When to remove infected osteosynthesis material?
Foot & Ankle
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UZ LEUVEN ORTHOPEDIE

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Complications in Orthopaedics and Traumatology
25-26 April 2019
Kursaal Oostende
INCA Meeting March 22, 2019
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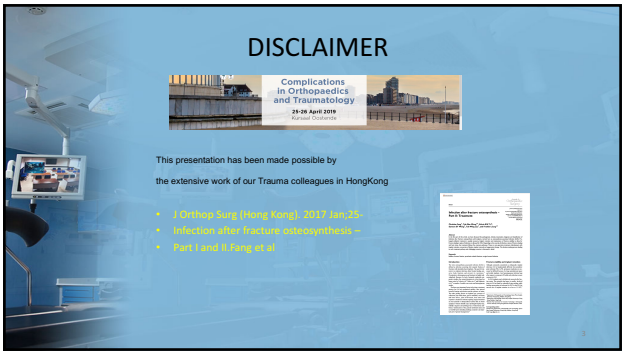
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Complications in Orthopaedics and Traumatology
25-26 April 2019
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This presentation has been made possible by
the extensive work of our Trauma colleagues in HongKong
J Orthop Surg (Hong Kong). 2017 Jan;25-
Infection after fracture osteosynthesis –
Part I and II.Fang et al
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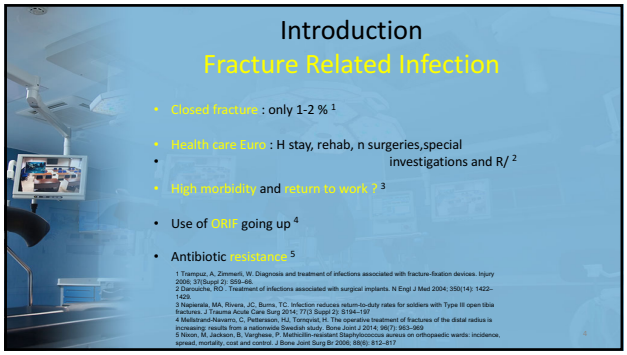
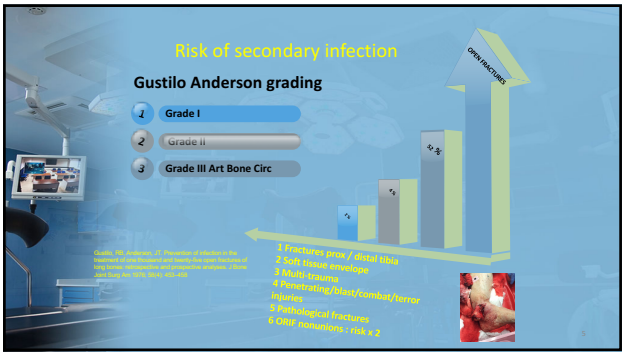
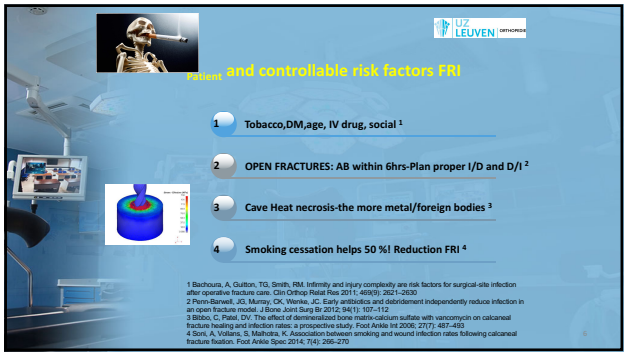

Introduction
Fracture Related Infection
Closed fracture : only 1-2 % [1]
Health care Euro : H stay, rehab, n surgeries,special investigations and R/ [2]
High morbidity and return to work ? [3]
Use of ORIF going up [4]
Antibiotic resistance [5]
1 Trampuz, A, Zimmerli, W. Diagnosis and treatment of infections associated with fracture-fixation devices. Injury 2006; 37(Suppl 2): S59–66.
2 Darouiche, RO . Treatment of infections associated with surgical implants. N Engl J Med 2004; 350(14): 1422–1429.
3 Napierala, MA, Rivera, JC, Burns, TC. Infection reduces return-to-duty rates for soldiers with Type III open tibia fractures. J Trauma Acute Care Surg 2014; 77(3 Suppl 2): S194–197.
4 Mellstrand-Navarro, C, Pettersson, HJ, Tornqvist, H. The operative treatment of fractures of the distal radius is increasing: results from a nationwide Swedish study. Bone Joint J 2014; 96(7): 963–969
5 Nixon, M, Jackson, B, Varghese, P. Methicillin-resistant Staphylococcus aureus on orthopaedic wards: incidence, spread, mortality, cost and control. J Bone Joint Surg Br 2006; 88(5): 612–617
4


Risk of secondary infection
Gustilo Anderson grading
1 Grade I
2 Grade II
3 Grade III Art Bone Circ
OPEN FRACTURES
1 Fractures prox / distal tibia
2 Soft tissue envelope
3 Multi-trauma
4 Penetrating/blast/combat/terror injuries
5 Pathological fractures
6 ORIF nonunions : risk x 2
5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Patient and controllable risk factors FRI
1 Tobacco,DM,age, IV drug, social [1]
2 OPEN FRACTURES: AB within 6hrs-Plan proper I/D and D/I [2]
3 Cave Heat necrosis-the more metal/foreign bodies [3]
4 Smoking cessation helps 50 %! Reduction FRI [4]
1 Bachoura, A, Guitton, TG, Smith, RM. Infirmity and injury complexity are risk factors for surgical-site infection after operative fracture care. Clin Orthop Relat Res 2011; 469(9): 2621–2630
2 Penn-Barwell, JG, Murray, CK, Wenke, JC. Early antibiotics and debridement independently reduce infection in an open fracture model. J Bone Joint Surg Br 2012; 94(1): 107–112
3 Bibbo, C, Patel, DV. The effect of demineralized bone matrix-calcium sulfate with vancomycin on calcaneal fracture healing and infection rates: a prospective study. Foot Ankle Int 2006; 27(7): 487–493
4 Soni, A, Voltans, S, Malhotra, K. Association between smoking and wound infection rates following calcaneal fracture fixation. Foot Ankle Spec 2014; 7(4): 266–270
6

PATHOGENESIS FRI

2

Gram positive	Gram negative	Polymicrobial
▪ MSSA and MRSA ▪ CNS : 80% MR ▪ Coryne and Cuti NOT CONTAMINANTS	▪ E Coli , E bacter/coc, Klebsiella,Proteus ▪ Multi-resistant Pseudomonas and Acinetobacter ▪ DTT=difficult to treat	▪ Open fractures ▪ Clostridium/aeromonas necrotizing ! ▪ Atypical slow growing:think imm compromised state / pathological fracture

Rilloch, V. Kerem-Yaniszik, R. Batirman-Igra, Y. Multidrug-resistant Pseudomonas aeruginosa: risk factors and clinical impact. Antimicrobial Agents and Chemotherapy 2008; 52(1): 43–49

BIOFILM FORMATION IN FRI

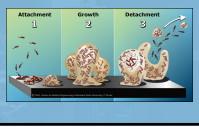
Stage 1 : from free-floating to adherence to metal surfaces

Stage 2 : multiply and start production polysaccaride matrix

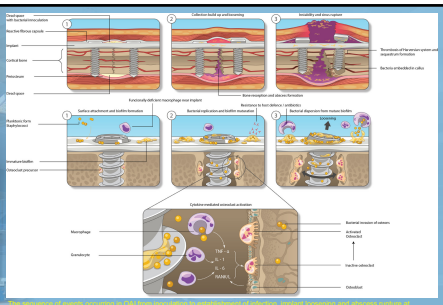
Stage 3 : development 3D architecture / quorum sensing / small colony variants

Stage 4 : maturation : inside dormant low metabolism ! (MIC x1000)

Stage 5 : colonization other sites



Costerton, JW, Lewandowski, Z, Caldwell, DE. Microbial biofilms. Annu Rev Microbiol 1995; 49(1): 711–745



The sequence of events occurring in GAI from inoculation to establishment of infection, implant loosening and abscess rupture at different magnifications, (refer to pathogenesis).

Fang, C., Wong, T.-M., Lau, T.-W., To, K. K., Wong, S. S., & Leung, F. (2017). Infection after fracture (osteosynthesis) – Part I: Pathogenesis, diagnosis and classification. Journal of Orthopaedic Surgery

Implant material and design

1 Foreign body versus host defences

2 Cytokine cascade ---------- tissue damage [1]

3 Surface topology, chemical composition, charge, hydrophobicity, physics

4 Stainless steel surface versus titanium microrough surface but none superior [2]

5 Internal dead spaces ! : cannulated nails/screws

6 MIPO better because of viability soft tissues

7 absorbable polymer = metal for FRI

1 Gristina, AG . Implant failure and the immuno-incompetent fibro-inflammatory zone. Clin Orthop Relat Res 1994; 298: 106–118
2 Rochford, ETJ, Richards, RG, Moriarty, TF. Influence of material on the development of device-associated infections. Clin Microbiol Infect 2012; 18(12): 1162–1167

INFECTION VERSUS FRACTURE (IN)STABILITY

Unstable ?

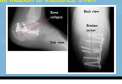
More chance for FRI : why ? Dead space/ disruption revasc/..

Infection > 2 weeks ?

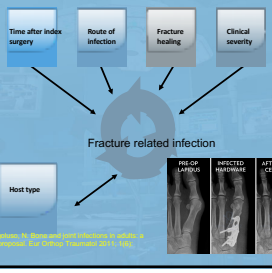
Leucocytes produce TNF-alpha, IL-1 and IL-6 stimulate osteoclasts via RANK (rec activ nucl factor kappaB)

Osteoclasts responsible for osteolucencies ---- mechanical failure

Schmidt, AH, Swiontkowski, MF. Pathophysiology of infections after internal fixation of fractures. J Am Acad Orthop Surg 2000; 8(5): 285–291



Classification FRI



Romanò, CL, Romanò, D, Logoluso, N. Bone and joint infections in adults: a comprehensive classification proposal. Eur Orthop Traumatol 2011; 1(4): 207–217

Classification FRI
Time after surgery

- Early/acute : within 2/52 : StaphA,Gr neg,Strept pyogenes
- Delayed : 3-10 weeks : CNS
- Late : > 10 weeks : StaphA,StaphE,Pseudo

Torbert, JT, Joshi, M, Moraff, A. Current bacterial speciation and antibiotic resistance in deep infections after operative fixation of fractures. Journal of Orthopaedic Trauma 2015; 29(1): 7–17

13

Classification FRI
Route of infection

- Exogenous : most common/adverse wound factors
- Contiguous: from cellulitis nearby
- Haematogenous : less than for PJI/check other septic foci and metal !

Zimmerli, W . Clinical presentation and treatment of orthopaedic implant-associated infection. J Intern Med 2014; 276(2): 111–119.

14

Classification FRI
Status Fracture Healing

- Type 1 : stable/progressive callus: AB and obs

- Type 2 : stable but no callus : DAIR and bio trigger
- Type 3 : unstable no callus : EXT FIX or special

Romano, CL, Romano, D, Logoluso, N. Bone and joint infections in adults: a comprehensive classification proposal. Eur Orthop Traumatol 2011; 1(4): 207–217

15

Classification FRI
HOST TYPE Cierny-McPherson

- Type A : no co-morb and no local adverse factors

- Type B : 1 or 2 local or systemic adverse
- Type C : 3 or more : amputation or supp

1 Cierny, G, Mader, JT, Penninck, JJ. A clinical staging system for adult osteomyelitis. Clin Orthop Relat Res 2003; 414: 7–24

2 McPherson, EJ, Woodson, C, Holtom, P. Periprosthetic total hip infection: outcomes using a staging system. Clin Orthop Relat Res 2002; 403: 8–15

16

HOST RISK STRATIFICATION

Table 1. Systemic and local factors that affect local immunity, metabolism and vascularity in the host physiological classification system adopted from Cierny et al.[189]

Adverse factors affecting immunity, metabolism and local vascularity	
Systemic	Local
Malnutrition	Chronic lymphedema
Renal, liver failure	Venous stasis
Alcohol abuse	Major vessel compromise
Immune deficiency	Arteritis
Chronic hypoxia	Extensive scarring
Malignancy	Radiation fibrosis
Diabetes mellitus	
Extremes of age	
Steroid therapy	
Tobacco abuse	

Systemic and local factors that affect local immunity, metabolism and vascularity in the host physiological classification system adopted from Cierny et al.

17

GOALS OF TREATMENT for FRI

- Eradicate infection
- Allow fracture healing
- Preserve function
- Prevent recurrence of infection

1 Torbert, JT, Joshi, M, Moraff, A. Current bacterial speciation and antibiotic resistance in deep infections after operative fixation of fractures. J Orthop Trauma 2015; 29(1): 7–17
2 Rightmire, E, Zurakowski, D, Vrahas, M. Acute infections after fracture repair: management with hardware in place. Clin Orthop Relat Res 2008; 466(2): 466–472

18

TREATMENT STRATEGY for FRI

- Mechanical stability S
- Time period between fixation vs infection T
- Presence of union U
- Implant type – Collections- non-viable bone(graft)-defect , joint involvement, host status and response to treatment I
- Optimization nutrition / co-morbidities C

Naique, SB, Pearse, M, Nanchahal, J. Management of severe open tibial fractures: the need for combined orthopaedic and plastic surgical treatment in specialist centres. J Bone Joint Surg Br 2006; 88(3): 351–357

STUYCK: stable/time/union/Implant/Coll and Comorb Keys to success

19

FRI IS NOT PJI

Periprosthetic joint infection	Fracture related infection
▪ Eradication tough because of joint space and large implants ▪ Late haematogenous infection ▪ argument 1 ▪ Success DAIR : 15-54 % in late PJI	▪ Once fracture union, implant removal possible ▪ Smaller dead space ▪ Living cartilage to be preserved ▪ Success DAIR : 56-86 %negative argument 1 ▪ Infection within 10 wks from index ▪ Fracture healing possible if STABLE and VASCULAR ▪ Fracture healing NOT POSSIBLE if UNSTABLE, DEFECT, LOOSE IMPLANT, SEQUESTRUM

IF STABLE HARDWARE AND IF NO COLLECTIONS AND IF TISSUE NECROSIS AND IF NO DEAD SPACE ⟶ FRACTURE HEALING CAN HAPPEN

Hofmann, CO, Bär, T, Buhren, V. The osteosynthesis implant and early postoperative infection: healing with or without removal of the material? Chirurg 1997; 68(11): 1175–180

20

Treatment strategy: acute infection < 2 weeks after index

- 25% of FRI
- SSI be careful !
- Deep collections ? By US or CT
- If SSI----- empirical IV AB
- If collection/discharge++/wound edge breakdown---- DAIR
- (debridement,AB,implant retention)

21

Treatment strategy: delayed infection before fracture healing: 3-10 after index

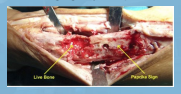
- DAIR : success union: 68-71%
- infection eradic : 50 % thus eventually METAL REMOVAL
- Failure DAIR : smoking,DM,co-morb,Pseudo, open fractures
- If DAIR fails : EXT FIX after metal out

Berkes, M, Obremskey, WT, Scannell, B. Maintenance of hardware after early postoperative infection following fracture internal fixation. J Bone Joint Surg Am 2010; 92(4): 823–828

22

Treatment strategy: late infection with non-union: > 10 weeks after index

- Not amenable for bracing or conservative R/
- Remove loose metal
- Remove sequestrum
- EXT FIXATION (if not possible use stable bridging implants)
- Succes fracture union : 66-100%
- Succes infection erad : up to 40 %



Olszewski, D, Strauber, PN, Studnon, C. The fate of patients with a "surprise" positive culture after nonunion surgery. J Orthop Trauma 2016 1; 30(1): e18–23

23

Treatment strategy: infection after fracture union

- Check union with CT-MARS
- Co-factualities : osteomyelitis,septic arthritis, soft tissue defects
- DAI-OUT = Debridement Antibiotics Implant Out

Al-Mayahi, M, Betz, M, Muller, DA. Remission rate of implant-related infections following revision surgery after fractures. Int Orthop 2013; 37(11): 2253–2258

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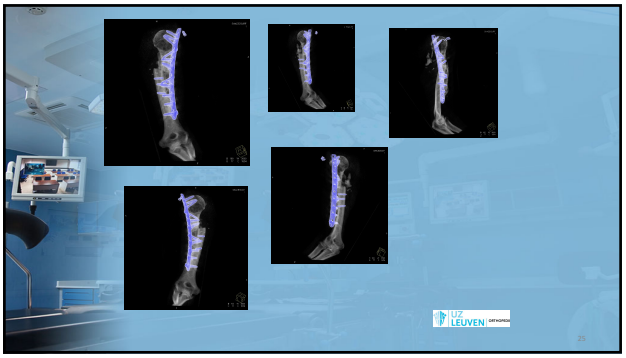
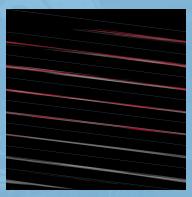


METAL ARTEFACT REDUCTION SEQUENCE



Surgical debridement

- Spare skin at wound margins
- Away with dead tissue, debris , pus and haematoma
- Assess fracture / implant stability
- Lift up or exchange implant (reduce biofilm burden)
- I/D and D/I : irrigate with N/S 9l hip/knee 3l foot/ankle
- AB spacers (Masquelet technique)
- Better primary wound closure than VAC exchanges (especially exposed bone)
- Second or third look every 3 days until
- Base with healthy bleeding bone and soft tissue
- Paprika or tomato sign ?

Rightmire, E. Zurakowski, D. Vrahas, M. Acute infections after fracture repair: management with hardware in place. Clin Orthop Relat Res 2008; 466(12): 466–472

FRI: conversion int to external fixators

- Failure of control even with repeated I/D
- Multiple adverse local / systemic factors
- RING EXTERNAL FIXATORS (ILIZAROV- Spatial Taylor Frame) best
- Conversion back to INTERNAL FIXATION OK once bact source control

Paley, D. Lamm, BM. Katsenis, D. Treatment of malunion and nonunion at the site of an ankle fusion with the Ilizarov apparatus. Surgical technique. J Bone Joint Surg Am 2006; 88(Suppl 1 Pt 1): 119–134

FRI: local antimicrobial therapy

- Common practice but no strong evidence
- Like PJI - minimum systemic toxicity
- Polymethylacrylate BEADS/SPACERS/RODS (PMMA)
- Masquelet technique
- PMMA curing HOT thus heatstable water soluble AB:
- Vanco Genta Imipenem – duo therapy best
- 40g PMMA mix with 4 g VANCO or 2 g Genta
- NO VACUUM MIXING
- AB elusion within few days !
- ALWAYS IV OR PO AB !! HIGH DOSE (not Floxapen 500mg tds)

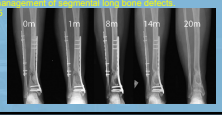
Obremskey, WT. Molina, CS. Collinge, C. Current practice in the initial management of open fractures among orthopaedic trauma surgeons. J Orthop Trauma. 2014 8; 28(8): e198–202

FRI: MASQUELET TECHNIQUE

- Antibiotic cement spacer-induced membrane
- 4-8 weeks
- Vascular biochamber rich in growth factors
- Second-stage cancellous bone grafting (with local AB)(or RIA)

Masquelet, AC, Begue, T. The concept of induced membrane for reconstruction of long bone defects. Orthop Clin North Am 2010; 41(1): 27–37

Donegan, DJ, Scolaro, J, Matuszewski, PE. Staged bone grafting following placement of an antibiotic spacer block for the management of segmental long bone defects. Orthopedics 2011; 34(11): e730–e735



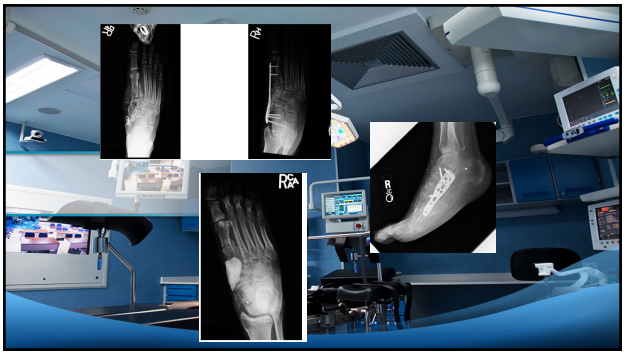
FRI: MASSIVE BONE DEFECTS

- DEBRIDE SEQUESTRUM !
- FIRST ERADICATE INFECTION !
- Defect < 4 cm : 2 stage PMAA AB cement spacer-induced membrane

- Segmental Defect > 4 cm : ILI-TRANSPORT (ORIF after docking can)
- : Papineau : open cancell bone grafting (
- slow and nursing intensive)
- : tibialization fibula
- : graft-induced Tib-Fib synostosis
- : Free vasc bone transfer

Wiese, A, Pape, HC. Bone defects caused by chronically infected bone, bone loss, infected nonunions, and nonunions. Orthop Clin North Am 2010; 41(1): 1-4

Chan, YS, Ueng, SW, Wang, CJ. Antibiotic-impregnated autogenic cancellous bone grafting is an effective and safe method for the management of small infected tibial defects: a comparison study. J Trauma 2008; 65(2): 246–253



FRI: SOFT TISSUE DEFECTS

- Prefer primary wound closure
- Do not leave bone/metal exposed
- Suck away / out haematoma and dead space (drains!)
- Free flaps : no tobacco-ethyl+drugs / organ/lung failure- DM->75yrs
- If needed , combine acute bone/soft tissue shortening and later distraction osteogenesis
- VAC or Neg Pressure Wound Therapy : bridging therapy
- : NO SUBSTITUTE for early wound closure and flap coverage

El-Rosasy, MA. Acute shortening and re-lengthening in the management of bone and soft-tissue loss in complicated fractures of the tibia. J Bone Joint Surg Br 2007; 89(1): 85–89

FRI: AFTER IM NAILING

- Delayed diagnosis and deep canal
- R/ pillars : stable,systemic AB,D/I, soft tissue coverage, staged bone defect R/
- Early infection : DAIR
- Delayed infection : DAI-EXCHANGE
- Late infection: DAI-OUT and EXT FIX
- : DAI-OUT and AB cement rod – new nail 2/12 later

- AB cement rod with PMMA-coated locking screws
- Reamer Irrigator Aspirator + AB cement rods : promising

Mouzopoulos, G, Kanakaris, NK, Kontakis, G. Management of bone infections in adults: the surgeon's and microbiologist's perspectives. Injury 2011; 42(Suppl 5): S18–23

Cox, G, Jones, E, McGonagle, D. Reamer-irrigator-aspirator indications and clinical results: A systematic review. Int Orthop 2011; 35(7): 951–956

FRI: JOINT INVOLVEMENT

- Poorly perfused dead space and fragile cartilage
- High energy (pilon tibial- peritalar)
- FRI is not PJI : debrid and immobilize ! Better control of infection !!--- Later capsular release
- Arthrodesis
- If joint replaced , two-stage with spacer!!
- Tumour prosthesis replacement : up to 25 % risk for infection
- Amputation : not a failure option but escape pathway!
- Special: amp distal to infection : mechanic/vasc reasons

Hulscher, JB, Te Velde, EA, Schoonhan, AH. Arthrodesis after osteosynthesis and infection of the sinks joint. Injury 2011; 32(2): 149–152

FRI: SYSTEMIC TREATMENT

- Empirical
- Targeted
- Long-term suppression
- Consider bio-availability, bone penetration and side effects

FRI: SYSTEMIC TREATMENT: EMPIRICAL AB

- NO penetration into haematoma/seroma/abscess/dead bone and tissue
- MIC = high dose especially if peri-implant or poor vasc
- MSSA : fluclox or first gen Ceph
- MRSA chance : Vanco or Teico
- DM, old age, imm comp,pelvic fract : 3rd gen Ceph CefTx

- Delayed/late infections: first deep culture/biopsy then AB
- Cave AB resistance and 'persisters'

FRI: SYSTEMIC TREATMENT:Targeted AB

- MRSA : > 50% !
- Multi-R : up to 30 % of FRI
- ONCE SENSITIVITIES KNOWN, NARROW SPECTRUM !
- Open fractures/imm comp : polymicrobial
- Staph and metal in place and early FRI: Clinda/Quinolone and Rifampicin 3/12
- NEVER USE RIFAMPICIN AS MONOtherapy (fast resistance)

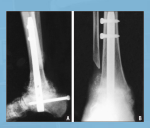
Zimmerli, W, Widmer, AF, Blatter, M. Role of rifampin for treatment of orthopedic implant-related staphylococcal infections: a randomized controlled trial. JAMA 1998; 279(19): 1537–1541

FRI: DURATION OF AB TREATMENT

- t1 : high dose IV AB at least 1/52 then oral if bio-available and favourable response (OVIVA trial)
- PICCC line if > 2/52 IV AB needed
- DAIR : minimum 6/52
- : 3/12 if no rapid response and adverse factors
- DAI-OUT : 3/52 (fracture healed)
- If clinic,CRP,Rx healing,implant OK : Stop AB
- In doubt : PET-CT

FRI: SYSTEMIC TREATMENT: failed eradication and long-term suppression

- Failure source control : FRI w/i 3/12 after AB stop
- No surgery possible/ incomplete # healing:supp R/
- Fracture healing can still occur
- If so, DAI-OUT best !

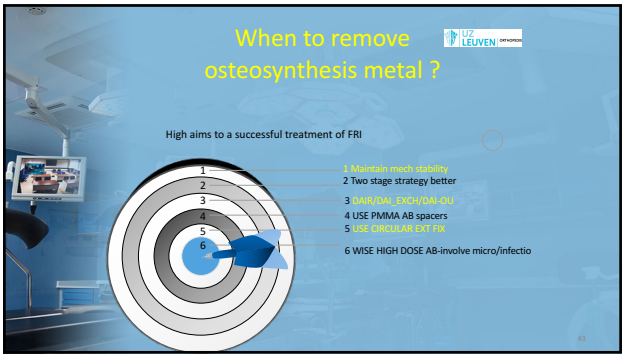


FRI: ONGOING DEVELOPMENTS

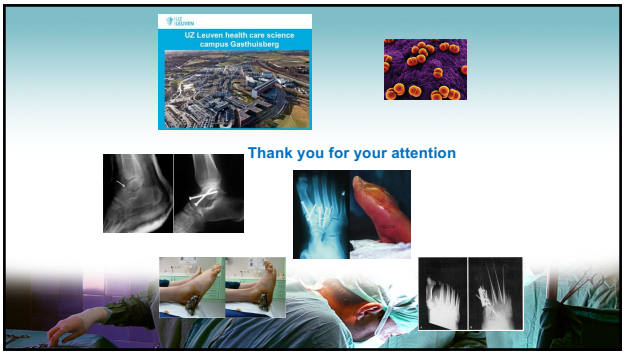
- POC-test : Leucocyte Esterase cfr.PJI
- Biofilm disruption by soni,electrics,laser
- Implant design: nansostreucture surface finish
- : polyethylene oxide
- : silver and copper
- : AB coating or AB gels or CSA-90 (cat ster antibiotic)

Moriarty, TF, Schlegel, U, Perren, S. Infection in fracture fixation: can we influence infection rates through implant design? J Mater Sci Mater Med 2010; 21(3): 1031–1035

Penn-Barwell, JG, Murray, CK, Wenke, JC. Local antibiotic delivery by a tobramycin spray is superior to PMMA bead deposit in reducing infection in an open fracture model. J Orthop Trauma 2014; 28(6): 370–375


When to remove osteosynthesis metal ?
UZ LEUVEN
High aims to a successful treatment of FRI
1
2
3
4
5
6
1 Maintain mech stability
2 Two stage strategy better
3 DAIR/DAI_EXCH/DAI-OU
4 USE PMMA AB spacers
5 USE CIRCULAR EXT FIX
6 WISE HIGH DOSE AB-involve micro/infectio

Clinical features and initial treatment
Investigations and Surgery
Antibiotic therapy
Aftercare
1. Non-operative
2. Implant retention
3. Conversion of fixation
4. Implant removal
5. Suppression


UZ Leuven health care science campus Gasthuisberg
Thank you for your attention