Scoliosis and metal allergy

MELISA® is a clinically validated blood test for metal hypersensitivity and may be used in two ways:
Firstly, to check pre-operatively for specific metal allergy in patients presenting with a history of suspected metal allergy (dermal reactions to jewellery, earrings, contact dermatitis, etc). Studies have shown patients who reacted to a single metal have an increased chance of co-sensitisation to another metal. [1,2,3] Given the complexity and high rate of complications associated with removing spinal rods, allergy testing prior to surgery should be considered in patients presenting with a history of metal allergy.
Secondly, post-operatively, when patients present with increased and persistent unexplained pain, sometimes after an initial pain-free period with no evidence of infection [4,5,6], usually within six months of implantation. MELISA can be used to confirm if metal allergy is responsible for the post-surgical symptoms, and will measure the strength of the allergy to particular metals [7,8].

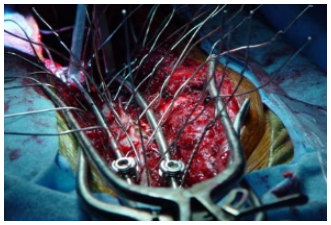
Life threatening metal allergy treated through "immunological camouflage" of implant
This scoliosis case report describes an innovative solution for patients with metal allergies needing implants. A young boy with syndromic scoliosis had metal rods implanted and developed severe post operative symptoms. MELISA testing showed that the boy was allergic to several metals found in the implant. Symptoms resolved after the rods were removed. Eventually the rods were "camouflaged" from the patient's immune system by an innovative carbon coating and the boy was able to tolerate the implant.
Zielinski et al, 2014 [28]

Metal allergy and spinal implants

In metal-on-metal total hip arthroplasty, cell-mediated hypersensitivity reactions (Type IV) are well recognized and reported and have become of increasing concern [9,10,11]. Although the frequency of hypersensitivity reactions is unknown, they are associated with poor outcomes and implant failures. Although fewer cases of hypersensitivity reactions have been reported after spinal implants, which may be down to the difficulty in diagnosis. However, the mechanisms leading to such reactions are similar to those described after hip arthroplasty [12,13,14].

Why use MELISA testing?

Studies show that lymphocyte transformation tests are better suited for diagnosing possible metal sensitivity than traditional patch testing. Implant-related hypersensitivity reactions are generally type-IV delayed hypersensitivity [15] and the relationship between skin hypersensitivity and systemic hypersensitivity is ill defined [15,16]. The accuracy of patch testing for titanium allergy in particular seems to be variable. Mayo Clinic failed to detect any positive reactions to titanium in over a decade of patch testing [17], despite several cases of titanium allergy published by others. [18,19]
Traces of other metals such as nickel and aluminium are found even in commercially pure titanium due to the production process [20,21]. Titanium has been shown to induce clinically relevant hypersensitivity which can be detected with MELISA testing [16]. Before testing, it is important to bear in mind that the screws, wires, bolts, etc. used in surgery may contain other metals than are present in the rods, and these metals should also be tested. This may be a problem for hypersensitive patients and could also lead to increased corrosion.



Corrosion *in vitro*

With stainless steel scoliosis implants, over 65% were found to have corroded after retrieval [22]. It is generally agreed that implants rely on an oxidative layer to prevent corrosion. When mechanical stresses are applied then this protective layer will break down and metal ions may be released. The corrosive process may accelerate once the alloys or metals are exposed to bodily fluids *in vitro*. Spinal implants are static, load-bearing devices and are subject to both tiny movements and to fretting – at least until fusion is finally achieved. As a consequence, metal ions are released and can be found in body fluids [23-25]. In one study 35% of patients with titanium spinal implants showed abnormal serum metal concentrations [25]. Locally, released titanium particles are taken up by macrophages and might initiate inflammation, activation of osteoclasts and cellular apoptosis as described in an animal model [26].

Thus in the clinical setting, the presence of titanium debris around corroding spinal implants could serve as the impetus for both late-onset inflammatory-infectious complications and long-term osteolysis [26]. As the use of dissimilar metals in spine instrumentation has increased, eg cobalt chromium alloys with titanium alloy screws Ti-6Al-4V screws so there is an increased risk of galvanic corrosion and the need for revision surgery due to metallosis [27].

Long term exposure to metal ions

Whilst a short term (12 month) rise in levels of titanium, aluminium and niobium in a paediatric cohort has been reported after scoliosis/kyphosis surgery, few studies have looked at the long term effects that corrosion may have [29]. Levels of nickel and chromium remain higher than normal levels four years post surgery – even when implants showed no sign of corrosion [30]. Studies link metal allergy from spinal devices to a variety of conditions including inflammatory arthritis [31], cauda equine syndrome [32] and the development of soft-tissue mass [33]. The causes of surgical site infections in scoliosis have been discussed at great length in the literature. Some authors suggest that allergy is a risk factor on the development of infectious complications associated with surgical treatment of idiopathic scoliosis [34].

References

1. Torres F, das Graças M, Melo M, Tosti A. *Management of contact dermatitis due to nickel allergy: an update.* Clinical, cosmetic and investigational dermatology. CCID2009;2:39-48
2. Mei-Eng Tu, Yu-Hung W. *Multiple allergies to metal alloys.* Original Research Article Dermatologica Sinica, 2011;29(2):41-43
3. Ruff CA, Belsito DV. T*he impact of various patient factors on contact allergy to nickel, cobalt, and chromate.* J Am Acad Dermatol. 2006;55(1):32-9
4. Willert HG, Buchhorn GH, Fayyazi A et al. *Metal-on-metal bearings and hypersensitivity in patients with artificial hip joints. A clinical and histomorphological study.* J Bone Joint Surg Am 2005;87(1):28-3
5. Shang et al. *Metal hypersensitivity in patient with posterior lumbar spine fusion: a case report and literature review.* BMC Musculoskeletal Disorders 2014;15:314
6. Zairi F, Remacle JM, Allaoui M, Assaker R. *Delayed hypersensitivity reaction caused by metal-on-metal total disc replacement: Case report.* Journal of Neurosurgery: Spine 2013;19(3):389-391
7. Sakellariou V et al. *Postoperative spinal infection mimicking systemic vasculitis with titanium-spinal implants.* Scoliosis 2011;6:20
8. Valentine-Thon E, Schiwara HW. V*alidity of MELISA® for metal sensitivity testing.* Neuroendocrinology Letters 2003; 24(1/2):57-64
9. Jacobs JJ, Hallab NJ, Skipor AK, Urban RM. *Metal degradation products: a cause for concern in metal-metal bearings?* Clin Orthop Relat Res 2003(417):139-147
10. Rushinga G, Goretsky M, Gustin T et al. *When it is not an infection: metal allergy after the Nuss procedure for repair of pectus excavatum.* Journal of Pediatric Surgery 2007;42:93-97
11. Adala R, Chakravarthy M, Srinivas V, Pai S. *Orthopaedic surgery in a patient with metal sensitivity.* J Cutan Aesthet Surg. 2011;4(1):67-68
12. Anderson PA, Kurtz SM, Toth JM. *Explant analysis of total disc replacement.* Semin Spine Surg 2006;18:109-116
13. Kurtz SM, Toth JM, Siskey R et al. T*he latest lessons learned from retrieval analyses of ultra-high molecular weight polyethylene, metal-on-metal, and alternative bearing total disc replacements.* Semin Spine Surg 2012;(24):57-70
14. Punt IM, Austen S, Cleutjens JPM et al. *Are periprosthetic tissue reactions observed after revision of total disc replacement comparable to the reactions observed after total hip or knee revision surgery?* Spine 2012;(37):150-159
15. Hallab N, Merritt, Jacobs J. *Metal sensitivity in patients with orthopedic implants*. The Journal of Bone and Joint Surgery 2001;83:428
16. Cambell P; metalsensitivity.com
17. Davis MD et al. *Patch testing with a large series of metal allergens: findings from more than 1,000 patients in one decade at Mayo Clinic.* Dermatitis 2011;22(5):256-71
18. Thomas P, Bandl WD, Maier S, Summer B, Przybilla B. *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
19. Evrard L, Waroquier D, Parent D. *Allergies to dental metals. Titanium: a new allergen.* Rev Med Brux 2010; 31(1):44-9
20. Schuh A, Thomas P, Kachler W et al. *Allergic potential of titanium implants.* Orthopade 2005;34(4):327-8, 330-3
21. Darvell, BW et al. *Contamination of titanium castings by aluminium oxide blasting.* J Dent 1995;23(5):319-22
22 Akazawa T et al. *Corrosion of spinal implants retrieved from patients with scoliosis.* J Orthop Sci 2005;10(2):200-205
23. Kim YJ, Kassab F, Berven SH et al. *Serum levels of nickel and chromium after instrumented posterior spinal arthrodesis.* Spine 2005;30(8):923-926
24. Del Rio J, Beguiristain J, Duart J. *Metal levels in corrosion of spinal implants.* Eur Spine J 2007;16(7):1055-1061
25. Kasai Y, Iida R, Uchida A. *Metal concentrations in the serum and hair of patients with titanium alloy spinal implants.* Spine 2003;28(12):1320-1326
26. Cunningham BW, Orbegoso CM, Dmitriev AE et al. *The effect of titanium particulate on development and maintenance of a posterolateral spinal arthrodesis: an in vivo rabbit model.* Spine 2002;27(18) 1971-1981
27. Panagiotopoulou VC et al. Assessment of corrosion in retrieved spine implants. J Biomed Mater Res B Appl Biomater. 2017 (March)
28. Zielinski J, Lacy TA, Phillips JH. *Carbon coated implants as a new solution for metal allergy in early-onset scoliosis: A case report and review of the literature.* Spine Deformity 2014;2:76-80
29. Cundy TP, Antoniou G, Sutherland LM, Freeman BJ, Cundy PJ. *Serum titanium, niobium, and aluminum levels after instrumented spinal arthrodesis in children.* Spine 2013;38:564-70
30. Kim Y et al. *Serum levels of nickel and chromium after instrumented posterior spinal arthrodesis.* Spine 2005; 15;30(8):923-6
31. Dörner T, Haas J, Loddenkemper C, von Baehr V, Salama A. *Implant-related inflammatory arthritis.* Nature Clinical Practice Rheumatology 2006;2:53-56
32. Zairi F, Remacle JM, Allaoui M, Assaker R. *Delayed hypersensitivity reaction caused by metal-on-metal total disc replacement.* J Neurosurg Spine. 2013;19(3):389-91
33. Guyer RD et al. *Early failure of metal-on-metal artificial disc prostheses associated with lymphocytic reaction: diagnosis and treatment experience in four cases.* Spine 2011;1:36(7):492-497
34. Grosman R, Vlach O, Leznar M. *Infections in surgery of idiopathic scoliosis* .Acta Chir Orthop Traumatol Cech 2002;69(3):175-178

Testing procedure

A blood sample can be sent to any licensed MELISA laboratory. Samples are time sensitive and should arrive within 24hrs (maximally 48hrs).

The blood sample should be kept at room temperature and sent in tubes sodium citrate light blue vacuette tubes. The amount of blood required depends on how many antigens are to be tested.

For adults, a screening of 10 metals, 36 ml (or 4 large 9ml tubes) of blood is needed.

Taking steroids or other immuno-suppressant drugs may affect the test results.

A questionnaire which helps to identify patients who are likely to benefit from MELISA testing can also be provided and evaluated. However, patient history alone is not sufficient to diagnose metal hypersensitivity [18].

MELISA®
DIAGNOSTICS

MELISA Diagnostics Ltd
t 020 8133 5166
f 020 8711 5958
e info@melisatest.com
w melisa.org