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EXPERIMENTAL PRURITUS IN THE UNAFFECTED SKIN OF PATIENTS WITH DIFFERENT ITCHING DERMATOSES

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Abstract. In 253 patients of both sexes under 60 years and with different pruriginous disorders, itching was elicited by intracutaneously applied 2–3 μg trypsin in the intact skin of the arm (i). The itch duration was prolonged in about half of the cases with diabetes mellitus, with "pruritus" and in 7 of 30 cases of urticaria. Similarly, prolonged itch duration was found in some of the patients with circumscribed neurodermatitis, lymphoma, and polycythemia vera and furthermore in some cases of acne, furunculosis, microbial eczema as well as hypostatic ulcus. On the other hand, no such reactivity could be registered in dermatitis herpetiformis or in lichen ruber planus. (ii). Prolonged itch latency was observed selectively in diabetes mellitus, in urticaria, in the acne-furunculosis group as well as in hypostatic ulcus.

In earlier experiments it could be shown that the intracutaneous application of trypsin provokes itching. The duration of itching is longer in the unaffected skin of most patients with atopic dermatitis and in subjects over 65 years with itching eczema or psoriasis. In older patients even the latency of trypsin itch is prolonged (9, 10). In present studies it was investigated whether pruritus might be elicited by intracutaneous trypsin administration on the intact skin, in itchy disorders, in patients below 60 years of age.

MATERIAL AND METHODS

253 patients of both sexes under 60 years were investigated, who suffered from the following diseases: 34 from diabetes mellitus, 14 from "pruritus" ("sine materia"), 5 from circumscribed neuroderma, 2 from polycythemia vera [complemented with 4 similar patients over 60 years and compared with respective older controls (10)], 5 from lymphoma and 2 cases with pronounced histologic evidence of the premycotic stage of granuloma fungoides. Furthermore, 30 patients with urticaria or edema, 4 with dermatitis herpetiformis, 7 with lichen ruber planus, 10 with acne or furunculosis, 4 with microbic eczema and 6 with hypostatic ulcer were investigated.

As controls, 50 patients with various eczematous lesions, 50 with psoriasis, 10 with mycotic infections, 20 patients with other non-itching dermatoses as well as 14 healthy persons (see Table I) were chosen.

The method consisted of the intracutaneous injection of 2–3 μg trypsin in 0.1 ml saline into at least three places on macroscopically intact skin of the arm. By this method two parameters of itching were recorded:

I. Itch duration, considered as prolonged if over 2 min.
II. Itch latency, considered as prolonged if over 30 sec.

RESULTS

The results of these investigations are given in Table I.

I. The itch duration was increased in about half of the cases with diabetes mellitus and with pruritus, and in about one-quarter of the urticaria cases. Similarly increased itch duration was found in some of the patients in the following disease categories: circumscribed neurodermatitis, lymphoma, acne/furunculosis, microbic eczema as well as hypostatic ulcus. Further, similar results were obtained in the 2 patients with polycythemia vera complemented and compared with older patients. By contrast, very few patients responding with prolonged itch duration were found in the groups of dermatitis herpetiformis and in lichen ruber planus and no such reactivity was found in the 2 patients with premycotic granuloma fungoides. In the 114 control patients the incidence of prolonged itch duration was about 2%.

II. The itch latency, which was under 1% in the control group was prolonged only in certain disease groups, as in urticaria, in diabetes mellitus, in the acne/furunculosis group as well as in hypostatic ulcus cases. Furthermore, polycythemia vera patients, under and over 60 years

Table I. *Experimental pruritus on the intact skin of 253 patients under 60 years with various itching disorders*

Patients/number of cases	(>2′)	I. Prolonged duration	II. Prolonged latency (>30″)
Diabetes mellitus	34	17	10
Urticaria	30	7	18
"Pruritus"	14	7	0
Acne/furunculosis	10	2	4
Lichen ruber planus	7	1	0
Hypostatic ulcus	6	2	3
Circumscribed neurodermatitis	5	2	0
Lymphoma	5	2	0
Microbic eczema	4	2	0
Dermatitis herpetiformis	4	1	0
Polycythema vera[a]	2	1	1
Premycotic granuloma fungoides	2	0	0
Control groups			
Eczema (excl. microbic)	50	2	0
Psoriasis	50	1	0
Other dermatoses	20	1	1
Healthy persons	14	0	0
Mycotic infections	10	0	0
[a] Polycythemia over 60 years	4	3	4
Controls over 60 years	58	27%	67%

also seem to show similar reactivity. No itch was elicited in the investigated patients by physiologic saline.

DISCUSSION

I. By an experimental itch method, the longer itch duration, i.e. the increased pruritus, could objectively be verified in diabetics. This was the case even in the presumably polyetiologic group of patients with uncertain pruritus and in about one-quarter of cases in urticaria. In relation to polycythemia vera, the small group complemented with older patients showed similar prolonged itch duration. As anticipated, this was the case even in some lymphoma patients, though not in the "praemycotic" cases. Whereas similar prolonged reactivity was found in patients with circumscribed neurodermatitis, it was of interest that several such reactions were observed in the following patient categories: acne/furunculosis, microbic eczema as well as hypostatic ulcus. The cause of these latter findings is at present unknown. The common factor in this group may assumedly be bacterial especially in pyococcal infections (or autosensitization?). In this context, the theory of Arthur & Shelley (1) on the possible role of bacterial proteases in producing itching should be mentioned. In dermatitis herpetiformis and in lichen ruber planus, the intense clinical itching could not be verified by present experimental itch studies. In the control group, the incidence of prolonged itching was relatively low. Furthermore, it was assumed that the skin disease of the 2 patients with "eczematous" lesions may correspond to a type of atopic dermatitis or of microbic eczema, i.e. according to previous (9) or present studies of diseases with prolonged itch duration.

In contrast to the well-known and common experience of clinical itching in the above-mentioned diseases, data on experimental tests for pruritus are lacking. On the other hand, the pruritogenic role of histamine and consequently the itching character of those diseases where histamine-liberation plays an important role, as in urticaria, is generally assumed. A good correlation was found between the parallel increase of histamine and basophils in the blood (4) on the one hand, and pruritus in polycythemia vera (6) on the other. However, if one analyses the findings of histamine levels e.g. or of basophils (2, 8) in different skin disorders, no strict parallelism between these and clinical itching may be demonstrated. This even concerns the relation of basophils in lymphoma (5) and the incidence of pruritus. According to Rothman & Shapiro (11), the cause of itching in lymphomas is the production of toxic substances due to cellular decomposition. More recently, a graft-versus-host reaction between leukemic and normal tissue cells, as eliciting pruritus, was discussed (3). In diabetes mellitus, the asteatotic dry skin is held as of basic importance for the pruritus in this disease (11). Furthermore, there seems to be no correlation between proteolytic activity in various skin disorders (as investigated by Steigleder et al. (12)), and pruritus.

II. A prolonged itch latency was selectively found in certain diseases, as in diabetes mellitus, in polycythemia vera, in more than half of the urticarial cases, and also in acne/furunculosis and in hypostatic ulcus.

All these findings are difficult to evaluate until the mechanism of pruritus is better understood. At present, the exact role and possible relation of proteolytic enzymes and histamine in eliciting itch is unclear. In the present investigations, however, an experimental test was given for the common clinical experience of intense pruritus in several disorders.

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