

North American Contact Dermatitis Group Patch-Test Results, 2001–2002 Study Period

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

Background: Allergic contact dermatitis is a significant cause of cutaneous disease affecting many individuals in the home and at the workplace. Patch testing is the most worthwhile diagnostic tool for the evaluation of patients with suspected allergic contact dermatitis.

Objective: This study reports the results of patch testing from January 1, 2001, to December 31, 2002, by the North American Contact Dermatitis Group (NACDG).

Methods: Patients were tested with an extended screening series of 65 allergens. A standardized patch-testing technique was used. Data from these patients were recorded on a standardized computer entry form and analyzed.

Results: Sixty-five allergens were tested on 4,913 patients. The top 10 allergens remain the same in this study period as in the 1999–2000 study period: nickel sulfate (16.7%), neomycin (11.6%), *Myroxylon pereirae* (balsam of Peru) (11.6%), fragrance mix (10.4%), thimerosal (10.2%), sodium gold thiosulfate (10.2%), quaternium-15 (9.3%), formaldehyde (8.4%), bacitracin (7.9%), and cobalt chloride (7.4%). Of the 4,913 patients tested, 69% had at least one positive allergic patch-test reaction. Of all patients, 15.8% had occupation-related dermatitis; 15.4% were determined to have irritant contact dermatitis, and 11.1% of the 15.4% had a relevant reaction to an occupational irritant. Of all patients tested, 16.7% had a relevant reaction to an allergen not in the NACDG standard series, and 5.5% had a relevant reaction to an occupational allergen not in the standard series.

Conclusion: Our findings once again reinforce the need for a more comprehensive group of diagnostic allergens than those found in the standard screening kits. The usefulness of patch testing is enhanced when a greater number of allergens are tested, especially nonstandard allergens occupationally encountered.

THE NORTH AMERICAN CONTACT DERMATITIS GROUP (NACDG) evaluates patients with suspected allergic contact dermatitis (ACD) and patch-tests them with the same screening allergens by way of a standardized technique so that trends in delayed-type contact sensitivity can be detected. Established allergens and newer chemicals are tested to determine the causes of ACD. Periodically, the results of this multicenter patch testing are published so that all interested parties might use the information to determine their own testing series and to determine which chemicals in topical products should be avoided.^{1–6}

Methods and Materials

Members of the NACDG patch-tested 4,913 patients from January 1, 2001, to December 31, 2002. All patients were

patch-tested with a screening series of 65 allergens (Chemo-technique Diagnostics AB, Malmö, Sweden). Patch testing was done with a standardized technique using Finn Chambers (Epitest Ltd Oy, Tuusula, Finland) on Scanpor tape (Norgesplaster A/S, Vennesla, Norway). The patches remained in place for 48 hours, and test sites were evaluated initially at 48 to 72 hours and again between 72 and 168 hours after placement.

A positive allergic reaction was interpreted as +, ++, or +++, manifested by erythematous papules, vesicles and/or a spreading reaction, sometimes with crusting and ulceration.^{1,7} The clinical relevance of the positive patch-test reactions was determined by the patient's history and clinical skin examination findings.⁷ Present relevance was divided into definite, probable, and possible relevance, based on previously defined criteria.

Relevance was considered definite if the reaction to a use test with the putative item containing the suspected allergen was positive or if a positive patch-test reaction to the object or product was obtained. Relevance was considered

From the North American Contact Dermatitis Group.

Address reprint requests to Dr. Melanie Pratt, 413-1095 Carling Avenue, Ottawa, ON, Canada K1Y 4P6; E-mail: kellypratt@sympatico.ca

probable if the substance identified by patch testing could be verified as present in the known skin contactants of the patient and if the clinical distribution fit. Relevance was considered possible if the patient was exposed to circumstances in which skin contact with materials known to contain the putative allergen likely occurred.⁷

The history, skin examination, and patch-test results were integrated to determine the following diagnostic groups: ACD, irritant contact dermatitis, atopic dermatitis, stasis dermatitis, nummular eczema, seborrheic dermatitis, other types of dermatitis, psoriasis, other dermatoses, and pompholyx.²

In this study period, the NACDG screening tray was expanded to include 65 allergens, increased from the previous 50 allergens. The new additions included hydrocortisone-17-butyrate (1% petrolatum [pet]); Disperse Blue 106 (1% pet); tetracaine (1% pet); lidocaine (15% pet); dibucaine (2.5% pet); prilocaine (2.5% pet); phenoxyethanol (1% pet); benzalkonium chloride (0.1% aqueous [aq]); dimethylol dihydroxyethyleneurea (4.5% aq); coconut diethanolamine (0.5% pet); Compositae mix (6% pet), consisting of 0.5% arnica, 2.5% German chamomile, 0.1% lactone, 0.9 % parthenolide, 1% tansy, and 1% yarrow; DL-alpha-tocopherol acetate (100% pet); ylang ylang oil (2% pet); jasmine absolute (2% pet); and black rubber mix (0.6% pet). In the current series, cinnamic aldehyde and N-isopropyl-N-phenyl-4-phenylenediamine were removed. The latter was replaced by black rubber mix (0.6% pet).

Results

Table 1 presents the results from the 2001–2002 study period as well as from previous NACDG study periods.^{1,7,8} A total of 4,913 persons were patch-tested with the 65 allergens in the NACDG screening tray over the 2-year period from January 1, 2001, to December 31, 2002. The patients' ages ranged from 2 to 97 years. Twenty-six percent of the patients had allergic rhinitis, 16% had atopic dermatitis, and 13% had a history of asthma. The majority of these patients worked as the following: homemakers (20.2%), retirees (14.2%), hospital workers (6.9%), construction workers (2.5%), restaurant workers (2.4%), and beauticians (1.3%).

The specific occupational categories were as follows: unemployed (36.8%, which included homemakers), managers and administrators (4.8%), nurses (3.4%), electrical workers (2.1%), hairdressers (1.4%), teachers (1.3%), assemblers (1.2%), and machinists (1%). The primary diagnoses were ACD (43.5%), irritant contact dermatitis

(13.3%), other types of dermatitis (14.7%), other dermatoses (9.9%), photodermatitis (1.1%), and psoriasis (2.7%).

The data show that 69% of the 4,913 tested patients had at least one allergic patch-test reaction; 16.7% of the 4,913 had relevant allergens not on the NACDG standard series, and 5.5% had relevant occupation-related allergens not on the NACDG standard tray.

The top 10 most frequent allergens remained the same when compared to the 1999–2000 results⁸; these were nickel sulfate (16.7%), neomycin (11.6%), *Myroxylon pereirae* (11.6%), fragrance mix (10.4%), thimerosal (10.2%), gold sodium thiosulfate (10.2%), quaternium-15 (9.3%), formaldehyde (8.4%), bacitracin (7.9%), and cobalt chloride (7.4%).

Of all patients evaluated, 15.4% had reactions to specifically identifiable relevant irritants, and 11.1% of the total had reactions to identifiable relevant irritants that were related to occupation. Some of the more frequent relevant irritants were detergents (2.4%), cosmetics (2.1%), soaps and cleansers (1.6%), liquids and lotions used for personal hygiene (1.8%), gloves (1.7%), fluids used in metalworking (1.3%), and glues and adhesives (1.8%).

The performance of the new allergens that were recently added for this 2001–2002 study period were as follows: 0.5% of patients tested reacted to hydrocortisone-17-butyrate, 3.0% to Disperse Blue dye, 0.6% to tetracaine, 0.7% to lidocaine, 0.9% to dibucaine, 0.1% to prilocaine, 2.8% to cocamidopropyl betaine, 4.3% to benzalkonium chloride, 1.1% to dimethylol dihydroxyethyleneurea, 1.0% to Compositae mix, 1.1% to DL alpha tocopherol, 0.5% to DL alpha tocopherol acetate, 1.1% to ylang ylang oil, 0.7% to jasmine absolute, 1% to black rubber mix, and 1.3% to coconut diethanolamine. Thus, among the newly added allergens, Disperse Blue 106, cocamidopropyl betaine, and benzalkonium chloride elicited the greatest number of positive allergic reactions.

It has been postulated that amidoamine, a by-product in the manufacturing of cocamidopropyl betaine (CAPB), may be the allergenic moiety in CAPB. In the 2001–2002 study period, patients were tested with both chemicals. The results revealed that 2.8% had positive reactions to CAPB as opposed to 2.3% who had positive reactions to amidoamine.

All three local anesthetics in the TRUE Test (Mekos Laboratories A/S, Hillerød, Denmark) "caine" mix (benzocaine, tetracaine, and dibucaine), as well as lidocaine, were tested individually in the 2001–2002 study period. Results revealed that 1.7% of the patients reacted to benzocaine, 0.6% reacted to tetracaine, 0.7% reacted to lidocaine, and 0.9% reacted to dibucaine.

Table 1. Test Substances Ranked by Frequency of Positive Reactions

Test Substance*	n	Reaction (%)			Relevance (%)				1994–1996		1996–1998		1998–2000	
		Pos	Unknown	Irritant	Definite	Probable	Possible	Past	Pos (%)	n	Pos (%)	n	Pos (%)	n
Nickel sulfate (2.5%)	4,901	16.7	0.7	0.4	1.6	10.3	37.5	33.0	14.3	3,108	14.2	3,429	16.2	5,827
Neomycin (20%)	4,904	11.6	0.4	0.2	4.6	14.2	13.5	29.0	11.6	3,104	13.1	3,436	11.5	5,822
Balsam of Peru (25%)	4,910	11.6	2.3	0.9	1.6	11.6	67.5	2.6	10.4	3,112	11.8	3,439	12.3	5,832
Fragrance mix (8%)	4,896	10.4	1.2	0.7	1.8	17.2	64.5	6.2	14.0	3,082	11.7	4,095	10.9	5,802
Thimerosal (0.1%)	4,899	10.2	0.4	0.5	0.6	1.2	5.4	26.4	10.4	3,075	10.9	4,087	10.8	5,795
Sodium gold thiosulfate (0.5%)	4,900	10.2	1.0	0.6	0.2	10.0	27.1	7.0	—	—	9.5	4,101	10.5	5,806
Quaternium-15 (2%)	4,910	9.3	0.3	0.1	3.1	25.5	55.7	4.1	9.2	3,110	9.0	3,436	9.2	5,832
Formaldehyde (1% aqs)	4,909	8.4	0.8	0.3	1.0	13.8	54.8	1.9	9.2	3,111	9.3	3,440	9.2	5,830
Bacitracin (20%)	4,900	7.9	0.2	0.2	7.8	18.2	16.6	30.4	9.1	3,079	8.7	4,103	9.2	5,812
Cobalt chloride (1%)	4,899	7.4	0.8	1.8	1.1	6.6	36.1	19.6	8.0	3,087	9.0	4,095	7.6	5,811
MDGN/PE (2.5%)	4,897	5.8	1.0	0.8	3.2	14.4	43.5	1.1	—	—	7.6	4,054	6.0	5,778
Carba mix (30%)	4,908	4.9	0.9	0.8	5.0	17.6	54.0	6.3	5.7	3,115	7.3	3,437	4.8	5,829
PPD (1%)	4,903	4.8	0.5	0.2	5.1	26.7	17.8	21.2	6.8	3,111	6.0	3,441	4.9	5,831
Thiuram (1%)	4,907	4.5	0.2	0.1	7.7	23.0	48.2	7.7	6.8	3,115	6.9	3,435	4.7	5,830
Potassium dichromate (0.25%)	4,913	4.3	1.2	0.9	1.9	12.3	41.2	6.6	2.0	3,106	2.8	3,440	5.8	5,833
Benzalkonium chloride (0.1% aqs)	4,892	4.3	1.5	2.8	0.9	5.2	20.8	8.5	—	—	—	—	—	—
Propylene glycol (30% aqs)	4,899	4.2	0.9	0.7	18.1	20.1	51.0	0.5	1.1	3,077	3.8	4,095	3.7	5,804
2-Bromo-2-nitropropane-1,3-diol (0.5%)	4,897	3.3	0.3	0.3	0.6	6.7	62.8	1.8	2.3	3,074	3.2	4,094	3.1	5,800
Diazolidinylurea (1% aqs)	4,897	3.2	0.3	0.1	5.1	27.8	58.2	1.9	3.7	3,060	2.9	4,094	2.6	5,778
Diazolidinylurea (1%)	4,897	3.1	0.3	0.1	4.7	26.0	62.7	1.3	3.9	3,085	3.7	4,096	3.0	5,802
Imidazolidinylurea (2%)	4,897	3.0	0.2	0.1	4.0	21.5	66.4	3.4	3.1	3,080	3.2	4,094	2.5	5,784
Tixocortol-21-pivalate (1%)	4,901	3.0	0.1	0.1	9.0	30.3	47.6	4.8	2.3	3,091	2.3	4,100	2.7	5,807
Disperse Blue 106 (1%)	4,888	3.0	0.5	0.4	0.0	10.3	45.5	5.5	—	—	—	—	—	—
Ethylenediamine dihydrochloride (1%)	4,909	2.8	0.1	0.1	6.5	6.5	15.2	23.9	2.9	3,113	2.6	3,439	2.5	5,831

continued

Table 1. Continued

Test Substance*	n	Reaction (%)			Relevance (%)				1994–1996		1996–1998		1998–2000	
		Pos	Unknown	Irritant	Definite	Probable	Possible	Past	Pos (%)	n	Pos (%)	n	Pos (%)	n
DMDM hydantoin (1%)	4,897	2.8	0.3	0.0	5.9	23.5	64.0	2.9	2.3	3,082	2.6	4,093	2.0	5,801
Cocamidopropyl betaine (1% aqs)	4,887	2.8	1.1	0.5	11.5	22.3	55.4	0.7	—	—	—	—	—	—
MDGN/PE (4%)	4,897	2.7	0.6	0.2	6.7	16.4	47.8	0.7	2.0	3,074	2.7	4,053	3.5	5,797
Colophony (20%)	4,908	2.6	0.1	0.1	5.5	3.9	36.7	20.3	2.6	3,113	2.0	3,443	2.5	5,833
Epoxy resin (1%)	4,909	2.3	0.1	0.1	27.2	21.9	11.4	13.2	2.2	3,114	1.9	3,439	2.7	5,832
MCI/MI (100 ppm aqs)	4,895	2.3	0.2	0.1	2.8	28.3	52.2	5.3	3.0	3,075	2.9	4,083	2.7	5,792
Amidoamine (0.1% aqs)	4,897	2.3	0.5	0.3	1.8	19.5	61.9	1.8	—	—	—	—	3.4	5,773
EU/MF resin (5%)	4,897	2.3	0.3	0.1	0.9	11.7	55.0	0.9	5.0	3,071	7.2	4,095	5.0	5,799
Lanolin (30%)	4,908	2.2	0.2	0.1	6.6	20.8	54.7	4.7	3.3	3,114	3.3	3,442	2.4	5,834
DMDM hydantoin (1% aqs)	4,897	2.2	0.2	0.1	3.6	27.3	57.3	4.5	2.1	3,064	1.9	4,093	1.6	5,767
p-tert-Butylphenol formaldehyde resin (1%)	4,911	1.9	0.1	0.1	3.2	9.5	34.7	7.4	2.7	3,114	1.8	3,442	1.6	5,832
Glyceryl thioglycolate (1%)	4,897	1.9	0.2	0.2	7.4	25.3	6.3	26.3	2.0	3,075	1.9	4,094	2.0	5,800
Imidazolidinylurea (2% aqs)	4,909	1.8	0.1	0.0	2.3	27.6	60.9	1.1	2.6	3,101	2.5	4,101	2.0	5,821
Benzocaine (5%)	4,908	1.7	0.1	0.1	6.0	14.3	19.0	17.9	2.6	3,112	2.0	3,444	1.7	5,833
Tolsylamide formaldehyde resin (10%)	4,897	1.6	0.1	0.0	10.4	19.5	40.3	9.1	1.6	3,077	1.5	4,097	1.3	5,800
Methyl methacrylate (2%)	4,900	1.4	0.1	0.0	5.6	25.4	26.8	22.5	1.2	3,080	1.6	4,099	1.4	5,812
Glutaraldehyde (1%)	4,878	1.4	0.2	0.6	4.5	35.8	9.0	13.4	2.2	3,076	2.6	4,094	1.9	5,802
Ethyl acrylate (0.1%)	4,899	1.3	0.1	0.1	9.4	17.2	32.8	20.3	1.8	3,074	1.3	4,095	1.3	5,802
Cocamidopropyl betaine (0.5%)	4,888	1.3	0.5	0.2	6.3	15.9	52.4	4.8	—	—	—	—	—	—
DL alpha Tocopherol	4,881	1.1	0.2	0.4	8.9	16.1	50.0	5.4	—	—	—	—	—	—
Budesonide (0.1%)	4,901	1.1	0.2	0.1	11.5	32.7	42.3	0.0	1.1	1,678	1.2	4,098	1.4	5,806
DMDHEU (4.5% aqs)	4,889	1.1	0.2	0.2	0.0	18.5	42.6	3.7	—	—	—	—	—	—
Ylang ylang oil (2%)	4,893	1.1	0.1	0.0	3.6	18.2	63.6	1.8	—	—	—	—	—	—
Black rubber mix (6%)	4,908	1.0	0.0	0.1	5.9	13.7	23.5	3.9	—	—	—	—	—	—
Compositae mix (6%)	4,887	1.0	0.1	0.1	5.9	25.5	35.3	3.9	—	—	—	—	—	—
Mercaptobenzo-thiazole (1%)	4,907	0.9	0.1	0.1	4.4	17.8	55.6	8.9	2.1	3,115	1.8	3,440	2.0	5,834
Dibucaine (2.5%)	4,891	0.9	0.2	0.2	0.0	8.7	6.5	21.7	—	—	—	—	—	—
Thioureas (1%)	4,897	0.8	0.0	0.0	18.4	15.8	44.7	2.6	0.7	3,075	1.3	4,098	1.1	5,807
Jasmine abs (2%)	4,900	0.7	0.2	0.2	0.0	9.4	78.1	3.1	—	—	—	—	—	—

continued

Table 1. Continued

Test Substance*	n	Reaction (%)			Relevance (%)				1994–1996		1996–1998		1998–2000	
		Pos	Unknown	Irritant	Definite	Probable	Possible	Past	Pos (%)	n	Pos (%)	n	Pos (%)	n
Mercapto mix (1%)	4,908	0.7	0.0	0.1	6.1	12.1	63.6	6.1	2.2	3,115	1.8	3,439	1.3	5,834
Lidocaine (15%)	4,892	0.7	0.2	0.1	5.9	5.9	14.7	11.8	—	—	—	—	—	—
Paraben mix (1%)	4,898	0.6	0.1	0.2	10.3	17.2	51.7	3.4	1.7	3,086	1.7	4,096	1.0	5,803
Sesquiterpene lactone (0.1%)	4,896	0.6	0.0	0.0	10.3	41.4	27.6	3.4	0.9	3,073	0.7	4,095	0.9	5,800
Benzophenone (3%)	4,899	0.6	0.1	0.1	7.4	33.3	18.5	3.7	—	—	—	—	0.6	5,800
PCMX (1%)	4,898	0.6	0.1	0.1	0.0	25.0	46.4	0.0	1.2	3,074	1.0	4,093	0.8	5,800
Tetracaine (1%)	4,891	0.6	0.2	0.1	0.0	3.6	17.9	7.1	—	—	—	—	—	—
Hydrocortisone-17-butyrate (1%)	4,888	0.5	0.2	0.1	0.0	22.7	59.1	0.0	—	—	—	—	—	—
DL alpha Tocopherol acetate	4,874	0.5	0.1	0.1	12.0	28.0	32.0	4.0	—	—	—	—	—	—
IPBC (0.1%)	4,897	0.3	0.1	0.2	7.7	0.0	53.8	0.0	—	—	—	—	0.4	5,770
PE (1%)	4,887	0.2	0.1	0.1	9.1	0.0	54.5	9.1	—	—	—	—	—	—
Prilocaine (2.5%)	4,890	0.1	0.1	0.1	0.0	0.0	50.0	25.0	—	—	—	—	—	—

abs = absolute; aqs = aqueous; DMDHEU = dimethylol dihydroxyethyleneurea; DMDM = dimethylol dimethyl; EU/MF = ethyleneurea/melamine formaldehyde; IPBC = iodopropynyl butyl carbamate; MCI/MI = methylchloroisothiazolinone/methylisothiazolinone; MDGN = methyldibromoglutaronitrile; PCMX = p-chloro-m-xenol; PE = phenoxyethanol; Pos = positive.

*All test substances (allergens) are in petrolatum, except those marked as in water (aqs).

The corticosteroid screening allergens were also expanded in the 2001–2002 study period. The results revealed that 3% of patients reacted to tixocortol-21-pivalate, 1.1% reacted to budesonide (0.1% pet), and 0.5% reacted to hydrocortisone-17-butyrate. Information regarding cross-reactivity among these steroid allergens was unavailable.

Discussion

The NACDG continues to evaluate the frequency of allergic reactions to established and new chemicals in an effort to make patch testing current and an effective tool in diagnosing ACD. Many allergens included in the NACDG standard series and not commercially available in the United States had positive-reaction rates of greater than 2%. Among these allergens (by decreasing frequency) are sodium gold thiosulfate, bacitracin, methyldibromoglutaronitrile/phenoxyethanol (Euxyl K400, Schülke & Mayr GmbH, Norderstedt, Germany), benzalkonium chloride, propylene glycol, 2-bromo-2-nitropropane-1, 3-diol (bronopol), diazolidinylurea, imidazolidinylurea, tixocortol-21-pivalate, Disperse Blue 106, dimethylol dimethyl (DMDM) hydantoin, cocamidopropyl betaine (and its putative contaminant, amidoamine), and ethyleneurea/melamine formaldehyde.

Euxyl K400 (0.4% methyldibromoglutaronitrile [MDGN] and 1.6% phenoxyethanol [PE]) in 2% petrolatum caused positive patch-test reactions in 5.8% of our patients. However, MDGN (0.4% in petrolatum) alone caused positive reactions in 0.7% of our group, and PE alone caused positive reactions in only 0.2%. The discrepancy between the number of reactions to Euxyl K400 and its individual constituents is curious but has a number of potential explanations. Chief among these are the following: (1) the combination is irritant, and the reactions are falsely interpreted; (2) the combination is mildly irritant and allows for the development of a positive patch-test reaction to a suboptimal concentration of the actual allergen (MDGN vs PE); and (3) the combination results in a chemical reaction that produces the actual allergen. The European experience with this preservative showed that significant numbers of consumers were sensitized to this chemical as a result of higher concentrations in leave-on products than have been allowed in the United States (where “leave-ons” have been restricted to a maximum MDGN concentration of 0.025%).⁹ The NACDG series for the 2003–2004 study uses MDGN (2% pet) alone. PE (1% pet) and MDGN (0.4% pet) have been dropped.

Tixocortol-21-pivalate (1% pet), a marker for some topical corticosteroid allergies, gave positive reactions in

3% of our patients. Budesonide 0.1% in petrolatum was added to the NACDG series in July 1998 and yielded positive reactions in 1.1% of patients tested in the 2001–2002 period. The European literature suggests that testing at a lower concentration may be more accurate because of the initial antiinflammatory and vasoconstrictive nature of corticosteroids. A lower concentration would reduce the effects of the steroid and make the testing more accurate. Therefore, budesonide 0.01% in petrolatum was added to our 2003–2004 series. Hydrocortisone-17-butyrate (2% pet) caused positive reactions in 0.5% of the study group. These three tests for corticosteroid allergy were a significant addition to the NACDG standard series. Previously, ACD from topical corticosteroids frequently went unrecognized and was misdiagnosed.¹⁰ In the new 2003–2004 series, we have expanded our corticosteroid screeners to include not only budesonide (0.01% pet) but also triamcinolone acetonide (1% pet) and clobetasol-17-propionate (1% pet).

In the 2001–2002 tray, several local anesthetics were added to determine whether the introduction of eutectic anesthetic preparations would result in a rise in allergic reactions to their constituents and because the literature suggested that individual “caine” antigens performed better than the mix did. Among our patients, 1.7% reacted to benzocaine, with a present and past combined relevance of 57.2%; 0.69% reacted to tetracaine, with a past and present relevance of 28.6%; 0.7% reacted to lidocaine, with a past and present relevance of 38.3%; and 0.9% reacted to dibucaine, with a present and past relevance of 36.9%. (Past and present relevance is a combined relevance. In this article, the present component includes definite, probable, and possible relevances. Definite relevance values are listed in Table 1.)

In the 2001–2002 study period, 2.8% of tested patients had positive reactions to CAPB while 2.3% had positive reactions to amidoamine. The present and past combined relevance of the CAPB reactions was 90.9% whereas the combined relevance of amidoamine reactions was 85%. In the 2003–2004 series, coconut diethanolamide was included also to expand the search for significant contact allergy to foaming agents in shampoos.

Thimerosal caused positive reactions in 10.2% of the patients. Present relevance was only 7.3%, and past relevance was 26.4%, which usually related to the use of ear and eye drops in childhood or perhaps to vaccination. Because of the very low present relevance, this allergen was dropped from the 2003–2004 series.

Gold sodium thiosulfate caused positive reactions in 10.2% of the group. It had a combined present relevance

of 37.3%, of which only 0.2% was definite. Its past relevance among our patients was 7%. Gold frequently caused persistent (> 6 weeks) indurated reactions. Given this and its low definite relevance, it will be dropped from the 2005–2006 tray.

In the 2001–2002 series, 1.1% of patients reacted positively to DL-alpha-tocopherol, and 0.5% reacted positively to DL-alpha-tocopherol acetate. All patients who reacted positively to DL-alpha-tocopherol acetate reacted to DL-alpha-tocopherol. Hence, the DL-alpha-tocopherol acetate formulation was dropped from the 2003–2004 series.

In the 2001–2002 series, iodopropynyl butyl carbamate (IPBC) (0.1% pet) was added. It caused positive reactions in only 0.3% of patients. Its combined present and past relevance was 61.5%. The correct concentration for testing this allergen remains to be determined. Several European investigators have recommended higher concentrations. In the new 2005–2006 tray, the NACDG will test IPBC at 0.1% and 0.5% in petrolatum. Of note, IPBC and carba mix do not appear to cross-react.

Compositae mix was added to the 2001–2002 series. It caused positive reactions in 1% of patients, as compared to the 0.6% of patients who had positive reactions to sesquiterpene lactone (SQL) mix. SQL mix had a combined present and past relevance of 87.7%; for the Compositae mix, this number was 70.6%.

Bacitracin caused positive reactions in 7.9% of patients. Previous studies found this topical antibiotic a significant allergen in patients with leg ulcers, with otitis media or externa, or with a history of prior dermatologic surgery.^{11,12} Bacitracin had a present and past relevance rate of 73%. In the 1999–2000 study period, it caused positive reactions in 9.2% of patients tested.

Ethyleneurea/melamine formaldehyde (EU/MF) was previously found to be the best screening agent for detecting ACD from permanent-press clothing.^{13,14} Patients sensitive to this textile resin often had dermatitis affecting areas covered with clothing although some of the reactions were generalized, and some patients had follicular patterns and/or nummular morphologies.¹³ The head and neck were often uninvolved, as were the palms, unless the patient worked in the textile industry. According to the 2001–2002 data, EU/MF caused positive reactions in 2.3% of the patients, with a 67.6% present and past relevance. In the 1998–2000 study period, EU/MF caused positive reactions in 5% of the patients.

Although EU/MF has been reported to be the best screening allergen for textile resin reactions,^{13,14} it is not used in clothing but rather in upholstery and carpeting and in industrial applications. Dimethylol dihydroxy-

ethyleneurea (DMDHEU) was added to the 2001–2002 series after a recent study revealed its value.¹⁵ The NACDG found that it caused positive reactions in 1.1% of patients, with a relevance of 64.8%. In contrast to EU/MF, DMDHEU is used as a textile resin in clothing.

Another significant frequent relevant textile allergen added to the 2001–2002 study series was Disperse Blue 106; 3% of patients had positive reactions, with a present and past relevance of 61.3%. Disperse Blue 106 is frequently used in synthetic fibers such as polyester, acetate, and nylon. Disperse dyes wash off easily. They are usually in the azo chemical class that cross-reacts with the hair dye para-phenylenediamine 20% of the time.¹⁶ In one recent study, Disperse Blue 106 was found to cause positive reactions in 80% of patients who were allergic to textile dyes.¹⁶

Cosmetics are an extremely important and common cause of ACD, especially on the eyelids, face, and hands. The NACDG screens with several formaldehyde-releasing preservatives in various concentrations and vehicles. Quaternium-15 was found to yield positive reactions in 9.3% of patients and had a past and present relevance of 87.6%. Formaldehyde was found to cause positive reactions in 8.4% of patients, with a 71.5% combined relevance rating. 2-Bromo-2-nitropropane-1,3-diol (bronopol) caused positive reactions in 3.3%, with a 71.9% combined relevance. Diazolidinylurea (1% aq) caused positive reactions in 3.2%, with a 93% positive combined relevance. Diazolidinylurea at 1% in petrolatum yielded positive reactions in 3.1%, with a 94.7% combined relevance. Imidazolidinylurea (2% pet) caused positive reactions in 3% and had a combined relevance of 95.3%. DMDM hydantoin at 1% in petrolatum caused positive reactions in 2.8%, with a 96.3% combined relevance. DMDM hydantoin at 1% in aqueous solution caused positive reactions in 2.2%, with a 92.7% combined relevance. Finally, imidazolidinylurea (2% aq) caused positive reactions in 1.8%, with a 91.9% combined relevance rating. All of these antigens remain in the 2003–2004 series. The combined present and past relevances are very high in this entire group, ranging from 71.5 to 96.3%.

Nonformaldehyde-releasing preservatives also accounted for ACD in our patients. Methylchloroisothiazolinone/methylisothiazolinone (Kathon CG, Rohm and Haas, Philadelphia, PA) caused positive reactions in 2.3% of patients, with an 87.6% present and past relevance rating.

Paraben mix caused positive reactions in only 0.7% of the group, with a present and past relevance of 82.6%, again confirming that parabens are not common cosmetic preservative allergens.

Benzalkonium chloride, a frequent preservative in eye drops and occasionally in cosmetics, disinfectants, and cleaners, caused positive reactions in 4.3%, with a present and past relevance of 35.4%.

Glutaraldehyde, an irritant and potential allergen in cold sterilization products used in dentistry, endoscopy, and uroscopy,¹⁷ caused positive reactions in 1.4% of patients, with a present or past relevance of 62.7%. Glutaraldehyde was an irritant 0.6% of the time.

Jasmine absolute and ylang ylang oil were added to the 2001–2002 series after an article by Larsen and colleagues suggested that the yield of relevant fragrance allergies would be enhanced by their inclusion.¹⁸ Jasmine absolute caused positive reactions in 0.7% whereas ylang ylang oil caused positive reactions in 1%. Cinnamic aldehyde, which was removed from the 2001–2002 study series, was reintroduced in the 2003–2004 series after reconsideration of its value. In the past, it caused positive reactions in 3.6% of patients studied (1999–2000 study period). Fragrance mix caused positive reactions in 10.4%, and *Myroxylon pereirae* (balsam of Peru) caused positive reactions in 11.6% of the group. The relevance of fragrance allergy is difficult to determine, and because this is done inconsistently, the relevance values are highly controversial.

Appropriate history, skin examination, and patch testing can lead to significant benefit in the diagnosis and care of patients with eczematous eruptions.^{19–21} Only a limited number of TRUE Test allergens are available in the United States. TRUE Test contains only 23 allergens and/or mixes. Our findings that 16.7% of the patients had relevant allergic patch-test reactions to supplemental allergens not in the NACDG standard series (which contains 65 allergens and/or mixes) and that 5.5% of reactions were related to occupation reinforce the need for a more comprehensive group of diagnostic allergens. If one were to consider the number of relevant allergens missed when only TRUE Test is used, the numbers would be far greater than when only the NACDG standard is used.²²

Patch testing remains a worthwhile diagnostic tool in the evaluation of patients with suspected ACD. The results need to be evaluated and interpreted skillfully and cautiously because of the difficulties in defining and recognizing allergic and irritant reactions and in determining the relevance of a patient's reactions to their dermatitis. Awareness of the changing trends in regard to what allergens should be used in patch testing and at what concentration and in which vehicle is imperative. The screening series is meant to evolve over time, based on

experience with previously tested allergens and the introduction of new ones.

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