

Allergy to surgical devices: Stents, staples, clips, coils, pins and contraceptive devices

Metal hypersensitivity and implanted medical devices

MELISA® is a clinically validated blood test, which can detect hypersensitivity to multiple metals from a single blood sample. Current research into the effects of metal hypersensitivity is generally focussed on the adverse health effects caused by metal devices in orthopaedics, especially metal-on-metal hip replacements. There is more limited research into allergy and smaller implanted devices, but researchers recommend pre-testing for metal allergy in patients with a history of dermal reactions to metals and in those, post-surgery who become symptomatic [1].

Stents

Researchers have identified that hypersensitivity to nickel and molybdenum - released from stents - may be one of the triggering mechanisms for in-stent restenosis [2,3,4]. Additional research into gold-plated stents showed a three-fold risk for restenosis when a gold-allergic patient was stented with a gold-plated stent [5]. Contraindications for metal allergic patients can be found on certain stents [6]. Surgeons may be aware of metal hypersensitivity but may consider screening unnecessary [7], or be unaware which metals are contained in alloys. [8] Other authors suggest that pre-screening prior to surgery is critical [9, 10].

Coronary stents are usually made from stainless steel (containing nickel), cobalt chromium, platinum chromium or Nitinol (nickel and titanium). Konishi et al suggest that an allergy to the stent should be considered as a possible cause of recurrent stent thrombosis in relatively young patients and that “a history of metal allergy should be meticulously explored before elective percutaneous coronary intervention” [3].

Staples and clips

Allergy to stainless steel clips used in surgery may appear as granulomas, which have been mistaken for recurrence of malignant tumours on scans [11]. Titanium is seen as a “biocompatible” alternative to traditional stainless-steel clips but there are reports of granulomas formed by hypersensitivity to titanium alloy staples and/or clips [12]. Titanium ear piercings have, in rare cases, generated granulomatous dermatitis which persisted 10 years after the original piercings were removed [13]. Chronic urticaria, along with abdominal pain and coughing were reported after a cholecystectomy using 10 tantalum clips. After these were removed, the patient’s symptoms resolved within 4-6 weeks [14]. A nickel-allergic patient suffered from headaches, fatigue, swollen lymph nodes and post operative pain following a cholecystectomy [15].

Breast clips are tiny radio-opaque markers (usually titanium) used to mark biopsies. There are only three cases of allergy reported, one patient had widespread dermatitis [16] and the others experienced both pain and local itching [17,18]. All patients’ symptoms resolved after removal. Metal-free breast markers have been developed [19].

Coils and pins

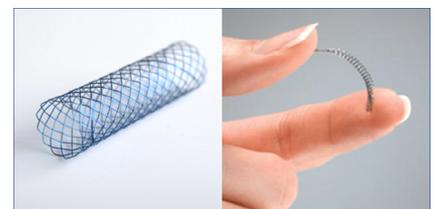
Coils used in surgery may be stainless steel, or titanium or platinum alloys. In one case report, 11 days after a coil embolization, the patient was readmitted as an emergency: with fever, seizures and impaired speech. Six days after surgery to replace the nickel-containing coil with a titanium alloy, the patient was able to leave and begin the process of rehabilitation [20].

Adverse reaction to titanium staples following cholecystectomy

Following gall bladder surgery, a 66-year old woman presented with diverse symptoms including: burning sensations in her arm, conjunctivitis, sinusitis and irregular bowel movements. She had previously exhibited an allergic reaction to titanium plates in her ankle including: oedema, slow wound healing and erythema. After MELISA testing for titanium allergy, her clips were removed. One month post-surgery, she reported being symptom free [34].

MELISA testing

MELISA is a clinically validated blood test used to detect delayed-type hypersensitivity to metals. The results are highly quantifiable and objective. A Stimulation Index above 3 is a Positive reaction and above 10 is Strongly positive.



FDA WARNING

This device contains nitinol, an alloy of nickel and titanium. Persons with allergic reactions to these metals may suffer an allergic reaction to this implant.

FDA recommend the following warning on Nitinol implants

Other researchers have suggested that nickel hypersensitivity may also present as chest pain, palpitations, oedema migraine, respiratory and digestive issues [21,22] and also as alopecia in a case where metal pins were used [23]. One patient with an embolization coil presented with a multitude of symptoms: pain, urticaria, tingling in his hands and feet, dizziness, “brain fog” and headaches. He tested positive to tungsten which made up 8% in his coil. All symptoms resolved after the coils were removed [24].

Symptoms of allergy vary widely: palpitations, severe pelvic pain, fatigue, night sweats, heavy legs and dermatitis were all present in a 34-year-old woman with nickel/palladium endovascular coils placed for pelvic congestion syndrome. The patient, who was bed-bound at times, was found to suffer from both palladium and nickel allergy. Again, all symptoms resolved after removal [25]. Dermal reactions to platinum coils have also been reported [26].

Contraceptive devices

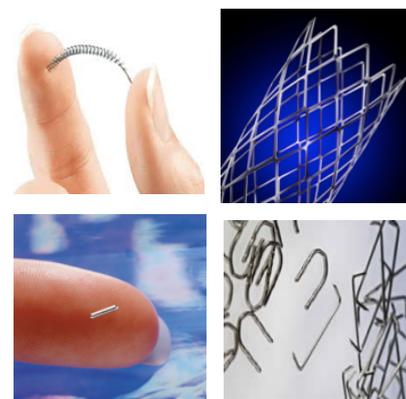
Older implanted contraceptive devices (IUDs) contain copper, and copper allergy is a contraindication to placement of these devices. Essure contains a nickel-titanium alloy, *in vitro* testing has shown that nickel is released from this device. Since 2002, more than 21,000 Essure “events” were reported to MedWatch, including pelvic pain, heavier periods, headache and fatigue, and the device was finally withdrawn. Yet only 4 cases of hypersensitivity have been published [27,28]. Patients who are allergic to nickel may have an allergic reaction to this device, especially those with a history of metal allergies. Additionally, some patients may develop an allergy to nickel if this device is implanted [29].

Allergy testing

Cutaneous and systemic hypersensitivity reactions to implanted metals are challenging to evaluate and treat. The incidence and prevalence of dermal and systemic hypersensitivity reactions are uncertain, as studies are limited. Complications related to metals may have been underestimated; a recent study showed that up to 5% of patients experience metal-related cutaneous complications post-implant placement [30]. Testing for titanium allergy is particularly problematic and it is generally believed that it is underdiagnosed, since traditional patch testing may give false negative results [31]. LTT-based tests like MELISA may provide a better solution for diagnosing implant-related sensitivity [32,33].

Accessing MELISA testing

- Locate your nearest MELISA laboratory and order a test kit
- Draw blood in 9ml sodium citrate Vacuette tubes and keep at room temperature
- Ship with a courier to arrive no later than 48 hrs of the draw
- Steroids or other immunosuppressant drugs may affect the test results and should be avoided where possible
- A questionnaire, which helps to identify patients who are likely to benefit from MELISA testing, can be provided, as well as tailor-made testing panels



Breast clips	Stents	Stainless steel staples	Titanium staples	Essure	Platinum coils	
Panel E	Various	Panel F	Panel E	Individual metals	Individual metals	
Aluminium	Stainless steel	Chromium	Aluminium	Chromium	Nickel	Iridium
Nickel trace*	Panel F	Managense	Nickel trace	Gold	Platinum	Palladium
Titanium**	Platinum/Chromium	Molybdenum	Titanium**	Iridium	Silver	Platinum
Vanadium	Chromium	Nickel	Vanadium	Manganese	Tin	Rhodium
	Manganese			Molybdenum	Titanium**	Ruthenium
	Molybdenum					Tungsten
	Platinum					
	Nitinol					
	Nickel					
	Titanium**					
	Cobalt Chromium					
	Panel F					

* Nickel trace means nickel may be present in amounts < 0.03%

** In MELISA, the titanium salts tested are titanium dioxide and titanium sulphate

References

1. Schalock, P. et al 2012. Hypersensitivity reactions to metallic implants – diagnostic algorithm and suggested patch test series. *Contact Dermatitis*. 66:4-19.
2. Koster, R. et al. 2000. Nickel and molybdenum contact allergies in patients with coronary in-stent restenosis. *Lancet*. 356:1895-7.
3. Konishi, T. et al. 2015. Stent thrombosis caused by metal allergy complicated by protein S deficiency. *Thromb J*. 1325(13);25.
4. Nakajima, Y., Itoh, T., Morino, Y. 2016. Metal allergy to everolimus-eluting cobalt chromium stents confirmed by positive skin testing as a cause of recurrent multivessel in-stent restenosis. *Catheter Cardiovasc Interv*. 87(4):E137-42
5. Svedman, C. et al. 2009. A correlation found between contact allergy to stent material and restenosis of the coronary arteries. *Contact Dermatitis*, 60(3):158-64.
6. Medtronic Resolute Integrity Zotarolimus-Eluting Coronary Stent System 2013 Rev1C. [Online] https://www.accessdata.fda.gov/cdrh_docs/pdf11/P110013S005c.pdf [Accessed 2022].
7. Gordon, B. & Moore, J. 2009. Nickel for your thoughts: Survey of the Congenital Cardiovascular Interventional Study Consortium (CCISC) for nickel allergy. *J Invasive Cardiol*. 21(7):326-9.
8. Univers, J et al. 2018. Systemic hypersensitivity reaction to endovascular stainless steel stent. *Journal of Vascular Surgery*; (67).
9. Guntani, A et al. 2020. Metallic allergy requiring removal of iliac stent: report of a case. *Surgical Case Reports* 6, Article number: 82
10. Nagura, S., Sakai, M., Obi, H. et al. 2022. Aortic valve replacement in a patient with self-reported systemic multiple metal allergy. *Gen Thorac Cardiovasc Surg*. 70:79-82.
11. Yüksel, M., Akgül, A., Evman, S. & Batirel, H. 2007. Suture and stapler granulomas: a word of caution. *J Cardiothorac Surg.*, Volume 31 (3), pp. 563-565.
12. Nihon-Yanagi, Y., Ishiwatari, T. & Otsuka, Y., 2015. A case of postoperative hepatic granuloma presumptively caused by surgical staples/clipping materials. *Diagn Pathol*, Volume 10, p. 90.
13. High, W. et al., 2006. Granulomatous reaction to titanium alloy: an unusual reaction to ear piercing. *Journal of the American Academy of Dermatology*, Volume 55(4), p. 716–720.
14. King, L., Fransway, A. & Adkins, R., 1993. Chronic urticaria due to surgical clips. *N Engl J Med*, Volume 329(21), pp. 1583-1584.
15. Luvsannyam E, et al. 2021. Diffuse Nickel Hypersensitivity Reaction Post-cholecystectomy in a Young Female. *Cureus* 13(8)
16. Tamai, K. et al., 2001. A case of allergic reaction to surgical metal clips inserted for postoperative boost irradiation in a patient undergoing breast-conserving therapy. *Breast Cancer*, 8(1):90-2.
17. Wegner, U. & Rainford, S., 2019. Adverse reaction regarding titanium-based marker clip: case report of a potential complication. *Int Med Case Rep J*. 2019; 12: 291–295.
18. Motton, Stéphanie et al. 2011. “Hurt eczematiforme column (chronicle) of the breast after implementation of a surgical clip.” *J Gynecol Obstet Biol Reprod*. 40(2):174-7.
19. Pinkney, D., Mychajlowycz, M. & Shah, B., 2016. A prospective comparative study to evaluate the displacement of four commercially available breast biopsy markers. *Br J Radiol*, p. 89.
20. Grande, A., Grewal, S., Tackla, R. & AJ, R., 2014. Life-threatening allergic vasculitis after clipping an unruptured aneurysm: Case report, weighing the risk of nickel allergy. *Surg Neurol Int*. 5(Suppl 4): S161–S164.
21. Goldenberg A, Jacob S, 2015. Update on systemic nickel allergy syndrome and diet. *Eur Ann Allergy Clin Immunol*. 47(1):25-6.
22. Morshedi, M. Kinney, T, 2014. Nickel hypersensitivity in patients with inferior vena cava filters: case report and literature and MAUDE database review. *J Vasc Interv Radiol*, 25(8):1187-91.
23. Ono, H., Takasuna, H. & Tanaka, Y., 2016. Alopecia due to an allergic reaction to metal head-pins used in a neurosurgical operation. *Surg Neurol Int* 07-Jan-2016;7
24. Clague, G., McGann, G. & Gilbert, H., 2012. An unusual allergy to platinum embolization coils. *Cardiovasc Intervent Radiol*, ;35(1):215-6.
25. Fahrni, J., Gloviczki, P., Friese, J. & Bakkum-Gamez, J., 2015. Hypersensitivity to nickel in a patient treated with coil embolization for pelvic congestion syndrome. *J Vasc Surg Venous Lymphat Disord*, 3(3):319-21.
26. Uwatoko, T. et al., 2015. Dermatitis caused by metal allergy after coil embolization for unruptured cerebral aneurysm. *BMJ case reports*: bcr2015011981.
27. Basko-Plluska, J., Thyssen, J. & Schalock, P., 2011. Cutaneous and systemic hypersensitivity reactions to metallic implants. *Dermatitis*, 22(2):65-79.
28. Baltus, T., Brown, J. & I, M., 2018. Delayed systemic allergic dermatitis following Essure insert: a case report. *Case Rep. Women Health*; 20:e00075.
29. MAUDE, 2017. FDA MAUDE Adverse Event Report. [Online] Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/Detail.cfm?MDRFOI_ID=3878099 [Accessed 2022].
30. Niki, Y., Matsumoto, H. & Otani, T., 2005. Screening for symptomatic metal sensitivity: a prospective study of 92 patients undergoing total knee arthroplasty. *Biomaterials*, pp. 26(9):1019-1026.
31. Hamann, C., 2018. Titanium. In: *Metal Allergy*. s.l.:Springer.
32. Hallab, N., 2017. Diagnosis of Metal Hypersensitivity in Orthopedics. *Operative Techniques in Orthopaedics*, pp. 168-177.
33. Hallab, N., Merritt, K. & Jacobs, J., 2001. Metal sensitivity in patients with orthopedic implants. *The Journal of Bone*, p. 83:428.
34. Tiesenga, F., Wang, J. & Crews, C., 2014. Adverse Reactions to Titanium Surgical Staples in a Patient After Cholecystectomy. *CRSLS MIS Case Reports*, pp. <http://crsls.sls.org/2014-03056/>