

生醫材料導論

Introduction of Biomaterials

金屬生醫材料

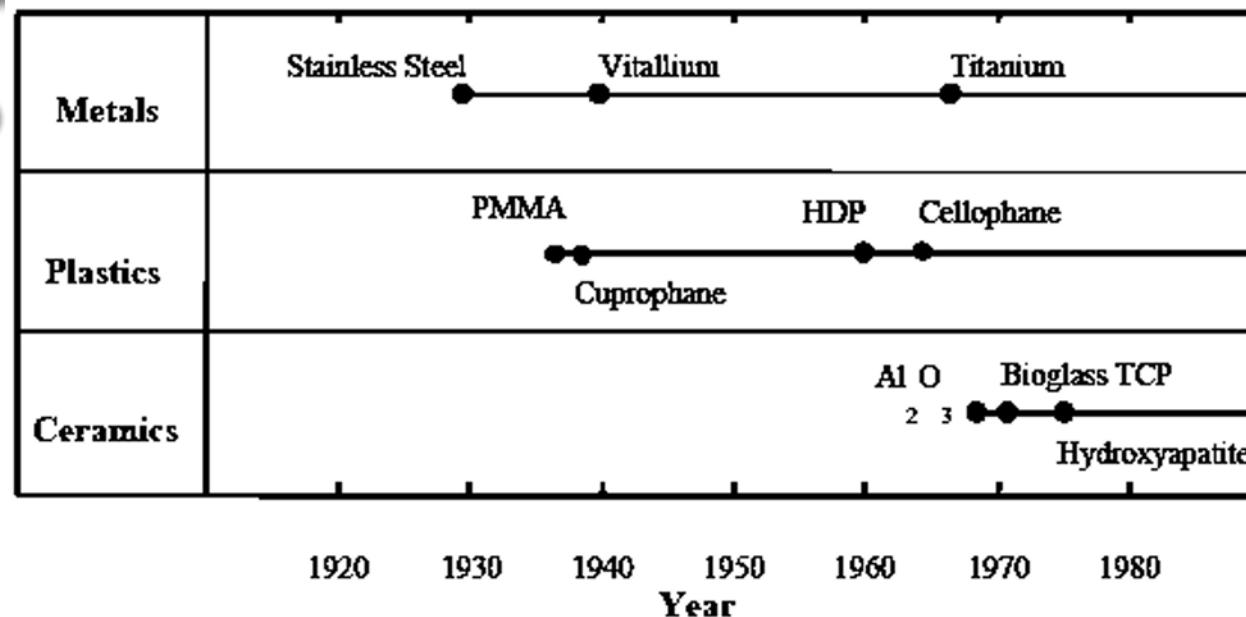
Metallic Biomaterials

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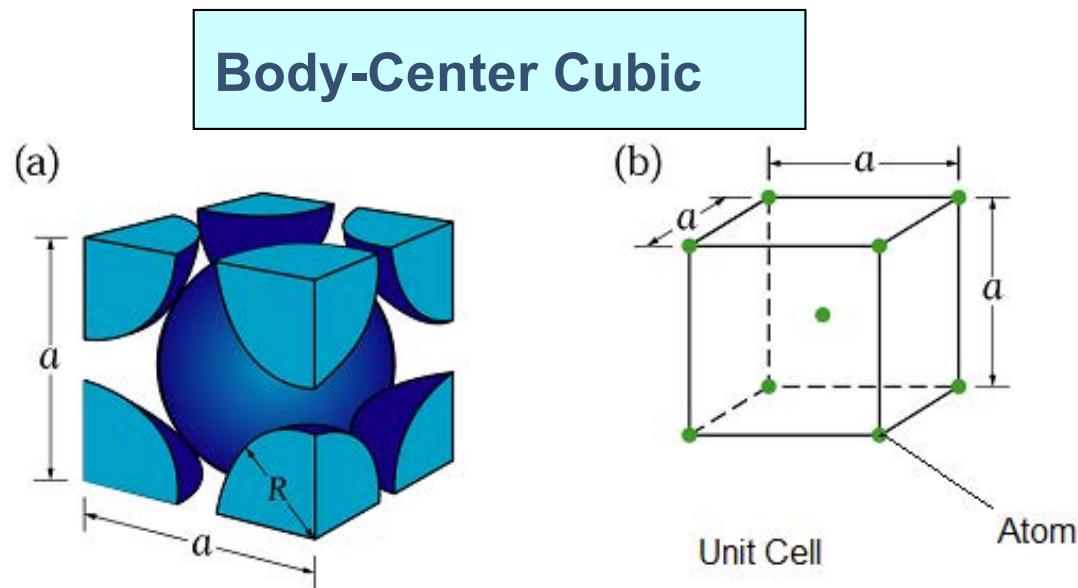
各類材料於生醫領域應用發展過程



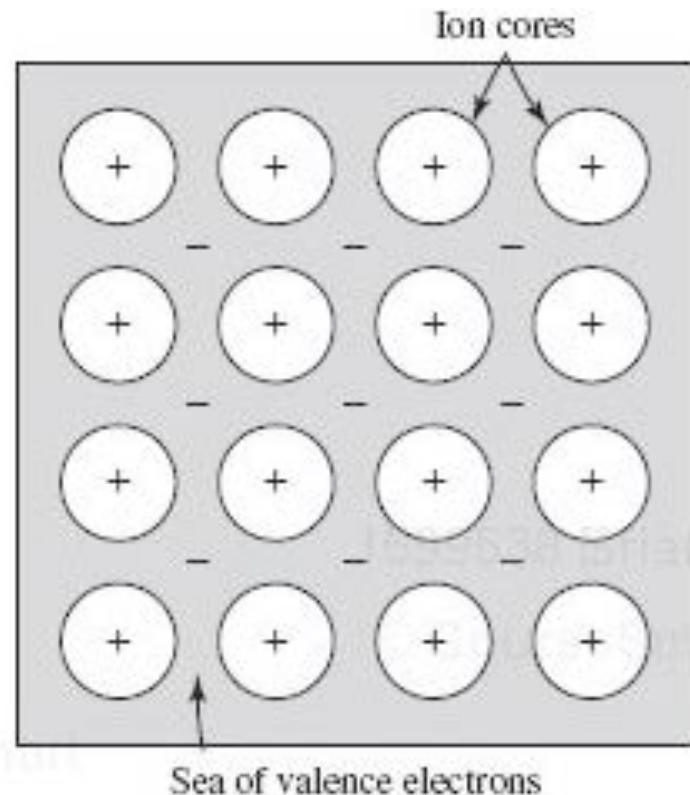
- The first metal alloy developed specifically for human use was the “**vanadium steel**” which was used to manufacture bone fracture plate and screws.
- Iron (Fe), chromium (Cr), cobalt (Co), nickel (Ni), titanium (Ti), tantalum (Ta)**鉭, **niobium (Nb)**鉻, **molybdenum (Mo)**, and **tungsten (W)**.
- The **biocompatibility** of the **metallic implant** is of considerable concern because these implants can **corrode** in an *in vivo* environment. The consequences of **corrosion** are the disintegration of the implant material, which will weaken the implant, and the harmful effect of corrosion products on the surrounding tissues and organs.

Metallic Biomaterials

Metals are crystalline



The body-centered cubic (bcc) crystal structure: (a) hard-ball model; (b) unit cell; and (c) single crystal with many unit cells.
Source: W. G. Moffatt, et al., *The Structure and Properties of Materials*, Vol. 1, John Wiley & Sons, 1976.



：良好的導電、導熱、機械強度

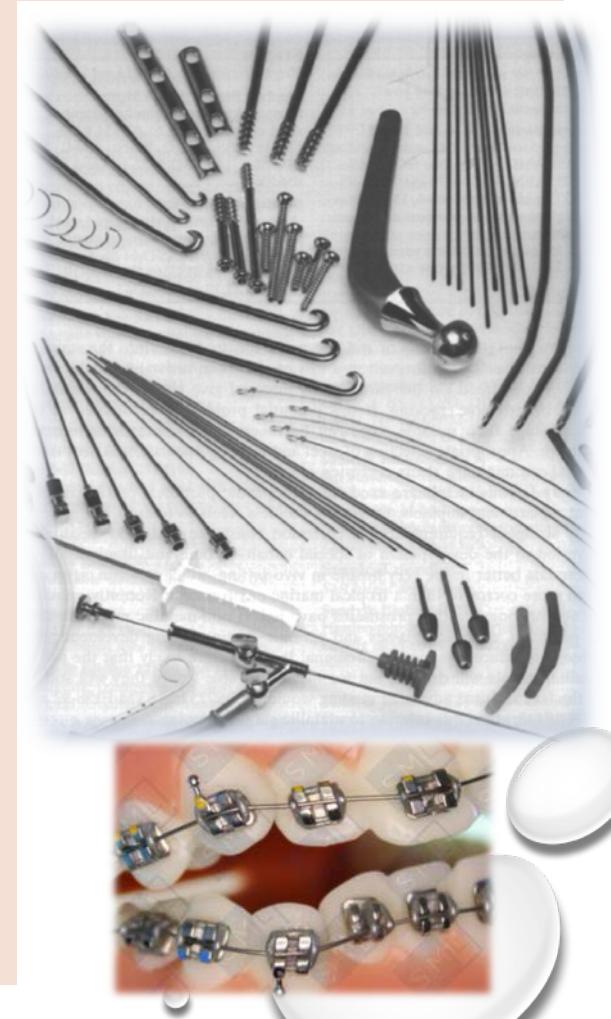
骨、牙科

Metallic Biomaterials

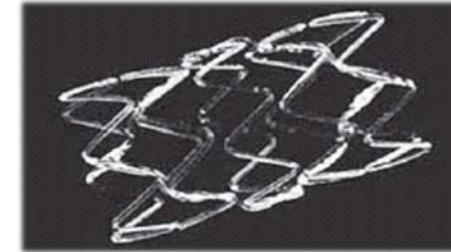
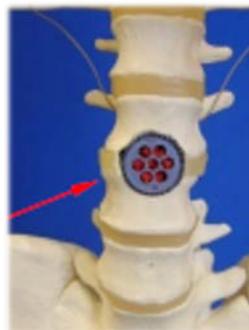
- Metals are used as biomaterials due to their excellent electrical and thermal conductivity and mechanical properties.
- Some metals are used as passive substitutes for hard tissue replacement such as total hip and knee joints; for fracture healing aids as bone plates and screws, spinal fixation devices, and dental implants because of their excellent mechanical properties and corrosion resistance.
- Some metallic alloys are used for more active roles in devices such as vascular stents, catheter guide wires, orthodontic arch wires, and cochlea implants.

血管

金屬延展、柔韌性



Metallic Biomaterials



腐蝕

Corrosion

- A natural process that converts a refined metal into a more chemically stable form such as **oxide**, **hydroxide**, or **sulfide**.
- It is the **gradual destruction of materials** (usually a metal) by chemical and/or **electrochemical reaction** with their environment.
- Corrosion engineering is the field dedicated to controlling and preventing corrosion.



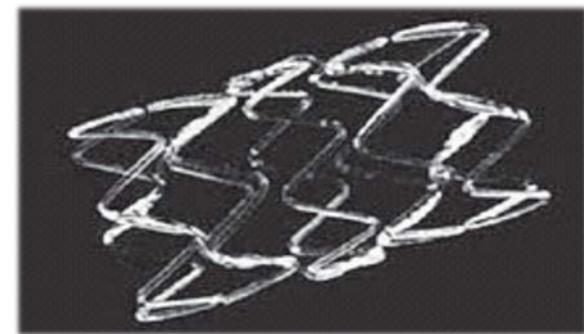
Hip joint replacement

Metallic Biomaterials

There are 3 main groups of metals used as biomaterials:

- **Stainless steels (不鏽鋼)**

碳少、鉻Cr↑、鎳Ni↑而耐腐蝕



- **Co-based alloys (鈷合金)**

- **Titanium-based alloys (鈦合金)**



Stainless Steels

不鏽鋼

200 (Cr-Ni)

400 (Cr)

300 (Cr-Ni-Mo)

500 (Low Cr)

- First stainless steel used for implant materials : 18-8 (Austenitic Stainless Steel), 18-8sMo stainless steel was introduced.
- Contains **Chromium (Cr)**, **Nickle (Ni)**, **Molybdenum(Mo)** to improve corrosion resistance in salt water.

提高耐腐蝕性

316L

- In the 1950s the **carbon content** of **316** stainless steel was **reduced from 0.08 w/o to 0.03 w/o** maximum for better **corrosion resistance** to chloride solution, and it became known as 316L.
- 316L and 316 stainless steel is the maximum content of carbon, that is, 0.03 and 0.08% 碳含量↓ 提高對氯化物溶液的耐腐蝕性

Table 5-1. Compositions of 316L Stainless Steel Surgical Implants (ASTM, 2000)

Element	Composition (w/o)
Carbon	0.030 max
Manganese	2.00 max
Phosphorus	0.025 max
Sulfur	0.010 max
Silicon	0.75 max
Chromium	17.00–19.00
Nickel	13.00–15.00
Molybdenum	2.25–3.00
Nitrogen	0.10 max
Copper	0.50 max
Fe	Balance

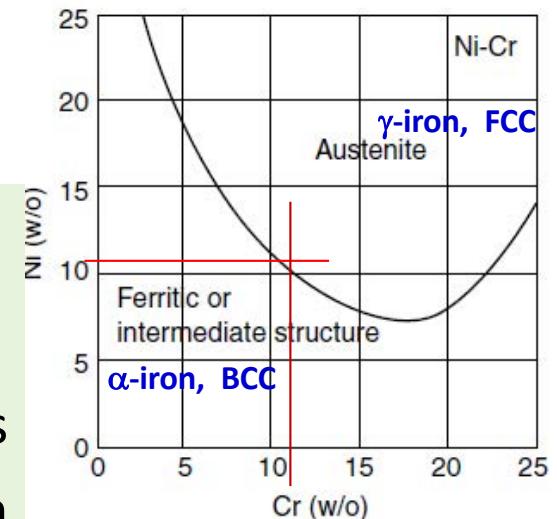
Stainless steels (F138 and F139 of ASTM).

Stainless Steels

- **Chromium** is a major component of corrosion-resistant stainless steel. (>11%)
- The chromium is a reactive element, but it and its alloys can be passivated to give excellent corrosion resistance. (Cr_2O_3)
- The inclusion of molybdenum enhances resistance to pitting corrosion in salt water.
- The **nickel** serves to stabilize the austenitic phase at room temperature and, in addition, to enhance corrosion resistance.

Corrosion

- Unwanted reaction of metal with environment, resulting in its continuous degradation to oxides, hydro-oxides and other compounds.



The effect of Ni and Cr contents on the **austenitic phase** of stainless steels containing 0.1 % Cr

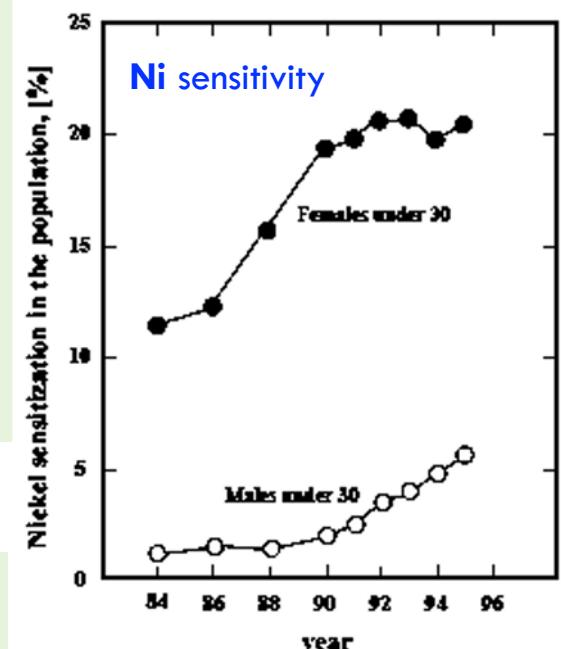


Fig. Frequency of nickel sensitization in the population

Trace elements in human body

- Barium 鈽
- Beryllium 鍍
- Boron 硼
- Cadmium 鎘
- Caesium 銫
- Chromium 鉻
- Cobalt 鈷
- Copper 銅
- Iodine 碘
- Fluorine 氟
- Iron 鐵
- Lithium 鋰
- Manganese 錳
- Molybdenum 鉬
- Nickel 镍
- Selenium 硒
- Strontium 鈦
- Tungsten 鑑
- Zinc 鋅

Functions of some trace elements

缺鐵

- Deficiencies iron

缺硼

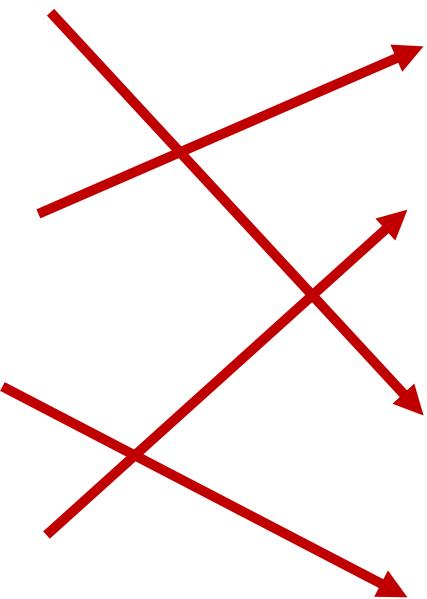
- Boron shortage

缺碘

- Less iodine

缺銅

- Copper shortage



- Osteoporosis (骨質疏鬆)

變白髮

- Hair greying

- Anemia (貧血)

- Thyroid imbalance(甲狀腺症)



Toxic Examples-Co, Cr & Ni

微量OK，但太多會致癌

carcinogenic hexavalent chromium,

- Although **Co** and **Ni** is an essential element for life in minute amounts, at **higher levels of exposure** it shows **mutagenic and carcinogenic effects**.
- In 1966, the addition of **cobalt compounds to stabilize beer foam** in Canada led to **cardiomyopathy**, which came to be known as beer drinker's cardiomyopathy.
- After nickel and chromium, **cobalt** is a major cause of contact dermatitis

永不妥協

• Erin Brockovich

Carcinogenic hexavalent chromium

Pacific Gas and Electric Company (PG&E)



Biocompatibility of Trace Elements

Most **trace elements** can be **tolerated** by the body in **minute amounts**, but **cannot be tolerated in large amounts** in the body, although they are essentials in cell function (Fe) and vitamin B12 (Co), crosslinking of elastin in the aorta (Cu) etc.

CoCr Alloys

- The two basic elements of the **CoCr** alloys form a solid solution of up to **65% Co**. *鉬 + 鉻 → 細晶粒 → 強度↑*
- The **molybdenum (Mo)** is added to produce **finer grains** which results in **higher strengths** after casting or forging.
- The **chromium(Cr)** enhances **corrosion resistance** as well as solid solution strengthening of the alloy. *(Cr₂O₃)*

TABLE 1.3 Chemical Compositions of Co-Cr Alloys

- CoCrMo** alloys (F75) - casting
- CoCrWNi** alloys (F90) - forging
- CoNiCrMo** alloys (F562) - forging
- CoNiCrMoWFe** alloys(F563) - forging

Element	CoCrMo (F75)		CoCrWNi (F90)		CoNiCrMo (F562)		CoNiCrMoWFe (F563)	
	Min.	Max.	Min.	Max.	Min.	Max.	Min.	Max.
Cr	27.0	30.0	19.0	21.0	19.0	21.0	18.00	22.00
Mo	5.0	7.0	—	—	9.0	10.5	3.00	4.00
Ni	—	2.5	9.0	11.0	33.0	37.0	15.00	25.00
Fe	—	0.75	—	3.0	—	1.0	4.00	6.00
C	—	0.35	0.05	0.15	—	0.025	—	0.05
Si	—	1.00	—	1.00	—	0.15	—	0.50
Mn	—	1.00	—	2.00	—	0.15	—	1.00
W	—	—	14.0	16.0	—	—	3.00	4.00
P	—	—	—	—	—	0.015	—	—
S	—	—	—	—	—	0.010	—	0.010
Ti	—	—	—	—	—	1.0	0.50	3.50
Co			Balance					

Source: American Society for Testing and Materials, F75-87, p. 42; F90-87, p. 47; F562-84, p. 150, 1992.

Casting (鑄造) 將金屬倒入模具

- The casting process consists of **pouring or injecting molten metal into a mold** containing a cavity with the desired shape of the casting.
- Metal casting processes can be classified either by the type of mold or by the pressure used to fill the mold with liquid metal.

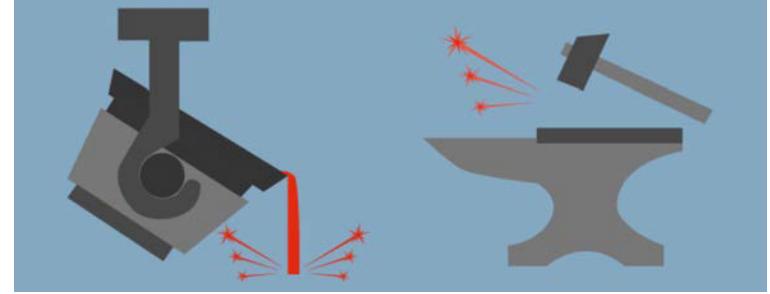
- Large and complex parts
- High production rate
- Design flexibility

Forging (鍛造) 壓力塑性

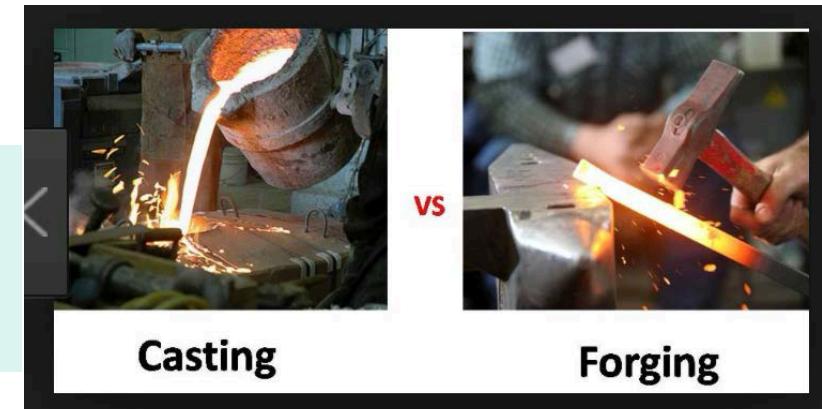
- Forging is a manufacturing process where **metal is shaped by plastic deformation under great pressure** into high strength parts.

- Good mechanical properties (yield strength, ductility, toughness)
- Reliability (used for critical parts)
- No liquid metal treatment

CASTING or FORGING?



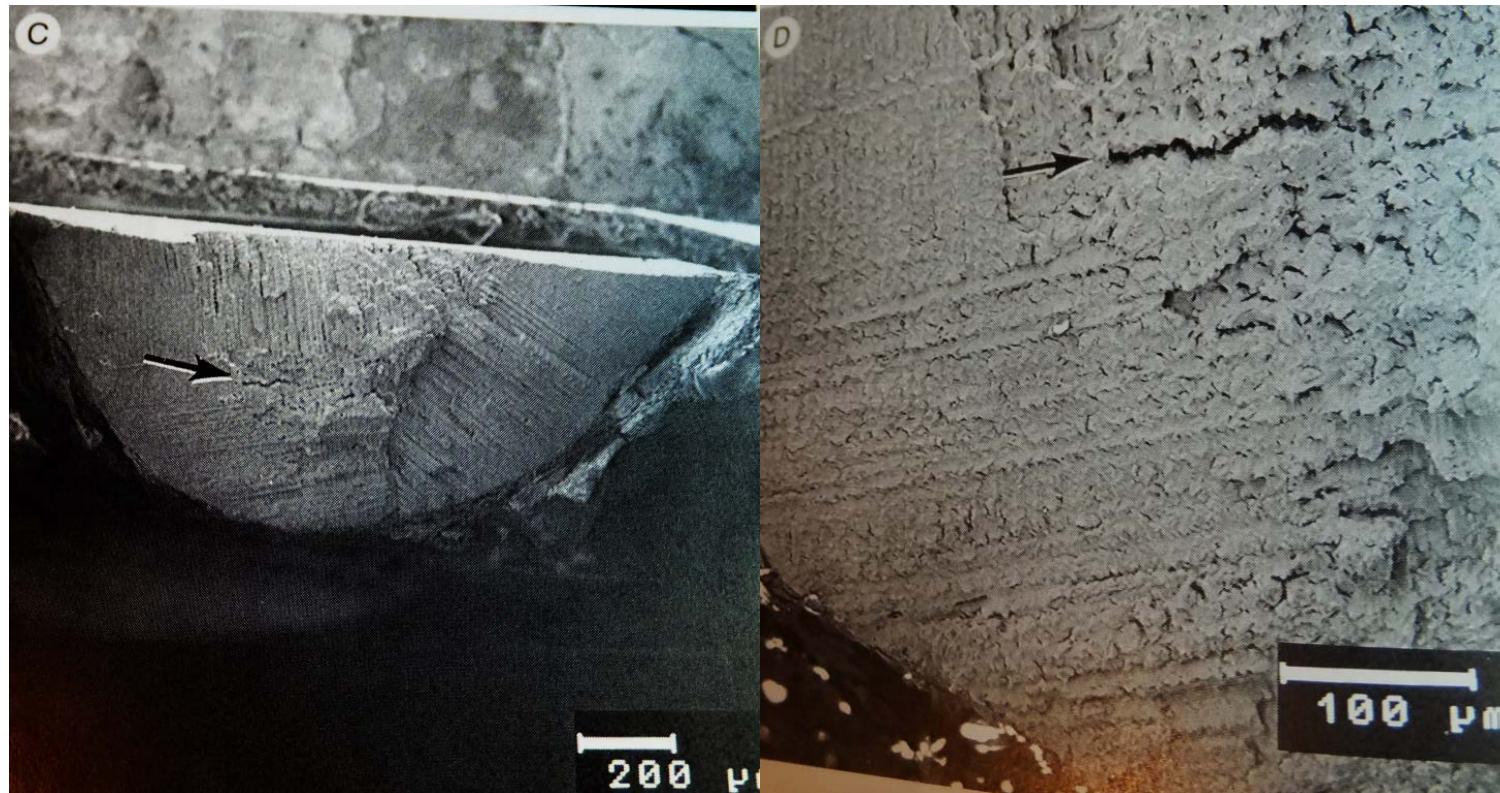
<http://www.dropforging.net>



<http://www.ekoendustri.com/assets/pdf/6.pdf>

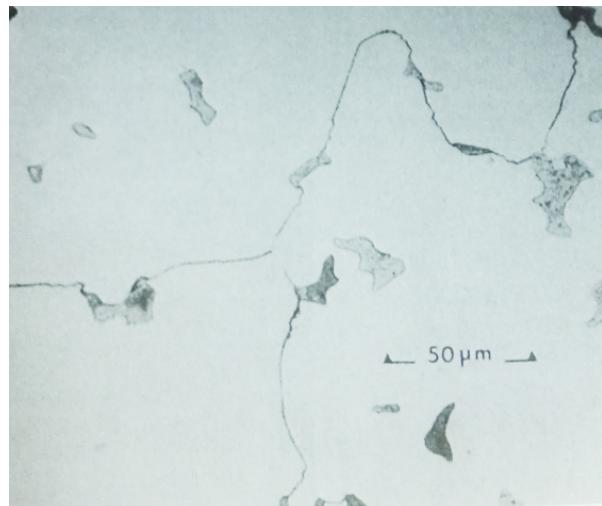
CoCr Alloys

Casting Defect

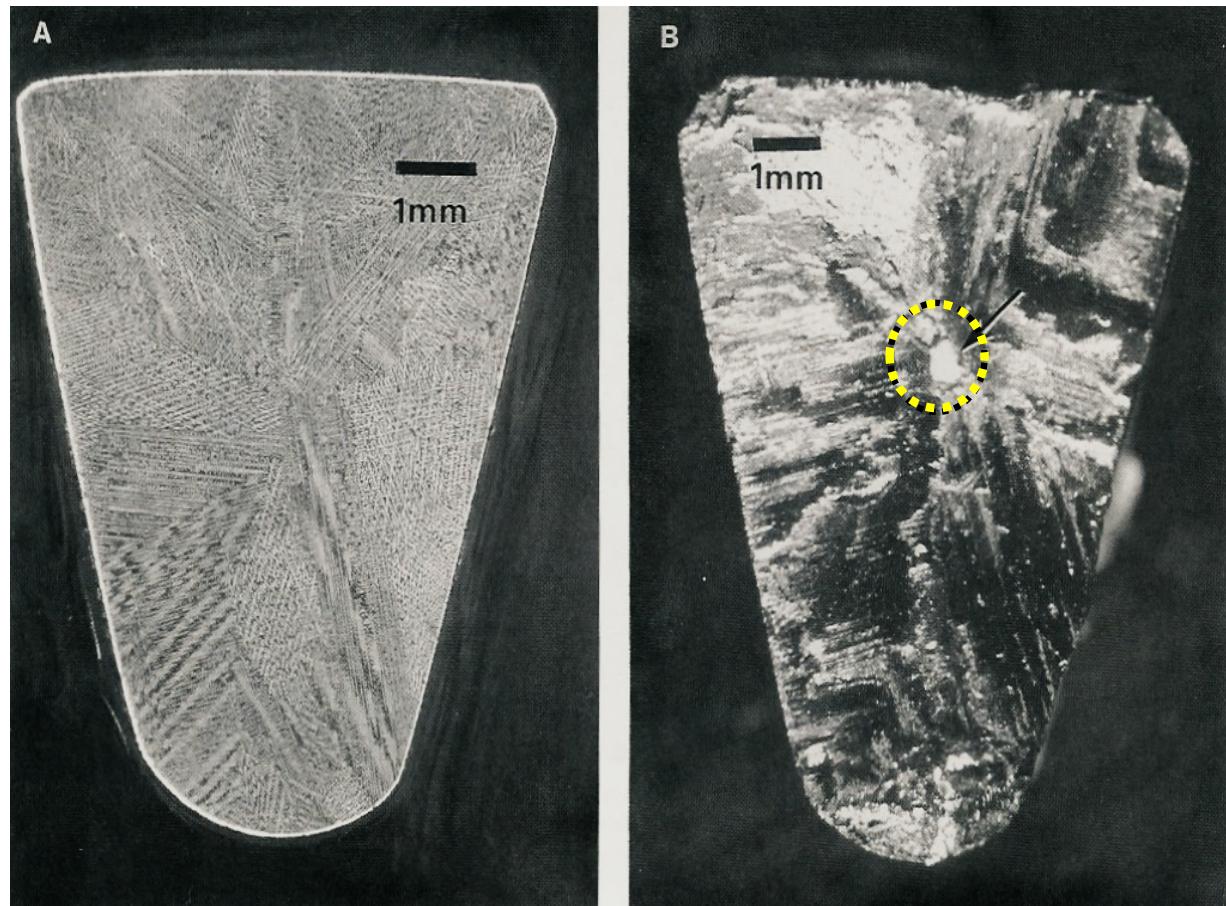


CoCr Alloys

Casting Defect



Microstructure of F75
(Casting)



Polished-etched view of a cast
ASTM F75 femoral hip stem. Note
dendrites and large grains

In vivo fracture initiated from
an inclusion formed during
the casting process

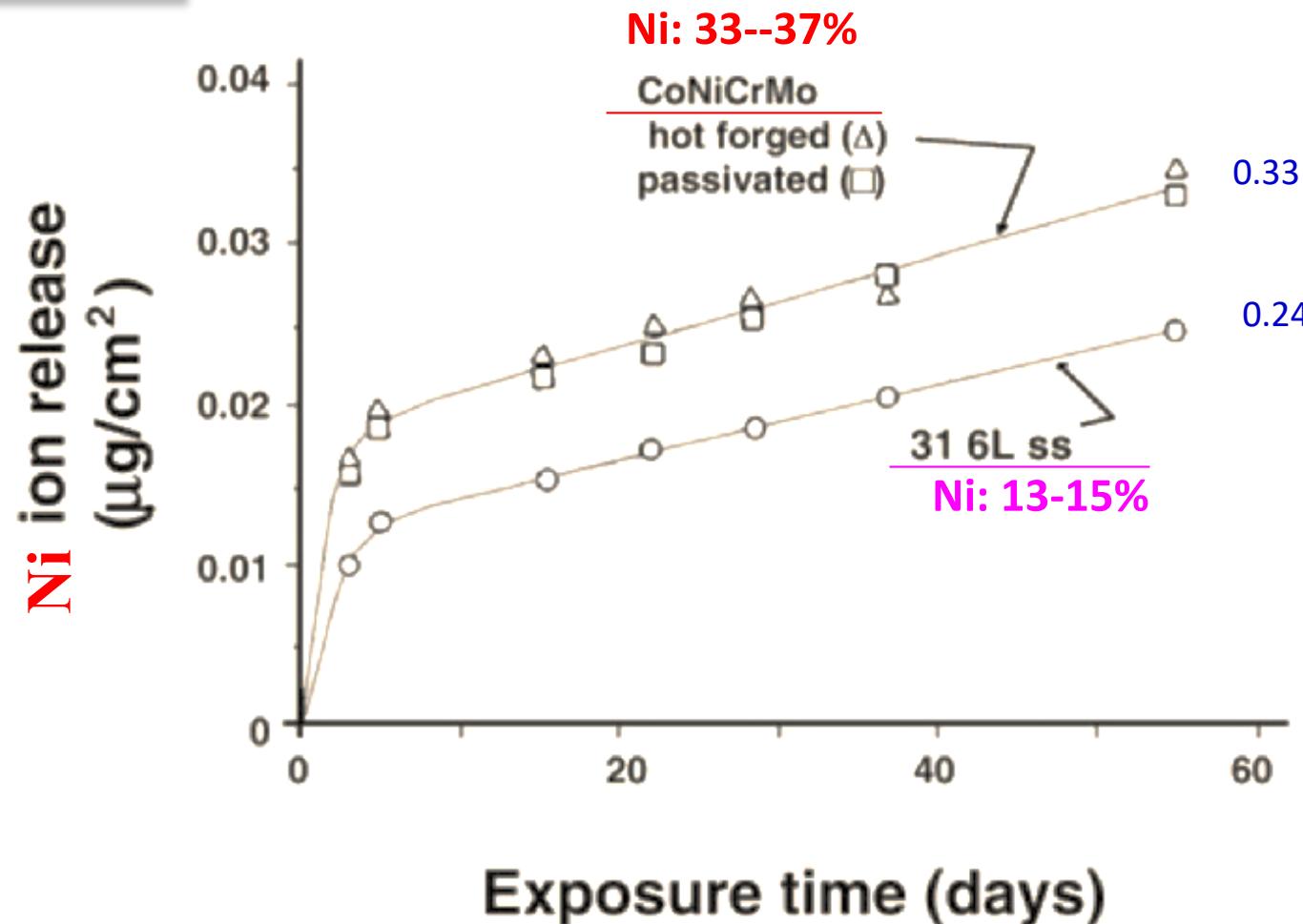
CoCr Alloys

Wear, corrosion, and fretting

抑制成骨細胞

- *In vitro* studies have indicated that particulate **Co** is **toxic** to **human osteoblastlike cell lines** and **inhibits synthesis** of **type-I collagen**, **osteocalcin** and **alkaline phosphatase** in the culture medium.
- Particulate **Cr** and **CoCr** alloy are well **tolerated** by **cell lines** with no significant toxicity. 可提升耐受性
又無毒
- The toxicity of metal extracts *in vitro* have indicated that **Co** and **Ni** extracts at **50%** concentration appear to be **highly toxic** since all viability parameters were altered after 24 h. However, **Cr** extract seems to be **less toxic** than **Ni** and **Co**. 副毒

CoCr Alloys

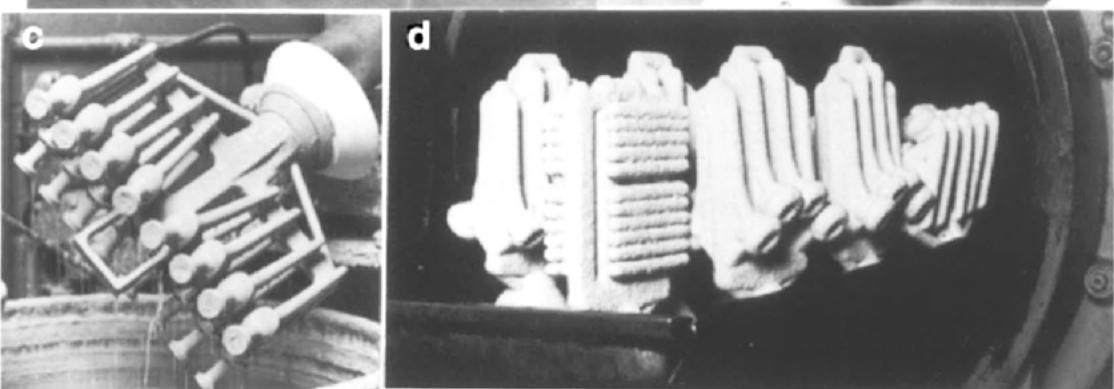
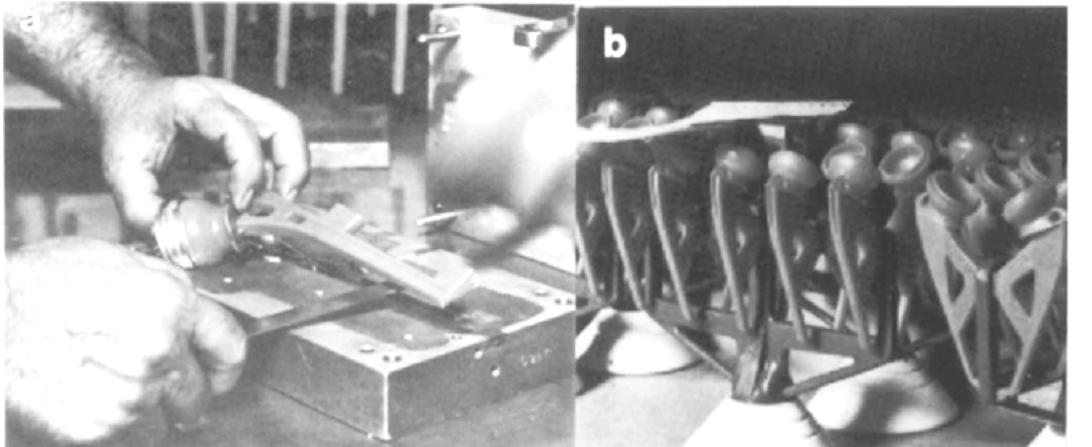


- The Ni release rate from CoNiCrMo alloy and 316L in 37°C Ringer's solution
- Ni release rate in both was about the same ($3 \times 10^{-10} \text{ g/cm}^2/\text{day}$)

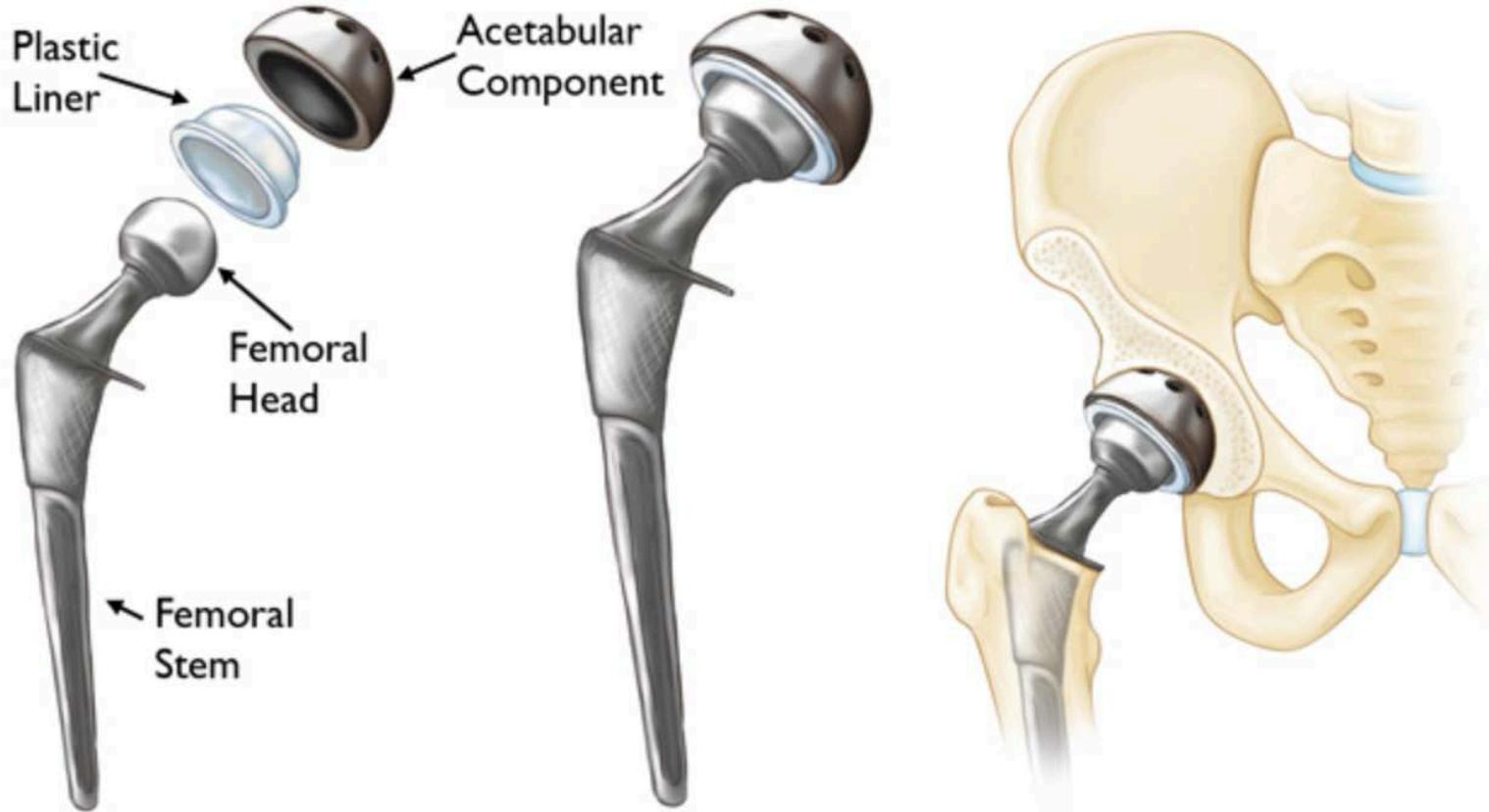
Manufacturing Implants Using Co-Based Alloys

Lost wax casting of femoral joint prosthesis

- (a) Injection of wax into a brass mold.
- (b) Wax patterns assembled for a ceramic.
- (c) Application of ceramic coating.
- (d) A hot pressure chamber retrieves the wax, leaving behind a ceramic coating.
- (e) Pouring molten metals into the preheated ceramic mold. (mold : 800-1000°C, alloy: >1300°C)



Hip joint replacement



(Left) The individual components of a total hip replacement. (Center) The components merged into an implant. (Right) The implant as it fits into the hip.

Ti and Ti-based Alloys

- Attempts to use titanium for implant fabrication date to the late 1930s
- Anti-corrosion (TiO_2)
- The **lightness** of titanium and good mechanochemical properties are salient features for implant application

	Stainless (316)	CoCrMo alloy	Titanium
Density (g/cm^3)	7.9	9.2	4.5

57% 49%



Ti and Ti-based Alloys

Pure Titanium

Four grade of unalloyed Ti

Table 5-5. Chemical Compositions of Pure Titanium (F67; ASTM, 2000)

Element	Grade 1	Grade 2	Grade 3	Grade 4
N	0.03	0.03	0.05	0.05
C	0.10	0.10	0.10	0.10
H	0.015	0.015	0.015	0.015
Fe	0.20	0.30	0.30	0.50
O	0.18	0.25	0.35	0.40
Ti		Balance		

All are in maximum % allowed.

Ti-6Al-4V Alloys

Aluminium (5.5–6.5 w/o)

Vanadium (3.5–4.5 w/o)

Table 5-6. Chemical Compositions of Ti6Al4V Alloys (ASTM, 2000)

Element	Wrought, forging (F136, F620)	Casting (F1108)	Coating (F1580)
N	0.05	0.05	0.05
C	0.08	0.10	0.08
H	0.012	0.015	0.015
Fe	0.25	0.30	0.30
O	0.13	0.20	0.20
Cu	–	–	0.10
Sn	–	–	0.10
Al	5.5–6.50	5.5–6.75	5.50–6.75
V	3.5–4.5	3.5–4.5	3.50–4.50
Ti		Balance	

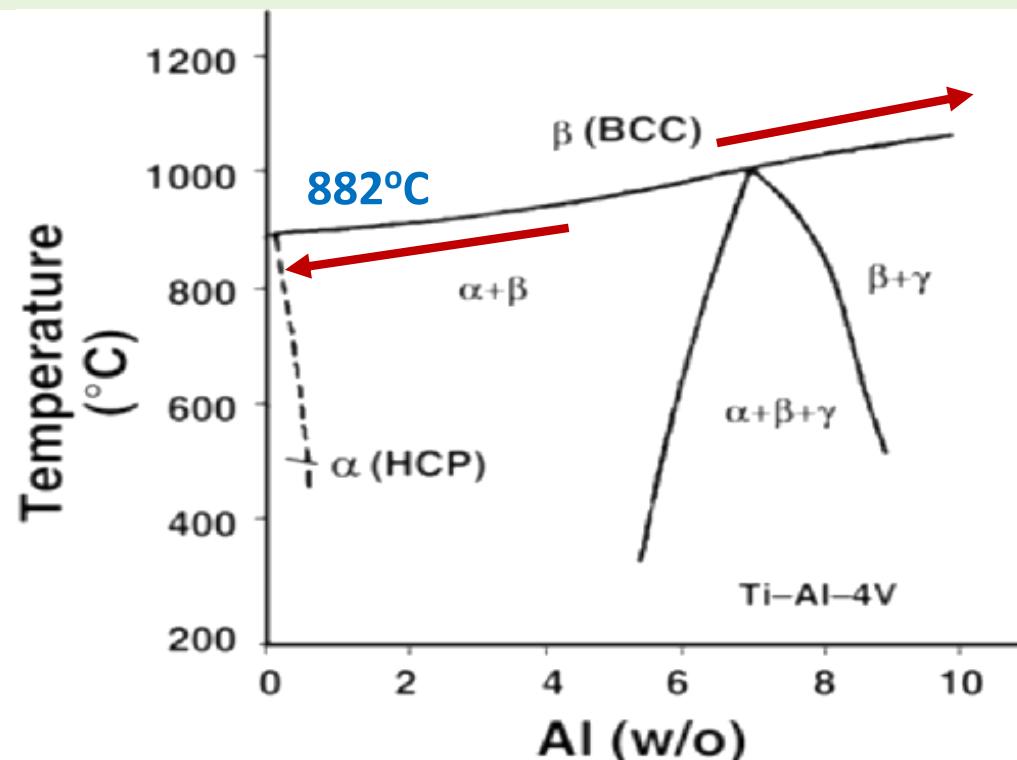
Another wrought Ti6Al4V alloy (F1472) is very similar to F136 alloy. All are in maximum % allowed.

Ti and Ti-based Alloys

Ti-6Al-4V Alloys

widely used to manufacture implants

1. Aluminum (Al) tends to stabilize the α phase, that is, increase the transformation temperature from α to β phase.
2. Vanadium (V) stabilizes the β phase by lowering the temperature of the transformation from α to β .



4V

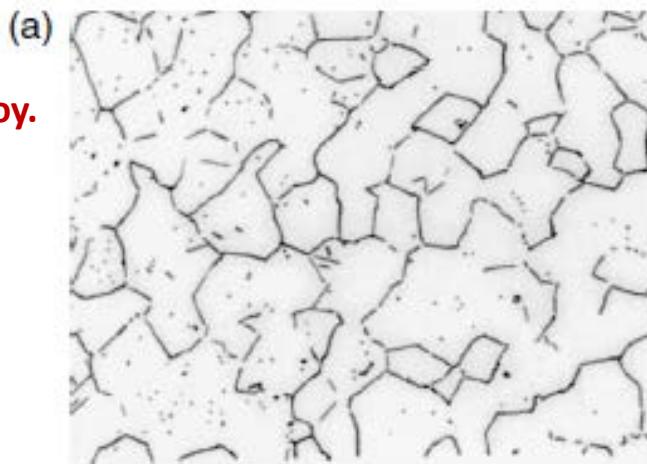


Ti and Ti-based Alloys

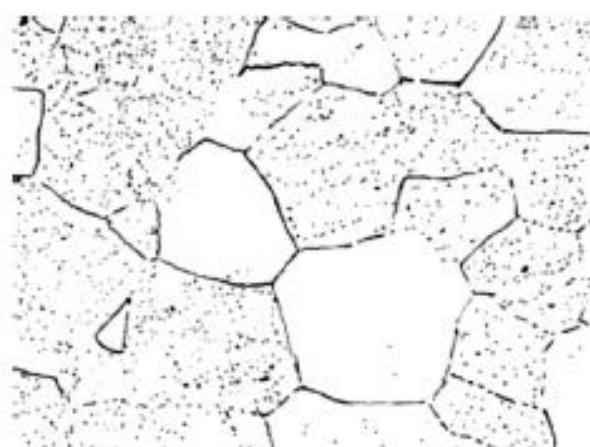
Ti6Al4V Alloys

Microstructure of Ti alloys

(a) Annealed α -alloy.

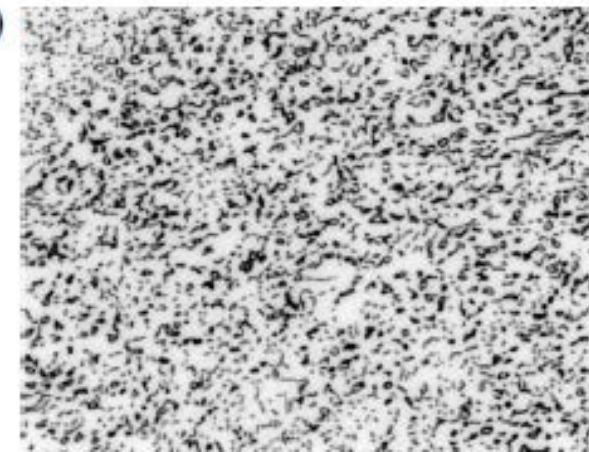


(c) β -alloy, annealed.

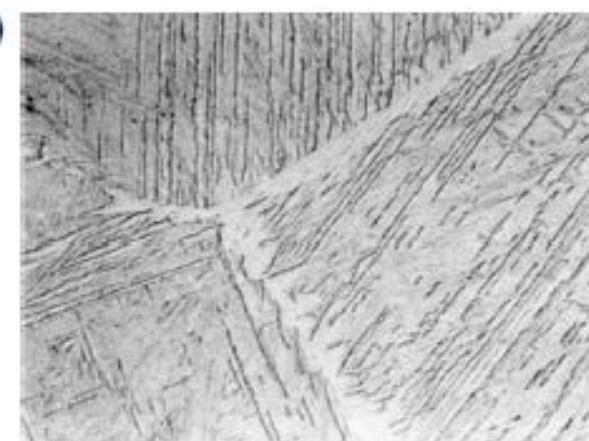


(500X)

(b) Ti6Al4V,
 α - β alloy, annealed



(d)



Ti13Nb13Zr with 13% Nb and 13% Zr

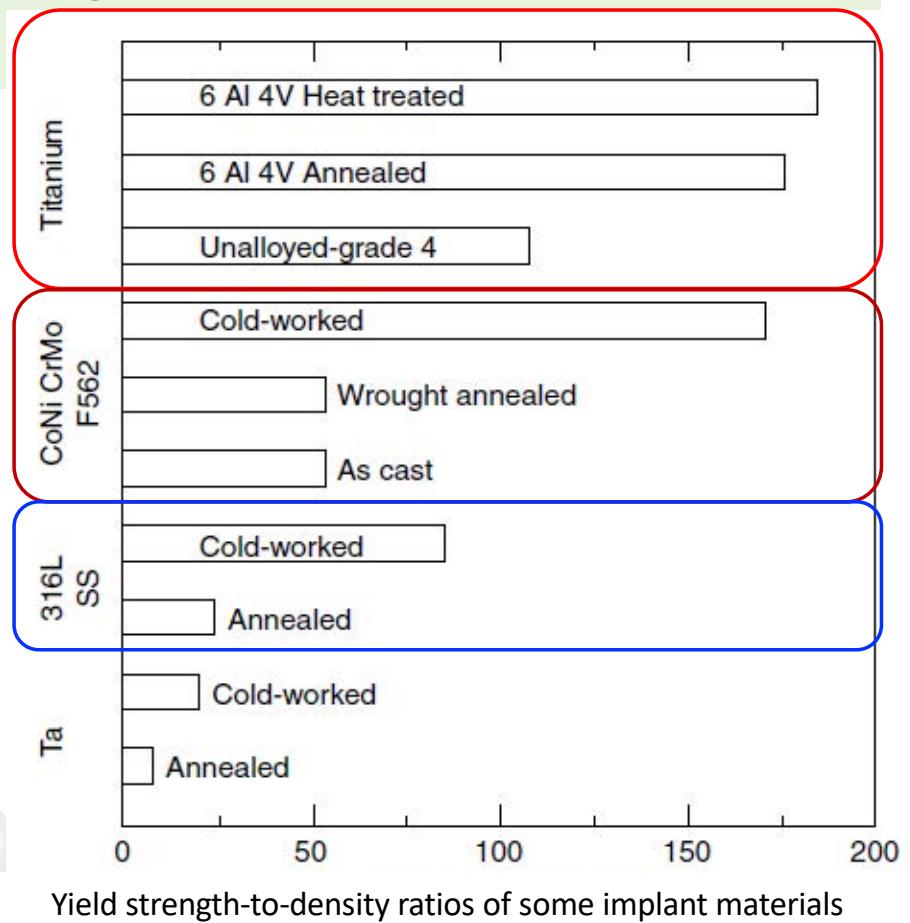
Ti and Ti-based Alloys

- Titanium alloy excels any other implant materials
鉢 (剪切強度 bad)
- Titanium has **poor shear strength**, making it less desirable for bone screws, plates, and similar applications.
- It also **tends to gall or seize** when in sliding contact with itself or another metal.

TABLE 1.7 Mechanical Properties of Ti and its Alloys (ASTM F136)

Properties	Grade 1	Grade 2	Grade 3	Grade 4	Ti6Al4V	Ti13Nb13Zr
Tensile strength (MPa)	240	345	450	550	860	1030
Yield strength (0.2% offset) (MPa)	170	275	380	485	795	900
Elongation (%)	24	20	18	15	10	15
Reduction of area (%)	30	30	30	25	25	45

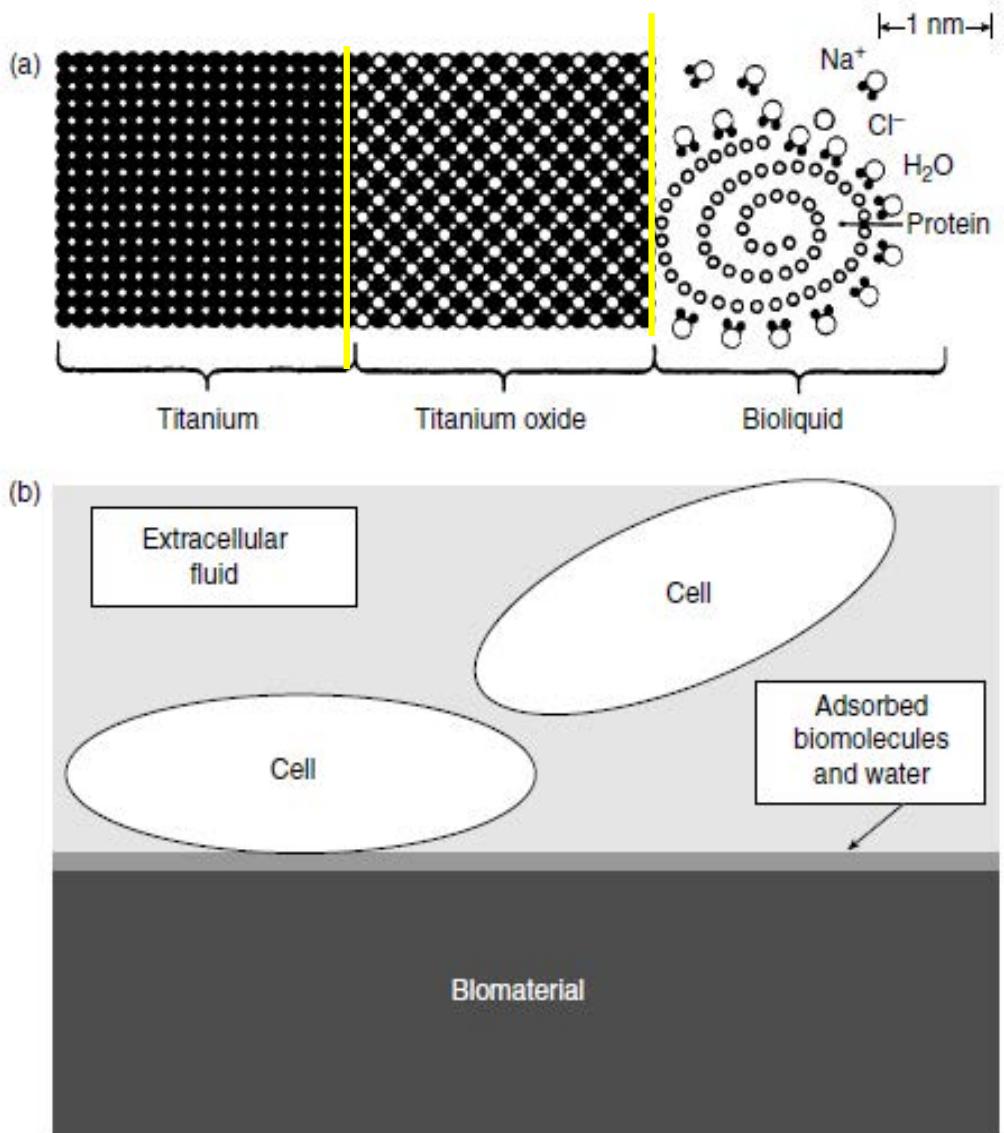
Source: American Society for Testing and Materials, F67-89, p. 39; F136-84, p. 55, 1992 and Davidson et al., 1994.



Ti and Ti-based Alloys

- Titanium derives its resistance to **corrosion** by the formation of a solid oxide layer.
 - Under *in vivo* conditions the **Titanium oxide (TiO_2)** is the only stable reaction product.
 - The oxide layer forms a thin adherent film and passivates the material.
- **Similar as Cr_2O_3**

Passivating oxide film



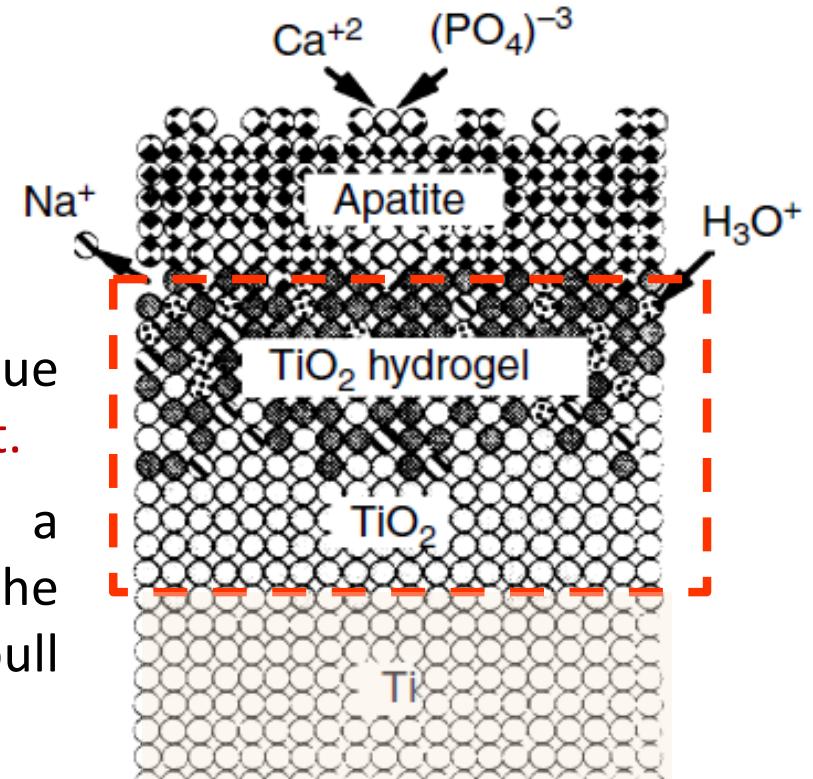
(a) Interface between a titanium implant and bioliquid and (b) the cell surface interaction [Kasemo and Lausma, 1988].

Ti and Ti-based Alloys

Osseo-integration

骨
整
合

- **Direct contact** without intervening soft tissue between viable remodeled bone and an implant.
- **Surface roughness** of titanium alloys have a significant effect on the bone apposition to the implant and on the bone implant interfacial pull out strength. 太粗糙 ⇒ 細胞數量減少
成骨
- The average roughness increased from 0.5 to 5.9 μm and the interfacial shear strength increased from 0.48 to 3.5 Mpa.
- On the **rougher surfaces**, there are **lower cell numbers**, **decreased rate of cellular proliferation**, and **increased matrix production** compared to smooth surface.
- Highest levels of osteoblast cell attachment are obtained with **rough sand blast surfaces** where cells differentiated more than those on the smooth surfaces.
- Chemical changes of the titanium surface following heat treatment is thought to form a **TiO₂ hydrogel layer on top of the TiO₂ layer**.
- The TiO₂ hydrogel layer may induce the apatite crystal formation.



Ti and Ti-based Alloys

Osseo-integration

8 week after implantation



Design Considerations

- Typically want to match **mechanical properties** of **tissue** with mechanical properties of **metal**.
- Have to consider how the **metal may fail *in vivo***
 - **Corrosion**
 - **Wear**
 - **Fatigue**
- Need to consider cost/price of raw materials

Metallic structure-properties

Mechanical Properties

Material	E (GPa)	σ_{yield} (MPa)	σ_b (MPa)
316L SS	190	221 - 1213	586 – 1351
Co-Cr alloys	210 – 253	448 – 1606	655 – 1896
Ti F67	110	485	760
Ti F136	116	896 – 1034	965 – 1103
Cortical Bone	15 – 30	30 – 70	70 - 150

Metallic structure-properties

Metallic **valence** gives following properties

- **Conductive** (thermally and electrically)
- **Ductile** (non-brittle, safe to be used in structure)
- **Strong** (good combination of strength and ductility)
- **Corrosion**

Hence, **corrosion** can introduce toxicity, and thus is a major concern.

Corrosion (腐蝕)

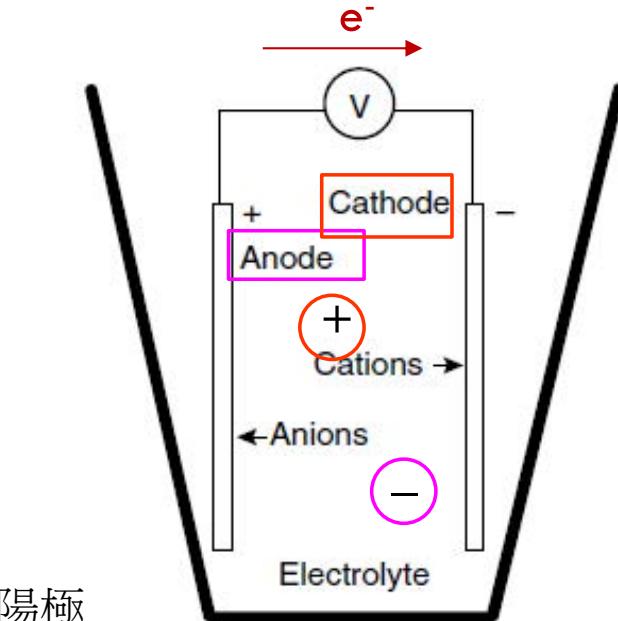
- Corrosion is the **unwanted chemical reaction** of a **metal** with its **environment**, resulting in its continued **degradation to oxides, hydroxides, or other compounds**.
- Tissue fluid in the human body contains **water**, **dissolved oxygen**, **proteins**, and various **ions** such as **chloride (Cl^-)** and **hydroxide(OH^-)**.
- The human body presents a very **aggressive environment** for metals used for implantation.
- Metallic biomaterials are good conductors in an electrolyte solution, leading to **galvanic corrosion**.
- Corrosion resistance of a metallic implant material is consequently an important aspect of its biocompatibility.

Corrosion (腐蝕)

Electrochemical Aspects

- Corrosion occurs when metal atoms become ionized and go into solution, or combine with oxygen or other species in solution to form a compound that flakes off or dissolves.
- The **electrolyte**, which contains **ions** in solution, serves to complete the electric circuit.
- The electrochemical cell is an **unwanted corrosion cell** for a biomaterial in the body.

Electroplating cell



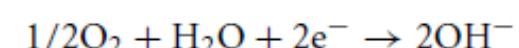
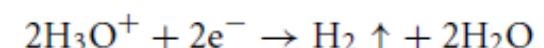
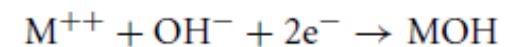
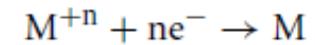
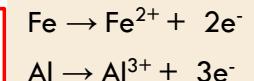
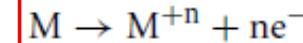
陽極

Anode

陰極

Cathode

Metal oxidize



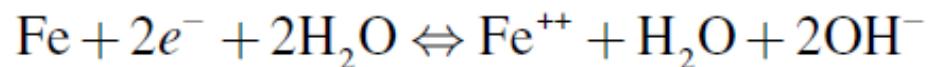
Corrosion (腐蝕)

Corrosion of iron

Electrochemical Aspects

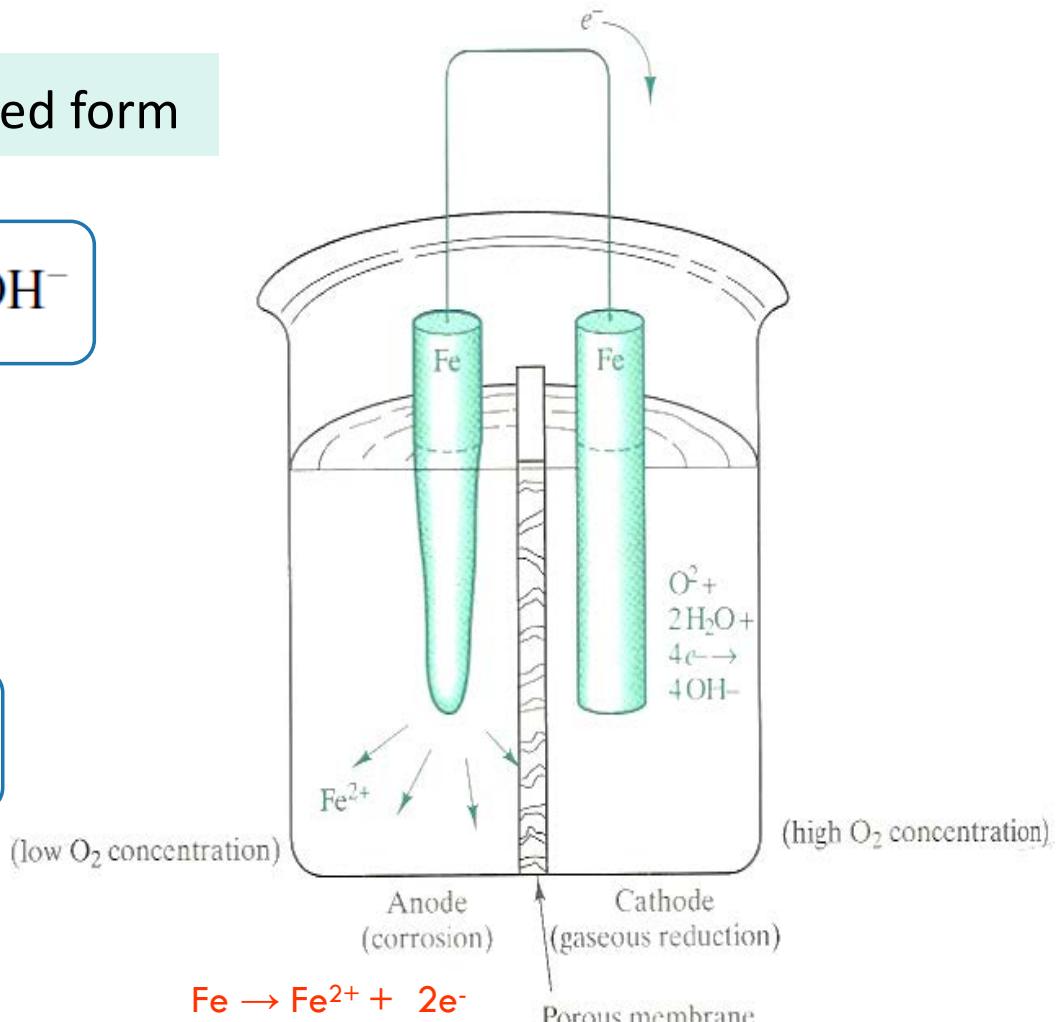
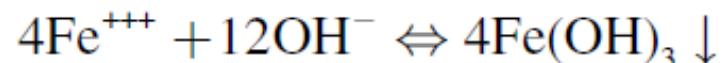
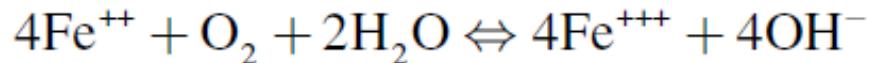
Metallic **iron** goes into solution in ionized form

ferrous (Fe^{2+})



Rust forming following reactions

ferric (Fe^{3+})



Corrosion (腐蝕)

Nernst potential

- Electrochemical measurements in which one electrode is a standard hydrogen electrode formed by bubbling **hydrogen** through a layer of finely divided **platinum black**. The potential of this reference electrode is defined to be **zero**.
- Two dissimilar metals** are present in the same environment, the **one** which is most **negative** in the galvanic series will become the anode, and bimetallic (or galvanic) corrosion will occur.

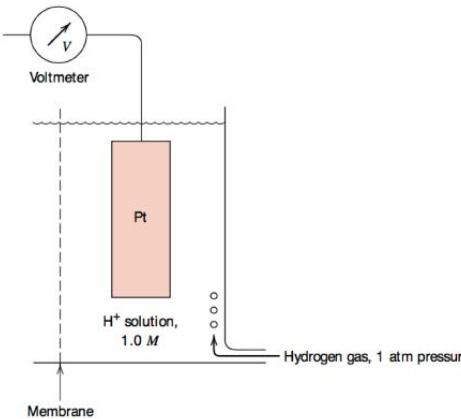


TABLE 1.10 Standard Electrochemical Series

Reaction	ΔE_0 [volts]
$Li \leftrightarrow Li^+$	-3.05
$Na \leftrightarrow Na^+$	-2.71
$Al \leftrightarrow Al^{+++}$	-1.66
$Ti \leftrightarrow Ti^{+++}$	-1.63
$Cr \leftrightarrow Cr^{++}$	-0.56
$Fe \leftrightarrow Fe^{++}$	-0.44
$Cu \leftrightarrow Cu^{++}$	-0.34
$Co \leftrightarrow Co^{++}$	-0.28
$Ni \leftrightarrow Ni^{++}$	-0.23
$H_2 \leftrightarrow 2H^+$	-0.00
$Ag \leftrightarrow Ag^+$	+0.80
$Au \leftrightarrow Au^+$	+1.68

E
Potential difference

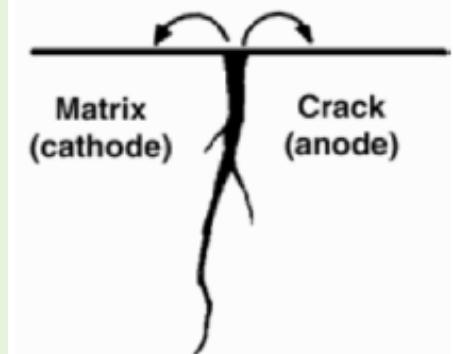
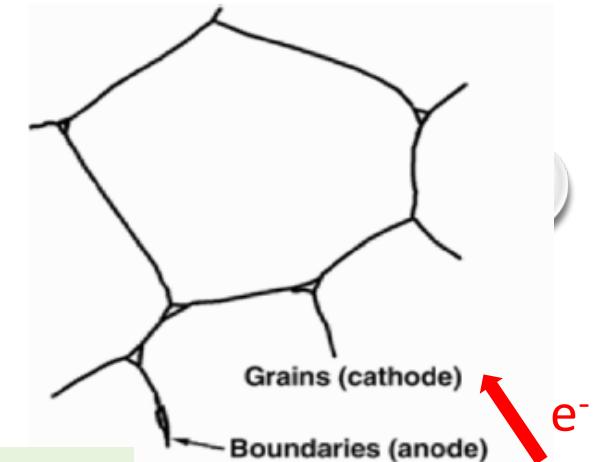
$$E = E_0 - (RT / nF) \ln(M^{n+}),$$

F : Faraday's constant
(96,487 C/mole)
n: number of moles of ions

Corrosion (腐蝕)

□ Galvanic corrosion 過凡尼腐蝕

- When two **dissimilar metals** are immersed in an **electrolyte** and electrically connected, **one metal corrodes preferentially to another**, a process called Galvanic corrosion
- **Galvanic corrosion** can be *much more rapid than the corrosion of a single metal.* Consequently, implantation of dissimilar metals (**mixed metals-alloys**) is to be avoided.
- Galvanic action can also result in corrosion within a single metal, if there is **inhomogeneity in the metal or in its environment.**



Corrosion (腐蝕)

□ Galvanic corrosion

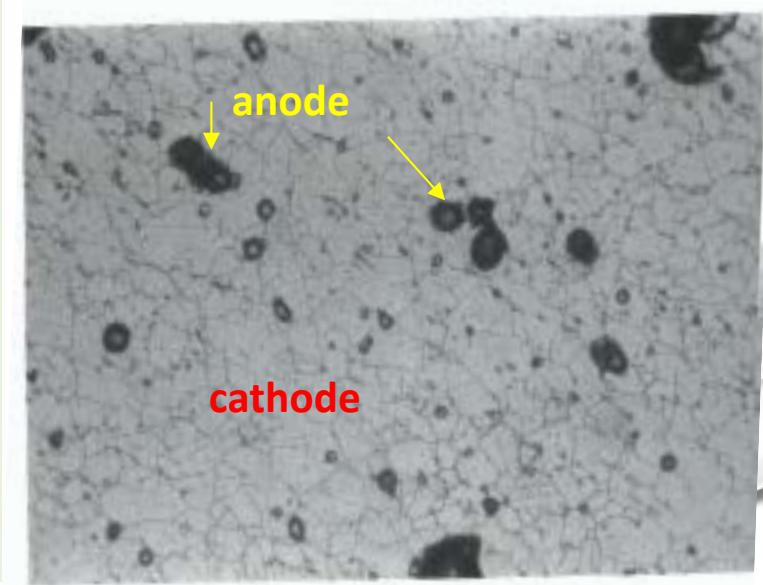
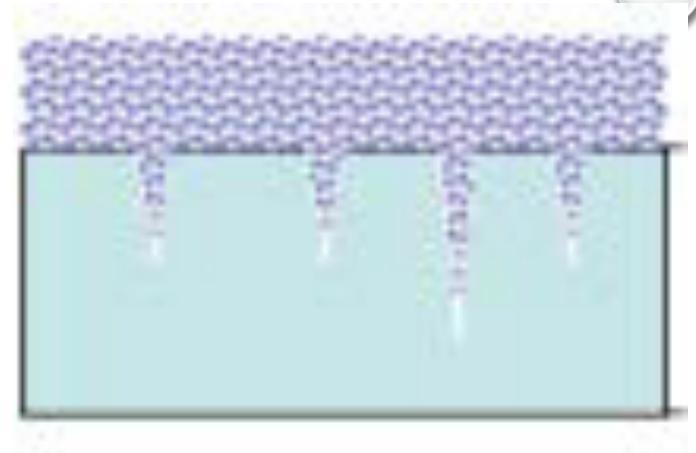
- Sea water is similar to the body fluid.
 - So the galvanic series for seawater can be used as a first approximation, although data in the body solution itself should be used if available
- The anodic metal will have a higher corrosion rate in the couple than in the freely corroding (uncoupled) condition.
- Galvanic corrosion is usually not a desired occurrence, it can be minimized by a number of methods.

- Select similar electrical potential metal
- Insulate the contact between dissimilar metal when possible
- Organic coating
- Install a third metal which is anodic to both metal (sacrificial anode)

Corrosion (腐蝕)

□ Pitting corrosion (孔蝕/斑蝕)

- Localized corrosion can occur as a result of **imperfections in the oxides layer**, producing small areas in which the protective surface is removed.
- These localized **spots** will actively corrode and pits will form in the surface of material.
- Resulted in a large degree of localized damage because the **small areas of active corrosion become the anode** and the entire remaining surface becomes the cathode.

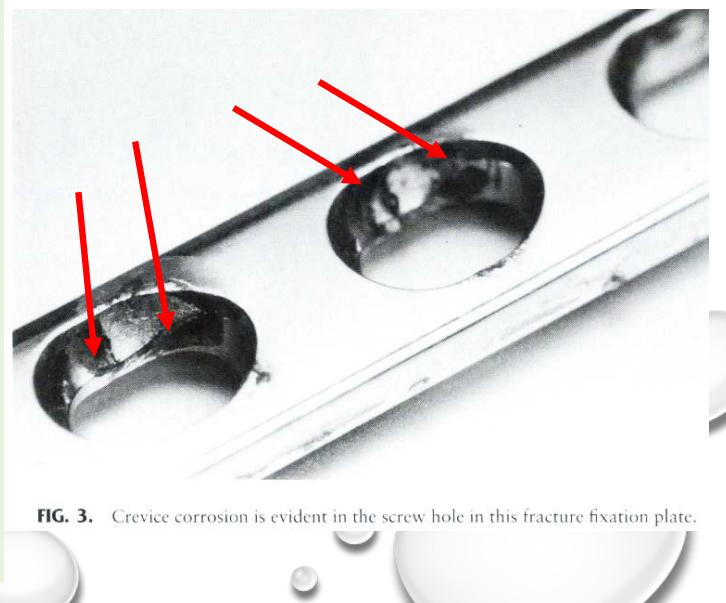
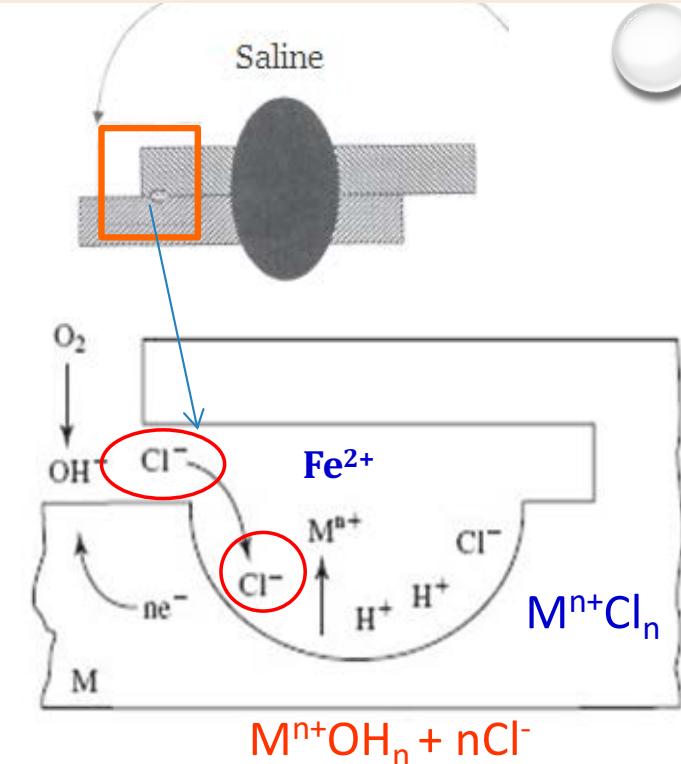


Pitting corrosion of stainless steels

Corrosion (腐蝕)

□ Crevice Corrosion (裂縫腐蝕)

- Accelerated corrosion can be initiated in a crevice by **restricted diffusion of oxygen** into the crevice.
- As the crevice becomes depleted of oxygen, the reaction is limited to metal oxidation balanced.
- In an aqueous **sodium chloride** solution, the metal ions with the crevice causes the influx of the chloride ions to balance the charge by forming the **metal chloride**.
- In the presence of **water**, the **chloride** will **dissociate** to its insoluble hydroxide and acid.
- Rapidly accelerate the corrosion by the **decrease** in **pH** causes further metal oxidation.



Corrosion (腐蝕)

□ Intergranular Corrosion

- Stainless steel rely on the formation of **chromium oxides (Cr_2O_3)** to passivate the surface .
- When **carbides** are form at the grain boundaries, the regions adjacent to the grain boundaries become depleted in chromium.
- The passivity of the surface in these regions is therefore affected and preferential corrosion can occur.

Cr: -0.56. V

Fe: -0.44 V

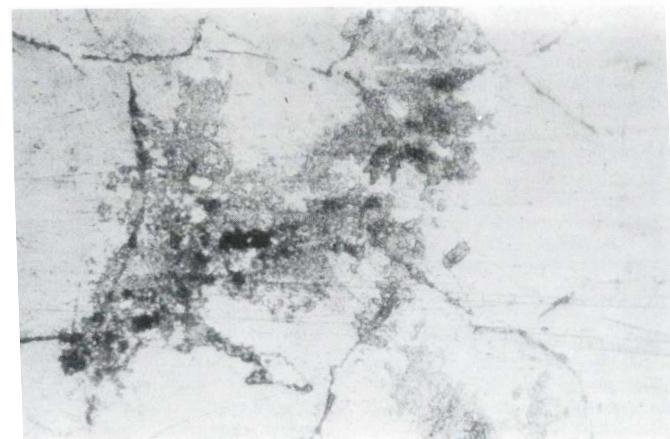
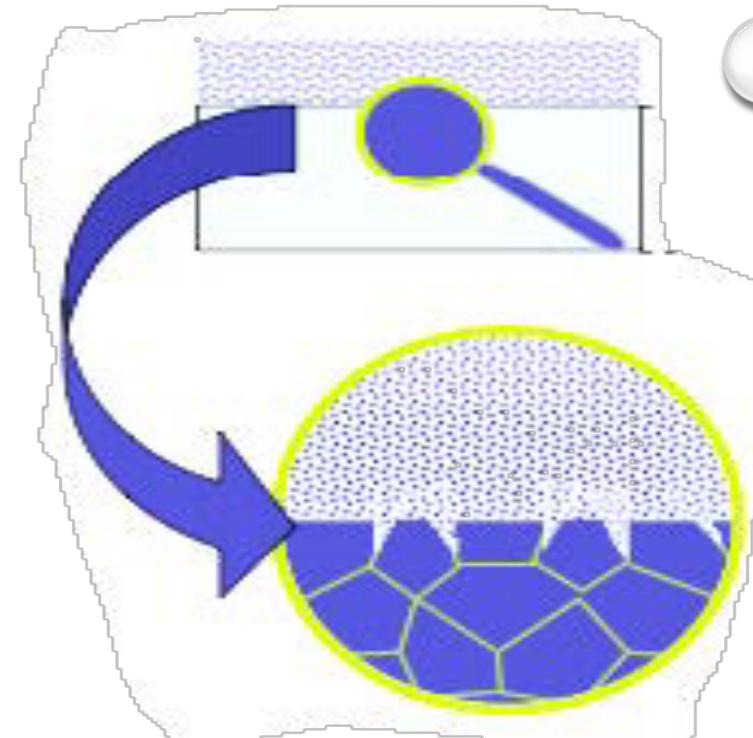


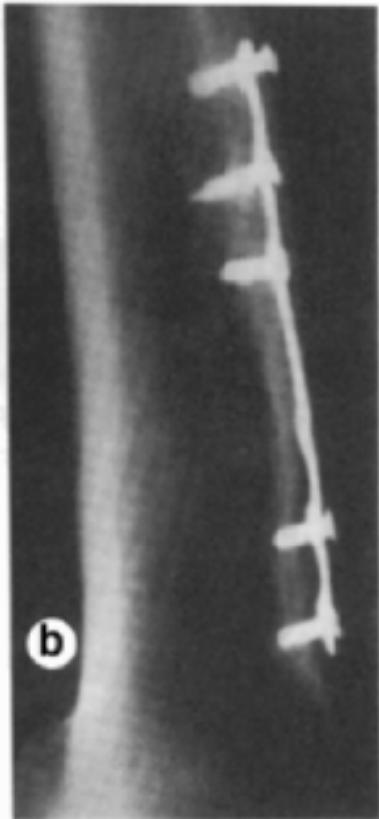
FIG. 4. Intergranular corrosion is demonstrated on this etched stainless steel specimen.

Corrosion

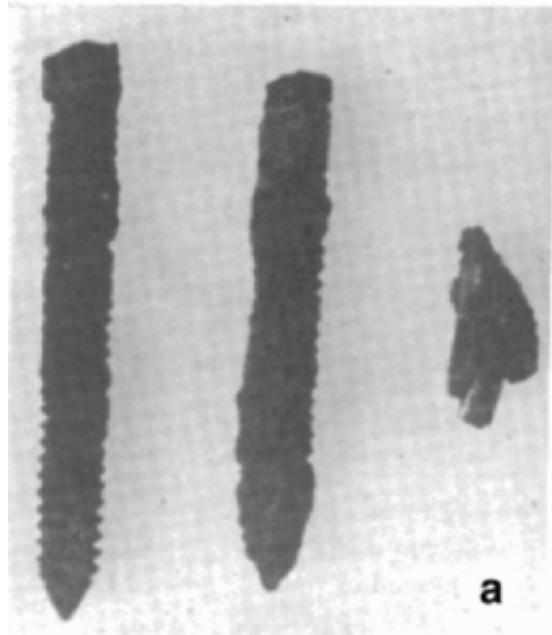
top view



side view



A Vanadium steel bone plate in place
for 30 years.



Wear (磨損/磨耗)

- Involves the **loss of material** in particulate form as a consequence of relative motion between two surfaces.
- Two materials placed together under load will only contact over a small area of the higher peaks or asperities.

Abrasion — 磨損

by which **a harder surface plow grooves in the softer material**

Adhesion — 黏著

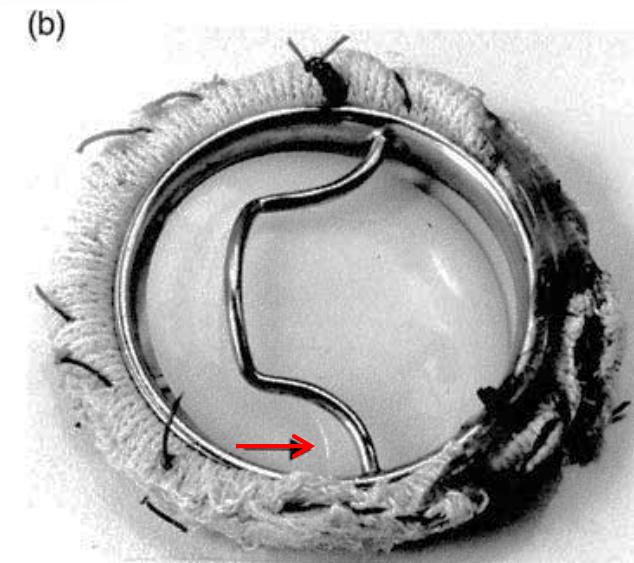
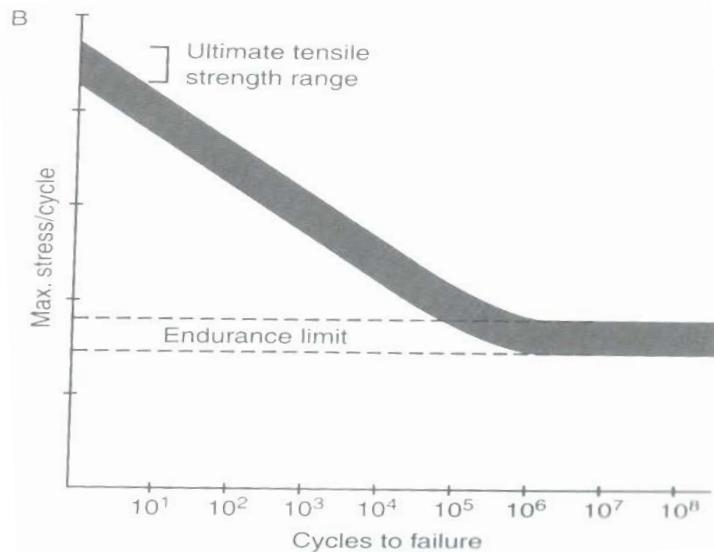
by which **a softer material is smeared onto a harder counter surface**, forming a transfer film

Fatigue — 疲勞

by which **alternating episodes of loading and unloading** result in **the formation of subsurface cracks** which propagate to form particles that are shed from the surface.

Fatigue (疲勞)

- Fatigue is progressive failure of a material due to the application of **cyclical stresses below the ultimate stress** of the material **causing crack propagation**.
- Crack usually starts at a stress concentrator or stress riser.



Fatigue (疲勞)

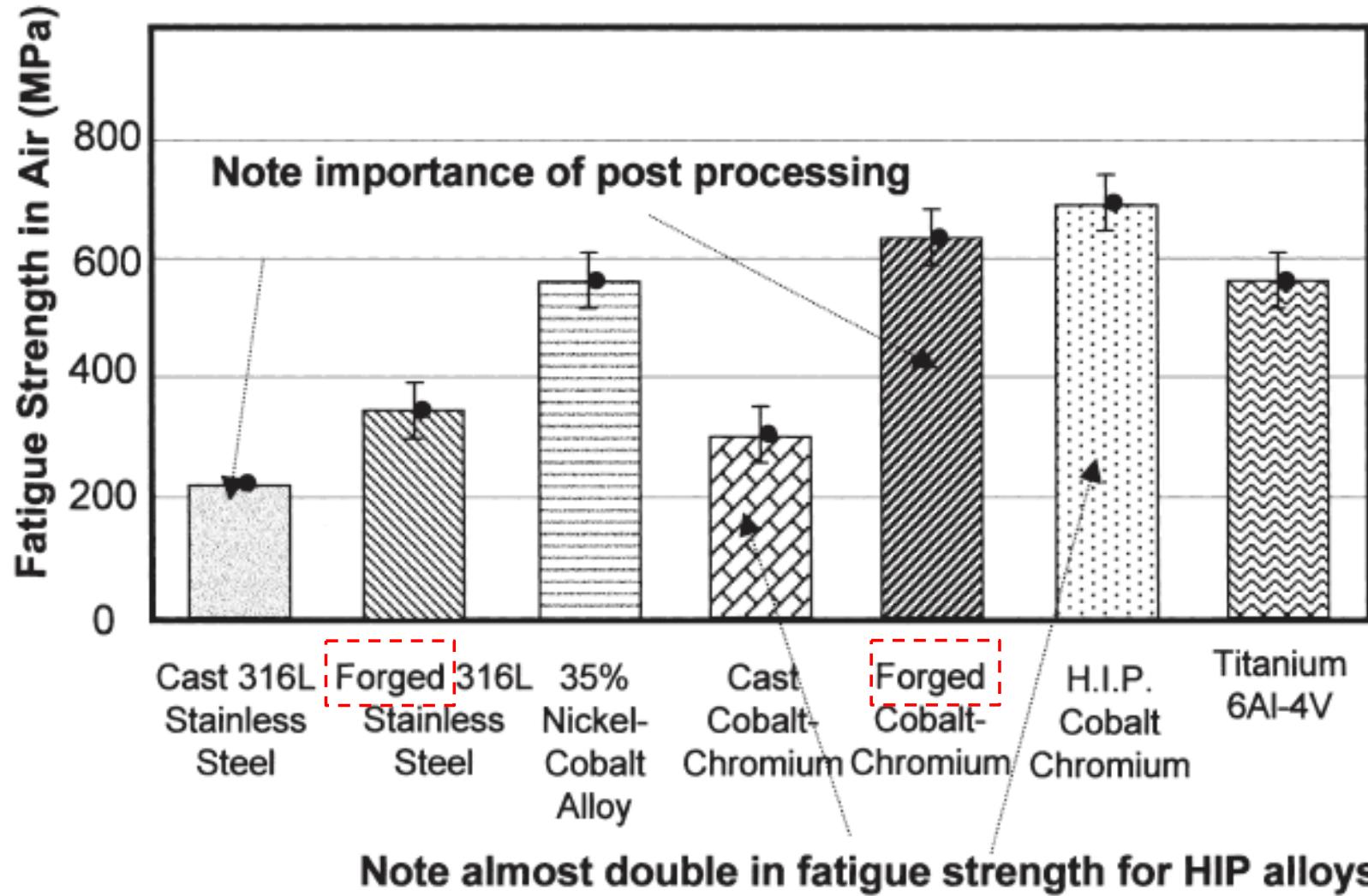


Fig. 4. Fatigue strength of some common implant alloys.

Fatigue (疲勞)

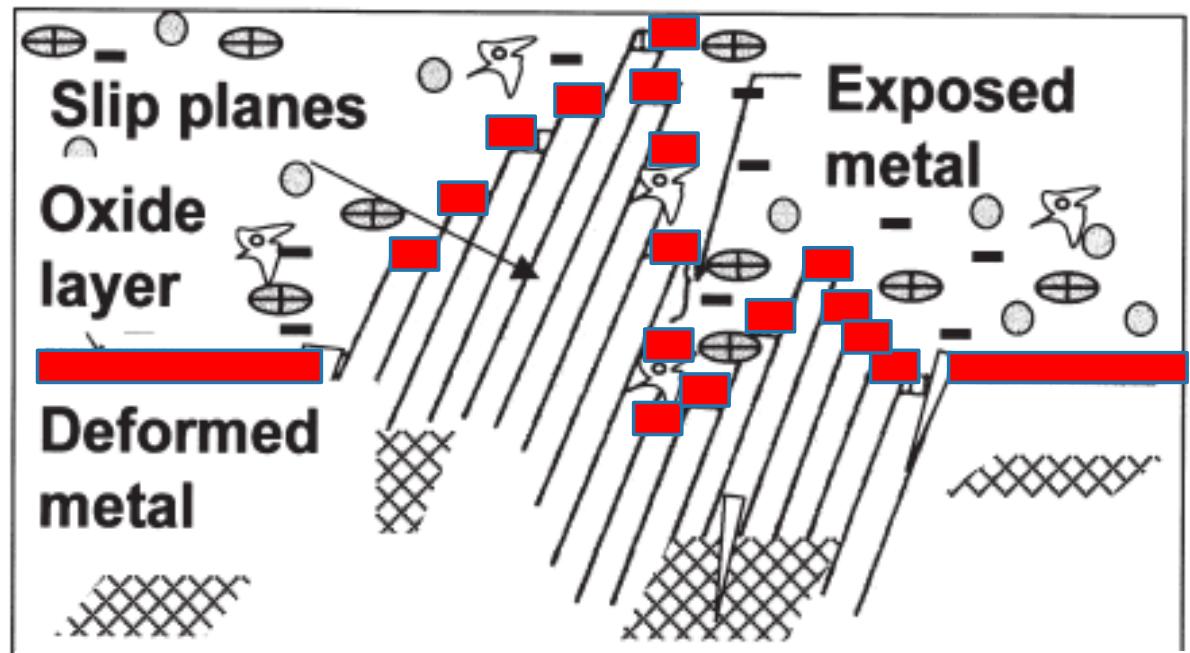
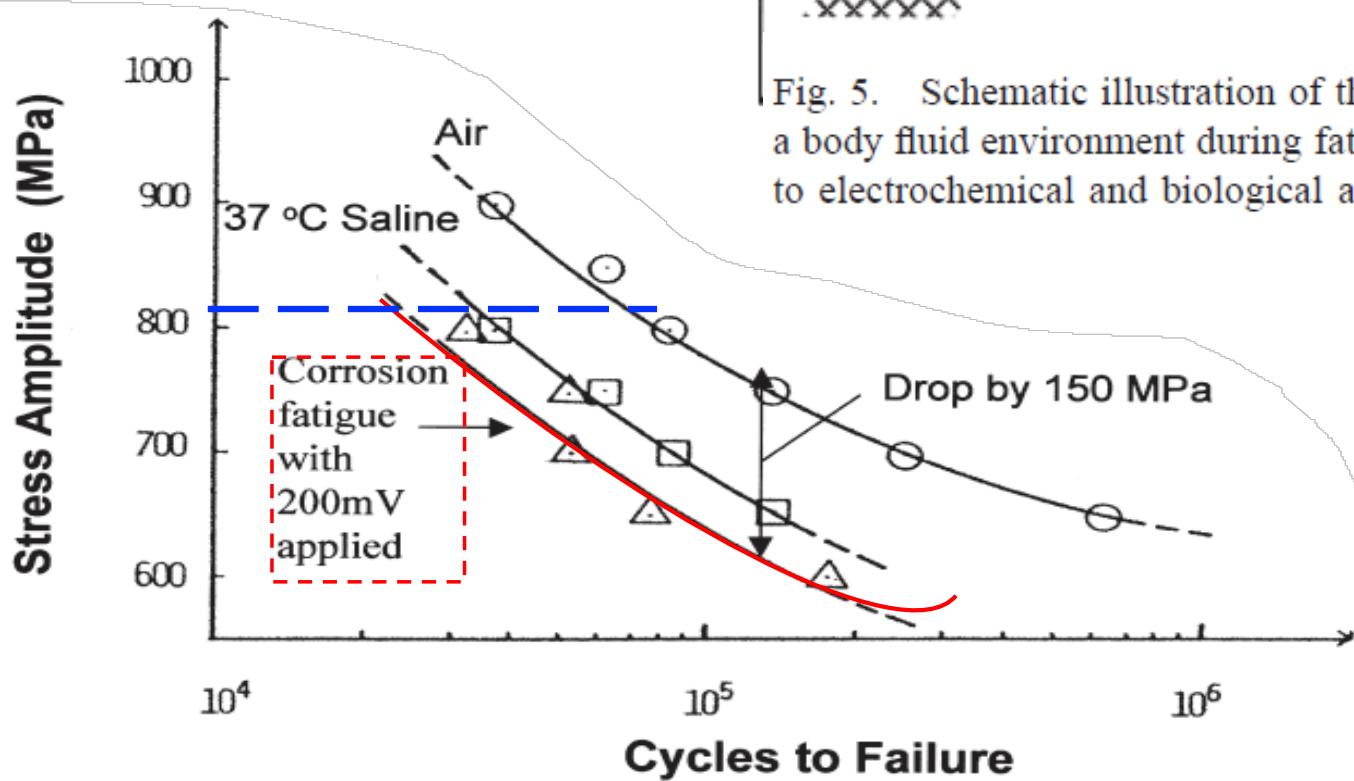


Fig. 5. Schematic illustration of the formation of fresh slip planes in a body fluid environment during fatigue, exposing unprotected regions to electrochemical and biological activities.

Fig. 6. Corrosion fatigue of 316L cold worked stainless steel (after Taira and Lautenschlager [27])

Failure with combination factors

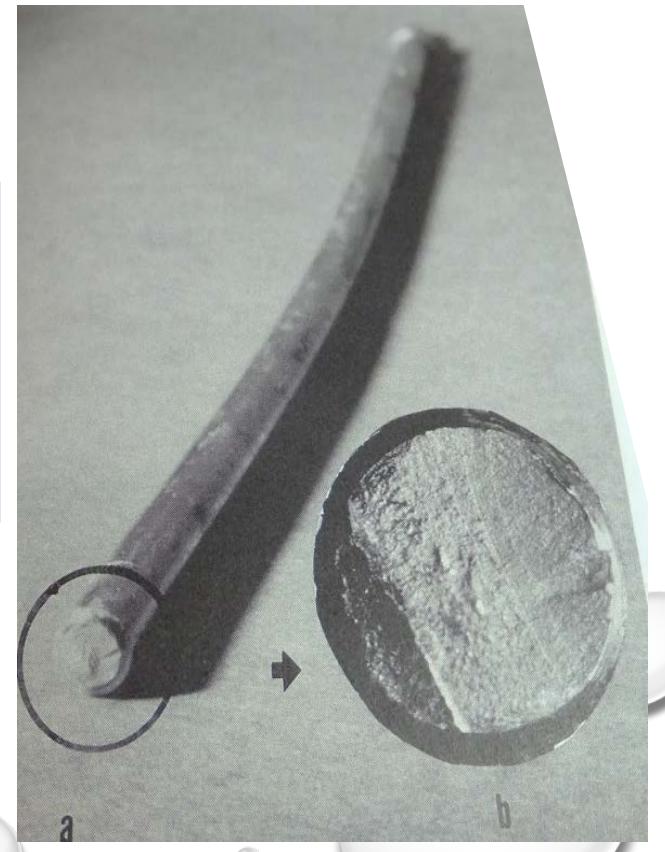
Surgery

The surgeon bent the rod to make it fit a bit better in the patient, but this **increase** the **bending moment** and **bending stress** on the rod.

Stress concentration

The **stress** at the ratchet end of the rod were serve enough to significantly increase stress at the first ratchet junction, which was indeed the eventual site of **fatigue fracture**.

Spinal fusion did not occur in the patient which contributed to relatively persistent loading of the rod over several month post implantation.



pH value vs. Corrosion

pH can change dramatically in tissue that has been injured or infected.

- Normal tissue fluid has pH of about 7.4
- In a wound, it can be as low as 3.5.
- In an infected wound, the pH can increase to 9.0

Minimization of Corrosion

1. Use appropriate metals (native or inert elements of the body)
2. Design alloys to minimize corrosion
3. Avoiding implantation of different types of metal in the same region.
4. In the manufacturing process, provide matched parts from the same batch of the same variant of a given alloy
5. In surgery, avoid contact between metal tools and the implant, unless special care is taken (to avoid surface damage)

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