

# Spinal implants

## Diagnosing type IV delayed hypersensitivity with MELISA® testing

MELISA® is a clinically validated blood test that may be used in two ways:

First, to check pre-operatively for specific metal allergy in patients presenting with a history of suspected metal allergy (e.g. dermal reactions to jewellery, contact dermatitis, etc.) to ensure the biocompatibility of the new implant [1]. Studies have shown patients who reacted to a single metal have an increased chance of co-sensitization to another metal, so patient-reported nickel allergy may indicate hypersensitivity to other metals [2,3,4].

Second, post-operatively or when planning revision surgery. When patients present with increased and persistent unexplained pain, unexplained neurologic symptoms or rashes, sometimes after an initial pain-free period with no evidence of infection [1,5,6,7]. MELISA can help diagnose if metal allergy is responsible for the post-surgical symptoms, and will measure the strength of the allergy to particular metals [8,9].

### 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 an increasingly important area for research [10,11]. Around 500,000 spinal instrumentation procedures are performed each year in the USA alone, compared to 400,000 for hip replacements. Analysis of spinal instrumentation is “surprisingly underdeveloped compared to the research of hip retrievals.” [12] However, the mechanisms leading to such reactions in spinal surgery are similar to those described after hip arthroplasty [13,14,15].

Galvanic corrosion may also be increased by the use of dissimilar metals in spine instrumentation eg cobalt chromium alloys with titanium alloy screws e.g. Ti-6Al-4V screws [12].

Spinal implants are all static load-bearing devices and are subject to movement. In consequence, metal ions are released and can be found in body fluids [16-18]. In one study, 35% of patients with titanium spinal implants showed abnormal serum metal concentrations [18]. Locally released titanium particles are taken up by macrophages and might initiate inflammation, activation of osteoclasts, and cellular apoptosis [19]. The presence of metal debris around corroding spinal implants could serve as the signal for both late-onset inflammatory-infectious complications and long-term osteolysis. [20]

### Why use MELISA testing?

- Repeat or revision spinal surgery is less likely to succeed than initial surgery [21,22].
- Failure rates in spinal surgery are generally high already, ranging between 10% and 40% [23,24].

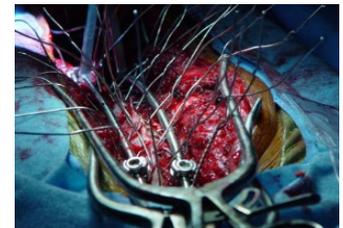
Reducing the risk of implant failure through metal allergy by testing prior to surgery is advantageous. Particularly in patients presenting with a history of skin reactions and atopic or autoimmune conditions.

Studies show that lymphocyte transformation tests, like MELISA, are better suited for diagnosing possible metal sensitivity than traditional patch testing. Implant-related hypersensitivity reactions are generally type-IV delayed hypersensitivity [25] and the relationship between skin hypersensitivity and systemic hypersensitivity is ill defined [25,26]. 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 [27], despite several cases of titanium allergy published by others. [28,29]

Traces of other metals such as nickel, vanadium and aluminium are found even in commercially pure titanium due to the production process [30,31]. Titanium has been shown to induce clinically relevant hypersensitivity which can be detected with MELISA testing [9,32].

### Life threatening metal allergy treated through “immunological camouflage” of implant

This case report describes an innovative solution for the placement of implants in severely metal allergic patients. 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. [33]



### 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 with sodium citrate.

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.

### References

- Hallab, Nadim J. Biological Responses to Spinal Implant Debris. Spine: April 1st, Volume 42, 2017.
- 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
- Mei-Eng Tu, Yu-Hung W. *Multiple allergies to metal alloys.* Original Research Article Dermatologica Sinica, 2011;29(2):41-43
- Ruff CA, Belsito DV. *The impact of various patient factors on contact allergy to nickel, cobalt, and chromate.* J Am Acad Dermatol. 2006;55(1):32-9
- 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
- Shang et al. *Metal hypersensitivity in patient with posterior lumbar spine fusion: a case report and literature review.* BMC Musculoskeletal Disorders 2014;15:314
- 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
- Sakellariou V et al. *Postoperative spinal infection mimicking systemic vasculitis with titanium-spinal implants.* Scoliosis 2011;6:20
- Valentine-Thon E, Schiwarz HW. *Validity of MELISA® for metal sensitivity testing.* Neuroendocrinology Letters 2003; 24(1/2):57-64
- 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
- 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
- Panagiotopoulou VC et al. *Assessment of corrosion in retrieved spine implants.* Journal of Biomedical Materials Research Applied Biomaterials 2018;106(2):632-638, )
- Anderson PA, Kurtz SM, Toth JM. *Explant analysis of total disc replacement.* Semin Spine Surg 2006;18:109-116
- Kurtz SM, Toth JM, Siskey R et al. *The 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
- 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
- Akazawa T et al. *Corrosion of spinal implants retrieved from patients with scoliosis.* J Orthop Sci 2005;10(2):200-205.
- 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
- Del Rio J, Beguiristain J, Duart J. *Metal levels in corrosion of spinal implants.* Eur Spine J 2007;16(7):1055-1061
- 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
- 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
- Ragab A, Deshazo RD. *Management of back pain in patients with previous back surgery.* Am J Med 2008; 121: 272-278.
- North RB, Kidd DH, Farrokhi F, et al. *Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: a randomized, controlled trial.* Neurosurgery 2005; 56: 98-106.
- North RB, Kidd DH, Zahurak M, et al. *Spinal cord stimulation for chronic, intractable pain: experience over two decades.* Neurosurgery 1993; 32: 384-394.
- Wilkinson HA. *The failed back syndrome: Etiology and therapy.* Philadelphia: Harper & Row, 1991.
- Hallab N, Merritt, Jacobs J. *Metal sensitivity in patients with orthopedic implants.* The Journal of Bone and Joint Surgery 2001;83:428
- Cambell P; metalsensitivity.com
- 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
- 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
- Evrard L, Waroquier D, Parent D. *Allergies to dental metals. Titanium: a new allergen.* Rev Med Brux 2010; 31(1):44-9
- Schuh A, Thomas P, Kachler W et al. *Allergic potential of titanium implants.* Orthopade 2005;34(4):327-8, 330-3
- Darvell, BW et al. *Contamination of titanium castings by aluminium oxide blasting.* J Dent 1995;23(5):319-22
- Müller K, Valentine-Thon E. *Hypersensitivity to titanium: clinical and laboratory evidence.* Neuro Endocrinol Lett. 2006 Dec;27 Suppl 1:31-5.
- 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