

## ALCOHOL DERMATITIS

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Few cases of contact allergy to lower aliphatic alcohols, have been described, as demonstrated by epicutaneous tests (3, 5, 6, 7, 9). This paper reports 3 observed cases of allergy to alcohols and reinvestigation of a patient described by Haxthausen (7) in 1944.

### Testing procedures

Al-test<sup>®</sup> units (8) were used and all tests were performed on the upper back. The patients were examined with the standard test series used at the various departments. All test materials were applied for 48 hours, the reactions were then read after removal and then again after 24 and 48 hours. Classification of a reaction as positive required the presence of erythema as well as infiltration and/or papules-vesicles.

The alcohols and aldehydes studied were those commercially available for laboratory use. Ethanol, methanol, and 1-propanol used were also purified by gas liquid chromatography to remove the impurities known to occur in most alcohols (6). Tests were performed with red wine (Côte du Rhone) and beer (Three Town, Sweden).

To establish the pattern of sensitivity, all the patients were tested with various lower alcohols and their corresponding al-

dehydes. The concentrations used were based on experience gained when testing other patients with dermatitis. Some of the substances were applied in serial dilutions to ascertain the degree of sensitivity.

### Case 1

A 60-year-old housewife, seen at the Department of Dermatology, Lund. *Heredity and previous illnesses.* No relevant information available. *Present illnesses.* On several occasions during the past 10 years she had had dermatitis of the fingers, wrists and thighs from metal wrist-straps, metal suspender clasps and a pair of green nylon gloves.

Three years previously she had been fitted with acrylic dentures. For 18 months she had burning, erythema and aphthae of the oral mucosa. When she occasionally discontinued to use the dentures for a fortnight, her oral discomfort improved but never disappeared. The patient drank beer almost every day and sometimes red wine, but never spirits. Routine patch testing produced positive eczematous reactions *inter alia* to all the 10 test solutions containing ethanol. She also reacted positively to a later patch test with ethanol. On repeated

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patch tests, in which alcohol was not used as a solvent, the patient was found to be allergic to nickel sulphate, cobalt chloride, oil of turpentine, p-phenylenediamine and p-aminoazobenzene. Liver function tests including transaminases, lactic acid dehydrogenase and bilirubin in serum, the bromsulphthalein test and serum electrophoresis were normal. The urinary excretion of coproporphyrins and uroporphyrins was normal. *Further course.* The patient avoided alcoholic beverages and the symptoms disappeared. When last seen five years later she reported that she had no recurrence in spite of continued use of the same denture.

#### Case II

A 55-year-old housewife, seen at the Department of Dermatology, Gothenburg. *Heredity and previous illnesses.* Her son had recurrent eczema. At 30 years she had transient joint pain. At 38 years she had dermatitis of the hands and lower arms. From the age of 40 onward she had recurrent bronchial asthma and vasomotor rhinitis. At 43 years ulcers developed on both ankles, and somewhat later eczema of both lower legs, which occasionally recurred and sometimes spread up the legs and even to the face. At an operation for varicose veins she had an exacerbation of the eczema ascribed to intolerance to the adhesive material used. *Present illnesses.* At 25 years of age the patient noticed that consumption of alcoholic beverages was followed by oral discomfort. Not only the consumption of spirits but also of beer was followed within 5–10 minutes by itching and burning in the oral cavity and swelling of the lips. Even after a few sips of an alcoholic beverage she felt "strange" and tired and had patchy facial flushes. She therefore avoided alcoholic beverages. She has no dentures. At 50 years dermatitis of the forearm was noticed when the skin was washed with alcohol before collection of a blood sample. Epicutaneous testing showed a distinct positive reaction to 70 per cent ethyl alcohol. At 55 years the patient had her first permanent wave. Already within a few hours she experi-

enced severe itching of the face and scalp. The following day the patient had dermatitis of the forehead, temples, neck and scalp. The dermatitis persisted for about a month. The lotion used for setting the hair contained alcohol. Epicutaneous testing in July 1966 revealed besides what is shown in table 1, positive reactions to balsam of Peru (25 % in petrolatum) and to Sudan red (1 % in petrolatum), a denaturant of alcohols for domestic and industrial use. *Further course.* During 2 years the patient avoided all contact with alcohol and all alcoholic beverages. During that period she has had no recurrences of dermatitis. She was subsequently fitted with dentures and had no oral symptoms.

#### Case III

A 55-year-old technician at a chemical pathology laboratory, seen at the Department of Dermatology, Linköping. *Heredity and previous illnesses.* No relevant information. At 24 years of age the patient had a diffuse dermatitis of the hands. The following years she had relatively mild recurrences which occasionally made her interrupt her work. At 47 years of age she had dermatitis mainly of the axillae. A patch test reaction to formaldehyde was positive. She avoided formalin and had no axillary dermatitis. *Present illnesses.* At 55 years of age she had acute bullous dermatitis of the palm of the left hand. She had been in frequent contact with ether and ethyl alcohol before the appearance of the dermatitis. One month later after re-exposure to alcohol, she again had an acute attack of bullous dermatitis of the hands. She had been exposed to different types of alcohol at work, mainly methanol which is a component of haematological stains. She is a teetotaller and has no oral symptoms. Patch testing showed a positive reaction to ethanol and other alcohols (Table 1). *Further course.* During the last 18 months she has avoided contact with alcohol by working at a special laboratory. During this time she has had no symptoms except after a gynaecological examination when she had pronounced reddening and itching of the

Table 1. Test results in four patients with alcohol allergy

Test substances	Patch test reactions in four patients			
	1	2	3	4
<b>I. Primary alcohol</b>				
Methanol	+	+	+	+
Ethanol	+	+	+	+
1-Propanol	+	+	+	+
1-Butanol	+	+	+	+
1-Pentanol	+	+	+	+
Methanol, chromatogr. prep.	+	+	+	+
Ethanol, chromatogr. prep.	+	+	+	+
1-Propanol, chromatogr. prep.	+	+	+	+
<b>II. Secondary alcohol</b>				
2-Propanol	-	+	+	-
2-Butanol	-	+	-	-
<b>III. Tertiary alcohol</b>				
2-Methyl-2-propanol	-	-	-	-
2-Methyl-2-butanol	-	-	-	-
<b>IV. Aldehyde</b>				
Methanal, 3 %	-	-	-	-
Ethanal, 2 %	-	-	-	-
Propanal, 2 %	-	-	-	-
2-Butanal, 2 %	-	-	-	-
2-Butenal, 0.01 %	+	-	-	-
<b>V. Beverage</b>				
Beer	+	+	+	+
Red wine	+	+	+	+

Purified alcohols were tested undiluted. Unpurified primary alcohols were tested in water dilutions of 10 and 1 %. All patients gave positive reactions with 10 % dilution and several reactions also appeared to 1 % dilution.

vagina and vulva. The symptoms were due to the use of exploration cream containing alcohol.

#### Case IV

A female physician, aged 48, seen at the Department of Dermatology, Finsen Institute, Copenhagen. *Heredity.* Father had psoriasis, mother lymphatic leukaemia in old age. *Present illnesses.* In 1943, while working at a surgical department, she developed dermatitis of both hands after

washing them with 60 per cent ethanol. Shortly afterwards she experienced a generalized erythema and a flare-up of previous eczematous patches about 12 hours after consumption of moderate amounts of wine and spirits. She was examined by Haxthausen and a few months later by Lomholt (7). Standard patch tests gave a positive reaction to iodine 0.5 per cent, the only test substance in alcoholic solution. Patch tests with methanol, ethanol and 1-propanol were positive, but a test with 2-propanol was negative as were tests with aldehydes and acids. Between 1943 and 1945 she had been a total abstainer. From 1945 to 1967 she took alcoholic beverages occasionally, and never more than two glasses of wine or one glass of brandy at a time. She had never experienced any recurrence of dermatitis, nor had she had any irritation of the mucous membranes of the mouth after ingestion of alcoholic beverages. She had no dentures. She used Eau de Cologne on the exposed areas of the neck every morning for several years without irritation. At re-examination in 1967 she was still highly sensitive to primary alcohols (see Table 1). In connection with patch testing in 1967 she complained of itching of the hands, which disappeared without treatment.

#### Results

The test results are given in Table 1. The reactions to stronger concentrations of alcohols were generally very strong. All patients were found to have reactions to commercial methanol, ethanol, 1-propanol, 1-butanol and 1-pentanol. Tests with chromatographically pure methanol, ethanol and 1-propanol were all positive. Of secondary alcohols 2-propanol gave positive reactions in two patients and 2-butanol in one patient. Tertiary alcohols were negative in all.

The aldehydes corresponding to methanol, ethanol, 1-propanol and 1-butanol, namely methanal (formaldehyde), ethanal (acetaldehyde), 1-propanal (propylaldehyde), and 1-butanal (butyraldehyde), gave negative test reactions. The only aldehyde which produced inflammatory test reac-



tion was 2-butenal (croton aldehyde) and only in one patient.

Testing with 2-butenal after complex formation (6) in case I gave a negative reaction.

Beer and red wine gave positive tests in all four patients.

## Discussion

All four patients reacted positively to several primary alcohols, an observation also made in previously published cases (3, 6, 7, 9). But since the alcohols conventionally used contain contaminants (6), unequivocal demonstration of allergy requires the use of purified preparations for the testing. In a previous investigation an allergic reaction could be demonstrated with certainty when using gas-liquid chromatographically purified ethanol in one patient (6). In the present investigation allergy to ethanol was demonstrated with purified ethanol in a further 4 patients. These patients were also tested with gas-chromatographically purified methanol and 1-propanol, so that allergy to these substances can also be regarded as established.

This is the first time that allergy to secondary alcohols has been demonstrated. However, the alcohols used were not purified and therefore the allergy cannot be regarded as established.

Fregert *et al.* (6) described a case of allergy to alcohol and co-existing allergy to ethanal. In the present four patients, however, allergy to aldehyde could not be demonstrated except in one who reacted to 2-butenal (croton aldehyde).

In all 4 patients the skin lesions were severe. In two of them oral symptoms were pronounced after consumption of alcohol and one also had skin symptoms after such beverages. Therefore, the possibility of allergy to alcohol should be considered in patients with stomatitis. One of our patients had her dentures exchanged without improvement, while avoidance of alcohol gave immediate relief.

It is noteworthy that 2 of our patients became sensitized after occupational exposure.

The duration of allergy to alcohol is illustrated by the persistent allergic reactions in the patient who had 24 years previously been examined by Haxthausen and by Lomholt. That patient had in the meantime limited her exposure and had had no clinical symptoms.

The allergic symptoms of our patients were of delayed type, but the oral symptoms occurred very soon after contact. Fisher (5) emphasizes that reaction to alcohol can occur very soon after application to the skin.

It is not properly understood how alcohol acts as an inflammation-producing substance in the patients studied. Since alcohols do not form covalent linkages, it is less likely that alcohol should form complete antigens (4). The co-occurrence of aldehyde-allergy in a previous case gave rise to the hypothesis that metabolites of alcohol might constitute the hapten. Since only one of our four patients had allergy to an aldehyde (croton aldehyde), this explanation seems less likely. It is well known that persons with Hodgkin's disease may have pathologic reaction to alcohol (1) and alcohol can change the metabolism of endogenous or exogenous substances (2). These observations should be born in mind also when searching for an explanation why some persons react with local inflammation to small amounts of a substance which is usually well tolerated when applied externally.

## SUMMARY

Four female patients with eczematous reactions to lower aliphatic alcohols are described. One of them had skin symptoms also after consumption of alcohol and 2 had severe symptoms of the oral mucosa. Testing with gas-chromatographically pure methanol, ethanol and 1-propanol showed positive reactions in all 4. They also reacted positively to unpurified 1-butanol. Of the secondary alcohols, 2 patients had reactions to 2-propanol and one to 2-butanol. None of the patients reacted to tertiary alcohol and only one patient reacted to croton aldehyde, which was one of the 5

aldehydes tested. All four reacted positively to patch test with beer and red wine.

One of our patients had been studied already in 1943 by Haxthausen and by Lomholt. The reactions then observed could be confirmed with use of gaschromatographically purified preparations and the patient reacted negatively to aldehyde and secondary alcohols in the same way as 24 years previously.

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