

ONLINE FIRST

The Effect of Patch Testing on Surgical Practices and Outcomes in Orthopedic Patients With Metal Implants

Natasha Atanaskova Mesinkovska, MD, PhD; Alejandra Tellez, MD; Luciana Molina, MD; Golara Honari, MD; Apra Sood, MD; Wael Barsoum, MD; James S. Taylor, MD

Objective: To determine the effect of patch testing on surgical decision making and outcomes in patients evaluated for suspected metal hypersensitivity related to implants in bones or joints.

Design: Medical chart review.

Setting: Tertiary care academic medical center.

Participants: All patients who had patch testing for allergic contact dermatitis related to orthopedic implants.

Intervention: Patch testing.

Main Outcome Measures: The surgeon's preoperative choice of metal implant alloy compared with patch testing results and the presence of hypersensitivity complications related to the metal implant on postsurgical follow-up.

Results: Patients with potential metal hypersensitivity from implanted devices (N=72) were divided into 2 groups depending on timing of their patch testing: preimplantation

(n=31) and postimplantation (n=41). History of hypersensitivity to metals was a predictor of positive patch test results to metals in both groups. Positive patch test results indicating metal hypersensitivity influenced the decision-making process of the referring surgeon in all preimplantation cases (n=21). Patients with metal hypersensitivity who received an allergen-free implant had surgical outcomes free of hypersensitivity complications (n=21). In patients who had positive patch test results to a metal in their implant after implantation, removal of the device led to resolution of associated symptoms (6 of 10 patients).

Conclusions: The findings of this study support a role for patch testing in patients with a clinical history of metal hypersensitivity before prosthetic device implantation. The decision on whether to remove an implanted device after positive patch test results should be made on a case-by-case basis, as decided by the surgeon and patient.

Arch Dermatol.

Published online February 20, 2012.

doi:10.1001/archdermatol.2011.2561

MORE THAN 1 MILLION lower extremity total joint replacements are completed yearly in the United States, and this number is expected to increase.^{1,2} The overwhelming majority were for osteoarthritis; other causes included inflammatory arthritis, posttraumatic arthritis, avascular necrosis, and postsepsis arthritis. The increasing need for orthopedic implants is secondary to multiple factors, including the population's increased life expectancy, obesity, expanding indications, and the desire of patients to maintain active lifestyles.³⁻⁶

See Practice Gaps at end of article

For bone implants to withstand the associated movement and stress, most implants are metal alloys, made from a mixture of 2 or more components.⁷ Nickel is a

commonly used metal in alloys because it grants necessary strength and durability to the implant. At the same time, nickel is the leading cause of contact dermatitis associated with metals, affecting up to 19% of the population evaluated with patch testing.⁸ Although the prevalence of contact allergy to metals is high, hypersensitivity complications associated with metal implants have been reported to be less than 0.1%.⁹ Potential allergic complications after implantation of orthopedic metal devices are cutaneous eruptions, chronic joint pain, edema, loosening, and joint failure.¹⁰⁻¹²

Objective criteria supporting a causative association between metal release from an orthopedic implant, metal allergy, and dermatitis overlying an implant have been proposed; however, the clinical decision-making process remains difficult.¹³ Patients are frequently referred to the dermatology department to rule out hypersensitivity reactions related to metal implants preoperatively or postoperatively if problems de-

Author Affiliations: Departments of Dermatology, Dermatology–Plastic Surgery Institute (Drs Atanaskova Mesinkovska, Molina, Honari, Sood, and Taylor), and Orthopedic Surgery, Orthopaedic and Rheumatologic Institute (Drs Tellez and Barsoum), Cleveland Clinic, Cleveland, Ohio.

Table 1. Prosthesis Tray Components

No.	Allergen	Material Source
1	Ammonium vanadate, 1% aq	Cleveland Clinic pharmacy
2	Ammonium heptamolybdate, 1% aq	allergEAZE MC240
3 ^a	Titanium powder, 1% pet	allergEAZE MC260
4	Palladium chloride, 2% pet	allergEAZE DM226
5	Copper sulfate, 2% pet	allergEAZE MC245
6	Aluminum chloride	Cleveland Clinic pharmacy
7	Manganese chloride, 2% aq	Cleveland Clinic pharmacy
8	<i>N,N</i> -Dimethyl-4-toluidine, 2% pet	allergEAZE DM225
9	Benzoyl peroxide, 1% pet	allergEAZE DM218
10	4,4-Diaminodiphenylmethane, 0.5% pet	allergEAZE PG296
11	Hydroquinone, 1% pet	allergEAZE PC626
12	Chlorhexidine digluconate, 0.5% aq	allergEAZE AP84
13	Tantal, 1% pet	allergEAZE MC255
14 ^b	Ammonium tetrachloroplatinate, 0.25% pet	allergEAZE DM217
15	Indium (III) chloride, 1% pet	allergEAZE MC249
16	Cobalt (II) chloride hexahydrate, 1% pet	allergEAZE NA21
17	Methyl methacrylate, 2% pet	allergEAZE NA49
18	Thimerosal, 0.1% pet	allergEAZE EM409
19	Bacitracin, 20% pet	allergEAZE NA11
20	Colophony, 20% pet	allergEAZE NA24
21	Neomycin sulfate, 20% pet	allergEAZE NA51
22	Formaldehyde, 1% aq	allergEAZE NA37
23	Nickel sulfate hexahydrate, 2.5% pet	allergEAZE NA52
24	Potassium dichromate, 0.25% pet	allergEAZE NA54
25	Gold sodium thiosulfate, 0.5% pet	Chemotechnique G005A
26 ^b	Gentamicin sulfate, 20% pet	allergEAZE AA419
27 ^c	Titanium dioxide, 10% pet	Chemotechnique T-040
28 ^b	Tin (II) chloride, 0.5% pet	allergEAZE DM230
29 ^b	Zirconium (IV) oxide, 0.1% pet	allergEAZE MC295
30 ^b	Ferrous sulfate, 5% pet	allergEAZE MC247
31 ^b	Ferrous chloride, 2% ethanol/glyc	allergEAZE MC246
32 ^c	Titanium (IV) oxide, 0.1% pet	allergEAZE MC256
33	Iridium, 1% pet	Chemotechnique MET-14
34	Iridium (III) chloride, 1% pet	Chemotechnique MET-13
35 ^b	Vanadium, 5% pet	Chemotechnique MET-22
36 ^b	Nickel sulfate hexahydrate, 5% pet	allergEAZE ST167
37 ^b	Tobramycin, 20% pet	Cleveland Clinic pharmacy
38 ^b	Tobramycin, 20% aq	Cleveland Clinic pharmacy
39 ^b	Vancomycin, 0.005% aq	Cleveland Clinic pharmacy
40 ^a	Titanium disc	Medtronic
41 ^a	Polyethylene disc	Medtronic

Abbreviations: aq, aqueous solution; glyc, glycerin; pet, petrolatum.

^aComponent added to the testing tray in 2006.

^bComponent added to the testing tray in 2008.

^cComponent added to the testing tray in 2007.

velop in an implant.¹⁴ Dermatologists commonly rely on patch testing to evaluate these patients for potential metal allergy. However, the effect of patch test results on the practices of the referring surgeons is unknown.¹⁵ With the exponential demand for orthopedic procedures, there is an obvious need for effective collaboration between dermatologists and surgeons to better identify patients at risk for complications due to metal hypersensitivity. In this study, we evaluated the role of patch testing in the decision-making process of referring surgeons and subsequent outcomes of patients with hypersensitivity to metals identified with the testing.

METHODS

This was an institutional review board–approved medical record review of patients who underwent patch testing for allergic contact dermatitis related to implantation of a metal in a bone or joint

in the Cleveland Clinic Department of Dermatology from January 1, 2003, through December 31, 2010. The dermatology patch test database was used to identify patients who had testing with a prosthesis-specific tray (n=94). Study patients included only those who had an orthopedic surgical procedure, with a minimum postsurgical follow-up of 6 weeks or longer (N=72).

Data recorded on these 72 individuals included demographics; self-reported history of atopy; clinical history of hypersensitivity to metals in costume jewelry, belts, buckles, watches, or dental implants; timing of referral; reason for referral and referring physician; location, onset, and nature of presenting symptoms; presence of dermatitis on examination; location of implanted metal; surgeon's choice of metal components implanted after patch test results; and patients' status on postoperative visits. Patients were divided into 2 main groups: pre-implantation (patch testing before the surgical implant) and postimplantation (patch testing after the surgical implant). Patients from the postimplantation group were evaluated for the presence of factors other than metal hypersensitivity to explain their presenting symptoms, such as infection or mechanical causes of failure. Investigations included imaging, synovial fluid aspirates, microbiologic testing, histopathological examination of periprosthetic tissue, and assessment of postoperative dressing material for cutaneous allergic reactions. All medical office notes were cross-referenced with surgical operative notes, postoperative hospital notes, and manufacturers' information sheets for completeness.

Patients who were taking long-term immunosuppressive medications were excluded, as were patients who had received patch testing related to cardiac or dental metal implants. One patient with a spinal stimulator and 2 patients with joint prosthesis were included in a previously published report.¹⁶ Two patients with Nuss bars were included in another publication.¹⁷

Statistical analysis was performed using 1-sided Fisher exact tests to calculate the association between self-reported history of hypersensitivity to metals and positive results of patch testing for hypersensitivity to metals.

DEVICES

All patients had implanted metal devices for orthopedic use, such as screws and plates for fracture fixation, partial or total arthroplasties of extremities, spinal stimulators, or Nuss bars for thoracic expansion. The operative procedure notes were analyzed to confirm site, type of implant, intraoperative events, and decision-making process. The manufacturers' technical sheets and serial number labels were used to confirm the metal components of the implanted joints, and this information was used to further analyze the relevance of patch testing results. A positive patch test to a certain metal was considered relevant if that metal was a component of the alloy that was surgically implanted or was going to be implanted.

PATCH TESTS

The patch testing procedures of allergens used in our study were performed by dermatologists according to the standards set by the North American Contact Dermatitis Group (NACDG).⁸ All patients had patch testing with both standard screening of the NACDG and prosthesis trays (**Table 1**). The patch tests were applied to unaffected skin on the upper back using chambers (Finn Chamber; Epitest Ltd) on acrylic-based adhesive medical tape (Scanpor; Norgespilster AIS). Patches were removed after 48 hours, and the reactions were evaluated on day 2 or 3 and again on day 6 or 7. Interpretation of patch test results was performed according to the NACDG guidelines.¹⁶

RESULTS

There were 31 patients in the preimplantation group and 41 patients in the postimplantation group. The demographic characteristics of the groups are presented in **Table 2**.

PREIMPLANTATION GROUP RESULTS

Patients in the preimplantation group were most often referred by their orthopedic surgeon because of a self-reported history of hypersensitivity to metals. Several patients in this group showed positive reactions to at least 1 metal (21 of 31 [68%]), with 15 patients reacting to more than 1 metal (**Table 3**). All 21 of these patients were significantly more likely to have a clinical history of metal hypersensitivity than were those without a positive result (7 of 10 [70%]) ($P=.03$).

The patch test results influenced the decision-making process of the referring surgeons (**Table 4**). In all patients who tested positive to metals, surgeons chose an implant that did not have that metal as a component. In 13 of these cases, the surgeons chose an implant that was different from their implant of choice. The 21 patients with implanted allergen-free hardware did not have skin eruptions or early joint loosening on surgical follow-up (**Table 4**). In the patients with negative results to the patch test, only 1 received an oxidized zirconium knee implant because of a self-reported history of metal intolerance.

POSTIMPLANTATION GROUP RESULTS

In the postimplantation group, the referring physicians recommended patch testing after excluding periprosthetic complications, such as infection and mechanical failure. The most common reason for patch testing referral in this group was chronic pain at the site of the implanted metal (24 of 41 patients [59%]) (**Table 5**). Clinical history of hypersensitivity to metals in this group was not a major factor for referral; nevertheless, patients with a positive patch test (8 of 15 [53%]) were significantly more likely to have a clinical history of metal hypersensitivity than were those with a negative patch test (5 of 26 [19%]) ($P=.03$).

Fewer positive patch test reactions to metal were identified (15 of 41 patients [37%]) in the postimplantation group. The most common positive results were documented for nickel, cobalt, palladium, and chromium; there were no positive reactions to gold (**Table 3**). Ten postimplantation patients had at least 1 relevant positive patch test to a metal that was a component of their implant. The details of their clinical findings are reported in **Table 6**. Among these patients, all who reported a history of metal hypersensitivity had a positive reaction to nickel ($n=7$). Nickel was the most frequently implicated relevant metal (7 of 10 [70%]), with dermatitis being the most common concern (4 of 10 [40%]). Six patients who had the potentially offending prosthesis explanted experienced alleviation of their symptoms. In contrast, 4 patients who did not have an implant revision operation continued to experience the related problems. The decisions to not remove the implant resulted from additional

Table 2. Clinical Characteristics of Patients Who Were Patch Tested to Identify Metal Hypersensitivity to an Orthopedic Metal Implant

Characteristic	No. (%) ^a	
	Preimplantation Group (n = 31)	Postimplantation Group (n = 41)
Age, y		
Mean (SD)	56.1 (15.4)	56.8 (16.49)
Median (range)	58 (14-80)	57 (14-81)
Sex		
Male	8 (26)	18 (44)
Female	23 (74)	23 (56)
Race		
White	29 (94)	38 (93)
Black	2 (6)	3 (7)
Clinical history of metal hypersensitivity	28 (90)	13 (32)
History of atopy	13 (42)	17 (41)
Type of orthopedic device		
Dynamic	24 (77)	28 (68)
Static	7 (23)	13 (32)
Type of prosthesis		
TKA	15 (48)	16 (39)
THA	9 (29)	6 (15)
Shoulder arthroplasty	0	2 (5)
Elbow arthroplasty	0	2 (5)
Spinal implant	3 (10)	6 (15)
Nuss bar	2 (6)	1 (2)
Rotator cuff device	1 (3)	3 (7)
Spinal stimulator	1 (3)	3 (7)
Osteosynthesis material	0	2 (5)
Referring service		
Orthopedic surgery	28 (90)	34 (83)
Pain management	1 (3)	2 (5)
Pediatric surgery	2 (6)	1 (2)
Neurosurgery	0	2 (5)
PCP	0	1 (2)
Self	0	1 (2)
Patch test to operation time, median (range), mo	1 (0.5-64)	NA
Operation to patch test time, median (range), mo	NA	21 (1-232)

Abbreviations: NA, not applicable; PCP, primary care physician; THA, total hip arthroplasty; TKA, total knee arthroplasty.

^aBecause of rounding, some percentages do not total 100%.

comorbidities ($n=2$) and preference of the patient to avoid an additional operation ($n=1$); 1 reason was not reported. Negative patch test results were documented in 26 patients. Nine of these patients underwent revision of the implanted prosthesis. Reasons for device revision or removal included infection ($n=4$), mechanical failure ($n=3$), arthrofibrosis ($n=1$), and patient choice ($n=1$).

COMMENT

The advent of orthopedic implants has transformed the treatment of bone and joint conditions by improving quality of life, increasing mobility, and reducing pain in affected patients.¹⁸ Most implants used in orthopedic operations are composed of metal alloys that contain classic contact allergens, such as nickel, cobalt, and chromium.¹⁹ The occurrence of potential allergic complications to a metal im-

Table 3. Results of Patch Testing to Identify Metal Hypersensitivity

Metal	No. (%)	
	Preimplantation Group (n = 31)	Postimplantation Group (n = 41)
Positive patch test to any metal	21 (68)	15 (37)
Nickel	16 (52)	10 (24)
Palladium	10 (32)	3 (7)
Gold	7 (23)	0
Cobalt	6 (19)	4 (10)
Chromium	4 (13)	3 (7)
Molybdenum	1 (3)	0
Indium	0	1 (2)

Table 4. Preimplantation Patients With Positive Patch Test Results Indicating Metal Hypersensitivity

Characteristic	No. (%) (n = 21)
Metal allergen avoided by surgeon	21 (100)
Alternative implant used on the basis of patch test results	13 (62)
Implant alloy used	21/21 (100)
Titanium alloy	11 (52)
Zirconium oxide	10 (48)
Complications postimplant	
Suture reaction	2 (10)
Nonspecific joint pain	1 (5)
Arthrofibrosis	1 (5)
Scar contracture	1 (5)
Dermatitis	0
Early loosening	0
Follow-up after operation, median (range), mo	12 (1.5-71)

plant depends on the immune status of the individual, the corrosion potential of the material, and the presence of underlying metal hypersensitivity.^{20,21}

The summary of our experience from this study suggests a role for patch testing before a surgical implant in patients who report a history of hypersensitivity to metals such as those found in costume jewelry, belt buckles, or watches. These patients should undergo patch testing with a dermatologist who has access to testing ingredients found in implanted metal alloys. Patch testing is important because additional metal sensitizers may be identified. Seventy-four percent of preimplantation patients showing metal hypersensitivity on patch testing had positive reactions to more than 1 metal patch test. Multiple metal coreactions in patients with positive patch tests to nickel (n=11) most commonly occurred with palladium (n=9), cobalt (n=4), gold (n=4), and chromium (n=1).

In this study, nickel was the most common relevant allergen in both groups. Nickel is an important component of orthopedic alloys that grants stability. The amount of nickel differs in implant alloys depending on its application. Orthopedic grades of alloys, such as stainless steel and cobalt-chromium, contain relatively high levels of nickel in comparison with titanium.²² Stainless steel is a commonly used alloy in plates and screws for inter-

Table 5. Clinical Findings in Postimplantation Patients

Clinical Finding	No. (%)	
	Patients With Clinically Relevant Patch Test Results (n = 10)	Patients With Negative or Nonrelevant Patch Test Results (n = 31)
Dermatitis	4 (40)	15 (48)
Localized	3 (30)	8 (26)
Generalized	1 (10)	7 (23)
Localized pruritus	2 (20)	3 (10)
Joint pain	6 (60)	18 (58)
Joint loosening	4 (40)	4 (13)
Impaired wound healing	1 (10)	2 (6)
Edema	2 (20)	7 (23)

nal fixation of bone fractures, spinal instrumentation, and Nuss procedures.²³ Its composition varies according to application standards and includes chromium, 19.5% to 22%; molybdenum, 2% to 3%; nickel, 9% to 33%; and less than 1% of niobium, manganese, carbon, and nitrogen.²⁴⁻²⁷ An advantage of stainless steel is the relatively low resistance to corrosion.^{28,29} Cobalt alloys are widely used in total knee replacement, sometimes hip replacement, and smaller endoprostheses. The composition of cobalt (Co-Cr-Mo) alloys includes cobalt, 64%; chromium, 28%; molybdenum, 6%; and nickel, 0.5% to 2.5%.⁷ In contrast, titanium alloys (Ti-6Al-4V, Ti-Mo12-Zr6-Fe2, and TiNb13Zr13) have a very low content of nickel (0.01%-0.03%), which typically results from the production process. Titanium alloys are frequently used in the femoral stem of hip prostheses, the tibial component in knee arthroplasties, for spinal fusion, and in osteosynthesis materials.^{7,19}

The choice of implant alloy depends on its application, therapeutic standards, and the surgeon's experience. In this study, the surgeons were cognizant of patch test results and dermatologist recommendations when selecting implants. The most commonly chosen allergen-free implants in this study were titanium alloys and oxidized zirconium-niobium (Oxinium; Smith & Nephew). Titanium implants are frequently used as an alternative prosthesis in primary hip arthroplasty in conjunction with a polyethylene- or ceramic-bearing surface.⁷ Titanium alloys, even the "nickel-free" variants, contain traces of nickel, with a theoretical possibility for hypersensitivity reaction.⁴ The oxidized zirconium-niobium alloy is coated with ceramic and oxygen that does not contain nickel; it is associated with fewer wear particles. It is a novel, more expensive alternative to the conventional cobalt-chromium alloys in knee arthroplasty.¹⁹ The drawbacks to using these "allergen-free" implants rather than conventional prostheses include lack of studies on long-term results and substantially higher costs.⁴

In the postimplantation group, the most commonly encountered symptoms in patients with relevant metal allergy were localized dermatitis, joint loosening, and joint pain. Aseptic loosening is the clinical manifestation of the body's reaction to wear debris generated from metal-on-metal or metal-on-polyethylene articulation.³⁰ The post-

Table 6. Details on Postimplantation Patients With Clinically Relevant Patch Tests Indicating Metal Sensitivity

Sex/ Age, y	Type of Implant (Metal Alloy) ^a	Symptoms	Cutaneous Findings Postimplant	Onset of Symptoms After Operation	Allergy History	Relevant Metal	Implant Removal/ Revision (Composition of New Implant) ^a	Outcome (Total FU After Revision)	Total FU After First Operation, mo
F/48	Fibular plate (SS)	D, E	Localized to prosthesis, pruritic erythematous plaques	Immediate	CMH, A	Ni	Device removed	D and E resolved (54 mo)	62
M/14	Nuss bar (SS)	D	Localized to prosthesis, pruritic erythematous patches	7 mo	None	Ni	Device removed	D resolved (1 mo)	23
M/18	Spinal fusion rod (SS)	D, W	Localized to prosthesis, focal granulation tissue, with fibrosis and erosions	<1 mo	A	Ni	Device removed	D resolved, wound healed (46 mo)	58
M/73	TKA, bilateral (Fem/Tib: Co-Cr-Mo)	D, P, E	Generalized, involving site of prosthesis, eczematous lichenified plaques	<1 mo	CMH	Ni	No revision	D and P persisted until last FU	179
F/50	TKA (Fem/Tib: Co-Cr-Mo)	P, W	None	2 mo	CMH	Co	No revision	P and W persisted until last FU	17
F/73	TKA (Fem/Tib: Co-Cr-Mo)	P, Lo, E	None	Progressive, <12 mo	CMH, A	Ni	No revision	P, E and Lo persisted until last FU	93
M/56	TKA (Fem/Tib: Co-Cr-Mo/ Ti-6Al-4V)	P, Lo, E	None	15 mo	CMH	Ni, Cr	No revision	P, Lo, and E persisted until last FU	36
M/70	TKA (Fem/Tib: Co-Cr-Mo)	P, Lo	None	Progressive, <12 mo	A	Cr	Revision (OZN)	P resolved, no recurrence of Lo (14 mo)	38
M/60	Shoulder arthroplasty (Met/screw: Ti-6Al-4V; Hum/Glen: SS)	P, Lo	None	Progressive, pain at <1 mo	CMH, A	Ni	Revision, (Ni-free Ti)	P resolved, no recurrence of Lo (12 mo)	36
F/55	THA (Acet: Ti-6Al-4V; Fem: Co-Cr-Mo; Insert: PE)	P, Lo	None	Pain at <1 mo	CMH	Ni	Revision (OZN)	P resolved, no recurrence of Lo (1.5 mo)	38

Abbreviations: A, atopy; Acet, acetabular component; Al, aluminum; bal, remaining balance; CMH, cutaneous metal hypersensitivity; Co, cobalt; Cr, chromium; D, dermatitis; E, edema at site of prosthesis; Fe, iron; Fem, femoral component; FU, follow-up; Glen, glenosphere; Hum, humeral component; Lo, joint loosening; Met, metaglene; Mo, molybdenum; Nb, niobium; Ni, nickel sulfate; OZN, oxidized zirconium-niobium; P, joint pain; PE, polyethylene; SS, stainless steel; THA, total hip arthroplasty; Ti, titanium; Tib, tibial component; TKA, total knee arthroplasty; V, vanadium; W, impaired wound healing; Zr, zirconium.

^aMetal composition of implants (weight percentage). SS: Cr (17-19), Ni (13-15), Mo (2.25-3), copper (0.5), manganese (2), and Fe (bal); Co-Cr-Mo alloy: Cr (27-30), Mo (5-7), Ni (1), manganese (1), Fe (<1), tungsten (<1), Al (<1), and Co (bal); Ti-6Al-4V: Al (5.5-6.75), V (3.5-4.5), Fe (<1), and Ti (bal); OZN: Zr (97.5) and Nb (2.5); Ni-free Ti: Fe (30) and Ti (32).

implantation patients with complications to a relevant metal implant who underwent a procedure to have it removed, revised, or both subsequently experienced resolution of their symptoms. Patients who did not undergo revision continued to experience symptoms. Thus, if patch testing supports a potential allergic causative association, removal of the offending implant should be considered. This may be generally easier with static devices. Dynamic devices should not be replaced or revised solely on the basis of a positive metal patch test unless there is severe impairment of function of the device or the joint.

The focus of this study was on hypersensitivity complications associated with implanted metals; however, other

implant components occasionally cause hypersensitivity reactions.³¹ For example, the implant may be lined with plastic that acts as artificial cartilage, or the hardware may require anchoring in the bone with cement, which can be acrylate-based or impregnated with antibiotics. Thus, in addition to metals, methyl methacrylate monomers, benzoyl peroxide, and gentamicin can act as potential causes of implant-related allergic reactions.^{32,33} In this study, positive patch test reactions to benzoyl peroxide and gentamicin were detected only in our postimplantation patients, which may reflect exposure to that material in their implant (**Table 7**). The other common nonmetal allergens in the postimplantation patients were bacitracin (n=4), bal-

Table 7. Patch Test Results for Common Nonmetal Allergens in Preimplantation and Postimplantation Patients

Positive Patch Test Result	No. (%)	
	Preimplantation Patients (n = 31)	Postimplantation Patients (n = 41)
Benzoyl peroxide	0	4 (10)
Gentamicin	0	3 (7)
Methyl methacrylate	0	0
Balsam of Peru	2 (6)	4 (10)
Thimerosal	4 (13)	3 (7)
Bacitracin	1 (3)	4 (10)
Neomycin	4 (13)	2 (5)

sam of Peru (n=4), thimerosal (n=3), and neomycin (n=2). Furthermore, patients with cutaneous eruptions who did not have a relevant positive patch test to a metal benefited from dermatology evaluation. The identified causes for the eruptions in these patients included benzoin in bandages (n=2), bacitracin used in wound irrigation (n=1), reticular telangiectatic erythema (n=3), infection (n=2), medication-induced dermatitis (n=1), palmoplantar keratoderma (n=1), prurigo nodularis (n=1), neurodermatitis (n=1), tumid lupus (n=1), psoriasis (n=1), and reflex sympathetic dystrophy (n=1).

In conclusion, the results of this study support the value of patch testing for patients with a clinical history of metal hypersensitivity before surgical implant in bone or a joint as a safe measure to avoid complications. The study confirms the need for surgeons and dermatologists to work together and establish guidelines with a goal to identify patients who would benefit from revisions of previously implanted metal. When interpreting these results, we are conscious of the study's limitations, such as the relatively small sample size and the lack of a comparative group for whom the surgeons disregarded the patch test results. Ultimately, a decision should be made on a case-by-case basis, as a careful choice of a device to be implanted minimizes the potential for complications. Patch testing remains a standard for evaluating patients with suspected metal allergy; however, it may not always result in a diagnosis, despite a high clinical suspicion. We acknowledge the lack of agreement on which specific allergens, especially which metal salts, should be used for patch testing when devising the prosthesis trays. Because many of the metals are not part of routine testing, there is always a possibility of false-positive (irritant) or false-negative reaction if the allergen concentration is too low to elicit a response. In vitro tests that measure proliferative response of lymphocytes to a patient's serum incubated with metals are another option but are performed only in a few laboratories.³⁴

Accepted for Publication: October 27, 2011.

Published Online: February 20, 2012. doi:10.1001/archdermatol.2011.2561

Correspondence: Natasha Atanaskova Mesinkovska, MD, PhD, Department of Dermatology, Dermatology-Plastic Surgery Institute, Desk A-61, Cleveland Clinic, Cleveland, OH 44195 (atanasn@ccf.org).

Author Contributions: All authors had full access to all the data in the study and take responsibility for the integrity and accuracy of the data analysis. *Study concept and design:* Atanaskova Mesinkovska, Tellez, Molina, Honari, Sood, and Taylor. *Acquisition of data:* Atanaskova Mesinkovska, Tellez, Molina, and Taylor. *Analysis and interpretation of data:* Atanaskova Mesinkovska, Tellez, Honari, Barsoum, and Taylor. *Drafting of the manuscript:* Atanaskova Mesinkovska, Tellez, and Molina. *Critical revision of the manuscript for important intellectual content:* Atanaskova Mesinkovska, Honari, Sood, Barsoum, and Taylor. *Administrative, technical, and material support:* Atanaskova Mesinkovska and Taylor. *Study supervision:* Honari, Sood, Barsoum, and Taylor.

Financial Disclosure: Dr Taylor has served as a consultant for the National Institute for Occupational Safety and Health; Betco, Inc; Shire Pharmaceuticals, plc; Novartis; Procter & Gamble; AMA Press; and the Consumer Product Safety Commission. He has received honoraria from the American Academy of Dermatology; Chinese Society of Dermatology; HMP Communications; Medicis Pharmaceutical Corporation; Hermal Pharmaceutical Laboratories Germany; BASF; UnitedHealthcare; Regent Medical Ltd; Uni-Tech Communications; Watson Pharmaceuticals; WebMD; and HOB Biotech/SmartPractice. Dr Taylor has had stock ownership in Amgen (sold in 2008); Bristol-Myers Squibb; GlaxoSmithKline; Johnson & Johnson; Keithley Instruments (sold in 2006); Merck & Co, Inc; Medco Health Solutions; Wyeth Pharmaceuticals (sold in 2009); and Renovo, plc. He has received grants from Guidant and Shire. His department is an investigator for Amgen; Astellas Pharma; Biogen Idec; Bristol-Myers Squibb; Eli Lilly and Company; Genentech; Lexington International; Johnson & Johnson; Novartis AG; Pfizer, Inc; Procter & Gamble; Centocor; Sovay Pharmaceuticals; and Wyeth Pharmaceuticals. Dr Barsoum has served as a consultant for Stryker Orthopaedics; Wright Medical Technology, Inc; and Shukla Medical. He is a member of the speakers' bureau for Stryker Orthopaedics. Dr Barsoum has stock ownership or options in OtisMed Corporation; Custom Arthroplasty Solutions; and Custom Orthopaedic Solutions, Inc. He has received grants from Stryker Orthopaedics; Zimmer; Salient Surgical Technologies; CoolSystems, Inc; and Orthovita, Inc. He has filed and received multiple patents. Dr Barsoum receives royalties from Stryker Orthopaedics; Exactech, Inc; Wright Medical Technology; and Shukla Medical. None of the financial relationships listed for Drs Taylor and Barsoum are directly relevant to the subject matter of this article.

Additional Contributions: We are indebted to James Bena, MS, from the Cleveland Clinic Foundation for assistance with statistical analysis. (Mr Bena received compensation for this assistance.)

REFERENCES

1. Kurtz S, Ong KM, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am.* 2007;89(4):780-785.
2. Joint Replacement Registry. American Academy of Orthopaedic Surgeons Web site. <http://www6.aaos.org/news/pemr/JointRegistry/JointRegistry.cfm>. Accessed November 30, 2011.

3. Holliday KL, McWilliams DF, Maciewicz RA, Muir KR, Zhang W, Doherty M. Lifetime body mass index, other anthropometric measures of obesity and risk of knee or hip osteoarthritis in the GOAL case-control study. *Osteoarthritis Cartilage*. 2011;19(1):37-43.
4. Bader R, Bergschmidt P, Fritsche A, Ansorge S, Thomas P, Mittelmeier W. Alternative materials and solutions in total knee arthroplasty for patients with metal allergy [in German]. *Orthopade*. 2008;37(2):136-142.
5. Räsänen P, Paavolainen P, Sintonen H, et al. Effectiveness of hip or knee replacement surgery in terms of quality-adjusted life years and costs. *Acta Orthop*. 2007;78(1):108-115.
6. Wearing SC, Hennig EM, Byrne NM, Steele JR, Hills AP. Musculoskeletal disorders associated with obesity: a biomechanical perspective. *Obes Rev*. 2006;7(3):239-250.
7. Dearnley PA. A review of metallic, ceramic and surface-treated metals used for bearing surfaces in human joint replacements. *Proc Inst Mech Eng H*. 1999;213(2):107-135.
8. Zug KA, Warshaw EM, Fowler JF Jr, et al. Patch-test results of the North American Contact Dermatitis Group 2005-2006 [published correction appears in *Dermatitis*. 2009;20(5):300]. *Dermatitis*. 2009;20(3):149-160.
9. Merritt K, Rodrigo JJ. Immune response to synthetic materials: sensitization of patients receiving orthopaedic implants. *Clin Orthop Relat Res*. 1996;326(326):71-79.
10. Willert HG, Buchhorn GH, Fayyazi A, et al. Metal-on-metal bearings and hypersensitivity in patients with artificial hip joints: a clinical and histomorphological study. *J Bone Joint Surg Am*. 2005;87(1):28-36.
11. Kubba R, Taylor JS, Marks KE. Cutaneous complications of orthopedic implants: a two-year prospective study. *Arch Dermatol*. 1981;117(9):554-560.
12. Niki Y, Matsumoto H, Otani T, et al. Screening for symptomatic metal sensitivity: a prospective study of 92 patients undergoing total knee arthroplasty. *Biomaterials*. 2005;26(9):1019-1026.
13. Thyssen JP, Menné T, Schalock PC, Taylor JS, Maibach HI. 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(3):473-478.
14. Reed KB, Davis MD, Nakamura K, Hanson L, Richardson DM. Retrospective evaluation of patch testing before or after metal device implantation. *Arch Dermatol*. 2008;144(8):999-1007.
15. Thyssen JP, Jakobsen SS, Engkilde K, Johansen JD, Søballe K, Menné T. The association between metal allergy, total hip arthroplasty, and revision. *Acta Orthop*. 2009;80(6):646-652.
16. Aneja S, Taylor JS, Billings SD, Honari G, Sood A. Post-implantation erythema in 3 patients and a review of reticular telangiectatic erythema. *Contact Dermatitis*. 2011;64(5):280-288.
17. Aneja S, Taylor JS, Soldes O, DiFiore J. Dermatitis in patients undergoing the Nuss procedure for correction of pectus excavatum. *Contact Dermatitis*. 2011;65(6):317-321. doi:10.1111/j.1600-0536.2011.01966.x.
18. Baron JA, Barrett J, Katz JN, Liang MH. Total hip arthroplasty: use and select complications in the US Medicare population. *Am J Public Health*. 1996;86(1):70-72.
19. Hallab N, Merritt K, Jacobs JJ. Metal sensitivity in patients with orthopaedic implants. *J Bone Joint Surg Am*. 2001;83(3):428-436.
20. Rau C, Thomas P, Thomsen M. Metal sensitivity in patients with joint replacement arthroplasties before and after surgery [in German]. *Orthopade*. 2008;37(2):102-110.
21. Gawkrödger DJ. Nickel sensitivity and the implantation of orthopaedic prostheses. *Contact Dermatitis*. 1993;28(5):257-259.
22. Schuh A, Thomas P, Kachler W, et al. Allergic potential of titanium implants [in German]. *Orthopade*. 2005;34(4):327-328, 330-333.
23. Rushing GD, Goretsky MJ, Gustin T, Morales M, Kelly RE Jr, Nuss D. When it is not an infection: metal allergy after the Nuss procedure for repair of pectus excavatum. *J Pediatr Surg*. 2007;42(1):93-97.
24. Thomas P, Schuh A, Ring J, Thomsen M. 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 Allergy and Clinical Immunology) [in German]. *Orthopade*. 2008;37(1):75-88.
25. Dearnley PA. A review of metallic, ceramic and surface-treated metals used for bearing surfaces in human joint replacements. *Proc Inst Mech Eng H*. 1999;213(2):107-135.
26. Thomas P, Thomsen M. Implant allergies [in German]. *Hautarzt*. 2010;61(3):255-262.
27. Gawkrödger DJ. Metal sensitivities and orthopaedic implants revisited: the potential for metal allergy with the new metal-on-metal joint prostheses. *Br J Dermatol*. 2003;148(6):1089-1093.
28. Gotman I. Characteristics of metals used in implants. *J Endourol*. 1997;11(6):383-389.
29. Haudrechy P, Mantout B, Frappaz A, et al. Nickel release from stainless steels. *Contact Dermatitis*. 1997;37(3):113-117.
30. Hallab NJ, Cunningham BW, Jacobs JJ. Spinal implant debris-induced osteolysis. *Spine (Phila Pa 1976)*. 2003;28(20)(suppl):S125-S138.
31. Granchi D, Cenni E, Tigani D, Trisolino G, Baldini N, Giunti A. Sensitivity to implant materials in patients with total knee arthroplasties. *Biomaterials*. 2008;29(10):1494-1500.
32. Haddad FS, Cobb AG, Bentley G, Levell NJ, Dowd PM. Hypersensitivity in aseptic loosening of total hip replacements: the role of constituents of bone cement. *J Bone Joint Surg Br*. 1996;78(4):546-549.
33. Treudler R, Simon JC. Benzoyl peroxide: is it a relevant bone cement allergen in patients with orthopaedic implants? *Contact Dermatitis*. 2007;57(3):177-180.
34. Hallab NJ. Lymphocyte transformation testing for quantifying metal-implant-related hypersensitivity responses. *Dermatitis*. 2004;15(2):82-90.

PRACTICE GAPS

ONLINE FIRST

The Role of Patch Testing in the Selection and Management of Metal Device Implants

Most dermatologists are familiar with patch testing, but expanded testing beyond standard trays is not ubiquitous. Patients with metal implants (orthopedic, dental, or cardiac devices) referred to dermatologists for patch testing present a unique challenge an important practice gap. How should we manage these patients? Who benefits from testing? What, if any, impact does patch testing have on implant selection or management?

Whether seeing the patient preoperatively to determine what metals the patient is allergic to or postoperatively to help manage issues of joint failure or device complications, the dermatologist must set realistic expectations

for the patient and referring physician about what information will be obtained through patch testing. For the patient undergoing testing prior to implant selection, the dermatologist must emphasize that the patch test detects current allergy but is not indicative of future allergy. In addition, limitations must be discussed. The patch test is a cutaneous test that does not recreate the environment in which the metal resides. Therefore, the testing might not recreate or elicit the same response as that of a metal within a joint space, for example. Coordinating the patch test procedure with a surgeon's timeline is yet another challenge.

The clinical situation is not always clear and depends on whether testing is done before or after implantation.