

Use of the North American Contact Dermatitis Group Standard 65-Allergen Series Alone in the Evaluation of Allergic Contact Dermatitis: A Series of 794 Patients

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Background: The “gold standard” for diagnosing allergic contact dermatitis is patch testing. Previous studies have not adequately addressed the validity and usefulness of the North American Contact Dermatitis Group (NACDG) Standard 65-allergen series alone as a screening tool in the evaluation of contact dermatitis.

Objective: The purpose of this study is to examine the usefulness of the NACDG series of 65 allergens as an exclusive screening method in the diagnosis of contact allergy.

Methods: A retrospective chart review of 794 patients referred for patch testing with the NACDG Screening Series with or without additional allergens was performed to determine the number of positive patch-test results. The study groups were analyzed to identify whether the positive reactions were to allergens in the NACDG Standard Series or to allergens in the supplementary group.

Results: Of the 794 patients patch-tested between July 1, 2004, and July 1, 2006, 590 (74.31%) had a positive reaction to either an NACDG patch-tested allergen or a supplemental allergen; 386 (65.42%) patients testing positive for an allergen were positive to an NACDG allergen only, and 534 (90.51%) of the total positive reactors were positive for at least one NACDG test allergen.

Conclusion: As a screening tool, the NACDG Standard Series is substantially more efficacious than are more limited standard series when used exclusively in the evaluation of patients with allergic contact dermatitis. More extensive testing, including testing with suspected supplementary allergens determined by thorough history and physical examination, can improve upon the NACDG series as a means to investigate the full causes of contact dermatitis in any individual patient.

ALLERGIC CONTACT DERMATITIS (ACD) is a common reason patients present to the dermatologist. Awareness and interest in ACD has risen steadily since World War II. Clinics for patch testing existed as early as the late 1800s, but following World War II, many new clinics opened, first in the United Kingdom and subsequently in the United States. However, as research and interest in ACD rose over time, it became apparent that researchers were using different methods and concentrations of allergens. Patch testing continued without any standardization that would allow for comparisons. The International Contact Dermatitis Research Group was formed in the late 1960s from an amalgamation of European organizations to coordinate and standardize patch testing worldwide. This organization inspired the formation of a domestic group, the North

American Contact Dermatitis Group (NACDG), which became active in the validation and efficacy studies needed to gain Food and Drug Administration (FDA) approval for commercial patch testing. The first system approved included 20 allergens in what was known as the Allergen Patch Test Kit (Hermal Pharmaceutical Labs, Oak Hill, NY) and was used in the United States before 1995. The most common test used for ACD screening today and the only FDA-approved patch test is the Thin-Layer Rapid Use Epicutaneous (T.R.U.E.) Test (Allerderm Laboratories, Petaluma, CA), which now contains 29 allergens. Since the 1980s, the NACDG has worked to study and test new allergens suspected in eliciting ACD. Their series began as 20 allergens, increased over time to 50 allergens, and had 65 allergens at the time of our study. All 28 of the 29 T.R.U.E. Test allergens were included in the NACDG series at the time of this study, with the exception of quinolone mix.

Patch testing aims to detect the allergens responsible for contact sensitivities in patients with ACD. The usefulness of patch testing has been confirmed in many studies,¹⁻³ and the validity of using an “expanded” series such as the NACDG Standard Series has been examined as

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DOI 10.2310/6620.2008.06061

well.⁴ Several authors have written specifically about the T.R.U.E. Test and its limitations as a standard screening series and have shown that the test is not adequate as a screening tool.⁵

The objective of this study was to investigate the percentage of allergens that are not detected if only the NACDG Screening Series, without the addition of suspected supplemental allergens, is used for patch testing. Previous studies have not adequately discussed whether the NACDG Screening Series is effective in comparison to more extensive testing with supplemental allergens.

Patients and Methods

The patients who were evaluated in this study were from the New York University Medical Center Ronald O. Perleman Department of Dermatology Skin and Cancer Center Contact Allergy Unit and the Dermatologic Associates Faculty Practice of the New York University School of Medicine. All patients were suspected of having ACD by their referring dermatologists. Male and female patients more than 16 years of age were included in the study. Patients requiring photopatch testing either alone or in conjunction with routine patch testing were excluded from the study. Patients who were patch-tested with allergen batteries that did not include the NACDG Standard Series were excluded from this analysis. In addition, pregnant women were not tested.

The study is a retrospective chart review done on 794 patients who received patch tests between July 1, 2004, and July 1, 2006. The study was designed, reviewed, and approved by the Internal Review Board at the New York University School of Medicine. The patch testing method used Finn Chambers (Epitest Ltd. Oy, Tuusula, Finland) and Scanpor tape (Alpharma AS, Norgesplaster, Vennesla, Norway) placed on the upper back as previously described.⁶ The location of the allergens was documented on a separate paper grid for interpretation. The 65 allergens of the NACDG Standard Series (Table 1), last updated in the period from 2001 to 2002, were placed on each patient.⁷ Patients were tested with supplementary allergens if deemed necessary by the clinician after an occupational and environmental history from the patient and a physical examination. Previous patch testing did not influence the assignment of allergens to be tested. The number of supplementary allergens ranged from none to 100. The average number of allergens (both NACDG standard allergens and supplementary allergens) tested on the patients was 86.40. Supplementary allergens were materials obtained from commercial and other sources

and included personal products that were tested without alteration.

The patches were removed 48 hours after placement, at which time an initial reading was performed. A final reading and interpretation was performed either on day 4 or day 7. Reactions were positive if scored according to NACDG criteria with a 1, 2, or 3 rating during initial readings and were then labeled allergic (score of 1) as the final interpretation. If a patient registered a negative reaction at the initial reading but subsequently had a positive reaction, the patients was also considered to be allergic on final interpretation. Macular erythema (score of 4) and irritancy (score of 5) were considered negative.⁸

Patient charts in the study were reviewed and analyzed for positive reactions to patch-tested allergens. All 794 charts were reviewed for positive reactions to NACDG standard allergens only, supplementary allergens only, at least one NACDG allergen and one supplementary allergen, at least one NACDG allergen, and either an NACDG allergen or a supplementary allergen.

Results

The results are summarized in Table 2. Between July 1, 2004, and July 1, 2006, 794 patients were patch-tested; 74.31% had at least one positive reaction, either to an NACDG standard allergen or a supplementary allergen. On average, there were 2.41 positive reactions per person, with an average of 86.40 patches tested per person. Of patients testing positive, 65.42% (386) were positive exclusively for NACDG standard allergens; 9.15% (54) of patients testing positive were positive exclusively for supplementary allergens, 25.08% of patients were positive for at least one NACDG and one supplementary allergen, and 90.51% of patients were positive for at least one NACDG standard allergen. This group, represented by column E in Table 2, is mutually exclusive of the data analyzed and included in columns A and C.

Discussion

The “gold standard” for identifying specific allergens that cause ACD is patch testing.⁹ In general, patients who are patch-tested during the course of their diagnosis and treatment experience a shorter postdiagnosis duration of disease than those who are not patch-tested.¹⁰ This is likely due to the early opportunities for interventions, such as avoidance of offending chemicals and products.

The results of this study show that the NACDG Standard Series of 65 allergens is comprehensive and may

Table 1. North American Contact Dermatitis Group Standard 65 Allergens

Benzocaine 5% pet	Propylene glycol 10% aq
Mercaptobenzothiazole 1% pet	Benzophenone-3 3% pet
Colophony 20% pet	Chloroxyleneol (PCMX) 1% pet
para-Phenylenediamine 1% pet	DMDM hydantoin 1% aq
Imidazolidinylurea 20% aq	Diazolidinylurea 1% aq
Jasmine absolute 2% pet	Ethyleneurea/melamine formaldehyde 5% pet
Lanolin alcohol 30% pet	Methyldibromoglutaronitrile/phenoxyethanol 2% pet
Carba mix 3% pet	Iodopropynyl butyl carbamate 0.1% pet
Neomycin sulfate 20% pet	dl- α -Tocopherol 100%
Thiuram mix 1% pet	Sodium gold thiosulfate 0.5% pet
Formaldehyde 1% aq	Ethyl acrylate 0.1% pet
Ethylenediamine dihydrochloride 1% pet	Glyceryl thioglycolate 1% pet
Epoxy resin 1% pet	Tosylamide/formaldehyde resin 10% pet
Quaternium-15 2% pet	Methylmethacrylate 2% pet
p-tert-Butylphenol formaldehyde resin 1% pet	Cobalt chloride 1% pet
Mercapto mix 1% pet	Tixocortol-21-pivalate 1% pet
IPPD 0.1% pet	Budesonide 0.1% pet
Potassium dichromate 0.25% pet	Hydrocortisone-17-butyrate 1% pet
<i>Myroxilon pereirae</i> (balsam of Peru) 25% pet	Disperse Blue 106 1% pet
Nickel sulfate 2.5% pet	Tetracaine 1% pet
Diazolidinylurea 1% pet	Lidocaine 15% pet
DMDM hydantoin 1% pet	Dibucaine 2.5% pet
Imidazolidinylurea 2% pet	Ylang ylang oil
Bacitracin 20% pet	Prilocaine 2.5% pet
Mixed dialkyl thioureas 1% pet	Cocamidopropyl betaine 1% aq
Methylchloroisothiazolinone/methylisothiazolinone 100 ppm aq	Phenoxyethanol 1% pet
Paraben mix 12% pet	Benzalkonium chloride 0.1% aq
Methyldibromoglutaronitrile 1% pet	Dimethylol Dihydroxyethyleneurea 4.5% aq
Fragrance mix 8% pet	Cocamide DEA 0.5% pet
Amidoamine 0.1% pet	Compositae mix 5% pet
2-Bromo-2-nitropropane-1,3-diol 0.5% pet	Glutaral 1% pet
Sesquiterpene lactone mix 0.1% pet	Dimethylaminopropylamine 1.0% aq
Thimerosal	

aq = aqueous; DEA = diethanolamine; DMDM = dimethylol dimethyl; IPPD = N-isopropyl-N'-phenyl-4-phenylenediamine; PCMX = p-chloro-m-xyleneol; pet = petrolatum; ppm = parts per million.

provide an adequate level of screening for ACD. In this case, 65.42% of the patients who had positive reactions were exclusively positive for an NACDG allergen alone.

Only 9.15% were positive for a supplemental allergen alone. However, 25.08% of patients were positive for at least one NACDG standard allergen and one supplemental

Table 2. Patch-Test Results by Positive Reactions to Series and Supplemental Allergens

	Positive Reaction Group				
	(A) NACDG Allergens Exclusively	(B) Supplemental Allergens Exclusively	(C) At least 1 NACDG and 1 Supplemental Allergen	(D) At least 1 NACDG or Supplemental Allergen	(E)* At least 1 NACDG Allergen
Patients with positive reactions	386/590 (65.42%)	54/590 (9.15%)	148/590 (25.08%)	590/794 (74.31%)	534/590 (90.51%)

NACDG = North American Contact Dermatitis Group.

*This group combines groups A and C.

allergen. If patients had not been tested with supplementary allergens, 34.23% of patients (see columns B and C in Table 2) would have had one or more allergens missed during the course of their diagnosis. Overall, 90.51% of patients who had positive reactions to an allergen had positive reactions to an NACDG standard allergen, showing that the allergens currently listed provide ample breadth of screening chemicals and lead to a high level of diagnosis in the majority of patients. The results of this study are in concordance with the biannual study done by the NACDG to evaluate the allergens included in their full standard series. In the evaluation done from 2001 to 2002, 69% of patients with a positive reaction had a positive result to one of the allergens in the series.⁷ The NACDG series provides a high level of screening and diagnostic sensitivity for contact allergens, but those patients (25%) who had positive reactions to supplementary allergens in addition to an NACDG standard allergen show that any one standard series may be incomplete for accurate diagnosis.

In the study by Saripalli and colleagues, 25% of patients testing positive for an allergen were positive for an allergen on the T.R.U.E. Test.⁵ Our study shows that using the entire NACDG series improves the allergen detection rate to 65%. Other authors, such as Larkin and Rietschel, have made the argument for patch testing to a larger sample of allergens,¹¹ but not all patients would benefit from extensive patch testing. It is critical to determine by clinical history which patients would benefit from a larger standard series with supplementary allergens versus those who might benefit from more-targeted allergen testing.¹² The risk in overtesting a patient is that by statistical chance alone, positive reactions may occur that may not be clinically relevant.¹³ Also, our study did not address the relevance of the positive patch-test reactions.

Interpretation of patch tests may be done by more than one physician, leading to interobserver bias; in this study, only two dermatologists (experienced in patch testing) participated in the reading, recording, and interpretation of the patch tests. We would expect a similar bias to occur in regard to those allergens in the NACDG Standard Series as well as those not included in the series. Potential confounding factors are thereby reduced although not eliminated. Another concern that may arise while assessing the results of this study is the high positive rate for patch testing in general. This is likely a consequence of the patient demographics and selection bias. The majority of the patients used in this study were referred from community dermatologists, likely causing the sample to have a higher percentage of patients experiencing positive results. However, even with the higher percentage of patients having positive results, it can be

gleaned that the chance the 65-allergen series will miss the diagnosis entirely is 9.15%, and the chance that it will underdiagnose is 25%.

Conclusion

Overall, our study shows that use of the North American Contact Dermatitis Group (NACDG) series detects all of the allergens in 65% of patients and at least one allergen in 90% of patients. The addition of supplementary allergens increases the diagnostic accuracy of patch testing in 34% of patients. Previous studies have shown that the NACDG series is more effective than the commercially available T.R.U.E. Test. The data from this study further point to the importance of adding supplementary allergens even to the already comprehensive set of allergens used in the NACDG series. A standard series is an important starting point for analyzing and screening for potential contact allergies, but the increased diagnostic accuracy in 34% of patients tested suggests that testing based on a detailed medical, environmental, and occupational history is critical for identifying the correct allergens.

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