

Systemic Contact Dermatitis from Propylene Glycol

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A 39-year-old woman presented with pruritic eczematous plaques on her face, neck, and right hand that she had had for approximately 2 months, following an abrasive injury caused by the deployment of an airbag in a car accident. Results of patch testing were positive for several medicaments and propylene glycol (PG). The patient's condition cleared after discontinuation of all topical products containing PG and her other identified allergens, but she noted flares of her contact dermatitis following the ingestion of foods containing PG. A subset of patients will have a recurrence of dermatitis after the ingestion of a contact sensitizer. Recurrent dermatitis despite complete avoidance of identified topical allergens and a history of recurrent eczema at the patch-test site are clues to the diagnosis of systemic contact dermatitis. Even weak patch reactions to PG, if they persist to a day-7 reading, should be considered potentially relevant. Avoidance of dietary PG includes attention to labels on food and medication and the avoidance of certain foods in restaurants when ingredients cannot be verified.

SYSTEMIC CONTACT DERMATITIS (SCD) after the ingestion, injection, or inhalation of a substance can occur after cutaneous sensitization. The reaction can take various forms, including (1) focal flares at sites of previous contact dermatitis, (2) baboon syndrome, (3) pompholyx, and (4) erythema multiforme, urticaria, or vasculitis.^{1,2} Symptoms of headache, fatigue, arthralgias, and diarrhea and/or vomiting may accompany the skin signs.¹ Symptom onset is typically less than a day after systemic exposure to the allergen.¹

In addition to propylene glycol, the allergens most commonly associated with SCD are fragrances and flavorings, foods and plants, medicaments, and (less commonly) preservatives. In regard to fragrances and flavorings, Salam and Fowler found that 47% of patients with positive patch-test reactions to balsam of Peru and/or fragrance mix experienced "complete or significant improvement" in their dermatitis following topical avoidance and adherence to a diet that avoided balsam of Peru whereas only 20% cleared with topical avoidance but no dietary modification.³ Besides flavoring agents, other comestibles that can cause SCD include garlic, various spices, and cashews.² Oral or parenteral medication-induced SCD can be particularly problematic for patients owing to the difficulty of finding a substitute

medication that does not cross-react. Antimicrobials are some of the more frequently reported offending agents.⁴⁻⁶ Besides propylene glycol, another substance with preservative properties that has been documented to cause SCD is ethylenediamine (EDA). Some patients with known sensitivity to EDA must avoid any medications that contain this compound. In this case, such medications include aminophylline (a mixture of theophylline and EDA) and hydroxyzine-family antihistamines (whose parent compound is EDA).⁷

Patch testing is widely accepted as the best way to diagnose contact dermatitis, and it can also be used in cases of suspected SCD. SCD may be diagnosed if a patient is found to flare at his or her patch-test site upon subsequent ingestion of the allergen. This is a type of recall phenomenon that occurred in the case described below.

Case Report

A 39-year-old white office worker with a history of latex allergy and hand dermatitis presented with pruritic, red, thin, scaly, and crusted plaques that she had had on her face and neck for approximately 2 months and on her right hand for several weeks. Two months prior to presentation, the patient had been in a car accident in which the air bag had deployed. Immediately after the accident, the patient noted a redness of her face, which she attributed to abrasions from the air bag. The patient self-treated with over-the-counter hydrocortisone, triple antibiotic ointment, and pimecrolimus cream. These offered no relief of her symptoms.

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After 1 week, the patient discontinued these treatments and sought consultation for her dermatitis. The initial history was significant for use of shampoo, conditioner, and facial scrub that contained propylene glycol and for use of mascara that contained Abitol (Chemotechnique Diagnostics, Malmo, Sweden).

On examination, the patient appeared well and afebrile. She had erythematous scaly plaques in her perioral area and on her upper eyelids bilaterally. She also had a sharply demarcated, round, and erythematous scaly plaque measuring approximately 4 cm on her left neck (Fig 1) and a diffuse eczematous plaque measuring approximately 2 cm on her right dorsal hand at the base of her third and fourth fingers.

Patch testing with a standard screening tray (extended from the standard North American Screening Series [Chemotechnique Diagnostics, Malmö, Sweden]) was performed; results are shown in Table 1. Tacrolimus 0.1% ointment was prescribed for the rash, and she was given information on how to avoid her allergens.

The dermatitis resolved but then recurred in the same areas shown in Figure 1 and at her propylene glycol patch-test site. The patient was instructed to avoid dietary propylene glycol. At follow-up appointments, she stated that she had experienced flares after consuming, (among other things) sour cream at a Mexican restaurant, macaroni and cheese at a delicatessen, packaged french-fried onion rings, vanilla ice cream, and cake. Onset of the rash was approximately 24 hours after she ate the



Figure 1. Lateral neck lesion. The patient presented with a sharply demarcated, round, and erythematous scaly plaque measuring approximately 4 cm on the left side of the neck. This unilateral lesion corresponded to the application site of a pimecrolimus cream containing propylene glycol after abrasion by an inflated airbag.

Table 1. Results of Patch Testing*

Tested Agent	Reading	
	Day 4	Day 7
Propylene glycol	Questionable	Questionable
Neomycin	—	Questionable
Bacitracin	+	+
Tixocortol pivalate	+++	+
Thimerosal	Questionable	Questionable
Abitol	Questionable	+

*Patch-test responses are graded according to the following criteria: questionable reactions exhibit homogeneous erythema without infiltration, + reactions exhibit infiltration with or without a few discrete papules, ++ reactions exhibit many discrete papules, +++ reactions exhibit coalescing vesicles or bullae, and irritant reactions exhibit a decrescendo pattern (weaker at late reading than at early reading) and a scorched morphology. Twenty percent of day-7 (late) patch-test reactions in our clinic are graded “questionable,” and these are often relevant; 1% of final readings are considered conclusively irritant in our clinic (Euxyl K400, cocamidopropyl betaine, and potassium dichromate account for the majority of this 1%).

offending product and was associated with malaise and nausea. She has subsequently remained clear for 3 or more months at a time but has developed several flares during a 1-year interval. The patient is able to trace each of the flares to inadvertent contact with or ingestion of propylene glycol.

Discussion

Propylene glycol often produces weak patch-test reactions; therefore, it is important that the clinician consider pretest suspicion of medicament allergy when determining relevance. Propylene glycol is a clear odorless liquid used as a vehicle in medicaments and cosmetic products for its moisturizing and solvent qualities. It also enhances penetration through the skin and is used in many topical medications, including corticosteroids. Propylene glycol may be used in cosmetic products at concentrations up to 50%.⁸

One case in which suspicion should be high is that of a dermatitis that worsens after use of a topical corticosteroid, since 58.5% of these products contain propylene glycol.⁹ Propylene glycol allergy is as common as corticosteroid allergy in our contact dermatitis clinic, where 2% of patients are patch test positive to budesonide and 2% to tixocortol pivalate.

Our patient found that personal care products containing dipropylene glycol also caused contact dermatitis in her case. Dipropylene glycol is commonly used in fragrances. The incidence of cross-reaction to a number

of other propylene glycol derivatives (including propylene glycol polymerized with polyethylene glycol or with dimethicone) is unknown.

Patch-test reactions to propylene glycol are often weak and difficult to distinguish from irritant reactions. Of the last 652 patients seen in our patch-test clinic, 7 (1%) had a day-7 propylene glycol reaction of + or greater, 7 (1%) had a day-7 reaction graded “questionable,” 7 (1%) had a day-3 or day-4 reaction of less than + that was lost at day 7, and 15 (2%) had a day-3 or day-4 reaction graded “questionable” and lost (negative) at day 7. In our clinic, irritant antigens commonly cause “questionable” reactions at the early reading that are “lost” (negative) at the final reading. For example, the antigens with the most “questionable” lost reactions are Euxyl K400 (Chemotechnique Diagnostics, Malmo, Sweden) and potassium dichromate; both are marginal irritants and often elicit patch-test reactions with irritant morphology. However, antigens with characteristically weak day-7 reactions are not necessarily irritant. Of the 70 items on our extended standard screening series, the following elicit “questionable” day-7 reactions more commonly than they elicit “+ or greater” reactions: ethyleneurea melamine formaldehyde resin, imidazolidinylurea, propylene glycol, carba mix, cocamidopropyl betaine, and dimethylol dimethyl (DMDM) hydantoin. Of these, only cocamidopropyl betaine and propylene glycol are generally considered marginal irritants, and in our experience, none of these commonly elicits a reaction of irritant morphology. We consider the “questionable” lost reactions to represent probable irritant reactions and a “+ or greater” reaction at day 3 or 4 and any positive reaction at day 7 to represent true allergy; this gives a total of 3% of subjects allergic to propylene glycol, as compared with the 4.2% found by the North American Contact Dermatitis Research Group for the 2001–2002 study period.¹⁰ However, we have found some patients with a questionable day-3 or day-4 reaction and a negative reaction at day 7 who did in fact have allergy to propylene glycol, and we suggest reconsideration of these weak “lost” reactions in patients whose conditions do not clear with the avoidance of other identified allergens.

Propylene glycol is used in foods for its humectant, preservative, and softening properties and as a solvent for flavorings and colors. It is also used in food processing to cool and freeze foods, to make inks used to print food packaging, and to clean equipment.¹¹ The chemical is not approved for use in the European Union as a “general-purpose food grade product or direct food additive”; however, it may be used as a “carrier and carrier solvent in

colors, emulsifiers, antioxidants and enzymes at a maximum content of 1 gram per kilogram of final foodstuff.”¹² These restrictions are based on a lack of data on the effects of dietary propylene glycol in humans and also on preliminary studies showing that the chemical may cause anemia in cats and (to a lesser extent) dogs. Propylene glycol is in fact not approved as an ingredient for cat food in the United States because it shortens red blood survival time.¹³

Some of the more common foods currently containing propylene glycol are salad dressings, sauces, sour cream, store-bought cakes, and cake mixes (Table 2). Some medications such as ibuprofen also contain propylene glycol.

There are several reported cases of SCD in response to propylene glycol. One involved a woman who experienced pruritic vulvitis upon receiving a solution of intravenous valium that was 40% propylene glycol after having reacted years earlier to K-Y Lubricating Jelly (Johnson and Johnson, Fort Washington, PA) (which no longer contains propylene glycol) that was used on her obstetrician’s glove.¹⁴ Several other cases involved patients who had flares at sites of previous contact dermatitis after ingesting foods containing propylene glycol.^{15,16} One study, conducted by Hannuksela and Forstrom, found that 8 of 25 patients with positive patch-test reactions to propylene glycol experienced “an extensive rash” following oral ingestion of propylene glycol capsules. These 8 patients consisted of all 4 of the patients with a positive patch-test reaction to a 2% propylene glycol solution plus 4 of 21

Table 2. Products That May Contain Propylene Glycol

<i>Type of Product</i>	<i>Examples</i>
Sauces	Steak sauce, horseradish, tartar sauce
Snack foods	Potato snacks, fried onion rings
Desserts	Cinnamon buns, donuts, cupcakes, ice cream
Dessert kits	Cake mix, brownie mix, cream pie mix
Salad dressings	Various flavors; sour creams
Potato salads	
Medications	Ibuprofen, acetaminophen, glucosamine/chondroitin sulfate, coated aspirin, many prescription medications (including clarithromycin, cetirizine solution, fosinopril, and dipyridamole)

patients who had positive patch-test reactions to 5% or 10% propylene glycol solutions. The patients were given 5 mL of propylene glycol the first day, followed by 15 mL the second day if they reported no symptoms after their first dose. Twelve patients with “various dermatoses” that did not include contact dermatitis reaction to propylene glycol were used as control subjects, and none of them showed any rash after ingesting propylene glycol.¹⁷

Conclusion

Propylene glycol can cause systemic contact dermatitis, and even weak late (day-7) reactions to propylene glycol may indicate relevant allergy rather than an irritant patch-test result. Recalcitrant dermatitis in a propylene glycol-allergic patient who is compliant with topical avoidance may indicate the need for a trial of a propylene glycol-restricted diet.

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