

Table 1. *The combined results of virus isolation, Tzanck smear and IF-test*

Virus isolation	Tzanck smear	IF-test	No. of patients
+	+	+	16
-	-	-	7
+	-	+	3
-	+	+	3
+	-	-	2
-	+	-	1
Total			32

slightly larger than leukocytes and in some up to five times this size. The latter were judged to be multinuclear giant cells. The most intense fluorescence was usually seen just below the cell membrane and in the cytoplasm, whereas nuclear fluorescence was weaker. In some slides, cells with a morphology similar to normal epithelial cells showed weak fluorescence. In no instance was this sufficiently intense as to be confused with specific fluorescence (Fig. 1). No fluorescence was seen in any of the slides from the control patients.

Table 1 shows the correlation between the results of virus isolation, IF-test and Tzanck smear. For 23 of 32 patients the results of the three techniques were identical.

The average duration of the eruption among patients with homogeneously positive tests was found to be 5 days, among those with homogeneously negative tests, 9 days.

### DISCUSSION

The diagnostic tests employed in this investigation proved to be almost equally sensitive (Table 1). However, it proved necessary to prepare two Tzanck smears from each patient in order to achieve this result.

20 of the 25 patients with positive diagnostic test results were identified using Tzanck smear as the sole diagnostic tool. The addition of virus isolation identified the remaining 5 patients. Combination of any two diagnostic tests used in this study will produce similar results. Although a combination of IF-test and Tzanck smear gave the poorest result, this combination identified 23 of the 25 patients in whom positive diagnostic tests were made.

IF-test was seen to be the single most sensitive diagnostic tool, and previous studies have shown

that distinction can be made between herpes simplex type 1 and 2 infections using this test (2, 7).

All three of the techniques employed gave consistently negative results for 7 patients. This might have been due to the fact that the average disease duration for this group of patients was 9 days, whereas it was 5 days in the group for whom homogeneously positive test results were found. The results of Tzanck smears and virus isolation are frequently negative in herpes simplex infections of more than 8 days' duration (8). It is also possible that not all of these patients had eruptions caused by HVH.

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### Effect of Cyproterone acetate on Skin Surface Lipids

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*Abstract.* Skin surface lipids in female patients with acne were examined before and after treatment with the oral

contraceptive SH 209 AB (2 mg cyproterone acetate and 0.05 mg ethinyl estradiol) by direct extraction with petrol ether and photometrical determination. A significant reduction in the skin surface lipids was seen, together with a remarkable alleviation of the disease.

**Key words:** Acne; Hormonal control; Skin surface lipids; Cyproterone acetate

Hormonal control of the activity of sebaceous glands consists of stimulation by androgens and inhibition by estrogens. Moreover, the sebaceous glands as well as the entire skin are important sites of androgen metabolism. Here, conversion of testosterone under pituitary control into the much more potent dihydrotestosterone results in the production of a more potent androgen (8). Elevated levels of androgens, increased formation of dihydrotestosterone, and genetically determined hypersensitivity of sebaceous glands to hormonal stimulation lead to a rise in sebaceous secretion as well as skin surface lipids and seborrhea, which is a major pathogenetic factor in acne vulgaris.

Knowledge of hormonal control of sebaceous secretion has encouraged experimentation with therapeutics interfering with this mechanism. Good results were obtained by combined administration of antiandrogens and estrogens as sequential therapy according to Hammerstein & Cupceancu (5), using a dosage of 100 mg cyproterone acetate with 0.05 mg ethinyl estradiol. Efforts to reduce the dosage were also successful. Therapy with the oral contraceptive SH 209 AB—kindly provided by Schering Co., Vienna—(combination of 2 mg cyproterone acetate with 0.05 mg ethinyl estradiol) resulted in defatting of seborrheic skin and improvement of acne vulgaris (3). In the present study an objective assessment of this finding was undertaken by investigating sebaceous secretion during the above-mentioned therapy through measurement of skin surface lipids.

## MATERIAL AND METHODS

### Patient material and therapeutic schedule

11 female patients between 16 and 34 years (average 18 years) suffering from severe papulopustular acne received for 3 months the preparation SH 209 AB in accordance with their menstrual cycle. In 3 patients treatment was continued with a commercially available sequential preparation containing ethinyl estradiol and *d*-norgestrel (Sequilar<sup>®</sup>, Schering, Vienna). No additional therapy was implemented.

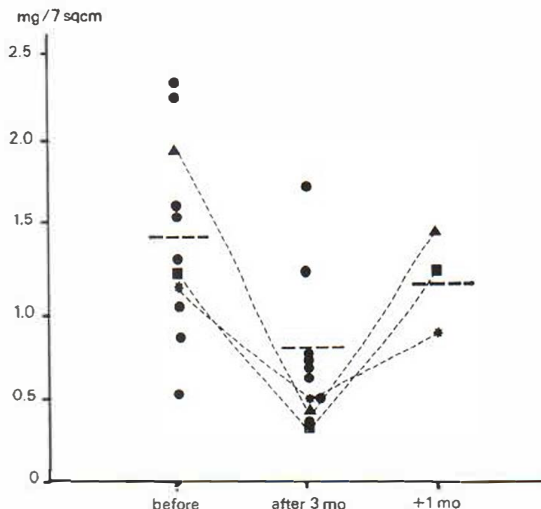


Fig. 1. ●, Skin surface lipids before and after treatment with SH 209 AB for 3 months; ▲■, skin surface lipids before and after 3-month therapy with SH 209 AB and subsequent treatment with a sequential contraceptive for one month.

### Quantitative lipid assay

In all patients the causal level (6) of untreated skin was determined quantitatively before and after treatment, using a modification of the method of Schirren & Honsig (9). The patients were told to cleanse their skin thoroughly on the day preceding measurement only with an alcoholic lotion and refrain from applying ointments or make-up. To reduce the risk of error to a minimum, the examinations were performed during the cool season, at room temperature (23°C), at the same time of day and in the middle of the menstrual cycle. Direct extraction of skin surface lipids was carried out by placing 4 tubes (standardized diameter) with 2 ml petrol ether each, on a cheek, covering an area of 7 cm<sup>2</sup>.

### Chemical analyses

The lipid extracts were pooled and evaporated under nitrogen to dryness. The lipids were determined photometrically (10). Aliquots of the lipid extracts were applied to a 20×20 glass plate coated with 0.25 mm silica gel G (Merck). For the purpose of separation and determination of the different lipid classes the plates were developed in a solvent system of hexane–diethylether–glacial acid (70:3:1.5-v/v/v) according to Erb & Böhle (2). After development (15 cm) the plates were sprayed with a solution of ammonium molybdate–perchloric acid and heated at 120°C for 20 minutes (7). For quantification of the different lipid classes the plates were determined densitometrically.

Statistical analysis was performed using the *t*-test.

## RESULTS

After 3 months of therapy with SH 209 AB, overall lipid values were significantly reduced in 10 pa-

tients, with an increase in one patient only. The "before" values ranged between 0.5 and 2.3 mg/7 cm<sup>2</sup> with a mean of 0.8. The reduction in mean values was 45.7%. Statistical analysis using the *t*-test showed a significance of  $p > 0.005$  (Fig. 1). No change in the proportionate composition of lipids was observed.

Reduction of surface lipids were accompanied in most cases by an improvement in the course of the disease. In 9 patients the acne improved significantly after 3 months of therapy, in one patient no amelioration was seen in spite of a reduction of the values from 1.25 to 0.65, and the patient whose values increased from 0.5 to 0.9 proved refractory to therapy.

All 3 patients whose treatment was continued with a sequential preparation containing *d*-norgestrel again showed a significant increase in lipid values.

## DISCUSSION

Of all antiandrogens tried so far that act by competitively inhibiting androgenic receptors, the synthetic hormone cyproterone acetate, derived from progesterone, has proved the most effective. By contrast, gestagens, which are derived from 19 nor-testosterone, still show considerable residual androgenic action. The combination of cyproterone acetate with estrogen does not interfere with the menstrual cycle and also offers the necessary contraceptive protection, since administration of cyproterone alone would cause feminization of the male fetus in the case of pregnancy. Moreover, the action of the combined drug is cumulative: estrogens reduce androgen synthesis, by means of central inhibition of gonadotropic secretion and also have an anti-inflammatory effect, so beneficial in acne vulgaris. The use of cyproterone acetate and estrogen in the treatment of acne rests on their sebostatic effect. Although sebaceous secretion shows wide individual differences and skin surface lipid values vary according to the method of determination (4), it is the currently accepted opinion that, collectively, acne patients have higher surface lipid values than healthy controls and that all cases of severe acne are associated with a significant seborrheic state (1). That seborrhea may exist without the development of acne vulgaris underlines the importance of additional factors, such as increased vulnerability of the follicular epithelium.

If the effectiveness of antibiotics used in the treatment of acne vulgaris is judged on the basis of the reduction of free fatty acid in the sebum, then the reduction of skin surface lipids is the parameter for an effective sebostatic therapy. As is demonstrated by the results of the present investigation, this reduction was obtained with SH 209 AB in 9 of 11 cases, accompanied by a significant improvement in the clinical picture, whereas treatment with a *d*-norgestrel-containing sequential preparation reversed the results. The low doses in the combination SH 209 AB allow for a treatment of acne vulgaris that is not associated with any higher risk than administration of oral contraceptives. This therapy is especially indicated for patients with acne vulgaris who also want to take an oral contraceptive, or in cases of acne vulgaris refractory to other forms of treatment.

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