1 Introduction

For a long time, the only means for combatting hirsutism were ablative surgery, the mechanical removal of body hair such as through shaving, plucking, waxing, chemical depilation and electrolysis, or simply bleaching. When glucocorticoids became available in the early 1950s, it was hoped that adrenal hirsutism and virilism could be treated by the suppressive action of these hormonal compounds upon adrenal androgen hypersecretion via a reduction in the release of pituitary ACTH. In fact, this was shown by Wilkins et al. (1950) to be true in the case of congenital adrenal hyperplasia (originally, congenital, adrenogenital syndrome). Since that time the use of glucocorticoids has become the method of choice for this type of inborn enzymatic disturbance.

Postpubertal adrenal hirsutism, on the other hand, was found only on occasion to respond well to corticoids, although normalization of the hypersecretion of adrenal androgens can be achieved in a considerable proportion of cases (Casey et al. 1966; Forbes 1965; Ismail et al. 1974). In contrast, Perlhoff et al. (1959) stated that prednisolone, in daily doses of 7.5–15 mg, resulted in fair to good improvement of hirsutism in all 45 women treated. Recently, Abraham et al. (1981) also reported satisfying results when dexamethasone treatment was restricted to women with hyperandrogenism of adrenal origin.

In the early 1960s there were a few reports on favourable effects of ovulation inhibitors on hirsutism (Maggiolo 1964; Mauvais-Jarvis and Decourt 1964; Casey et al. 1966). Again, it was possible to reduce the increased secretion and/or excretion of androgens and their metabolites with oral contraceptives (OCs) in most of the cases, but improvement of hirsutism, if any, was rather limited. The vast majority of contraceptive formulations at that time, as well as those available today, contained as the progestational component derivatives of 19-nor-17α-ethinyl-androstan, now known as estranes. With the exception of norethynodrel, however, all progestogens of this category exert weak androgenic side effects. Consequently, it is a question of the balance between the administered androgenic activities and the reduced endogenous androgen production which determines whether hirsutism, acne and the other signs of hyperandrogenism improve, remain unchanged or even deteriorate under OCs. More recently, with the advent of low-dose OCs and new progestogens, the chances of improving hirsutism by means of ovulation inhibitors have become better (Cullberg et al. 1985).
In the late 1960s, the 17α-acetoxyprogesterone derivatives, the so-called pregnanes, were used more widely as the progestational component of the contraceptive pill. The beneficial effects upon hirsutism and other signs of hyperandrogenism were reported to be somewhat better, but altogether they were also disappointing. The obvious superiority of pregnanes compared to estranes in this respect is readily explained by their lack of androgenic partial effects. According to animal experiments, some of these compounds even exert antiandrogenic effects.

In men, the antiandrogenic partial effect of a progestogen is difficult to evaluate. So far, it has been attributed mainly to chlormadinone acetate and to its closely related derivative cyproterone acetate (CPA), which is thought to be more powerful in this respect. It remains an open question whether other drugs with a 17α-acetoxy-progesterone structure, such as megestrol acetate and medroxyprogesterone acetate, possess antiandrogenic properties of clinical relevance in humans. In fact, the sole intramuscular administration of 100 mg medroxyprogesterone acetate every 15 days has been reported to definitively improve hirsutism (DeOliveira 1976). As in the case of a very few earlier papers on the sole use of progestogens in this field, the communication quoted remained without confirmation.

17α-methyl-B-nortestosterone (benorterone) was the first antiandrogen successfully tried in women for the treatment of hirsutism, acne and seborrhoea (Zarate et al. 1966; see Fig. 1). Although it was obviously more effective in reducing the signs of androgenization than ovulation inhibitors, this compound was soon withdrawn from clinical trials “pending further animal experimentation” (Dalla Pria et al. 1970). “The expense of manufacturing this agent and stringent requirements of the Food and Drug Administration for further safety testing resulted in loss of interest by the manufacturers in promoting this agent” (Greenblatt and Gambrell 1985).

![Fig. 1. Weight of facial hair obtained by shaving in a hirsute woman before and during treatment with benorterone. Significance versus pre-treatment values: *p<0.05; **p<0.01 (Zarate et al. 1966)