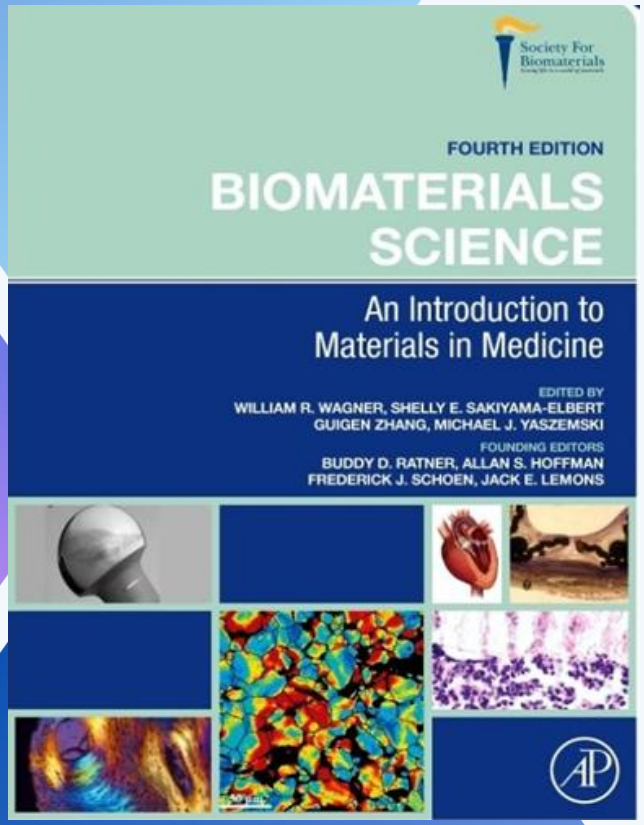


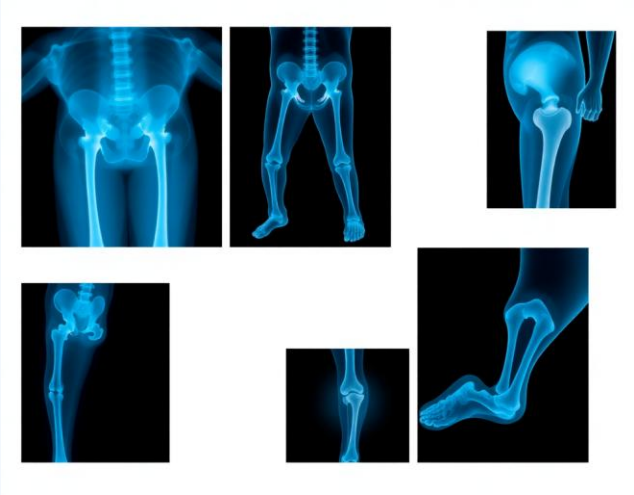
Orthopedic Applications of Biomaterials

Nadim James Hallab & Joshua J. Jacobs

Department of Orthopedic Surgery, Rush University Medical Center, Chicago, IL, United States

An in-depth review based on Chapter 2.5.4 for advanced studies in biomaterials.

The Success of Orthopedic Biomaterials

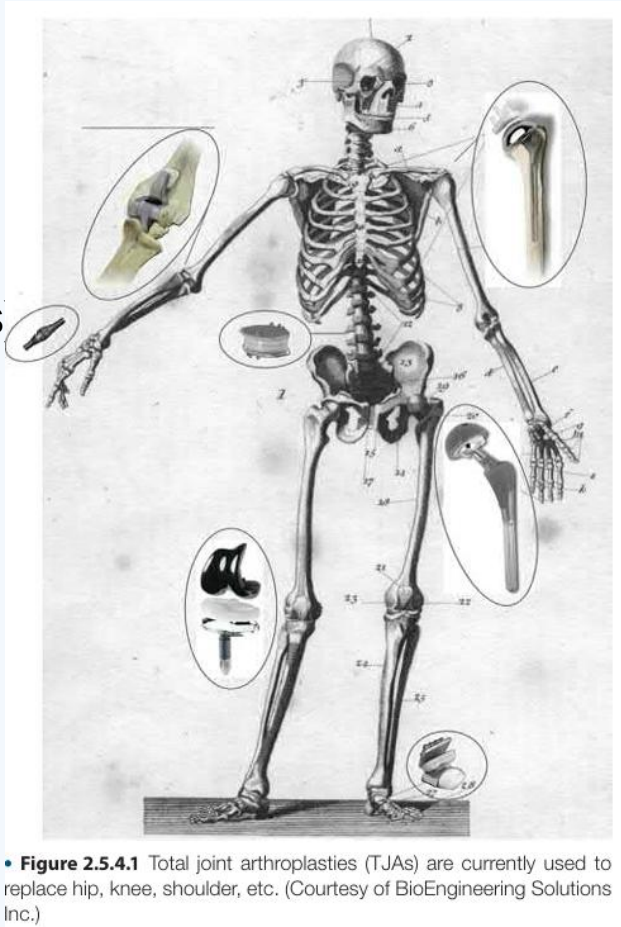


Orthopedic biomaterials have achieved remarkable success in restoring mobility and enhancing the quality of life for millions of individuals annually.

These materials form the basis of a wide range of medical devices designed to address musculoskeletal issues.

Categories of Orthopedic Implants

- Reconstructive Implants (e.g., Total Joint Replacements
- Fracture Management Products
- Spinal Products
- Rehabilitation Products
- Arthroscopy Products
- Casting Products



• **Figure 2.5.4.1** Total joint arthroplasties (TJAs) are currently used to replace hip, knee, shoulder, etc. (Courtesy of BioEngineering Solutions Inc.)

Primary Clinical Applications

The use of orthopedic products generally falls into three main functional categories:

- Fracture Fixation Enhancement
- Joint Replacement
- Dynamic Stabilization
- Lenghtening and bone modeling

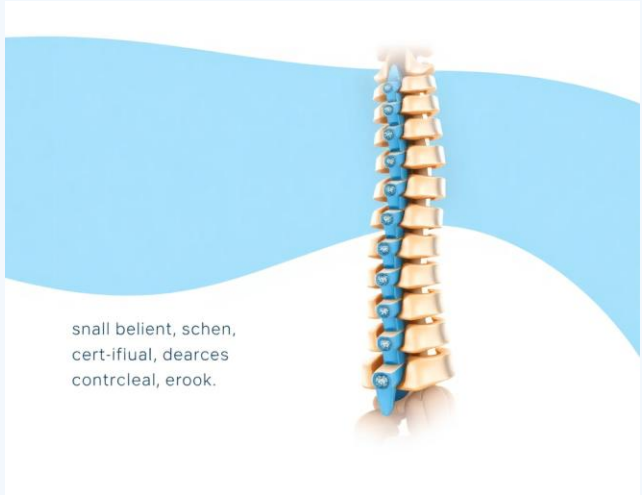
Application 1: Joint Replacement (Arthroplasty)

- Hip Arthroplasty
- Knee Arthroplasty
- Spine Arthroplasty
- Ankle Arthroplasty
- Shoulder Arthroplasty
- Elbow Arthroplasty
- Wrist Arthroplasty
- Finger Arthroplasty

The medical term ***arthroplasty*** refers to a surgical procedure, also known as *joint replacement surgery*, where a damaged or diseased joint is surgically replaced with an artificial joint (prosthesis).

This surgery is performed to relieve pain, improve function, and restore the range of motion in joints, most commonly the hip, knee, and shoulder.

Application 3: Dynamic Stabilization Devices



This is a newer category of orthopedic implants designed to stabilize a joint, particularly the spine, while preserving a degree of motion. An example is a spine stabilization device.

The Orthopedic Biomaterials Market

A Dominant and Growing Sector

- Worldwide market dominated biomaterial sales at approximately $24 billion in 2007.
- Expected annual growth rate of 7% - 9%.
- Trauma fracture management products totaled ~$3.7 billion in 2007.
- Knee and hip joint replacements accounted for $10 billion in 2007.
- Revision procedures are growing at an accelerated rate, indicating a need for improved implant longevity.

Fundamentals: Biomaterials & Bone

Primary Orthopedic Biomaterials

Orthopedic biomaterials are generally limited to those materials capable of withstanding significant cyclic load-bearing applications. The three primary classes are:

Metals

Polymers

Ceramics

Why Metals Dominate Load-Bearing Roles

Metals have uniquely provided the combination of material properties necessary for most load-bearing roles in fracture fixation and total joint arthroplasty (TJA).

- High Strength
- Ductility
- Fracture Toughness
- Hardness
- Corrosion Resistance
- Formability
- Biocompatibility

Surgical Specialty Categories

The use of orthopedic biomaterials generally falls into one of three surgical specialty categories:

- Upper Extremity
- Spine
- Lower Extremity

Each specialty is typically divided into three general sub-categories: pediatric, trauma, and reconstruction.

Most Common Orthopedic Biomaterials: Metals

Material	Primary Use(s)
Ti alloy (Ti-6%Al-4%V)	Plates, screws, TJA components (non-bearing surface)
Co-Cr-Mo alloy	TJA components
Stainless steel	TJA components, screws, plates, cabling

Most Common Orthopedic Biomaterials: Polymers

Material	Primary Use(s)
Polymethylmethacrylate (PMMA)	Bone cement
Ultra-high-molecular-weight-polyethylene (UHMWPE)	Low-friction inserts for bearing surfaces in TJA

Most Common Orthopedic Biomaterials: Ceramics

Material	Primary Use(s)
Alumina (Al_2O_3)	Bearing surface TJA components
Zirconia (ZrO_2)	Bearing surface TJA components

Key Design Concerns for New Biomaterials

- The material must not adversely affect its biological environment (Biocompatibility).
- The material must not be adversely affected by the surrounding host tissues and fluids (Biostability/Corrosion Resistance).
- New materials must exceed the performance of present materials (Performance Improvement).

The Importance of "Form-Function"

Understanding the interrelationship between the structure and properties of the natural tissues being replaced is critical.

An appreciation of the "form-function" relationship in calcified tissues provides insight into implant design and material selection.

Structure and Properties of Calcified Tissues

All calcified tissues in the human body share common components: the principal protein component, collagen, and an inorganic component, hydroxyapatite [OHAp, $Ca_{10}(PO_4)_6(OH)_2$].

The organization of these components in compact cortical bone can be understood through four levels of organization.

Level 1: Molecular Organization

This level involves the collagen triple helical structure (tropocollagen) and the crystallography of hydroxyapatite (OHAp).

- OHAp forms a hexagonal unit cell.
- Crystallite size in bone is very small (approx. 2nm x 20nm x 40nm), leading to X-ray diffraction line broadening.
- The presence of a Ca-bearing compound led to the development of osteophilic ceramic materials.

Level 2: Ultrastructural Organization

This is the structural level observed with Transmission Electron Microscopy (TEM) or high-magnification Scanning Electron Microscopy (SEM).

- The precise collagen-OHAp organization is not fully understood.
- OHAp appears to be both inter- and intrafibrillarly located within the collagen.
- Elastic properties at this level can be modeled as a two-component system.

Level 3: Microstructural Organization

At this level, fibrillar composites form larger structures like fibers and fiber bundles, which then pack into lamellar-type units.

- Observable with SEM and optical microscopy.
- This is the level typically referred to as "bone tissue" or discussed in histology.
- Composite analysis can be used to model elastic properties, but the modeling is highly complex.

Level 4: Macroscopic Organization

This level pertains to the overall structure of a bone sample or a large section of bone, as observed with the naked eye.

The Challenge: A Complex Natural Material

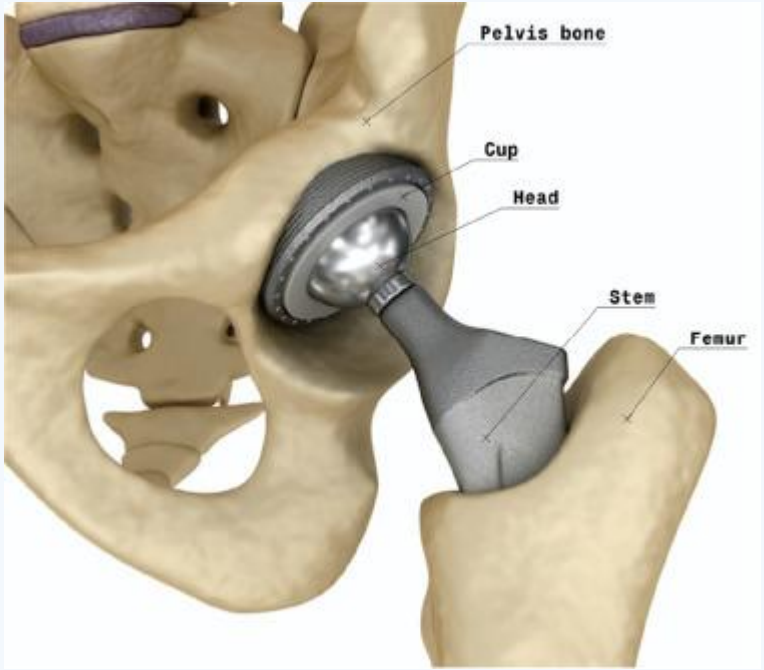
Bone is *anisotropic*, *inhomogeneous,* and *viscoelastic* due to its significant collagen content.

Duplicating these complex properties with long-lasting synthetic biomaterials remains an unrealized goal.

The history of orthopedic biomaterials is characterized by eliminating poorly performing materials rather than creating perfect bone-mimetic synthetics.

A Case Study in Biomaterial Evolution:

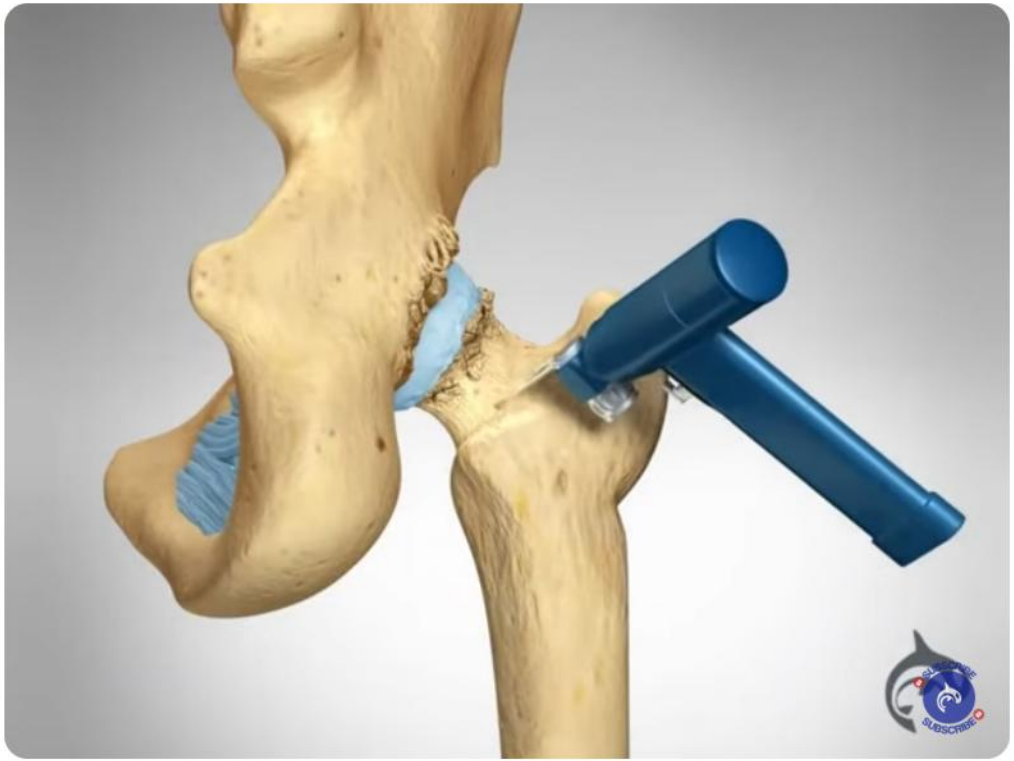
Total Hip Arthroplasty (THA)



THA: A Case Study for Biomaterial Evolution

The history of total hip replacement is one of the best illustrations of how an implant has evolved over a century to its current successful status, primarily due to advances in biomaterials science.

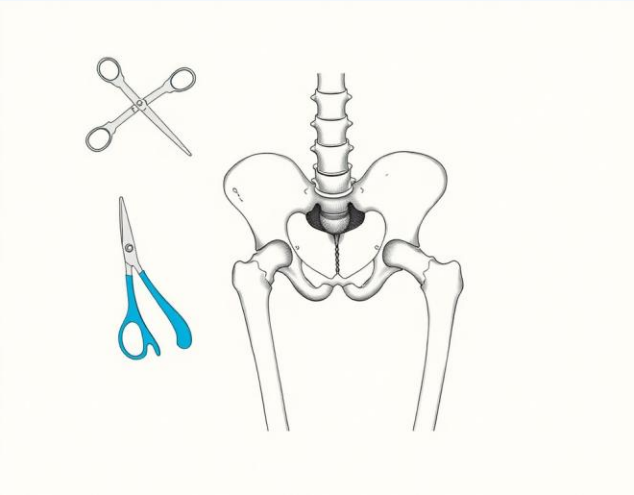
Many biomaterial-related issues impacting THRs are applicable to all other orthopedic implants.



Total Hip Replacement (Arthroplasty) - 3D Animation (No Narration)

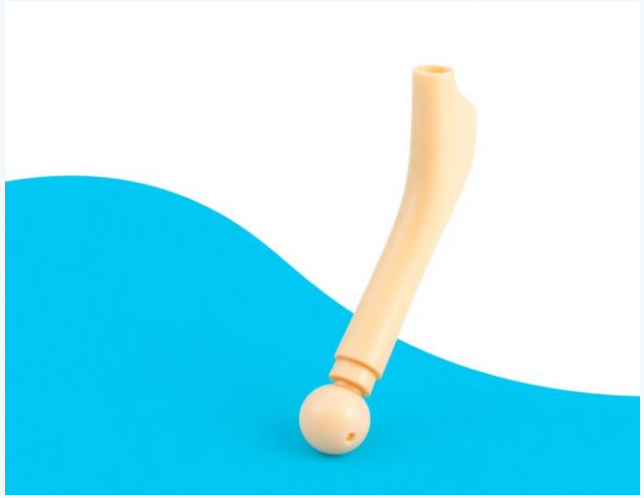
https://youtu.be/i3iOYz24sXo?si=9jZx-ocIzy64WvRL

Earliest Attempts (1820s - 1880s)



- 1820s: Focused on simply removing affected femoral and acetabular bone (osteotomy).
- 1830s-80s: Ghastly attempts at interpositional membranes using materials like wooden blocks and animal soft tissues (e.g., pig).

The First Prosthetic Hip (1890)



In 1890, Professor Themistocles Gluck of Berlin published a description of a carved ivory femoral head replacement.

He used bone-cement-like materials such as pumice and plaster of Paris to secure the implant.

Mold Arthroplasty: A New Era (1923)

Marius Smith-Peterson ushered in the modern era of TJA with his "mold" arthroplasty.

- Inspired by a shard of glass in a patient's back with a benign synovial-like membrane around it.
- Initial mold was made of glass, designed to fit between the femoral head and acetabulum.
- Aimed to prompt a "tissue-engineered" synovial/cartilage-like layer.

Material Evolution of Mold Arthroplasty

1923-1938

Efforts focused on improving the fracture resistance of the glass mold using materials like:

- Early polymers (Celluloid, Bakelite)
- Improved glass (Pyrex)

1939

A major breakthrough occurred with the use of the first suitable metal, a cobalt alloy termed Vitallium.

This provided the necessary corrosion resistance for improved biocompatibility and performance.

The Landmark Study on Metals (1937)

Venable, Stuck, and Beach published a landmark article systematically analyzing the electrolytic effects of various metals on bone and tissue.

- Metals tested included aluminum, copper, iron, nickel, gold, stainless steel, and others.
- They concluded that Vitallium (a Co-Cr alloy) was superior in corrosion resistance and mechanical properties.
- This set the standard for selecting future metallic alloys for implants.

Femoral Head & Short-Stem Prostheses

Around the same time, prostheses designed to replace only the femoral head emerged.

- Early materials included ivory (Gluck, 1890) and rubber (Delbet, 1919).
- Hey Groves used an ivory nail to replace the femoral articular surface.
- Harold Bohlman designed a Co-Cr alloy femoral head with a short stem in 1937.

The Judet Brothers' PMMA Prosthesis (1946)

The Judet brothers in Paris popularized a short-stemmed prosthesis manufactured from polymethylmethacrylate (PMMA), presumed to be inert.

Initial good results were followed by problems of implant fracture and excessive wear debris, leading to loss of favor by the early 1950s.

Transition to Vitallium and Long Stems

Vitallium (Co-Cr alloy) eventually replaced acrylic in several other short-stem designs (e.g., Wiles, Peterson, Thompson).

However, short-stem designs were subject to high shear stress, leading to early loosening. This prompted the development of longer stems to provide less stress concentration and better load transfer.

Popular Long-Stem Prostheses (1950s)

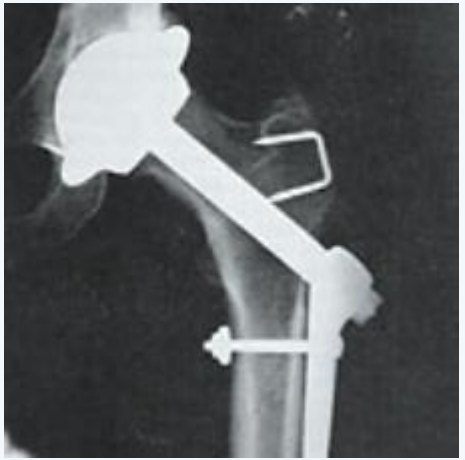
The designs of Frederick R. Thompson and Austin T. Moore became popular in the 1950s.

- Cast in Vitallium (Co-Cr alloy).
- Required removal of the femoral head but only part of the neck.
- Moore's design included fenestrations for bone growth and a vane for rotational stability.
- Their continued use today, with slight variations, is a testament to their successful design.

The First Total Hip Replacement Arthroplasty

Philip Wiles is credited with the first THA in 1938.

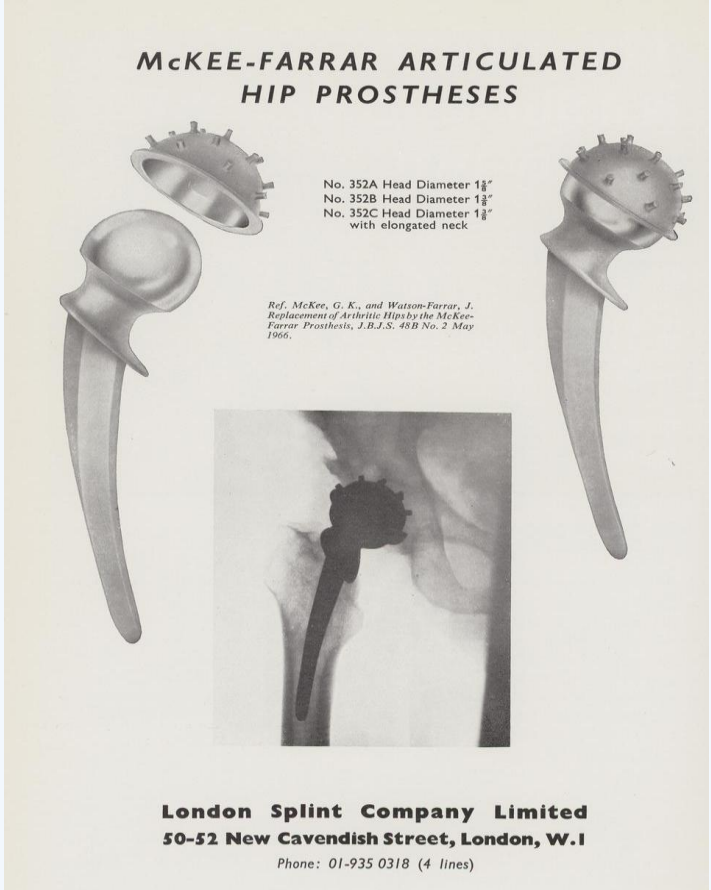
- Used a stainless steel ball secured with a bolt and a stainless acetabular liner secured with screws.
- Results were disappointing due to poor corrosion resistance of early stainless steel and high stress concentrations.



The McKee-Farrar Prosthesis (1951)

Developed by G.K. McKee and J. Watson-Farrar, this was a successful adaptation of Wiles' design.

- Initially used a stainless steel cup and a Thompson long-stem, but it failed rapidly due to corrosion.
- Switched to a cobalt-chrome alloy with greater success.
- Evolved to include a true spherical head undercut at the neck to reduce impingement and increase mobility.



Milestone: Acrylic Bone Cement (PMMA)

The popularization of acrylic bone cement in the 1950s was a major milestone.

- First used by Sven Kiar in 1950 to attach a plastic prosthesis.
- Dramatically reduced the rates of loosening associated with metal-on-metal THA.
- Designs like the McKee-Farrar were adapted with studded surfaces to maximize mechanical fixation with cement.

Charnley's "Low-Friction Arthroplasty"

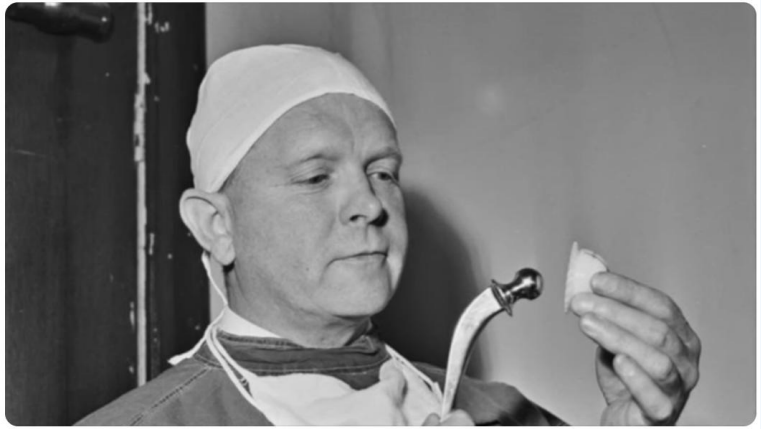
In the 1960s, Sir John Charnley identified high frictional forces in metal-on-metal joints as a cause of debris and loosening.

His goal was to create a "low-friction" joint.

Charnley's Material Journey: From Failure to Success

- **First Attempt (PTFE/Teflon):** Used shells of PTFE on both sides, resulting in immediate failures due to massive debonding and wear debris.
- **Second Attempt (Thick Teflon):** A thick Teflon cup articulating on a small head also failed due to excessive wear and severe inflammation.
- **Success (HDPE/UHMWPE):** In 1962, Charnley replaced Teflon with high-density polyethylene. While not as frictionless, it was 1000 times more wear-resistant.

The Charnley Prosthesis: The Modern Blueprint



Sir John Charnley and the Birth of Total Hip Arthroplasty

https://youtu.be/KIsReErL1Mw?si=qc0kOWAkik4cNOTE

The 1962 metal-on-polyethylene design became the basis for future designs and remains the most popular form of THA performed today.

The history Dr Sir Charnley of total hip replacement is one of the best illustrations of how an implant has evolved to its current successful status and changed the future, primarily showing the insight of advances in biomaterials science.

Innovations and Acknowledging the Community

- **Design Modifications:** Muller (variable neck sizes), Ling, Aufranc, Harris, Galante (geometrical modifications, modularity, porous coatings).
- **A Broader View:** The success of THA is not due to one person but is an example of evolution through the work of many scientists and physicians in materials technology, biomechanics, immunology, and more.

Total Hip Replacement Surgery | Inside the OR

https://youtu.be/AwH1ZACzB6A?si=mZdcPpDhuQU4wzlv

Contrast: Total Disc Arthroplasty (TDA)

In contrast to the long history of THA,

TDA is a relatively recent development,
with the goal of replacing spine fusion to restore mobility and eliminate pain.

Early TDA: The Ball-and-Socket Concept


Figure 2.5.4.

- First disc arthroplasties were Co-alloy spheres implanted in the 1950s without fixation.
- A decade later, stainless steel spheres termed "Fernström balls" were used.
- Attempts with PMMA balls had disastrous results.

The Modern Era of TDA: The SB Charité

The era of modern disc arthroplasty began in 1982 with the development of the SB Charité disc in Berlin.

- It applied Charnley's low-friction principle from THA.
- Consisted of a UHMWPE sliding core articulating between two metal endplates.
- Endplates had teeth-like projections for fixation to the vertebral bodies.

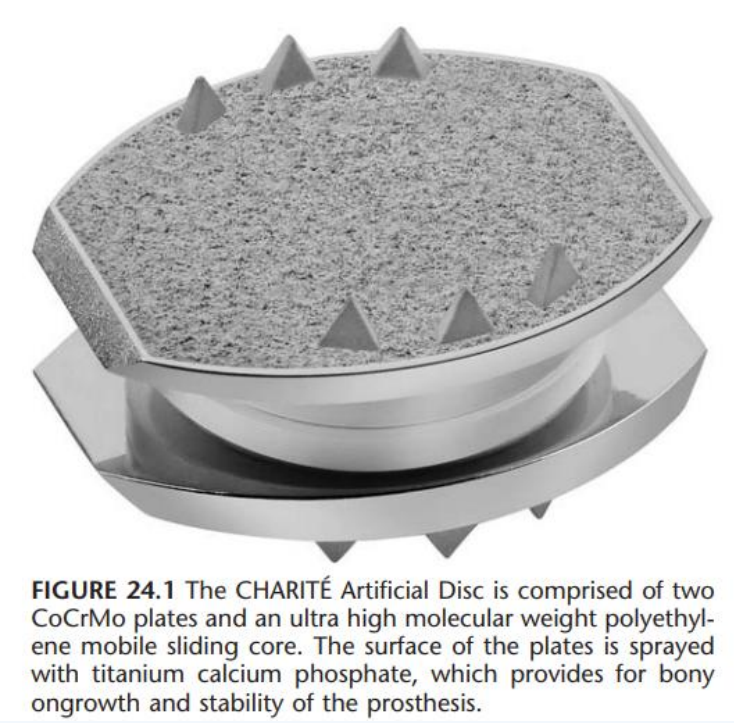


FIGURE 24.1 The CHARITÉ Artificial Disc is comprised of two CoCrMo plates and an ultra high molecular weight polyethylene mobile sliding core. The surface of the plates is sprayed with titanium calcium phosphate, which provides for bony ongrowth and stability of the prosthesis.

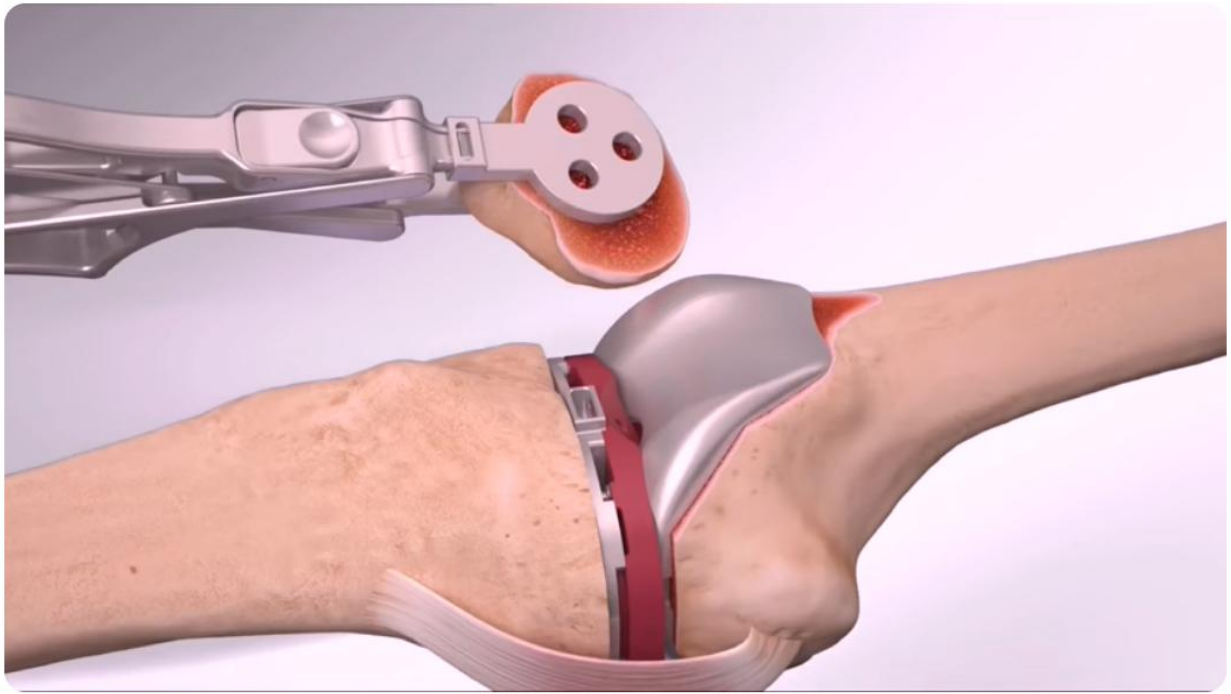
Clinical Neurosurgery • Volume 53, 2006The CHARITE´ Artificial Disc: Design History, FDA IDE Study Results, and Surgical Technique

Current TDA Designs and Technologies

Current TDA designs utilize various articulation technologies, and their long-term clinical success remains under close evaluation.

- Polymer-on-Metal
- Polymer-on-Polymer
- Metal-on-Metal
- All-Elastic Core Technology

Total Knee Arthroplasty



Total Knee Replacement (TKR) - Animation

https://youtu.be/wt_renA2mrw?si=m_G2hxBydVwO5G0z

Manufacturing Total Knee Implant

From Image To Implant

https://youtu.be/08hCiKSB3m8?si=HXwZ6ARGqVmoUa-D

Current Biomaterials in Arthroplasty

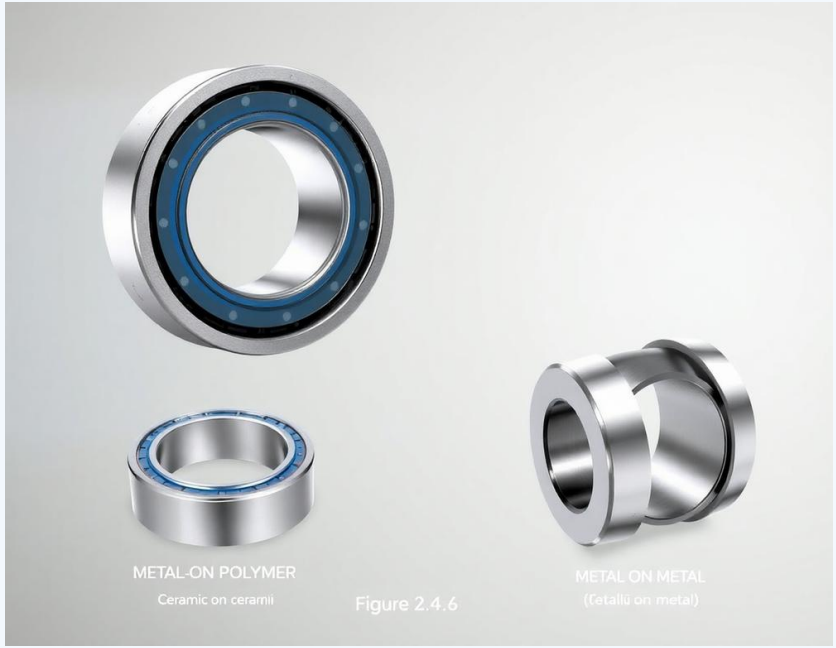
The Archetype of a Modern Total Hip Implant

The typical THA today consists of:

- A Ti or Co-Cr alloy femoral stem (cemented or press-fit).
- A modular Co-Cr alloy or ceramic head.
- An UHMWPE or ceramic acetabular cup/liner.
- A Ti or Co-Cr alloy acetabular shell.

Hundreds of variations exist, creating a challenge for surgeons to select the optimal implant for a specific patient.

Bearing Couples in Modern TJA



The choice of articulating surfaces, or bearing couple, is a critical decision in TJA.

Polymers in Orthopedics

Polymers are most commonly used as:

Articulating Surfaces

e.g., Ultra-High-Molecular-Weight Polyethylene (UHMWPE). Requires low friction and low wear rates.

Fixation Cement

e.g., Polymethylmethacrylate (PMMA). Requires appropriate mechanical properties and in-vivo curing.

Ultra-High-Molecular-Weight Polyethylene (UHMWPE)

Chosen by Charnley after the failure of Teflon, UHMWPE became the standard bearing surface in THA.

Primary Problem: Wear Debris

The wear of the polyethylene bearing produces billions of submicron-sized wear particles annually, which can lead to osteolysis (bone loss).

Improving UHMWPE: Cross-Linking

To improve wear resistance, modern UHMWPE is highly cross-linked, typically using gamma irradiation (2.5-5.0 Mrad).

- Cross-linking improves wear resistance but can negatively affect other properties like tensile strength.
- Heat treatment is used after irradiation to reduce residual free radicals and minimize oxidation.
- While accepted as superior, long-term performance data is still being gathered.

Polymethylmethacrylate (PMMA) Bone Cement

Popularized by Charnley, PMMA acts as a "grouting" material to fix components and distribute loads more uniformly from the implant to the bone.

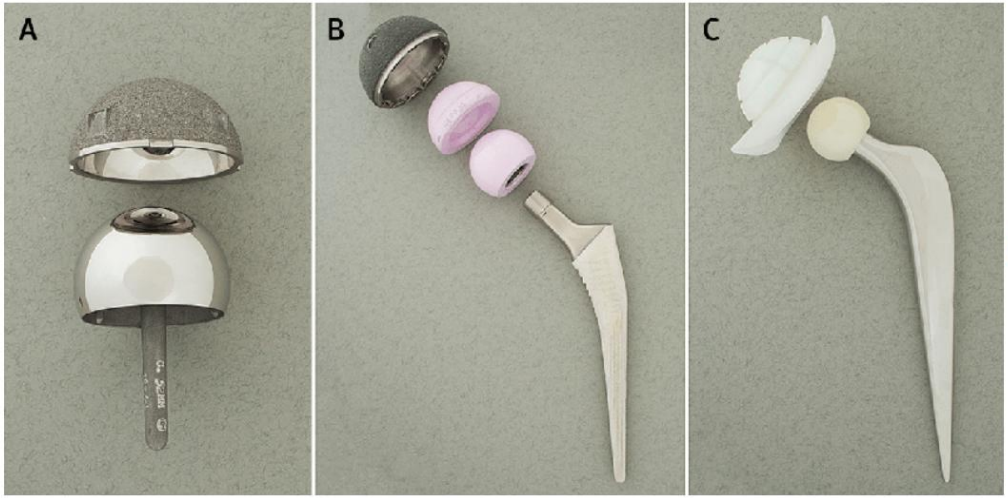
It serves as a structural interface, accommodating the modulus mismatch between a high-modulus metal prosthesis and lower-modulus bone. PMMA remains the method of choice for cemented fixation.

Ceramics in Orthopedics

Ceramics have played an increasing role, with the first FDA approval for a ceramic-on-ceramic hip implant in 2003.

Primary Advantage: **Superior Wear Resistance**

Ceramic-on-ceramic and ceramic-on-polymer bearings offer lower wear rates compared to traditional metal-on-polymer bearings. They are also inert, stiff, and have low friction.



| Illustration of (A) resurfacing implant; (B) ceramic-on-ceramic, large head, uncemented implant (components disassembled); and (C) ceramic-on-polyethylene, small head, cemented implant (head assembled with stem)

Common Orthopedic Ceramics: Alumina & Zirconia

Alumina (Al_2O_3)

Used in orthopedics for over 30 years. The first ceramic couple was implanted in 1970 by Pierre Boutin.

Zirconia (ZrO_2)

Introduced in 1985 as an alternative with enhanced mechanical properties compared to alumina.

Challenges with Ceramics

Early concerns about **fracture** toughness have been addressed by improving ***manufacturing*** (e.g., hot isostatic pressing, HIP), ***lowering grain size***, and ***increasing purity***.

However, mechanical integrity is extremely dependent on manufacturing quality, as evidenced by a major recall of zirconia heads in 2001 due to a change in the sintering process.

Bioactive Ceramics and Coatings

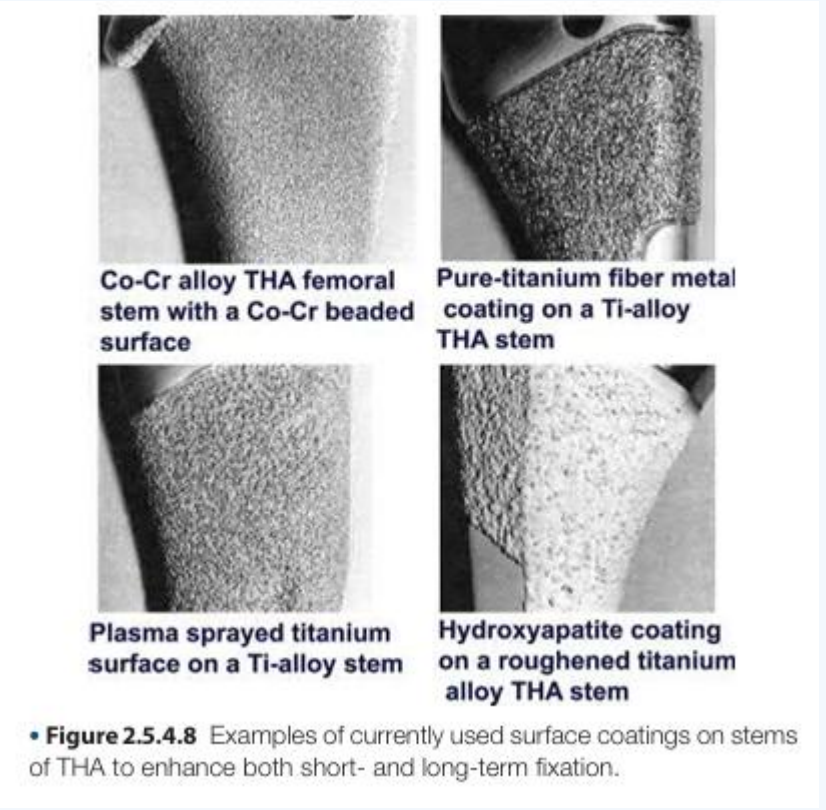
Certain ceramics and glass ceramics are "***osteophilic***," *meaning bone-forming cells* (osteoblasts) will lay down bone in direct apposition to the material.

- ****Bioglasses**:** Special compositions that form a bond with bone through a controlled surface reaction.
- ****Hydroxyapatite*** (OHAp):** The naturally occurring inorganic component of bone. Used as a cladding on metal prostheses to provide fixation via direct bone bonding, as an alternative to PMMA.

Surfaces and Coatings for Fixation

A variety of surface coatings are used to enhance bone ingrowth and fixation:

- Roughened Titanium
- Porous coatings (CoCr or Ti beads)
- Titanium wire mesh (fiber mesh)
- Plasma-sprayed Titanium
- Bioactive materials (Hydroxyapatite)
- Osteogenic growth factors (e.g., TGF-beta) are in development.



• **Figure 2.5.4.8** Examples of currently used surface coatings on stems of THA to enhance both short- and long-term fixation.

Deep Dive: Metal Alloys

The Three Principal Metal Alloys

Implant alloys were originally developed for maritime and aviation uses where ***high strength and corrosion resistance*** are paramount. Three alloy families dominate orthopedics:

- Titanium-based alloys
- Cobalt-based alloys
- Stainless steel alloys

High corrosion resistance is the key property that has led to their widespread use as load-bearing implant materials.

Stainless Steel Alloys (e.g., 316LVM)

Among the first metals used in orthopedics (1926). The most common form is 316LV, an austenitic steel with low carbon content, formed under vacuum.

- Mechanical properties are generally less desirable than other alloys (lower strength, lower corrosion resistance).
- Possess greater ductility, making them popular for cable fixation components.
- **A low-cost alternative** to Ti and Co alloys.

Cobalt-Chromium Alloys

Two types are predominantly used:

- **Cobalt-chromium-molybdenum (CoCrMo - ASTM F75):** The dominant alloy for total joint components due to its excellent wear properties.
- **Cobalt-nickel-chromium-molybdenum (CoNiCrMo - ASTM F562):** Promises increased corrosion resistance but raises concerns of **nickel toxicity/immunogenicity**.

Properties of Cobalt-Chromium Alloys

- Generally cast into their final shape (investment casting) as they are susceptible to work-hardening.
- The strongest, hardest, and most fatigue-resistant of the common implant metals.
- Care must be taken as **finishing treatments** (e.g., sintering porous coatings) **can reduce fatigue strength**.

Titanium Alloys

Developed for the aviation industry, two alloys dominate orthopedic use:

- **Commercially Pure Titanium (CPTi - ASTM F67):** **High corrosion resistance** and ductility. Often used for porous coatings (e.g., fiber metal).

- **Ti-6Al-4V (ASTM F136):** **Superior mechanical properties**. Used for TJA stems.

Properties of Titanium Alloys

- **Pros:** High corrosion resistance (passive TiO_2 film),
  lower stiffness (modulus) closer to bone,
  potentially reducing stress shielding.

- **Cons:** Particularly sensitive to geometrical factors (notch sensitivity),
  relatively soft compared to Co-Cr alloys,
  poor wear and frictional properties.

- Due to poor wear resistance, Ti alloys are seldom used for articulating surfaces.

Newer Alloys: Zirconium and Tantalum

Zirconium (Zr) and Tantalum (Ta) are ***refractory metals known for their chemical stability and high melting points***.

Alloys like oxidized zirconium (e.g., Oxinium) offer high strength, wear resistance (10x Co-Cr), and enhanced biocompatibility due to a stable, hard surface oxide layer.

They are gaining popularity, especially in cases of ***metal hypersensitivity***.

Composition of Common Metal Alloys (%)

Alloy	Ni	Co	Cr	Ti	Mo	Fe
Stainless Steel (F138)	10-15.5	*	17-19	*	2-4	61-68
CoCrMo (F75)	<2.0	61-66	27-30	*	4.5-7.0	<1.5
CoNiCrMo (F562)	33-37	35	19-21	<1	9.0-11	<1

Composition of Common Metal Alloys (cont.)

Alloy	Ti	Al	V	Fe	Ni
CPTi (F67)	99	*	*	0.2-0.5	*
Ti-6Al-4V (F136)	89-91	5.5-6.5	3.5-4.5	*	*
45TiNi	45	*	*	*	55

Electrochemical Properties (Corrosion Resistance)

Alloy	Corrosion Potential (mV)	Passive Current Density (μA/cm²)	Breakdown Potential (mV)
Stainless Steel (F138)	-400	0.56	200-770
Co-Cr-Mo (F75)	-390	1.36	420
CPTi (F67)	-90 to -630	0.72-9.0	>2000
Ti-6Al-4V (F136)	-180 to -510	0.9-2.0	>1500

Note: More negative potential = more reactive. Lower current density & higher

Biomaterial Degradation I: Wear

The Primary Clinical Concern: **Aseptic Osteolysis**

Implant loosening due to ***aseptic osteolysis*** (bone loss not caused by infection) accounts for over 75% of TJA implant failures.

This process is primarily driven by the host's biological response to implant degradation products, namely ***wear debris*** and ***corrosion products***.

Mechanisms of Wear Debris Generation

Wear is the loss of material as particles due to relative motion between two surfaces. Three primary processes **cause wear**:

- **Abrasion**:** A harder surface "plows" grooves in a softer material.
- **Adhesion**:** A softer material is smeared onto a harder counter-surface, forming a transfer film that can then be shed.
- **Fatigue**:** Cyclic loading and unloading cause subsurface cracks that propagate and release particles.

Characterizing Wear Rates

After an initial "wearing-in" period with a high wear rate, the rate decreases and becomes linearly dependent on force and distance.

Steady-State Wear Equation: $V = K * F * x$

- **V:** Volumetric wear (mm^3/year)
- **K:** Material constant for the couple
- **F:** Contact force (N)
- **x:** Distance of relative travel (mm)

Variability of In Vivo Wear Rates

Clinically, **implant wear rates** (typically ~0.1 mm/year for CoCr-on-UHMWPE) ***increase with:***

- Physical activity
- Patient weight
- Size of the femoral head (e.g., 32mm vs 28mm)
- Roughness of the metallic counterface
- Oxidation of the polyethylene

Wear in Spine Arthroplasty (TDA)

Metal-on-Polymer TDA

In vitro wear rates range from 2 to 20.8 mm^3 per million cycles. This is about 10-fold less wear than seen in conventional THA/TKA.

Metal-on-Metal TDA

In vitro wear rates are even lower, around 0.93 - 1.26 mm^3 per million cycles, similar to MoM hip replacements.

Summary: Wear as a Primary Factor

The generation of particulate wear debris is a primary factor affecting the long-term performance and longevity of total joint replacements. This debris induces an inflammatory foreign-body response that can lead to bone loss and implant loosening.

Biomaterial Degradation II: Corrosion

Introduction to Electrochemical Corrosion

Corrosion occurs to some extent on all metallic implants and is undesirable for two main reasons:

- The ***degradative process may reduce the structural integrity*** of the implant.
- The release of ***degradation products*** (metal ions) ***is potentially toxic to the host***.

It often occurs through a synergistic combination of electrochemical dissolution and mechanical wear.

Factors Influencing Corrosion

Corrosion is a multifactorial phenomenon dependent on:

- **Geometric Variables:** e.g., crevices in modular tapers.
- **Metallurgical Variables:** e.g., surface microstructure, oxide composition.
- **Mechanical Variables:** e.g., stress, relative motion (fretting).
- **Solution Variables:** e.g., pH, proteins, enzymes in body fluids.
- **Mechanical Loading Environment:** e.g., degree of movement, contact forces.

Thermodynamic Driving Force for Corrosion

The tendency for a metal to corrode (oxidize) is a thermodynamic driving force related to the change in Gibbs Free Energy (ΔG).

$$\Delta G = -nF\Delta E$$

A more negative potential (E) of a metal in solution indicates a greater tendency to react and corrode.

Kinetic Barriers to Corrosion

While thermodynamics determines *if* corrosion can happen,
kinetics determines *how fast* it happens.

Kinetic barriers physically limit the rate of corrosion. The most important kinetic barrier for orthopedic alloys is the formation of a passive oxide film on the metal surface.

The Role of Passivating Oxide Films

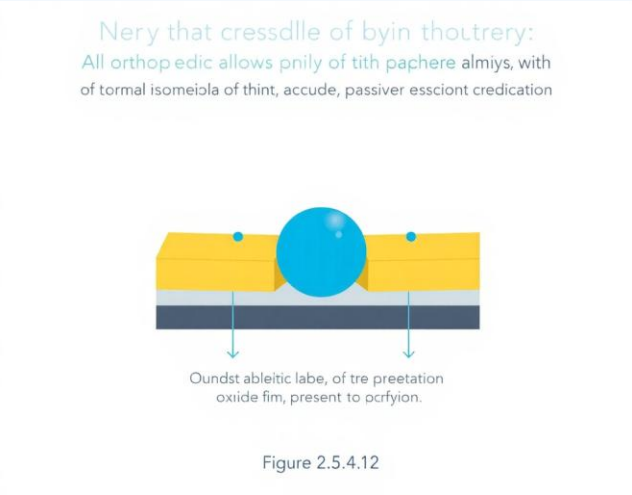


Figure 2.5.4.12

Most orthopedic alloys rely on spontaneously formed passive films (metal oxides) to prevent significant corrosion. These films act as a barrier to the transport of metallic ions and/or electrons.

Characteristics of Oxide Films (Part 1)

- **Very Thin:** Typically 5-70 Å. The electric field across them is immense (10^6-10^7 V/cm).
- **Semiconductors:** They have an atomic defect structure (e.g., vacancies) that determines ionic and electronic transport. Fewer defects (like in TiO_2) mean better corrosion resistance.
- **Mixed Oxides (Spinels):** Oxides like $(Cr_2O_3)CoO$ can form on Co-Cr alloys, offering higher strength and better resistance to ion diffusion.

Characteristics of Oxide Films (Part 2)

- **Adherence (Pilling-Bedworth Ratio):** The mismatch between the metal and oxide lattice determines if the oxide will adhere or flake off (spall).
- **Morphology:** Films are not smooth sheets but often consist of needle or dome shapes.
- **Mechanical Fragility:** Films can be abraded or fractured by fretting or stress. When this happens, fresh metal is exposed, and rapid repassivation (or corrosion) occurs.

Fretting Corrosion / MACC

Mechanically Assisted Crevice Corrosion

This occurs at junctions of implant components (e.g., modular tapers) due to small-scale relative motion (1-100 µm) from cyclic loading.

Mechanical abrasion of the oxide layer within a crevice alters the local chemistry (e.g., lowers pH), which further accelerates corrosion. This process releases bioreactive corrosion products.

Debris Types: Particles and Ions

The degradation products of orthopedic implants are one of two basic types:

Particulate Debris

Solid particles of metal, ceramic, or polymer ranging from submicron to millimeter size. Primarily generated by mechanical wear.

Soluble Debris (Ions)

Metal ions (or nanoparticles) that are released through corrosion and bind to proteins, allowing systemic transport.

Particulate Debris: Size and Shape

The size and shape of wear debris are specific to the implant materials.

- **Hard-on-Hard (e.g., Metal-on-Metal):** Produces smaller (submicron), fairly round debris.
- **Hard-on-Soft (e.g., Metal-on-Polymer):** Produces larger (micron-sized), more elongated debris.

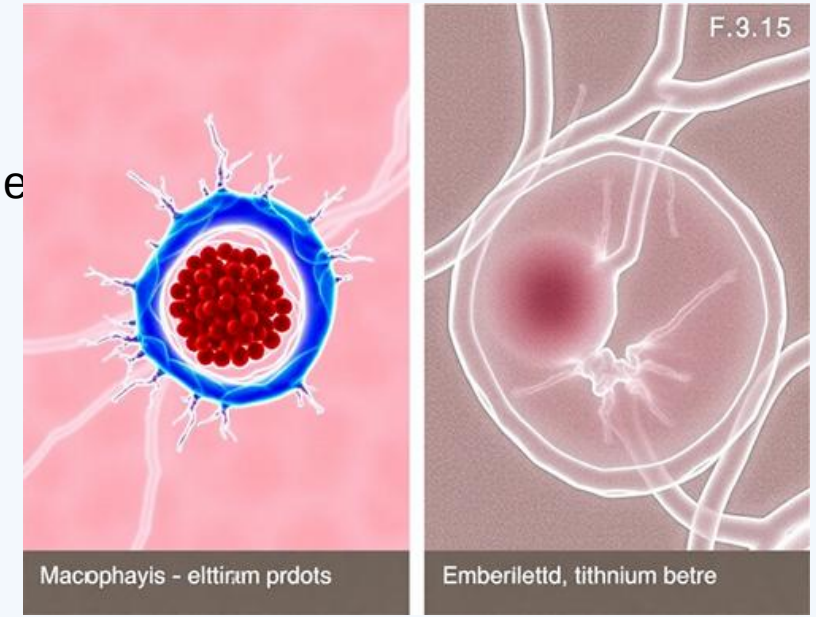
Histological Identification of Debris: SS and Co-Base

- **Stainless Steel:** Tissues show iron-containing granules (hemosiderin-like) and larger "microplates" of a chromium compound.
- **Cobalt-Base Alloys:** The principal corrosion product is a chromium-phosphate hydrate. These particles can be found at modular junctions and within tissues, and can participate in third-body wear.

Histological Identification of Debris: Ti-Base

Unlike SS and Co-alloys which form precipitated corrosion products, titanium degradation results in tissue discoloration from metallic debris that has the same elemental composition as the parent alloy.

This wear debris presents an enormous surface area for further electrochemical dissolution, contributing to systemic elevations in titanium levels.



Particle Characterization: Number vs. Volume

The "average size" of particles depends on the method of evaluation.

- **Number Basis (e.g., SEM/TEM):** The majority of particles are in the nanometer to submicron range.
- **Volume Basis (e.g., LALLS):** A few very large particles can comprise a significant portion of the total mass (volume) of debris, even though they are few in number.

Particulate Debris Bioreactivity

The inflammatory response to debris depends on several particle characteristics. A theoretical "Pro-inflammatory Index" can be considered:

Index = K_load * K_shape * K_material

Reactivity Factor 1: Particle Load

Greater particle load (concentration of phagocytosable particles) increases inflammation. This depends on both the total volume of debris and the size of the particles. A given mass of small particles will result in far greater numbers than the same mass of large particles.

Reactivity Factor 2: Aspect Ratio (Shape)

Elongated particles (fibers) are generally more pro-inflammatory than round particles. This has been well-established in studies of materials like asbestos. However, a specific threshold aspect ratio for implant debris has not been defined.

Reactivity Factor 3: Chemical Reactivity (Material)

There is a growing consensus that metal particles are more pro-inflammatory than polymers.

This may be because metals are capable of corroding and releasing ions that can induce hypersensitivity, cytotoxicity, and DNA damage.

Metal Ions (Soluble Debris)

Chemically active metal ions are released from implants, bind to proteins, and can disseminate into the bloodstream and remote organs.

Following TJA, levels of circulating metals (e.g., Co, Cr, Ti) have been shown to increase significantly above normal baseline levels.

Sources of Elevated Metal Ions

Articular Wear

Wear of the bearing surface, especially in Metal-on-Metal (MoM) hips, is a major source of Co and Cr ions.

Fretting Corrosion

Mechanically assisted crevice corrosion at modular junctions (e.g., head-neck taper) is another significant source.

Corrosion at Modular Junctions

Corrosion at the head-neck taper of a modular hip implant is a significant clinical issue.

Local & Systemic Effects of Degradation

Local Effect: Osteolysis

Implant debris limits longevity by causing a local inflammatory response that leads to bone erosion (osteolysis) and implant loosening. This occurs as either diffuse cortical thinning or focal cyst-like lesions.

Normal bone maintenance (balance of osteoblast and osteoclast activity) is disrupted.

The Osteolytic Cascade

Debris-induced inflammation is largely mediated by macrophages, which secrete inflammatory cytokines (IL-1β, TNFα, IL-6), prostaglandins (PGE_2), and enzymes that promote bone resorption and decrease bone formation.

Mediators like RANKL (promotes osteoclast formation) and osteoprotegerin (inhibits it) are also key factors.

How Does Sterile Debris Provoke Inflammation?

For decades, it was unclear how sterile, non-biological implant debris could trigger an immune response. Recent progress has implicated a specific intracellular danger-signaling pathway.

The Inflammasome Pathway

The inflammasome is an intracellular multi-protein complex that senses "danger-associated molecular patterns" (DAMPs), including sterile stimuli like implant debris, asbestos, and silica.

Activation of this pathway is a key mechanism explaining how cells transduce sterile challenges into an inflammatory response.

Inflammasome Activation Mechanism

- Debris is phagocytosed by a macrophage.
- The particle causes lysosomal damage/destabilization.
- This leads to an increase in reactive oxygen species (ROS).
- The NALP3 inflammasome complex is activated.
- Activated caspase-1 is produced.
- Caspase-1 cleaves pro-cytokines into their active forms (e.g., IL-1β), which are then released.

Particle Migration and Granulomas

Particulates generated at the articular surface can migrate to the bone-implant interface, even in remote regions of the implant.

When present in sufficient amounts, they induce an inflammatory foreign-body granulation tissue that can invade the interface and cause osteolysis.

Sex Differences in Reactivity

Recent studies suggest potential sex-based differences in response to implant debris.

- CoCrMo debris induced significantly more osteolysis in female mice than male mice.
- No sex-based difference was observed for UHMWPE particles in the same models.
- Clinical observations report higher failure rates for women with some MoM THA designs.

This may be due to the complex, pleotropic effects of metal debris (e.g., toxicity, adaptive immunity) that are not present with polymer debris.

Systemic Effects: Metal Ion Toxicity

The release and systemic distribution of metal ions is a concern due to the known potential toxicities of the elements used in implant alloys.

- **Cobalt:** Polycythemia, cardiomyopathy, hypothyroidism.
- **Chromium:** Nephropathy, hypersensitivity, carcinogenesis.
- **Nickel:** Eczematous dermatitis, hypersensitivity, carcinogenesis.
- **Vanadium:** Cardiac/renal dysfunction, hypertension.
- **Aluminum:** Anemia, osteomalacia, neurological dysfunction.

Metal Concentrations in Remote Organs

Postmortem studies of subjects with Co-base alloy TJA components have shown significant increases in Co and Cr concentrations in the:

- Heart
- Liver
- Kidney
- Spleen
- Lymphatic Tissue

Similarly, patients with Ti-base alloy implants show elevated Ti, Al, and V levels in remote organs.

Metal in Liver & Spleen (µg/g dry wt)

Organ	Group	Cr	Co	Ti
Liver	Normal	<14	120	100
Liver	TJA	1130	15,200	560
Spleen	Normal	10	30	70
Spleen	TJA	180	1600	1280

Systemic Particle Distribution

Lymphatic transport is a major route for the dissemination of wear debris. Particles are found in regional lymph nodes, and may further disseminate to the liver and spleen.

Accumulation of particles can induce lymphadenopathy, fibrosis, necrosis, and granulomas in these remote organs.

Immunological Concerns

Hypersensitivity ("Metal Allergy")

Released metal ions, while not sensitizers on their own, can act as haptens by forming complexes with native proteins. These metal-protein complexes can then be recognized by the immune system as antigens (allergens), triggering an immune response.

The Immune Mechanism: Type IV DTH

Implant-associated metal sensitivity is generally a Type IV Delayed-Type Hypersensitivity (DTH) response.

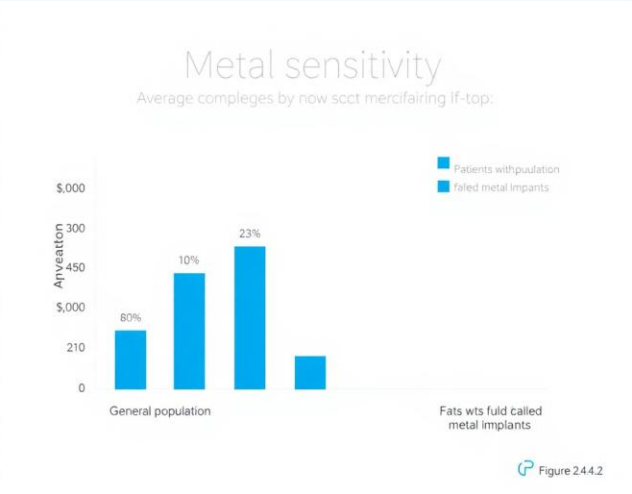
- This is a cell-mediated response, not an antibody-mediated one.
- Sensitized T-lymphocytes, upon re-exposure to the metal antigen, release cytokines.
- These cytokines recruit and activate large numbers of macrophages.
- This self-perpetuating response can create extensive tissue damage and inflammation.

Common Metal Sensitizers

Dermal hypersensitivity to metal is common, affecting 10-15% of the population.

- **Most Common:** Nickel (Ni)
- **Also Common:** Cobalt (Co), Chromium (Cr)
- **Occasional:** Tantalum (Ta), Titanium (Ti), Vanadium (V)

Incidence of Metal Sensitivity in Implant Patients



Correlation with Implant Failure

- The incidence of metal sensitivity in patients with a well-functioning implant is ~25% (twice the general population).
- The incidence in patients with a FAILED implant is ~50-60% (more than five times the general population).
- This has led to speculation that immunological processes may be a factor in implant loosening.

It remains unclear if sensitivity *causes* loosening, or if loosening (and increased debris) *causes* sensitivity.

Testing for Metal Sensitivity

Patch Testing

The traditional dermatological test. Involves applying metal salt solutions to the skin. Concerns exist about its representativeness and potential to sensitize the patient.

Metal-LTT

An in-vitro blood test (Lymphocyte Transformation Test) that measures the proliferative response of a patient's lymphocytes to metal antigens. It is considered more quantitative and is gaining popularity.

Carcinogenesis

The carcinogenic potential of implant debris remains an area of concern and investigation.

Evidence for Carcinogenesis

- **Animal Studies:** Have documented that implant metals (Co, Cr, Ni) can act as carcinogens, causing sarcomas in rats and dogs.
- **Epidemiological Studies:** Some early, smaller studies implicated implants in causing cancer 10-20 years post-op. However, larger, more recent studies have found no significant increase in cancers like leukemia or lymphoma.
- **Confounding Factors:** Differences in populations with and without implants make interpretation difficult.

Current View on Carcinogenic Risk

Causality has not been established in human subjects. It remains unknown if metal release from orthopedic implants is carcinogenic in humans.

Compared to the millions of devices implanted yearly, the incidence of cancer at the site of implantation is relatively rare. However, continued monitoring and large long-term epidemiological studies are required.