Octocrylene: Preventing or Causing the Summertime Blues?

Summertime. And the living is easy—especially when your patients wisely protect themselves from photaging and photocarcinogenesis by the generous application of sunscreen products. But what if your patients are among the growing number of individuals who develop skin reactions to sunscreens? In recognition of this trend, the American Contact Dermatitis Society selected benzophenones (in 10% petrolatum from allergEAZE, SS506) as the 2014 Allergen of the Year. However, this group of structurally related ultraviolet (UV) filters, which protect against UVB and some UVA radiation, are not the only potential sensitizers in products intended to protect the skin from harmful solar radiation.

Another chemical filter, an ester in the cinnamate family known as octocrylene, was introduced to the consumer market about 15 years ago. Since then its use in both sunscreens and in cosmetics has increased dramatically. In a 12-year cross-sectional study of sunscreen products in the United States, octocrylene, combined with butyl methoxydibenzoylmethane, was found in none of the products tested in 1999. By 2003, the percentage had increased to 18% and by 2009 octocrylene was identified in more than half of the products tested. Furthermore, its use in cosmetic products tested increased from 0% to 23% across the same time span. In the United Kingdom and Europe, the use of octocrylene may be even more widespread: It was found in 91% of tested sunscreens in the United Kingdom, 85% in Switzerland, and more than 80% in the Netherlands.

By itself octocrylene offers relatively poor UV protection. However, it was introduced to sun-protective products because it has several desirable properties. First, it can help increase the sun protection factor (SPF) of a product when it is combined with other chemical UV filters. Second, its photostability is excellent, and it helps keep other photoabsorbers from breaking down. It also improves the water-resistance of sunscreens. Finally, its miscibility with a variety of cosmetic oils allows it to be used in gel sunscreens. All of these features help improve the performance of sunscreens.

So what is the allergenicity potential of octocrylene? Based on the murine local lymph node assay, it is a moderate sensitizer. The frequency of contact dermatitis related to octocrylene, however, is unclear. In the few reported series, the percentage of patients testing positive has ranged from 1.3 to 20%. Many reported cases have been from France, Belgium, Italy, and Spain; altogether, more than 100 cases in adults and about 2 dozen cases in children can be found in the literature. This pattern of responding suggested that sensitization is age-dependent. In fact, children seem to be susceptible to primary sensitization via direct use of sunscreen on their skin. In contrast, adults who react to octocrylene tend to exhibit photoallergic contact dermatitis. They also have an interesting history.

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More than 80% of adults sensitized to octocrylene have exhibited previous photosensitization to the nonsteroidal anti-inflammatory drug (NSAID) ketoprofen from the use of topical medications. Furthermore, ketoprofen photosensitivity also appears to lead to benzophenone-3 photocontact allergy (17-64% of cases)—perhaps not surprisingly because the two chemicals share a benzophenone moiety. Yet, structural similarity between ketoprofen and octocrylene is minimal; the latter lacks a benzophenone substructure. There is, however, a fascinating twist. In the skin aminolysis and hydrolysis of octocrylene may lead to benzophenone. Whether the clear co-reactivity of octocrylene with ketoprofen would more appropriately be considered cross-sensitivity awaits further analysis, but the connections are intriguing, especially since octocrylene-sensitive patients also tend to co-react with benzophenone-3.

Clearly, the life cycle of octocrylene as an allergen is still in its early stages. But with the widespread use of octocrylene in so many products, now estimated to include more than 80% of sunscreens and more than 20% of daily skin care cosmetics in the U.S. and Europe, it would be no surprise if the number of cases continued to mount. As of 2010 in France, access to ketoprofen was restricted to a prescription-basis only and patients had to be informed about the risk of developing photocontact allergy. This regulation was enacted in response to concern about the interaction between the NSAID and octocrylene. The restriction may reduce the number of cases of adult sensitization to octocrylene in the future, but the potential for continued sensitization will have to be monitored. No regulatory action has been taken, but a joint task force (European Society of Contact Dermatitis and European Society for Photodermatology) has recommended that octocrylene (available from allergEAZE in 10% petrolatum, SS982) be included in a baseline series of photoallergens.

What’s the bottom line for patch test practitioners? As de Groot and Roberts note in their excellent review article on which this summary is based, three patient groups should be considered candidates for photopatch testing: those with reactions to sunscreens, those with reactions to NSAIDs, and those suspected of photoallergic contact dermatitis. Patch testing with this allergen in carefully selected patients can help you help your patients chase away at least one potential cause of summertime blues!

In Bondage with Octyl-2-Cyanoacrylate

In 1998, the U.S. Food and Drug Administration approved the use of octyl-2-cyanoacrylate (2-OCA) as a topical skin adhesive. It was marketed as Dermabond® with the intent to replace sutures and staples for the closure of skin incisions and lacerations. Scarcely 10 years ago, Dermatology Clinics, featured an article on the indications for using 2-OCA. The authors noted that the applications discussed likely represented only the beginnings of how this adhesive would be used in cutaneous medicine. They were right. Since then the popularity of 2-OCA has expanded to almost every conceivable surgical field. It has been used to close a variety of surgical incisions: joint replacements, breast augmentations/reductions, abdominoplasties, and maxillofacial incisions to name a few. It has also been used in the treatment of complex genital skin defects and sutureless pediatric circumcisions, to stop bleeding at hemodialysis sites, and to dress external ventricular drain sites in patients in neurological intensive care units. One article even noted that it could be used to close a “myriad” of pediatric incisions. Almost universally, the use of 2-OCA in these surgical contexts has been associated with cosmetic outcomes as good as or better than those associated with sutures or staples. It reaches maximum bonding strength in 2.5 minutes, and its closure strength is equivalent to that of healed tissue at 7 days. By promoting healing, it also helped shorten hospital stays and lower reoperation and readmission rates. Furthermore, it garners high marks in terms of both patient and surgeon satisfaction. As a result it is rapidly becoming the standard for wound closure.

These desirable qualities have spurred the use of 2-OCA in a variety of noncutaneous applications such as a pediatric tongue repair, cleft lip repair, and closure of postparoidectomy salivary fissures. Deeper within the body it has been used for vascular repairs and to repair cerebrospinal fluid leaks and thoracic duct injuries incurred during neck dissections. It has been applied to anastomotic sites to prevent postoperative pancreatic fistulas after pancreaticoduodenectomy and to uterine incisions. It has also been used experimentally in animal models to explore other potential uses such as peripheral nerve repair and to strengthen colorectal anastomoses and reduce subsequent leakage. It has even been combined with sodium bicarbonate to stabilize and reduce bilateral fractures of the zygomatic arch. In vivo studies to determine the biological effects would be the logical next step.

Despite the apparent benign nature of 2-OCA, reports of allergic contact dermatitis are beginning to appear in the literature. Recently, McDonald and Buckley reported two cases in the British Journal of Dermatology. One case involved a woman who developed severe, pruritic dermatitis 3 weeks after a hip replacement. The outbreak was refractory to strong steroids and persisted 3 months. She patch tested positive to Dermabond and to 2-hydroxyethyl methacrylate and negative to methyl cyanoacrylate. Despite her previous use of false nails that contained acrylates, her delayed reaction led the authors to conclude that her case represented primary sensitization from her surgical exposure. In the second case Dermabond was applied to a woman who underwent two radiofrequency treatments for varicose veins 3 months apart. Within 36 hours of her second treatment, she developed severe itching and erythematous blistering that persisted 2 weeks. Upon patch testing this patient had positive reactions to Dermabond and n-2-butyl cyanoacrylate. Her course suggested that she was likely sensitized on the occasion of her first treatment.

Although symptoms along an incision site sealed with 2-OCA might be highly suggestive of allergic contact dermatitis in a patient with no fever or other signs of infection, patch testing may still be in order because polymerized cyanoacrylates degrade and release formaldehyde. Therefore, a reaction to free formaldehyde may need to be ruled out. If a reaction to 2-OCA is identified, suggested treatments include removal of the adhesive and short-term use of topical steroids, followed, of course, by avoidance of the allergen in the future.

The rapidity and reactivity of the cyano group in 2-OCA were originally thought to preclude it from becoming a sensitizer because the hapten should be isolated to the keratinocytes and never reach immunomodulators. To date few cases have been reported, but their number could grow if the adhesive is used in noncutaneous applications that increase its potential for molecular penetration and hence sensitization. Indeed, a quick look at online anecdotal reports by individuals seeking relief for cutaneous rashes associated with a surgical incision might raise questions about how often reactions to 2-OCA already go unrecognized. Whether the widespread acceptance of the use of this adhesive to treat pediatric patients has the potential to increase the likelihood of sensitization also bears close surveillance.

McDonald BS, Buckley DA. Severe dermatitis from Dermabond® surgical glue. Brit J Dermatol 170: 735-758, 2014

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Although allergic contact dermatitis is the most common cause of periorbital dermatitis, other underlying conditions can be responsible. Periorbital dermatitis can reflect atopic eczema, airborne contact dermatitis, and irritant contact dermatitis. Periorbital rosacea, psoriasis vulgaris, and allergic conjunctivitis also may need to be ruled out. Even if you suspect allergic contact dermatitis as the cause of periorbital dermatitis, the list of potential allergens is challenging enough to illustrate why patch test clinicians must be more than a little Sherlockian to identify the culprit.

A recent study by Landeck and coworkers, however, helps clarify the most common causative allergens. In their 10-year, retrospective cross-sectional analysis of the largest sample reported to date with standardized historical data collected across 57 centers, 4.7% (4779) of 101,403 individuals investigated had periorbital dermatitis. Females (81.1%) were affected significantly more often than males, and occupational causes were unusual. Patients with periorbital dermatitis in response to an environmental allergen were significantly younger than control patients; the reverse was true of patients whose periorbital dermatitis was thought to be related to ophthalmic medications. Patients using topical ophthalmic medications also had the highest rate of allergic contact dermatitis (34.7%). Overall, the findings were consistent with those reported previously.

The frequency of allergic contact dermatitis in the patients with periorbital symptoms paralleled that of the general population. Metals, fragrances, and preservatives were the most common types of allergens. Not surprisingly, that ubiquitous allergen, nickel, topped the list as the most common allergen in 17.5% of the sample. It is worthwhile remembering that the transfer of nickel ions to the area around the eyes from contact with items like coins and jewelry is not the only avenue for exposure. Eye cosmetics can also contain nickel as an unintended consequence of the manufacturing process. Glasses and even eyelash curlers are other potential sources. Among fragrance allergens the highest percentage of patients tested positive to Fragrance Mix 1 (6.2%) and to Myroxylon pereierrae (5.3%). With 8.5% of patients reacting to phenyl mercuric acetate, it was the leading allergen of the preservatives with one caveat: The authors note that the concentration tested could also be an irritant, and such reactions could have been misinterpreted as weak positive reactions. If so, the percentage represents an overestimation. It is worth noting that after the test concentration of phenylmercuric acid was decreased, the number of positive reactions decreased, and such reactions could have been misinterpreted as weak positive reactions. If so, the percentage represents an overestimation. It is worth noting that after the test concentration of phenylmercuric acid was decreased, the number of positive reactions decreased dramatically.

Overall, the authors conclude that patch testing should be applied routinely to the diagnosis of periorbital dermatitis. Clinicians challenged by a patient with periorbital dermatitis can be confident about patch testing with the knowledge that about 95% of the 36 most common allergens identified in this patient group are covered by T.R.U.E. TEST and allergEAZE allergens while others are under development.


The December 2013 issue of all things contact dermatitis was primarily devoted to the potent allergen para-phenylenediamine (PPD), which is used widely in hair dyes. We also noted that PPD is not the only allergen in hair dyes. A recent article, the first survey of allergens present in hair dye products available to consumers for home use in the United States, underscores that point and adds an exclamation point: Of 107 products included in the study, 106—or 99%—contained more than one potent sensitizer!

Altogether, 30 different potent sensitizers were identified in the 107 products. The average number of allergens present in the dyes was 6. Resorcinol, which was present in 89% of the products, was the most common potential allergen followed by PPD, which was identified in 78%. Based on earlier reports, resorcinol was also the top potent sensitizer in hair dye products in Spain (81%) and Sweden (82%). In contrast, PPD was present in only 50% of the products evaluated in Spain and in only 16% of those from Sweden. Interestingly, the rate of positive reactions to PPD in patch test patients is significantly lower in northern countries compared to elsewhere in Europe, but whether this finding reflects a connection with the presence of PPD in hair dye is unknown. m-aminophenol and p-aminophenol were present in 75% and 60% of the dyes, respectively.

The graying of the U.S. population has the potential to increase opportunities for exposure to the potent allergens in hair dyes. In one study more than 50% of respondents cited the desire to conceal gray hair as their reason for coloring their hair. Given the prevalence of potent allergens in these dyes, clinicians must remain alert to related symptoms of allergic contact dermatitis, which may involve the scalp, hands, and regions near the eyes and mouth in consumers and may be especially prominent on the hands in hairdressers even if they wear gloves while applying the product to clients’ hair. Nor is hair dying restricted to women; many men do as well.

As the authors of this report note, of the 30 potent allergens identified in hair dye products, only PPD is included on the baseline series recommended by the North American Contact Dermatitis Group or on that of the European Series. Some practicing clinicians may not need to patch test to some of these potent hair dye allergens on a regular basis. As a result, even if the allergen is commercially available, purchasing an entire syringe may exceed the use pattern of a practice and may not be the cost effective choice. To help remedy that situation, we are happy to introduce the SmartPractice Allergen Bank dedicated to compounding special orders. For more information, please visit our website at www.smartpracticeallergenbank.com to learn more about this exciting and unique new service designed to help you with your diagnostic challenges.