Immunological Responses to Metal-containing Medical Devices in Orthopedic Patients

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Scope of the Problem

► US: >1 million joint replacements/year
► Main recipients
  ▪ 65-84 y/o – largest Medicare expenditure
  ▪ 45-64 y/o – significant increase since 2000
► Joint replacements are cost effective
► Estimates: 4 million/year by 2030
  ► Aging of US population
  ► Demand to maintain mobility
Projected Rates of Increase

BMC Musculoskeletal Disorders. 2019; 20: 90. Published online 2019 Feb 23.

Growth in number of total knee replacements from 2003 to 2030. #TKA for 2003–2013 based on reports to AOANJRR. Number of procedures from 2014 on based on projections.

Growth in number of total hip replacements from 2003 to 2030. #THA for 2003–2013 based on reports to AOANJRR. Number of procedures from 2014 on based on projections.
10% of all joint replacements will fail

3 Main Causes of Joint Failure:
- Immune-mediated*
- Infection
- Mechanical

Contributing factors:
- Obesity
- Cigarette smoking
- Osteoporosis

*However, need to suspect it first.
Why is sensitization a concern?

- **Stainless steel**
  - Nickel 14-28%
  - Chromium 12-18%
  - Manganese 5%

- **Cobalt/chromium**
  - Cobalt 60%
  - Chromium 30%
  - Molybdenum 5%
  - Nickel 0.5-2%

- **Titanium alloy**
  - Titanium 90%
  - Aluminum 6%
  - Vanadium 4%

- **Oxinium**
  - Zirconium 95%
  - Niobium 5%

- **Nitinol**
  - Titanium 55%
  - Nickel 45%

- **Coatings**
  - Tantalum
  - Hydroxy apatite not a problem

- **Bone cement**
  - Poly methyl methacrylate
  - Benzoyl peroxide
  - DMPT
  - Hydroquinone

- **Antibiotics**
  - Bacitracin
  - Gentamicin
  - Tobramycin
► Started in Oct 2010

► Total patients = 2500 / n=1500 enrolled in study

► Criteria: referred by their orthopedic surgeon
  ▪ Preop: history of skin reactions to jewelry, belt buckles, jean snaps, gel nails, skin glue, topical antibiotics.
  ▪ Postop: Implant failure not due to infection or mechanical issues.

► Evaluation: H & P, patch testing*
  ▪ NiLPT, CoLPT

*Still the gold standard to diagnose metal sensitization
Pre-operative Findings

- Approximately 70% of patients with pre-operative history of metal reactivity are sensitized to a metal:
  - Nickel
  - Cobalt (30% of Nickel allergic are sensitized to Cobalt)
  - Chromium

- Bone cement allergy is rare in this group (≈10%), and most are sensitized to other methacrylates (2-HEMA).
Post-operative Findings

► ≈ 50% of patients with joint failure, referred by their orthopedist who has already ruled out infection and mechanical issues, are sensitized to one or more components of their joint replacement:
  - ≈ 25% to a relevant metal: nickel, cobalt, chromium (titanium)
  - ≈ 21% to bone cement
  - ≈ 4% to a metal and to bone cement
Patients revised due to allergy greatly improve

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Implant Allergy n=35</th>
<th>No Implant Allergy n=26</th>
<th>p</th>
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<tbody>
<tr>
<td>No, or mild symptom</td>
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<tr>
<td>Revision to non-allergic implant</td>
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<td>n=22</td>
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<td>Other surgery or no Revision</td>
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<td>n=13</td>
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<td>Revision to new implant</td>
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<td>n=13</td>
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<td>Good or better ROM</td>
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<td>Overall doing better</td>
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</table>

No or mild Pain: 15 (68%) vs 1 (8%) 0.001

No or mild Swelling: 14 (64%) vs 3 (23%) 0.035

No or mild Instability: 16 (73%) vs 3 (23%) 0.006

Good or better ROM: 13 (59%) vs 3 (23%) 0.078

Overall doing better: 16 (73%) vs 1 (8%) 0.0003
Implications for Practice

► Sensitization to implant components is one of 3 common causes of joint replacement failure.
  ▪ Need research/data collection on actual # and rates.

► Nickel, cobalt, and chromium, and rarely titanium are the most common metal culprits.
  ▪ Need research on specific metals and alloys.

► Sensitization to bone cement, and/or skin glue, also important.

► Antibiotics such as bacitracin, gentamicin, or tobramycin may be added to bone cement or surgical irrigation, and can cause transient inflammation and pain.
Recommendations based on these data:

► **Preoperative:**
  - Patients with a history of skin reactions to jewelry, metals, gel nails, skin glue, or Gorilla Glue, should undergo preoperative testing, with the choice of implant based on results.

► **Postoperative:**
  - Patients with the first episode of joint failure, not caused by infection or mechanical issues, should be tested for allergy to implant components, and use those results to select replacement hardware.
Questions?

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