

Should Macular Erythema Reactions Be Counted as Positive Allergic Patch-Test Reactions?

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Background: Positive allergic patch-test results are generally described as erythematous papules, vesicles, or a spreading reaction with crust and ulceration. This description excludes milder reactions, including macular erythema.

Objective: Our aim was to investigate the prevalence and relevance of reactions graded as macular erythema at Mayo Clinic.

Methods: Between January 2001 and June 2004, patients suspected of having allergic contact dermatitis were patch-tested with our institution's standard patch test, a screening series of 68 to 72 allergens. In total, 2,823 patients were patch-tested with 193,530 allergen applications. Reactions were interpreted with the North American Contact Dermatitis Group scale, including and excluding reactions graded as macular erythema. Irritant reactions were excluded from calculations. For this study, scores for current, questionable, and past relevance were combined.

Results: On day 5, with the exclusion of reactions graded as irritant, 7,274 allergen applications were associated with reactions, including 3,082 (42.4%) that were graded as macular erythema. Of the macular erythema reactions, 2,430 (78.8%) were graded as relevant. The rate of reaction in our patients was 2.2% if macular erythema was excluded, 3.8% if all macular erythema reactions were included, and 3.4% if only those macular reactions deemed relevant were included.

Conclusion: Patch-test reactions rated as macular erythema are common and may be of clinical relevance. For the purposes of patient education, they should not be disregarded. Consideration should be given to including these reactions when reporting patch-test results.

PATCH TESTING involves placing allergens on the skin (usually on the back) on day 1, removing the allergens after approximately 48 hours, and interpreting the cutaneous reaction. An initial reading is performed after the allergens are removed on day 3 (ie, 48 hours after allergen placement), and a second reading is performed usually on day 5, 6, or 7. The first and second readings are essential for deciding whether the reaction to an allergen is more likely to be irritant (the reaction usually decreases between the two readings) or allergic (the reaction usually increases between the two readings). Other factors may be important in deciding whether a reaction is irritant or allergic. The relevance of the patch-test reaction is determined in the context of the patient's history and skin examination findings.¹

The North American Contact Dermatitis Group (NACDG) includes North American physicians who specialize in patch testing and provides expert guidance and a

reference point for others who perform patch testing. Periodically, the NACDG reports the results of patch testing with a standard series.¹⁻⁴ The NACDG grades a reaction as a negative reaction; as macular erythema; as erythema, infiltration, and possibly papules; as erythematous papules or vesicles (or both); as spreading blisters or crust with ulceration (or both); or as an irritant reaction.¹ A positive allergic patch-test reaction is "generally interpreted to be" a reaction manifested by erythematous papules, vesicles, or a spreading reaction with crust and ulcerations.¹⁻⁴ This definition of an allergic patch-test reaction, however, does not explicitly recognize macular erythema, which is the grade between the grade for a negative reaction and the grade for erythema, infiltration, and possibly papules. The NACDG may grade a reaction as questionable (macular erythema) but may also interpret that questionable reaction as allergic (Dr. James G. Marks, personal communication, July 2004), although this is not documented in the reports from NACDG.¹⁻⁴

Anecdotally, we noted that many of the reactions we saw at our institution were interpreted as macular erythema—reactions that showed erythema but no evidence of infiltration, papules, or vesicles. Many of these reactions were thought to be relevant.

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Table 1. Patch-Test Reactions Graded as Macular Erythema on Day 5

Relevancy	Frequency (n = 3,082)	%
Missing values	51	1.65
Allergic reactions		
Not relevant	601	19.50
Past relevance	88	2.86
Questionable relevance	1,180	38.29
Relevant	1,162	37.70

If these reactions are common and relevant, we wondered, why are they excluded from (or not explicitly included in) the definition of a positive allergic patch-test reaction? Furthermore, if they are not important, should patients be advised to disregard them? In an attempt to answer these questions, we retrospectively examined the prevalence of these reactions and whether they were deemed relevant by physicians in our institution's practices.

Methods

We analyzed the results from patch testing with our institution's standard series, a screening series of 68 to 72 allergens, over 3.5 years (between January 2001 and June 2004) at Mayo Clinics in Arizona, Florida, and Minnesota. Patients suspected of having allergic contact dermatitis were evaluated and then patch-tested with a standard series of allergens (mean number of allergens, 68.55; median, 69; standard deviation, 4.49) purchased from Chemotechnique Diagnostics AB (Malmö, Sweden) and from our institu-

tion's pharmacy. This standard series is similar to that used by the NACDG. A total of 2,823 patients were patch-tested with 193,530 allergen applications. The patients were patch-tested with a standardized technique (previously outlined by the NACDG)²⁻⁴ using Finn Chambers (Epitest Ltd Oy, Tuusula, Finland) on Scanpor tape (Norgesplaster A/S, Vennesla, Norway). The patches were removed 48 hours after initial placement (ie, on day 3), and test sites were evaluated twice (initially on day 3 and again on day 5, 6, or 7). The reactions were interpreted with the NACDG grading scale. After patch testing was completed, the results were entered into a *Uniface* database (March Hare Software Ltd., London, UK) and analyzed.

Reaction rates were studied in three ways: (1) exclusion of macular erythema reactions, (2) inclusion of macular erythema reactions, and (3) inclusion of macular erythema reactions deemed to be relevant. The relevance of the patch-test reactions was determined in the context of the patient's history and skin examination findings. For the purposes of this study, current, questionable, and past relevance scores were combined into one score.

Results

The results of patch testing are summarized in Tables 1 and 2. On day 5, with the exclusion of reactions graded as irritant, 7,274 allergen applications were associated with reactions, including 3,082 (42.4%) that were graded as macular erythema. Of the macular erythema reactions, 2,430 (78.8%) were graded as being of relevance (current, questionable, and past relevance were combined).

Table 2. Top 10 Allergens Leading to Macular Erythema Reactions

Allergen*†	No. of Patients Tested	No. of Patients with Reactions (%)	
		Positive Nonmacular Erythema Reactions	Macular Erythema Reactions
Balsam of Peru, 25%	2,734	195 (7.1)	223 (8.2)
Fragrance mix, 8%	2,770	173 (6.2)	165 (6.0)
Benzalkonium chloride, 0.1% aqueous	2,753	97 (3.5)	163 (5.9)
Cobalt chloride, 1%	2,643	205 (7.8)	136 (5.1)
Potassium dichromate, 0.25%	2,718	102 (3.8)	135 (5.0)
Gold sodium thiosulfate, 0.5%	2,523	234 (9.3)	131 (5.2)
Nickel sulfate hexahydrate, 2.5%	2,737	406 (14.8)	121 (4.4)
<i>Dermatophagoides</i> mix, 20%	745	183 (24.6)	111 (14.9)
Neomycin sulfate, 20%	2,779	256 (9.2)	106 (3.8)
Methyldibromo glutaronitrile	2,753	93 (3.4)	94 (3.4)
phenoxyethanol, 1.5%			

*Allergens are listed in decreasing order of macular erythema frequency.

†Allergens were in petrolatum unless otherwise noted.

The rate of reaction in our patients was 2.2% if macular erythema was excluded, 3.8% if all macular erythema reactions were included, and 3.4% if only those macular reactions deemed relevant were included.

Discussion

In the patients studied, the rate of positive allergic patch-test reactions was 2.2%, 3.8%, or 3.4%, depending on whether the macular erythema reaction rate was included or excluded and whether relevance was taken into account. Which of these rates is correct?

The question is not simply academic, because it raises the very practical concern as to what patients should be told about their macular erythema reactions. Should they be told to ignore the reactions that are graded as macular erythema? Should they be told to avoid all allergens associated with macular erythema or only those allergens deemed to be of relevance by the consulting physician?

We propose that macular erythema reactions be subject to the same scrutiny for relevance as are stronger reactions (infiltration and papules, erythematous papules or vesicles) and should not be categorically deemed negative. For example, a macular erythema reaction should be considered relevant in a patient who demonstrates macular erythema to fragrance mix and whose dermatitis clears on cessation of the use of eau de toilette and flares on re-exposure to the fragrance. In contrast, a macular erythema reaction should not be considered relevant in a patient who has a macular erythema reaction to Disperse Blue 126 and who can comfortably wear all colors of various synthetic fabrics. Further, we propose that in reports of patch-test reaction rates, macular erythema reactions of relevance be explicitly included in the calculation of allergic patch-test reactions.

We recognize the shortcomings of our study. Although we excluded irritant reactions in these calculations (ie, reactions that diminished between the first and second

readings and other reactions that were thought by our physicians to be irritant reactions), some of the reactions may have represented irritant reactions. However, the strengths of this study include the large number of patients studied and the use of a standardized means of grading patch-test reactions (overseen by our institution's Contact Dermatitis Core Group).

Conclusion

Patch-test reactions that are graded as macular erythema are common (42.4% of all reactions, in our experience) and are often of clinical relevance. Therefore, reactions that are graded as macular erythema should not be discounted when counseling patients, and consideration should be given to explicitly including these reactions when reporting patch-test results.

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References

1. Marks JG, Belsito DV, DeLeo VA, et al. North American Contact Dermatitis Group standard tray patch test results (1992 to 1994). *Am J Contact Dermat* 1995;6:160–5.
2. Pratt MD, Belsito DV, DeLeo VA, et al. North American Contact Dermatitis Group patch-test results, 2001–2002 study period. *Dermatitis* 2004;15:176–83.
3. Marks JG Jr, Belsito DV, DeLeo VA, et al. North American Contact Dermatitis Group. North American Contact Dermatitis Group patch-test results, 1998 to 2000. *Am J Contact Dermat* 2003;14:59–62.
4. Marks JG, Belsito DV, DeLeo VA, et al. North American Contact Dermatitis Group patch test results for the detection of delayed-type hypersensitivity to topical allergens. *J Am Acad Dermatol* 1998;38:911–8.