## SECTION VIII.

## MEDICAL DEVICE REPORTS AND ADVERSE EVENTS FROM THE LITERATURE

## METAL/METAL SEMI-CONSTRAINED TOTAL HIP PROSTHESES

**Inclusive dates: January 1, 1992 to March 31, 2005.**

A reasonable effort was made to find all adverse reports made for these devices under the Medical Device Reporting (MDR) regulations. A search of the publicly available information yielded fifty nine reports filed for metal/metal semi-constrained total hip prostheses. However, it is possible that a small number of additional reports could have been made using improper product codes, erroneous device descriptions, etc. In addition, the FDA may have access to additional reports made after March 31, 2005.

A review of the published literature was performed to provide a summary of the device related adverse events reported for metal/metal hip prostheses.

A. MDR Reports

A summary of the fifty four MDR reports obtained for a metal/metal hip prosthesis is provided below. There were no vigilance reports obtained from searches conducted of the databases available for the member states comprising the European Economic Community (EEC).

| | |
|---|---|
| Manufacturer: | Sulzer Orthopaedics, Inc.<br>9900 Spectrum<br>Austin, TX 78717 |
| Device Description: | Acetabular Insert 28x55 Metasul APR |
| MDR Report Key: | 29355620-2000-00012 |
| Product Code: | KWA |
| Report Date: | 4/24/2000 |
| Catalog No.: | 4340-28-055 |
| Device Lot No.: | 1251199 |
| Event Description: | Allegedly the anti-rotation pin became dislodged from the polyethylene acetabular insert. |
| Patient Outcome: | Hospitalization. |
| Device Description: | Acetabular Insert 28x49 Metasul APR |
| MDR Report Key: | 2935620-2000-00062 |
| Product Code: | KWA |
| Report Date: | 11/6/2000 |
| Catalog No.: | 4340-28-049 |

Device Lot No.: 1303668
Event Description: Pin in Metasul insert came out after 1.5 years
Patient Outcome: Hospitalization

Device Description: Acetabular Insert 28x49 Metasul APR
MDR Report Key: 2935620-2000-0075
Product Code: KWA
Report Date: 12/8/2000
Catalog No.: 4340-28-049
Device Lot No.: 1297149
Event Description: Patient underwent Total Hip Arthroplasty (THA) on 2/4/98. Revised three times due to dislocations. Underwent last THA on 11/7/00—insert and ball head replaced.
Patient Outcome: Unknown

Device Description: Acetabular Insert 28x49 Metasul APR
MDR Report Key: 2935620-2001-0003
Product Code: KWA
Report Date: 1/23/2001
Catalog No.: 4340-28-049
Device Lot No.: 1230114
Event Description: It was reported on 11/13/00 that there was a sudden clunk in hip and patient could not walk. X-ray in ER showed disassociation of Metasul insert from APR II shell. Patient experienced 2 heavy falls, one on her back in March 2000 and one fall forward.
Patient outcome: Unknown

Device Description: Acetabular Insert 28x49 Metasul APR
MDR Report Key: 2935620-2001-01058
Product Code: KWA
Report Date: 5/10/2001
Catalog No.: 4340-28-049
Device Lot No.: 1427124
Event Description: When Dr. impacted insert into shell it did not seat. When insert pulled out for inspection the locking pin missing. Resulted in 30 minute delay in surgery.
Patient Outcome: Unknown

Device Description: Acetabular Insert 28x49 Metasul APR
MDR Report Key: 2935620-2001-01162
Product Code: KWA
Report Date: 6/18/2001
Catalog No.: 4340-28-049
Device Lot No.: 1299668

Event Description: Metasul insert dislocation after 4 years, significant metalosis and severe pain
Patient Outcome: Revision surgery

Device Description: Acetabular Insert 28x49 Metasul APR
MDR Report Key: 2935620-2001-01193
Product Code: KWA
Report Date: 5/23/2001
Catalog No.: 4340-28-049
Device Lot No.: 1303666
Event Description: Revision surgery
Patient Outcome: Unknown

Device Description: Acetabular Insert 28x49 Metasul APR
MDR Report Key: 2935620-2001-01806
Product Code: KWA
Report Date: 12/12/2001
Catalog No.: 4340-28-049
Device Lot No.: 1302992
Event Description: Anti-rotation pin dislocated from insert
Patient Outcome: Unknown

Device Description: Acetabular Insert 28x49 Metasul APR
MDR Report Key: 2935620-2002-00048
Product Code: KWA
Report Date: 2/11/2002
Catalog No.: 4340-28-049
Device Lot No.: 1181945
Event Description: Plaintiff alleged the Metasul insert loosened from APR II shell
Patient Outcome: Unknown

Device Description: Acetabular Insert 28x49 Metasul APR
MDR Report Key: 2935620-2002-00141
Product Code: KWA
Report Date: 4/15/2002
Catalog No.: 4340-28-049
Device Lot No.: 1322215
Event Description: Disassociation of insert 2 yrs 9 mo after initial surgery
Patient Outcome: Unknown

Device Description: Acetabular Insert 28x49 Metasul APR
MDR Report Key: 2935620-2003-00135
Product Code: KWA
Report Date: 6/10/2003
Catalog No.: 4340-28-049

Device Lot No.: 1230114
Event Description: Patient felt pain due to dislocation.
Patient Outcome: Revision surgery 6/5/03

Device Description: Acetabular Insert 28x49 Metasul APR
MDR Report Key: 2935620-2003-00142
Product Code: KWA
Report Date: 6/25/2003
Catalog No.: 4340-28-049
Device Lot No.: 1322216
Event Description: Dislocation
Patient Outcome: Revision surgery

Device Description: Acetabular Insert 28x49 Metasul APR
MDR Report Key: 2935620-2003-00279
Product Code: KWA
Report Date: 11/26/2003
Catalog No.: 4340-28-049
Device Lot No.: 1230114
Event Description: Dislocation of Metasul insert
Patient Outcome: Revision surgery

Device Description: Acetabular Insert 28x49 Metasul APR
MDR Report Key: 2935620-2004-00005
Product Code: KWA
Report Date: 1/13/2004
Catalog No.: 4340-28-049
Device Lot No.: 1299671
Event Description: Dislocation of Metasul insert
Patient Outcome: Unknown

Device Description: Acetabular Insert 28x51 Metasul APR
MDR Report Key: 2935620-2001-01841
Product Code: KWA
Report Date: 12/5/2001
Catalog No.: 4340-29-051
Device Lot No.: 1245308
Event Description: Dr reported patient with pain. Disassocation of liner from shell
Patient Outcome: Unknown

Device Description: Acetabular Insert 28x51 Metasul APR
MDR Report Key: 2935620-2002-00069
Product Code: KWA
Report Date: 2/20/2002
Catalog No.: 4340-29-051

Device Lot No.: 1181946
Event Description: Advised on an APR Metasul acetabular liner disassociation.
Patient Outcome: Revision surgery 2/26/02

Device Description: Acetabular Insert 28x51 Metasul APR
MDR Report Key: 2935620-2002-00106
Product Code: KWA
Report Date: 3/15/2002
Catalog No.: 4340-29-051
Device Lot No.: 1245308
Event Description: Implant breakage. Patient reported pain.
Patient Outcome: Revision surgery

Device Description: Acetabular Insert 28x51 Metasul APR
MDR Report Key: 2935620-2003-00143
Product Code: KWA
Report Date: 6/19/2003
Catalog No.: 4340-29-051
Device Lot No.: 1303680
Event Description: Dislocation of APR Metasul insert.
Patient Outcome: Unknown

Device Description: Acetabular Insert 28x53 Metasul APR
MDR Report Key: 2935620-1999-00011
Product Code: KWA
Report Date: 3/5/1999
Catalog No.: 4340-29-053
Device Lot No.: 1272471
Event Description: Anteverted cup and posterior impingement
Patient Outcome: Unknown

Device Description: Acetabular Insert 28x53 Metasul APR
MDR Report Key: 2935620-2000-00030
Product Code: KWA
Report Date: 7/21/2000
Catalog No.: 4340-29-053
Device Lot No.: 1187760
Event Description: Impingement between femoral stem and acetabular insert.
Patient Outcome: Revision surgery

Device Description: Acetabular Insert 28x53 Metasul APR
MDR Report Key: 2935620-2001-1531
Product Code: KWA
Report Date: 8/23/2001
Catalog No.: 4340-29-053
Device Lot No.: 1348667-B

Event Description: APR insert disengaged 9 mo post surgery
Patient Outcome: Unknown

Device Description: Acetabular Insert 28x53 Metasul APR
MDR Report Key: 2935620-2001-01765
Product Code: KWA
Report Date: 11/6/2001
Catalog No.: 4340-29-053
Device Lot No.: 1245313
Event Description: Disassociation of liner from cup
Patient outcome: Unknown

Device Description: Acetabular Insert 28x53 Metasul APR
MDR Report Key: 2935620-2003-00202
Product Code: KWA
Report Date: 7/9/2003
Catalog No.: 4340-29-053
Device Lot No.: 1348666
Event Description: Metasul insert dislocation
Patient Outcome: Unknown

Device Description: Acetabular Insert 28x55 Metasul APR
MDR Report Key: 2935620-2000-00012
Product Code: KWA
Report Date: 4/24/2000
Catalog No.: 4340-29-055
Device Lot No.: 1251199
Event Description: Anti-rotation pin dislodged from Polyethylene acetabular liner
Patient Outcome: Unknown

Device Description: Acetabular Insert 28x55 Metasul APR
MDR Report Key: 2935620-2001-01192
Product Code: KWA
Report Date: 5/23/2001
Catalog No.: 4340-29-055
Device Lot No.: Unknown
Event Description: Disassociation of left Metasul acetabular liner
Patient Outcome: Revision Surgery

Device Description: Acetabular Insert 28x55 Metasul APR
MDR Report Key: 2935620-2003-00282
Product Code: KWA
Report Date: 12/17/2003
Catalog No.: 4340-29-055
Device Lot No.: 1223168

Event Description: Polyethylene spinning, locking mechanism
Patient Outcome: Revision surgery

Device Description: Acetabular Insert 28x57 Metasul APR
MDR Report Key: 2935620-2002-00105
Product Code: KWA
Report Date: 3/15/2002
Catalog No.: 4340-29-057
Device Lot No.: 1181949
Event Description: Disassociation of an APR Metasul insert
Patient Outcome: Revision surgery

Device Description: Acetabular Insert 28x59 Metasul APR
MDR Report Key: 2935620-2002-00026
Product Code: KWA
Report Date: 1/28/2002
Catalog No.: 4340-29-059
Device Lot No.: 1230120
Event Description: Disassociation of APR acetabular insert.
Patient Outcome: Patient fell in September 2001

Device Description: 28x55 Std Metasul Insert I-O
MDR Report Key: 2935620-2001-01060
Product Code: KWA
Report Date: 5/14/2001
Catalog No.: 4372-28-055
Device Lot No.: 1417750
Event Description: Patent complained of hearing and feeling a "pop"
Patient Outcome: Hip dislocated, revision surgery

Device Description: 28x55 Std Metasul Insert I-O
MDR Report Key: 2935620-2003-00246
Product Code: KWA
Report Date: 6/16/2000
Catalog No.: 4372-28-055
Device Lot No.: 1426338-A
Event Description: Delay in surgery
Patient Outcome: Unknown

Device Description: 28x57 Std Metasul Insert I-O
MDR Report Key: 2935620-2000-00045
Product Code: KWA
Report Date: 6/16/2000
Catalog No.: 4372-28-057
Device Lot No.: 1330653

Event Description: Patient weight-bearing just one week then developed debilitating pain. Deep infection reported
Patient Outcome: Device explanted at surgery on 6/1/00.

Device Description: 28x61 Std Metasul Insert I-O
MDR Report Key: 2935620-1999-00048
Product Code: KWA
Report Date: 12/2/1999
Catalog No.: 4372-28-061
Device Lot No.: 1324824
Event Description: Liner would not seat in shell.
Patient Outcome: Unknown

Device Description: Co-Cr Head 12/14 Neck Neutral 28mm Metasul
MDR Report Key: 2935620-2002-00178
Product Code: KWA
Report Date: 6/4/2002
Catalog No.: 7340-28-000
Device Lot No.: 1426357
Event Description: Hip dislocated. Patient originally had recall Inter-Op shell
Patient Outcome: This was the second revision for this patient

Device Description: Co-Cr Head 12/14 Neck Neutral 28mm Metasul
MDR Report Key: 2935620-2003-00062
Product Code: KWA
Report Date: 3/4/2003
Catalog No.: 7340-28-000
Device Lot No.: 1171205
Event Description: Patient revised on 4/23/01
Patient Outcome: Unknown

Device Description: Co-Cr Head 12/14 +4mm Neck 28mm Metasul
MDR Report Key: 2935620-2001-01186
Product Code: KWA
Report Date: 6/8/2001
Catalog No.: 7340-28-400
Device Lot No.: 1327368-F
Event Description: Revision of femoral head on 12/11/99
Patient Outcome: Unknown

Device Description: Co-Cr Head 12/14 +4mm Neck 28mm Metasul
MDR Report Key: 2935620-2002-00393
Product Code: KWA
Catalog No.: 7340-28-400
Device Lot No.: 1409774
Event Description: Second revision required because of hip instability

Patient Outcome: Patient operated on 10-01-01

Device Description: Acetabular Insert 28x53 mm Metasul APR
Report Date: 12/15/04
MDR Report Key: 2935620-2004-00113
Product Code: KWA
Catalog No.: 4340-28-053
Device Lot No.: 1245313
Event Description: Acetabular insert dissociation. The shell was well fixed. At the time of surgery the insert was out of the shell. The metal pin was broken and the poly plug and lip liner had sheared off.

Device Description: Acetabular Insert 28x49 mm Metasul APR
Report Date: 12/15/04
MDR Report Key: 2935620-2004-00114
Product Code: KWA
Catalog No.: 4340-28-049
Device Lot No.: 1245303
Event Description: On January 23, 2004, the patient experienced a sudden onset of pain and instability in the right hip. The primary surgery had been performed on October 23, 1996. No significant causative event occurred prior to the onset of pain/instability. X-Ray examination confirmed disassociation of APR Metasul liner. Patient was admitted to hospital and APR Metasul liner revised to a polyethylene liner on January 28, 2004.

Manufacturer: Biomet
Airport Industrial Park
Warsaw, IN 46580

Device Description: M2A Modular Head Prosthesis
MDR Report No.: 1825034-2002-00129
Product Code: KWA
Report Date: 11/8/2002
Catalog No.: 11-173660
Device Lot No.: 698740
Event Description: Report from hospital indicated five of eleven cases of hip replacement procedures resulted in post-operative infections. No information that infections are related to devices used.
Patient outcome: Unknown

Device Description: M2A Modular Head
MDR Report No. 1825034-2003-0001

Product Code: KWA
Report Date: 1/7/2003
Catalog No. : 11-173661
Device Lot. No.: 321210
Event Description: Patient experienced pain, osteophytes removed.
Modular head component exchanged.
Patient outcome: Revision surgery

Device Description: M2A M/H Radial Solid Shell
MDR Report No. 1825034-2003-0034
Product Code: KWA
Report Date: 1/6/2003
Catalog No.: 15-104090
Device Lot No.: 986560
Event Description: Hip dislocated, acetabular components and
Modular head replaced.
Patient outcome: Revision surgery

Device Description: M2A M/H Radial Solid Shell
MDR Report No.: 1825034-2003-00035
Product Code: KWA
Report Date: 1/6/2003
Catalog No.: 15-105004
Device Lot No.: 916180
Event Description: Hip dislocated, acetabular components and
Modular head replaced.
Patient Outcome: Revision surgery

Device Description: M2A M/H Radial Solid Shell
MDR Report No.: 1825034-2003-00036
Product Code: KWA
Report Date: 1/6/2003
Catalog No.: 11-173670
Device Lot No.: 816160
Event Description: Hip dislocated, acetabular components and
Modular head replaced.
Patient Outcome: Revision surgery

Device Description: M2A Modular Head
MDR Report No.: 1825034-2003-0001

Device Description: M2A Ringloc LP Custom Liner
MDR Report No.: 1825034-2004-00041
Product Code: KWA

Report Date: 3/22/2004
Catalog No.: CP 160602
Device Lot No.: 394100
Event Description: Multiple dislocations, resulted in disassociation of liner component---acetabular liner replaced.
Patient Outcome: Revision surgery

Device Description: M2A Taper Liner
MDR Report No.: 1825034-2004-00106
Product Code: KWY
Report Date: 12/21/2004
Catalog No.: 15-105004
Device Lot. No.: 916140
Event Description: Patient underwent left revision total hip arthroplasty in 2001. Due to dislocation, closed reduction performed in 2004. Following multiple dislocations, left revision arthroplasty Performed in 2004. Metallosis of adjacent tissue was noted and Acetabular components were replaced.
Patient Outcome: Unknown

Device Description: M2A Modular Head
MDR Report No.: 1825034-2004-0017
Product Code: KWA
Report Date: 12/21/2004
Catalog No.: 11-163670
Device Lot No.: 889090
Event Description: Patient underwent left revision hip replacement in 2001. Due to Dislocation closed reduction performed in January 2004. Following multiple dislocations, left revision hip arthroplasty performed 2 weeks later. Metallosis of the adjacent tissue was noted and acetabular components were replaced.
Patient outcome: Unknown

Device Description: M2A T-Universal 2 hole Shell
MDR Report No.: 1825034-2004-00073
Product Code: KWA
Report Date: 8/20/2004
Catalog No.: 15-103654
Device Lot No.: 513150
Event Description: Patient underwent total hip arthroplasty in 2000. Due to loosening, revision performed in 2004 to replace acetabular components.
Patient outcome: Unknown

Device Description: M2A Taper Liner 37/28mm
MDR Report No.: 1825034-2004-00074

Product Code: KWA
Report Date: 8/20/2004
Catalog No.: 15-105000
Device Lot No.: 011380
Event Description: Patient underwent total hip arthroplasty in 2000. Due to loosening revision performed in 2004 to replace acetabular components.
Patient outcome: Unknown

Device Description: M2A Modular Head Prosthesis
MDR Report No.: 1825034-2004-00075
Product Code: KWA
Report Date: 8/20/2004
Catalog No.: 11-163662
Device Lot No.: 11-163662
Event Description: Patient underwent total hip arthroplasty in 2000. Due to loosening revision performed in 2004 to replace acetabular components.
Patient outcome: Unknown

Device Description: M2A Taper Liner 37x28mm
MDR Report No.: 1825034-2004-00071
Product Code: KWA
Report Date: 8/17/2004
Catalog No.: 15-105000
Device Lot No.: 674440
Event Description: Patient underwent total hip arthroplasty in 2000. Operative report indicates that loose acetabular components were replaced during revision surgery in 2003.
Patent outcome: Unknown

Device Description: M2A Modular Head Prosthesis
MDR Report No.: 1825034-2004-00072
Product Code: KWA
Report Date: 8/17/2004
Catalog No.: 11-163663
Device Lot No.: 724130
Event Description: Patient underwent right total hip arthoplasty in 2000. Operative Report indicates loose acetabular components were replaced during revision surgery in 2003.
Patient outcome: Unknown

Device Description: M2A T-Universal 2-Hole Shell
MDR Report No.: 1825034-2004-00070
Product Code: KWA
Report Date: 8/17/2004

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|---|---|
| Catalog No.: | 15-103656 |
| Device Lot No.: | 710160 |
| Event Description: | Patient underwent right total hip replacement in 2000. Operative report indicates that loose acetabular components were replaced during revision surgery in 2003. |
| Patient outcome: | Unknown |

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|---|---|
| Device Description: | M2A Modular Head |
| MDR Report No.: | 1825034-2005-00010 |
| Product Code: | KWA |
| Report Date: | 1/4/05 |
| Catalog No.: | 11-173663 |
| Device Lot No.: | 819060 |
| Event Description: | It was reported that patient underwent total hip arthroplasty on November 6, 20002. Due to multiple dislocations revision was performed November 18, 2004. Acetabular components were replaced. |
| Patient outcome: | Unknown |

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|---|---|
| Device Description: | M2A 38 mm Cup |
| MDR Report No.: | 1825034-2005-0009 |
| Product Code: | KWA |
| Report Date: | 1/4/05 |
| Catalog No.: | RD118852 |
| Device Lot No.: | 634220 |
| Event Description: | It was reported that patient underwent total hip arthroplasty on November 6, 2002. Due to multiple dislocations, revision was performed November 18, 2004. Acetabular components were replaced. |
| Patient outcome: | Unknown |

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|---|---|
| Device Description: | Alternate Bearing Surface Liner 10 Degree |
| MDR Report No.: | 1825034-2005-00019 |
| Product Code: | KWA |
| Report Date: | 2/21/05 |
| Catalog No.: | RD157015 |
| Device Lot No.: | 619210 |
| Event Description: | Patient underwent right total hip arthroplasty on May 27, 1998. Onset of right hip pain noted in July, 2004 and patient underwent revision surgery on February 3, 2005. Surgeon noted osteolysis involving proximal femur and acetabulum. |
| Patient outcome: | Unknown |

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|---|---|
| Device Description: | Alternate Bearing Modular Head Taper 1 |
| MDR Report No.: | 1825034-2005-00020 |
| Product Code: | KWA |

Report Date: 2/21/05
Catalog No.: RD157606
Device Lot No.: 300670
Event Description: Patient underwent right hip arthroplasy on May 27, 1998. Onset of right hip pain noted in July, 2004 and patient underwent revision surgery on February 3, 2005. Surgeon noted osteolysis involving proximal femur and acetabulum.
Patient outcome: Unknown

Manufacturer: DePuy Orthopaedics, Inc.
P.O. Box 988
Orthopaedic Drive
Warsaw, IN 46581-0988

Device Description: Ultamet MOM Insert 54 OD x 36 ID
MDR Report Key: 0202391C-1
Product Code: KWA
Report Date: 12/13/2002
Catalog No.: 121887354
Device Lot No.: YMD 59
Event Description: Package split—inner plastic portion—no revision surgery
Patient outcome: unknown

Device Description: Ultamet MOM Insert 52 ID x 36 ID
MDR Report Key: 0300405C-2
Product Code: KWA
Report Date: 3/3/2003
Catalog No.: 121887352
Device Lot No.: 1070181
Event Description: Metal insert locked into shell off axis and could not be removed from acetabular shell. Delay in surgery
Patient outcome: unknown

Device Description: Ultamet MOM Insert 62 OD x 36 ID
MDR Report Key; WPC 354-2003
Product Code: KWA
Report Date: 12/22/2003
Catalog No.: 121887362
Device Lot No.: YHT 84
Event Description: Metal insert did not seat properly, surgery extended 30 minutes.
Patient outcome: Unknown

B. Summary of Published Adverse Events from the Literature

A survey of the published literature resulted in the following adverse events reported for these devices.

1. Wagner, Michael and Heinz Wagner. "Preliminary Results of Uncemented Metal on Metal Stemmed and Resurfacing Hip Replacement Arthroplasty."; Clin. Orthop., No. 329S (1996): S78-S88.

   This article reports on a series of 70 patients in Europe with metal/metal semi-constrained total hips implanted during 1990-1992. There was one early dislocation with the patient refusing further treatment; one late infection requiring removal of the prosthetic implant components. Periarticular calcification in two patients requiring reoperations was also reported.

2. Dorr, L. D., K. R. Hilton, Z. Wan, G.D. Markovich, and R. Bloebaum, Ph.D. " Modern Metal on Metal Articulation for Total Hip Replacments."; Clin. Orthop., No. 333 (1996): 108-117.

   This article reports on a series of 54 patients treated in the U.S. with metal on metal semi-constrained total hips from 1991-1994. There was one infection and two dislocations; one of these dislocations required revision of the prosthesis three years postoperatively.

3. Weber, B.G. " Experience With the Metasul Total Hip Bearing System."; Clin. Orthop., No. 329S (1996): S69-S77.

   This article reports on a series of 110 patients treated in Europe with metal on metal semi-constrained total hips from 1988-1992. There were five early failures attributed to loosening reported. There were two additional complications of trochanteric bursitis (one case) and painful ectopic ossification (one case), neither case required reoperation.

4. Hilton, K.R., L.D. Dorr, Z. Wan and E.J. McPherson. " Contemporary Total Hip Replacement With Metal on Metal Articulation."; Clin. Orthop. No. 329S (1996): S99-S105.

   This article updates a previous report by Dorr, et al. (See ref. 2) There was one additional dislocation reported for this series.

5. Doorn, P.F., J.M. Mirra, P.A. Campell, and H.C. Amstutz. "Tissue Reaction to Metal on Metal Total Hip Prostheses."; Clin. Orthop. No. 329S (1996): S187-S205.

   Nine metal/metal hip implants retrieved from nine patients underwent histological evaluation to study the tissue reaction around the prostheses. Four McKee-Farrar, one APR and one Apollo metal/metal total hip prostheses and three McMinn

metal/metal total surface replacement hip prostheses were evaluated. The duration of implantation ranged between seven months and 25 years. Implants were retrieved due to aseptic loosening (4), pain (2), dislocation (1), femoral fracture (1) and death (1). While many of the common tissue responses to metal/polyethylene articulations were also noted for the metal/metal devices, however, overall these reactions appeared less intense.

6. Iida, H., E. Kaneda, H. Takada, K. Uchida, K. Kawanabe, and T. Nakamura. "Metallosis Due to Impingement Between the Socket and the Femoral Neck in a Metal-on-Metal Bearing Total Hip Prosthesis: A Case Report."; J Bone Joint Surg. Vol. 81(A) (1999): 400-3.

   This article reports on a single patient who suffered a failure of her metal-on-metal hip prosthesis 12 months following her surgery. The patient had no prior history of dislocation or other major complication. The prosthesis was shown to be loose on x-rays at 12 months and osteolysis was suspected in the calcar and trochanter regions of the femur. Examination of the retrieved titanium alloy femoral prosthesis and the cobalt-chromc alloy acetabular prostheses revealed markings consistent with impingement between the socket and the femoral neck during maximum hip flexion. Histological examination of the psuedocapsular tissue revealed particles of titanium, but cobalt and chromium were not detected. The authors concluded that the source of the metal debris was from the femoral prosthesis. The authors further concluded that this type of complication can occur anytime, without symptoms or associated complications and questioned the use of titanium in the manufacture of this implant.

7. Campell, P., H. McKellop, R. Alim, J. Mirra, S. Nutt, L. Dorr, and H.C. Amstutz. "Metal-On-Metal Hip Replacements: Wear Performance and Cellular Response to Wear Particles." In Cobalt-Based Alloys for Biomedical Applications. ASTM STP 1365., editors J.A. Disegi, R.L. Kennedy and R. Pilliar, (1999) 193-209. West Conshohocken, PA: ASTM publishers.

   This article reports on 20 second generation metal-on-metal hip prostheses retrieved from patients after use ranging from nine months to 6.5 years. The specific aims of this study of retrieved devices were to examine the amount of wear, study the histological appearance of the periprosthetic tissues and characterize the wear particles generated *in vivo*. There were 10 total hip and 10 surface replacement hip prostheses configurations available for evaluation. Implants were made available due to a variety of reasons including loosening, debonding, component breakage, infection and death.

   Eighteen of the 20 retrieved prostheses had at least one component measured for wear. For those components in which wear could be measured, the amount of wear ranged from 3-32 microns. Two of the total hip prostheses exhibited clusters of micropits in the main bearing area, but these did not appear to be associated with high wear.

Histological evaluation revealed metallosis occurred in five cases. Impingement of the titanium alloy femoral components with the acetabular shell, debonding of the porous coating and breakage of the femoral component were cited as the likely causes in four of these cases. For the fifth case, discoloration was likely due to cobalt-chrome particles released during the wear-in phase of the components. The histology for another case revised due to distal femoral osteolysis, was inconsistent with wear-induced osteolysis. Extensive necrosis was noted for two other cases, but no clear association between necrosis and metal wear particles could be made. Except for the five metallosis cases, there were fewer macrophages and wear particles than is typically seen in tissues around metal-polyethylene hip prostheses. Two consistent forms of cobalt-chrome particles were noted. One was a dense elongated form that commonly had a defined edge. The second, and the most common, form had less defined edges with a non-homogeneous, amorphous texture. Particle size was comparable between the total hip and surface replacement hip prostheses.

Conclusions are summarized as follows: 1) wear of the metal-on-metal articulations was substantially lower than for metal-polyethylene articulations, 2) third body damage was noted in varying degrees on all components, 3) histology and particle morphology were consistent with the low wear of these bearings, 4) cellular reaction to the metal particles could be described as mild, and 5) further histopathological studies and measurements of *in vivo* wear of metal-on-metal total hip replacements are recommended.

8. Albrecht-Olsen, P, Owen-Falkenberg, T, Burgaard, P, Andersen, PB. Nine-Year Follow-up of the Cementless Ring Hip. *Acta Orthop Scand*, 60:1:77-80, 1989.

   Albrecht-Olsen et al. reviewed 238 Ring prostheses implanted during the period 1968-1979. Of those cases, 127 with a median follow-up of 9 years were available for evaluation with 90% of those patients demonstrating excellent/good results upon self assessment. Using the Charnley scale, 87% had a pain score of 4 or greater (score of 6 = no pain), 76% had a motion score of 4 or greater, and 57% had a walking score of 4 or greater. The author cites an infection rate of 2.5% (6 deep infections, 16 superficial infections). Four dislocations were also encountered. At the time of this evaluation, 17% (n=40) of the patients had been revised, mainly due to pain. Overall results predicted an 81% survival rate at 12 years, comparable to outcomes seen with metal-on-polyethylene articulation

9. Almby, B, Hierton, T. Total Hip Replacement: A Ten-Year Follow-up of an Early Series. *Acta Orthop. Scand.*, 53:397-406, 1982.

   Almby reported on 93 patients receiving the Muller device, 57% of which had been followed for more than 10 years. Using the Charnley scale (6 possible points in each category), 90% had pain rating of 4 or better or a range of motion greater than 100°. Nine deep infections were reported. Thirty patients died (26 unrelated to device, 1 embolus, 1 ileus, 1 renal failure, 1 septic). Twenty-nine patients were revised (19 aseptically loose, 7 septically loose, 4 stem fractures, 1 fracture).

Twenty-three acetabular and 16 femoral components showed signs of loosening. Femoral loosening was secondary to calcar resorption and cement settling in most cases. Survivorship in this series was calculated to be approximately 80% at 5 years and 57% at 10 years.

10. Andrew, T.A., Berridge, D, Thomas, A, Duke, RNF. Long-term Review of Ring Total Hip Arthroplasty. *Clinical Orthopedics and Related Research*, 201:111-122, 1980.

    Andrew presented his results of 116 Ring patients followed for 8 years. Using the Harris scoring system (100 points possible), 33% of the patients had 80 points or greater with another 13% exhibiting total scores of 70-80. Using the Ring evaluation, 49% of the patients rated excellent or good. Two deep infections and 4 dislocations were encountered. Other complications included grade IV heterotopic ossification (5), fracture (4), embolic event (7), and sciatic palsy (1).

11. Djerf, K, Wahlstrom, O. Total Hip Replacement Comparison Between the McKee-Farrar and Charnley Prostheses in a 5-Year Follow-up Study. *Acta Orthop. Scand.*, 105:158-162, 1986.

    Djerf presents results on 107 McKee-Farrar and 70 Charnley devices with 5 years followup. Analysis revealed 94% of patients to have no pain and 78% to have improved flexion. Unrelated death occurred in 12% of the patients. Six infections (3.4%) and 4 dislocations (2.3%) were reported. Other complications included trochanteric problems (2.8%), nerve injury (1.7%), deep venous thrombosis (1.7%), pulmonary embolus (0.6%), fracture (0.6%), and ossification (0.6%). Loosening was evident in 32% of the cases. Analyses showed no significant difference in the outcomes of either implant.

12. August, AC, Aldam, CH, Pynsent, PB. The McKee-Farrar Hip Arthroplasty: A Long Term Study. *Journal of Bone and Joint Surgery*, 68B:4:520-527, Aug. 1986.

    Results of 175 patients with the McKee-Farrar device at an average 13.9 years of follow-up are presented by August. Using the Harris evaluation, the average total score was 76.4, with 48.9% having excellent/good outcomes. On self assessment, 90% of the patients rated themselves as having a satisfactory outcome. Sixty-four patients were revised, mainly for loosening, stem fracture and bone fracture. Over 50% of the stems and cups showed signs of looseness radiographically. Additionally, the cup showed signs of protrusion in 62.5% of rheumatoid patients. Heterotopic ossification (grade IV) was reported in 2.7% of the cases. August calculated survival at 84.3% at 14 years and 27.5% at 20 years.

13. Jantsch, S, Schwagerl, W, Zenz, P, Semlitsch, M, Fertschak, W. Long-term Results After Implantation of McKee-Farrar Total Hip Prostheses. *Acta Orthop. Scand.*, 110:230-237, 1991.

Jantsch analyzed followup at 14 years in a series of 248 patients with 330 McKee-Farrar devices. Only 56% of the patients were followed clinically to this period (24% died, 17% untraceable, 3% refused participation). Using the Mayo rating system, 48% of the patients were found to have excellent/good ratings (62% if revisions are excluded). Based on radiographs available, 34% of the cups and 26% of the stems were unstable. There were 36 retrievals (22 cup and stem, 7 cup, 7 stem).

14. McKee, GK, Chen, SC. The Statistics of the McKee-Farrar Method of Total Hip Replacement. *Clinical Orthopedics and Related Research*, 95:26-33, Sept. 1973.

    McKee reports on four series of patients treated with the various iterations of the McKee-Farrar device from 1956-1971. Postoperative outcome improved through each design iteration, with approximately 89% achieving excellent or good outcomes in the 1965-69 series (4-7 year followup) and 97% achieving excellent or good outcomes in the 1971 series (2 year or less followup). Retrievals have occurred in 4% of the 1965-69 series and 0% of the 1971 series. Fifteen (15) deaths were reported in the 1965-69 series; two were reported in the 1971 series. The reported rate of infection was 4% in the 1965 series and 0% in the 1971 series. Two dislocations (2%) were also reported in each of these series. Other complications include pulmonary embolus, deep venous thrombosis, shaft perforation, hematoma and heterotopic ossification.

15. Ring, P. Press-Fit Prostheses: Clinical Experience. *Osteoarthritis in the Young Adult Hip: Options for Surgical Management.* Pp. 220-232, edited by D Reynolds and M Freeman, Churchill Livingstone Publishing, 1989.

    Ring presents results on 106 metal-metal Ring prostheses with 7-17 years followup. Postoperatively, 83% were assessed as excellent/good clinically. Outcomes of the various design iterations is again presented in this article. Thirteen retrievals have occurred (7 femoral failures, 2 pelvic failures, 3 combination failures, 1 ankylosis). Survivorship of patients implanted from 1968-73 was 81% at 18 years; survivorship was 95% at 16 years for those implanted from 1972-79.

16. Schmalzried, TP, Szuszczewicz, ES, Akizuki, KH, Petersen, TD, Amstutz, HC. Factors Correlating with Long Term Survival of McKee-Farrar Total Hip Prostheses. *Clinical Orthopedics and Related Research*, 329S:48-59, Aug. 1996.

Thirteen McKee-Farrar patients (15 devices) with an average follow-up of 23.7 years are presented by Schmalzried. The average Harris hip score of these patients was 86 with 11 patients having an excellent/good rating. These patients outscored a matched metal-on-poly control population on the SF-36 Health Status questionnaire. Activity levels were also reported to exceed the averages for this age population. The only complication reported is that of lysis in three femurs and one acetabulum.

17. Zaoussis, AL, Patikas, AF. Experience with Total Hip Arthroplasty in Greece, the First 20 Years: A Particular Reference to Long-Term Results with the McKee-Farrar Technique. *Clinical Orthopedics and Related Research,* 246:39-47, Sept. 1989.

Zaoussis presents results on 38 McKee Farrar patients followed for 12-20 years, with 26 having greater than 15 years followup. At the time of this evaluation, 45% were found to have very good outcomes. Fifty-three percent (53%) of the patients were pain free and 79% had 60-90° range of motion. Three infected components and four loose components were retrieved. There have been five dislocations (all in one patient). Nine components show looseness. Other complications include five peroneal nerve palsies, one cortical perforation and one ossification.

18. Archibald, MJ, Jacobs, JJ and Black, J. Alternative Bearing Surfaces in Total Joint Arthroplasty. *Clinical Orthopaedics and Related Research,* 379:12-21, Oct. 2000

This review article describes the local effects of metal and ceramic particles, which appear similar to that seen with ultrahigh molecular weight polyethylene. Volumetric wear of metal particles is generally reduced but this effect may be mitigated by the finer particles generated by metal-on-metal wear. The systemic effects of these particles are largely unknown. All particle types can elicit a cell response that varies with cell type and the specific response measured. According to the authors, additional investigation is needed to identify the potential beneficial or harmful effects of alternative bearing surfaces.

19. Brodner, W et al. Serumcobalt- und Serumchromspiegel bei zwei chronish niereninsuffizienten Patientinnen mit Hüftotalendoprothese und Metall-Metall-Gleitpaarung. Z Orthop Ihre Grenzgeb 138:425-429, 2000

The influence of chronic renal failure on serum cobalt and serum chromium in two patients with metal-on-metal bearing (Metasul) and cementless total hip arthroplasty (Alloclassic) were investigated. Maximum values were found to be more than 100-fold elevated when compared to the reported median serum cobalt concentrations in patients with the same prosthesis type and no known renal disease. The authors concluded that chronic renal failure seems to be responsible for the marked elevation of serum cobalt and serum chromium. In their opinion, metal-on-metal bearings in THA should not be inserted in patients with chronic renal failure.

20. Hallab, N et al. Metal Sensitivity in Patients with Orthopaedic Implants. JBJS 83-A(3):428-436, 2001

Specific types of implants with a greater propensity to release metal *in vivo* may be more prone to induce metal sensitivity. Failures of total hip prostheses with metal-on-metal bearing surfaces have been associated with a greater prevalence of metal sensitivity than have those of similar designs with metal-on-ultra-high molecular weight polyethylene bearing surfaces. In contrast, other studies have indicated that, after total joint replacement with metallic components, some patients show an induction

of metal tolerance---that is, a previously detected metal sensitivity abates after implantation of a metal containing prosthesis. Until the roles of delayed hypersensitivity and humoral immune responses to metallic orthopaedic implants are more clearly defined, the risk to patients may be considered minimal.

21. Tharani, BS et al. The Risk of Cancer Following Total Hip or Knee Arthroplasty. JBJS 83-A(5):774-780, 2001

    There has been concern that metal-on-metal total joint replacements may be associated with an increased risk of cancer because of an increased exposure to metal particles or ions. The risk of cancer after metal-on-metal total hip replacement has been assessed specifically in only one epidemiological study. In that study, the relative risk of cancer was reported to be 0.95 (95 % confidence interval, 0.79 to 1.13), suggesting that there is no apparent increased risk of cancer after metal-on-metal total hip arthroplasty. In addition, the risk of sarcoma after metal-on-metal total hip replacement was found to be 0.00 (95 % confidence interval, 000 to 6.59). However, those same authors found the relative risk of hematopoietic cancer to be 1.59 (95 % confidence interval, 082 to 2.77) following metal-on-metal total hip replacement and 3.77 (95 % confidence interval, 0.96 to 17.6) for leukemia when metal-on-metal implants were compared with metal on polyethylene implants. From an epidemiological perspective, these data are limited because of the small number of patients (579) who underwent metal-on-metal total hip replacement. Because this number is small and the numbers of both observed and expected cases are also small, the strength of the probability analysis is quite limited. In their summary, the authors noted that the available data do not support a causal link between total hip or knee arthroplasty and the development of cancer. Although it is biologically possible for the materials used in total joint replacement to induce malignant generation, this relationship has not been demonstrated.

22. Lombardi, AV. Short-Term Results of the $M^2$ a-Taper Metal-on-Metal Articulation. J. Arthroplasty 16(8) Suppl. 1:122-128, 2001

    A polyethylene-free metal-on-metal acetabular system was designed in an effort to improve total hip arthroplasty (THA) longevity. Minimum 2- year follow-up results involving 72 polyethylene (PE) liner THAs and 78 metal liner THAs from a multicenter, randomized, controlled, investigational device exemption study was reported. Mean Harris hip scores of 95.54 (PE liner group) and 95.23 (metal liner group) were reported at mean follow-up intervals of 3.29 and 3.23 years. Radiographic evaluation revealed no evidence of early failure. No acetabular components were revised or were pending revision. No statistically significant differences in the data were calculated between liner types except for the immediate postoperative (P=.0415) and minimum 2-year follow-up (P=.0341) angles of inclination. The $M^2$ a-taper metal-on-metal articulation may represent a viable alternative for THA in younger, higher demand patients.

23. Harding, I. et al. Serum Levels of Cobalt and Chromium in a Complex Modular Total Hip Arthroplasty System. J. Arthroplasty 17(7):893-95, 2002

This study measured the serum cobalt and chromium levels in patients with an Oxford Universal Hip (Corin, Cirencester, UK), which has a modular sliding mechanism; patients with a similarly manufactured hip with no sliding mechanism; and a control group. Loosening was excluded clinically and radiographically. Arthroplasty patients had statistically higher levels of serum cobalt and chromium than controls, but there was no significant difference in levels between the implanted groups. Although it is not known what the long-term effects of chronic low-grade exposure to these ions are, the levels are many orders below the toxic range.

24. Brodner, W, et al: Serum Cobalt Levels After Metal-on-Metal Total Hip Arthroplasty. JBJS (Am), 85:2168-2173, 2003

A total hip arthroplasty was performed without cement in 100 consecutive patients who have either unilateral osteoarthritis or unilateral osteonecrosis. Fifty patients were randomized to be treated with Metasul metal-on-metal articulation, and fifty patients with a ceramic-on-polyethylene bearing. Blood samples were taken before the operation and at multiple time points for five years after the operation. Serum cobalt concentrations were measured with atomic absorption spectrometry. In the metal-on-metal group, the median serum cobalt concentration was 1μg/L at one year after surgery and 0.7 μg/L at five years. The median of the serum cobalt concentrations measured from 3 to 12 months did not differ from the median of subsequent measurements. The median serum cobalt level in the control group of patients treated with ceramic-on-polyethylene articulation was below the detection limit at all time points. The authors did not determine what serum cobalt levels reflect or whether they corresponded to wear of the articulating metal surfaces. They believed that there was little doubt that renal function influences serum metal concentrations. However, they did not believe that routine determination of serum metal levels or routine monitoring of renal function is needed for patients with metal-on-metal articulation. They do recommend careful follow-up with monitoring of serum cobalt concentrations as well as renal function when renal disease develops in a patient with a metal-on-metal articulation. Until more information is available, the authors are concerned about patients with high levels of serum cobalt, and believe it prudent to observe such patients. They recommend informing patients that, so far, elevated serum cobalt concentrations after total hip replacement with a metal-on-metal articulation have not been linked to adverse health reactions but the effects of long-term elevation of serum cobalt levels are not yet known.

25. Reinisch, G, et al: Retrieval Study of Uncemented Metal-Metal Prosthesis Revised for Early Loosening. *Biomaterials*, 24:1081-1091, 2003

A tribologic assessment was performed on 22 metal-metal hip prostheses from a single manufacturer, following removal for early aseptic loosening after a mean service life of 32 months (range 12-59 months). The mean linear wear rate was 7.6μm/year (range , 2.9 –12.8 μm/year). This was below the rates previously observed in other metal-metal combinations. A novel contour analysis technique using a coordinate measuring machine showed the mean volumetric wear rate to be 2.02 $mm^3$ /year (range, 0.55—3.74 $mm^3$ /year), which corresponds to a mean gravimetric wear rate of 16.9 mg/year (range, 4.6—

31.4 mg/year). The mean clearance of 39.8 μm (range 30-50 μm) was within the optimal range for hard-hard bearing combinations. Evidence of abrasive, adhesive, and third-body wear was found on all bearing surfaces. The tribologic assessment did not indicate manufacturing defects as a cause for early loosening. Equally third-body wear was too low to be considered a causative factor for early loosening.

26. Brown, SR et al: Long-term Survival of McKee-Farrar Total Hip Prostheses. *Clin Orth Rel Res* 402:157-163, 2002

The long-term results of 153 consecutive McKee-Farrar total hip arthroplasties done in 129 patients by one surgeon between 1969 and 1973 were evaluated. The average age of the patients at implantation surgery was 61 years (range 28-85 years) and these patients were observed as many as 28 years. Primary diagnosis included osteoarthritis (49% of implants), rheumatoid arthritis (38%), and other conditions (13%). During the 28 years of followup , five implants were revised for infection and 14 implants were revised for aseptic loosening. Survivor analysis of the McKee-Farrar prostheses had a 20-year probability of implant survivorship of 84%, and a 28-year survivorship of 74%, Excellent long-term results were seen. Given the inherent problems associated with implant wear debris, especially polyethylene wear particles, second generation metal-on-metal bearing implants may offer a viable alternative to current designs. Their excellent long-term survival may infer particular suitability for use in younger patients.

27. Signorello LB et al: Nationwide Study of Cancer Risk Among Hip Replacement Patients in Sweden. J Natl Cancer Inst 93:1405-10, 2001

The authors conducted a nationwide cohort study in Sweden to examine cancer incidence among 116,727 patients who underwent hip replacement surgery during the period from 1965 through 1994. Through record linkage to the Swedish Cancer Register, they identified all incident cancers through 1995 in this population (693,954 person-years of observation). For each cancer type, the observed number of cases was divided by that expected in the general Swedish population to produce standardized incidence ratios (SIRs). Relative to the general population, the cohort had no overall cancer excess (SIR=1.10; 95% confidence interval [CI] = 0.99 to 1.03). However, they observed elevated SIRs for prostate cancer (SIR=1.16; 95% CI = 1.11 to 1.22) and melanoma (SIR=1.15; 95% CI = 1.10 to 1.20) and a reduction in stomach cancer risk (SIR=0.83; 95% CI = 0.75 to 0.92). Longer-term followup (>15 years) revealed an excess of multiple myeloma (SIR=1.86; 95% CI =1.01 3.11) and a statistically nonsignificant increase in bladder cancer (SIR=1.42; 95% CI = 0.98 to 1.99). There was no material increase in risk for bone or connective tissue cancer for either men or women in any followup period. The conclusion was that in this, the largest study to date, hip implant patients had similar rates of most types of cancer in those in the general population. There was no mention of whether the devices studied were metal or metal or polyethylene on metal.

28. Campbell PA et al: Positive Cytokine Production in Failed Metal-on-Metal Total Hip Replacements. Acta Orthop Scand 73(5):506-512, 2002

Tissues surrounding failed conventional total hips have been shown to produce inflammatory cytokines that can induce osteoclastic bone resorption. The authors evaluated the cytokine profiles of tissues from 5 failed metal-on-metal total hip replacements. Serial frozen sections were stained using immunohistochemical and in situ hybridization techniques. As compared to a group of 5 metal-polyethylene hip tissues, they found fewer CD68 positive macrophages, and lower levels of transforming growth factor beta TGF-β and tumor necrosis factor alpha TNF-α, but no differences in CD3 positive lymphocytes, IL-1βIL-6 and PDGF-α in the metal –on-metal tissues. This may be due, in part, to the presence of wear particles from sources other than the bearing surfaces. Thus, cytokines associated with bone resorption and implant loosening may occur in total hips despite the use of alternative bearing materials.

29. Dorr, LD et al: Total Hip Arthroplasty with Use of the Metasul Metal-on-Metal Articulation. JBJS 82-A(6):789-798, 2000

Between 1991 and 1994, seventy patients had a total hip replacement with the Metasul metal-on-metal articulation and a cemented Weber cup. Fifty six patients had complete clinical and radiographic data four to 6.8 years after the operation. There was one mechanical failure (2 percent). Thirty six of 47 patients who completed the patient self assessment form rated their result as excellent; seven, as very good; two, as good; one, as fair; and one, as poor. Wear could not be measured on radiographs because of the metal-on-metal articulation. No hip had radiographic evidence of acetabular osteolysis and two hips had calcar resorption, but there was no other evidence of focal osteolysis. From their four to seven year experience with the device the authors feel that the clinical results are similar to those of total hip replacements with a metal-on-polyethylene articulation. They believe the device may have a role in reducing the wear that occurs with total hip replacement and that the device appears particularly indicated for younger patients.

30. Savarino, L, et al: Ion Release in Patients with Metal-on-Metal Hip Bearings in Total Joint Replacement: A Comparison with Metal-on-Polyethylene Bearings. J Biomed Mater Res. 63(5):467-74, 2002

This study compared ion release in the serum of two groups of patients who had the same type of stable cementless prosthesis, but different bearing: 26 with metal-on-metal (Group A), and 15 with metal-on-PE bearing (Group B). The follow-up was 14-38 months for group A and 18-34 months for group B. The serum concentration of chromium (Cr), cobalt (Co) and molybdenum (Mo) was measured. Twenty two patients before surgery were used for comparison group (Group C). The reference values were obtained from a population of twenty two healthy subjects (Group D). Their findings indicate that metal-on-metal bearings produce a significantly higher systemic release of cobalt and chromium (ng/ml) when compared with levels found in metal-on-PE, pre-surgery, and reference groups. Such a high release should induce to improve the bearing materials or, at least, to study the biologic fate of metal ions and consequently their long-term effects. In such a way a risk-to-benefit ratio for the patient could be established.

31. Adami, G, et al: Cobalt Blood Levels after Total Hip Replacement: A New Follow-up Study in Trieste (Italy). Annali di Chimica 93:1-9, 2003

According to the authors there is little information in the literature regarding cobalt and chromium release following metal-on-metal total hip replacement. This is due to the fact that blood levels can change depending on physical and working activity, individual feeding and metabolism. The results obtained confirm the presence of an increase of cobalt in the blood of patients after THR, while the chromium levels are almost alike; average values in patients operated are 4.1±1.5μg/L for cobalt (0.3±0.1μg/L in the control group) and 4.5±2.9μg?l for chromium (4.7±2.4μg/L in the control group). In spite of the cobalt values that stand below the concentration generally considered dangerous, the difference between the two examined groups points out that a risk exists for the health of these patients. These results must be confirmed by further studies, providing better information and more reliable and biocompatible materials.

32. MacDonald, S.J. et al: Metal-on-Metal Versus Polyethylene in Hip Arthroplasty: A Randomized Clinical Trial. Clin Orth & Rel Res 406:282-296, 2003

A prospective, randomized blinded clinical trial was done to evaluate polyethylene versus metal bearing surfaces in total hip replacement. Forty one patients were randomized to receive either a metal (23 patients) or a polyethylene (18 patients) insert. The femoral and acetabular components were identical with the acetabular insert the only variable. Patients were assessed preoperatively and postoperatively using radiographs, multiple outcome measures (Western Ontario MacMaster University Score, Harris hip score, Short Form-12), erythrocyte metal ion analysis (cobalt, chromium, titanium). Patients were followed up for a minimum of two years (mean 3.2 years; range, 2.2-3.9 years). There were no differences in radiographic outcomes or outcome measurement tools between patients. Patients receiving a metal-on-metal articulation had significantly elevated erythrocyte and urine metal ions compared to patients receiving a polyethylene insert. Patients who had metal-on-metal inserts had on average a 7.9 fold increase in erythrocyte cobalt, a 2.3 fold increase in erythrocyte chromium, a 1.7 fold increase in erythrocyte titanium, a 35.1 fold increase in urine cobalt, a 17.4 fold increase in urine chromium, and a 2.6 fold increase in urine titanium at 2 years follow-up. Patients receiving a polyethylene insert had no change in erythrocyte titanium, urine cobalt or urine chromium and a 1.5 fold increase in erythrocyte cobalt, a 2.2 fold increase in erythrocyte chromium, and a 4.2 fold increase in urine titanium. Forty-one percent of patients receiving metal-on-metal articulations had increasing metal ion levels at the latest follow-up. The clinical significance of this remains unknown. Only through thorough long-term clinical analysis will appropriate conclusions be valid. Metal-on-metal total hip replacements perform well clinically; however, only with time will the risk to benefit ratio become clear.

33. Reinisch, G., et al: Retrieval Study of Uncemented Metal-Metal Hip Prostheses Revised for Early Loosening. Biomaterials 24:1081-1091, 2003

A tribologic assessment was performed on 22 metal-metal hip prostheses from a single manufacturer, following removal for early aseptic loosening after a mean service life of 32 months (range, 12-59 months). The mean linear wear rate was 7.6μm/year (range, 2.9-12.8 μm/year). This was below the rates previously observed in other modern metal-metal articulations. A novel contour analysis using a coordinate measuring machine showed the mean volumetric wear rate to be 2.02 $mm^3$ /year (range, 0.55-3.74 $mm^3$ /year), which corresponds to a mean gravimetric wear rate of 16.9 mg/year (range, 4.6-31.4 mg/year). The mean clearance of 39.8 μm (range, 30-50 μm) was within the optimal range for hard-hard bearing combinations. Evidence of abrasive, adhesive, and third-body wear was found on all bearing surfaces. The tribologic assessment did not indicate manufacturing defects as a cause of early loosening. Equally, third-body wear was too low to be considered a causative factor for early loosening. The implants investigated were uncemented total hip prostheses with a metal-metal bearing combination, from a single manufacturer (Plus Endoprothetik AG, Rotkreus, Switzerland).

34. Lhotka, C, et al: Four-year Study of Cobalt and Chromium Blood Levels in Patients Managed with Two Different Metal-on-Metal Total Hip Replacements. J Orth Res 21:189-195, 2003

In 259 patients with total hip replacement, blood cobalt and chromium concentrations were measured with atomic absorption spectrophotometry over a period of four years after arthroplasty. Of the patients enrolled in the study, 131 had been managed with a METASUL cobalt-chromium alloy metal-on-metal bearing combination, while 128 had been given a SIKO-MET-SM21 cobalt-chromium alloy metal-on-metal combination. The control group consisted of 31 age- and gender-matched subjects. Compared with the controls, all of the patients had higher cobalt and chromium levels. Cobalt concentrations were up to 50 times higher, while chromium concentrations were up to 100 times higher. Both systems showed evidence, in the whole-blood samples, of wear debris production by the implants. Therefore, patients managed with metal-on-metal bearing combinations should be carefully monitored in order to ensure that any local or systemic complications are detected early on. According to the authors, the cause and effect relationship between metal wear debris and local or systemic disease has not been conclusively proved, although complications from metal wear products are a subject of concern. Any metal-on-metal bearing combination used in joint replacements must, therefore, be designed and manufactured in such a way as to produce minimal debris.

35. Clarke, MT, et al: Levels of Metal Ions after Small- and Large-Diameter Metal-on-Metal Hip Arthroplasty. JBJS (Br) 85-B:913-917, 2003

Metal-on-metal bearings for hip arthroplasty are increasing in popularity but concern remains regarding the potential toxicological effects which these bearings release. The serum levels of cobalt and chromium in 22 patients who had undergone MOM resurfacing arthroplasty were compared with a matched group of 22 patients who had undergone 28 mm MOM total hip arthroplasty (THA). At a median of 16 months (7to 56) after resurfacing arthroplasty, the authors found the median serum levels of cobalt and chromium to be 38nmol/l (14 to 44) and 53 nmol/l (23 to 165) respectively. These were

significantly greater than the levels after 28 mm MOM THA which were 22 nmol/l (15 to 87, p=0.021) and 19 nmol/l (2 to 58, p <0.001) respectively. Since the upper limit for normal patients with implants is typically 5 nmol/l, both groups had significantly raised levels of metal ions. MOM bearings of large diameter, however, result in a greater systemic exposure of cobalt and chromium ions than bearings of small diameter. This may be of relevance for potential long-term side effects. It is not known to what extent this difference is due to corrosion of the surfaces of the component or of the wear particles produced.

36. Clarke MT, et al: Dislocation after Total Hip Replacement in Relation to Metal-on-Metal Bearing Surfaces. JBJS (Br) 85-B650-4, 2003

Metal-on metal (MOM) is a commonly used bearing noted for its "suction fit" when lubricated. A clinical study was conducted to compare the rate of dislocation of MOM bearings with those of ceramic-on-polyethylene (COP) bearings and found that one MOM bearing dislocated in a series of 109 hips (0.9%) compared with nine of 145 hips (6.2%) in the COP group (p=0.02), An in vitro investigation was performed comparing the peak forces generated during forced separation of the two bearings of the same dimensions at velocities from 1 to 50 cm/s. This revealed that the MOM bearing generated significant resistance to separation at all velocities (maximum mean 24N), whereas the COP did not (maximum mean 1.9N, p<0.001). The authors conclude that MOM bearings are more stable to dislocation than COP bearings as a result of the interfacial forces provided by a thin, lubricating fluid.

37. Savarino, L, et al: Ion Release in Stable Hip Arthoplasties using Metal-on-Metal Articulating Surfaces; A Comparison Between Short- and Medium-Term Results. J Biomed Mater Res 66A(3):450-456, 2003

The use of metallic heads articulating with metallic cups could solve the problem of polyethylene (PE) wear in total hip replacement (THR) with metal-on-PE bearings. A conspicuous release of metal ions from new models on metal-on-metal bearings has been found in the short-term, but it is yet unclear whether the medium-term corrosion rate is high, or, on the contrary, it becomes negligible, because of the continuous surface finishing. The purpose of the study was to compare the serum ion values (nanograms per milliliter) in 15 patients with metal-on-metal stable prosthesis (Group A), in the short-term (subgroup $A_1$; mean follow-up; 24 months) and medium term (subgroup $A_2$; mean follow-up: 52 months), in order to determine whether the ion release decreased with time of implant. Chromium (Cr), cobalt (Co), molybdenum (Mo) and Aluminum (Al) were analyzed. Twenty-two presurgical patients were used for comparison (Group B). The reference range was obtained from a population of 27 healthy subjects (Group C). Co and Cr levels in the medium term (subgroup $A_2$) were not decreased in comparison with the short-term values (subgroup $A_1$) and were significantly higher ($p< 0.001$) than presurgical and reference values. Otherwise, Mo and Al concentrations were not significantly increased in comparison with reference values. In conclusion, despite the apparent advantage of metal-on-metal coupling especially in younger patient populations, there is a major concern about the extent and duration of the relevant "internal" exposure

to Cr and Co ions. This exposure should be carefully monitored, in order to clarify the biologic effects of ion dissemination and, consequently, to identify risks concerning long-term toxicity of metals.

38. Campbell, P. et al: Autopsy Analysis Thirty Years After Metal-on-Metal Total Hip Replacement. JBJS 85-A(11):2218-2222, 2003

This report describes an autopsy retrieval to assess the distribution of wear products in the tissues immediately surrounding as well at a distance from a McKee Farrar metal-on-metal bearing total hip replacement after nearly 30 years in situ. The patient had been highly satisfied with the results of arthroplasty because her hip was free of pain and did not limit her function. Radiographs demonstrated good positioning and fixation of the implant with no evidence of loosening or osteolysis. Blood and urine samples were obtained for measuring cobalt and chromium ions. Following the patient's death in 1999, the left hip joint with surrounding acetabular and femoral bone, pseudocapsular tissue and the prosthesis were removed en bloc. Tissue samples were obtained from the liver, spleen, left kidney, left inguinal and abdominal lymph nodes, and muscle of the left thigh. Whole blood was aspirated from the bladder for analysis of ion content. Tissue analysis of the membrane present within the femoral canal revealed fibrous tissue containing histiocytes and giant cells with spaces consistent with dissolved bone cement. Capsular tissues were fibrous, with areas of adipose or necrotic tissue. A distinct inflammatory zone on the edge facing the implant contained macrophages, giant cells, blood vessels and wear particles of cobalt-chromium and polymethylmethacrylate. Lymphocytes and plasma cells were rare and polymorphonuclear leukocytes were absent. No histological abnormalities were noted in any organ samples. It was not possible to obtain serum levels of cobalt or chromium ions. The liver samples contained measurable levels of cobalt and chromium that were higher than those found in control samples. According to the authors it was difficult to assess the possible clinical implications of ion levels of cobalt and chromium in the urine, blood, and liver without validated threshold levels of toxicity, carcinogenicity, and other possible systemic effects. Studies that have examined the rates of cancer in patients who had total hip replacements, including those who had metal-on-metal prostheses, have demonstrated conflicting results, but there is a consensus that longer and broader studies need to be carried out.

39. Brodner W. et al: Serum Cobalt Levels After Metal-on-Metal Total Hip Arthroplasty JBJS 85-A(11):2168-2173, 2003

Systemic cobalt dissemination from the Metasul Co-28Cr-6Mo-0.2C metal-on-metal total hip prosthesis has been demonstrated in the first year after implantation. This study was designed to monitor the serum cobalt concentrations in patients during the first five years after total hip arthroplasty. Fifty patients were randomized to be treated with a metal-on-metal articulation and fifty with a ceramic-on polyethylene bearing. The femoral stem was made from Ti-6Al-7Nb alloy, and the threaded acetabular cup from commercially pure titanium. Blood samples were taken before the operation and at multiple time points for five years thereafter. Serum cobalt concentrations were measured with atomic absorption spectrometry. In the metal-on-metal group, the median serum cobalt

concentration was 1 µg/L at one year after surgery and 0.7 µg/L at five years. The median of the serum cobalt concentrations measured from three to twelve months did not differ from the median of subsequent measurements, with the numbers available. The median serum cobalt level in the control group of patients treated with the ceramic-PE articulation was below the detection level at all time points. In their conclusion the authors noted that systemic cobalt release was demonstrated throughout the five year study period and that median serum cobalt concentrations were found to be slightly above the detection limit and remained in a constant range. The serum cobalt concentrations did not reflect a so-called run-in wear period of the metal-on-metal articulations. The authors did not believe that routine determination of serum metal levels or routine monitoring of renal function is necessary for patients with metal-on-metal articulations. They do regard end-stage chronic renal diseases a contraindication. The authors also believe that allergy to cobalt or chromium or advanced age are reasons to avoid metal-on-metal hip replacements. They recommend informing patients that, so far, elevated serum cobalt concentrations after total hip replacement with a metal-on-metal articulation have not been linked to adverse health reactions but the effects of long-term elevation of serum cobalt levels are not yet known.

40. Lombardi, AV et al: Mid-Term Results of a Polyethylene-Free Metal-on-Metal Articulation. J. Arthroplasty 19(7) Supp 2:42-47, 2004

One hundred ninety-three patients (195 hips) were enrolled into this prospective, randomized, controlled multi-center investigational device exemption study. Ninety eight patients (99 hips) with 46 polyethylene liners and 53 metal liners had minimum 5-year followup (mean 5.7 years). Average followup , Harris hip score improvement, and radiographic analysis were not statistically different between groups. No stress shielding or osteolysis was observed in either group. Three polyethylene liners and no metal liners had acetabular radiolucencies >1 mm in 1 or more zones. There were no device related complications, no acetabular revisions performed, and none pending in either group. Based on these mid-term results, the authors conclude that a metal-on-metal articulation represents a viable alternative in young, high-demand, active patients. The device used was a $M^2$ a Taper Metal-on-Metal Articulation (Biomet Orthopaedics, Warsaw, IN).

41. Jacobs, M. et al: Three-to Six Year Results with the Ultima Metal-on-Metal Hip Articulation for Primary Total Hip Arthroplasty. J. Arthroplasty 19(7) Supp 2:48-52, 2004

One hundred seventy- one primary total hip arthroplasties were evaluated in a prospective, randomized study. Ninety-five involved a metal-backed cup with an all-metal liner and 76 involved a metal backed polyethylene cup that was used as the control. All were implanted with an S-ROM cementless femoral component with a 28-mm head. The mean followup period was 3.7 years (range 3.0-5.7). The average postoperative Harris hip score was 95.4 (range 65-100) for the metal-on-metal group and 96.1 (range 65-100) for the metal- on- polyethylene group. Radiographic results were not statistically different between the two groups. Early results show metal-on-metal articulation has been successful to date and justify continued clinical use.

42. Naudie, D et al: Metal-on-Metal Versus Metal-on-Polyethylene Bearings in Total Hip Arthroplasty. J. Arthroplasty 19(7) Supp 2:35-41, 2004

This is a report of a case- control study performed to investigate the hypothesis that metal-on-metal (MOM) bearings reduce the risk of aseptic component loosening when compared with metal-on-polyethylene (M-PE) bearings. Cases were identified from a computerized joint database as patients who had received a primary total hip arthroplasty using an MOM or M-PE bearing and had documented revision or radiographic loosening of the stem or cup. Multiple controls were matched to each case for gender, age, diagnosis, hospital, operation date, followup, stem type and cup design. Odds ratios were determined to identify the risk of component loosening for either bearing surface. In all, 505 cases and 1,605 controls were identified. MOM bearings demonstrated a lower risk of aseptic stem and/or cup loosening that M-PE bearings; however, this was not statistically significant.

43. Ladon, D et al: Changes in Metal Levels and Chromosome Aberrations in the Peripheral Blood of Patients after Metal-on-Metal Hip Arthroplasty. J Arthroplasty 19(8) Supp 3:78-87, 2004

A prospective study was performed to investigate changes in metal levels and chromosome aberrations in patients within 2 years of receiving metal-on-metal hip arthroplasties. There was a statistically significant increase of cobalt and chromium concentrations, with a small increase in molybdenum, in whole blood at 6, 12, and 24 months after surgery. There was also a statistically significant increase in both chromosome translocations and aneuploidy in peripheral blood lymphocytes at 6, 12, and 24 months after surgery. The changes were generally progressive with time, but the change in aneuploidy was much greater than in chromosome translocations. No statistically significant correlations were found in secondary analyses between chromosome translocation indices and cobalt or chromium concentration in whole blood. Although the clinical consequences of these changes, if any, are unknown, future epidemiological studies could usefully include direct comparisons of patients with implants of different composition. A total of 95 patients with Metasul metal-on-metal total hip arthroplasty were recruited to provide data for this study.

44. Huk, OL et al: Induction of Apoptosis and Necrosis by Metal Ions *In Vitro,* J. Arthroplasty 19 (8) Supp 3:84-87, 2004

There has been a renewed interest in the use of metal-on-metal (MOM ) implants for total hip arthroplasty. It is well known, however, that the MOM articulation generates both metal particles and ions. The physiologic effects of these ions is poorly understood and their potential toxicity remains a cause for concern. In the present study, murine J774 macrophages were incubated with $Co^{2+}$ and $Cr^{3+}$ ions and the mode of cell death (apoptosis/necrosis) was evaluated *in vitro* by transmission electron microscopy and cell death ELISA. Overall, results demonstrated that the mode of cell death was dependent on the ion concentration and incubation time. Indeed, at short incubation times (24 h),

the noninflammatory process of apoptosis was predominant. At longer incubation times (48h), however, necrosis was predominant at higher ion concentrations. According to the authors, the effect of metal particles and ions on remote organs beyond the hip joint is poorly understood, however, and deserves close scrutiny by the orthopaedic community.

45. Hallab, NJ et al: Immune Responses Correlate with Serum-Metal in Metal-on-Metal Hip Arthroplasty. J Arthroplasty 19(8) Supp 3:88-93, 2004

Cell- mediated hypersensitivity associated with metal components may be related to levels of implant debris. The authors tested this hypothesis by comparing lymphocyte reactivity to soluble Co, Cr, Ni and Ti of patients with metal-on-polyethylene and metal-on-metal arthroplasties with healthy controls, and patients with osteoarthritis. The metal-on-metal group (n=9) demonstrate significantly elevated Co and Cr concentrations (13- and 58 fold, $P<0.5$, respectively) and significantly elevated lymphocyte reactivity to Co (SI>5, $P<.004$) and Ni (SI >2.5, $P<.01$) when compared to controls (n=12) and subjects with metal-on-poly implants (n=7). These elevated *in vivo* metal levels demonstrated positive linear correlation with lymphocyte reactivity supporting our hypothesis that lymphocyte metal induced reactivity increases with increased metal exposure. These results represent the first direct link between *in vivo* metal exposure and lymphocyte reactivity. Whether this lymphocyte reactivity to metal debris is etiologically linked to poor implant performance remains uncertain.

46. Long, WT et al: An American Experience with Metal-on-Metal Total Hip Arthroplasties—A Seven Year Follow-up Study, J Arthroplasty 19(8) Supp 3:29-34, 2004

This study reviews the clinical performance of 161 hip arthroplasties (154 patients) with the Metasul metal-on-metal articulation and an uncemented modular acetabular component. Between 1995 and 2002 clinical evaluation and radiographic follow-up of patients included Harris hip scores, patient self-assessment, and radiographs. Twelve operative site complications (7.5%) included 6 revision operations (3.7%) and 3 other complications (1.9 %) not needing reoperation. Six revision operations (3.7%) included 1 femoral revision for aseptic loosening (0.06%) and 5 acetabular revisions (3.1%). One cup revision was for recurrent dislocation, 1 for disassociation of the acetabular insert from the cup, 1 for infection, and 2 for unexplained pain. Histologic evidence did not support the diagnosis of metal hypersensitivity in either case of unexplained pain, and 1 had relief following spine surgery. A focal radiolucency, identified as calcar resorption, was observed in 9 patients. Metal ion levels were not tested in patients as part of these studies. The authors note that after 40 years of use, there is no evidence that metal-on metal articulations have been a cause of cancer. The strength of this study is that it confirms that the high incidence of early aseptic loosening has been improved with this modern metal-on-metal articular system.

47. Delaunay, CP: Metal-on-Metal Bearings in Cementless Primary Total Hip Arthroplasty. J Arthroplasty 19(8) Supp 3:35-40, 2004

One hundred cementless titanium primary total hip arthroplasties with 28 mm Metasul bearings were prospectively studied (osteoarthritis in 76% of hips, mean age 59.6 years). Ninety-eight were reviewed after a 6-year average follow-up (range, 17-126 months) with clinical results graded excellent and good in 97%. One femoral component was revised for aseptic loosening at 7.8 years. Postoperative cobalt level was higher than the upper "normal" value (5μg/L in whole blood) for 16 cases. No significant relationship could be established between cobalt concentration increase and any demographic or surgical data, including activity level, except anteversion of the cup >25°. In this early experience, impingement due to a head sleeve has been the main cause of dislocation and failure, and systemic cobalt survey appeared to be a good indicator of metal-on-metal bearing mechanical behavior. According to the author, the absence of detectable wear and, above all, the lack of relationships among increased cobalt level, age and high patient activity are encouraging findings for continued use of metal-on-metal bearings in young and/or active patients.

48. MacDonald, SJ: Can a Safe Level of Metal Ions in Patients with Metal-on-Metal Total Hip Arthoplasties Be Determined? J Arthroplasty 19(8) Supp 3:71-77,2004

The single most significant obstacle preventing a broader application of metal-on-metal hip arthroplasties continues to be the concerns regarding elevated metal ion levels in the blood and urine of patients with this bearing. A safe level for metal ions has yet to be defined for patients with metal-on-metal hip arthroplasties. A review of occupational exposure data gives some insight; however, longitudinal studies of large numbers of patients with metal-on-metal implants will ultimately be required to answer specific clinical concerns. The author notes that there can be no doubt that patients with metal-on-metal implants will be exposed to elevated levels of metal ions locally, in their blood and in their urine. The outstanding question remains the clinical impact of these elevated ion levels. According to the author, there is no conclusive evidence for a detrimental clinical effect. Furthermore, to date, from current publications there is no evidence that prolonged exposure to elevated metal ions produced from a metal-on-metal arthroplasty results in a statistically significant increase in risk of cancer development in these patients.

49. Brodner, W et al: Does the Placenta Inhibit the Passage of Chromium and Cobalt After Metal-on-Metal Total Hip Arthroplasty? J Arthroplasty 19(8) Supp 3:102-106, 2004

Umbilical cord serum and corresponding maternal serum of 3 women with uncemented Metasul total hip arthroplasties were analyzed for cobalt and chromium. The women were an average 3.8 (range 2-5) years after hip surgery. At the time of delivery, the maternal chromium concentrations were 1.6 μg/l, 0.5 μg/l, and 0.9 μg/l, respectively, and the maternal cobalt concentration was 1 μg/l in the first woman and below the detection limit in the other 2. Cobalt and chromium concentrations of the 3 umbilical cord sera were below the detection limit. This indicates that ---with regard to the detection limit in our laboratory---we were unable to observe a passage of cobalt and chromium ions from metal-on-metal articulations across the placenta at the time of delivery.

50. Migaud, H et al: Cementless Metal-on-Metal Hip Arthroplasty in Patients Less than 50 Years of Age. J Arthroplasy 19(8) Supp 3:23-28, 2004

Thirty nine cementless hip arthroplasties using metal-on-metal articulation (Metasul) were consecutively implanted in 30 patients less than 50 years of age and compared to a matched control group (by age, diagnosis, Devane activity, and Harris hip scores) of cementless arthroplasties using ceramic-on polyethylene articulation. The Harris hip score at follow-up (minimum 5 years) for the metal-on-metal was 94.9 (range 74-100). After the same follow-up, the results with the ceramic-on-polyethylene were significantly worse; 9 osteolyses and 7 surgical revisions related to wear (none in the metal-on-metal). Five year survival rates were 97% ±2% for the ceramic-on-polyethylene and 100 % for the metal-on-metal. The metal-on-metal may be recommended to prevent wear problems in younger and more active patients; however, a longer follow-up is required to confirm this encouraging data.

51. Campbell, P et al: Biologic and Tribologic Considerations of Alternative Bearing Surfaces. Clin Orthop 418:98-111, 2004

Patients who are young or active or both who require total joint replacement pose a unique challenge; their high activity demands wear-resistant bearings that will perform for decades, without suffering from the adverse effects of accumulated wear products. The authors discuss the tribologic and biologic properties of newly introduced bearing materials for hip prostheses. The new polyethylenes (PE) are intended to address the aseptic loosening problem by reducing the volume of submicron PE particles to a level well below that historically associated with osteolysis. However, choosing among the several variations of the cross-linked thermally stabilized PEs is confounded by conflicting opinions regarding the optimum balance between long-term wear resistance and mechanical strength, and regarding potential effects of differences in morphologic features of the submicron-sized wear particles on their relative osteolytic potential. Metal-on-metal bearings have clinically proven wear resistance and the advantage of self-polishing, but the long-term biologic effects of metallic ions remain unknown. Ceramic-on ceramic bearing have the advantage of high biocompatibility and usually very low wear, but fracture remains a rare but catastrophic complication. The choice of an appropriate bearing couple should be made after a thorough consideration of the relative risks and potential benefits of each of these materials.

52. MacDonald, SJ: Metal on Metal Total Hip Arthroplasty. Clin Orth 429:86-93, 2004

According to the author, metal on metal bearings are having a resurgence in clinical applications for total hip and knee resurfacing technologies. The most noteworthy advantage is the improved wear characteristics seen in vitro on wear simulators and in vivo with retrieved implants. All bearings have disadvantages, and a metal-on-metal bearing is no exception. Concerns exist regarding the generation of metal ions seen in the blood and urine of patients. These elevated metal ions have theoretical, although not

proven, risks related to carcinogenic and biologic concerns. Additionally, concerns exist regarding hypersensitivity, increased incidence of instability and increased costs. Specific patient selection issues arise with metal-on-metal implants. The current generation of implants has only early and mid-term results available, with no long-term series yet published. Therefore, although a metal bearing may be considered a viable alternative to either polyethylene or ceramic implants, outstanding and unresolved issues continue to exist with this bearing, as they do with the alternatives.

53. Davies, AP et al: An Unusual Lymphocytic Perivascular Infiltration in Tissues Around Contemporary Metal-on-Metal Joint Replacements. JBJS 87-A (1):18-27, 2005

Tissue samples obtained from hips with metal-on-metal implants displayed a pattern of well-demarcated tissue layers. A prominent feature, seen in seventeen of twenty five tissue samples, was a pattern of perivascular infiltration of lymphocytes. In ten of the tissue samples obtained from hips with metal-on-metal prostheses, there was also an accumulation of plasma cells in association with macrophages that contained metallic wear debris particles. The surfaces of tissues obtained from hips with metal-on-metal prostheses were more ulcerated than those obtained from hips with other types of implants, particularly in the region immediately superficial to areas of perivascular lymphocytic infiltration. The lymphocytic infiltration was more pronounced in samples obtained at the time of revision because of aseptic failure than in samples retrieved at the time of autopsy or during arthrotomy for reasons other than aseptic failure. Total joint replacement and surface replacement designs of metal-on-metal prostheses were associated with similar results. Tissue samples obtained from hips with metal-on-polyethylene implants showed far less surface ulceration, much less distinction between tissue layers, no pattern of lymphocytic infiltration, and no plasma cells. The inflammation was predominantly histiocytic. Tissues retrieved from hips undergoing primary joint replacement showed dense scar tissue and minimal inflammation. The pattern and type of inflammation seen in periprosthetic tissues obtained from hips with metal-on-metal and metal-on-polyethylene implants are very different. At the present time, the authors do not know the prevalence or clinical implications of these histologic findings, but suggest that they may represent a novel mode of failure for some metal-on-metal joint replacements.

54. Dorr, LD et al: The Argument for the Use of Metasul as an Articulation Surface in Total Hip Replacement. Clin Orth Rel Res 429:80-85, 2004

Metasul metal- on- metal articulations have been used for 15 years in approximately 300,000 total hip replacements. The authors have used Metasul articulations in three clinical studies and have shown clinical success as measured by Harris Hip Scores and patient self-assessment. The authors have noted the usual mechanical complications. The only complications have been mechanical, including two cup loosenings and 24 dislocations in a total of 582 patients (619 hips; 3.8%) who had Metasul articulations and were included in these studies. In the randomized study, the group who had Metasul articulations had no clinical results or complications different from the control ceramic-

on-polyethylene group. Authors of retrieval results in the literature report low annual linear wear rates and no consequences of elevated Co ion levels. Currently, the scientific evidence of the results using the Metasul articulation would recommend its continued use in any patient who does not have compromised renal function.

55. Dumbleton, JH and Manley, MT: Metal on Metal Total Hip Replacement-What Does the Literature Say? J. Arthroplasty 20(2):174-187, 2005

Second generation metal-on-metal (M/M) total hip replacements were introduced into clinical use in the late 1980s and demonstrate equivalent survivorship to conventional metal-on-polyethylene prostheses. Wear rates are comparable to those of first generation designs that survived for a long time in the body. Biological effects from metal ions remain a concern. Patients with both first and second generation M/M hips have higher levels of cobalt and chromium in their blood and urine than either patients with metal-on-polyethylene devices or unoperated patients. Concerns include the potential for acquired hypersensitivity, mutagenicity, and carcinogenicity. However, reports of proven adverse effects are scant. Prospective, randomized trials with follow-up in excess of 15 years will be needed to differentiate between the performance and effects of M/M and other bearing combinations. According to the authors, the literature does not address the long-term risks with M/M bearings. It appears reasonable to assume that the biological risk is higher than for metal-on-polyethylene, ceramic-on-polyethylene, or ceramic-on-ceramic bearings because of a demonstrated higher level of metal ion release. It also appears reasonable to assume that the risk increases with time of implantation.

56. Park, Y-S et al: Early Osteolysis Following Second Generation Metal-on-Metal Hip Replacement. JBJS 87-A (7):1515-21, 2005

The authors analyzed 165 patients (169 hips) who had undergone primary cementless total hip replacement with a contemporary (Ultima-DePuy) metal on metal bearing cup design between 2000 and 2002. After a minimum duration of follow-up of 23 months, nine patients (10 hips) had an osteolytic lesion localized to the greater trochanter. Skin patch tests for hypersensitivity to metals were performed on the nine patients and on nine randomly selected patients with total hip replacements who did not have osteolytic changes and who were matched to the study cohort for age and gender. Microbiological cultures, histopathologic examinations, and immunohistochemical analysis were performed on samples of periprosthetic tissue that were collected during revision arthroplasy on two hips with early osteolysis. The patients with early osteolysis had a significantly higher rate of hypersensitivity reaction to cobalt compared with controls ($p=0.031$). The retrieved periprosthetic tissues showed no evidence of metallic staining, but histologic analysis revealed a perivascular accumulation of CD3-positive T-cells and CD68-positive macrophages and an absence of both particle-laden macrophages and polymorphonuclear cells. Immunohistochemical analysis demonstrated that bone-resorbing cytokines such as IL-1β and TNF-α were produced mainly by infiltrating lymphocytes and activated macrophages. According to the authors, these findings raise the possibility that early osteolysis in patients with this second generation metal-on-metal hip replacement is associated with abnormalities consistent with delayed-type

hypersensitivity to metal. A prospective study in which a large group of patients is evaluated with multiple diagnostic methods is needed in order to establish whether there is a causal relationship between metal hypersensitivity and osteolysis.

57. Clarke, MT et al: Long-Term Clinical, Radiological and Histopathological Follow-Up of a Well-Fixed McKee-Farrar Metal-on-Metal Total Hip Arthroplasty. J. Arthroplasty 20(4):542-6, 2005

The authors present a unique postmortem case of a well-fixed metal-on-metal, McKee-Farrar total hip arthroplasty implanted 30 years previously that was clinically asymptomatic in life. The total hip arthroplasty was found to be well fixed without evidence of loosening, wear particle formation or adverse tissue reactions. Although a full tribological bearing analysis of this retrieval was hindered by the lack of pre-implantation measurements, the data available would support a low estimated linear wear rate of less than 2μm per year. This wear rate is in agreement with data from in vitro simulation where large diameter MOM bearings have achieved similar wear rates under a variety of simulator conditions. For contemporary MOM bearings, a deviation from roundness of less than 10 μm, surface roughness less than 0.05 μm and diametric clearance between 50 and 250 μm are considered desirable. This case highlights the observation that when the tribological conditions are met, MOM bearings are tolerated by the host and can function for long periods with little wear.