the particular components of the flora which predominate depend on that interaction and on the degree of hydration of the keratin (2, 6). The ability to distinguish between the infective agents is important in terms of therapy, but the results described here suggest that no single clinical feature, except perhaps erythema, will enable the distinction to be made easily.

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Effect of Betamethasone Valerate on the Normal Human Facial Skin Flora

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Abstract. Eighteen volunteers were randomly divided into two groups and allocated either an active corticosteroid preparation (Betamethasone valerate) or the basal formulation only (placebo). The cream was applied to the face twice daily for one month. The treated area was sampled by the scrub-wash method immediately before treatment began and after 2 and 4 weeks, and microorganisms were enumerated and identified. Application of either cream produced a very slight increase (≤ 0.5 log cycle) in the skin flora during the first 2 weeks of treatment. There were no significant differences in the changes occurring between volunteers treated with placebo and those on the steroid formulation. The results are discussed in relation to theories of pathogenesis of perioral dermatitis and steroid acne.

Key words: Steroid; Skin microflora; Perioral dermatitis

This work was undertaken in connection with a study of patients suffering from perioral dermatitis (PD). The condition is of uncertain aetiology, but responds to tetracycline therapy, suggesting a possible role for microorganisms. No obvious pathogens have been consistently isolated from lesions of PD, but disturbances in the numbers or balance of the normal flora have not been investigated. Misuse of corticosteroid creams may be the precipitating factor for PD and we have therefore investigated the effect of steroid cream on the normal skin flora of the face in healthy volunteers. Since the aetiology of steroid acne is also poorly understood, the study may cast some light upon this clinical entity.

METHODS

Subjects and treatment schedule

Eighteen healthy medical students (11 male, 7 female) volunteered to participate. The study was conducted in a double-blind manner, and each student was randomly allocated to either treatment A (betamethasone valerate) or treatment B (vehicle only). Volunteers were instructed to apply a small amount of cream to the side of of the face midway between the mouth and the ear at night and in the morning after washing.

Microbiology

Samples were taken by the scrub-wash method (15) before treatment commenced and after 2 and 4 weeks of treatment. Numbers of bacteria in the scrub-wash fluid were determined by the method of Miles & Misra (9). Aerobic bacteria were cultured on heated blood agar plates (Oxoid Columbia agar base +5% horse blood) at 37°C for 48 hours.

Propionibacteria were cultured on Oxoid Reinforced Clostridial Medium agar + furazolidone 6 μg/ml (RCMF) for one week at 37°C in an Oxoid anaerobic jar (80% N_2+10% H_2+10% CO_2). Numbers of the yeast *Pityrosporum* were determined by the membrane filtration method of Mulvany (10).

Gram-positive, catalase-positive cocci were differen-

Table I. *LOG number of microorganisms/cm² skin before and during treatment (geometric mean count ± SEM)*

	Treatment group, $n=10$			Placebo group, $n=8$		
Time	0	2	4	0	2	4
Propionibacteria	4.36±0.52	4.72±0.52	4.46±0.73	4.8 ±0.45	5.09±0.37	4.67±0.38
Staphylococci	3.74±0.36	4.24±0.40	4.54±0.31	4.55±0.32	5.03±0.25	4.82±0.25
Pityrospora	2.76±0.52	3.11±0.45	3.15±0.56	2.12±0.64	2.18±0.67	2.67±0.62

tiated as micrococci or staphylococci on the basis of colony morphology, reaction on erythromycin/glycerol medium (13) and reaction in the modified oxidase test (4). Aerobic coryneforms were recognized by colony morphology, Gram stain and catalase reaction. Colonies growing on RCMF anaerobically were presumed to be skin propionibacteria: Gram and catalase reactions of representative colonies were always checked.

RESULTS

Ten volunteers were treated with active preparation and 8 with placebo. All of the subjects were colonized with staphylococci and propionibacteria and all but 2 with the yeast *Pityrosporum* as well. Micrococci were consistently present in only 3 subjects, appearing transiently in a further 3. Aerobic coryneforms were consistently present in only 2 subjects, appearing transiently in a further 5. No comment can be made on the micrococci and coryneforms due to the small amount of data obtained. One subject treated with the placebo preparation became colonized with *Klebsiella* during treatment.

Table 1 shows the mean counts/cm² skin of staphylococci, propionibacteria and pityrospora initially and during treatment. There were no significant differences between the counts of treatment and placebo subjects before treatment commenced (Mann-Whitney U-test). Counts tended to increase very slightly (<0.5 log cycle) during the first 2 weeks of application of either preparation. These increases were significant ($p<0.05$) in the cases of staphylococci and propionibacteria in the steroid-treated group (Wilcoxon paired test). The upward trend in counts of staphylococci continued in the treatment group only but was not significant between weeks 2 and 4. The number of staphylococci in the placebo group were reduced during this period ($p<0.05$ Wilcoxon paired test). These changes, though statistically significant, were small and probably of little practical significance. When the treatment and placebo groups were compared, no significant differences were found between the groups for changes in level of any of the microorganisms at any time (Mann-Whitney U-test).

Counts of *Pityorsporum* fluctuate more widely than those of bacteria: this is partly due to the insensitivity of the membane filtration technique where the lowest detectable count is 3.4×10^2 yeasts/cm² skin. Counts below this level register as 0, so changes may seem to be greater than they actually are if the skin is colonized at a low level.

DISCUSSION

Despite wide useage of topical steroid preparations in dermatology, little is known of their effect on the normal microflora of the skin. Interest has centred on the appropriateness of combined antibiotic–steroid therapy in various clinical situations. Marples et al. (1973) studied the effects of topical steroid on experimental human skin infections with *Staphylococcus aureus* and *Candida albicans* (8). Multiplication of these organisms was not affected by the steroid, though the symptoms of infection were ameliorated. Leyden & Kligman (1977) treated lesions of atopic dermatitis secondarily infected with *S aureus* with 0.025% fluocinolone acetonide cream (6). Mean counts of total aerobes and *S. aureus* did not change significantly after one week, although there was a downward trend (1 log cycle) attributed to the skin becoming more normal and less suitable for multiplication of *S. aureus*. Our results are compatible with these studies in that the steroid seemed to have little effect on the numbers of microorganisms present.

Steroid acne is possibly due to hyperkeratinization of the acroinfundibulum (5) but, surprisingly, bacteriological studies in this clinical entity are

lacking. Our study shows no marked effect on the propionibacteria but on the other hand does not exclude some change in the pilosebaceous duct organisms or an effect following longer application of the steroid.

It is now generally accepted that misuse of potent topical steroids is important in the aetiology of PD (14) but the mechanism by which steroids cause the condition is not clear. Some authors suggest that an infective process is involved in PD, possibly because steroid treatment alters conditions locally to allow growth of organisms which do not normally form part of the skin flora. *Candida albicans* was implicated in one case study (2) but this seemed to be an isolated incident. Fusiform bacilli were seen in biopsies, but not cultured, in another series of patients (3). Evidence for and against involvement of fusiforms was reviewed by Rockl & Schubert (12). Routine bacteriology on skin swabs of the kind reported in several studies shows only that there is no obvious pathogen present in the majority of patients. None of the steroid-treated sites in our study yielded organisms other than normal skin flora: the one volunteer colonized by *Klebsiella* from week 2 was in the placebo group. Our procedures would not recover fusobacteria (the study was not designed by precipitate PD and the sampling site was not next to the mouth, which is the presumed site of origin of fusiforms). Preliminary studies have shown that *Fusobacterium* dies quickly in the scrub-wash fluid we used for sampling the skin.

If abnormal organisms are not involved, perioral dermatitis might result from steroid treatment upsetting the ecological balance between normal facial organisms (1). Our data lend little support to this concept. No really distinctive changes occurred in our steroid-treated group. In a pilot study where bacteria were identified to species level, there were no indications of shifts of species within a genus during steroid treatment (data not presented). It is possible that some change in the population of aerobic coryneforms is important: our data were not suggestive of such a change but the numbers studied were very small. Prolonging treatment beyond a month might eventually cause changes in the skin flora.

What other effect of steroids on the skin flora could be implicated in perioral dermatitis? Raab (1976) showed that glucocorticoids at various concentrations culd both stimulate and inhibit metabolism of *S. aureus*, *S. albus* and *C. albicans* *in vitro* (11). In vivo modification of microbial metabolism by steroids might result in some effect on the skin. Alternatively, the microflora might be capable of metabolizing the steroid preparation to produce compounds which irritate the skin in some way. Leyden et al. (1981) have recently suggested that aerobic coryneforms may be able to synthesize steroids from cholesterol in apocrine sweat to produce body odour (7). It is also possible that the clinical response of PD to tetracycline is entirely unrelated to the antibacterial activity of the drug. These possibilities will be further investigated.

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