

Allergic contact dermatitis caused by isopropyl alcohol: a missed allergen?

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Summary

Background. Isopropyl alcohol is a secondary alcohol, a structural isomer of propanol, that is widely used as an industrial solvent and as a preservative and antiseptic in the clinical environment. It is known to be a mild irritant for the eyes and mucous membranes, but is considered to be a weak and infrequent sensitizer.

Objectives. To show that isopropyl alcohol should be considered as a potential allergen in patients with eczema who have contact with this substance.

Materials and methods. We present a series of 1450 patients patch tested with isopropyl alcohol during the period 1992–2011.

Results. Forty-four patients showed an allergic response to isopropyl alcohol. Four cases presented as occupational hand eczema. Fourteen cases were seen in patients with leg ulcers. Twenty-six patients presented with eczematous lesions following the use of products containing isopropyl alcohol to disinfect previous skin lesions. Eighty-four per cent of the patients showed sensitization to three or more allergens. Relevance was present in 84% of the patients.

Conclusions. We report here the first large case series of contact allergy to isopropyl alcohol, which demonstrates that sensitization to this substance might not be as uncommon as previously thought.

Key words: allergic contact dermatitis; biocides; hand washing; isopropyl alcohol; rubbing alcohols.

Alcohols are classified into primary, secondary and tertiary alcohols, on the basis of the number of carbon atoms linked to the carbon atom that bears the hydroxyl group. Isopropyl alcohol (CAS 67-63-0), or isopropanol (Fig. 1), is a secondary alcohol, a structural isomer of propanol, that can be produced by combining water and propene. It is a clear and flammable liquid that has a moderate evaporation rate and is complete miscible with most solvents. It is widely used as an industrial solvent

and cleaning fluid, and is present in many products, such as lacquers, inks, and thinners, as well as in household products. In the EU, it is approved for use in cosmetics as a solvent, an antifoaming agent, a perfuming agent, and a viscosity controller (1).

Because of its antimicrobial activity (including multidrug-resistant pathogens, *Mycobacterium tuberculosis*, non-envelope virus, and a variety of fungi), isopropyl alcohol is highly valued as a preservative (it is a less toxic alternative to formaldehyde and other related chemicals) and as an antiseptic in the clinical environment, being included in many solutions, gels and foams for this purpose (2). These preparations are used to achieve skin antiseptics before invasive procedures (i.e. venous puncture or vaccination) and to disinfect wounds, and, more recently, have been used as an alternative to hand

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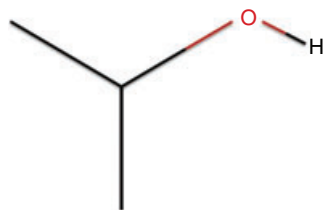


Fig. 1. Chemical structure of isopropyl alcohol.

washing for routine medical hygiene (3–5). There is no reported resistance to isopropanol-based products.

We present here a series of 44 patients with proved allergic contact dermatitis caused by isopropyl alcohol.

Material and Methods

From 1 January 1992 to 15 January 2011, a total of 11 490 patients (7585 females) were patch tested in Leuven. One thousand four hundred and fifty of them were also tested with isopropyl alcohol ('as is', pharmaceutical grade), as the history had revealed exposure to this. Patch testing and readings were performed according to the International Contact Dermatitis Research Group criteria (i.e. 2 days of occlusion, readings on D2 and D4, and sometimes also later), using their standard score from + to +++ (6). The test materials used were van der Bend® patch-test chambers (Van der Bend®, Brielle, The Netherlands) applied on the back with Micropore™ (3M Health Care®, Borken, Germany), and fixed with Mefix® (Mölnlycke Health Care®, Göteborg, Sweden) as adhesive tape.

Rare weak reactions that suggested irritancy, such as erythema without infiltration, were not taken into account in this study. Present relevance was only considered when the patient's dermatitis correlated with the exposure to isopropyl alcohol and dramatically improved or cleared when it was avoided. The significance of the association between positive responses to isopropyl alcohol and to other allergens was analysed with the chi-square test.

Results

Forty-four (3%) of the 1450 cases patch tested with isopropyl alcohol showed a clear positive response (Table 1). The MOAHLFA scores of both the total population investigated during this period and those reacting to isopropyl alcohol are given in Table 2.

Of the 44 patients, 32 were women (72%) and 12 were men (28%), the median age being 56.6 ± 15 years, ranging from 23 to 78 years. Four cases

were occupational, all presenting with hand eczema: a mechanic who had used isopropyl alcohol to degrease metals, and three nurses who had developed dermatitis following the use of medicinal products containing it. The median age of this occupational group was 32 years. Forty cases were considered to be non-occupational: 14 patients presented with leg ulcers and/or leg eczema (median age 64 years). The remaining 26 patients (median age 54 years) had been referred because of eczematous lesions following the use of products containing isopropyl alcohol to clean and/or disinfect previous skin lesions.

The patch test results with isopropyl alcohol showed a + response in 25 patients (57%), a ++ response in 16 (36%) patients, and a +++ response in 8 patients (18%; Fig. 2). Several patients had also been tested with other alcohols (Table 1): 42 with propylene glycol (10% aqueous solution), 15 (35%) of whom had a positive response; and 12 with ethanol (70% aqueous solution), 7 (58%) of whom had a positive response. In 84% of the patients, positive responses to three or more allergens were observed, indicating multiple sensitization. The more common concomitant reactors were fragrances (45%), corticosteroids (23%), and lanolin (wool alcohols) (34%). None of these associations was statistically significant in the isopropanol-tested subjects. Relevance of the positive responses to isopropyl alcohol was present in 37 patients (84%). Four of 7 with unknown relevance for isopropyl alcohol reacted to corticosteroids. Table 3 shows the causal products containing isopropyl alcohol with present relevance in our patients.

Discussion

Isopropyl alcohol is considered to be a mild irritant for the eyes and mucous membranes, and it is supposed to promote only minor skin barrier changes following chronic exposure (5). According to murine local lymph node assay studies, isopropyl alcohol is considered to be a non-sensitizer (7). However, several isolated cases of contact allergy to isopropyl alcohol have been previously reported in the literature (8–17). The International Chemical Safety Card of isopropyl alcohol (ILO) (ICSC number 0554, last reviewed March 1999 (18)) states that long-term or repeated skin exposure may 'defat the skin', without any additional explanation. The European Chemical Substances Information System does not recommend that any risk phrase should be included for this substance with regard to potential skin side effects (neither the R38: Irritating to skin, nor the R43: May cause sensitisation by skin contact). As a consequence, most Material Safety Data Sheets concerning products containing isopropyl alcohol do not consider it as a potential sensitizer (19–22).

Table 1. Cases of isopropyl alcohol contact allergy

Sociodemographic and clinical variables							Alcohols tested (D4)				Concomitant reactions		
Case	Sex	Age (years)	Atopic skin	Location	Occupational	MS	ISO	PG	ETH	Present relevance	Fragrances	Steroids	Lanolin
1	F	34	No	Leg	No	No	+	—	NT	Yes	No	No	Yes
2	M	39	No	Hand	Yes	No	+	—	NT	Yes	No	No	No
3	F	67	No	Leg	No	Yes	+	—	++	No	Yes	Yes	Yes
4	F	23	No	Hand	Yes	No	+	—	NT	Yes	No	No	No
5	F	54	No	Face	No	Yes	++	+	NT	Yes	No	No	Yes
6	F	72	No	Leg	No	Yes	++	++	++	No	Yes	No	Yes
7	F	62	No	Leg	No	Yes	++	++	++	Yes	Yes	Yes	Yes
8	F	49	No	Leg	No	Yes	++	++	NT	No	No	Yes	Yes
9	F	57	No	Leg	No	Yes	++	++	NT	Yes	Yes	Yes	Yes
10	M	63	No	Leg	No	Yes	+++	—	NT	Yes	No	No	No
11	F	74	No	Leg	No	Yes	++	++	+	Yes	Yes	Yes	Yes
12	F	61	No	Hand	No	Yes	+	—	—	Yes	No	No	Yes
13	F	66	No	Leg	No	Yes	+++	++	NT	Yes	Yes	Yes	No
14	F	69	No	Face	No	Yes	+	++	NT	Yes	Yes	No	No
15	F	59	No	Leg	No	Yes	++	—	NT	Yes	Yes	No	Yes
16	F	34	Yes	Hand	Yes	Yes	+	—	NT	Yes	No	No	No
17	F	44	No	Trunk	No	Yes	++	—	—	Yes	Yes	No	No
18	M	71	No	Trunk	No	Yes	+++	+++	NT	Yes	No	No	No
19	F	56	No	Face	No	Yes	+	—	++	No	No	Yes	Yes
20	F	32	No	Face	No	Yes	++	++	NT	Yes	No	No	No
21	F	35	No	Trunk	No	Yes	++	++	NT	Yes	No	No	Yes
22	F	53	No	Hand	No	Yes	+	+	+	Yes	Yes	No	No
23	F	60	No	Face	No	Yes	++++	+	NT	Yes	No	No	No
24	M	57	No	Trunk	No	Yes	++	—	NT	Yes	Yes	No	No
25	F	38	Yes	Hand	No	Yes	++	—	NT	Yes	Yes	No	No
26	F	74	No	Genital	No	Yes	+	+	NT	Yes	No	No	No
27	M	76	No	Face	No	No	+	—	NT	Yes	No	No	No
28	M	53	No	Hand	No	No	+	NT	NT	Yes	No	No	No
29	F	63	No	Arm	No	Yes	+	—	+	Yes	Yes	Yes	No
30	M	65	No	Hand	No	Yes	+	—	NT	Yes	Yes	No	No
31	F	31	No	Spread	No	Yes	++	—	—	Yes	No	Yes	No
32	F	71	No	Leg	No	Yes	+	—	NT	Yes	No	No	Yes
33	M	45	Yes	Spread	No	Yes	++	—	—	No	No	No	No
34	F	46	No	Hand	No	Yes	+	—	NT	No	Yes	No	No
35	M	61	No	Arm	No	Yes	++	—	NT	Yes	No	No	No
36	F	34	No	Hand	No	Yes	++	—	NT	Yes	Yes	No	No
37	F	68	No	Neck	No	Yes	+	—	NT	Yes	Yes	No	No
38	M	78	No	Leg	No	Yes	+	+	—	Yes	Yes	No	Yes
39	F	58	No	Face	No	Yes	+	—	NT	No	Yes	Yes	No
40	F	51	Yes	Neck	No	No	+	—	NT	Yes	No	No	No
41	F	74	No	Leg	No	Yes	+	—	NT	Yes	Yes	No	Yes
42	M	57	No	Hand	No	Yes	+	—	NT	Yes	No	No	No
43	M	79	No	Leg	No	Yes	+	—	NT	Yes	No	No	No
44	F	34	No	Hand	Yes	No	+	NT	NT	Yes	No	No	No

ETH, ethanol; F, female; ISO, isopropyl alcohol; M, male; MS, multiple sensitization; NT, not tested; PG, propylene glycol.

Allergic contact dermatitis caused by isopropyl alcohol was first described in 1968 (8). Since then, other cases have been published, usually in a young, healthy population who reacted to swabs used to disinfect the skin before venepuncture. Unfortunately, only a few cases (8, 10–12, 15) have been adequately studied and patch tested with isopropyl alcohol (Table 4), and most of the

patients were only tested with the swab 'as is' (4, 14, 16, 17). Positive patch test responses to isopropyl alcohol without clinical relevance have also been reported (9, 23).

Curiously, none of the 44 patients described here presented with skin lesions after the use of a medical swab applied on healthy skin; this leads to the suspicion that only those cases with a clear causal association

Table 2. MOAHLFA scores of the overall group of patients tested from 1 January 1992 to 15 January 2011 compared with MOAHLFA scores of the patients tested with isopropyl alcohol (n = 1450) and MOAHLFA scores of the isopropyl alcohol-positive patients (n = 44)

	Isopropyl alcohol-positive patients (n = 44) (%)	Isopropyl alcohol-tested patients (n = 1450) (%)	Overall sample (n = 11 490)
Male	27	31	34
Occupational	9	21	15
Atopy	9	20	22
Hand	27	42.5	38
Leg	32	7	3
Face	16	26	34
Age >40 years	77	51	49

**Fig. 2.** Strong patch test response (+++) to isopropyl alcohol on day 2.

between the dermatitis and exposure to isopropyl alcohol-containing swabs were reported. Therefore, most cases might go undiagnosed, as isopropyl alcohol is not

Table 3. Products containing isopropyl alcohol with present relevance in our cases

Commercial name	Provider	Active drugs
Hexomedine transcutaneous® Hexomedine solution®	Sanofi Aventis®, Diegem, Belgium	Hexamidine
Hibitane concentrate® Hibitane tincture®	AstraZeneca®, Brussels, Belgium	Chlorhexidine
HAC cutaneous solution®	AstraZeneca®, Brussels, Belgium	Chlorhexidine
Flexium gel®	Melisana® S.A., Brussels, Belgium	Etofenamate
Mobilat gel®	NeoCare® S.A., Brussels, Belgium	Purified suprarenal extract Acetylsalicylic acid
Hibiscrub solution®	Mölnlycke Health Care® NV/SA, Antwerp, Belgium	Chlorhexidine
Diprosone lotion®	MSD®, Brussels, Belgium	Betamethasone
Hirudord gel®	STADA®, Bad Vilbel, Germany	Heparinoids
Dax Alcolgel®	Multimedi®, Meerhout, Belgium	—
Sterilium®	Bode Chemie®, Hamburg, Germany	—

suspected by dermatologist to be a sensitizer, and is thus rarely tested.

Combining our results with previously published experience, we think that patients sensitized to isopropyl alcohol may be divided into four main groups: (i) older patients with chronic wounds, especially leg ulcers and/or leg eczema; (ii) patients with acute wounds who applied an isopropyl-alcohol containing product; (iii) younger

Table 4. Cases published in the literature with proven relevance for isopropyl alcohol

No	Author	Sex	Age (years)	Occupational	Localization	Product	Concomitant reactions
1	Wasilewski (8)	F	20	No	Arm Hand	Swab with 70% isopropyl alcohol	None
2	Kurwa (10)	F	48	No	Elbow	Swab with 70% isopropyl alcohol	Lanolin
3	Ludwig and Hausen (12)	F	45	No	Back (patch tested on a volunteer)	Hair lotion	Other primary and secondary alcohols Aldehydes
4	Jensen (11)	M	28	No	Arm	Swab with 70% isopropyl alcohol	Propylene oxide
5	Kwon et al. (15)	F	36	No	Forearm	Swab with 67% isopropyl alcohol	Dodecyl diaminoethyl-glycine

F, female; M, male.

patients with otherwise healthy skin who react to isopropyl alcohol-based swabs applied to disinfect the skin prior to invasive procedures; and (iv) occupational cases suffering from hand eczema though daily contact with isopropyl alcohol. Patients from groups (i) and (ii) usually present with sensitization to multiple allergens, especially fragrances, corticosteroids, and lanolin. Patients from groups (iii) and (iv) often react only to isopropyl alcohol. Many of our patients also reacted to ethanol, a primary alcohol. Cross-reactions between ethanol and other primary alcohols are commonly reported, but it is uncommon for primary alcohols to cross-react with secondary or tertiary alcohols (24). Patients may, of course, become sensitized to both substances individually. The same is true for propylene glycol, which is a diol that is also included in many preparations containing isopropyl alcohol. Both propylene glycol and ethanol present concomitant reactions to corticosteroids (25), and for ethanol this was suggested (26) to result from the formation of certain common intermediate metabolites, such as acetaldehyde. Our cases presented with the typical profile of a polysensitized patient with chronic wounds, such as leg ulcers (27, 28), in whom contact allergy to corticosteroids is also frequently observed (29).

Allergic contact dermatitis caused by isopropyl alcohol has special relevance at the present time, as this substance is being recommended for daily use as an alternative to

hand washing in both clinical and non-clinical fields. The World Health Organization recommends the use of alcohol-based handrubs in its guidelines on hand hygiene in healthcare (2). It also recommends that handrubs should be readily available in the clinical environment, either through dispensers close to the point of care, or in small bottles for on-person carriage. These preparations may be also used to clean other medical devices, such as stethoscopes (30). This means that large numbers of health professionals are being regularly exposed to isopropyl alcohol. Moreover, it is considered to be less irritant than normal hand washing, which may improve adherence to the regimen (31). Furthermore, it is not unusual to see handrubs designed to be used in domestic environments (especially after the influenza A epidemic). As a result, more new cases are expected to appear in the near future.

Conclusion

We report here the first large series of cases of contact allergy to isopropyl alcohol, which demonstrates that sensitization to this substance might not be as uncommon as previously thought. This allergen should be tested in all patients being investigated for their dermatitis and who have skin contact with products containing it. Otherwise, most of the cases will go undiagnosed.

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