Usure de Matériel et infection: l'exemple des prothèses articulaires

L Bernard, CHU Tours

12ème journée Maurice RAPIN

Jeudi 13 octobre 2011

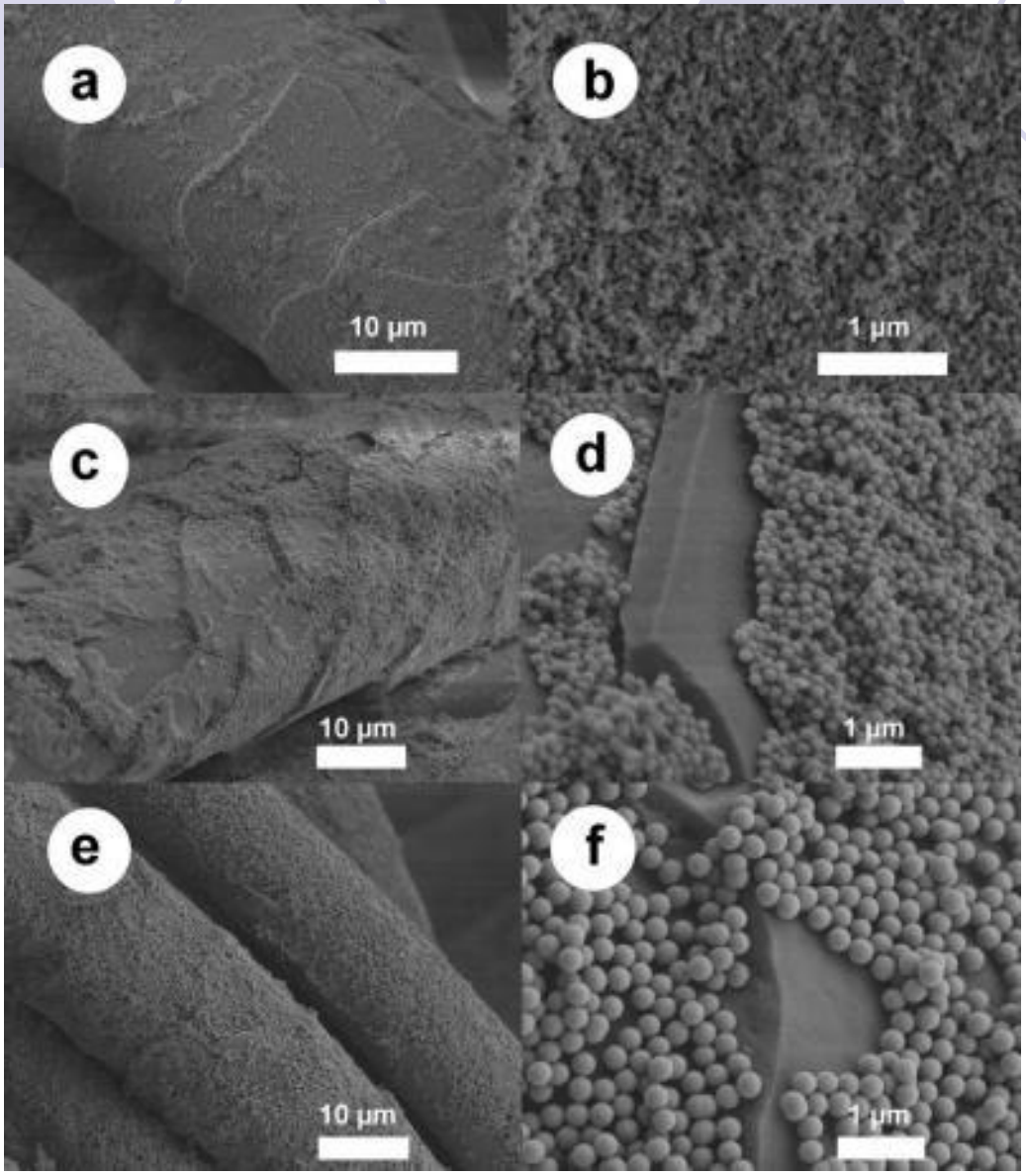
LES BIOMATERIAUX ORTHOPEDIQUES

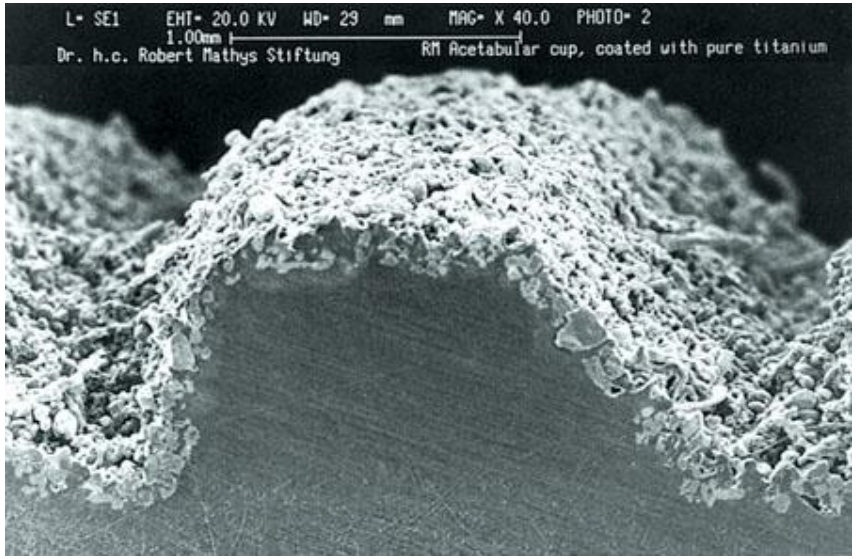
Surface métallique (1)

Plus ou moins lisse

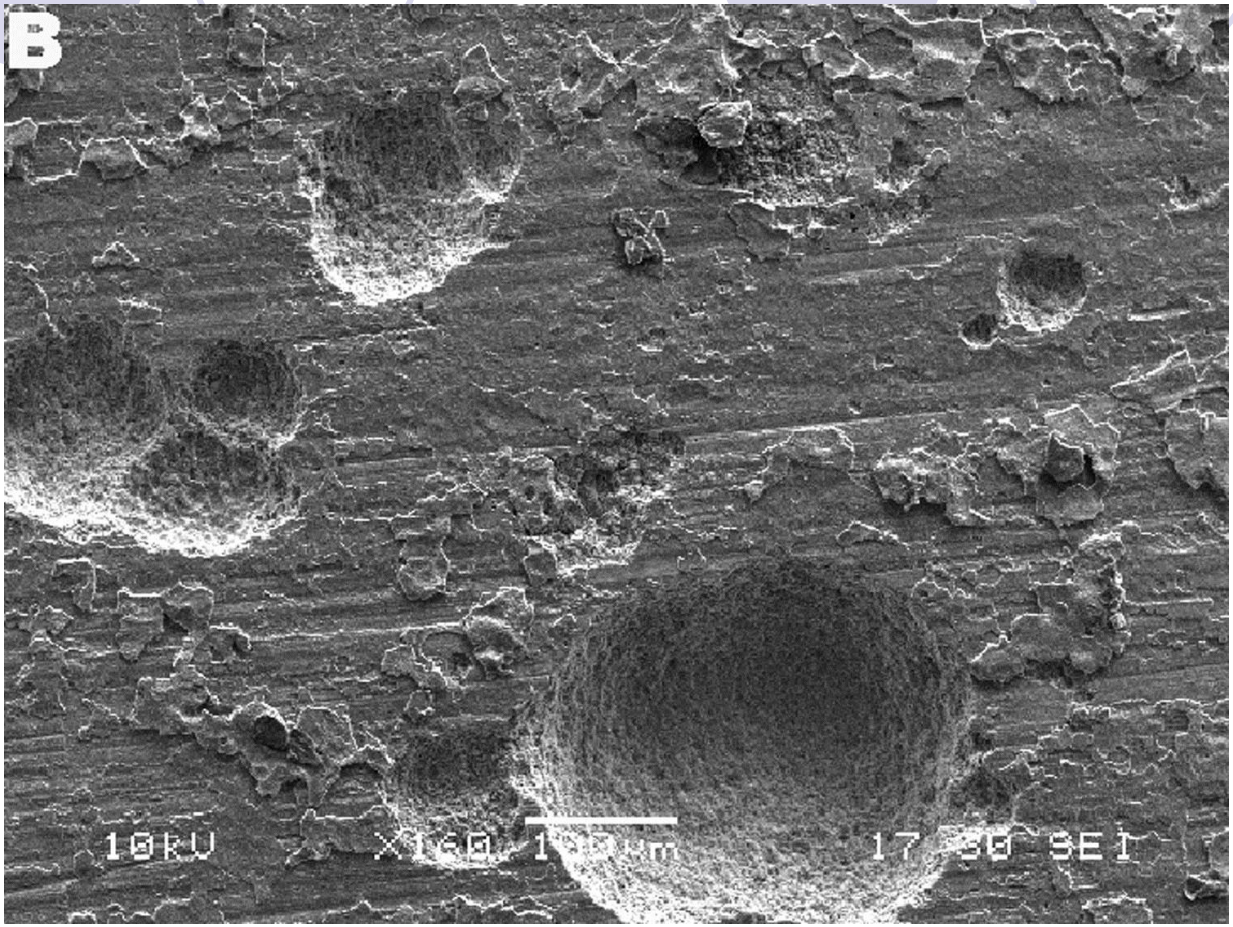
- n’est pas un support inerte.
- Plusieurs types de matériaux: métal ou alliages métalliques (acier, chrome, cobalt, titane), polyéthylènes, céramique.
- Hautes énergies de surface, sites moléculaires insaturés.
- Oxydes des surfaces métalliques (acier, chrome, cobalt, titane)

  interagissent avec les glycoprotéines tissulaires et les structures membranaires des cellules


a
10 µm
b
1 µm
c
10 µm
d
1 µm
e
10 µm
f
1 µm



R. Lemaire
Centre Hospitalier Universitaire de Liège



Pitting corrosion of Ti-6Al-4V hip prosthesis in-vivo (Rodrigues, 2009, JBMR-B)

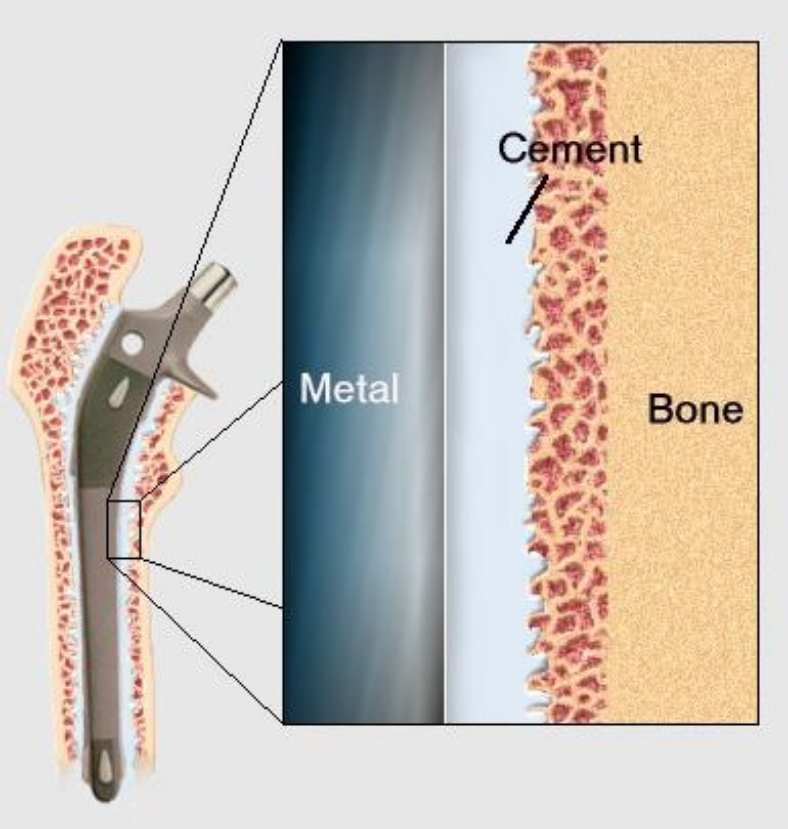
Surface métallique (2)

- Phénomènes physiques, ioniques, électrophysiologiques,

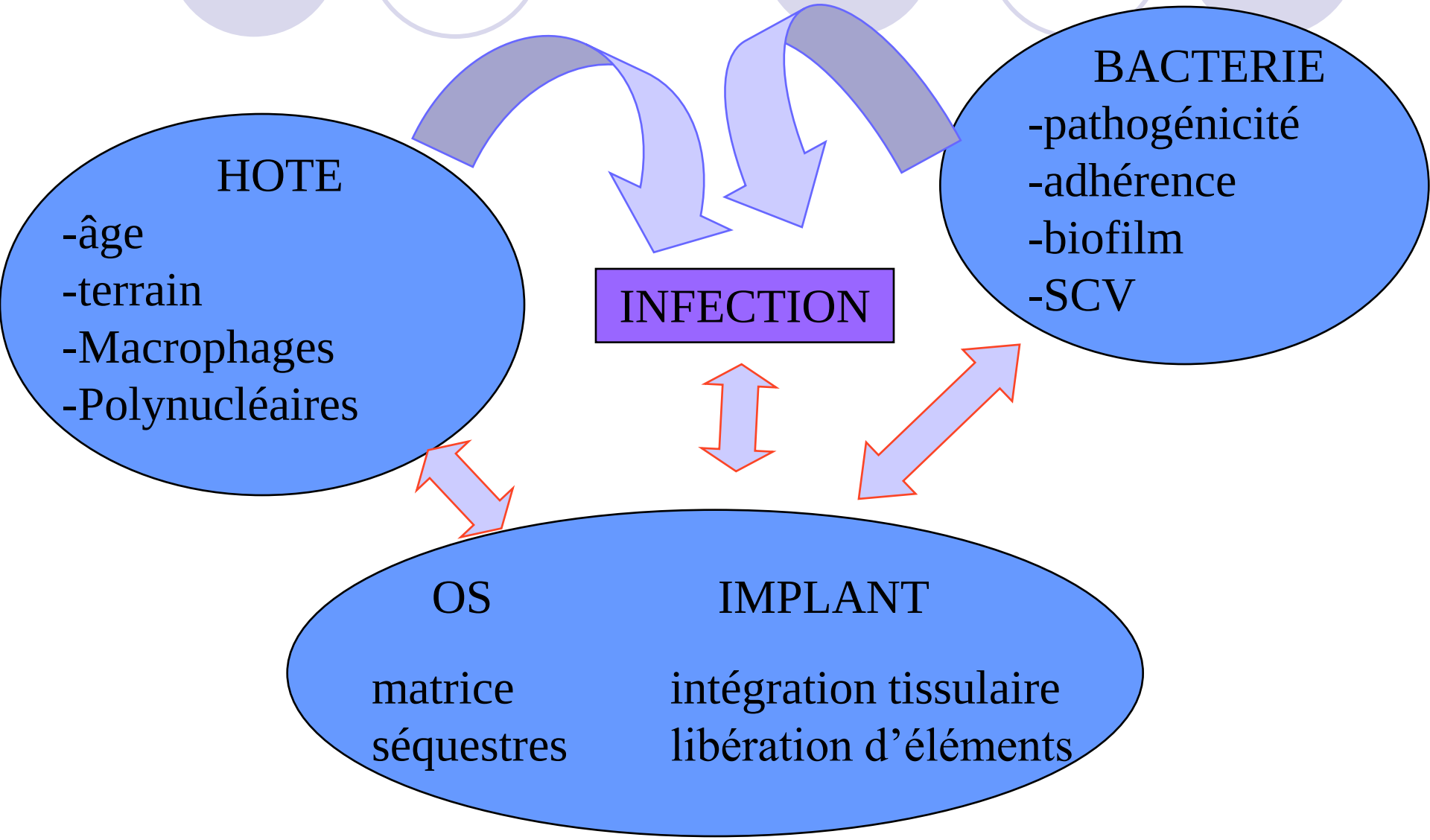
  biochimiques et moléculaires

- processus d'intégration de l'implant,
- processus d'usure de l'implant
- conditions de constitution et de persistance de l'infection bactérienne.

interface réactive avec son environnement.


Cement
Metal
Bone

INFECTION OSSEUSE SUR MATERIEL



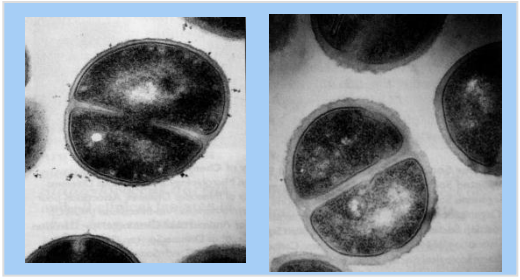
Stratégies adaptatives des bactéries/implant

LA BACTERIE:
Stratégie adaptative / implant

- La bactérie: pouvoir pathogène, résistance aux ATB
- Biofilm
- Bactéries quiescentes (Small colonies variant)

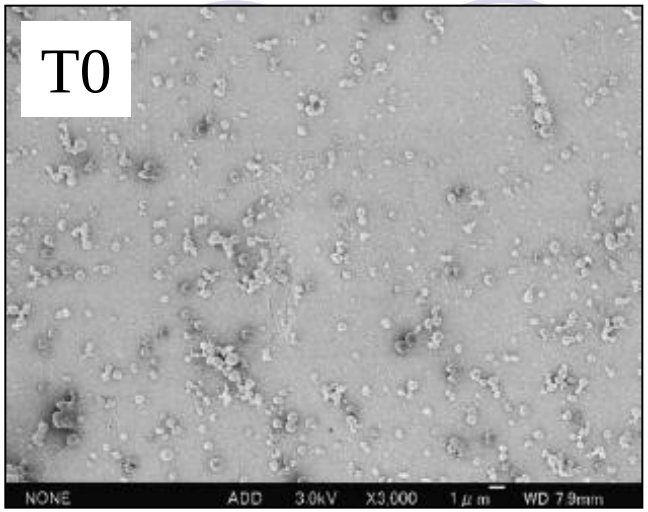
1- La bactérie: *S. aureus*

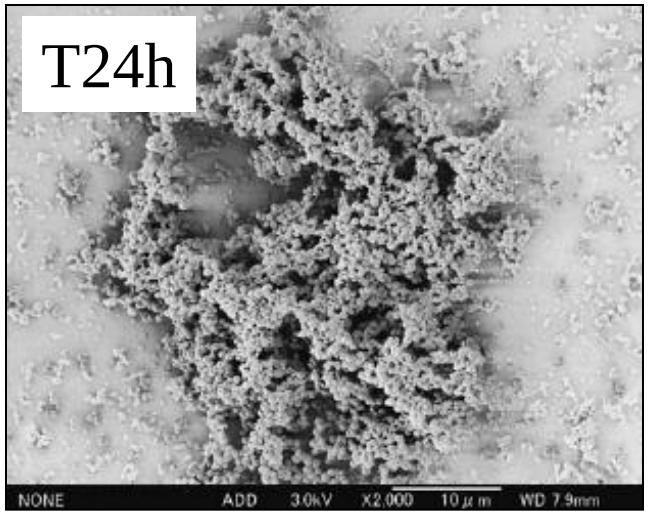
- Adhésion
- Pouvoir pathogène
- Présence intracellulaire
- Résistances aux antibiotiques

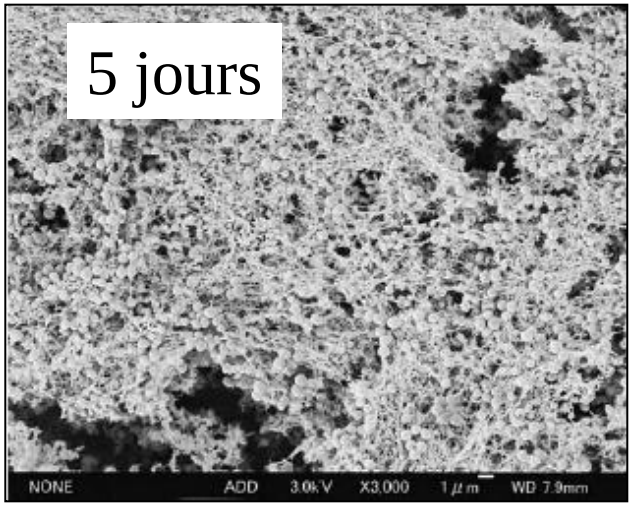


2 Stratégie adaptative: Biofilm

Cinétique de colonisation du matériel par un biofim

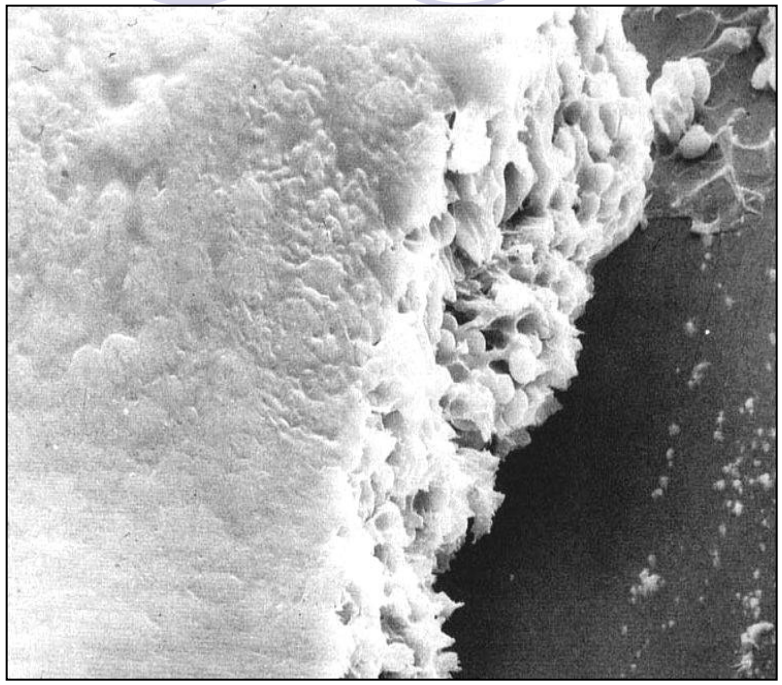




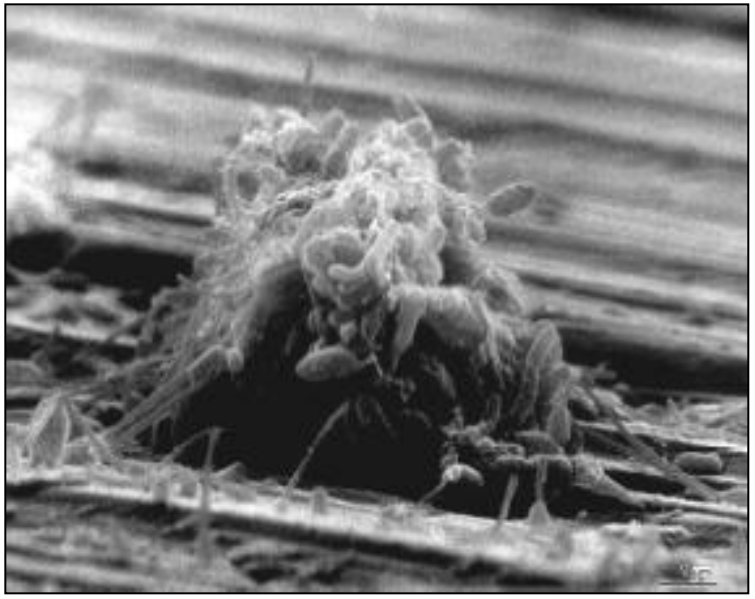


Nishimura S. J Orthop Sci. 2006 ;11:46-50.

Biofim sur une surface métallique
Microscope électronique à balayage

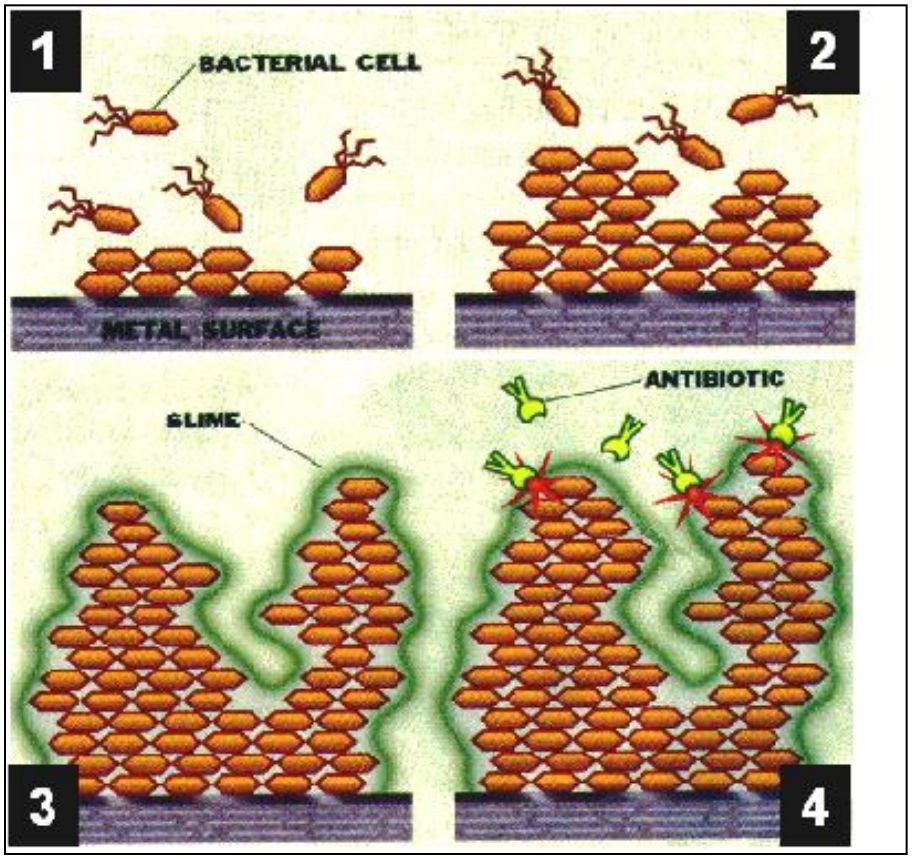


Infections Associated with Indwelling Medical Devices. Waldvogel, FA, Bisno AL, 3rd ed. (2000)



Sutherland IW.
Trends Microbiol. 2001;9:222-7.

Biofilm



Business Week, Science & Technology
Licking E, (2000)

1 Slime « Glue »

- substance polysaccharidique
- sécrétée par les bactéries
- armature d'exopolymères « ancrage »

  riche en eau, en ADN, en protéines,

  molécules de signalisation

2 Quorum sensing:

- réseaux de communication inter- cellulaires

  régulant passage transitionnel en phase stationnaire/ croissance

3 Stratégie adaptative: **Bactéries quiescentes**

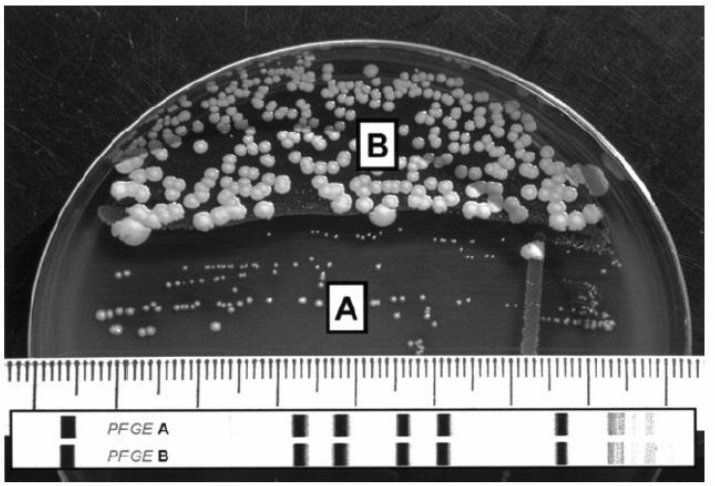
Petites colonies

ou Small Colony Variants

Bactéries quiescentes : importance clinique

- 5 cas/83 IPOA (2002 – 2005)
  - 2 patients bactériémiques
  - 1 patient : ± IPOA bilatérale
  - Durée antibiothérapie : 4 à 22 mois
  - 100% d'échec
  - Puis changement en 2 T

P. Sendi, CID 2006 : 43:961-7



Bactéries quiescentes

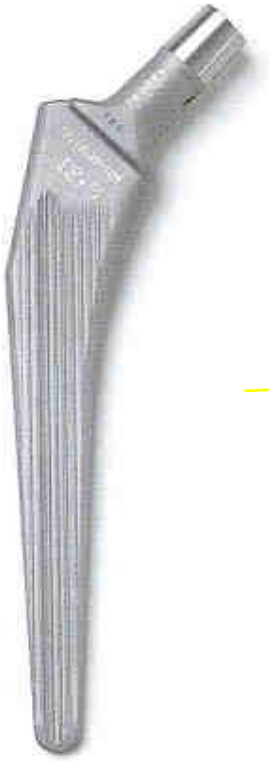
- **↘ Taille (1/10)**
- **Croissance lente (7j)**
- **↘ Pigmentation**
- **↘ hémolyse**
- **↗ R aux aminoglycosides**
- **Gêne = *fem*A**

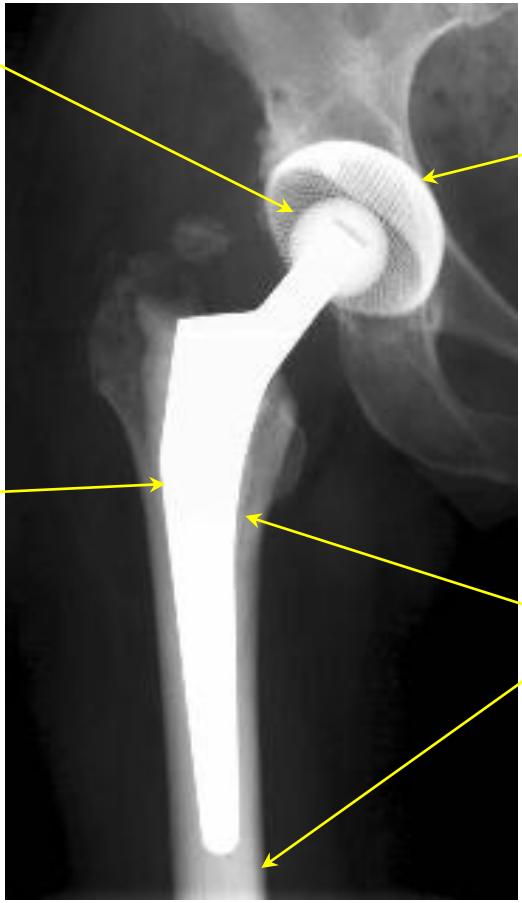
DEFICIT PHAGOCYTAIRE DANS LES INFECTIONS SUR MATERIEL

Prothèse de hanche: composants

Tête
métal

Cupule
titane et polyéthylène

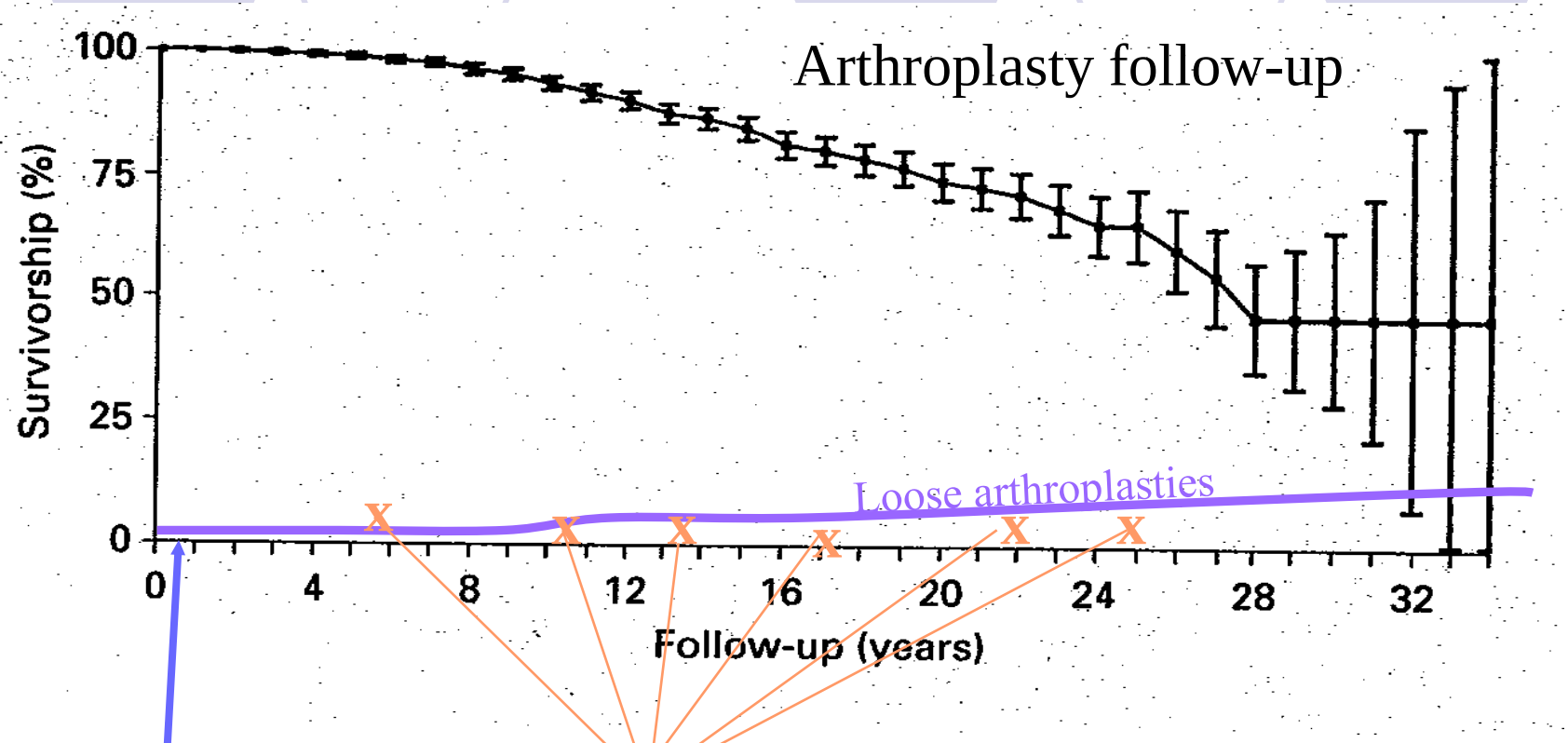




Ciment
méthyl-méthacrylate

Tige
alliage chrome-cobalt

When does prosthetic infection occur ?



Type I

Acute and early just after surgery (< 1 m)

Type II

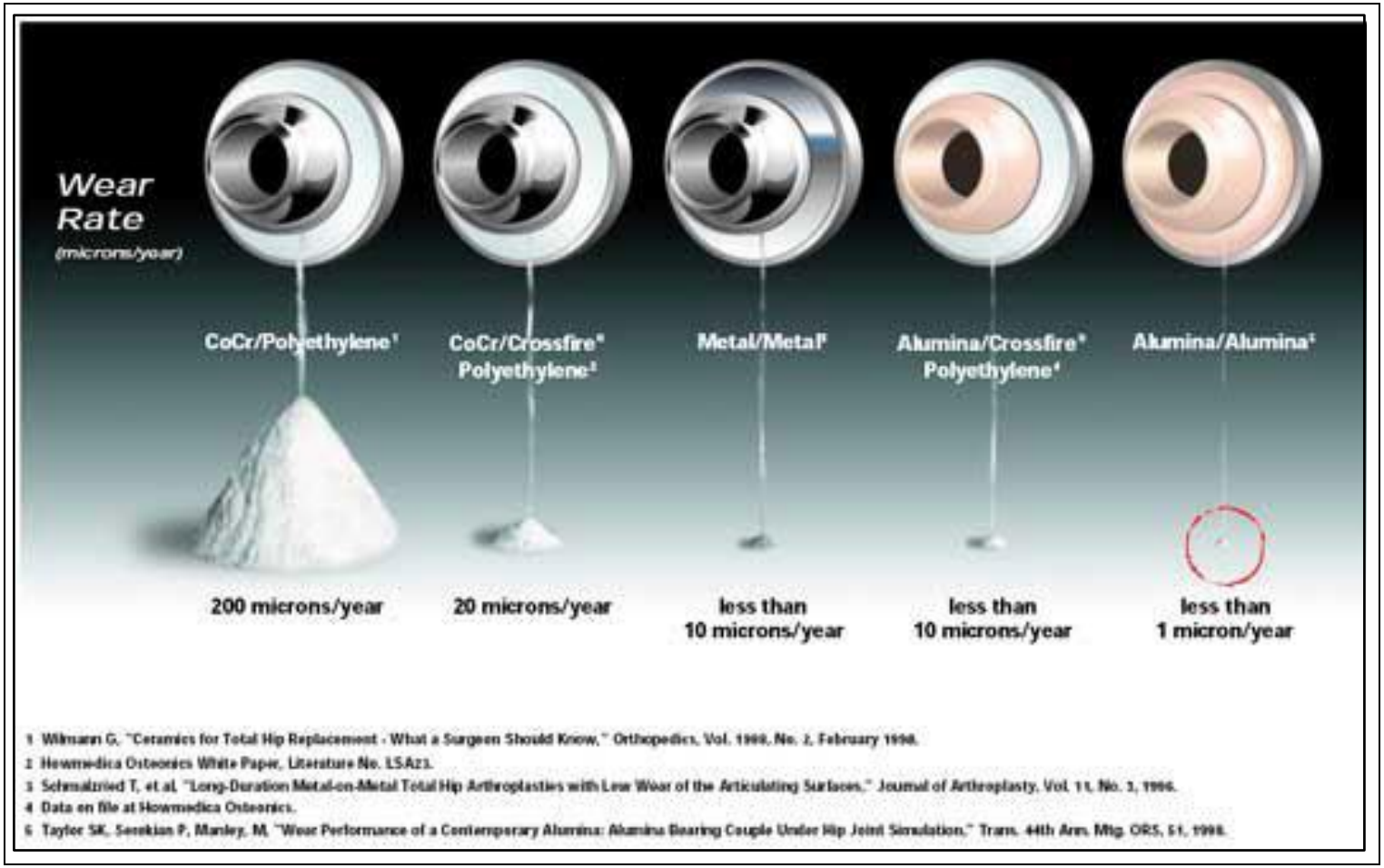
Chronic and later prosthesis with pain

Type III:

Acute and late hematogenous route prosthesis without pain

Prothèse de genou

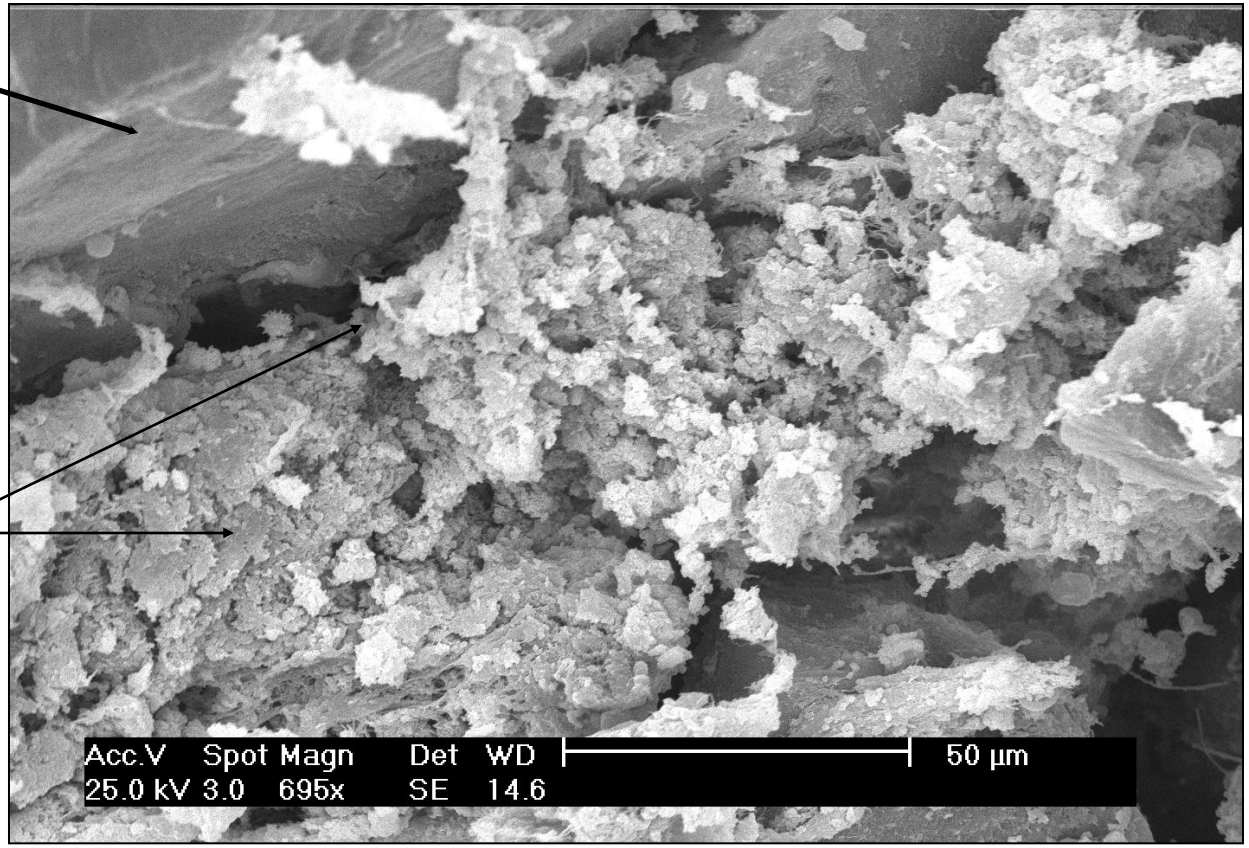
Illustration de l'usure des différents composants de prothèses articulaires en fonction du temps (Source : www.stryker.com)



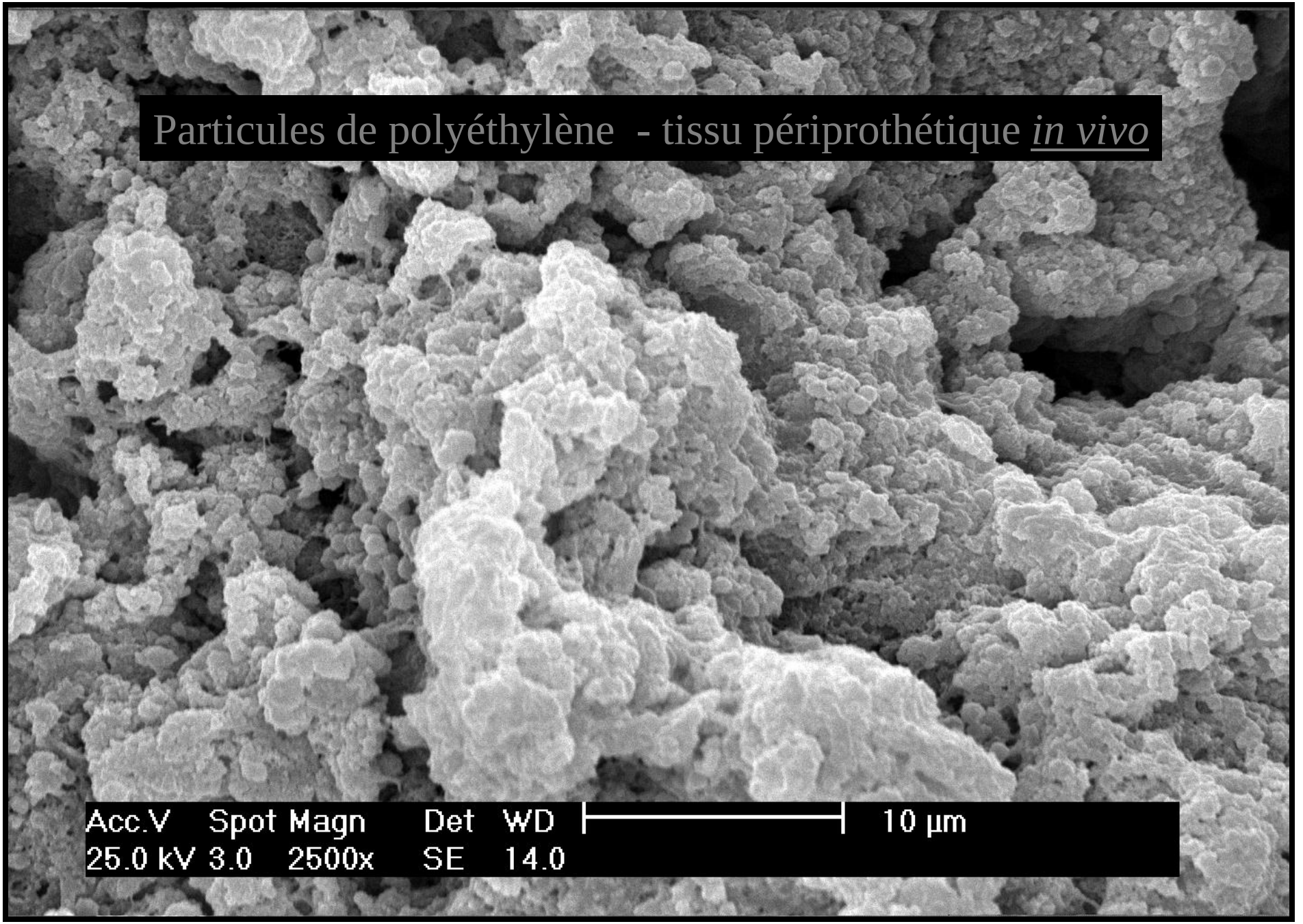
Aseptic Loosening (microscopic analysis)

neocapsule

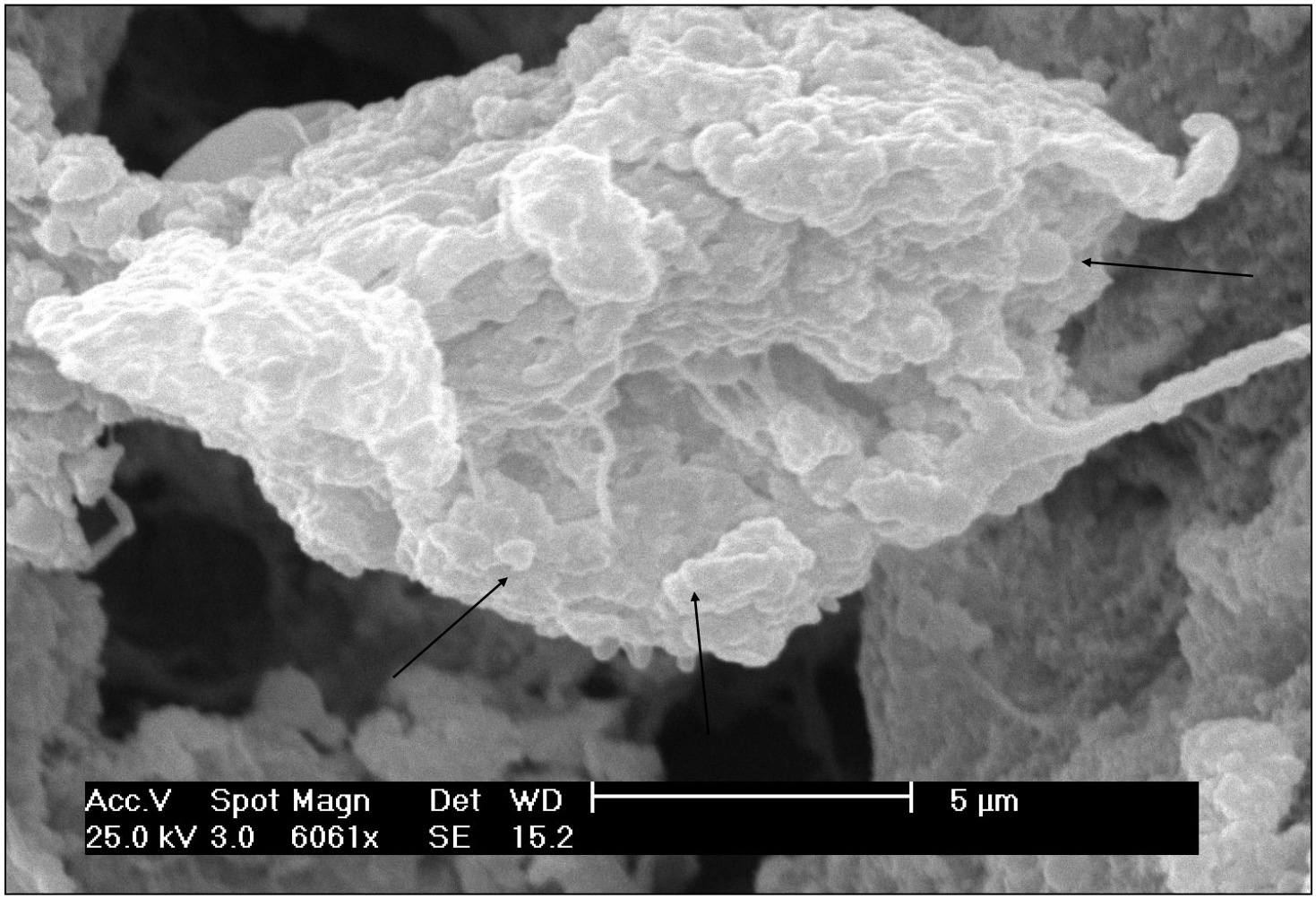
Polyethylene particles



MEB x 695

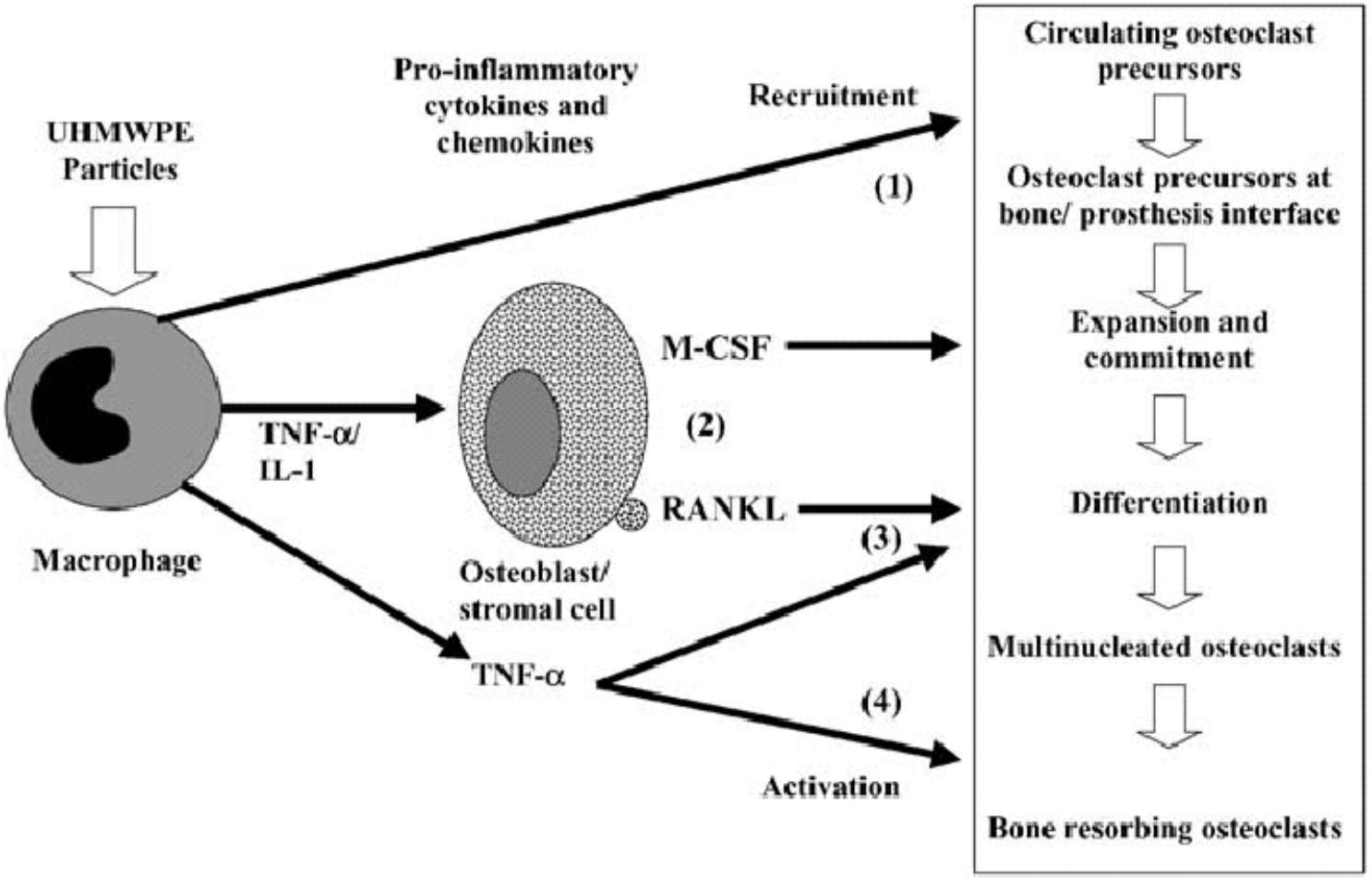

Particules de polyéthylène - tissu périprothétique *in vivo*
Acc.V Spot Magn Det WD 10 µm
25.0 kV 3.0 2500x SE 14.0

Aseptic Loosening (microscopic analysis)



MEB x 6061

Mécanisme immunologique du descellement aseptique de prothèse articulaire



E. Ingham, J. Fisher / Biomaterials 26 (2005) 1271–1286

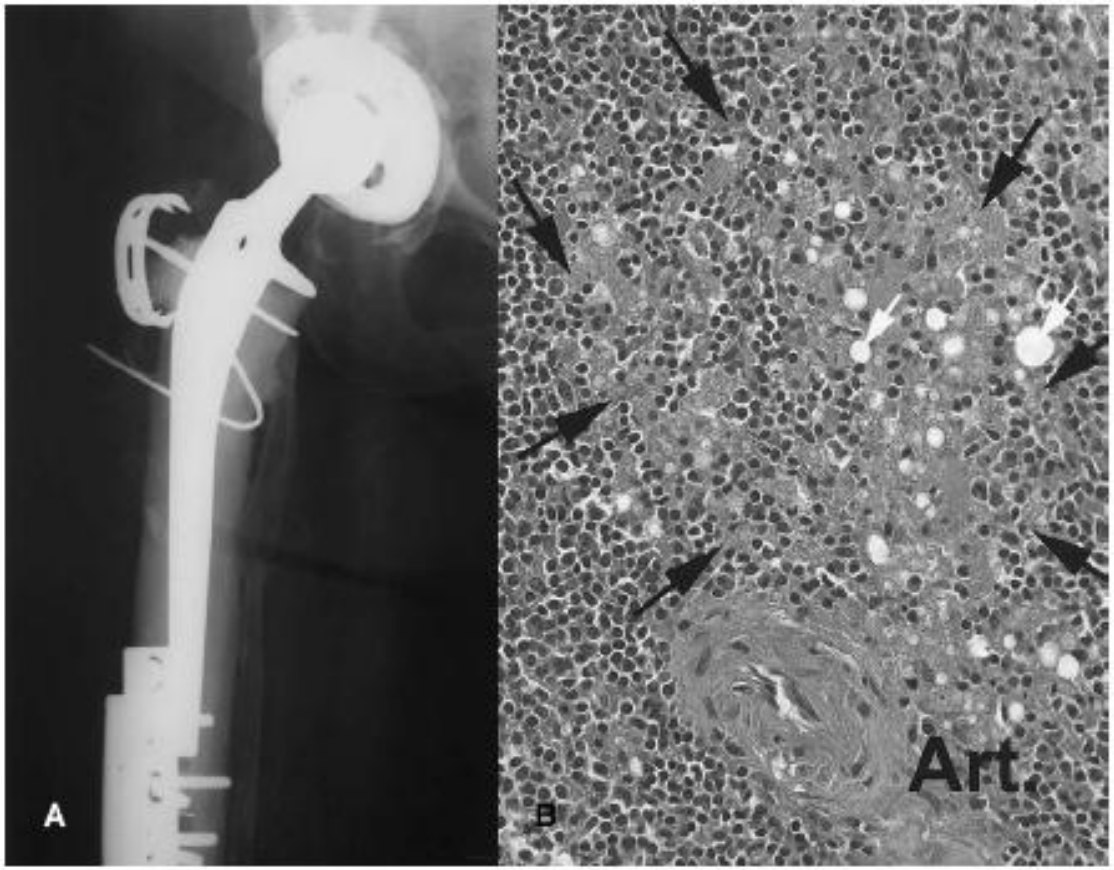


Fig. 2. Patient 28. (A) Radiograph demonstrates allograft-prosthesis composite with fixation plates and cobalt-chromium-nickel-tungsten alloy cable grip system with broken cable 1.7 years prior to the death of this patient. (B) Postmortem photomicrograph of white pulp of the spleen shows aggregate of macrophages (black arrows) containing abundant submicrometer particles of cobalt-chromium-nickel-tungsten alloy generated by the cables. Lipid droplets (white arrows) consistent with deposition of dietary saturated hydrocarbons such as mineral oil were also present. Art. = splenic arteriole. (Hematoxylin and eosin; original magnification ×200).

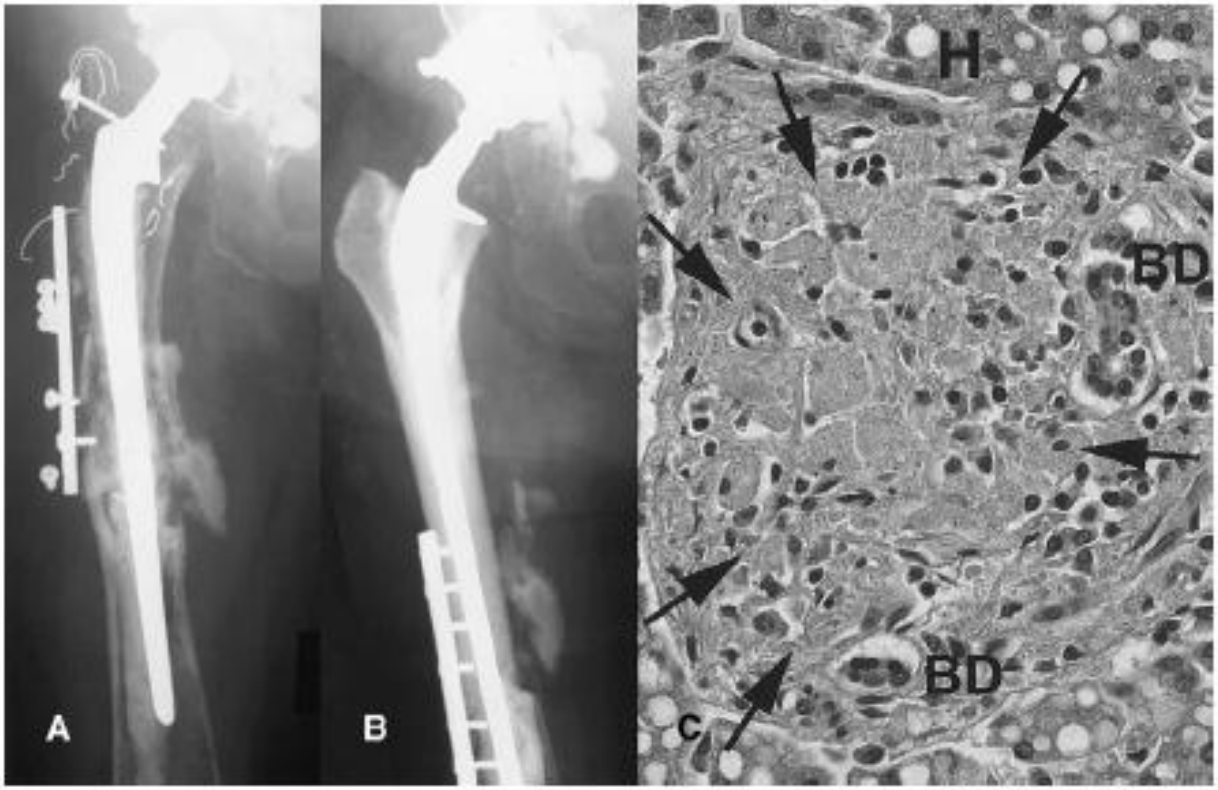
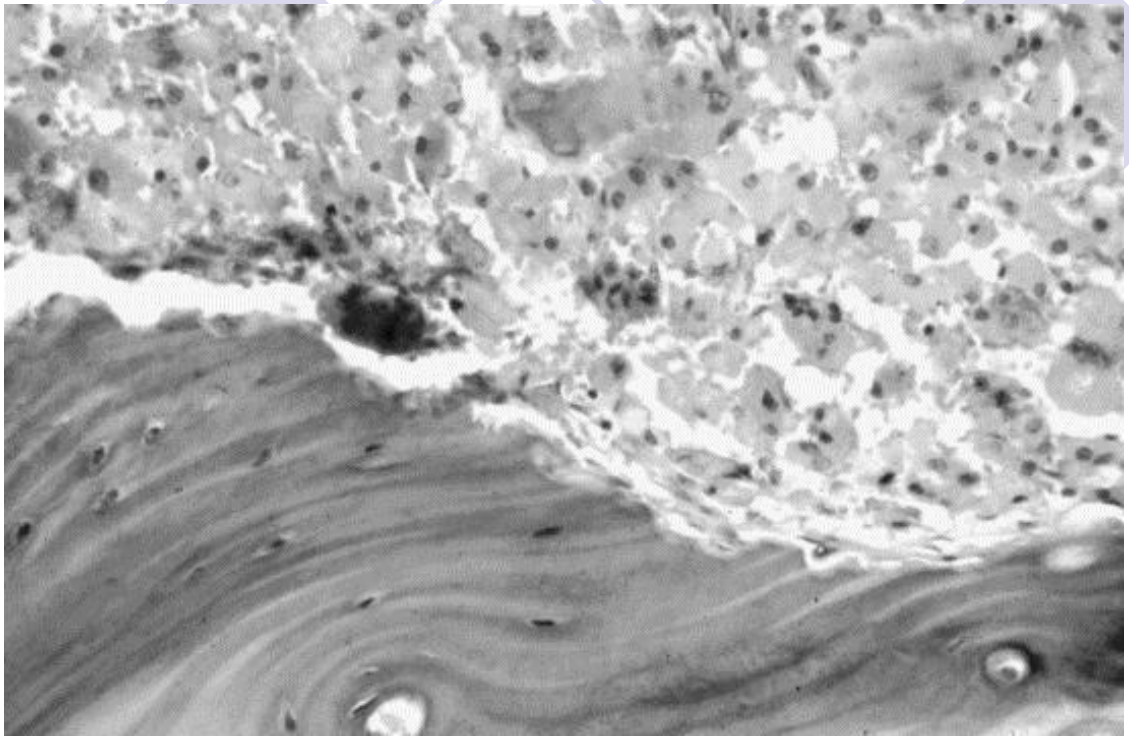
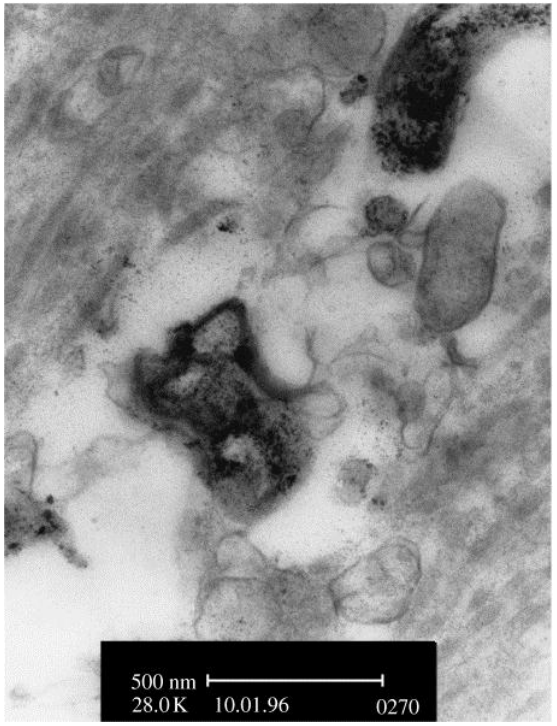


Fig. 1. Patient 30. (A) Preoperative radiograph of failed reconstruction for periprosthetic fracture showing loose and broken stainless steel hardware 12 years prior to this patient's demise. (B) Radiograph 10.5 years following successful reconstruction of the same femur using an allograft-prosthesis composite. (C) Postmortem photomicrograph of liver reveals cluster of pale-staining macrophages (arrows) containing minute stainless steel particles (presumably, some of which were generated 12 years earlier) filling the central portion of a portal tract. BD = bile ductule; H = hepatocytes. (Hematoxylin and eosin; original magnification ×300).

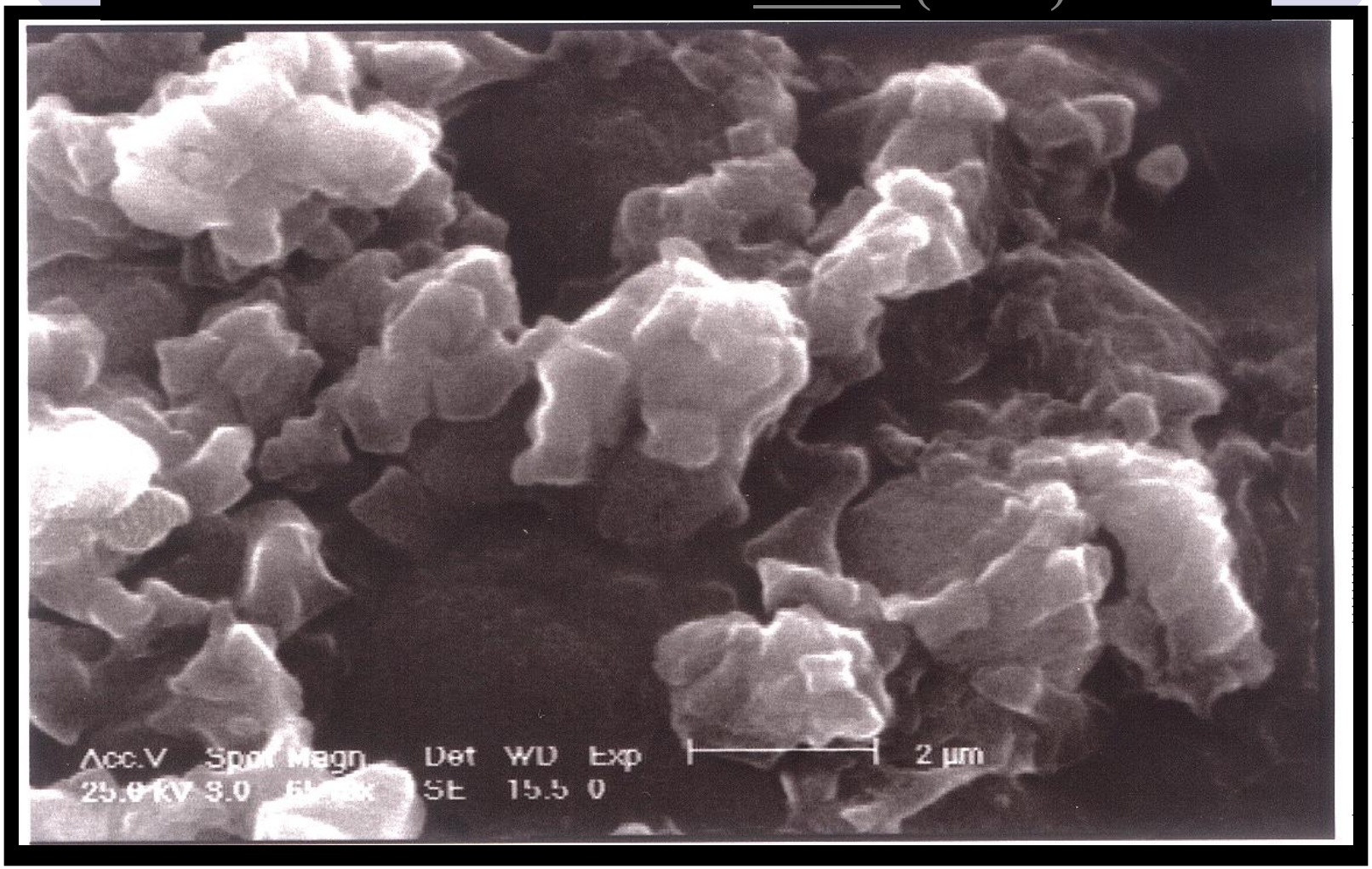


Revell PA.. J R Soc Interface. 2008 Nov 6;5(28):1263-78.



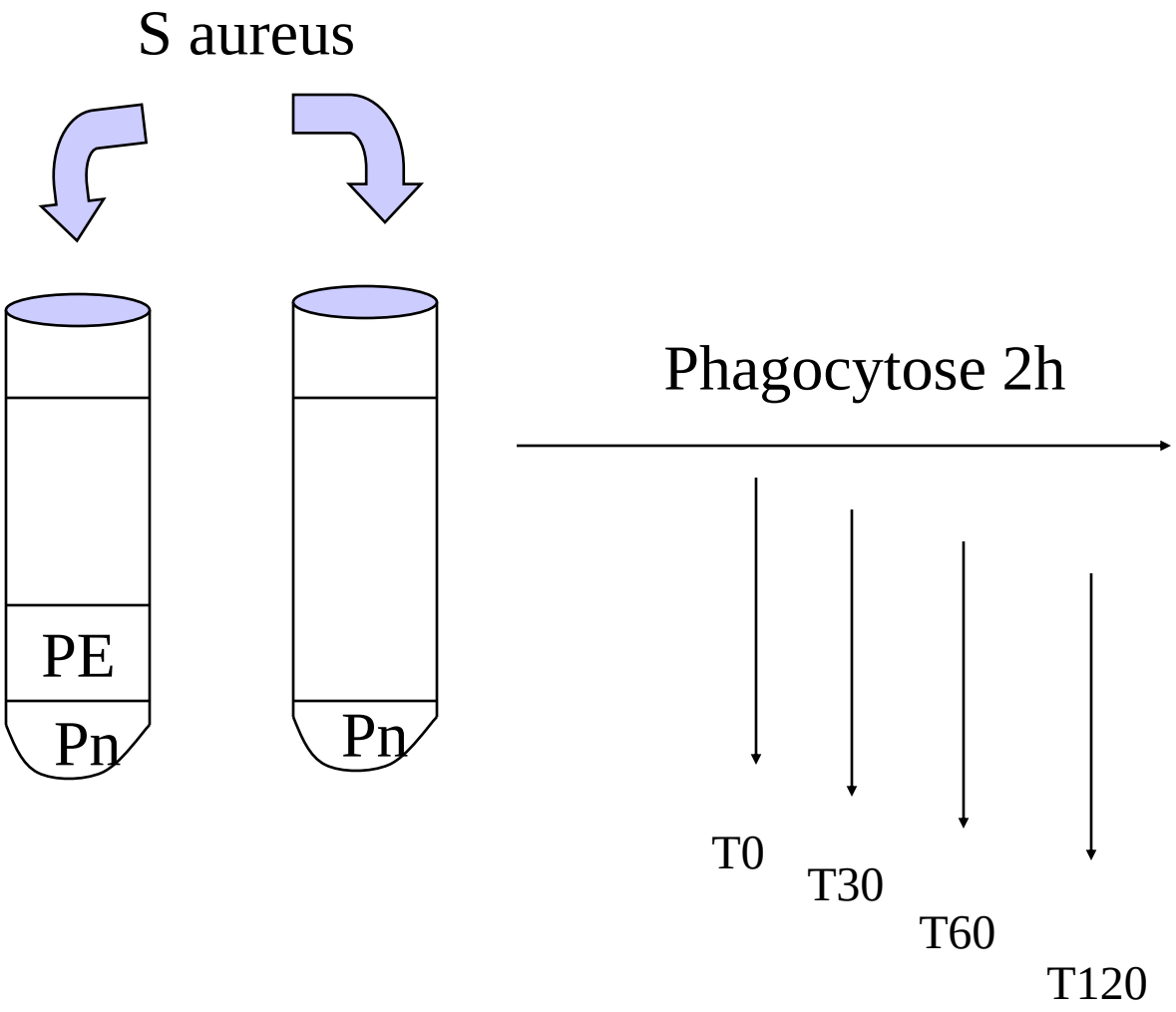
Transmission electron micrograph
to show the presence of numerous nanoparticles of CoC

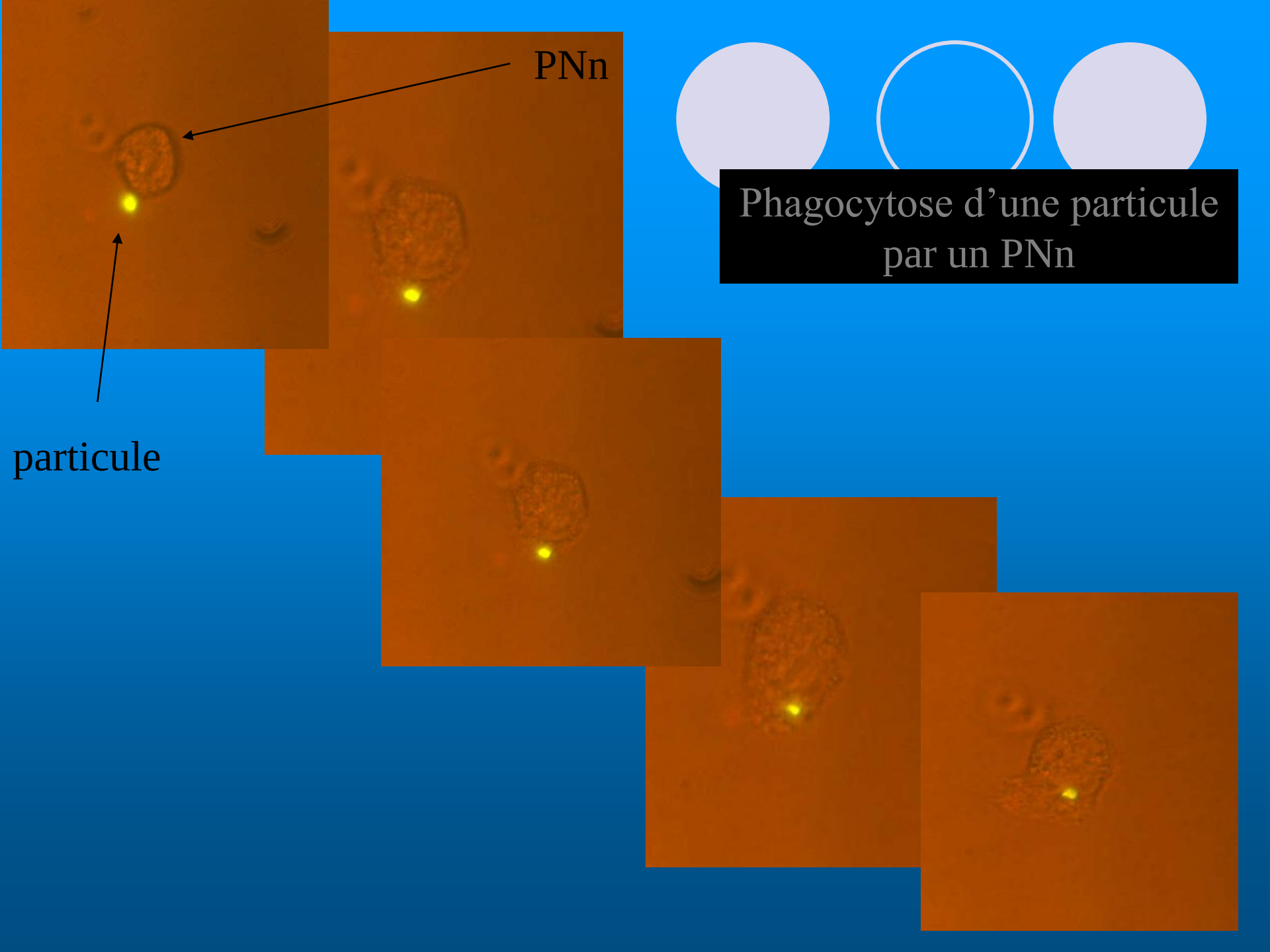
Particules de HDPE *in vivo* (MEB)



Particules de HDPE *in vitro* (MEB)

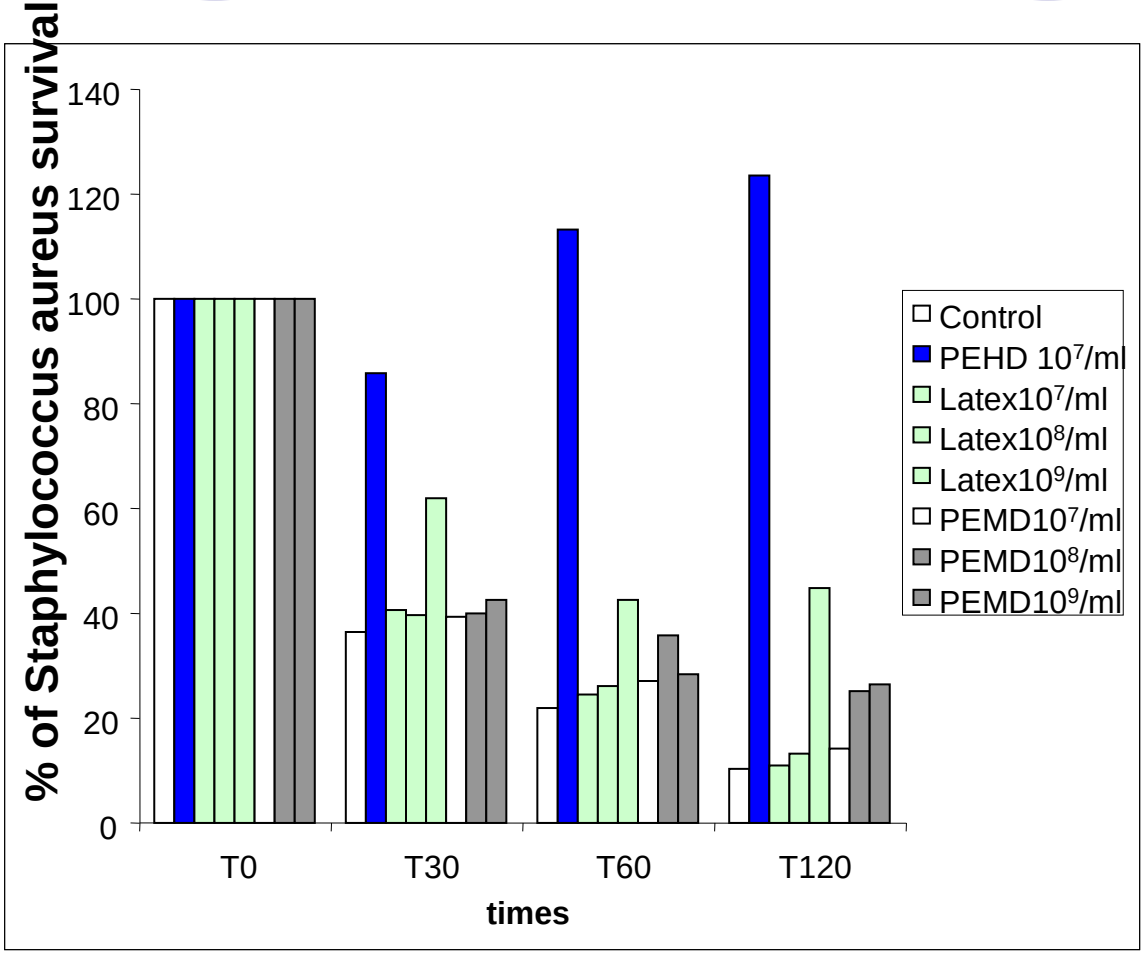
Test de « killing bactérien »



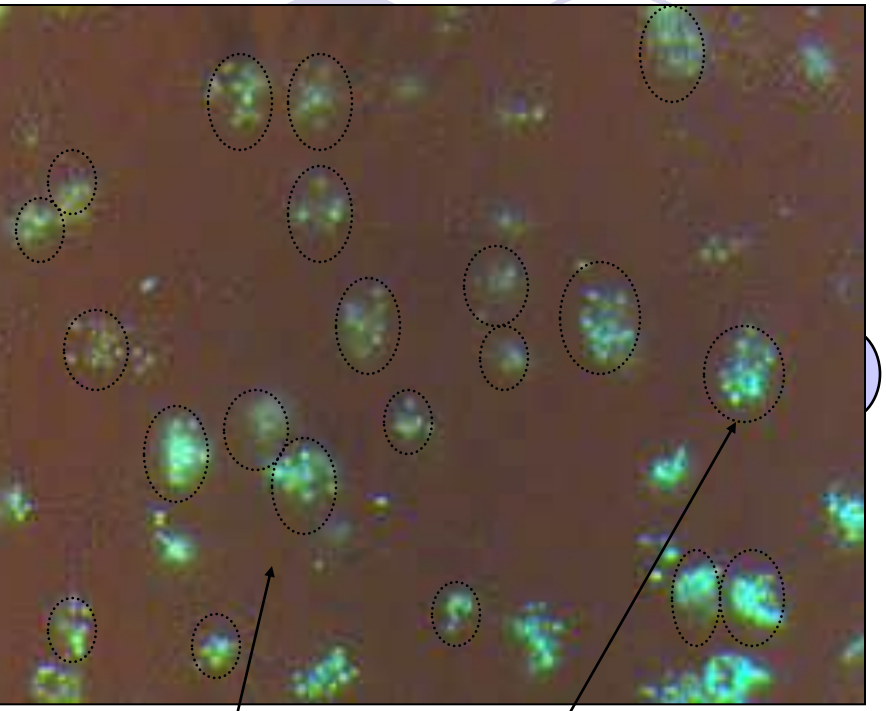


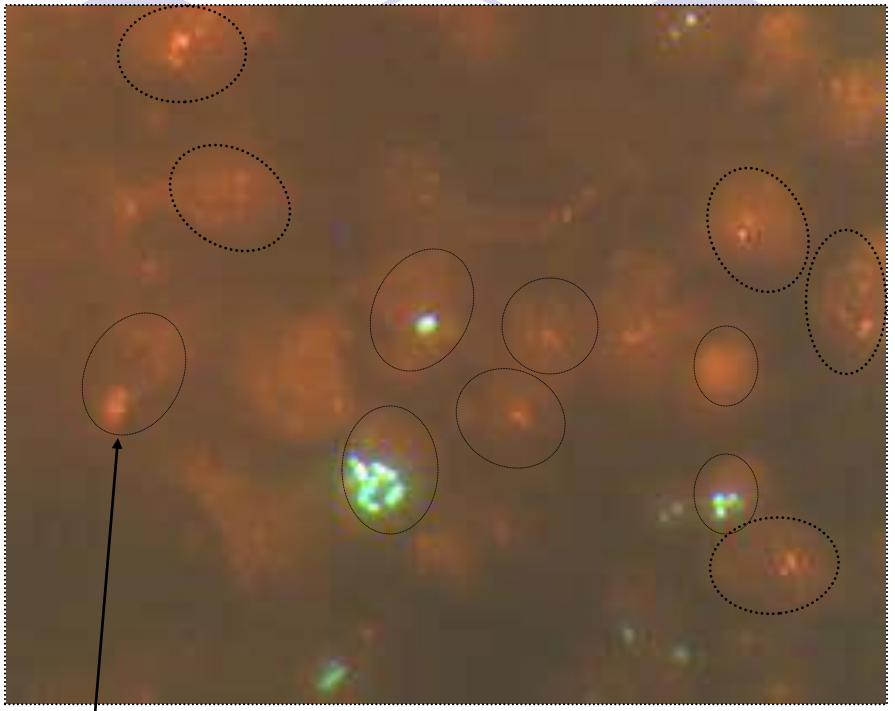
Phagocytose d’une particule par un PNn

« Killing » de *S.aureus* par les polynucléaires en présence de particules de STRUCTURES DIFFERENTES



Bernard L, Vaudaux P, Merle C, Stern R, Huggler E, Lew D, Hoffmeyer P. Biomaterials. 2005 Sep;26(27):5552-7.





Polynuclear cell

Staphylococcus (green-FITC)

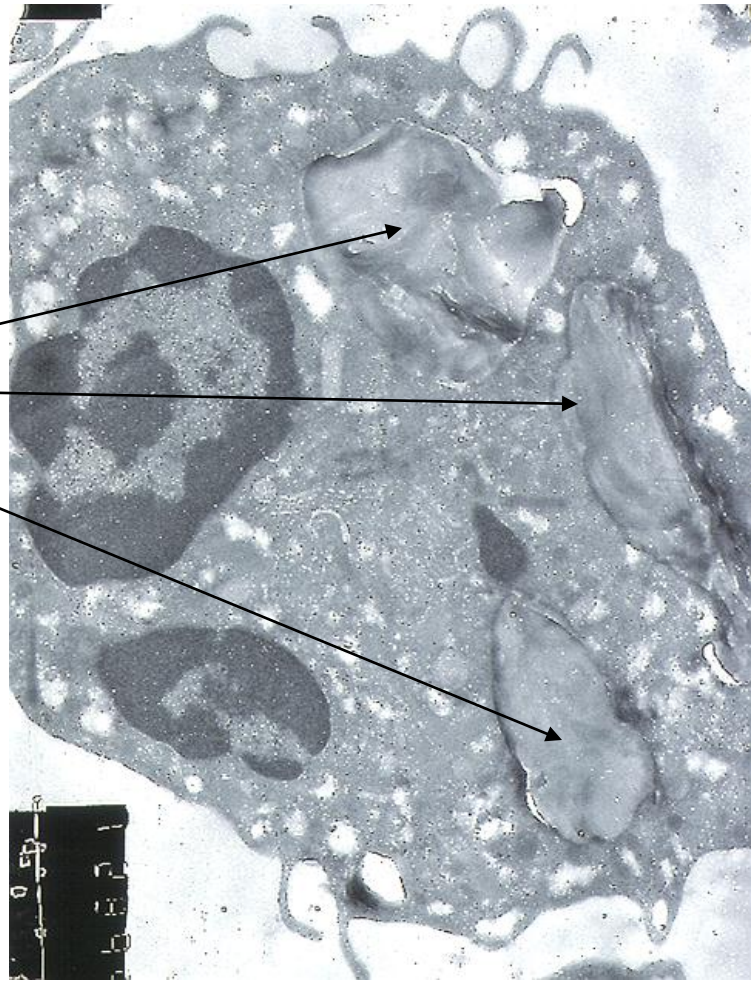
Polyethylene particle (red-rhodamin)

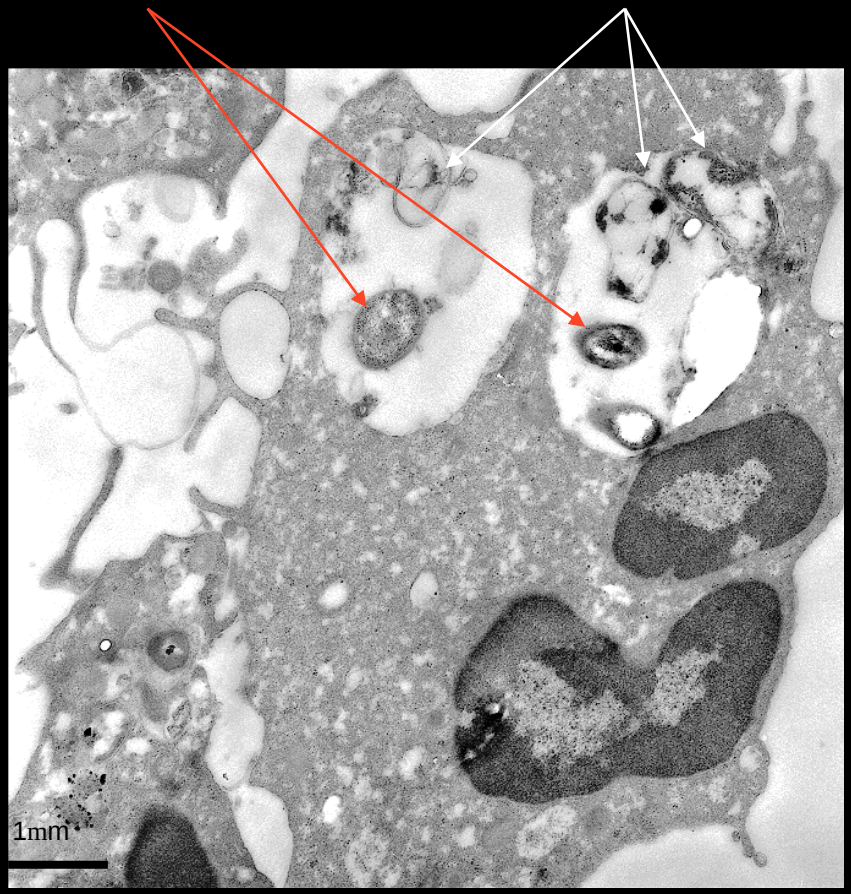
Double-staining fluorescence assay to measure polynuclear phagocytosis of Staphylococcus aureus in presence or absence of polyethylene particles

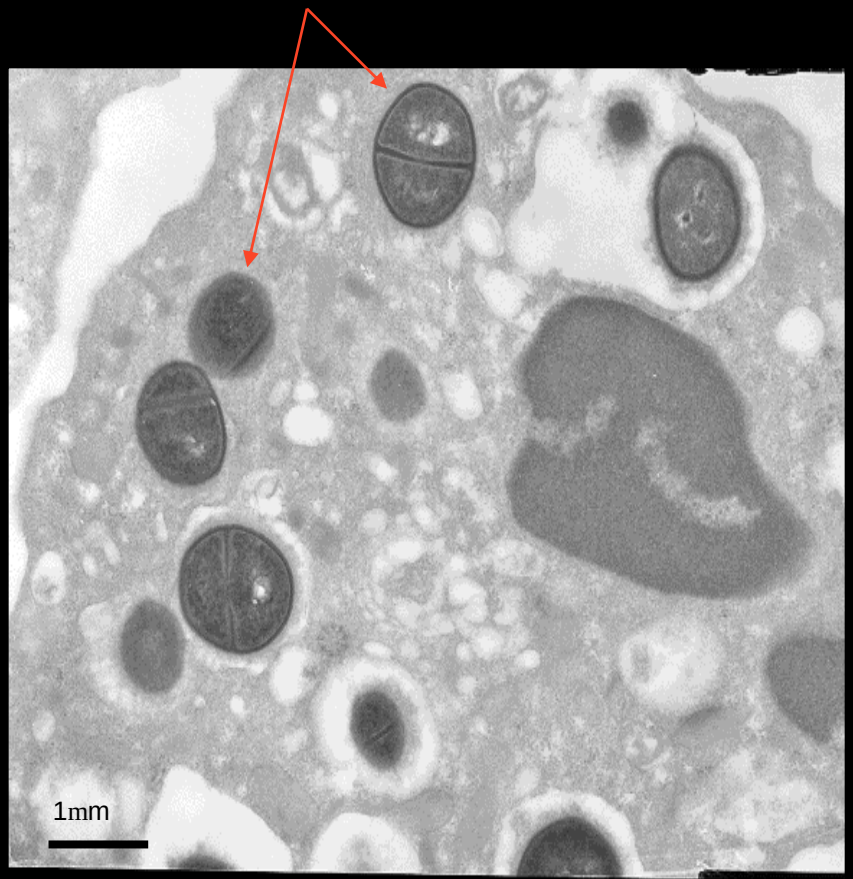
Bernard L, Vaudaux P, Huggler E, Stern R, Fréhel C, Francois P, Lew D, Hoffmeyer P.
FEMS Immunol Med Microbiol. 2007 Apr;49(3):425-32

Polynuclear neutrophils from Aseptic Loosening (microscopic analysis)

Polyethylene wear




1mm


1mm

Et l'interface METAL-METAL ???

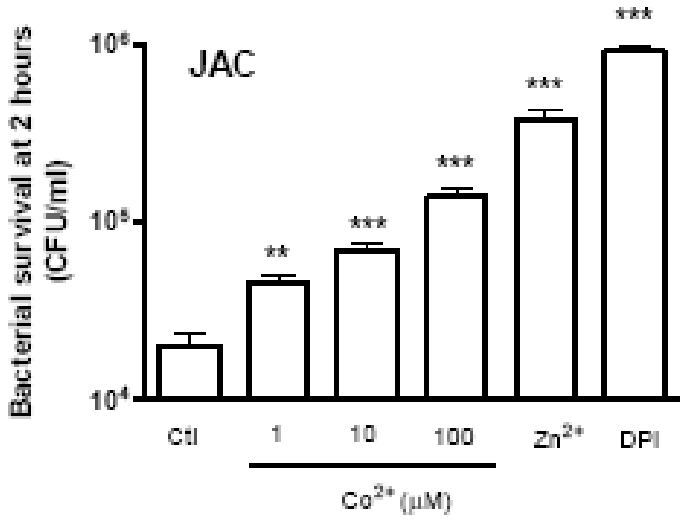
The potential role of cobalt ions released from metal prosthesis on the inhibition of Hv1 proton channels and the decrease in Staphyloccocus epidermidis killing by human neutrophils.

Daou S, El Chemaly A , Chritofilopoulos P, Bernard L, Hoffmeyer P, Demaurex N
Biomaterials. 2010 Dec 6.

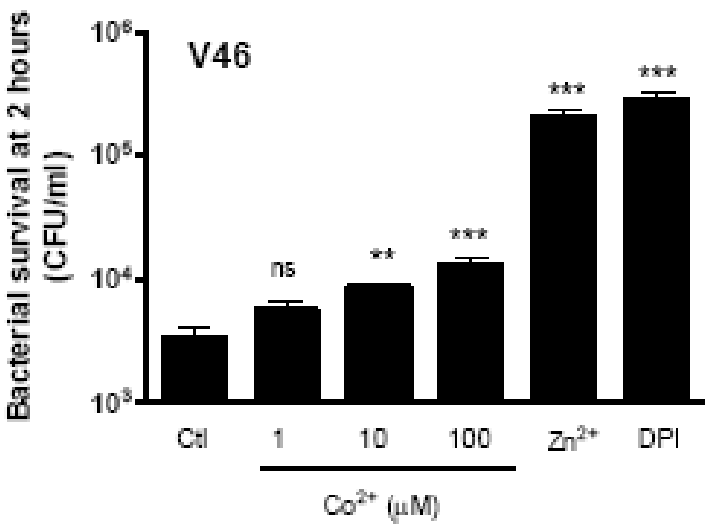
Case	sex	Patient age (years)	Prosthesis age (years)	Diagnosis	Blood [Co2+] µM	Tissues [Co2+] µM	Articular liquid [Co2+] µM
Metal / Metal total hip arthroplasty							
1	M	79	5	Aseptic loosning	0.119	108	na
2	F	72	> 15	Aseptic loosning	0.617	410	16.4
3	M	80	4	Chronic pain	0.142	51	na
4	F	85	2	Chronic bruise	0.007	99	2.18
5	M	65	4	Chronic pain	0.012	8.2	0.134
6	F	68	2	Aseptic loosning	0.043	48	na
7	M	79	2	infection	0.136	6	0.175
8	M	72	15	Aseptic loosning	0.017	19.25	0.021
9	M	72	12	Aseptic loosning	0.014	154	na
10	M	81	14	Aseptic loosning	0.011	12.5	na
11	M	79	2	Aseptic loosning	0.010	37	0.408
12	M	81	3	Aseptic loosning	0.144	19	13
13	M	66	2	Chronic pain	0.053	15	na
14	F	51	4	Chronic pain	na	3.14	na
15	M	36	4	Aseptic loosning	0.008	0.767	na
16	M	61	6	Aseptic loosning	0.024	0.379	2.13
17	F	45	18 months	Chronic pain	0.020	2	na
18	M	36	2	Aseptic loosning	0.011	0.09	na
19	M	43	2	Aseptic loosning	0.021	7.15	na
Polyethylene / Ceramic total hip arthroplasty							
20	M	77	8 months	infection	0.050	0.253	0.109
21	F	69	2	Aseptic loosning	na	0.209	0.009
22	M	68	10	Aseptic loosning	0.010	39	na
23	M	79	4	Aseptic loosning	0.009	0.95	na
24	F	62	16	Aseptic loosning	0.010	0.037	na
25	F	62	18	Aseptic loosning	0.008	0.059	na
26	F	73	3	Aseptic loosning	0.025	0.584	na

Alliages Chrome-Cobalt

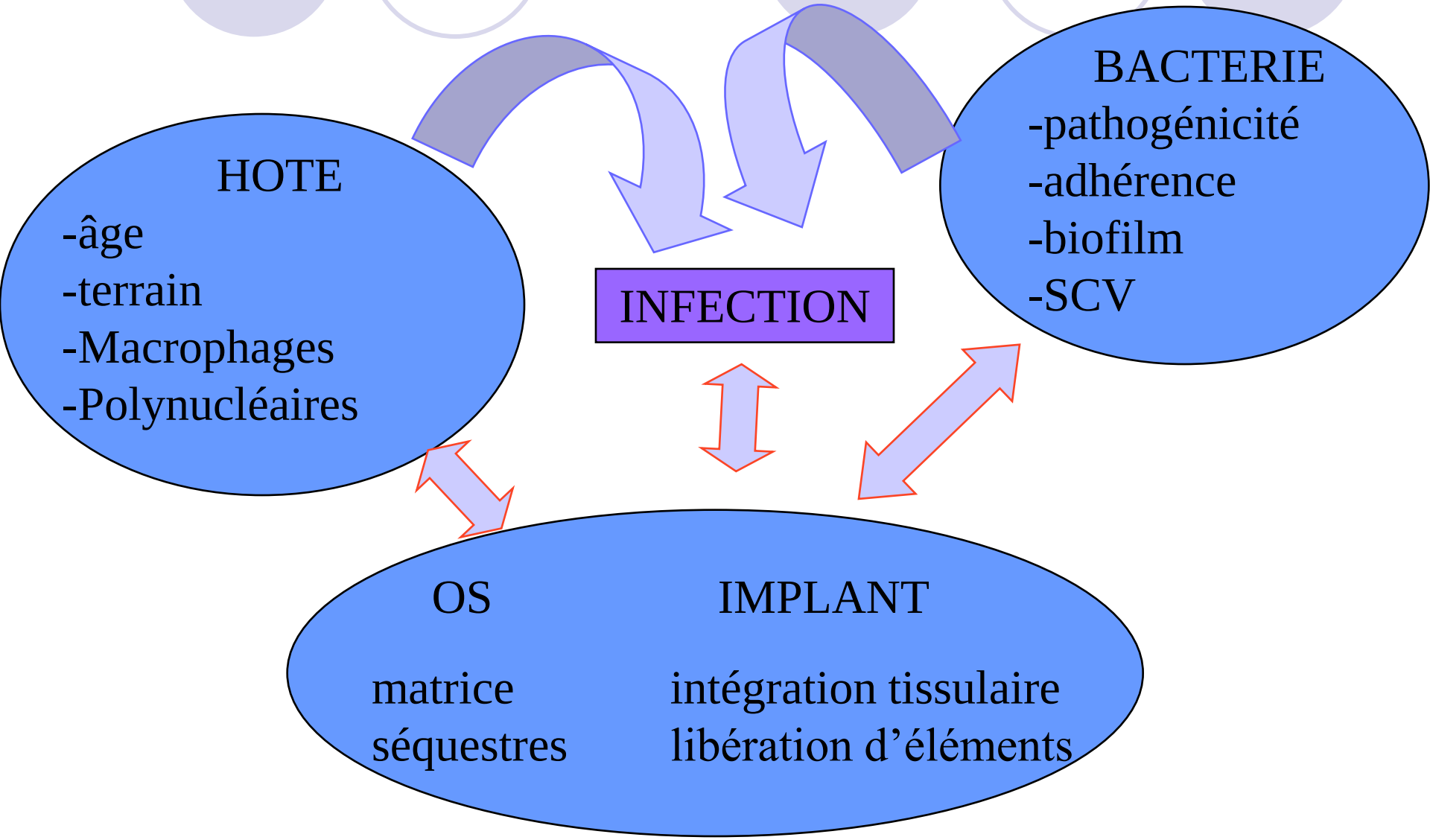
C

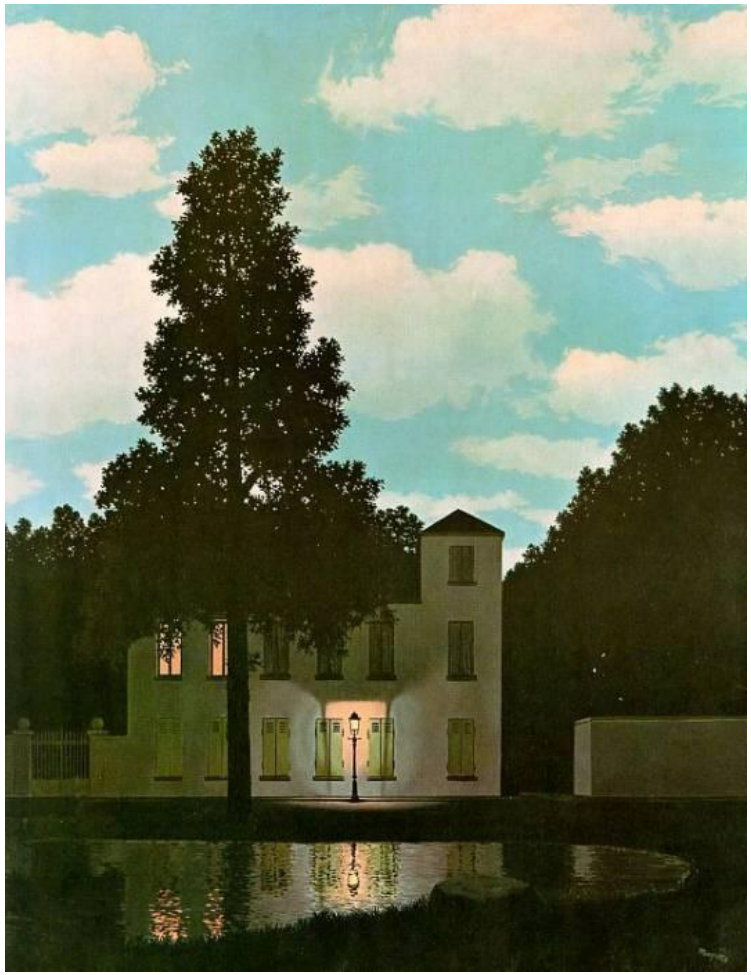

JAC
Bacterial survival at 2 hours (CFU/ml)
10^6
10^5
10^4
**
***
***
***
***
Ctl
1
10
100
Zn^{2+}
DPI
Co^{2+} (μM)

D


V46
Bacterial survival at 2 hours (CFU/ml)
10^6
10^5
10^4
10^3
ns
**
***
***
***
Ctl
1
10
100
Zn^{2+}
DPI
Co^{2+} (μM)

INFECTION OSSEUSE SUR MATERIEL





Merci

"Chercher des voies nouvelles.
fournir les moyens d'y progresser.
pour ainsi féconder l'avenir."