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SHARING EXPERTISE

Metal Hypersensitivity

Diagnosis – Procedure – Implant Materials

Metal Hypersensitivity

It has been discovered that a possible contact allergy to implant materials or the components contained in bone cement may lead to implant intolerance. Endoprostheses are known to release metal ions into the human body. This can lead to immune reactions in patients who are at risk of a hypersensitive reaction. Symptoms that have been described include eczema, impaired wound healing, bruising, pain, restricted movement and loosening of the implant.
The most common allergenic metals are nickel, cobalt and chromium. People have also been known to exhibit sensitivities to certain components of cement, such as acrylate and gentamicin.
With between 10 % and 15 % of the population allergic to metals, it would appear that such sensitivities are relatively high; (1) however, the number of patients which develop an intolerance to implant materials is much lower than reactions on the skin.

Incidence of skin reactions to metals (2)

- General population 10 %
- Patients with a well functioning prosthesis 25 %
- Patients with a loose prosthesis or pain 60 %

Hypersensitivities associated with implants are generally of type IV hypersensitivity [Gell and Coombs classification (4)]: A T-cell-mediated, delayed type hypersensitivity (DTH).

Contact allergy after endoprosthesis (3)

239 patients experiencing implant complications, 181 of whom with knee or hip endoprostheses, underwent contact allergy investigation. (3)

- Reaction to nickel 21.3 %
- Reaction to cobalt 10.9 %
- Reaction to chromium 5.0 %
- Reaction to components contained in bone cement 24.8 %

Among patients with endoprosthetic complications, the incidence of contact allergies to metals and potentially to components in bone cement is higher than among the general population. (2)

Diagnosis

The criteria for diagnosing a metal implant allergy have not yet been defined conclusively, such that differential diagnoses (infection) have to be excluded and several test methods have to be considered at the same time.

The standard allergological diagnosis should include an **epicutaneous test,** if possible with **histological evaluation** of the tissue surrounding the implant. Additional information can be provided by the **lymphocyte transformation test (LTT).**

Histological evaluation

Periimplantary tissue collected arthroscopically from total knee replacement patients should be fixed in formalin and subjected to further immunohistological investigation for inflammatory cell infiltration, foreign body reaction or infection-associated changes.6 In the specific case of loosening of the endoprosthesis, the following consensus classification is described for (immune) histological testing of tissue. (6)

- Type I (wear particle induced) refers to an infiltration consisting predominantly of macrophages and multinucleated giant cells.
- Type II (infectious) may indicate a pronounced or minimal infection with chronic granulomatous inflammation.
- Type III (combined) is a combination of both wear particle induced and infections.
- Type IV (indeterminate) refers to a clinical picture with fewer cells, but high collagen fibre.

Lymphocyte transformation test (LTT)

The LTT shows, by means of inducible T-cell proliferation following the in-vitro addition of antigens, that the donor's blood lymphocytes 'recognise' the antigen added to the cell culture (sensitization). This figure is shown in comparison to the negative control of unstimulated cultures in a ratio, which is referred to as the stimulation index (SI). An SI>2 indicates sensitivity. The test can show whether a patient is sensitive to metals (7); however, a sensitivity does not necessarily mean an allergy.

Epicutaneous testing

Test metals are administered to the skin and the results read after 2, 3 and in some cases 7 days. Suspect metals (nickel, chromium and cobalt) are tested in a standard series of tests. Components of bone cement should also be tested if cement was used to attach the implant.
The test compounds are standardized to detect a contact allergy; to nickel, for instance. However, the results may be affected by altered immune reactions or immunotolerance. Although the test is conducted on the skin and therefore only has limited applicability to subcutaneous tissue, the results are at least able to identify hypersensitive persons. More detailed exploration would then be required for clinical relevance.

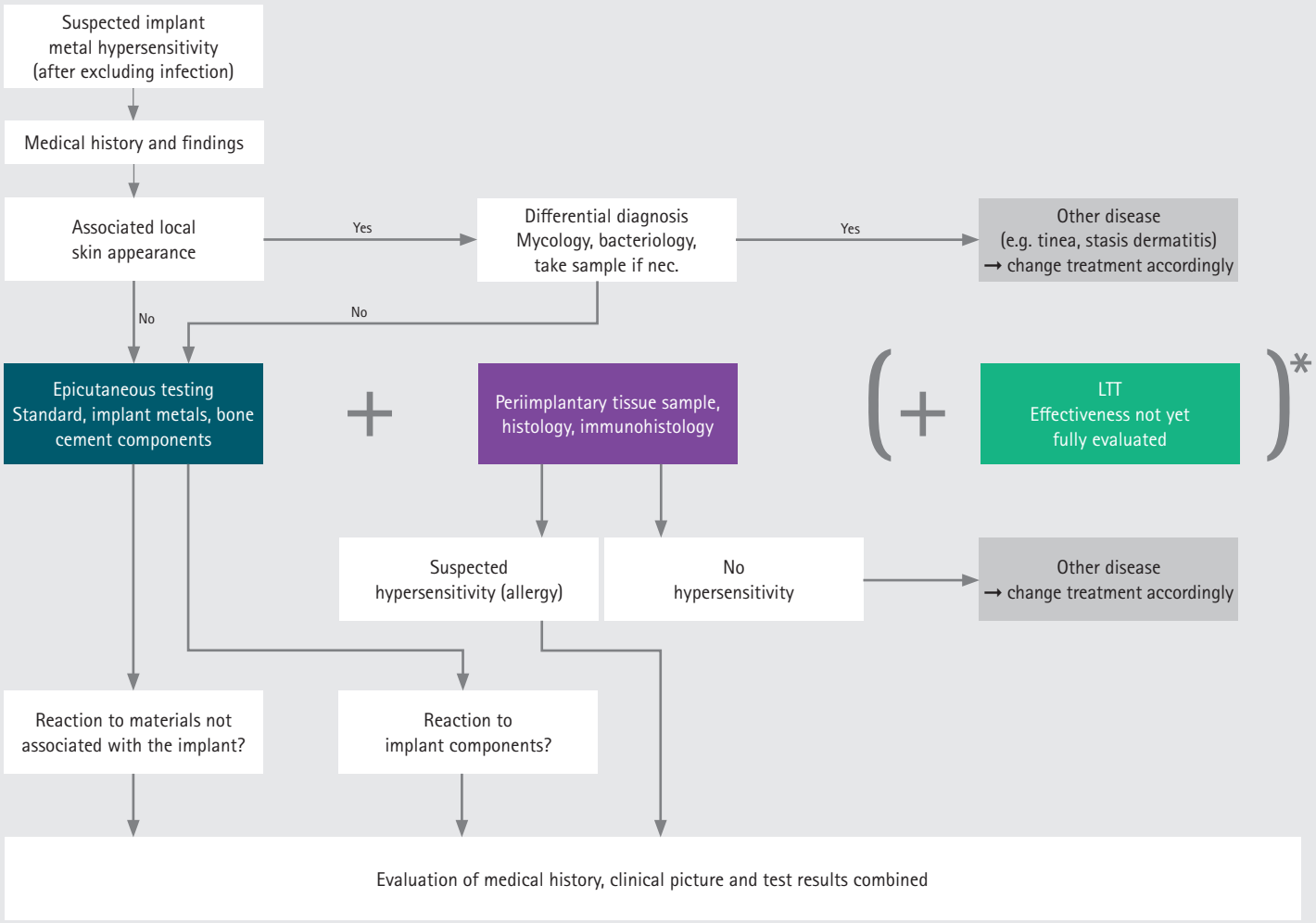
Patch testing using metal discs is no longer recommended for the following reasons (5):

- Because it is not standardized, false-negative or false-positive reactions may arise and it is unclear which metal the individual is reacting to.
- The test discs can rub and press down on the skin, causing skin irritation that leads to false-positive results.

In view of the above, B. Braun no longer offers patch test discs.

Metal Hypersensitivity Investigation Procedure

The Implant Hypersensitivity Working Group of the DGOOC (German Association of Orthopaedics and Orthopaedic Surgery) came up with an procedure for clarifying a suspected metal hypersensitivity, as described below.



* LTT as a further scientific approach (effectiveness still under evaluation)

Chart: Metal hypersensitivity investigation procedure as defined by the Implant Hypersensitivity Working Group (5)

AESCULAP® Implant Materials

Materials	ISODUR® F	ISODUR® C	ISOTAN® F	PLASMAPORE® coating
ISO standard	ISO 5832-12	ISO 5832-4	ISO 5832-3	ISO 5832-2
Alloy base	Cobalt	Cobalt	Titanium	Titanium
Alloy type	CoCrMo	CoCrMo	Ti6Al4V	Ti
Carbon	≤ 0.35	≤ 0.35	≤ 0.08	≤ 0.10
Silicium	≤ 1.0	≤ 1.0	–	–
Manganese	≤ 1.0	≤ 1.0	–	–
Cobalt	Residual	Residual	–	–
Chromium	26.0 - 30.0	26.5 - 30.0	–	–
Molybdenum	5.0 - 7.0	4.5 - 7.0	–	–
Nickel	≤ 1.0	≤ 1.0	–	–
Vandium	–	–	3.5 - 4.5	–
Aluminum	–	–	5.5 - 6.7	–
Iron	≤ 0.75	≤ 1.0	≤ 0.3	≤ 0.3
Titanium	–	–	Residual	Residual
Nitrogen	≤ 0.25	–	≤ 0.05	≤ 0.05
Oxygen	–	–	≤ 0.2	≤ 0.45
Hydrogen	–	–	≤ 0.015	≤ 0.0125

Table: Constituent substances of alloys used in implant components

AS Coating

Multilayer ceramic coating made from zirconium nitride and various intermediate layers (ZrN-CrN-CrCN-Cr)

- Knee implants: complete portfolio
- Hip implants: AS CoreHip®

ISODUR® F

- Knee implants: Extension stems, obturator, augmentation, tibia univation
- Hip implants: Metal heads, Dual Mobility Insert, cemented stems

ISODUR® C

- Knee implants: Columbus®, e.motion®, VEGA System®, femur univation, EnduRo
- Hip implants: Bipolar Cup (REF-INDEX „K“)

PLASMAPORE® µCaP is idential to PLASMAPORE®, but with a layer of 15 µm Dicalciumphosphate

ISOTAN® F

- Hip implants: Cementless stems, Plasmacup®, Screwcup SC, Plasmafit®, Plasmafit® Revision, Structan®

PLASMAPORE® coating

- Hip implants: Bicontact®, PLASMAPORE®, Excia®, Plasmacup®
- Cementless knee implants: Columbus®, e.motion®, CoreHip®, Plasmafit®, Prevision®

PLASMAPORE® µ-CaP coating

- Hip implants: Metha®, Excia®
- Knee implants: e.motion®

Literature

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