# Pacemaker allergy

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**Contact point**

# PACEMAKER ALLERGY

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Allergic complications following pacemaker insertion are rare. However, when they do occur, they usually mimic pacemaker infection, which may lead to multiple device replacements and increased morbidity burden (1, 2). Reactions can take the form of dermatitis localized in the area above implantation and, uncommonly, generalized or remote site dermatitis (1, 2).

**CASE REPORT**

In 2011, a 64-year-old female had a pacemaker implanted in the left pectoral region to treat intermittent second-degree AV block (Mobitz II) and presyncope. The pacemaker was made by Medtronic (*DDD Medtronic Sensia SED01*). The device pulse generator, device controller-monitor and leads were coated with various materials (polyurethane, polysulfone, silicone rubber, titanium, parylene coated titanium, platinum iridium, nickel MP35N) to reduce infections and reaction. The leads were made of nickel alloy (MP35N) isolated with silicone rubber.

Ten months later, the patient presented with localized swelling, redness and purulent drainage in the implanted area. She had no fever and laboratory data showed no signs of infection. Bacterial swabs and cultures of the material taken were negative. Over the next two years, she was treated with many different antibiotics. Repeated bacterial swabs were mostly negative. Coagulase-negative staphylococci (*Staphylococcus species*) were isolated on two occasions. Between 2013 and 2014, the patient underwent five repositions of the old pacemaker system and re-implantation to the different site on the left chest wall. Every time, 6 – 8 weeks after the procedure, the skin overlying the generator became "infected" and the patient received antibiotics, despite negative bacterial swabs and/or cultures. During that period, the patient felt constantly tired; had palpitations and vertigo; and could not perform everyday activities. Her ECG showed persistent signs of arrhythmia. Her medical history revealed costume jewelry eczema for the past 20 years. In 2009 she had hysterectomy and adnexectomy due to uterine fibroids. For years she has been treated for arterial hypertension, bronchial asthma and chronic gastritis.

The patient presented to our Department because of persistent vulvar pruritus that has begun in 2011, a few months after the implantation of the pacemaker. She was treated with various local corticosteroids and neutral creams, which temporarily relieved the symptoms. Clinical examination revealed vulvar eczema (chronic lichen simplex) and persistent "infection" on the left chest wall (figure 1). We performed patch test to the baseline series, titanium dioxide, titanium, titanium nitride, molybdenum and methyl-methacrylate. Patch testing to nickel sulfate (5% pet) showed a positive reaction "+" at day 2 and "++" at day 3 and day 7. The specific manufacturer's patch test substances were not tested because they were not available to us. In the lymphocyte transformation test (LTT), the patient's lymphocytes showed markedly enhanced proliferation *in vitro* to nickel.

The prednisone therapy (initial dose of 30 mg tapered down over 2 weeks) had no effect on the left chest wall skin lesion, however vulvar eczema temporarily disappeared.

We suspected pacemaker systemic contact allergy, and we recommended removal of all pacemaker systems and the implantation of a new pacemaker system.

The removal of the old pacemaker device and placement of a new one (the same brand and type of pacemaker device but nickel-free) resulted in the complete resolution of her symptoms: vulvar eczema cleared and skin lesion on the left chest wall disappeared. At the follow-up controls after 3, 6 and 12 months, *in vitro* hyper-reactivity to nickel disappeared. The patient has now been free of cardiac and dermatological symptoms for over 18 months.

**DISCUSSION**

Pacemaker component allergy is a relatively rare cause of erythema, pain and swelling at the site of an implanted pacemaker (3). Clinical presentation includes skin lesions that are often confused with pacemaker infection or necrosis (4, 5). Clinicians tend to suspect a low-grade bacterial infection prior to performing an allergy test to confirm the presence of an allergy. Chua *et al.* have showed that 32% of patients with clinical signs and symptoms of implantable electrophysiological cardiac devices

infection had negative tissue and swab cultures, and they responded well to total device removal and antibiotics (6).

The time taken to develop sensitivity varies from months to years. The exact pathological mechanism is unclear, but delayed-type hypersensitivity reaction is possible (2).

Pacemakers are made of two implanted components: generator and leads. Generators are mostly covered with titanium capsule (2). Leads are attached to the capsule through the pacemaker header (2). In our case, leads were insulated wires made of MP35N alloy, composed of nickel, cobalt, chromium, and molybdenum. MP35N is an age-hardenable nickel-cobalt base alloy with a unique combination of properties: ultra-high strength, toughness, ductility and outstanding corrosion resistance (7). There have been several reported cases of allergic sensitivity to these encasing materials, including titanium, nickel, polyurethane, epoxy, mercury, cadmium, chromium, silicone, polychloroparaxylene, and cobalt (3, 4, 8-14).

Nickel is the most frequent allergen found when patch-testing patients with allergic contact dermatitis. Our patient had vulvar eczema that started a few months after the pacemaker implantation. Vien and Menné described a 37-year-old woman who had severe anogenital dermatitis, which was suspected to be a systemic contact dermatitis due to nickel (15). Her patch test showed a "++" reaction to nickel. Placebo-controlled oral challenge with 2.5 mg nickel produced a severe flare of her anogenital dermatitis after 2 days. Following a low-nickel diet for 2 months, the dermatitis disappeared (15). In another patient, lichenified plaques on forearms, thighs, and legs developed 2 years after pacemaker insertion (16). A stainless steel screw was exposed to tissues. That patient's patch test results were positive to nickel, cobalt, and chromate (16). Landwehr and van Ketel described a patient with a long history of hand dermatitis and with sensitivity to metal objects in whom pompholyx developed two days after the implantation of a pacemaker with a stainless steel case (12). Her patch test showed a positive reaction to nickel sulphate (12).

The patch test is a gold standard for the evaluation of delayed type allergy. The LTT shows reactions to circulating lymphocytes, and it more accurately reflects immune reactions within the body (1, 17). Fifty-six individuals with Ti implants, systemic symptoms and negative patch test results had a positive Ti LTT (17). In 54 cases, the patients had complete resolution of symptoms following the removal of metal implants (17). The same happened in our case where we suspected nickel systemic contact sensitivity. Thomas *at al* reported about a patient in whom impaired fracture healing and eczema localized to the perioperative area developed following titanium-based osteosynthesis (18). Patch tests to the metals were negative, but LTT showed markedly enhanced proliferation *in vitro* to titanium. After removal of the titanium material, the fracture healed and the eczema cleared. As in the Thomas study, we also noticed that *in vitro* hyper-reactivity to nickel disappeared after the pacemaker re-implantation.

**CONCLUSION**

Contact allergy to pacemaker is often unrecognized. A failure to diagnose may lead to multiple unnecessary surgical interventions. Once infection has been excluded, allergy testing must be performed. Patch test should be performed to the baseline allergens and the specific biomaterials used in device. The role of LTT is not well defined, but it could be a useful tool when systemic metal sensibility is suspected. Although pacemaker contact sensitivity is rare, its recognition is very important to the pacemaker-dependent patient.

**REFERENCES:**


1. 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(1):4-19.
2. Honari G, Ellis SG, Wilkoff BL, et al. Hypersensitivity reactions associated with endovascular devices. Contact Dermatitis 2008;59:7-22.
3. Shittu M, Shah P, Elkhalili W, et al. A Rare Case of Recurrent Pacemaker Allergic Reaction. Heart Views 2015;16(2):59-61.
4. Tamenishi A, Usui A, Oshima H, et al. Entirely polytetrafluoroethylene coating for pacemaker system contact dermatitis. Interact Cardiovasc Thorac Surg 2008;7(2):275-277.
5. Syburra T, Schurr U, Rahn M, et al. Gold-coated pacemaker implantation after allergic reactions to pacemaker compounds. Europace 2010;12(5):749-750.
6. Chua JD, Wilkoff BL, Lee I, *et al.* Diagnosis and management of infections involving implantable electrophysiologic cardiac devices. Ann Intern Med 2000; 17;133(8):604-608.
7. Nickel alloys. Alloy MP35N* (UNS R30035). (Available from http://www.finetubes.co.uk/uploads/docs/Alloy_MP35N.pdf) accessed on July 21 2016.
8. Iguchi N, Kasanuki H, Matsuda N, et al. Contact sensitivity to polychloroparaxylenecoated cardiac pacemaker. Pacing Clin Electrophysiol 1997;20:372–373.
9. Hayes D L, Loesl K. Pacemaker component allergy: case report and review of the literature. J Interv Card Electrophysiol 2002;6:277–278.
10. Skoet R, Tollund C, Bloch-Thomsen PE. Epoxy contact dermatitis due to pacemaker compounds. Cardiology 2003;99:112.
11. Andersen KE. Cutaneous reaction to an epoxy-coated pacemaker. Arch Dermatol 1979;115:97–98.
12. Landwehr AJ, van Ketel WG. Pompholyx after implantation of a nickel-containing pacemaker in a nickel-allergic patient. Contact Dermatitis 1983;9(2):147.
13. Brun R, Hunziker N. Pacemaker dermatitis. Contact Dermatitis 1980;6:212–213.
14. Abdallah H I, Balsara R K, O'Riordan A C. Pacemaker contact sensitivity: clinical recognition and management. Ann Thorac Surg 1994:57:1017–1018.
15. Veien NK, Menné T. Systemic contact dermatitis. In: Contact Dermatitis, 5th edition, Johansen J D, Frosch P, Lepoittevin J P (eds): Berlin, Heidelberg, Springer, 2011: pp. 347-360.
16. Tilsley DA, Rotstein H. Sensitivity caused by internal exposure to nickel, chrome and cobalt. Contact Dermatitis 1980;6(3):175-178.
17. Hallab NJ, Caicedo M, Epstein R, et al. In vitro reactivity to implant metals demonstrates a person-dependent association with both T-cell and B-cell activation. J Biomed Mater Res A 2010;92(2):667-82.
18. Thomas P, Bandl WD, Maier S, *et al*. Hypersensitivity to titanium osteosynthesis with impaired fracture healing, eczema, and T-cell hyperresponsiveness in vitro: case report and review of the literature. Contact Dermatitis 2006;55(4):199-202.


**Figure 1**

A 64-year-old female patient with 4 years' history of repeated local swelling, redness and purulent drainage on the site of pacemaker implanted area