

# Common Contact Allergens Associated with Eyelid Dermatitis: Data from the North American Contact Dermatitis Group 2003–2004 Study Period

Robert L. Rietschel, Erin M. Warshaw, Denis Sasseville, Joseph F. Fowler Jr, Vincent A. DeLeo, Donald V. Belsito, James S. Taylor, Frances J. Storrs, C.G. Toby Mathias, Howard I. Maibach, James G. Marks Jr, Kathryn A. Zug, and Melanie Pratt

**Background:** Allergic contact dermatitis can be manifest as an eruption confined to the eyelids. In regard to this specific presentation, only limited information on which to base the selection of patch tests for proper evaluation is available.

**Objective:** To identify the contact allergens most frequently found to be both patch test positive and relevant when only the eyelids are involved.

**Methods:** Data collected from 2003 to 2004 by the North American Contact Dermatitis Group (NACDG) were analyzed for relevant allergens in the setting of dermatitis on the eyelids only. Data on eyelid dermatitis patients whose relevant allergens were not among the 65 allergens used for screening during this study period were also tabulated.

**Results:** Data showed that 268 patients had only eyelid dermatitis and a final diagnosis of allergic contact dermatitis. In 193 (72%) of these, reactions were of current relevance and were identified from a screening series of 65 allergens. The top 26 allergens identified 65% of cases (175 cases). Gold was the most frequently encountered allergen (22 of 175 cases [12.5%]). Of the 268 cases, 33 showed relevant reactions to an allergen that was not among the 65 NACDG standard screening allergens. No specific allergen was identified in the remaining 42 cases.

**Conclusion:** The top 26 allergens identified in this study represent a potential eyelid dermatitis screening series.

DERMATITIS confined solely to the eyelids is a distinct clinical event. Although there are causes of pure eyelid dermatitis other than contact dermatitis, the purpose of this analysis was to describe specific allergens that should be given consideration in this setting.

## Methods

The North American Contact Dermatitis Group (NACDG) collects data on patients patch-tested at 13 sites in the United States and Canada. The methods of the NACDG have previously been published.<sup>1</sup> Collected information includes identification of the site of dermatitis. Up to three sites can

be specified on our data collection instrument. For this study, only patients with a single site of dermatitis were included, and that site was “eyelids.” Group members must specify a final diagnosis; for this analysis, the final diagnosis had to be allergic contact dermatitis. Data on whether allergens that produce an allergic response are considered to be of possible, probable, or definite current relevance or of past relevance are also collected. Definitions of relevance used by the NACDG have been published.<sup>2</sup> During the study period from 2003 to 2004, the NACDG tabulated the cases in which the identified relevant allergens were not part of our screening series of 65 allergens. The general source of these allergens (but not the allergen per se) was coded and was available for analysis.

Inclusion criteria included (1) eyelid dermatitis listed as the only site, (2) a final diagnosis of allergic contact dermatitis, and (3) a positive patch-test reaction of possible, probable, or definite current relevance. These criteria were chosen because an allergen found to be of past relevance might not be linked to the current eyelid problem. An example would be a case in which the patient had eyelid dermatitis and was patch test positive for nickel but in which the investigator determined that this was not of current

*From the Southern Arizona VA Health Care System, Tucson, AZ; Minneapolis VAMC, Minneapolis, MN; University of Louisville, Louisville, KY; St. Luke's Roosevelt Hospital Center, New York, NY; University of Missouri, Kansas City, MO; Cleveland Clinic, Cleveland, OH; Oregon Health Science University, Portland, OR; University of California San Francisco, San Francisco, CA; Milton S. Hershey Medical Center, Hershey, PA, and Dartmouth-Hitchcock Medical Center, Lebanon, NH.*

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relevance to the eyelids but was of past relevance to an earlobe problem not currently active. Cases in which the eyelids were the sole site of dermatitis and the relevant allergen was not among the standard 65 allergens were also included in this tabulation. Those patients with eyelid dermatitis and a positive patch-test reaction that was not considered relevant were excluded. Similarly, patients with eyelid dermatitis whose final diagnosis was other than allergic contact dermatitis (such as atopic dermatitis) were excluded.

## Results

During the 2003–2004 study period, the NACDG patch-tested 5,145 patients with the 65 screening allergens selected for routine use; 268 patients (5.2%) met the study criteria of having only eyelid dermatitis and a final diagnosis of allergic contact dermatitis. The top 26 relevant allergens are listed in Table 1; these allergens identified 65% (175) of the cases. A total of 193 cases (72%) of relevant allergy were identified by the 65 screening-series allergens. There were 33 cases in which an allergen other than one of the 65 screening-series allergens yielded a positive reaction; in those cases, we collected data on the source of the allergen but not on the exact allergen (Table 2). The remaining 42 cases of eyelid dermatitis yielded positive patch-test results that were of past or uncertain relevance. Although there are many causes of eyelid dermatitis other than contact allergy, these allergens are the allergens most commonly encountered in our practices. Allergens that identified two or fewer cases include potassium dichromate, ethylenediamine, benzophenone-3, para-phenylenediamine, black rubber mix, diazolidinylurea, imidazolidinylurea, Compositae mix, tea tree oil, paraben mix, iodopropyl butyl carbamate, and cocamide diethanolamine.

## Discussion

There have been eyelid dermatitis studies that report on the contact allergens identified, but some of these reports include cases of dermatitis at sites other than eyelids.<sup>3,4</sup> In the report by Valsecchi and colleagues, only 54 of 150 cases involved eyelids only, and patch-test information on that subset was not presented separately.<sup>3</sup> In Guin's report, eyelid dermatitis was a "primary or secondary complaint," which is problematic if our interest is in contact allergens when only the eyelids are dermatitic.<sup>4</sup> One study (of 25 cases of eyelid dermatitis) that distinguished patients with facial dermatitis did provide a list of the most frequently encountered contact

**Table 1.** Top 26 Relevant Contact Allergens for Patients with Pure Eyelid Dermatitis

| Allergen                                                           | % Relevant Positive Reactions* (N) |
|--------------------------------------------------------------------|------------------------------------|
| Gold sodium thiosulfate 0.5% pet                                   | 8.2 (22)                           |
| Fragrance mix 8% pet                                               | 7.1 (19)                           |
| Balsam of Peru ( <i>Myroxylon pereirae</i> ) 25% pet               | 6.3 (17)                           |
| Nickel sulfate 2.5% pet                                            | 6.0 (16)                           |
| Neomycin 20% pet                                                   | 3.3 (9)                            |
| Methyldibromoglutaronitrile 2% pet                                 | 3.0 (8)                            |
| Quaternium-15 2% pet                                               | 3.0 (8)                            |
| Methylchloroisothiazolinone/<br>Methylisothiazolinone (100 ppm) aq | 2.2 (6)                            |
| Cobalt chloride 1% pet                                             | 1.9 (5)                            |
| DMDM hydantoin 1% aq                                               | 1.9 (5)                            |
| Amidoamine 0.1% aq                                                 | 1.9 (5)                            |
| Cocamidopropyl betaine 1% aq                                       | 1.9 (5)                            |
| Thiuram mix 1% pet                                                 | 1.9 (5)                            |
| Bacitracin 20% pet                                                 | 1.5 (4)                            |
| Cinnamic aldehyde 1% pet                                           | 1.5 (4)                            |
| d- $\alpha$ -Tocopherol acetate 100%                               | 1.5 (4)                            |
| Tosylamide formaldehyde resin 10% pet                              | 1.5 (4)                            |
| Propylene glycol 30% aq                                            | 1.5 (4)                            |
| Tixocortol pivalate 1% pet                                         | 1.5 (4)                            |
| Formaldehyde 1% aq                                                 | 1.1 (3)                            |
| Colophony 20% pet                                                  | 1.1 (3)                            |
| Ylang ylang oil 2% pet                                             | 1.1 (3)                            |
| Lanolin 30% pet                                                    | 1.1 (3)                            |
| Ethyl acrylate 0.1% pet                                            | 1.1 (3)                            |
| Methylmethacrylate 2% pet                                          | 1.1 (3)                            |
| Budesonide 0.1% pet                                                | 1.1 (3)                            |
| Total                                                              | 175/268                            |

aq = aqueous; DMDM = 1,3-dimethylol-5,5-dimethyl; N = size of population studied; pet = petrolatum; ppm = parts per million.

\*Defined as of definite, possible, or probable current relevance (excludes past relevance).

allergens.<sup>5</sup> Those allergens, listed in Table 3, contrast with the mixed facial and eyelid allergens reported by Valsecchi and colleagues, in whose report 65.3% of 150 cases of eyelid dermatitis with or without other areas of involvement were deemed allergic contact dermatitis. Reactions to nickel and fragrance mix occurred more frequently in those patients with eyelid dermatitis than in the 1,008 other patch-tested individuals who did not have eyelid involvement.<sup>3</sup> However, nickel sensitivity was not statistically significantly more frequent among women with eyelid dermatitis than among women without eyelid dermatitis.<sup>3</sup> Of the 25 cases of eyelid dermatitis without other areas of dermatitis, 72% were due to allergic contact dermatitis, and the most common relevant allergen was fragrance.<sup>4</sup> In a separate study of 609 German patients with periorbital eczema, 52% had a relevant

**Table 2.** Sources of Eyelid Dermatitis in Patients whose Allergen Was Not in the Screening Series

| Source                                        | No. of Cases |
|-----------------------------------------------|--------------|
| Cosmetics and beauty products (not specified) | 14           |
| Moisturizers and lotions                      | 5            |
| Topical antibiotics                           | 3            |
| Jewelry                                       | 2            |
| Perfumes and fragrances                       | 1            |
| Artificial nails                              | 1            |
| Insects and arachnids                         | 1            |
| Recreational and athletic equipment           | 1            |
| Sealants (industrial type)                    | 1            |
| Adhesives, glues, bonding agents              | 1            |
| Undeclared                                    | 3            |
| Total                                         | 33           |

contact allergen, and reactions to fragrance mix occurred less frequently in these patients than in patients who had other areas of involvement.<sup>6</sup> Nethercott and colleagues studied 79 patients who had eyelid dermatitis; of that group, 78.5% of the cases involved only the eyelids.<sup>7</sup> In that study, 46% had allergic contact dermatitis. In contrast to the other study, nickel and cobalt were less frequently identified as allergens in the eyelid group when compared to dermatitis cases without eyelid involvement whereas cinnamic alcohol, diazolidinylurea, and neomycin sulfate occurred as allergens more frequently.<sup>7</sup> These previously published studies indicate that one half or more of eyelid dermatitis cases may be due to allergic contact dermatitis. Reactions to nickel and fragrance mix are either over- or underrepresented in eyelid dermatitis cases, depending on the study.

In this analysis, we found 22 cases of eyelid dermatitis caused by gold. Gold was the most common allergen that accounted for pure eyelid dermatitis. The NACDG has previously reported that 9.5% of 4,101 patch-tested patients

were allergic to gold and that the most common sites of dermatitis in gold-allergic patients were the hands (29.6%), face (19.3%), and eyelids (7.5%).<sup>8</sup> Ehrlich and Belsito found that 7 of 15 gold-allergic patients cleared their dermatitis by not wearing gold jewelry.<sup>9</sup> In 3 of 7 cases, discontinuation of gold jewelry was the only behavior modification, and facial and eyelid dermatitis were the main problems.<sup>9</sup> In Guin's study, 33 patients were allergic to gold; he noted that some cases were relevant.<sup>4</sup> These data support a trial of gold jewelry avoidance in the setting of eyelid dermatitis and a positive patch-test reaction to gold.

In our series, fragrances and preservatives were found to be the main cosmetic allergens, and their presence on this list is no surprise.<sup>10</sup> Nickel was the fourth most common allergen, and eyelash curlers would be a possible source of exposure. Thiuram can also be found in the rubber components of eyelash curlers and in foam makeup sponges. Cocamidopropyl betaine (CAPB) and amidoamine (an impurity of CAPB) can be found in shampoos, and allergy to them in shampoos presents as eyelid dermatitis.<sup>11</sup> The fingernail polish allergen tosylamide formaldehyde resin is commonly considered in the evaluation of eyelid dermatitis, but it was a minor factor in this series, representing only 1% of cases (4 of 268).

The allergens listed in Table 1 would constitute a reasonable screening series for the evaluation of patients with eyelid dermatitis without other areas of involvement.

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**Table 3.** Previously Published Data on Common Contact Allergens Associated with Eyelid Dermatitis

|                                          | Positive Cases              |                                   |
|------------------------------------------|-----------------------------|-----------------------------------|
|                                          | UK 1996 <sup>5</sup> (n=25) | Italy 1992 <sup>3</sup> (n = 150) |
| Patient Population                       |                             |                                   |
| Eyelids only                             | 25                          | 54                                |
| Eyelids + other site                     | —                           | 96                                |
| Allergens                                |                             |                                   |
| Fragrance, 5                             |                             | Nickel, 63                        |
| Toluenesulfonamide formaldehyde resin, 3 |                             | Kathon CG, 15                     |
| Amerchol L 101, 3                        |                             | Fragrance, 12                     |
| Chloramphenicol, 2                       |                             | Diaminodiphenylmethane, 11        |
| Own cosmetics, 2                         |                             | Thimerosal, 11                    |

n = size of sample studied; UK = United Kingdom.

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