of anovulatory fertility. The general paradigm is to begin with the easiest to manage therapies, and if these do not result in ovulation or pregnancy in a reasonable period of time, to move on to more elaborate therapies. Clomiphene Citrate-Clomiphene citrate is still the first line of therapy for ovulation induction in women with PCOS, although the argument has been made that metformin is preferable. The standard clomiphene regimen is 50 mg/day for 5 days beginning on cycle day 3-5 following spontaneous or progesterin-induced bleeding. Metformin in doses of 1500-1700 mg/day significantly increases rates of spontaneous ovulation and clomiphene-induced ovulation compared to placebo or placebo and clomiphene. Another alternative to standard clomiphene citrate therapy is to treat with a short course of dexamethasone 0.5-2 mg daily together with clomiphene citrate. It reduces adrenal androgen production thereby reducing peripherally produced estrogens and estrogen negative feedback on FSH secretion. Dexamethasone may ameliorate the steroidogenic effect of insulin in the ovary by inducing ovarian insulin resistance, and thereby paradoxically improving the likelihood of ovulation. Gonadotropins are options for women unresponsive to standard or modified clomiphene citrate stimulation therapies or to metformin alone.

**Surgical Ovulation Induction**

The final option in treating...
Hirsuitism

clomiphene citrate resistant PCOS is surgical ovulation induction. Recently there has been great interest in using laparoscopic methods to surgically induce ovulation in women with PCOS. Electrocautery or laser is used to produce multiple burns in the ovarian capsule, or ovarian tissue may be excised with scissors. All laparoscopic methods of ovulation induction result in similar rates of ovulation and pregnancy. The advantage of laparoscopic ovulation induction in PCOS is that it may result in long-term ovulation without any other therapy.

Non-Medical Therapy - Medical therapy with OCP and antiandrogens will decrease production of new terminal hair in androgen dependent sites. However, it will not immediately affect hair already present, and it will not affect hair growth at androgen independent sites. Therefore different means of mechanical hair removal have been employed in combination with medical therapy to achieve optimal results. Shaving and epilation are fast, simple and inexpensive means of temporary hair removal. However, hair quickly regrows at a normal rate and the cosmetic results are typically unappealing to women for use on the face. Epilation includes plucking and waxing and involves removal of the hair from the bulb which may lead to inflammation. Chemical depilatories are a painless method but temporary method of hair removal that generally last slightly longer than shaving without bristly regrowth of hair. All chemical depilatories act by breaking disulfide bonds in hair causing it to break off at or just beneath the surface of the skin. The most common side effect is an irritative dermatitis. Electrolysis is a permanent method of hair removal that utilizes electrical current to destroy the hair follicle. Lasers – It is one of the better alternatives available today for hair removal. This allows for selective destruction of the follicle without damaging nearby structures. Photodynamic therapy utilizes light and a chemical photosensitizer to permanently destroy the hair follicle. The best studied is the topical use of aminolevulinic acid (ALA). The advantage of photodynamic therapy is the ability to quickly treat larger areas and use on more skin types.

Hirsutism and Endometrial cancer: - Hyperandrogenic, anovulatory women have normal estrogen levels and are constantly exposed to estrogen stimulation of endometrial proliferation. Without the periodic progesterone-induced inhibition of proliferation and differentiation to secretory endometrium that occurs after ovulation, they are at risk to develop endometrial hyperplasia and carcinoma. A threefold increased risk of endometrial cancer in anovulatory women has been reported. Increased serum levels of insulin are also associated with an increased risk of endometrial cancer. It is critical that hyperandrogenic women undergo therapy to prevent endometrial hyperplasia or carcinoma. If a patient has been anovulatory for more than a year, an endometrial biopsy is recommended before instituting therapy. The oral contraceptive pill (OCP) is an excellent choice, as it both inhibits endometrial proliferation and reduces ovarian androgen production, thus ameliorating the consequences of hyperandrogenism. If a progestin is used alone, studies in postmenopausal women receiving estrogen suggest it should be give for 12-14 days every month to minimize the risk of endometrial hyperplasia. Insulin-sensitizing drugs may also decrease the risk of endometrial cancer in PCOS by lowering insulin levels and increasing the frequency of ovulation.

CONCLUSION : The many manifestations of hirsutism are complex and heterogeneous. Body weight is the major determinant of insulinemia, insulin sensitivity, and ovarian hyperandrogenism, independent of PCOS, and central obesity in association with insulin resistance is a strong predictor of Coronary artery disease in South Asians. The dangerous increase in the prevalence of obesity and its related complications that we are witnessing in Asia, and the documented efficacy of lifestyle interventions and weight loss on hyperandrogenism, ovulation, fertility indicate that lifestyle modifications should be used as primary prevention strategy to treat these disorders. Pharmacologic approaches should be used only if such measures fail. The use of the traditional age-old Indian therapy has also been attempted in PCOS but lifestyle and weight loss essentially produce the desired results. However, larger, randomized, multicentric trials are required to support the documented efficacy of these drugs. Research work and clinical studies in this regard have been conducted only in individual setups within cities in India or among Asian migrant populations. However, no multicentric study that is representative of the prevalence and manifestations of hirsutism has been carried out throughout India. Future studies in this direction would help to highlight the magnitude of the problem and its severity in this part of the world.

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