

Is benzyl alcohol a significant contact sensitizer?

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Abstract

Background

Benzyl alcohol is a widely used preservative, solvent, and fragrance material. According to published data, it is a rare sensitizer in humans.

Objectives

To identify characteristics and sensitization patterns of patients with positive patch test reactions to benzyl alcohol and to check the reliability of the patch test preparation benzyl alcohol 1% pet.

Patients and Methods

Retrospective analysis of data from the Information Network of Departments of Dermatology (IVDK), 2010-2019.

Results

Of 70,867 patients patch tested with benzyl alcohol 1% pet., 146 (0.21%) showed a positive reaction, most of them (89%) only weak positive. The number of doubtful and irritant reactions significantly exceeded the number of positive reactions. Reproducibility of positive test reactions was low. Among benzyl alcohol-positive patients, compared to benzyl alcohol negative patients, there were significantly more patients with leg dermatitis (17.8% vs. 8.6%), more patients aged 40 years or more (81.5% vs. 70.5%), and more patients who were tested because of a suspected intolerance reaction to topical medications (34.9% vs. 16.6%). Concomitant positive reactions were mainly seen to fragrances, preservatives, and ointment bases.

Conclusions

Sensitization to benzyl alcohol occurs very rarely, mainly in patients with stasis dermatitis. In view of our results, benzyl alcohol cannot be regarded as a significant contact allergen, and therefore marking it as skin sensitizer 1B and labelling it with H 317 is not helpful.

Keywords

Benzyl alcohol, CAS 100-51-6, clinical epidemiology, contact allergy, patch testing.

1. Introduction

Benzyl alcohol (CAS 100-51-6) is a widely used preservative, solvent, and fragrance material. Animal and in vitro experiments do not clearly and unequivocally indicate that benzyl alcohol is a skin sensitizer [1,2]. In some Human Repeated Insult Patch Test (HRIPT) studies with high concentrations of benzyl alcohol, sensitization could be induced. From these studies, a No Observed Effect Level (NOEL) of 5,906 $\mu\text{g}/\text{cm}^2$ was derived [1,2]. When patch tested in skin clinics as part of preservative and fragrance test series, benzyl alcohol 1% in petrolatum (pet.) elicits positive reactions in less than 1%, mostly even in less than 0.5%, of the patients [2,3; for additional references see online supplemental information]. Remarkably, patch test studies using higher test concentrations (5% or 10% pet.) did not yield significantly higher reaction frequencies [3]. In the course of the European Chemicals Agency (ECHA) consultation on harmonised classification and labelling, the German Federal Institute for Occupational Safety and Health (BAuA) proposed classifying benzyl alcohol as skin sensitizer category 1B and labelling it with the hazard statement H 317 ("May cause an allergic skin reaction") [1].

Against this background, we regard it necessary to summarize data from the Information Network of Departments of Dermatology (IVDK) concerning benzyl alcohol. The IVDK holds the world's largest contact allergy database including benzyl alcohol patch test data of more than 70,000 patients. We comprehensively analyse this data in order to describe the role of benzyl alcohol as skin sensitizer in humans, characterize its sensitizing properties based on clinical data, and check the diagnostic reliability of the routinely used patch test preparation benzyl alcohol 1% pet.

For this purpose, we

- describe the reaction pattern and determine the Reaction Index (RI) and Positivity Ratio (PR) [4,5],
- evaluate concomitant reactivity to the irritant control sodium lauryl sulphate (SLS) [6],
- check the reproducibility of positive patch test reaction to benzyl alcohol 1% pet.,
- compare population characteristics of patients with and without positive patch test reactions to benzyl alcohol 1% pet., respectively, and
- compare concomitant reactions to other allergens in these two patient groups.

2. Data and Methods

The IVDK is a network of currently 57 departments of dermatology in Germany, Switzerland, and Austria, dedicated to clinical epidemiology of contact allergy. Patients' medical histories, clinical data, and patch test results are recorded in local databases in the participating centres and, after pseudonymization, transmitted to the IVDK central office at the University Medical Centre of Göttingen twice a year. Data are subjected to standardized quality control, added to the central IVDK database, and analysed according to international standards [7].

All IVDK members are also members of the German Contact Dermatitis Research Group (DKG). Patch testing and evaluation of reactions is performed according to DKG guidelines [8,9]. For the present data analysis, patch test reactions at day 3 (D3) were considered. In a few exceptional cases, when a patch test reading was performed at D4 instead of D3, this reading was selected. Readings coded as +, ++ or +++, i.e. positive reactions with erythema, infiltration, papules and/or (coalescing) vesicles were rated as positive. Most patch test preparations, including benzyl alcohol 1% pet., were purchased from Almirall Hermal, Reinbek, Germany until 2013, and from SmartPractice Europe, Greven, Germany from 2014 on. Some of the other patch test preparations mentioned below were bought from Chemotechnique, Vellinge, Sweden.

Percentages of proportions of items from the patients' medical histories and of reaction frequencies in subgroups of patients are presented together with exact 95% confidence intervals (CIs). Statistical significance of differences on a 5%-level was concluded from non-overlapping 95%-CIs. Reaction Indices (RIs) and Positivity Ratios (PRs) were calculated according to the published formulae [4,5,10]. Data was managed and analysed using the statistical analysis software SAS®, version 9.4 (SAS Institute, Cary, NC, USA).

3. Results

In the years 2010 to 2019, altogether 117,279 patients were patch tested in the departments of dermatology joining the IVDK, in the course of 121,100 consultations. Benzyl alcohol 1% pet. was patch tested in 70,867 patients. Patch test results are presented in table 1. There were 146 positive reactions (0.21%). RI was -0.44, PR was 89%.

Patients with a positive reaction to benzyl alcohol 1% pet. ($n = 146$) had a total of 1,004 positive reactions to any allergen preparation. Thus, the average count of positive reactions per patient was 6.88. The median was 5 positive reactions. For comparison: Among benzyl alcohol-negative patients ($n=70,347$), 36,785 (52.3%) had at least one positive patch test reaction to any of the allergen preparations tested. Altogether, there were 104,720 positive test reactions in these patients. On average, every patient had 2.85 positive reactions (median: 2).

In 67,338 patients patch tested with benzyl alcohol 1% pet., sodium lauryl sulphate (SLS) was tested at 0.25% in water (aq.) as an irritant control. Of these patients, 13,276 (19.7%) had an irritant reaction to SLS 0.25% aq. Benzyl alcohol 1% pet. elicited a positive patch test reaction in 137 patients (0.2%). The proportion of benzyl alcohol-positive patients was significantly ($p = 0.02$; χ^2 test) higher among those with an irritant reaction to SLS ($38 / 13,276 = 0.29\%$) than among those not reacting to SLS ($99 / 54,062 = 0.18\%$).

Benzyl alcohol 1% pet. was patch tested more than once during the 10-year period 2010 – 2019 in 1,184 patients. There were 23 non-negative reactions, and of these, only 2 had the same reaction intensity in both tests (one doubtful reaction, one weak positive reaction). Only 1 out of 4 positive reactions in the first patch test could be reproduced on a later occasion. In table S1 in the online supplemental information, patch test results of the first and the last patch test, respectively, are cross-tabulated in detail.

Table 2 gives a comparison of population characteristics of patients with a positive patch test reaction ($n = 146$), patients with a doubtful or irritant reaction ($n=374$), and those with a negative patch test reaction ($n = 70,437$) to benzyl alcohol 1% pet. There were no significant differences between benzyl alcohol-negative patients and those with a doubtful or irritant reaction, as far as the items presented are concerned. Among patients reacting positively to benzyl alcohol, there were – compared to those with a negative reaction – significantly more patients with leg dermatitis (17.8% vs. 8.6%), more patients aged 40 years or more (81.5% vs. 70.5%), and more patients who were tested because of a suspected intolerance reaction

to topical medications (34.9% vs. 16.6%). In addition, patch testing obviously was performed more targeted in benzyl alcohol-positive patients: they had the highest proportions of patients tested under the suspicion of allergic contact dermatitis (and not in order to exclude contact sensitization), and of patients with a final diagnosis of allergic contact dermatitis. On the other hand, benzyl alcohol-positive patients had the lowest share of hand dermatitis patients and of patients suffering from occupational dermatitis.

A comparative illustration of the reaction frequencies to other contact sensitizers observed in the three groups of patients is given in table 3. Only those allergens are listed which were tested in at least 90% of the patients of each group, in order to avoid a selection bias. The listing is limited to those allergens which elicited positive reactions in at least 7 benzyl alcohol-positive patients (5% of the patients of this group). When comparing patients with a positive reaction to benzyl alcohol 1%pet. (n=146) to benzyl alcohol-negative patients (n=70,437), frequencies of sensitization to a number of allergens were significantly increased. All of these allergens belong to 3 groups: fragrances, preservatives / antiseptics, and ointment bases. Frequencies of sensitizations to other ubiquitous contact allergens such as metals (nickel, cobalt, chromium) did not differ significantly.

4. Discussion

The pattern of patch test reactions to benzyl alcohol 1% pet. is not satisfactory with regard to its diagnostic discriminatory power. The number of doubtful and irritant (i.e. unwanted) test reactions exceeds the number of positive reactions by far, resulting in a negative RI. Almost 90% of the positive reactions are only weak positive, as indicated by a PR of 89%. With a RI of -0.44 and a PR of 89%, benzyl alcohol 1% pet. is a typical “problematic allergen” [11]. It is suspected that a considerable proportion of positive reactions to such allergen test preparations false positive. This suspicion is underlined by the finding that patients whose skin tends to show irritant reactions easily – as indicated by a positive patch test with SLS 0.25% aq. – have significantly more positive reactions to benzyl alcohol 1% pet. than those with a negative SLS test. The third finding characterizing benzyl alcohol 1% pet. as a rather unreliable test preparation is the low reproducibility. Out of 4 positive reactions, only 1 could be reproduced in a second patch test.

On the other hand, there are significant differences between patients reacting positively to benzyl alcohol 1% pet. and those who don't, which convincingly indicates that not *all* positive reactions are false-positive. The analysis of the total number of positive patch test reactions in patients with negative and positive reactions to benzyl alcohol, respectively, revealed that patients reacting to benzyl alcohol tend to be poly-sensitized. This may indicate a particular susceptibility for contact sensitization, special circumstances when sensitization to benzyl alcohol was acquired, a particular way of concomitant allergen exposure, or a combination of these factors. Considering the fact that patients with leg dermatitis are over-represented among those with a positive test reaction to benzyl alcohol, it can be assumed that a considerable proportion of these patients suffer from stasis dermatitis caused by chronic venous insufficiency. In these patients, various topical medications and skin care products are being applied on inflamed skin (with impaired epidermal barrier). This increases the risk of contact sensitization due to dermal “danger signals” being present because of the inflammation, and a high exposure to a combination of various contact allergens (emulsifiers, fragrances, preservatives) in the topical medical preparations [12].

When comparing frequencies of reactions to other allergens between patients reacting to a particular allergen and those who do not, one has to be aware that generally patients who are sensitized to one substance tend to acquire sensitization to other allergens, too [13,14]. This means, it is generally to be expected that reaction frequencies to all allergens are higher in the “positive” group. This can be seen

from table 3, where proportions of positive reactions to all allergens are highest in the group of patients with a positive reaction to benzyl alcohol.

However, some special pattern can be recognized. When comparing patients with a positive reaction to benzyl alcohol 1% pet. to benzyl alcohol-negative patients, we find a dramatic increase in sensitization to balsam of Peru, fragrance allergens such as fragrance mixes I and II, Jasmine absolute, and Ylang ylang oil, and propolis among those reacting to benzyl alcohol. In case of balsam of Peru and propolis, this was to be expected, because benzyl alcohol is present in both of these natural extracts [15]. As far as the fragrance allergens are concerned, this is probably due to co-exposure to benzyl alcohol and fragrances in topical medications and body care products. This explanation also holds true for the – less pronounced – increased proportion of positive reactions to ointment bases and emulsifiers as well as other preservatives and skin antiseptics among the benzyl alcohol positive patients.

5. Conclusion

The first – and most important – finding is that positive patch test reactions to benzyl alcohol are very rare (0.2%), even in a clinical dermatitis patient population.

Secondly, considering the low diagnostic performance of the test preparation benzyl alcohol 1% pet., it is very probable that the correct proportion of truly sensitized patients is even lower.

Nevertheless, there are a few cases of contact allergy to benzyl alcohol as can be seen from the analyses of patient characteristics and concomitant reactions. A considerable proportion of the cases of sensitization is due to particular exposure and skin conditions, especially in stasis dermatitis patients.

In order to verify if patients with positive patch test reactions to benzyl alcohol are truly sensitized, or whether they react to consumer products containing benzyl alcohol within the legal concentration limits, repeated open application tests (ROAT) or provocative use tests (PUT) could be performed. However, considering the very limited number of patients with a (reproducible) positive patch test reaction and the fact that most of the patients reacting to benzyl alcohol are poly-sensitized, this would be a very time-consuming and complex undertaking, which seems not justified in view of the extremely low importance of benzyl alcohol as contact sensitizer.

In view of these results, benzyl alcohol cannot be regarded as a significant contact allergen. In our opinion, categorizing benzyl alcohol as skin sensitizer 1B and labelling benzyl alcohol with H 317 according to Annex VI of Regulation (EC) No 1272/2008 is not justified.

The definition of “low/moderate” frequency of sensitization leading to category 1B includes a sensitization rate of < 1.0% in unselected dermatitis patients and/or < 2.0% after aimed patch testing. Our data would easily fit into this category. However, no lower threshold of this category is defined, and hence every substance eliciting a contact allergy reaction in only 1 individual must be categorized as 1B. This means, almost no substance can be classified as non-sensitizing, which is a general problem of the category definition. Currently, the CLP Regulation (Regulation (EC) No 1272/2008 on the classification, labelling and packaging of substances and mixtures) is being revised. In this context, there is a public consultation [16] giving the opportunity of bringing this problem to the attention of the EU authorities.

Category 1 (A or B) and the hazard statement H 317 are intended to warn the user / consumer of risks. Extending their application to even extremely rare allergens such as benzyl alcohol may severely compromise its warning character and therefore appears to be rather counterproductive.

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Table 1. IVDK, 2010-2019: patch test results with benzyl alcohol 1% pet.

Reaction	n (patients)	% (patients)
Negative	70,347	99.27
Doubtful (erythema or few follicular papules only)	278	0.39
+	130	0.18
++	14	0.02
+++	2	0.00
Irritant	96	0.14
Total	70,867	100.0

Table 2. Selected population characteristics of three groups of patients with different patch test reactions to benzyl alcohol 1% pet. Proportions are presented as percentages, together with the corresponding 95% confidence intervals [in brackets].
Items with significantly increased reaction frequencies among benzyl alcohol-positive patients when compared to benzyl alcohol-negative patients are marked in bold.

	Reaction to benzyl alcohol 1% pet.		
	negative (n=70,347)	doubtful or irritant (n=374)	positive (n=146)
<i>MOAHLFA-Index</i>			
Males	36.3 [35.9 – 36.6]	38.5 [33.5 – 43.6]	32.9 [25.3 – 41.1]
Occupational dermatitis	21.2 [20.9 – 21.5]	22.5 [18.3 – 27.0]	12.3 [7.5 – 18.8]
Atopic dermatitis	27.2 [26.9 – 27.5]	25.9 [21.6 – 30.7]	24.7 [17.9 – 32.5]
Hand dermatitis	37.0 [36.7 – 37.4]	35.6 [30.7 – 40.6]	24.0 [17.3 – 31.7]
Leg dermatitis	8.6 [8.4 – 8.8]	7.5 [5.0 – 10.6]	17.8 [12.0 – 25.0]
Face dermatitis	18.3 [18.0 – 18.6]	19.8 [15.9 – 24.2]	12.3 [7.5 – 18.8]
Age >= 40 years	70.5 [70.2 – 70.9]	71.1 [66.2 – 75.7]	81.5 [74.2 – 87.4]
<i>Suspected allergen sources</i>			
Cosmetics	47.9 [47.5 – 48.3]	47.1 [41.9 – 52.3]	53.4 [45.0 – 61.7]

Topical medications	16.6 [16.3 – 16.8]	19.3 [15.4 – 23.6]	34.9 [27.2 – 43.3]
Disinfectants	11.6 [11.4 – 11.8]	9.9 [7.1 – 13.4]	13.7 [8.6 – 20.4]
Gloves	11.7 [11.5 – 11.9]	11.8 [8.7 – 15.5]	10.3 [5.9 – 16.4]
Perfume, deodorant etc.	3.7 [3.6 – 3.9]	4.3 [2.5 – 6.9]	4.1 [1.5 – 8.7]
<i>Indication for patch testing</i>			
Suspected allergic contact dermatitis	41.2 [40.8 – 41.6]	41.2 [36.1 – 46.4]	50.7 [42.3 – 59.0]
Exclusion of allergic contact dermatitis	38.0 [37.7 – 38.4]	36.9 [32.0 – 42.0]	32.2 [24.7 – 40.4]
<i>Final diagnosis</i>			
Allergic contact dermatitis	24.8 [24.5 – 25.1]	28.9 [24.3 – 33.8]	49.3 [41.0 – 57.7]

Table 3. Frequencies of positive patch test reactions in three groups of patients with different patch test reactions to benzyl alcohol 1% pet. Reaction frequencies are presented as age- and sex-standardized percentages of positive reactions, together with the corresponding 95% confidence intervals [in brackets].

Allergens with significantly increased reaction frequencies among benzyl alcohol-positive patients when compared to benzyl alcohol-negative patients are marked in bold.

Allergen	Percent positive reactions		
	negative (n = 70,347)	doubtful or irritant (n = 374)	positive (n = 146)
Benzyl alcohol 1% pet.	0	0	100.0
Balsam of Peru 25% pet.	6.3 [6.1 - 6.5]	13.0 [9.8 - 16.3]	48.0 [37.1 - 58.9]
Fragrance mix I 8% pet.	7.5 [7.3 - 7.7]	12.2 [8.6 - 15.8]	27.8 [18.8 - 36.8]
Jasmine absolute 5% pet.	1.2 [1.1 - 1.3]	4.9 [2.7 - 7.1]	22.3 [14.5 - 30.1]
Ylang ylang (I + II) oil 10% pet.	2.2 [2.1 - 2.4]	5.2 [3.1 - 7.3]	23.6 [14.4 - 32.7]
Nickel sulphate 5% pet.	16.0 [15.7 - 16.3]	14.5 [10.5 - 18.6]	16.6 [9.5 - 23.7]
Fragrance mix II 14% pet.	4.4 [4.2 - 4.6]	9.3 [6.3 - 12.2]	13.9 [6.9 - 20.8]
Propolis 10% pet.	3.3 [3.2 - 3.5]	5.4 [3.3 - 7.5]	11.5 [6.5 - 16.4]
Methyldibromo glutaronitrile¹	2.9 [2.8 - 3.0]	5.4 [3.1 - 7.7]	12.0 [5.4 - 18.5]
Octyl gallate 0.3% pet.	1.7 [1.6 - 1.8]	3.9 [1.8 - 6.1]	12.1 [4.3 - 20.0]
Amerchol L-101 50% pet.	3.1 [2.9 - 3.2]	8.4 [5.2 - 11.5]	9.7 [3.7 - 15.6]
Lanolin alcohols 30% pet.	2.2 [2.1 - 2.3]	6.7 [4.1 - 9.3]	11.6 [3.4 - 19.7]
Propylene glycol 20% aq.	1.5 [1.4 - 1.7]	4.7 [2.5 - 6.8]	13.7 [4.5 - 22.9]
Triclosan 2% pet.	0.3 [0.2 - 0.3]	0.6 [0.0 - 1.3]	8.2 [2.9 - 13.6]
MCI/MI 0.01 % aq.	4.6 [4.4 - 4.7]	4.3 [2.0 - 6.6]	9.9 [2.7 - 17.0]
Cetearyl alcohol 20% pet.	0.7 [0.6 - 0.8]	4.9 [2.7 - 7.1]	7.8 [1.4 - 14.1]
Colophony 20% pet.	3.7 [3.6 - 3.9]	4.2 [2.1 - 6.4]	6.5 [2.2 - 10.9]
Potassium dichromate 0.5% pet.	3.7 [3.5 - 3.8]	6.6 [3.7 - 9.5]	8.7 [1.5 - 15.8]
Cobalt chloride 1% pet.	5.7 [5.5 - 5.9]	6.6 [3.9 - 9.4]	8.5 [2.3 - 14.6]
Sorbic acid 2% pet.	0.5 [0.5 - 0.6]	1.0 [0.1 - 1.9]	6.9 [1.7 - 12.1]
Methylisothiazolinone 0.05% aq.	4.9 [4.8 - 5.1]	5.1 [2.6 - 7.7]	5.2 [1.0 - 9.5]
HICC ² 5% pet.	1.8 [1.7 - 1.9]	3.3 [1.7 - 4.9]	6.5 [0.3 - 12.7]
Turpentine oil 10% pet.	1.1 [1.0 - 1.2]	1.6 [0.3 - 2.9]	4.9 [0.7 - 9.0]
Thiuram mix 1% pet.	2.5 [2.4 - 2.6]	4.4 [2.3 - 6.4]	4.8 [0.8 - 8.8]
Coconut diethanolamide 0.5% pet.	0.6 [0.5 - 0.7]	2.3 [0.5 - 4.0]	3.6 [1.2 - 6.0]
Chlorohexidine digluconate 0.5% aq.	0.3 [0.3 - 0.4]	1.5 [0.2 - 2.9]	5.6 [0.6 - 10.6]

Sodium benzoate 2% pet.	0.3 [0.2 - 0.3]	1.0 [0.0 - 2.1]	4.3 [0.4 - 8.2]
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¹ Methylidibromo glutaronitrile was patch tested at 0.2% pet. and 0.3% pet. during the study period.

² HICC; Hydroxyisohexyl 3-cyclohexene carboxaldehyde

Contact sensitization to benzyl alcohol – summary of published IVDK data.

All diagnostic patch tests were done with benzyl alcohol 1% in petrolatum (pet.).

Patient population	Study period	Patients with positive reactions	Additional data (further remarks see below)	Ref.
11,373 patients tested with the DKG preservative series	1990 – 1994	0.4 % (n=46)	0.55 % doubtful and irritant reactions (n=62); RI = - 0,1	[17]
65,398 patients tested with the DKG preservative series	1996 – 2007	0.34% (n=223)	RI = - 0.15; PR = 75% men: 0.23% positive (n=55 / 24,175) women: 0.41% positive (n=168 / 41,223)	[18]
79,770 patients tested with the DKG preservative series	1996 – 2009	0.32% (n=258)	RI = - 0.23; PR = 76% men: 0.22% positive (n=64 / 29,519) women: 0.39% positive (n=194 / 50,251)	[19]
17,740 patients tested with preservatives	2006 – 2009	0.17% (n=31)	SEQ = 0.30	[20]
37,744 patients tested with the DKG preservative series	2009 – 2013	0.21% (n=78)	RI = - 0.4; PR = 95%	[21]
69,623 patients tested with the DKG preservative series	2009 – 2018	0.21% (n=145)		[22]
23,257 patients tested with fragrance series no. 43*	2005 – 2008	0.24% (n=56)	0.53% doubtful and irritant reactions (n=123); RI = - 0.37; PR = 87.5%	[23]
2,257 patients tested with fragrance series no. 43*	2010 – 2014	0.2% (n=5)		[24]
3,191 patients tested with fragrance series no. 43*	2016 – 2018	0.1%		[25]
2,166 consecutive patients	2003	0.3% (n=7)	0.6% doubtful and irritant reactions (n=13); RI = - 0.3; PR = 43%	[26]
1,059 consecutive patients	2005 – 2008	0.1% (n=1)	1% doubtful and irritant reactions (n=11)	[23]

DKG; Deutsche Kontaktallergie-Gruppe (German Contact Dermatitis Research Group).

RI; Reaction Index. PR; Positivity Ratio.

* Fragrance series no. 43; DKG patch test series with fragrances to be declared if in cosmetics.

Additional remarks

- [17]: For comparison: A total of 11,120 patients were tested with 2-phenoxyethanol 1% pet.; 14 positive reactions (0.1%), 52 doubtful and irritant reactions; RI = - 0.6.
- [18]: The high number of doubtful and irritant reactions and the high proportion of weak positive reactions among the total of positive reactions indicates the possibility that there are false-positive reactions which additionally puts the low reaction frequency into perspective.
- [19]: An epidemiologically relevant decrease (> 10%) of the proportion of positive reactions to benzyl alcohol was seen from 1996 to 2009. Sensitization to benzyl alcohol was associated with leg dermatitis. Indeed, among patients reacting to benzyl alcohol, there were significantly less men, occupational dermatitis patients, hand and face dermatitis patients, but significantly more leg dermatitis patients and patients aged 40 years or more, when compared to the remainder of the total test population.
Reaction frequencies to other widely used preservatives for comparison:
Methyldibromo glutaronitrile – 2.4%; MCI/MI – 2.2%; Iodopropynyl butylcarbamate – 0.9%.
- [20]: Frequencies of sensitization to various preservatives observed in the IVDK, 2006 – 2009, were compared to the number of leave-on cosmetic / body care products purchased at random during the same time period containing the corresponding preservatives. The proportions of patients sensitized to a particular preservative among all patients sensitized to one of the preservatives investigated was divided by the proportion of products containing this preservative among all 3,451 products in order to calculate a “sensitization exposure quotient” (SEQ). The lowest SEQ, indicating a very low frequency of sensitization despite frequent use in leave-on products, was found for phenoxyethanol (SEQ = 0.06). Benzyl alcohol ranked second (SEQ = 0.30). For comparison: The SEQ for Methylchloroisothiazolinone / Methylisothiazolinone (MCI/MI) was 9.0, and Bronopol had an SEQ of 13.0 which was the highest value found.
- [22]: Reaction frequencies to other widely used preservatives for comparison:
Methylisothiazolinone – 5.0%; MCI/MI – 4.6%; Iodopropynyl butylcarbamate – 1.3%.
- [26]: Sensitization to benzyl alcohol was associated with leg dermatitis (29%). A closer look at the data reveals that this means 2 out of 7 patients, which is a proportion of 29%; however, the 95% confidence interval (95%-CI) ranges from 4% to 71%, illustrating that this is not significant at all. Proportion of leg dermatitis patients in the test population was 11%.

Table S1. Reproducibility of patch tests with benzyl alcohol 1% pet.

		2 nd test					
		neg.	?	f	+	ir.	total
1 st test	neg.	1,161	7	1	2	3	1,174
	?	2	1	0	0	0	3
	f	0	0	0	0	0	0
	+	3	0	0	1	0	4
	ir.	3	0	0	0	0	3
	total	1,169	8	1	3	3	1,184

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