

MEASUREMENT OF SKIN THICKNESS: A COMPARISON OF TWO IN VIVO TECHNIQUES WITH A CONVENTIONAL HISTOMETRIC METHOD

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Two in vivo techniques which are rapid, inexpensive, and reproducible have been investigated. The first is a standardized radiological (xerographic) technique which we have shown is capable of detecting small degrees of dermal atrophy after the application of topical corticosteroid preparations for only one month. The second technique employs the Harpenden Skinfold Caliper used in an unconventional manner so as to exclude subcutaneous fat. We have shown that this too is capable of detecting dermal atrophy from the application of topical corticosteroids and that there is a strong correlation between the two techniques ($r = 0.82$, $p < 0.001$). Histometric techniques, on the other hand, give inaccurate and erroneous results for dermal thickness.

The prolonged usage of topical corticosteroids almost inevitably leads to clinically obvious atrophy [1]. Such atrophy is most clearly seen in patients with rosacea [2] where corticosteroids exacerbate the wasting of the papillary dermis prevalent in that disorder. The relationship between the potency of corticosteroids and their atrophogenicity is not clear and is hampered by the paucity of methods for assessing the latter. Simple methods for measuring dermal thickness and hence atrophogenicity would be helpful not only in choosing the most suitable treatments for individual patients but also in screening new corticosteroid preparations. This study compares a newly established radiological technique with one employing Harpenden Skinfold Calipers. A conventional histometric method has also been investigated.

MATERIALS AND METHODS

Radiological Method

The recent modification [3] of Black's [4] original technique was used. Briefly, soft tissue x-rays were directed at the flattened flexor aspect of the forearm and detected by a light- and radiation-sensitive selenium-coated plate. To ensure that the skin was flat and that the rays were in fact parallel, a perspex block was used to flatten the area to be measured. After exposure the plates were processed in a Rank Xerox 125 system which resulted in a permanent positive image. The band due to the skin was easily distinguished and its thickness measured using a magnifying lens incorporating a measuring graticule (Fig. 1).

Harpenden Skinfold Caliper Method

The instrument was not used in the conventional manner described by Tanner [5]. Instead,

the smallest possible skin fold was raised (minimal skin fold) and measured (Fig. 2). At least 8 readings were taken at each site to be measured and the skin thickness was calculated from the mean of these readings.

Application of Corticosteroid Preparations

Normal healthy volunteers were instructed to apply the material to be tested twice daily to one forearm and a placebo to the other. The choice of forearms for test or placebo material was randomized and blind in all experiments of this type. The duration of application was 4 weeks unless otherwise indicated. Each subject was instructed to apply 100 gm of both test and placebo preparations over this time period.

Histometric Method

Nine volunteers applied betamethasone-17-valerate, hydrocortisone, hydrocortisone-17-butyrate, and a placebo preparation to different sites on the forearm for 4 weeks. At the end of this period 4-mm punch biopsies were taken, fixed in 10% formalin, processed by routine histologic methods, and embedded in paraffin wax. Sections prepared from the embedded tissue were stained in hematoxylin and eosin and the mean epidermal thickness measured [6]. The dermal thickness was also measured using a microscope incorporating an eyepiece measuring graticule.

RESULTS

Radiological Method

As previously reported [3] Clobetasol propionate (0.05%) produced a mean atrophy of 17% after 4 weeks of application. The skin was found to have recovered when the subjects were again x-rayed 8 weeks after they had stopped using the steroid preparation. The results obtained with this and other corticosteroids using this technique are

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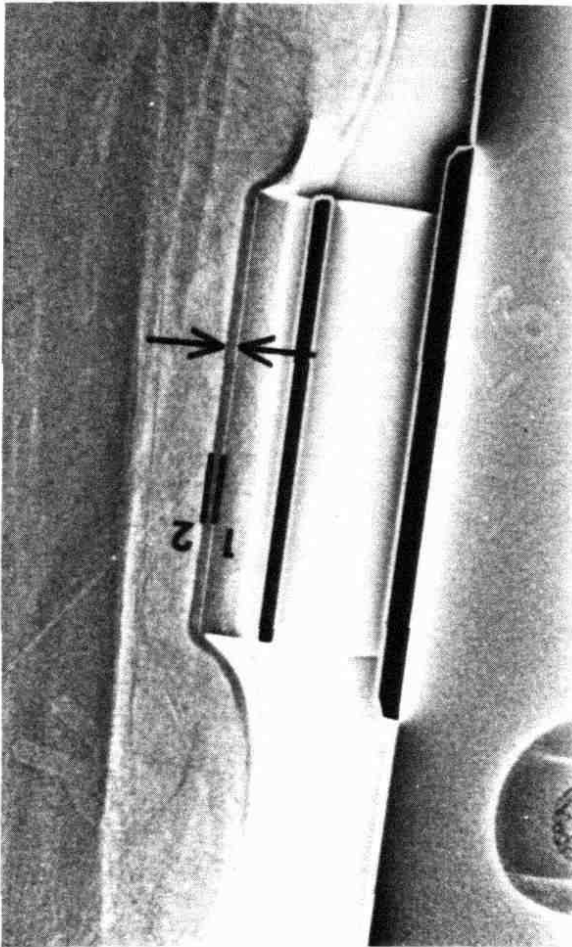


FIG. 1. Xerogram of forearm demonstrating the shadow produced by the skin. The two parallel lines 1 and 2 are superimposed on the lines representing the skin-perspex and the skin-subcutaneous tissue interfaces, respectively. Thus the skin thickness is obtained by measuring the width of the band between the two arrows.

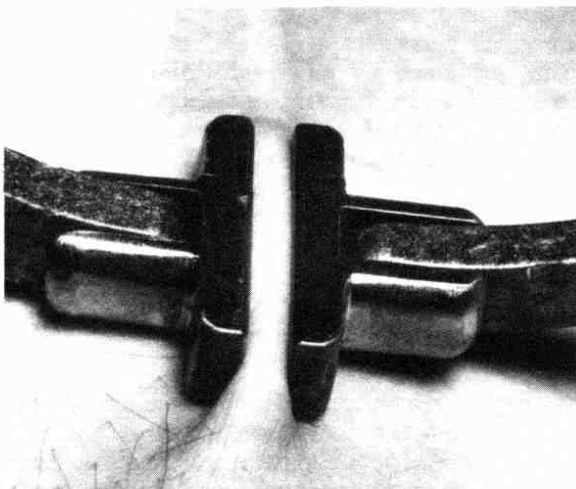


FIG. 2. Minimal skin fold raised and measured by the Harpenden Skinfold caliper.

given in Table I. Only one compound tested produced no atrophy over the period of application and that was hydrocortisone-17-valerate. Perhaps surprisingly, both hydrocortisone and betamethasone-17-valerate produced similar degrees of atrophy under the conditions of this study.

Harpenden Skinfold Caliper Method

A comparison between the normal skin thickness values for forearms obtained by the radiological and caliper method is given in Table II. As can be seen, the results for female subjects are identical whereas the values given by the calipers for males are slightly higher. The ability to detect corticosteroid-induced atrophy with this method is demonstrated in Table III. Measurements taken after 28 days of application of 0.025% fluocinolone acetonide indicated that a mean dermal atrophy of 7% was produced. The results obtained by x-raying the same subjects are given in Table IV. Again a mean atrophy of 7% was observed. Similar values were obtained when the results were corrected for measurements taken prior to the period of application. However, individual variations were noted. For example, subject #8 showed no difference between placebo and test arm as judged by the caliper technique but a marked difference (-18%) by the x-ray technique. Such discrepancies

TABLE I. Summary of results obtained using a radiological method

Corticosteroid	No. of subjects	Time of application (weeks)	Mean of percentage changes observed in subjects (% atrophy)
Clobetasol propionate 0.05%	9	4	17
Hydrocortisone-17-butyrate 0.1%	4	4	13
Hydrocortisone-17-butyrate 0.1%	3	7	13
Hydrocortisone 1%	7	4	7
Hydrocortisone 1% ^a	6	5	4
Betamethasone-17 valerate 0.1%	8	4	6
Hydrocortisone-17 valerate 0.2%	6	4	1

^a This represents a second, completely independent experiment using 1% hydrocortisone.

TABLE II. Normal range for dermal thickness (mm)

	Male	Female
Caliper technique	1.15 ± 0.11 ^a (11 subjects)	0.93 ± 0.10 (9 subjects)
X-ray technique	1.04 ± 0.10 (20 subjects)	0.91 ± 0.15 (19 subjects)
X-ray technique (Black 1969)	1.30 ± 0.02	1.10 ± 0.005

^a Means ± SD.

are probably due to a combination of the inherent errors of the methods used and the inclusion of some subcutaneous tissue in the caliper reading. Despite these individual variations a high degree of correlation ($r = 0.82$, $n = 3$, $p < 0.001$) was found between the values obtained for the skin thickness using both techniques (Fig. 3).

Histometric Method

No meaningful values for dermal thickness could be obtained using this method (see *Discussion*). Only the values for mean epidermal thickness (Tab. V) gave useful data. As can be seen, a rank order was obtained which corresponds approximately to the clinical efficacy of these compounds.

DISCUSSION

The histometric method which at first sight may appear relatively easy and straightforward was

TABLE III. *Dermal atrophy after fluocinolone acetonide treatment—caliper results*

Using paired case analysis the difference between test and placebo was significant at $0.02 > p > 0.01$.

Subject	Skin thickness at 4 weeks (mm)		% Change
	Placebo arm	Test arm	
1.	0.95	0.82	-14
2.	0.85	0.72	-15
3.	1.07	0.99	-7
4.	0.86	0.72	-16
5.	0.76	0.79	+4
6.	1.10	1.06	-4
7.	1.15	1.07	-5
8.	0.98	0.98	0
Means \pm SD	0.97 ± 0.14	0.89 ± 0.15	-7

TABLE IV. *Dermal atrophy after fluocinolone acetonide treatment—x-ray results*

Using paired case analysis the difference between test and placebo was significant at $0.05 > p > 0.02$.

Subject	Skin thickness at 4 weeks (mm)		% Change
	Placebo Arm	Test Arm	
1.	0.95 ^a	0.85	-10
2.	0.74	0.65	-12
3.	1.10	1.03	-6
4.	0.70	0.76	+8
5.	0.89	0.84	-6
6.	1.10	0.95	-14
7.	1.04	1.04	0
8.	0.95	0.78	-18
Means \pm SD	0.93 ± 0.15	0.86 ± 0.14	-7

^a Each value for skin thickness is the mean value obtained from 8 readings taken along the block in contact with the forearm skin.

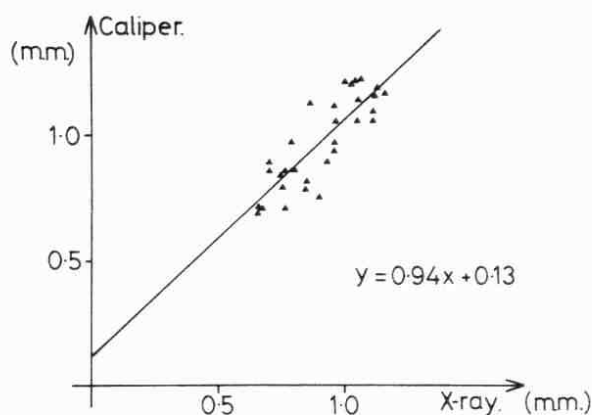


FIG. 3. Scatter diagram showing the caliper measurements (y axis) and the x-ray measurements (x axis) with the regression line $y = 0.94x + 0.13$. Correlation coefficient $r = 0.82$ ($n = 32$, $p < 0.001$).

TABLE V. *Effect of corticosteroids on epidermal thickness*

Betamethasone 17-valerate vs placebo $p = 0.01$; betamethasone-17-valerate vs hydrocortisone $p = 0.05$; other comparisons not statistically significant.

Material	Mean epidermal thickness (expressed as number of cells) \pm SD
Control	4.46 ± 0.78
Placebo	4.33 ± 0.61
Hydrocortisone	3.89 ± 0.71
Betamethasone-17-valerate	3.07 ± 0.47
Hydrocortisone-17-butyrate	3.45 ± 0.62

found in practice to be fraught with difficulties. Firstly, a full-thickness biopsy could not always be obtained with the size of biopsy acceptable to volunteers. Secondly, removal of connective tissue constituents undoubtedly occurs during histologic processing which results in shrinkage of the specimen. Thirdly, perfect orientation of the specimen prior to sectioning is difficult to achieve and is necessary to avoid large errors.

On the other hand, both the radiological and caliper methods proved to be simple and reasonably accurate in use. Individual variations between the two methods were observed. Furthermore, there is no doubt that the caliper measurement of skin thickness does give slightly higher values than the x-ray method. Nevertheless, this study indicates that the Harpenden Skinfold Caliper can provide an accurate, easy, and inexpensive way of measuring skin thickness changes due to treatment and as such should prove useful in both clinical and investigative situations.

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