Clinical Testing for Metal-on-Metal Prosthetic "Wear and Tear"

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February 8th, 2013

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

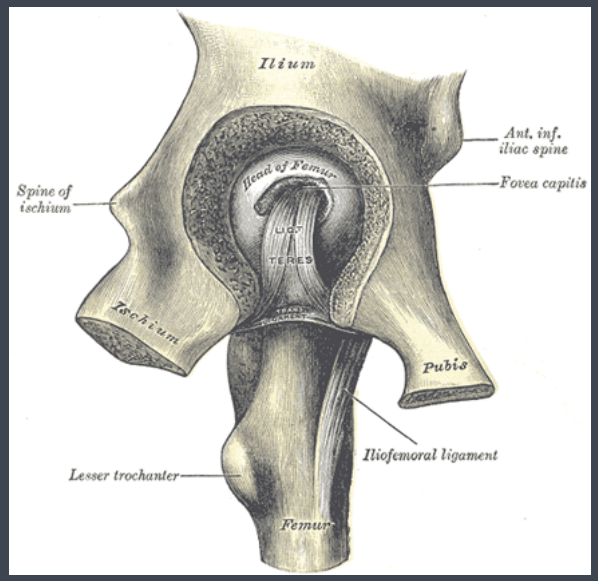
What are the current controversies surrounding hip replacements?

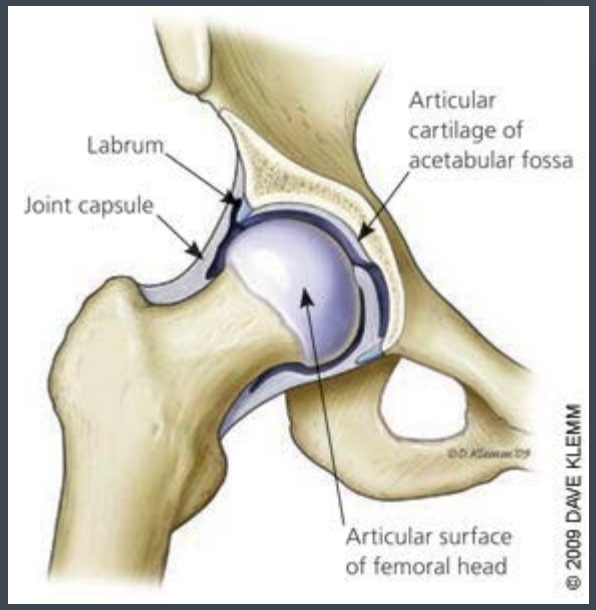
Is there a valid concern due to elevated Cr and Co concentrations found after hip replacements?

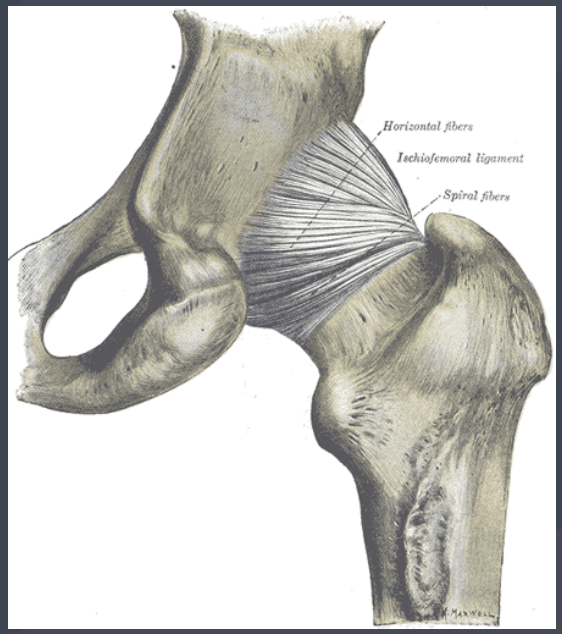
Which sample is best for studying joint failure?

Can peripheral measures be used to non-invasively monitor joint failure?

Anatomy of the Hip and Joint

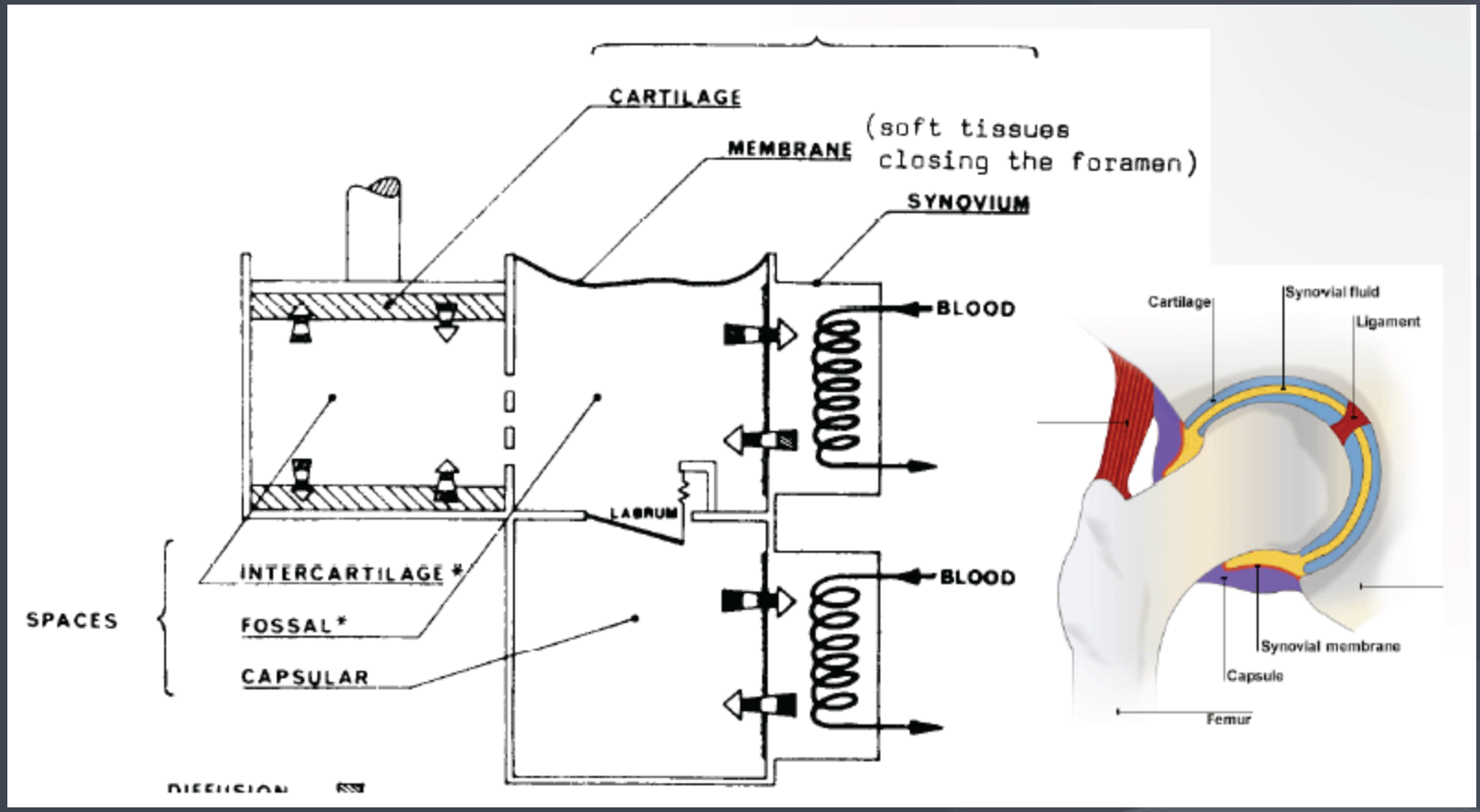






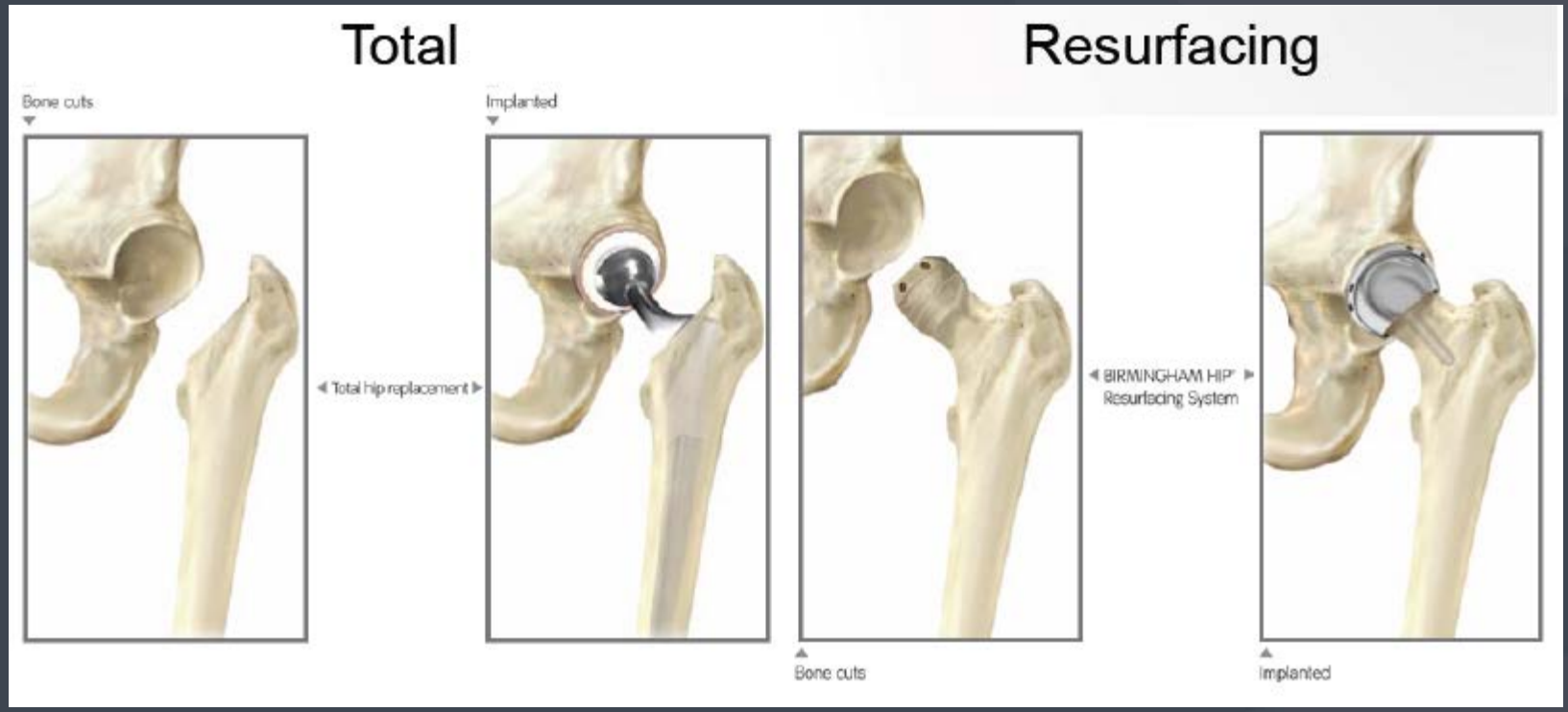
http://www.theodora.com/anatomy/coxal_articulation_or_hip_joint.html

Synovial Fluid in the Joint



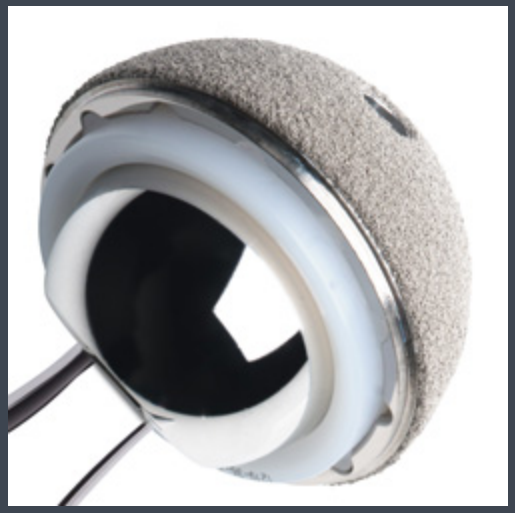
Afoke et al., 1984

Total vs. Resurfacing



http://activejointsortho.com/procedure.htm

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

http://www.hipreplacement.com/DePuy/technology/implants/bearings/index.html

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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

http://taylormartino.com/injury-news/depuy-hip-recall

A Wrinkle in Time

The number of complaints filed with the FDA between 2006 and 2010.

887

2004

DePuy introduces their ASR Acetabular System

2005

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+.

- August 5 – FDA 510k approval of DePuy ASR Acetabular System (cup sizes 44mm – 62mm)[2]

2006

12

The number of complaints to FDA regarding the DePuy ARS Acetabular System in 2006.[3]

- March 24 – First complaint to FDA of ASR Acetabular malfunction – ASR failed during surgery while being checked by surgeon.[3]

2007

87

The number of complaints to FDA regarding the DePuy ARS Acetabular System in 2007.[3]

- Australian Orthopaedic's National Joint Replacement Registry (NJRR) reports the revision rate for DePuy ASR Acetabular System is over 2 times the normal rate.[4]
- September 27 – DePuy settles case paying $84,796,800 for bribing surgeons to use DePuy devices. DePuy signs Corporate Integrity Agreement with Department of Health and Human Services.[5,6]

2008

239

The number of complaints to FDA regarding the DePuy ARS Acetabular System in 2008.[3]

- DePuy files 510k with FDA for ASR XL Modular Acetabular System (cup sizes 64mm – 70mm)
- July 2 – FDA approval on ASR XL Modular Acetabular System
- Australia's NJRR re-identifies DePuy ASR still having a higher than normal revision rate[4]
- 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[7]

2009

424

The number of complaints to FDA regarding the DePuy ARS Acetabular System in 2009.[3]

- DePuy sends brochure to doctors describing importance of proper cup position for its ASR system. But does not address any specific concerns for its ASR system
- Australia's NJRR continues to report DePuy ASR still having a higher than normal revision rate[5]
- DePuy withdraws ASR from Australian market for "comercial reasons"
- DePuy announces it will discontinue the ASR system based on claims of "declining demand" but does not device

2010

125

The number of complaints to FDA regarding the DePuy ARS Acetabular System in 2010.[3]

- In a February interview with New York Times DePuy states ASR's performance is equal to that of competition
- DePuy issues formal recall in the United States of their ASR Systems in a letter dated March 6
- April 10 – DePuy maintains in the New York Times the ASR System is safe despite the recall
- May 25 – FDA issues alert on DePuy ASR Systems
- August 24 – Johnson & Johnson announce that DePuy issues worldwide recall on their ASR Systems, 5 months after U.S. recall of product

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

http://zimmerduromcup.legalview.com/; http://burnetti.com

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 PROSTHESES

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

Ann. rheum. Dis. (1969), **28**, Supplement p. 29

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 PROSTHESES

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

376 BRITISH MEDICAL JOURNAL 15 NOVEMBER 1975

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

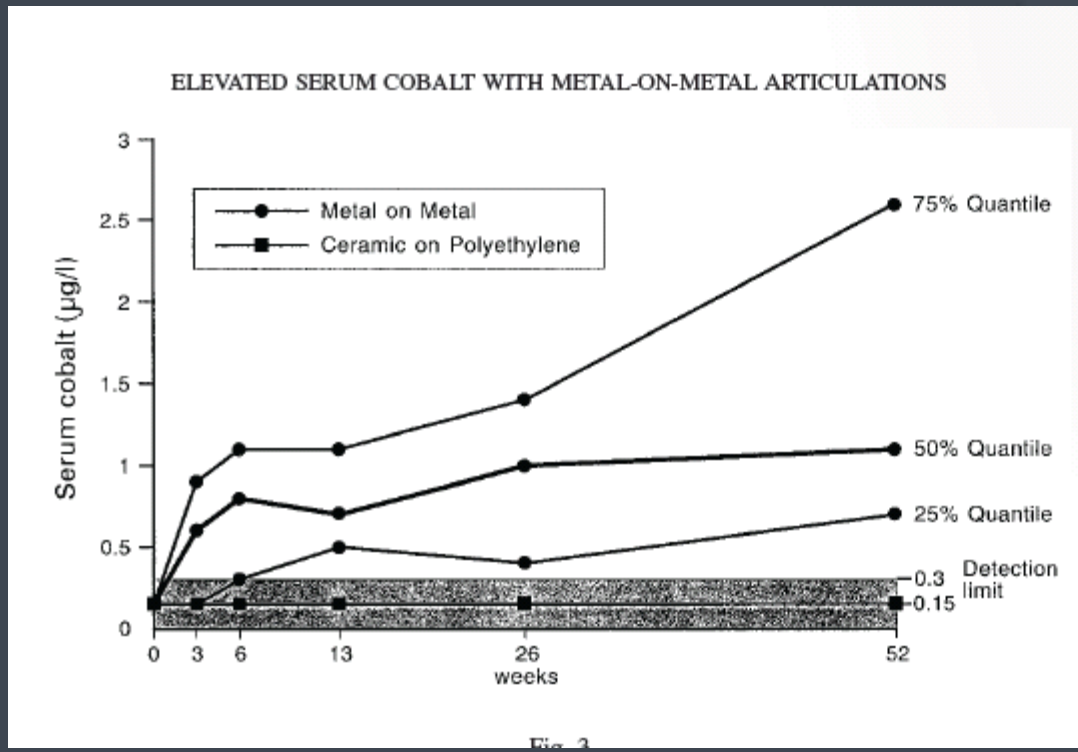
What are the current controversies surrounding hip replacements?

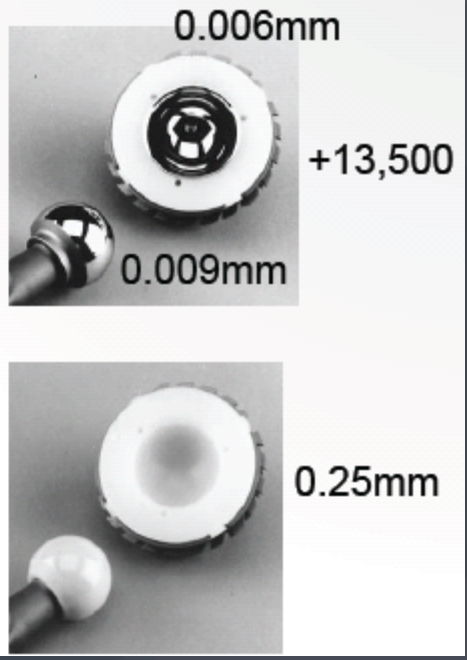
Is there a valid concern due to elevated Cr and Co concentrations found after hip replacements?

Which sample is best for studying joint failure?

Can peripheral measures be used to non-invasively monitor joint failure?

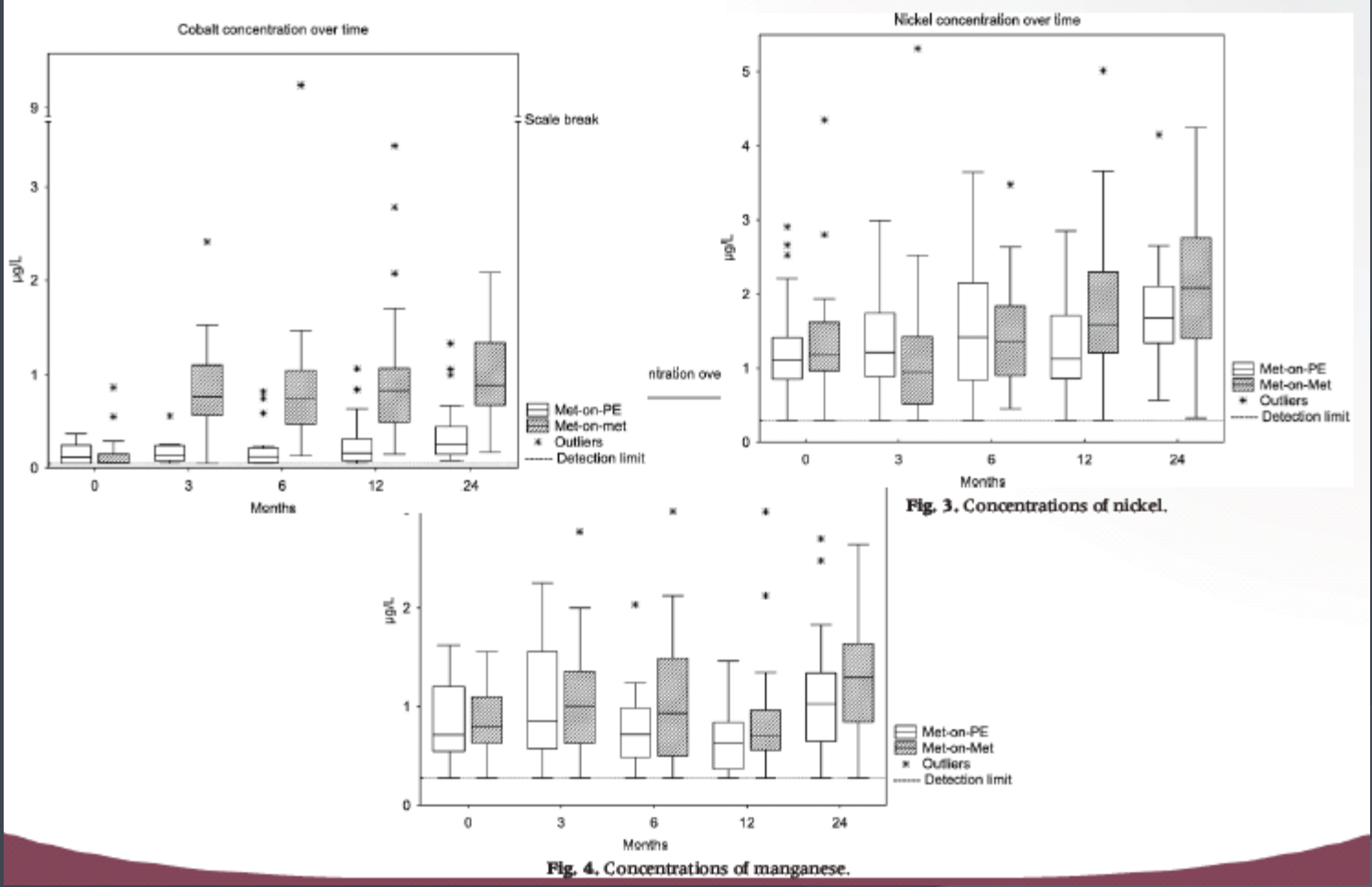
CoPE vs. MoM





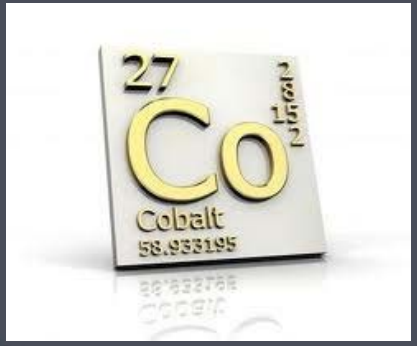
Brodner W, Bitzan P, Meisinger V, et al. *J Bone Joint Surg Br, 1997.* ***79(2): p. 316-21.***

CoPE vs. MoM; Distributions



Dahlstrand H, Stark A, Anissian L, et al. *The Journal of Arthroplasty, 2009.* ***24(6): p. 837-845.***

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

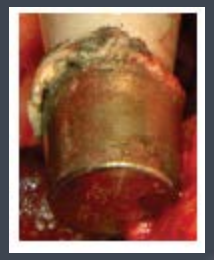
- Cr^{+3} released
- Found in the serum
- Relatively non-toxic

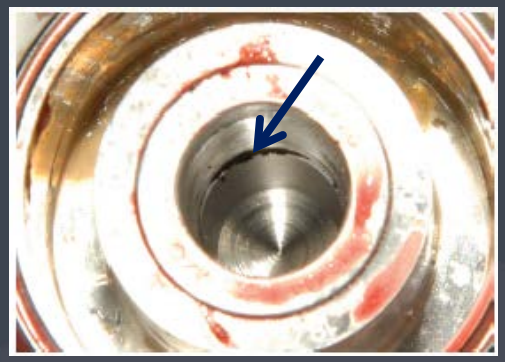
http://depositphotos.com/6285057/stock-photo-Chromium-form-Periodic-Table-of-Elements.html

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





Lavigne M, Belzile EL, Roy A, et al. *J Bone Joint Surg Am, 2011.* ***93 Suppl 2: p. 128-36.***

Arthroprosthetic cobaltism

Systemic

- Tower SS, *Arthroprosthetic cobaltism: neurological and cardiac manifestations in two patients with metal-on-metal arthroplasty: a case report. J Bone Joint Surg Am, 2010. 92(17): p. 2847-51.*

Tower SS. *J Bone Joint Surg Am, 2010.* ***92(17): p. 2847-51.***

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

Tower SS. *J Bone Joint Surg Am, 2010.* ***92(17): p. 2847-51.***

Medicine and Healthcare Products Regulatory Agency (UK)

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

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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

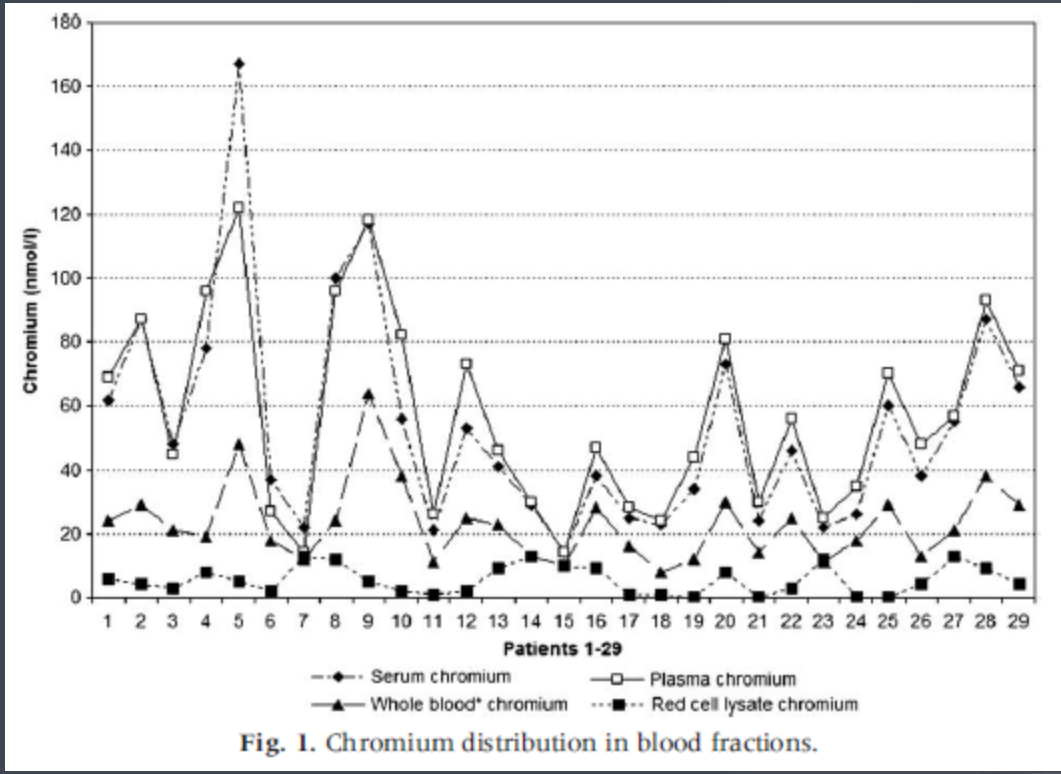

Fig. 1. Chromium distribution in blood fractions.

Walter LR, Marel E, Harbury R, et al.. *The Journal of Arthroplasty, 2008.* ***23(6): p. 814-821.***

Sample Choice: Cobalt

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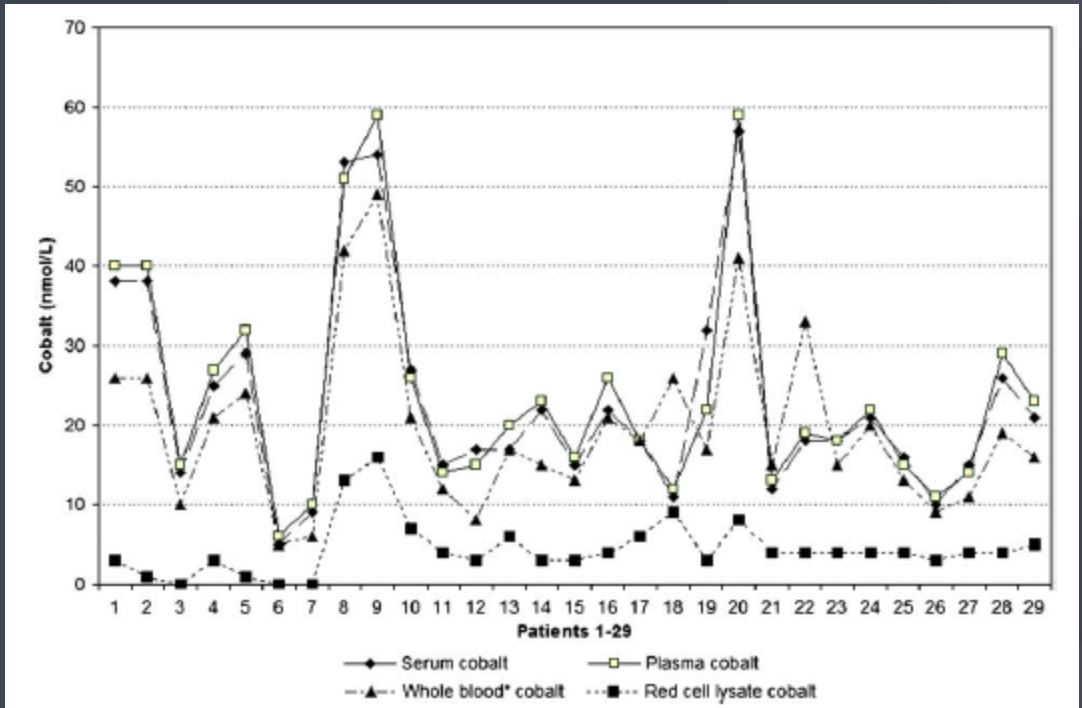


Fig. 2. Cobalt distribution in blood fractions.

Walter LR, Marel E, Harbury R, et al.. *The Journal of Arthroplasty, 2008.* ***23(6): p. 814-821.***

Results Across Studies

Whole blood:

Study	Chromium (µg/L)	Cobalt (µg/L)
Lavigne et al 2011	1.3 (0.08 to 20.7)	1.29 (0.27 to 13.0)
Walter et al 2008	4.03	2.9

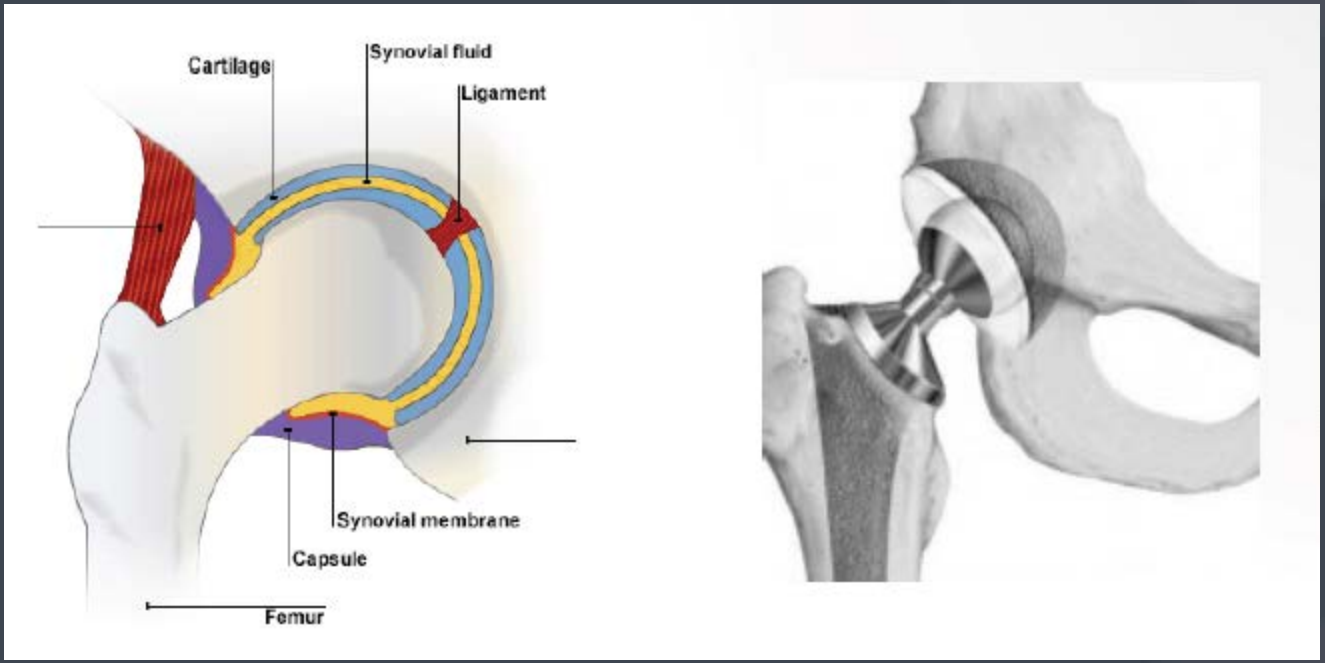
Serum/Plasma:

Study	Chromium (µg/L)	Cobalt (µg/L)
Walter et al 2008	8.8	3.2
De Smet et al 2008	3.35 33.9	3.2 33.8

Joint Fluid:

Study	Chromium (µg/L)	Cobalt (µg/L)
Davda et al 2011	1400 (0 to 263,298)	1100 (0 to 14,285)
Langton et al 2010	8000 (1000 to 46,000)	5000 (0 to 10,000)
De Smet et al 2008	179.5 (19 to 661) 5136.5 (155 to 29,080)	106.25 (13 to 769) 2185 (110 to 5120)

Synovial Fluid Exchange



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

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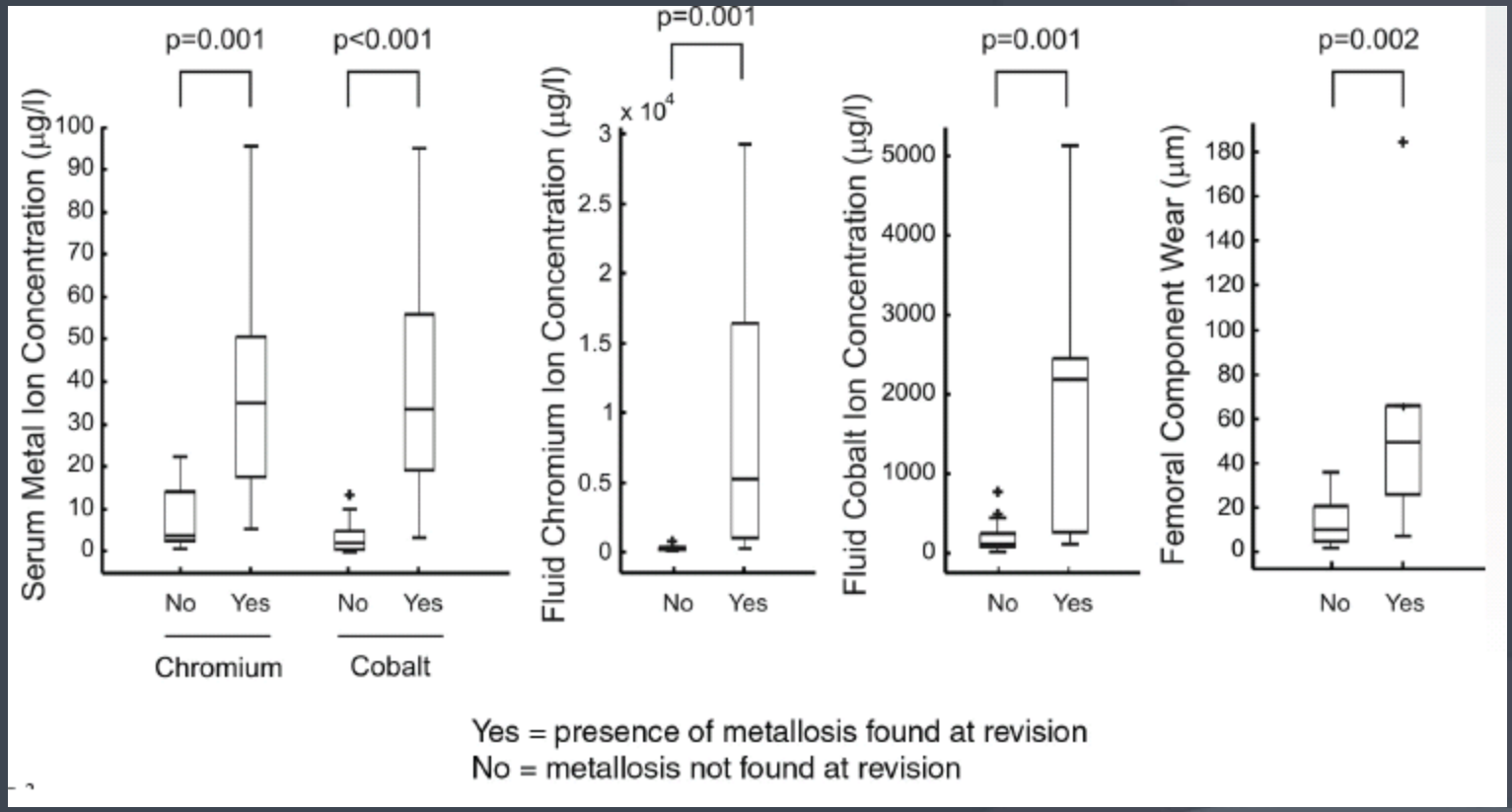
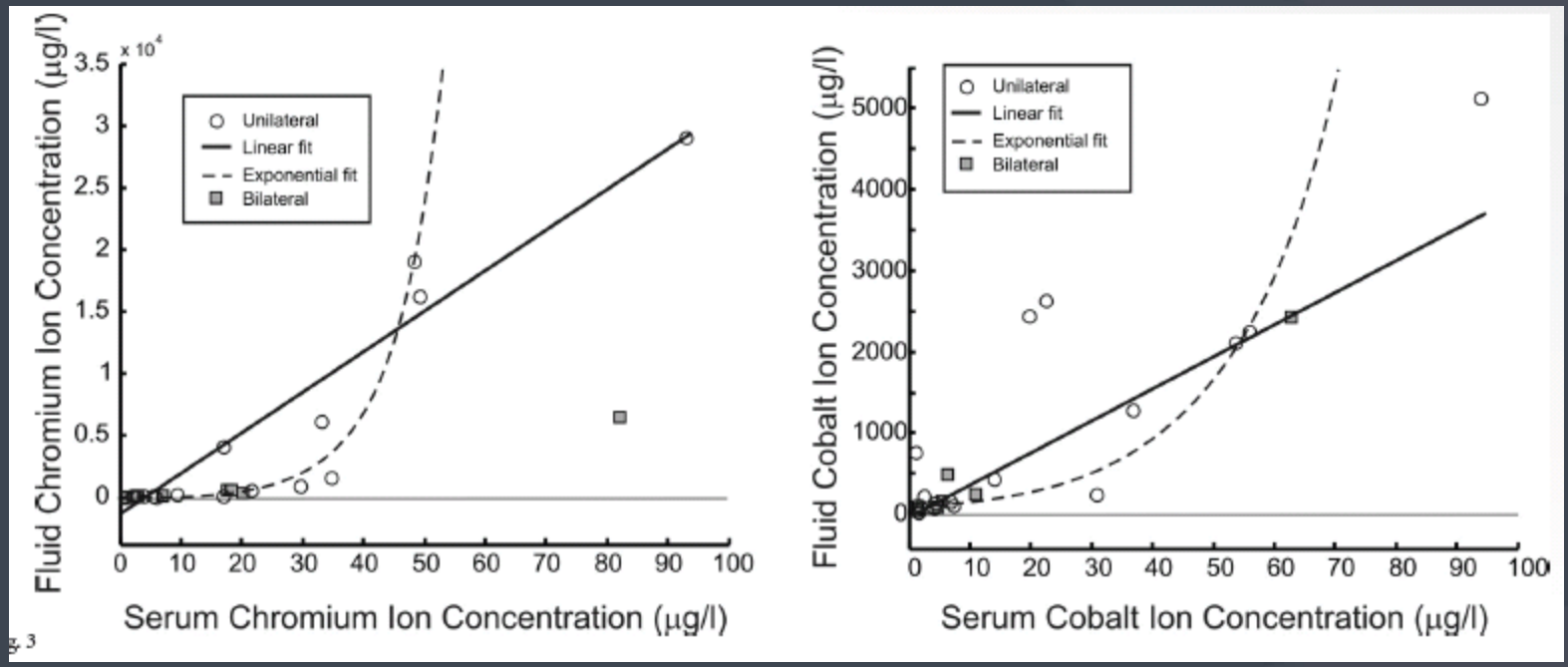
Serum vs. Joint Fluid: Distributions



De Smet K, De Haan R, Calistri A, et al.. *J Bone Joint Surg Am, 2008.* ***90 Suppl 4: p. 202-8.***

Serum vs. Joint Fluid: Correlation



De Smet K, De Haan R, Calistri A, et al. *J Bone Joint Surg Am, 2008.* ***90 Suppl 4: p. 202-8.***

Serum vs. Femoral Wear

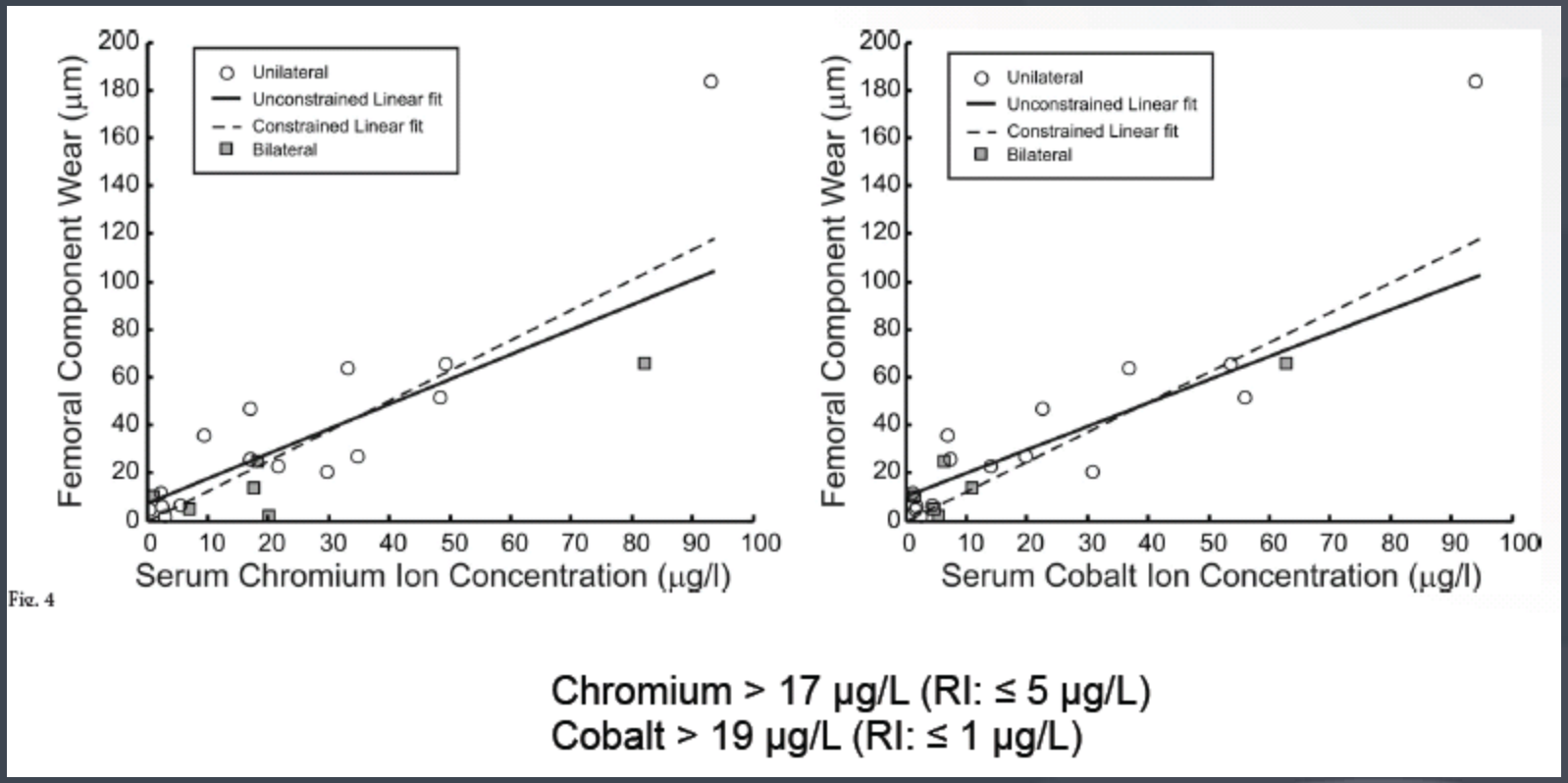


Fig. 4

Chromium > 17 µg/L (RI: ≤ 5 µg/L)
Cobalt > 19 µg/L (RI: ≤ 1 µg/L)

De Smet K, De Haan R, Calistri A, et al. *J Bone Joint Surg Am, 2008.* ***90 Suppl 4: p. 202-8.***

Whole Blood vs. Joint Fluid

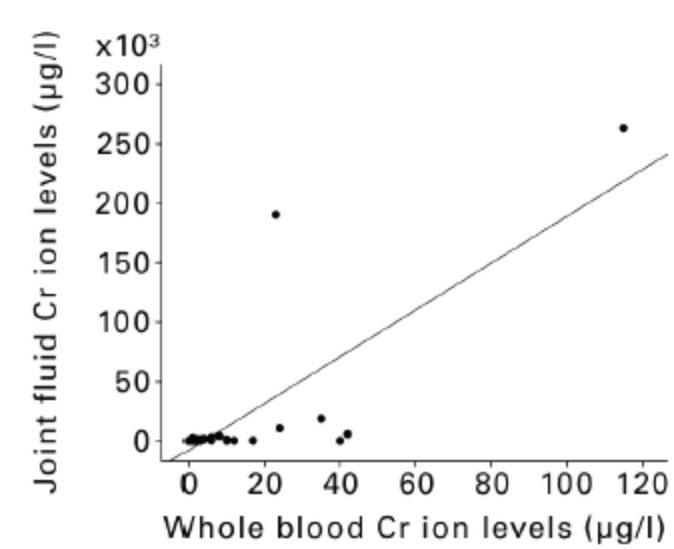


Fig. 6a

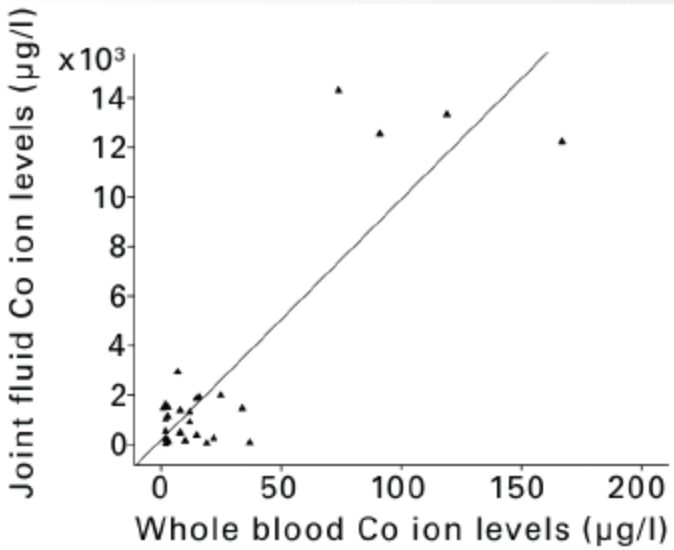


Fig. 6b

Davda K, Lali FV, Sampson B, et al. *J Bone Joint Surg Br, 2011.* ***93-B(6): p. 738-745.***

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