

Short Communication

## Systemic Contact Dermatitis and Patch Testing in Patients Receiving Orthopedic Implants

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**Key Words:** Systemic Contact Dermatitis; Patch Testing; Metal Allergies; Prosthetics; Orthopedic Implants

### Introduction

Contact dermatitis is defined as a cutaneous inflammatory response to an allergen. While cutaneous reactions to metals such as chromium, cobalt, and nickel are common causes of contact dermatitis, cutaneous reactions to implanted orthopedic devices is a rare finding [1]. Contact dermatitis presents as an erythematous rash on exposed areas of the skin while sparing unaffected areas. Orthopedic implants are typically placed within the deep tissue and away from the superficial skin, however they can produce an immune reaction called systemic contact dermatitis (SCD). SCD results from prior cutaneous sensitization to an allergen that results in an immune reaction upon re-exposure via systemic routes, namely through orthopedic implants. Clinically, the secondary cutaneous reaction associated with SCD can manifest as contact dermatitis amongst other cutaneous manifestations including urticarial rashes and impaired wound healing [2].

The hypersensitivity reaction encountered in contact dermatitis associated with orthopedic implants is an immune response to the composite particles released systemically by the orthopedic implant due to corrosion or natural wear and tear. Metal particles can serve as haptens, which can form complexes with endogenous proteins that act as antigens to activate circulating lymphocytes. Activation of these lymphocytes induces immediate formation of antibodies and antibody-antigen immune complexes (classically known as type II and III hypersensitivity reactions) in addition to cell-mediated or delayed-type hypersensitivity reactions (type IV hypersensitivity reaction) [3]. Type IV hypersensitivity reactions involve the activation of CD4<sup>+</sup> Th1 lymphocytes, which release cytokines that recruit the other inflammatory cells to the site of the orthopedic implant.

### Patch Testing

Assessing pre-test probability of eliciting hypersensitivity reaction after implantation of orthopedic hard ward remains a major challenge. Patch testing is the most common tool used to assess metal allergies. Common metals utilized in prosthetics include nickel, cobalt, chromium, and titanium alloys [4]. The American Contact Dermatitis Society (ACDS) recommended core allergen series “ACDS standard” and North American 80 Comprehensive Series (NAC-80) both tests for nickel, cobalt, chromium, and gold [1]. However, options to assess for allergic reactions to other metals such as titanium, palladium, tin, copper, aluminum, and silver must be ordered separately.

The results of patch testing for the purpose of orthopedic implant material selection has been listed in a chart review conducted by Mesinkovska et al. where all patients (n= 7) had pre- and postoperative patch testing performed [5]. Mesinkovska et al. determined that positive preoperative patch testing results ultimately influenced the decision making process regarding the choice of orthopedic implant material. Results from this review demonstrated that all patients with positive

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**Sub Date:** January 31<sup>th</sup>, 2018, **Acc Date:** February 6<sup>th</sup> 2018, **Pub Date:** February 8<sup>th</sup> 2018.

**Citation:** Calvin T Sung, Alfred Lee, Natalia E Jacobs, Peter Gust, Erica Hwang and Randolph Jacobs (2018) Systemic Contact Dermatitis and Patch Testing in Patients Receiving Orthopedic Implants. Int J Drug Disc 2: 007.

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patch tests who received allergen-free implants were free of post-operative hypersensitivity symptoms, and that six out of ten patients who had positive post-implantation patch testing results experienced resolution of hypersensitivity symptoms after implant removal. Preoperative patch testing plays a significant role in patients with a clinical history of metal allergies, however the decision to remove implants after positive post-implant patch testing should be considered on a case-by-case basis [5].

Patch testing is currently the most widely used and regarded as the best test for metal hypersensitivity reactions. Out of the 119 dermatologists surveyed by Schalock et al [6], 54% felt that pre-operative patch testing should be performed in patients with a clinical history of metal hypersensitivity versus 38% that felt that patch testing should be omitted in lieu of substitution of a non-allergenic implant based on clinical history alone. An even smaller minority, 8%, believed that the evaluation of metal hypersensitivity should be foregone altogether. Krecisz et al [7] examined patient history, dermatological examination, and patch testing in both pre- and postoperative patients (n=108) and demonstrated the importance of preoperative patch test screening in patients that report symptoms of metal hypersensitivity and recommended that patients with confirmed metal hypersensitivity should be provided with non-allergenic orthopedic implants.

Pre-operative patch testing is a convenient and simple way to predict the likelihood of developing metal hypersensitivity after orthopedic implant placement, particularly in patients predisposed to contact dermatitis or other cutaneous hypersensitivity reactions. Metal ions are not the only culprit for eliciting hypersensitivity reactions in orthopedic implants. There are several non-metal components. For example, components of bone cement, an essential part of successful implantation of orthopedic hardware, such as benzoyl peroxide, toluidine, and gentamycin have been known to elicit cutaneous reactions that resemble contact dermatitis. According to Bircher et al [8], five patients experienced edema, pruritic, and implant failure after either shoulder or knee joint replacement. Interestingly, these patients were all found to be allergic to benzoyl peroxide. Thus, it is essential to recognize that non-metal components of orthopedic implants are very much capable of eliciting hypersensitivity reactions. Similarly, the questionnaire issued by Schalock et al. [6] to 119 dermatologists revealed that 82% of the respondents also evaluated the glue and plastic components of orthopedic implants postoperatively to complement the assessment of metal hypersensitivity reactions.

Patient history is an important role in the decision-making process. According to Bloemke et al.[1, 9], out of the 139 patients with malfunctioning orthopedic implantation devices, 14% self-reported cutaneous metal hypersensitivity; 22% (19/86) amongst females and 2% (1/53) amongst males, which places these patients at risk for experiencing an allergic reaction to implanted orthopedic devices. They concluded that use of implants that lack chromium, cobalt, and nickel, which has allergic prevalence rates of 2.3%, 6.2%, and 15.5%, respectively, in the North American population.

In a patient presenting with hypersensitivity to an orthopedic implant device, the most definitive treatment is the prevention and substitution with a non-allergenic device [10]. Identifying patients with hypersensitivity-related implant failure is clinically significant in terms of outcomes. Complications assessed by Oxford hip score and post-operative complication rates were worse in patients who required surgical revision due to metal hypersensitivity than those of other causes (infection, recurrent dislocations, and a vascular necrosis). Therefore, early intervention in patients with identifiable metal hypersensitivities may result in better outcomes in the case revision surgery is indicated [11].

Other options exist for predicting the occurrence of metal hypersensitivity reactions in patients receiving orthopedic implant devices including in vitro peripheral lymphocyte proliferation testing (lymphocyte transformation test, or LTT), which assess the peripheral blood lymphocyte proliferation in blood with and without the addition of the metal antigen in question after incubation. Lymphocyte transformation testing is performed by incubating peripheral lymphocytes both with and without addition of a metal antigen, then comparing the reactions and obtaining a stimulation index, which indicates T-cell reactivity [12]. Stander et al. [13] reported the sensitivity and specificity of LTT in comparison to patch testing to be 88% and 96%, respectively. Though LTT has been shown to be a viable alternative to patch testing, it is not widely used due to the relatively narrower range of detectable metals, increased cost, lack of standardization, and more limited laboratory access, therefore patch testing remains the gold standard for metal hypersensitivity testing and should be used in the clinical setting [6,12,14].

Contact dermatitis in association with orthopedic implantation devices is a rare but clinically significant problem with poor long-term outcomes if not addressed properly. While early intervention is key in the management of selected cases of post-implantation contact dermatitis, patch testing plays a key role in preventing complications of implant metal hypersensitivity in those with a clinically evident history of metal hypersensitivity in the first place.

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