Induction of Skin Blanching by Hydrogen Peroxide

Sir,
Hydrogen peroxide in a unique stabilized lipid cream base (1, 2) has biological effects on the skin. In two earlier studies, the application of a 2% and 1% hydrogen peroxide cream prior to UVA exposure on a sunbed was found to prevent white spots on anoxic pressure areas from developing, the resulting pigmentation being almost uniform (3, 4). At the same time, for some of the subjects in these studies, washing off the hydrogen peroxide cream with water just prior to exposure to UV light revealed the occurrence of a temporary skin blanching. The aim of the present study was to further investigate this local blanching reaction to epicutaneously applied hydrogen peroxide cream, in different groups of subjects.

MATERIAL AND METHODS

Subjects
In the study participated 30 healthy persons with no signs of skin disorder (13 men, 17 women; age 23–61 years), 30 patients with psoriasis vulgaris (16 men, 14 women; age 21–84 years) and 30 patients with atopic dermatitis (9 men, 21 women; age 17–45 years). All were Caucasians.

Cremes applied
An active and a placebo cream were employed. The active cream contained hydrogen peroxide (2%), 1-glycerol monomyristate (21%), 1-glycerol monolaurate (7%) and water (70%); the ingredients of the placebo cream were the same except that hydrogen peroxide was lacking. The two creams were not identifiable by sight or smell and were supplied in identical tubes, each provided with a code sign and marked either “left” or “right”.
For each subject, one of the creams was applied to the left forearm and the other to the right, symmetrical normal-looking areas of the ventral forearm skin being involved. Which forearm received the active cream was varied randomly and was of equal frequency within the groups, as a double-blind principle was employed. To an area previously marked by a template 3×2 cm in size about 5 mm of the ointment was applied on each arm and was first rubbed on lightly for 2 min and then washed off gently with lukewarm water. Immediately afterwards, both arm areas were observed in daylight for at least 20 min and the skin temperature was measured with a digital thermometer, both within the area treated and a few centimetres from it.

RESULTS
In 19 of the 30 healthy subjects, use of the hydrogen peroxide cream induced skin blanching which appeared almost immediately after the cream had been washed off. The blanching was confined to the treated area and lasted for 7–15 min.
Among the patients with psoriasis, 21 of 30 showed a similar blanching reaction, which lasted for 5–12 min after the cream had been washed off.
In the atopic group the hydrogen peroxide cream caused a blanching reaction in all but 2 cases. The blanching lasted for 8–20 min and, in 3 of the patients, the blanched area exceeded the cream-treated area by 0.5 cm.
In none of the three groups did the placebo-treated contralateral areas show any blanching reaction.

In both the hydrogen peroxide- and the placebo-treated areas, a drop in surface temperature of up to 3°C was noted just after the cream had been washed off. After about 2 min the temperature had risen to the same value as for the untreated control sites a few centimetres away. The occurrence vs. non-occurrence of a blanching reaction was not found to be correlated with changes in skin surface temperature.

DISCUSSION
Blanching of the skin has been observed after the application of a variety of different substances. There is a well-known blanching reaction caused by corticosteroids, often used as a topical test for the determination of corticosteroid activity.
A blanching of the skin after the application of an anaesthetic cream containing lidocaine and prilocaine has also been reported. The mechanism behind this reaction is unknown (5).
A transient blanching reaction to white soft paraffin that has likewise been observed has been attributed to the presence of propylene glycol (6). The cream used in the present study did not contain this substance.
A whitening of the skin after exposure to solvents has been reported as well. This skin blanching does not correspond to any decrease in blood flow found on the basis of laser Doppler flowmetry but to changes in structure and to the removal of skin lipids (7).
A blanching of the skin after contact with a 3% solution of hydrogen peroxide was reported in 1977 (8). The blanching was temporary, disappearing after 10–30 min. The phenomenon was found in all members of a group of healthy whites but was not found to occur in the skin of blacks. The authors proposed that the topical application of hydrogen peroxide induces a transient vasoconstriction of vessels in the superficial dermis. In the present study skin blanching occurred in about 2/3 of both the healthy subjects and the patients with psoriasis, and in nearly all of the atopic patients. No correlation between the blanching reaction and changes in skin temperature could be shown. However, the mechanism behind the skin blanching caused by hydrogen peroxide is still unknown.

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Received April 6, 1994.

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Stevens-Johnson Syndrome Induced by Clofibrate

Sir,

Clofibrate and other fibric acid derivatives are commonly prescribed for the treatment of hyperlipidaemia. Skin rashes have been reported in about 2% of patients (1), including severe generalized erythema (2), urticaria (3), purpura (4) and vesiculobullous eruptions (5). Clofibrate-induced erythema multiforme has previously been reported in one patient 12 months after taking the drug (6). The Committee on Safety of Medicine in the United Kingdom has had a report of one other case of erythema multiforme associated with the use of the drug (personal communication). This is the first report of a patient who developed Stevens-Johnson syndrome.

A 33-year-old man was found to have hypertriglyceridaemia of 5.23 mmol/l (normal <1.86) on routine testing. He was commenced on 500 mg three times daily of clofibrate by his general practitioner. Ten days later, he developed a high fever, generalized malaise and severe pain on swallowing. He also had a severe generalized erythematous rash, affecting the entire skin and mucous membranes. There was no past medical or other drug history of note.

Examination revealed an ill-looking patient with a temperature of 38°C. He had bilateral conjunctivitis and marked ulcerative lesions on the lips, oral and nasal mucosa as well as the genitalia. There were tense erythematous patches of varying sizes in the entire trunk and limbs. Vesicles, bullae and target lesions were noted in the extremities.

Apart from a leucocytosis of 15×10⁹/l, blood, urine and viral cultures were all negative. There was no rise in the titre for mycoplasma.

A skin biopsy of a typical lesion on the right thigh showed epidermal cell necrosis and desquamation, basal cell hydroptic degeneration with numerous cytid bodies and marked oedema, telangiectasia and perivascular infiltrates of polymorphs and eosinophils in the upper and mid dermis. The diagnosis of Stevens-Johnson syndrome was established and clofibrate was discontinued on admission to hospital.

The patient was treated with intravenous fluids initially, and 40 mg of oral prednisolone daily was given subsequently 48 h after admission because of increasing painful dysphagia. Seven days later, he could tolerate oral fluids and there was gradual improvement in the skin and mucous membranes. Prednisolone was tailed off over 10 days and the skin lesions gradually and completely resolved over 20 days. There was no recurrence of any rash at follow-up after 3 months.

The lack of other etiological factors, especially infections, the close temporal relationship between the onset of the syndrome and the commencement of clofibrate as well as the improvement on drug withdrawal strongly suggest drug-induced Stevens-Johnson syndrome. The patient was not rechallenged with the drug because of the severity of the syndrome.

Though clofibrate-induced serious skin diseases are rare, clofibrate should be included in the list of drugs capable of inducing Stevens-Johnson syndrome.

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Received April 12, 1994.

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