

LETTER TO THE EDITOR

A Case of an Allergic Reaction to a Spinal Cord Stimulator: Identification of the Antigen With Epicutaneous Patch Testing, Allowing Successful Reimplantation

To the Editor:

LD, a 50-year-old Caucasian woman with a known allergy to costume jewellery, had an Advanced Neuromodulation Systems (ANS) Series 90 spinal cord stimulator (SCS) system consisting of two epidural Octrode leads and a receiver in her left buttock implanted for persistent buttock and leg pain after a L5/S1 disc prolapse, discectomy, and fusion. A radio-frequency transmitter was clipped to her belt, with a lead from this terminating in a rubber antenna held over the receiver by an adhesive pad. She reported good pain relief, with 12 hours stimulation providing 12 hours carryover pain relief and no untoward problems during the first four months.

LD presented five months post implantation to report a mild rash over the receiver, which was initially thought to be unrelated to the stimulator.

At seven months post implantation, the rash over the left buttock was marked and getting worse, despite topical and oral steroids, phenol cream, antihistamines, and topical barriers to the antenna and assistance from a dermatologist. The rash had spread from the left buttock, and she now had a mirror-image rash on the right buttock unrelated to any implanted hardware as shown in Figure 1.

At eight months, the rash had become a generalized erythematous papular rash involving her neck, trunk, both groins and arms, both buttocks with a serous exudate weeping from the receiver site in the left buttock as shown in Figure 2. A copy of an ANS clinical bulletin released in April 2000 advising practitioners about case reports of allergic reactions to SCS and pacemakers was given to me by the company technicians (1).

Nine months after insertion the whole SCS system was removed because of local symptoms, generalized rash, and likely wound dehiscence despite maximal therapy. A visual inspection after removal found a subtle split in one of the leads between the anchor and receiver.

Microscopy and culture of receiver capsular tissue revealed a few polymorphs, but no bacteria were seen or cultured. A swab of the receiver site showed a moderate amount of degenerative cell debris but again no pus cells or bacteria.

Histopathology of tissue from around the lead anchor found unremarkable nonspecific fibrous tissue. Tissue taken from the receiver capsule showed a rich vascular fibrous tissue surface beneath which was a lesser vascular fibrous area showing scattered lymphoid follicles. There was no evidence of any acute inflammatory infiltrate, granuloma, or epithelium. The appearances were consistent with the fibrous reaction surrounding an implanted capsule.

The rash progressively disappeared after explantation without additional treatment as seen at two months, and the rash had gone completely at three months as shown in Figure 3.

However, she was again troubled by persistent severe radiating low back pain, and she was keen to have another SCS implanted if possible. The clinical challenge was to identify the allergen and then determine if a different SCS could be safely inserted given her apparent allergic response to an implanted device.

Skin testing performed by an allergy specialist using an "Australian standard panel" confirmed her known allergy to costume jewelry and nickel. There was no response to other allergens in the test panel.

I then patch tested her with SCS material supplied by ANS and Medtronic. Epicutaneous patch testing for 36 hours with the four items of test material supplied by ANS (a formal test kit was not available) (Table 1) and again for another 36 hours with an 11-item Medtronic test kit (Table 2) were negative with no rash, itching, or skin reaction. She was then patch tested with sutures and material taken from a time-expired Series 90 stimulator system (Table 3) and developed widespread itch and rash at five days that was maximal around the receiver. Further patch testing confirmed that only the silicone shavings from the "header block" and "boot sleeve" in the Series 90 system produced a systemic allergic response and 3 mm wheal around the test material. There was no reaction to the silicone lead anchor, epoxy shavings, or other material.

Having identified a likely allergen, I repeated epicutaneous patch testing for two weeks with the 11-item Medtronic test kit using aluminum chambers (Finn Chambers, Tuusula, Finland) and then for another two weeks with a "dummy" implanted pulse generator (IPG) (Genesis IPG, ANS, Plano, TX, USA) without the parylene coating (with opsite control) without producing a rash, itch, or reaction to any component.

We elected to implant a Medtronic stimulation system because the 11-item Medtronic test kit gave more information, and I was more confident that result from the Medtronic test panel was a true negative reaction than the result from the 4-item ANS test panel and

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Figure 1. Left and right buttocks at seven months.

“dummy” Genesis IPG. Furthermore, ANS advised against implanting another ANS system because the patient had experienced such a strong and generalized reaction to implanted silicone compounds.

In January 2003 a Medtronic Synergy dual lead SCS system, components of which had been found to be unreactive on skin testing, was implanted and continues to be well tolerated nine years later and provide pain relief in 2012.

DISCUSSION

Allergic reactions to implanted devices have been ascribed to a variety of compounds, including epoxy, mercury, cadmium, platinum, silicone, polyurethane, titanium, nickel, chromium, polychloroparaxylene (parylene), and cobalt.

Silicones are generally made from silanes, which are analogous to hydrocarbons with a similar basic structure $\text{SiH}_3(\text{SiH}_2)_n\text{SiH}_3$ using a SiH_4 (silane) building block. Similar substitutions can occur with Cl for H. Silicones are generally made by reacting chlorosilane with water. Silicone elastomers have a Si-O-Si backbone with the general formula $\text{SiH}_3(\text{OSiH}_2)_n\text{OSiH}_3$ and require the formation of large molecular weight polymers. They can be fluids, gels, or solids. Additives may include peroxides used during the curing process, fillers such as silica to improve tensile strength, platinum, aluminum trihydrate to improve flame retardant properties. Carbon black can be used to improve electrical conductivity. Heat stability can be improved by the addition of ferric oxide; titanium dioxide and various organometals can be used for pigments. Silicone is one of the most biocompatible materials, and true allergy to silicone is considered to be extremely rare.

ANS could not tell me the exact mix of their silicones. ANS advised me that the silicones used to make the boot, header block, and connectors of their stimulators were all the same basic compounds with slightly different mix factors to accommodate hardness and molding issues.

Although the stability and low toxicity of silicone allows use in many medical applications, the small changes in “mix factors” used in the various components made from silicone may explain why a patient will react to one compound but not to another. In May 2004 ANS advised me that the “test material” I had been given in 2002 had been for the ANS “Renew” and “Genesis” SCS products and not the

earlier Series 90 SCS product, which had been implanted. This belatedly offered an explanation for the lack of observed reaction with this ANS test material and highlights the need for model-specific test kits. The test panel itself also needs to be a complete panel, not just the external material in case of leakage or lead fracture as in this case to allow exposure to internal material to be tested.

In addition to medical products, silicone is found in many household items such as soaps, hand lotions, nail polishes, chewing gum, waterproof coatings, lubricants, and even processed foods. Therefore allergy to silicone can occur even without implanted silicone.

Contact dermatitis is an inflammatory skin reaction that may be allergic or irritant in origin. Irritant contact dermatitis is a non-specific, nonimmunological reaction to noxious cutaneous agents, whereas allergic contact dermatitis is usually a delayed hypersensitivity (Type IV) T lymphocyte mediated event but may have an IgE hypersensitivity (Type I) component. Initial sensitization takes 10–14 days from initial contact, and once sensitized to a chemical allergic contact dermatitis develops within hours to several days of exposure (e.g., Mantoux tuberculin sensitivity test that is read at 48–72 hours). The reasons why LD presented five months post implantation three pacemakers and three cochlear implants extruded months or years post implantation is not clear (2–4).

Patch testing has been used to determine the causative agent in contact dermatitis since the 1930s and the Finn chambers method of patch testing has been used since the 1970s; however, the utility and reproducibility of patch testing to identify allergic reactions to implanted material has not been determined. A positive patch test will usually appear over 48–96 hours, but reactions to metals may not appear until 7–14 days. The size of the skin test reaction is measured at 48 hours, 5–6 days, and again at 11–14 days. The threshold for a “clinical” reaction is > 2 mm palpable induration, with larger reactions providing more certainty.

I used the patch testing to identify the allergen and then to find a nonreactive system. Patch testing also can be used to be custom-built systems without the allergen. Do we need to retest patients once we have identified the allergen? Could we rely on detailed model-specific data sheets produced by the device manufacturer? Clinically the confidence gained from identifying an allergen(s) and showing the patient, clinician, and payer that a new system is unlikely to produce an allergic response justifies the effort of retesting. However, knowing the allergen and having detailed information on

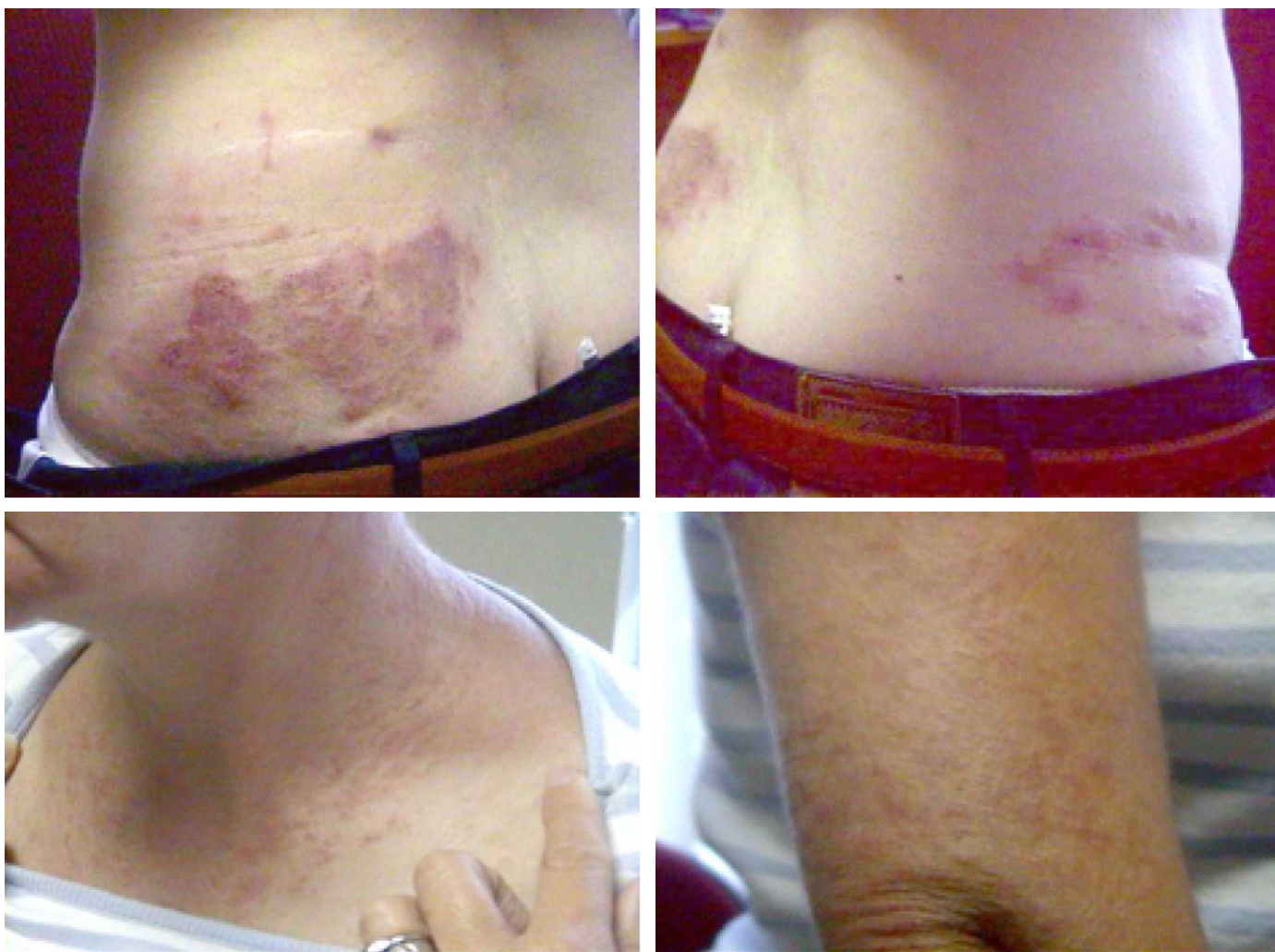


Figure 2. Both buttocks, neck, and arm nine months post implant just before removal.

the materials used to make each stimulator would allow an informed choice on a suitable device to be made. From personal experience, retesting is desirable as it reduced the anxiety for all parties involved.

A PubMed literature review found 12 reports of allergic reaction to implanted pacemakers and 5 case reports of allergic reactions to SCS systems, 1 case report of allergy to a ventriculoperitoneal shunt, 1 allergy to a drug pump and 2 case reports of allergy to cochlear implants.

Andersen reported cutaneous reaction to an epoxy-coated pacemaker (5). Gensch and Schmitt described circumscribed erythema that developed suddenly over a pacemaker (6). Abdallah et al. described the appearance of vesicular skin lesions overlying pacemakers three to eight months after insertion that was patch skin tested positive for titanium and polyurethane sensitization (3). Maushagen et al. described circumscribed erythema overlying a pacemaker containing silicone and absent during intervals without silicone. Patch testing did not identify an allergen, and it was thought to be a foreign body reaction (7). Moini et al., in a case report and review, described the limited response to local steroid and removal of the allergen as the only effective treatment (8). Iguchi et al. reported proven contact sensitivity to the polychloroparaxylene (parylene) pacemaker coating that was managed by wrapping the pacemaker in a polytetrafluoroethylene sheet prior to

implantation to prevent further skin reactions (9). Yamauchi et al. also reported dermatitis due to a titanium pacemaker (10). Hayes and Loesl described a violent reaction to polyurethane and positive patch test to parylene and managed the patient with a specially made pulse generator fully coated with silicone (11). They highlighted the need for the test material to contain every component of the implanted system. Tamenishi et al. also described the successful use of polytetrafluoroethylene sheets coating the pacemaker and pericardial leads to prevent pacemaker contact dermatitis (12). Skoet et al. described the delayed onset two years after implantation of a mild cutaneous reaction over the pacemaker that became worse six years post implant with redness and swelling spreading to the neck (4). Patch testing revealed a positive reaction to epoxy resin. They discussed a possible role for topical tacrolimus and pimecrolimus before explantation.

Mironer et al. described the progressive onset of erythema and edema eight days after the implantation of a Medtronic SynchroMed drug pump in a patient who previously had a SCS (13). The erythema and edema spread from the pump pocket to involve the left leg. Infection was excluded, and symptoms completely resolved within 18 hours of explantation.

Oprea et al. described a similar story of allergic response to the silicone of an implanted pacemaker in a 12-year-old girl that was



Figure 3. Left buttock two and three months post explantation.

Table 1. ANS test material.

Urethane pellets	Silicone rubber (#1137)
Silicone rubber (#40076)	Silicone rubber (type c)
Plus Micropore tape control	

Table 2. Medtronic test kit.

Silicone rubber (MDX-70)	Polyurethane (80A)
Silicone rubber (ETR-50)	Titanium
Silicone rubber adhesive	Polyurethane (75D)
Epoxy	Polysulfone (amber)
Parylene	Polysulfone (beige)
Platinum iridium	Plus Micropore tape control

Table 3. Test material from time-expired ANS Series 90 stimulator.

1 × Series 90 SCS lead	1 × Series 90 Quatrode receiver
3 lead screws	Antennae
Black silk sutures	Polysorb suture
Ethibond suture	Plus Op-site control

confirmed using a model-specific test kit supplied by the manufacturer after a negative response to a standard test panel (14). This patient was successfully implanted with a specially designed silicone-free pacemaker. Oprea et al. emphasized the key to the diagnosis was a specific patch test kit supplied by the manufacturer. Our experience confirms the need for a model-specific test kit to identify the allergen and implant a nonreactive system. Syburra described a case of recurrent pacemaker rejection and reimplantation due to wound necrosis (15). Titanium patch testing was negative. They successfully implanted a custom-built gold-plated pacemaker with polyurethane leads. These cases demonstrate the successful use of an alternative strategy of using custom-built

systems without the known allergen or a custom-built system made with completely different materials.

Hussain et al. described an allergic response to a silicone ventriculo-peritoneal shunt that was replaced by a polyurethane catheter and system that continued to function for more than eight years (16).

Nosbaum et al. described a nickel-induced systemic allergic dermatitis from an implanted sacral nerve stimulator (17). McKenna and McClean described the use of topical steroids to control eczema from a Medtronic X-trel RF SCS in a patient with a history of contact dermatitis from “cheap metals” (18). Patch testing to a European standard series found a positive reaction to nickel. “Rubber,” glues, “plastic” series, the antennae and adhesive pads all tested negative. Our case showed a similar lack of response to a standard test series other than nickel.

Kemler et al. described a case of recurrent SCS rejection where an unknown stimulator had been removed for suspected infection (19). The unidentified replacement also was rejected and removed. Subsequent patch testing with test samples and material taken from the IPG failed to identify an allergen. Negative patch testing that fails to identify an allergen in the setting of failed implants due to inflammatory reaction is of no prognostic benefit and meant this patient could not safely have another implant. Our case demonstrated the potential benefit of epicutaneous skin testing when an allergen was identified, and the proposed implant was nonreactive.

Ochani et al. described a woman with a complex regional pain syndrome who developed burning pain and erythema over the leads and tenderness over the implanted IPG (20). Pain and erythema over the lead were worse during stimulation. Culture and histopathology were not performed, but epicutaneous patch testing was positive for platinum, silicone, and polyurethane, highlighting the possibility of multiple allergies. Explantation resulted in symptomatic improvement.

Puri et al. described erythema and pruritus with serous discharge over a cochlear implant. Patch testing was positive to LSR-30 silicone encasing the Nuclear Contour and Med-el devices but not to the LSR-70 silicone in the Advanced Bionics device (21). Symptoms resolved with device explantation and did not return after inserting a proven nonreactive Advanced Bionics system. Kunda et al. reported on the delayed presentation of silicone allergy in three

cochlear implants (2). They then described negative patch testing on one patient that had a positive skin prick reaction to room temperature vulcanizing (RTV) silicone adhesive, another patient patch test positive to RTV silicone adhesive, and a third patient with unproven but suspected silicone allergy that were all successfully managed with custom-made devices without the known allergen or made from different silicones.

Delaplace et al. reported burning sensation and cutaneous inflammation that began for months post implantation and resolved with explantation (22). They also described another case with pruriginous erythema over the neurostimulator that was patch test positive for two types of silicone that was successfully managed with topical steroids.

Allergic reactions to implanted SCS and similar devices are rare, complex, distressing, and expensive complications. The literature describes allergies to many materials used to make these devices. Many authors have emphasized the key to the diagnosis was a specific patch test kit supplied by the manufacturer. The literature shows reimplantation of new off-the-shelf devices that do not have the allergen, custom-made devices without the allergen, and the use of devices coated with polytetrafluoroethylene sheets can prevent recurrent allergic reactions.

CONCLUSION

This case shows that although epicutaneous patch testing is an imperfect tool, it identified the allergenic substance, and the lack of response to a model-specific test panel correctly predicted the subsequent long-term viability of an alternative product.

Clinical management of this case would have been facilitated by the availability of a model-specific test kit (i.e., for the ANS Series 90 stimulator), and knowledge that the materials used in the Series 90 stimulator were different to those used in the new ANS devices. Seven- to fourteen-day patch testing with a model-specific test kit may increase the chance of finding the allergen and increase the probability that "no reaction" will correctly predict a successful implant.

RECOMMENDATIONS

Patch test kits be available for all implanted devices.

Test kits should include a complete panel of material used in manufacturing the device.

Documentation should relate test material to device(s) and describe the test procedure.

Test material should be appropriately sized and shaped to be worn by patients for up to two weeks.

Test kits should contain specific technology to hold samples on skin for a prolonged period, e.g., "Finn Chambers."

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REFERENCES

1. AdvancedNeuromodulationSystems Inc. Allergic reaction to spinal cord stimulator, 2000. p. 1.
2. Kunda LD, Stidham KR, Inerra MM, Roland PS, Franklin D, Roberson JB, Jr. Silicone allergy: a new cause for cochlear implant extrusion and its management. *Otol Neurotol* 2006;27:1078–1082.
3. Abdallah HI, Balsara RK, O'Riordan AC. Pacemaker contact sensitivity: clinical recognition and management. *Ann Thorac Surg* 1994;57:1017–1018.
4. Skoet R, Tollund C, Bloch-Thomsen PE. Epoxy contact dermatitis due to pacemaker compounds. *Cardiology* 2003;99:112.
5. Andersen KE. Cutaneous reaction to an epoxy-coated pacemaker. *Arch Dermatol* 1979;115:97–98.
6. Gensch EG, Schmitt CG. [Circumscribed reticular telangiectatic erythema following implantation of a heart pacemaker]. *Hautarzt* 1981;32:651–654.
7. Maushagen E, Reichle B, Simon H. [Circumscribed erythema after cardiac pacemaker implantation]. *Z Kardiol* 1994;83:340–342.
8. Moini C, d'Alterroche A, Cosnay P, Vaillant L, Babuty D, Delhomme C et al. [Contact dermatitis following cardiac pacemaker implantation]. *Arch Mal Coeur Vaiss* 1996;89:253–256.
9. Iguchi N, Kasanuki H, Matsuda N, Shoda M, Ohnishi S, Hosoda S. Contact sensitivity to polychloroparaxylene-coated cardiac pacemaker. *Pacing Clin Electrophysiol* 1997;20 (2 Pt 1):372–373.
10. Yamauchi R, Morita A, Tsuji T. Pacemaker dermatitis from titanium. *Contact Dermatitis* 2000;42:52–53.
11. Hayes DL, Loesl K. Pacemaker component allergy: case report and review of the literature. *J Interv Card Electrophysiol* 2002;6:277–278.
12. Tamenishi A, Usui A, Oshima H, Ueda Y. Entirely polytetrafluoroethylene coating for pacemaker system contact dermatitis. *Interact Cardiovasc Thorac Surg* 2008;7:275–277.
13. Mironer YE, Flandry RE, Grumman S. Local erythema and edema of soft tissue after intrathecal morphine pump implant: an unusual complication. *Pain Dig* 1998;8:171–172.
14. Oprea ML, Schnoring H, Sachweh JS, Ott H, Biertz J, Vazquez-Jimenez JF. Allergy to pacemaker silicone compounds: recognition and surgical management. *Ann Thorac Surg* 2009;87:1275–1277.
15. Syburra T et al. Gold-coated pacemaker implantation after allergic reactions to pacemaker compounds. *Europace*, 2009.
16. Hussain NS, Wang PP, James C, Carson BS, Avellino AM. Distal ventriculoperitoneal shunt failure caused by silicone allergy. Case report. *J Neurosurg* 2005;102:536–539.
17. Nosbaum A, Rival-Tringali AL, Barth X, Damon H, Vital-Durand D, Claudy A et al. Nickel-induced systemic allergic dermatitis from a sacral neurostimulator. *Contact Dermatitis* 2008;59:319–320.
18. McKenna KE, McCleane G. Dermatitis induced by a spinal cord stimulator implant. *Contact Dermatitis* 1999;41:229.
19. Kemler MA, Barendse GA, van Kleef M. Recurrent rejection of a spinal cord stimulation system. *Contact Dermatitis* 2000;42:304–305.
20. Ochani TD, Almirante J, Siddiqui A, Kaplan R. Allergic reaction to spinal cord stimulator. *Clin J Pain* 2000;16:178–180.
21. Puri S, Dornhoffer JL, North PE. Contact dermatitis to silicone after cochlear implantation. *Laryngoscope* 2005;115:1760–1762.
22. Delaplace M, Maitre F, Dufour T, Landrieux I, Gauthier P, Jebira P et al. [Two cases of cutaneous erythema following spinal cord stimulation]. *Ann Dermatol Venerol* 2010;137:297–300.