

Immediate reactions to patch tests with balsam of Peru

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Closed patch tests with balsam of Peru gave rise to nine immediate reactions among 121 patients with different dermatoses and to 10 reactions among 57 patients with chronic urticaria. Among compounds of balsam of Peru, cinnamic aldehyde, cinnamic acid, benzoic acid and benzaldehyde also gave the same reactions. The reactions could not passively be transferred with serum from patients. They were abolished by antihistamine given before testing, and by pretreatment with compound 48/80.

Balsam of Peru and cinnamic aldehyde did not provoke new symptoms when given orally to patients.

Key words: Balsam of Peru – chronic urticaria – immediate reactions – patch test.

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Urticarial reactions have occasionally been reported with closed patch tests but more commonly with open patch tests. A series of different substances have been responsible, e.g. ammonium persulphate (Calnan & Shuster 1963, Fisher & Dooms-Goossens 1976), cetyl and stearyl alcohols (Gaul 1969), 2-hydroxy-4 methoxy-benzoephnone-5-sulphonic acid (Ramsay et al. 1972), monomylamine (Tharp 1973), cephalosporin (Tuft 1975), cobalt chloride (Smith et al. 1975), diethyltoluamide (Maibach & Johnson 1975). In recent years, the term contact urticaria has often been used for these reactions, since the substance involved is possibly the cause of the patient's dermatological condition. In many cases the precipitating substances have been food products and in a number of patients the reactions have arisen only on chronically inflamed skin (Hjorth & Roed-Peterson 1976, Maibach 1976). In a short report Friis & Hjorth (1973) described immediate

reactions to patch tests with balsam of Peru. We have also found that balsam of Peru in a closed patch test can produce urticarial reactions, especially in patients with urticaria. In this article we present the results of an investigation designed to demonstrate the mechanism mediating these reactions.

Materials and Methods

The investigation was conducted on adult patients of both sexes with chronic urticaria, i.e. with continuous or recurrent symptoms of more than 3 months' duration and with varying dermatoses.

Test procedure. A closed patch test was applied to the upper part of the back for a period of 30 min. The result was read immediately after removal and after every hour until the reaction disappeared. In a number of patients a conventional 48-h closed patch test was also performed. The

result was read 24 h after removal of the test.

Test substances. Balsam of Peru: 1.56, 3.12, 6.25, 12.5 and 50 % in petrolatum:

Components of balsam of Peru
(in petrolatum)

Benzoic acid	5 %
Benzaldehyde	5 %
Cinnamic aldehyde	2 %
Cinnamic alcohol	2 %
Cinnamic acid	5 %
Methyl cinnamate	0.5 %
Benzyl benzoate	5 %
Benzyl salicylate	2 %
Benzyl cinnamate	5 %
Eugenol	5 %
Vanillin	10 %

Screening set of chemicals according to the International Contact Dermatitis Research Group (Fregert et al. 1969).

Provocation tests. Peroral provocation with balsam of Peru and cinnamic acid was performed using capsules containing 25 mg balsam of Peru and 25 mg cinnamic acid. Reactions were noted during the 24 h subsequent to the administration of 1 capsule of the respective substances.

Effect of an antihistamine. Clemastine 2 mg was given orally 12 and 2 h before testing with the serial dilution of balsam of Peru. The test was removed after 30 min and the reaction was observed for 1 h.

Pretreatment with compound 48/80. Compound 48/80 was diluted to 0.1 mg/ml and 0.1 ml injected intradermally into one of the patient's forearms. The site was reinjected two more times at about a 10-h interval. After the third injection a 30-min closed patch test was applied to the injection site and to a contralateral saline control site.

Passive transfer. Passive transfer was accomplished by injecting 0.1 ml of freshly prepared sera from two patients with urticarial reactions to balsam of Peru into the

Table 1. Immediate reactions to balsam of Peru among 57 patients with chronic urticaria

	No. pos	No. neg.	Total No. tested
Males	10	20	30
Females	6	21	27
Total	16	41	57

forearm of eight adult volunteers. Twenty-four hours later a 30-min closed patch test was applied to the injection site and to a contralateral control site.

Results

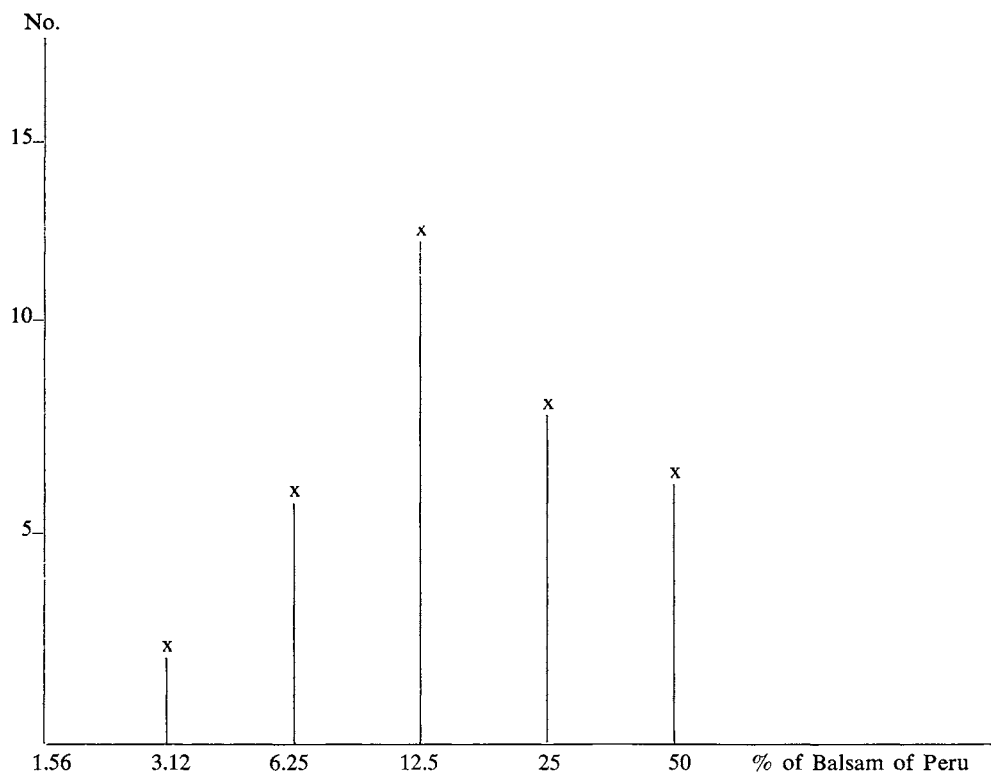
Balsam of Peru gave rise to nine urticarial reactions in 121 patients with diversely differing dermatoses, and to 16 reactions in 57 patients with recurring urticaria (Table 1). Tests performed using a standard series without balsam of Peru in 33 patients with varying diagnoses gave rise to no urticarial reaction.

The distribution of the 25 patients with regard to diagnoses and sex is presented in Table 2. With the exception of the 16 reactions in patients with urticaria, a further four reactions were observed in patients with allergic contact dermatitis and one in atopic dermatitis, non-specific eczema, drug reaction, psoriasis and erysipelas, respectively. Balsam of Peru precipitated no reactions in these patients after a conventional 48-h closed patch test.

Table 2. Immediate reactions to balsam of Peru according to diagnosis and sex

	Immediate reactions No.	Urticaria No.	Different diagnosis No.
Males	14	10	4
Females	11	6	5
Total	25	16	9

Table 3. Eight patients tested with different concentrations of balsam of Peru



In seven patients repeat testing was performed. In five cases the urticarial reaction could be reproduced after a duration of 3–12 months; in two cases it had disappeared after 6 and 9 months, respectively. The significance of the concentration of the balsam of Peru is presented in Table 3, which shows that 12.5 % and 25.0 % gave rise to the majority of the

reactions. The reaction appeared earliest 10 min after application of balsam of Peru and normally after 20 min. The reaction faded within 2 h. Among the components of balsam of Peru, Table 4 shows that cinnamic aldehyde, cinnamic acid, benzoic acid and benzaldehyde also gave rise to urticarial reactions. One patient showed no reaction for any component.

Table 4. Five patients tested with four components of balsam of Peru

	Concentration	1	2	Patient 3	4	5	Total No. reactions
Cinnamic aldehyde	2 %	1	1	1	—	1	4
Cinnamic acid	5 %	1	1	1	—	—	3
Benzoic acid	5 %	1	1	—	—	1	3
Benzaldehyde	5 %	—	1	—	—	—	1

Table 5. Number of immediate reactions before and after treatment with clemastine

	Conc. %	Before	After
Balsam of Peru	3.12	2	—
	6.25	3	—
	12.5	3	—
	25.0	4	1
Cinnamic aldehyde	2	2	2
Cinnamic acid	5	3	1
Benzoic acid	5	2	—
Benzaldehyde	5	1	—

Provocation with 25 mg balsam of Peru and 25 cinnamic acid failed to precipitate urticaria or other skin changes in four patients with urticaria and in one with allergic contact dermatitis.

Passive transfer with serum from two patients to eight normal volunteers was negative. The effect of antihistamine was shown in Table 5. The reactions were not always inhibited but were diminished. In the experiment with 48/80 no reaction appeared at the injected site but an urticarial response appeared at the control site.

Discussion

This urticarial reaction does not seem to be antigen-antibody mediated since it is not possible to induce passive transfer with serum, which is in contrast to Maibach & Johnson's (1975) successful transfer of urticaria to diethyltoluamide. The reaction also seemingly lacks an aetiological significance in our cases since oral exposure to balsam of Peru and cinnamic aldehyde failed to evoke a reaction and did not worsen the patients' symptoms. It belongs to that type of reaction which Hjorth & Roed-Petersen (1976) and Maibach (1976) have described, and which in general has been termed contact urticaria. Maibach & Johnson (1975) make three major sub-

divisions of contact urticaria; non-immunologic, and those of uncertain mechanism. Our cases seem to belong to the last group. Histamine release probably occurs since the reaction arises rapidly and is inhibited by antihistamine and compound 48/80. The similar reaction was briefly mentioned by Friis & Hjorth in 1973. They used patch tests containing 1.25–10.0 % balsam of Peru in liquid paraffin for 20 min and observed urticarial reactions mainly with the higher concentrations. We used a test series of 1.56 to 50 % balsam of Peru and the majority of reactions occurred at 12.5 % and did not increase in frequency at a greater concentration. Possibly, this could depend upon the eventuality that the maximum quantity of evoking and thus possibly skin penetrating substance(s) is attained at 10–12.5 %. The substances comprising balsam of Peru which also gave rise to urticarial reactions were cinnamic aldehyde, cinnamic acid, methyl cinnamate, benzaldehyde and benzoic acid. One of the patients tested, however, did not react to any of these substances. A possible explanation of these immediate reactions is that these and other substances in balsam of Peru have a weak histamine releasing effect which is most of all evident in testing individuals with recurring urticaria.

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