

Benzyl Alcohol Allergy: Importance of Patch Testing with Personal Products

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Benzyl alcohol is a weak sensitizer found in a wide array of plants and plant products, foods, cosmetics, and medications. Delayed contact dermatitis reactions as well as immediate, urticarial, and systemic reactions have been reported to occur with its use in these various formulations. We present the case of a woman with allergic contact dermatitis from benzyl alcohol and provide a brief review of allergy to this chemical.

BENZYL ALCOHOL is an aromatic alcohol found in many naturally occurring plant products such as balsam of Peru. It is also a component of essential oils such as hyacinth, jasmine, and ylang-ylang oils and of foods such as apricots, cranberries, cocoa, honey, mushrooms, and snap peas.¹⁻³ In topical preparations, benzyl alcohol may function as a preservative, solvent, and/or anesthetic, as well as a viscosity-decreasing agent. Its structure consists of an aromatized benzene ring with an attached hydroxylated carbon (Fig 1). Its physical and chemical properties suit its use as a preservative in medical solutions, over-the-counter medications, topical creams and lotions, fragrances, and cosmetics.²

In 1998, the Food and Drug Administration listed benzyl alcohol as an ingredient in 322 cosmetic formulations, including baby toiletries, mascaras, hair dyes, and other skin care products.¹ The Danish Product Register, a European chemical database, listed benzyl alcohol as a chemical primarily found in hardeners, paints and lacquers, photographic developers, toiletries, and products containing binders.⁴ Despite its widespread use, reports of allergy to benzyl alcohol are relatively rare.⁵ We report a patient with an allergy to benzyl alcohol, discuss the importance of patch testing with personal products and the investigation of synonyms, and present a brief review of the literature regarding benzyl alcohol.

Case Report

A 57-year-old obese woman with a 10-year history of persistent pruritic dermatitis on her arms and legs presented to the University of Minnesota Occupational and Contact Dermatitis Clinic for patch testing. The dermatitis on her legs had been complicated by several bouts of cellulitis requiring oral and parenteral antibiotics. This presumed stasis dermatitis had also been treated with numerous topical antibiotic and corticosteroid preparations. At the time of patch testing, she was using fluocinonide 0.05% ointment, pimecrolimus 1% cream, and hydrocortisone 2.5% cream. She did not wear support stockings, and her 28-year career as a receptionist was thought to be unrelated to her dermatitis. Patch testing approximately 10 years previously had shown reactions to lanolin and neomycin, both of which the patient was successfully avoiding.

Patch testing was performed with an expanded standard series (64 antigens, with neomycin and lanolin removed) and with preservative, vehicle, corticosteroid, and cosmetic series. In addition, 20 personal products were also tested. The patch-test results are listed in Table 1, and key reactions are shown (Fig 2). Based on these results as well as those from prior patch testing, the patient was diagnosed with allergic contact dermatitis to benzyl alcohol, class B corticosteroids, bacitracin, neomycin, lanolin, fragrance, and Euxyl K400 (Schülke & Mayr GmbH, Norderstedt, Germany). Because of doubtful reactions to mupirocin ointment and paraben mix, repeat patch testing with these antigens was recommended. The patient's dermatitis improved after discontinuing the use of benzyl alcohol-containing products and institution of hydrocortisone 2.5% ointment and petroleum jelly.

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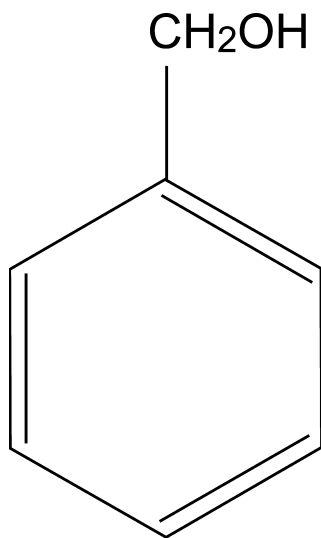


Figure 1. Structure of benzyl alcohol.

The presence of benzyl alcohol in one of this patient's personal products, Aveeno Moisturizing Lotion (Johnson & Johnson, New Brunswick, NJ), would have been missed if she had not been patch-tested with the actual product. Further investigation using the dictionary prepared by the Cosmetic, Toiletry and Fragrance Association (CTFA) revealed that phenylcarbinol, listed on the ingredient label of Aveeno Moisturizing Lotion (Fig 3), is a synonym for benzyl alcohol. Other synonyms for benzyl alcohol are benzenemethanol, benzylic alcohol, phenylmethanol, phenylmethyl alcohol, α -toluene, and hydroxytoluene.^{1,6} In 2001, the CTFA mandated that when this compound is used as an active ingredient in over-the-counter medications, the name "benzyl alcohol" should be listed,⁷ but this patient's Aveeno Moisturizing Lotion had likely been packaged before 2001. Had the patient not been tested with the actual product, we would have likely missed this synonym on the label. A review of the label of Aveeno Moisturizing Lotion in February 2005 showed that the term "benzyl alcohol" is now in use on the label.

Discussion

One of the first reports of adverse reactions to benzyl alcohol involved toxicity. In the early 1980s, 16 neonates were admitted to a neonate intensive care unit with suspected benzyl alcohol toxicity thought to be a result of catheter flushing with normal saline containing benzyl alcohol as a preservative.⁸ It was hypothesized that the toxicity resulted from the inability of the newborns' immature livers to eliminate toxic metabolites of benzyl alcohol. Since

then, intravenous fluids and medications containing benzyl alcohol have been banned from use in newborns.⁹

For topical products, the CTFA Cosmetic Ingredient Review Expert Panel concluded in 2001 that studies regarding toxicity, sensitization, mutagenicity, carcinogenicity, and reproductive and developmental effects in adults support the safety of benzyl alcohol. The panel's clinical recommendation was that benzyl alcohol could be used safely in cosmetics for adults at concentrations up to 5% (up to 10% for hair dyes). However, owing to a lack of data, the panel was unable to reach an agreement on the safety of inhaling benzyl alcohol and its derivatives.¹

Epidemiology

The prevalence of allergy to benzyl alcohol is unknown. This antigen is neither on the North American Contact

Table 1. Patch-Test Results

<i>Products Causing Positive Reactions*</i>	<i>Products Causing Pertinent Doubtful Reactions</i>
Benzyl alcohol	Walsporin ointment (Walgreen Co., Deerfield, IL)
Bactroban Cream [†] (GlaxoSmithKline)	Paraben mix
Moisturel lotion [†] (Westwood-Squibb, Montreal, QC)	
Aveeno Moisturizing Lotion [†]	
Hydrocortisone cream 2.5% [†]	
Elidel cream [†] (Novartis)	
Hydrocortisone cream 1% [†]	
Clotrimazole cream [†]	
Amcinonide [‡]	
Budesonide [‡]	
Nutraderm lotion (Healthpoint Ltd., Fort Worth, TX) [§]	
Balsam of Peru	
Methyldibromoglutaronitrile/ phenoxyethanol	
Bacitracin	
Amerchol L-101	
Lanolin [#]	
Neomycin [#]	

*+, ++, or +++.

[†]Contained benzyl alcohol.

[‡]Class B corticosteroid.

[§]Contained parabens and fragrance.

^{||} Cross-reacts with benzyl alcohol.

[#]Previous patch-test reactions.

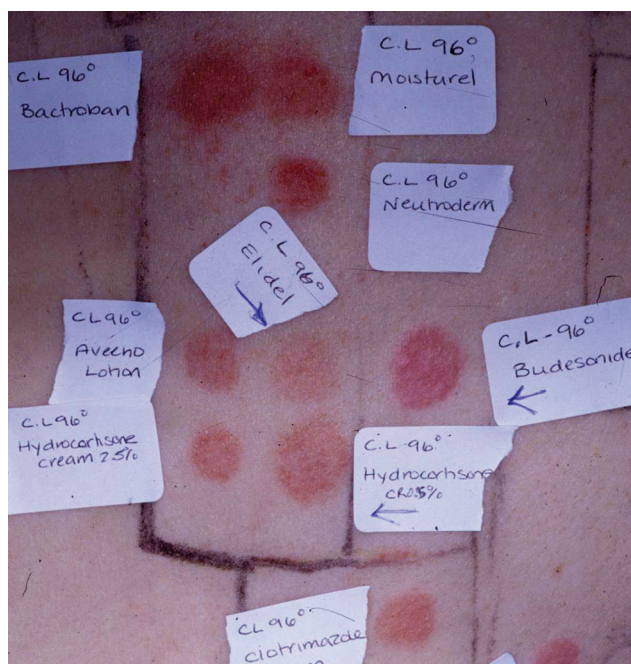


Figure 2. Key patch-test reactions.

Dermatitis Group standard series nor on the European screening series, so prevalence information from large cross-sectional databases is not available. A Belgian study of common antimicrobial component allergens ranked benzyl alcohol as the twelfth most frequent allergen in antimicrobials; 25 (0.3%) of 8,521 patients had a positive patch-test reaction to benzyl alcohol.¹⁰ In spite of a low prevalence, allergic contact dermatitis from benzyl alcohol is well documented.

Type IV Delayed-Type Hypersensitivity Reactions

There have been numerous case reports of delayed-type allergic contact dermatitis following the use of various topical medicaments that contain benzyl alcohol as a preservative. These cases have mostly presented as a chronic dermatitis that worsened into an acute localized eczema after the addition of a benzyl alcohol-containing formulation. Recently, Sestini and colleagues described a woman who developed allergic contact dermatitis from numerous topical medications used for chronic vulvovaginitis. Positive patch-test reactions were found to Bactroban Cream (GlaxoSmithKline, Research Triangle, NC) and Gyno Canesten cream (Bayer AG, West Haven, CT), both of which contain benzyl alcohol, as well as to 5% benzyl alcohol in petrolatum.¹¹ Shaw reported a man who developed severe swelling of his ear 4 hours after using an earmold impression material for a hearing aid. The impression material

contained benzyl alcohol, and subsequent patch testing with benzyl alcohol 0.9% in saline yielded positive results. The result of prick testing with benzyl alcohol 1% was negative.³

Antimycotic agents have been well documented as culprits of benzyl alcohol allergy. One report from Japan described a woman treated with an antifungal cream for tinea pedis that did not improve until she was treated with a steroid-only preparation. Closed patch tests resulted in strong reactions to benzyl alcohol 5%, which was a component of the antifungal cream.¹² Wurbach and colleagues reported on a patient with recurrent tinea cruris and tinea corporis that developed into a widespread eczematous rash (including involvement of the eyelids) after the application of several topical antifungal creams. Patch testing in this patient confirmed contact allergy to benzyl alcohol, which was verified as an ingredient in two of the antifungal preparations.¹³ Podda and colleagues described another patient with tinea pedis who developed pruritic

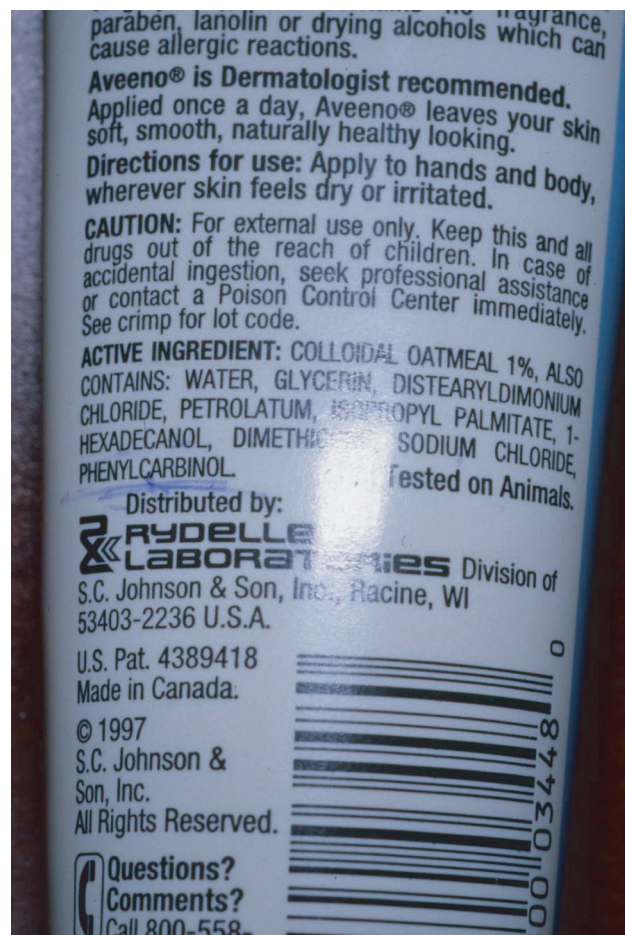


Figure 3. Label of Aveeno Moisturizing Lotion.

papules and redness after starting to use a new antifungal cream. Patch tests and use tests revealed positive reactions to both the antifungal cream (which contained benzyl alcohol) and benzyl alcohol 5% in petrolatum.¹⁴ Li and Gow described a woman with vulval lichen sclerosus et atrophicus and chronic dermatitis who was hospitalized owing to increasing discomfort following the use of antifungal and corticosteroid creams. Patch-test results were positive for benzyl alcohol as well as for a corticosteroid cream that contained benzyl alcohol as a preservative.¹⁵ Corazza and colleagues reported on a man with a history of atopic dermatitis who developed an acute eczematous flare that was unresponsive to topical corticosteroids, antibiotics, and antipruritics. Patch testing revealed positive reactions to a commercial lotion that contained benzyl alcohol, to purified benzyl alcohol, and to essence bouquet, which the authors confirmed (via gas chromatography) to contain a high concentration of benzyl alcohol.⁶ Aguirre and colleagues reported on two patients who developed dermatitis following the use of a topical preparation used widely in Spain for treatment of musculoskeletal injuries. Both patients had very strong reactions to the spray (as is) and to benzyl alcohol 1% in petrolatum, which was a component of the spray propellant.¹⁶ In another case, a woman developed a localized reaction after being treated with a sclerosing agent for varicose veins. Subsequent patch testing showed a very strong positive reaction to benzyl alcohol 5% in petrolatum, which was confirmed as an ingredient of the sclerosing agent.¹⁷

Vascular insufficiency, in the form of venous stasis and stasis dermatitis, may predispose individuals to develop allergic contact dermatitis from topical products, including those containing benzyl alcohol. Lazzarini described a woman with stasis dermatitis who developed worsening edema and pruritus of her legs 72 hours after treatment with a corticosteroid cream (amcinonide 0.1%) and wet dressings. The result of patch testing with purified corticosteroids was negative, but positive reactions were noted to benzyl alcohol 5% in petrolatum and isopropyl palmitate 2.0% in petrolatum (both components of the commercial amcinonide 0.1% cream) as well as to the commercial amcinonide 0.1% cream itself.¹⁸

There has been one case report of a man with a history of lichen nitidus who developed scalp and hair depigmentation following the use of a hair rinse that contained benzyl alcohol as a solubilizing agent. Although he had a positive patch-test reaction to benzyl alcohol 5%, no depigmentation was observed at the test site for 2 years. Postinflammatory depigmentation and vitiligo could not be excluded.¹⁹

Cases of benzyl alcohol allergy resulting from occupational exposures have also been described. Most recently, there have been two reports of occupational airborne exposures to a benzyl alcohol-containing epoxy resin that resulted in contact dermatitis. In both cases, remission of symptoms occurred when these patients stopped working for an extended period. Patch testing revealed very strong reactions to a two-part glue containing benzyl alcohol and epoxy resin, as well as to epoxy resin and benzyl alcohol tested separately.²⁰ In a different case, a metal grinder developed a pruritic dermatitis after the use of a new cutting oil that contained an almond-scented reodorant called vanillal S 10026, which consisted of 80% benzyl alcohol and 20% vanillal. Patch testing yielded positive reactions to benzyl alcohol 1% in petrolatum and to vanillal S 10026.²

Type I Immediate Reactions

In 1985, Emmons and Marks found contact urticaria on open testing with benzyl alcohol (5% in petrolatum) in 7 of 15 patients who had eczematous dermatitis, 10 of 16 patients who had a history of cosmetic sensitivity, and 15 of 19 controls. Positive reactions included wheals, erythema, and pruritus. None of these patients had a delayed-type positive reaction on patch testing. The authors suggested that benzyl alcohol may produce nonimmunologic contact urticaria.²¹

In a report of two patients who had positive patch-test reactions to benzyl alcohol in perfume and aftershave lotion, Fisher was unable to demonstrate positive reactions to 1% benzyl alcohol in saline by scratch or by intradermal or subcutaneous injections.²² Edwards, however, reported a woman who was found to have a coexistent contact urticarial response and a type IV delayed vesicular reaction to the benzyl alcohol 1% in her sunscreen. She also had an immediate response to the sunscreen product itself.²³ Hausen reported another patient who developed angioedema after using a lip balm that contained benzyl alcohol. Subsequent patch testing showed a strong reaction to benzyl alcohol, but immediate testing was not performed.²⁴

Immediate reactions have been attributed to the presence of benzyl alcohol used as a preservative in injectable medications. Hausen reported a patient who had episodes of urticaria that developed after the patient consumed one to two packets of sweets containing benzyl alcohol and after injection of a medication containing benzyl alcohol. Results of both patch and immediate tests were positive to benzyl alcohol.²⁴ In a separate report, Guin and Goodman described a woman with unresponsive stasis dermatitis who

had been using bacteriostatic saline soaks that contained benzyl alcohol as a preservative. A 10 cm urticarial wheal developed within 1 hour at the benzyl alcohol patch-test site but faded by day 6. Prick tests were not performed.²⁵

Although rare, generalized reactions after injections of vitamin B₁₂, corticosteroids, and gallium 67 (all of which contained benzyl alcohol as a preservative agent) have also been reported. Grant and colleagues described a patient who experienced a sudden onset of nausea, fatigue, and diffuse angioedema shortly after intramuscular injection of vitamin B₁₂. Results of skin-prick tests for vitamin B₁₂ and diluents were negative. However, a wheal and flare reaction was noted 15 minutes after intradermal injections of vitamin B₁₂ with 0.9% benzyl alcohol as well as to normal saline containing benzyl alcohol. No reactions were noted to injections of vitamin B₁₂ that either contained parabens as a preservative or contained no preservative.²⁶ In another report, a patient with a history of atopy developed generalized urticaria soon after two corticosteroid injections for tendinitis. Both preparations were tested on the patient. Although results of prick and intradermal tests of diluted (1:10) aqueous betamethasone dipropionate/betamethasone disodium phosphate and methylprednisolone sodium succinate were negative, tests with undiluted forms of these corticosteroids produced strong reactions. Benzyl alcohol was a preservative in both preparations. Although the result of prick testing for benzyl alcohol 1% aqueous was negative, intradermal testing of benzyl alcohol 1% aqueous yielded a strong reaction.²⁷ In another report, a generalized reaction was noted in a welder who had received a gallium 67 injection, which contained benzyl alcohol, for silicosis testing. That evening, the patient developed severe pruritus and arthralgias, followed by a rash the next day. The result of patch testing with benzyl alcohol 5% was negative whereas the results of prick tests were positive.²⁸

Cross-Reactions

Benzyl alcohol frequently cross-reacts with balsam of Peru, parabens (including benzylparabens), and benzyl cinnamate.^{2,12,13,22,24} Hausen reported three patients who were found to be allergic to balsam of Peru and benzyl alcohol by patch testing. Benzyl alcohol was found to be one of the 20 constituents of balsam of Peru with which these individuals were tested. It was discovered that these patients were prone to eating large amounts of sweets, which seemed to correlate with dermatitis flares. It is possible that degradation products such as cinnamates and benzoates could also explain these reactions.²⁴

Summary

We describe a woman with chronic dermatitis who had positive patch-test reactions to numerous products containing benzyl alcohol. Of note, she was found to have a reaction to Aveeno Moisturizing Lotion, the label of which listed a synonym of benzyl alcohol. Our patient was also found to have an allergy to balsam of Peru, a known cross-reacting substance that contains benzyl alcohol. This case highlights the importance of patch testing with personal products and the investigation of antigen synonyms.

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