Pathology of Femoral Loosening

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Outline

- ✓ Causes of loosening
- ✓ Historical perspective
- ✓ Mechanism of loosening and osteolysis
- ✓ Possible therapeutic interventions

Causes of femoral stem loosening

- ✓ Aseptic loosening
- ✓ Infection
- ✓ Fracture

Other causes of loosening

- ✓ Stem fracture
- ✓ Hypersensitivity to bone cement or its constituents
  - ✓ Haddad et al, 1996
- ✓ Hypersensitivity to metal
  - ✓ Evans et al 1974

Aseptic loosening

- ✓ Charnley recognised loosening of THRs in 1960s
- ✓ Initially attributed it to infection
- ✓ Histology: caseating granuloma with sterile pus

Historical perspective

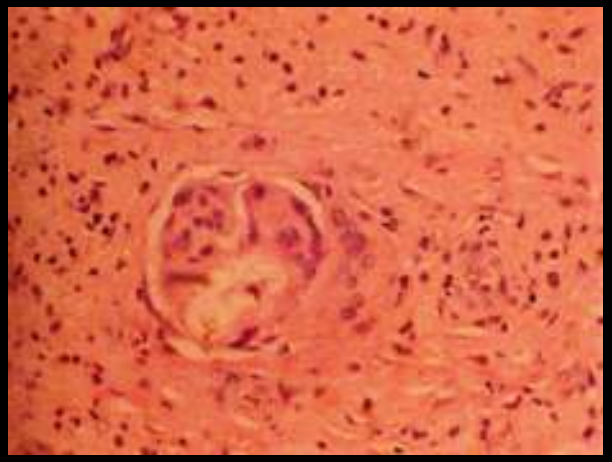
- ✓ Charnley implanted finely divided PTFE subcutaneously into his own thigh
- ✓ 3 months later this formed a palpable nodule
- ✓ Changed over to UHMWPE cups

Historical perspective

- ✓ Despite these observations, bone cement was blamed- ‘cement disease’
- ✓ Willert and Semlitsch proposed that aseptic loosening is caused by excessive wear of the poly liner

Current understanding

- UHMWPE wear- accepted as a major cause of osteolysis and aseptic loosening (NIH consensus statement 1994, 2000)

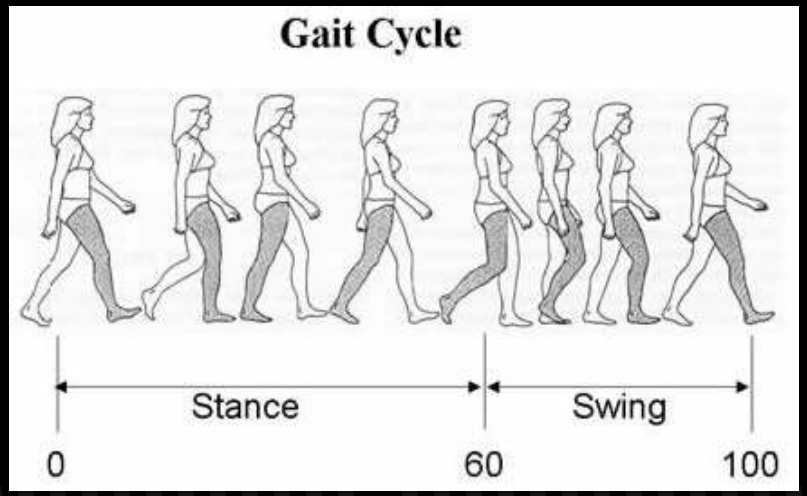


Magnitude of wear

- ✓ Depends on the distance the femoral head slides against the cup (2cm/step)
- ✓ 1 million cycles/year = 2463m^2
- ✓ Area of 7 basketball courts

Magnitude of wear

- 500,000 submicron particles may be generated with each gait cycle
  - McKellop, Clin Orthop, 1995



Loosening and Osteolysis

- ✓ Aseptic loosening and osteolysis are historically considered separate processes… but biologically are identical

- ✓ Cemented stems may mechanically de-bond initially

Aseptic loosening

- Essentials for osteolysis:
  - Generation of wear particles
  - Access of particles to periprosthetic bone
  - Cellular response to debris

Sources of wear particles

- ✓ Poly particles from UHMWPE cup (90%)
- ✓ Metal particles from fretting of modular head
- ✓ PMMA particles
- ✓ Braided wires and cables

Size does matter!

- ✓ Submicron poly particles are thought to be responsible for activating macrophages leading to osteolysis

- ✓ Particles >10μ do not lead to osteolysis

Access of wear debris to bone

- ✓ Segments of femur/acetabulum not in contact with joint space can still have access to joint fluid: ‘effective joint space’

Schmalzried, Jasty and Harris

Effective Joint Space

- ✓ Fluid in the hip is subjected to high pressures during activities of daily living

- ✓ This fluid gets dispersed along the path of least resistance, which in turn depends on the type of fixation, implant design and bone remodelling around the implant

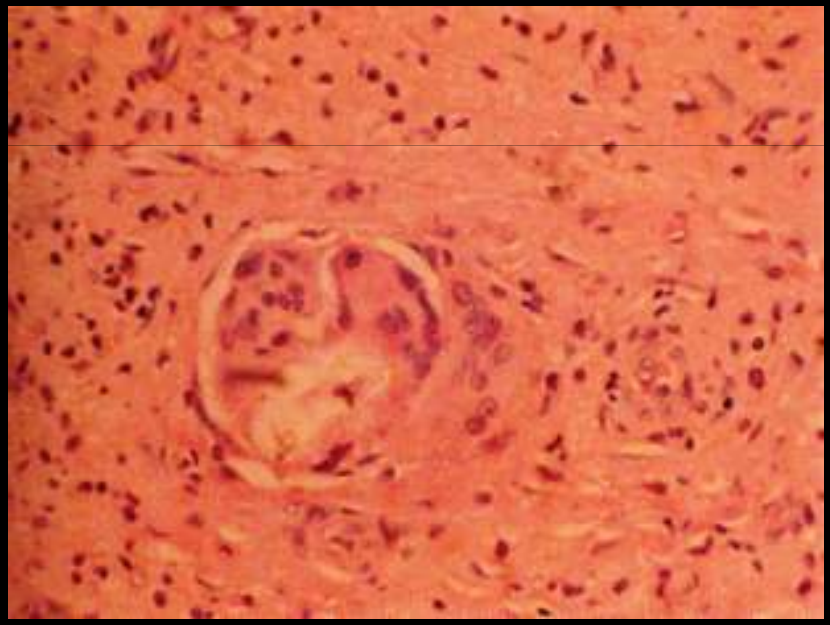
Cellular response to debris

- ✓ Goldring (1983) described synovium like membrane surrounding loose THR components

- ✓ These membranes contain macrophages that could produce collagenases and PGE2.

Histology of soft tissue membrane

- ✓ Foreign body granuloma

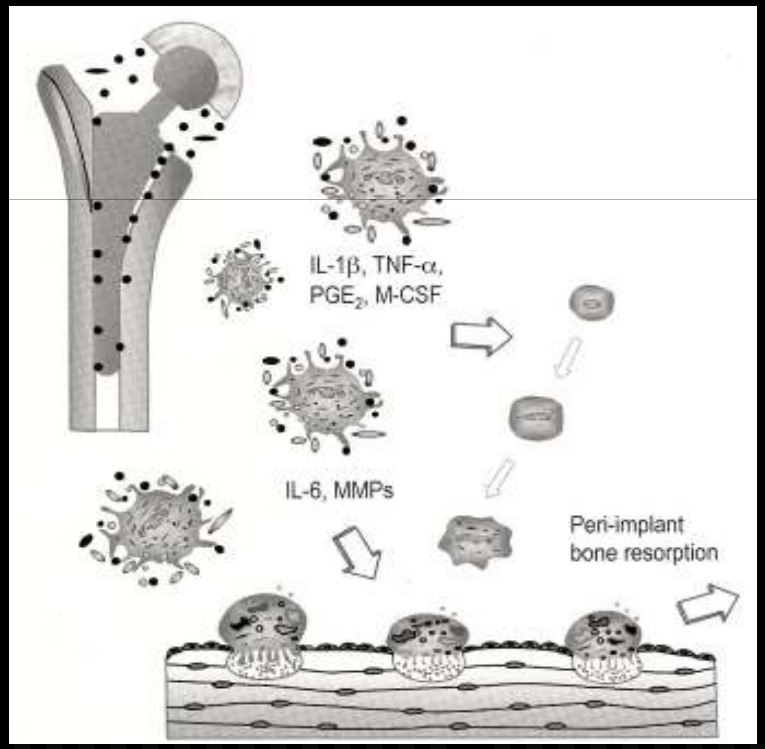


Histology

- ✓ Response to biomaterials that are incapable to being degraded
- ✓ Principal cell type in the granuloma is the macrophage
- ✓ Lymphocytes are not prominent

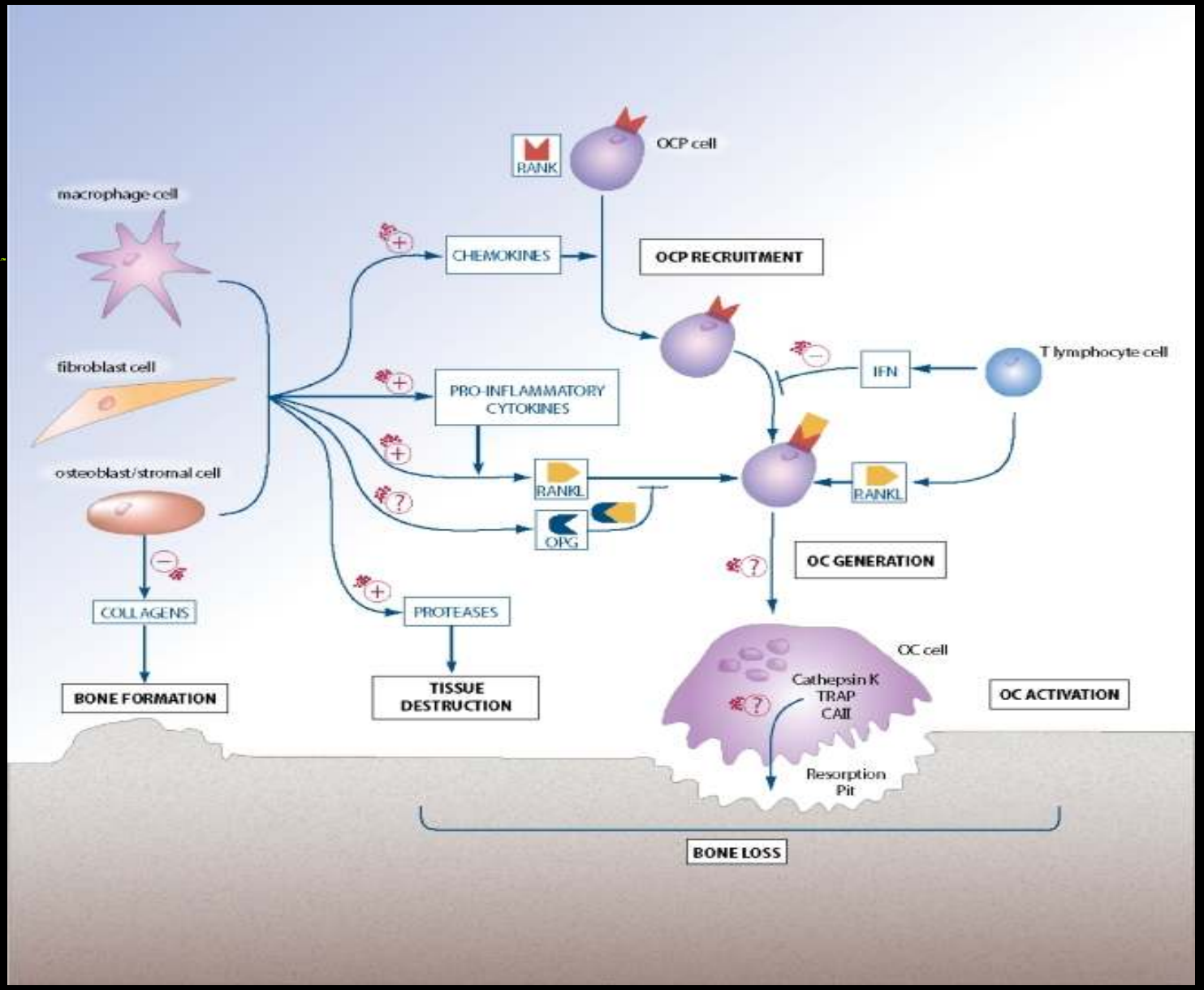
Cellular response

- Cytokines secreted by macrophages
  - IL-1
  - IL-6
  - TNFά
  - PDGF
  - VEGF
  - $TGF\beta_1$



Osteoclast differentiation

- 3 regulators
  - RANK (receptor for activation of NFkB)
    expressed on the surface of osteoclast precursors
  - RANKL (receptor activator of NFkB ligand)
    expressed by marrow stromal cells
  - OPG (osteoprotegerin)
    glycoprotein secreted by stromal cells

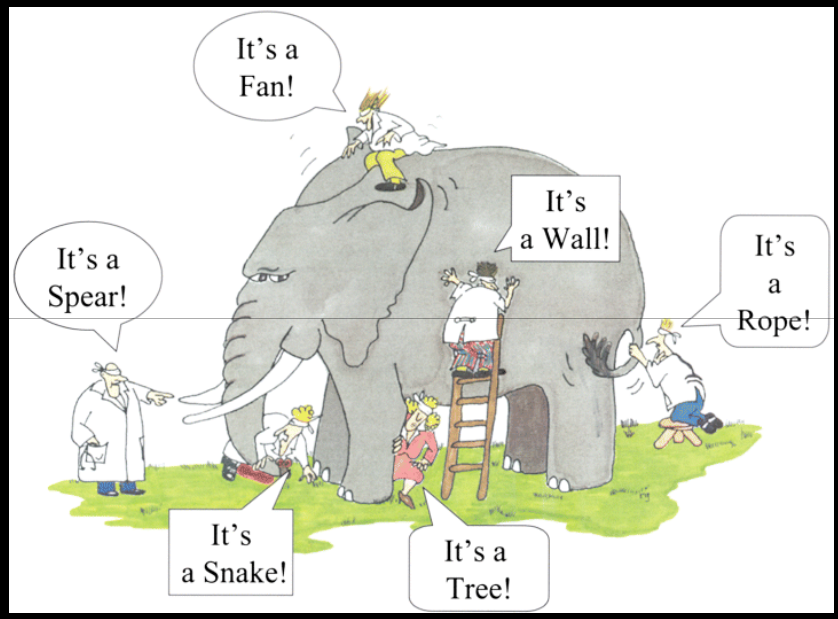

RANK
OCP cell
macrophage cell
CHEMOKINES
OCP RECRUITMENT
fibroblast cell
PRO-INFLAMMATORY CYTOKINES
IFN
T lymphocyte cell
osteoblast/stromal cell
RANKL
RANKL
OPG
OC GENERATION
COLLAGENS
PROTEASES
OC cell
Cathepsin K
TRAP
CAII
BONE FORMATION
TISSUE DESTRUCTION
OC ACTIVATION
Resorption Pit
BONE LOSS

Role of lymphocytes?

- ✓ Jasty et al injected PMMA powder into immunocompetent and immunodeficient mice
- ✓ All mice showed a foreign body reaction (macrophage & giant cells), irrespective of immune status

Genetic susceptibility?

- Aseptic loosening may be related to genetic expression of matrix metalloproteinase-1
  - Malik et al, 2007



Type of femoral stem and osteolysis

Cemented stems and loosening

- ✓ Polished collarless stems e.g. Exeter, CPT
- ✓ Matte finish (rough stems) with collars e.g. Charnley elite

Exeter stem

- ✓ Double taper stems subside in cement mantle by a few mm
- ✓ Stem wedges into the cement
- ✓ Axial forces are converted into radial compressive forces

Rough cemented stems

- ✓ Implant-cement-bone acts as a composite beam
- ✓ Require perfect bonding at both interfaces

Failure of cemented stems

Polished stems

Rough surface stems

Poor cement mantle

De-bonding between cement-stem-bone interfaces

Access to wear particles

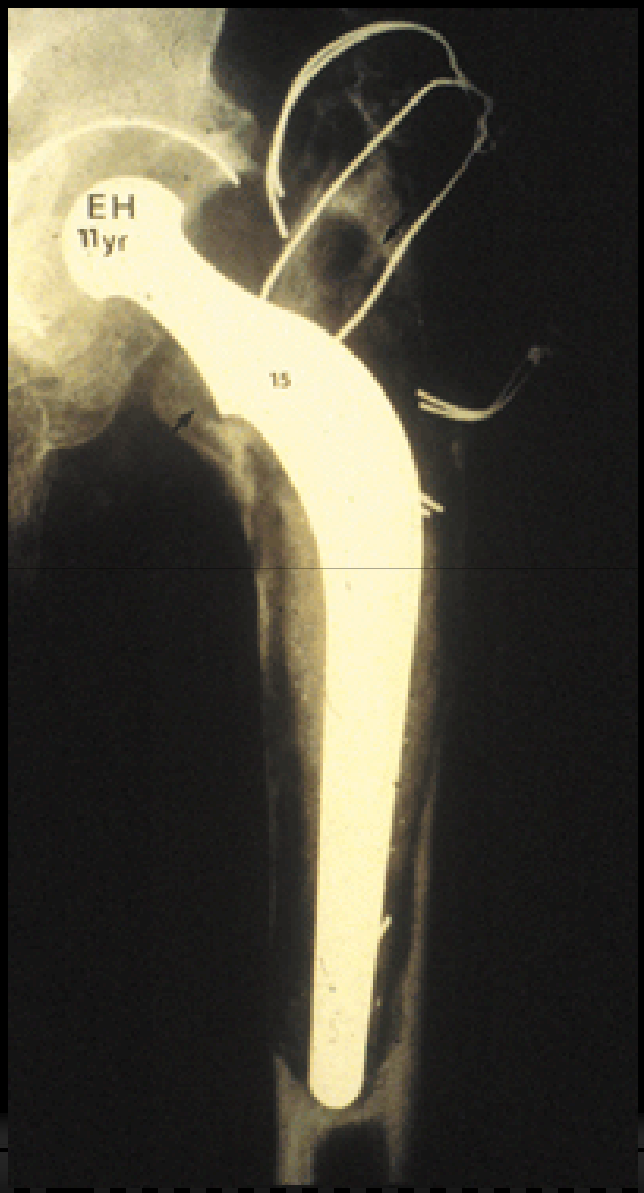
Loosening

Cement mantle

- ✓ Good cement mantle is a essential to prevent aseptic loosening

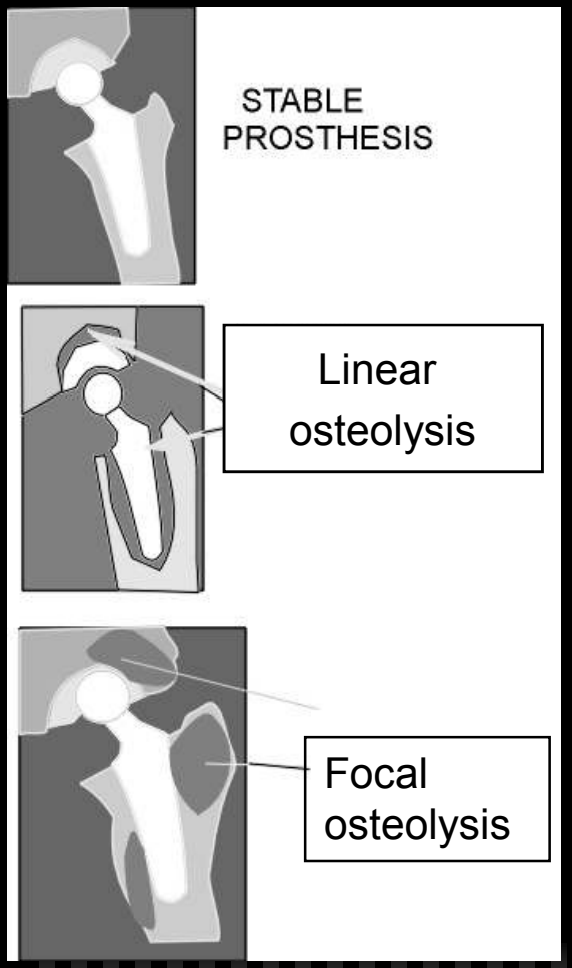
Linear osteolysis

- ✓ All around prostheses with poor cementation
- ✓ Confined to proximal femur with modern cementation techniques
  - ✓ Mulroy and Harris, JBJS 1990



Osteolysis in cemented THR

- ✓ Focal osteolysis in cemented THR occurs distally
- ✓ May be due to the high pressures forcing particles into the cement-stem interface.



Uncemented stems

- ✓ 2 stages of fixation
- ✓ Initial intra-operative stabilisation
- ✓ Osteo-integration from on/in-growth

Uncemented stems

- ✓ Patch coated (e.g. Harris Galante-1 stem)
  - ✓ Higher incidence of distal osteolysis and loosening
- ✓ Circumferentially coated (e.g. Synergy, Accolade, Corail)

Failure of uncemented stems

Early failure

Poor intra-op stability or failure of bony ingrowth

Late failure

Fatigue fractures of bridging trabeculae

Access to wear particles

Loosening/ osteolysis

How can we reduce aseptic loosening?

- ✓ Reduce wear
- ✓ Minimise access of wear debris to bone
- ✓ Block cellular response to wear debris

Reduce wear

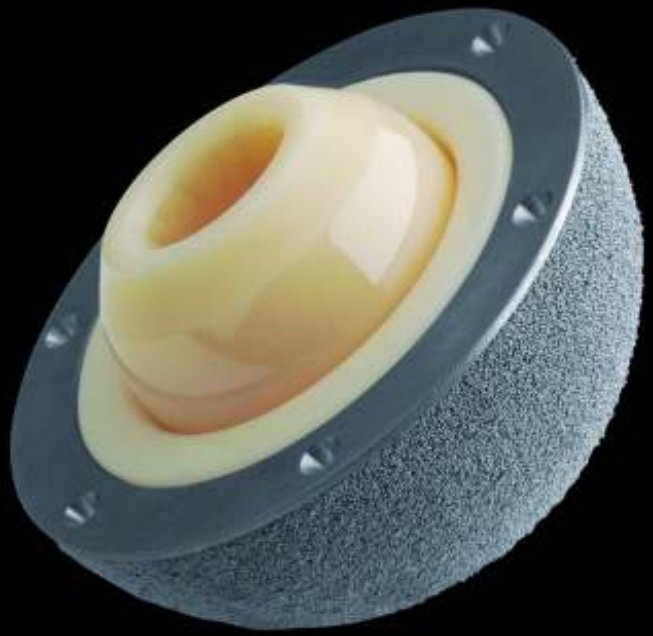
- ✓ Smaller diameter heads
- ✓ Avoid thin poly cups
- ✓ Minimise motion between metal shell and poly liner

Reduce wear

- ✓ Avoid abrasions on the surface of femoral head/ poly cup
- ✓ Meticulously remove cement particles to avoid third body wear
- ✓ Use highly cross-linked poly

Reduce wear

- ✓ Use alternative bearing surfaces



Minimise access of wear particles to bone

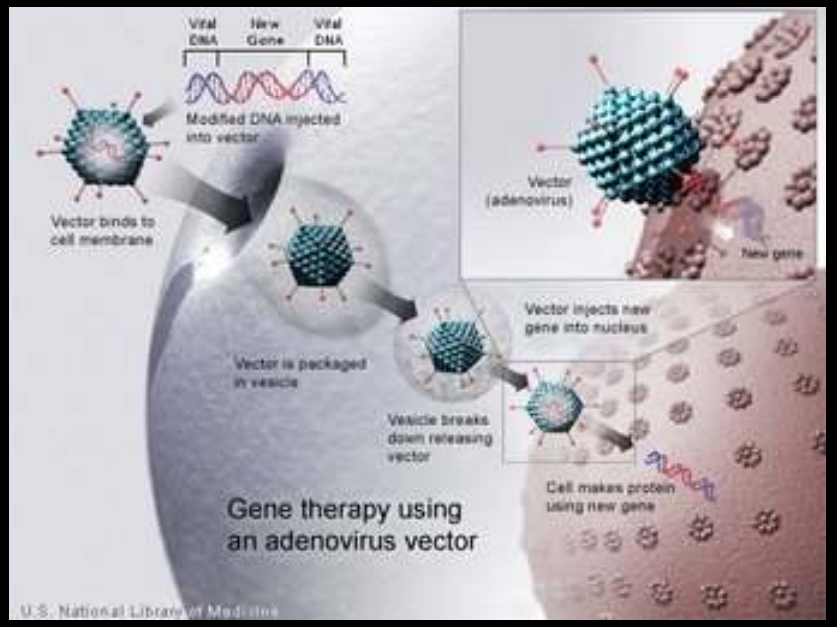
- ✓ Select implant designs with a good track record
- ✓ Good cementation technique
- ✓ Avoid metal shells with screw holes if possible

Block cellular response to wear debris

- ✓ NSAIDS
- ✓ Anti TNF therapy (Etanercept)
- ✓ Bisphosphonates
  - ✓ May be effective to prevent stress shielding

Block cellular response to wear debris

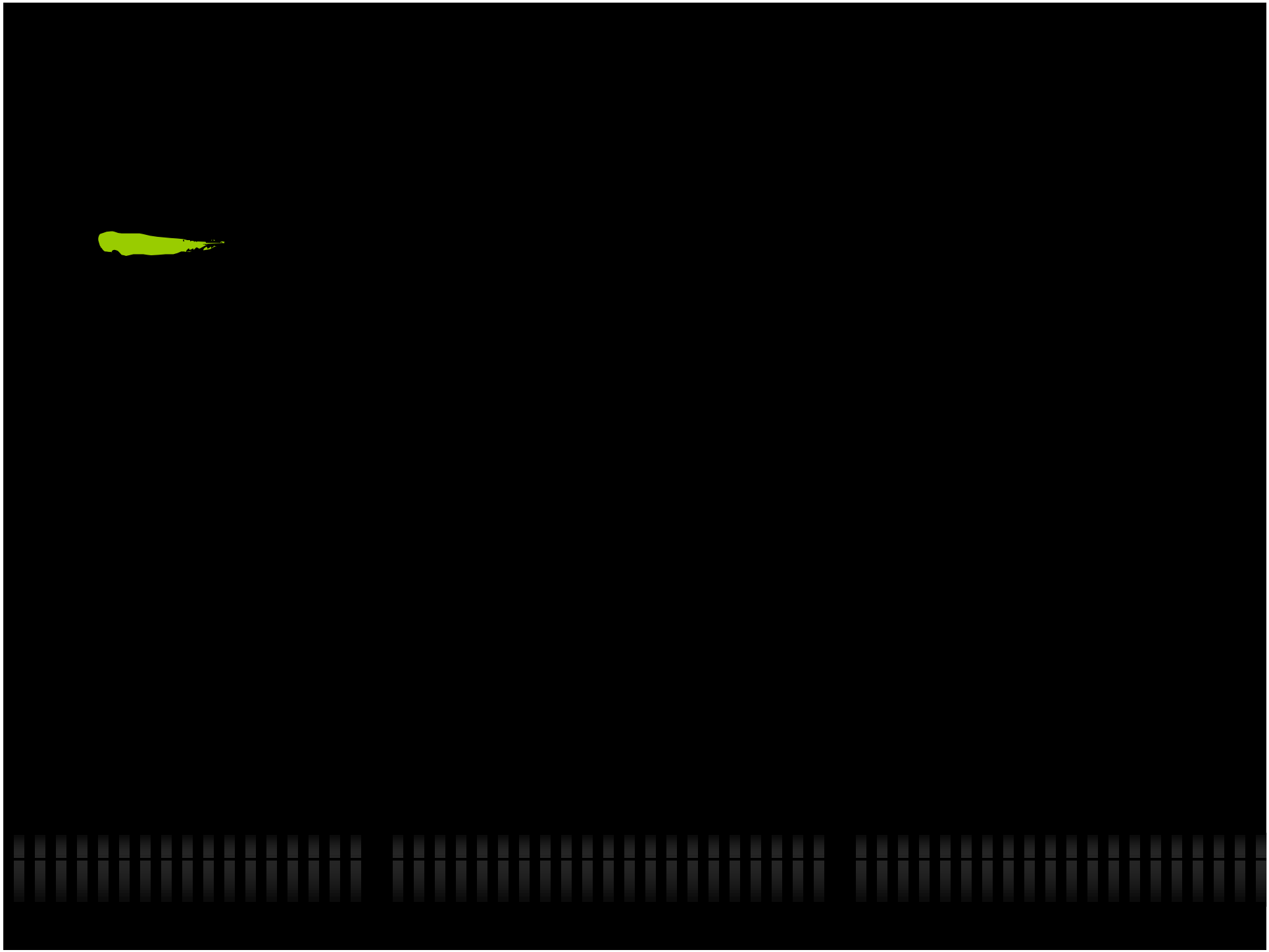
- ✓ Gene therapy
  - ✓ Adenoviral vector to transduce OPG gene in mice
  - ✓ Experimental stage



Summary

- ✓ Poly wear is the major cause of osteolysis
- ✓ Osteolysis can be minimised by reducing wear and blocking access of wear particles to bone
- ✓ Medical intervention has failed to control osteolysis

Thank you

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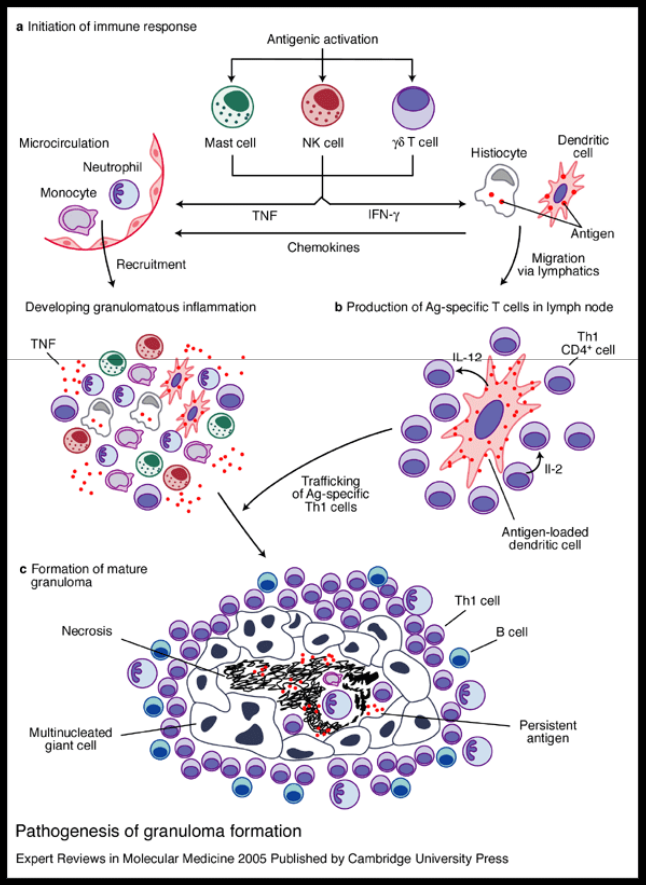
GA

Formation of granuloma



Pathogenesis of granuloma formation

Expert Reviews in Molecular Medicine 2005 Published by Cambridge University Press

- ✓ Wear particles- ingested by macrophages- activate T and B lymphocytes, secrete IL-1, IL6, PGE2, TNFalpha- recruit osteoclasts- bone resorption

- Cross linked poly liners reduce wear by 90%; but, the debris is more inflammatory to macrophages

- However, clinical results have shown decreased osteolysis with cross linked poly.
  - JBJS(Am) 2007

Definition

- A radiographically demonstrable change in the mechanical integrity of the load carrying cemented femoral component, esp. fractured cement and an intersurface gap the produces a radiolucent zone in cement-stem or cement-bone interface.
  - Gruen, McNeice and Amstutz

Why do polished tapered stems work?

- ✓ Minimal wear at cement stem interface
- ✓ Controlled subsidence prevents access of joint fluid containing wear particles

Mechanical theory of loosening

- In cemented stems, failure at prosthesis cement interface (cement fracture) occurs before formation of membrane between cement bone interface
  - Jasty et al
- Not necessarily true with tapered polished stems
  - Ling et al

Uncemented stems

- ✓ Proximal fix e.g. Accolade
- ✓ Distal fix e.g. Eschelon
- ✓ Extensively coated e.g. Corail

Loosening of cemented stems

- ✓ Linear/ focal osteolysis around cemented stems depends on the access and distribution of particulate wear debris