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Complications after TKA : Allergy

Diagnosis and options for re-surgery

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Complications & Failures

- Total Knee Arthroplasty (TKA)
- Excellent clinical outcomes
- Improvement in quality of life
- However
- Significant number of failures
- Revision rate: 2% at 5 years¹

- Infection (26.1%)²
 - Aseptic Loosening (23.1%)
 - Instability (9.2%)

....

- Femoro-patellar complications (8.9%)
- Metal allergies (0.5%)



- Release of metal ions (produced by corrosion)
 - oxidized and reabsorbed
 - capable of interacting with the immune system
 - and triggering immunotoxic effects
 - including delayed hypersensitivity reactions.¹
 - Main metal allergens: nickel, cobalt, chrome
 - Less common: vanadium, titanium, manganese.





Metal allergies (0.5%

• But .. Controversal topic¹

Literature



Some authors are questioning the existence of this pathological entity as a cause for failed TKA.^{2,3}

- 1: Matar HE, Porter PJ, Porter ML. Metal allergy in primary and revision total knee arthroplasty : a scoping review and evidence-based practical approach. Bone Jt Open. 2021
- 2 : Thomas P, von der Helm C, Schopf C, Frommelt L L, GollwitzerH. Patients with intolerance reactions to total knee replacement: Combined assessment of allergy diagnostics, periprosthetic histology, and periimplant cytokine expression pattern. Biomed Res Int. 2005;2015:910156.
- 3: Mitchelson AJ, Wilson CJ, Mihalko WM, Grupp TM, Manning BT, Dennis DA, Goodman SB, Tzeng TH, Vasdev S, Saleh KJ. Biomaterial hypersensitivity: is it real? Supportive evidence and approach considerations for metal allergic patients following total knee arthroplasty. Biomed Res Int. 2015

From a histopathological perspective :

- Implant-associated pathologies involving the Synovial-Like Interface Membrane (SLIM) are categorized in accordance with the consensus classification of joint implant related pathologies^{1,2,3,4}

- **SLIM type VI** describes adverse local tissue reactions in implant materials, including allergy and hypersensitivity.

Table I The international expanded classification of the synovial-like interface membrane (SLIM).

SLIM type	Description
I	Wear-induced synovitis
II	Infection-induced synovitis
111	Mixed synovitis
IV	Indifferent (not wear-induced, not infection-induced) synovitis
V	Prosthesis-associated arthrofibrosis
VI	Adverse local tissue reactions to implant materials (allergy/ hypersensitivity)
VII	Local osseous pathologies

^{1:} Matar HE, Porter PJ, Porter ML. Metal allergy in primary and revision total knee arthroplasty : a scoping review and evidence-based practical approach. Bone Jt Open. 2021

^{2 :} Krenn V, Morawietz L, Perino G, et al. Revised histopathological consensus classification of joint implant related pathology. Pathol Res Pract.

^{3 :} Goldring SR, Jasty M, Roelke MS, Rourke CM, Bringhurst FR, Harris WH. Formation of a synovial- like membrane at the bone- cement interface. Its role in bone resorption and implant loosening after total hip replacement. Arthritis Rheum. 1986

^{4:} Pap G, Machner A, Rinnert T, et al. Development and characteristics of a synovial-like interface membrane around cemented tibial hemiarthroplasties in a novel rat model of aseptic prosthesis loosening. Arthritis Rheum. 2001

Diagnosis

• Diagnosis of exclusion.

First, rule out infection ++ and mechanical causes.

Aspecific symptoms :

Clinically:

- Contact eczema
- Pain
- Effusions
- Stiffness
 - •••

Radiologically:

- Loosening



Diagnosis

- Main issue: absence of universally recognized tests.¹
- In vivo tests :
- → Patchs-tests

Reliable for examining sensitivity to implant components²

Possibility of simultaneously testing multiple haptens²

Corrosion products released by the prosthesis circulate and reach skin appendages³

Causal relationship ... ?

1: Jacobs JJ, Hallab NJ. Loosening and osteolysis associated with metal-on-metal bearings: A local effect of metal hypersensitivity? J Bone Joint Surg Am. 2006

2: Granchi D, Cenni E, Trisolino G, Giunti A, Baldini N. Sensitivity to implant materials in patients undergoing total hip replacement. J Biomed Mater Res B Appl Biomater. 2006

3 : Coleman RF, Herrington J, Scales JT. Concentration of wear products in hair, blood, and urine after total hip replacement. Br Med J. 1973

• In vitro tests :

\rightarrow Lymphocyte transformation tests (LTT) ^{1,2}

Based on the reaction of immune cells to the metal-protein complex

Benefit in indeterminate or negative patch test results in a patient strongly suspected of having metal hypersensitivity³

Causal relationship ... ?

Not available in France...

1: Granchi D, Ciapetti G, Savarino L, Stea S, Filippini F, Sudanese A, Rotini R, Giunti A. Expression of the CD69 activation antigen on lymphocytes of patients with hip prosthesis. Biomaterials. 2000

2 : Valentine-Thon E, Schiwara HW. Validity of MELISA for metal sensitivity testing. Neuro Endocrinol Lett. 2003

3: Schalock PC, Menné T, Johansen JD, Taylor JS, Maibach HI, Lidén C, Bruze M, Thyssen JP. Hypersensitivity reactions to metallic implants - diagnostic algorithm and suggested patch test series for contact Dermatitis. 2012

\rightarrow Synovial biopsies

No correlation with LLT testing¹

Can act as a **confirmatory test** before revision surgery is considered



1 : Yang S, Dipane M, CH L, Schmalzried TP, McPherson EJ. Lymphocyte transformation testing (LTT) in cases of pain following total knee arthroplasty: Little relationship to histopathologic findings and revision outcomes. J Bone Joint Surg Am. 2019

2: Biant LC, Bruce WJ, van der Wall H, Walsh WR. Infection or allergy in the painful metal-on-metal total hip arthroplasty? J Arthroplasty. 2010





- Most used method by manufacturers ++
- Addition of a **coated layer** on cobalt-chromium standard implants.
- Titanium-nitride (TiN)
- Zirconia nitride
- Titanium niobium nitride

Addition of a coated layer on cobalt-chromium standard implants.
Titanium-nitride (TiN)

Heterogeneous data in the literature

*Mohammed et al*¹ : **305** TiN TKA : **95%** survival for any revision at 10y FU *Breugem et al*² : **1031** TiN TKAs : **95.1%** survival for any revision at 4y FU

Song et al³: 7% of tibial aseptic loosening in mobile-bearing TiN TKAs at 5y FU Lionberger et al⁴ : 6% of tibial aseptic loosening

^{1:} Mohammed A, Metcalfe A, Woodnutt D. Medium-term outcome of titanium nitride, mobile bearing total knee replacement. Acta Orthop Belg. 2014

^{2 :} Breugem SJM, Linnartz J, Sierevelt I, Bruijn JD, Driessen MJM. Evaluation of 1031 primary titanium nitride coated mobile bearing total knee arthroplasties in an orthopedic clinic. World J Orthop. 2017 3 : Song SJ, Lee HW, Bae DK, Park CH. High Incidence of Tibial Component Loosening After Total Knee Arthroplasty Using Ceramic Titanium-Nitride-Coated Mobile Bearing Prosthesis in Moderate to Severe Varus Deformity: A Matched-Pair Study Between Ceramic-Coated Mobile Bearing and Fixed Bearing Prostheses. J Arthroplasty. 2020 13

^{4 :} Lionberger D, Conlon C, Wattenbarger L, Walker TJ. Unacceptable failure rate of a ceramic-coated posterior cruciate-substituting total knee arthroplasty. Arthroplast Today. 2019

Coated implants

- Addition of a coated layer on cobalt-chromium standard implants.
- Zirconia nitride

 Observational Study
 > Orthop Traumatol Surg Res. 2022 Sep;108(5):103320.

 doi: 10.1016/j.otsr.2022.103320. Epub 2022 May 13.

Beneficial effect of a zirconium-nitride-coated implant in total knee arthroplasty revision for suspected metal hypersensitivity

Yassine Bulaïd¹, Az-Eddine Djebara², Ramy Belhaouane¹, Eric Havet¹, Massinissa Dehl¹, Patrice Mertl¹

Affiliations + expand

PMID: 35577273 DOI: 10.1016/j.otsr.2022.103320



Mean Follow-up: 3.8y

- Survivorship: **93%** - 3 revisions including 1 for tibial aseptic loosening

- Significant functional improvement
- No short term complications₁₄





Titanium implants

> Knee. 2020 Oct;27(5):1519-1524. doi: 10.1016/j.knee.2020.08.007. Epub 2020 Aug 27.

Ten-year outcomes of a nitrided Ti-6Al-4V titanium alloy fixed-bearing total knee replacement with a highly crosslinked polyethylene-bearing in patients with metal allergy

Stefano Marco Paolo Rossi ¹, Loris Perticarini ², Mario Mosconi ³, Matteo Ghiara ⁴, Francesco Benazzo ⁵

Affiliations + expand PMID: 33010769 DOI: 10.1016/j.knee.2020.08.007



Interesting results and survival rates :

Survival rate of 97.2% at 5 years and 95.1% at 10 years.

Significant improvements in range of motion (ROM), Knee Society Scoring (KSS) and Hospital for Special Surgery (HSS) knee scores were registered at final follow-up (P < 0.0001).





Ceramic implants

- Oxinium (zirconium+niobium)
- biologically inert with similar physical properties to titanium
- used for femoral implants
- with titanium tibial base plate

Comparative Study > J Bone Joint Surg Am. 2002:84-A Suppl 2:129-35. doi: 10.2106/00004623-20020002-00018.

Polyethylene wear performance of oxidized zirconium and cobalt-chromium knee components under abrasive conditions

Michael D Ries¹, Abraham Salehi, Kirstin Widding, Gordon Hunter

Affiliations + expand PMID: 12479351 DOI: 10.2106/00004623-200200002-00018



Ceramic implants

• Oxinium (zirconium+niobium)

> J Bone Joint Surg Am. 2017 Feb 15;99(4):275-283. doi: 10.2106/JBJS.16.00092.

Twelve-Year Outcomes of an Oxinium Total Knee Replacement Compared with the Same Cobalt-Chromium Design: An Analysis of 17,577 Prostheses from the Australian Orthopaedic Association National Joint Replacement Registry

Christopher J Vertullo ¹, Peter L Lewis, Stephen Graves, Lan Kelly, Michelle Lorimer, Peter Myers Affiliations + expand PMID: 28196029 DOI: 10.2106/JBJS.16.00092

> <u>Cumulative percent revision at 12 years:</u> 11,608 TKA with **CoCr femoral** components Vs 5,969 TKA with **Oxinium** femoral components.

More femoral loosening in patients
 ≥75 years old (p = 0.033)

4.8% (95% CI, 4.2% to 5.4%) vs **7.7%** (95% CI, 6.2% to 9.5%)

Conclusions

- Diagnosis of allergy on TKA is based on a body of evidence: a prosthesis that has never been painless, in the absence of infection (repeated aspirations), recurrent loosenings on the X-Rays sometimes supported by eczematous skin reactions near the prosthesis.
- Skin patch testing / LTT are reasonable screening tests
 +/- synovial biopsies as confirmatory test
- Ultimately, revision can confirm the diagnosis provided that components made of a different metal than the one suspected to cause the allergy are available, and histology finds a specific synovitis.

- Multiple "hypoallergenic" implants are available, and can be divided into coated implants, titanium implants and ceramic implants.
- **Coated implants** are the most commonly used among manufacturers.
- Few high-sample-size studies exist on TKA revisions with hypoallergenic prostheses.
- Creation of a **registry** of theses specific prostheses would be relevant.



Thank you for your attention



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