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Prolactin response to thyrotropin-releasing hormone was normal in the hirsute women. No significant relationship between prolactin and steroid hormones values. On the other hand, mean dehydroepiandrosterone and its sulfate, and androstenedione were higher in the group of ten hirsute women with slightly elevated prolactin concentrations than in the group with normal concentrations, but the difference was not significant. Thus serum prolactin is often slightly elevated in hirsute women with ovarian hyperandrogenism (Buvat et al., 1982).

Urinary Steroids in hirsutism:

The amounts of androstenediol (the main metabolite of dihydrotestosterone) and testosterone glucuronide excreted in the urine of 17 normal men, ten normal women and ten women with idiopathic hirsutism were measured by Mauvais-Jarvis et al., in 1973. In women with idiopathic hirsutism. The mean urinary excretion of testosterone was in the normal range for women, whereas
the mean excretion of androstanediol was elevated to levels found in normal men. This elevation is compatible with an extensive transformation in extrahepatic tissues of testosterone or other androgen precursors to androstanediol. Most hirsute patients have elevated androgens levels upon thorough evaluation. If only urinary 17-Ketosteroids are measured, only 15% of hirsute women will have elevated values (Maroulis et al, 1977), and it is not always clear what these values signify (Judd et al, 1977).
Adrenal and Ovarian vein catheterization

To determine the origin of the excessive testosterone, percutaneous bilateral adrenal and ovarian vein catheterization were performed and effluent blood samples obtained for androgen measurement. Kirschner and Jacobs, (1971) found that in 9 of the 13 women studied, the major source of androgen was ovarian. In the remaining four women, androgen originated from both the ovaries and adrenal glands. Following dexamethasone administration there was a decrease in plasma testosterone and androstenedione in the four women whose androgen originated from both adrenals and ovaries and also in three out of the nine women whom androgen originated from the ovaries.

Rosenfield et al, (1972) using dexamethasone suppression criteria, concluded that 85% of oligomenorrheic hirsute women had excessive ovarian production of androgens, and Kirschner et al, (1976) using catheterization criteria, concluded that 90% of a group of predominately oligomenorrheic hirsute
women had excessive ovarian androgen production.

Givens et al, (1974) found that an elevation of serum testosterone levels without an elevation of urinary 17-Ketosteroid levels points to the presence of an ovarian lesion because the adrenal does not convert precursors to testosterone. However, exceptional adrenal tumours possess pathways of testosterone biosynthesis without directly oversecreting enough androstenedione or dehydroepiandrosterone to cause an elevation of urinary 17-Ketosteroid levels.

Abraham et al, (1976), Maroulis et al, (1981) found that the evaluation of hirsutism must include the measurement of plasma levels of androgen. Among the adrenal androgens, dehydroepiandrosterone sulfate is a good choice to study because it attains the highest levels in normal individuals, its levels remain relatively constant despite the diurnal variation of other adrenal androgens, it suggests specifically adrenal rather than ovarian disease, and its levels have been
found to be elevated in patients with adrenal androgen excess of various causes.
Treatment of Hirsutism

Treatment of hirsutism depends of course upon the cause of the excess androgen secretion in the individual case. There are various methods of suppressing the excess androgen production after locating its source. They can be summarized in the following:

Dexamethasone:

Dexamethasone can be used to suppress the excess androgen production of adrenal origin, but as the source of androgen excess in hirsute women is usually the ovaries, it is rarely used alone but usually in combination of other drugs which suppress the ovarian androgen. Dexamethasone is usually preferred than other steroids because it is a potent steroid and has least of side effects.

Nightly dexamethasone administration resulted in prompt and sustained suppression of cortisol, dehydroepiandrosterone and androstenediol. The
nocturnal rises of these hormones were also completely suppressed. The amount of suppression was equal to or greater than that reported earlier with short term, high dose dexamethasone administration in both hirsute and normal women using only morning samples (Bardin et al, 1968; Abraham et al, 1976; and Judd et al, 1977). Also nightly dexamethasone administration was associated with reduction of serum androstenedione and testosterone and obliteration of their diurnal fluctuations. The magnitude of these reductions was less than were reported by earlier investigators using short term, large dose dexamethasone administration using only morning samples (Turbridge et al, 1973; Abraham et al, 1975; and Judd et al, 1977).

Rosenfield et al., (1980) found that a single 0.5 mg dose of dexamethasone at bed time is the usual starting dose and it is adjusted depending upon the androgen level. This generally lessens adrenal secretion for most of the day. Therapy at this level usually does not impair recovery of adrenal reserve. However, cortisol levels
should be measured while the patient is receiving dexamethasone and if the morning cortisol level is less than \(0.003\text{mg/loooml}\), the patient would be at risk of developing cushingoid changes and should be advised to increase medication in times of stress. Dexamethasone doses over 0.75 mg/day are likely to result in cushingoid changes over a long period of time.

Lachelin et al. (1982) found that nightly dexamethasone administration for one month resulted in marked suppression of dehydroepiandrosterone, testosterone, androstenediol and cortisol. For testosterone the mean percent decreases of the twenty-four hours transverse means were 15% and 46% for the polycystic ovarian disease and normal subjects, respectively. For androstenedione the mean percent decreases were only 7% and 20%, respectively. The diurnal variation of all steroids disappeared with dexamethasone.

HoYuen and Mincey, in 1983 found that the administration of glucocorticoids to hyperandr-
ogonic hirsute women resulted in a significant suppression of androstenedione plasma levels and 17-ketosteroid excretion. Although statistically insignificant, testosterone and luteinizing hormone concentrations declined to a mean of 65% and 51% of pretreatment values, respectively. Clinically, beneficial effects were observed on the hirsutism & menstrual dysfunction in these women.

Oral Contraceptive:

Since oral contraceptives have been used by many workers to suppress excess androgen secretion by the ovary and in locating the source of androgen excess in hirsute patient, use was made of this to treat these patients. Since the ovaries have been found to be the main source of androgen excess rather than the adrenal, oral contraceptives pill seem to be a useful drug in treatment of such condition. The choice of the suppressing agent may be critical.

Estrogen alone is a poor suppressant of
lutenizing hormone in hirsute women (Kirschner et al., 1970). Plasma testosterone is increased and not decreased in hirsute women given norgestrel 1 mg-mestranol 0.08 mg (Easterling et al., 1974).

Further investigation is needed to evaluate the relative effectiveness of various progestin-estrogen combinations in suppressing androgenic hormones in hirsutism.

The effectiveness of two oral contraceptives in suppressing plasma androstenedione (A), testosterone (T), luteinizing hormone (LH) and follicle stimulating hormone (FSH) and in stimulating testosterone-estradiol-binding globulin (TEBG) was evaluated in 39 hirsute women by Givens et al., in 1976. Twenty seven hirsute women received norethindrone 2 mg, mestranol 0.1 mg (Group I) and 12 received norgestrel 0.5 mg - ethinyl estradiol 0.05 mg (Group II).

Hormone assays were performed before treatment and at the end of 3 weeks of therapy.
subjectively reported a decrease in the rate of hair growth and/or a decrease in the amount of facial hair.

Gordon et al., (1970) showed that medroxyprogesterone reduced the plasma levels of testosterone in both normal men and women.

Correa de Oliveira et al., in 1975 treated 24 hirsute female patients with 100 mg of depo-medroxy progesterone acetate intramuscularly by every 15 days. Twenty-three showed definite improvement from their abnormal hair growth. All patients with initially elevated 17-Ketosteroids in 24-hours urine collected, showed a decrease of these metabolites with treatment. In eleven patients the initial plasma testosterone level was elevated and returned to normal values with treatment. The first patient who was submitted to this therapy stopped the treatment for five months and started having abnormal hair growth again. With other patients after initial treatment with depo-medroxy progesterone acetate i.m., they started using contraceptive
pills containing medroxy progesterone, this maintained the reduced ectopic hair growth. The most important side effect was amenorrhea.

**Cyproterone acetate:**

Cyproterone acetate is an antiandrogen, the chemical structure of which is similar to that of chlormadinone. The acetylated compound has strong progestogenic activity in addition to its antiandrogenic activity (Vokaer and Kridelka, 1963).

The antiandrogen properties arise from the drug's competition with testosterone at endorgan receptors (Vioget et al, 1968; Neumann, 1971).

It is contraindicated in liver disease. It influences the enzymatic activity of the liver, especially the glucuronid transferase (Elert, 1969), although, Burchardt and Agrapidakis (1972) found no liver damage after three and half years treatment.
There is a number of studies of its effect in hirsute women. Hammerstein and cupoeanu, (1969) recommended a sequential regime of cyproterone acetate (C A ) with 100 to 200 mg daily from the 5th to the 14th days of menstrual cycle and .05mg of ethinyl-estradiol from the 5th to 25th days of the cycle. Ethinyl-estradiol was used to inhibit ovulation to obviate the possibility of pregnancy during treatment because intrauterine feminization of male fetuses after administration of cyproterone acetate to pregnant rats has been reported (Hamada et al, 1963).

Ismail et al, in 1974 using the above regime, reported a marked reduction in hirsutism after 12 months of therapy. There was a significant increase in the rate of hair growth following cessation of cyproterone acetate alone, but not ethinyl-estradiol. Both plasma and urinary testosterone levels were reduced during therapy.

Different figures of success reported, using cyproterone acetate in treatment of


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