

Systemic Contact Dermatitis and Allergy to Biomedical Devices

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Abstract Systemic contact dermatitis (SCD) refers to a skin condition where an individual who is cutaneously sensitized to an allergen will subsequently react to that same allergen or a cross-reacting allergen via the systemic route. It occurs to allergens including metals, medications, and foods. There has been recent interest in metal allergy as it relates to the implantation of devices such as orthopedic, dental, cardiac, and gynecologic implants. This review will briefly address all causes of systemic contact dermatitis with a special and expanded focus on metal implant allergy. We present literature on SCD to various metal biomedical devices, patch testing for diagnosis of metal allergy pre and post implantation and treatment.

Keywords Systemic contact dermatitis · Allergic contact dermatitis · Metal allergy · Orthopedic implant · Dental implant · Dental amalgam · Stent · Pacemaker · Intrauterine devices · Biomedical devices

Introduction

Systemic Contact Dermatitis (SCD) refers to a skin condition where an individual who is sensitized to an allergen via the cutaneous route will subsequently react to that same allergen or a cross-reacting allergen via the systemic route (oral, intravenous, intramuscular, inhalational, transmucosal or transcu-

taneous) [1•, 2]. It can manifest as a rash at the previous site of dermatitis, rash at the site of previous positive patch test, hand dermatitis, erythroderma, vasculitis-like lesions and symmetrical intertriginous and flexural exanthema [1•, 3]. In the 1980s, it was described as “Baboon syndrome” by Andersen et al. for its erythematous lesions on the buttocks, inner thighs and axilla [4]. It occurs to allergens including metals, medications and foods including plants and herbal products usually within 1–2 days of exposure.

SCD to Foods. Plant members of the Compositae family (chamomile, feverfew, chrysanthemum) and Anacardiaceae family (poison ivy, poison oak, mango tree, cashew nut tree) are responsible for many cases of SCD to foods. Members of the Compositae family are frequently used in cosmetics and topical medications [5]. Patients sensitized to chamomile have reported reactions with ingestion of chamomile teas [6–8]. Patients allergic to Balsam of Peru (BOP) can react after the ingestion of foods and spices including tomato-based products, colas, cinnamon, vanilla, ketchup, cough syrup, candies and toothpastes [9]. In a series of seven pediatric patients with difficult to treat atopic dermatitis suspected of having allergic contact dermatitis, 60–80 % improvement in rash was seen on a low Balsam of Peru diet [10]. In a retrospective review of patients positive to BOP and fragrance mix, 47 % on a low BOP diet had significant to complete resolution of their dermatitis while only 20 % had complete/significant improvement with fragrance or other allergen contact avoidance only [11]. SCD has also been identified to propylene glycol (PG) [12] which is used as a vehicle in various forms of medications (topical, oral, injection), foods and cosmetic products for its moisturizing and solvent qualities. Foods that contain PG include creamers, caffeine beverages, snack foods, dairy products and soups; a PG avoidance diet has been proposed in patients with systemic contact dermatitis who do not respond to contact avoidance [13•].

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SCD to Medications. Medications that have caused SCD include those that have both a topical and systemic form including aminoglycosides, corticosteroids, and ethylenediamines [1•]. Neomycin is the 2nd most common positive allergen on patch testing in North America [14]; it is highly cross-reactive with gentamycin and patients sensitized through the skin, likely due to its frequent inclusion in over-the-counter topical antibiotic preparations may react to orally administered aminoglycosides [15]. Other medications implicated in SCD include diclofenac, hydroxyquinoline, penicillin, nystatin, vitamins C and B6, and acetylsalicylic acid [2]. A separate classification [16] has been proposed for patients developing a symmetric drug-related intertriginous and flexural exanthema (SDRIFE) who do not have a history of cutaneous sensitization.

SCD to Metals. Of the metals, nickel, mercury, gold, cobalt, copper, chromium and aluminum have been reported to cause SCD [2]. Nickel is the most common patch test allergen [14, 17] and routes of exposure include coins, jewelry, tools, clothing, utensils, nickel-plated objects (phones, laptops) and food. Canned foods, cocoa, chocolate, soy, legumes, herring, salmon, shellfish, cashews and mackerel are examples of foods with high nickel content [18]. Sensitization to nickel likely also occurs via ear [19] and body piercings. In Europe, following the institution of EU Nickel Directive, the prevalence of nickel allergy decreased in Danish young women; the prevalence of nickel allergy and dermatitis was higher in female patients pierced prior to 1990 than those pierced after this date [20•].

Allergy to Metals in Biomedical Devices

Wear and corrosion of metal implants leads to release of free ions which can deposit in periprosthetic sites as well as extracutaneously in liver, spleen and kidney tissue [21–26]. This has been shown for both stainless steel (iron, chromium, molybdenum, and nickel) and titanium devices (vanadium and aluminum) [27]. Intravascular devices and joint prostheses are typically comprised of nitinol, chromium/cobalt alloy, or stainless steel. Nitinol releases the least amount of free nickel, while stainless steel releases the greatest amount [28]. Much of the literature regarding metal ion exposure relates to the putative deleterious effects of nickel or other composite metal ions, depending on the prosthesis used, although there is a lack of in vivo data that the presence of metal ions results in systemic symptoms. It has been hypothesized that free nickel may conjugate with proteins as a hapten, and can act as a superantigen [29, 30] or lead to recruitment of ICAM-1 [31] and result in fibrosis or neointimal hyperplasia (the latter hypothesized as a mechanism of re-stenosis in cardiovascular

devices). Systemic or localized cutaneous reactions can be attributed in part to type IV, delayed hypersensitivity reactions [25, 32, 33]. Nickel allergy may be somewhat more challenging to attribute entirely to implantation, as it is so prevalent in consumer items. Lastly, it has been proposed that the development of aseptic lymphocytic vasculitic associated lesions (ALVAL) may also be due to a delayed hypersensitivity reaction localized to the joint when metal ions are released from the prosthesis [34]. Another mechanism of how the innate immune system may be contributing to orthopedic implant failure is the role of debris stimulating toll-like receptors (TLRs) [35] which have been found around the interface membrane in aseptic loose total hip replacements [36]. Nickel has been recently shown to stimulate TLR4 [37] in a species-specific mechanism via non-conserved histidines at positions 456/458 of the TLR4 molecule.

SCD to Orthopedic Implants

Older orthopedic implants of the 1960s–1970s were comprised of stainless steel (8–35 % nickel, 20 % chromium, 45 % other metals) or chromium/cobalt/molybdenum steel alloy [38, 39]. These first generation metal-on-metal implants are prone to corrosion and mechanical wear, leading to deposition of metals including nickel, cobalt, and chromium in the blood, urine, and hair, and resulted in higher rates of metal sensitization [40–42]. Newer implants are made of titanium or oxallium, which contain at most trace amounts of nickel and no cobalt or chromium; or vitallium, a newer chromium/cobalt alloy [43–47]. These newer implants are purported to have a lower rate of postoperative instability [47]. There have been reports, however, of elevated serum and urine concentrations of cobalt and chromium in patients undergoing implantation with a newer generation prosthesis [48–51].

Metal implant sensitivity has been described in a number of case reports. To date, there are more than 55 cases describing allergic contact dermatitis secondary to orthopedic implants which have been summarized elsewhere [52•], in addition to sporadic cases of erythema [53], vasculitis [54], and urticaria [55]. Non-cutaneous reactions to orthopedic implants including implant failure and ALVALs [56–58] have also been described.

Metals reported responsible for systemic contact dermatitis include nickel, cobalt, chromium, and, rarely, titanium [59–61]. Up to one-fifth of patients with sensitivity preoperatively may later develop ACD upon re-exposure to the same metal [32]. These findings were supported in a recent review by Granchi et al., who published a meta-analysis of 22 observational studies [62] in which metal sensitization was analyzed pre- and post-joint implantation. Rates of sensitization to metals were higher in patients with a failed implant as compared to those with a well-functioning device,

although PT results did not appear to be predictive of joint failure [63].

There are some data to support that metal implantation may lead to de novo sensitization, although there is a lack of statistical support [23, 45, 64]. Patients undergoing hip or knee arthroplasty who had patch testing (PT) pre- and 1-year post-implantation had a new sensitization rate of 6.5 % which was not statistically significant [65]. In a European study [66], where PT was also preformed pre- and post-implantation, there was no statistically significant change in positive PT results, although five patients did develop a positive PT result post-implantation, all of whom were symptomatic. Non-metals, such as silicon and components of bone cement including but not limited to acrylates, benzoyl peroxide, N,N-dimethyl-p-toluidine, and gentamicin, also warrant investigation when considering implant allergy [67, 68••].

It has been proposed that up to 5 % of joint arthroplasty failures may be attributable to type IV hypersensitivity reactions, particularly with the older implants [32]; however, there is a lack of confirmatory data. A retrospective study of 356 patients undergoing total hip arthroplasty (THA) showed that rates of revision among patients with THA were no different in nickel-allergic patients than those without nickel allergy. Additionally, the rates of development of nickel allergy did not appear to be increased in patients with nickel implants [69]. These statistics warrant confirmation with long-term prospective studies in this field.

SCD to Endovascular Devices

The data on the role of metal allergy in cardiac stent implantation relate to in-stent restenosis. Bare metal stents are made of stainless steel and have higher rates of in-stent restenosis than drug-eluting stents. Although theoretically possible, there are limited data to suggest that patients with a nickel allergy have a higher rate of in-stent restenosis, and the evidence has not been reproducible [70–75]. Molybdenum and manganese have also been implicated in very small-scale studies, and there was question as to the concentration of metal salts used for PT [28, 71, 76, 77]. There is, however, a slightly higher in-stent restenosis rate with gold-coated stents which was demonstrated very early on in clinical trials [78–80]. Additionally, there is a higher risk of the development [81] of ACD to gold in patients with these stents [82]. For these reasons, these stents are no longer used. Lastly, there have been four isolated reports of fatal coronary thrombosis after placement of a Cypher® drug-eluting stent. Eosinophilic infiltration and poor intimal healing was found upon autopsy. While no allergen has been identified to date, the eosinophilic predominance on histology suggests a possible allergic explanation for stent failure [83, 84].

Two devices are commonly used for repair of patent foramen ovale (PFO) and atrial septal defects (ASD), Amplatzer® (nitinol wire mesh with Dacron) [85] and CardioSEAL® (cobalt alloy and polyester fabric) [86]. One study assessed serum nickel levels in 67 patients who underwent Amplatzer® placement, and found a statistically significant increase in serum nickel content within 1 month [87]. There are only a few case reports of non-cutaneous reactions with implantation of these devices; in one patient a positive PT reaction was seen to the Amplatzer® device [88]. In another patient [89], who displayed fever and shortness of breath in the absence of infection 2 months after implantation, PT was positive to nitinol, and her symptoms resolved with removal of the PFO occluder [89]. Further investigation as to whether these devices induce sensitization or cause SCD is warranted.

SCD to Pacemakers

Allergic reactions to pacemakers are rare. Titanium is the most common metal responsible for pacemaker-induced dermatitis, and typically presents as eczematous dermatitis overlying the pacemaker site [90–93]. The use of polytetrafluoroethylene (PTFE) covers typically results in resolution of the dermatitis and has proven beneficial long term [91, 94]. There may be a slight increased rate of infection with the use of these covers, although this has not been demonstrated in large scale [95]. There has been a case of systemic, septic-like symptoms (in the absence of infection) to a pacemaker without a dermatitis which resolved with removal of the implant. Patch testing revealed a strong positive to cobalt, which was a component in the metal implant [96]. There has also been a case of dermatitis secondary to a silicone component in the pacemaker, which was proven by patch testing, and resolved with the use of a silicone-free pacemaker device [97]. All components of the pacemaker should be taken into account when evaluating for pacemaker-induced dermatitis. One must also take into consideration other non-allergic skin findings that have been reported with pacemaker implantation including telangiectasias and infection-related causes of inflammation [28]. Treatment of pacemaker dermatitis may include use of topical corticosteroids, replacement of device that does not include suspected allergens, and using PTFE sheet [28]. An extensive review of case reports of contact allergy including local and systemic reactions to pacemakers is presented elsewhere [28].

SCD to Pectus Repair

There have been a few case reports of contact allergy to the stainless steel bar after Nuss repair for pectus excavatum [98, 99]. Nuss reported that 2.9 % of 1015 patients who underwent the procedure were reported to have “bar allergy” [99], which

lead to a prospective study following 50 patients who underwent the Nuss procedure. Of these, 4 had wound dehiscence and 1 tested positive to nickel. No patients required removal of the bar and no patients tested positive to the stainless steel disc provided by the manufacturer. The authors suggested that metal allergy may play a role in wound dehiscence or overlying dermatitis and a history of confirmed metal allergy may be taken into consideration prior to bar placement [100].

SCD to Dental Implants

Type 4 hypersensitivity reactions to dental materials may present as stomatitis, lichenoid reactions of the oral mucosa, and burning or pain experienced by the patient [101, 102]. Of these, the most frequent manifestation seen in conjunction with ACD is a lichenoid reaction [52] which may be reticular, atrophic, erosive, or plaque-like in nature. Dental amalgam is an alloy that is composed of metals including mercury; it is the most common dental filling used worldwide for over 100 years due to its strength, durability, and inexpensiveness [103]. Common reactions to amalgam are oral lichenoid lesions on the mucosa that is in contact with the amalgam [103]. Lesions are most commonly seen on buccal mucosa or tongue unilaterally and are not symmetrical; patients may be asymptomatic or have pain with hot or spicy foods [103]. PT should include 5 % amalgam and 1 % ammoniated mercury with a delayed reading at 10–14 days [103]. Following a PT-positive result, only amalgams in close contact to the lichenoid lesion should be removed; if PT is negative but suspicion is still high, either the crown may be covered to limit amalgam contact with the mucosa or a single amalgam can be removed to check if healing is induced [103].

In a retrospective review of 206 patients [104] who had PT preformed to investigate contact allergy to dental metals, 28 (27 F; 1 M) patients had at least one positive PT result. The highest number of PT-positive results was for gold, palladium, and nickel ($n=10$ for each metal). In this study, the diagnoses yielding the highest number of PT-positive results were stomatitis and lichen planus. The results were deemed relevant in 7 out of 9 patients with lichen planus and 7 out of 8 patients with stomatitis. In another retrospective study from Israel [105], looking at PT results in 121 patients (103 with facial and oral involvement) suspected of having ACD to dental materials, the most common allergens detected were gold, nickel, mercury, palladium, cobalt, and 2-hydroxyethyl methacrylate. These patients had presented most commonly with cheilitis and perioral dermatitis, burning mouth, and lichenoid reaction. Most of the reactions to mercury appeared relevant to the authors, while gold and nickel positives were of uncertain clinical relevance.

A case of isolated lichen planus of the lip [106] in a 47-year-old male was attributed to SCD from metals (nickel,

cobalt) and food (cinnamic aldehyde, cinnamyl alcohol); he improved with low nickel/cobalt/balsam of peru diet and avoidance of flavored toothpastes and mouthwashes. Another presentation of SCD was seen in a 46-year-old atopic woman with cheilitis, stomatitis, and dermatitis [107] on her right forearm and forehead after an oral surgical implantation of titanium on the maxillary bone near to her dental amalgams. PT was positive to dental amalgam (++), nickel sulphate and palladium chloride (+++). The patient returned with bilateral leg dermatitis after receiving an entire maxillary prosthesis of chromium-cobalt alloy.

Although uncommon, there are reported cases of SCD to zinc. A 61-year-old male [108] presenting with generalized vesicular rash was PT-positive to zinc chloride (++). The patient's dermatitis improved with replacement to zinc free fillings. In another case report [109], a 37-year-old Japanese male with a 1-year history of pruritic widespread skin eruptions had dental fillings 3 months prior to onset of rash. He was PT-positive to zinc (+) and had a positive lymphocyte stimulation test to zinc. Overall removal of the zinc-containing fillings led to improvement of the rash with brief flare-ups associated with each procedure.

A 15-year-old female who developed an erythematous dermatitis on face, neck, scalp, arms, and wrists 40 days after placement of orthodontic appliances [110], was found to be PT-positive to nickel (++). Removal of the appliances led to resolution of symptoms within 6 months and sustained symptom-free interval after 2 years. Another teenager developed eczema on palms, soles, scalp, abdomen, and legs with vesicles around the lips after placement of bands on the maxillary molars and use of extra-oral face bow [111]. He was PT-positive to cobalt and nickel and resolution of the eczema occurred after discontinuation of the face bow and removal of the bands.

In another case report [112], a 71-year-old female who had dental amalgams and dental plate placed 8 years prior to the onset of an eczematous dermatitis was PT-positive to potassium dichromate. With removal of her dental plate, her symptoms resolved almost completely, and with reintroduction of the plate her symptoms recurred.

SCD to Contraceptive Devices (Intrauterine Devices)

Intrauterine devices (IUD) are made of copper sulfate. Reports of reactions to these copper-containing devices are rare in the literature [52] consisting mostly of individual case reports; in one reported case of SCD to IUD [113], a patient developed urticaria and angioedema of eyelids and labia 6 months after placement. She was positive to copper sulfate on PT and lymphocyte-stimulating test; removal of the device resulted in complete resolution of her symptoms.

Since 2002, a nitinol-containing (alloy of 55 % nickel and 45 % titanium with trace chromium in the outer coil) device

called Essure®, which is implanted in the fallopian tubes during an in-office procedure, has been approved by the FDA for permanent contraception [52, 114]. There have been case reports of symptoms to this device, one in a 40-year-old woman [115] presenting with anogenital itch and erythematous macular papular rash in genital and flexural areas and in a 27-year-old woman [116] who developed itch without a rash within 1 week of device placement. The diagnosis was confirmed with positive PT result for nickel (+) in both patients, and total clearance of symptoms occurred with removal of the implant in both cases.

A review of female patients with suspected nickel hypersensitivity from 2001 through 2010 who had Essure® implanted was undertaken [114]. Records from adverse events reported to the manufacturer (Conceptus), the Manufacturer and User Facility Device Experience (MAUDE) database, and clinical trials found 63 possible reports of nickel hypersensitivity. Of these 63 patients, 20 had PT and 13 were PT-positive to nickel. Nine of the 13 PT-positive patients had their device removed, and symptom resolution occurred in 4 out of 9. In 2 patients, the device was removed but symptoms remained, and in another 2 patients symptom resolution was unknown. Considering over 400,000 Essure® kits have been used since its introduction, the incidence of suspected nickel hypersensitivity to this device is very small (0.014 %) [114]. However, a contraindication to placement of this device is a known hypersensitivity to nickel (www.accessdata.fda.gov/cdrh_docs/pdf2/P020014c.pdf). Patients with suspected history of nickel allergy should be patch tested prior to placement of this device [115].

Evaluation of Metal Hypersensitivity

Prior to Placement of Metal Device

The tools available for evaluation of metal hypersensitivity include patient history of metal reactions, the lymphocyte transformation test, and patch testing. It is important, however, to note that patients with a negative history may still be PT-positive, and those who report history of metal allergy may be PT-negative [65, 117]. Thus, history alone is not of sufficient reliability to diagnose metal allergy.

Many experts do not believe that performing PT in patients without a history of reaction to metals is indicated prior to placement of a metal implant [68•]. Those patients with a history of metal hypersensitivity should be screened if the history is of “sufficient magnitude to cause concern to the patient or healthcare provider” [118]. If PT is preformed prior to surgery in a patient with suspected metal sensitivity, and there is a positive result, should an alternative implant be chosen? The answer is not clear cut from the literature. There is evidence that patients [69] with known metal hypersensitivity do not have a

greater risk of surgical revision following hip arthroplasty than those who do based on a Danish case control study. An older study [61], followed 18 patients with metal allergy who were implanted with a metal to which they were PT-positive; none of these patients developed complications. However, patients with positive PT reactions to metals and bone cement components and history of metal hypersensitivity display shorter lifespans of their implants [68•].

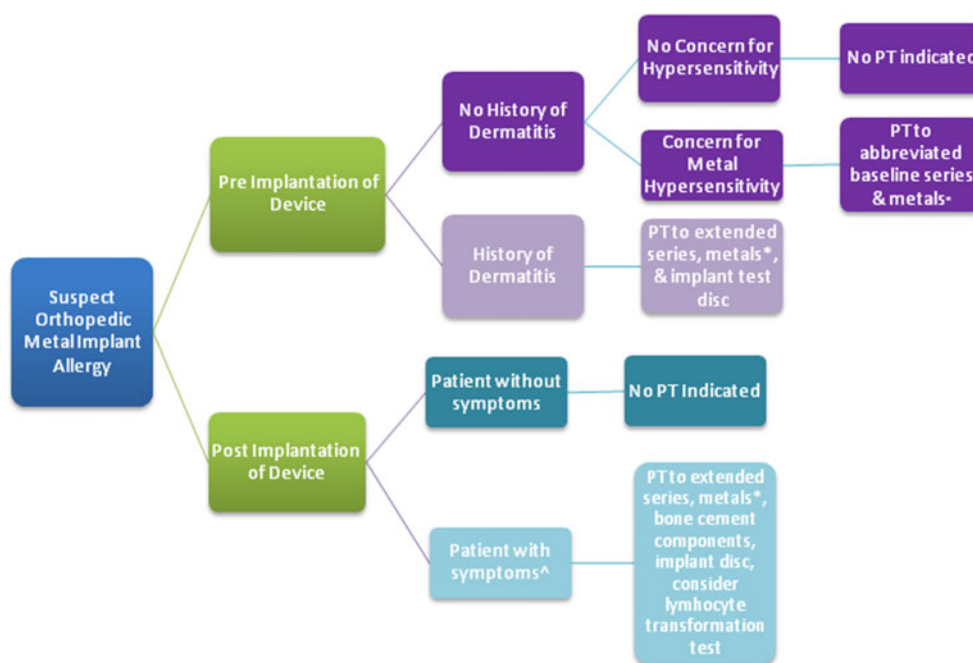
In vitro assays such as the lymphocyte transformation test are also part of the evaluation for metal hypersensitivity. This assay measures the proliferation of lymphocytes from peripheral blood in the presence and absence of an allergen [68•]; it is reported as a stimulation index. These assays are limited based on the need for expert interpretation, are not universally available, have a limited number of potential allergens that can be tested, and a need for rapid transport based on the limited lifespan of the lymphocytes [68•]. While this assay has added to the literature and our understanding of metal hypersensitivity, the gold standard for the evaluation of type 4 cell-mediated allergy to metals remains the patch test.

What to Test to Pre-implantation

PT should be targeted to the contents in the biomedical device. There are various suggested series to use for patch testing to metals prior to placement of metal implants [68•] (please refer to Fig. 1). Honari et al. [28], propose testing the following for endovascular implants along with a patch-testing kit if available from manufacturer of the product: ammonium molybdate, bacitracin, chlorhexidine, cobalt chloride, colophonium, formaldehyde, gold, indium, iridium, manganese, methyl methacrylate, neomycin, nickel, palladium, polydimethylsiloxane, potassium dichromate, tantalum powder, titanium dioxide, and titanium powder. A group from Mayo [59], who tested 44 patients (22 pre-op) proposed screening with a wide series including: acrylates, metals (aluminum, amalgam, beryllium, cadmium, chromium, cobalt, copper, ferric chloride, gold, manganese, mercury, molybdenum, nickel, palladium, potassium dichromate, tin, titanium alloy, vitallium, and zinc), and other agents including bone cement components (4-tert-butylphenol, bisphenol, epoxy resin, ethylene glycol, hydroquinone, and tetraethylene glycol). Both groups do suggest the addition of a baseline series along with the above metals when performing PT [28, 59]. If the patient has a history of dermatitis, an expanded baseline panel is suggested instead of an abbreviated baseline series [28, 68•].

A concise metal series is proposed by Schalock et al. [68•] depending on which implant is placed (dental, orthopedic pre- and post-implantation, intravascular stent, pacemaker, and gynecological) that can be tailored based on an individual's history. It references other components for testing, including acrylates and antibiotics (bone cement components), and offers advice on vehicles, concentrations,

Fig. 1 Hypersensitivity reactions to orthopedic metallic implants: diagnostic algorithm and suggested patch test series for clinical use. *LTT* Lymphocyte transformation test, *PT* patch test, *Pre-Implant* pre-implantation of metal device, *Post-Implant* post-implantation of metal device. *Metals: Aluminium, Chromium, Cobalt, Iron, Manganese, Molybdenum, Nickel, Niobium, Phosphorus, Silicon, Tantalum, Titanium, Tungsten, Vanadium, Zirconium. ^Symptoms: Patients may present with joint loosening, joint pain, and/or rash beginning weeks to months after implantation (erythema, induration, papules or vesicles) above site of implantation (Adapted from Schalock et al. [68••])



commercial availability of allergens, and cited evidence for allergen use [68••].

Post-placement of Metal Device

In those patients who experience joint loosening, joint pain, and rash above site of implantation of a metal device suspicious for metal hypersensitivity, PT should be considered [118]. A European group [118] have identified criteria that support a causative association between metal allergy and metal dermatitis overlying implant: these include (1) a dermatitis beginning weeks to months after implantation, (2) an eruption overlying the implant with erythema, induration, papules or vesicles, (3) positive patch results to a metal used in the implant, (4) positive in vitro testing to metals (lymphocyte transformation test), (5) a dermatitis that is resistant to medical therapy, and (6) complete recovery after removing the implant.

Testing for bone cement components is recommended in pre-implantation PT, but it is especially important in post-implantation symptomatic patients as there are data that sensitivity to acrylates, antibiotics, initiators, and stabilizers contribute to metal implant complications [67, 119, 120]. If available, testing with sample kits obtained from the manufacturer can be considered. However, one must note that both false positive results (from pressure effect) and false negative results can be seen [68••], and thus these kits should not be the only products tested when evaluating a patient. Also, the yield tends to be low; in Reed's series [59], none of the 22 patients tested with metal disc from manufacturer had a positive result.

It, however, is not recommended that action be taken in a patient with a positive PT test without symptoms [68••]. In

patients who have PT, post-joint placement only, it is often difficult to tease out whether the allergy caused in fact the joint problem or vice versa [121].

Treatment

Treatment for patients with symptoms and positive PT results is controversial. There is no current guideline available to determine who requires removal of implant. One option reported in a case report for a male with nickel sensitivity to PFO closure device, is to offer a 21-day course of corticosteroids [122]. Treatment with topical CS has also been tried for sites of dermatitis. It is also important to consider other sources of exposure to these metals in the environment and in foods, and these should be optimized prior to the consideration of implant removal. In patients with symptoms and positive PT result, one must consider if removal of the implant is reasonable and can be safely accomplished. These decisions should be tailored to the individual patient in dialogue with the surgeon, weighing risks and benefits. Options post-implantation with a symptomatic patient and a positive PT result include removing the implant, replacing the implant with a non-allergenic alloy, and coating the metal with polytetrafluoroethylene [68••].

Conclusions

Systemic contact dermatitis is rare but should be considered in special populations; it is seen in context of reactions to foods, metals, and medications. Allergic reactions to biomedical devices are seen with orthopedic implants, dental implants,

endovascular stents, and intrauterine contraceptive devices. Evaluation of the patient with metal allergy is dependent on whether or not the patient is seen pre- or post-implantation. Patch testing is the gold standard for diagnosis of contact dermatitis; relevant metals in the device should be part of the testing series. All external sources, including food and environmental exposures, should be optimized in terms of avoidance measures, and optimal skin care regimens should be executed, prior to consideration for implant removal.

Compliance with Ethics Guidelines

Conflict of Interest Marcella Aquino has been treasurer and a board member of the Long Island Allergy & Asthma Society; has served as principal investigator on a clinical trial for Merck & Co.-SPIRO; has served as a sub-investigator on clinical trials for Novartis, Genentech, Baxter, and Dyax. Corp.; has been paid for giving lectures by the ACAAI; has had travel expenses covered/reimbursed for travel to meetings by the ACAAI; and has had travel expenses covered/reimbursed for travel to investigators' meetings by Merck & Co.

Tania Mucci declares that she has no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- Of importance
- Of major importance

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