Metal Hypersensitivity

A surgeon’s guide to understanding metal sensitivity and the methods of testing.

Metallic alloys commonly used in artificial joints undergo corrosion when in contact with biological systems. This electrochemical process leads to the release of metallic ions into the patient’s body. In a metal sensitive patient, these ions form complexes with proteins and trigger an immune response.

Common metal sensitizers include: nickel, cobalt, chromium
- Occasional responses to beryllium, tantalum, titanium and vanadium have been reported

Dermal hypersensitivity to metal is common, affecting 10% to 15% of the population.

Frequency of skin sensitivity to metals:
- General population: 10%
- Patients with stable total joints: 25%
- Patients with loose total joints: 60%

Implant related hypersensitivity reactions are generally type-IV delayed-type hypersensitivity (DTH).

Testing for Metal Hypersensitivity

Currently there is no generally accepted test for the clinical determination of metal hypersensitivity to implanted devices. Historically, testing for delayed-type hypersensitivity (DTH) has been conducted in vivo by skin testing and in vitro by lymphocyte transformation testing (LTT) and leukocyte migration inhibition (LMI) testing.

Patch Test
Patch testing involves incorporating an antigen in a carrier and exposing this to dermal tissue by means of an affixed bandage for 48-96 hours. There are concerns about the applicability of skin testing to the study of immune responses to implants. One concern is the short length of the test because typical reports of eczemic reactions to orthopaedic implants occur after weeks to months of constant exposure. There are also concerns that patch testing could possibly be affected by immunological tolerance or by impaired host immune response and the testing could induce hypersensitivity in the patient.

Lymphocyte Transformation Test (LTT)
LTT is a measure of the proliferative response of lymphocytes following activation. A radioactive marker is added to isolated lymphocytes along with the desired challenge agent. On the sixth day, radiisotope uptake is measured with use of liquid scintillation. The proliferation factor, or stimulation index, is calculated with use of measured radiation counts per minute (cpm):

\[
\text{proliferation factor} = \frac{\text{mean cpm with treatment}}{\text{mean cpm without treatment}}
\]

LTT is less popular than patch testing, but has been well established as a method for testing metal sensitivity in a variety of clinical settings.

Leukocyte Migration Inhibition (LMI) Test
LMI testing involves the measurement of mixed-population leukocyte migration activity. Leukocytes in culture actively migrate in a random pattern, but they can be attracted preferentially to chemotactants. In the presence of a sensitizing antigen, leukocytes migrate more slowly, losing the ability to recognize chemotactants and are said to be migration-inhibited. Migration testing may lack the sensitivity for detecting a DTH response at certain times over the course of a hypersensitivity reaction.

MELISA® Allergy Blood Test

MELISA® is a blood test which measures cellular hypersensitivity (type IV allergy) to metals and other low-molecular allergens. MELISA® has been validated by an independent laboratory and the results are published.

MELISA® measures the patient’s lymphocyte reaction to allergens by two separate technologies. First by the uptake of radioisotope by dividing lymphocytes and second by classical evaluation by microscopy. The level of reactivity is measured as a stimulation index. A value over 3 indicates a positive reaction to a given allergen. Results are available within 10 days.

Several testing panels are offered with prices ranging from $367.00 to $997.00*. Custom panels are also available.

The materials tested include: aluminum, beryllium, cadmium, calcium titanate, chromium, cobalt, copper, gold, indium, inorganic mercury, lead, methyl mercury, molybdenum, nickel, niobium, palladium, phenyl mercury, platinum, silver, tantalum, thimerosal, tin, titanium dioxide, titanium trichloride, tungsten, vanadium and zirconium.

Lab Locations
- Pharmasan Labs
  Osceola, WI
  Phone: +1 715-294-2144
  Fax: +1 715-294-3921
  Website: www.neuroscienceinc.com/MELISA
  Email: Gottfried.Kellermann@neurorelief.com
- Health Diagnostics and Research Institute
  South Amboy Medical Center, South Amboy, NJ
  Phone: +1 732-721-1234
  Fax: +1 732-525-3288
  Email: e.valentine-thon@web.de

For more information: www.melisa.org

Orthopedic Analysis, LLC Metal LTT

The Orthopedic Analysis LLC Metal LTT Assay is performed by isolating lymphocytes and other important immune cells from the patient’s blood. Isolated immune cells are divided up in a culture dish and exposed to different metals. Cells are cultured for about one week in the presence of metals that are found in different types of orthopedic implant materials. The amount of proliferation is measured since lymphocytes will expand in number as a reaction to a threat.

Results are available 10 days following the blood draw.

Two testing panels are offered with prices ranging from $350.00 to $500.00*.

The materials tested include: aluminum, chromium, cobalt, iron, molybdenum, nickel, vanadium, zirconium, bone cement, particles of bone cement, cobalt-alloy particles and titanium-alloy particles.

Lab Location
- Orthopedic Analysis, LLC
  Department of Orthopedic Surgery
  Rush University Medical Center
  Chicago, IL
  Phone: 312-733-7121
  Website: www.orthopedicanalysis.com

Aesculap Implant Materials

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<th>Percent Weight Composition*</th>
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Additional Resources