CHAPTER 35

The Treatment of Acne

J. R. MARSDEN and S. SHUSTER

A. Introduction

There is a direct relationship between the severity of acne and the rate of sebum excretion (CUNLIFFE and SHUSTER 1969a; BURTON and SHUSTER 1971) and increased sebum production is the primary causal factor (SHUSTER 1985). Secondary bacterial colonisation of the pilo-sebaceous follicle with mainly Propionibacterium acnes (MARPLES 1974) results in the characteristic inflammatory lesions. Consequently acne responds best to drugs which reduce sebum production, followed in effectiveness by anti-microbials. There is little evidence for the opinion that obstruction of the pilo-sebaceous ducts is causally related to acne (see SHUSTER 1985) although several treatments are alleged to work by unblocking them. Despite its simplicity, failure of treatment is common; and this is as often due to inadequate explanation by the doctor as to misunderstanding by the patient. The slow onset of action of most acne treatments and the persistence with which they need to be used (LANCET 1982) needs emphasising from the outset. There is no evidence that dietary, sexual, hygienic or cosmetic practices affect the severity of acne.

Because of toxicity the most potent sebostatic drugs are used only in severe acne, whereas anti-microbials are used in all grades of severity. There is a major placebo effect in acne (FRY and RAMSAY 1966; POCHI and STRAUSS 1973; CHRISTIANSSEN et al. 1974) which probably explains the alleged effects of many available treatments.

B. Sebostatic Drugs

Although sebum production in humans is mainly due to endocrine modulation (SHUSTER and THODY 1974; THODY and SHUSTER 1989 and Chap. 14 Volume I) because many hormones are involved complete control of acne by endocrine mechanisms is not feasible. The alternative of non-endocrine inhibition of sebaceous cells is proving a more satisfactory approach.

I. Endocrine Inhibitors

1. Anti-androgens

Although it is clear that many hormones affect sebaceous gland function, the largest contribution is that of androgens (SHUSTER 1982). Hence anti-androgens are the most effective endocrine sebaceous inhibitors and they work either by di-
rect competition for the cytosolic androgen receptor (e.g. cyproterone acetate, cimetidine, flutamide) or by inhibiting the intracellular interconversion of androgens. Although the conversion of testosterone to dihydrotestosterone by 5α-reductase is generally believed to be critical for the sebaceous response to androgen (see Chaps. 14, 15 Volume I) dihydrotestosterone is only a weak androgen agonist in the human sebaceous gland (Cooper et al. 1979) where its role is dubious (Shuster 1982). Thus, the reason patients with 5α-reductase deficiency do not develop acne (Peterson et al. 1977) is likely to be a developmental effect of dihydrotestosterone in early life and not a modulatory effect on sebum production in the adult (Shuster 1982).

Cyproterone acetate (CPA) is the most potent anti-androgen and reduces sebum excretion rate (SER) by a maximum of 65–70% by 4 weeks of treatment with 100 mg/day (Burton et al. 1973) with commensurate improvement in acne apparent by 8 weeks (Marsden et al. 1984a). The response is dose related with a negligible effect with doses less than 10 mg/day. Thus, it is probable that any therapeutic action of commercially available low dose CPA preparations is due to their oestrogen content. Its action is to reduce sebaceous lipogenesis with little qualitative change in lipid composition (Marsden et al. 1984a). The unwanted effects of CPA include reduction in libido and potency (which restricts its use in males to short periods only) and breast tenderness, weight gain and mild adrenal suppression (Chapman 1982). In females it is combined with ethinyloestradiol both to prevent conception, as CPA feminises male foetuses, and to reduce its progestogenic effects. A suitable regimen CPA 50–100 mg/day from day 5 to day 14 of the menstrual cycle, and 50 μg ethinyloestradiol from day 5 to day 25 (Hammerstein and Cupceanu 1969). The long-term side effects of this treatment are unclear and it is progestogenic (Lancet 1983). Other anti-androgens, e.g. cimetidine (Lyons et al. 1979), spironolactone (Keahey et al. 1983) or 17α-methyltestosterone (Strauss and Pochi 1970) have only a small effect and topical anti-androgens which could minimise the unwanted effects of systemic treatment are surprisingly ineffective (Strauss and Pochi 1970; Simpson et al. 1979; Lyons and Shuster 1982). In the case of topical CPA this is presumably because its action is due to a metabolite (Lyons and Shuster 1983).

2. Oestrogens and Oral Contraceptives

Ethinyloestradiol 250 μg given cyclically reduces SER by about 40% (Pochi and Strauss 1973), and has a modest therapeutic effect; 50 μg, the dose used in several oral contraceptive pills, would be expected to reduce SER by about 20%, with little therapeutic effect. However, the greater the dose or potency of progestogen in the contraceptive pill, the smaller the decrease in SER and the most suitable combination in this respect if 50 μg ethinyloestradiol and 1 mg norethisterone acetate (Pye et al. 1977).

3. Corticosteroids

Prednisone can reduce SER in females because of suppression of adrenal androgen production, but the effect is too small to be useful on its own. Prednisone