

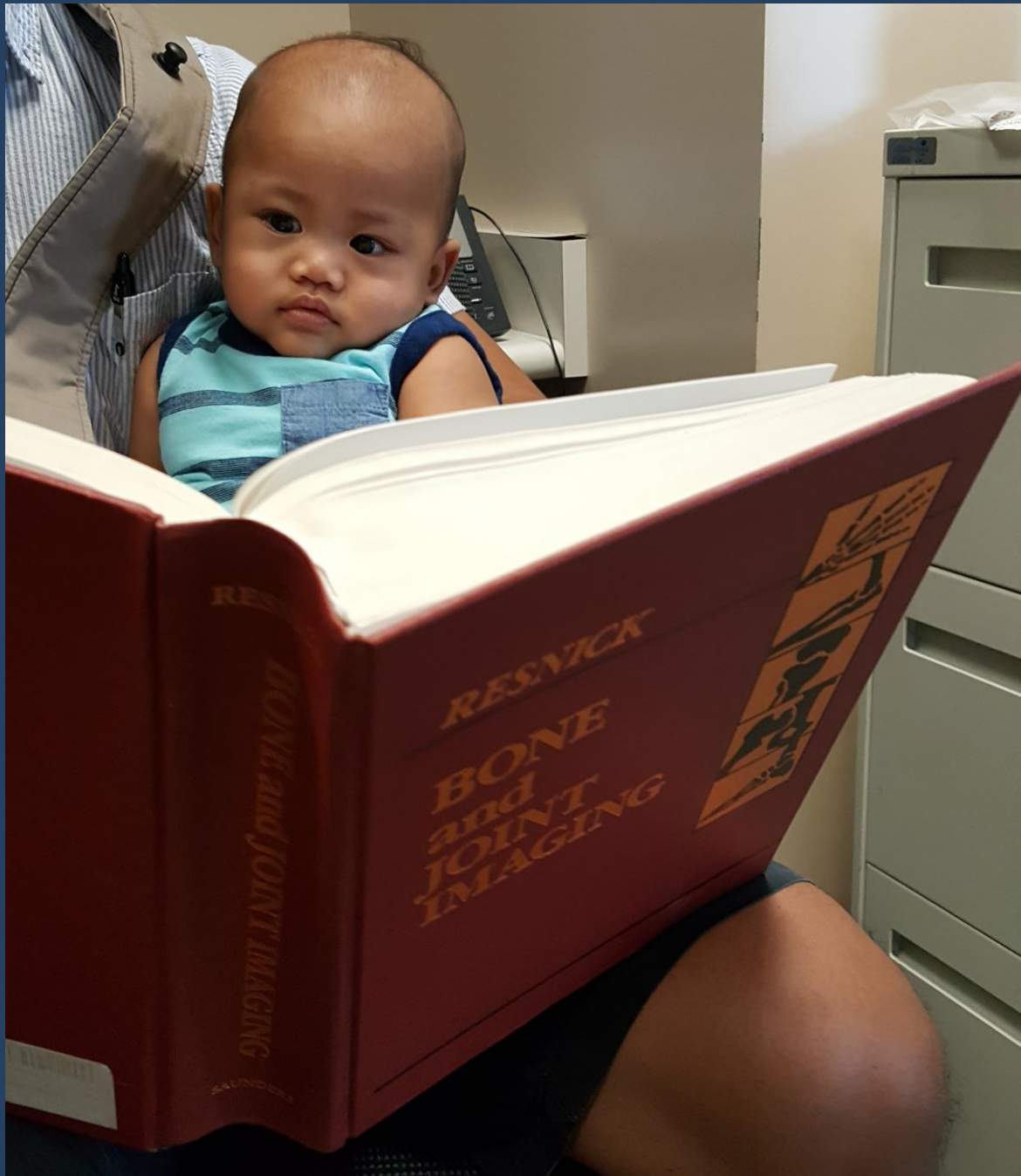


**ADVERSE REACTION TO METAL  
DEBRI**  
**Hip Arthroplasty**

Peachy Mae T. Piana, MD

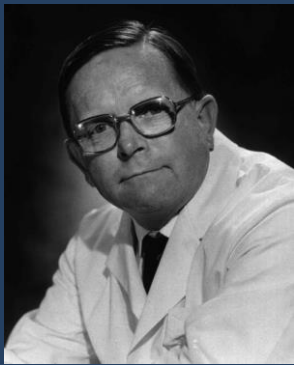
# OUTLINE

- History of Total Hip Arthroplasty
- MoM Prosthesis
- Production of Metal Particles
- Defining Terminology: Metallosis, ARMD, ALTR, ALVAL, pseudotumor, periprosthetic reactive masses
- Etiology of ARMD
- Risk Factors of ARMD
- Presentation
- Management of patients with MOM prosthesis
- Imaging findings
- Differential Diagnosis
- Treatment



# PAST: Hip Arthroplasty

- 1891: Earliest recorded attempt in Germany
  - use of ivory to replace femoral heads to treat TB
- Late 19<sup>th</sup> and early 20<sup>th</sup> century: Interpositional arthroplasty
  - utilizing various tissues (fascia lata, skin, pig bladders submucosa) between articulating surfaces of the arthritic hip
- 1925: Marius Smith-Petersen and Philip Wiles
  - first stainless steel total hip prosthesis that was fitted to bone with bolts and screws



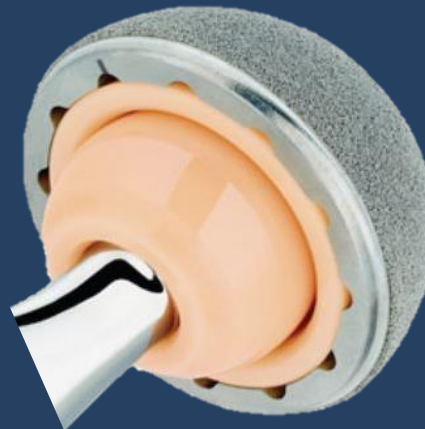
# PAST: Hip Arthroplasty

- 1953: George McKee
  - First to use a metal-on-metal prosthesis on a regular basis
  - Modified Thompson stem + one-piece cobalt-chrome socket as the new acetabulum
  - 28 year survival rate of 74%
  - Fell out of favor in mid-1970's due to local effects of metal particles seen during revision surgery for prosthetic failure
- 1960's: **Sir John Charnley** – Father of modern THA
  - Low friction arthroplasty- small femoral head reduces wear due to its smaller surface area
  - Metal femoral stem + polyethylene acetabular component and acrylic bone cement

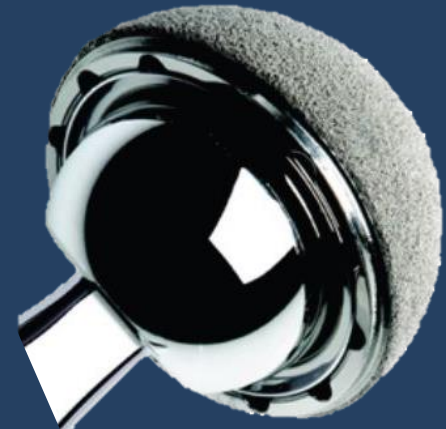
# PRESENT: Modern Bearing Surfaces



Metal on Polyethylene  
(MoP)



Ceramic on Ceramic  
(CoC)



Metal on Metal  
(MoM)

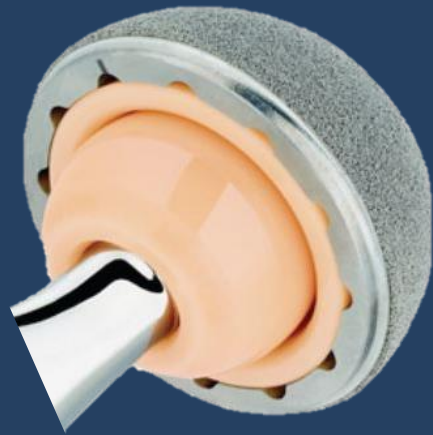
# PRESENT: Modern Bearing Surfaces



Metal on Polyethylene  
(MoP)

- Advantages:
  - Most commonly used
  - Large volume of evidence to support use
  - Predictable lifespan
  - Cost effective
- Disadvantage
  - Polyethylene debris leading to aseptic loosening
  - Particle Disease
  - High debris particles, high reactivity

# PRESENT: Modern Bearing Surfaces



Ceramic on Ceramic  
(CoC)

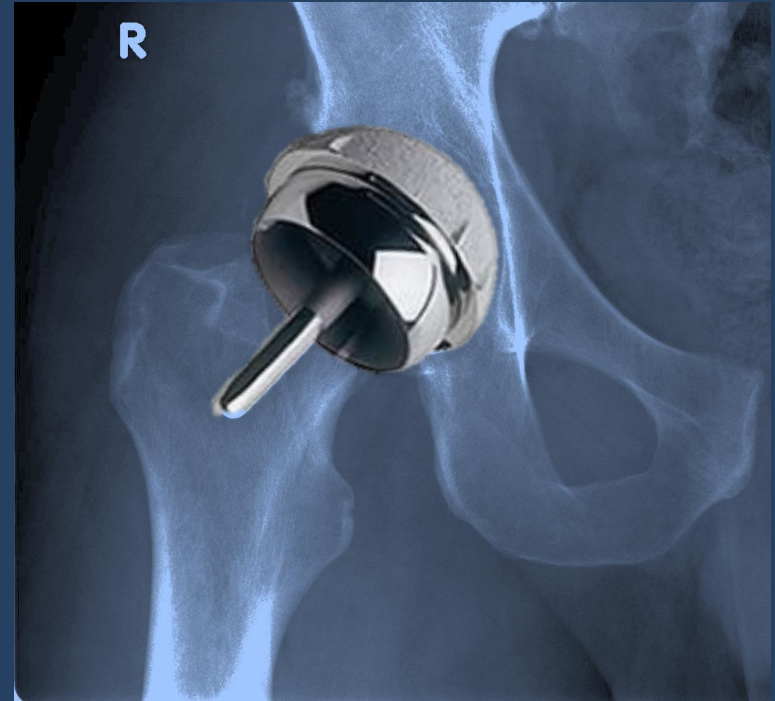
Ceramic on Metal (COM)-Not shown

Ceramic on Polyethylene (CoP)- Not shown

- 1970: French surgeon Pierre Boutin
- Developed to address problems of friction and wear
- Benefits:
  - Low friction
  - Low debris particles
  - Inert debris
  - Good choice for young and active patients due to reduced wear
- Disadvantages
  - \$\$\$\$
  - High fracture rate of first generation ceramic bearings
  - Produce noise on movement



# MoM Prosthesis



# PRESENT: Modern Bearing Surfaces



Metal on Metal  
(MoM)

- Advantages of THA:
  - Smooth and hard surface
  - Wear rate of MoM 60x less than MoP
  - Potentially longer lifespan than polyethylene due to reduced wear
  - Large femoral head → increase stability and lower dislocation rate
- Traditionally used to treat painful osteoarthritis particularly in young active patients with good bone stock (men aged <65 yrs and women aged <60 yrs)
- HRA: conserves bone and lead to improved revision outcomes

# Failing MOM prosthesis

- ~1 in 5 MoM hip replacements revised 10-13 years after insertion
  - Higher risk in larger head sizes ( $\geq 36$  mm)
- ~13% of hip resurfacing revised 10 yrs after insertion
- MoP revised <4% of cases 10 yrs after insertion

What is causing the increased revision rates of MoM prosthesis?

Metallosis

&

Adverse Reaction to Metal Debris  
(ARMD)

# Production of Metal Particles



- Mechanical wear of bearing surfaces
- Corrosion
- Trunnionosis (modular junctions)

# Production of Metal Particles



- Mechanical wear of bearing surfaces
  - Abrasion from normally positioned metallic WB surfaces

# Production of Metal Particles



- Mechanical wear of bearing surfaces
  - Edge loading from abnormally positioned acetabular component

# Production of Metal Particles



- Mechanical wear of bearing surfaces
  - Edge loading from abnormally positioned acetabular component



# Production of Metal Particles



- Mechanical wear of bearing surfaces
  - Neck on cup impingement

# Production of Metal Particles



## **PINCER TYPE IMPINGEMENT:**

Excessive anteversion of acetabular component resulting in impingement of metal liner and notching on the posterior aspect of the femoral stem.

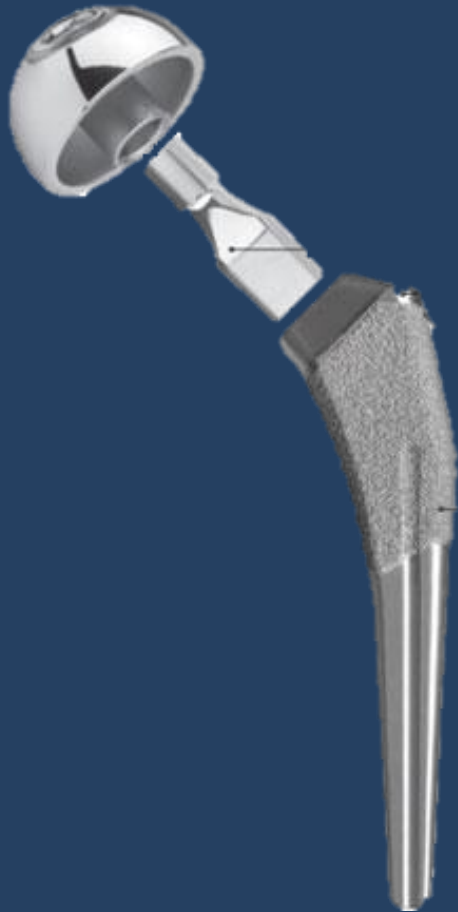
- Mechanical wear of bearing surfaces
  - Neck on cup impingement
    - **Pincer type:** inadequate removal of acetabular osteophytes and malposition of acetabular components
    - **CAM type:** small head-to-neck ratio
    - **Mix type**
    - Occur early or late following loosening and substantial rotation of acetabular cup

# Production of Metal Particles



- Corrosion
  - Deterioration of metal through an electrochemical process of oxidation and reduction reactions producing metal ions
  - Most common form is rust
  - Requirement for metal components to have high corrosion resistance by formation of a passive surface film to prevent oxidation
    - Disrupted in vivo by fretting and micromotion
  - Tribocorrosion: complex interaction where corrosion hastens wear and vice versa
  - Metal release from corrosion can cause particle deposition within local tissues & elevated serum metal levels causing metallosis & adverse reaction to metal debris
  - Prevalence of corrosion among retrieved specimens ranged from 0%-57% at 0.5-5.5 years

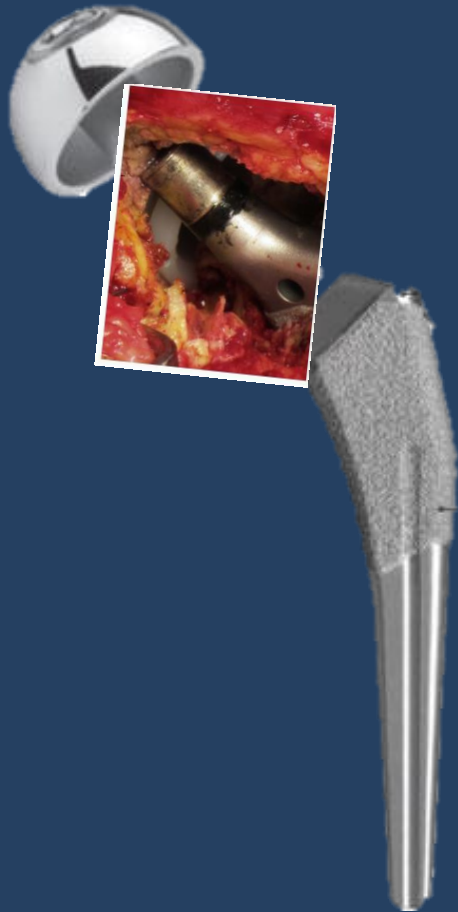
# Where does wear & corrosion occur in non-MoM THA?



- Adverse reaction to metal debris have been typically defined in the context of the bearing surfaces of MoM hip arthroplasty
- But similar findings have been more recently described in non-MoM prosthesis...
- **TRUNNIONOSIS:** Wear and/or corrosion at a tapered modular interface with resultant metal ion release most commonly at the head-neck junction.

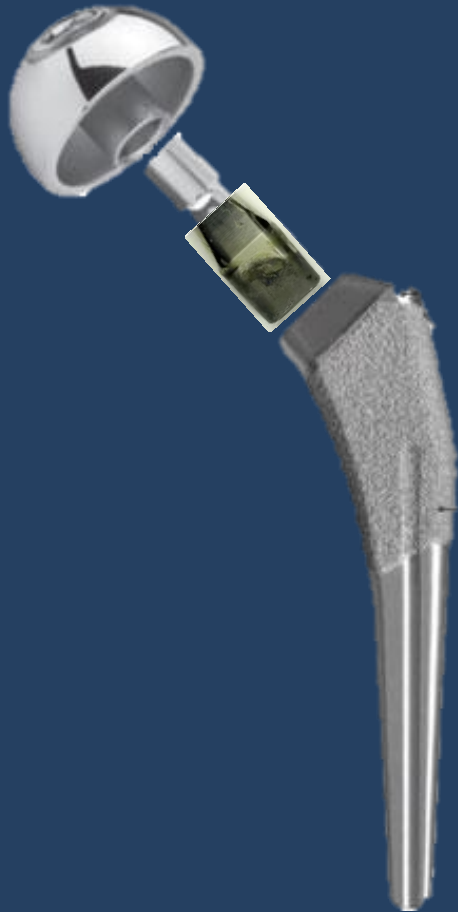
**MODULAR DESIGN**

# Where does wear & corrosion occur in non-MoM THA?



- Trunnion originates from the French word *trognon* meaning stump; a pin or pivot on which something can be rotated or tilted
- Trunnion- cylindrical protrusion forming one half of a modular interface
- Modular interfaces
  - \*Head-Neck junction
  - Neck-Body junctions
  - Mid-Stem junctions
- Thought to account for the adverse reaction to metal debris regardless of bearing surface

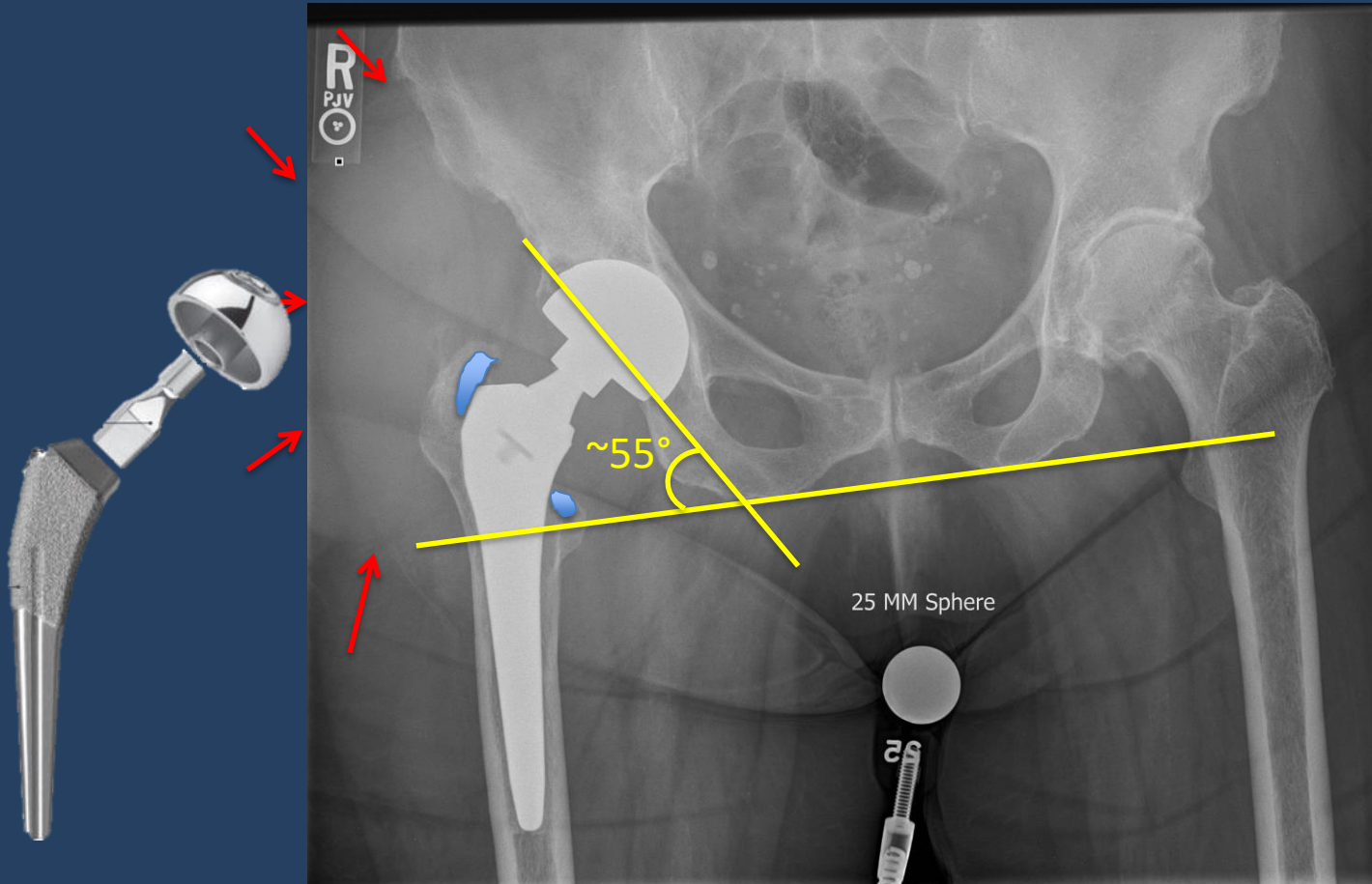
# Where does wear & corrosion occur in non-MoM THA?



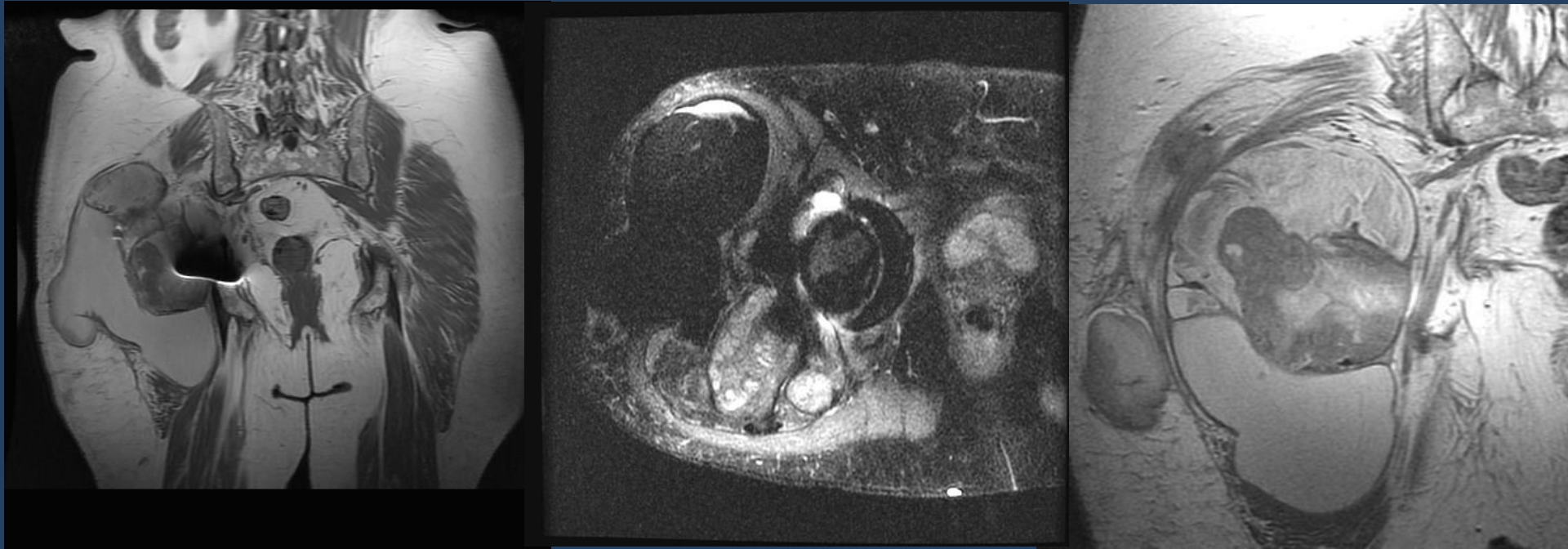
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- Thought to account for the adverse reaction to metal debris regardless of bearing surface

CASE: 81 yo F with **Wright medical Mom with a large femoral head and Profemur Z modular femoral neck THA** in 2011 with worsening right hip pain.  
NI WBC. NI Serum Chromium. Elevated Serum Cobalt at 13.1  $\mu\text{g/L}$  (nl  $\leq 1$ ).



ALTR to MoM with a large femoral head &  
modular femoral component THA.



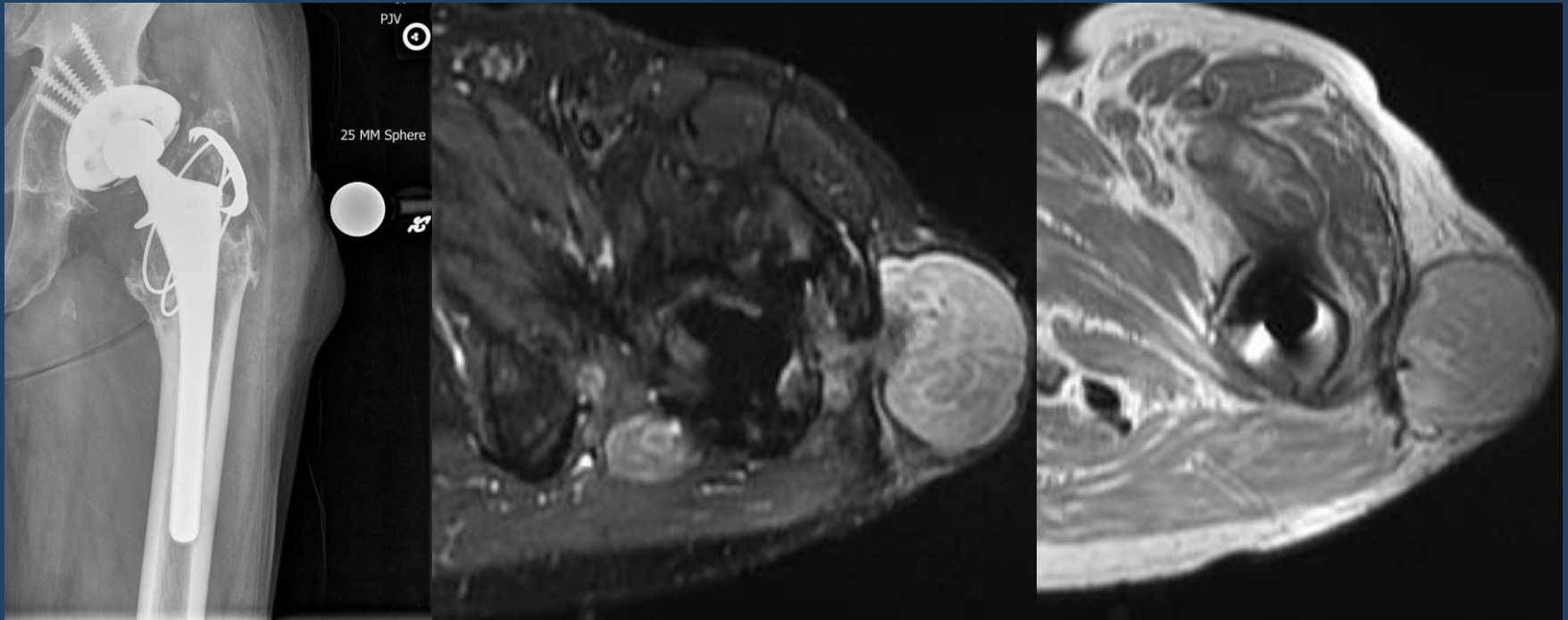


# ALTR to MoM with a large femoral head & modular femoral neck THA.



CASE: 69-year-old with **MoP** present with a left hip mass nearly tripled in size over the last 2 years.

**Serum Cobalt = 11.9 microgram/L (<=1). Serum Chromium serum= 3 microg/L (<=5)**



Particle disease with polyethylene wear-induced synovitis  
VS  
Particle disease with ARMD through metal corrosion???

# CONFUSING TERMINOLOGY

- ALTR- Adverse Local Tissue Reaction
- ARMD- Adverse Reaction to Metal Debris
- Metallosis
- ALVAL- Aseptic Lymphocytic Vasculitis-Associated Lesions
- Periprosthetic reactive mass
- Inflammatory pseudotumor

???!?



?

# ALTR/ARMD

?

Metallosis  
(FB Reaction)

ALVAL  
(Type 4

Delayed Hypersensitivity Reaction)

True Metal Allergy  
(Type 1 Hypersensitivity)

ALTR = ARMD = ALVAL = Pseudotumors

Metallosis

ALTR/ARMD/ALVAL/Pseudotumor

# Metallosis

- Chronic inflammatory process caused by the infiltration of periprosthetic soft tissues and bone by metallic debris from mechanical wear--> aseptic fibrosis, local necrosis or loosening of a device.
- Described in total hip, total shoulder, total knee and unicompartmental knee arthroplasties.
- Increased frequency in titanium prostheses compared to chromium-cobalt prosthesis suggesting increased propensity for wear
- Grossly appears as oily black fluid in the joint and grey/black discoloration of the periprosthetic soft tissue

# Metallosis Pathophysiology



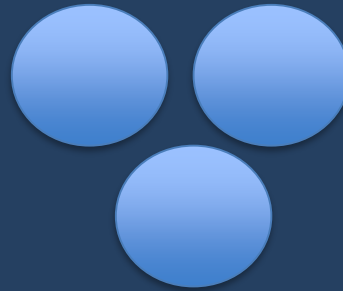
# Metallosis Pathophysiology



# Metallosis Pathophysiology

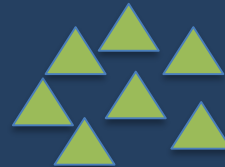


METAL PARTICLES

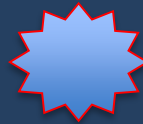


FOREIGN BODY RESPONSE

MACROPHAGES  
MULTINUCLEATED GIANT CELLS



RELEASE OF CYTOKINES



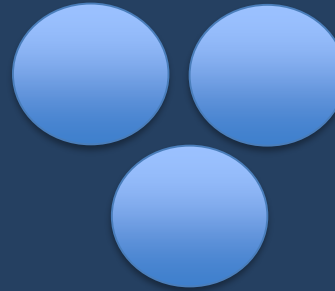
ACTIVATE OSTEOCLAST



# Metallosis Pathophysiology

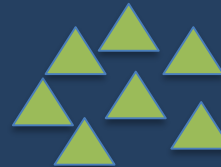


METAL PARTICLES

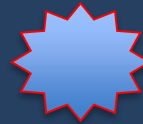


FOREIGN BODY RESPONSE

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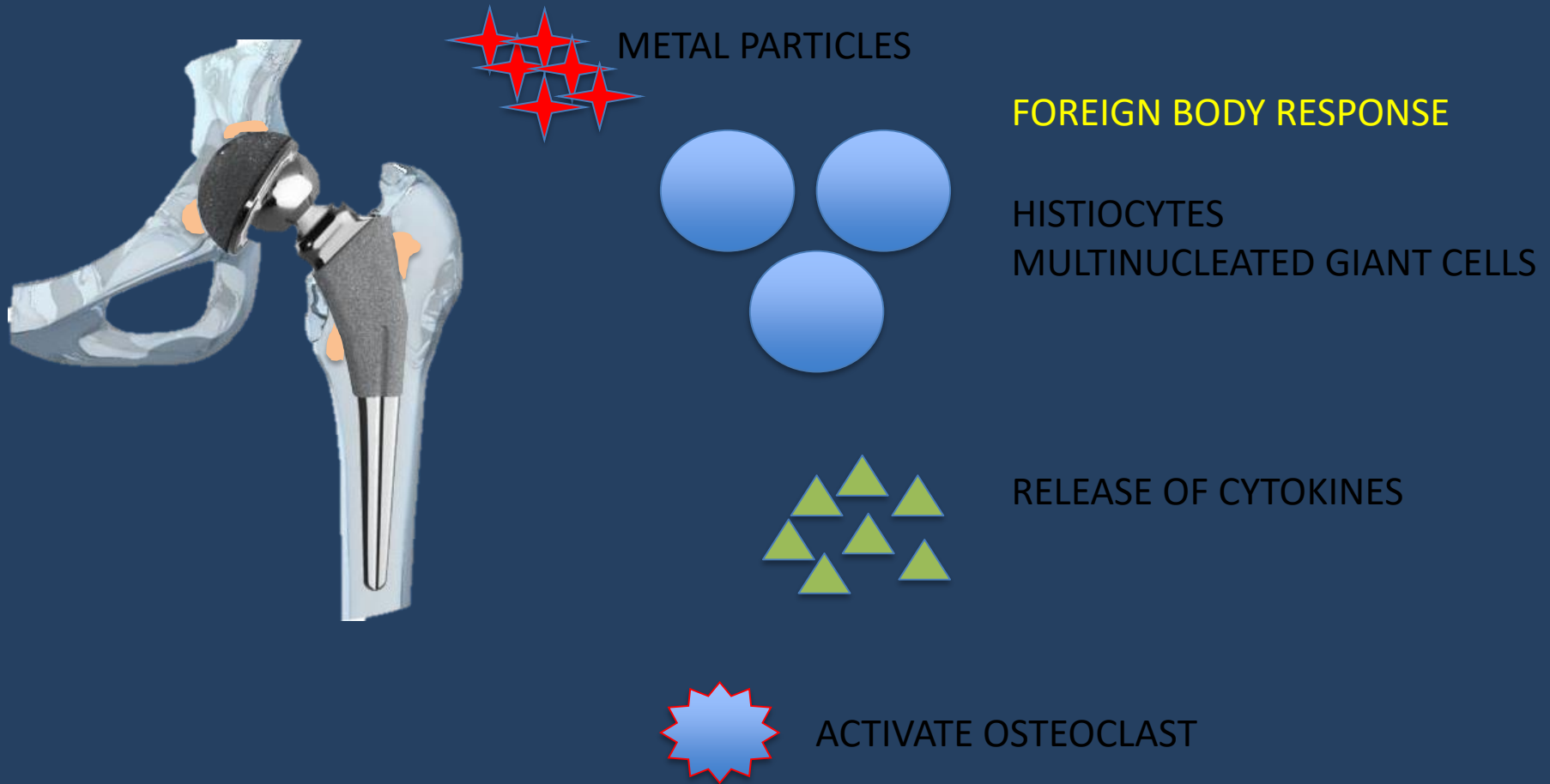


RELEASE OF CYTOKINES

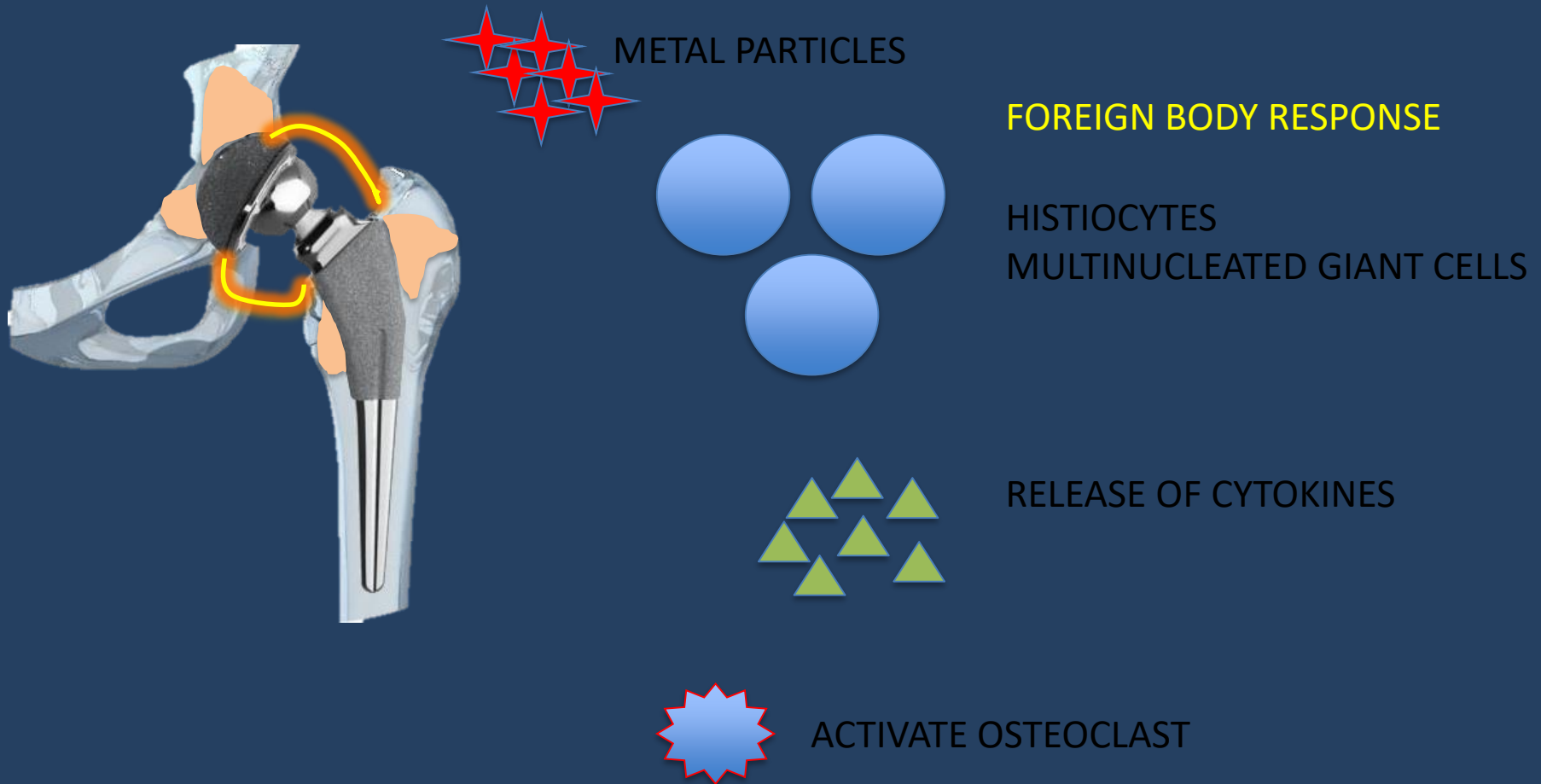


ACTIVATE OSTEOCLAST

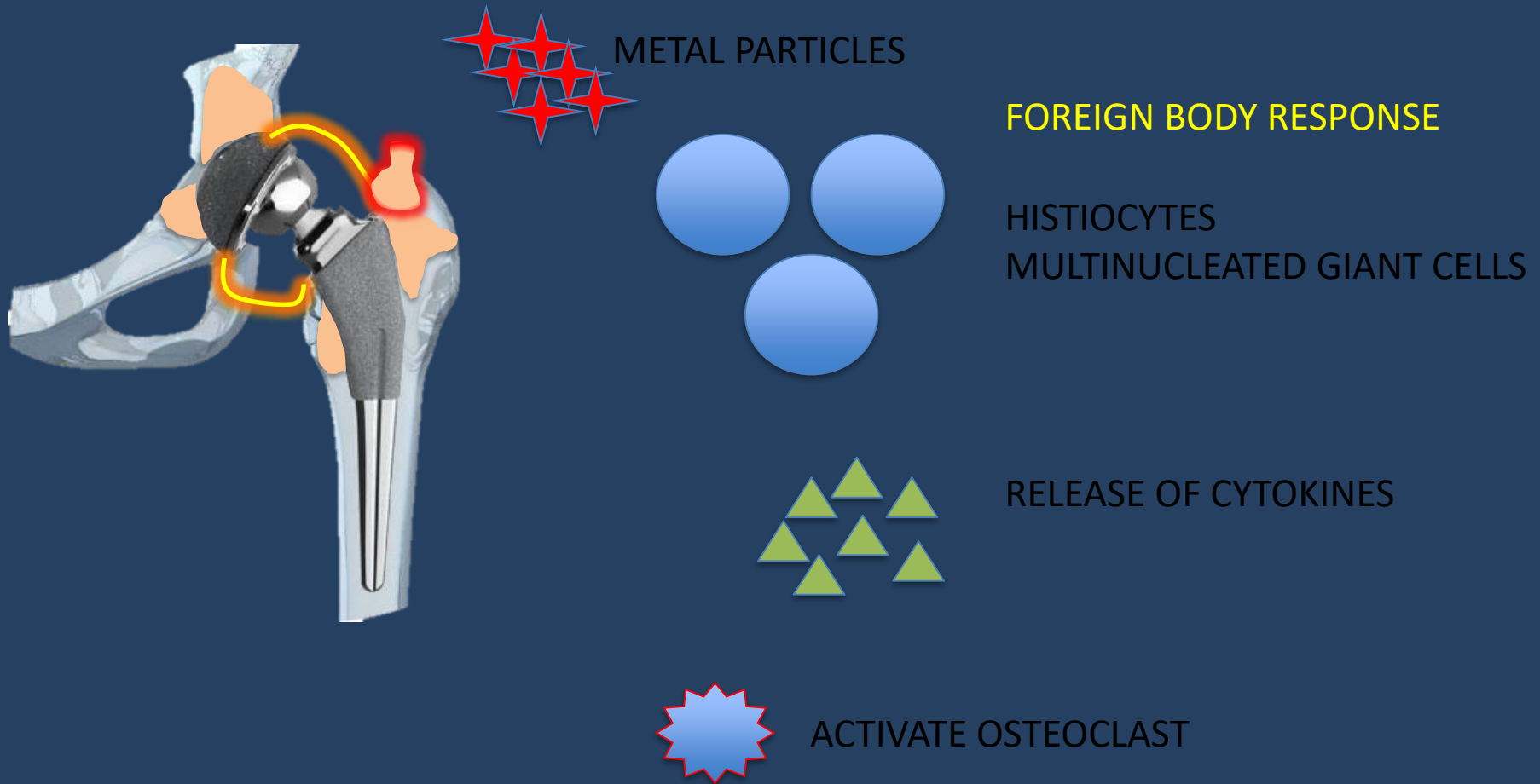
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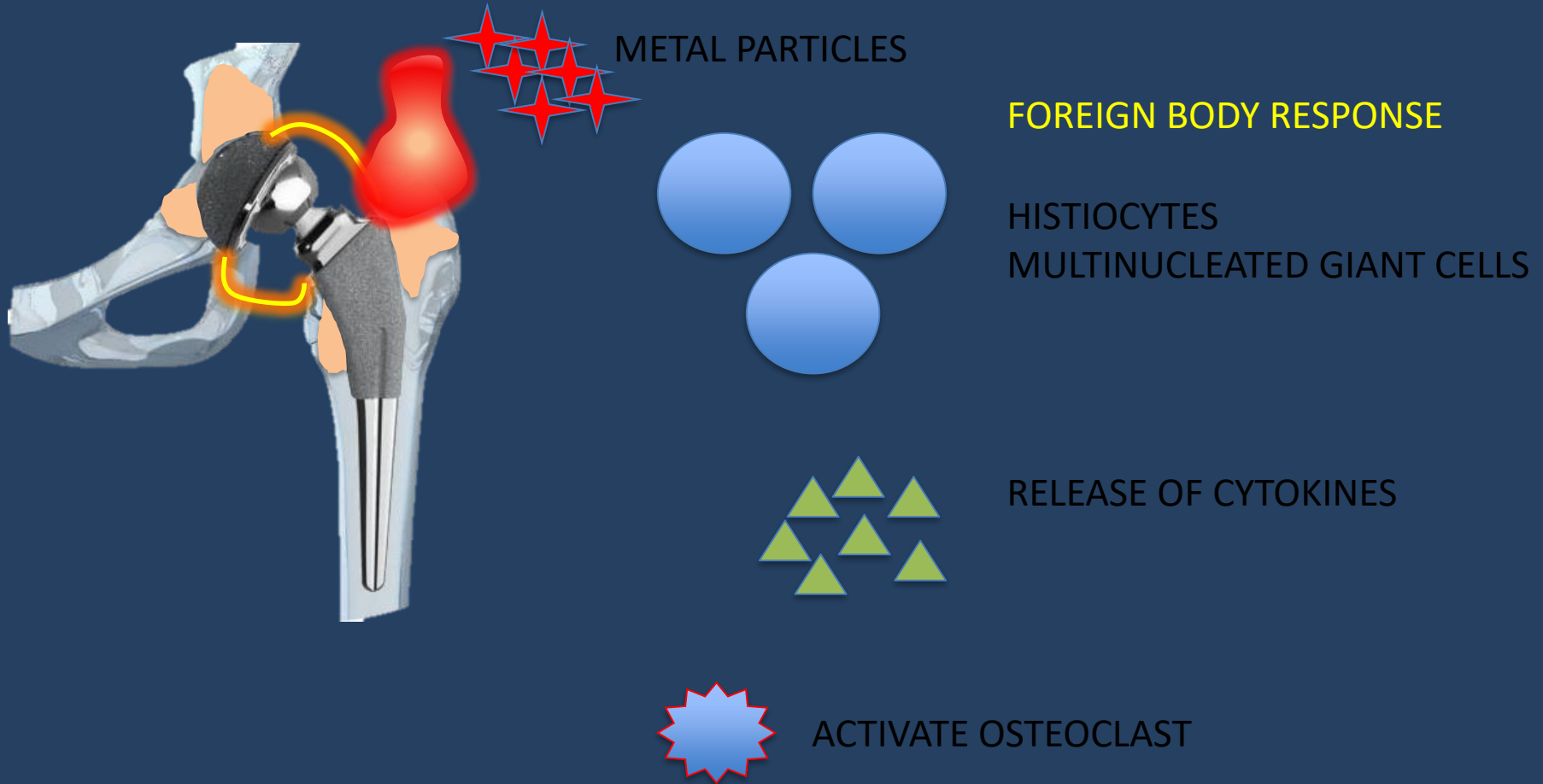
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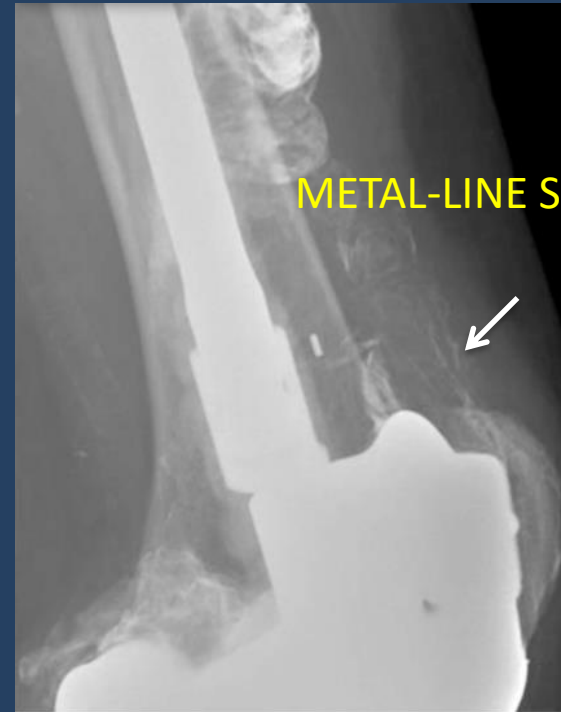
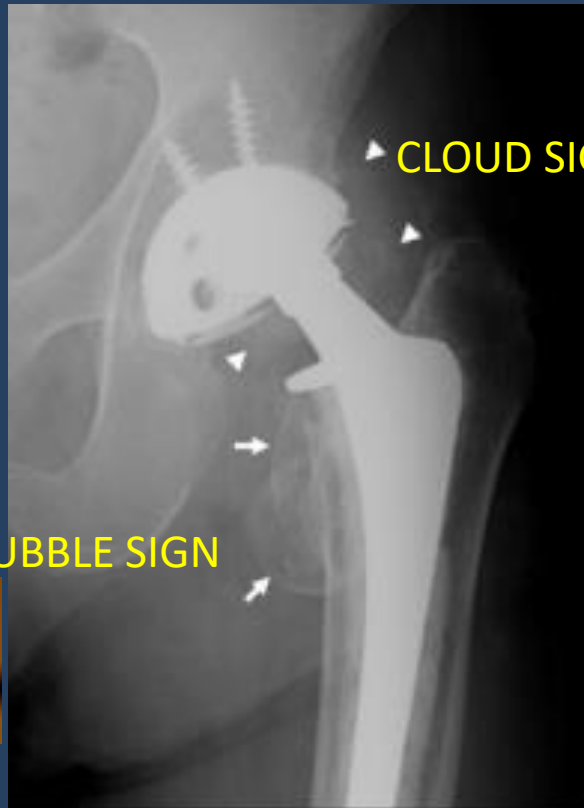
# Metallosis Pathophysiology



# Metallosis Pathophysiology



# Imaging Findings: Metallosis



BUBBLE SIGN

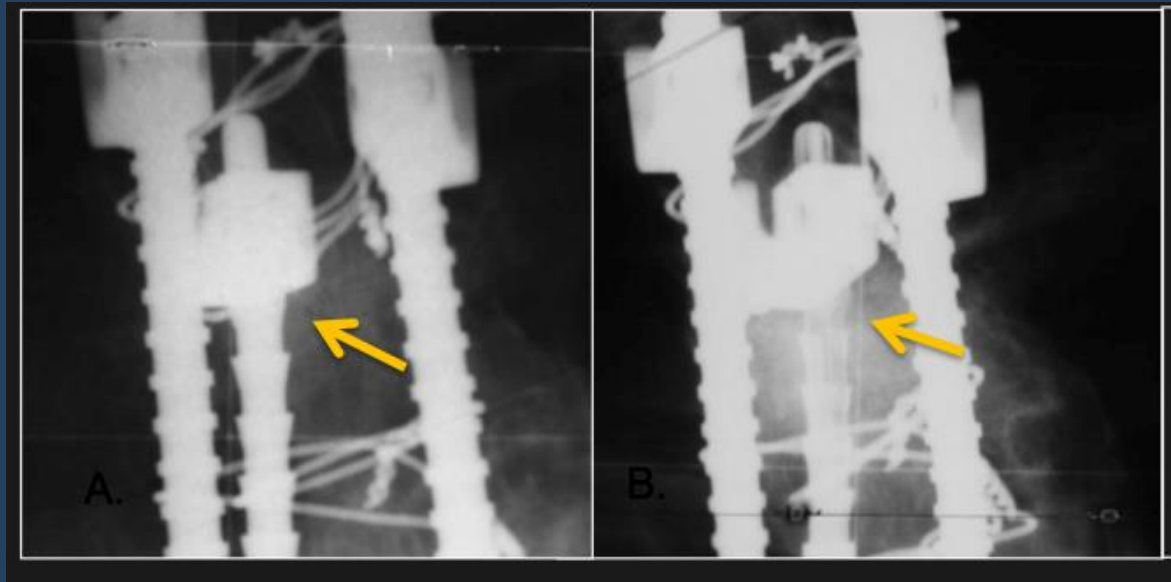
CLOUD SIGN

METAL-LINE SIGN



# Imaging Findings: Metallosis

## METAL FADE SIGN



POST-OP

7 YEARS AFTER SURGERY

# Adverse local tissue reaction (ALTR)

- Umbrella term describing all periprosthetic adverse reaction
- Spectrum of abnormality include osteolysis, periprosthetic soft tissue masses/pseudotumors, to extensive necrosis.



# Adverse Reaction to Metal Debris (ARMD)

- Often used synonymously with ALTR, inflammatory pseudotumor, ALVAL.
- Umbrella term describing all periprosthetic reactions attributable to metal alloy
- Spectrum of abnormality include asymptomatic small cysts to large soft tissue masses/pseudotumors.

## Inflammatory Pseudotumor/ Periprosthetic Reactive Mass:

- Imprecise definition and correspond to a wide variety of imaging appearances
- Describes the **clinical** and **radiologic** presentation of an aseptic periprosthetic solid or cystic mass.
- Can be seen in foreign body reactions such as in particle disease or metallosis as well as in ARMD/ALTR.

# ALVAL

Aseptic

Lymphocyte mediated

Vasculitis

Associated

Lesions

# Aseptic lymphocytic vasculitis-associated lesions (ALVAL)

- **Histologic diagnosis** describing the unique cellular change that occur in **aseptic** periprosthetic masses in response to metal ions namely cobalt and chromium ions.
- Believed to be a **T-lymphocyte** mediated **type IV hypersensitivity reaction** with tissue damage occurring as a result of cytotoxic T cells and activated monocytes/macrophages.

# METALLOSIS vs ARMD

- Wear related
  - Foreign body reaction to metal debris
  - Predominantly macrophage and MNGC-mediated response
  - Osteolysis
  - >Titanium
- Metal sensitivity
  - Type-IV delayed hypersensitivity reaction to metal ions
  - Predominantly lymphocyte-mediated response
  - Soft tissue damage, necrosis and pseudotumor formation
  - >Chromium and Cobalt

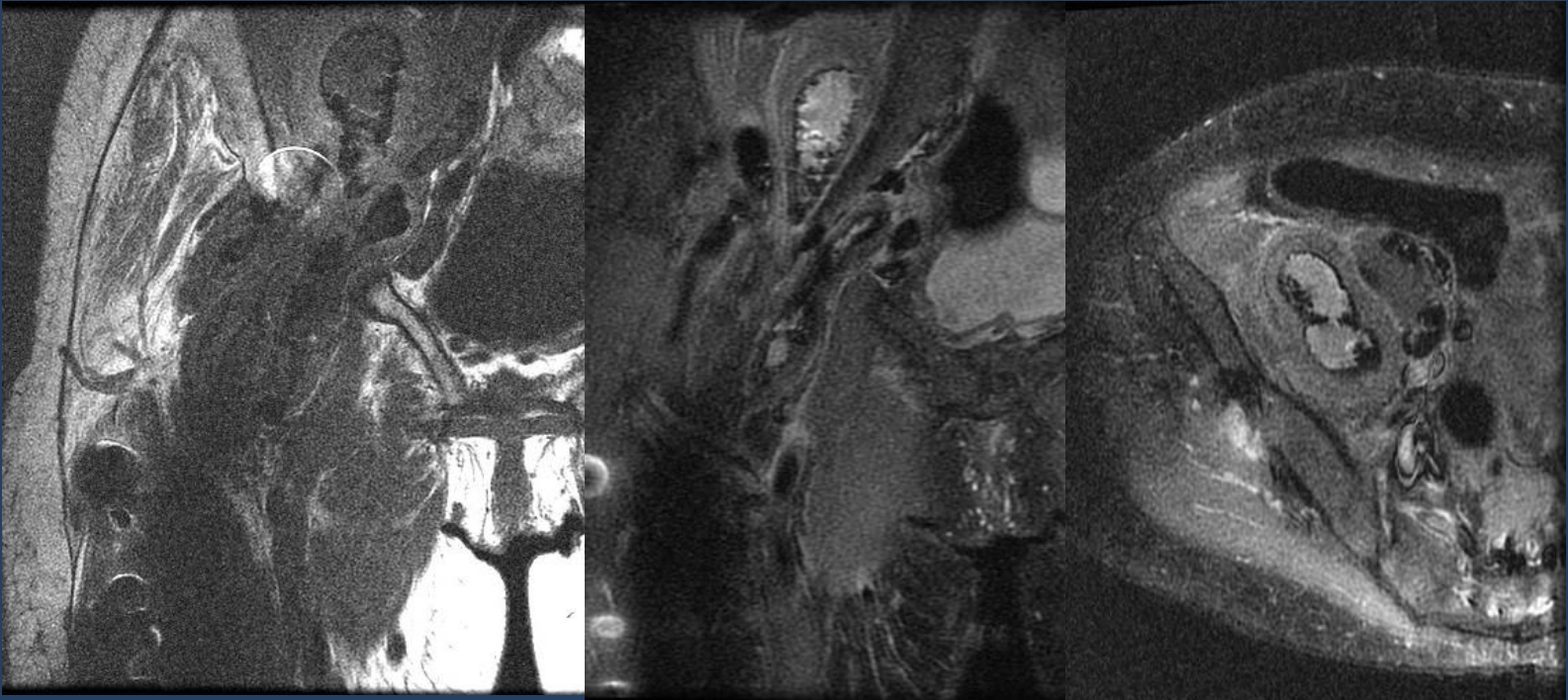
Same spectrum of disease vs separate process?  
Usually an overlap between the two: metallosis is frequently seen in joints with ARMD.

CASE: 71 yo M with **MoM THA** 8 yrs ago presents with vague right hip and buttock pain as well as decreased ROM of the hip.



Chromium= 17.2 elevated (<5) ug/L  
Cobalt= 67.1 elevated (<1 ug/L)

CASE: 71 yo M with MoM THA 8 yrs ago presents with vague right hip and buttock pain as well as decreased ROM of the hip.



**Metallosis with ARMD**

Unfortunately, it is not that simple...

Pseudotumors in ARMD found to be  
also wear related!



## **Histological Features of Pseudotumor-like Tissues From Metal-on-Metal Hips**

**Pat Campbell PhD, Edward Ebramzadeh PhD,  
Scott Nelson MD, Karren Takamura BA,  
Koen De Smet MD, Harlan C. Amstutz MD**

- 32 samples from 32 revised MoM hip replacements with pseudotumor-like reactions
- Used a 10 point grading scale to rank the degree of ALVAL by examining synovial lining integrity, inflammatory cell infiltrates, and tissue organization.
- Quantified implant wear
- Cases divided into pts suspected of having HIGH WEAR vs METAL HYPERSENSITIVITY based on clinical, radiographic, and retrieval findings

**Table 1.** Histologic scoring criteria for ALVAL score

Points	Synovial lining
0	Intact synovial lining
1	Focal loss of synovial surface, fibrin attachment may occur
2	Moderate to marked loss of synovial surface, fibrin attachment
3	Complete loss of synovium, abundant attached fibrin and /or necrosis of lining tissue
Points	Inflammatory infiltrate
0	Minimal inflammatory cell infiltrates
1	Predominantly macrophages, occasional lymphocytes may occur
2	Mix of macrophages and lymphocytes, either diffuse and/or small (< 50% of hpf) perivascular aggregates
3	Mix of macrophages and lymphocytes, large (> 50% hpf) perivascular aggregates may occur
4	Predominantly lymphocytes, mostly in multiple, large (> 50% hpf) perivascular aggregates, follicles may be present
Points	Tissue organization
0	Normal tissue arrangement
1	Mostly normal tissue arrangement, small areas of synovial hyperplasia, focal necrosis may occur
2	Marked loss of normal arrangement, appearance of distinct cellular and acellular zones, thick fibrous layers may occur
3	Perivascular lymphocytic aggregates mostly located distally, thick acellular areas may occur

Sum  
Low = 0–4  
Moderate = 5–8  
High = 9–10

Results of the semiquantitative evaluation of histologic features for cases revised for suspected high wear and for unexplained pain/suspected metal sensitivity.

Variable (p value)	Suspected wear related		Suspected metal sensitivity	
	Average	SD	Average	SD
ALVAL score (p < 0.001)	3.6	2.5	8.5	1.4
Macrophages (p < 0.001)	2.7	0.5	1.7	0.5
Lymphocytes (p = 0.001)	1.4	0.6	2.5	0.7
Metal particles (p = 0.008)	1.5	0.7	0.7	0.5
Necrosis (p = 0.29)	1.0	0.7	1.4	0.7
Tidemark (p = 0.03)	0.2	0.4	0.7	0.5

# Conclusion

- Pseudotumors from ARMD can be seen in both high wear (metal reactivity) and low wear (metal sensitivity).
- Histologic features including synovial integrity, inflammatory cell infiltrates, tissue organization, and metal particles may help differentiate these causes.
- Metal sensitivity should be considered in patients with painful hips with periprosthetic masses if high-wear is excluded.

# RISK FACTORS FOR ADVERSE REACTION TO METAL DEBRI



SURGEON

Acetabular  
malpositioning



PATIENT

Female  
Preoperative  
sensitization to metal?



HARDWARE

MoM  
Modular Design non-MoM  
Optimize fit of femoral head  
and acetabulum

Campbell et al. Histological Features of Pseudotumor-like Tissues From Metal-on-Metal Hips. Clin OrthopRelat Res (2010) 468:2321-2327.

Bestic et al. Current Concepts in Hip Arthroplasty Imaging: Metal-on-Metal Prostheses, Their Complications, and Imaging Strategies. Semin Roentgenol. 2013 Apr;48(2):178-86.

# CLINICAL PRESENTATION

- Suspect in MoM, MoP, and THA with modular components
- Variable presentation including asymptomatic, mild discomfort, severe hip pain, palpable mass, dislocation, and neuropathy
- May present months or years after surgery

# LABORATORY WORKUP

- Serum cobalt and chromium levels
- No correlation was found between serum cobalt and/or chromium ion levels and the extent of necrosis, degree of macrophage infiltration, or ALVAL score.
- Patients with markedly elevated metal ions tend to have high ALVAL score.
- Although high ion levels are elevated in most MoM failures, a normal metal ion level does not exclude the diagnosis.

# RADIOLOGIC WORKUP



# RADIOGRAPHS

- Standard imaging exam
- Baseline and follow-up XR most useful in evaluating component position and integrity
- Easy diagnosis of common complications
  - Mechanic loosening/subsidence, osteolysis, periprosthetic fracture, and heterotopic ossification
- Pseudotumor typically no XR finding

CASE: 61 yo F s/p **MoM THA** 4.5 yrs ago with vague anterior hip discomfort and clunking with activity.

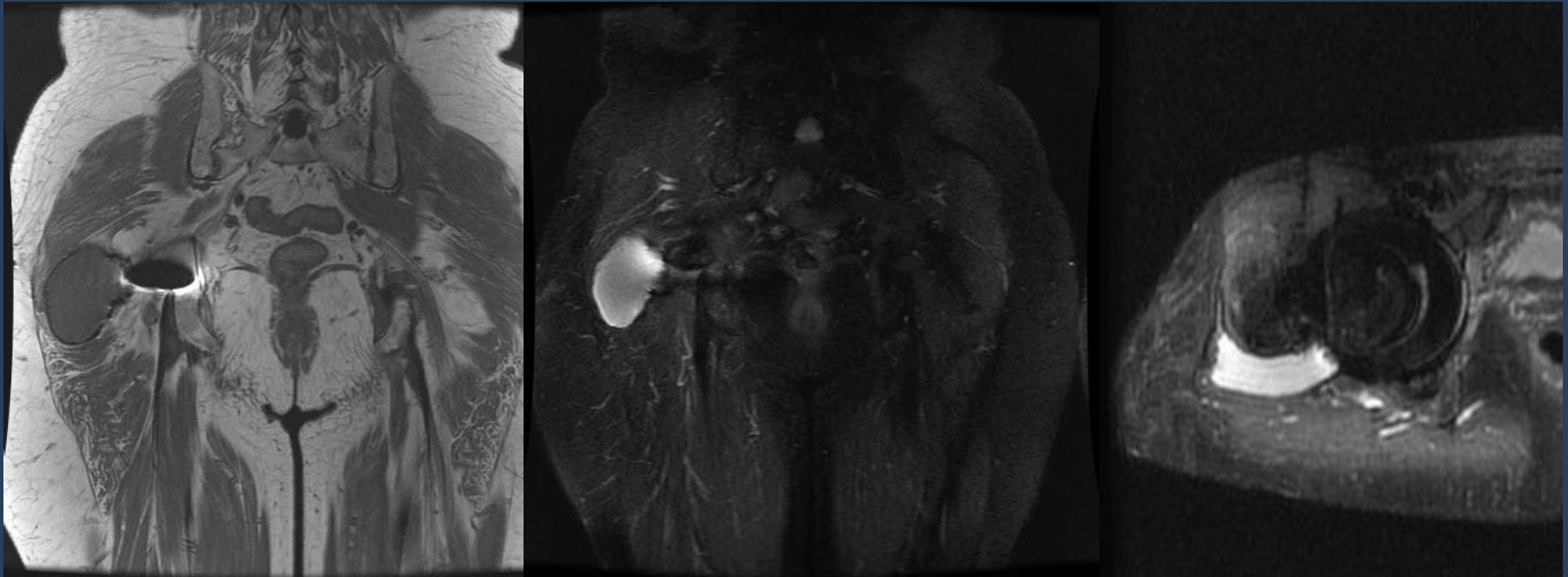


Negative XR

Serum Cobalt 21.4

Serum Chromium  
16.7  $\mu\text{g}/\text{L}$  (nl  $\leq 1$ ).

CASE: 61 yo F s/p **MoM THA** 4.5 yrs ago with vague anterior hip discomfort and clunking with activity.



**SURGICAL FINDINGS:**

1. Severe adverse reaction to metal debris
2. Abnormal membranous bursa
3. Small osteolysis around the acetabulum.

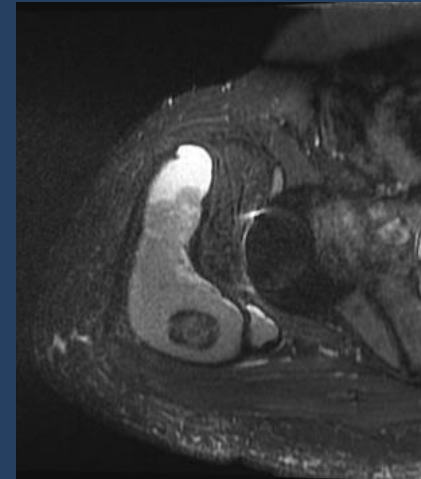
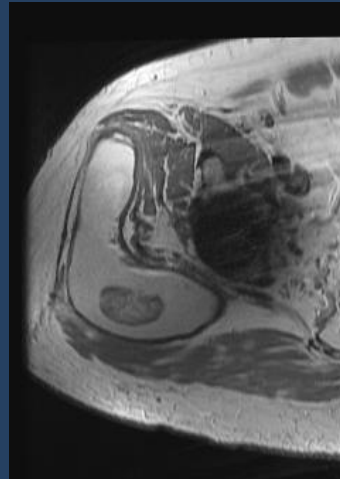
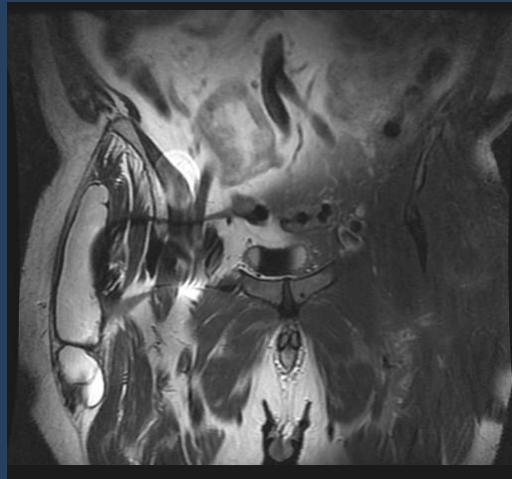
**PATHOLOGY:** Fibrous tissue with chronic inflammation and numerous histiocytes containing metal particles.

CASE: 71 yo M with **MoM THA** 8 yrs ago presents with vague right hip and buttock pain as well as decreased ROM of the hip.



**Negative XR???**

CASE: 71 yo M with **MoM THA** 8 yrs ago presents with vague right hip and buttock pain as well as decreased ROM of the hip.



Aspiration: 20 cc of very dark brown fluid, looks like dirty engine oil consistent with ARMD/Metallosis.

Teaching point:  
**WINDOW** for ST abnormality.

# ULTRASOUND

- Useful screening tool as it avoids metal-related artifacts
- Smaller lesions closer to hardware may be better appreciated than in US
- Operator dependent
- MRI still more sensitive particularly when using metal susceptibility reduction techniques
- Aspiration/Biopsy guidance

# CT

- Evaluating extent of osteolysis, cement interfaces, heterotopic ossification and metallosis
- Limited by beam hardening artifact from hardware
- Not a good screening tool for ARMD given poor ST resolution

# MRI

- Preferred over CT in evaluating periprosthetic abnormalities owing to superior soft tissue differentiation
- Metal susceptibility artifact reduction protocol
  - Lower magnetic field strength
  - Increasing bandwidth
  - Substituting STIR for FS sequences
  - Increasing frequency encoding gradient strength
  - Using fast spin echo with a long echo train and short echo time rather than GRE
  - Reducing voxel size
  - Using a higher-resolution matrix
  - Using thinner imaging sections
  - Selectively orienting the frequency and phase encoding gradients
  - Aligning the primary magnetic field with the longitudinal axis of the components
  - Artifacts most easily reduced by increasing the amplitude of the frequency encoding gradient either by increasing the receiver bandwidth or decreasing the pixel size
  - Increasing the bandwidth can result in >90% artifact reduction



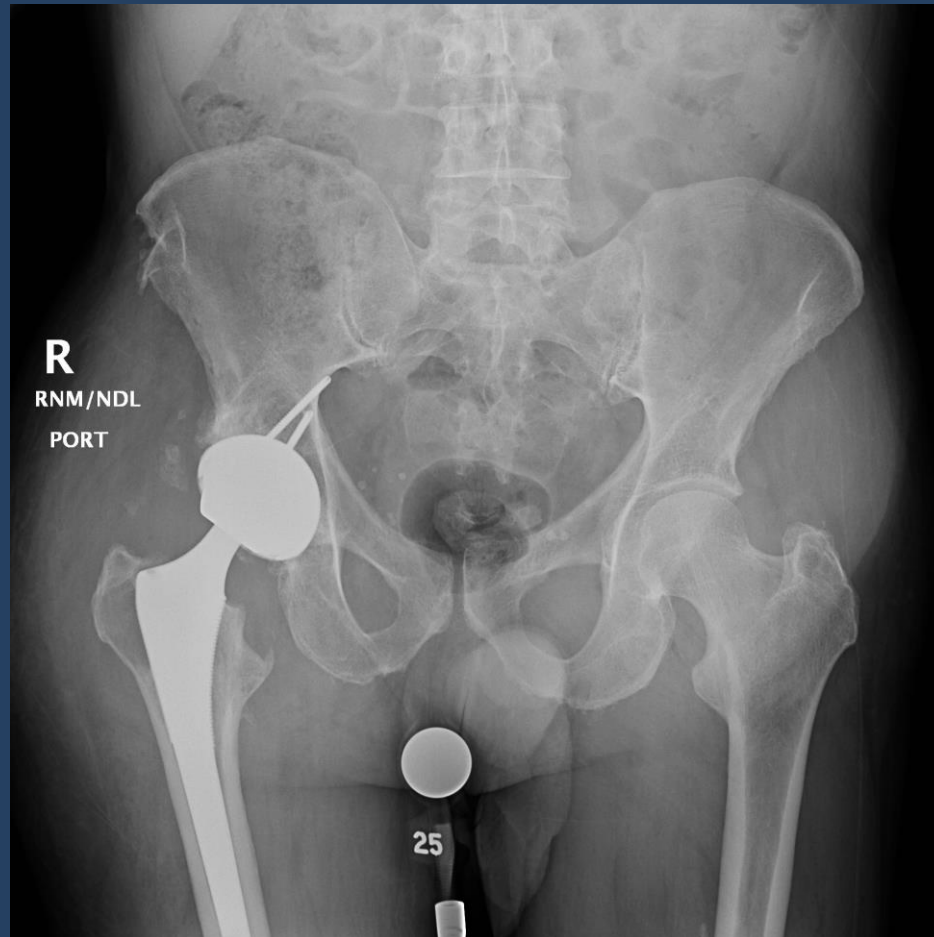
# MRI grading system

- Various MRI grading systems have been proposed to attempt to stratify the severity of periprosthetic pseudotumors
  - Size, composition, cyst wall thickness, and regional tissue abnormalities, etc
- Prognostic significance remain to be validated
- Maximal synovial thickness (Median 13.6 mm/12 mm) and synovial volumes (Median 62778 mm<sup>3</sup>/50428 mm<sup>3</sup>) determined on MRI correlated with high ALVAL scores and severe intraoperative tissue damage
  - 94% sensitivity, 87 % specificity for detecting ALVAL
  - 90% sensitivity, 86% specificity for quantifying intraoperative tissue damage

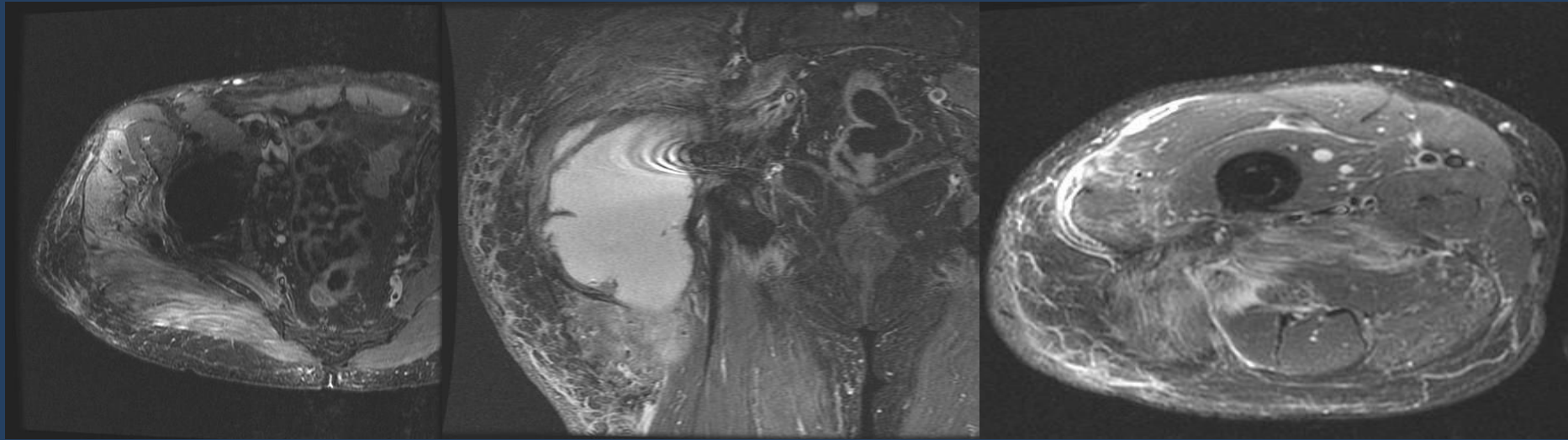
# Differential Diagnosis of Periprosthetic Masses

- ALTR/AMRD
- Infection
- Tumor

CASE: Status post **MoM THA** 8 years ago with recurrent hip pain and swelling worsening over the last couple of weeks radiating to the right scrotum. Recently on steroids for polymyalgia rheumatica.

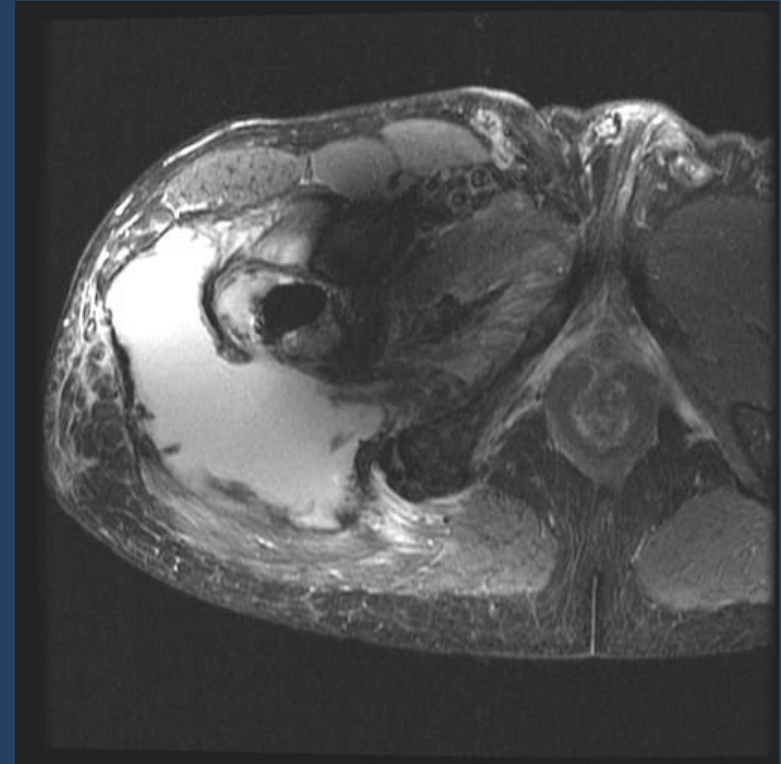
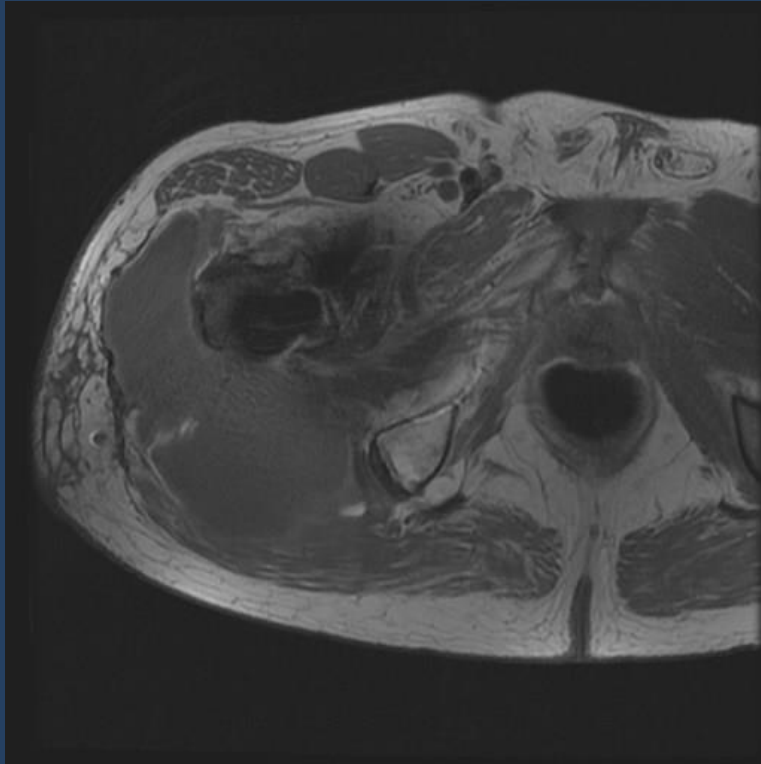


CASE: Status post **MoM THA** 8 years ago with recurrent hip pain and swelling worsening over the last couple of weeks radiating to the right scrotum. Recently on steroids for polymyalgia rheumatica.



MoM... is this another case of ARMD???

CASE: Status post **MoM THA** 8 years ago with recurrent hip pain and swelling worsening over the last couple of weeks radiating to the right scrotum. Recently on steroids for polymyalgia rheumatica.



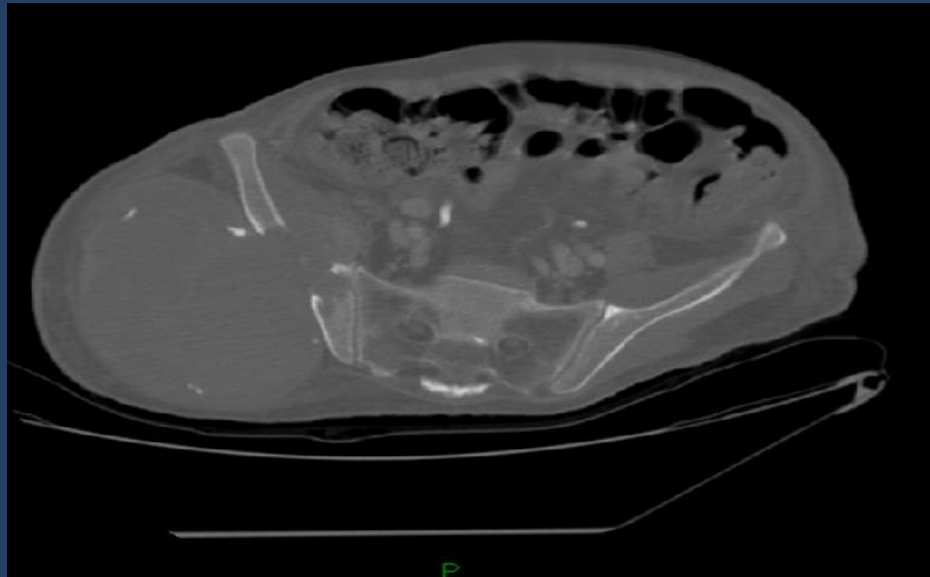
**LARGE ABSCESS** with osteomyelitis  
ASPIRATION: ~ 240 mL of brownish, purulent,  
foul smelling fluid. >300,000 WBC's.

CASE: Status post cementless revision right THA 21 yrs ago presents with hip pain.



7 months later

# Missed diagnosis of angiosarcoma ultimate resulting in patient's death.



- Periprosthetic malignancy such as primary sarcoma or metastatic cancer is a very rare yet reported event in the setting of previous hip replacement.
- Delay in diagnosis will likely leading to catastrophic consequences when not diagnosed in a timely manner.

# TREATMENT

- Symptomatic pseudotumors candidate for revision
- Management of smaller lesions that are asymptomatic is less clear
- Depends on source of wear or corrosion
  - MoM bearing wear → MoP or CoM
  - Head-Neck interface corrosion → Ceramic femoral head or removal of femoral stem to provide a virgin femoral trunnion
- Avoid Co and Cr revision components as ARMD typically arise from reactions to Co and Cr debris.
  - Use Ti alloy and CoC or CoXLP bearing surfaces
- Outcomes for revision are generally poor, particularly if associated with extensive tissue destruction.
- Early revision should be considered in symptomatic patients to limit extent of soft tissue destruction



# TEACHING POINTS

- Terminology is confusing. Know your referrers to make sure that you are using the same language.
- ARMD can be both related to metal reactivity and metal sensitivity
- ALTR often do not have signs of osseous abnormality or hardware failure especially if related to metal sensitivity.
- Look at ST WINDOW on XR!!!
- Don't forget infection and neoplasm as differentials.

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