

Metal Hypersensitivity Reactions to Implants: Opinions and Practices of Patch Testing Dermatologists

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Background: Cutaneous metal hypersensitivity reactions (MHR) are common but rare with implanted devices.

Objectives: This study aimed to characterize the opinions of dermatologists who are actively evaluating/advising patients with MHR.

Methods: A questionnaire was distributed to all individuals who attended the European Society of Contact Dermatitis (ESCD) 2012 and the American Contact Dermatitis Society 2013 meetings.

Results: A total of 119 individuals responded with a participation rates of 10% (ESCD) and 32% (American Contact Dermatitis Society). Ninety-six percent of the respondents evaluate MHR and 91% were attending physicians. Orthopedic and dental devices were common problems compared with cardiovascular devices. Patch testing is the top choice for evaluating MHR. Lymphocyte transformation and intradermal tests are rarely used. Eighty-two percent of the respondents evaluate plastic/glue components in symptomatic patients postimplant. Most dermatologists use a tray specifically for joint allergy or a history-based custom array of allergens. Those patients with a strong clinical history of metal allergy should be evaluated before metal implantation (54%), whereas others forgo evaluation and recommend a titanium implant based on history alone (38%). Diagnostic criteria for postimplant reactions were evaluated. Eight percent of the respondents felt that no evaluation was necessary, with ESCD respondents being significantly more likely to not recommend evaluation ($P = 0.001$).

Conclusions: Metal hypersensitivity reactions consultation requests are common for preimplant and postimplant issues. Patch testing is currently the best test for MHR.

BACKGROUND

Hypersensitivity reactions to metal exposures are common, and nickel, cobalt, and chromium remain some of the most common allergens on patch test series worldwide. The recent North American Contact Dermatitis Group data from 2009–2010 had nickel, cobalt, and chromium in their most prevalent allergens at 15.5%, 6.2%, and 2.3%, respectively.¹ Allergic contact dermatitis after cutaneous exposure to, for example, jewelry, belt buckles, fasteners, leather, and other metal-releasing everyday items is not only common but often relatively straightforward to clinically diagnose and solve. Patch test reactivity to other metals such as molybdenum, manganese, and

titanium occurs less commonly but occasionally plays important roles in metal hypersensitivity reactions (MHR) to implanted metallic devices. However, MHR to implants, whether dental, cardiac, or orthopedic, are often much more difficult to diagnose and manage because the cause-and-effect relationship is complex and often difficult to determine. Although MHR to cardiac stents initially were of much concern,² there seems to be minimal support for in-stent restenosis of bare stainless steel devices,^{3,4} whereas gold-plated stents increased the risk for chest pain and restenosis after placement.⁵ Moreover, MHR to static and dynamic orthopedic devices are controversial in almost every aspect, and recent review articles and comments published in the dermatology journals have addressed the great complexity and provided practical suggestions for their diagnosis and management.^{6–12} Because of the increasing age of Western populations as well as the number of implantations, a growing number of patients are referred to dermatologists for metal patch testing either before or after surgery. At present, there is little evidence-based guidance for the correct work-up of patients with MHR to implants, and physicians are left with the experience and consensus agreements provided by their peers. Dermatologists who only occasionally manage patients suspected with MHR to implants

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TABLE 1. Metal Implant Hypersensitivity Survey

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1. Do you evaluate patients with suspected metal hypersensitivity reactions to metallic implants (eg, orthopedic prostheses or plates, cardiac stents, pacemakers, dental devices)?

☐ YES☐ NO

Comments: _____

2. What percent of your metal hypersensitivity patients fall into each of the following categories?

Device Type

Share of Metal Patients

Dental

%

Cardiovascular (eg, pacemakers, stents, occluders)

%

Implanted orthopedic (eg, total hip/knee replacements, plates)

%

Other metal devices

%

TOTAL

100%

3. Which evaluation method(s) do you typically use to evaluate metal hypersensitivity reactions to implanted devices? Use a scale of 1 to 7, where 1 is never and 7 is always.

Method

1 (Never)

2

3

4

5

6

7 (Always)

Patch testing

Lymphocyte transformation test (LTT) or similar in vitro test

Intradermal testing

4. When you patch test for evaluation of implanted metal hypersensitivity reactions, do you use a specific tray/series for that purpose (eg, device allergy tray)?

☐ Yes, I have a standard series that I use in all my patients with metal implant hypersensitivity reactions.☐ No, based on the medical history and the content of the implant, I pick specific allergens every time.☐ No, I only use the European/North American baseline series (or similar standard screening series).

5. How should a patient with a medical history of moderate to severe metal dermatitis be managed before implantation of a medical device? (Check all that apply.)

☐ Patch testing and/or in vitro testing (LTT or similar) should be performed to identify metal hypersensitivity.☐ The patient and the treating surgeon should be advised to use low allergenic alloys, eg, titanium alloys.☐ No need for patch testing or in vitro testing; the treating surgeon should not be advised against any specific alloys.

6. Do you patch test to plastics/glues when evaluating a patient with hip/knee implant problems?

☐ YES☐ NO

Comments: _____

Survey continues on other side.

7. When evaluating a patient with a suspected hypersensitivity reaction after device implant, what do you feel is supportive of a relevant metal allergy? (Check all that apply.)

☐ Chronic dermatitis beginning weeks to months after metallic implantation☐ Eruption overlying the metal implant☐ Morphology consistent with dermatitis (erythema, induration, papules, vesicles)☐ Systemic allergic dermatitis reaction☐ Histology consistent with allergic contact dermatitis☐ Positive patch test reaction to a metal used in the implant☐ Positive in vitro test to metals, eg, the lymphocyte transformation test☐ Dermatitis reaction is therapy resistant☐ Complete recovery after removal of the offending implant☐ Other (please specify) _____

8. Do you think that a patient with a positive allergic reaction on patch testing (eg, nickel sulfate), symptoms from the implanted joint (eg, pain), and an implanted device that contains the allergenic metal in question should have the device removed?

☐ YES☐ NO

Comments: _____

9. How many individual patients are patch tested in your clinic each year?

☐ 1–50☐ 51–100☐ 101–150☐ 151–200☐ 201–300☐ >300

(Continued on next page)

TABLE 1. (Continued)

10. Which of the following is your primary practice environment, and in what country?

- ☐ Hospital
- ☐ Academic (research)
- ☐ Academic (clinical)
- ☐ Private practice
- ☐ Other (please specify) _____
- Country in which you work: _____

11. What is your primary professional role?

- ☐ Physician
- ☐ Resident (in training)
- ☐ Nurse or nurse practitioner
- ☐ Medical student
- ☐ Researcher
- ☐ Other (please specify) _____

Please place your completed survey in the box in the ACDS table by the end of the meeting or

Complete the survey online at: <https://www.surveymonkey.com/s/ACDS2013>

Distribution of the questionnaire is supported by the Annual Meeting committee of the ACDS.

Thank you for taking time to complete this survey! We value your opinions.

may therefore benefit from the opinions of physicians with a special interest in MHR because they may relate this to their own practice.

OBJECTIVES

Through summarizing the opinions of active patch testing dermatologists attending recent patch test conferences in Malmö, Sweden, and Miami, Fla, regarding opinions on MHR, we characterize how these reactions are currently being evaluated by a subset of patch testers, the criteria used for diagnosis and the type of management recommendations being given.

METHODS

The participants of the 11th Congress of the European Society of Contact Dermatitis (ESCD) (June 2012) and the 24th Annual Meeting of the American Contact Dermatitis Society (ACDS) (March 2013) were provided the same questionnaire, evaluating opinions about MHR in patients with implant. Participants to these conferences include a mixture of practicing dermatologists, medical students, nurses, skin biologists, occupational physicians, toxicologists, employees from regulatory affairs in governmental agencies, employees from pharmaceutical companies, manufacturers of diagnostic products, and employees from industry (eg, fragrance and hair dyes). The survey tool is available in Table 1. The ESCD survey was placed on each auditorium chair before a combined morning session, and the ACDS survey was provided to all participants as part of their registration package. The survey data were tabulated using surveymonkey.com's online tools. The

χ^2 test and Fisher exact test, where appropriate, were used to calculate differences between the groups.

RESULTS

A total of 119 responses were received. The total number of participants responding from the ESCD and ACDS meetings were 46 of 450 (10%) and 73 of 217 (34%), respectively. Because we were eager to achieve a high sample size, we spoke to many participants and learned that mainly the dermatologists chose to complete the survey, whereas nonphysicians, occupational physicians, and nonphysicians replied that the survey was not relevant to them. Although we cannot exclude that some participants attending both conferences could have completed the survey twice, it is our impression from attending these conferences and from speaking to the participants that it was only done once. Moreover, not every respondent answered every question. The total respondents are provided for each individual question in the appropriate data table. The country of origin and practice data for the ACDS and ESCD respondents are summarized in Table 2. In general, the ACDS respondents were mostly from North America (55%) and the ESCD respondents from Europe (77%), although both meetings were decidedly international. The respondents were overwhelmingly attending-level physicians (91% for both meetings). Although 72% worked in academic or hospital settings, 28% of the respondents were in private practice. Reported patch testing volumes were greater or equal to 100 patients per year in 83% of the respondents, with 43% of the total testing were more than 300 per year.

In question 1, 96% of the respondents (112/119) evaluate patients with suspected MHR reactions to metallic implants. This number was the same for both the ACDS and ESCD meetings.

TABLE 2. Respondent Characterization

Country of Origin of Respondents						
ESCD (n = 35)			ACDS (n = 73)			
Australia	2 (6)		Australia	4 (5)		
Belgium	2 (6)		Belgium	2 (3)		
Canada	1 (3)		Brazil	4 (5)		
Denmark	4 (11)		Canada	6 (8)		
Germany	1 (3)		Denmark	3 (4)		
Mexico	1 (3)		Mexico	1 (1)		
Netherlands	3 (9)		Netherlands	3 (4)		
Poland	1 (3)		Poland	1 (1)		
Portugal	2 (6)		Portugal	2 (3)		
Romania	1 (3)		Romania	1 (1)		
Spain	1 (3)		Sweden	3 (4)		
Sweden	3 (9)		UK	8 (11)		
UK	7 (20)		USA	33 (45)		
USA	6 (17)					
Practice Setting						
ESCD (n = 44)			ACDS (n = 73)			
Hospital	22 (50)			13 (18)		
Academic (research)	1 (2)			8 (11)		
Academic (clinical)	11 (25)			32 (44)		
Private practice	10 (23)			26 (36)		
Other (please specify)	0 (0)			0 (0)		
Patients Evaluated per Year (n = 118)						
	1–50	51–100	101–150	151–200	201–300	>300
ACDS	6 (8.22)	14 (19.18)	12 (16.44)	13 (17.81)	9 (12.33)	19 (26.03)
ESCD	1 (2.22)	1 (2.22)	4 (8.89)	3 (6.67)	9 (20)	27 (60)
Average, %	5	11	13	12	16	43

Values are presented as n (%).

The data from questions 2 to 6 are summarized in Table 3.

In question 2, the types of metal devices evaluated were primarily orthopedic devices (33.3%–33.6%), dental devices (28.4%–31.9%), and cardiovascular devices (20.7%–21.6%). Other devices were evaluated by 15% of the respondents, and the specific types of devices were not recorded.

In question 3, the respondents were allowed to respond with a number between 1 (never) and 7 (always) for the use of patch testing, lymphocyte transformation test (LTT), and intradermal testing. Patch testing was the most commonly used modality for the evaluation of MHR, and no difference was observed among ACDS and ESCD conference participants.

In question 4, 60% (58%–62%) of the patch testers used a standard series for all patients with MHR, and 33% (32%–33%) of the patch testers based their patch testing trays on the patient's history and picked specific allergen trays for each patient. Only 7% (4%–10%) of the respondents used a "standard" screening series alone for patients with MHR. No difference among ACDS and ESCD conference participants was noted.

In question 5, 54% (46%–61%) of the respondents believed that a patient with suspected moderate to severe metal dermatitis should undergo patch testing and/or LTT before implantation of a metallic device. Thirty-eight percent (36%–42%) of the respondents feel that it is adequate to counsel the surgeon and patient that a titanium device is adequate. Overall, although 8% felt that no testing or changes in management would be necessary, significantly more ESCD participants (12%) replied so when compared with the ACDS participants (4%; $P = 0.001$).

In question 6, 82% (80%–84%) of the respondents evaluate for plastic and glue components when testing patients suspected to have a MHR to a hip or knee device.

Questions 7 and 8 were used to evaluate respondents' opinions on the utility of Thyssen³ diagnostic criteria for MHR. A total of 9 criteria were presented, and the data were split into 4 minor and 5 major criteria (Table 4). A recently published article analyzing these results concluded that in the challenging situation of a symptomatic or failing orthopedic device, applying the criteria may be useful for guiding decision making.⁸

TABLE 3. Respondent Data Summary**Question 2: Types of Metal Devices Evaluated, % (n = 107)**

	Dental Devices	Cardiovascular (eg, Pacemakers, Stents, Occluders)	Implanted Orthopedic Devices (eg, Total Hip/ Knee Replacements, Plates)	Other Metal Devices
ACDS	28.43	21.57	33.33	16.67
ESCD	31.90	20.69	33.62	13.79
Average	30	21.5	33.5	15

Question 3: Which Type of Evaluation(s) Used to Evaluate MHR? (n = 116)

Patch testing*							
	1	2	3	4	5	6	7
ACDS	0 (0)	1 (1.41)	0 (0)	1 (1.41)	3 (4.23)	7 (9.86)	59 (83.10)
ESCD	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4.44)	43 (95.56)
Lymphocyte transformation test or similar in vitro test*							
	1	2	3	4	5	6	7
ACDS	49 (87.50)	3 (5.36)	3 (5.36)	1 (1.79)	0 (0)	0 (0)	0 (0)
ESCD	37 (82.22)	3 (6.67)	0 (0)	3 (6.67)	1 (2.22)	0 (0)	1 (2.22)
Intradermal testing*							
	1	2	3	4	5	6	7
ACDS	51 (89.47)	3 (5.26)	3 (5.26)	0 (0)	0 (0)	0 (0)	0 (0)
ESCD	34 (77.27)	6 (13.64)	1 (2.27)	2 (4.55)	0 (0)	1 (2.27)	0 (0)

Question 4: Do You Have a Specific MHR Patch Testing Tray? (n = 116)

	Yes, I Have a Standard Series That I Use in All My Patients With Metal Implant Hypersensitivity Reactions	No, Based on the Medical History and the Content of the Implant, I Pick Specific Allergens Every Time	No, I Only Use the European/ North American Baseline Series (or Similar Standard Screening Series)
ACDS	41 (57.75)	23 (32.39)	7 (9.86)
ESCD	28 (62.22)	15 (33.33)	2 (4.44)
Average, %	60	33	7

Question 5: How Should a Patient With Moderate to Severe Metal Dermatitis Be Managed Before Implantation of a Metal Device? (n = 114)

	Patch Testing and/or In Vitro Testing (LTT or Similar) Should Be Performed to Identify Metal Hypersensitivity	The Patient and the Treating Surgeon Should Be Advised to Use Low Allergenic Alloys, eg, Titanium Alloys	There Is No Need for Patch Testing or In Vitro Testing. The Treating Surgeon Should Not Be Advised Against Any Specific Alloys
ACDS	53 (60.92)	31 (35.63)	3 (3.45)
ESCD	31 (46.27)	28 (41.79)	8 (11.94)
Average, %	54	38	8

Question 6: Do You Evaluate for Plastics and Glues When Evaluating for Hip/Knee MHR? (n = 115)

	Yes	No
ACDS	56 (80)	14 (20)
ESCD	38 (84.44)	7 (15.56)
Average, %	82	18

Values are presented as n (%), unless specified otherwise.

*A scale of 1 to 7, where 1 is never and 7 is always.

TABLE 4. Question 7: Diagnostic Criteria for MHR (Adapted From Schalock and Thyssen¹⁰)**Major**

Eruption overlying the metal implant
 Positive patch test reaction to a metal used in the implant
 Complete recovery after removal of the offending implant
 Chronic dermatitis beginning weeks to months after metallic implantation

Minor

Dermatitis reaction is therapy resistant
 Morphology consistent with dermatitis (erythema, induration, papules, vesicles)
 Systemic allergic dermatitis reaction
 Histology consistent with allergic contact dermatitis
 Positive in vitro test to metals, eg, the lymphocyte transformation test

Questions 9 to 11 are demographic and practice data, which are summarized in Table 2. The ESCD participants tended to manage a higher number of patients with metal implant than participants from the ACDS meeting ($P = 0.0004$).

DISCUSSION

The need for evaluation of MHR is common among patch testers around the world. In this survey, which encompassed opinions of 119 participants from 2 international conferences and who came from 16 countries worldwide, 96% of those who were surveyed evaluated patients with suspected implanted metal reactions of various types, although this may be an overestimate because of response bias. In both ESCD and ACDS, the average respondent works in an academic/hospital setting with a relatively high number of patients tested each year. Our total response rate of all of those attending the meeting was relatively low (participation rate unknown). It is therefore clearly the opinions and habits of the selected conference participants that we present and not the general attitudes of all patch testers. We saw that those respondents with an interest in MHR and implant failure completed the questionnaire, whereas participants, for example, from industry, nursing staff, toxicologists, and regulators would be much less likely to complete the survey. The results are therefore interesting because they are the first to quantitatively and qualitatively assess the practice of leading patch testers.

Evaluations for reactions to dental devices and implanted orthopedic devices were nearly equal, with 30% and 33.5% of the patients evaluated by ACDS and ESCD meeting participants, respectively. Cardiovascular devices and other implanted metal devices were less common. In any case, these numbers are important because they support the general impression that cardiac issues in MHR constitute a smaller challenge. Keep in mind that the question of MHR is typically being asked by our referring health care providers and patients; patch testers are then performing evaluations for a variety of types of metal implants. Thus, the

results only reflect patients who were referred to patch testers and not patient groups with MHR, causing morbidity in general.

Evaluation for implanted orthopedic devices is controversial. Both preimplantation evaluation for those patients with a history significantly concerning for MHR and postimplant morbidity such as pain, implant loosening, and aseptic lymphocyte-dominated vasculitis-associated lesion have evoked much discussion in the orthopedic and dermatologic communities. But once testing is completed, the results need to be reported to the patient and the consulting physician. There are widely varying opinions regarding patient counseling. Interestingly, the practice differs dramatically among survey respondents, emphasizing heterogeneous attitudes in the dermatological community. Thus, 54% of the respondents believe that a patient with suspected moderate to severe metal dermatitis should undergo patch testing and/or LTT before implantation of a metallic device. Thirty-eight percent of the respondents feel that it is adequate to counsel the surgeon and patient that a titanium device is sufficient. Eight percent of the respondents felt that no testing or changes in management would be necessary. None of these opinions is evidence based, although they are completely different actions with different socioeconomic and health consequences. Overall, there seemed to be a slightly more conservative approach among ESCD participants because significantly more replied that they refrain from patch testing patients with a history of allergic contact dermatitis to metals. Whether this is explained by the fact that more ACDS participants worked in a private setting is unclear. In addition, it may illustrate some of the differences between European and non-European patch testers because of different legal and health care systems. Nonetheless, a simple approach to patients with a history of MHR is that of the German Implant Allergy Working Group (AK 20) of the DGOOC (German Association of Orthopedics and Orthopedic Surgery), DKG (German Contact Dermatitis Research Group), and DGAKI (German Society for Allergology and Clinical Immunology). They recommend titanium-based osteosynthesis materials for patients with MHR and in elective hip replacements, a ceramic/polyethylene articulation.¹³ There is some evidence collected by Carlsson and Möller¹⁴ that patients with MHR have the same risk of device reactivity as nonallergic individuals. In their study, 18 patients with confirmed nickel, cobalt, or chromium allergy were prospectively identified, and their metal allergy was confirmed before implantation of a metallic orthopedic device. No changes in management were made based on the information from patch testing and confirmation of metal allergy. These patients were exposed to a device containing their allergen for a mean of 6.3 years with no reported complications. In addition, a recent case report described a woman with chromium, cobalt, and nickel allergy who underwent bilateral total knee arthroplasty. The surgeon feared MHR to the implant and therefore chose to use a titanium-niobium alloy. However, by mistake, such an alloy was only inserted in 1 of the knees, whereas a chromium-cobalt alloy was inserted in the other. After a 2-year follow-up, there were no signs of device failure.¹⁵

Several studies have reported results of preimplant and postimplant patch testing with mixed results. Atanaskova and colleagues¹⁶ reported the results of 72 patients after patch test evaluations for suspected MHR. Of the 31 patients tested preimplant, 21 were metal allergic and had no hypersensitivity complications after orthopedic implant. Of the 41 patients tested postimplantation, 10 had metal hypersensitivity, and of the 10 patients with metal hypersensitivity, 6 had symptom resolution after device removal. In both groups, patient history of MHR was predictive of a positive patch test. Reed and colleagues¹⁷ presented similar patient data, but only the preimplantation group was felt to benefit. Of the 22 patients in this group, 5 had a positive patch test to a proposed device. None of the postimplantation group with symptoms had MHR.

Respondents were asked to evaluate the Thyssen⁷ diagnostic criteria for MHR. These 9 criteria were presented, and the resulting data were split into 4 minor and 5 major criteria (Table 4). The authors' recent article analyzing these results concluded that in the challenging situation of a symptomatic or failing orthopedic device, applying the criteria may be useful for guiding decision making.¹⁰ Kubba and colleagues¹⁸ have also suggested criteria for those patients with postimplant cutaneous reactions. They found in a group of 19 patients that the likelihood of the skin reaction being related to a MHR was higher when the metal device is static, there is a reported history of MHR, the reaction is local to the implant, and the reaction is eczematous, persistent, and developed after the implant.

Although these reports certainly illustrate that most patients with a metal allergy will do well, despite implant allergen exposure, these authors do not feel that ignoring the information regarding symptomatic metal allergy is always warranted or safe. Ignoring these reactions may expose a very small number of patients to the morbidity of a failing device, the increased cost of management, and the complications related to replacing a failed device. Moreover, in some cases, ignoring a patient with known allergies to metals with subsequent complications has led to legal action against the treating physicians in the United States. In our opinion and that of 54% of the respondents, a complete evaluation of patients with very strong reactions to metals before implantation of a metallic device should be considered.^{8,10,11,19}

Probably most controversial is the question of which test is the right test. At this point, this likely is the patch test, but whether a type IV reaction is actually occurring in the peri-implant environment remains to be proven. Theories for and against this are discussed in detail in 2 recent reviews.^{9,19} In summary, patch testing is currently considered the criterion standard for evaluating cutaneous type IV hypersensitivity reactions by most dermatologists. Its use for evaluation of MHR to implanted metal devices, however, is less established.⁹ The immunology of reactions surrounding implanted metal devices is not completely clear, and the types of reactions seem to be a mix of types. Type IV reactions seem to be partially implicated and there are likely common pathways and cell types involved in skin, mucous membrane, and bone reactions.¹⁹ Considering this, the patch test is the best test for

implanted metal reactions at this time.^{8,11,12} The popularity of the patch test is also reflected in the opinions of most patch testers responding, with 89% always using patch testing and 83% to 85%, respectively, never using LTT or intradermal testing to evaluate MHR. Explanations for the low or modest use of LTT include poor access to laboratories that can perform it, transportation time causing T-cell inactivity, price, lack of standardization, and the fact that many metals cannot be properly tested yet. The intradermal test was also infrequently used by respondents. Intradermal testing for metal hypersensitivity, although rarely performed, may in some cases be a useful indicator of MHR.^{20–24} However, intradermal testing may also result in false-positive reactions, and their use should be carefully considered.

Choice of allergens when performing evaluations for MHR is also important. Most patch testers used a standard tray and a specific metal hypersensitivity panel to evaluate patients with this question. We did not ask our respondents to define their standard series or their metal hypersensitivity panel. Sixty percent of the patch testers used a standard series for all patients with MHR, and 33% of the patch testers based their patch testing trays on the patient's history and picked specific allergen trays for each patient. Either approach, if carefully performed, is, in our opinion, appropriate and will likely completely evaluate the patient. Seven percent of the respondents only used a standard screening series alone for patients with MHR. The use of a basic screen alone for all patients should be avoided because it is insufficient. Although most screening or standard series do contain nickel, cobalt, and chromium, the less common but still important allergens will be missed.¹⁹ Suggested patch testing allergen panels for clinical use have been recently reviewed by Schallock et al.¹⁹

A separate but important question is that of reactions to the glue components used in the placement of dynamic orthopedic devices such as hip or knee replacements. Allergic reactions to bone cement components were reported in 25% of the patients in 1 series.²⁵ The common allergenic components that should be evaluated in a symptomatic dynamic orthopedic device include the glue components methyl methacrylate, N,N-dimethyl-p-toluidine, and benzoyl peroxide.⁶ Antibiotics such as gentamicin, tobramycin, clindamycin, or erythromycin are also added into the glue mixture.²⁶ In addition to MHR, allergic reaction to these added antibiotics and glue components may also contribute to device failure. In 1 series, of the 15 patients with aseptic loosening of a total hip replacement, 7 were allergic to N,N-dimethyl-p-toluidine.²⁷ Eighteen percent of the respondents did not routinely test for these components. Although that number is relatively low, there does seem to be room for improvement in the choice of allergens that some experts are using for MHR and failing orthopedic devices. Only this way will the patients be sufficiently evaluated.

CONCLUSIONS

Consultation requests to patch testing dermatologists regarding the evaluation of metal allergy are common and increasing in

many centers. The device types that are being questioned include primarily orthopedic, dental, and cardiovascular devices. Patients are clinically split into preimplantation or symptomatic post-implantation groups. Most respondents feel that evaluation before implantation is desirable for patients with a significant history of MHR, and a large minority follow the German recommendation to use a titanium device without testing. Implanting potentially allergenic metal(s) in a device for these patients is not desirable. Major and minor criteria for diagnosing MHR in patients with postimplantation are available and likely are helpful in choosing patients needing further evaluation or at least to get an impression of the cause-and-effect relationship.¹⁰

Our bias after careful review of the data available to date and that of our respondents is that the patch test remains the criterion standard for identifying type IV delayed-type reactions on the skin and mucous membranes and likely the best available test for orthopedic and cardiac device screening and diagnosis. However, we acknowledge that the test is not ideal. In addition, using a standard tray and implanted device tray as well as evaluating for glue components is necessary for most patients.

There is a wide variety of opinions on who to evaluate, how they should be evaluated, and if it is even necessary. This survey summarizes current common practices among patch testing dermatologists worldwide. There is still much to be learned, and further evidence-based studies are necessary to delineate the true prevalence of MHR reactions, the actual pathophysiology of the reactions, and the best way to accurately evaluate our patients to minimize the morbidity of patients with MHR. This study showed that although there are minor differences, patch testers experience the same challenges worldwide. It emphasized that a joint global initiative is necessary to improve our understanding.

REFERENCES

1. Warshaw EM, Belsito DV, Taylor JS, et al. North American Contact Dermatitis Group patch test results: 2009 to 2010. *Dermatitis* 2013;24:50–59.
2. Köster R, Vieluf D, Kiehn M, et al. Nickel and molybdenum contact allergies in patients with coronary in-stent restenosis. *Lancet* 2000;356:1895–1897.
3. Thyssen JP, Engkilde K, Menné T, et al. No association between metal allergy and cardiac in-stent restenosis in patients with dermatitis—results from a linkage study. *Contact Dermatitis* 2011;64:138–141.
4. Honari G, Ellis SG, Wilkoff BL, et al. Hypersensitivity reactions associated with endovascular devices. *Contact Dermatitis* 2008;59:7–22.
5. Svedman C, Tillman C, Gustavsson CG, et al. Contact allergy to gold in patients with gold-plated intracoronary stents. *Contact Dermatitis* 2005;52:192–196.
6. Basko-Plluska JL, Thyssen JP, Schalock PC. Cutaneous and systemic hypersensitivity reactions to metallic implants. *Dermatitis* 2011;22:65–79.
7. Thyssen JP, Menné T, Schalock PC, et al. Pragmatic approach to the clinical work-up of patients with putative allergic disease to metallic orthopaedic implants before and after surgery. *Br J Dermatol* 2011;164:473–478.
8. Schalock PC. Pragmatism and the evaluation of metal hypersensitivity reactions. *Dermatitis* 2013;24:104–105.
9. Crawford GH. The role of patch testing in the evaluation of orthopedic implant-related adverse effects: current evidence does not support broad use. *Dermatitis* 2013;24:99–103.
10. Schalock PC, Thyssen JP. Patch testers' opinions regarding diagnostic criteria for metal hypersensitivity reactions to metallic implants. *Dermatitis* 2013;24:183–185.
11. Honari G, Taylor JS. Commentary on Crawford, et al, The role of patch testing in the evaluation of orthopedic implant-related adverse effects: current evidence does not support broad use. *Dermatitis* 2013;24:108–111.
12. Thomas P. Patch testing and hypersensitivity reactions to metallic implants: still many open questions. *Dermatitis* 2013;24:106–107.
13. Thomas P, Schuh A, Ring J, et al. Orthopedic surgical implants and allergies: joint statement by the Implant Allergy Working Group (AK 20) of the DGOOC (German Association of Orthopedics and Orthopedic Surgery), DKG (German Contact Dermatitis Research Group) and DGAKI (German Society for Allergology and Clinical Immunology). *Orthopade* 2008;37:75–88.
14. Carlsson A, Möller H. Implantation of orthopaedic devices in patients with metal allergy. *Acta Derm Venereol* 1989;69:62–66.
15. Thienpont E, Berger Y. No allergic reaction after TKA in a chrome-cobalt-nickel-sensitive patient: case report and review of the literature. *Knee Surg Sports Traumatol Arthrosc* 2013;21:636–640.
16. Atanaskova Mesinkovska N, Tellez A, Molina L, et al. The effect of patch testing on surgical practices and outcomes in orthopedic patients with metal implants. *Arch Dermatol* 2012;148:687–693.
17. Reed KB, Davis MD, Nakamura K, et al. Retrospective evaluation of patch testing before or after metal device implantation. *Arch Dermatol* 2008;144:999–1007.
18. Kubba R, Taylor JS, Marks KE. Cutaneous complications of orthopedic implants. A two-year prospective study. *Arch Dermatol* 1981;117:554–560.
19. Schalock PC, Menné T, Johansen JD, et al. Hypersensitivity reactions to metallic implants—diagnostic algorithm and suggested patch test series for clinical use. *Contact Dermatitis* 2012;66:4–19.
20. Baik JJ, Yoon YB, Park HS. Cobalt-induced occupational asthma associated with systemic illness. *J Korean Med Sci* 1995;10:200–204.
21. Leguy-Seguin V, Jolimoy G, Coudert B, Pernot C, et al. Diagnostic and predictive value of skin testing in platinum salt hypersensitivity. *J Allergy Clin Immunol* 2007;119:726–730.
22. Morris DL. Intradermal testing and sublingual desensitization for nickel. *Cutis* 1998;61:129–132.
23. Yamauchi R, Morita A, Tsuji T. Pacemaker dermatitis from titanium. *Contact Dermatitis* 2000;42:52–53.
24. Herbst RA, Lauerma AI, Maibach HI. Intradermal testing in the diagnosis of allergic contact dermatitis. A reappraisal. *Contact Dermatitis* 1993;29(1):1–5.
25. Thomas P, Schuh A, Eben R, et al. Allergy to bone cement components. *Orthopade* 2008;37:117–120.
26. Kuehn KD, Ege W, Gopp U. Acrylic bone cements: composition and properties. *Orthop Clin North Am* 2005;36:17–28.
27. Haddad FS, Cobb AG, Bentley G, et al. Hypersensitivity in aseptic loosening of total hip replacements. The role of constituents of bone cement. *J Bone Joint Surg Br* 1996;78:546–549.