

From the Division of Gerontology, Washington University School of Medicine,
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STUDIES IN PASSIVE TRANSFER OF SKIN
SENSITIZING ANTIBODIES (ATOPIC REAGINS).
THE EFFECTS OF TOPICAL
ADMINISTRATION OF STEROIDS ON THE
SKIN OF OLD INDIVIDUALS

By

MICHAEL SCHWARTZ
Copenhagen

During the last few years several investigators have brought evidence for a direct effect of steroids on the senile human skin. M. A. Goldzieher (3) has described regeneration of the atrophic epidermis and regenerative changes of the elastic fibers of the cutis, following inunction of the skin with estrogen ointment. J. W. Goldzieher (4) showed that both estrogen and androgen are directly capable of causing regeneration of the senile epidermis. Studies of the effects of parenteral and topical administration of steroids on the elastic properties of senile skin were performed by Chieffi (1). This author found an improvement in the elastic properties in the skin of women treated locally with estrogen in oil; parenteral administration of estrogen had no effect on the skin elasticity in females, and testosterone, parenterally or topically administered, was without any effect in males.

In a previous investigation (7) we have shown that the wheals induced by passive transfer of a skin sensitizing antibody (Hay fever reagin) were significantly larger in old

individuals than in younger ones using the antibody in a high concentration. This age variation was thought to be best explained by a presumption of a slightly diminished blood circulation in the skin with increasing age. Considering the above mentioned investigations on the local effect of steroids on the senile human skin, we have found it of interest to try, if we could, to influence the demonstrated effect of age on the urticarial wheal induced by passive transfer by topical application of steroids on the skin.

METHODS

The technique of the passive transfer tests, as well as the preparation of the antibody (serum) solutions used in this study, were essentially the same as reported in a recent investigation (7). Four different serum solutions were used: 10 %, 1 %, 0.5 % and 0.2 %. The skin of the front side of the forearm was used throughout ; 0.1 ml. of each of the serum solutions was injected intradermally, the strongest solution most proximal. The antigen (0.05 ml. Timothy extract, 1000 Nitrogen units) was injected into each of the four sensitized skin sites after a period of 24 hours; the reactions were read 20 minutes later and the transverse diameter (in mm.) of the wheals was measured.

EXPERIMENTAL

Twenty-seven individuals, 14 men and 13 women over 50 years of age were studied. All were inmates of the St. Louis City Infirmary Hospital. No individual with skin disease was included in the study.

The local treatment of the skin was as follows: an area of approximately 80 sq. cm. of the front side of the forearm was used and treatment was given three times a week for 6 weeks. The 14 men were treated with 25 mg. of testosterone propionate in 1 ml. of sesame oil, the 13 women with 1 mg. of estradiol benzoate (6000 R.U.) in 1 ml. of sesame oil. The

TABLE 1

Size of wheals (in mm.) induced by passive transfer of atopic hay fever reagin after 6 weeks of topical application of testosterone (left arm) and sesame oil (right arm) in 14 elderly males.

Serum concentration	Left arm				Right arm			
	10 %	1 %	0.5 %	0.2 %	10 %	1 %	0.5 %	0.2 %
Age								
79	13	7	0	0	14	6	0	0
70	12	5	0	0	14	9	5	0
61	9	0	0	0	11	0	0	0
67	11	8	0	0	13	9	0	0
88	13	10	0	0	13	9	0	0
86	15	9	5	0	14	8	5	0
85	15	11	7	0	16	12	6	0
72	11	4	0	0	12	7	0	0
74	9	0	0	0	10	0	0	0
64	13	8	4	0	13	9	6	0
74	13	8	0	0	12	7	0	0
85	13	8	0	0	13	9	0	0
80	12	0	0	0	13	0	0	0
79	9	5	0	0	12	5	0	0

Mean age—76.1 yrs.

TABLE 2

Size of wheals (in mm.) induced by passive transfer of atopic hay fever reagin after 6 weeks of topical application of estrogen (left arm) and sesame oil (right arm) in 13 elderly females.

Serum concentration	Left arm				Right arm			
	10 %	1 %	0.5 %	0.2 %	10 %	1 %	0.5 %	0.2 %
Age								
79	12	6	0	0	13	5	0	0
77	17	11	9	6	16	11	6	0
56	14	9	6	0	16	10	7	0
79	12	7	0	0	12	6	0	0
74	11	6	0	0	11	6	0	0
57	20	11	7	0	18	11	7	0
69	15	9	5	0	18	11	9	0
70	12	5	0	0	12	6	0	0
63	15	8	4	0	14	7	6	0
77	5	0	0	0	5	0	0	0
63	14	9	0	0	14	7	0	0
70	18	12	0	0	18	8	0	0
74	17	11	9	6	16	11	6	0

Mean age—70.0 yrs.

TABLE 3

Mean values of $\left[\frac{\text{Diameter (mm.)}}{2} \right]^2$ for wheals induced by passive transfer of an atopic reagin in elderly males and females after 6 weeks of treatment with, respectively, testosterone and estrogen (left arm) and sesame oil (right arm).

Antibody (serum) concentration	Males		Females	
	Left arm	Right arm	Left arm	Right arm
10 % ...	41.6	41.7	52.3	53.2
1 % ...	12.4	12.2	18.3	16.8
0.5 % ...	1.6	2.4	5.5	5.5
0.2 % ...	0	0	1.4	0

oil was massaged into the skin as far as this was possible. Sometimes it was necessary to let the last of the oil dry into the skin. Only the left arm was treated with the steroid compound, the right arm being treated with sesame oil alone to serve as a control. After 6 weeks of treatment the passive transfer tests were performed simultaneously on the right and left arms.

The results are given in table 1 (men) and table 2 (women) where the transverse diameter of the wheals for the four different antibody concentrations are recorded for each individual.

As will be seen from tables 1 and 2 there is no indication of any effect of estrogens in the female group or testosterone in the male group. The wheals are of essentially the same size on the right and left arms. A calculation of the mean values of the figure $\left[\frac{\text{Diameter (in mm.)}}{2} \right]^2$ which gives an expression of the area of the wheals, is given in table 3 and shows the same result. From Table 3 the previously described difference in size of the wheal between men and women (7), the latter demonstrating the larger wheal, is again recognized.

DISCUSSION

The wheals induced by the passive transfer tests in this study were of the same size-order as that found in another

study (7) and considerably larger than those obtainable in younger individuals considering the 10 per cent serum solution. It was not possible, however, under the conditions of the experiment, to demonstrate any effects on the wheal included by passive transfer, from the topical application of the steroids.

The reason why old individuals will demonstrate larger wheals than younger ones is obscure. We have mentioned the possibility that the wheal (using an antibody with a high titer) becomes larger with increasing age because of a gradually diminishing blood circulation in the skin. The histamine (H-substance) released by the antigen-antibody reaction causes the wheal through a local effect on the blood vessels which dilate and become permeable. If the blood circulation through the skin is completely stopped there will appear no wheal at all, but if the blood circulation is only diminished, for instance by slight stasis, the wheal induced by histamine becomes larger than with a normal circulation of blood through the skin (5).

It has been found that testosterone, parenterally administered, will increase the cutaneous vascularity of the skin in castrates (2). Estrogen, too, affects the capillaries and venules of the skin causing a vasodilatation, but the rate of blood flow through the skin was found to be unaltered (6). A local hyperemia of the skin was demonstrated in mice after local application of estradiol by Selye (8).

Our study does not tell us if any vascular changes were obtained by the local application of the hormones, only that there could not be observed any effect on the wheals. The local steroid treatment was not particularly massive, but presumably strong enough to create a fairly high local concentration. A more intensive local steroid treatment should be tried as well as the effects of parenterally administered steroids.

It must be admitted, however, that the cause of the larger wheal in old people may be something quite different from circulation changes in the skin and not at all influenceable by any steroid treatment.

SUMMARY

The wheals induced by passive transfer of a skin sensitizing antibody (Hay fever reagin), known to be larger in old individuals than in younger ones, was not influenced by topical administration of estrogen to women or testosterone to men.

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Author's Address:

Bispebjerg Hospital, Copenhagen NV, Denmark.

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