MEDICAL PRACTICE

Gynaecology in General Practice

Hirsutes

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In hirsutes there is an excessive growth of hair occurring on the face, breasts, limbs, or abdomen. In women such hair growth may present either without other abnormalities or be accompanied by other features of virilization such as hypertrophy of the clitoris; deepening of the voice; acne; breast atrophy; muscle hypertrophy; thinning of the scalp hair with temporal recession; and oligomenorrhoea or amenorrhoea.

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The potent androgen testosterone may be derived from either the ovary or adrenal cortex but contributes little to the 17-ketosteroids excreted in the urine. Other androgens of adrenal origin are the major precursors of the total urinary 17-ketosteroids. Estimation of plasma and urinary testosterone levels is now more readily available from routine laboratories and should be obtained whenever significant virilization is present. The ranges of normal values will depend on the precise techniques used and will vary from one laboratory to another.

Aetiology

The major conditions associated with hirsutes and virilism are shown in the Table.

Common Causes of Hirsutes

Cause		Urinary		Plasma Testosterone
		17-Ketosteroids	17-Ketogenic Steroids	
Constitutional	Familial	N	N	N
	Idiopathic	N	N	N
Physiological	Menopause	N	N	N
Iatrogenic	Corticosteroids: cortisone or hydrocortisone	↓	↓	N or ↓
	Corticosteroids: synthetic	↓	↓	
	ACTH	↑	↑	N or ↑
	Androgens	N	N	↑ N or ↓
	Progestogens	N or ↓	N or ↓	↓
Adrenocortical	Congenital adrenal hyperplasia	↑	↑	N or ↑
	Adenoma or carcinoma	↑	N or ↑	N or ↑
	Cushing's syndrome	N or ↑	↑	N or ↑
Ovarian	Polycystic ovary syndrome	N or ↑	N	N or ↑
	Tumours: arrhenoblastoma	N or ↑	N	
	Tumours: hilus cell tumour	N or ↑	N	↑
Pituitary	acromegaly	N or ↑	N	N or ↓
Gonadal maldevelopment—e.g., intersexual states, gonadal dysgenesis		N or ↓	N	N or ↓
Miscellaneous	Anorexia nervosa	↓	↓	N or ↓
	Porphyria	N	N	N

N = Normal
↑ = raised
↓ = reduced

CONSTITUTIONAL AND "PHYSIOLOGICAL" HIRSUTES

In many patients complaining of hirsutes there are no other signs of virilization and no evidence of disease is found. Hence presumably these patients show a constitutional predisposition to excess hair growth. There is frequently a family history of hirsutes in these patients. It is also not unusual for facial hair to appear at the menopause.

IATROGENIC HIRSUTES

Androgen therapy may cause virilism and be reversible on stopping treatment. Administration of steroids—particularly the progestogens to pregnant women—may result in virilization of the fetus.

OVARY

Polycystic Ovary Syndrome

Polycystic ovaries are frequently found in patients with hirsutes and mild virilism. Since there may be irregular menstruation or primary amenorrhoea rather than secondary amenorrhoea—and obesity is by no means always present—the eponym "Stein-Leventhal Syndome" is confusing and uninformative. Some use this term to refer to the complete "obesity-hirsutes-secondary amenorrhoea" complex, while others understand it to include only some of the features. Patients with polycystic ovaries usually ovulate infrequently and often present with infertility, though they may sometimes have had a previous pregnancy. Enlargement of the clitoris is usually not marked. But there may be uterine hypoplasia in nulliparous women. There is bilateral ovarian enlargement in most patients but it may be asymmetrical and not detectable by routine clinical examination.

Virilizing Ovarian Tumours

Virilizing ovarian tumours are rare and include arrhenoblastomas and hilus cell tumours. They are often small and may not be detectable unless the ovaries are split open.

ADRENAL CORTEX

Cushing's Syndrome and Adrenal Tumours

In Cushing's disease (due to excessive pituitary ACTH production and consequent bilateral adrenal hyperplasia) hirsutes and virilism may be present in addition to the features normally associated with overproduction of corticosteroids. In tumours of the adrenal cortex, particularly carcinomas but also some adenomas, virilism is usually more definite and there may be no "Cushingoid" features. The adrenal virilism is due to excessive production of adrenal androgens, such as dehydroepiandrosterone, androsterone, and testosterone.

Congenital Adrenal Hyperplasia

Congenital adrenal hyperplasia is due to deficiency of an enzyme in the metabolic pathway for the synthesis of cortisol (hydrocortisone), though the synthesis of other adrenal steroids may also be affected. As a result of the enzyme defect plasma cortisol levels tend to fall, leading to increased ACTH production and adrenocortical hyperplasia. The hyperplastic adrenals synthezise precortisol compounds in great excess and their metabolites are androgenic. If the condition is manifest in utero and the fetus is female it may be born with abnormal external genitalia of a male type (female pseudohermaphroditism)—a varying degree of labial fusion obscuring a persistent urogenital sinus with considerable enlargement of the clitoris, so that the appearance is that of apparent hypospadias and cryptorchidism; occasionally there is a penile urethra. It is evident that the incorrect sex may be ascribed to the child. If untreated, more extensive virilism develops. Sometimes there is in addition a "salt-losing" state and the infant develops dehydration, hyponatraemia, and circulatory failure; this is presumably due to mineralocorticoid deficiency. Virilism due to this type of enzyme deficiency may not be seen in the neonate but may develop in infancy, adolescence, or indeed in adults. Boys most commonly present early with the salt-losing state or with precocious puberty, usually in infancy.

Investigations

The urinary 17-ketosteroids represent, in the main, the metabolic breakdown products of adrenal androgens and only a small proportion is derived from testosterone. It is quite possible, therefore, to have a testosterone-secreting tumour in a patient in whom the 17-ketosteroid excretion is normal. A raised 17-ketosteroid excretion is seen in patients with congenital adrenal hyperplasia, adrenal tumours with or without Cushing's syndrome and also not infrequently in the polycystic ovary syndrome. With the exception of autonomous adrenocortical tumours and Cushing's syndrome the urinary excretion of 17-ketosteroids is suppressed during a three-to five-day course of dexamethasone (0·5 mg given each six hours by mouth), indicating their ACTH dependence. The adrenal contribution to the polycystic ovary syndrome is not understood, but undoubtedly the raised levels of 17-ketosteroids often found in this condition are largely dependent upon adrenocortical function. Plasma testosterone levels are often somewhat raised in these conditions, and are suppressed with dexamethasone unless an autonomous adrenal tumour is present.

The finding of a raised level of pregnanetriol in the urine confirms the diagnosis of congenital adrenal hyperplasia, since this product reflects the degradation of the abnormal corticosteroids which accumulate in this condition. In Cushing's syndrome plasma cortisol and urinary 17-ketogenic steroids are not suppressed by dexamethasone, 2 mg per day, but are usually suppressed to at least 50% of their basal level on a dosage of 8 mg per day given for 48 hours, unless an adenoma or carcinoma of the adrenal is present.

If congenital adrenal hyperplasia is suspected at the birth of a child with an ambiguous pattern of genitalia nuclear sex must be determined immediately—initially from the presence or absence of Barr bodies in cells obtained from a buccal smear and subsequently by full chromosome assessment from culture of peripheral leukocytes.

RADIOLOGICAL INVESTIGATIONS

If an adrenal tumour is suspected intravenous pyelography may show that one kidney is displaced. Selective arterial or retrograde venous angiography usually shows an abnormal pattern of blood vessels suggesting an adrenal tumour and indicates the side of the lesion.

Assessment of the size of the ovaries is facilitated by gynaecography—that is, the introduction of carbon dioxide into the pelvic cavity via the cervix and tubes, or transabdominally to outline the gonads. An *x*-ray film will then demonstrate the ovaries and uterus (Figs. 1 & 2). About half of enlarged ovaries cannot be detected by routine clinical examinations even by the experienced practitioner and gynaecography has become a routine part of the investigation

of a hirsute patient unless the cause is obviously not ovarian. Laparoscopy or pelvic peritinoscopy at the same session allows visualization and sometimes biopsy of the affected ovaries.

Unilateral ovarian enlargement is not always seen with virilizing ovarian tumours, for these may be small. If virilization is at all appreciable, especially if accompanied by amenorrhoea, assessment of plasma or urinary testosterone is essential. If such assays cannot be obtained then laparotomy should be performed.

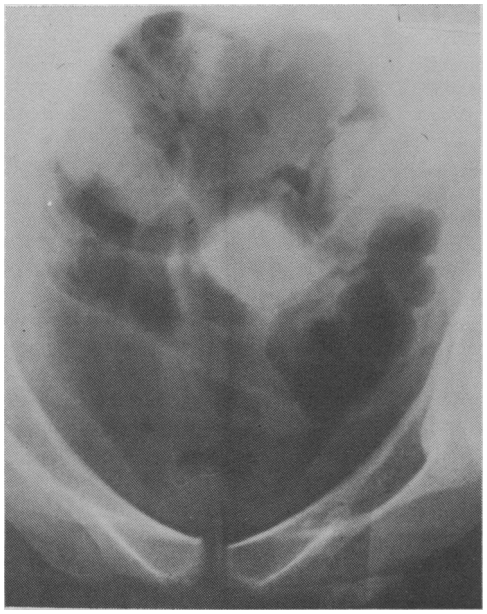

FIG. 1—Gynaccogram of patient with the polycystic ovary syndrome.

FIG. 2—Ovaries of the same patient at operation.

Treatment

When hirsutes is due to ovarian or adrenal tumours these are removed when possible, while bilateral adrenalectomy is generally preferred as the treatment for Cushing's syndrome due to adrenal hyperplasia. In congenital adrenal hyperplasia both the production of ACTH by the pituitary and hormones by the adrenal cortex should be suppressed with a corticosteroid such as prednisolone until the urinary 17-ketosteroid excretion is in the low-normal range and the pregnanetriol excretion less than 2 mg per day. A larger dose may be required initially, but eventually a dose in the range of 7·5 to 10 mg per day suffices. This is best administered in divided doses, with much of the total (about half) given before retiring as this will more effectively suppress the rise in ACTH which normally occurs during the second half of sleep.

Eradication of the cause of excess androgen production usually reverses many of the features of virilism, and menstruation returns. If the virilism has occurred during development in utero, or during the early growing period, the bone formation may remain android in type. Surgical correction of genital abnormalities may be required—for example, clitoridectomy or vaginoplasty. Unfortunately, once established, hirsutes often regresses only slowly, if at all. If it persists, local therapy is required.

OVARIAN STIMULATION OR SUPPRESSION

Treatment of the polycystic ovary syndrome is difficult and may be unrewarding. Ovulation and conception can be induced in many patients using clomiphene or human menopausal gonadotrophin, but this does not affect the hirsutes. Surgical treatment (wedge resection of the ovaries) may result in regular menstruation and ovulation, though the condition often returns and only rarely results in diminution of hair growth. In many patients with this syndrome the urinary 17-ketosteroids and plasma testosterone levels may be suppressed with prednisolone therapy, and this treatment often results in regular ovulation and menstruation. Alternatively, ovarian function may be suppressed with the contraceptive pill. At present it is impossible to predict reliably which patient is more likely to respond to corticosteroids and which to treatment with the contraceptive pill. Sometimes the best results are obtained when both treatments are given together.

If withdrawal bleeding does not occur regularly in those patients on the pill it should be discontinued. A diminution in the hirsutes is not infrequently seen with either form of treatment and failing this it often does not progress. Treatment should be continued for at least a year before being abandoned. If successful it should be stopped after two years for reassessment. Many patients with this syndrome, however, continue to suffer embarrassment from hirsutes and must seek local treatment.

LOCAL COSMETIC TREATMENT

Simple bleaching, plucking, or shaving of facial hair or depilatory waxes and creams are used by many patients in whom no cause for the hirsutes has been found or in whom treatment has not been fully effective. If the facial hirsutes is not extensive removal of the hair and destruction of the follicle by electrolysis is used. All these methods for local removal of facial hair may be aided by the twice daily application of an oestrogen cream (for example, dienoestrol 0·01%).