

Histological aspects of skin reactions to propylene glycol

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In view of the increased use of dermatological preparations containing a high concentration of propylene glycol (PG) for use under occlusive dressings, patch tests were performed with pure PG in a group of 98 out-patients at a skin clinic. No indication of a possible allergic contact dermatitis to PG could be found in the history of any of these patients. In 11 of them, the patch test reactions after a 48-h application were positive. In eight cases the reaction was scored as one plus, in two cases as two plus, and in the remaining case a three plus reaction was observed. In view of the negative history of all patients, the observed reactions were considered to be of a primary irritant nature.

Histological examination of the positive patch tests revealed some definite quantitative differences between one and two plus reactions on the one hand and a three plus reaction on the other. The findings suggest that the application of high concentrations of PG under occlusive dressings may give rise to skin reactions of a primary irritant character which may closely simulate an allergic reaction.

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Several reports have recently drawn attention to the marked germicidal efficiency of concentrated propylene glycol (PG) solutions and to their potential value as a topical antimicrobial agent. The effectiveness of a 90 % PG solution against a spectrum of microorganisms tested suggests that there might be a therapeutic benefit when concentrated PG solutions could be used as a vehicle for topically applied medication (Olintzky 1965). Barr (1965) stated that PG possesses many properties which make it an ideal vehicle for dermatological formulations.

Based on these data several preparations have become commercially available, consisting of steroid preparations in which PG, in concentrations up to 80 %, is used as a

dermatological vehicle. It must be noted, however, that patch test reactions to PG have been reported by several authors and the literature on the subject was reviewed recently by Hannuksela et al. (1975).

In one of these publications Warshaw & Herrmann (1952) reported positive patch test reactions to PG in 138 (nearly 16 %) of 866 subjects who attended the clinic for various allergic or possibly allergic dermatoses. The patch tests were performed with PG pure, 50 % and 10 % dilutions in water. Although they could not decide whether or not the positive reactions to PG were due to specific allergic sensitization, it appeared more likely to the authors that primary irritation was the cause of the patch test reaction. It is suggested that excessive

local dehydration of the skin following PG application may be an important factor predisposing to the reactions. The incidence of positive reactions to PG furthermore showed a seasonal fluctuation, in as much as the incidence was at its minimum during a period of hot and humid weather and significantly higher during the cooler and less humid season. Warshaw & Herrmann (1952) suggested that the augmented sweat and sebum production in a hot period contributed to the increased tolerance of the skin for PG.

Allergic reactions to PG have been reported in 38 patients treated with topical applications containing PG (Huriez et al. 1966); 17 (45 %) had positive patch test reactions with PG 38 % in water. Of a control group of 145 eczematous patients, who according to their history had never been treated with PG, six (4 %) reacted positively.

Hannuksela et al. (1975, 1976) reported patch test results in a total of 1556 cases of eczema. Reactions to undiluted PG were seen in 12.5 % of those tested. Of these, according to the authors, 70 % of the reactions were morphologically of a primary irritant type and 30 % were allergic in appearance. Ultimately, however, in only four out of 1556 tested patients were the observed patch test reactions considered by the authors to be of genuine allergic origin. The patch test results were interpreted by them as follows: Reactions with redness, with or without infiltration, maximum on the first day, were regarded as of toxic, primary irritant type. On the other hand, reactions with infiltration with or without vesiculation extending to a considerably larger area than that of the test chamber used by the authors, with their maximum on the second day or later after application, were considered allergic. These descriptions suggest, in our opinion, that macroscopically a differentiation of patch test reactions

to PG may sometimes give rise to difficulties.

None of the previously mentioned authors performed biopsies in a systematic way in order to facilitate the differentiation of primary irritant and allergic patch test reactions to PG.

The object of the present investigation was to study the histological aspects of reactions occurring when high concentrations of PG are applied on the skin as patch tests.

In view of the fact that in dermatological practice patch tests are commonly read after 48 h of application – in accordance with the standard procedure of the International Contact Dermatitis Research Group – the histological investigation was performed on skin which had been exposed to PG during that period of time.

Materials and Methods

A group of 98 consecutive out-patients with eczematous eruptions of the hands, presumably of a contact allergic nature, were patch tested with pure PG. None of the patients had any history of a possible allergic contact dermatitis to PG.

PG was applied to the skin of the back with Silver Patch® testers (van der Bend, Brielle). The time of exposure of the skin to PG was 48 h. The patch tests were performed in the months of November, December and April, during a cool climatic period. The reactions were scored 48 h after the application in the following way: Reactions with definite redness without infiltration were scored as a one plus reaction. Reactions consisting of definite erythema and with marked infiltration were scored two plus. Vesiculation was scored as three plus. With consent of the patient a biopsy was taken from all patch tests which was scored as a one, two or three plus reaction. The material was fixed in neutral

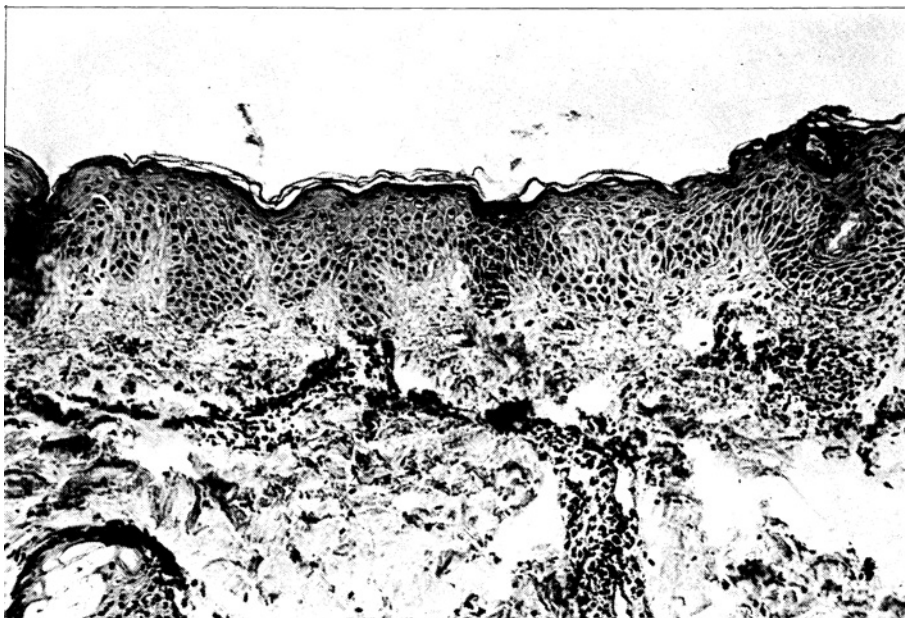


Fig. 1. Histological aspect of a one plus reaction to propylene glycol. The surface epithelium does not show any damage. There is slight spongiosis. A mononuclear cell infiltrate is present around the blood vessels in the upper layers of the dermis. There is also some oedema. H. E. 200X.

formalin, dehydrated and embedded in paraffin. Four micron sections were cut and stained routinely with hematoxylin and eosin. The biopsies were examined without previous knowledge of the result of the patch test.

Results

Patch tests

Patch test reactions were positive in 11 of 98 patients. The reaction consisted of a marked erythema without infiltration in eight cases. This reaction was noted as one plus. In all eight cases skin biopsies were obtained.

A marked erythema associated with infiltration of the skin was noted in two cases. These reactions were scored as two plus. Biopsies were performed in both cases. In one patient erythema and infiltration as

well as vesiculation could be noted and this reaction was recorded as three plus. A biopsy was taken.

From these patients five (three with the one plus reaction and two with the two plus reaction) were retested in June and July 1976 during a spell of extremely hot weather. This time all patch tests remained negative.

Histological examination

The results of histological examination in eight patients with one plus reactions can be summarized as follows (Fig. 1):

In general the surface epithelium did not show any damage. In a few cases spongiosis was seen. A mononuclear cell infiltrate was observed around the vessels in the upper layers of the dermis. No polymorphonuclear leucocytes were present, and no mast cells were seen. The infiltrate was not present



Fig. 2. Histological aspect of a three plus reaction to propylene glycol. The surface epithelium shows spongiosis and patchy necrosis, associated with infiltration of polymorphonuclear leucocytes. In the dermis a perivascular mononuclear infiltrate and some oedema are present. H. E. 80X.

around the appendages. The upper dermis showed oedema in some cases (Fig. 1). Histological examination of the biopsies of two plus reactions was made in two patients. In general the results were almost identical to those of the one plus reaction. In retrospect, the mononuclear perivascular infiltrate was perhaps somewhat increased in the two plus reaction. In both reactions spongiosis of the surface epithelium was noted.

The upper layers of the dermis showed severe oedema and there was a fairly heavy perivascular mononuclear infiltrate. No infiltration was seen around the skin appendages (Fig. 2).

Discussion

In view of the completely negative history of contact with PG-containing topically ap-

plied medication, none of the patch test reactions to PG in this group of patients was considered to be of allergic origin.

All observed reactions were attributed to a primary irritant effect caused by the patch testing technique, namely, application under tight occlusion for 48 h. Hence the combination of patch test results and the patient's history will be conclusive in most cases.

Problems may arise, however, if high concentrations of PG are applied to the skin under occlusion for reasons other than patch testing. For instance this may be the case when ointments containing PG in high concentration are applied repeatedly to the skin under occlusive dressings in the treatment of certain dermatoses. It is interesting that this problem was mentioned by Warshaw & Herrmann in 1952, at a time when

occlusive dressings had not reached the level of popularity which they have gained in recent years. Warshaw & Herrmann stated: "Fortunately, externally applied products containing PG are usually applied without any form of occlusive dressing". Our findings suggest the distinct possibility, that in some of the patients treated in this manner, the development of untoward skin reactions of a primary irritant character may be expected, which in some cases may closely simulate an allergic contact reaction. This adverse effect of PG may be expected only when high concentrations are applied under occlusion. Lower concentrations of this apparently rare sensitizing compound may have advantages in local therapeutics if this makes use of other probably more frequently sensitizing preservatives superfluous.

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