THE EFFECT OF FORMULATION ON THE CLINICAL RESPONSE TO TOPICAL FLUOCINOLONE ACETONIDE.

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In selecting the best bases for topical application of drugs, Williams (1964) has stressed the need for " much clinical study by many investigators over many years ". Penetration, defined by Goldsmith and Hellier (1954) as entry of a drug into the skin from a topically applied medicament, is likely to be different in normal and diseased skins. Kalz and Scott (1956) studied the therapeutic action of hydrocortisone in a variety of bases. They came to the conclusion that the differences they observed were not determined primarily by any specific influence of the bases on penetration, but rather depended on the compatibility of the base with the skin disease and its particular location. Jarrett (1961) has suggested that each type of skin disorder probably alters penetration in a different manner thus making a particular medicament from a particular vehicle more or less available to epidermal cells.

In a different context, the particle size of the drug itself has been shown to exert a profound influence on therapeutic effect. Studies on griseofulvin (Atkinson *et al.*, 1962 ; Duncan *et al.*, 1962) have shown that a microcrystalline powder is a significantly more efficient therapeutic agent orally than the original coarse powder.

McKenzie and Stoughton (1962) described a blanching test which compared a local vasoconstrictor action of topically applied corticosteroids and which appeared to be directly related to the potency of these drugs. Sarkany *et al.* (1965), using similar techniques, have shown that the vehicle plays a part in the percutaneous absorption of steroids, but there is inconclusive evidence to demonstrate the role that the particle size of the drug plays in skin penetration.

Barrett *et al.* (1965) have found that the percutaneous penetration of fluocinolone acetonide is significantly improved when the drug is " micronized ", and that this penetration is even further improved by using a vehicle in which the fluocinolone acetonide is soluble and therefore dispersed in molecular division. Björnberg and Hellgren (1965) in a double-blind comparison, have also shown the molecular dispersion to be a therapeutically superior preparation.

This report describes clinical studies in a total of 50 patients with chronic bilateral inflammatory dermatoses (eczema or psoriasis). The object was to assess the relative therapeutic merits of a preparation (A) containing a solution of fluocinolone acetonide in propylene glycol dispersed in soft paraffin and another (B) containing microcrystalline fluocinolone acetonide powder simply suspended in soft paraffin.

Investigation.

The applications were labelled according to a code and their identity was not revealed until the investigation had been completed. The allocation of treatments was randomized and assessment was therefore "double blind". The clinician indicated whether both sides had shown the same response or which side had responded better.

Table I.—*Comparison of Preparations A and B.*

		Eczema	Psoriasis.	Total.
Patients showing better response on side treated with	preparation A	14	9	23
	preparation B	3	3	6
Equal response on either side :	Improved	7	12	19
	Not improved	1	1	2
		25	25	50

Discussion.

The results are shown in Table I. Of the 25 eczema patients, 8 (32%) showed equal results with both treatments, and one of these showed no improvement with either preparation. In the remaining 17 eczema patients there was a better result from the fluocinolone acetonide molecular dispersion in 14 (82%) than was obtained with the fluocinolone acetonide microcrystalline suspension. Only 3 patients showed a better result from the microcrystalline preparation. This is a statistically significant difference at the 2% level ($P<0{\cdot}02$).

In the psoriasis patients, 13 (52%) of the 25 showed no difference in response on the two sides, and one of these showed no improvement with either treatment. Of the remaining 12 (48%), 9 (36%) showed better results with the molecular dispersion, and again only 3 patients (12%) showed better results with the microcrystalline formulation. The difference in these results is statistically significant at the 15% level ($P<0{\cdot}15$).

In view of the above results, a statistical analysis was made of the combined eczema and psoriasis groups. Twenty-one of the 50 patients (42%) showed no difference between the two preparations, but 23 of the remaining 29 patients (79%) showed better results with the fluocinolone acetonide in molecular dispersion than with the microcrystalline preparation. The difference in the number of patients showing this better result is highly statistically significant ($P<0{\cdot}005$).

Summary.

An ointment formulation of 0·025% fluocinolone acetonide dissolved in propylene glycol and dispersed in soft paraffin was compared with 0·025% of microcrystalline fluocinolone acetonide suspended in soft paraffin. In a double-blind paired comparison in 50 patients with chronic bilateral lesions, statistical analysis of the results showed that the former was significantly more effective.

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