ΜΕΤΑΠΤΥΧΙΑΚΟ ΠΡΟΓΡΑΜΜΑ ΛΟΙΜΩΞΙΟΛΟΓΙΑΣ Δ' ΠΑΝΕΠΙΣΤΗΜΙΑΚΗΣ ΠΑΘΟΛΟΓΙΚΗΣ ΚΛΙΝΙΚΗΣ ΕΚΠΑ ΠΓΝ «ΑΤΤΙΚΟΝ»

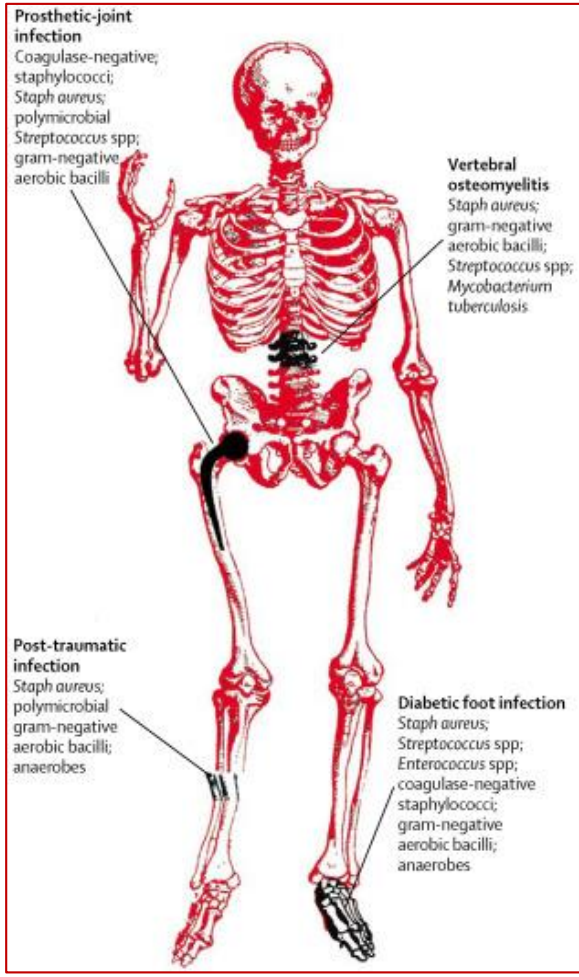
ΧΕΙΡΟΥΡΓΙΚΗ ΑΝΤΙΜΕΤΩΠΙΣΗ ΟΣΤΙΚΩΝ ΛΟΙΜΩΞΕΩΝ

ΣΤΑΥΡΟΣ Δ. ΓΟΥΜΕΝΟΣ

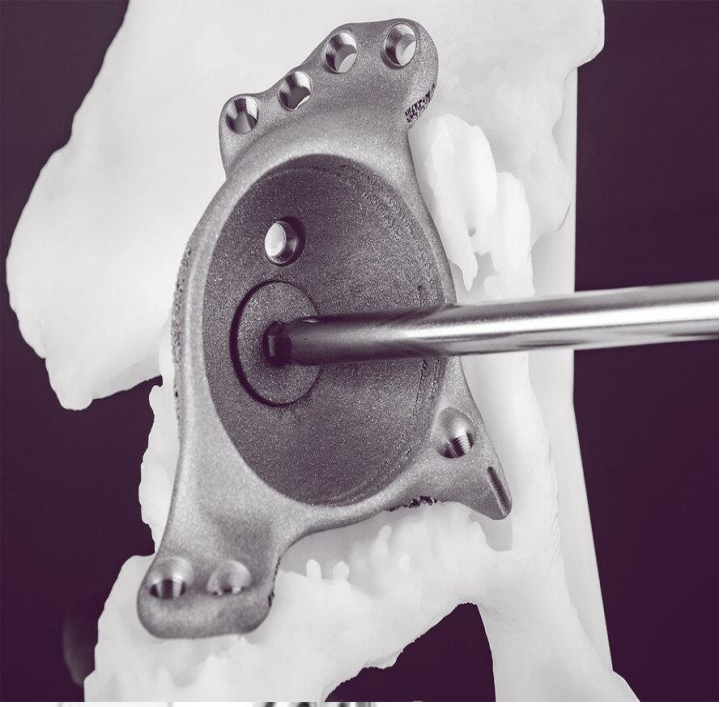
ΕΙΔ/ΝΟΣ Α' ΠΑΝΕΠΙΣΤΗΜΙΑΚΗΣ ΟΡΘΟΠΑΙΔΙΚΗΣ ΧΕΙΡΟΥΡΓΙΚΗΣ ΚΛΙΝΙΚΗΣ ΕΚΠΑ ΠΓΝ «ΑΤΤΙΚΟΝ»

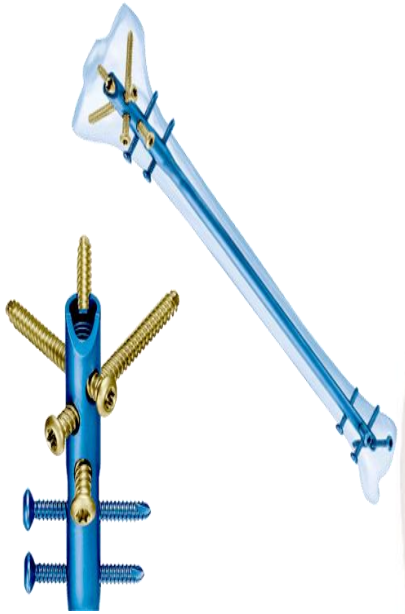
ΠΑΘΟΦΥΣΙΟΛΟΓΙΑ ΟΣΤΙΚΩΝ ΛΟΙΜΩΞΕΩΝ

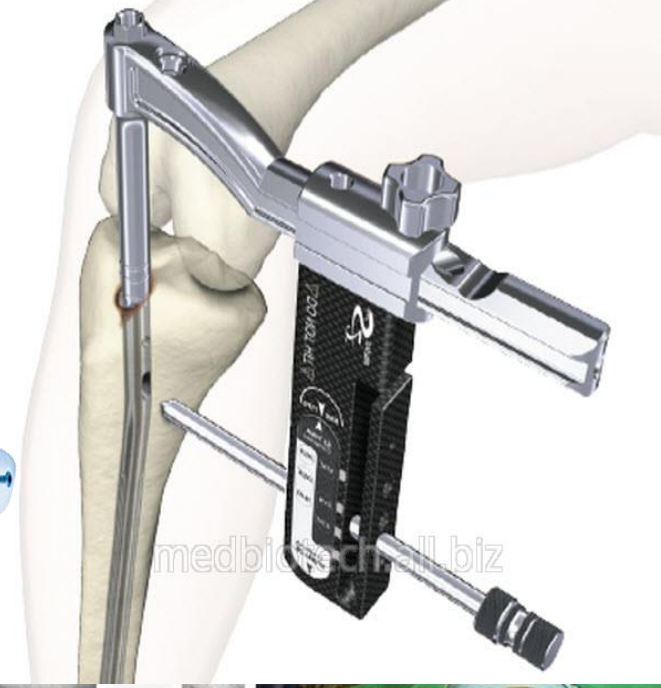
- **Αιματογενής**
- **Δευτερογενής λόγω νευραγγειακής δυσπραγίας**
- **Κατά συνέχεια ιστικού τραύματος / χειρουργικής παρέμβασης → fixation related or prosthetic joint infection**

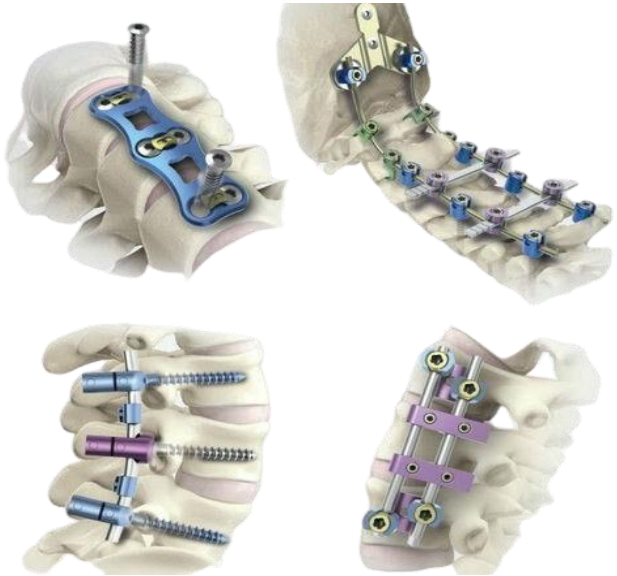


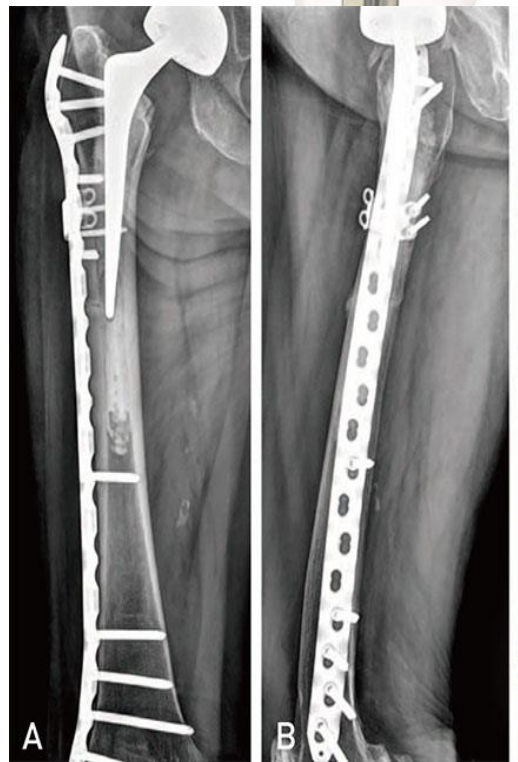
Lew DP & Waldvogel FA. Osteomyelitis. *Lancet* 2004, 364:369-79.






medbiotechmall.biz

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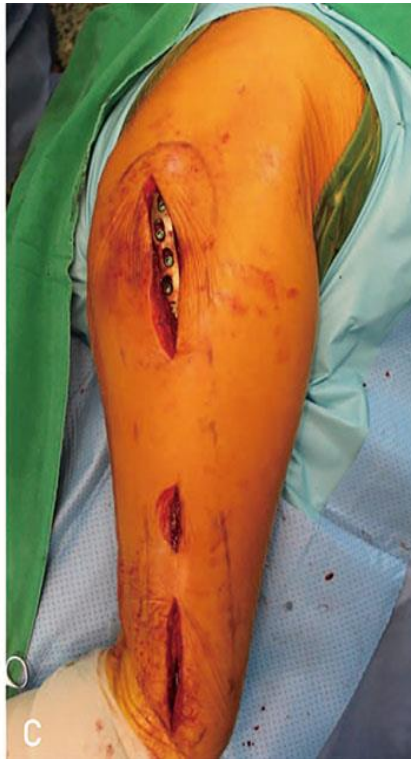
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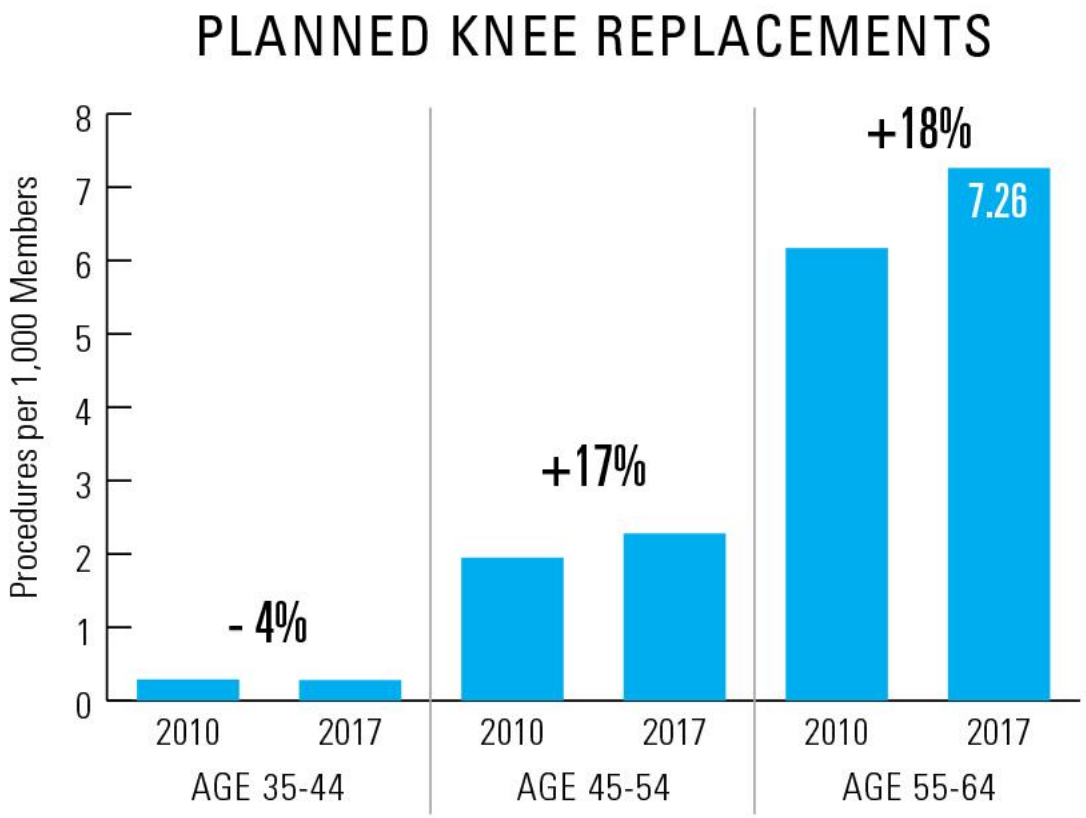
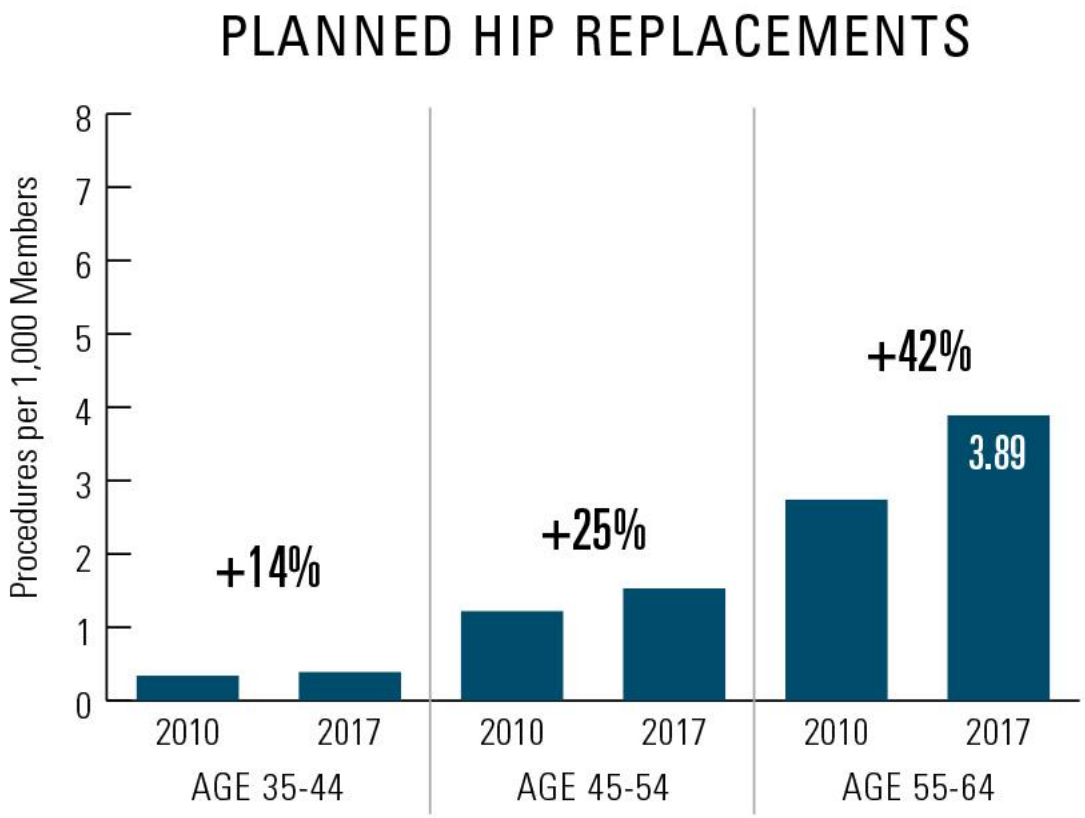
Η ΑΥΞΗΣΗ ΤΩΝ ΑΡΘΡΟΠΛΑΣΤΙΚΩΝ ΟΔΗΓΕΙ ΣΕ ΑΥΞΗΣΗ ΤΩΝ ΛΟΙΜΩΞΕΩΝ ΚΑΙ ΤΩΝ ΑΝΑΘΕΩΡΗΣΕΩΝ

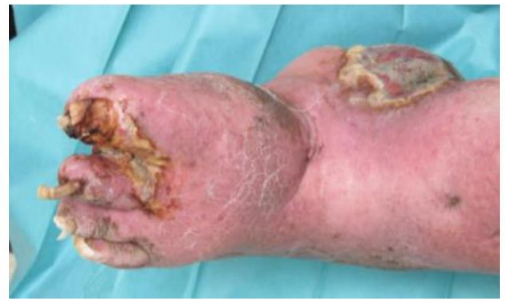




Planned knee and hip replacement surgeries are on the rise in the U.S. (Blue Cross Blue Shield)

BG Klinikum Hamburg

Osteomyelitis



The patient´s risk factors:

- age > 65 years
- obesity, malnutrition
- nicotine / alcohol dependency
- chronic diseases (cardio-vascular, allergies, circulatory disorder)
- Diabetes mellitus
- low immunity, immun-suppressive therapy
- rheumatic diseases
- accompanying infections (bladder, pneumonia..)
- damages caused by radiation
- catheter, artificial ventilation, hospitalization

REDUCING THE RISK FOR POSTOPERATIVE INFECTION

Minimization of perioperative duration

Less invasive approach

Use of antibiotic-loaded PMMA cement

Intraoperative complications

Type of implant

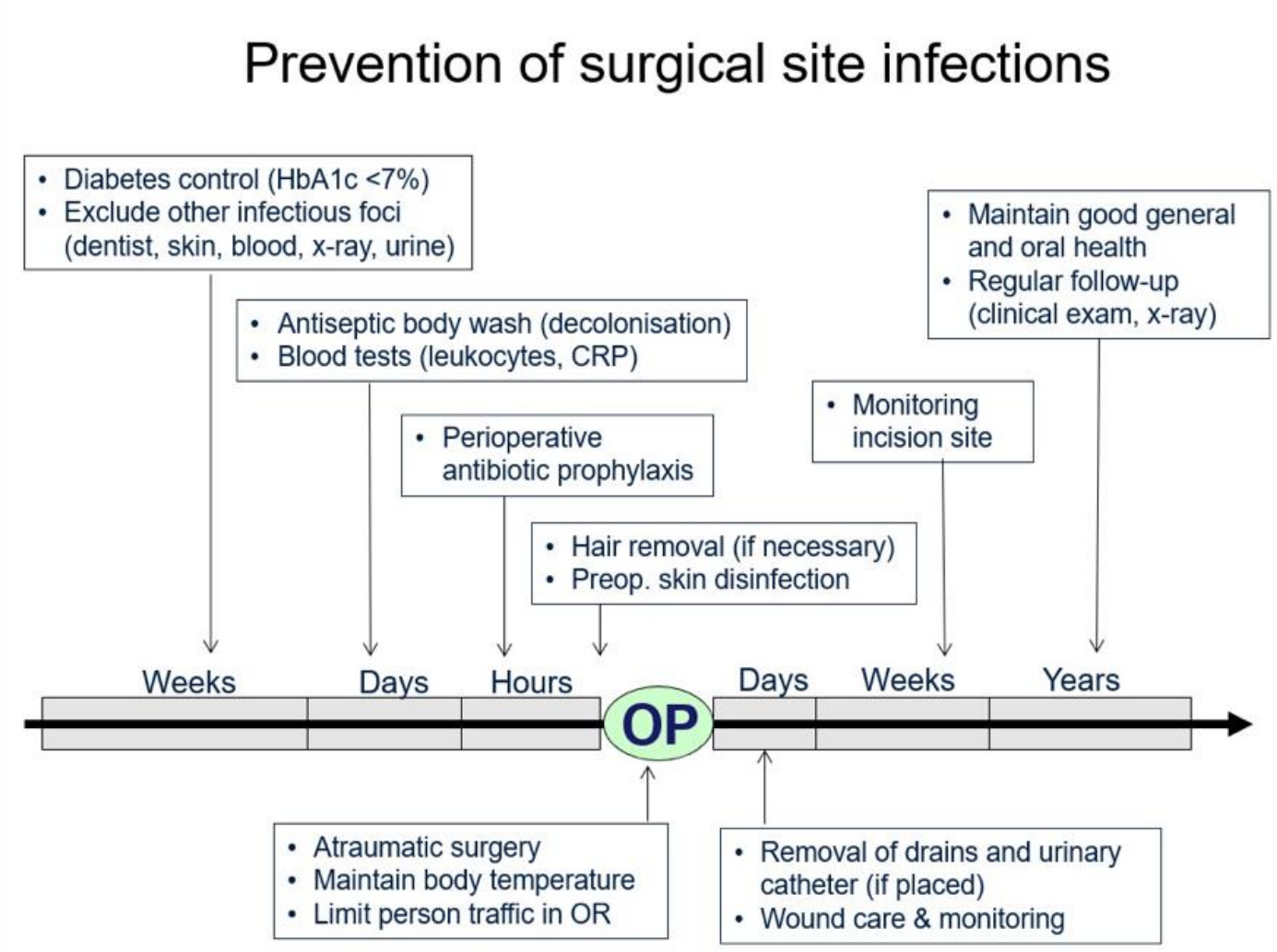
Optimization of indication for surgery

Point of time of surgical intervention

Rao N, et al. J Arthroplasty 2010

Parvizi J, et al. Acta Orthop 2011

BG Klinikum, Hamburg , Osteomyelitis

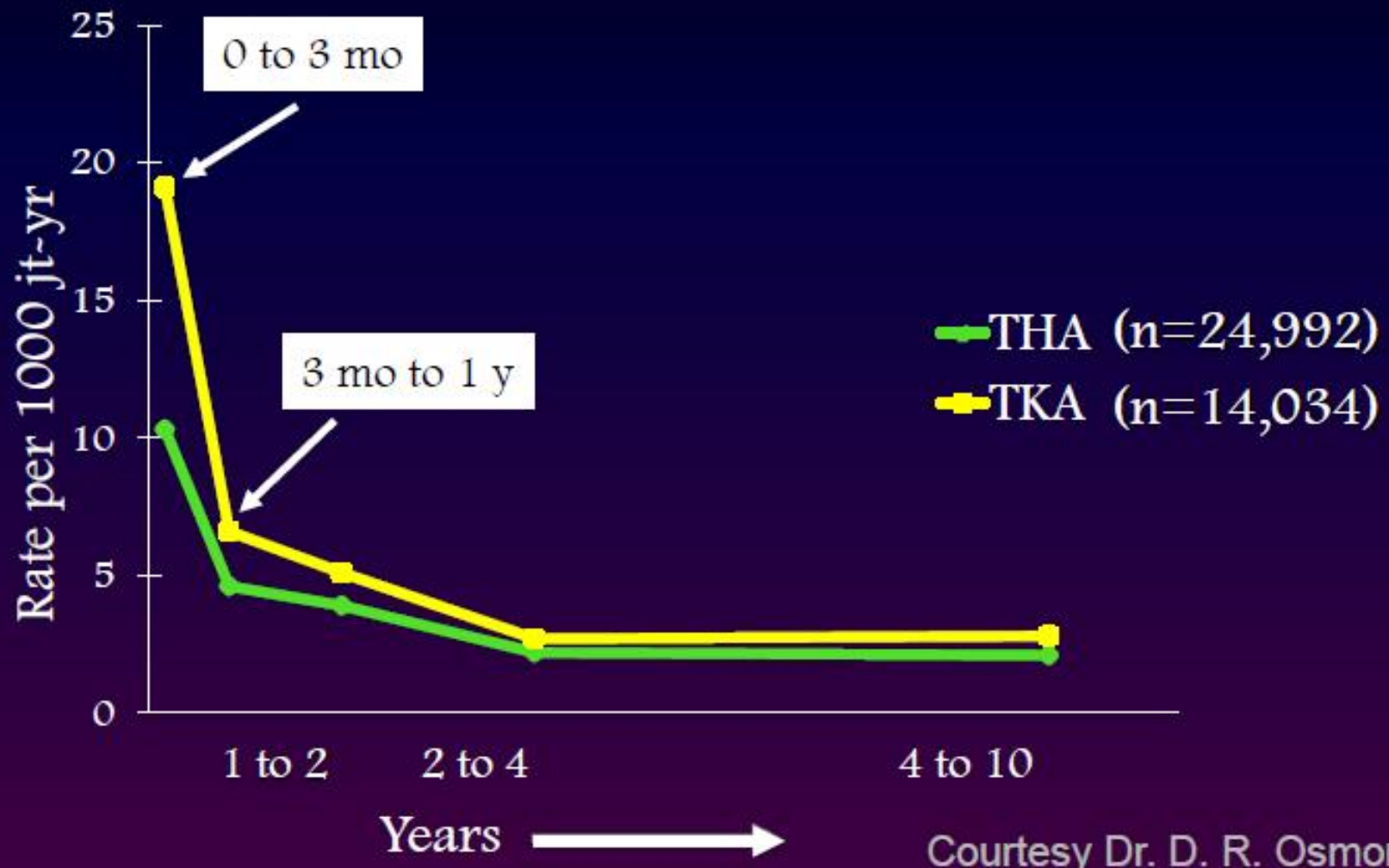


Allegranzi B, et al. New WHO recommendations on preoperative measures for surgical site infection prevention: an evidence-based global perspective. *Lancet* 2016

ΚΑΤΗΓΟΡΙΑ ΛΟΙΜΩΞΕΩΣ	ΧΡΟΝΙΚΗ ΕΝΑΡΞΗ ΜΕΤΑ ΤΗΝ ΕΠΕΜΒΑΣΗ	ΚΥΡΙΑ ΠΑΘΟΓΟΝΑ ΑΙΤΙΑ	ΚΛΙΝΙΚΗ ΕΙΚΟΝΑ
Πρώιμη μετεγχειρητική (early) **- οξεία** **- υποξεία**	**≤ 2 – 4 εβδ**	***S.aureus*** ***Streptococcus* spp** **Gram αρνητικά βακτηρίδια,** **Coagulase negative *Staphylococci*)**	Συνήθως συμπτώματα / σημεία οξείας φλεγμονής (πυρετός, ρίγος, τοπικά σημεία φλεγμονής και διαταραχής επούλωσης στο δέρμα ή την περιοχή της τομής), οργανωμένες συλλογές
Ενδιάμεσης χρονιότητας και Όψιμη χρονία (delayed)	**≥ 4 εβδομ – 10 εβδ** **> 10 εβδ**	**Coagulase negative *Staphylococci*,** ***Propionibacterium* spp,** ***S. aureus*** **Αναερόβια βακτήρια**	Αβληχρότερη εικόνα, επίμονο ή επιδεινούμενο άλγος, δυσκαμψία, οίδημα, πυρετός <30%, πιθανώς συρίγγιο, με ή χωρίς χαλάρωση ή θραύση του υλικού, ψευδάρθρωση
Όψιμη αιματογενής (late) - οξεία **- χρονία**	**> 2 έτη**	***Streptococcus* spp** ***S.aureus*** **Gram αρνητικά βακτηρίδια (*E. coli*)**	Οξείας ή υποξείας ενάρξεως φλεγμονή, δυσλειτουργία μιάς άρθρωσης που προηγουμένως λειτουργούσε καλώς, συνοδός ή απομεμακρυσμένη άλλη πηγή λοίμωξης πχ από δέρμα, ουροποιητικό ή αναπνευστικό σύστημα, οδόντες ή μετά από σήψη, ψευδάρθρωση

Zimmerli W, Sendi P. Orthopaedic biofilm infections. *APMIS* 2017, 125:353–64

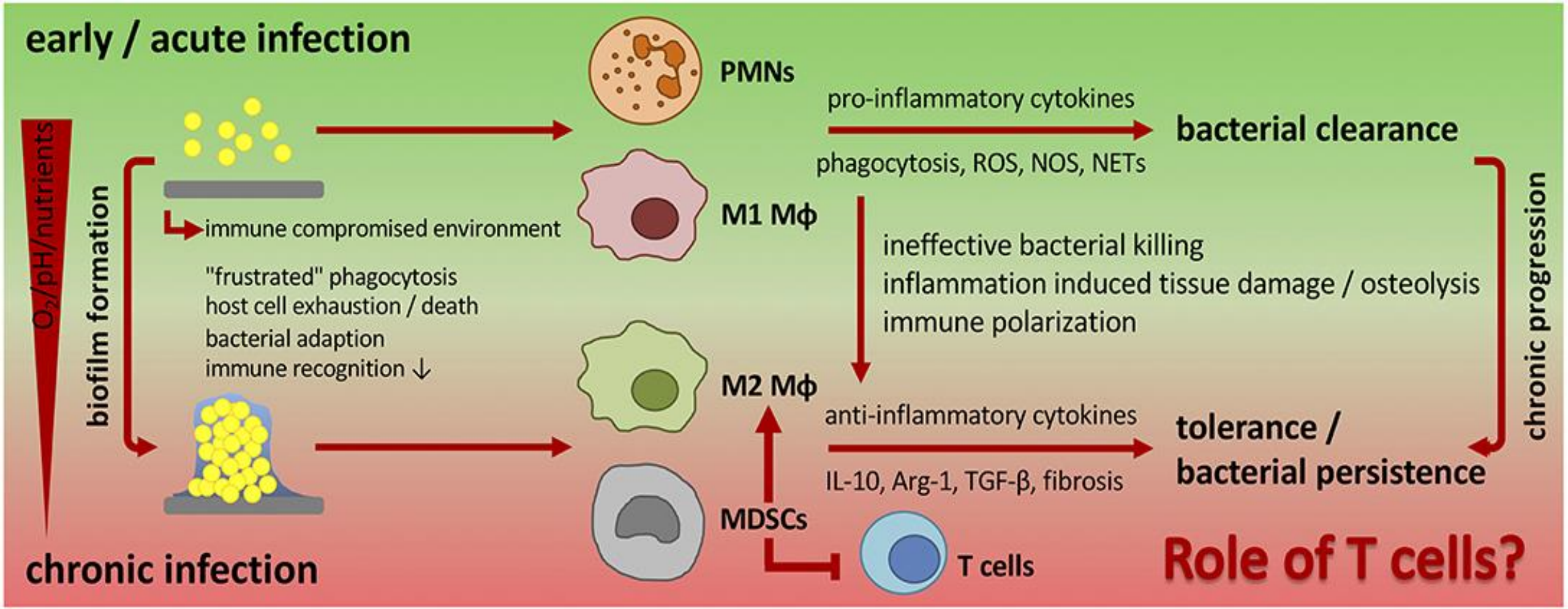
Epidemiology and Microbiology
Incidence Rate of Prosthetic Joint Infection at Mayo Clinic 1969-1991



Courtesy Dr. D. R. Osmon

BIOFILM MATURATION

acute → chronic



Seebach E & Kubatzky KF. Chronic implant-related bone infections—Can immune modulation be a therapeutic strategy? *Front Immunol* 2019, 10: 1724.

INTERNATIONAL WOUND INFECTION INSTITUTE

Contamination[26]	Colonisation[26]	Local infection		Spreading infection[22, 23]	Systemic infection[22, 23]
All wounds may acquire micro-organisms. If suitable nutritive and physical conditions are not available for each microbial species, or they are not able to successfully evade host defences, they will not multiply or persist; their presence is therefore only transient and wound healing is not delayed	Microbial species successfully grow and divide, but do not cause damage to the host or initiate wound infection	Covert (subtle) signs of local infection:[2, 27-36] ■ Hypergranulation (excessive 'vascular' tissue) ■ Bleeding, friable granulation ■ Epithelial bridging and pocketing in granulation tissue ■ Wound breakdown and enlargement ■ Delayed wound healing beyond expectations ■ New or increasing pain ■ Increasing malodour	Overt (classic) signs of local infection:[2, 27, 28, 35, 36] ■ Erythema ■ Local warmth ■ Swelling ■ Purulent discharge ■ Delayed wound healing beyond expectations ■ New or increasing pain ■ Increasing malodour	■ Extending in duration +/- erythema ■ Lymphangitis ■ Crepitus ■ Wound breakdown/ dehiscence with or without satellite lesions ■ Malaise/ lethargy or non-specific general deterioration ■ Loss of appetite ■ Inflammation,	■ Severe sepsis ■ Septic shock ■ Organ failure ■ Death

Surgical site

Wound

Clinical suspicion

Early diagnosis

Immediate intervention

TRADITIONAL LABORATORY METHODS

Microscopy

- Histology needed to confirm infection, but positive results may support empirical therapy while waiting for histology results in rapidly evolving cases
- May allow presumptive diagnosis of mucormycosis (ribbon-like, irregular, non-septate/pauci-septate, non-dichotomous branching hyphae) vs. aspergillosis/fusariosis (septate, dichotomous branching hyphae of uniform width)
- Does not allow genus/species identification and susceptibility testing

Culture

- Reduced sensitivity and reduced specificity (non-sterile, contaminated wound)
- Positive results may support therapy in rapidly evolving cases with necrotizing lesions and hemodynamically unstable patients
- Essential since it allows species identification and antifungal susceptibility testing

Histology

- It allows proven diagnosis of invasive mold infection of post-traumatic wound
- Detection of necrosis, white blood cells infiltration, and angioinvasion
- It allows presumptive diagnosis of mucormycosis (ribbon-like, irregular, non-septate/pauci-septate, non-dichotomous branching hyphae) vs. aspergillosis/fusariosis (septate, dichotomous branching hyphae of uniform width), further supported by possible identification through immunohistochemistry or polymerase chain reaction techniques, where available

TRADITIONAL LABORATORY MARKERS

Number of circulating WBCs and neutrophils → ↓ specificity

C-reactive protein and Erythrocyte sedimentation rate (ESR) → ↑ sensitivity

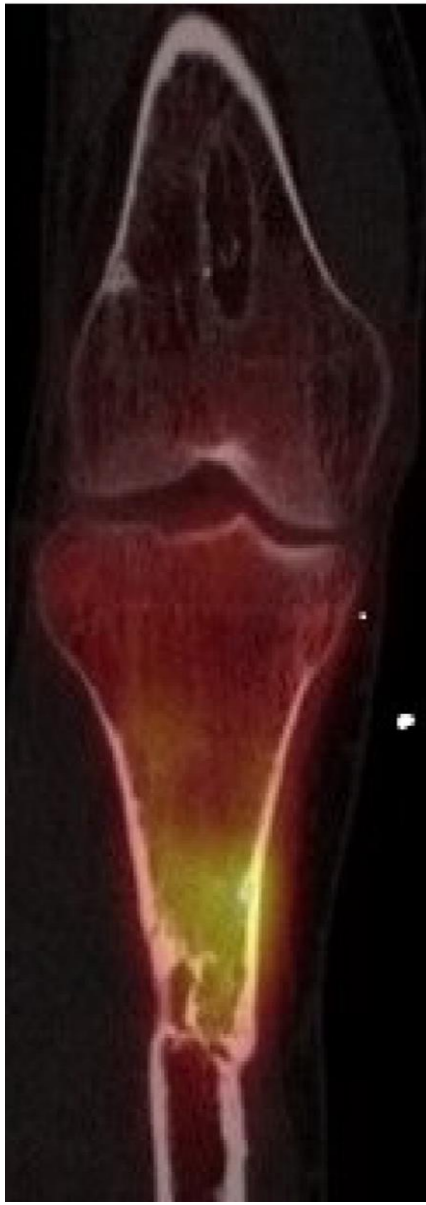
Sequential measurements of CRP → disease and therapy monitoring

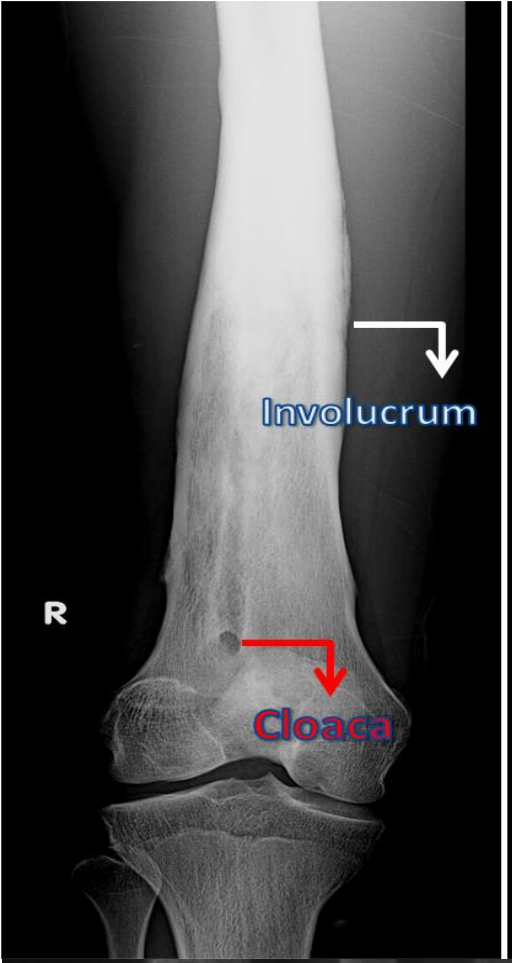
Normal CRP and ESR levels are a strong indicator of absence of infection.

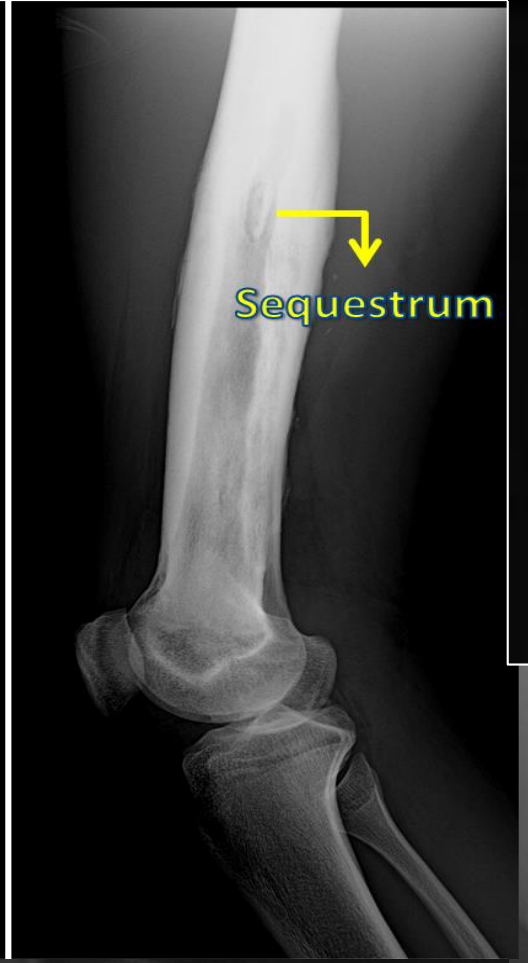
Shuman E, et al. Infect Dis Clin N Am 2012
Del Pozo JL, et al. N Engl J Med 2009

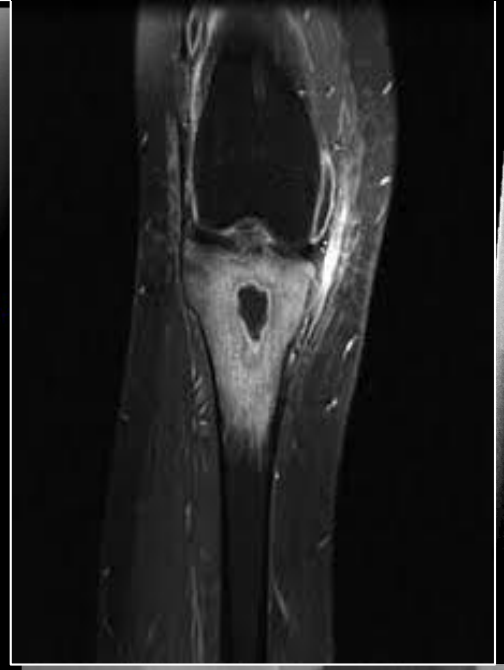
IMAGING

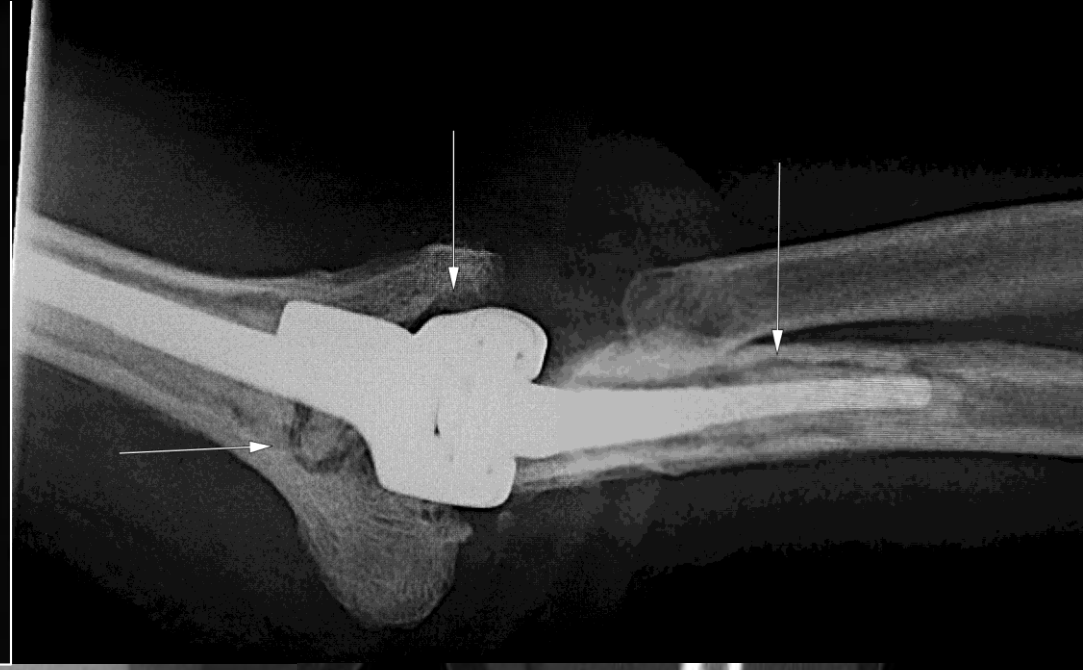
- Ultrasound → Fluid → Aspiration
- Plain X-ray → “Most important source of information”
- CT → Bone necrosis (sequestrum and involcrum) and biopsy
- CT + contrast → Effusion / Absess
- MRI → Bone marrow edema and soft tissue involvement extent
- PET-CT → implant associated → disease activity plus anatomy
- Scintigraphy (Tc, Ga, In) → ↑Sensitivity , ↓Specificity

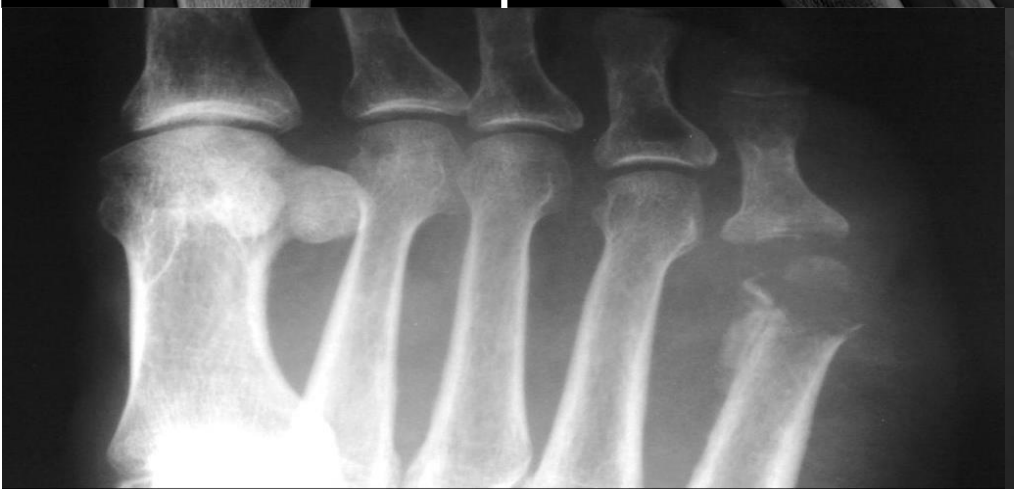


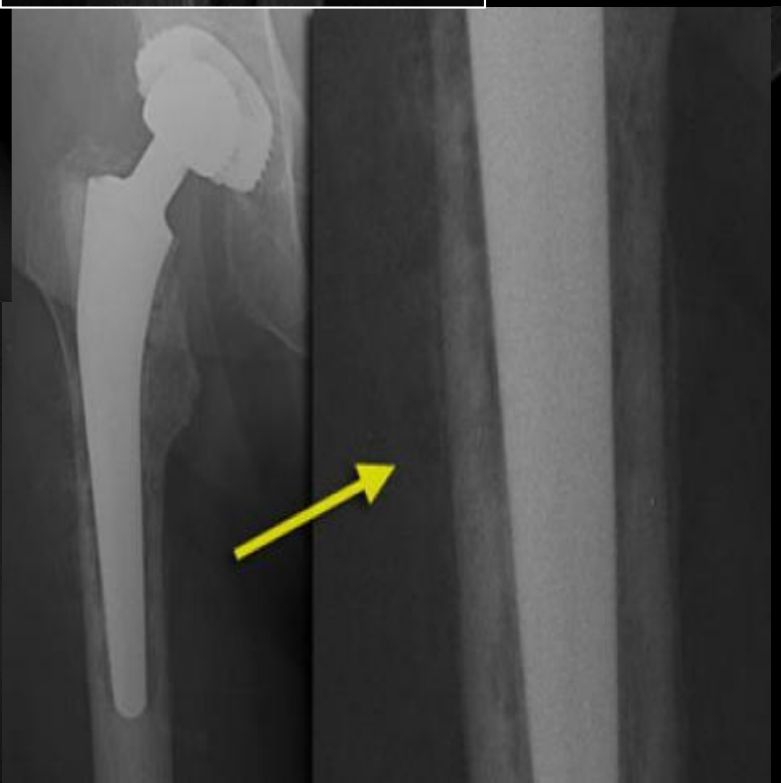

Involucrum
R
Cloaca

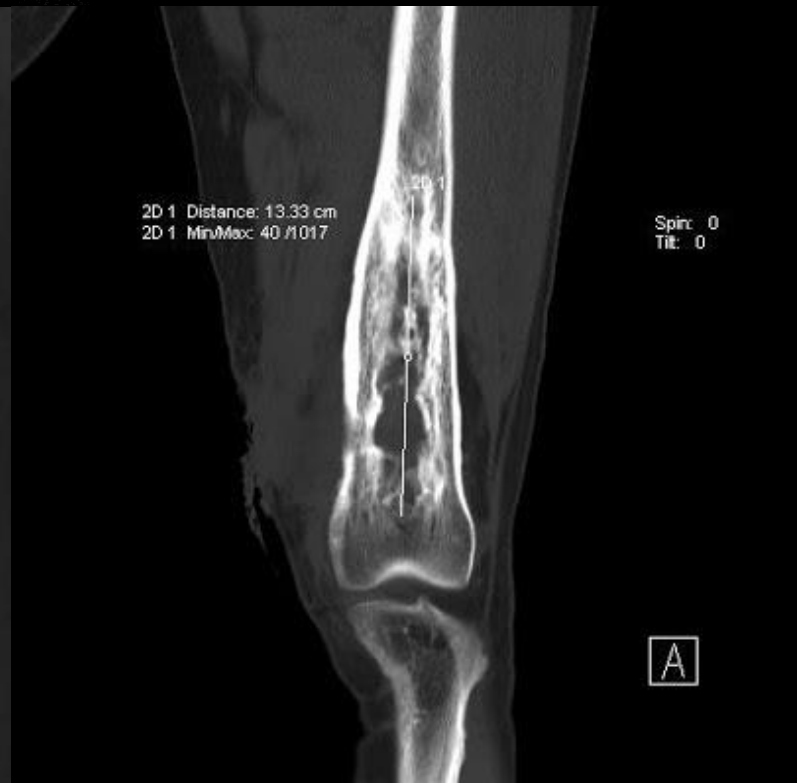

Sequestrum










2D 1 Distance: 13.33 cm
2D 1 Min/Max: 40 /1017
Spin: 0
Tilt: 0
A

IMAGING

“You only see what you look for… and you only look for what you know…”

Learning Radiology (2nd edition)

ΠΕΡΙΠΡΟΘΕΤΙΚΕΣ ΛΟΙΜΩΞΕΙΣ

- **Τουλάχιστον 3 - 6 ιστικά και οστικά δείγματα από την περιοχή διεπαφής του υλικού.**

- **ΟΧΙ λήψη καλλιεργειών με στυλεούς!**

American Academy of Orthopaedic Surgeons. The diagnosis of periprosthetic joint infections of the hip and knee, guideline and evidence report, 2010

- **Ιστική ομογενοποίηση των δειγμάτων προ καλλιέργειας → Αυξημένη διαγνωστική ικανότητα**

Redanz et al. *DMID* 2015

ΜΙΑ ΜΟΝΑΔΙΚΗ ΘΕΤΙΚΗ ΚΑΛΛΙΕΡΓΕΙΑ ΠΙΘΑΝΟΤΑΤΑ ΑΞΙΟΛΟΓΕΙΤΑΙ ΕΦΟΣΟΝ ΥΠΑΡΧΕΙ:

- Ιδιαίτερα παθογόνος μικροοργανισμός πχ *Staphylococcus aureus*
- Περιπροθετικό πυώδες εξίδρωμα
- Συρίγγιο μέχρι την άρθρωση
- Ταχεία ανάπτυξη παθογόνου στην καλλιέργεια
- Θετική Gram χρώση

Shuman E, et al. *Infect Dis Clin N Am* 2012

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

Journal of Clinical Microbiology

Improved Diagnosis of Periprosthetic Joint Infection by Multiplex PCR of Sonication Fluid from Removed Implants

Yvonne Achermann, Markus Vogt, Michael Leunig, Jürg Wüst and Andrej Trampuz

J. Clin. Microbiol. 2010, 48(4):1208. DOI: 10.1128/JCM.00006-10.
Published Ahead of Print 17 February 2010.

The 2010 Award of the Swiss Society of Hospital Hygiene (SSHH) & the Swiss Society for Infectious Diseases (SSI)

Molecular techniques for diagnosing prosthetic joint infections

John C. Hartley* and Kathryn A. Harris

Department of Microbiology, Virology and Infection Prevention and Control, Great Ormond Street Hospital for Children NHS Foundation Trust, Great Ormond Street, London WC1N 3JH, UK

***J Antimicrob Chemotherapy* 2014**

Prosthetic Joint Infection Diagnosis using Broad-Range PCR of Biofilms Dislodged from Knee and Hip Arthroplasty Surfaces using Sonication

Eric Gomez, Charles Cazanave, Scott A. Cunningham et al, Mayo Clinic, USA

Journal of Clinical Microbiology 2012

Evaluation of the FilmArray® Blood Culture (BCID) Panel on Biofilms Dislodged from Explanted Arthroplasties for Prosthetic Joint Infection Diagnosis

Shawn Vasoo,[1,2,3] Scott A Cunningham,[3] Kerryl E Greenwood-Quaintance,[3] Jayawant N Mandrekar,[4] Arlen D Hanssen,[5] Matthew P Abdel,[5] Douglas R Osmon,[1] Elie F Berbari,[1] Robin Patel[1,3]

International Journal of Infectious Diseases 99 (2020) 108–116

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Detecting the presence of bacteria in low-volume preoperative aspirated synovial fluid by metagenomic next-generation sequencing

Xinyu Fang[a,1], Yuanqing Cai[a,1], Tengbin Shi[a], Zida Huang[a], Chongjing Zhang[a], Wenbo Li[a], Chaofan Zhang[a], Bin Yang[b], Wenming Zhang[a,*], Zhenpeng Guan[c,**]

[a] Department of Orthopaedic Surgery, The First Affiliated Hospital of Fujian Medical University, Fuzhou, China
[b] Department of Laboratory Medicine, The First Affiliated Hospital of Fujian Medical University, Fuzhou, China
[c] Department of Orthopedic Surgery, Peking University Shougang Hospital, Beijing, China

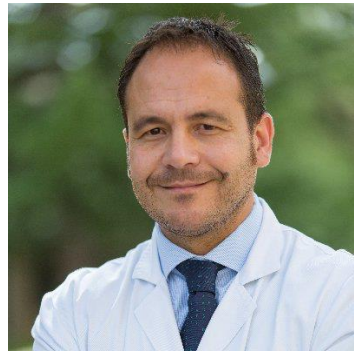
Diagnosing Periprosthetic Joint Infection

Has the Era of the Biomarker Arrived?

Carl Deirmengian MD, Keith Kardos PhD, Patrick Kilmartin, Alexander Cameron, Kevin Schiller, Javad Parvizi MD

Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

ΚΡΙΤΗΡΙΑ ΔΙΑΓΝΩΣΗΣ ΠΕΡΙΠΡΟΘΕΤΙΚΗΣ ΛΟΙΜΩΞΗΣ



1. **Συρίγγιο,** που επικοινωνεί με την περιοχή των εμφυτευμάτων (**Β-ΙΙΙ**)
2. **Πύον** πέριξ της αρθρώσεως/αρθροπλαστικής (**Β-ΙΙΙ**)
3. **Ιστολογική απόδειξη** οξείας φλεγμονής των περιπροθετικών ιστών (**Β-ΙΙ**)
4. Απομόνωση του ίδιου **μικροοργανισμού** από τουλάχιστον **δύο** καλλιέργειες
   - από υγρό αρθροκέντησης ή
   - από διεγχειρητικά περιπροθετικά δείγματα (**Β-ΙΙΙ**)

   ή

   απομόνωση ιδιαίτερα παθογόνου μικροοργανισμού πχ *S.aureus* από **μία** καλλιέργεια
   - από υγρό αρθροκέντησης ή
   - από περιπροθετικό ιστό διεγχειρητικά (**Β-ΙΙΙ**)
5. PJI μπορεί να υφίσταται, ακόμη κι αν τα κριτήρια αυτά δεν εκπληρούνται **(Β-ΙΙΙ)**

IDSA Guidelines, CID 2013

Del Pozo J, Patel R, et al. *N Engl J Med* 2009

DIADNOSTIC CRITERIA FOR PJI

Major criteria (at least one of the following)	Decision
Two positive cultures of the same organism	Infected
Sinus tract with evidence of communication to the joint or visualization of the prosthesis	

		Minor Criteria	Score	Decision
Preoperative Diagnosis	Serum	Elevated CRP *or* D-Dimer	2	≥6 Infected
		Elevated ESR	1	
	Synovial	Elevated synovial *WBC count or LE*	3	**2-5 Possibly Infected [a]**
		Positive alpha-defensin	3	
		Elevated synovial PMN (%)	2	0-1 Not Infected
		Elevated synovial CRP	1	

	Inconclusive pre-op score *or* dry tap [a]	Score	Decision
Intraoperative Diagnosis	Preoperative score	-	≥6 Infected
	Positive histology	3	**4-5 Inconclusive [b]**
	Positive purulence	3	
	Single positive culture	2	≤3 Not Infected

Parvizi J, et al. The 2018 definition of periprosthetic hip and knee infection: An evidence-based and validated criteria. *J Arthroplasty* 2018, 33:1309-14 (MSIS)

DIADNOSTIC CRITERIA FOR PJI

Bone biopsy remains the gold standard method for the identification of the pathogen causing PJI (Level of evidence 4)

Sinus tract and purulent discharge are clear signs of prosthetic joint infection (Level of evidence 5)

Antibiotic therapy should be discontinued before biopsy (Level of evidence 5)

In case of fever, blood cultures should always be performed in patients suspected to have prosthetic joint infection to identify the causative bacteria (Level of evidence 4)

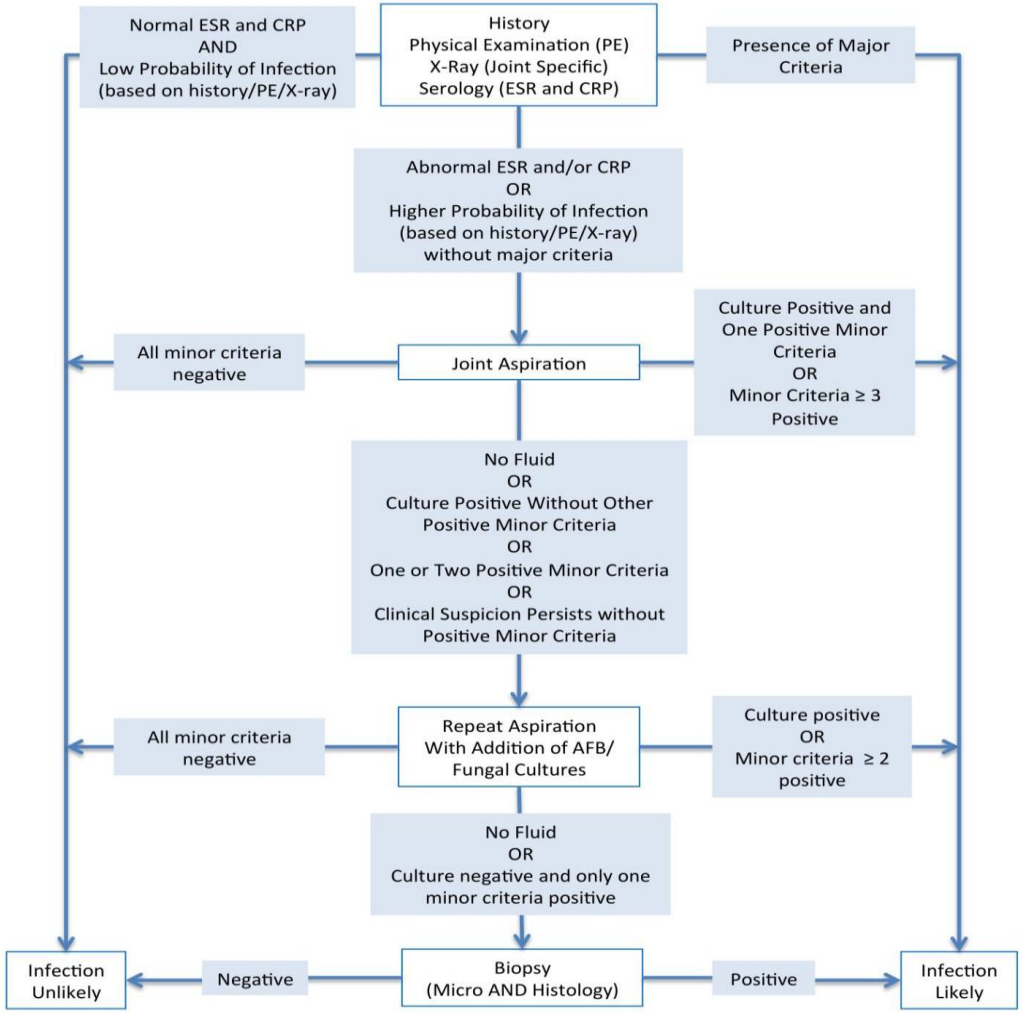
CRP, ESR, and WBC counts should always be performed in patients suspected of having peripheral bone infection for diagnostic purposes (Level of evidence 4)

Glaudemans AWJM, et al. Consensus document for the diagnosis of peripheral bone infection in adults: a joint paper by the EANM, EBJIS, and ESR (with ESCMID endorsement). *Eur J Nucl Med Mol Imaging* 2019, 46: 957-70

AAOS
American Academy of Orthopaedic Surgeons

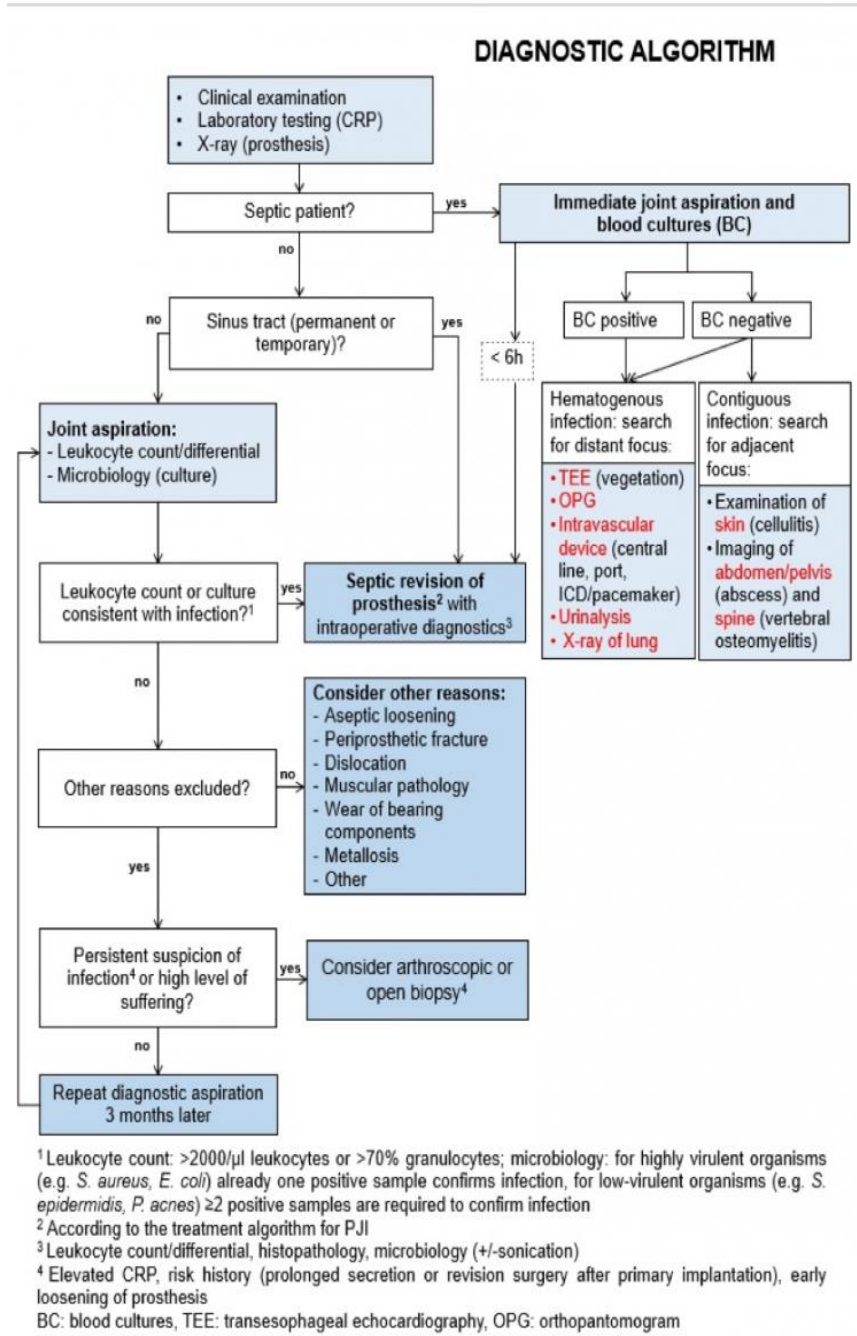
Major Criteria:
- Sinus tract communicating with the joint

Minor Criteria:
- Culture
- Leukocyte Esterase
- Synovial White Blood Cell Count
- Synovial Neutrophil Percentage



AO Recon

Adapt. By Trampuz A., Charite, Berlin. Pro-implant foundation_Course for Prosthetic implant infections 2020



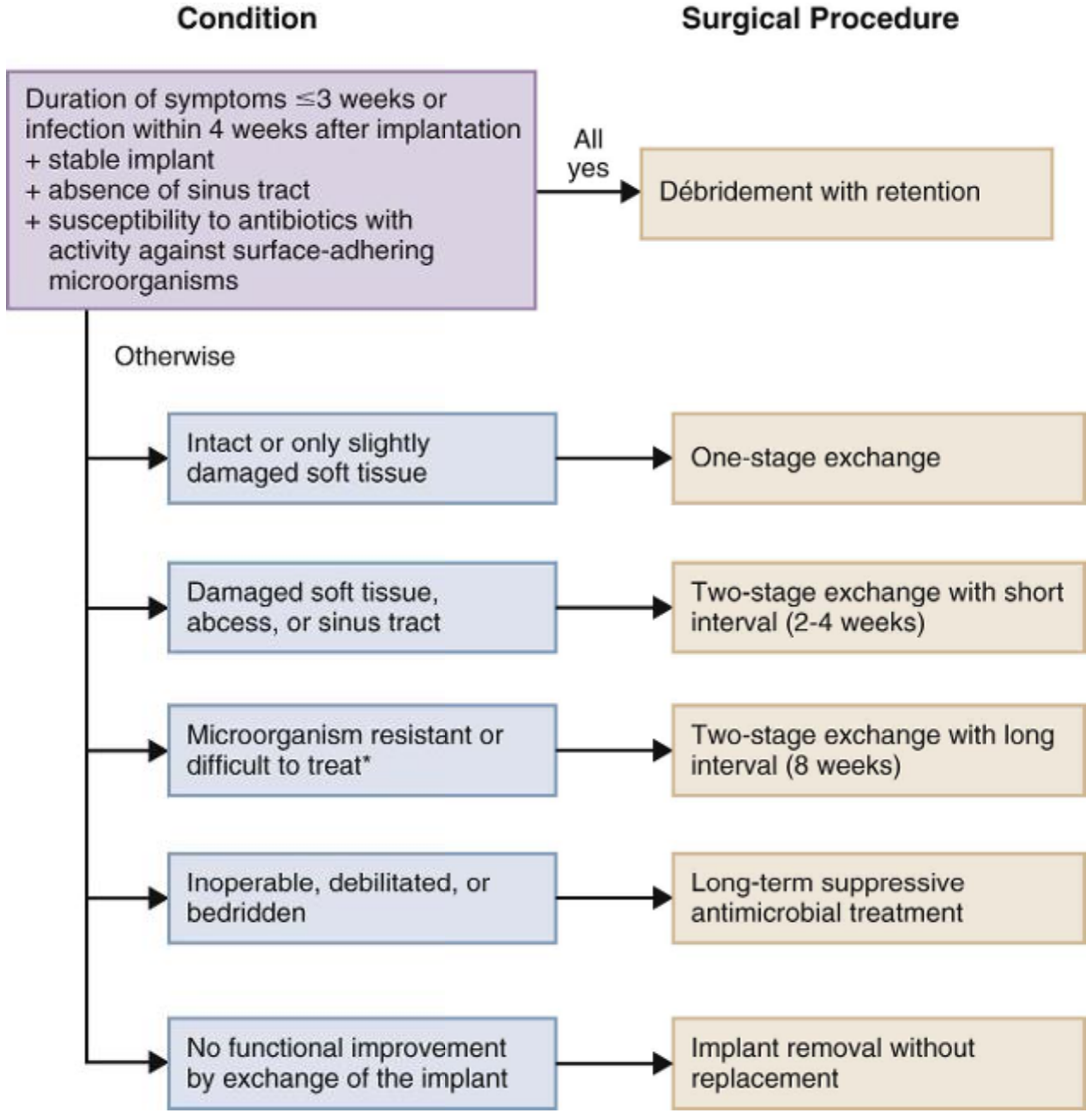
[1] Leukocyte count: >2000/µl leukocytes or >70% granulocytes; microbiology: for highly virulent organisms (e.g. *S. aureus, E. coli*) already one positive sample confirms infection, for low-virulent organisms (e.g. *S. epidermidis, P. acnes*) ≥2 positive samples are required to confirm infection
[2] According to the treatment algorithm for PJI
[3] Leukocyte count/differential, histopathology, microbiology (+/-sonication)
[4] Elevated CRP, risk history (prolonged secretion or revision surgery after primary implantation), early loosening of prosthesis
BC: blood cultures, TEE: transesophageal echocardiography, OPG: orthopantomogram

ΣΧΕΔΙΑΣΜΟΣ ΑΝΤΙΜΕΤΩΠΙΣΗΣ ΠΕΡΙΠΡΟΘΕΤΙΚΗΣ ΛΟΙΜΩΞΗΣ

- Χειρουργικός καθαρισμός, διατήρηση πρόθεσης + αντιβιοτικά → ***DAIR***
- Αντικατάσταση αρθροπλαστικής σε 1 στάδιο (one stage revision) ± σταθεροποιητικό υλικό (cement) με αντιβιοτικό + αντιβιοτικά IV
- Αφαίρεση αρθροπλαστικής με όψιμη επανατοποθέτηση (αντικατάσταση σε 2 στάδια) ± σταθεροποιητικό υλικό (cement) με αντιβιοτικό + αντιβιοτικά IV
- Απλή αφαίρεση με καθαρισμό + αντιβιοτικά IV
- Αρθρόδεση (fusion)
- Ακρωτηριασμός
- Χρόνια κατασταλτική αγωγή (>6 μήνες- πολλά έτη)

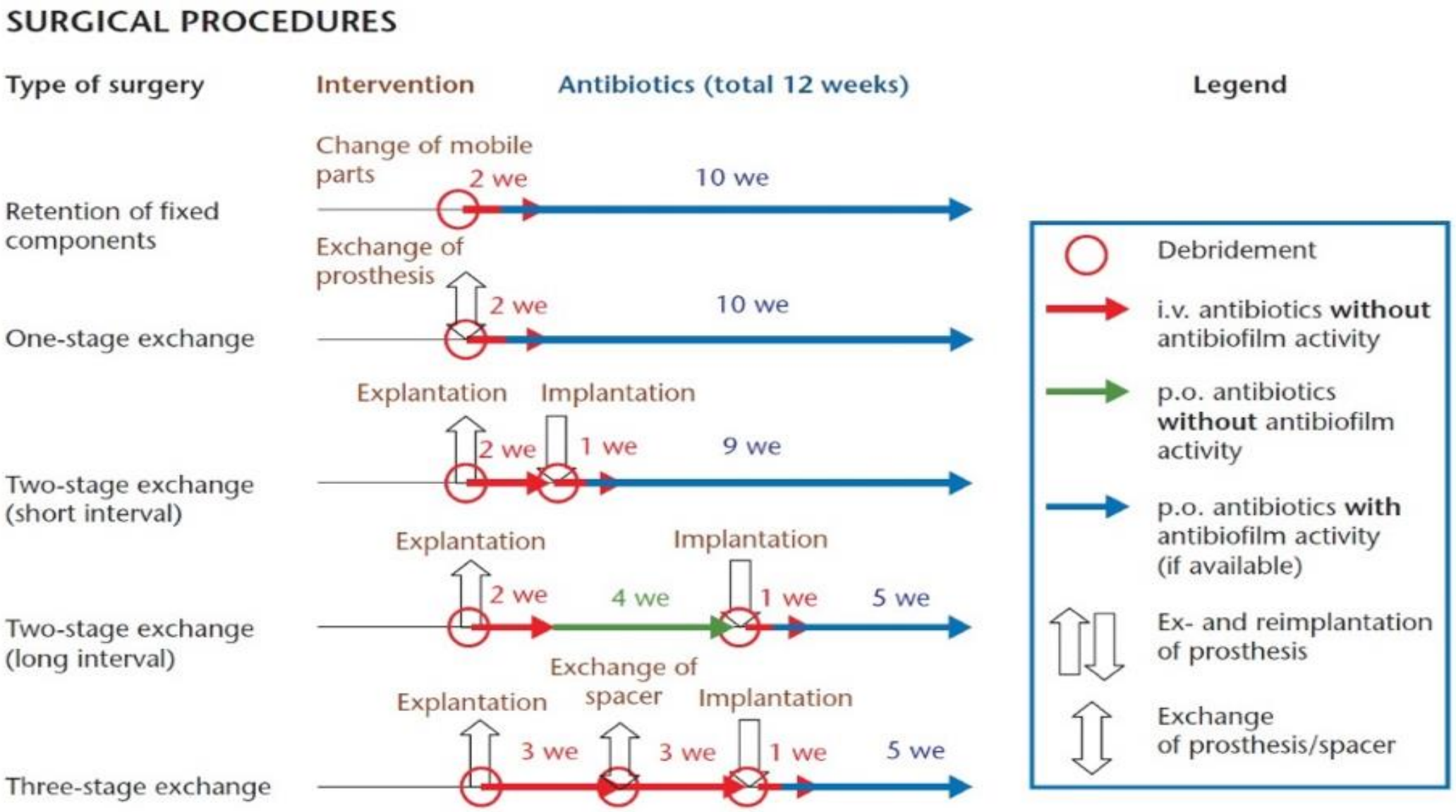
Zimmerli W & Sendi P. Orthopaedic implant-associated infections. *In: Principles and Practice of Infectious Diseases*, 2015 p.1328-40

Surgical treatment algorithm for prosthetic joint infections.



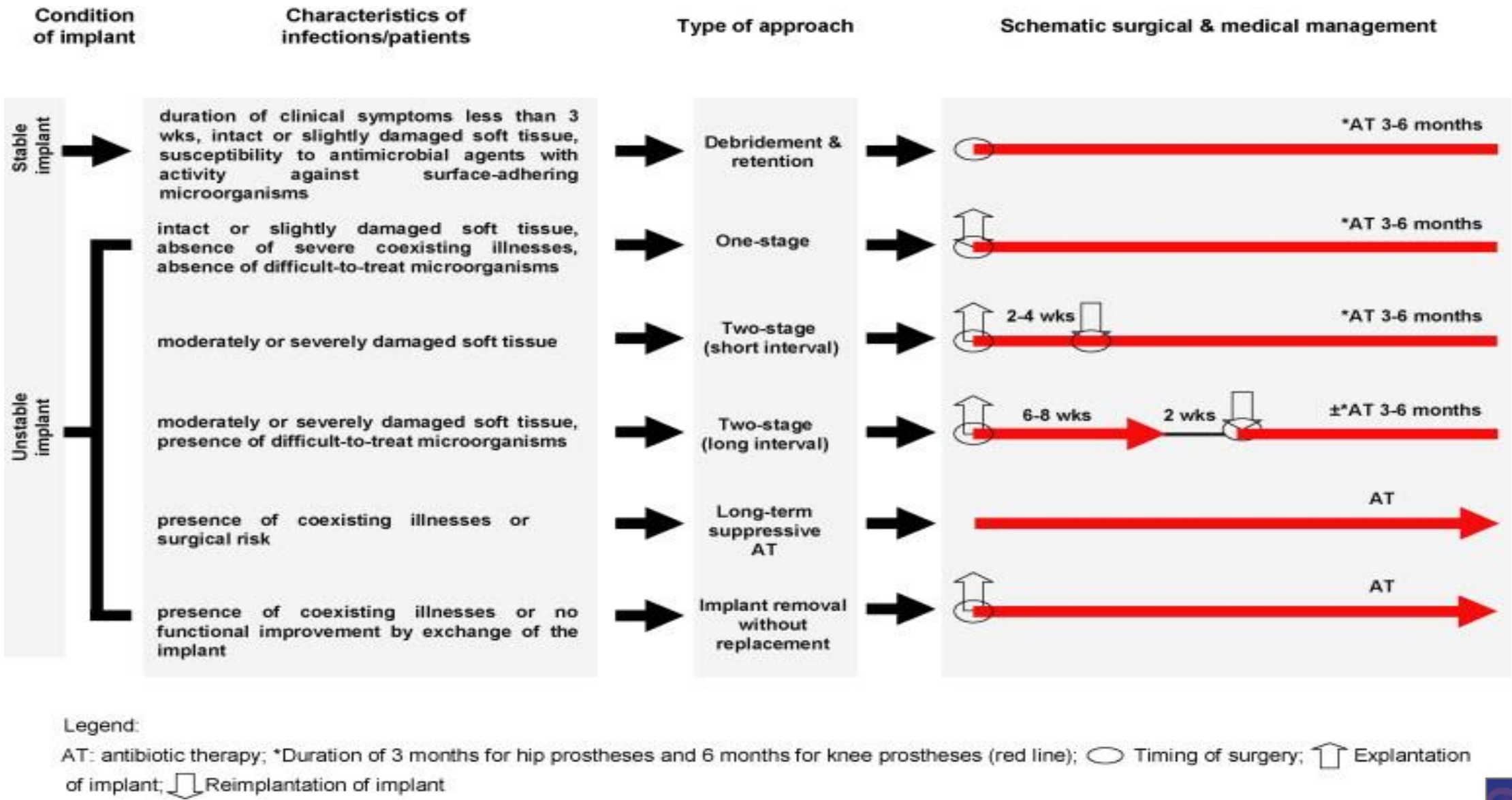
Difficult-to-treat microorganisms include microorganisms resistant to antibiotics with good oral bioavailability, rifampin-resistant *staphylococci, enterococci*, and quinolone-resistant gram-negative bacilli and fungi.

Zimmerli W & Sendi P. Orthopaedic implant-associated infections. *In: Principles and Practice of Infectious Diseases*, 2015 p.1328-40



AO Recon

Adapt. By Trampuz A. , Charite, Berlin. Pro-implant foundation_Course for Prosthetic implant infections 2020

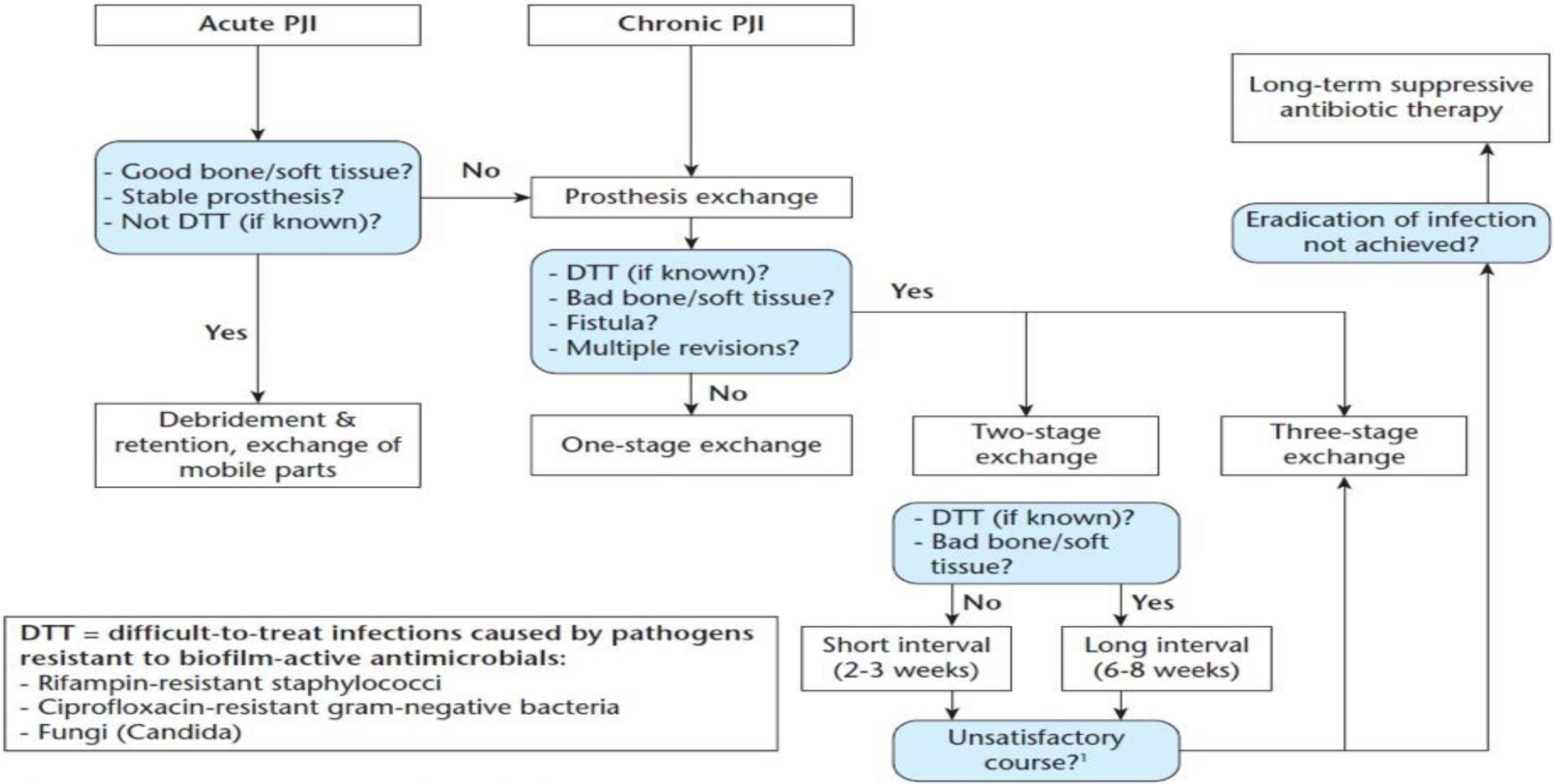


Legend:

AT: antibiotic therapy; *Duration of 3 months for hip prostheses and 6 months for knee prostheses (red line); ⬭ Timing of surgery; ⇧ Explantation of implant; ⇩ Reimplantation of implant

Leone S, et al. Consensus document on controversial issues on the diagnois and treatment of prosthetic joint infections. *Int J Infect Dis* 2010, 14: 67-77

TREATMENT ALGORITHM

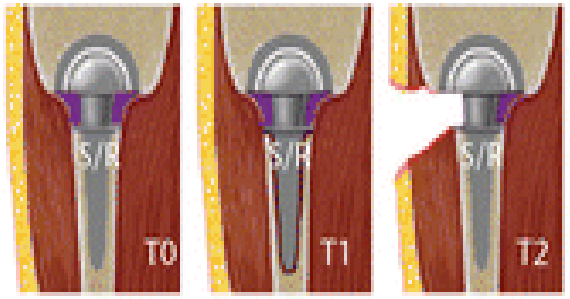


[1] Clinical signs of infection, elevated CRP, intra-operative pus, compromised tissue

*AO Recon*_Adapt. By Trampuz A., Charite, Berlin. Pro-implant foundation_Course for Prosthetic implant infections 2020

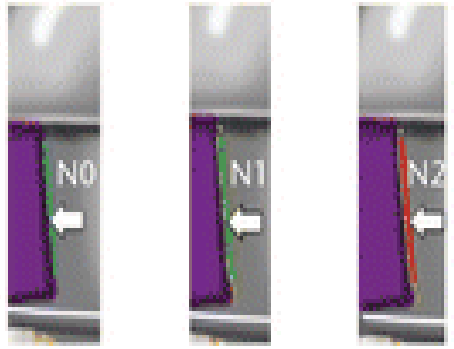
A FUNCTIONAL CLASSIFICATION SYSTEM

TNM Classification System for Prosthetic Joint Infections



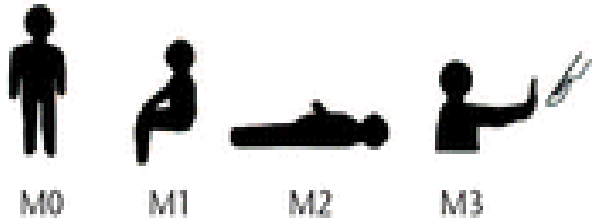
T — Tissue and Implant conditions

T0	a	Stable standard implant without important soft tissue defect
	b	Stable revision implant without important soft tissue defect
T1	a	Loosened standard implant without important soft tissue defect
	b	Loosened revision implant without important soft tissue defect
T2	a	Severe soft tissue defect with standard implant
	b	Severe soft tissue defect with revision implant



N — Non-human cells (bacteria and fungi)

N0	a	No mature biofilm formation *(former: acute)*, directly postoperatively
	b	No mature biofilm formation *(former: acute)*, late haematogenous
N1	a	Mature biofilm formation *(former: chronic)* without "difficult to treat bacteria"
	b	Mature biofilm formation *(former: chronic)* with culture negative infection
N2	a	Mature biofilm formation *(former: chronic)* with "difficult to treat bacteria"
	b	Mature biofilm formation *(former: chronic)* with polymicrobial infection
	c	Mature biofilm formation *(former: chronic)* with fungi



M — Morbidity of the patient

M0		Not or only mildly compromised (Charlson Comorbidity Index: 0-1)
M1		Moderately compromised patient (Charlson Comorbidity Index: 2-3)
M2		Severely compromised patient (Charlson Comorbidity Index 4-5)
M3	a	Patient refuses surgical treatment
	b	Patient does not benefit from surgical treatment
	c	Patient does not survive surgical treatment

r — reinfection

If the infection involves a previously infected implant, the situation is considered as "reinfection" and an "r" is put in front of the classification, e.g. rT1aN1aM2

Volker Alt, *et al. Bone Joint Res* 2020, 9:79–81

ANTIMICROBIAL TREATMENT (IV/PO) OF COMMON MICROORGANISMS CAUSING PJIs (B-III)

MICROORGANISM	PREFERRED TREATMENT iv	ALTERNATIVE TREATMENT iv/po	Comments
MSSA /MSSE	Cefazolin Nafcillin Flucloxacillin Ceftriaxome ?	Vancomycin Daptomycin Linezolid	± Rifampicin
MRSA / MRSE	Vancomycin	Daptomycin Linezolid	± Rifampicin

Osmon DR et al. IDSA Clinical Practice Guidelines. Clin Infect Dis 2013
Parvizi J & Gehrke T. International Consensus Meeting on Periprosthetic Joint Infection, 2013

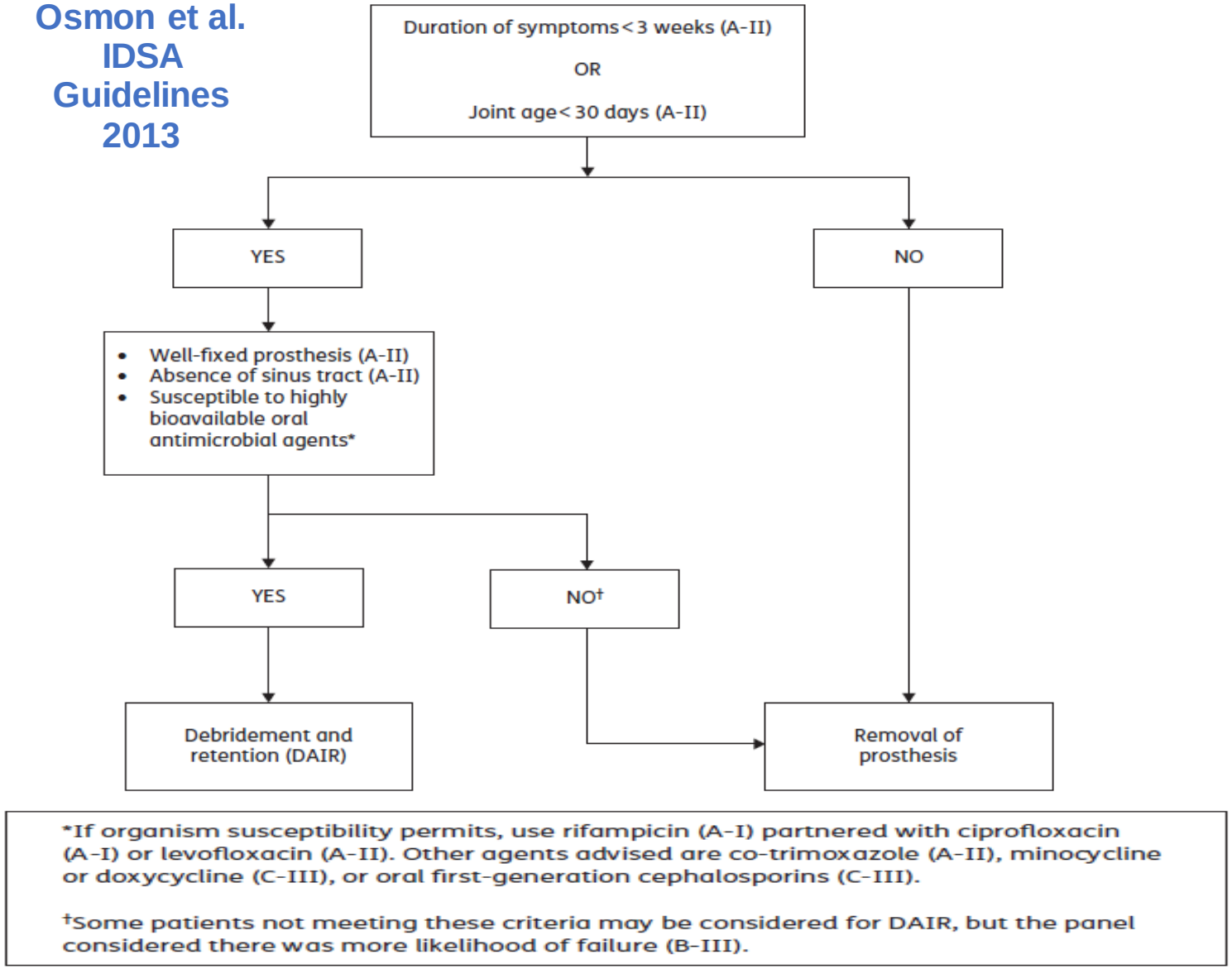
ANTIMICROBIAL TREATMENT (IV/PO) OF COMMON MICROORGANISMS CAUSING PJIs (B-III)

MICROORGANISM	PREFERRED TREATMENT iv	ALTERNATIVE TREATMENT iv/po	Comments
β-hemolytic Streptococci	Penicillin G Ampicilline Ceftriaxone	Vancomycin	
Enterococci	Penicillin G Ampicilline	Vancomycin Daptomycin Linezolid	± aminoglycoside Ampicilline +Rif Linezolid + Rif Ciprofloxacin + Rif
Gram - negative	Cefepime Fluoroquinolones Ertapenem		
Pseudomonas aeruginosa	Cefepime Meropenem	Ciprofloxacin Ceftazidime	
Propionibacterium acnes	Penicillin G Ceftriaxone	Clindamycin Vancomycin	

Osmon DR et al. IDSA Clinical Practice Guidelines. Clin Infect Dis 2013
Parvizi J & Gehrke T. International Consensus Meeting on Periprosthetic Joint Infection, 2013

IMPLANT RETENTION

Osmon et al. IDSA Guidelines 2013



Guo-Xin Qu, et al. Debridement, antibiotics, and implant retention for periprosthetic knee infections: a pooling analysis of 1266 cases. *J Orthop Surg Res* 2019

"Success rate 71-80 % (<3w , no MRSA)"

"Immunocompromise, MRSA infection, poor condition of local soft tissues and failure of one DAIR procedure should prompt revision arthroplasty."

Sultan Naseer Qasim, et al. *SICOT J* 2017

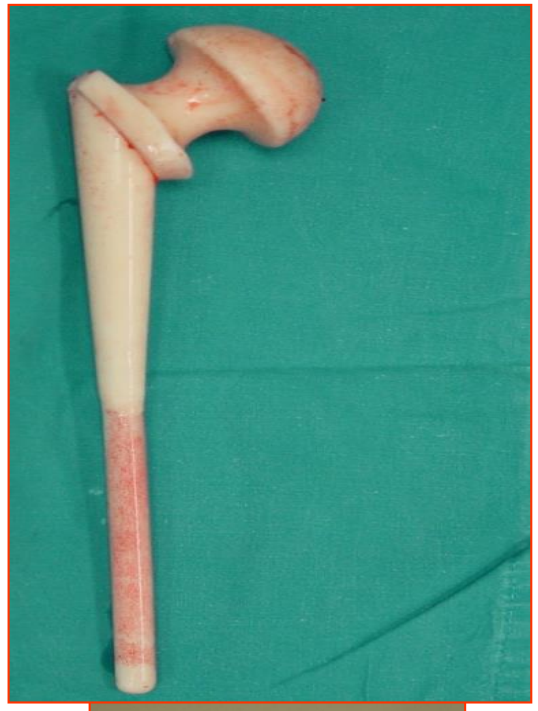
PREDICTORS OF DAIR FAILURE

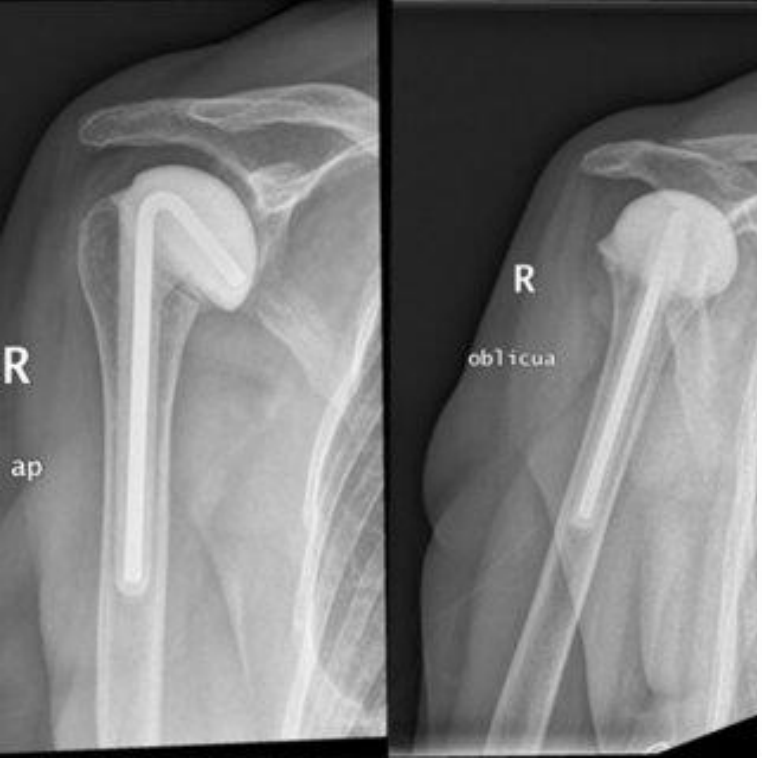
• No mobile parts exchange	Urikarte et al. *Hip Pelvis* 2019
• Total knee arthroplasty	Kunutsor et al. *J Infection* 2018
• Hematogenous PJI	Iza et al. *J Orthop Surg Res* 2019
• Long symptom duration	Kunutsor et al. *J Infection* 2018
• Fracture total hip arthroplasty	de Vries, *JBJI* 2019
• Immunocompromise	Segawa et al. *J Bone Joint Surg Am* 1999
• Bone loss & soft tissue necrosis	Segawa et al. *J Bone Joint Surg Am* 1999
• Sinus tract	Marculescu et al. *Clin Infect Dis* 2006
• *MRSA / Staph. aureus*	Triantafyllopoulos et al. *J Arthroplasty* 2014
• High virulence microorganisms	Azzam et al. *J Arthroplasty* 2010
• Ambiguous susceptibility to biofilm active Rx	Zimmerli et al. 2015
• Number of debridement	Geurts et al. *Acta Orthop* 2013

STAGED TREATMENT PROTOCOL

Temporary functional reconstruction (spacers)

- Local antibiotic delivery-extremely high local concentrations → vanco + genta
- Obliterate dead space.
- Simultaneously preserve space for definitive reconstruction
- Maintain ligament balance and soft tissue envelope and functional length
- PMMA-static
- PMMA-articulating
- Composite – metal, PMMA

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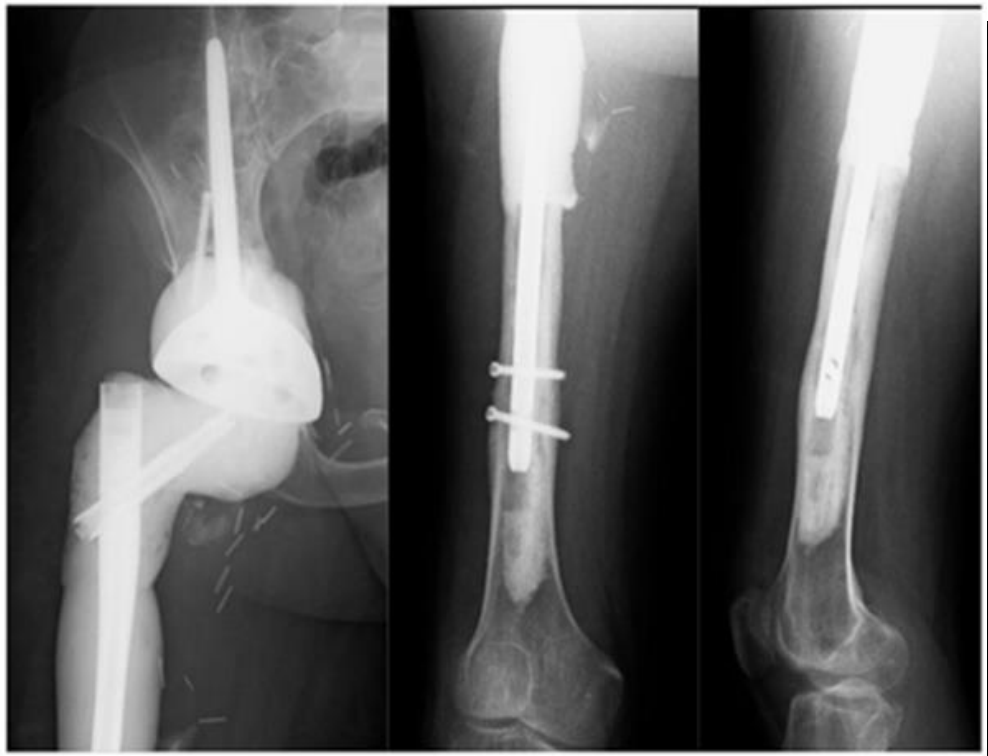
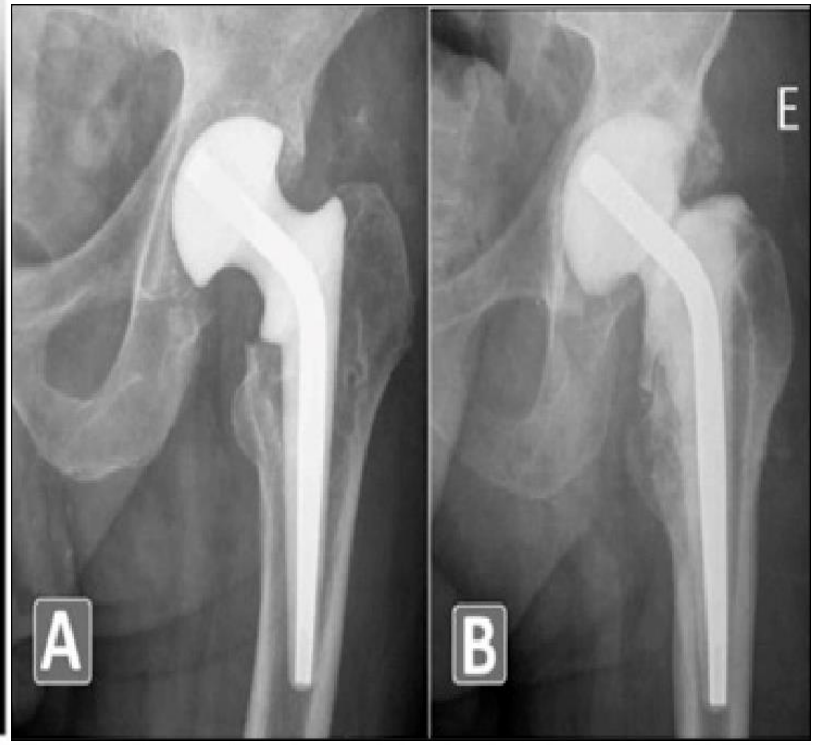
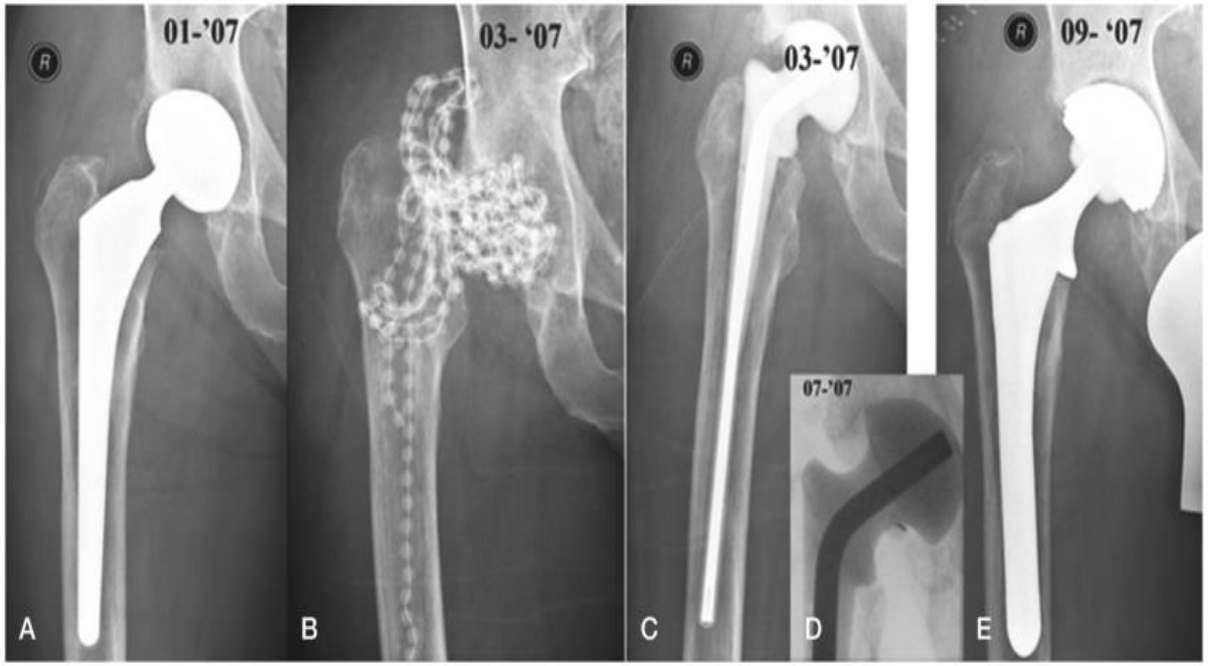



A
B
E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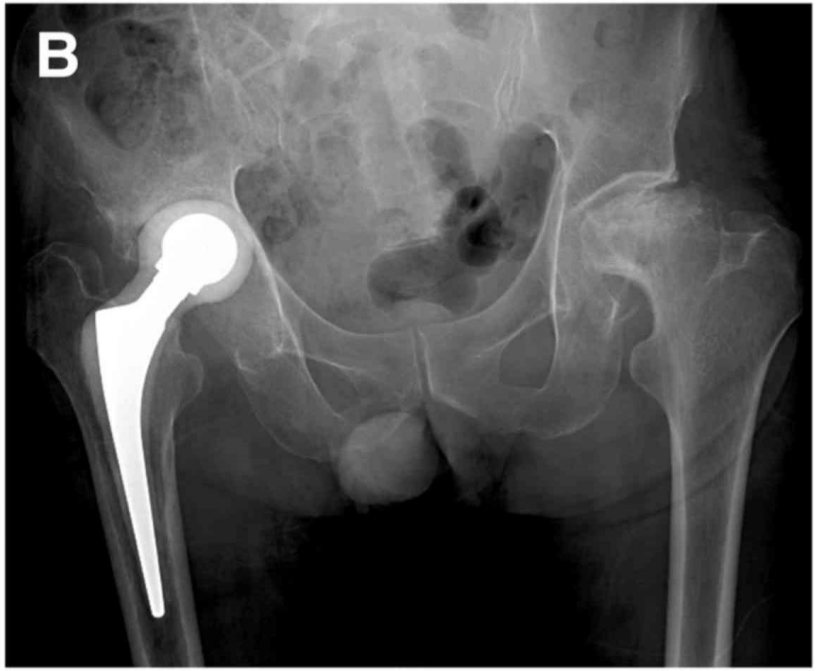
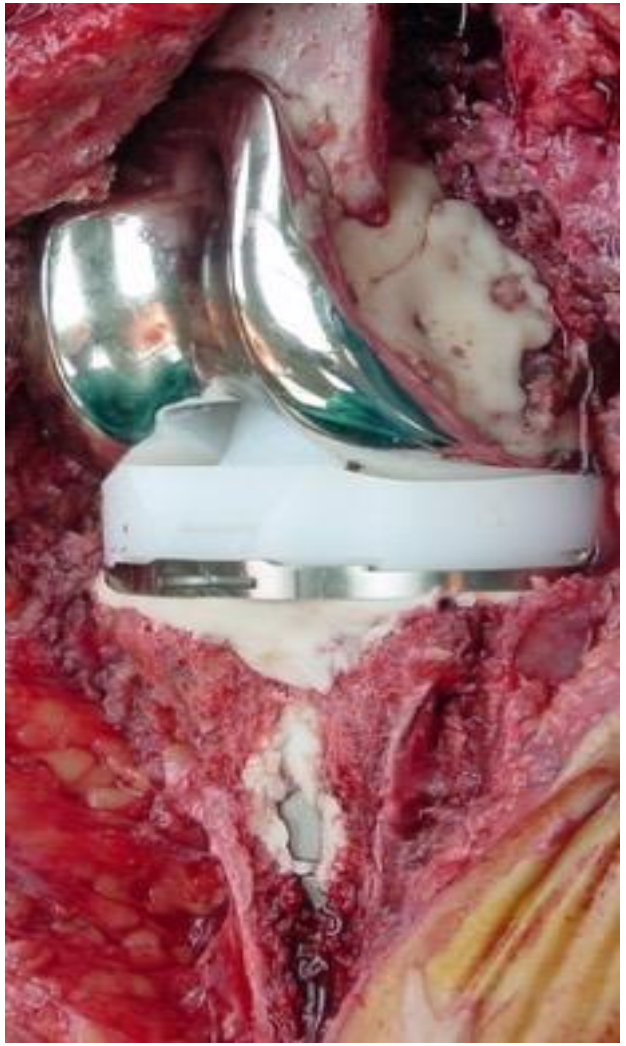
A

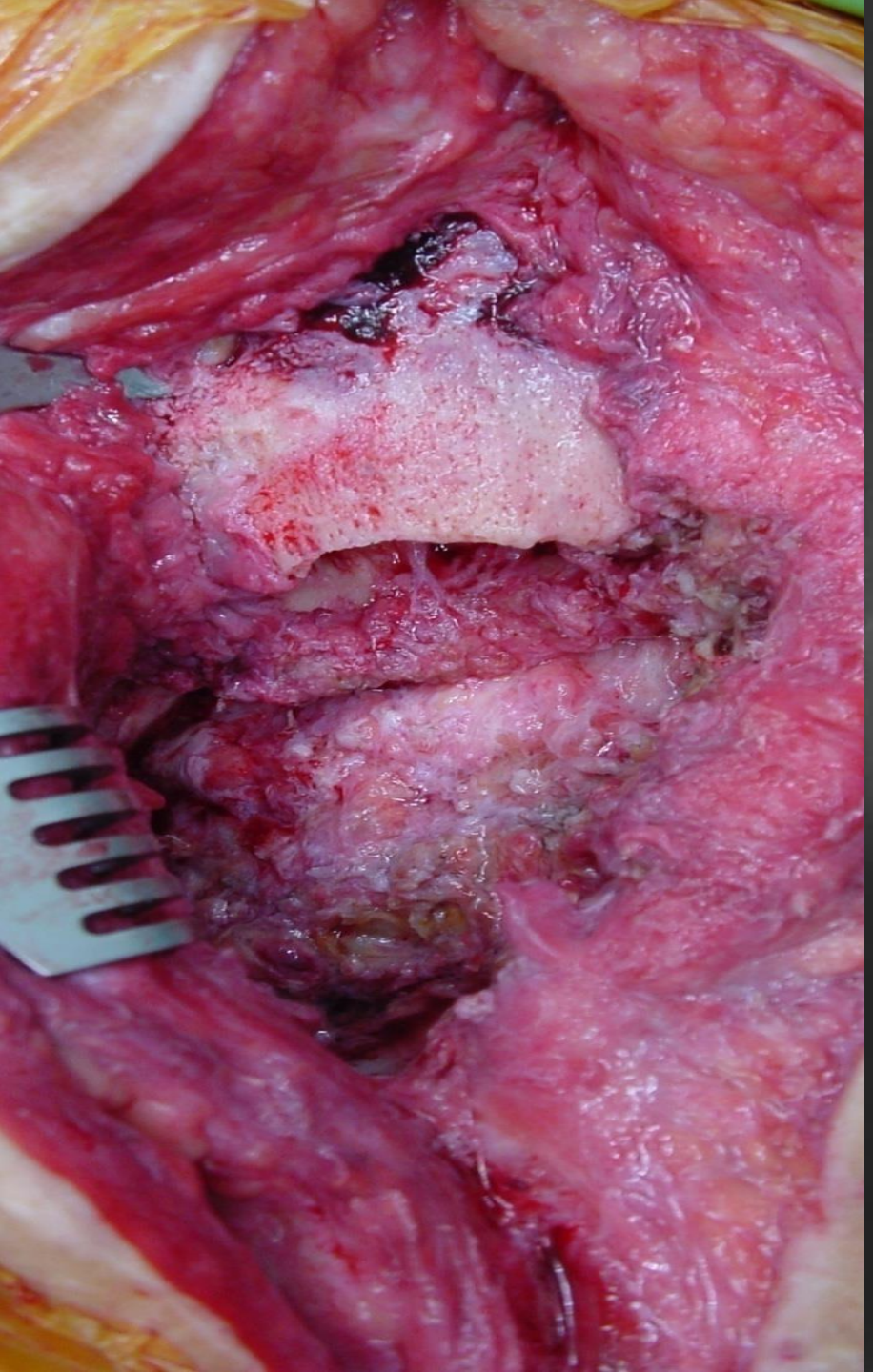

B

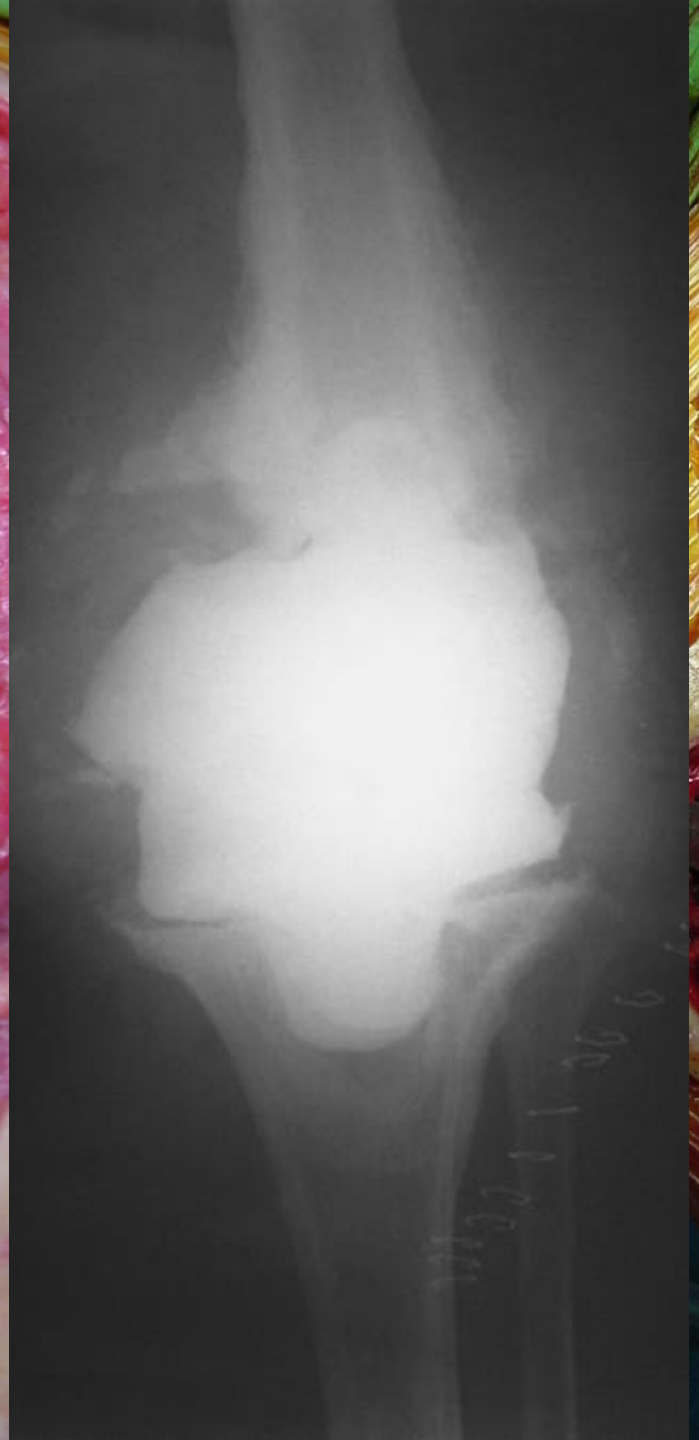
OUTCOMES OF PJI OVER TIME 2000 - 2016

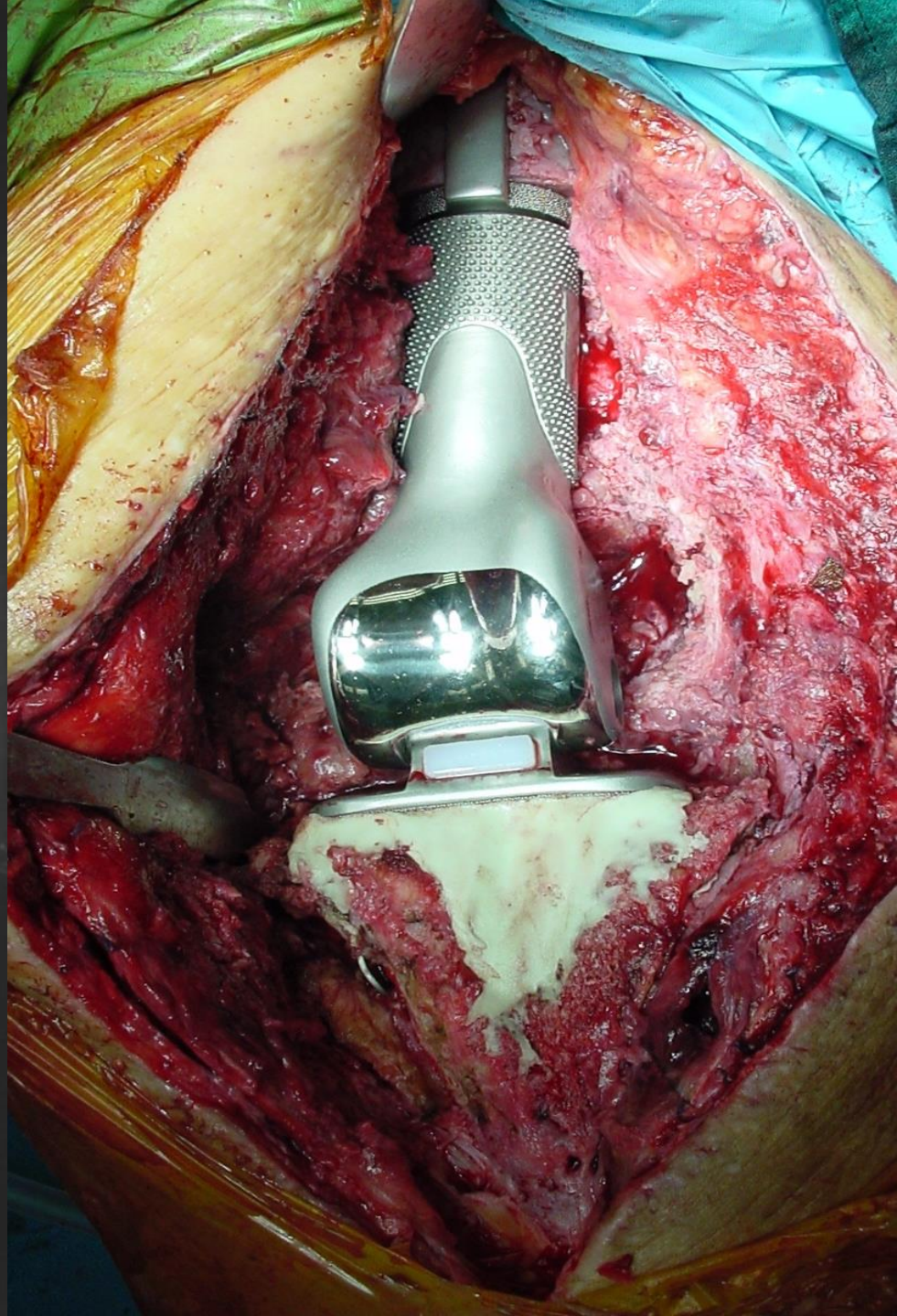
- Retrospective 17 years 2000-2016 (550 pts)
- 2-stage and DAIR (Debridement, Antibiotics, Implant Retention)
  - 123 patients not included as they did not have re-implantation
- Minimum 1 year follow-up
- Overall - 2-stage failure rate 19.8%
- **No difference in outcomes over 17 years - adjusted to age, sex, comorbidities**

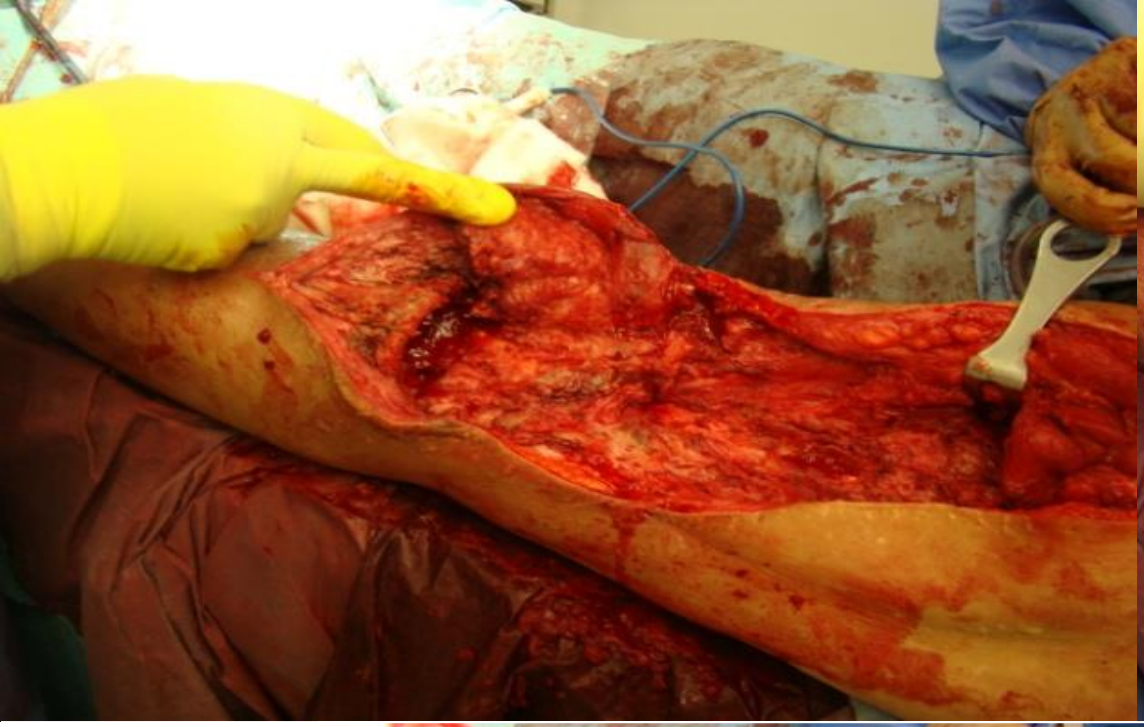


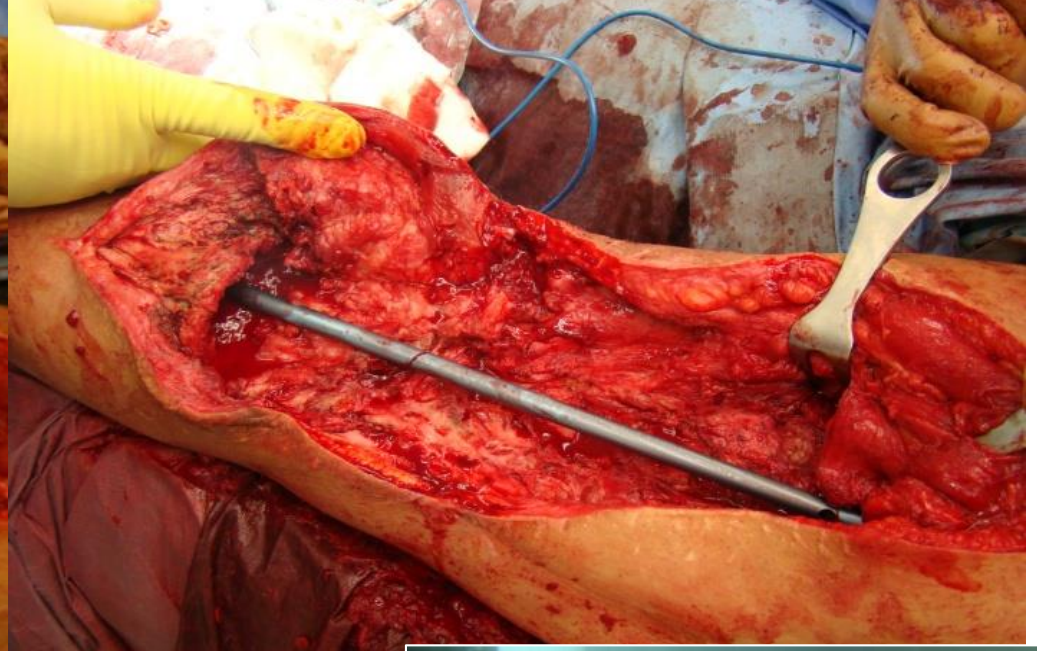
Goswami et al. MSIS. 2019

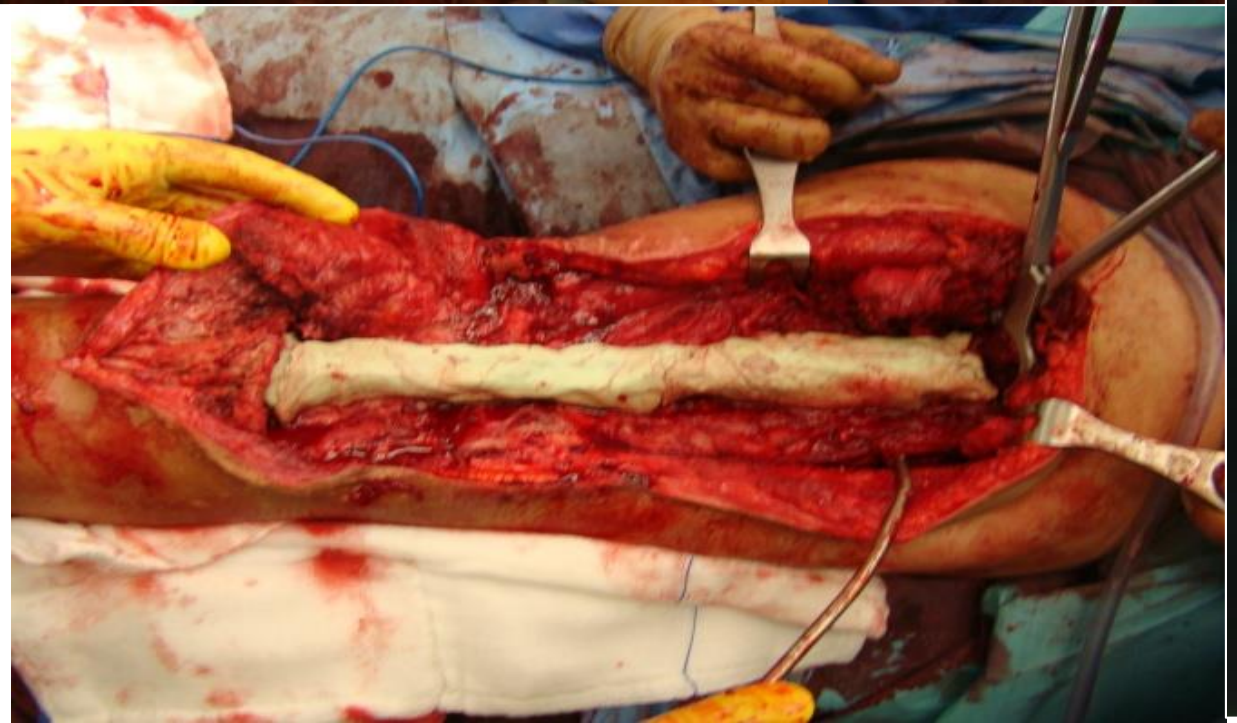


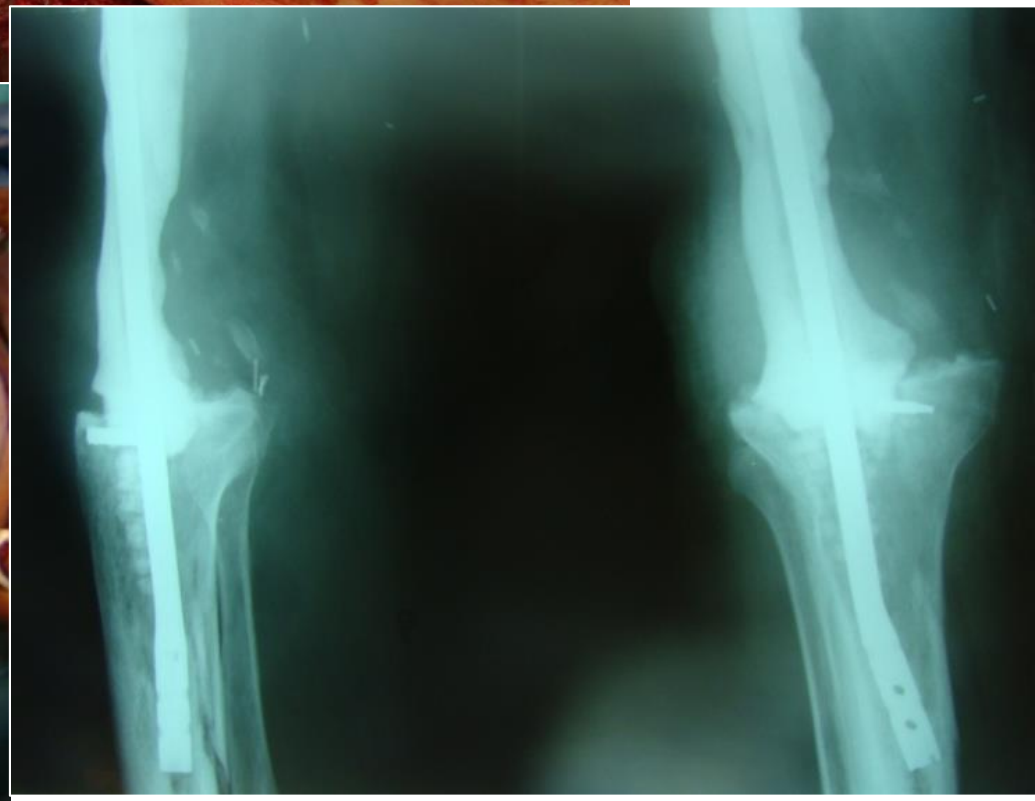


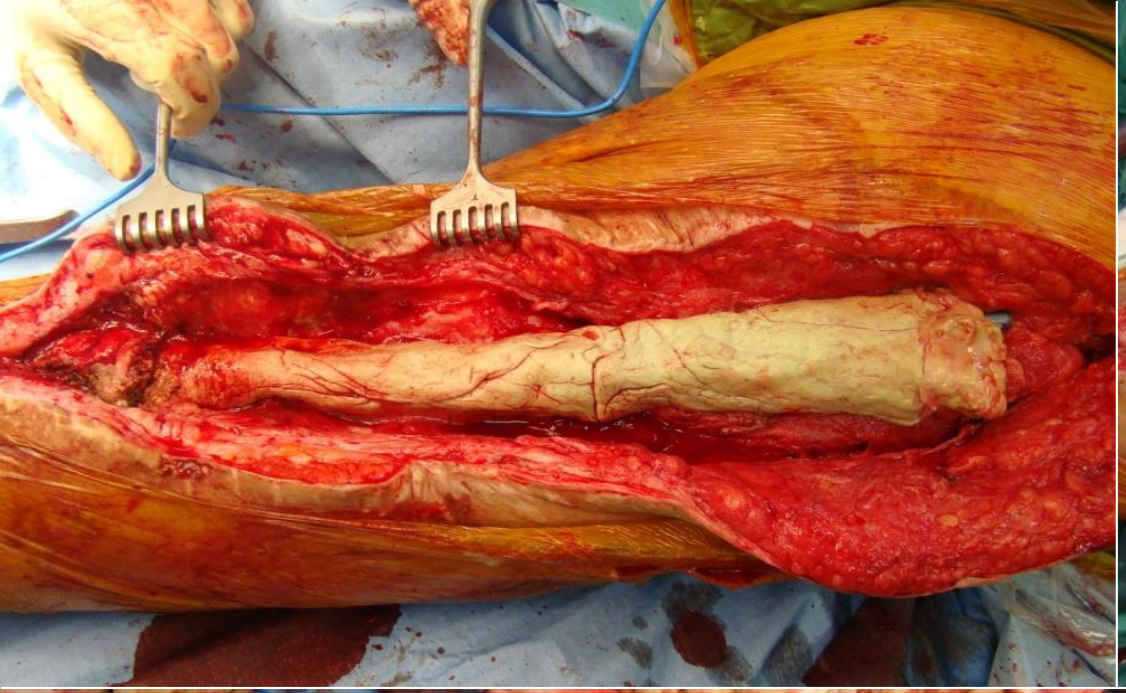
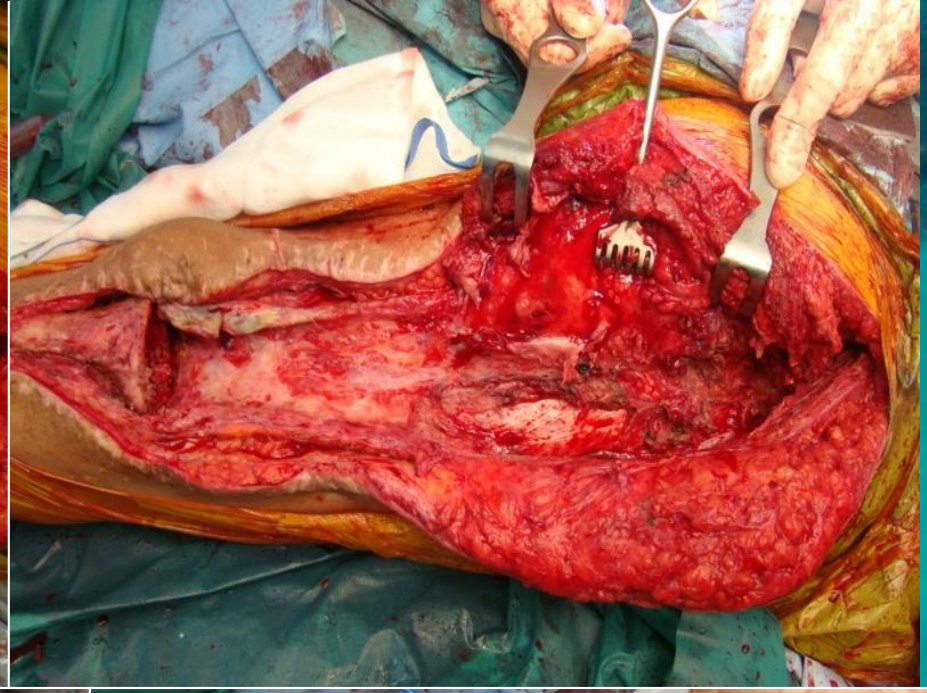
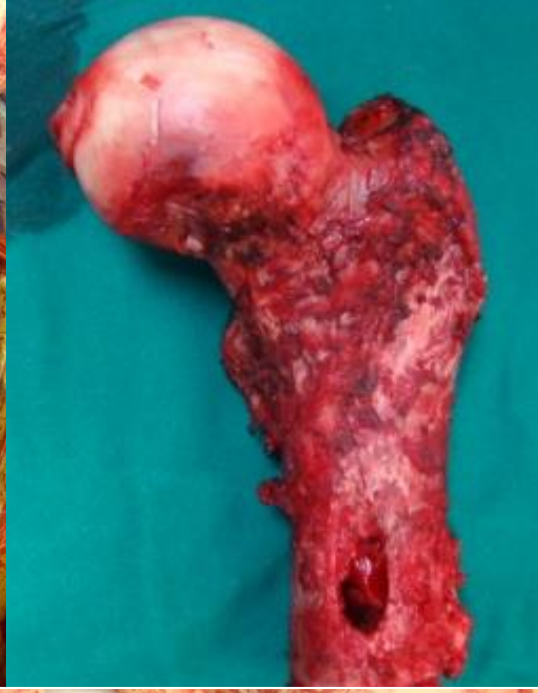
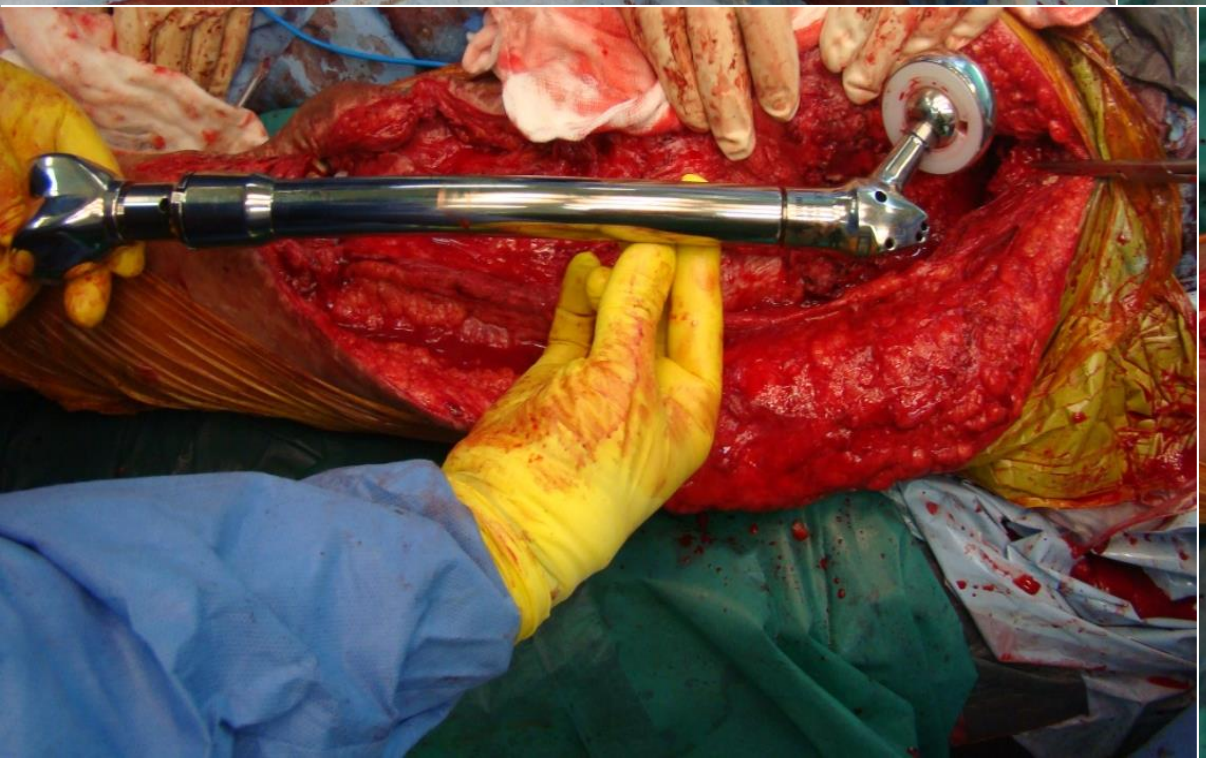
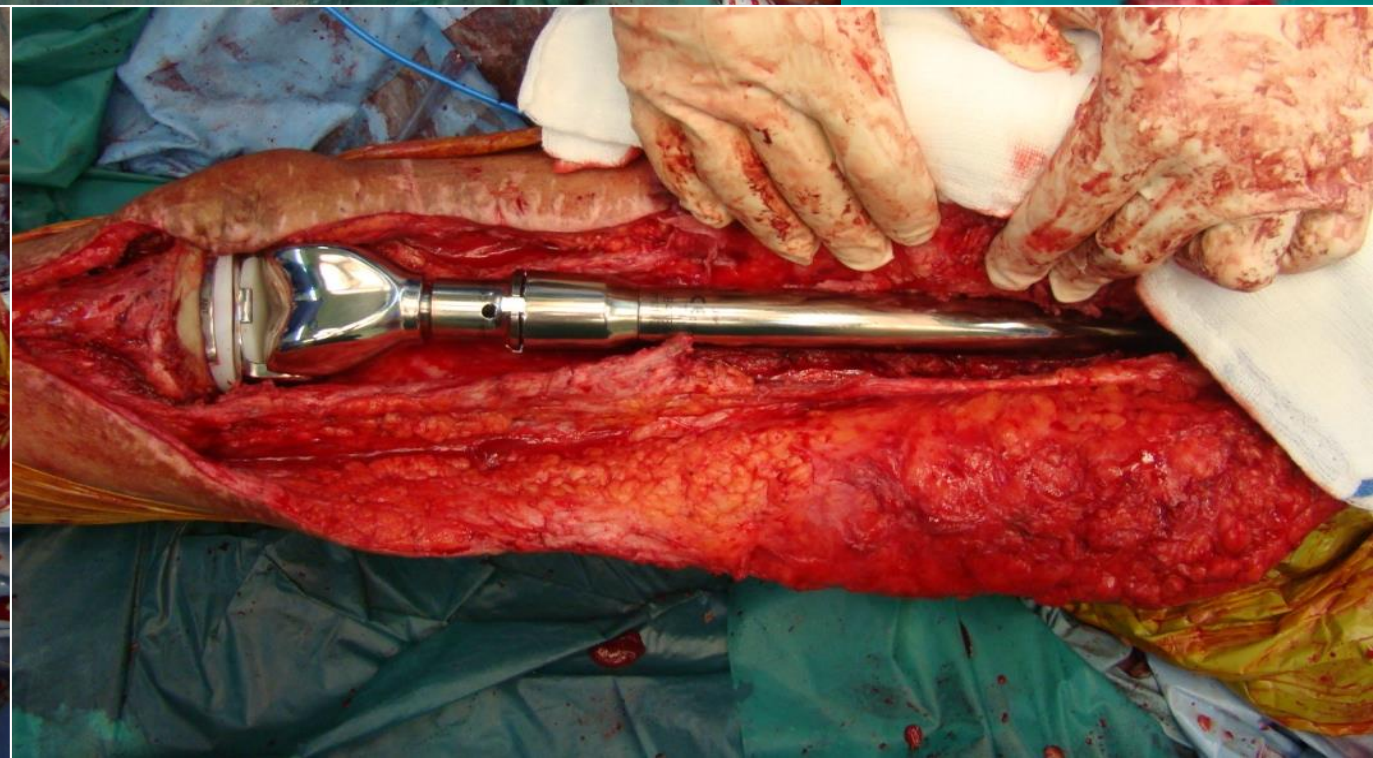






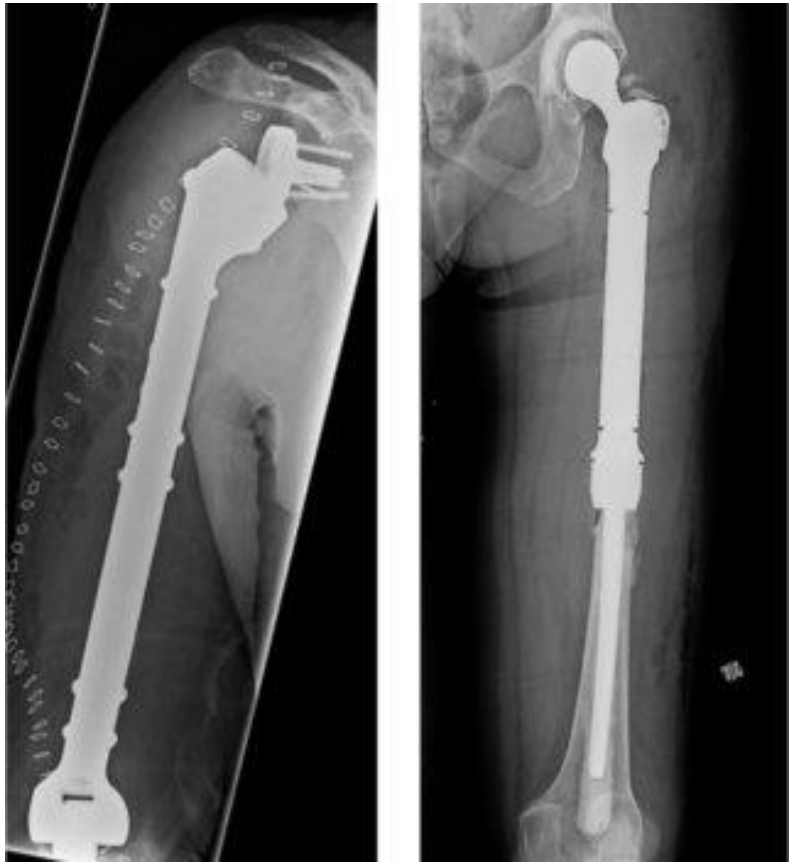




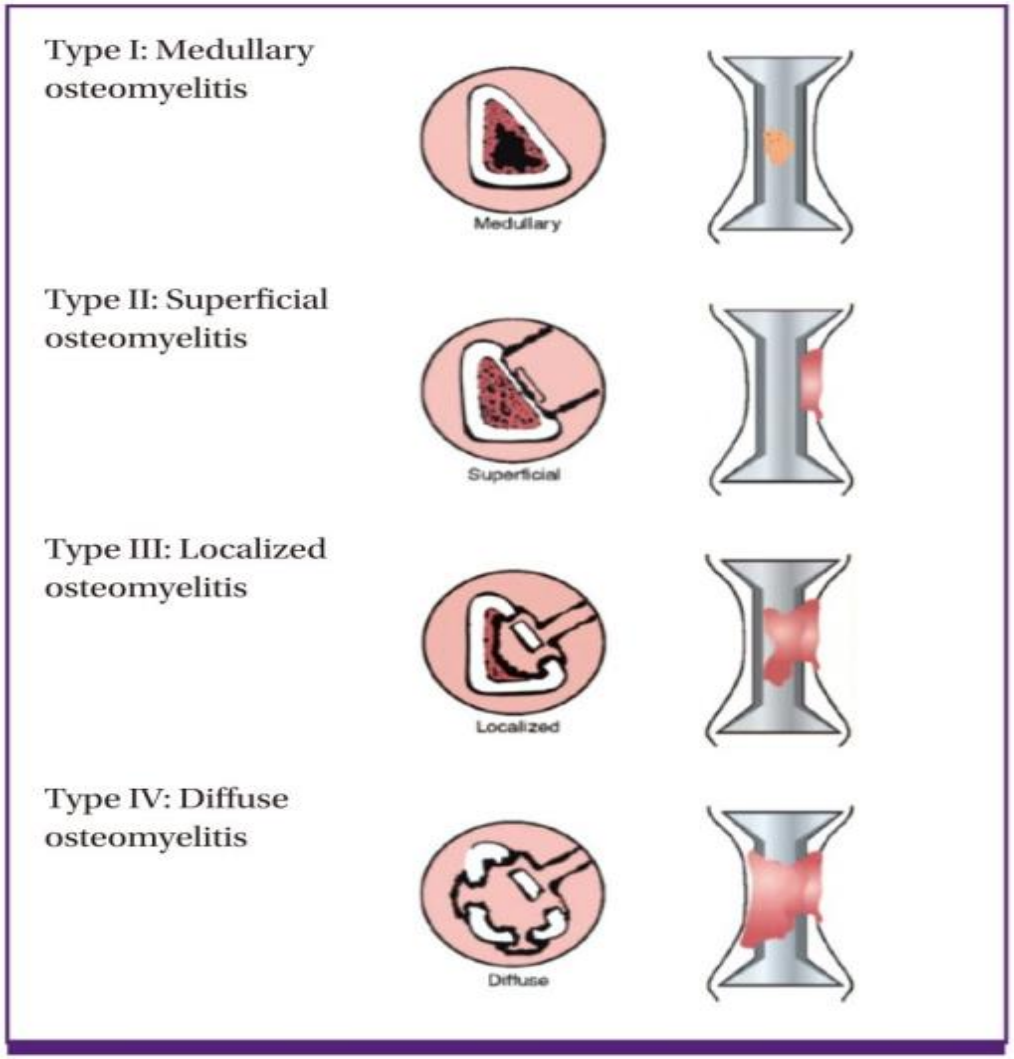
SILVER-COATED VS TITANIUM MEGAPROSTHESES

- 51 pts, silver-coated megaprosthesis
  - proximal femur, n = 22; proximal tibia, n = 29
- 74 pts , uncoated titanium megaprosthesis
  - proximal femur, n = 33; proximal tibia, n = 41
- The infection rate
  - 17.6% in the titanium group
  - 5.9% in the silver group
- 38.5% of pts in the titanium group with infection had amputation



Hardes et al, *J Surg Oncol* 2010

CIERNY & MADER CLASSIFICATION



Anatomic type

Type 1	Medullary osteomyelitis (nidus is endosteal). No dead space management. Etiology often hematogenous, post-intramedullary rod.
Type 2	Superficial Osteomyelitis. Limited to surface of bone. No dead space management but needs soft tissue coverage
Type 3	Localized osteomyelitis. Full thickness of cortex. Complex dead space management, simple osseous stabiliization
Type 4	Diffuse osteomyelitis. Circumference of cortex. Biomechanically unstable. Complex dead space and osseous management.

Physiologic host

A Host	Normal host. Normal immune system. Normal vascularity.
B Host	Bs: systemic compromise Bl: local compromise Bsl: systemic and local compromise
C Host	Treatment morbidity worse than present condition with low prognosis for cure.

THE CLASSIC

A Clinical Staging System for Adult Osteomyelitis

George Cierny III, MD; Jon T. Mader, MD; and Johan J. Penninck, MD

Jon Terry Mader (Fig 1) was born on March 21, 1944 in Madison, WI. He earned his BA and MD degrees at Wabash College at Indiana University in 1966 and 1970, respectively. He trained in Internal Medicine at the University of Texas Medical Branch in Galveston, TX and made his career there in the Division of Infectious Disease in the Department of Internal Medicine. At the time of his death on October 25, 2002, he had risen to the positions of Professor of Medicine, Professor of Pathology, and Adjunct Professor of Orthopaedic Surgery. During his life, he published more than 145 peer-reviewed papers on osteomyelitis, antibiotic therapy, hyperbaric oxygen, joint infections, the foot in patients with diabetes, and the use of the Ilizarov technique for the treatment of musculoskeletal infections. He also was the principle investigator in numerous funded research projects and the coauthor of Musculo-Skeletal Infection. He died when the book was in its final stages of production.

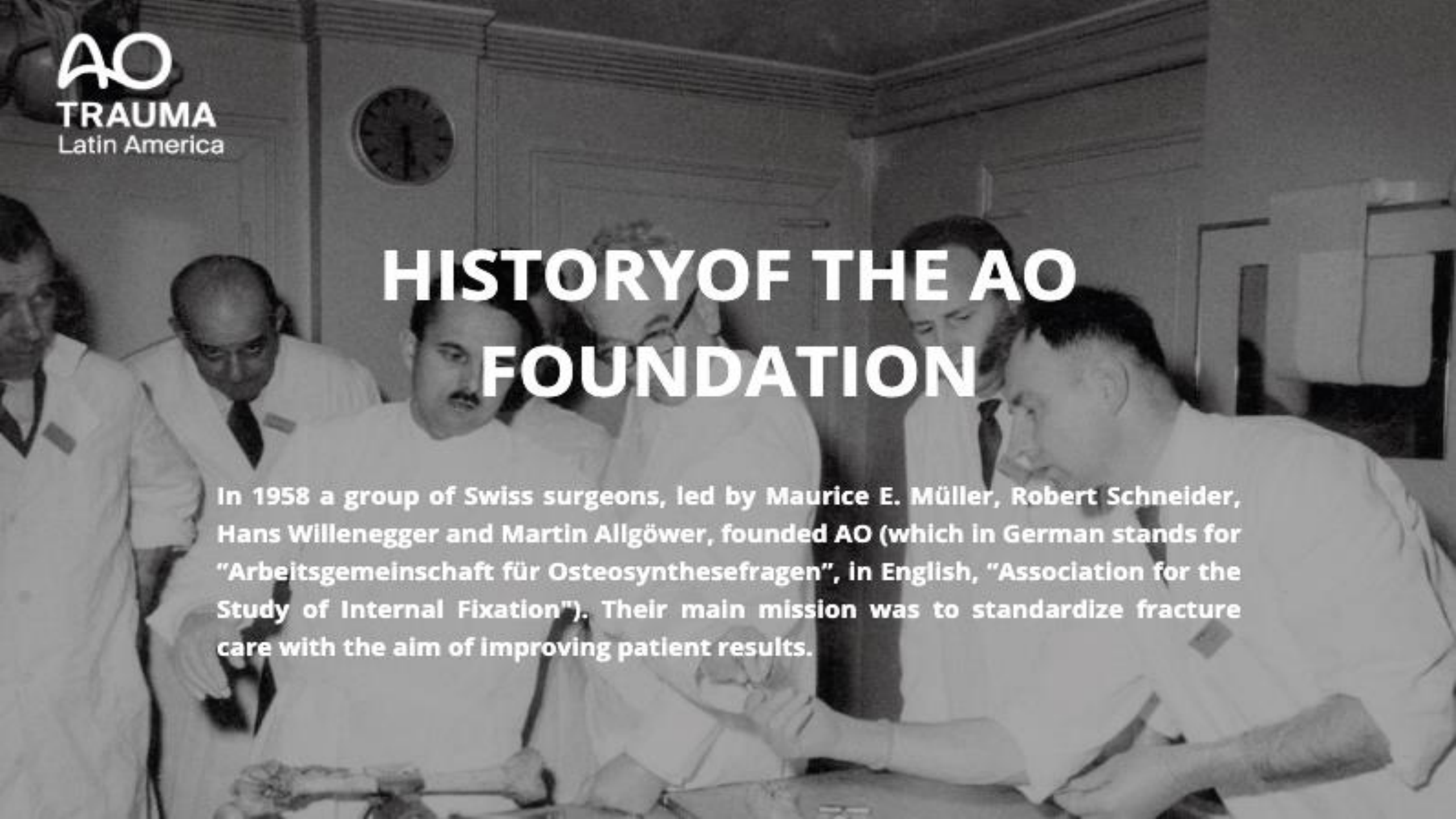
In addition, Dr. Mader was a gifted athlete, Eagle Scout, captain in the U.S. Naval Reserve, and regarded with respect and affection by his patients and colleagues.

Henry H. Sherk, MD

Cierny G, Mader JT, Pennick H. A clinical staging system of adult osteomyelitis. *Contemp Orthop* 1985, 10:17-37

AO TRAUMA Latin America

HISTORYOF THE AO FOUNDATION



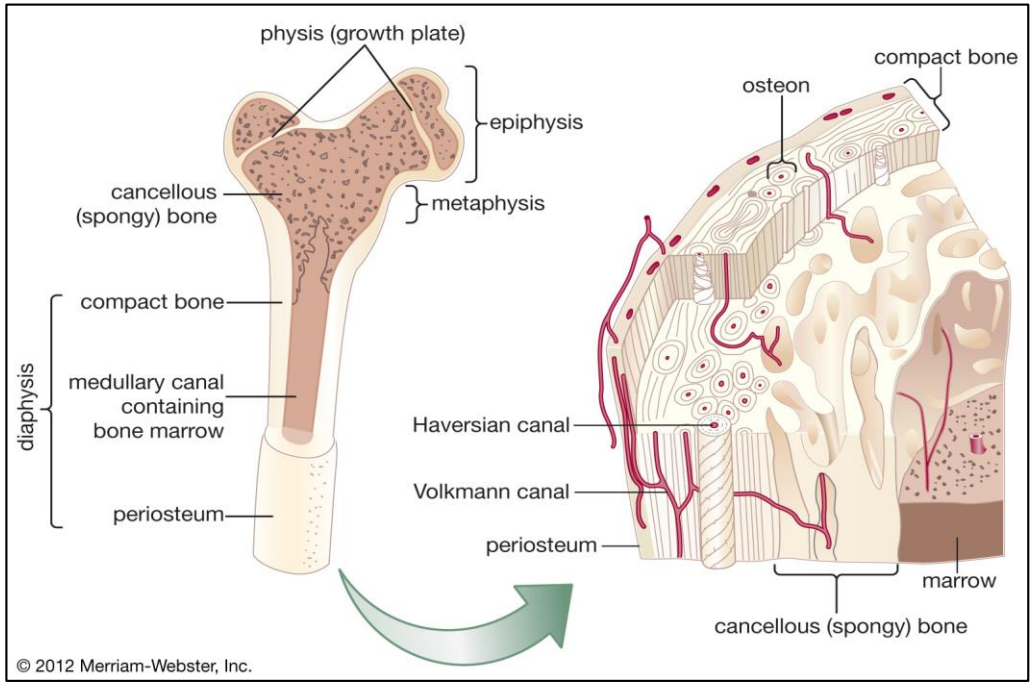
In 1958 a group of Swiss surgeons, led by Maurice E. Müller, Robert Schneider, Hans Willenegger and Martin Allgöwer, founded AO (which in German stands for "Arbeitsgemeinschaft für Osteosynthesefragen", in English, "Association for the Study of Internal Fixation"). Their main mission was to standardize fracture care with the aim of improving patient results.

AO Principles

“ Any necrotic and avascularized tissue must be debrided, in order to prevent the formation of biofilm…”

Antibiotics
Immune cells

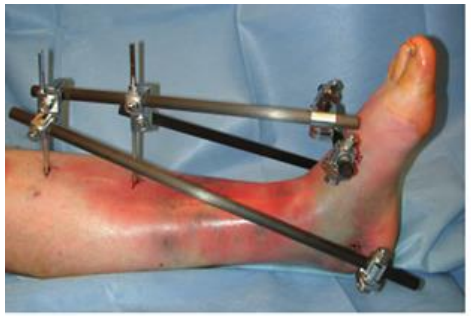
“ Vital muscle and periosteum must be preserved and left in contact with the bone, so that antibiotics reach the site…”



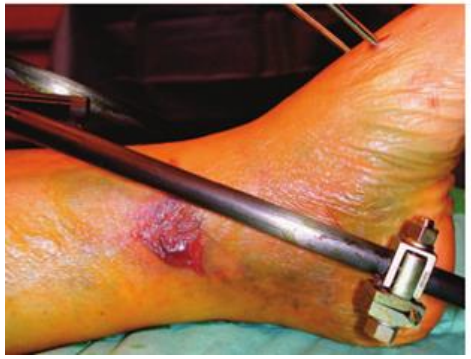
AO Principles

envelope

" Consider soft tissue damage and cover (envelope)…A fracture is considered a soft tissue injury plus bone discontinuity…" → **Timing !**



Closed fracture with severe soft-tissue injury, joint-bridging external fixator



Skin wrinkling after 7 days

PJI after planned surgery = 0.1-2%
FRI after fracture fixation = 1-5%

(BF Klinikum, Hamburg, Osteomyelitis)

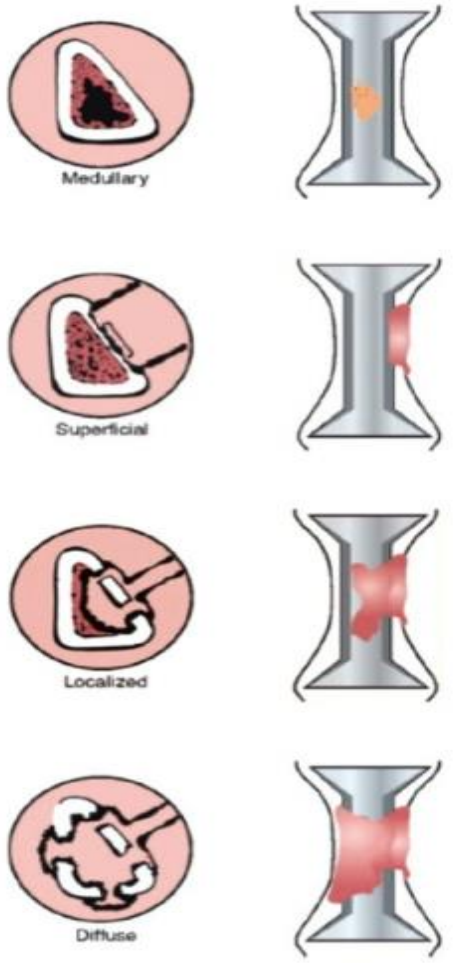
AO Principles

FRI : 1. ORIF → Plating

Bone fragments devascularization

→ least invasive approach

✓ Subcutaneous Vs Submuscular/subfascial



2. Intramedullary nailing

Endosteal necrosis, diaphyseal osteomyelitis, septic pseudarthrosis, purulence from fracture site

3. External fixation

Pin track infection, ring sequestra from high energy drilling

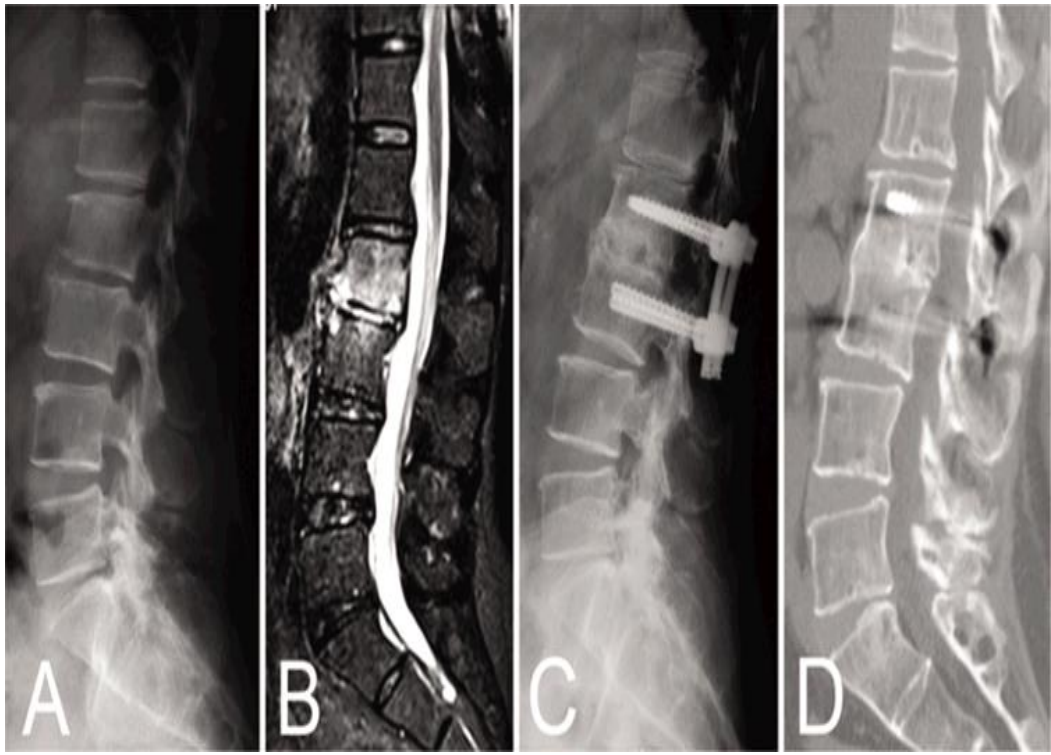
AO Principles

Instability

"In case of FRI the primary goals are :
1. fracture fixation and **2. prevention of chronic osteomyelitis…"**

"Administration of antibiotics without concomitant surgery fails to eradicate the infection…"

Instability ⇌ Infection

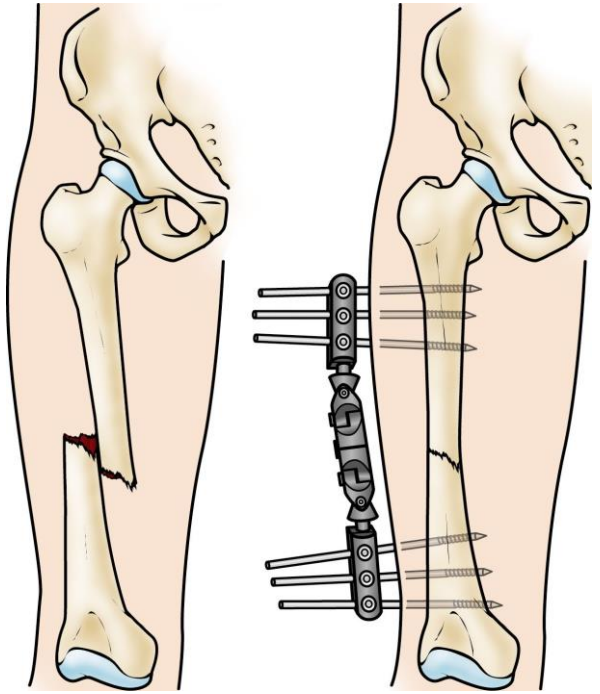


J Neurosurgery, Spine vol. 23

AO Principles

Stabilization

1. Initiation of fracture healing
2. Functional patient aftercare
3. Easier wound care
4. Stability for soft tissue healing
5. Maintains or restores length, alignment and rotation
6. Early weight bearing



AO Principles

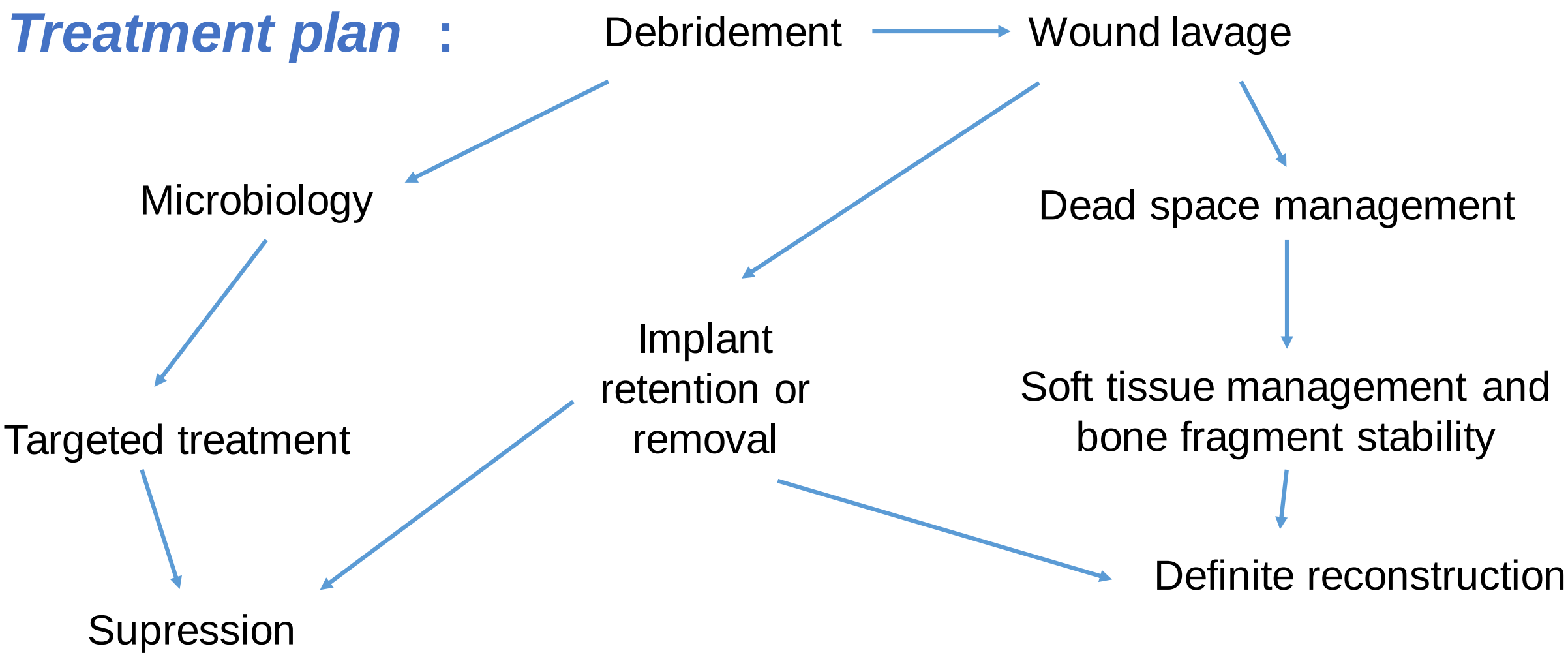
hematoma

“Early infections need to be distinguished from wound dehiscence and necrosis of the wound edges as well postoperative hematoma…”

”A painful or fluctuating hematoma requires immediate drainage and debridement…”

“Time is tissue…”

AO Principles



AO Principles of Fracture Management _ Acute and chronic infections (2017)

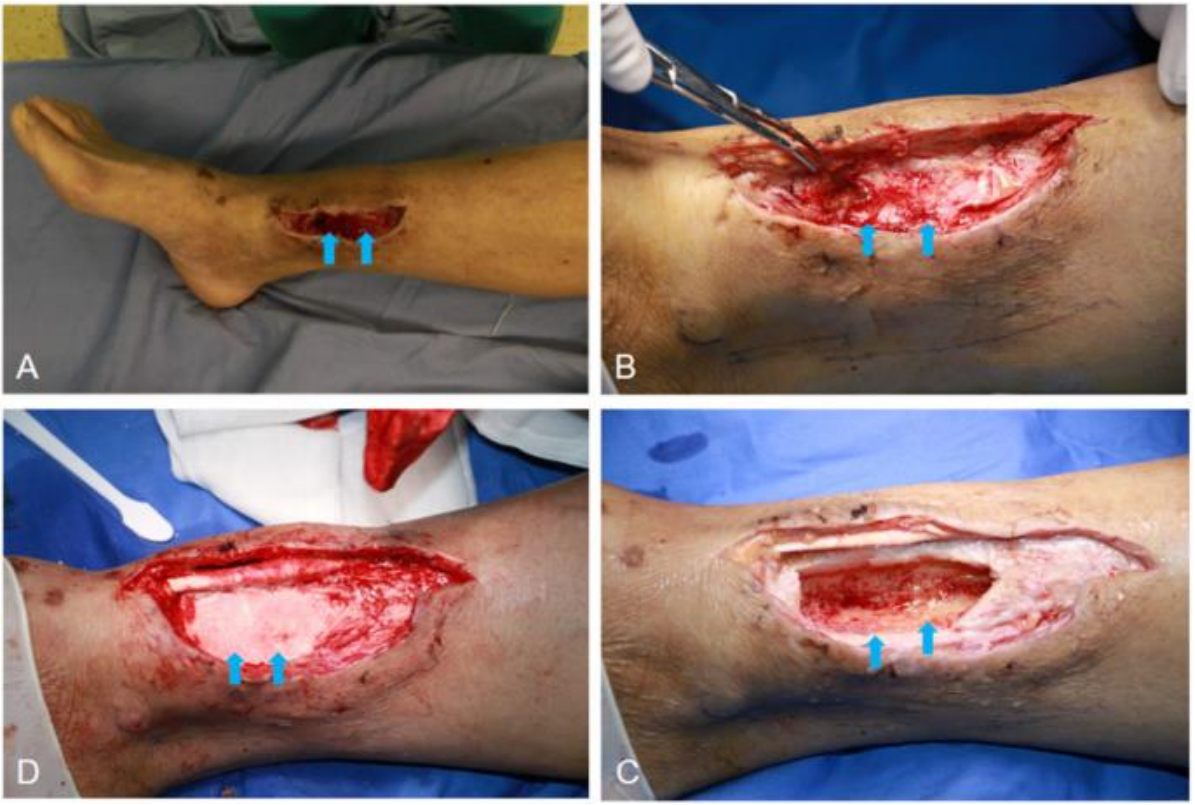
AO Principles

Debridement

1. In case of a sinus → infuse methylene blue
2. Excise skin wound margins
3. Remove hematoma
4. Abscess membrane
5. Excessive granulation tissue removal
6. Necrotic and devascularized tissue
7. Dead bone splints and sequestra (paprika sign)
8. Tissue sample from bone-implant interface
9. Rigorous surgical site irrigation → reduce cfu 10^6
10. 2nd debridement and irrigation after 24-48h → 10^6
11. Wound closure over suction drain or
    negative pressure wound treatment or cement beads
12. In case of bone loss → antibiotic loaded cement spacer

AO Principles

Debridement



AO Principles

Implant retention in FRI

”The entire implant should be considered infected with a biofilm covering through its entire length, width and depth…”

“Fracture healing will not take place in presence of infection without mechanical stability…”

Stable implant

- **YES → Retain until bridging → Supression**
- **NO → Remove and Ex-Fix → Eradication**

AO Principles

Infected Intramedullary nails

Nail

Retain , if stable / bridging / sensitive micro → In the end remove nail and ream

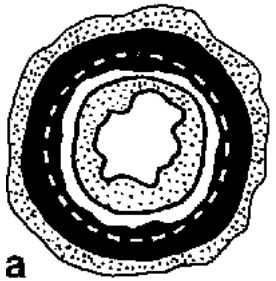
Remove and ream the canal 0.5-1.5mm to a distal opening (RIA : Reamer – Irrigator – Aspirator)

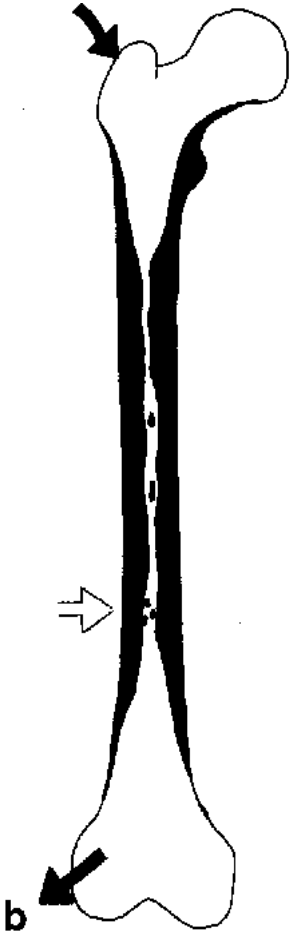
One stage nail exchange

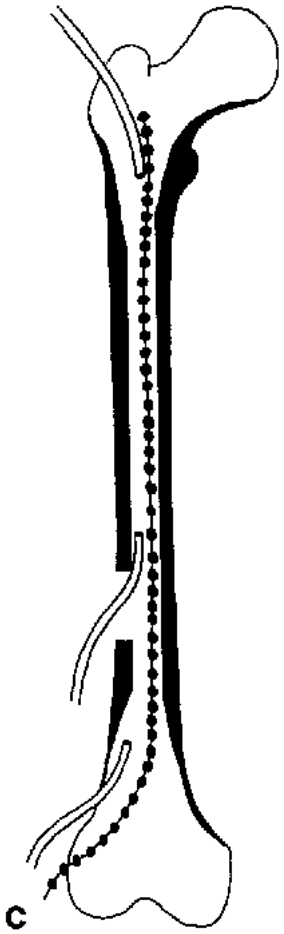
Two-stage nail exchange → antibiotic cement beads / antibiotic loades nail + Ex-Fix

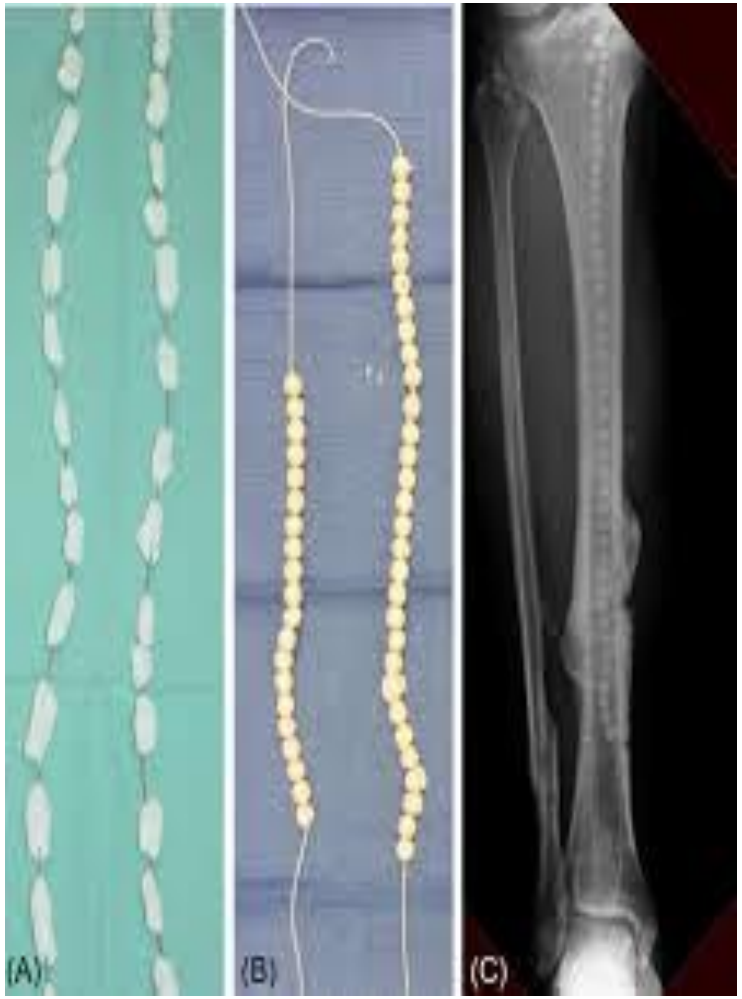
AO Principles

Infected Intramedullary nails



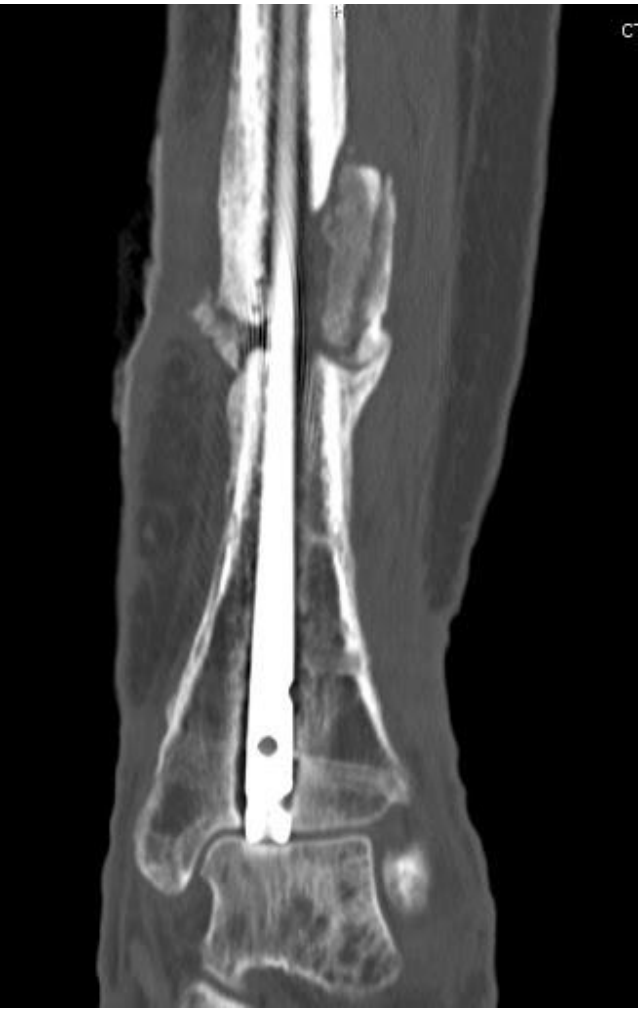


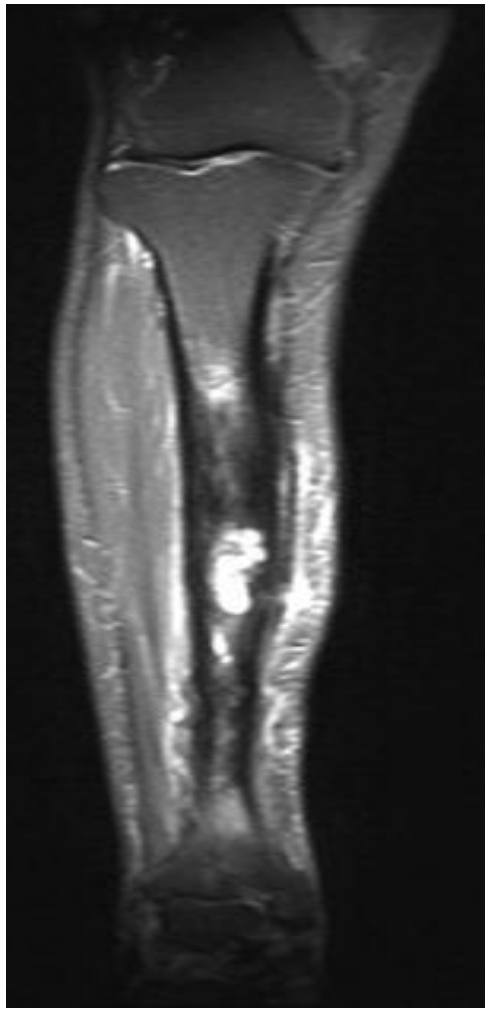


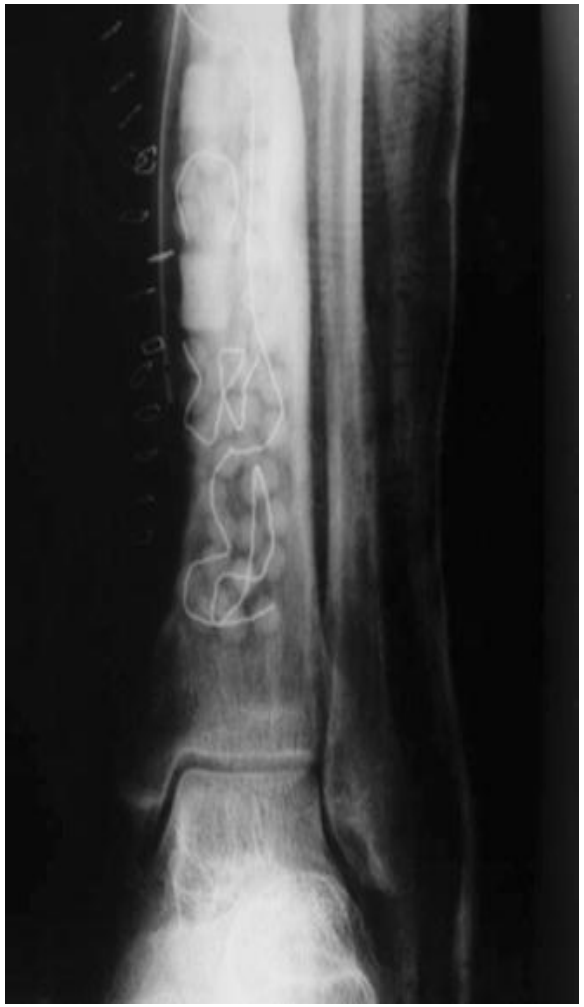


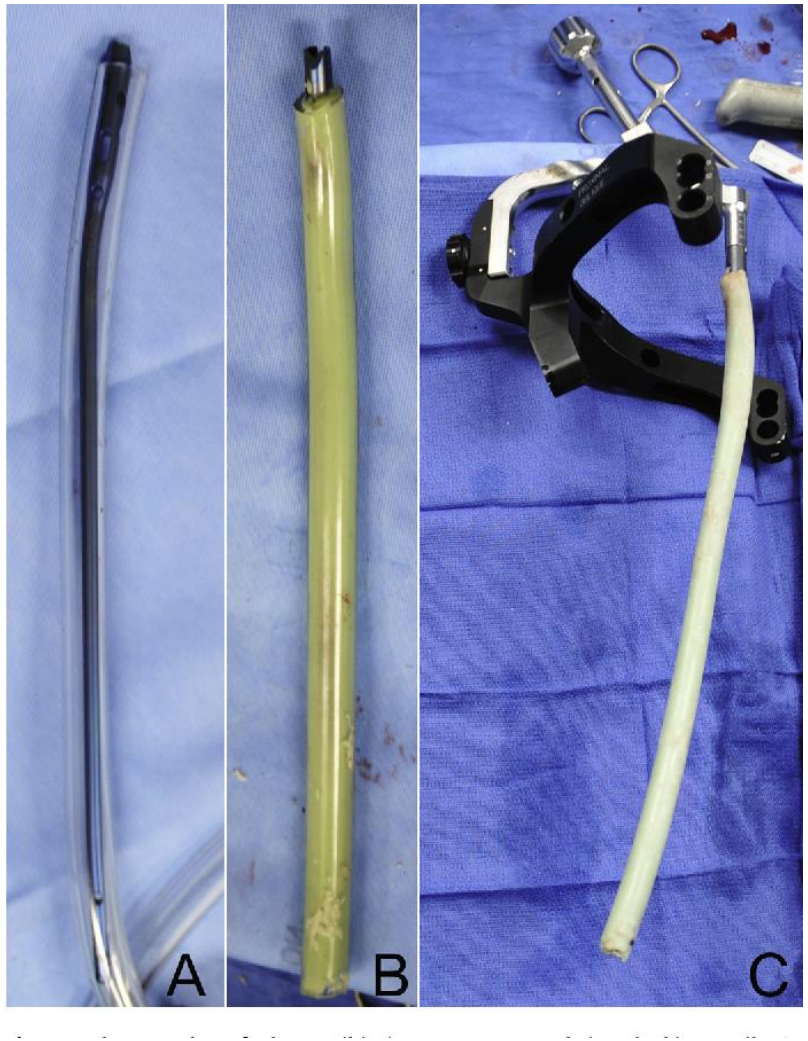
AO Principles

Infected Intramedullary nails





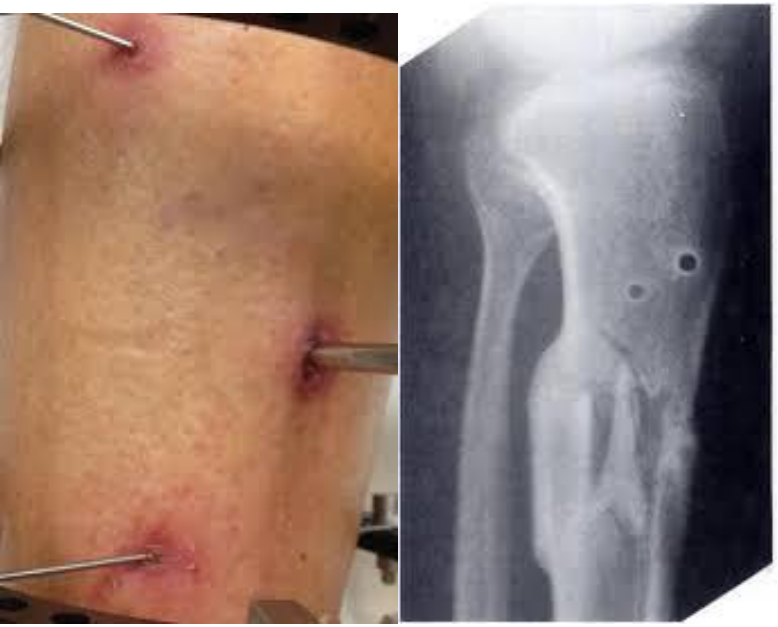




AO Principles

Pin track infection

External fixation → Pin track infection and ring sequestra



Remove and replace the pin
Perform curettage and remove sequestra
Irrigate and take tissue cultures from insertion site
Do not remove the Ex-Fix

AO Principles

Bone defects

Defect

If < 5-6 cm → Delayed cancellous bone graft (ilium)
✓ sterile biopsy and/or decortication

If > 10 cm

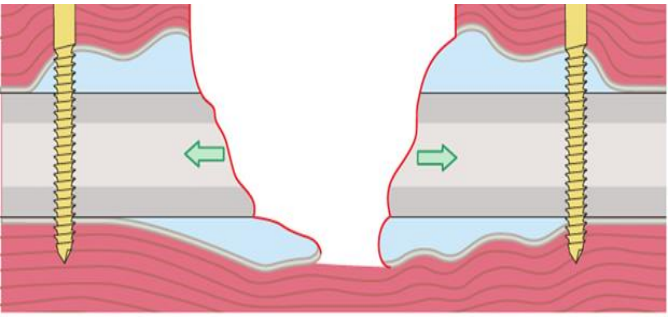
Distraction osteogenesis → allows for correction! (Ilizarov, Taylor frame, etc)

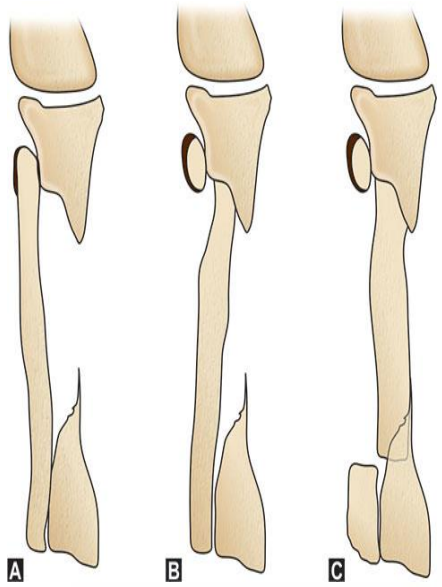
Masquelet technique
(spacer → membrane → late grafting plus nail/plate → 1-2 years

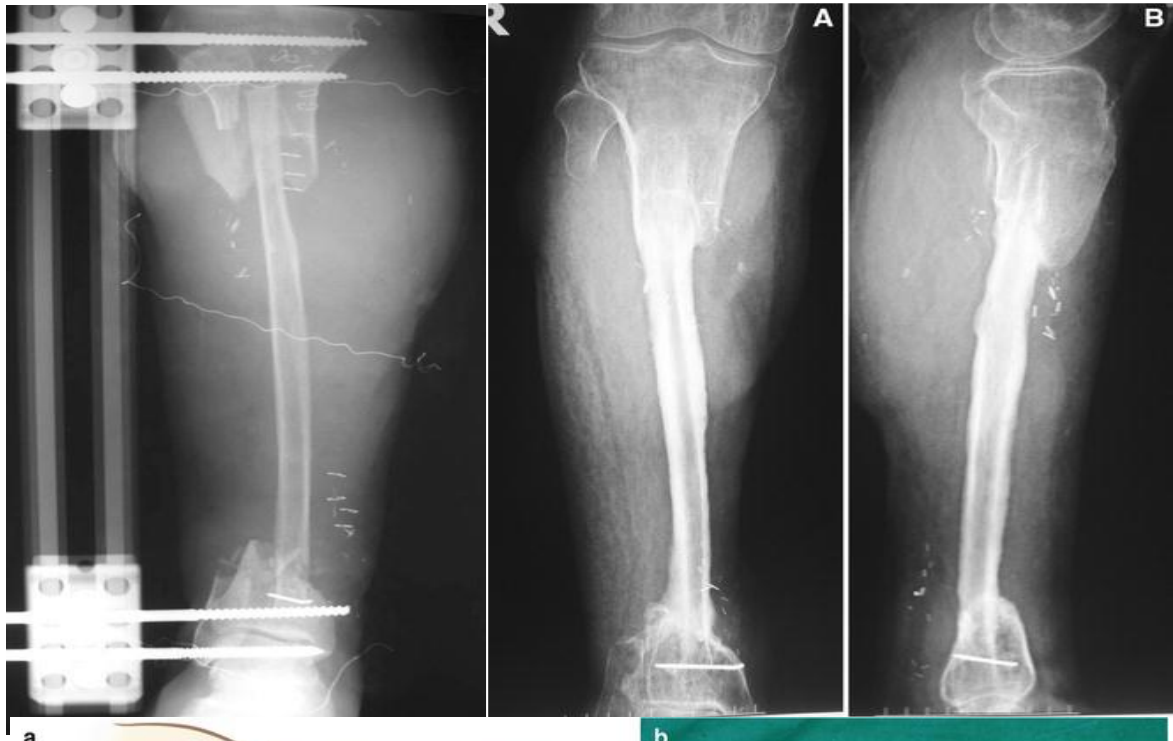
Free vascularized strout graft (Ilium, fibula)

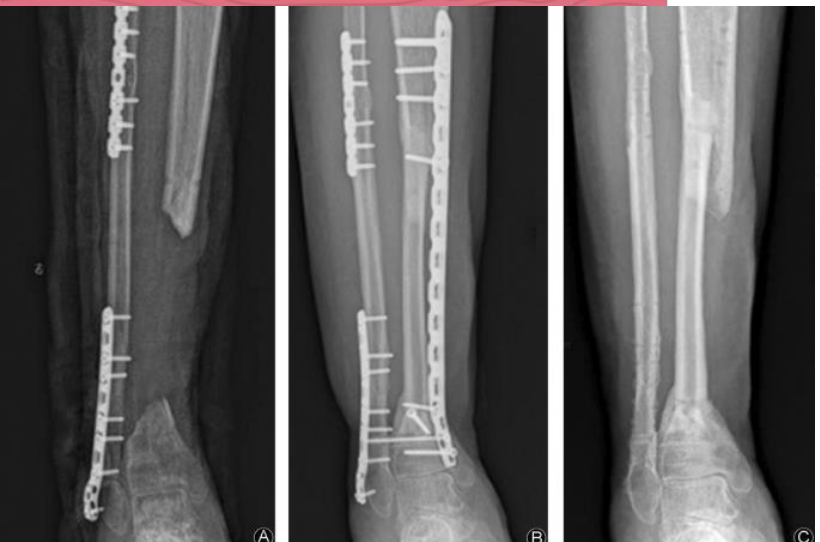
BONE GRAFTING TECHNIQUES

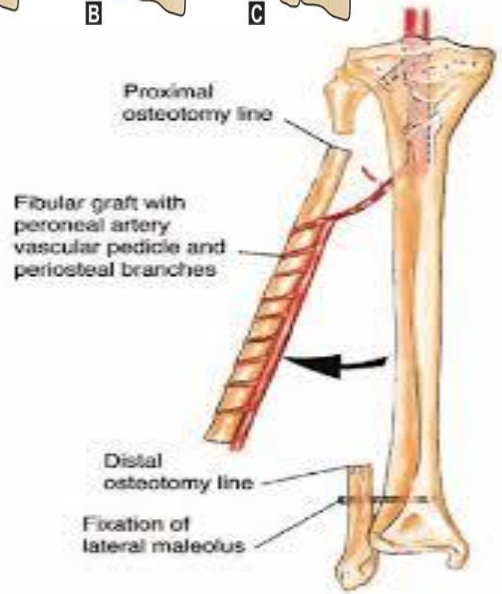
Free or vascularized graft

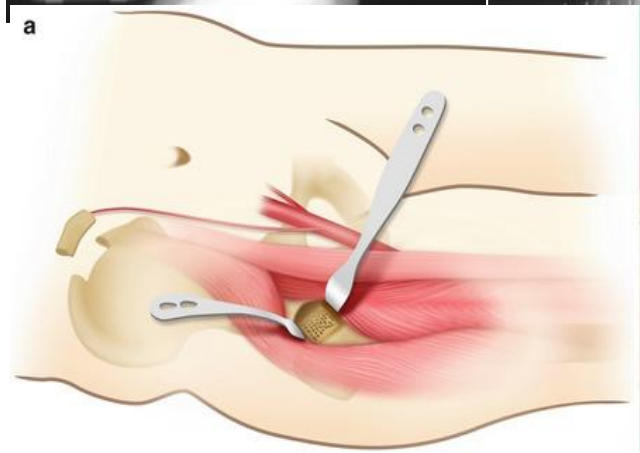


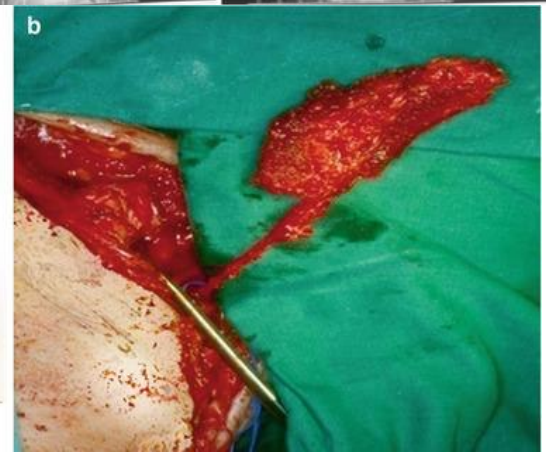






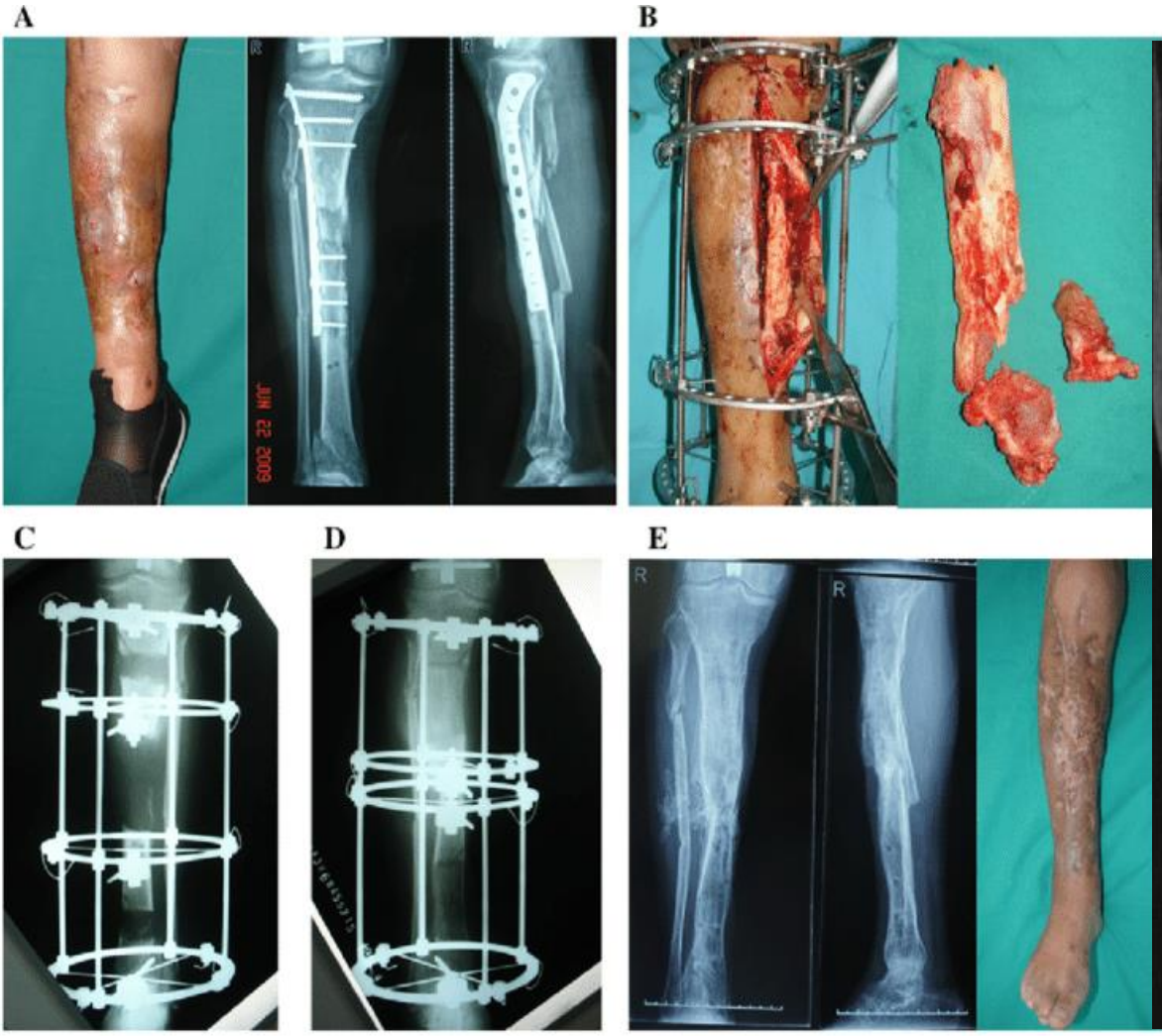


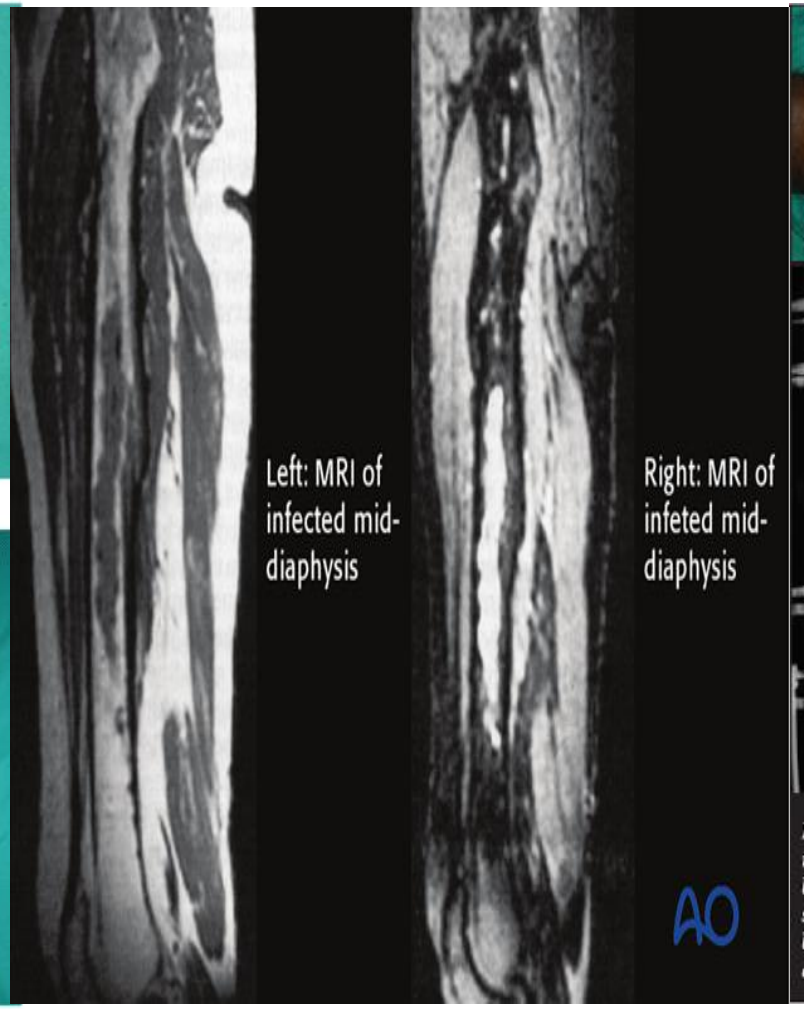




BONE GRAFTING TECHNIQUES

Distraction osteogenesis





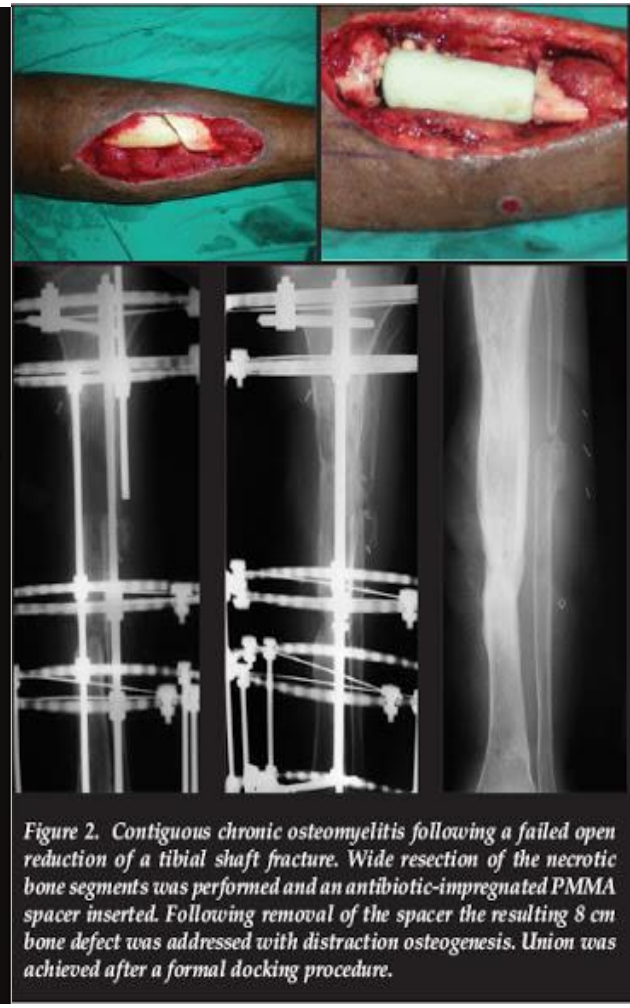
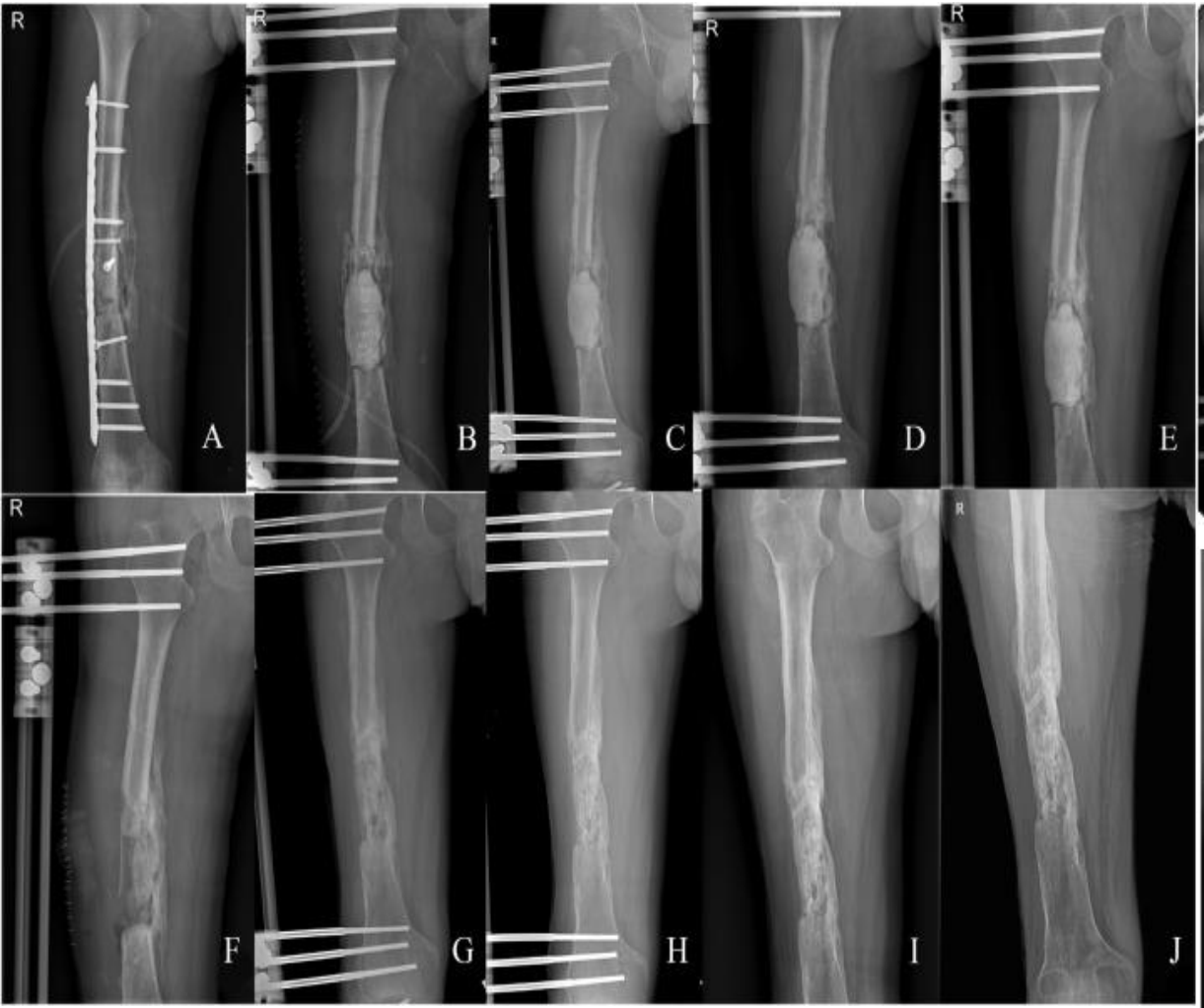
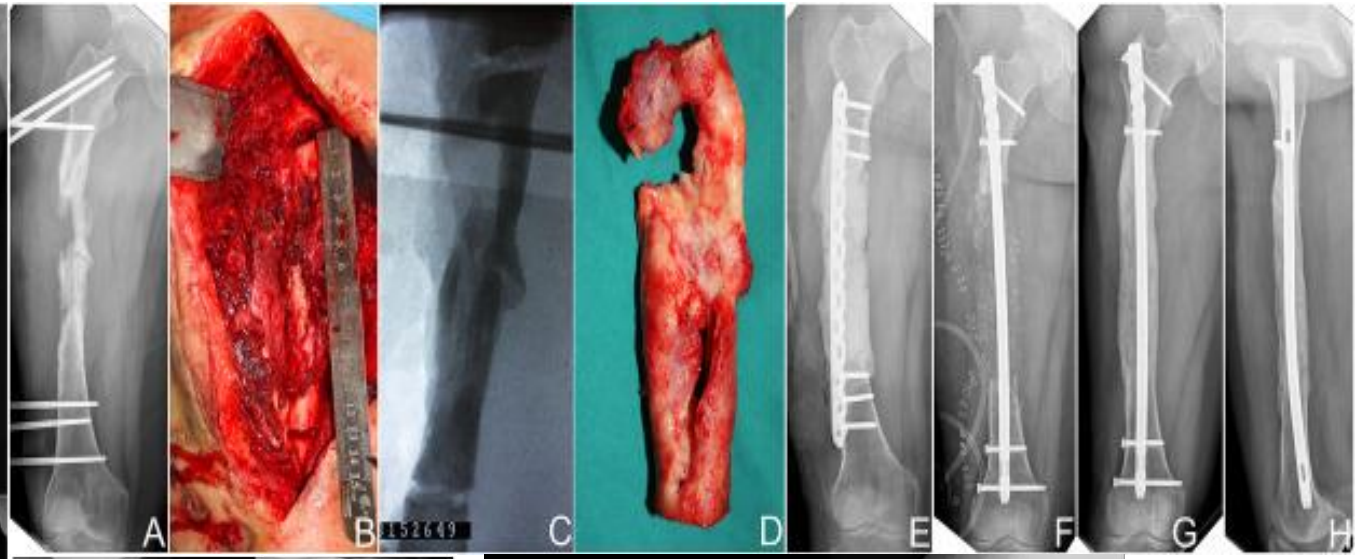


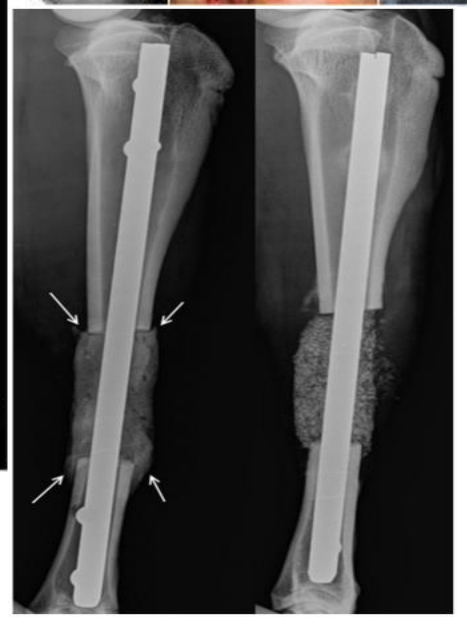
Figure 2. Contiguous chronic osteomyelitis following a failed open reduction of a tibial shaft fracture. Wide resection of the necrotic bone segments was performed and an antibiotic-impregnated PMMA spacer inserted. Following removal of the spacer the resulting 8 cm bone defect was addressed with distraction osteogenesis. Union was achieved after a formal docking procedure.

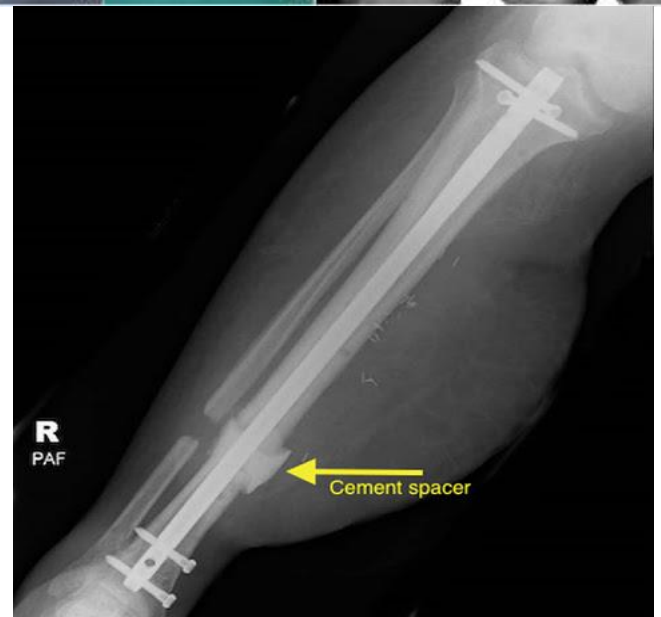
BONE GRAFTING TECHNIQUES

Masquelet technique









AO Principles

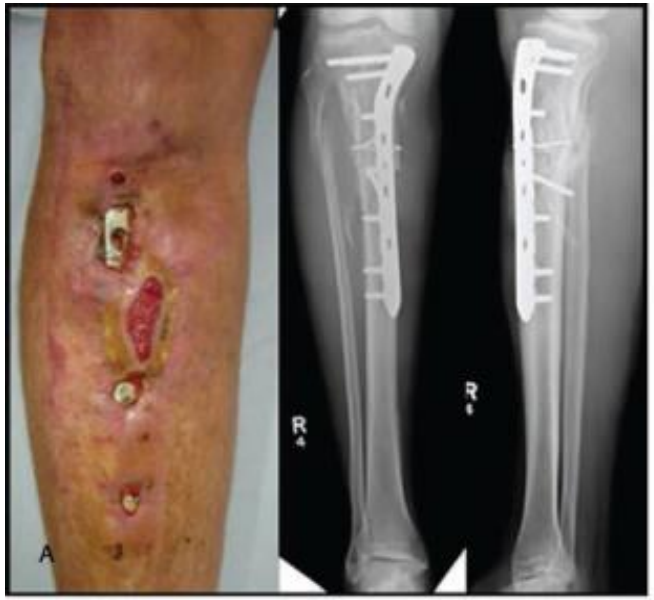
Flaps

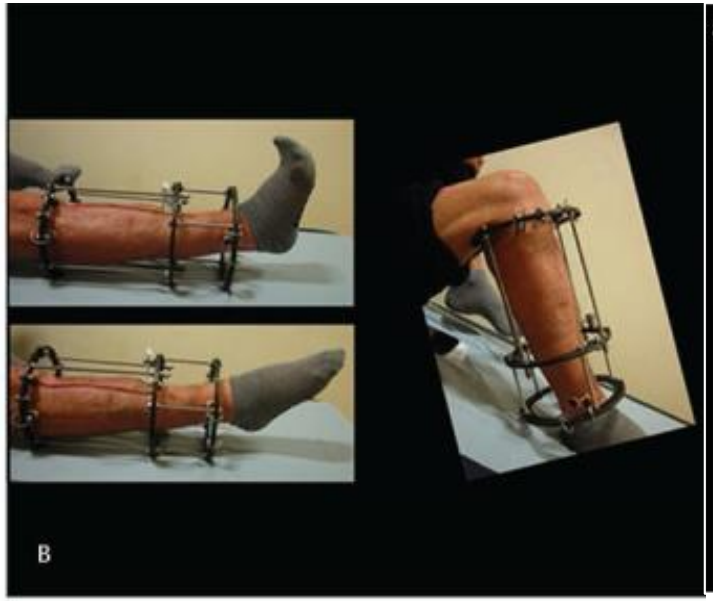
“If a bone graft must be applied, the establishment of healthy soft tissue cover (flap) should precede grafting. Placement of a flap over an infected bed will result in necrosis of the flap…”

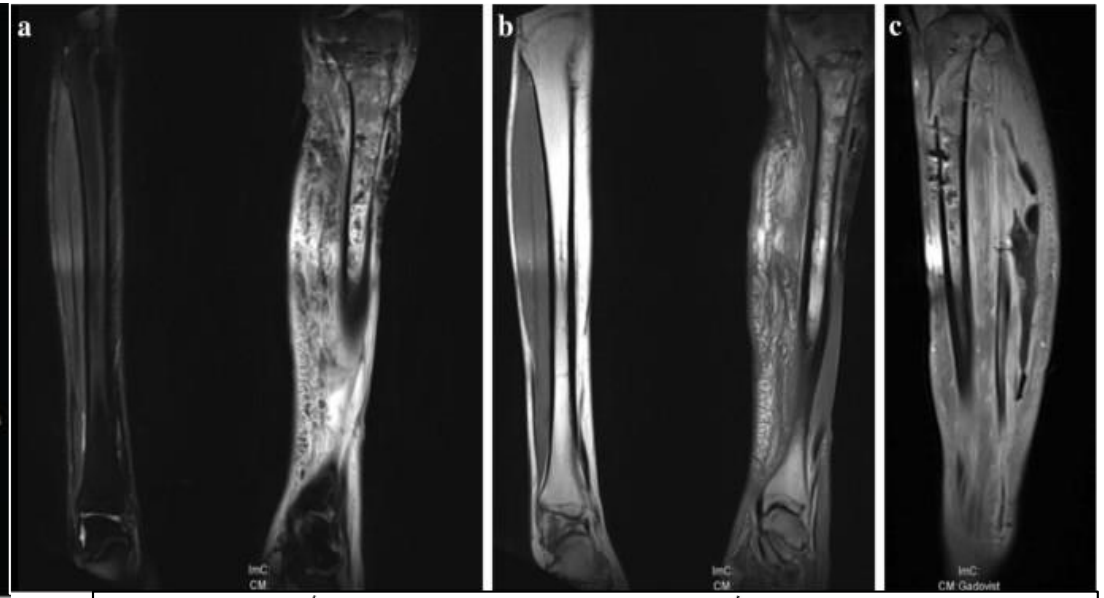
“Negative pressure wound therapy should not be a surrogate for early flap cover…the earliest the better…if successful…”

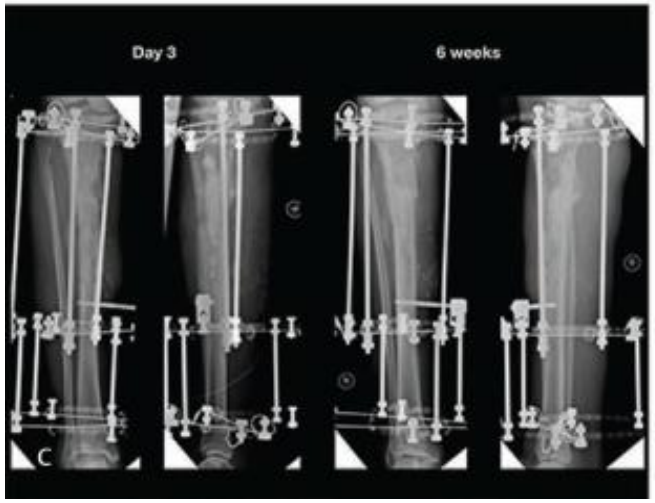
BONE GRAFTING TECHNIQUES

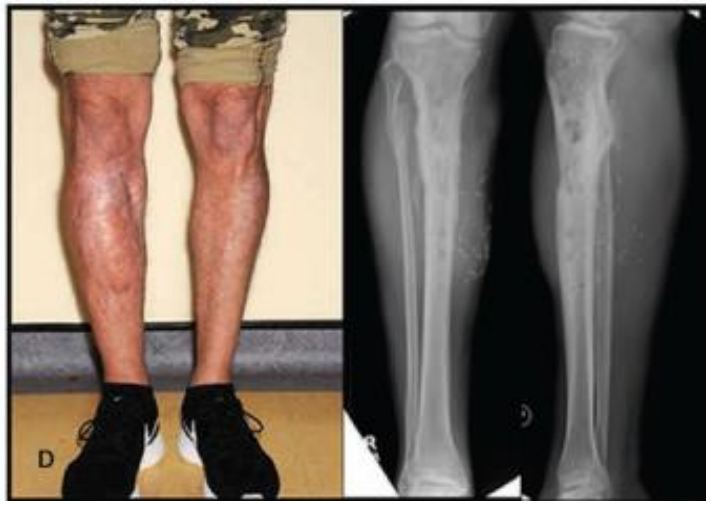
Bone and soft tissue defects

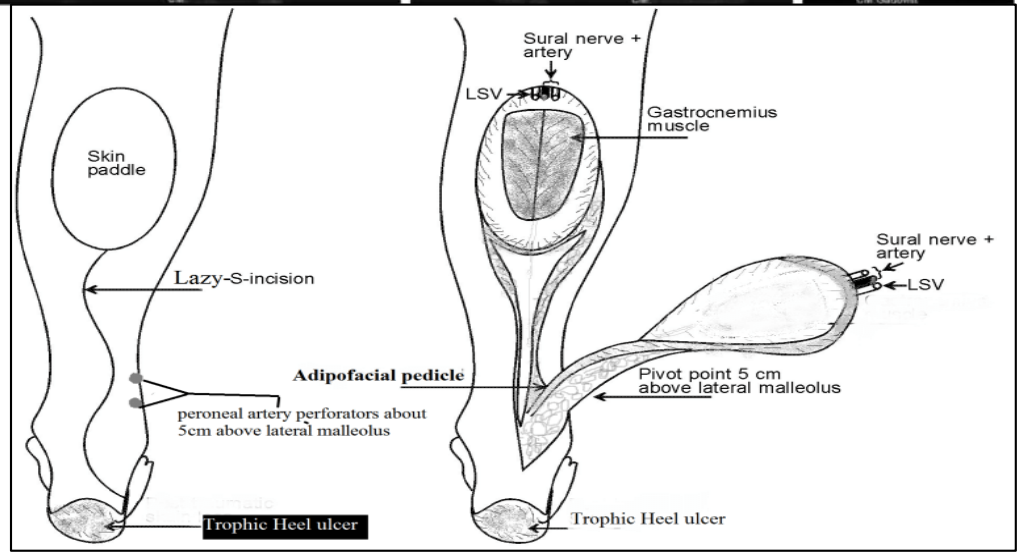




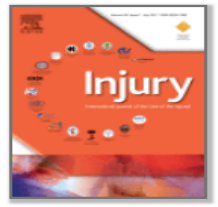








Injury
Volume 48, Issue 7, July 2017, Pages 1616-1622



Full length article

Masquelet technique versus Ilizarov bone transport for reconstruction of lower extremity bone defects following posttraumatic osteomyelitis

Kai Tong [a], Ziyi Zhong [a], Yulan Peng [b], Chuangxin Lin [c], Shenglu Cao [a], YunPing Yang [a], Gang Wang [a]

“In the treatment of segmental lower extremity bone defects following posttraumatic osteomyelitis, both IBT and MT can lead to satisfactory bone results while MT had better functional results, especially in femoral cases. IBT should be preferred in cases of limb deformity and MT may be a better choice in cases of periarticular bone defects.”

BG Klinikum Hamburg

Treatment of osteomyelitis and the reconstruction of bone defects

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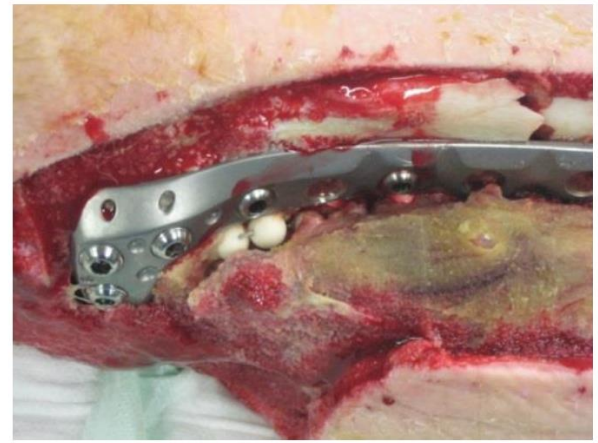
Department of Septic Trauma and Orthopedic Surgery
BG-Unfallkrankenhaus Hamburg
Ärztlicher Direktor: Prof. Dr. C. Jürgens

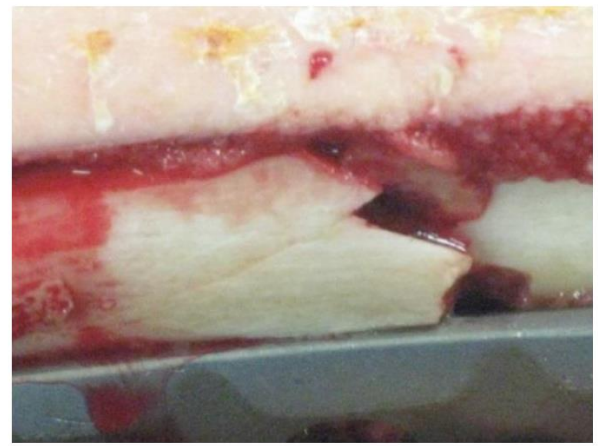
BG Klinikum Hamburg

Osteomyelitis

Primary goal of the therapy:

- long lasting stop of the infection
- closure of soft tissue defects
- reconstruction of bone defects
- stability of the extremity
- an extremity allowing full weight-bearing
- pain reduction
- professional reintegration





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Osteomyelitis

Our therapy/our algorithm: al least 2-stage-surgery

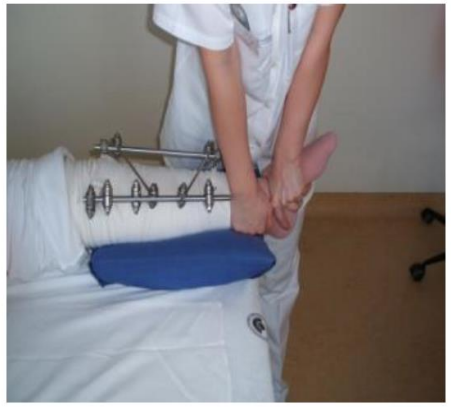
1rst.operative step: treatment of the infection

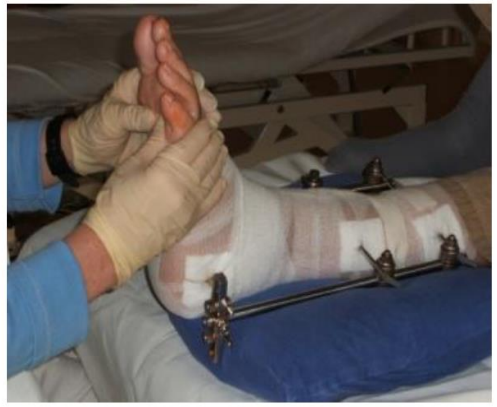
2nd operative step: treatment of the soft tissue defects

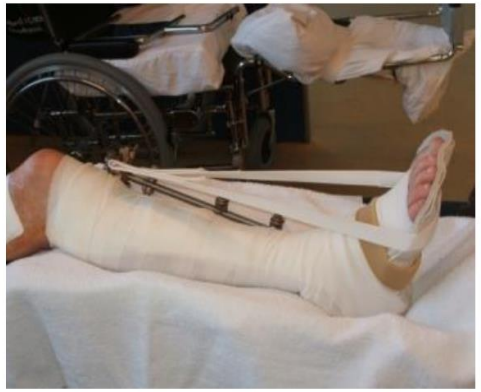
3rd operative step: treatment of the bone defects

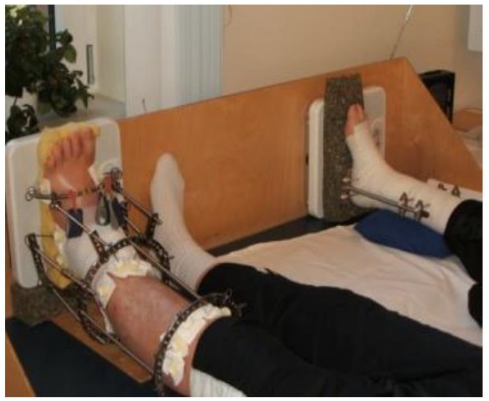
4th step: social and professional reintegration

Physiotherapy all the time!









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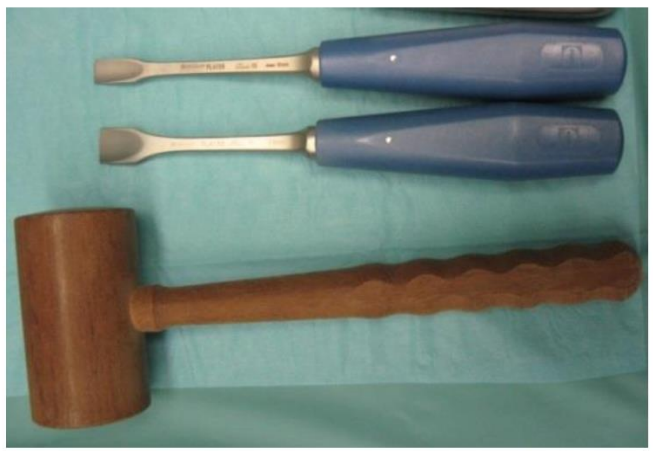
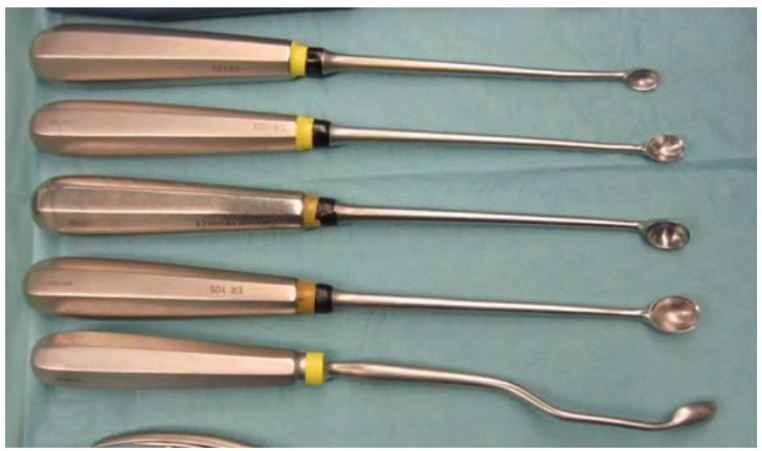
Osteomyelitis

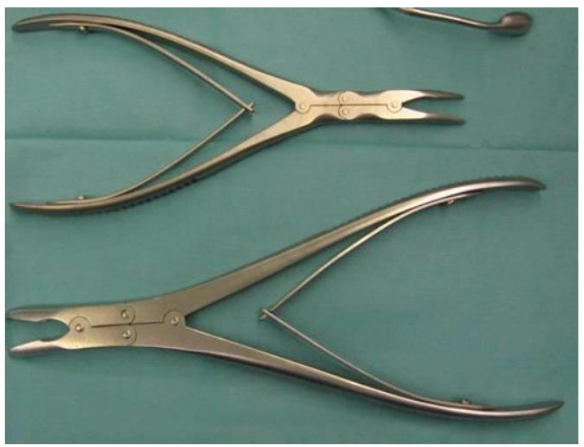
1st operative step:

- removal of every foreign body
- radical sequestrectomy
- implantation of local antibiotic carriers
- stabilization (external fixator)
- short term antibiotic therapy

Important for the successful therapy: radical sequestrectomy !

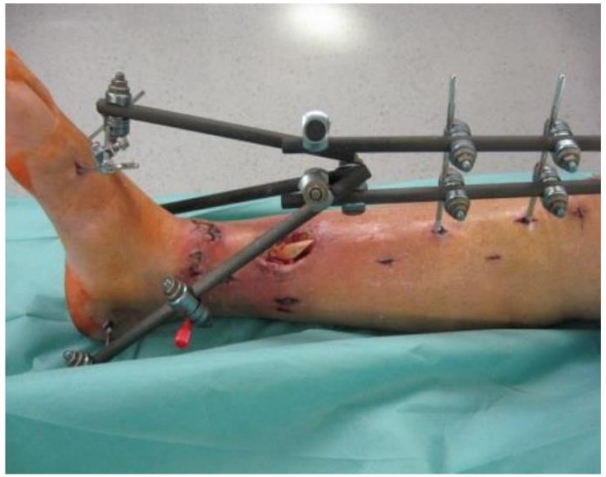


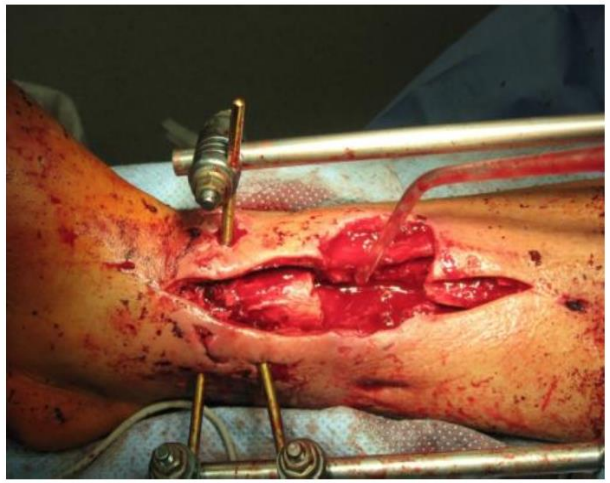


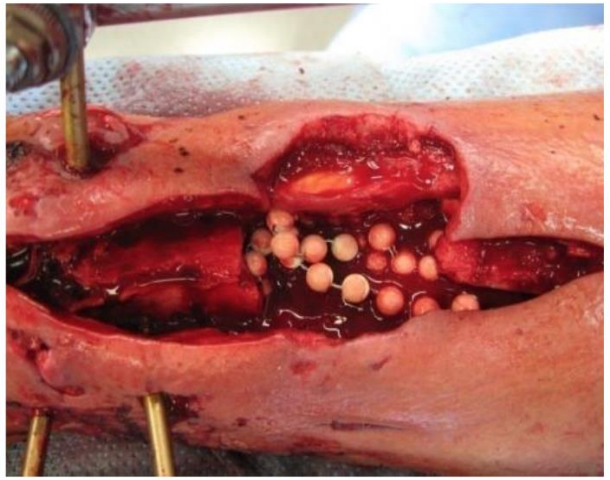


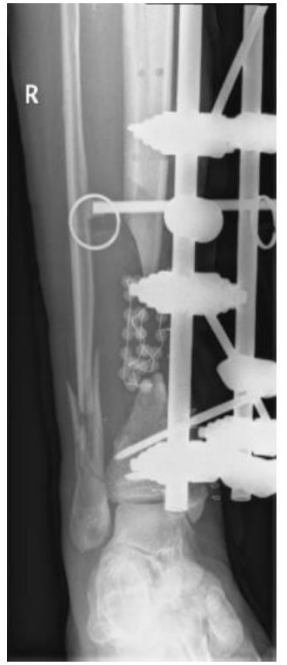
BG Klinikum Hamburg

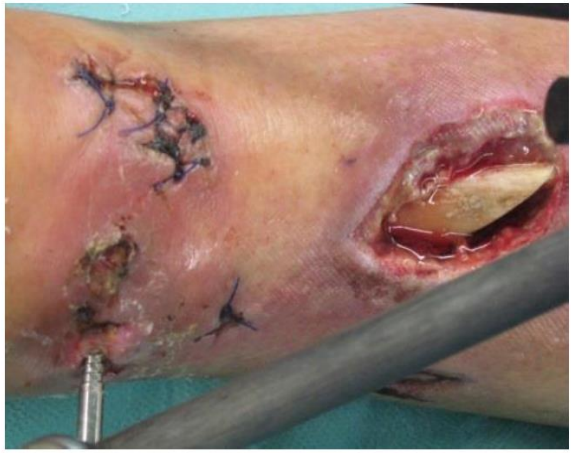
Osteomyelitis

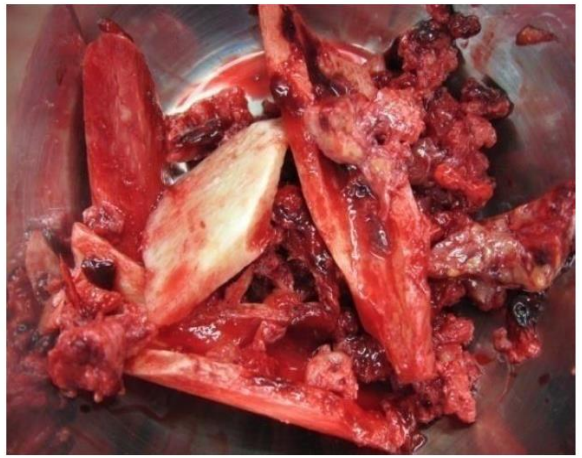


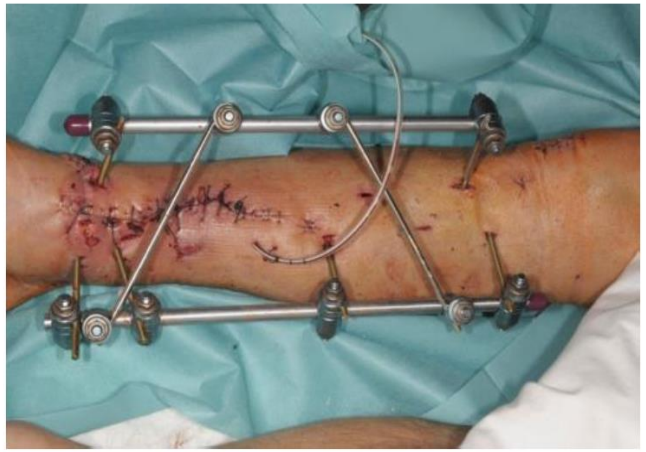


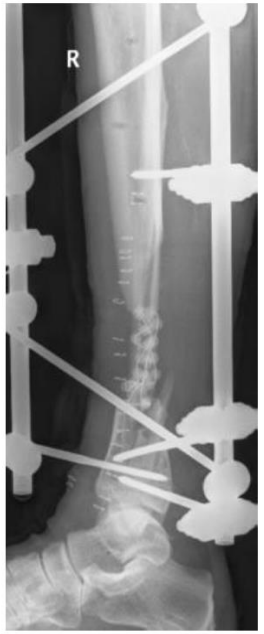












BG Klinikum Hamburg

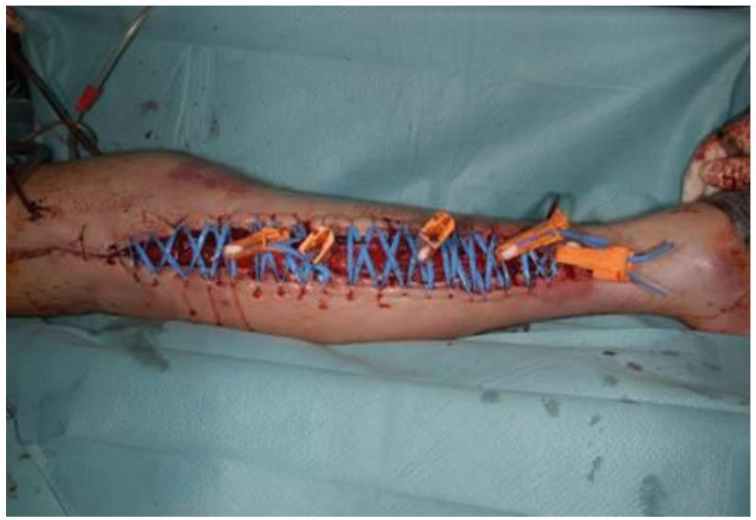
Osteomyelitis

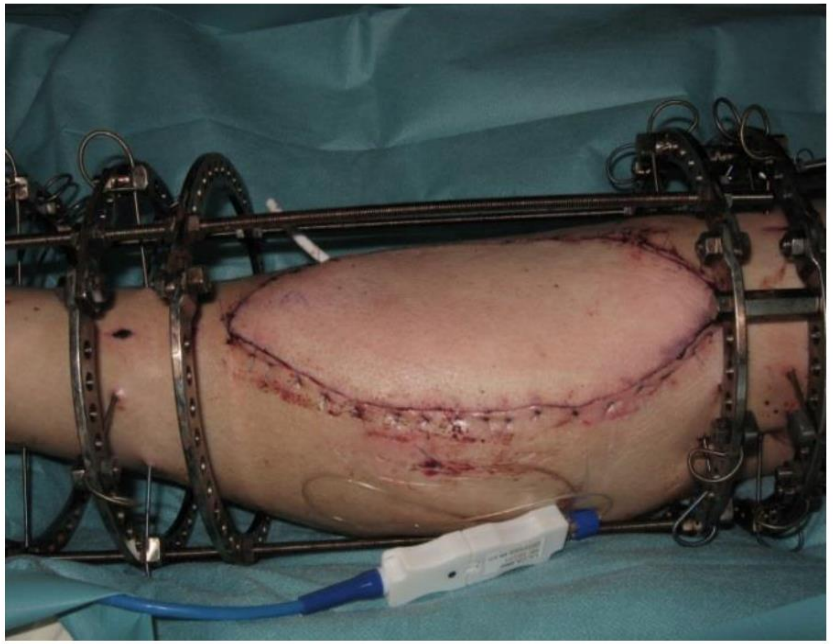
2nd operative step:

Treatment of soft tissue defects

- as early as possible
- as stable as possible

- Co-operation with plastic surgeons in case of large defects
- Split skin, dermato-distraction, free flap





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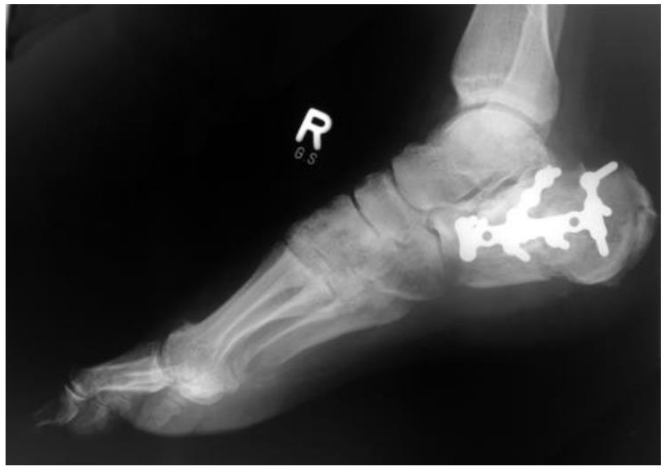
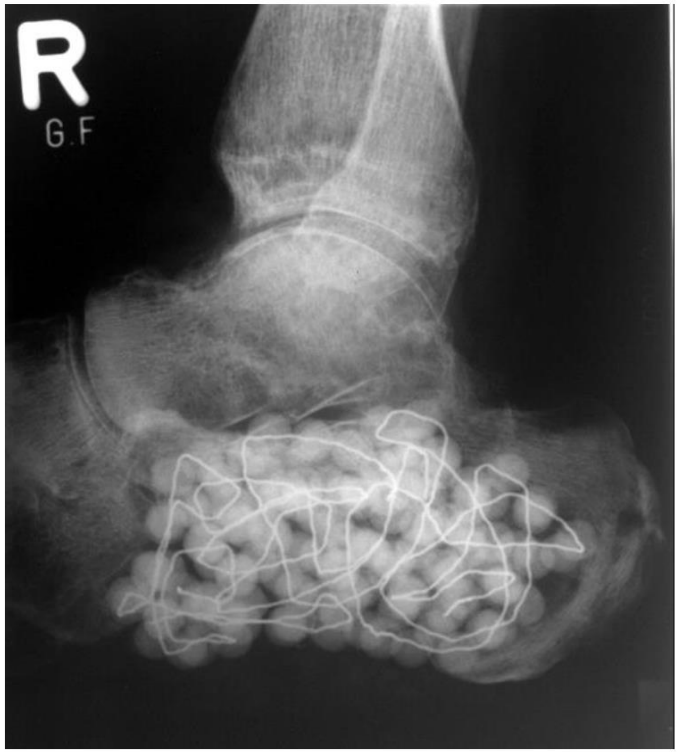
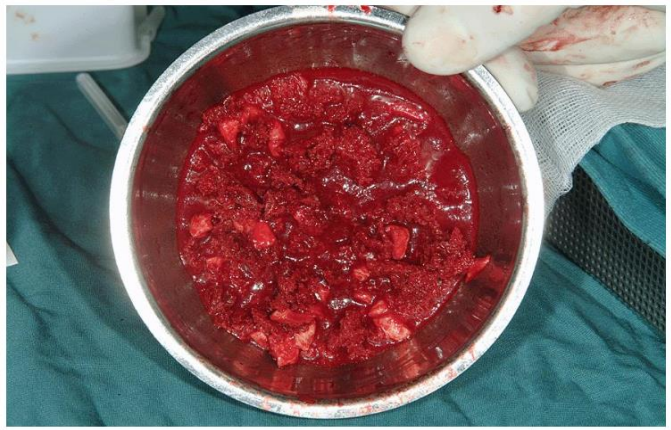
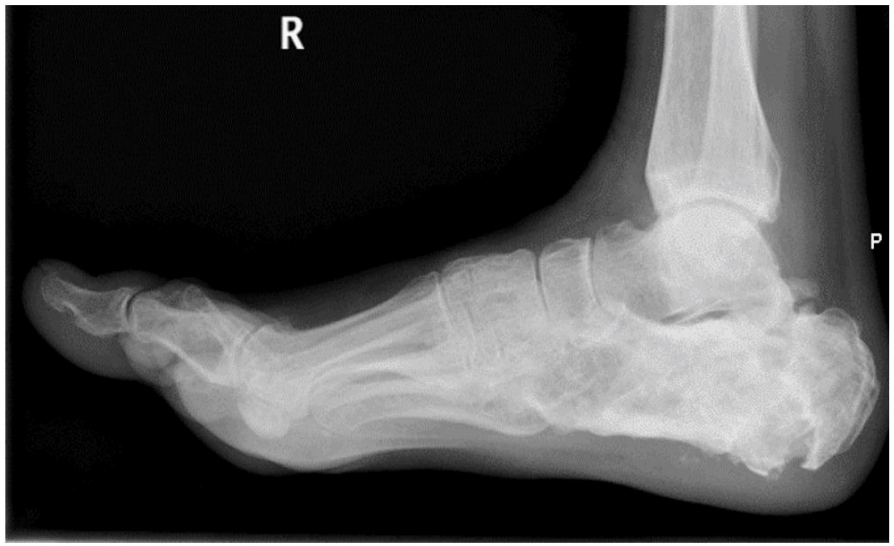
Osteomyelitis



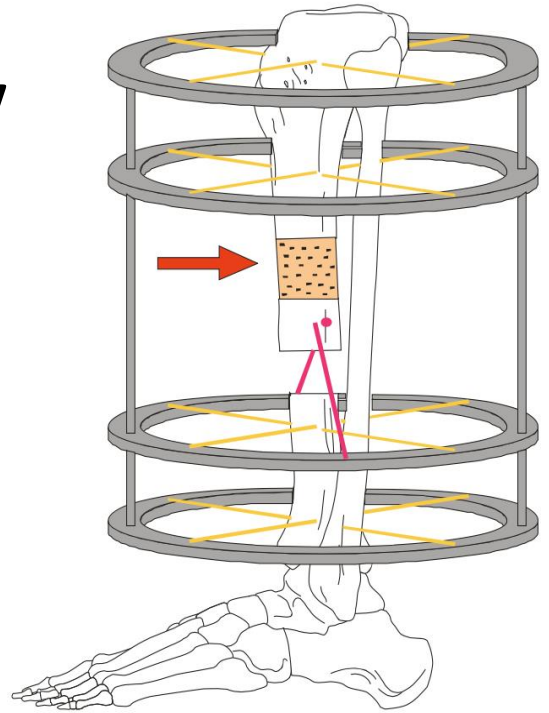


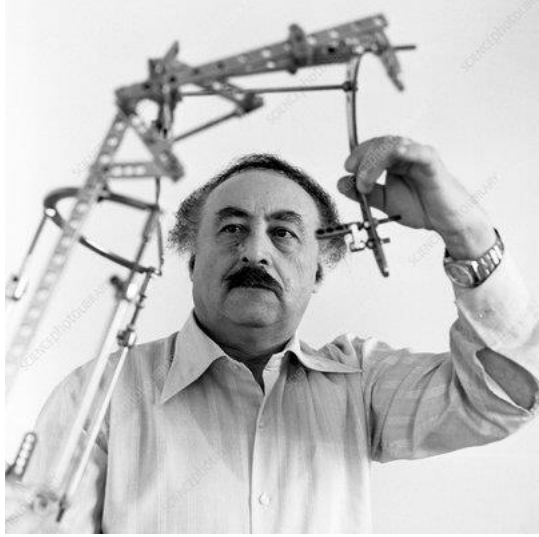


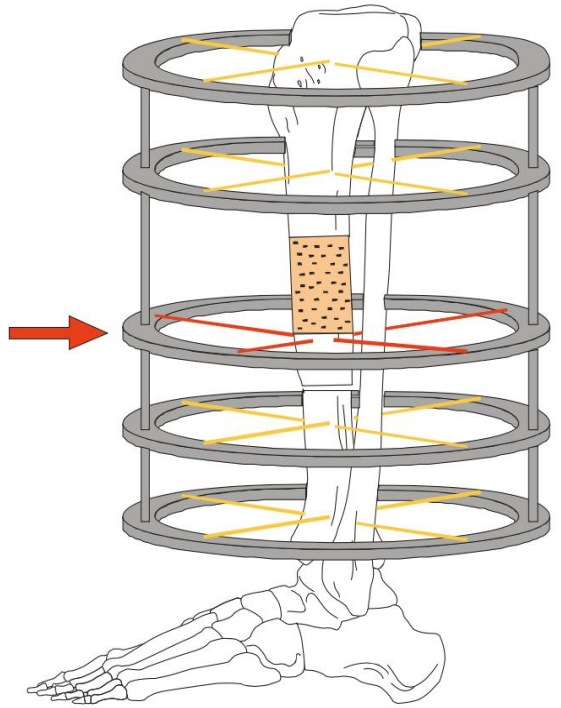


BG Klinikum
Hamburg

Dr. Gavril Ilizarov







The Taylor frame

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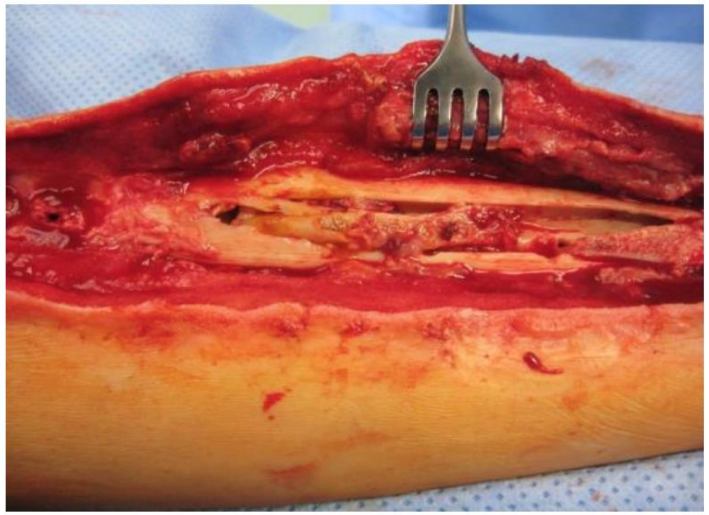
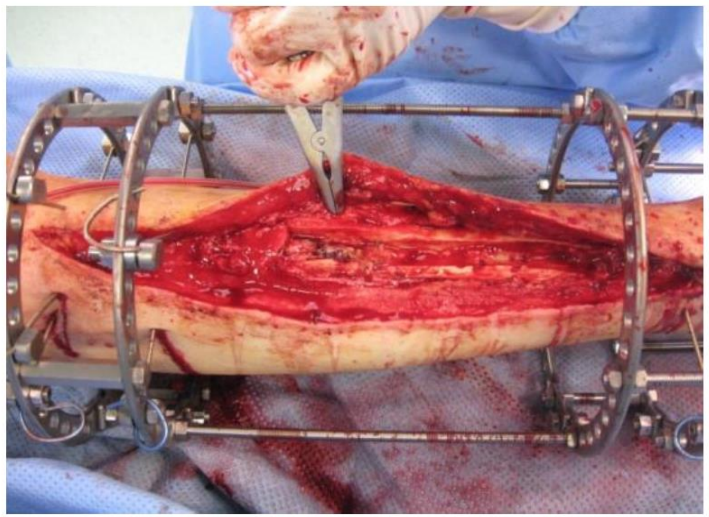
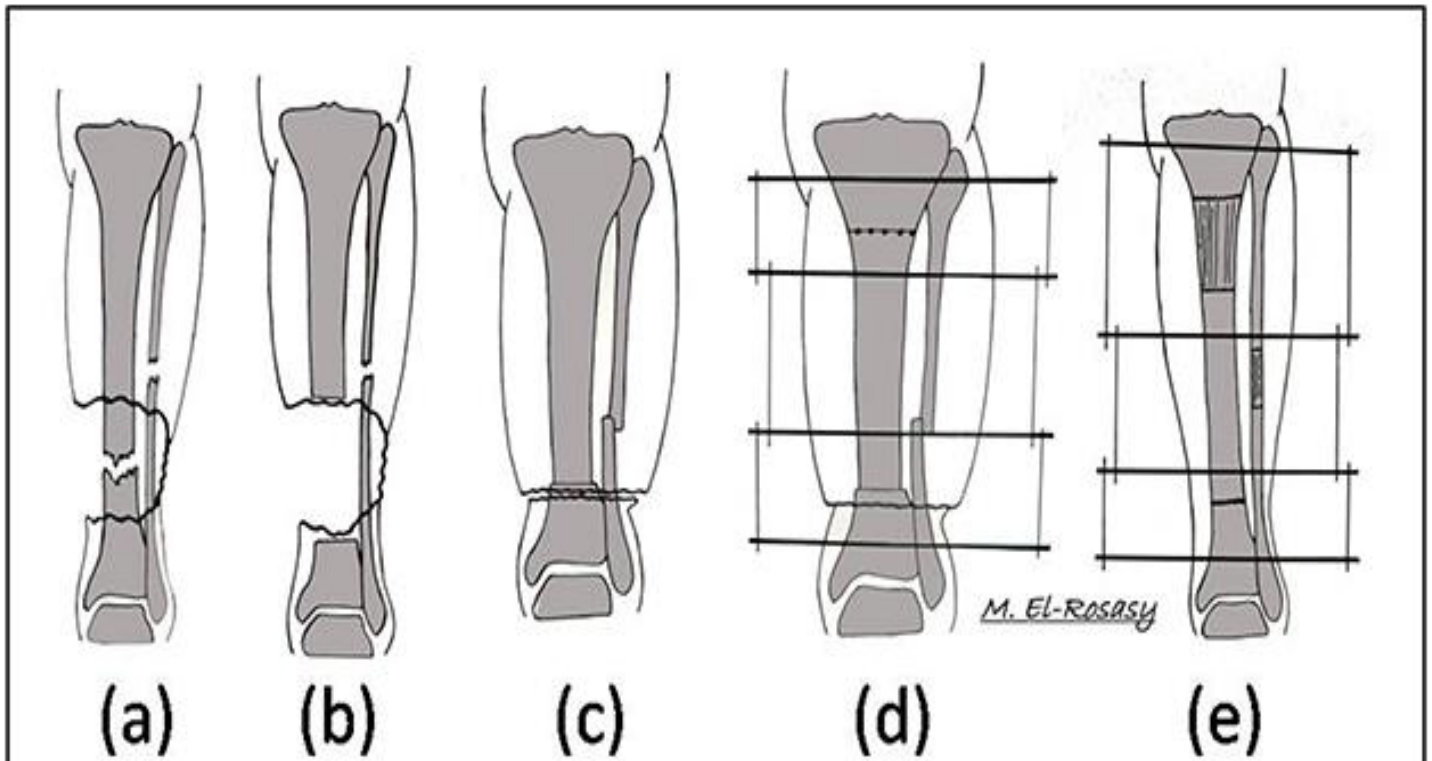
Osteomyelitis







Technique of acute limb-shortening and re-lengthening:
(a) soft tissue defect with exposure of bones; (b) resection of infected and dead tissues with the result of osteocutaneous defect, (c) acute limb-shortening to close the defect; (d) application of external fixator and metaphyseal lengthening osteotomy; (e) limb lengthening to restore length.

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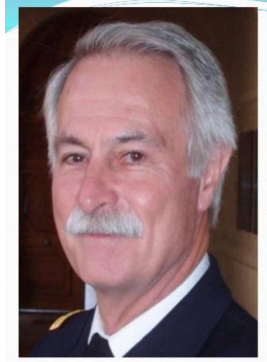
Osteomyelitis



Alain Masquelet

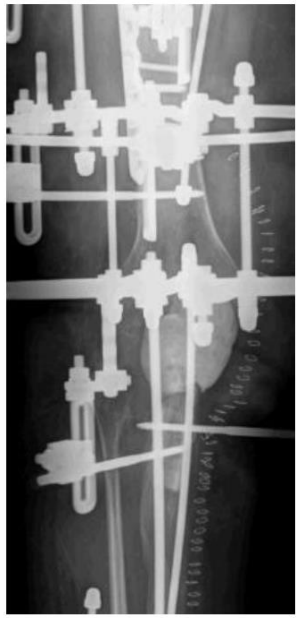
Ortopedista frances
Profesor Adscrito de la Universidad de Paris
Equipo de cirugia de Hospital Universitario de Avicena Paris .

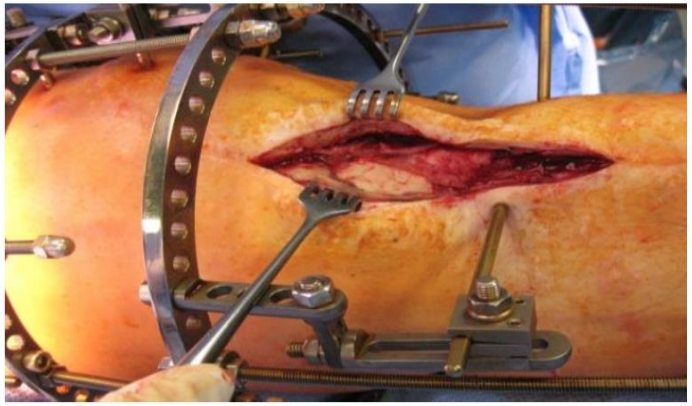
Masquelet-technique

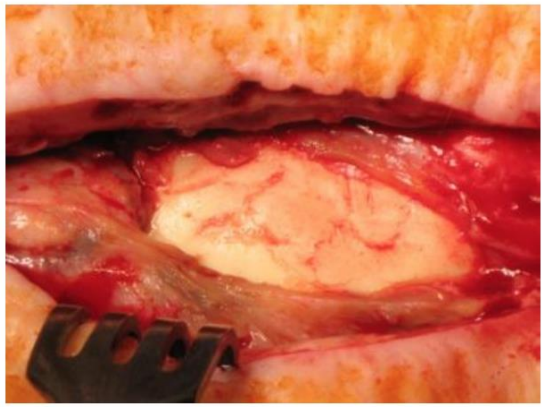
Complete fullfilling of the defect with acrylic cement (mixed with antibiotics, overlapping the bone-ends, intramedullar, soft-tissue-management)

Induced membrane:

- contains cells, which produce growth-faktors like bone morphogenic protein (BMP-2) and transforming growth factor ß-1 (TGF ß-1) (Dumont et al 2008)
- revascularises bone graft and minimizes the resorbtion of bone graft (Giannoudis et al 2011)







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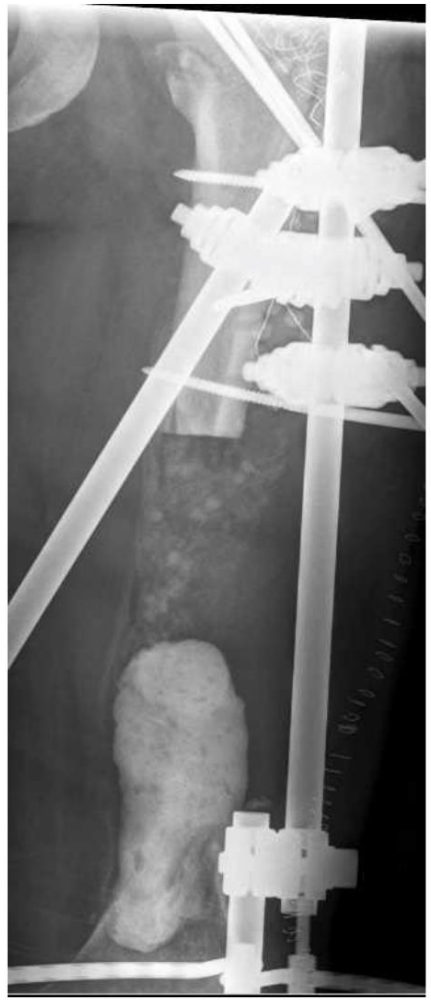
Osteomyelitis

After 6 and 12 weeks cancellous bone graft from the the posterior iliac crest, combined with PerOssal® and Vancomycin



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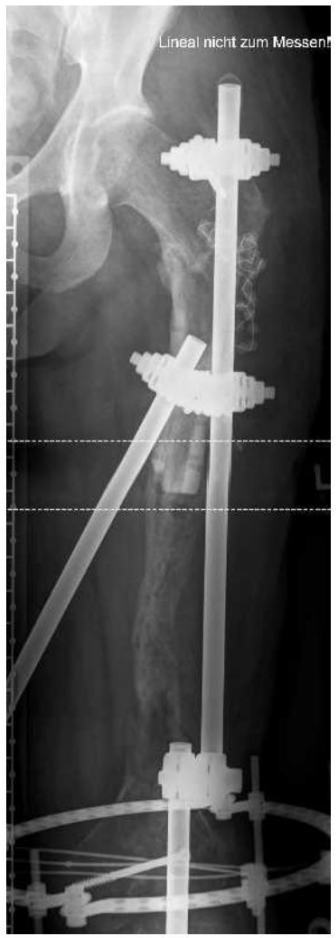
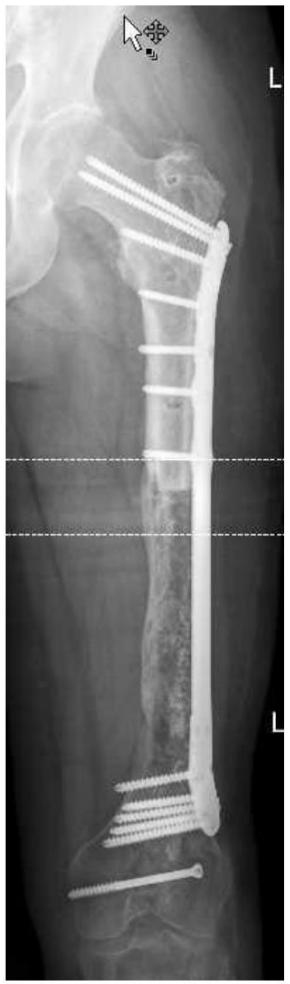
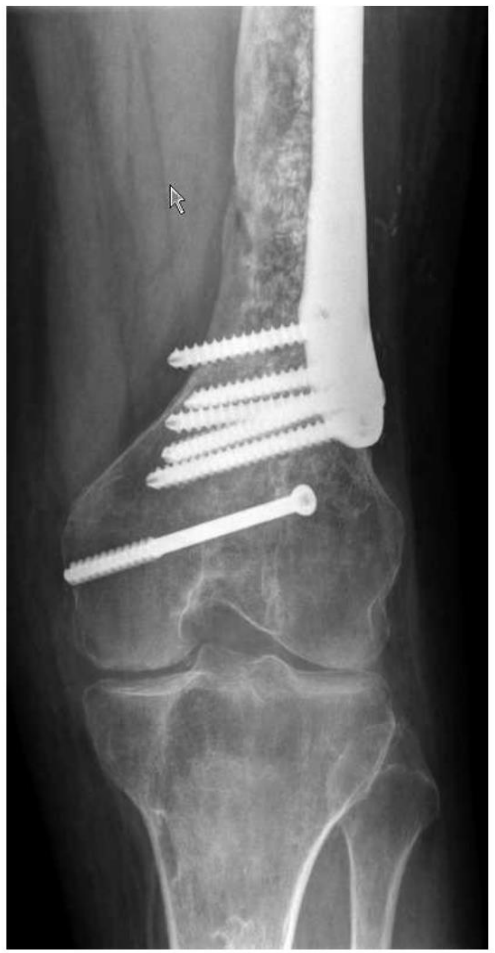
Osteomyelitis

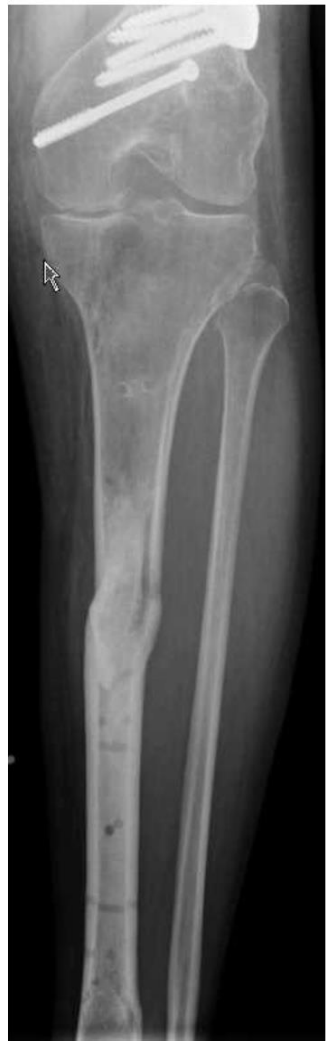
6 weeks later partial removal of the external fixator.

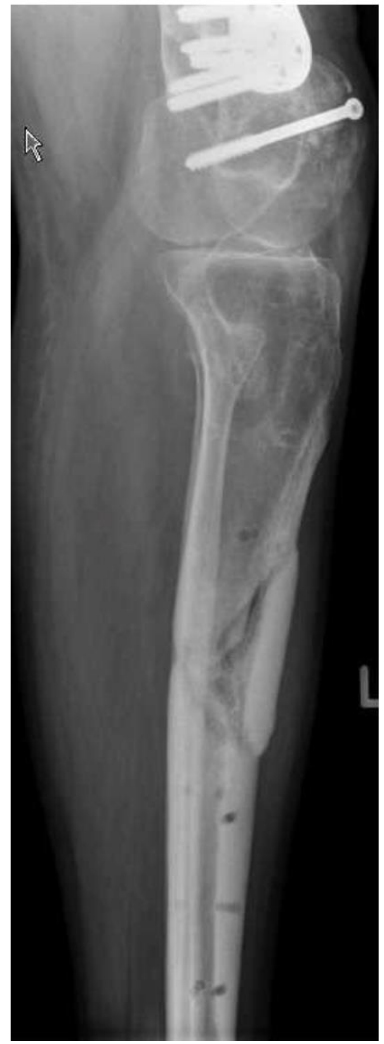
Then internal stabilization with a custom made angular stabil plate (Litos®) and cancellous bone graft (left tibial head) combined with BonAlive®











SEPTIC ARTHRITIS

Monoarthritis : Knee > Hip (Knee + Hip >85%)

Joint aspiration → Gold standard + fastest method

1. Cell count 2. Microbiology 3. Crystals

Gram stain → ↓Sensitivity Vs ↑Specificity

Margaretten, *Jama* 2007

“Time is cartiladge”

Ochsner 2016

SEPTIC ARTHRITIS

Treatment principles :

1. **Joint decompression**
2. **Systemic antibiotics for 4-6w (↑ perfusion rate of synovia)**
3. **Physiotherapy**
4. **Lavage but not antiseptics**

Mathews et al. *Lancet* 2010

“Dilution is the solution to pollution”

SEPTIC ARTHRITIS

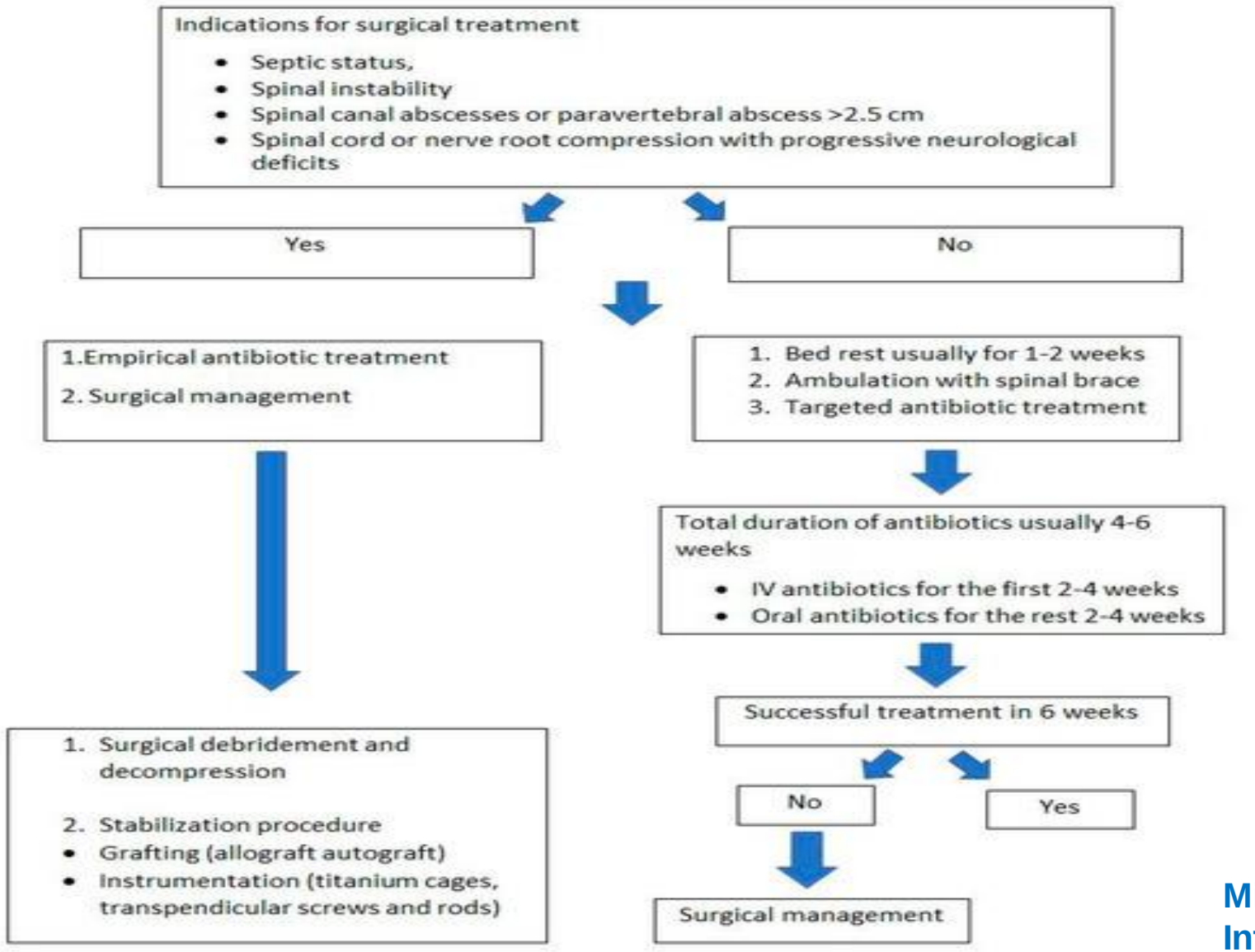
Arthroscopy → **Synovitis → Conservative treatment**

Fibrinous deposits & Synovial tissue overgrowth/ debri → Cartiladge compromise → Synovectomy

Repetition in 48-72h → If no remission → Arthrotomy

Conen A, et al. AOTrauma, *Thiemeverlag* 2016

SPONDYLODISCITIS



Microorganisms : Spinal Infections_An Update


Death by PowerPoint
(and how to fight it)
Ευχαριστώ πολύ!