

Propylene Glycol

Sharon E. Jacob, MD,* Andrew Scheman, MD,† and Maria A. McGowan, MD*

Propylene glycol (PG), an emollient and emulsifier found in cosmetics, medications, and food, has been granted the dubious honor of being named the American Contact Dermatitis Society's Allergen of the Year for 2018. Allergic and irritant contact dermatitis and systemic cutaneous reactions to PG, which has become an increasingly common ingredient, have been documented. Propylene glycol is as contentious as it is ubiquitous because it acts as both a weak sensitizer and an irritant, confounding the results of positive patch tests. This report serves to increase awareness about PG sensitization and appropriate testing and evaluation of PG patch tests.

Propylene glycol (PG) is a common ingredient in many cosmetics, topical skin preparations, medications, and foods. Propylene glycol's potential as a contact allergen has long been recognized, and the first study of patch tests to PG was performed in the 1950s.¹ However, the significance of PG as a contact allergen has been ambiguous. Patch tests to PG are often weak and can be difficult to differentiate from irritant reactions. However, PG has also been demonstrated to cause systemic contact dermatitis. With increasing prevalence of PG in cosmetics and medications, especially topical corticosteroids, it is of special importance that dermatologists should be aware of how PG sensitivity manifests and how to identify unexpected sources.

EPIDEMIOLOGY AND CLINICAL PICTURE

Estimates on the prevalence of PG allergy range from 0.8% (10% PG in aqueous solution) to 3.5% (30% PG in aqueous solution).²⁻⁴ The North American Contact Dermatitis Group (NACDG) data from 1996 to 2006 showed that the most common site for PG contact dermatitis was the face (25.9%), followed by a generalized or scattered pattern (23.7%).² Personal care products, such as creams, lotions, and cosmetics were associated with reactions in

12.8% of these patients and were the most common source of PG, accounting for 53.8% of identified sources of PG.² This was followed by topical corticosteroids at 18.3%.² Few reactions (4.2%) were deemed to be occupational, relegating PG as an infrequent cause of occupational dermatitis.²

Over time, there has been a reported increase in the use of PG in personal care products in the United States. In a 1994 safety assessment, the Cosmetic Ingredient Review noted use of PG in 5676 products listed in the Voluntary Cosmetic Registry; in the Cosmetic Ingredient Review 2012 update, this Voluntary Cosmetic Registry reported 9094 products containing PG.⁵ These data are similar to the data from December 15, 2016, in the American Contact Dermatitis Society (ACDS) Contact Allergy Management Program, which showed PG present in 1301 (37.8%) of 4674 products (A. Scheman, personal communication on C.A.M.P. data, December 2016). Propylene glycol is found in most topical gel preparations.⁶ Historically, it was included in the NACDG patch test set in 1992 at 10% in aqueous solution. However, this was increased to 30% in aqueous solution in 1996.

FOODSTUFFS AND MEDICATIONS

Propylene glycol is also found in many foods. It can be found in many packaged foods (prepackaged coffee, creamers, drink mixes, breakfast foods, desserts, snacks, prepared meals, mixes, seafood/meat breading/marinades/glazes [including premarinated ham/turkey], dried soup/bouillon, most fast food).⁶ It can also be found in some bread (bread, bagels, rolls, breadsticks, bread mixes), canned beans, bacon, dairy products (cream cheese, yogurt, sour cream, dips/spreads, cheese, whipped cream), many condiments, and occasional frozen vegetables. Propylene glycol can be found in many artificial flavor extracts and artificial food coloring products.⁶ Regarding medications, PG is often found in coated pills, gelcaps, liquids, chewables, and lozenges.⁷ Noncoated pills are most likely to be free of PG.^{6,7}

CO-REACTIONS

The NACDG data showed Balsam of Peru (24.8%), fragrance mix (17.0%), and formaldehyde (16.9%) to be the most common

From the *Department of Dermatology, Loma Linda University, CA and †Northwestern University, Chicago, IL.

Address reprint requests to Sharon E. Jacob, MD, Department of Dermatology, Loma Linda University, Faculty Medical Offices, 11370 Anderson St, Suite 2600, Loma Linda, CA 92354. E-mail: sjacob@contactderm.net.

S.E.J. is founder and CEO of Dermatitis Academy, an open-access contact dermatitis learning forum, E-source; served as coordinating principal investigator on the safety and efficacy of T.R.U.E. Test (Smart Practice, Phoenix, AZ) panels 1.1, 2.1, and 3.1 in children and adolescents, Pediatric Research Equity Act (PREA-1) trial; and has served as a consultant for Johnson & Johnson. M.A.M. has no relevant disclosures. A.S. is director of the American Contact Dermatitis Society Contact Allergy Management Program database.

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concomitant positive patch tests (PPTs) to PG.² Propylene glycol also co-reacted with substances associated with topical medications, such as bacitracin (14.1%), neomycin sulfate (13.6%), and tixocortol (10%).² It is important to note that these co-reactants are not cross-reactions and are likely due to co-sensitization from cosmetics and topical medications.

CONTROVERSY

Propylene glycol is one of the more controversial substances on standard patch test trays, with some literature suggesting that weak PG reactions are almost entirely irritant and others claiming relatively high significance of all PPTs to PG.^{2,3} This controversy lies in the fact that patch testing for PG is often confounded by its potential for irritation and frequently weak hypersensitivity reactions.⁸ This has led to various concentrations of PG for patch testing. The NACDG initially tested PG at 10% in aqueous solution. In 1996, this was changed to 30% in aqueous solution.⁵ Starting in January 2013, the NACDG added 100% PG to their standard screening tray. Based on the subsequent results and expert opinion, the NACDG recommended that 30% PG in aqueous solution be dropped as a screening agent since 100% PG had a relatively low rate of irritancy but significantly improved efficacy of discerning PPT.⁹ From 1992 to 2002, the Information Network of Departments of Dermatology used 20% in aqueous solution.³ It has been suggested that stronger concentrations be used in patients who test negative but have high suspicion of PG allergy.¹⁰ However, regardless of whether reactions are irritant or allergic, almost all reactions are clinically relevant to affected patients. That is, because concentrations of PG in topical products are often less than 30%, a patch test reaction to 30% PG is likely to be clinically relevant whether the patch test reaction is caused by allergy or irritancy.

PATCH TESTING

Propylene glycol is included in several patch test series, including the North American, ACDS Recommended Allergen Series, Cosmetic series, and International Comprehensive Baseline Series (a series based on the NACDG data).^{11,12} In the United States, it is typically applied as 30% PG in aqueous solution, although in the Cosmetic series (Chemotechnique Diagnostics, Vellinge, Sweden), it is applied as 5% PG in petroleum.¹¹ Interestingly, it is not included in the cutaneous adverse drug reaction series or corticosteroid series,¹¹ despite extensive documentation of its relevance to reactions associated with systemic drugs and topical corticosteroids. In addition, although it is included in the ACDS core series based on the data from the NACDG, it is not a part of the International Standard Series, based on studies by the International Contact Dermatitis Research Group, T.R.U.E. Test, or European Standard Series.^{11–14}

Because PG can act as an irritant, weak reactions present at 48 hours, which are gone or almost gone at 96 hours (decrecendo reactions), are often false-positive irritant reactions. On the other

hand, a lack of reaction or weak reaction at 48 hours followed by a stronger reaction at 96 hours (crescendo reaction) is more likely to indicate contact allergy. However, this may also be misleading because some substances, including PG, may present as “late irritants.”¹⁵ Well-demarcated margins of erythematous reactions or reactions that occur in less than 24 hours are suggestive of irritant reactions.¹⁶ Weak reactions may be relevant, especially if they are late (ie, day 7).^{8,16} It has also been suggested that “weak lost” reactions may be relevant, and PG should be reconsidered as a contact allergen in patients with positive reactions on days 3 or 4 but negative reactions on day 7.¹⁷

CONCLUSIONS AND RECOMMENDATIONS

Propylene glycol has become ubiquitous in topical and systemic products. While allergic contact dermatitis to PG may have a low prevalence, many patients manifest some form of sensitivity. Despite the relative controversy of PG as an irritant versus an allergic reactant, any reaction is relevant to the patients whose skin is compromised by PG. Patch testing is the criterion standard to evaluate for allergic contact dermatitis, but evaluation of patch tests may be challenging because of the frequently weak nature of PPT to PG. It is therefore important that clinicians should be familiar with how PPT to PG presents.

REFERENCES

1. Warshaw TG, Herrmann F. Studies of skin reaction to propylene glycol. *J Invest Dermatol* 1952;19(6):423–430.
2. Warshaw EM, Botto NC, Maibach HI, et al. Positive patch-test reactions to propylene glycol: a retrospective cross-sectional analysis from the North American Contact Dermatitis Group, 1996 to 2006. *Dermatitis* 2009;20(1):14–20.
3. Lessmann H, Schnuch A, Geier J, et al. Skin-sensitizing and irritant properties of propylene glycol. *Contact Dermatitis* 2005;53(5):247–259.
4. Wetter DA, Yiannias JA, Prakash AV, et al. Results of patch testing to personal care product allergens in a standard series and a supplemental cosmetic series: an analysis of 945 patients from the Mayo Clinic Contact Dermatitis Group, 2000–2007. *J Am Acad Dermatol* 2010;63(5):789–798.
5. Fiume MM, Bergfeld WF, Belsito DV, et al. Safety assessment of propylene glycol, tripropylene glycol, and PPGs as used in cosmetics. *Int J Toxicol* 2012;31(Suppl 5):245S–260S.
6. FoodFacts.com. The Rak Foundation for Nutritional Awareness. Available at: <http://www.foodfacts.com/>. Accessed February 3, 2017.
7. Scheman A, Cha C, Jacob SE, et al. Food avoidance diets for systemic, lip, and oral contact allergy: an american contact alternatives group article. *Dermatitis* 2012;23(6):248–257.
8. Lowther A, McCormick T, Nedorost S. Systemic contact dermatitis from propylene glycol. *Dermatitis* 2008;19(2):105–108.
9. DeKoven JG, Warshaw EM, Belsito DV, et al. North American Contact Dermatitis Group patch test results 2013–2014. *Dermatitis* 2017;28(1):33–46.
10. Marks JG, Elsner P, DeLeo VA. *Contact and Occupational Dermatology*. 3rd ed. St Louis, MO: Mosby; 2002.

11. Chemotechnique Diagnostics. International Standard Series. Available at: <http://www.chemotechnique.se/products/series/international-standard-series/>. Accessed January 26, 2017.
12. Oakley A. Baseline series of patch test allergens. 2008. Available at: <https://www.dermnetnz.org/topics/baseline-series-of-patch-test-allergens>. Accessed January 26, 2017.
13. Chemotechnique Diagnostics. Bakery Series. Available at: <http://www.chemotechnique.se/products/series/bakery-series/>. Accessed January 26, 2017.
14. Schalock PC, Dunnick CA, Nedorost S, et al. American Contact Dermatitis Society Core Allergen Series: 2017 update. *Dermatitis* 2017;28(2):141–143.
15. Frosch PJ, Menné T, Lepoittevin JP. *Contact Dermatitis*. 4th ed. Berlin, Germany: Springer; 2006:1136.
16. Carlson S, Gipson K, Nedorost S. Relevance of doubtful (“equivocal”) late patch-test readings. *Dermatitis* 2010;21(2):102–108.
17. Pootongkam S, Nedorost ST. Focus on propylene glycol. *The Dermatologist* 2013;21(8). Available at: <http://www.the-dermatologist.com/content/focus-propylene-glycol>.