

p-Phenylenediamine

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p-PHENYLENEDIAMINE, the allergen of the year? Why now?

Granted, p-phenylenediamine (PPD) has been the leading permanent hair coloring agent or oxidative hair dye in most of the Western world since its introduction in the 1880s,¹ and it has been a problematic agent almost since its debut. Because of its allergic potential, it was banned in France and Germany from 1906 until the 1980s to 1990s, when it was again allowed for use in member states of the European Union.

So why now?

PPD was chosen this year because a number of changes have occurred recently in the clinical aspects of dealing with allergy to this antigen. These include the recognition of new patterns of exposure that lead to increased sensitization potential; increased usage by women and even men of the “baby boomer” generation in an attempt to stave off the appearance of aging; a broadening array of cross-reacting substances; reports of high levels of sensitization in certain ethnic groups; and new substitutes that will likely allow those who are sensitive to continue to alter the color of their hair.

Scope of the Problem

The primary route of exposure to PPD is through hair color, among consumers as well as among hairdressers. Allergy to the PPD in the consumer usually presents as a dermatitis of the face near the hair line and neck and may involve the eyelids, often sparing the scalp. In more severe cases, scalp dermatitis and more generalized eruptions may occur.² Immunoglobulin E (IgE)-mediated contact urticaria and anaphylaxis have been reported,^{3,4} as have lymphomatoid reactions.⁵ Theoretically, once oxidized, the PPD is no longer allergenic, but in reality, it is likely that the PPD is almost never completely oxidized.

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Although the number of individuals that use hair dyes seems to be increasing, the incidence of positive patch-test reactions to this antigen among consumers at this point seems to have remained constant or to have even decreased slightly over the past decade (Table 1^{6–10}). In the biannual reports from the North American Contact Dermatitis Group, the incidence of positive patch-test results in their population of tested individuals has actually decreased from almost 7% to just less than 5% between 1994 to 1986 and 2001 to 2002.^{6–9} A similar rate of incidence of approximately 5% was also reported by the Mayo Clinic group in their 1998–2000 test population.¹⁰

In contrast, reactions caused by occupational exposure appear to be increasing. Comparing the periods of 1980 to 1993 and 1994 to 2003, a study of more than 600 hairdressers found that the incidence of reactions to PPD increased from 45.9% to 58.0%.¹¹

In addition to reactions related to hair coloring, PPD and related substances may be used to dye textiles and fur and can therefore be a cause of textile or clothing dye dermatitis. Testing with PPD alone, however, will not identify most individuals who are allergic to textile dyes.¹²

A number of chemically related compounds have been associated with cross-reactivity to PPD (Table 2). These include a number of commonly used medications, including a relatively new cyclooxygenase-2 (COX-2) inhibitor (celecoxib), sunscreen agents, and antioxidants used in the manufacture of rubber products, such as N-isopropyl-N'-phenyl-p-phenylenediamine—agents in the black rubber mix patch-test allergen. The latter are more likely to cause problems in the workplace but may also be used in garments. These agents color the rubber black or grey.

Aging Population

“Many graying baby boomers find themselves lingering in the hair dye aisles...wistfully eyeing boxes displaying the

Table 1. Incidence of Positive Patch-Test Responses to p-Phenylenediamine

<i>Center Years</i>	<i>% Positive</i>
NACDG	
1994–1996	6.8
1996–1998	6.0
1998–2000	4.9
2001–2002	4.8
Mayo Clinic	
1998–2000	4.9

NACDG = North American Contact Dermatitis Group.
Adapted from Marks JG et al⁶; Marks JG et al⁷; Marks JG et al⁸; Pratt MD et al⁹; Wetter DA et al.¹⁰

colors their hair once was.”¹³ Two of every five American women color their hair. The number of men who use this cosmetic procedure is unknown but has certainly grown within the last decade. In a recent Danish survey, almost 20% of the male respondents had used hair color.¹⁴ In addition, many younger individuals, both men and women, decide to change the color of their hair. This is a huge market and a growing population of individuals exposed to all varieties of hair coloring agents, the majority of which contain PPD or cross-reacting substances (Table 3).^{2,12}

Ethnic Differences

Fisher was the first to suggest that PPD was a more important allergen for black persons than for white individuals.¹⁵ More recently, a study comparing the incidence of reactions to specific allergens between white and black patch-test subjects from the Cleveland Clinic reported that black men had a statistically higher incidence of PPD

Table 2. Chemicals That May Cross-React with p-Phenylenediamine

<i>Product Class</i>	<i>Chemicals</i>
Sunscreens	PABA and padimate O
Antifungives	Sulfonamides and p-aminosalicylic acid
Diuretics	Thiazides
Anesthetics	Benzocaine and related “caines”
Textile dyes	Azo dyes
Antidiabetics	Sulfonylureas
COX-2 inhibitors	Celecoxib
Rubber accelerators	N-isopropyl-N'-phenyl-p-phenylenediamine
Black rubber mix	

COX-2 = cyclooxygenase-2; PABA = para-aminobenzoic acid.

Table 3. Oxidative Dye Components Related to p-Phenylenediamine

p-Phenylenediamine diamine
p-Toluenediamine
p-Aminodiphenylamine
2,4-Diaminoanisole
o-Amino-phenol
1,4-Benzenediamine
1,4-Phenylenediamine
p-Aminoaniline

allergy than white men had.¹⁶ In a larger population studied by the North American Contact Dermatitis Group, of 45 antigens tested over a 6-year period, only PPD was found to cause a higher incidence of positive reactions in black patients than in white patients. In fact, the incidence among the black patients was so high as to make PPD one of the most common allergens in those individuals, rivaling nickel and neomycin in incidence of reaction. The reason for this difference is presently undefined; although it may be a true genetic difference, it is most likely related to patterns of use. It has been suggested that the difference is due to the fact that black persons are likely to use darker shades of dye, which contain higher concentrations of PPD.¹⁷

In some ethnic groups, facial hair is considered an essential part of religious observance. Hsu reported on eight Arabic men with facial dermatitis found to be due to PPD allergy related to the dyeing of beard hair.¹⁸

As the population of the United States changes with the increasing diversity of racial and ethnic groups, these differences in reaction patterns will certainly play a greater role in the clinical presentation of PPD allergy.

New Route of Exposure

Henna has been used for centuries in certain cultures as body paint and more recently as a hair coloring agent. It has been noted to be a very low-level sensitizer.¹² At the same time, body tattooing has enjoyed increased acceptance among the youth of many cultures, including those in the West. A recent phenomenon is “temporary tattooing,” in which the tattoo colors the stratum corneum and lasts until that layer is shed. Such tattoos are usually referred to as henna tattoos or black henna tattoos. Recently, reports of reaction to these temporary henna tattoos have become common. In the vast majority of such cases, the offending allergen has been found to be PPD. The level of PPD in these products is much higher than that found in hair color.^{19–23}

Because of PPD's high sensitization potential, the application of PPD to the skin is not an approved use. Since sensitization to PPD from tattoos is likely to be lifelong, we will likely see a population of individuals who will respond adversely to their attempts at hair coloring as they age. Because sensitization from such high concentrations in these tattoos leads to a very low threshold for elicitation, testing with the standard 1% concentration may lead to severe reactions, and it has been suggested that testing be done with concentrations of 0.01 to 0.30%.²⁴

Prevention

Although labeling mandated by the Food and Drug Administration has required salons and home users to test oxidative dyes before use, such testing is not always carried out. Recent evidence suggests that such testing should be encouraged as it appears to be predictive and could provide adequate secondary prevention if properly used.²⁵

Even more impressive is the development of new hair dyes that contain FD & C and D & C dyes and that appear to have very low levels of cross-reactivity with PPD and its other chemically related oxidative dyes.²⁶ One of these products, Elumen Hair Color (Goldwell Cosmetics, Linthicum Heights, MD), comes in a range of colors and lasts on the hair for 4 to 6 weeks. Such products are now available in the United States as salon products. We routinely recommend these agents to our PPD-sensitive patients. To safeguard against possible cross-reactivity, we always test with the agents before allowing their use.

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