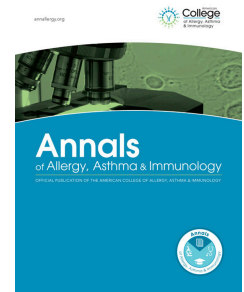


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## Experience in patch testing: A 6-year retrospective review from a single academic allergy practice

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## INTRODUCTION

Contact dermatitis is an inflammatory cutaneous reaction induced by an exogenous agent coming into direct contact with the skin and is characterized by pruritic, well-defined, eczematous dermatitis with vesicles, or erythematous papules.[1-3] Irritant contact dermatitis (ICD) accounts for >80% of cases and occurs as a result of direct damage to the skin by physical agents or chemicals without prior sensitization.[4] Only 20% of cases of contact dermatitis have an underlying allergic mechanism. Allergic contact dermatitis (ACD) is a delayed, type IV (T-cell mediated) hypersensitivity reaction occurring in susceptible individuals with prior sensitization.[5] Typically, the sensitization phase takes 10-14 days, and re-exposure to the allergen causes dermatitis most often localized to the site of contact. Subsequent exposures often lead to more severe dermatitis and a much more rapid onset.[5] An estimated 25-40% of individuals will experience an allergic skin disease at some point during their lifetime.[6] Previous studies have estimated the prevalence of contact dermatitis to range from 12.5-40.6%, and rates appear to be on the rise.[7, 8] A recently published large cross-sectional study in Europe determined the prevalence of ACD to be 27%.[9]

Patients with suspected ACD are commonly referred to dermatologists for evaluation, and more recently there has been an increase in referrals to allergy practices.[10, 11] Clinical history may provide clues for potential allergens and should include time of onset and possible contact with allergens/irritants, clinical pattern, working environment, leisure activities, domestic products, skin care products, reactions to jewelry/clothing, and history of previous dermatitis.[12] Clinical information is oftentimes not enough to identify which allergen(s) may be the cause of ACD, and studies have shown that history and physical exam alone have only

modest sensitivity (76%) and specificity (76%).[13, 14] Patch testing remains the gold standard for diagnosis and has been performed since the 1800s with little change in the procedure.[15] Patch testing should be performed in patients with acute, subacute, or chronic dermatitis if allergy is suspected; in those with persistent dermatitis despite treatment; and when dermatitis has a distribution suggestive of contact dermatitis such as the eyelids/face/extremities.

Performing PT early in disease onset has been demonstrated to be cost effective, and previous studies have shown that patch testing allows for identification of relevant allergens, early resolution of symptoms, and, ultimately, improved quality of life in affected individuals.[16, 17]

The Thin-Layer Rapid Use Epicutaneous (T.R.U.E.) Test (SmartPractice, Phoenix, AZ) is a standardized, pre-loaded patch testing system. It is the only FDA-approved, commercially available patch test in the United States, currently with 35 allergens and a negative control.

Although T.R.U.E. Testing is relatively easy to use, it does have limitations, including the relatively small number of allergens tested and the inability to customize the panel on the basis of an individual's exposure history. The North American Contact Dermatitis Group (NACDG), is a group of dermatologists in Canada and the United States who collect and report data from patch testing using a standardized screening series, currently comprised of 70 allergens. This series can change slightly every two years, based on trends. The American Contact Dermatitis Society (ACDS) has recommended a Core Allergen Series of 80 allergens that can be adjusted based on physician and patient needs/exposures. As compared to T.R.U.E. Test, the NACDG screening series and ACDS panels require that the allergens be individually loaded into a chamber system manually. A previous study has shown that TRUE testing can miss up to 26.7% of allergens that are detected by NACDG.[18]

We sought to report on patch test findings from a single academic allergy practice, including positive patch testing results, history of atopy, referral source and also whether or not using an extended panel of allergens increased sensitivity of patch testing.

## METHODS

This study is a retrospective chart review on patients evaluated for ACD between April 2010 and April 2016 at a tertiary care academic allergy practice. A total of 585 patients were patch tested during this period, primarily by a single physician and occasionally by a second physician. Patient charts were analyzed for positive reactions on patch testing, and demographics were reviewed for all patients undergoing patch testing which included: age, sex, race, atopic history (i.e., asthma, allergic rhinitis, and atopic dermatitis), referral source, occupation and location of dermatitis.

Patch testing included a combination of either a) T.R.U.E. Test allergens; b) NACDG screening series of allergens; or c) supplementary allergens such as patient's personal products or metal tray (when indicated or requested by referring physicians). The patch testing method used Finn Chambers or AllergEAZE patch system on Scanpor tape applied to the upper aspect of the patients back. The patches remained in place for 48 hours, at which time the patient returned for patch removal and was assessed after 20-30 minutes for any reactions. A final reading and interpretation took place 96 hours after patch application as described in practice parameters.[3] Reactions were then scored according to the International Contact Dermatitis Research Group (ICDRG)[19]: Negative (-/0); doubtful with faint erythema only (?+), weak positive with mild, non-vesicular erythema (1+); strong positive reaction with vesicular erythema, infiltration and papules (2+); and extremely positive with intense erythema and blister/bullae formation (3+). A

reaction scored as 1+ or greater was considered positive. Reactions were determined to be clinically relevant or irrelevant based on patient history and physician judgement.

Categorical variables are expressed as percentages and associations among categorical variables was assessed by chi-square tests or Fisher's Exact Test if expected values in more than one cell was less than 5. Normally distributed continuous scale variables are expressed as mean and standard deviation with tests between groups by Student's t-test. Minitab 17 software was used.

The study was reviewed and approved by the Internal Review Board at the Albany Medical College prior to chart review.

## RESULTS

### *Patient Demographics*

Patient demographics are provided in Table 1. A total of 585 patients were patch tested during the 6-year review period. The majority of patients undergoing patch testing were female (71.7%) and Caucasian (78%). The mean age was 48.7 years old and ranged from 4 to 92 years (SD = 18.1 years). Three hundred thirty-nine patients (58%) reported a history of atopy, including 17.2% with a history of atopic dermatitis, 38.5% with a history of allergic rhinitis, and 29.3% with a history of asthma. Nearly half (44%) of patients were referred for testing by a dermatologist. A total of 369 (63%) were determined to have positive patch test results (reactions scored as 1+ or greater were considered positive).

Of the patients with positive patch results, 270 (73%) were female and 213 (57%) reported a history of atopy, including 65 (17.6%) with history of atopic dermatitis. The

extremities were the most common site of dermatitis (82%), followed by the face/head/neck (74.5%) and the trunk (49%). The most commonly reported occupations in this group were office work/education, retired/unemployed, and healthcare workers (Table 2).

#### *Patch Test Results*

Patients underwent patch testing to T.R.U.E. test allergens, an expanded series (NACDG) of allergens, and/or supplemental allergens including their own products. Five-hundred forty-eight (94%) were tested to an extended series (NACDG screening series) of allergens during the study period, and 37 (6%) were tested to only the T.R.U.E. Test allergens. A total of 260 patients were additionally tested to their own products, or supplemental allergens such as specialized metal tray but only 68 (26%) were found to be positive to these supplemental products. One hundred forty-five patients (24.7%) were positive to only one allergen, 90 patients (15%) were positive to 2 or more allergens, and 121 patients (20.6%) were positive to 3 or more allergens.

The 10 most common positive allergens in this study were: nickel sulfate, gold sodium thiosulfate, methylchloroisothiazolinone (CI+ ME-isothiazolinone), thimerosal, bacitracin, quaternium-15, cobalt dichloride, p-phenylenediamine (PPD), propylene glycol, and fragrance mix. The results were compared to recent data reported by the NACDG series and data reported from Camacho-Halili et al (table 3). With the exception of gold sodium thiosulfate and thimerosal, which are only present in T.R.U.E. test, the most commonly positive allergens were part of the NACDG extended series.

A total of 314 patients (54% of total tested), were found to be positive to allergen(s) from the T.R.U.E. Test. Ninety-one patients (15.5% of total tested) were positive to allergen(s) from

both the T.R.U.E. Test and extended allergen series. Of the 185 patients with negative testing on T.R.U.E. Test, 20 (10.8%) were found to be positive to extended series of allergens.

## DISCUSSION

Individuals with suspected ACD are commonly referred to dermatologist and more recently allergists for evaluation. Patch testing remains the gold standard for diagnosis of ACD, and early identification of culprit allergens leads to shorter duration of disease. [17, 20] Several studies have been published on performing patch testing in the dermatology literature [21-24], whereas large studies from allergy practices remain scarce. [25] To the best of our knowledge this is the largest report on patch test findings at a single academic allergy practice described in the allergy literature to date.

Approximately half (44%) of the patients were referred by a dermatologist specifically for PT, as our allergy group is one of the only practices in our area performing testing. Once testing was completed, patients were subsequently followed and managed by their dermatologist. This provided us with the unique opportunity to work with the dermatology colleagues in our community and highlights the role that allergists can play in evaluating ACD. Also patch tests were placed by only a small number of specially training medical staff, and predominantly read by one board-certified allergist.

Most patients who underwent patch testing were female (71.7%), Caucasian (78.1%), with an average age of 48.4 years, which is consistent with previous studies in both dermatology and allergy literature.[21, 25-27] Furthermore, females were much more likely to have positive patch test (73%). This is thought to be due to increased exposure to cosmetics, personal care products, nickel present in body piercings, and some have even suggested hormonal influences

as a potential explanation.[8, 28, 29] Similar to previous studies, the most common occupations reported in those with positive patch testing were office or educational employees, followed by retirees and those employed in the health care field.[25, 26]

A history of atopy (allergic asthma, allergic rhinitis, or atopic dermatitis) was reported in more than half (58%) of those who underwent patch testing. Atopic dermatitis (AD) was present at similar frequencies in those with positive vs negative patch testing (17.6% vs 16.6%). The correlation between atopic dermatitis and allergic contact dermatitis remains uncertain. Aquino et al reported on the evidence for and against the role of contact allergy in those with atopic dermatitis in a recently published review article.[30] Several early studies suggested that patients with AD are less likely to develop ACD.[31-33] This was based on the finding that patients with AD stimulated with strong antigens including dinitrochlorobenzene (DNCB), p-nitrosodimethylamine (NDMA), and Rhus oleoresin, developed sensitization at much lower rates when compared to healthy controls. More recent studies, however, have shown that patients with AD have similar if not increased rates of positive patch testing.[25, 34-37] This finding has been especially important in the pediatric population in which AD is common, and ACD has similar presentation and may be missed. Silny et al evaluated the prevalence of positive PT in those diagnosed with atopic dermatitis and found much higher rates in those with AD (45%) compared to healthy controls (14%).[38] This is likely due to the loss of barrier function in those with atopic dermatitis and subsequently increased risk for sensitization.

The top 10 most frequent positive allergens in this study were composed of three metals (nickel sulfate, cobalt dichloride and gold sodium sulfate), four preservatives (CI+ME-isothiazolinone, thimerosal, quaternium-15, and propylene glycol), one antibiotic (bacitracin), PPD, and fragrance mix. Nine of the 10 top allergens were part of the T.R.U.E. Test panel of

allergens (nickel sulfate, gold sodium sulfate, Cl+ME-Isothiazolinone, thimerosal, bacitracin, quaternium-15, cobalt dichloride, PPD, and fragrance mix) and the remaining allergen, propylene glycol, is present in the NACDG screening series of allergens.

It is not surprising that preservatives made up the most common category of positive allergens in this study. Preservatives are frequently used in cosmetics and personal care products to decrease contamination. They are categorized as either formaldehyde releasers (e.g., formaldehyde, quaternium-15, diazolidinyl urea, imidazolidinyl urea, and DMDM hydantoin) or non-formaldehyde releasers (e.g., methylchloroisothiazolinone/methylisothiazolinone, parabens, and thimerosal).[39] It is estimated that up to 20% of personal care products in the United States contain a formaldehyde releaser as a preservative.[40] Cl+ Me-isothiazolinone, which was the 3<sup>rd</sup> most common positive allergen in this study, contains both methylchloroisothiazolinone (MCI) and methylisothiazolinone (MI). These substances are common non-formaldehyde preservatives used in personal care products including bath products, makeup baby products (shampoos and wipes), hair care products, nail care products, deodorants, and sunscreens.[41] These allergens should be considered in patients with history of reaction to cosmetics, sunscreen or with facial dermatitis. Quaternium-15, the 6<sup>th</sup> most positive allergen, is a formaldehyde-releaser commonly found in cosmetics, wrinkle-resistant fabrics, cleaning products, and personal care products. Propylene glycol is a preservative commonly used in emollient creams, lotions, cosmetics, fragrances, hair care and oral care products and is part of the NACDG screening series of allergens.[39]

Metals are common sensitizers, nickel has repeatedly been shown to be the most common allergen in screening series. [18, 25-27, 37] Nickel sulfate, gold sodium thiosulfate, and cobalt

dichloride were the first, second, and seventh most common positive allergens in this study, respectively. Nickel is quite ubiquitous, and is often used in jewelry, coins, tools, belt buckles, metal fasteners, braces, and eye glasses. The European Union has instituted regulations to limit the nickel content in items that are likely to come into direct contact with the skin and similar changes are currently being advocated for in the United States.[42] A large, epidemiological survey conducted in Europe to determine the prevalence of sensitization to metals in the general population revealed that Sweden had the lowest prevalence of nickel sensitization out of the 5 countries surveyed.[43] This was attributed to long standing regulations the Swedish government had instituted regarding nickel content in ear-piercing materials.[44] Cobalt is often a co-sensitizer with nickel, so it is not surprising that it is also among the top 10 allergens. Interestingly, gold sodium thiosulfate was the second most common allergen in our cohort. Gold was named the contact allergen of the year in 2001 by The American Journal of Contact Dermatitis.[45] Gold sodium thiosulfate (75 mcg gold/cm<sup>2</sup> in hydroxypropyl cellulose gel vehicle; T.R.U.E. Test package insert) is currently part of the standardized T.R.U.E. Test panel of allergens, but was removed from NACDG screening series after 2004 due to persistent positive test reactions and patient concern.[46, 47] Fifteen percent of our patients tested positive to gold sodium thiosulfate. The NACDG previously reported prevalence rates to gold of 8.7% during their study period from 2003-2004.[46] Our group has previously reported on the high rates of clinically irrelevant patch testing to gold and discovered that only 3.2% of those with positive patch testing to gold had history that was suggestive of clinical reactivity.[48] The clinical relevance of gold has been previously questioned, with prior studies reporting clinical relevance in only 10-15% of cases.[49, 50] Despite the low rates of clinical relevance, gold still remains an important allergen, especially in certain clinical circumstances. In particular, in those

presenting with facial and/or eyelid dermatitis, those with exposure to gold dental materials, those with suspected jewelry allergy, or those with a history of occupational exposure. Moreover, it is important for those interpreting patch testing to take a thorough history especially when a patient is found to be positive to gold and to properly counsel patients as to whether the positive test is clinically relevant to circumvent unnecessary avoidance and anxiety.

P-phenylenediamine (PPD) was the 8<sup>th</sup> top allergen and is a coloring agent that is often used in hair dyes, body painting such as black henna tattoos, leather, rubber, and textiles. It is a common sensitizer and an important cause of ACD in hairdressers and those who have their hair dyed. PPD should be considered in patients with facial or scalp dermatitis.

Fragrance mix I, which is part of the T.R.U.E. Test, is composed of 8 different elements (geraniol, hydroxycitronellal,  $\alpha$ -amylcinnamaldehyde, eugenol, cinnamaldehyde, cinnamyl alcohol, isoeugenol, oak moss), and was the 10<sup>th</sup> top positive allergen. Fragrances are commonly added to household items, topical medications and cosmetics, and it is estimated that fragrances account for 1.8%-4.2% of ACD in the general population.[51] Fragrance mix I is estimated to detect up to 80% of cases of fragrance sensitivity.[52] Fragrance mix II was added to the NACDG screening series after 2006 in an attempt to increase sensitivity and has six components (hexyl cinnamic aldehyde, coumarin, farnesol, hydroxyisohexyl 3-cyclohexane carboxaldehyde, and citral).

We compared our most common positive allergens, with the recently published NACDG[27] results and patch testing results from Camacho-Halili et al[25], who reported on patch testing in 427 patients from 3 separate allergy practices over a 5 year period (Table 4). In all 3 studies, nickel sulfate was the most commonly positive allergen, with similar prevalence

rates (16.3% vs. 17.5% vs. 15.1%). Gold sodium thiosulfate was the second most common positive allergen in our cohort but was not included in the patch test panels for the other two studies. Similar to the NACDG and Camacho-Halili study, fragrance mix, and PPD were amongst the top 10 allergens. Thimerosal, which is also included in the T.R.U.E. Test panel but not NACDG screening series of allergens, and cobalt chloride, which is included in both T.R.U.E. Test and NACDG screening series were found at similar rates in both this study and the Camacho-Halili study. Cl<sup>+</sup> Me-isothiazolinone, which is part of the T.R.U.E. Test panel of allergens, was the third most positive allergen in our study and was also part of the top 10 allergens from the NACDG study. The remaining top allergens in this study were, Quaternium-15 and Propylene glycol. These allergens were not part of the top 10 allergens in the other two studies, and Quaternium-15 is included in the T.R.U.E. Test and Propylene glycol in the NACDG series.

In those patients with positive patch testing, 85% were positive to T.R.U.E. Test allergens. However, T.R.U.E. Test would have missed 10.8% of patients tested who were positive to allergens only included in an extended series (e.g. NACDG screening series) which is lower than previous studies reporting 12.5-26.7% of patients may be missed by using T.R.U.E. Test alone.[18, 25] In a recently published multicenter study from North America over 4800 patients underwent patch testing with a screening series of 70 allergens the T.R.U.E. Test would have hypothetically missed 24.1-34% of reactions that were detected by the NACDG screening series.[26] T.R.U.E. Test may be an appropriate screening series, but relying on it solely as opposed to using an extended panel such as the NACDG or ACDS series may miss identification of clinically significant allergen(s).

Unfortunately, in most cases the clinical relevance of positive patch testing was not determined in our study, as patients returned to their referring dermatologist/physician after testing. All patients positive to thimerosal and the majority of patients positive to gold in our study (96.8%) were irrelevant allergens based on patient history. Positive nickel on patch testing showed past, but not present relevance in a majority of patients. Previous studies have shown patch testing not only identifies relevant allergens in ACD, it also leads to earlier resolution of symptoms, and improved quality of life in affected individuals. [16, 27, 53] In a recently published retrospective study of 156 patients from the United Kingdom, 64.3% of individuals with positive patch test results were determined to be of current clinical relevance, all of which noted complete resolution or significant improvement in dermatitis following 3-4 months of allergen avoidance.[54]

Similar to other studies published on patch testing, the present study was a retrospective medical record review, which is inherently associated with limitations, including that data extracted from medical charts may have been incomplete. Other limitations identified include that testing was performed at a single academic center in one geographic region of the United States, leading to lack of diversity. Also, the number of allergens tested changed over the period of the study, and thus patients were not all tested with a uniform extended panel. Our study is also limited by the lack of follow-up information on patients (i.e., clinical improvement following removal of identified allergens) who underwent testing as most returned to their referring provider for follow-up. Strengths of this study include its relatively large patient population, with a robust range of ages and occupations. Also, the majority of patch tests were interpreted by a single board-certified allergist, and occasionally a second (both with several

years of experience in patch testing), limiting the operational error and variability that can occur with several individuals placing and interpreting the test.

In conclusion, contact dermatitis is an important cutaneous condition encountered by both dermatologists and allergists. Patch testing remains the gold standard for early identification of culprit allergens and is considered a safe and practical method for diagnosis of ACD. As more allergists evaluate for ACD and perform patch testing, it is important to continue to report on findings in the allergy literature. Currently, the T.R.U.E. Test is the only standardized, FDA-approved panel of allergens available for patch testing and is a reasonable screening test. However, our study and previous studies have shown that the use of an extended panel (i.e., NACDG screening series, ACS, supplemental) can increase the diagnostic accuracy of patch testing and can be crucial in patient management and treatment.

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Table 1: Patient Characteristics: Demographics

| Characteristic                     | N (%)<br>(N= 585)     |
|------------------------------------|-----------------------|
| <b>Sex</b>                         |                       |
| Female                             | 419 (71.7)            |
| <b>Age (Range, 4-92 years old)</b> |                       |
| Mean age (SD)                      | 48.7 (+/- 18.1 years) |
| <b>History of atopy*</b>           | 339 (58)              |
| Atopic dermatitis                  | 101 (17.2)            |
| Allergic rhinitis                  | 225 (38.5)            |
| Asthma                             | 171 (29.3)            |
| <b>Race</b>                        |                       |
| White                              | 457 (78.1)            |
| Black                              | 29 (5)                |
| Asian                              | 24 (4.1)              |
| Hispanic                           | 6 (1)                 |
| Not reported/other                 | 69 (11.8)             |
| <b>Dermatology Referral</b>        | 258 (44)              |
|                                    |                       |

\*Exceeds 100% as some patients reported more than 1 atopic condition

Table 2: Positive Patch Test Patient Characteristics

| Characteristic           | N (%)<br>N = 369 |
|--------------------------|------------------|
| <b>Sex</b>               |                  |
| Female                   | 270 (73)         |
| <b>History of atopy*</b> | 213 (57)         |
| Atopic dermatitis        | 65 (17.6)        |
| Allergic rhinitis        | 138 (37.3)       |
| Asthma                   | 101 (27.3)       |
| <b>Location*</b>         |                  |
| Extremities              | 304 (82.3)       |
| Head/Neck                | 275 (74.5)       |
| Trunk                    | 181 (49)         |
| <b>Occupation</b>        |                  |
| Office work/Education    | 170 (46)         |
| Health care              | 46 (12.5)        |
| Beauty industry          | 8 (2.2)          |
| Food service             | 11 (3)           |
| Retired/Not working      | 73 (19.8)        |
| Construction/maintenance | 14 (3.8)         |
| Not reported             | 47 (12.7)        |

\* Exceeds 100% as some patients reported >1 location involved

Table 3: Positive allergens from our series

| Allergen                        | No. (%) of patients tested | No. (%) positive |
|---------------------------------|----------------------------|------------------|
| Nickle Sulfate                  | 585 (100)                  | 96 (16.28)       |
| Gold Sodium Thiosulfate         | 416 (71.1)                 | 62 (14.9)        |
| Cl+ Me-Isothiazolinone          | 585 (100)                  | 54 (9.23)        |
| Thimerosal                      | 416 (71.1)                 | 28 (6.73)        |
| Bacitracin                      | 585 (100)                  | 38 (6.5)         |
| Quaternium-15                   | 585 (100)                  | 34 (5.81)        |
| Cobalt Dichloride               | 585 (100)                  | 32 (5.47)        |
| p-Phenylenediamine              | 585 (100)                  | 29 (4.96)        |
| Propylene glycol                | 555 (94.9)                 | 23 (4.14)        |
| Fragrance mix                   | 585 (100)                  | 24 (4.1)         |
| Neomycin Sulfate                | 585 (100)                  | 23 (3.93)        |
| Formaldehyde                    | 585 (100)                  | 20 (3.42)        |
| Neomycin Sulfate                | 585 (100)                  | 23 (3.93)        |
| Formaldehyde                    | 585 (100)                  | 20 (3.42)        |
| HEMA                            | 385 (65.8)                 | 13 (3.38)        |
| Carba mix                       | 585 (100)                  | 17 (2.91)        |
| Propolis                        | 385 (65.8)                 | 11 (2.86)        |
| 2-Bromo-2-Nitropropane-1,3-diol | 585 (100)                  | 14 (2.39)        |
| Ethyl acrylate                  | 169 (28.9)                 | 4 (2.37)         |
| Lauryl glucoside                | 385 (65.8)                 | 9 (2.33)         |
| K Dichromate                    | 585 (100)                  | 12 (2.05)        |
| Balsam of Peru                  | 585 (100)                  | 12 (2.05)        |
| Ethylenediamine Dihydrochloride | 585 (100)                  | 11 (1.88)        |
| Colophony                       | 585 (100)                  | 11 (1.88)        |
| Iodopropynyl butyl carbamate    | 555 (94.9)                 | 10 (1.81)        |
| Diazolidinyl Urea               | 585 (100)                  | 10 (1.71)        |
| Tixocortol-21-Pivalate          | 585 (100)                  | 10 (1.71)        |
| Budesonide                      | 585 (100)                  | 10 (1.71)        |
| Imidazolidinyl Urea             | 585 (100)                  | 9 (1.54)         |
| Methyl methacrylate             | 555 (94.9)                 | 8 (1.44)         |
| Wool Alcohol                    | 416 (71.6)                 | 6 (1.44)         |
| Composite Mix II                | 555 (94.9)                 | 7 (1.24)         |
| Caine Mix                       | 416 (71.6)                 | 5 (1.2)          |
| Parthenolide                    | 416 (71.6)                 | 5 (1.2)          |
| p-tert Butylphenol              | 585 (100)                  | 7 (1.2)          |
| Formaldehyde Resin              |                            |                  |
| Cinnamal/cinnamic aldehyde      | 555 (94.9)                 | 6 (1.08)         |

|                                          |            |          |
|------------------------------------------|------------|----------|
| Hydrocortisone-17-Butyrate               | 585 (100)  | 6 (1.03) |
| Disperse Blue 106                        | 585 (100)  | 6 (1.03) |
| Chloroxylonol (PCMX)                     | 555 (94.9) | 5 (0.90) |
| Thiuram Mix                              | 585 (100)  | 5 (0.85) |
| Benzyl EtOH                              | 385 (65.8) | 3 (0.78) |
| Cocamide DEA                             | 385 (65.8) | 3 (0.78) |
| Tea Tree Oil                             | 385 (65.8) | 3 (0.78) |
| Cananga odorata oil                      | 385 (65.8) | 3 (0.78) |
| Glutaral/Glutaraldehyde                  | 555 (94.9) | 4 (0.72) |
| Mixed diakyl thiourea                    | 555 (94.9) | 4 (0.72) |
| Ethyleneurea                             | 555 (94.9) | 4 (0.72) |
| Dimethylol dihydroxyoxy-<br>Ethyleneurea | 555(94.0)  | 4 (0.72) |
| Paraben Mix                              | 585 (100)  | 4 (0.68) |
| Epoxy Resin                              | 585 (100)  | 4 (0.68) |
| Mercaptobenzothiazole                    | 585 (100)  | 4 (0.68) |
| Fragrance Mix II                         | 169 (28.9) | 1 (0.59) |
| Benzocaine                               | 169 (28.9) | 1 (0.59) |
| Benzophenone-3                           | 555 (94.9) | 3 (0.54) |
| Glyceryl monothioglycolate<br>(GMTG)     | 555 (94.9) | 3 (0.54) |
| Toluenesulfonamide<br>formaldehyde       | 555 (94.9) | 3 (0.54) |
| Triamcinolone acetonide                  | 555 (94.9) | 3 (0.54) |
| Lyril                                    | 385 (65.8) | 2 (0.52) |
| dL Alpha Tocopherol                      | 385 (65.8) | 2 (0.52) |
| Clobetasol-17-propionate                 | 385 (65.8) | 2 (0.52) |
| Black rubber mix                         | 416 (71.1) | 2 (0.48) |
| Cocamidopropylbetaine                    | 555 (94.9) | 2 (0.36) |
| Desoximethasone                          | 385 (65.8) | 1 (0.26) |
| Lidocaine                                | 385 (65.8) | 1 (0.26) |
| Quinolone Mix                            | 416 (71.1) | 1 (0.24) |
| DMDM hydantoin                           | 555 (94.9) | 1 (0.18) |
| Desquiterpene lactone mix                | 555 (94.9) | 1 (0.18) |
| Sesquiterpene lactone mix                | 555 (94.9) | 1 (0.18) |
| Methyl-dibromo Glutaronitrile            | 585 (100)  | 1 (0.17) |
| Mercapto Mix                             | 585 (100)  | 1 (0.17) |

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Table 4: Comparison of Top Ten Positive Allergens

| Our study (% positive)             | NACDG standard series (% positive) (Dekoven et al) <sup>27</sup>      | Allergy study (% positive) (Camacho-Hallali et al) <sup>25</sup>                                  |
|------------------------------------|-----------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| 1. Nickle sulfate (16.3)           | 1. Nickle sulfate (17.5)                                              | 1. Nickle sulfate (15.1)                                                                          |
| 2. Gold sodium thiosulfate (14.9)* | 2. Methylisothiazolinone 0.2% aq (13.4)                               | 2. Fragrance mix I (10.1)                                                                         |
| 3. Cl+Me-Isothiazolinone (9.2)     | 3. Fragrance mix, 8% pet (11.3)                                       | 3. p-Phenylenediamine (8.8)                                                                       |
| 4. Thimerosal (6.7)*               | 4. Formaldehyde 2% aq (8.4)                                           | 4. Thimerosal (7)                                                                                 |
| 5. Bacitracin (6.5)                | 5. Methylchloroisothiazolinone/ Methylisothiazolinone mix 0.01% (7.3) | 5. Cobalt Dichloride (6.5)                                                                        |
| 6. Quaternium-15 (5.8)             | 6. Myroxylon pereirae resin (Balsam of Peru) (7)                      | 6. Neomycin sulfate (6.5)                                                                         |
| 7. Cobalt Dichloride (5.5)         | 6. Neomycin (7)                                                       | 7. Glutaraldehyde (4.4)                                                                           |
| 8. p-phenylenediamine (5)          | 8. Bacitracin (6.9)                                                   | 8. Balsam of Peru (4.2)                                                                           |
| 9. Propylene glycol (4.1)          | 9. Formaldehyde 1% aq (6.4)                                           | 9. Thiuram mix (3.9)                                                                              |
| 10. Fragrance mix (4.1)            | 9. p-phenylenediamine (6.4)                                           | 10. Disperse blue, wool alcohols (lanolin), carba mix, and ethylene diamine dihydrochloride (2.3) |

\*Gold sodium thiosulfate, and Thimerosal not currently included in NACDG (only TT)