

Toluene-2,5-Diamine Sulfate: The 2025 American Contact Dermatitis Society Allergen of the Year

Kayla Tran, BA; Brandon L. Adler, MD; JiaDe Yu, MD, MS

PRACTICE POINTS

- Toluene-2,5-diamine sulfate (PTDS) is a widely used alternative to para-phenylenediamine (PPD) that is itself a potent and likely underreported allergen.
- As high cross-reactivity has been reported, consider testing for both PTDS and PPD and possible delayed patch test reading.
- Allergic contact dermatitis to PTDS may manifest with erythema, edema, and/or pruritus, similar to PPD.
- Prevention entails avoidance of PTDS/PPD if sensitized, use of proper hand protection, and recommendation of alternative products.

The American Contact Dermatitis Society named toluene-2,5-diamine sulfate (PTDS) the 2025 Allergen of the Year. Toluene-2,5-diamine sulfate is widely used as an alternative to para-phenylenediamine (PPD) in hair dyes but is itself a potent and likely underreported contact allergen. Cross-reactivity with PPD is common. Allergic contact dermatitis to PTDS manifests similarly to PPD reactions and disproportionately affects hairdressers and individuals who frequently use hair dye. Clinical recommendations include patch testing for PTDS and PPD (with consideration of delayed readings), occupational prevention, and use of safer dye alternatives where appropriate.

to para-phenylenediamine (PPD) in oxidative and permanent/semipermanent hair dyes, PTDS has emerged as a potent contact allergen with substantial cross-reactivity to PPD. In this article, we discuss PTDS as both a PPD alternative and a contact allergen as well as the clinical features of allergic contact dermatitis (ACD) to PTDS and practical recommendations for management in at-risk populations.

Background

Toluene-2,5-diamine sulfate is a compound formed by combining 2,5-diaminotoluene (PTD) with sulfuric acid, making it more water soluble and potentially less irritating than PTD alone.² In this article, the terms *PTDS* and *PTD* will be used interchangeably due to their structural similarity.

Toluene-2,5-diamine sulfate commonly is used in oxidative and permanent/semipermanent hair dyes as an alternative to PPD, the most common hair dye contact allergen.³ Toluene-2,5-diamine sulfate also is a component used in color photography development and in dyes used for textiles, furs, leathers, and biologic stains.⁴ The prevalence of PTDS contact allergy likely is underreported due to its absence in routine patch test series such as the Thin-Layer Rapid Use Epicutaneous (T.R.U.E.) test (Smart Practice) and the American Contact Dermatitis Society Core 90 Series.

Cross-Reactivity Between PTDS and PPD

There is substantial cross-reactivity between PTDS and PPD, necessitating careful avoidance and alternative dye

The American Contact Dermatitis Society selected toluene-2,5-diamine sulfate (PTDS) as the 2025 Allergen of the Year.¹ Widely used as an alternative

Kayla Tran is from the School of Medicine, Virginia Commonwealth University, Richmond. Dr. Adler is from the Keck School of Medicine, University of Southern California, Los Angeles. Dr. Yu is from the Department of Dermatology, Virginia Commonwealth University Health System, Richmond. Kayla Tran has no relevant financial disclosures to report. Dr. Adler has received research grants from AbbVie and Dermavant and income from UpToDate. Dr. Yu has served as a consultant, advisory board member, and/or investigator for AbbVie, Arcutis, Astria, Dermavant, Eli Lilly and Company, iRhythm, Johnson & Johnson, Kiehl's/L'Oréal, LEO, the National Eczema Association, O'Glancee, Pfizer, Sanofi, SmartPractice, and Sol-Gel and has received honorarium from UpToDate.

Correspondence: JiaDe Yu, MD, MS, Department of Dermatology, Virginia Commonwealth University Health System, 9109 Stony Point Dr, PO Box 980538, Richmond, VA 23235 (jia.de.yu@vcuhealth.org).

Cutis. November 2025;116(5):167-169. doi:10.12788/cutis.1288

selection. The rate of cross-reactivity between these compounds is high, with some estimated to be more than 80% among patch tested individuals.⁵⁻⁹ In some cases, patients with a contact allergy to PPD are able to tolerate dyes containing PTDS. Studies conducted in Canada and Europe showed that 31.3% to 76.3% of patients with a contact allergy to PPD also had an allergy to PTDS or PTD.^{7,8,10} Stronger reactions to PPD also seem to be associated with an increased risk for cross-reaction.¹¹

Clinical Manifestation of ACD to PTDS

In the literature, case reports of ACD caused by PTDS are rare. The clinical manifestations of PTDS-ACD will closely mirror those described in PPD-ACD or PTD-ACD, reflecting the cross-reactivity between these aromatic amines. Generally, ACD to components in hair dyes manifests as a pruritic, erythematous, edematous, eczematous rash that can affect the margins of the scalp, ears, face, and/or neck. Severe cases can extend beyond the initial area of contact, potentially resulting in widespread involvement and systemic symptoms.¹² Notably, the scalp often is spared, which may be attributable to protection provided by sebum or the hair itself covering the scalp.¹³

Two case reports described ACD of the eyebrows after application of PTD-containing hair dye.^{14,15} One patient developed severe bullous ACD involving the eyebrows and eyelashes with concurrent conjunctivitis,¹⁴ and the other experienced erythema, edema, burning, itching, and exudation at and around the eyebrows.¹⁵ The latter patient had prior exposure to PPD from a black henna tattoo, which may have led to an initial sensitization and subsequent cross-reactivity to PTD in the hair dye.

Another case report described a patient with erythema, edema, and scaling of the face, neck, and arms within 1 week of exposure to a new hair dye at a salon.¹⁶ Patch testing revealed a positive reaction to PPD on day 3, despite it not being a component of the hair dye. On day 7, the patient showed a delayed reaction to PTD, which was confirmed to be present in the dye.¹⁶ The implications of these findings are twofold. First, delayed patch test readings beyond day 5 could provide more sensitive interpretation. Second, this case highlights the cross-reactivity between these related compounds.

Hairdressers and users of hair care products are most commonly affected by PTDS contact allergy. Though hairdressers generally are at a higher risk, prevalence for PTD sensitization in a European patch tested population showed rates of 20% in hairdressers and 30.8% in consumers.¹⁷ The North American Contact Dermatitis Group reported PTDS sensitization in fewer than 2% of 4121 patients patch tested across 13 North American centers over a period of 1 year.¹⁸ This suggests potential underutilization of the more specific panels that include PTDS.

Hairdressers are at an increased risk of contact allergy to PTDS due to occupational exposure and are at higher risk for hand dermatitis due to frequent exposure to water. In a review of epidemiologic studies published

between 2000 and 2021, the pooled lifetime prevalence of hand eczema in hairdressers was 38.2% compared to an estimated lifetime prevalence of 14.5% in the general population.¹⁹ Higher risk for hand eczema can increase the risk for sensitization to contact allergens including PPD and PTDS due to impaired barrier function, allowing allergen penetration through disrupted skin.²⁰

Strategies for Management and Avoidance

Patients with suspected contact allergy to PTDS should avoid this compound and related dye chemicals such as PPD due to the high risk for ACD and frequent cross-reactivity. While PTDS-allergic patients should avoid products containing PPD, some patients allergic to PPD may be able to tolerate exposure to PTD or PTDS.^{7,8,10} Regardless, any suspected contact allergy should be supported by patch testing with PTDS and PPD to confirm sensitization. Patch test readings for PTDS/PTD could be delayed beyond day 5 if clinical suspicion is high and early patch test reading is noncontributory; however, more studies are needed to establish that later readings are more reliable for PTDS.

Occupational risk reduction in hairdressers is essential. Hairdressers as well as at-home users of hair dyes should be properly informed by their dermatologist or other trained health care professional about PTDS and PTD as potent allergens and should be provided with information on potential alternatives. They also should be counseled on proper skin protection, including single-use gloves and careful hand care through gentle cleansing and use of barrier creams to protect skin integrity and prevent contact dermatitis. Nitrile rubber gloves offer the best protection when handling hair dyes. Polyvinyl chloride or natural latex rubber gloves also may be sufficient; however, polyethylene gloves should be avoided, as they have been shown to have the fastest time to penetration.²¹ Gloves should be properly sized, and reuse should be avoided.

Because PTDS and PTD frequently are used in semipermanent and permanent hair dyes, temporary hair dyes (eg, henna-based dyes) may be safer alternatives, as they infrequently contain these allergens. Food, Drug, and Cosmetics (FD&C) and Drug and Cosmetics (D&C) dyes also are used in some semipermanent hair dyes and seem to have low cross-reactivity to PPD; therefore, these may be used in patients allergic to PTDS or PTD.²² However, these dyes require frequent reapplication, which may be unfavorable to some patients. Gallic acid-based hair dyes have been shown to be safe alternatives in patients with contact allergy to PTDS or PTD, though pretesting is recommended with a repeat open application test.²³ The PPD derivative 2-methoxymethyl-para-phenylenediamine (ME-PPD) has reduced sensitization potential. In simulated hair dye use conditions, cross-reactivity to ME-PPD in patients with PPD contact allergy was 30% compared with 84% for PPD.²⁴ However, in an open-use test in 25 PPD-allergic individuals, ME-PPD was

reactive in 84% (21/25) and ME-PPD 2% patch testing was positive in 48% (12/25), suggesting that ME-PPD could be a potential alternative but is not universally tolerated.²⁵

It is important to note that products purporting to be natural or botanical are not inherently safe and may themselves be allergenic.²⁵ Patients should attempt a repeat open application test or patch testing prior to use of an alternative dye.

Given the prevalence of PTDS allergy, the fact that some PPD-allergic individuals may be able to tolerate hair dyes containing PTDS (assuming it tests negative), and the substantial quality of life and socioeconomic impacts of hair dye allergy, PTDS should be considered as an addition to standard patch test screening series.¹

Final Thoughts

While initially popularized as an alternative to PPD in semipermanent and permanent hair dyes, PTDS now is emerging as a contact allergen with well-documented cross-reactivity to PPD. Dermatologists should consider patch testing for PTDS (and PPD) in individuals who regularly encounter this compound. This will guide further counseling and recommendations.

REFERENCES

- Atwater AR, Botto N. Toluene-2,5-diamine sulfate: allergen of the year 2025. *Dermatitis*. 2025;36:3-11. doi:10.1089/derm.2024.0384
- National Center for Biotechnology Information. PubChem Compound Summary for 2,5-diamintoluene sulfate (CID 22856). Accessed Oct. 2, 2025. https://pubchem.ncbi.nlm.nih.gov/compound/2_5-Diaminotoluene-sulfate
- Søsted H, Rustemeyer T, Gonçalves M, et al. Contact allergy to common ingredients in hair dyes. *Contact Dermatitis*. 2013;69:32-39. doi:10.1111/cod.12077
- Burnett CL, Bergfeld WF, Belsito DV, et al. Final amended report of the safety assessment of toluene-2,5-diamine, toluene-2,5-diamine sulfate, and toluene-3,4-diamine as used in cosmetics. *Int J Toxicol*. 2010;29 (3 suppl):61S-83S.
- Schmidt JD, Johansen JD, Nielsen MM, et al. Immune responses to hair dyes containing toluene-2,5-diamine. *Br J Dermatol*. 2014;170:352-359. doi:10.1111/bjd.12676
- Yazar K, Boman A, Lidén C. Potent skin sensitizers in oxidative hair dye products on the Swedish market. *Contact Dermatitis*. 2009;61:269-275. doi:10.1111/j.1600-0536.2009.01612.x
- Fautz R, Fuchs A, van der Walle H, et al. Hair dye-sensitized hairdressers: the cross-reaction pattern with new generation hair dyes. *Contact Dermatitis*. 2002;46:319-324. doi:10.1034/j.1600-0536.2002.460601.x
- Vogel TA, Heijnen RW, Coenraads PJ, et al. Two decades of p-phenyl-enediamine and toluene-2,5-diamine patch testing—focus on co-sensitizations in the European baseline series and cross-reactions with chemically related substances. *Contact Dermatitis*. 2017;76:81-88. doi:10.1111/cod.12619
- Skazik C, Grannemann S, Wilbers L, et al. Reactivity of in vitro activated human T lymphocytes to p-phenylenediamine and related substances. *Contact Dermatitis*. 2008;59:203-211. doi:10.1111/j.1600-0536.2008.01416.x
- LaBerge L, Pratt M, Fong B, et al. A 10-year review of p-phenylenediamine allergy and related para-amino compounds at the Ottawa Patch Test Clinic. *Dermatitis*. 2011;22:332. doi:10.2310/6620.2011.11044
- Thomas BR, White IR, McFadden JP, et al. Positive relationship—intensity of response to p-phenylenediamine on patch testing and cross-reactions with related allergens. *Contact Dermatitis*. 2014;71:98-101. doi:10.1111/cod.12255
- Helaskoski E, Suojalehto H, Virtanen H, et al. Occupational asthma, rhinitis, and contact urticaria caused by oxidative hair dyes in hairdressers. *Ann Allergy Asthma Immunol*. 2014;112:46-52. doi:10.1016/j.anai.2013.10.002
- Mukkanna KS, Stone NM, Ingram JR. Para-phenylenediamine allergy: current perspectives on diagnosis and management. *J Asthma Allergy*. 2017;10:9-15. doi:10.2147/JAA.S90265
- Søsted H, Rastogi SC, Thomsen JS. Allergic contact dermatitis from toluene-2,5-diamine in a cream dye for eyelashes and eyebrows—quantitative exposure assessment. *Contact Dermatitis*. 2007;57:195-196. doi:10.1111/j.1600-0536.2007.01105.x
- Romita P, Foti C, Mascia P, et al. Eyebrow allergic contact dermatitis caused by m-aminophenol and toluene-2,5-diamine secondary to a temporary black henna tattoo. *Contact Dermatitis*. 2018;79:51-52. doi:10.1111/cod.12987
- Bregnhøj A, Menne T. Primary sensitization to toluene-2,5-diamine giving rise to early positive patch reaction to p-phenylenediamine and late to toluene-2,5-diamine. *Contact Dermatitis*. 2008;59:189-190. doi:10.1111/j.1600-0536.2008.01407.x
- Uter W, Hallmann S, Gefeller O, et al. Contact allergy to ingredients of hair cosmetics in female hairdressers and female consumers—an update based on IVDK data 2013-2020. *Contact Dermatitis*. 2023;89:161-170. doi:10.1111/cod.14363
- DeKoven JG, Warshaw EM, Reeder MJ, et al. North American Contact Dermatitis Group patch test results: 2019-2020. *Dermatitis*. 2023;34:90-104. doi:10.1089/derm.2022.29017.jdk
- Havmose MS, Kezic S, Uter W, et al. Prevalence and incidence of hand eczema in hairdressers—a systematic review and meta-analysis of the published literature from 2000-2021. *Contact Dermatitis*. 2022;86:254-265. doi:10.1111/cod.14048
- CDC. About skin exposures and effects. Published December 10, 2024. Accessed October 13, 2025. <https://www.cdc.gov/niosh/skin-exposure/about/index.html>
- Havmose M, Thyssen JP, Zachariae C, et al. Use of protective gloves by hairdressers: a review of efficacy and potential adverse effects. *Contact Dermatitis*. 2020;83:75-82. doi:10.1111/cod.13561
- Fonacier L, Bernstein DI, Pacheco K, et al. Contact dermatitis: a practice parameter—update 2015. *J Allergy Clin Immunol Pract*. 2015;3(3 suppl):S1-S39. doi:10.1016/j.jaip.2015.02.009
- Choi Y, Lee JH, Kwon HB, et al. Skin testing of gallic acid-based hair dye in paraphenylenediamine/paratoluenediamine-reactive patients. *J Dermatol*. 2016;43:795-798. doi:10.1111/1346-8138.13226
- Blômeke B, Pot LM, Coenraads PJ, et al. Cross-elicitation responses to 2-methoxymethyl-p-phenylenediamine under hair dye use conditions in p-phenylenediamine-allergic individuals. *Br J Dermatol*. 2015;172:976-980. doi:10.1111/bjd.13412
- Schüttelaar ML, Dittmar D, Burgerhof JGM, et al. Cross-elicitation responses to 2-methoxymethyl-p-phenylenediamine in p-phenylenediamine-allergic individuals: results from open use testing and diagnostic patch testing. *Contact Dermatitis*. 2018;79:288-294. doi:10.1111/cod.13078
- Tran JM, Comstock JR, Reeder MJ. Natural is not always better: the prevalence of allergenic ingredients in "clean" beauty products. *Dermatitis*. 2022;33:215-219. doi:10.1097/DER.0000000000000863