Periprosthetic Joint infection "PJI"

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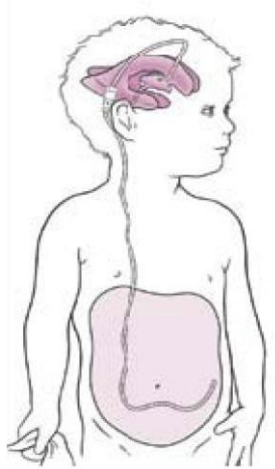
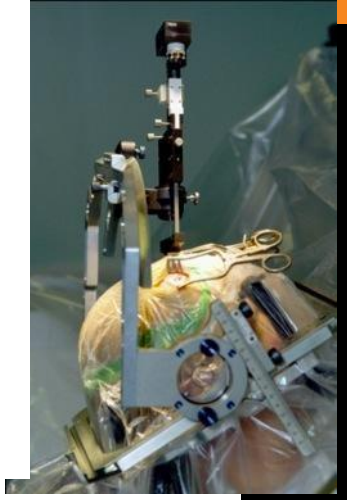
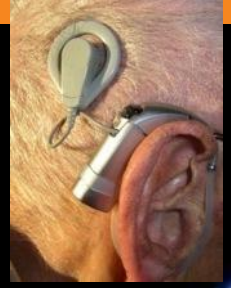
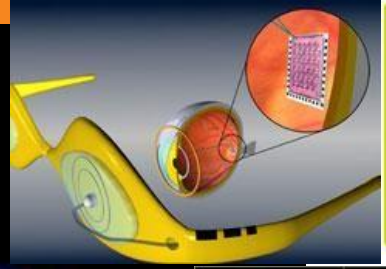
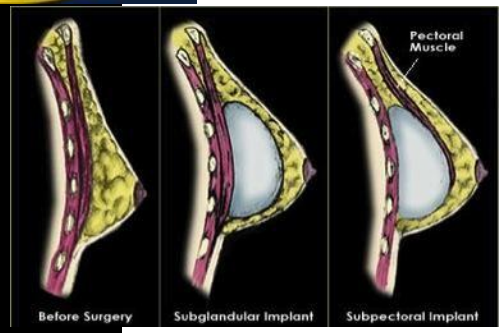
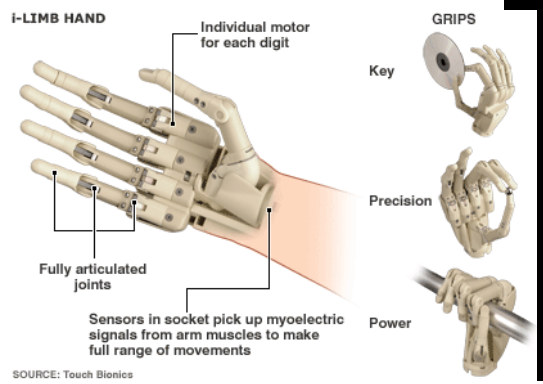
DISCLOSURE

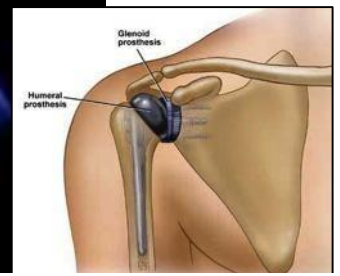
No disclosures relevant to this presentation

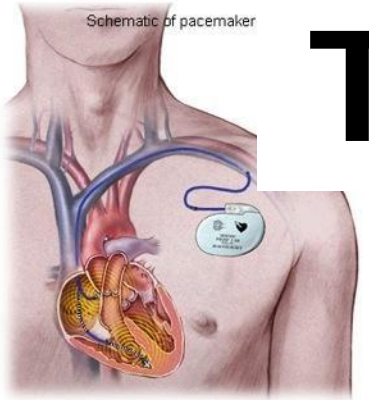






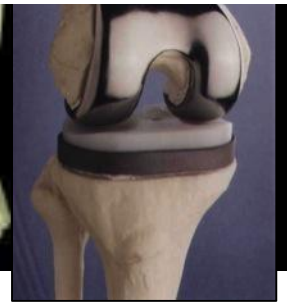
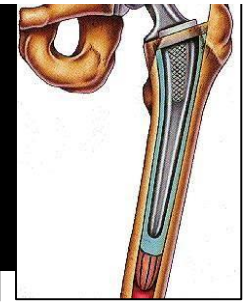
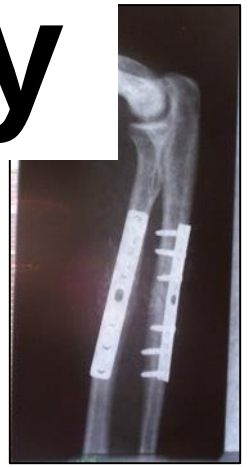






The bionic society

Quality of life!!

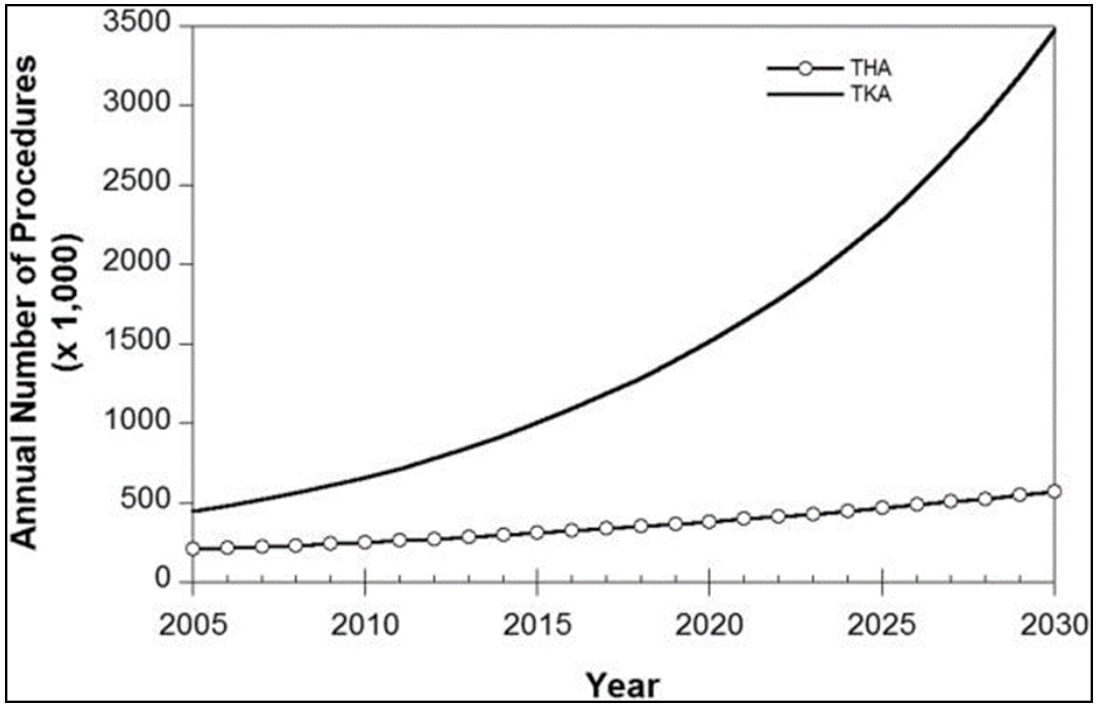
Overview

- Definition
- Management
- Biofilm = enemy
- Challenges
- Future trends

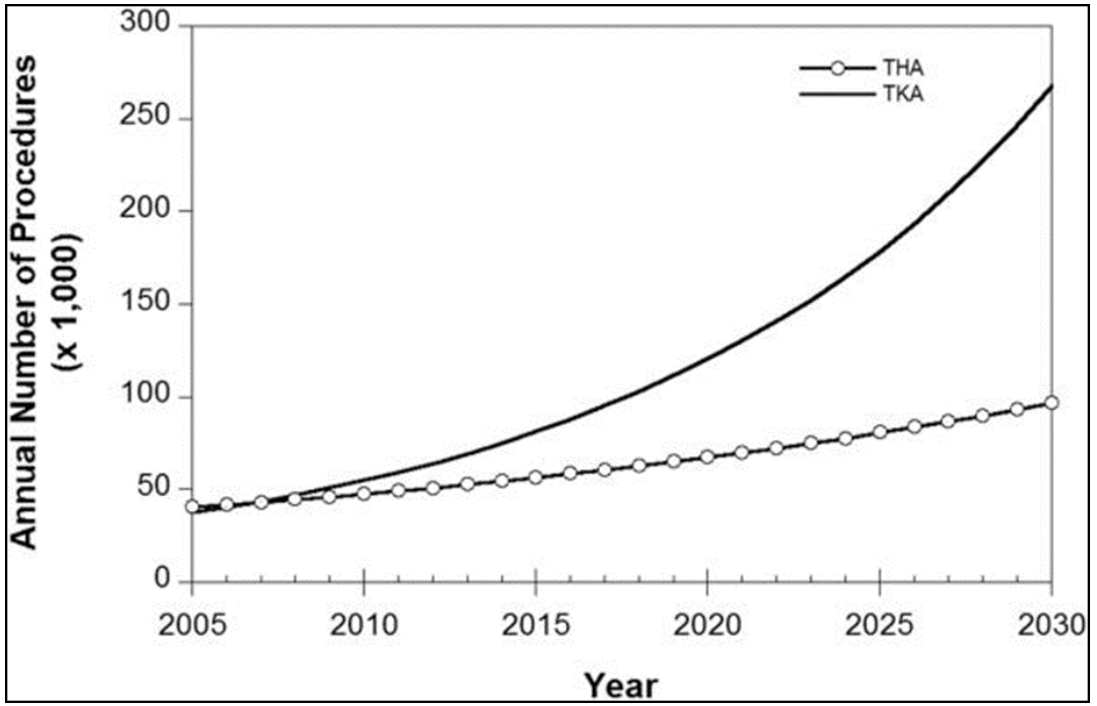
- Deep PJI is one of the most common causes for implant failure and revisions, with dramatic medical and socioeconomic implications.

- PJI is a tremendous burden for individual patients as well as global health care

- Appropriate recognition and management are critical to preserve/restore function and prevent exces morbidity.



primary

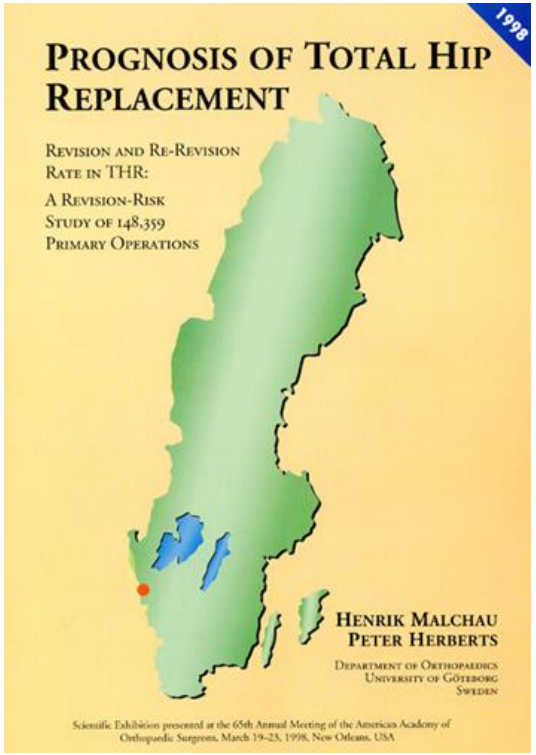


revision

Projections of Primary and Revision Hip and Knee Arthroplasty in the United States from 2005 to 2030.
Kurtz, Steven; Ong, Kevin; Lau, Edmund; Mowat, Fionna; Halpern, Michael; MPH, MD

Journal of Bone & Joint Surgery - American Volume.
89(4):780-785, April 2007.
DOI: 10.2106/JBJS.F.00222

Swedish Hip registry 2016



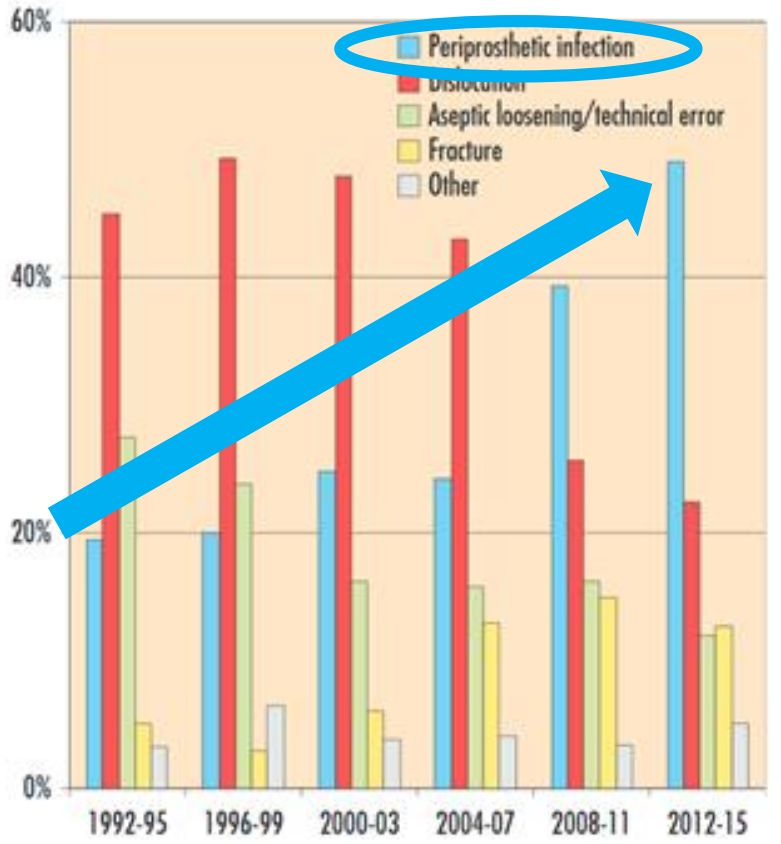


Figure 1. Distribution of the causes of reoperation within two years after the primary operation, divided into six time intervals between 1992 and 2014.

By 2030 over 60% of all total joint revisions will be because of PJI

The Impact of Infection After Total Hip Arthroplasty on Hospital and Surgeon Resource Utilization

Kevin J. Bozic and Michael D. Ries
J Bone Joint Surg Am. 2005;87:1746-1751. doi:10.2106/JBJS.D.02937

	Group 1 (Revision Arthroplasty for Infection)† (N = 29)	Group 2 (Revision Arthroplasty for Aseptic Loosening)† (N = 27)	Group 3 (Primary Arthroplasty)† (N = 29)
No. of hospitalizations	3.6 ± 2.1	1.2 ± 0.5	1.2 ± 0.4
Total no. of days in hospital	28.2 ± 20.9	8.1 ± 5.3	6.2 ± 2.4
Total no. of operations	3.690 ± 2.222	1.407 ± 0.888	1.0 ± 0.2
Total hospital costs *(US$)*	96,166 ± 60,664	34,866 ± 15,547	21,654 ± 4291
No. of outpatient visits	54.6 ± 35.1	[illegible]	[illegible]
Total outpatient charges *(US$)*	48,348 ± 27,965	16,411 ± 9478	8519 ± 4185

2.8X

4.8X

Definition by MSIS

Definite PJI exists when:

Major

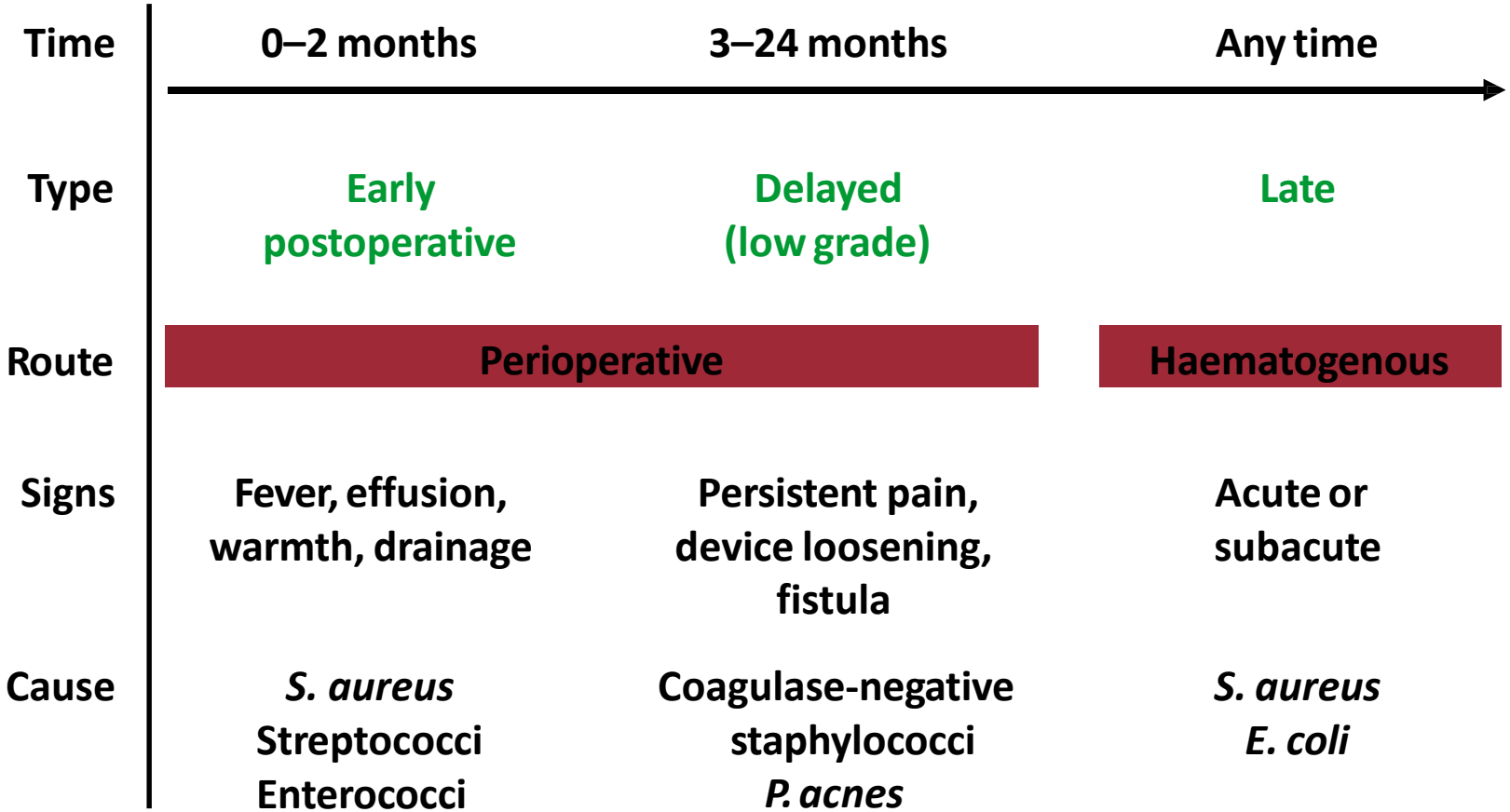
- There is a sinus tract communication with the prosthesis; or
- A pathogen is isolated by culture from at least 2 separate tissue or fluid samples, obtained from the affected prosthetic joint; or

Minor

- 4 of following 6 criteria exist:
  1. Elevated ESR and CRP concentration,
  2. Elevated synovial leucocyte count,
  3. Elevated synovial neutrophil percentage (PMN%),
  4. Presence of purulence in the affected joint,
  5. Isolation of a microorganism in 1 culture of periprosthetic tissue or fluid,
  6. >5 neutrophils per HPF in 5 HPF's observed from histologic analysis op periprosthetic tissue at x400

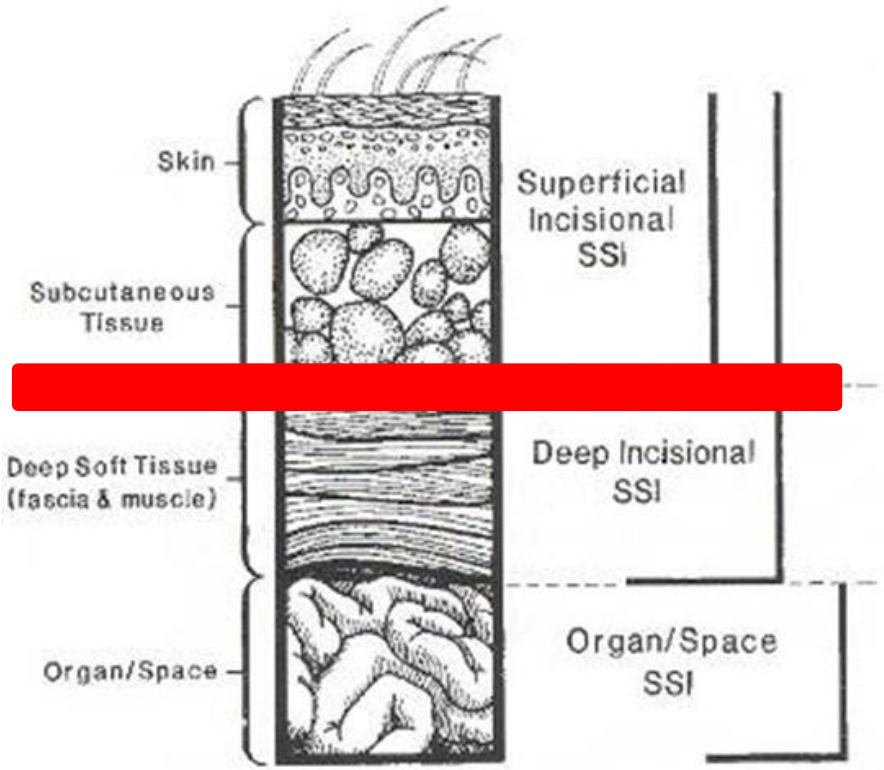
Clin Orthop Relat Res. 2011 Nov; 469(11): 2992–2994

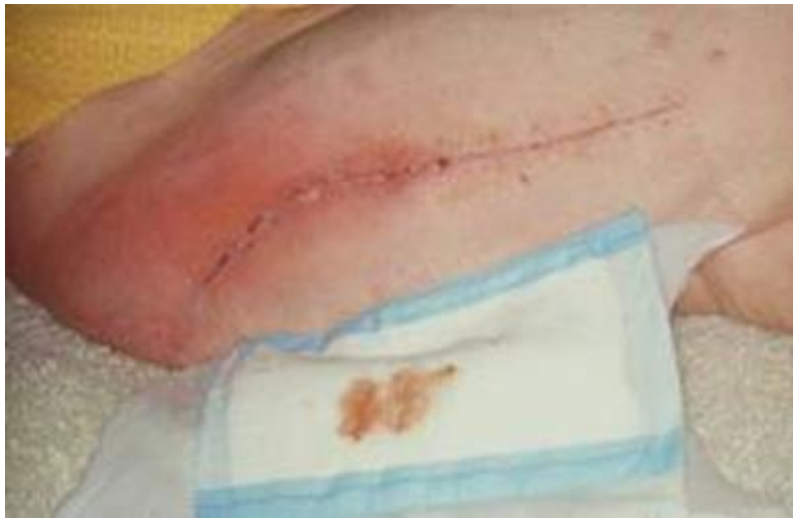
Three types of implant infection



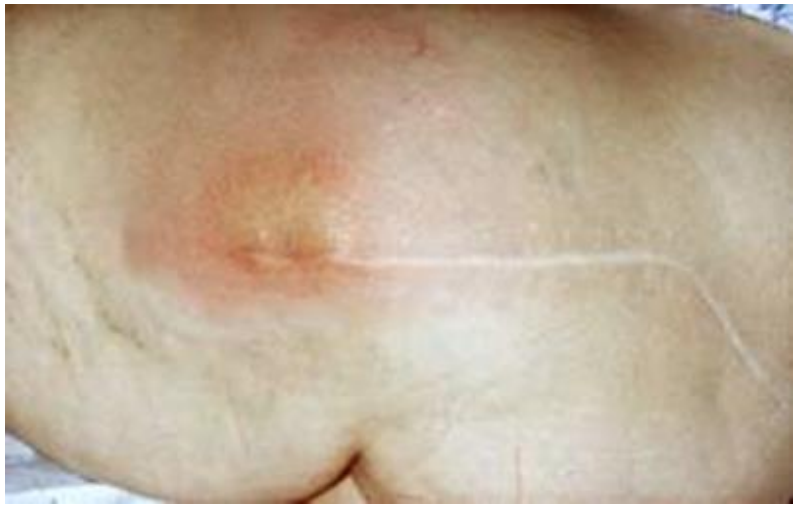
Zimmerli W NEJM 2004 Trampuz A Injury 2006

Definition

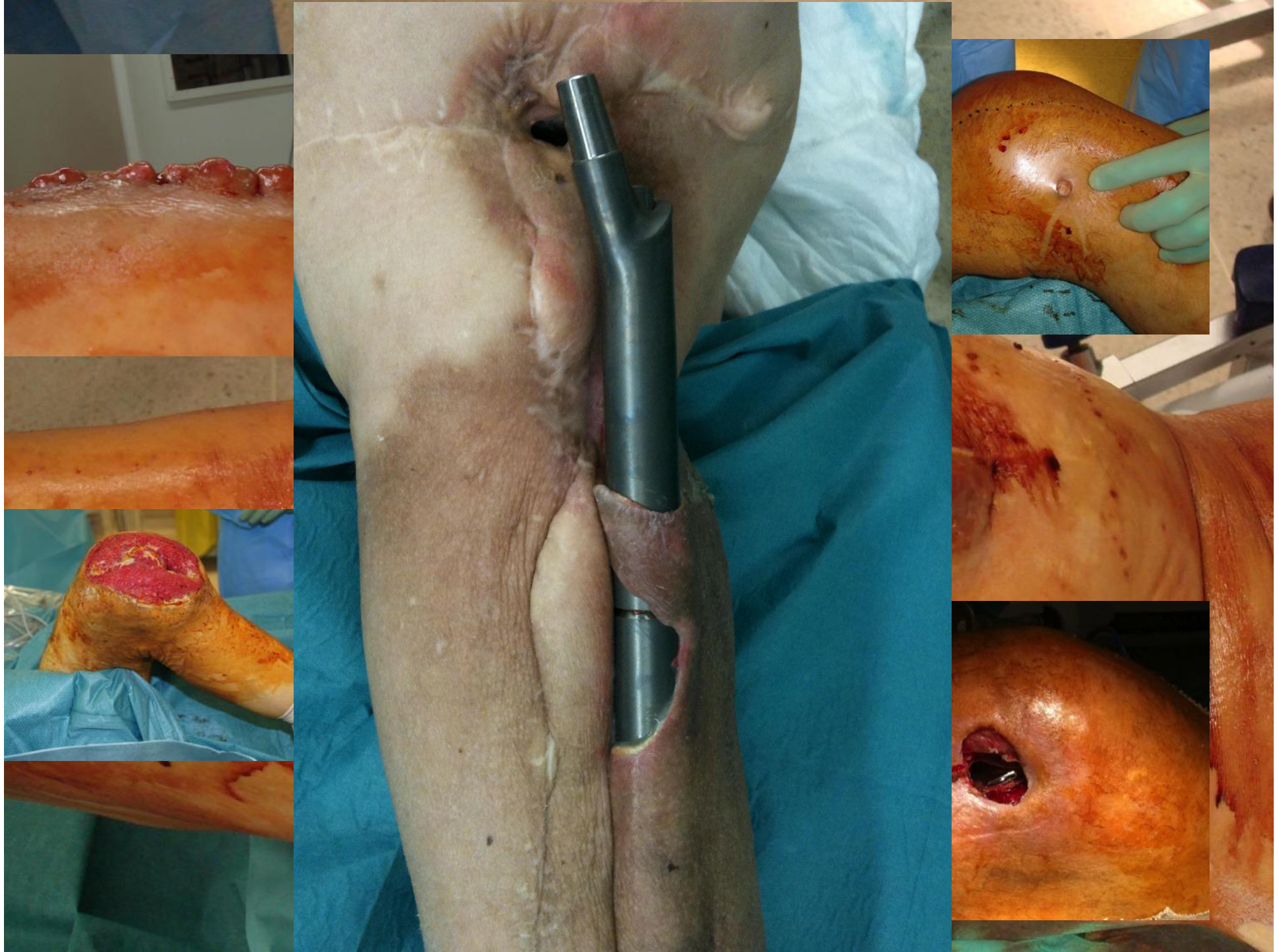




Superficial



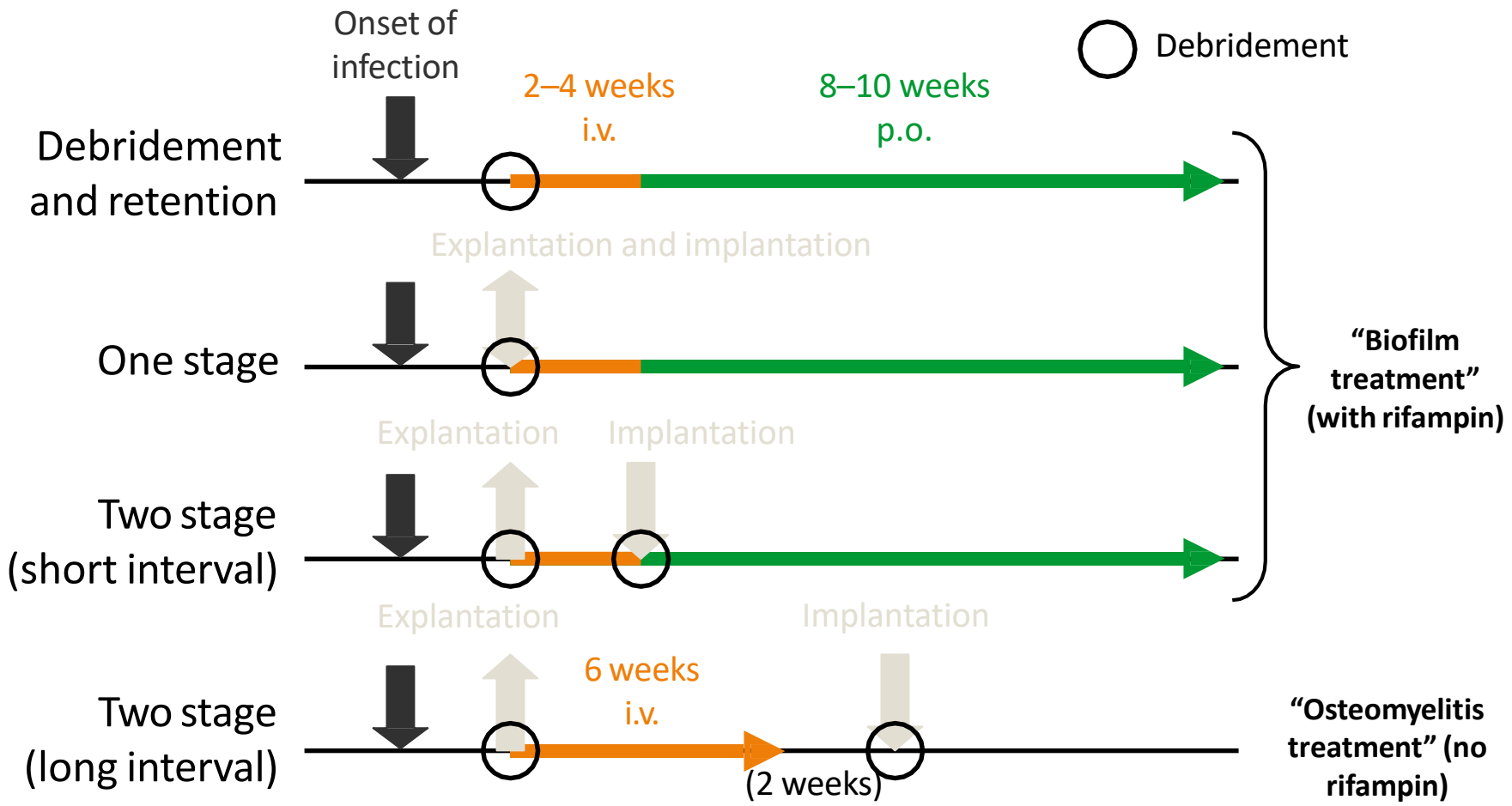
Deep



Treatment strategies

- In situ treatment : DAIR : debridement, antibiotics & implant retention
- One-step exchange
- Two-step exchange
- Definitive removal : Girdlestone / arthrodesis
- Long-term suppressive antibiotic therapy

Treatment infected TJA

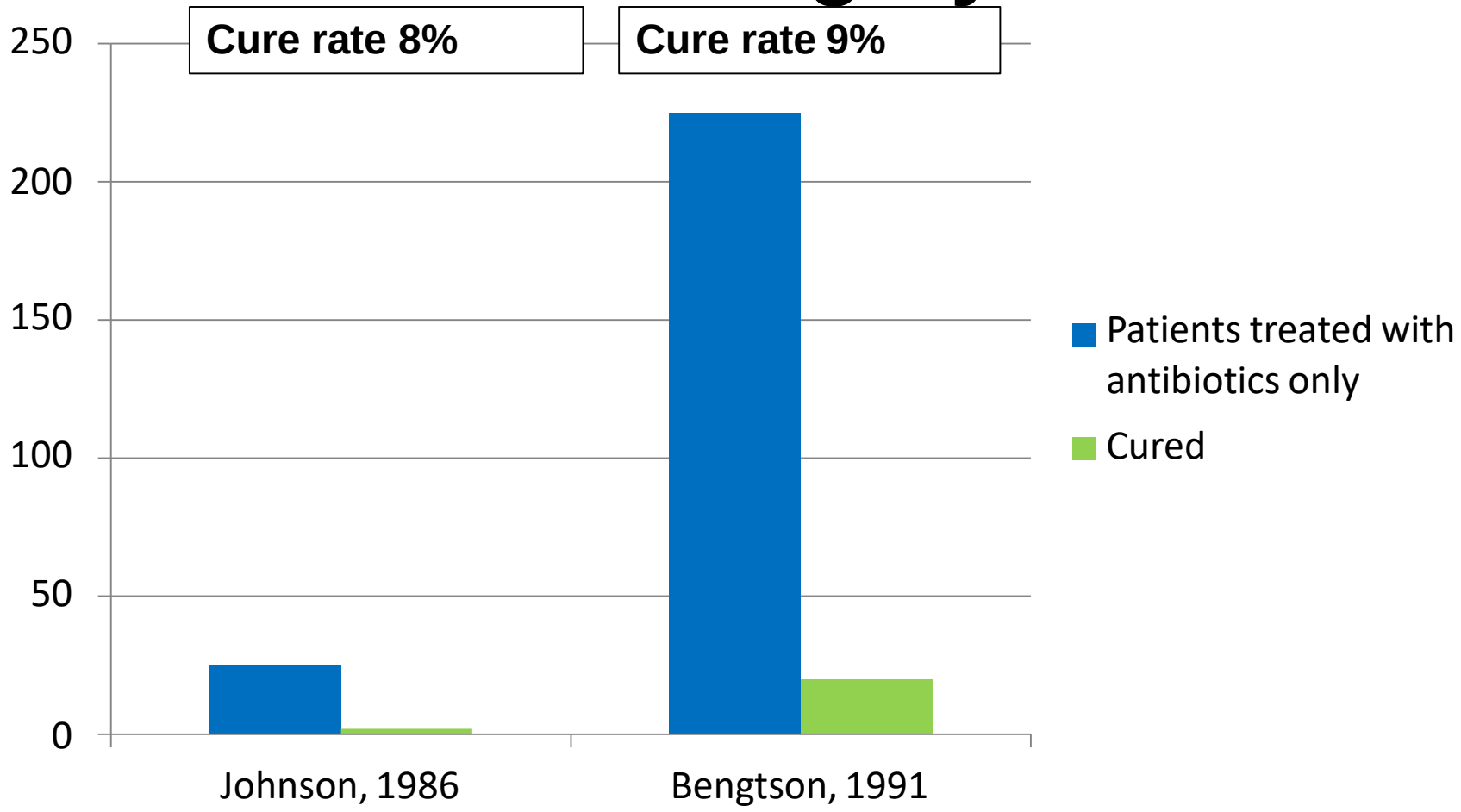


Zimmerli W *et al*. *N Engl J Med* 2004

Borens O et al. Rev Med Suisse 2009

Treatment concept:
Surgery and Antibiotics

Error: antibiotic treatment without surgery



J Bone Joint Surg Br 1986; Bengtson et al. Acta Orhop Scand1991

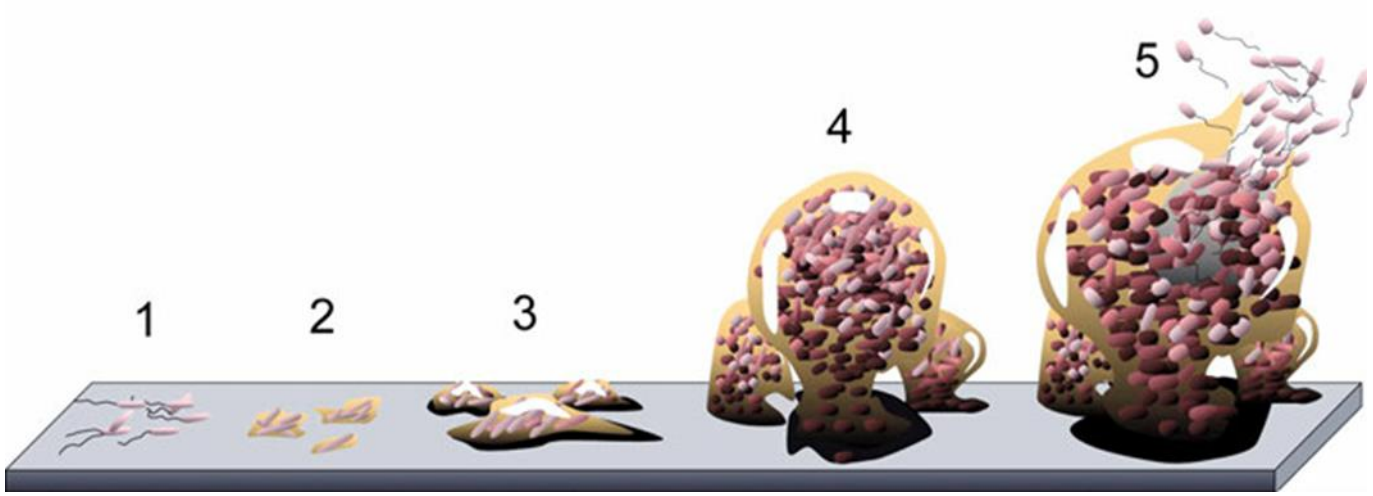
What are we fighting? BIOFILM!

- One of the most resistant forms of life on Earth
- Most bacteria in nature live in biofilm communities

Hot, acidic pools in Yellowstone National Park

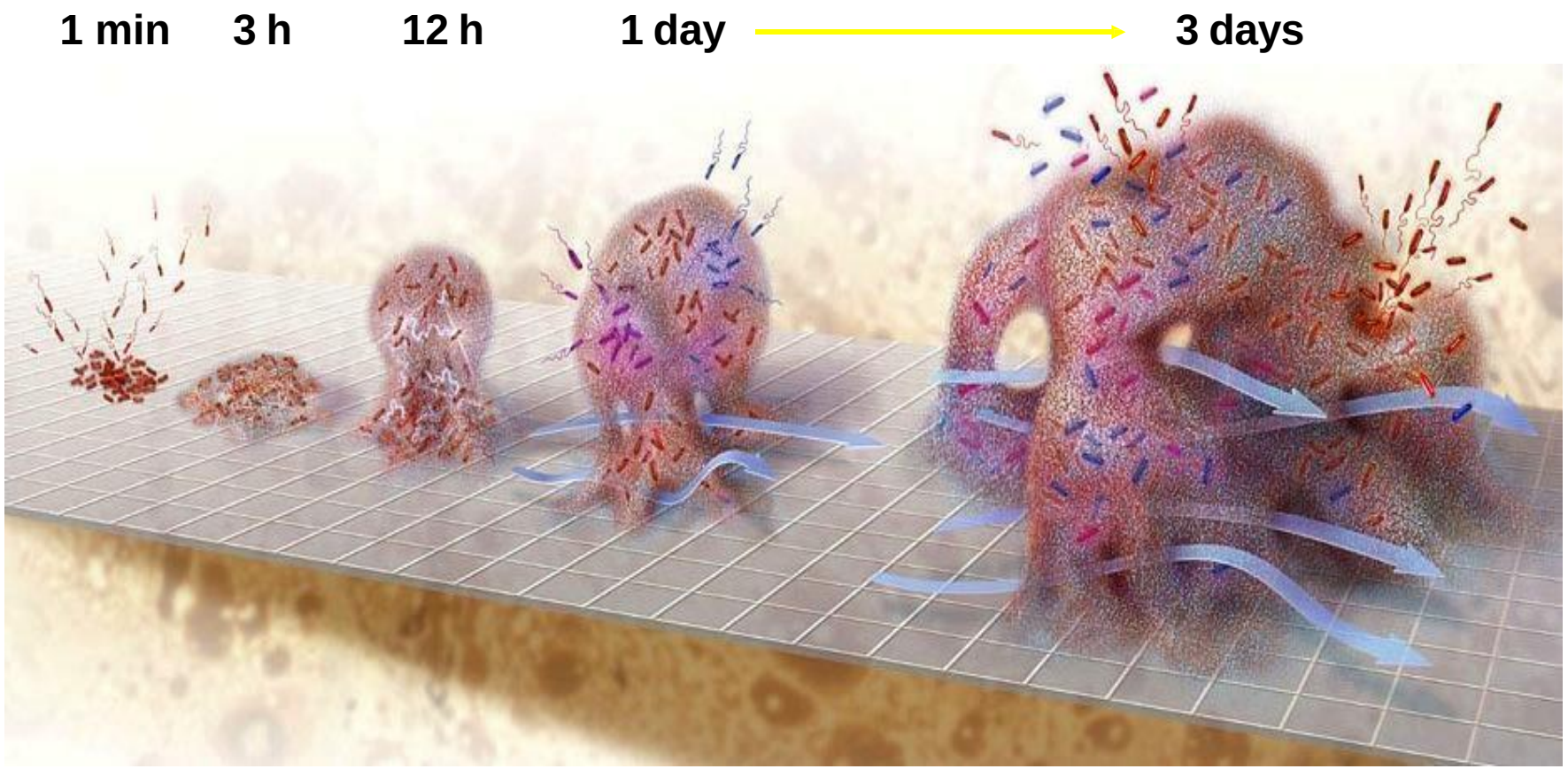
Glaciers in Antarctica

What are we fighting? BIOFILM!



- Dynamic concept
- Reduced antimicrobial susceptibility
  - Low growth rate
  - “persisters”
  - Micro-environent that impairs antimicrobial activity
- Bacteriae also protected from host immune system

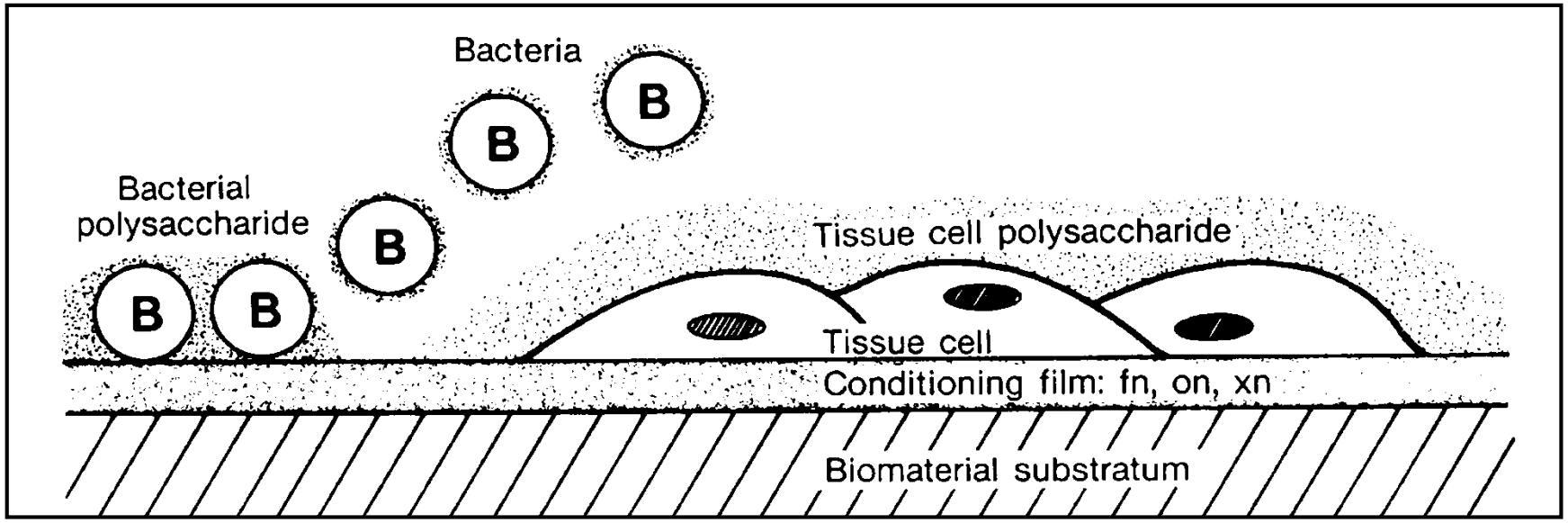
Biofilm: The race for the surface



Gristina AG. Biomaterial-centered infection: microbial adhesion versus tissue integration. Science 1987;237:1588-95

Biofilm: The race for the surface

Microbial adhesion and biofilm formation compete with tissue integration of host

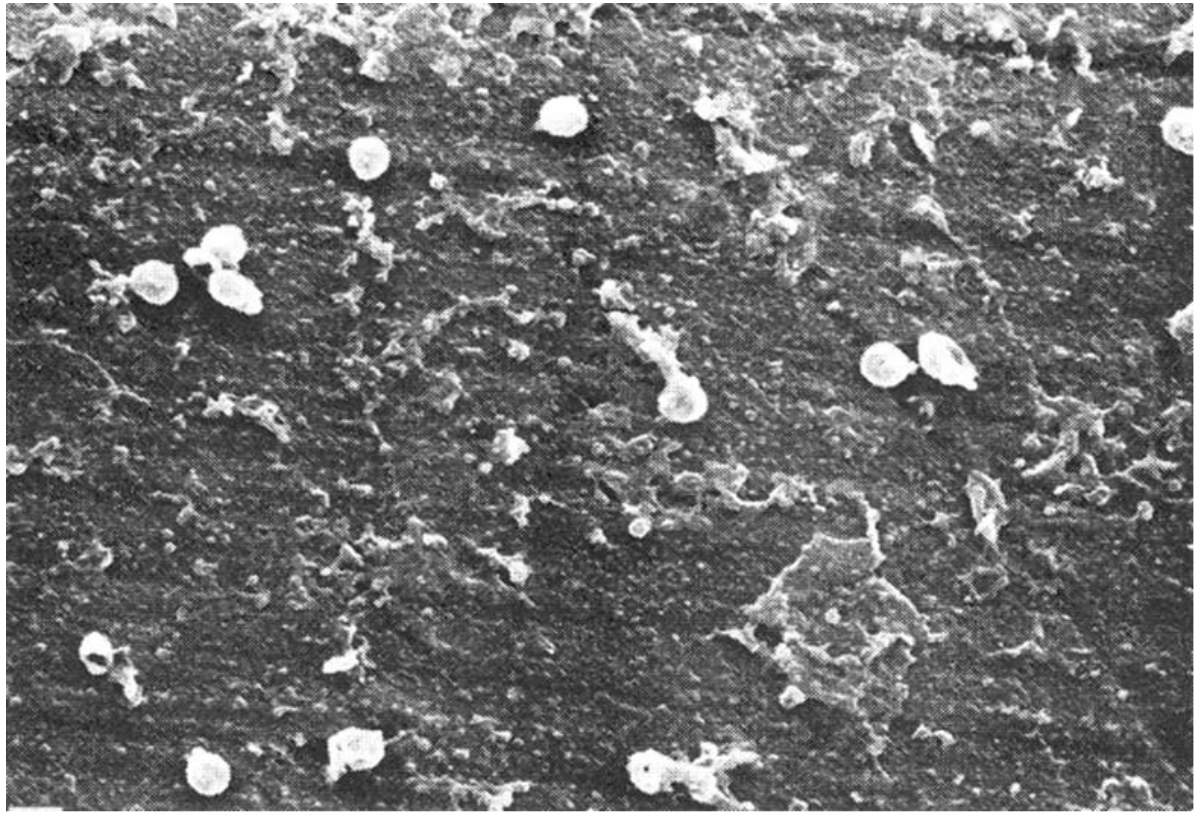


Tissue cells win	➔	**infection risk <**
Bacteria win	➔	**formation biofilm on implant**

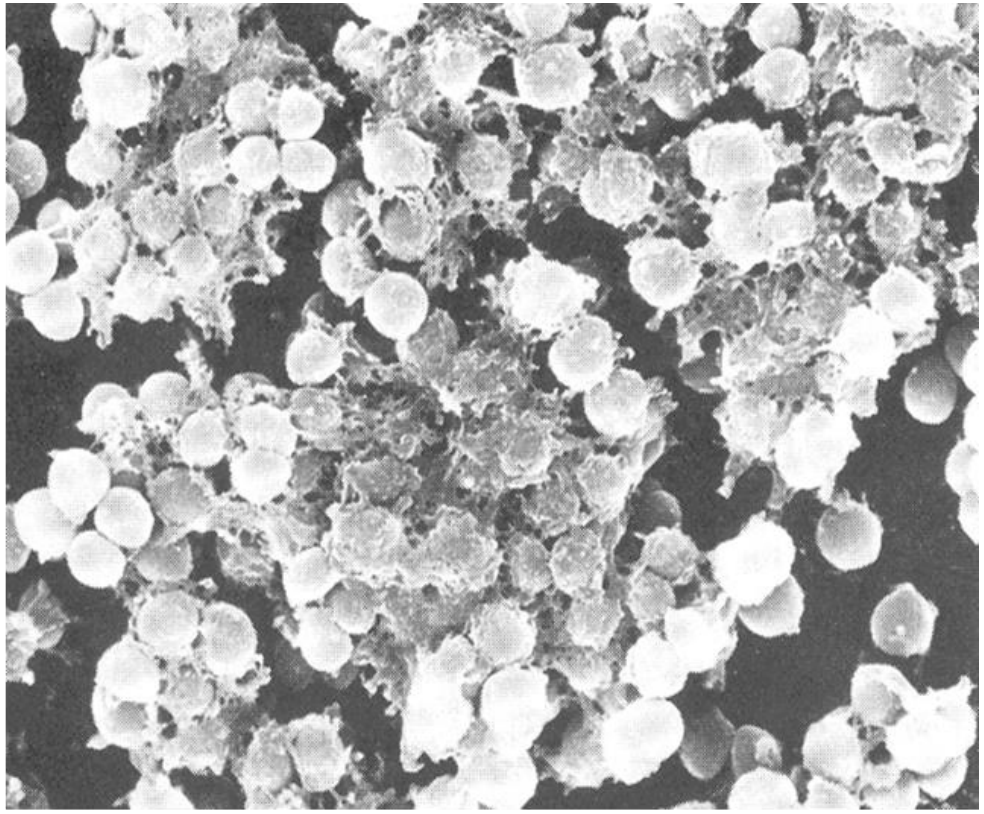
* Gristina R. Biomaterial-centered infection: microbial adhesion versus tissue integration. Science 237:1588-95,1987.

** Gristina AG, Shibata Y, Giridhar G, Kreger A, Myrvik QN. The glycocalyx, biofilm, microbes, and resistant infection. Semin Arthroplasty. 1994 Oct;5(4):160-70. Review.

Biofilm: The race for the surface



2 h incubation



12 h incubation

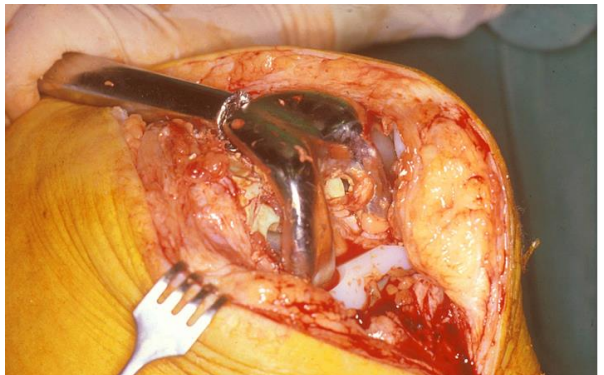
Biofilm: The race for the surface

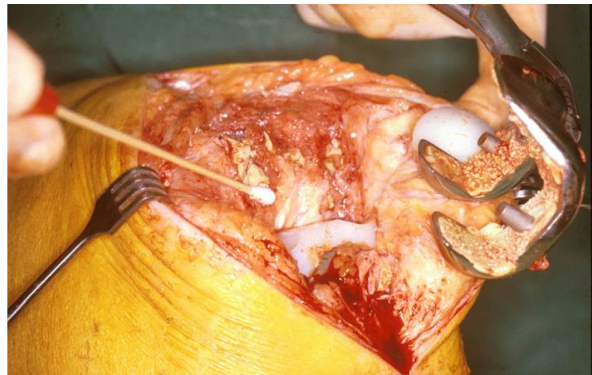
Bacteria attached to biomaterials are securely anchored and hardly reachable for immune response cells and antibiotics

Polymers	**predeposition for *st.epidermidis***
Metals	**predeposition for *st.aureus***
Relative risk	**CrCo > stainless steel > titanium**

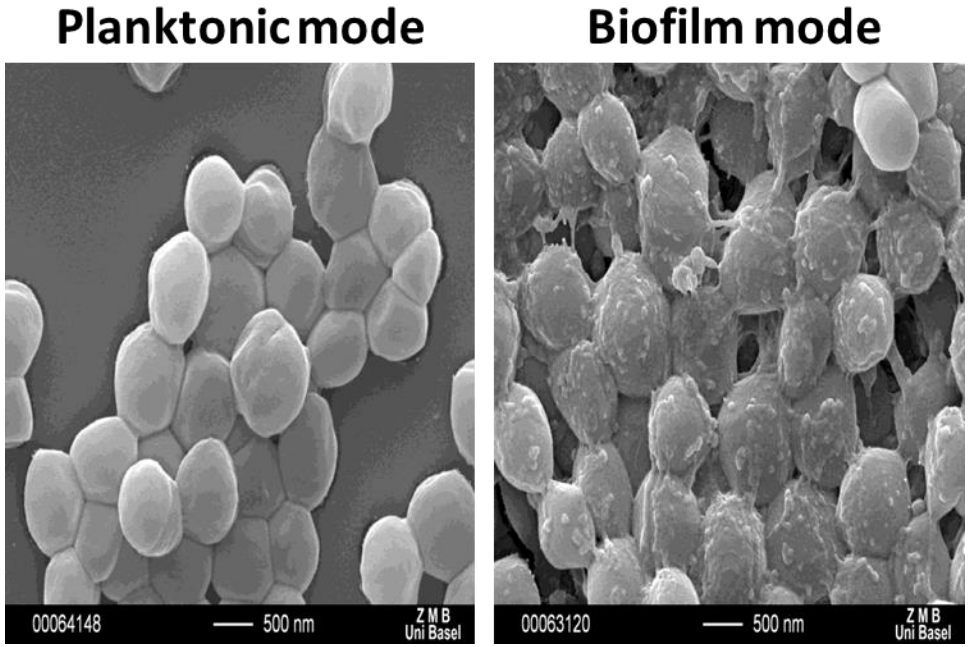
Biomaterials infections are hard treat

Eventually implant removal may be necessary



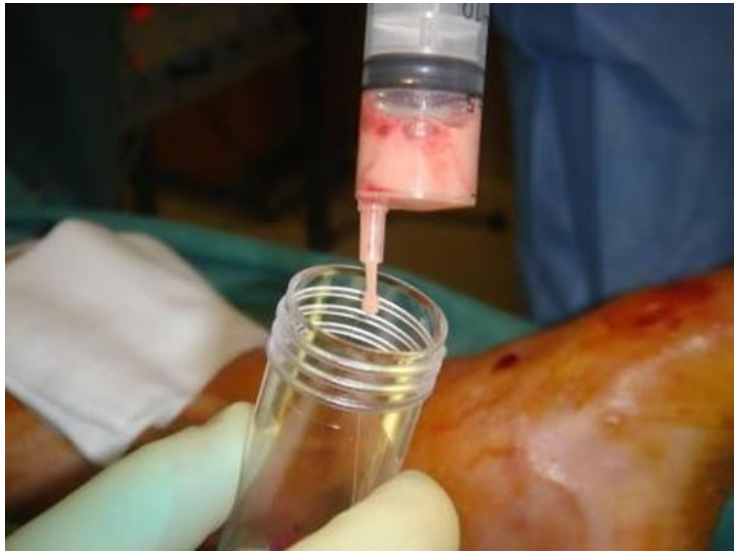


Biofilm Challenges



Diagnostics

- With joint aspiration/swabs/tissue cultures we find planktonic bacteria
- We cannot remove biofilm bacteria
- Sensitivity is not high enough!



Biofilm Challenges

Diagnostics

- Sonication

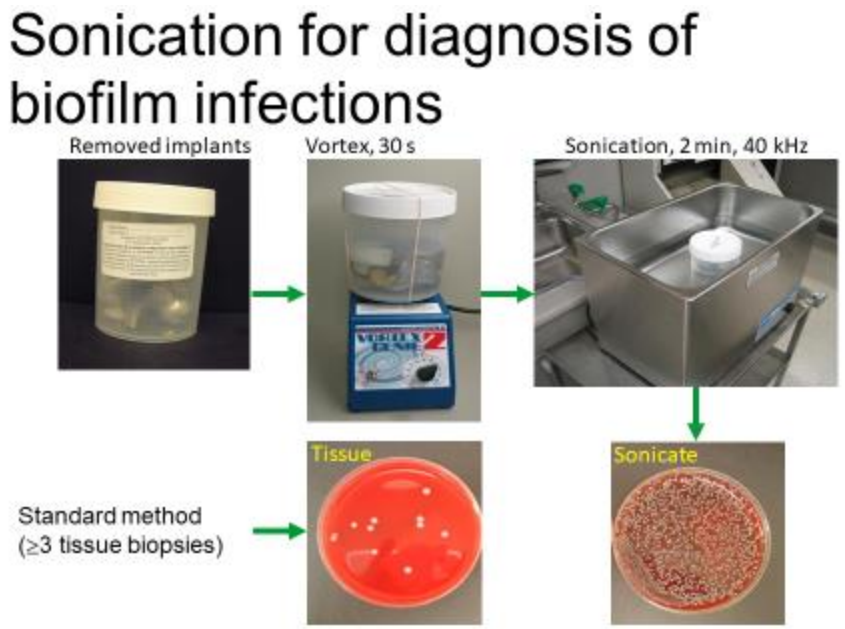
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Sonication of Removed Hip and Knee Prostheses for Diagnosis of Infection

Andrej Trampuz, M.D., Kerryl E. Piper, M.S., Melissa J. Jacobson, A.S., Arlen D. Hanssen, M.D., Krishnan K. Unni, M.D., Douglas R. Osmon, M.D., Jayawant N. Mandrekar, Ph.D., Franklin R. Cockerill, M.D., James M. Steckelberg, M.D., James F. Greenleaf, Ph.D., and Robin Patel, M.D.

N ENGL J MED 357;7 WWW.NEJM.ORG AUGUST 16, 2007



Trampuz N Engl J Med 2007

Results of sonication study

846 implants
(367 joint prostheses + 479 fracture fixation devices)

Microbiologic test	Aseptic cases (n = 675)	Infected cases (n = 171)
Tissue culture	**26 (4%)**	**126 (74%)**
Sonicate culture	**30 (5%)**	**152 (89%)**

p <0.001

Problem : still high numbers of false positive and false negative

Trampuz N Engl J Med 2007

Biofilm Challenges

Diagnostics

- Sonication

Problems

- Risk of contamination : multi-step procedure
- Operator dependent procedures

1. Harvesting of samples in operation
2. Transport of harvested samples to lab
3. Inserting physiological solution in container
4. Sonicating the samples
5. Collecting the fluid after sonication
6. Centrifuging the fluid
7. Culturing bacteria pellet in solid media or broth

Biofilm Challenges

Diagnostics

- Sonication

Problems

Gram -

JOURNAL OF CLINICAL MICROBIOLOGY, May 2010, p. 1720–1725 Vol. 48, No. 5
0095-1137/10/$12.00 doi:10.1128/JCM.01562-09

Escherichia coli Variants in Periprosthetic Joint Infection: Diagnostic Challenges with Sessile Bacteria and Sonication▽

Parham Sendi,[1,2]* Reno Frei,[3] Thomas B. Maurer,[4] Andrej Trampuz,[5]†
Werner Zimmerli,[1] and Peter Graber[1]

Unit of Infectious Diseases, Basel University Medical Clinic, Liestal,[1] University Clinic for Infectious Diseases, University Hospital Bern and University of Bern, Bern,[2] Clinical Microbiology, University Hospital Basel, Basel,[3] Clinic of Orthopedic Surgery, Cantonal Hospital, Liestal,[4] and Department of Biomedicine, University Hospital Basel, Basel,[5] Switzerland

Biofilm Challenges

Diagnostics

- Dislodging of biofilm
  DTT : dithiotreitol → to dissolve the polysaccharide matrix of the biofilm and detach the bacteriae

Biofilm Challenges

Diagnostics

- DTT

JOURNAL OF ORTHOPAEDIC RESEARCH June 2013 DOI 10.1002/jor.22423

Use of Dithiothreitol to Improve the Diagnosis of Prosthetic Joint Infections

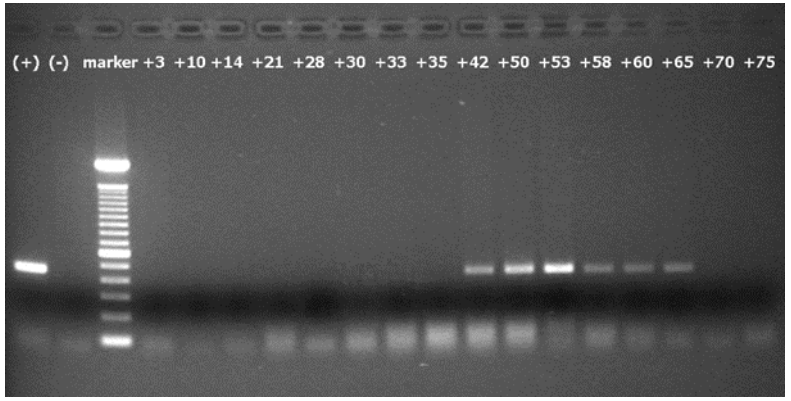
Lorenzo Drago,[1,2] Valentina Signori,[1] Elena De Vecchi,[1] Christian Vassena,[1] Elisa Palazzi,[1] Laura Cappelletti,[1] Delia Romanò,[3] Carlo Luca Romanò[3]

Methods: Periprosthetic tissue samples (n=5-8).
Removed implants aseptically divided into two parts and transported to the laboratory and randomly processed by sonication or DTT.
Diagnosis of infection according Spangehl criteria

[Spangehl M et al. (1999) J Bone Joint Surg. 81: 672-83].

Results	Tissue Cultures	Sonication	DTT
Sensitivity	**71.4%**	**71.4%**	**85.7%**
Specificity	**76.5%**	**94.1%**	**94.1%**
Positive predictive value	78.9%	93.7%	94.7%
Negative predictive value	68.4%	72.7%	84.2%

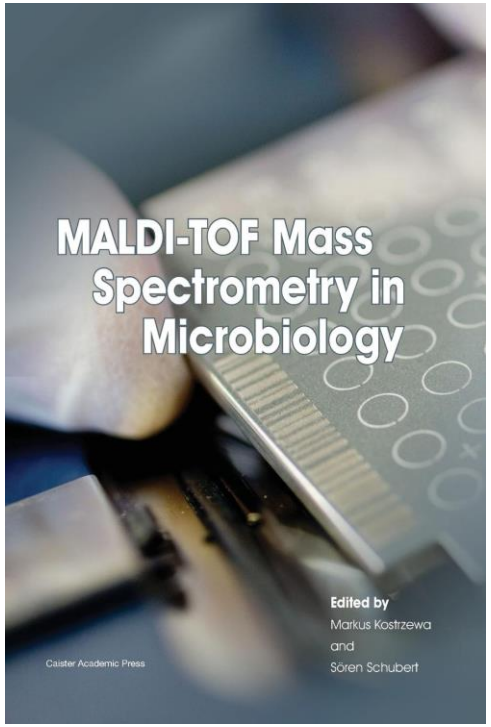
Biofilm Challenges



Diagnostics

- PCR
- MALDI-TOF
- Calorimetry

→ Pathogen identification <24h



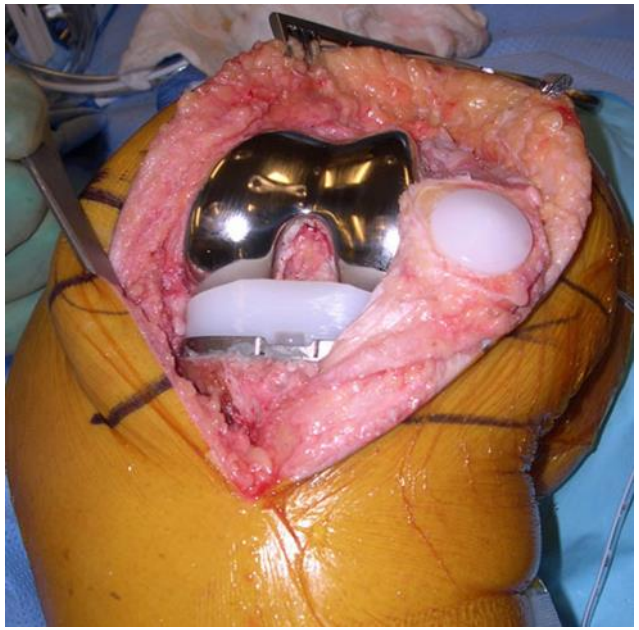
Biofilm Challenges

Treatment

- GOAL =
  - Reduce bacterial load
  - Breakdown of biofilm in order to force bacteriae in planktonic state and make them susceptible

- Ways to do this =
  - Do it early
  - Change all modular parts
  - Mechanically disrupt biofilm

Biofilm Challenges



Treatment

- **DAIR : time is running and biofilm is coming fast**
  - Succes-rate DAIR ↓
    - With time (4w : 90%, 8w : 80%, > 8w : 50%)
    - Deterioration of soft tissue
    - “difficult-to-treat” bacteria : resistance / high MIC
      eg. Enterococcus : never DAIR
    - After revision

Biofilm Challenges

Treatment

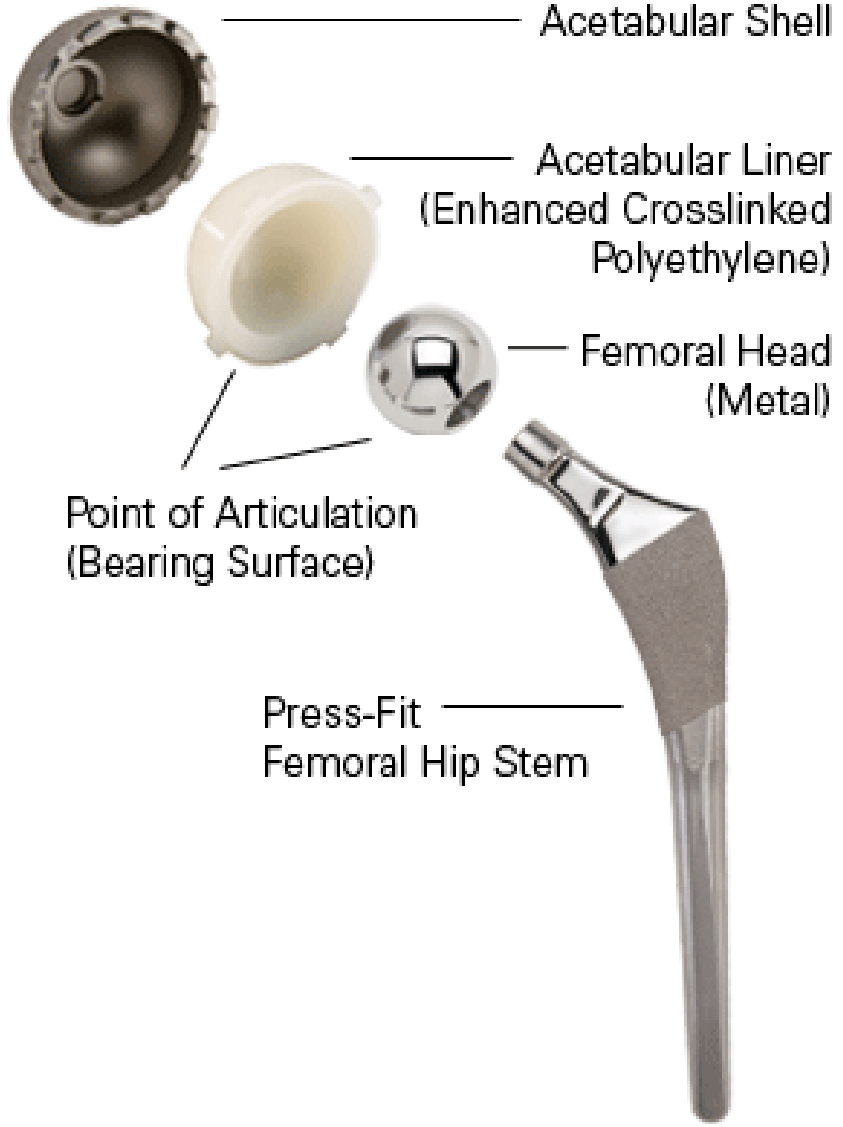
- **DAIR**

CHANGE THE MODULAR PARTS!

Polyethylene Insert Exchange Is Crucial in Debridement for Acute Periprosthetic Infections following Total Knee Arthroplasty

J Knee Surg 2017;30:36–41.

Cure rate 93% versus 30% (p=0,0001)



Biofilm Challenges

Treatment : CHANGE THE MODULAR PARTS!

Oxford study

- Exchange modular parts : 10y survival 86% vs 68% (p=0.02)

- Combi:
  - Early + exchange : 90% (78-100%)
  - Early + no exchange : 81% (67-95%)
  - Late + exchange : 79% (60-98%)
  - Late + no exchange : 52% (31-73%)

Biofilm Challenges

Treatment : DISRUPTION OF BIOFILM

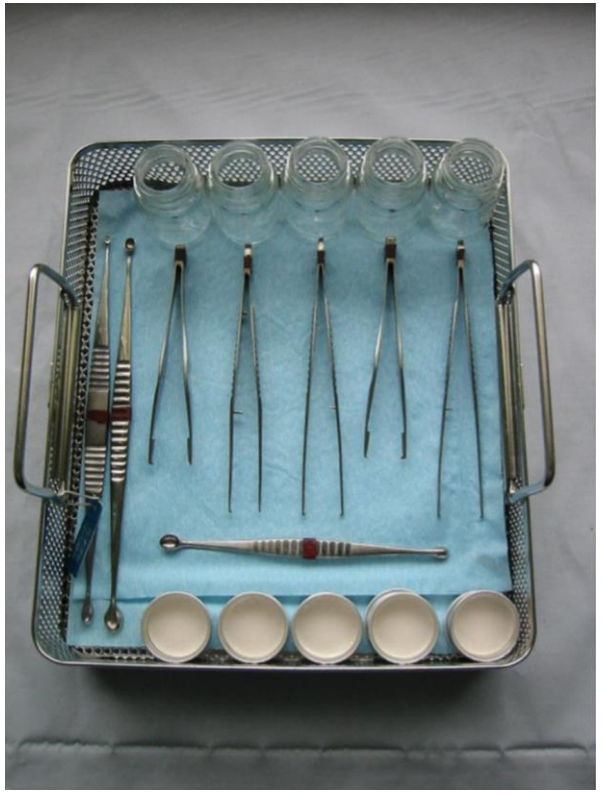
Biofilm Challenges

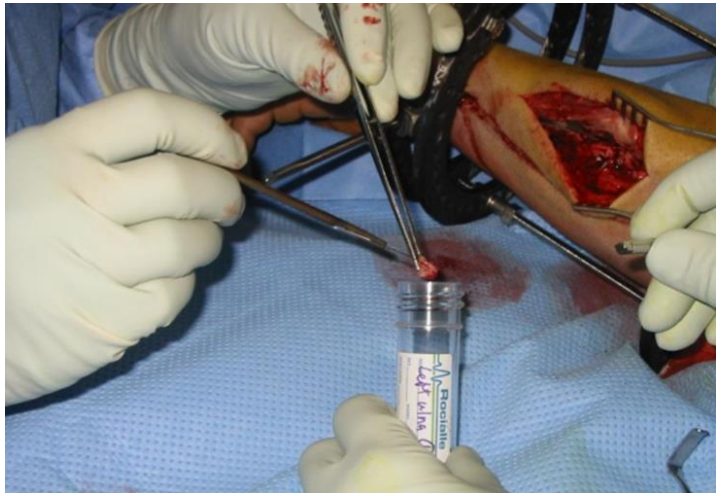
Treatment

DISRUPTION OF BIOFILM

Other Challenges ; Cultures

- Instruct your orthopaedic surgeon!
- Separate instruments
- Obtain ≥ 3 tissue specimens
- No-touch technique
- No swabs, no sinus tract cultures





Other Challenges ; Antibiotics

- AB's are not anti-inflammatory drugs → should not be given to combat erythema

- Never give AB unless infection is confirmed and adequate work-up performed

- Systemic AB
  - AB in the wrong way (oral monotherapy with AB with low bio-availability ; penicillin,…)
  - Rifampicin : no rifa / rifa monotherapy /…
  - AB too long / too short

Other Challenges ; Antibiotics

Drug	Oral bioavailability	Bone penetration
Amoxicillin/clavulanic acid or ampicillin/sulbactam	15% (AUC 6x lower with PO dose)	**7%**
Cefuroxim, cefadroxil	10% (AUC 10x lower with PO dose)	**12 %**
Ciprofloxacin	70%	**48%**
Levofloxacin	100%	**77%**
Rifampin	80%	**51%**
Co-trimoxazole	85%	**55%**
Clindamycin	**90%**	**45%**

Other Challenges ; Antibiotics

Risk factors for rifampicin resistance

Characteristics	Cases ($n = 48$)	Controls ($n = 48$)	P value[a]
Treatment			
Treated with any antibiotics	44 (91.7 %)	30 (62.5 %)	0.001[f]
Treated with rifampin	41 (85.4 %)	20 (41.7 %)	<0.001[f]
Rifampin always adequate[b]	25	15	
Rifampin inadequate	16	5	
Monotherapy and/or	4	3	
Empiric therapy[c] and/or	6	1	
Other reasons[d]	7	1	
Treatment with high bacterial load	34 (70.8 %)	13 (27.1 %)	<0.001[f]
<2 weeks iv antimicrobial treatment	12	4	
No surgical debridement	7	1	
No iv and no surgical debridement	15	8	

Achermann Y et al. Infection. 2013;41:431-437

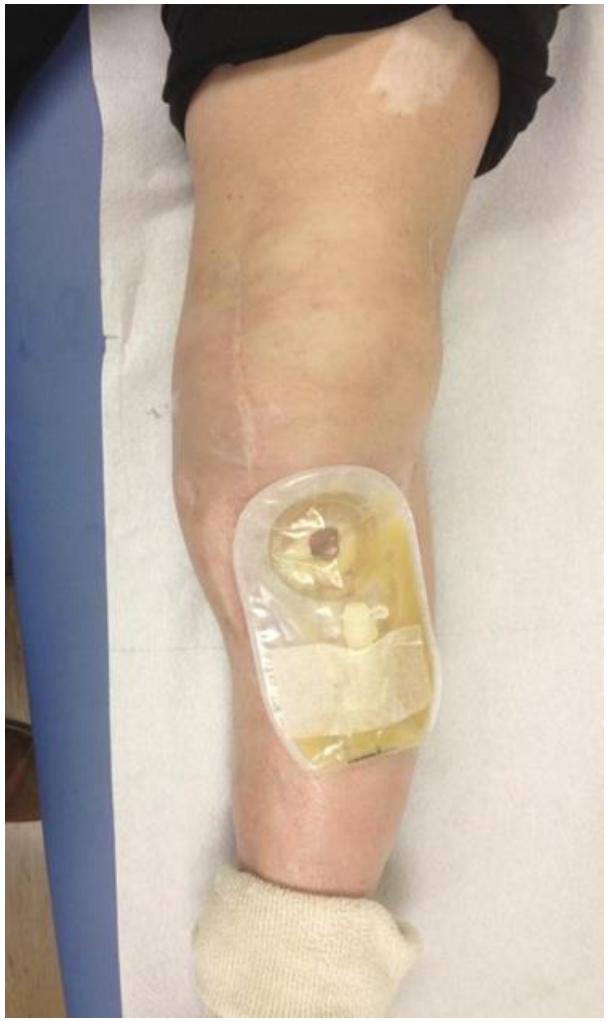
Other Challenges ; Soft tissue management

If you don’t solve the problem…

- Iatrogenic fistula
- Longterm VAC treatment

Inadequate soft tissue management will lead to

- Superinfection
- Multiresistent pathogens



Other Challenges ; Soft tissue management

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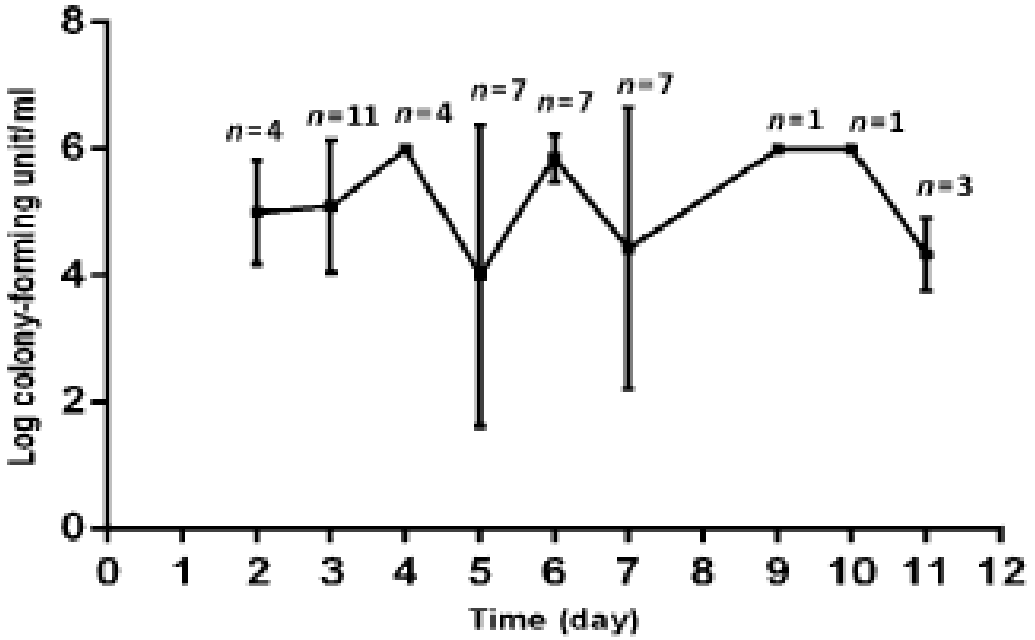
Original Research-Clinical Science

High bacterial load in negative pressure wound therapy (NPWT) foams used in the treatment of chronic wounds

Erlangga Yusuf MD, PhD, Xavier Jordan MD, Martin Clauss MD, Olivier Borens MD, Mark Mäder MD, PhD, Andrej Trampuz MD

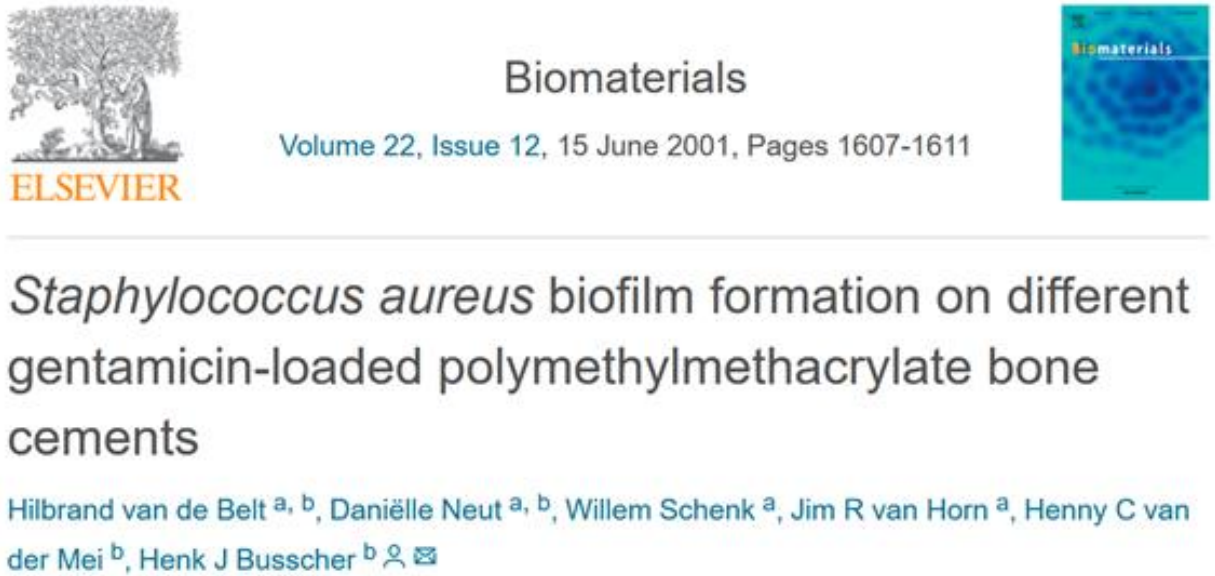
View issue TOC
Volume 21, Issue 5
September-October 2013
Pages 677-681



Probably no indication for use of VAC in bone/implant infections

Other Challenges ; Spacer contamination

- Over time : biofilm can & wil form on spacers



- Possibly induction of resistent strains

Future trends

Anti-infection coatings

J Orthop Surg Res. 2015; 10: 157.
Published online 2015 Oct 1.
doi: 10.1186/s13018-015-0294-5
PMCID: PMC4591707

Antibacterial coating of implants in orthopaedics and trauma: a classification proposal in an evolving panorama

Carlo Luca Romanò, Sara Scarponi, Enrico Gallazzi, Delia Romanò, and Lorenzo Drago

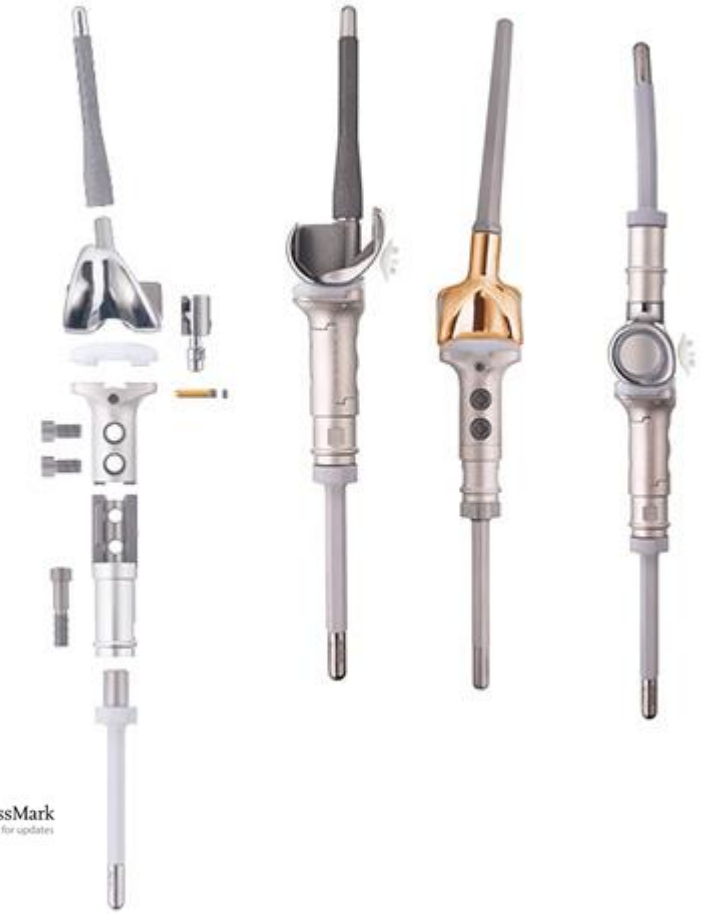
A list of requirements to be fulfilled by the "ideal" antibacterial implant coating strategy

Requirements	Fulfillments			
Safety	No systemic toxicity	No local toxicity	No detrimental effects on bone healing	No unwanted long-term side effects
In vitro activity	No cytotoxicity or genotoxicity	Proven bactericidal and antibiofilm activity on different surfaces	Large spectrum	No induction of resistance
Efficacy	Proven in vivo	Case series	Multicenter trials	Randomized trials
Ease-of-use	Easy handling	Versatility	Resistance to press-fit insertion	Storage
Market	Acceptable cost	Large availability	Easy to manufacture	Overcomes regulatory issues

Future trends

Anti-infection coatings

- Au, Ag,…



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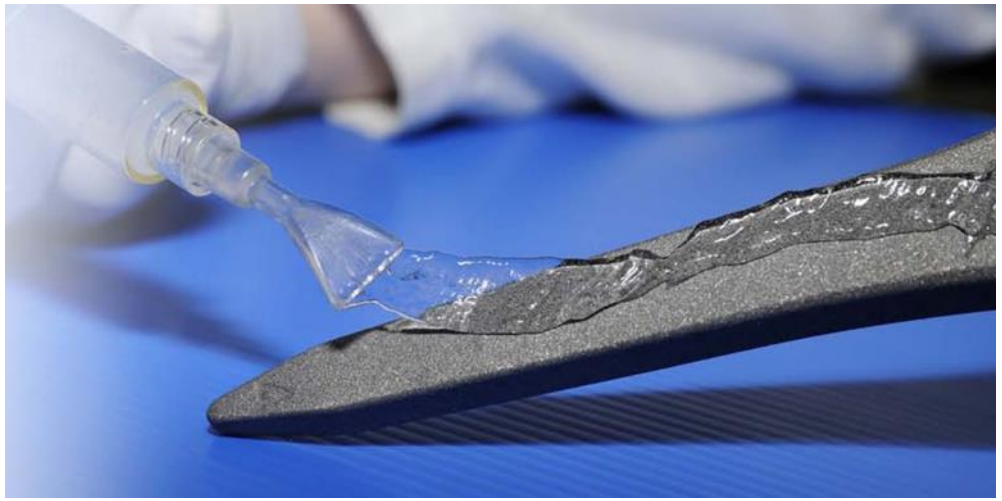
Preventing Implant-Associated Infections by Silver Coating

Richard Kuehl,[a,b] Priscilla S. Brunetto,[c] Anne-Kathrin Woischnig,[a] Massimo Varisco,[c] Zarko Rajacic,[a] Juerg Vosbeck,[d] Luigi Terracciano,[d] Katharina M. Fromm,[c] Nina Khanna[a,b]

Future trends

Anti-infection coatings

- Biomolecular coatings
  - cfr Hydrogel : hyaluronic acid + polylactic acid (DAC®)



Future trends

Not adressed in this talk :

- Prevention
- Diagnostics
- Imaging

So let’s join forces and battle this challenge together

microbiology →

← ortho