Clinical Testing for Metal-on-Metal Prosthetic “Wear and Tear”

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Disclosures

None
Objectives

Compare heavy metal analysis in synovial fluid with venous sampling for monitoring metal-on-metal joint failure.

List common health concerns associated with elevated chromium or cobalt blood levels.

Explain the relationship between the degree of metal-on-metal wear in joint replacements and heavy metal blood and serum concentrations.
Four central questions

What are the current controversies surrounding hip replacements?

Is there a valid concern due to elevated Cr and Co concentrations found after hip replacements?

Which sample is best for studying joint failure?

Can peripheral measures be used to non-invasively monitor joint failure?
Anatomy of the Hip and Joint

http://www.theodora.com/anatomy/coxal_articulation_or_hip_joint.html
Synovial Fluid in the Joint
Total vs. Resurfacing
Bearing Types

- metal head
- metal-base alloy
- polyethylene lined acetabular cup

- metal head
- metal-base alloy
- metal acetabular cup

- ceramic head
- metal-base alloy
- polyethylene or ceramic lined acetabular cup
Four central questions

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MoM DePuy 2010 Recall

Issued in August of 2010, the voluntary recall included implants since 2003 of:
• ASR™ XL Acetabular System (below; available 2005)
• DePuy ASR™ Hip Resurfacing Platform
  • Only approved for use outside US and was not commercially available in the US

Potential Impact
• 93,000 implants
• 1 in 8 failure rate within 5 years post implant
• 1st US lawsuit filed June 15, 2010
### A Wrinkle in Time

<table>
<thead>
<tr>
<th>Year</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>DePuy introduces their ASR Acetabular System</td>
</tr>
<tr>
<td>2005</td>
<td>DePuy files for a FDA 510k Application of Approval for ASR Acetabular System saving DePuy time and money. Filing for a 510k costs $4,400, versus filing for a FDA Permanent Application of Approval costing $250,000.</td>
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<tr>
<td>2006</td>
<td>August 5 - FDA 510k approval of DePuy ASR Acetabular System (cups sizes 44mm – 62mm)</td>
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<td>2007</td>
<td>The number of complaints to FDA regarding the DePuy ASR Acetabular System in 2007:</td>
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<tr>
<td></td>
<td>• Australian Orthopedic National Joint Replacement Registry (NJRR) reports the revision rate for DePuy ASR Acetabular System is over 2 times the normal rate.</td>
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<tr>
<td></td>
<td>• September 27 – DePuy settles case paying $4,725,000 for doctors to use DePuy devices. DePuy signs Corporate Integrity Agreement with Department of Health and Human Services.</td>
</tr>
<tr>
<td>2008</td>
<td>The number of complaints to FDA regarding the DePuy ASR Acetabular System in 2008:</td>
</tr>
<tr>
<td></td>
<td>• DePuy files 510k with FDA for ASR XL Modular Acetabular System (cup sizes 64mm – 70mm)</td>
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<tr>
<td></td>
<td>• July 2 – FDA approval on ASR XL Modular Acetabular System</td>
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<tr>
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<td>• Australia’s NJRR reports DePuy ASR still having a higher than normal revision rate.</td>
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<td>• National Joint Registry of England and Wales reports that over 3 years, DePuy’s ASR system has worst revision rate at 7.5% versus a 4.5% average</td>
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<tr>
<td>2009</td>
<td>The number of complaints to FDA regarding the DePuy ASR Acetabular System in 2009:</td>
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<tr>
<td></td>
<td>• DePuy sends brochure to doctors describing importance of proper cup positioning for its ASR system.</td>
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<td>• DePuy issues recall for ASR XL system in the United States of their ASR Systems in a letter dated March 6</td>
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<td>• April 10 – DePuy maintains its the New York Times letter stating that the ASR is safe despite the recall</td>
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<tr>
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<td>• May 25 – FDA issues alert on DePuy ASR Systems</td>
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<tr>
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<td>• August 24 – Johnson &amp; Johnson announce that DePuy issues worldwide recall on their ASR Systems, 5 months after U.S. recall of product</td>
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<tr>
<td>2010</td>
<td>The number of complaints to FDA regarding the DePuy ASR Acetabular System in 2010:</td>
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<tr>
<td></td>
<td>• In a February interview with New Yor Times, DePuy’s states ASR’s performance is equal to that of competition.</td>
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<tr>
<td></td>
<td>• DePuy issues formal recall in the United States of their ASR Systems on a letter dated March 6</td>
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<td>• April 10 – DePuy maintains the New York Times letter stating that the ASR is safe despite the recall</td>
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The number of complaints filed with the FDA between 2006 and 2010:

**887**
Zimmer Durom Cup Recall

Initially blamed surgeons for poor technique

July 2008, recalled Metasul Durom Acetabular components
- Lack of bony ingrowth causing poor cup position

Other devices
- Wright Profemur Hip Implant
- Cormet Hip Resurfacing System
- Birmingham Hip Resurfacing System

Do I have a lawsuit.com

Metal on Metal Hip Replacement Recall
History of Elevated Co & Cr

1936 - Vitallium

1970’s - MoPE

1990’s – CeroPE

2000’s – MoM

STUDY OF THE WEAR PARTICLES PRODUCED FROM COBALT-CHROMIUM-MOLYBDENUM-MANGANESE TOTAL JOINT REPLACEMENT PROSTHESSES

M. A. R. FREEMAN, S. A. V. SWANSON, AND J. C. HEATH


Concentration of Wear Products in Hair, Blood, and Urine after Total Hip Replacement

R. F. COLEMAN, J. HERRINGTON, JOHN T. SCALES

British Medical Journal, 1973, 1, 527-529

LABORATORY TESTS ON TOTAL JOINT REPLACEMENT PROSTHESSES

S. A. V. SWANSON, M. A. R. FREEMAN and J. C. HEATH, LONDON, ENGLAND

THE JOURNAL OF BONE AND JOINT SURGERY VOL. 55 B, NO. 4, NOVEMBER 1973

Incidence of metal sensitivity in patients with total joint replacements

M W ELVES, J N WILSON, J T SCALES, H B S KEMP

British Medical Journal, 1975, 4, 376-378
Four central questions

What are the current controversies surrounding hip replacements?

Is there a valid concern due to elevated Cr and Co concentrations found after hip replacements?

Which sample is best for studying joint failure?

Can peripheral measures be used to non-invasively monitor joint failure?
CoPE vs. MoM

CoPE vs. MoM; Distributions

Cobalt

Normal function
Constituent of B$_{12}$

Pharmacokinetics
No single organ accumulation
50/50 distribution between blood and serum

Toxicity
Cardiac, Thyroid, Polycythemia

Elimination
Most eliminated within days via kidneys (some years)

Relevance to MoM implants
2:1 ratio in bearings (Co:Cr)
Metal of concern in bearing failure
Levels known to be higher in patients with functioning MoM bearings

http://depositphotos.com/6285057/stock-photo-Chromium-form-Periodic-Table-of-Elements.html
Chromium

Normal function
Glucose metabolism

Pharmacokinetics
Cr\(^{+3}\) vs. Cr\(^{+6}\)
Cr\(^{+6}\) rapidly taken up by cells then converted to Cr\(^{+3}\)

Toxicity
Cr\(^{+3}\) (little to none)
Cr\(^{+6}\); Kidneys, Carcinogen; GI; Liver

Elimination
Varies with Cr species

Relevance to MoM implants
• Cr\(^{+3}\) released
• Found in the serum
• Relatively non-toxic

http://depositphotos.com/6285057/stock-photo-Chromium-form-Periodic-Table-of-Elements.html
Complications with Joint Failure

Adverse Reaction to Metal Debris (ARMD) – [Local]

• Metallosis:
  • Infiltration of periprosthetic soft tissues and bone by metallic debris resulting from wear of joint arthroplasties (osteolysis typically occurs)

• Aseptic Lymphocyte-dominated Vasculitis-Associated Lesion (ALVAL)
  • Dense perivascular inflammatory infiltrate
  • Metal ion / native protein hapten formation

• Pseudotumor
  • Necrotic vs. Wear-particle
  • Cystic, solid tumors

Arthroprosthetic cobaltism

Systemic

Case Report: 49 y/o M

3 mo. Progressing pain, rash
11 mo. Fluid accumulation, dyspnea
   • Serum Co = 50 µg/L (RI: ≤ 1 µg/L)
18 mo. Anxiety, headaches, irritability, fatigue, tinnitus, and hearing loss
   • Serum Co = 35 µg/L
30 mo. Pain at rest, hip creaking, hand tremor, incoordination, cognitive decline, and depression
36 mo. Visual changes, optic nerve atrophy
   • Serum Co = 122 µg/L
43 mo. Revision arthroplasty conducted. Diastolic dysfunction by ECG, metallosis, necrosis, lymphocytic infiltrates
   • Serum Co = 83 µg/L; CSF Co = 2.2 µg/L; JF Co = 3200 µg/L

1. Follow up patients at least annually for five years (more if symptomatic)
2. Investigate patients with painful MoM replacements. Tests should include cobalt and chromium in levels and imaging.
3. Consider Cr and Co testing in patients with:
   • Poor positioning identified by radiological assessment
   • Patients with small component size after resurfacing
   • Surgeon concern is present
4. If Co or Cr is > 7 µg/L, perform a follow-up test after 3 months
5. Consider revision surgery in cases of soft tissue reactions, fluid collections or tissue masses.
FDA Recommendations

Surgeons:

- Ion assessment in asymptomatic patients is not recommended
- Advise of potential for systemic metal ion effects
- *IF* ion levels are assessed, interpret in the overall clinical context.
- Watch for elevations over time – indicative of wear
- Determine other potential sources of exposure
- Serial measurements if adverse reaction to metal is noted
- Use the same sample (dealer’s choice between serum or blood)
- No threshold value of ions as a trigger for intervention or revision
Four central questions

What are the current controversies surrounding hip replacements?

Is there a valid concern due to elevated Cr and Co concentrations found after hip replacements?

Which sample is best for studying joint failure?

Can peripheral measures be used to non-invasively monitor joint failure?
Sample Choice: Chromium

Urine
Hair
Whole Blood
RBCs
Serum
Plasma
Joint Fluid

Fig. 1. Chromium distribution in blood fractions.
Sample Choice: Cobalt

Urine
Hair
Whole Blood
RBCs
Serum
Plasma
Joint Fluid

Results Across Studies

<table>
<thead>
<tr>
<th>Whole blood:</th>
<th>Chromium (µg/L)</th>
<th>Cobalt (µg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lavigne et al 2011</td>
<td>1.3 (0.08 to 20.7)</td>
<td>1.29 (0.27 to 13.0)</td>
</tr>
<tr>
<td>Walter et al 2008</td>
<td>4.03</td>
<td>2.9</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Serum/Plasma:</th>
<th>Chromium (µg/L)</th>
<th>Cobalt (µg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walter et al 2008</td>
<td>8.8</td>
<td>3.2</td>
</tr>
<tr>
<td>De Smet et al 2008</td>
<td>3.35</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>33.9</td>
<td>33.8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Joint Fluid:</th>
<th>Chromium (µg/L)</th>
<th>Cobalt (µg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Davda et al 2011</td>
<td>1400 (0 to 263,298)</td>
<td>1100 (0 to 14,285)</td>
</tr>
<tr>
<td>Langton et al 2010</td>
<td>8000 (1000 to 46,000)</td>
<td>5000 (0 to 10,000)</td>
</tr>
<tr>
<td>De Smet et al 2008</td>
<td>179.5 (19 to 661)</td>
<td>106.25 (13 to 769)</td>
</tr>
<tr>
<td></td>
<td>5136.5 (155 to 29,080)</td>
<td>2185 (110 to 5120)</td>
</tr>
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</table>
Synovial Fluid Exchange

http://www.bbc.co.uk/bitesize/standard/biology/the_body_in_action/movement/revision/3/
Four central questions

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Can peripheral measures be used to non-invasively monitor joint failure?
Serum vs. Joint Fluid: Distributions

Yes = presence of metallosis found at revision
No = metallosis not found at revision

Serum vs. Joint Fluid: Correlation
Serum vs. Femoral Wear

Chromium > 17 μg/L (RI: ≤ 5 μg/L)
Cobalt > 19 μg/L (RI: ≤ 1 μg/L)
Whole Blood vs. Joint Fluid

![Graphs showing comparison between whole blood and joint fluid levels of Cr and Co](image-url)
Conclusions

Is there valid concern?
• Malpositioned or failing joints can release significant levels of chromium and cobalt
• Arthroprosthetic cobaltism

Which sample type is best?
• Serum
• Joint Fluid

Can peripheral measures be used to non-invasively measure joint failure?
• Annual measurements are recommended
• < 1 µg/L is typical in a normal functioning prosthesis
• Correlation and predictability is not well defined