Induction of Acne by Topical Steroids*

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Summary. An acneforme eruption was regularly induced in human adult male volunteers by topical application of corticosteroid solutions and various commercial creams. Within 7 to 14 days smooth, firm, dome-shaped, reddish papules of rather uniform size appeared followed by comedones several weeks later. Factors promoting the development of steroid acne were (I) high concentrations, (II) continuous occlusion, (III) young adults below age 30, (IV) whites in preference to blacks, (V) history or signs of acne, (VI) applications to acne areas of face and upper back. Increased formation of horny cells was demonstrated by radiolabelling with $^3$H-thymidine, $^3$H-glycine and $^3$H-histidine. Histologically, the first event was a focal degeneration of the follicular epithelium with the formation of a circumscribed intra- and perifollicular abscess.

An acneform eruption is one of the most characteristic side effects of prolonged therapy with ACTH or corticosteroids [22]. Acne is a classic feature of Cushing’s syndrome from adrenocortical hyperplasia. With the widespread use of steroids as immunosuppressives in preventing

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graft rejection and in controlling "autoimmune" disorders, steroid acne has now become a commonplace.

Oral corticosteroids are sometimes used in acne conglobata to reduce nodulo-cystic lesions [1, 5, 7]. Moreover, topical application is increasingly finding favor [6, 10, 19, 25, 27, 29]. For example, Tye and Fisher secured good to excellent results in 52 of 61 patients by applying fluocinolone acetonide (Synalar®) 4 to 5 times daily in conjunction with hot compresses [26]. The severer cases benefited most. On the other hand Fulton and Kligman found that 7 of 12 patients treated by nightly occlusive application of high strength (0.5%) triamcinolone acetonide (Aristocort®) experienced alarming flares. An initial improvement gave way after a couple of months to outcroppings of inflammatory papules and comedones [9].

Topical high strength steroids can elicit acneform eruptions in unusual sites. Pascher et al. observed comedones on the scalps of 5 of 28 alopecia areata patients in whom 0.2% fluocinolone acetonide (Synalar®) was being used to restore hair growth [12]. Steroids have begun to be incorporated in anti-acne medications, chiefly hydrocortisone in the US, but more potent ones are making a debut in Europe.

The objectives of this study were to develop a human model of topical steroid acne and to compare the process clinically and histologically to acne vulgaris.

**Materials and Methods**

*Subjects.* These were healthy adult male prison volunteers. More than 350 subjects participated over a 3 year period.

*Steroids.* Initially we used crystalline fluocinolone acetonide in equal parts of ethanol and propylene glycol in rather concentrated solutions. Later we discovered that certain proprietary formulations were quite suitable. The bulk of the study was conducted with Synalar® Cream 0.025%.

*Applications.* Solutions and cream were applied to the skin under strict occlusion continuously for three to four weeks. The test site, 4 x 4 cm or 10 x 10 cm on the acne prone areas of the upper back or chest, was covered with polyethylene plastic film and sealed to the skin with overlapping strips of impermeable plastic tape (3M Blenderm®, Minnesota Mining Co). Control sites were treated with Hydrophilic ointment, USP, applied in the same way. This was subsequently omitted when neither clinical nor histological studies gave evidence of acne.

*Sebum Production.* The gravimetric cigarette method of Strauss and Pochi [24] was utilized to measure sebum production in a 10 cm² area of forehead over a 3 h period. This was done twice before and once weekly during a four week exposure to steroid. The subjects rested quietly in air-conditioned rooms [4].

*Histology.* 74 full thickness specimens of skin were excised at various times from 6 days to 3 months. These were formalin fixed and semi-serially sectioned. The Brown-Brenn modification of Gram's stain was used to visualize bacteria.

*Autoradiographs.* A volume of 0.1 ml physiologic saline containing 5–10 μCi of ³H-thymidine (³H-TdR), (spec. act. 2.6 Ci/mM or 6.0 Ci/mM; New England