EBJIS 2019

38th Annual Meeting of the European Bone and Joint Infection Society

12 - 14 September 2019 · Antwerp · Belgium

www.ebjis19.org

EBJIS 2019

38th Annual Meeting of the European
Bone and Joint Infection Society

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Member benefits

- Preferential EBJIS Annual Meeting registration fee
- Become an EBJIS Fellow: Apply now for the annual Travelling Fellowship program **www.ebjis.org/fellowship**
- Submit manuscript to the EBJIS Journal www.jbji.net/ms/submit. EBJIS Members receive 30% of discount
- Access all EBJIS Newsletters and all the recent news related to Bone and Joint Infection
- Access the EBJIS Annual General Assembly with voting rights on key decisions.
- Access the EBJIS Forum community, that encourages discussion and collaboration between the EBJIS Members on clinical cases
- The Executive Committee support Members who organise Infection meetings and promote them among our Members and in the EBJIS website
- Apply for a Country Delegate position – a Committee which serves to improve the promotion of the EBJIS in Europe, to facilitate contacts with interested colleagues and to encourage Bone and Joint Infection centres in Europe
- Apply for being a Member of the EBJIS Abroad Committee, which is a new Committee to design and deliver education on Bone and Joint Infection in Resource-Poor Regions.

Annual membership fee: € 130

Join now the European Bone and Joint Infection Society and experience new opportunities on volunteering and being on the other side of the board table

Information and registration through the EBJIS website
www.ebjis.org/membership

For further details, contact us here: info@ebjis.org

European Bone & Joint Infection Society
EBJIS

Welcome

Dear participants,
Dear colleagues,

It is a great pleasure to welcome you to the 38th Annual Meeting of the European Bone and Joint Infection Society in Antwerp.

During the 2,5 conference days, you will experience a diverse programme that includes keynote sessions, free paper sessions, industry symposia and poster presentations. You will get a unique opportunity to meet experts within the field and be updated on bone and joint infection research happening across Europe.

The main conference theme is:
From basic science to clinical practice: the importance of translation science in the development of concepts on infection prevention and treatment.

The topics of the conference are:

- *Prevention of Muscular Skeletal Infections*
- *Fracture-Related Infection: current concepts on diagnostics and treatment*
- *Diabetic foot infection: vascularisation and soft tissue management*
- *Optimizing PJI diagnosis strategy*
- *Strategies against Biofilm related infections*
- *Spinal infections*

Furthermore, we have arranged some exciting social events, so you will get the chance to experience the historical side of the second European port in the shadow of the gothic Cathedral of Our Lady and have a taste of nature and green oasis next to the meeting center.

We hope you will enjoy the conference and your stay in Antwerp!

On behalf of the Local Organising Committee and the EBJIS Executive Committee,

Olivier Cornu
Conference Chair

Martin McNally
President of EBJIS

Organisation

EBJIS Executive Committee

President	Martin McNally
Vice President	Rihard Trebse
Past President	Klaus Kirketerp-Møller
General Secretary	Charles Vogely
Treasurer	Martin Clauss
Members	Alex Soriano
	Ricardo Sousa
Country delegates Chair	Christof Wagner

Local Organising Committee

Chair	Olivier Cornu
Members	Guy Putzeys
	Jeroen Neyt
	Willem-Jan Metsemakers

General information

CONFERENCE WEBSITE
www.ebjis19.org

CONFERENCE VENUE
Flanders Meeting & Convention Center
Koningin Astridplein 20
2018 Antwerp
Belgium

BADGES
The conference name badges must be worn at all times during the conference. Access to the conference venue will not be granted without the name badge issued by the conference organisers.

ENTITLEMENTS FOR PARTICIPANTS
Admission to all scientific sessions and industry symposia, admission to exhibition, conference bag with programme- and abstract book, CME credits, coffee breaks and lunch, welcome reception on Thursday 12/9, farewell lunch on Saturday 14/9 and certificate of attendance.

CME CREDITS
The conference has been accredited 14 European CME credits (ECMEC) by the European Accreditation Council for Continuing Medical Education (EACCME). In order to obtain the CME credits please log your attendance each day after 14.00 by scanning your badge at the logging stations in the registration area. CME Credits certificate and certificates of attendance can be downloaded from the conference website under registration. You will receive an email with more information and the link to download the certificate after the conference.

CLOAK ROOM
A cloak room located near the exhibition area will be available throughout the conference.

Opening hours:

Thursday 12 September	7.00 - 17.45
Friday 13 September	7.45 - 19.15
Saturday 14 September	7.45 - 14.30

CONFERENCE LANGUAGE
The conference will be held in English.

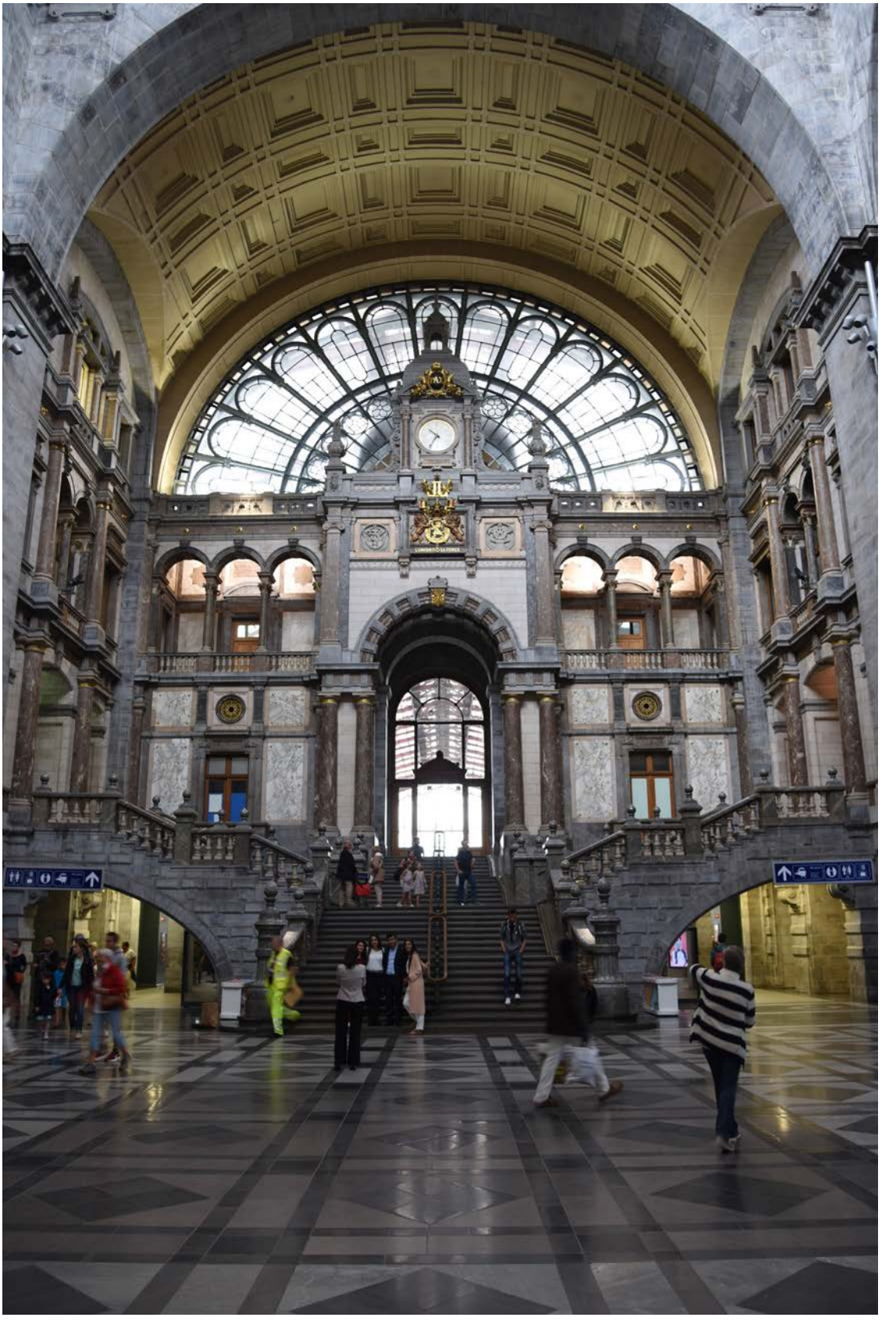
INFORMATION FOR SPEAKERS
Bring your presentation to the Speakers' Preview room at the venue.
An assistant will help you upload the presentation to the computer. Please make sure to upload your presentation at least 30 min. before your session starts. Please bring your presentation on a USB stick.
We do not allow the use of personal laptops for presentations. At the end of the conference, all presentations will be deleted in order to secure that no copyright issues will arise.

SPEAKERS' PREVIEW ROOM (STANLEY ROOM)

Opening hours:

Thursday 12 September	7.30 - 16.30
Friday 13 September	7.45 - 17.00
Saturday 14 September	8.00 - 11.00

WIFI
Free access to the WIFI at the conference venue is provided.
Connect to "KMDA Free" and sign up with your e-mail address.



Social events

WELCOME RECEPTION
Date 12 September 2019
Time 18.00 - 20.00
Place Grand Café Horta
Hopland 2
2000 Antwerp

The Welcome Reception will take place at the Grand Café Horta of Antwerp at 18:00-20.00. Make sure to be there for an evening full of surprises.
NB: The reception is included in the registration fee.

EBJIS GALA DINNER
Date 13 September 2019
Time 20.00 - 23.00
Place Marble Hall at the conference venue
NB: Please enter through the entrance to the Zoo located a few meters away from the conferences venue on the Koningin Astridplein square.

The gala dinner will take place in the beautiful Marble Hall located at the conference venue. The Marble Hall is the historical heart of the complex and one of the architectonic highlights of Art Nouveau in Belgium.

The dinner includes an aperitif and a 3-course dinner. You will also be invited to join an evening walk in the beautiful Antwerp zoo located right by the Marble Hall!
NB: The dinner is not included in the registration fee.

CONFERENCE SECRETARIAT
CAP Partner
Nordre Fasanvej 113, 2
DK-2000 Frederiksberg
Denmark

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SOCIAL MEDIA

Find EBJIS on Facebook
Search for "European Bone and Joint Infection Society"

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Search for "EBJIS Non Profit Organization"

Programme overview

Thursday 12 September 2019

	Room: Queen Elizabeth Hall	Room: Okapi room 1&2
07.00	**Registration**	
08.30 - 08.50	Welcome & Opening Ceremony	
08.50 - 09.45	**Key session 1:** Fracture-related infection: current concepts I	
09.50 - 10.50	**Key session 2:** Fracture-related infection: Current concepts II	Free Papers A: Microbiological diagnosis
10.50 - 11.20	Coffee, poster visit and exhibition	
11.20 - 13.15		Country Delegates Meeting (This meeting is by invitation only)
11.20 - 12.50	Free Papers B: Clinical research on fracture PJ related infection/DAIR	Free Papers C: Basic and translational research
12.50 - 14.00	Lunch	
12.55 - 13.55	Industry Symposium A in Okapi Room 3	Industry Symposium B
14.00 - 15.00	**Key session 3:** Bacterial-Implant Interactions	Free papers D: Clinical research on antimicrobial efficacy and tolerance
15.00 - 15.50	Free Papers E: Clinical research on Diabetic foot infection/Trauma	**Key session 4:** EBJIS abroad project
15.50 - 16.20	**Coffee, poster visit and exhibition**	
16.20 - 17.20	**Key Session 5:** Battles / Questions in debate Pro /Contra	Free Papers F: Infections treatment in developing countries
18.00 - 20.00	Welcome Drinks Reception at Grand Café Horta Address: Hopland 2 - 2000 Antwerp	

Friday 13 September 2019

	Room: Queen Elizabeth Hall	Room: Okapi room 1&2
7.45 -	Registration	
08.30 - 09.30	**Key Session 6:** Innovation in treatment of biofilm related Infection	Free Papers G: Clinical research on PJ related infection /one stage/two stage
09.30 - 10.30	**Key Session 7:** Improvement in microbiological diagnosis	Free Papers H: Clinical research on OA infection - diagnostic management
10.30 - 11.00	Coffee, poster visit and exhibition	
11.00 - 11.50	ICM Philly - Follow up	Free Papers I: Clinical research on fracture related infection (11:00-11:55)
11.55 - 12.25	New diagnostic criteria for PJI - EBJIS Executive Committee	
12.25 - 12.50	JBJI/MSIS symposium Top 5-10 best papers published in the JBJI	
12.50 - 14.00	Lunch	
12.55 - 13.55	Industry Symposium C in Okapi Room 3	Industry Symposium D
14.00 - 15.00	**Key Session 8:** Outpatient parenteral antimicrobial therapy	**Key Session 9:** How to prevent OA infection better?
15.00 - 16.00	Free Papers J: Infection and Hospital / Health care management	Free Papers K: Miscellaneous
16.00 - 16.30	Coffee, poster visit and exhibition	
16.30 - 17.30	**Key session 10:** Battles / Questions in debate Pro /Contra	Free papers L: Basic and translational research
17.45 - 19.00		General Assembly (for EBJIS members, by invitation only) NB! This meeting takes place at Okapi room 1&2.
20.00 - 23.00	EBJIS Gala Dinner Marble Hall at the congress venue	

Saturday 14 September 2019

	Room: Queen Elizabeth Hall	Room: Okapi room 1&2
9.00 - 10.00	**Key Session 11:** Bacteriophage therapy	Free Papers M: Clinical research on PJI prevention
10.00 - 10.30	Coffee, poster visit and exhibition	
10.30 - 12.00	Best Papers Session	
12.05 - 12.30	Honorary lecture: Will bacteria overcome humans?	
12.30.12.45	Closing Remarks & Prizes	
12.45 - 14.00	Farewell lunch	

Thursday 12 September 2019

Room: Queen Elizabeth Hall			
7.00		Registration	
8.30 - 8.50		Welcome & Opening Ceremony	Olivier Cornu & Martin McNally
8.50 - 9.45		**Key session 1:** **Fracture-related infection: current concepts I**	**Chairs:** **Martin McNally & Willem-Jan Metsemakers**
8.50 - 9.05		Current concepts on Diagnosis	Geertje Govaert
9.05 - 9.20		Problems of classifying Fracture-related infections	Mario Morgenstern
9.20 - 9.35		General treatment principles	Willem-Jan Metsemakers
9.35 - 9.45		Discussion	
9.50 - 10.50		**Key session 2:** **Fracture-related infection: Current concepts II**	**Chairs:** **Andrej Trampuz & Guy Putzeys**
9.55 - 10.10		Key aspects of soft tissue management	Alex Ramsden
10.10 - 10.25		Local antimicrobial strategies and dead space management	Marc Hanschen
10.25 - 10.40		Key aspects of antibiotic therapy	Andrej Trampuz
10.40 - 10.50		Discussion	
10.50 - 11.20		Coffee - Posters - Exhibition	
11.20 - 12.50		**Free Papers B:** **Clinical research on fracture PJ related infection/DAIR (10 x 6 min + 2 min)**	**Chairs:** **Martin Clauss & Jean-Cyr Yombi**
11.20 - 11.28	FP7	Early debridement, antibiotics and implant retention (DAIR) procedures in complicated wound healing after total joint arthroplasty – are elevated synovial fluid leukocyte counts accurate in differentiating superficial from deep infections?	André Dias Carvalho
11.28 - 11.36	FP8	DAIR procedure in prosthetic joint infection: predictive tools of failure	Olivier Cornu
11.36 - 11.44	FP9	Management of early periprosthetic joint infection with debridement-irrigation, antibiotic therapy and implant retention: postoperative positive suction drainage fluid culture is a predictive factor of failure	Benoît Villain
11.44 - 11.52	FP10	Debridement, antibiotics and implant retention is still a viable treatment option in early periprosthetic joint infection presenting more than six weeks after index arthroplasty	Claudia Löwik
11.52 - 12.00	FP11	No difference in 1-year re-revision rate after debridement antibiotics and implant retention (dair) by timing of dair procedure for total hip and knee arthroplasty in acute postoperative infections based on Dutch registry data	Jakob van Oldenrijk
12.00 - 12.05		Discussion	

Room: Okapi room 1&2			
		Registration	
9.50 - 10.50		**Free Papers A: Microbiological diagnosis (6 x 6 min + 2 min)**	**Chairs: Hector Rodriguez-Villalobos & Bridget Atkins**
9.50 - 9.58	FP1	Improved microbiological diagnosis of prosthetic joint infections by using beadmill processing of tissue samples and blood culture bottles	Karlien Vanhouteghem
9.58 - 10.06	FP2	Preoperative cultures of synovial fluid poorly predict the intraoperatively detected pathogen in PJI	Nora Renz
10.06 - 10.14	FP3	Diagnostic value of the unyvero implant and tissue infection (iti) multiplex pcr system for ruling out prosthetic joint infection in 200 unsuspected revisions of knee and hip arthroplasty	Jon Goosen
10.14 - 10.22	FP4	Advantages in diagnostics of orthopedic implant infection using incubation of explants	Arnold Suda
10.22 - 10.30	FP5	Mid-infrared spectroscopy for a rapid diagnosis of septic arthritis: a multi-centric study	Jerome Bernard
10.30 - 10.38	FP6	Diagnosis of stapylococcus spp. prosthetic joint infections with bacteriophage k based met	Andrej Cör
10.38 - 10.50		Discussion	
		Coffee - Posters - Exhibition	
11.20 - 13.15		Country Delegates Meeting (This meeting is by invitation only)	
		Free Papers C: Basic and translational research (10 x 6 min + 2 min)	**Chairs: Olivier Borens & Françoise Van Bambeke**
11.20 - 11.28	FP17	In vitro activity of fosfomycin, ciprofloxacin, gentamicin and their combinations against escherichia coli and pseudomonas aeruginosa biofilms	Lei Wang
11.28 - 11.36	FP18	Antimicrobial effect of cerament-g® on bacterial isolates, with various levels of gentamicin resistance, found in fracture-related infection; an in vitro study	Hans Bezstarosti
11.36 - 11.44	FP19	Prolonged cefazolin release from hydrogel-impregnated bone chips	Guy Putzeys
11.44 - 11.52	FP20	Double-dose pharmacokinetics of cefuroxime in porcine intervertebral disc and vertebral cancellous bone – a randomized microdialysis study	Pelle Emil Hanberg
11.52 - 12.00	FP21	Diversity of cutibacterium strains involved in prosthetic joint infections and ability to produce biofilm: cutibacterium acnes ia1 and ii phylotypes belonging to slst-type d1 or k1 produce more biofilm!	Stéphane Corvec
12.00 - 12.05		Discussion	

Room: Queen Elizabeth Hall			
12.05 - 12.13	FP12	Serial aspirations & intra-articular antibiotic injections for non-operative management of chronic pji: introducing the concept of biofilm training	Edward J. McPherson
12.13 - 12.21	FP13	Good outcome after prosthetic joint infection treated with debridement and retention of the prosthesis: a prospective registration of 99 patients	Øystein Espeland Karlsen
12.21 - 12.29	FP14	Outcome of dair (debridement, antibiotics and implant retention) procedures for infected total hip and knee replacements in a tertiary referral center	F.R.H.A. Nurmohamed
12.29 - 12.37	FP15	The use of antibiotic loaded calcium sulphate beads in lower limb periprosthetic joint infection	Zulfiqar Minhas
12.37 - 12.45	FP16	Implant stability of total hip arthroplasty after debridement and implant retention for periprosthetic joint infection	Martin Clauss
12.45 - 12.50		Discussion	
12.50 - 14.00		**Industry Symposium A (12.55 - 13.55) in Okapi Room 3 & Lunch**	
14.00 - 15.00		**Key session 3: Bacterial-Implant Interactions**	**Chairs: Mario Morgenstern & Christine Dupont**
14.00 - 14.15		Bacterial adhesion: How and Where ?	Martin Andersson
14.15 - 14.30		Biofilm eradication in infection models	Hervé Poilvache
14.30 - 14.45		Bacterial-Implant Interface and clinical relevance	Thomas Bjarnsholt
14.45 - 15.00		Discussion	
15.00 - 15.50		**Free Papers E: Clinical research on Diabetic foot infection/Trauma (5 x 6 min + 2 min)**	**Chairs: Klaus Kirketerp-Møller & Dan Putineanu**
15.00 - 15.08	FP33	Treatment and outcomes of calcaneal osteomyelitis in adults: a systemic review	Marta Sabater Martos
15.08 - 15.16	FP34	Season as a predictor for the incidence of surgical site infections after orthopedic trauma surgery of the lower leg, ankle and foot	Fay Sanders
15.16 - 15.24	FP35	Beside infection, do not forget to manage peripheral arterial disease in diabetic charcot foot.	Laura Orioli
15.24 - 15.32	FP36	Negative-pressure wound therapy in fracture-related infection: the influence on tissue culture results and outcome. Preliminary results from a single centre series	Melissa Depypere

Room: Okapi room 1&2			
12.05 - 12.13	FP22	In vitro evaluation of bacterial adhesion and biofilm formation to metallic cerclage wire versus polymer cerclage system	Margarita Veloso
12.13 - 12.21	FP23	Study of the effect of pulsed-washing on the antibiotic susceptibility of staphylococcus aureus biofilms	Hervé Poilvache
12.21 - 12.29	FP24	Isothermal microcalorimetry detects the presence of persister cells in a staphylococcus aureus biofilm after vancomycin treatment	Maria Eugenia Butini
12.29 - 12.37	FP25	Development of antibodies that enhance immune clearance of staphylococcus aureus biofilms	Lisanne de Vor
12.37 - 12.45	FP26	Phage therapy and bacterial reservoirs in bone and joint infections: evaluation of the efficacy of an assembly of three bacteriophages on staphylococcus aureus embedded in biofilm or internalized in osteoblasts	Camille Kolenda
12.45 - 12.50		Discussion	
		Industry Symposium B (12.55 - 13.55) in Okapi Room 1&2 & Lunch	
		Free papers D: Clinical research on antimicrobial efficacy and tolerance (6 x 6min + 2min)	**Chairs: Jean-Cyr Yombi & Alex Soriano**
14.00 - 14.08	FP27	Tolerance and microbiological efficacy cefepim or piperacillin/tazobactam in combination with vancomycin as empirical antimicrobial therapy of prosthetic joint infection	Claire Triffault-Fillit
14.08 - 14.16	FP28	Tigecycline versus colistin in the treatment of carbapenem-resistant acinetobacter baumannii osteomyelitis	Vladimir Cordeiro Carvalho
14.16 - 14.24	FP29	Efficacy and safety of intravenous fosfomycin in patients with periprosthetic joint infection: preliminary results from the proof study - a prospective multicenter study	Svetlana Karbysheva
14.24 - 14.32	FP30	Long-term linezolid use (>28 days) in patients with orthopedic infections is generally safe and well tolerated	Denise Telgt
14.32 - 14.40	FP31	Real life efficacy and safety of dalbavancin monotherapy as salvage treatment in bone and joint infection	Illes Gabriela
14.40 - 14.48	FP32	Predisposing factors for multidrug-resistant gram-negative prosthetic joint infections: the role of prior use of antibiotics and the nonelective arthroplasty due hip fracture.	Raquel Bandeira
14.48 - 14.54		Discussion	
15.00 - 15.50		**Key session 4: EBJIS abroad project**	**Chairs: Ricardo Sousa & Jan Noyez**
15.05 - 15.15		Point of view of EBJIS	Ricardo Sousa
15.15 - 15.25		Point of view of emerging countries	Loic Fonkoue
15.25 - 15.35		EBJIS Collaborations abroad	Martin McNally
15.35 - 15.50		Discussion	

Thursday 12 September 2019

Room: Queen Elizabeth Hall			
15.32 - 15.40	FP37	Bone transport and tibio-talar arthrodesis for distal tibia post-traumatic infection	Boštjan Sluga
15.40 - 15.50		Discussion	
15.50 - 16.20		Coffee - Posters - Exhibition	
16.20 - 17.30		**Key Session 5:** **Battles / Questions in debate Pro /Contra**	**Chairs:** **Eric Senneville & Jeroen Neyt**
		Battle 1: Delay for Rifampicin Introduction: immediate or delayed?	Delayed:P Sendi /Pro: E. Berbari
16.20 - 16.25		Moderator (present question/voting system)	
16.25 - 16.37		Immediate vs. Delayed	
16.37 - 16.47		Discussion	
16.47 - 16.55		Voting & Conclusion	
		Battle 2: Antibiotic free window period ?	No: A Trampuz / Yes: B. Atkins
16.55 - 16.57		Moderator (present question)	
16.57 - 17.09		Pro vs Contra	
17.09 - 17.19		Discussion	
17.19 - 17.30		Voting & Conclusion	
18.00 - 20.00		**Welcome Drinks Reception at Grand Café Horta** Address: Hopland 2 - 2000 Antwerpen	

Room: Okapi room 1&2			
		Coffee - Posters - Exhibition	
		Free Papers F: Infections treatment in developing countries (7 x 6 min + 2 min)	**Chairs: Ricardo Sousa & Jan Noyez**
16.20 - 16.28	FP38	Is the management of open leg fractures in a hospital facility in ivory coast a problem and why?	Kouassi Kouamé Jean-Eric
16.28 - 16.36	FP39	Vascularized fibula flap in the management of bone loss secondary to osteomyelitis in children.	Antonio Loro
16.36 - 16.44	FP40	Chronic osteomyelitis: prognostic and therapeutic aspect in the service of pediatric surgery chu gabriel touré	Sidi Yaya Traore
16.44 - 16.52	FP41	The example of bones and joints infections in cameroun shows the need to curb the antibiotic resistance in developing countries	Loïc Fonkoue
16.52 - 17.00	FP42	Intramedullary osteomyelitis cierny-mader type 1. Localized and diffuse diaphyseal infection	Leon Mora
17.00 - 17.08	FP43	Unexpected osteoarticular tuberculosis: review of outcomes following biofilm-targeted surgical management	Ruth Corrigan
17.08 - 17.16	FP44	Infection after osteosynthesis: good results in bad bugs	Aditya Menon
17.16 - 17.30		Discussion	

Friday 13 September 2019

Room: Queen Elizabeth Hall		
7.45 -	Registration	
08.30 - 09.30	**Key Session 6:** **Innovation in treatment of biofilm related Infection**	**Chairs:** **Alex Soriano &** **Françoise Van Bambeke**
8.30 - 8.45	Drug delivery systems for application in biomaterials associated infections	Ana Bettencourt
8.45 - 9.00	Antibiotic delivery systems	David Eglin
9.00 - 9.15	Innovative pharmacological strategies	Tom Coenye
9.15 - 9.25	Discussion	
9.30 - 10.30	**Key Session 7:** **Improvement in microbiological diagnosis**	**Chairs:** **Bridget Atkins &** **Hector Rodriguez-Vilalobos**
9.35 - 9.50	Differential diagnosis of prosthetic joint infections	Yvonne Achermann
9.50 - 10.05	Microbiological diagnosis: what do we need, and how do we achieve it?	Maria Dudareva
10.05 - 10.20	The Antibiofilmogram	Frederic Laurent
10.20 - 10.30	Discussion	
10.30 - 11.00	Coffee - Posters - Exhibition	
11.00 - 11.50	**ICM Philly - Follow up**	**Chairs:** **Andrej Trampuz &** **Jeroen Neyt**
11.00 - 11.15	What to retain from ICM Philly	Thorsten Gehrke
11.15 - 11.30	Where I disagree and why ?	Eric Senneville
11.30 - 11.40	TBD	Martin Clauss

Room: Okapi room 1&2			
7.45 -		Registration	
		Free Papers G: Clinical research on PJ related infection /one stage/two stage (6 x 6min + 2min)	**Chairs: Maite Van Cauter & Martin Clauss**
8.30 - 8.38	FP45	Diagnosing chronic periprosthetic joint infection : definition matter	Maxime Huard
8.38 - 8.46	FP46	Epidemiology, microbiological diagnosis, and clinical outcomes in prosthetic joint infection: results from the prospective brazilian-implant cohort study (brics)	Mauro Salles
8.46 - 8.54	FP47	The (de)terminator PJI treatment flowchart	Jeroen Neyt
8.54 - 9.02	FP48	Minimum four years follow-up results after single-stage revision in the management of chronic prosthetic-joint infection after total hip arthroplasty: retrospective analysis	Raquel Afonso
9.02 - 9.10	FP49	The use of massive protheses in the periprosthetic joint infections. A series of 58 patients treated in one or two stages	Gérard Giordano
9.10 - 9.18	FP50	Is one-stage revision surgery for infected the preferably when using vancomycin containing bone graft?	Gösta Ullmark
9.18 - 9.24		Discussion	
		Free Papers H: Clinical research on OA infection - diagnostic management (6 x 6min + 2min)	**Chairs: Jeroen Neyt & Christof Wagner**
9.30 - 9.38	FP51	Performance of synovial fluid D-Lactate test for accurate diagnosis of periprosthetic joint infection	Svetlana Karbysheva
9.38 - 9.46	FP52	The use of pet-ct reduce mortality in patients with implant related infection associated staphyloccocus aureusbacteremia (sab)	Jean-Cyr Yombi
9.46 - 9.54	FP53	Clinical evaluation of synovial alpha defensin and synovial c-reactive protein in the diagnosis of periprosthetic joint infection	Hernan Prieto
9.54 - 10.02	FP54	Seronegative hip and knee prosthetic joint infections: is erythrocyte sedimentation rate a helpful adjunct to c-reactive protein?	Ana Ribau
10.02 - 10.10	FP55	Combined biomarker analysis in pji diagnosis – a useful tool or not to recommend?	Sebastian Klim
10.10 - 10.18	FP56	Is a positive intra-operative culture associated with poor results in presumed aseptic revision of total hip and knee arthroplasties?	Mattia Loppini
10.18 - 10.30		Discussion	
		Coffee - Posters - Exhibition	
11.00 - 11.55		**Free Papers I: Clinical research on fracture related infection (6 x 6 min + 2 min)**	**Chairs: Mario Morgensten & Peter Reynders**
11.00 - 11.08	FP57	Antibiotic treatment and microbiological findings in complex fracture-related infections; a systematic literature review	Hans Bezstarosti
11.08 - 11.16	FP58	Outcomes in culture negative and culture positive osteomyelitis	Apoorva Khajuria
11.16 - 11.24	FP59	Multi-drug (mdr) and extensively drug-resistant (xdr) gram negative osteosynthesis-associated osteomyelitis (oao) of the lower extremities: a multi-centre international study	Efthymia Giannitsioti

Room: Queen Elizabeth Hall			
11.40 - 11.50		Discussion	
11.55 - 12.25		**New diagnostic criteria for PJI - EBJIS Executive Committee** Speakers: Rihard Trebse and Alex Soriano	**Chair: Martin McNally**
12.25 - 12.50		**JBJI/MSIS symposium** **Top 5-10 best papers published in the JBJI**	**Chairs: Parham Sendi, Elie Berbari**
12.50 - 14.00		**Industry Symposium C (12.55 - 13.55) in Okapi Room 3 & Lunch**	
14.00 - 15.00		**Key Session 8:** **Outpatient parenteral antimicrobial therapy**	**Chairs:** **Alex Soriano & Xavier Holemans**
14.00 - 14.15		NHS experience (OPAT: the current picture, the vision and the patient experience)	Bridget Atkins
14.15 - 14.30		Lyon experience (Products (agents & devices) – types, routes, transport, storage, administration)	Tristan Ferry
14.30 - 14.45		Belgian experience (How should we evaluate OPAT and governance of OPAT – what are our markers for success?)	Caroline Briquet
14.45 - 14.55		Discussion	
15.00 - 16.00		**Free Papers J:** **Infection and Hospital / Health care management** **(6 x 6min + 2min)**	**Chairs:** **Rihard Trebse &** **Jean-Cyr Yombi**
15.00 - 15.08	FP63	Implementing oviva: 18 months experience in a specialist orthopaedic hospital	Tariq Azamgarhi
15.08 - 15.16	FP64	Treatment of prosthetic-joint infections: the role of the surgeon	Arnaud Fischbacher
15.16 - 15.24	FP65	The financial burden of treating osteomyelitis in the uk	Jamie Ferguson
15.24 - 15.32	FP66	Risk assessment of resistance development by antibiotic loaded bone cement - is it a clinical concern?	Christof Berberich
15.32 - 15.40	FP67	The prosthesis protect project: improving patient care by implementing a regional prospective quality registry for PJI	Henk Scheper
15.40 - 15.48	FP68	Highly variable effect of sonication as a method to dislodge biofilm embedded staphylococcus epidermidis, in vitro	Erik Thorvaldsen Sandbakken
15.48 - 16.00		Discussion	
16.00 - 16.30		Coffee - Posters - Exhibition	

Room: Okapi room 1&2			
11.24 - 11.32	FP60	Does the BACH classification of long bone osteomyelitis correlate with patient reported outcome measures following surgery?	Andrew Hotchen
11.32 - 11.40	FP61	Three years use of an antibiotic-loaded bone substitute for orthopaedic infections	Anders Joensson
11.40 - 11.48	FP62	Polymicrobial infections and microbial patterns in septic nonunions – a descriptive analysis of 42 cases	Markus Rupp
11.48 - 11.55		Discussion	
		Industry Symposium D (12.55 - 13.55) in Okapi Room 1&2 & Lunch	
		Key Session 9: How to prevent OA infection better?	**Chairs: Maya Hites & Charles Vogely**
14.00 - 14.15		Individual and environment control	Mike Reed
14.15 - 14.30		Does one dose fit all?	Maya Hites
14.30 - 14.45		CDC guidelines	Elie Berbari
14.45 - 14.55		Discussion	
		Free Papers K: Miscellaneous (6 x 6min + 2min)	**Chairs: Charles Vogely & Xavier Holemans**
15.00 - 15.08	FP69	Risk factors for cutibacterium acnes spinal implant infection: a case-control study	Stephane Corvec
15.08 - 15.16	FP70	Is extended trochanteric osteotomy during two-stage revision of the hip a safe procedure?	Giorgio Cacciola
15.16 - 15.24	FP71	Local bone antibiotic delivery using porous alumina ceramic: clinical and pharmacological experience	Eric Denes
15.24 - 15.32	FP72	Knee arthrodesis for the salvage of infected total knee arthroplasty predicting failure and the need for amputation	Antonia Chen
15.32 - 15.40	FP73	Is combined antibiotic therapy in spacers superior to monotherapy with an aminoglycoside? – an analysis of positive cultures during the second stage	Andre Dias Carvalho
15.40 - 15.48	FP74	Outcome of two stage surgery: “hone your work carefully; spare no effort”	Ines Pastor
15.48 - 16.00		Discussion	
		Coffee - Posters - Exhibition	

Friday 13 September 2019

Room: Queen Elizabeth Hall		
16.30 - 17.30	**Key session 10:** **Battles / Questions in debate Pro /Contra**	**Chairs:** **Alex Ramsden & Guy Putzeys**
	Battle 1: Early versus late flap in open fracture	**Early: Thierry Begue,** **Late: Olivier Barbier**
16.30 - 16.35	Moderator (present question/voting system)	
16.35 - 16.47	Early vs. Late	
16.47 - 16.55	Discussion	
16.55 - 17.00	Voting & Conclusion	
	Battle 2: Local antibiotic: promoting bacteral resistance?	**Yes: Alex Soriano / No: Olivier Borens**
17.00 - 17.02	Moderator (present question)	
17.02 - 17.14	Pro vs. Contra	
17.14 - 17.22	Discussion	
17.22 - 17.30	Voting & Conclusion	
17.45 - 19.00		
20.00 - 23.00	**EBJIS Gala Dinner. Marble Hall at the congress venue**	

Room: Okapi room 1&2			
		Free papers L: **Basic and translational research** **(6 x 6min + 2min)**	**Chairs:** **Charles Vogely &** **Christine Dupont**
16.30 - 16.38	FP75	Antibiotic-loaded hydrogel outperforms clinical gold standard treatment in a large animal model of methicillin-resistant staphylococcus aureus implant-associated osteomyelitis	Andrew Foster
16.38 - 16.46	FP76	Bone cement with microencapsulated rifampicin: a new strategy against periprosthetic joint infection	Pablo Sanz Ruíz
16.46 - 16.54	FP77	Extensive debridement is fundamental for the success of an absorbable gentamicin loaded bio-composite	Louise Kruse Jensen
16.54 - 17.02	FP78	High-energy focused extracorporeal shockwave therapy in addition to conventional treatment: results from an in vivo rabbit model of fracture related infection	Jan Pützler
17.02 - 17.10	FP79	Antimicrobial silver-modification for locking plates shows uneventful fracture healing and good biocompatibility – results of an experimental study in rabbits	Volker Alt
17.10 - 17.18	FP80	Local concentrations of gentamicin obtained by microdialysis after a controlled application of a gentacoll sponge in a porcine model	Maja Thomassen
17.18 - 17.24		Discussion	
17.45 - 19.00		**General Assembly** (for members of EBJIS, by invitation only) NB! This meeting takes place at Okapi room 1&2.	

Saturday 14 September 2019

Room: Queen Elizabeth Hall			
9.00 - 10.00		**Key Session 11: Bacteriophage therapy**	**Chairs: Andrej Trampuz & Jean-Paul Pirnay**
9.05 - 9.20		"From phage biology to phage therapy"	Rob Lavigne
9.20 - 9.35		Optimal delivery method	Fintan Moriarty
9.35 - 9.50		Current clinical evidence	Willem-Jan Metsemakers
9.50 - 10.00		Discussion	
10.00 - 10.30		Coffee - Posters - Exhibition	
10.30 - 12.00		**Best Papers (10 x 6 min + 2 min)**	**Chairs: Olivier Cornu & Martin McNally**
10.30 - 10.40		Travelling Fellowship Report	
10.40 - 10.48	BP1	Non-steroidal anti-inflammatory drug administration impairs antibiotic treatment of orthopedic device-related infection in a rat model	Marc Antoine Burch
10.48 - 10.56	BP2	Efficacy of sb-1 bacteriophage in treating and preventing methicillin-resistant staphylococcus aureus in a galleria mellonella model of implant-associated infection	Mariagrazia Di Luca
10.56 - 11.04	BP3	Development of a two-stage animal model to evaluate new therapeutic strategies in the treatment of infected non-unions	Holger Freischmidt
11.04 - 11.12	BP4	Operating room ventilation and the risk of revision due to infection after total hip arthroplasty - assessment of validated data in the norwegian arthroplasty register 2005- 2015	Håkon Langvatn
11.12 - 11.20	BP5	Antimicrobial peptides eradicate bacteria, including persisters, in antibiotic-treated mature biofilms	Henk Scheper
11.20 - 11.28	BP6	The value of serum inflammatory markers in the diagnosis of fracture related infections	Irene Katharina Sigmund
11.28 - 11.36	BP7	Guideline for preclinical studies of bone infections	Louise Kruse Jensen
11.36 - 11.44	BP8	Joint infection (pji) – is this correctly recorded as a 'reason for revision' on the national joint registry?	Irrum Afzal
11.44 - 11.52	BP9	The risk of periprosthetic joint infection during bacteremia	Meeri Honkanen
11.52 - 12.00	BP10	The terminal complement pathway identifies prosthesis infection in periprosthetic tissue samples	Ann-Kathrin Meinshausen
12.00 - 12.05		Discussion	
12.05 - 12.30		**Honorary lecture: Will bacteria overcome humans?**	**Fernando Baquero**
12.30.12.45		**Closing Remarks & Prizes**	**Olivier Cornu & Martin McNally**
12.45 - 14.00		Farewell lunch	

Room: Okapi room 1&2			
9.00 - 10.00		**Free Papers M:** **Clinical research on PJI prevention** **(6 x 6min + 2min)**	**Chairs:** **Jean-CyrYombi &** **Olivier Borens**
9.00 - 9.08	FP81	Cutibacterium avidum persists in the groin area despite surgical skin antisepsis: a potential risk factor for periprosthetic joint infections	Steven Maurer
9.08 - 9.16	FP82	Iodine impregnated incision drape does not prevent infection in knee arthroplasty surgery – 12 months follow-up in a cohort of 1187 patients	Anne Brun Hesselvig
9.16 - 9.24	FP83	Reduced wound leakage and prosthetic joint infections in arthroplasty with modified wound closure	Ramon Roerdink
9.24 - 9.32	FP84	Universal decolonisation with polyhexanid prior to hip and knee joint arthroplasty. A regional multicenter time series analysis with regressional analysis.	Tobias Kramer
9.32 - 9.40	FP85	Prevention of early periprosthetic joint infections in a university hospital	Tina Wik
9.40 - 9.48	FP86	The impact of untoward events during primary or revision total hip or knee arthroplasty surgery	Rihard Trebse
9.48 - 10.00		Discussion	

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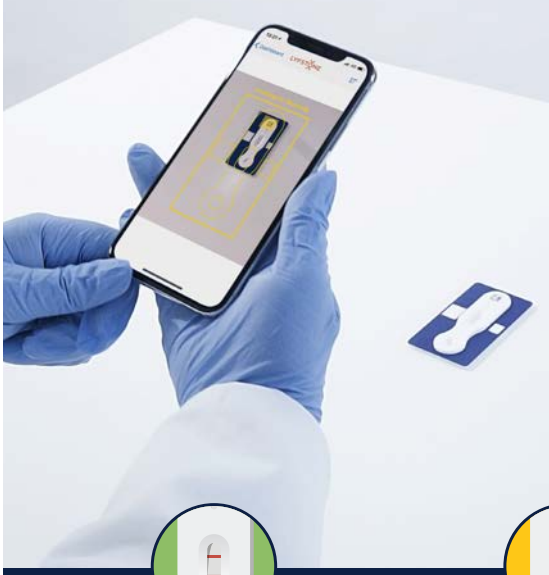

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SEP 12

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Industry Symposia

Industry Symposia A

Thursday, 12 September, 12.55-13.55 Room: Okapi 3

- Evaluation of a lateral flow test measuring synovial fluid Calprotectin for the diagnosis of prosthetic joint infection
- Development and Validation of a Correction Factor for Blood Contamination in Synovial Fluid used for a Point of Care Test for Infection
- Early Clinical Results of Prospective Calprotectin POC testing in Revision Total Knee Arthroplasty

Speakers:
Iain McNamara
Alison K. Klika
Viktor Krebs

Industry Symposia B

Heraeus

Thursday, 12 September, 12.55-13.55 Room: Okapi 1 & 2

Myths and truths of antibiotic use in PJI

Speakers:
Pablo Sanz Ruiz
Tamsin Oswald
Andrej Trampuz
Christof Berberich

Industry Symposia C

ZIMMER BIOMET

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Friday 13 September 2019 - 12.55-13.55 Room: Okapi 3

Update on ICM & new topics in PJI diagnostics

Moderator: T. Gehrke

12.55	Welcome	*T. Gehrke*
13.00	ICM update on PJI diagnostics with Alpha Defensin	*T. Gehrke*
13.10	The negative culture – how often – what's next	*M. Wouthuyzen-Bakker*
13.20	Fungal Infection – importance	M. Wouthuyzen-Bakker
13.30	New diagnostical tools: what is coming up?	*T. Gehrke*
13.40	Discussion All	
13.55	End	

Speakers:
Thorsten Gehrke
Marjan Wouthuyzen-Bakker

Industry Symposia D

Friday 13 September 2019 - 12.55-13.55 Room: Okapi 1 & 2

Optimizing Outcomes in the Management of Bone Infection

Speakers:
Mr. Martin McNally, Oxford UK
Dr. Willem-Jan Metsemakers, Leuven, Belgium
Mr. Jamie Ferguson, Oxford UK

Exhibitor directory

Platinum Partners

Company	Contact details	Company description
Biocomposites	**Biocomposites Ltd** www.biocomposites.com Booth 1	"At Biocomposites, we are distinct in that our team of specialists is singularly focused on the development of innovative calcium compounds for surgical use. We are proud to be driving improved outcomes across a wide range of clinical applications, in musculoskeletal infection, trauma, spine and sports injuries, for surgeons and patients alike."
BONESUPPORT™	**BONESUPPORT AB** www.bonesupport.com Booth 2	BONESUPPORT™ is an orthobiologic company specializing in the development of innovative injectable bone graft substitutes that remodel into bone within 6 to 12 months. Used in more than 35,000 patients, and includes the only CE marked injectable antibiotic eluting bone graft substitutes; CERAMENT®IG with gentamicin, and CERAMENT® V with vancomycin.
Heraeus	**Heraeus Medical GmbH** www.heraeus.com Booth 3	Heraeus Medical stands for delivering value to the patient, the healthcare professional and the healthcare system through innovation and evidence based medicine in Implant Fixation, Infection Management and regenerative treatments for bone, cartilage and soft tissue. Over the years the company built up extensive experience in the field of therapeutic support for PJI with local antibiotics and is a reliable and committed partner in all aspects that deal with the management of musculoskeletal infections.

Gold Partners

Company	Contact details	Company description
LYFSTONE	**Lystone AS** www.lyfstone.com Booth 8	Lyfstone AS have developed an informative and functional Calprotectin biomarker for the orthopaedic market. The CE-IVD labelled Lyfstone® Calprotectin for synovial fluid, a test designed to give results within 15 minutes, serves as a diagnostic aid for screening of suspected PJI patients in a near patient setting or laboratory.
ZIMMER BIOMET Your progress. Our promise.®	**Zimmer Bionet** www.zimmerbiomet.com Booth 5	Founded in 1927 and headquartered in Warsaw, Indiana, Zimmer Biomet is a global leader in musculoskeletal healthcare. We design, manufacture and market orthopaedic reconstructive products; sports medicine, biologics, extremities and trauma products; office based technologies; spine, craniomaxillofacial and thoracic products; dental implants; and related surgical products.

Silver Partners

Company	Contact details	Company description
bonalive	**Bonalive Biomaterials Ltd** www.bonalive.com Booth 19	At the intersection of technology and human biology, Bonalive® granules reduces the need for antibiotics in the resolution of chronic bone infections. Bonalive Biomaterials provides patients and surgeons with well-proven and safe bone regenerative products in orthopedics, trauma, spine, septic bone and ear surgery. It's time to heal smarter. #SmartHealing
KCI AN ACELITY COMPANY	**KCI** www.acelity.com Booth 21	KCI, an Acelity Company, is a global advanced wound care company committed to developing innovative healing solutions for customers and patients across the wound care continuum. We deliver value through solutions that aim to speed healing and lead the industry in quality, safety and customer experience, offering unparalleled service to support clinicians in the management of patients and therapies.

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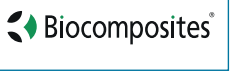
Exhibitor directory

Exhibitors

Company	Contact details	Company description
	**aap Implantate AG** www.aap.de Booth 9	aap Implantate AG is a globally operating medical device company, developing, manufacturing and marketing trauma products for orthopedics. Our three innovative patent protected platform technologies include the anatomical plating system LOQTEQ® (launched), the antibacterial silver coating technology (clinical trial in preparation) and the resorbable magnesium implant technology (under development).
	**European Cell and Tissue Bank** www.ectb.eu Booth 6	European Cell and Tissue Bank is a non-profit association, based in Austria. In compliance with the EU directives, we procure, store, processes and distribute tissue, and offer with OSTEOmycin™, a human bone allograft, impregnated with antibiotics (Vancomycin or Tobramycin). OSTEOmycin™ for simultaneously preventing infection and biofilm while reconstructing of bone defects
	**G21 S.r.l.** www.g-21.it Booth 18	G21 is a leading developer and manufacturer of bone cements and acrylic resins with years experience in orthopedics, oncology orthopedics and minimal invasive spine surgery. We are proud to affirm our unique and complete range of products for PJI care, in particular our custom modular spacer SpaceFlex for hip, knee and shoulder .
	**Molzym** www.molzym.com Booth 20	Molzym is manufacturer and supplier of innovative products for molecular microbiology and diagnostics. The product portfolio ranges from DNA isolation kits based on the proprietary MolYsis™ technology, ultra-clean, DNA-free PCR reagents to complete diagnostics solutions for the culture-independent detection of bacteria and fungi from body fluids and tissues (SepsiTest™-UMD, Micro-Dx™).
	**NuVasive Specialized** www.nuvasive.com Booth 11	NuVasive is a world leader in minimally invasive, procedurally-integrated solutions. From complex spinal deformity to limb length discrepancy and non-union solutions, NuVasive is transforming surgery with innovative technologies designed to deliver reproducible surgical outcomes. The PRECICE® system provides remote control technology for the treatment of limb length discrepancies and non-unions.
	**Stryker** www.stryker.com Booth 16	Stryker is one of the world's leading medical technology companies and, together with our customers, is driven to make healthcare better. We offer innovative products and services in Orthopaedics, Medical and Surgical, and Neurotechnology and Spine that help improve patient and hospital outcomes.
	**Tecres S.p.a.** www.tecres.it Booth 7	Tecres has got thirty-five years of experience as manufacturer of bone cements for orthopaedics. Cemex bone cements and Spacer, the unique temporary antibiotics-loaded prostheses for two-stage septic revision, are successfully sold worldwide. These products are available also in the combination Vancomycin-Gentamicin. CalCEMEX is our innovative reinforced bone substitute.

1 

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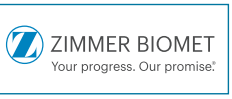
5 

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Exhibition floor plan

[FP1] IMPROVED MICROBIOLOGICAL DIAGNOSIS OF PROSTHETIC JOINT INFECTIONS BY USING BEADMILL PROCESSING OF TISSUE SAMPLES AND BLOOD CULTURE BOTTLES

Karlien Vanhouteghem[1], Olyslaegers Christophe[2], Fortems Yves[2], Van Eynde Elke[2], Willems Philippe[1], Van Schaeren Jef[1], Vanherendael Bruno[1]

[1]*GZA Hospitals, Antwerp, Belgium, Department of Laboratory Medicine*
[2]*GZA Hospitals, Antwerp, Belgium, Department of Orthopaedic surgery and Traumatology*

Aim: Microbiological culture of intraoperative periprosthetic tissue samples (IPTS) is one of the main criteria in diagnosing prosthetic joint infections (PJI) as stated by different guidelines. The current techniques are labor-intensive, prone for contamination and show low sensitivity. The aim of this study was to evaluate the added value of beadmill processing of IPTS and culturing in blood culture bottles (BCBs) over the conventional method of standard agar and broth alone.

Method: We conducted a single-center prospective study from May 2017 to January 2018 at the GZA Hospitals, a secondary care hospital (1012 beds) in Antwerp, Belgium. IPTS from patients undergoing revision arthroplasty were consecutively processed. Each IPTS was aseptically divided in two equal parts: one was processed by direct inoculation on agar and in broths (non-homogenized method); the other was transferred in a sterile vial with saline solution and glass beads (EOLabs), homogenized using a mechanic cell disruptor for 30s (Disruptor genie, Scientific Industries), 2mL of the suspension was inoculated in (an)aerobic BCBs, agar plates and broths (homogenized method). Agar plates were incubated for 4d; broths and BCBs in BacT/Alert (bioMerieux) for 14d. Micro-organisms were identified using MALDI-TOF MS (Bruker). Sensitivity (Se) and specificity (Sp) were calculated against the IDSA definition of PJI for different culture sets: non-homogenized and agar/broth; homogenized processing and agar/broth, agar/broth/BCB, agar/BCB. Ethics committee approved the study.

Results: Overall, 122 IPTS from 32 episodes from 29 patients were included; 14 subjects met the IDSA PJI criteria. No difference (Se71.4%,Sp88.8%) was observed between the conventional method and the homogenized method for the agar and broth set. An increased sensitivity was observed for the homogenized method with addition of BCBs (Se85.7%) in contrast to agars and broths alone (Se71.4%). The homogenized method with BCBs and agar plates showed an excellent specificity and positive-predictive value, indicating the lower contamination risk and facilitating the microbiological diagnosis. Adding broths to this combination increases the false positivity rate (Sp94.4%). A false positivity rate of 15/122 IPTS was observed for broths alone, in contrast to 2/122 for BCBs alone. Also, one case (1/14) would have been missed when using the homogenized method with agars and broths alone.

Conclusions: Beadmill processing of IPTS and culturing in BCBs is a sensitive and highly specific culture method for diagnosis of PJI. The superior specificity versus conventional methods minimizes false positive results, which frequently lead to erroneous clinical decisions. Furthermore, this makes semi-automated laboratory processing possible.

[FP2] PREOPERATIVE CULTURES OF SYNOVIAL FLUID POORLY PREDICT THE INTRAOPERATIVELY DETECTED PATHOGEN IN PJI

Nora Renz[1;2], Philipp Schulz[1], Constantin Dlaska[1;3], Andrej Trampuz[1]

[1]*Charité – Universitätsmedizin Berlin, Center for Musculoskeletal Surgery, Berlin, Germany*
[2]*Inselspital, Infectious Diseases Department, Bern, Switzerland*
[3]*Orthopaedic Research Institute of Queensland, Australia*

Aim: Surgical and antimicrobial treatment of periprosthetic joint infections (PJI) depends largely on the causative pathogen. We assessed the pathogen detection rates and the concordance of preoperative synovial fluid culture and culture of intraoperative samples harvested during revision surgery in patients with PJI.

Method: Culture-positive PJI cases treated at our institution from 02/2011 to 07/2018, for which culture results from preoperative (synovial fluid) and intraoperative samples (periprosthetic tissue, synovial or sonication fluid) were available, were retrospectively assessed. For organisms belonging to the resident skin flora (coagulase-negative staphylococci, cutibacteria and corynebacteria) significant growth was considered, if the identical pathogen grew in ≥2 samples or >50 cfu/ml sonication fluid. For other pathogens (S. aureus, streptococci, enterococci, fungi and gram-negative rods) or patients under antimicrobials, any growth was considered positive. We determined the pathogen detection rate in preoperative and intraoperative cultures and compared it in different subgroups using Fisher's exact test. Furthermore, we assessed the concordance of preoperative and intraoperative cultures.

Results: We included 167 culture-positive PJI cases (76 hip and 91 knee joints). Coagulase-negative staphylococci (n=55, 33%), Staphylococcus aureus (n=34, 20%) and streptococci (n=22, 13%) were the most common pathogens. In 17 cases (10%) polymicrobial infection was found. The pathogen(s) grew in synovial fluid in 105 cases and in intraoperative samples in 146 cases (63% vs. 87%, p<0.001). 49 patients received antibiotics before aspiration and/or surgery. No differences were observed comparing hip and knee prostheses, primary and revision prostheses or patients receiving or not receiving antibiotics before sampling. Congruent results of preoperative and intraoperative cultures were found in 85 cases (concordance 51%). In 14 cases (8%), the pathogen was detected preoperatively only, in 59 cases (35%) the pathogen was found intraoperatively only; in 3 cases an additional pathogen was found preoperatively, in 6 cases an additional organism was found intraoperatively. Pathogen detection was significantly better in intraoperative compared to preoperative cultures in low-virulent pathogens (87% vs 36%, p<0.001), polymicrobial infections (88% vs. 47%, p<0.001) and delayed/late PJI (>3months; 92% vs 64%, p<0.001). There was no difference regarding detection rate of high-virulent pathogens (88% vs 83%) and in early postoperative PJI (<3 months, 91% vs. 73%).

Conclusions: As concordance of preoperative and intraoperative microbiological results was 51%, surgical and antimicrobial treatment should not be selected based on preoperative synovial fluid cultures only. An additional pathogen was found intraoperatively in 39%.

[FP3] DIAGNOSTIC VALUE OF THE UNYVERO IMPLANT AND TISSUE INFECTION (ITI) MULTIPLEX PCR SYSTEM FOR RULING OUT PROSTHETIC JOINT INFECTION IN 200 UNSUSPECTED REVISIONS OF KNEE AND HIP ARTHROPLASTY

Jon Goosen[1], Anouk Jacobs[2], Petra Heesterbeek[2], Saskia Susan[2], Frans Bovendeert[2], Jacques Meis[3]

[1]*Sint Maartenskliniek, Orthopaedic surgery, Ubbergen, Netherlands*
[2]*Sint Maartenskliniek, Ubbergen, Netherlands*
[3]*Canisius Wilhelmina Hospital, Nijmegen, Netherlands*

Aim: Currently, despite a thorough diagnostic work up, around ten percent of the presumed aseptic revisions turn out to have unexpected positive cultures during the revision procedure[1]. The purpose of this study was to evaluate the negative predictive value (ruling out) of the automated multiplex PCR Unyvero i60 implant and tissue infection (ITI) cartridge (U-ITI) system for the detection of microorganisms in synovial fluid obtained intraoperatively.

Methods: A prospective study was conducted with 200 patients undergoing a one-stage knee or hip revision. In all patients six intraoperative tissue cultures were taken and a sample of synovial fluid which was analyzed as a culture and with the multiplex PCR U-ITI system. The primary outcome measure was the negative predictive value (NPV) of the multiplex PCR U-ITI system compared to the intraoperative tissue cultures to reliable rule out an infection.

Results: The NPV of the multiplex PCR U-ITI system of synovial fluid compared to tissue cultures in knee and hip revisions was 95.7% and 92.5%, respectively. In addition, cultures require several days for growth whereas the automated mPCR U-ITI system provides results within five hours.

Conclusions: The multiplex PCR U-ITI system is a quick additional test to conventional cultures in presumed aseptic knee and hip revisions for reliable ruling out of an underlying infective cause. With this simple test antibiotic overtreatment as well as undertreatment after one-stage revision arthroplasty can be avoided which can directly result in a reduction in length of hospital stay, hospital costs and possible antibiotic resistance development.

1. Jacobs AM, Benard, M, Meis JF, Van Hellemondt G, Goosen JH. The unsuspected prosthetic joint infection: incidence and consequences of positive intra-operative cultures in presumed aseptic knee and hip revisions. Bone Joint J. 2017 Nov;99-B(11):1482-1489.

[FP4] ADVANTAGES IN DIAGNOSTICS OF ORTHOPEDIC IMPLANT INFECTION USING INCUBATION OF EXPLANTS

Arnold Suda[1], Nadine Landua[1], Thomas Miethke[2]

[1]*University Medical Center Mannheim, Department for Orthopaedics and Trauma Surgery, Germany*
[2]*University Medical Center Mannheim, Department of Microbiology, Mannheim, Germany*

Aim: Diagnostics of orthopedic implant infection remains challenging and often shows false negative or inadequate results. Several methods have been described to improve diagnostic methods but most of them are expensive (PCR) or not accessible for all hospitals (sonication). Aim of this study was to evaluate the results of incubation of orthopedic explants compared to biopsies and punction fluid using conventional microbiological methods.

Method: In this prospective study, we included patients who received septic or aseptic orthopedic implant removal in a single University hospital between July and December 2018. A part of the explant as well as minimum 2 tissue biopsies or additional punction fluid were put in a bouillon and incubated for 11 days. Patient´s records with co-morbidities, use of antibiotics and demographic data were evaluated. The results were analyzed. The study was approved by the ethical committee.

Results: 94 patients were included in this study (43 females, 51 males, mean age 54 years). We detected statistically significant more pathogens in the bouillon with explants compared to biopsies (p=0,0059). We found the same results with pedicle screws (n=11, p=0,039) and endoprosthesis (n=56, p=0,019). Patients after osteosynthesis (p=27) showed same results but statistically not significant (p=0,050). Use of antibiotics did not have influence on the diagnostic result as well as co-morbidities. In 38 patients (40,4%), additional bacteria could be detected in explant´s bouillon. Most common pathogens were Staph. aureus, E. faecalis, Staph. epidermidis and Micrococcus luteus, mixed infections could be found in 9%.

Conclusions: In this study we could show that incubation of orthopedic implants has advantages in diagnostics of pathogens in infected endoprosthesis, osteosynthesis and spondylodesis. This method is simple compared to PCR or sonication and as cheap as incubation of tissue samples but in 40% of the cases, additional pathogens can be detected. We recommend to incubate removed screws, hip endoprosthetic heads or inlays in bouillon to optimize diagnostics and to detect all pathogens.

[FP5] MID-INFRARED SPECTROSCOPY FOR A RAPID DIAGNOSIS OF SEPTIC ARTHRITIS: A MULTI-CENTRIC STUDY

Albert Jean-David[1], Le Corvec Maena[2], Martin Antoine[3], Guennoc Xavier[3], David Claire[4], Hoang Sylvie[4], Guedes Claudie[4], Hoppe Emmanuel[5], Benoit Le Goff[6], Jousse-Joulin Sandrine[7], **Jerome Bernard**[2], Sire Olivier[8], Guggenbuhl Pascal[1], Olivier Loreal[9]

[1]*CHU Sud de Rennes, Rheumatology, Rennes, France*
[2]*DIAFIR, Research, Rennes, France*
[3]*CH de Saint-Brieuc, Rheumatology, Saint-Brieuc, France*
[4]*CH de Bretagne Atlantique, Rheumatology, Vannes, France*
[5]*CHU de Angers, Rheumatology, Angers, France*
[6]*CHU de Nantes, Rheumatology, Nantes, France*
[7]*CHU de Brest, Rheumatology, Brest, France*
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Background: Septic arthritis diagnostic is an emergency which implies a treatment with antibiotics and hospitalization. The diagnosis is based on the cytobacteriological examination of the synovial fluid (SF), but direct bacteriological examination is insensitive, and the result of the culture is obtained only after several days. Therefore, there is still a need for a rapid, simple and reliable method for the positive diagnosis of septic arthritis. Such method must allow avoiding both unrecognized septic arthritis leading to major functional consequences, and overdiagnosis that will induce unnecessary expensive hospitalization and unjustified treatment. Mid-infrared (MIR) spectroscopy, that gives a metabolic profiling of biological fluids, has been proposed for early and fast diagnosis.

Objectives: To confirm [(1)] the MIR spectroscopy to discriminate SF samples from patients with septic arthritis from other causes of joint effusion.

Methods: Synovial fluids from 402 patients referred for suspected arthropathies were prospectively collected in six hospitals and stored at -80°C. The infrared absorption spectrum was acquired for each of the frozen samples using a chalcogenide fiber biosensor. The most informative spectral variables were selected and then used to develop an algorithm. Then, the algorithm has been validated on independent synovial fluids collected straight after arthrocentesis from 86 patients.

Results: The calibration (n=402) and validation (n=86) cohorts consists of synovial fluid samples from patients exhibiting various etiologies. These samples (n=488), by using SF bacteriological analysis and culture and 16S PCR analysis were classified as septic arthritis (n=43) or non-septic arthritis (n=443). On the calibration cohort, the performances of the algorithm show a sensitivity of 90%, a specificity of 90%, a NPV of 99% and a PPV of 41%, the area under the ROC curve (AUROC) was 0.95. On the validation cohort, the performances of the algorithm show a sensitivity of 92%, a specificity of 81%, a NPV of 98% and a PPV of 46%, the area under the ROC curve (AUROC) was 0.90.

Conclusions: This study confirms the diagnostic performances of MIR spectroscopy for the discrimination between septic and non-septic synovial fluids. The high negative predictive value and the very short time (within ten minutes) required to obtain the result makes it possible to quickly rule out an infection diagnosis.

References: (1). J-D Albert et al., Joint Bone Spine, 2016, 83, 318-323.

[FP6] DIAGNOSIS OF STAPYLOCOCCUS SPP. PROSTHETIC JOINT INFECTIONS WITH BACTERIOPHAGE K BASED METHODS

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Background: Currently, the gold standard for the microbiological diagnosis remains the culturing of preoperative aspirated joint fluid and intraoperative periprosthetic tissue samples, which give false negative results in about 7 % of cases. Lytic bacteriophages are viruses that specifically infect and lyse bacteria within their replication cycle.

Aim: The aim of our study was to explore possibilities for the use of bacteriophage K for the detection of live *Staphylococcus* spp. bacteria in sonicate fluid of infected prosthetic joints, to possibly contribute to the development of a faster, more sensitive, specific and at the same time economical and handy method for the establishment of the right diagnosis.

Material and methods: Sonicate fluid samples obtained from 104 patients with revision arthroplasty were analysed. After the optimisation two indirect phage-based methods were used: a) bioluminescence detection of bacterial intracellular ATP released by bacteriophage K mediated lysis and b) q-PCR with primers specific for bacteriophage K DNA. The results were compared with classical microbiological cultivation methods.

Results: With both methods the analysis of sonicate fluid and the analysis of its over-night culture achieved 100 % specificity and predictive value, as there were no false positive results. The sensitivity of the methods was lower when analysing sonicate fluid samples directly, without cultivation. The sensitivity of qPCR detection was higher (81.25 %) compared to the sensitivity of ATP detection (62.5 %) in sonicate fluid directly as a result of 3 false negative results with the qPCR method compared to 6 false negatives with the ATP detection method. The sensitivity of the methods was significantly improved (to 94.12 %) with overnight cultivation of sonicate fluid samples prior to analysis, with no difference in detection between the methods. With both methods, with pre-cultivation of sonicate fluid samples, only one of the tested samples resulted in a false negative result. However, the same sample was negative even when tested with standard microbiological methods. In this patient, only the microbiological cultivation of the periprosthetic tissue sample was positive. The bioluminescence method took 3h with a limit of detection (LOD) in the bacterial concentration range of 10^3 CFU/mL. The method with qPCR took 4h and had a LOD of 10^2 CFU/mL.

Conclusion: Detection of staphylococci within sonicate fluid with bacteriophage K based methods is a rapid, sensitive and specific approach.

[FP7] EARLY DEBRIDEMENT, ANTIBIOTICS AND IMPLANT RETENTION (DAIR) PROCEDURES IN COMPLICATED WOUND HEALING AFTER TOTAL JOINT ARTHROPLASTY – ARE ELEVATED SYNOVIAL FLUID LEUKOCYTE COUNTS ACCURATE IN DIFFERENTIATING SUPERFICIAL FROM DEEP INFECTIONS?

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Aim: Treatment of complicated wound healing after total joint arthroplasty is controversial. What exactly constitutes prolonged wound drainage is matter of debate and recommendations to manage it vary considerably. Nonoperative measures are often recommended. If drainage persists, surgery may be indicated. To further intricate decision-making, differentiating superficial from deep surgical site infection is also controversial and inherently complex. Specific cutoffs for synovial fluid leukocyte count and blood C-reactive protein(CRP) in the acute stage have been suggested as a way to superficial infection requiring superficial wound washout from deep infection requiring a formal debridement, antibiotics and implant retention(DAIR) procedure. The goal of this study is to analyze clinical and laboratory findings of an institutional protocol of "aggressively" proceeding with formal DAIR in all patients with complicated wound healing

Method: Our indications for DAIR in suspected acute postoperative periprosthetic joint infection (PJI) are: 1)prolonged wound drainage and CRP upward trend after day-3; 2)persistent wound drainage by day-10 regardless of CRP; 3)wound healing disturbance (e.g."superficial" infection, "superficial" skin necrosis) anytime in early postoperative weeks. We retrospectively evaluated patients undergoing DAIR in the first 60 postoperative days between 2014-2018. Patients without multiple deep tissue cultures obtained intraoperative were excluded. Deep infection was defined by at least two positive deep tissue cultures or one positive deep culture and positive leukocyte count (>10,000 cells/mL or >90% PMN).

Results: A total of 44 DAIR procedures were included. Deep infection was confirmed in 79.5%(35/44) of cases. Mean CRP in infected cases was 93mg/L with 63%(19/30) of them below the 100 mg/L threshold. Unfortunately, only a small proportion of cases (10/44) had synovial fluid leukocyte counts available. Mean leukocyte count was 15,558 cells/mL and mean proportion of PMN was 65.3%. Of these ten, six confirmed deep infections were below the proposed >10,000 cells/mL or >90% PMN cutoff.

Conclusions: Early diagnosis of acute postoperative PJI is often hampered by its very subtle presentation. This study confirms that more often than not, deep infection is present when facing complicated wound healing after total joint arthroplasty, supporting our institutional "aggressive" protocol. We have been surprised by the number of confirmed acute PJI with low blood CRP levels and low synovial leukocyte counts. We hypothesize that the proposed acute PJI specific thresholds may lead to misinterpret a significant proportion of cases as superficial infections thus compromising timely intervention. The findings of this study lack confirmation in larger cohorts

[FP8] DAIR PROCEDURE IN PROSTHETIC JOINT INFECTION: PREDICTIVE TOOLS OF FAILURE

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Background: DAIR is an attractive treatment for PJI. The purpose of this study is to determine predictive factors of failure.

Materials and Methods: We reviewed all DAIR procedures for hip PJI performed between 2002-2017 (n=69). Data recorded included all factors correlated with treatment failure. KLIC score and an adapted McPherson score (sum of three criteria where the lower score is three for 3 A and the higher is 9 for 3 C) were analyzed.

Results: Infection eradication for early PJI (< 4 weeks) was achieved in 68% of patients and was correlated with treatment success (p=0.01). Success rate was only 37.5% in hematogenous infection and 28% in late infection. KLIC score (p=0.036), McPherson adapted score (threshold value 5.5/9) (p=0.01), CRP (with a cut-off value at 73.5 mg%) (p=0.025) and late PJI (p=0.031) were significantly predictive of failure treatment. For the KLIC score, patients with a score of ≤2, >2-3.5, >4-6.5, ≥7, respectively obtained a rate of failure of 33.3%,60%,71% and 100%.

We have established an equation in order to predict failure treatment. This tool predicts treatment failure when Logit P (equation result) is >0.476 with a sensitivity of 80% and a specificity of 83% (p = 0.05).

Conclusions: KLIC and adapted McPherson scores predict outcome of DAIR and should help making the decision in PJI treatment. Tsang et al, demonstrates that symptoms lasting for less than 7 days represent a significant threshold. Despite 80% of our patients operated within 7 days, the analysis wasn't significant. It seems that a DAIR procedure done promptly is not the only condition required for success and some others factors influence the outcome of treatment.

Logit P = 0.376 - (0.0533 * Kidney failure) + (0.933 * Age) + (0.640 * BMI) + (1.111 * Tobacco) + (0.031 * Fistula) + (0.164 * Deep infection) - (0.366 * Revision) - (2.684 * Exchange of the modular component) - (2.685 * Early PJI) + (1.243 * Hematogen PJI) + (0.127 * Polymicrobial PJI) - (0.309 * Staphylococcus aureus) + (0.393 * MRSA) + (0.907 * Resistance to quinolons/rifampicin) + (3.789 * CRP >73,5mg/L) - (2.578 * Onset of symptoms > 7days)

[FP9] MANAGEMENT OF EARLY PERIPROSTHETIC JOINT INFECTION WITH DEBRIDEMENT-IRRIGATION, ANTIBIOTIC THERAPY AND IMPLANT RETENTION: POSTOPERATIVE POSITIVE SUCTION DRAINAGE FLUID CULTURE IS A PREDICTIVE FACTOR OF FAILURE

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Introduction: Success rate after Debridement-Irrigation, Antibiotic Therapy and Implant Retention (DAIR) for treatment of Acute Haematogenous (AH) and Early Post-surgical (EP) periprotsthetic joint infection (PJI) varies widely among published studies. Prosthesis exchange is recommended to treat PJI after a failed DAIR. However, no early postoperative prognostic factors permitting to identify future failures have been described.

Aim: Identify early prognostic factor of failure after DAIR in order to propose efficient treatment before onset of chronic PJI.

Hypothesis: Positive suction drainage fluid culture is a strong early predictive factor of failure.

Methods: We conducted a retrospective study, with a minimum 2 years follow-up. Twenty-two consecutive patients (78 years-old +/-10) with EPPJI: i.e. infection within 1 month after joint replacement (n=12; 55%) or AHPJI: i.e. acute haematogenous infection with less than 2 weeks evolution (n=10; 45%) were included. The involved prostheses were: Total Knee Arthroplasty (n=12; 55%), Total Hip Arthroplasty (n=7 ; 32%) and Hip Hemi-Arthroplasty (n=3 ; 14%).

DAIR was indicated for each patient. Suction drainage fluid was systematically analysed at day 1, 3 and 5 postoperative.

Failure of the procedure was defined as: need for iterative surgery to control PJI or suppressive antibiotherapy to control PJI or death related to PJI.

Results: At 2 years follow-up, failure rate after DAIR was 55%. Only positive suction drainage fluid culture was statistically associated with treatment failure (p=0,039).

Neither type of prosthesis: knee prosthesis vs hip prosthesis (Odds Ratio (OR)=1 ; IC95%[0.14 ; 7.21]) nor type of fixation : cemented vs uncemented prothesis (OR=4,39 ; IC95%[0.29 ; 269]) were associated with treatment failure.

In addition, type of bacteria causing PJI and especially *S. aureus* (OR=3,1 ; IC95%[0.42; 28.61]), type of infection (OR= 1,47 ; IC95%[0.21 ; 11.37]), delay between onset of symptoms and DAIR (OR= 1,63 ; IC95% [0.21 ; 14.85]) or retaining of modular component (OR= 1.32 ; IC95% [0.17 ; 10.59)) were not associated with a higher rate of failure.

Conclusion: Positive suction drainage fluid culture could be an early postoperative predictive factor of failure after open Irrigation-Debridement, Antibiotic Therapy and Implant Retention for EPPJI and AHPJI.

[FP10] DEBRIDEMENT, ANTIBIOTICS AND IMPLANT RETENTION IS STILL A VIABLE TREATMENT OPTION IN EARLY PERIPROSTHETIC JOINT INFECTION PRESENTING MORE THAN SIX WEEKS AFTER INDEX ARTHROPLASTY

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Aim: Treatment success of debridement, antibiotics and implant retention (DAIR) is in early periprosthetic joint infection (PJI) is largely dependent on the presence or absence of a mature biofilm. In what time interval a mature biofilm develops is still unclear, and therefore, the time point at which DAIR should be disrecommended remains to be established. This large multicenter trial evaluated the failure rates of DAIR for different time intervals from index arthroplasty to DAIR in early PJI.

Method: We retrospectively evaluated patients with early PJI treated with DAIR between 1996 and 2016. Early PJI was defined as a PJI that developed within 90 days after index arthroplasty. Patients with hematogenous infections, arthroscopic debridements and a follow-up less than one year were excluded. Treatment failure was defined as 1) any further surgical procedure related to infection 2) PJI-related death, or 3) long-term suppressive antibiotics, all within one year after DAIR.

Results: A total of 769 patients were analyzed. Treatment failure occurred in 294 patients (38.2%), and was highest in the early (0-2 weeks) and late (6-12 weeks) post-surgical course: 0-2 weeks: 42.0% (95/226); 2-4 weeks: 37.8% (143/378); 4-6 weeks: 29.0% (29/100), and 6-12 weeks: 41.5% (27/65). Exchange of modular components was performed to a lesser extent in the early compared to the late post-surgical course (40.7% vs 63.2%, $p<0.001$). The percentage of positive cultures obtained during DAIR decreased according to the time interval from index arthroplasty to DAIR: 0-2 weeks: 88.6%; 2-4 weeks: 86.5%; 4-6 weeks: 75.1%; and 6-12 weeks: 63.2%, $p<0.001$. The causative microorganisms and the duration of symptoms were comparable between groups (6.7 days, SD ± 5.9, $p=0.135$).

Conclusions: Although failure rates increase when a DAIR is performed more than six weeks after index arthroplasty, DAIR is still a viable treatment option in these patients in case DAIR is performed as soon as symptoms of infections arise and modular components can be exchanged.

[FP11] NO DIFFERENCE IN 1-YEAR RE-REVISION RATE AFTER DEBRIDEMENT ANTIBIOTICS AND IMPLANT RETENTION (DAIR) BY TIMING OF DAIR PROCEDURE FOR TOTAL HIP AND KNEE ARTHROPLASTY IN ACUTE POSTOPERATIVE INFECTIONS BASED ON DUTCH REGISTRY DATA

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Aim: Debridement Antibiotics and Implant Retention(DAIR) is a procedure to treat a periprosthetic joint infection(PJI) after Total Hip Arthroplasty(THA) or Total Knee Arthroplasty(TKA). The timing between the primary procedure and the DAIR is likely a determinant for its successful outcome. There are few retrospective studies correlating timing of a DAIR with success (1,2). However, the optimal timing of a DAIR and the chance of success still remains unclear. We aimed to assess the risk of re-revision within one year after a DAIR procedure and to evaluate the timing of the DAIR in primary THA and TKA. An estimation of the chance of a successful DAIR will help clinicians and patients in their decision-making process in case of an acute postoperative PJI.

Method: We used data from the Dutch Arthroplasty Register(LROI) and selected all primary THA and TKA in the period 2007-2016 who underwent a DAIR within 12 weeks after primary procedure. A DAIR was defined as a revision for infection in which only modular parts were exchanged. A DAIR was successful if not followed by a re-revision within 1 year after DAIR. The analyses were separated for THA and TKA procedures.

Results: 207 DAIRs were performed <4 weeks after THA of which 41(20%) received a re-revision within 1 year; 87 DAIRs were performed between 4-8 weeks of which 15(17%) were re-revised and 11 DAIRs were performed >8 weeks and 2(18%) received a re-revision.

126 DAIRs were performed <4 weeks after TKA of which 27(21%) received a re-revision within 1 year; 68 DAIRs were performed between 4-8 weeks of which 14(21%) were re-revised and 15 DAIRs were performed >8 weeks and 3(20%) received a re-revision.

Conclusions: There was no difference in 1-year re-revision rate after a DAIR procedure by timing of DAIR procedure for total hip and knee arthroplasty based on Dutch registry data.

[FP12] SERIAL ASPIRATIONS & INTRA-ARTICULAR ANTIBIOTIC INJECTIONS FOR NON-OPERATIVE MANAGEMENT OF CHRONIC PJI: INTRODUCING THE CONCEPT OF BIOFILM TRAINING

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Aim: We outline a treatment protocol for subjects with chronic periprosthetic joint infections (PJI) who elected not to have surgery. We developed a method of serial "fluid-depleting" aspirations with intra-articular gentamycin injections to affect the population of the biofilm community. We have experienced many treatment failures, as expected, but have also had a group of subjects who responded exceptionally well, requiring no surgical intervention. Our longest follow-up is 10 years.

Method: From June 2009 to December 2018, 372 clinical cases of chronic PJI involving primary and revision TKA and THA were treated. Of these, 25 subjects were treated with an active suppression protocol, in lieu of surgery. The protocol entailed frequent aspirations and intra-articular antibiotic injections to quell the PJI inflammatory response. All aspirations were performed by the treating surgeon in the orthopaedic clinic without fluoroscopic guidance. Based on a subject's response to the protocol, he/she was identified as 1 of 3 classifications: 1) Ongoing Treatment – Biofilm Trained (OTBT), 2) Ongoing Treatment – Biofilm Untrained (OTBU), and 3) Treatment Failure (TF). OTBT subjects showed no clinical signs of infection. Serum biomarkers (CRP, ESR) remained consistently normal and subjects were not on oral suppressive antibiotics. Aspiration analysis and cultures remained negative. Maintenance treatment consisted of a fluid-depleting aspiration with an intra-articular gentamycin injection every 12-16 weeks. OTBU subjects showed improved clinical symptoms, lowered serum biomarkers, and lowered WBC counts, but still demonstrated objective signs of infection. TF subjects did not respond to the protocol and showed unchanged/worsening clinical symptoms.

Results: Of the 25 subjects, 8 were THA's and 17 were TKA's. Of these cases, 21 (84%) were endoprosthetic replacements. 8 subjects (32%) were classified as OTBT, 6 (24%) as OTBU, and 11 (44%) as TF. All TF subjects were treated with a two-stage exchange protocol.

Conclusions: This study is the first describing the potential of modifying bacterial biofilm in a chronic PJI. While our success rate was modest (32%), "Biofilm Trained" subjects demonstrated dramatic changes. Subjects led normal lives, only minimally disrupted by an aspiration and injection every 3-4 months. In the future, we are looking at different agents to modify the enveloping biofilm, including a pre-aspiration injection of EDTA to disrupt the biofilm surface, followed by injecting benevolent bacteria to transform the biofilm to a benevolent state. If able to achieve such a state in a consistent fashion, the impact on the patient and healthcare communities would be enormous.

[FP13] GOOD OUTCOME AFTER PROSTHETIC JOINT INFECTION TREATED WITH DEBRIDEMENT AND RETENTION OF THE PROSTHESIS: A PROSPECTIVE REGISTRATION OF 99 PATIENTS

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Aim: Debridement, antibiotics and implant retention (DAIR) has become the preferred treatment in early prosthetic joint infections (PJI) and acute haematogenous PJI, but the success rates have been varying. The aim of this study was to evaluate the outcome of a high quality DAIR procedure performed according to a consistently applied surgical protocol in early PJI's and acute haematogenous PJI's in hip and knee.

Methods: We performed a prospective multicentre study in 8 hospitals in Norway. A standardized DAIR protocol was used in all patients. An empirical intravenous regimen containing cloxacillin and vancomycin was given until definitive microbiological results were known. Antibiotics were given in total for 6 weeks. The primary outcome measure was infection control. Factors that could affect the outcome were also studied.

Results: Out of 99 patients included, 82 were finally analysed. 68/82 patients were successfully trreated (82,9% (CI: 74,4%-90,2%)). We found that DAIR following an infected revision arthroplasty was associated with poor outcome (59%) compares to DAIR following a primary arhroplasty (89%, p=0,007).

Conclusion: The success rate of a standardized DAIR-procedure with 6 weeks of antibiotic treatment was good in PJI following primary prosthesis. The success rates following revision surgery infections are poor, and other treatment options should be considered.

[FP14] OUTCOME OF DAIR (DEBRIDEMENT, ANTIBIOTICS AND IMPLANT RETENTION) PROCEDURES FOR INFECTED TOTAL HIP AND KNEE REPLACEMENTS IN A TERTIARY REFERRAL CENTER

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Aim: To retrospectively evaluate infection eradication rate of DAIR procedures performed in our tertiary referral center. We analyzed whether the outcome was influenced by time of infection after arthroplasty, type of previous surgery or causative pathogen.

Methods: We retrospectively collected data of 87 patients treated with DAIR for periprosthetic joint infections after (revision) hip (n=52) and knee (n=35) arthroplasty between 2011 and 2017. Patients were divided into 3 groups: acute early infections (occurring <4 weeks, 27 cases), late chronic infections (occurring >4 weeks postoperative, 12 cases) and acute haematogenous infections (occuring >3 months after surgery with symptoms less than 4 weeks, 48 cases). Primary outcome was successful infection eradication after treatment within one year. Eradication failure was determined as unplanned subsequent surgery because of persistent infection, use of suppressive antibiotics or signs of infection at one year follow-up.

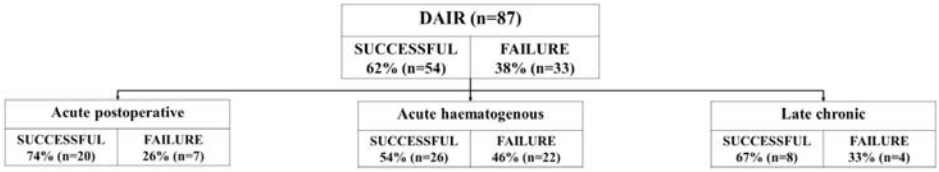

Figure 1.

Results: The success rates of DAIR in different types of prosthetic joint infection are shown in figure 1

Patients treated with DAIR (n=29) after previous treatment with DAIR, one- or a two-stage revision showed a success of 48% versus 69% in patients treated with DAIR after primary arthroplasty (n=58). A majority of the patients had a monomicrobial PJI (72.4%) versus polymicrobial (22%), while 6% were culture negative. The most frequently cultured causative pathogen in monomicrobial infections was *Staphylococcus aureus (18%) followed by Staphylococcus epidermis (13%). Patients with Staphylococcus aureus* infections had a success rate of 56% compared to 72% for *Staphylococcus epidermis infections*.

Conclusion: Our study shows that good results can be expected when DAIR is performed in patients with acute and late chronic PJI, 74% versus 67% respectively. Interestingly, in half of the patients who received a secondary DAIR, the prosthesis could still be retained. Lastly, specific causative organisms can lead to a lower success rate of DAIR.

[FP15] THE USE OF ANTIBIOTIC LOADED CALCIUM SULPHATE BEADS IN LOWER LIMB PERIPROSTHETIC JOINT INFECTION

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Introduction: Antibiotic loaded absorbable calcium sulphate beads (ALCSB) are an increasingly popular adjunct in the treatment of musculoskeletal infections including osteomyelitis and peri-prosthetic joint infections (PJI). Limited data exist regarding the clinical indications and biochemical outcomes of ALCSB in PJI cases.

Aims: To determine the proportion of organisms that were sensitive to the gentamicin and vancomycin that we add to the ALCSB as a part of our treatment protocol and to determine the prevalence of post-operative hypercalcaemia when used for treatment of hip and knee DAIR (debridement and implant retention) and revision arthroplasty for PJI.

Methods: A retrospective review of 160 hip and knee revisions using ALCSB performed between June 2015 and May 2018 at a tertiary unit was performed. 10-40 cc of ALCSB was used for each case containing vancomycin and gentamicin. Data recorded included patient demographics, comorbidities, indication for surgery, operative intervention, microbiological results and serum biochemistry for calcium levels.

Results: The cohort consisted of 91 males and 69 females, with a mean age of 69.0 years (21.3 to 93.1) and mean BMI of 34.7(12.6 to 48.1). 56 (35%) had single-stage revision, 45 (28.1%) had first stage revision, 35 (21.9) had DAIR, 19 (11.9%) had second stage revision and 5 (3.1%) other procedures.

Organisms included staphylococcus aureus (30.0%), culture-negative (27.5%), staphylococcus epidermidis (18.1%), and pseudomonas aeruginosa (3.1%). 54.3% were sensitive to both vancomycin and gentamicin, 25.0% to vancomycin only and 8.6% to gentamicin only.

11.9% (19/160) of patients had transient post-operative hypercalcaemia (normal range 2.2-2.7mmol/L), peaking at day 6-7 and resolved with hydration by day 10 postoperatively. Preoperatively, 26.9% had albumin <35 g/L and 49.3% had some degree of renal impairment with an eGFR <90 ml/min.

Conclusion: The use of ALCSB allows local delivery of vancomycin and gentamicin in lower limb PJI. Organisms were sensitive to this antibiotic combination in 88% cases. Care must be taken to monitor calcium for 10 days post-operatively.

[FP16] IMPLANT STABILITY OF TOTAL HIP ARTHROPLASTY AFTER DEBRIDEMENT AND IMPLANT RETENTION FOR PERIPROSTHETIC JOINT INFECTION

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Aim: Debridement and implant retention (DAIR) is a valuable option for treating periprosthetic joint infection (PJI), provided that the criteria of the Infectious Diseases Society of America guidelines are fulfilled. The inflammation caused by infection and the surgical impact of DAIR may influence implant stability. In this study, we investigated the sequelae of DAIR on implant survival after total hip arthroplasty (THA).

Method: THAs from our database implanted between 1984 and 2016 were included in a retrospective double-cohort study. THAs were exposed (DAIR cohort) or not exposed to DAIR (control cohort). The control cohort comprised patients matched 3:1 to the DAIR cohort. The outcome—implant failure over time—was evaluated for (i) revision for any reason, (ii) aseptic loosening of any component, and (iii) radiographic evidence of loosening.

Results: Fifty-seven THAs (56 patients) were included in the DAIR cohort and 170 THAs (168 patients) in the control cohort. The mean follow-up periods in the DAIR and control cohorts were 6.1 (SD 4.7) and 7.8 (SD 5.5) years, respectively. During follow-up, 20 (36%) patients in the DAIR cohort and 54 (32%) in the control cohort died after a mean of 4.1 (SD 4.7) and 7.2 (SD 5.4) years, respectively. Revision for any reason was performed in 9 (16%) DAIR THAs and 10 (6%) control THAs ($p = 0.03$) and for aseptic loosening of any component in 5 (9%) DAIR THAs and 8 (5%, $p = 0.32$) control THAs, respectively. Radiological analysis included 56 DAIR THAs and 168 control THAs. Two (4%) stems and 2 (4%) cups in the DAIR cohort and 7 (4%) and 1 (0.6%) in the control cohort, respectively, demonstrated radiological signs of failure ($p = 1$).

Conclusions: THAs exposed to DAIR were revised for any reason more frequently than were THAs in the control cohort. The difference in revisions for aseptic loosening was not statistically significant. There was no statistically significant difference in radiographic evidence of loosening of any component between cohorts.

[FP17] IN VITRO ACTIVITY OF FOSFOMYCIN, CIPROFLOXACIN, GENTAMICIN AND THEIR COMBINATIONS AGAINST ESCHERICHIA COLI AND PSEUDOMONAS AERUGINOSA BIOFILMS

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Aim: Ciprofloxacin is recommended as anti-biofilm therapy for *P. aeruginosa* periprosthetic joint infection. With ciprofloxacin monotherapy, resistance in gram-negative bacteria was observed. Therefore, we evaluated *in vitro* synergistic activity of fosfomycin, ciprofloxacin and gentamicin combinations against biofilms formed by *P. aeruginosa* strains.

Method: *P. aeruginosa* ATCC 27853 and 7 clinical isolates were used. MIC values were determined by Etest. Biofilms were formed on porous sintered glass beads for 24h and exposed to antibiotics for further 24h. Viability of bacteria on the glass beads after antibiotic treatment was detected by cfu counting of the sonicated beads. The minimum biofilm eradication concentration (MBEC) was defined as the lowest concentration of antibiotic required to kill biofilm cells (no colonies on plate counts; <20cfu/mL). Synergistic activity against biofilm was evaluated by calculation of the fractional inhibitory concentration index (FICI). According to it, synergism was defined as MBEC reduction by 2-fold compared to the lowest MBEC of single substance.

Results: Table 1 summarizes the antimicrobial susceptibility of planktonic (MIC), biofilm bacteria (MBEC) and synergism. Most strains were susceptible to tested antibiotics, except Pa6 (resistant to gentamicin) and Pa7 (resistant to ciprofloxacin). The biofilm susceptibility to each antibiotic varied widely among clinical isolates. Among 8 tested isolates, synergism was observed in 4 isolates (50%) with fosfomycin/ciprofloxacin, in 5 isolates (62.5%) with fosfomycin/ciprofloxacin and 6 isolates (75%) with ciprofloxacin/gentamicin.

Conclusions: The gentamicin/ciprofloxacin combination showed the highest activity against *P. aeruginosa* biofilms, flowed by fosfomycin/gentamicin and fosfomycin/ ciprofloxacin combination.

Table 1. MIC, MBEC and synergistic anti-biofilm activity for fosfomycin (FOS), ciprofloxacin (CIP) and gentamicin (GEN) against *P. aeruginosa* strains.

Strain	MIC (µg/mL)			MBEC (µg/mL)			Antibiotic Combination Synergism		
	FOS	CIP	GEN	FOS	CIP	GEN	FOS+CIP	FOS+GEN	GEN+CIP
ATCC 27853	8	0.25	1	>1024	512	16	-	+	+
Pa1	32	0.19	1.5	>1024	4	8	+	+	+
Pa2	48	0.064	1.5	>1024	32	32	-	+	+
Pa3	8	0.125	2	>1024	16	16	+	+	+
Pa4	16	0.125	3	>1024	8	16	+	+	+
Pa5	32	0.094	2	>1024	256	128	-	-	+
Pa6	24	0.19	128(R)	>1024	16	>1024	+	-	-
Pa7	48	12(R)	1.5	>1024	>1024	16	-	-	-

R, resistant (according to EUCAST breakpoints); +, synergism; -, no synergism

[FP18] ANTIMICROBIAL EFFECT OF CERAMENT-G® ON BACTERIAL ISOLATES, WITH VARIOUS LEVELS OF GENTAMICIN RESISTANCE, FOUND IN FRACTURE-RELATED INFECTION; AN IN VITRO STUDY

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Aim: Fracture-related infection (FRI) is a serious complication after trauma. More often resistant micro-organisms are cultured. Gentamicin covers a wide variety of causative agents for FRI. A bio-absorbable antibiotic carrier, Cerament-G®, combines dead space management with local release of gentamicin in a one-stage approach. The achieved tissue concentrations of locally applied antibiotics are 4-8 thousand times higher than after systemic administration. Does Cerament-G® have antimicrobial activity towards bacteria that are not susceptible to systemic gentamicin administration.

Method: The four most often cultured bacterial species found in FRI were used; *Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa,* and *Enterobacter cloacae*. For each species, four different isolates were obtained, each with a different susceptibility for gentamicin. This susceptibility, expressed in the minimal inhibitory concentration (MIC), varied from completely susceptible (MIC 0,064 mg/L - 4mg/L), minimal resistance (4mg/L – 16mg/L), moderate resistance (8 mg/L – 96 mg/L) to high resistance (24 mg/L - >1024 mg/L), depending on each different organism. Antimicrobial activity of Cerament-G® was determent by a Kirby-Bauer test, according to the EUCAST disc protocol. Each test was done in five-fold for each of the 16 cultured isolates, four of each species. The zone of inhibition (ZOI), obtained by the test, was compared between each bacterial isolate and within each of the four separate species.

Results: Cerament-G® shows antimicrobial activity against *S. aureus*, *S. epidermidis, P. aeruginosa* and *E. cloacae*. ZOI-values varied from 11 to 44 mm. It was negatively correlated with the MIC; the higher the MIC, the less the antimicrobial effect of Cerament-G®. Between bacterial isolates with the same MIC, within the same species, there was no significant difference in ZOI between the five-fold repetitions of the test, indicating an accurate test. The ZOI of the different bacterial isolates (with different MIC's), belonging to the same bacterial species, differed significantly. Of all 16 isolates, only the *S. aureus* with a MIC of >1024 mg/L did not show antimicrobial activity of Cerament-G®; ZOI =0mm.

Conclusions: This study shows that Cerament-G® has antimicrobial activity against bacterial isolates, resistant to gentamicin when systemically treated. This confirms that the cut-off point for systemic application is not very useful for the local use of Cerament-G® and emphasizes the need for optimization and change of current antibiotic protocols to increase the durability and sustainability of antibiotic FRI treatment.

[FP19] PROLONGED CEFAZOLIN RELEASE FROM HYDROGEL-IMPREGNATED BONE CHIPS

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Aim: Allograft bonechips used in complex bone reconstruction procedures are associated with an increased infection risk. The perioperative use of systemic cefazoline is standard to prevent infection, but is less effective in the presence of avascular bonegrafts. Bone chips have been described as a carrier for local delivery of antibiotics, but impregnation with cefazolin in a prophylactic setting has not been described. We aimed to obtain a prolonged cefazolin release from bone chips to maximize the prophylactic effect.

Method: Three types of bone chips were evaluated: fresh frozen, decellularized frozen and decellularized lyophilized. Bone chips were incubated with 20 mg/ml cefazolin or treated with liquid hydrogel containing either 1 mg/ml fibrin or 1 mg/ml collagen and 20 mg/ml cefazolin. The cefazolin hydrogel was distributed in the porous structure by short vacuum treatment. Bone chips with cefazolin but without hydrogel were incubated for 20 min- 4h under atmospheric pressure or under vacuum. Cefazolin elution of bone chips was carried out in fetal bovine serum and analyzed by Ultra Performance Liquid Chromatography – Diode Array Detection.

Results: Without hydrogel, cefazolin release was limited to 4 hours. When vacuum was applied during impregnation, elution of cefazolin exceeding the MIC (minimal inhibitory concentration) from decellularized lyophilized bone chips was obtained for 36 hours. Use of a collagen hydrogel and vacuum treatment resulted in a high concentration at 24 hours, but did not support prolonged release for any of the three types of tested bone chips. In contrast, combination of decellularized frozen bone chips with fibrin hydrogel resulted in an initial release of 533 µg/ml, declining to the MIC at 72 hours, while no longer measurable after 92 hours. Such elution profile is desirable, since high initial levels are important to maximize antibacterial action whereas the complete washout prevents antibiotic resistance. By increasing the cefazolin concentration during impregnation, elution above the MIC could be obtained for 120 hours. Impregnated bone chips stored at -20° C for 3 months performed similar to freshly impregnated bone chips.

Conclusions: Bone chips processed with the described hydrogel-based impregnation protocol allows tunable delivery of cefazolin for a local prophylactic effect.

[FP20] DOUBLE-DOSE PHARMACOKINETICS OF CEFUROXIME IN PORCINE INTERVERTEBRAL DISC AND VERTEBRAL CANCELLOUS BONE – A RANDOMIZED MICRODIALYSIS STUDY

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Aim: "Cefuroxime is a time-dependent antibiotic widely used as intravenous perioperative prophylaxis in spine surgery. A previous study has indicated that a single dose of cefuroxime provided insufficient spine tissue concentrations for spine procedures lasting more than 2-3 hours. Due to the fact that postoperative pyogenic spondylodiscitis is associated with prolonged antimicrobial therapy and high relapse rates, we aimed to evaluate if a twofold increase of standard dosage of 1.5g cefuroxime given as one double dose or two single doses with 4-hours intervals will lead to sufficient cefuroxime spine tissue concentrations throughout the dosing interval."

Method: "This is preliminary data for 8 out of 16 female pigs. Data from all 16 pigs will be included for the conference. Eight pigs were randomized into two groups: Group A received one double dose of cefuroxime (3g) as a bolus, and Group B received two single doses of cefuroxime (2x1.5g) with 4-hours intervals. Measurements were obtained from plasma, subcutaneous tissue (SCT), vertebral cancellous bone and the intervertebral disc (IVD) for 8-hours thereafter. Microdialysis was applied for sampling in solid tissues. The cefuroxime concentrations were determined using ultra-high performance liquid chromatography"

Results: "The time with concentrations above the minimal inhibitory concentration (T>MIC) for the clinical breakpoint MIC for *Staphylococcus aureus* of 4 µg/ml, was superior in all compartments when administering cefuroxime as two single doses with 4-hours intervals. For the target MIC of 4 µg/ml, the mean T>MIC in all compartments ranged between 53-73% and 85-95% for Group A and B, respectively. For both groups the area under the concentration-curve (AUC) was higher for plasma compared to the remaining compartments, and the lowest AUCs were found in the vertebral cancellous bone and the IVD. There were no differences in AUC between the two groups. Furthermore, the maximal concentrations were lower for both vertebral cancellous bone and IVD compared to both SCT and plasma. When comparing the two groups, higher maximal concentrations were found in all compartments for Group A. Tissue penetration was incomplete and delayed for all compartments and comparable between the two groups."

Conclusions: "Despite comparable pharmacokinetic results between the two groups, Group B exhibited superior T>MIC in all compartments for the clinical breakpoint MIC for *Staphylococcus aureus* of 4 µg/ml. As such administration of cefuroxime as two single doses with 4-hours intervals provided sufficient cefuroxime spine tissue concentrations for a minimum of 85% of an 8-hour dosing interval, which may be acceptable for most spine procedures."

[FP21] DIVERSITY OF CUTIBACTERIUM STRAINS INVOLVED IN PROSTHETIC JOINT INFECTIONS AND ABILITY TO PRODUCE BIOFILM: CUTIBACTERIUM ACNES IA1 AND II PHYLOTYPES BELONGING TO SLST-TYPE D1 OR K1 PRODUCE MORE BIOFILM!

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Aim: *Cutibacterium acnes* (CA) is one of the crucial actors in spine instrumentation or shoulder prosthesis. Its population is subdivided into 6 major phylotypes: IA1, IA2, IB, IC, II and III. Recent methods for discriminating subpopulations within CA phylotypes highlight the predominance of SLST types H1 to 6 or K1 to 20 in bone and joint infection (BJI). The impact of their ability to produce a biofilm during the development of the infection (with resistance / tolerance to antibiotics used for treatment) remains little studied.

Method: The purpose of this study was to determine whether the ability to establish a biofilm varied according to the different subtypes of clinical strains of CA previously characterized and involved in BJI (hip, knee and shoulder prosthesis). The BioFilm ring test (BioFilm Control®) method with index determination, called BFI (BioFilm Index) inversely proportional to the level of biofilm production was used (BFI = 0.00 indicates a high production of biofilm *versus* BFI = 20.00 indicates zero production). The BFI was determined after 3 h (T3) and 6 h (T6) incubation. The strains used came from patients, 5 belonging to the IA1 phylotype (SLST A1 and D1 types) and 4 to different phylotypes (IA2, IB, II and III).

Results: The results show that the kinetics of establishment of an early CA biofilm turns out to be phylotype dependent. The most productive strains are those belonging to phylotype II (BFI T3 = 5.73, BFI T6 = 0.00) and to type SLST D1 belonging to phylotype IA1 (BFI T3 = 4.07, BFI T6 = 0.00). The other strains did not demonstrate saturated BFI, even after 6 h of incubation

Conclusions: The exact role of CA, as well as its ability to produce a biofilm in the pathophysiology of BJI, remains poorly understood and the prolonged use of antibiotics to treat these infections is necessary, especially if devices have not been removed, with potential risk of increasing antibiotic resistance and therapeutic failures. CA's different phylotypes demonstrate different biofilm production capabilities, which could have an impact on the antibiotic efficacy suggesting the interest of effective anti-biofilm molecules on metabolically less active strains.

[FP22] IN VITRO EVALUATION OF BACTERIAL ADHESION AND BIOFILM FORMATION TO METALLIC CERCLAGE WIRE VERSUS POLYMER CERCLAGE SYSTEM

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Aim: To evaluate bacterial adhesion and biofilm formation to metallic cerclage wire versus polymer cerclage system (SuperCable®)

Methods: Experimental *in vitro* study to evaluate quantitative bacterial adherence to different cerclage wire materials. Two types of cerclage wires were compared: a metallic versus a polymer based wire (SuperCable®).

A two-centimeter cerclage wire piece of each material was included in 2 mL of tryptic soy broth (TSB) culture media, inoculated with 10 microliters of a 0.5 McFarland of a *Staphylococcus epidermidis* strain and cultivated at 37°C during 2h for adhesion and 48h for biofilm formation. After this time, the cerclages were washed using a 1% phosphate buffered saline (PBS) and sonicated in new culture medium. After sonication, dilutions of each culture were spread in TSB agar and incubated 37°C during 24h. The number of colonies were counted and the cfu/cm2 was calculated.

Results: There were no differences in the number of colonies counted at 2 hours. At 48 hours, the polymer cerclage system showed a clinically and statistically reduction of 95.2% in the biofilm formation of *S. epidermidis*.

The highest bacterial counts were observed in metallic cerclages after 48h.

Conclusion: In *in vitro* conditions, the polymer cerclage system may offer decreased biofilm formation compared with metallic cerclage wires. However, there are many other factors in *in vivo* conditions that could play a role in bacterial adhesion to cerclage wires. Further research is needed in order to recommend the use of polymer cerclage systems for septic revision surgery.

[FP23] STUDY OF THE EFFECT OF PULSED-WASHING ON THE ANTIBIOTIC SUSCEPTIBILITY OF STAPHYLOCOCCUS AUREUS BIOFILMS

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Aim: Irrigation is a major step during debridement surgery in the context of Prosthetic Joint Infections (PJI), but its effects on biofilms are poorly described. The present study aims at evaluating the effect of PW alone or followed by antibiotics on MSSA and MRSA biofilms grown on Ti6Al4V coupons in-vitro.

Method: Strains: 1 reference (MSSA: ATCC25923; MRSA: ATCC33591) and 2 clinical MSSA and MRSA isolated from PJI. Biofilm culture: Coupons were incubated for 24h at 37°C with bacteria (starting inoculum ~6.6Log_{10}CFU/mL in TGN [TSB + 1% glucose + 2% NaCl]), under shaking at 50rpm. Treatment: Half of the coupons were irrigated with 50mL physiological serum from 5cm using a Stryker Interpulse; the coupons were then either analysed (ControlT0 and PWT0) or reincubated for 24h in TGN or TGN containing flucloxacillin (MSSA) or vancomycin (MRSA) at MIC or 20mg/L. Analysis: Coupons were rinsed twice with PBS. Biomass was measured by crystal violet (CV) assay. CFUs were counted after recovering bacteria from coupons using sonication and TSA plating.

Results: Antibiotics alone: Flucloxacillin reduced CFU and biomass for ATCC25923 and 611 but not 578 (Fig b and d). Vancomycin had no statistically significant effects on CFUs for all MRSA and only a weak effect on biomass for 676. Irrigation alone markedly reduced CFUs and biomass for all strains but had no persistent effect after 24h reincubation in TGN. PW + antibiotics: Antibiotics prevented bacterial regrowth after PW when used at their MIC and further decreased CFUs when used at 20 mg/L.

Conclusions: PW alone has a transient effect on coupon colonisation by *S. aureus* biofilms. Vancomycin at therapeutic concentrations is ineffective and flucloxacillin has a strain-dependent effect. In combination, these treatments show synergistic effects, indicating the importance of irrigation followed by high antibiotic doses for ODRI.

MRSA

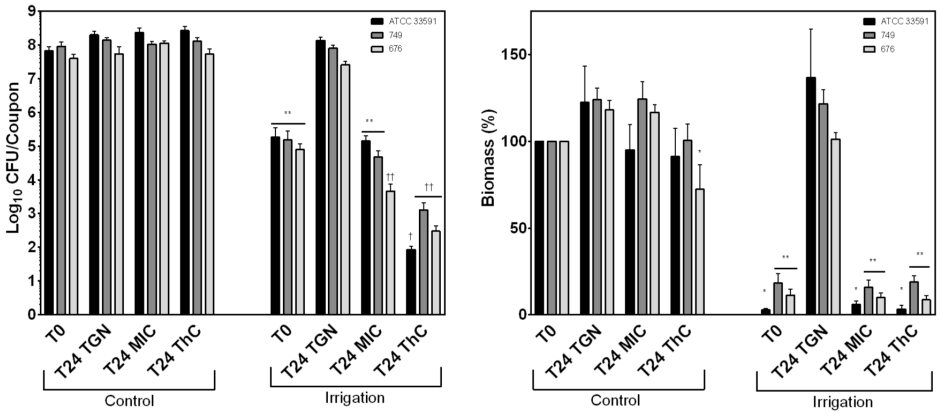

Fig a) Log_{10} CFU counts; fig b) Biomass assays normalized as percentage of T0 control. Control: Control samples; Irrigation: samples irrigated with 50 mL of 0,9% NaCl; T0: extemporaneously analysed; T24 TGN: 24h reincubation in TGN; T24 MIC: 24h reincubation in TGN with VAN at MIC; T24 ThC: 24h reincubation in TGN with VAN at 20mg/L. *:p<0,05 when compared to T0 control; **:p<0,001 when compared to T0 control; †:p<0,05 when compared to T0 irrigation; ††:p<0,001 when compared to T0 irrigation. 2-way ANOVA followed by Holm-Sidàk test. n=4 for all conditions.

MSSA

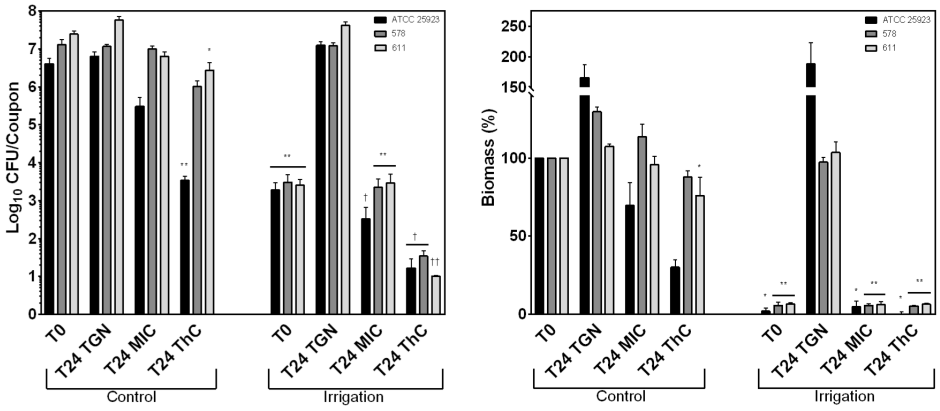

Fig a) Log_{10} CFU counts; fig b) Biomass assays normalized as percentage of T0 control. Control: Control samples; Irrigation: samples irrigated with 50 mL of 0,9% NaCl; T0: extemporaneously analysed; T24 TGN: 24h reincubation in TGN; T24 MIC: 24h reincubation in TGN with FLX at MIC; T24 ThC: 24h reincubation in TGN with FLX at 20mg/L. *:p<0,05 when compared to T0 control; **:p<0,001 when compared to T0 control; †:p<0,05 when compared to T0 irrigation; ††:p<0,001 when compared to T0 irrigation. 2-way ANOVA followed by Holm-Sidàk test. n=4 for all conditions.

[FP24] ISOTHERMAL MICROCALORIMETRY DETECTS THE PRESENCE OF PERSISTER CELLS IN A STAPHYLOCOCCUS AUREUS BIOFILM AFTER VANCOMYCIN TREATMENT

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Aim: Most orthopedic infections are due to the microbial colonization of abiotic surfaces, which evolves into biofilm formation. Within biofilms, persisters constitute a microbial subpopulation of cells characterized by a lower metabolic-activity, being phenotipically tolerant to high concentrations of antibiotics. Due to their extreme tolerance, persisters may cause relapses upon treatment discontinuation, leading to infection recalcitrance hindering the bony tissue regeneration. Using isothermal microcalorimetry (IMC), we aimed to evaluate *in vitro* the presence of persisters in a methicillin-resistant *Staphylococcus aureus* (MRSA) biofilm after treatment with high concentrations of vancomycin (VAN) and their ability to revert to a normal-growing phenotype during incubation in fresh medium without antibiotic. Moreover, the ability of daptomycin to eradicate the infection by killing persisters was also investigated.

Method: A 24h-old MRSA ATCC 43300 biofilm was exposed to 1024 µg/ml VAN for 24h. Metabolism-related heat of biofilm-embedded cells, either during or after VAN-treatment, was monitored in real-time by IMC for 24 or 48h, respectively. To evaluate the presence of VAN-derived "persisters" after antibiotic treatment, beads were sonicated and detached free-floating bacteria were further challenged with 100xMIC VAN (100 µg/ml) in PBS+1% Cation Adjusted Mueller Hinton Broth (CAMHB).. Suspensions were plated for colony counting. The resumption of persister cells' normal growth was analysed by IMC on dislodged trated cells for 15h in CAMHB. Activity of 16 µg/ml daptomycin was assessed against persister cells by colony counting.

Results: When incubated with 1024 µg/ml VAN, MRSA biofilm produced undetectable heat, suggesting a strong reduction of cell viability and/or cellular metabolism. However, the same samples re-inoculated in fresh medium produced a detectable and delayed metabolism-related heat signal, similarly to that generated by persister cells. The following exposure to 100xMIC VAN resulted in neither complete killing nor bacterial growth, strongly supporting the hypothesis of a persistent phenotype. IMC analysis indicated that VAN-treated biofilm cells resumed normal growth with a ~3h-delay, as compared to the untreated growth control. Daptomycin treatment yielded a complete eradication of persister cells selected after VAN treatment.

Conclusions: Hostile environmental conditions (*e.g.* high antibiotic bactericidal concentrations) select for persister cells in MRSA biofilm after 24h-treatment *in vitro*. A staggered treatment vancomycin/daptomycin allows complete biofilm eradication. These results support the use in clinical practice of a therapeutic regimen based on the combined use of antibiotics to kill persisters and eradicate MRSA biofilms. IMC represents a suitable technique to detect persisters and characterize in real-time their reversion to a metabolically-active phenotype.

[FP25] DEVELOPMENT OF ANTIBODIES THAT ENHANCE IMMUNE CLEARANCE OF STAPHYLOCOCCUS AUREUS BIOFILMS

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Aim: "Implant associated Staphylococcus aureus infections are often difficult to treat due to the formation of biofilms on prosthetic material. Biofilms are bacterial communities adhered to a surface with a self-made extracellular polymeric substance that surrounds resident bacteria. In contrast to planktonic bacteria, bacteria in a biofilm are in an adherent, dormant state and are insensitive to most antibiotics. In addition, bacteria in a biofilm are protected from phagocytic cells of the immune system. Neutrophils play a crucial role in clearing bacterial pathogens. They recognize planktonic bacteria via immunoglobulin (Ig) and complement opsonisation. In this study, we aim to evaluate what is the role of complement and IgG in the recognition and binding of S. aureus biofilms by human neutrophils. Furthermore, we evaluate if monoclonal antibodies (mAbs) recognizing biofilm structures can enhance recognition of S. aureus biofilms via the human immune system."

Method: "We produced a set of 20 recombinant mAbs specific for S. aureus antigens. Using flow cytometry and ELISA-based methods we determined the binding of these mAbs to planktonic S. aureus and in vitro S. aureus biofilms. Following incubation with IgG/IgM depleted human serum we determined whether mAbs or a pool of human IgG can react with the human complement system after binding to biofilm. In a co-culture system of biofilm and celltrace labeled human neutrophils, we studied attachment of neutrophils. Confocal microscopy was used to visualize the location of antibody binding and neutrophils in the biofilm 3D structure."

Results: "We show that mAbs directed against wall teichoic acid (a glycopolymer on the S. aureus cell wall) and polymeric-N-acetyl-glucosamine (major constituent of the Staphylococcus biofilm extracellular matrix) bind S. aureus biofilms in a dose-dependent manner. This interaction was specific since no binding was observed for control antibodies (recognizing the hapten DNP). Attachment of neutrophils to biofilms was completely dependent on IgG but not complement opsonisation, but attached neutrophils have an inactive morphology showed by confocal microscopy. No products of complement activation could be detected upon incubation with human serum and the mAbs or IgG pool, in contrast to planktonic S. aureus."

Conclusions: " Having established that our mAbs can bind biofilms but complement opsonisation is not induced, we will now study if we can engineering these antibodies to enhance complement deposition. A combination of complement and antibody opsonisation may improve recognition and clearance of biofilms by phagocytic immune cells."

[FP26] PHAGE THERAPY AND BACTERIAL RESERVOIRS IN BONE AND JOINT INFECTIONS: EVALUATION OF THE EFFICACY OF AN ASSEMBLY OF THREE BACTERIOPHAGES ON STAPHYLOCOCCUS AUREUS EMBEDDED IN BIOFILM OR INTERNALIZED IN OSTEOBLASTS

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Aim: *Staphylococcus aureus* is the first causative agent of bone and joints infections (BJI). It causes difficult-to-treat infections because of its ability to form biofilms, and to be internalized and persist inside osteoblastic cells. Recently, phage therapy has emerged as a promising therapy to improve the management of chronic BJI. In the present study, we evaluated the efficacy of an assembly of three bacteriophages previously used in a clinical case report (Ferry, 2018) against *S. aureus* in *in vitro* models of biofilm and intracellular osteoblast infection.

Methods: Using HG001 *S. aureus*, the bactericidal activities of the assembly of the three bacteriophages (Pherecydes Pharma) used alone or in association with vancomycin or rifampicin were compared by quantifying the number of viable bacteria in mature biofilms and infected osteoblasts after 24h of exposure.

Results: The activity of bacteriophages against biofilm-embedded *S. aureus* was dose-dependent. Synergistic effects were observed when bacteriophages were combined to antibiotics at the lowest concentrations, with no significant bactericidal activity in monotherapy. In the human osteoblast infection model, we were able to show that phage penetration into osteoblasts was only possible when the cells were infected, suggesting a *S. aureus* dependent Trojan horse mechanism. The intracellular inoculum in osteoblasts treated with bacteriophages or vancomycin was significantly higher than in cells treated with lysostaphin, used as control condition of rapid killing of bacteria released in the extracellular media after death of infected cells and absence of intracellular activity. These results suggest that bacteriophages are probably both i) inactive in the intracellular compartment and ii) unable to kill all bacteria released after cell lysis into the extracellular medium fast enough to prevent them from reinfecting other osteoblasts. Conversely, the intracellular inoculum recovered from cells treated with vancomycin+bacteriophages was significantly lower than the one inside cells treated with vancomycin or bacteriophages alone, suggesting that this combination allowed a better control of released bacteria in the extracellular media. Finally, bacteriophages did not increase the activity of rifampicin in this model.

Conclusion: In conclusion, we showed that the bacteriophages tested were highly active against *S. aureus* in mature biofilm but had no activity against bacteria internalized in osteoblasts. Additional studies using animal models of BJI and well-conducted clinical trials are needed to further evaluate phage therapy and its positioning in the management of these infections.

[FP27] TOLERANCE AND MICROBIOLOGICAL EFFICACY CEFEPIM OR PIPERACILLIN/ TAZOBACTAM IN COMBINATION WITH VANCOMYCIN AS EMPIRICAL ANTIMICROBIAL THERAPY OF PROSTHETIC JOINT INFECTION

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Aim: " The use of piperacillin/tazobactam with vancomycin as empirical antimicrobial therapy (EAT) for prosthetic joint infection (PJI) has been associated with an increased risk of acute kidney injury (AKI), leading to propose cefepim as an alternative since 2017 in our reference center. The present study compared microbiological efficacy and tolerance of these two EAT strategies."

Method: " All patients with PJI empirically treated by vancomycin-cefepim (n=90) were prospectively enrolled in an observational study, and compared with vancomycin-piperacillin/tazobactam-treated historical controls (n=117), regarding: i) the proportion efficacious empirical regimen (i.e., at least one of the two molecules active against the identified organism(s) based on *in vitro* susceptibility testing); and ii) the incidence of empirical therapy-related adverse events (AE), classified according to the Common terminology criteria for AE (CTCAE)."

Results: "Among the 146 (67.3%) documented infections, the EAT was considered as efficacious in 99 (99.0%) and 66 (98.5%) in the piperacillin-tazobactam and cefepim-treated patients, respectively (p=0.109). The rate of adverse events, and in particular AKI, was significantly higher in the vancomycin-piperacillin/tazobactam (n=38 [32.5%] and 32 [27.6%]) compared to the vancomycin-cefepim (n=13 [14.4%] and 5 [5.7%]) group (p=0.003 and <0.001, respectively; Figure). Of note, sex, age, and the proportion of patients receiving other nephrotoxics were similar among piperacillin/tazobactam- and cefepim-treated patients. However, in comparison with patients receiving cefepim, a higher modified Charlson's comorbitidy index (4 [IQR, 3-5] versus 2 [IQR, 2-4], p<0.001) has to be acknowledged, mainly related to a higher prevalence of baseline chronic renal injury (n=62, 53.4% versus n=34, 38.6%; p=0.035)."

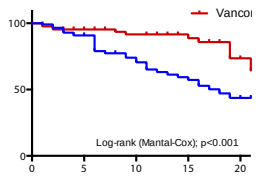

Figure – Kaplan-Meier curve analysis of adverse events (A) and AKI (B)-free survival in patients receiving piperacillin/tazobactam or cefepim in combination with vancomycin as empirical antimicrobial therapy for PJI.

Conclusions: " The empirical use of vancomycin-cefepim in PJI was as efficient as vancomycin-piperacillin/tazobactam, and was associated with a significantly lower incidence of AKI."

[FP28] TIGECYCLINE VERSUS COLISTIN IN THE TREATMENT OF CARBAPENEM-RESISTANT ACINETOBACTER BAUMANNII OSTEOMYELITIS

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Aim: To compare outcomes and incidence of adverse events (AE) of colistin versus tigecycline for treatment of patients with carbapenem-resistant *Acinetobacter baumannii* (CRAB) osteomyelitis.

Method: Retrospective study. Records of 111 patients with microbiologically confirmed CRAB osteomyelitis were analyzed. Colistin (34 cases) and tigecycline (31 cases) were the main drugs used for treatment of extremely-drug resistant (XDR) isolates. Patients who received these two antimicrobials were compared according to baseline features (sex, age, length of hospital stay, Charlson index, presence of comorbidities or immunosuppression, previous renal disease, smoking, alcoholism or use of illicit drugs, previous orthopedic surgery on affected limb, topography of infection, classification of osteomyelitis, ASA score, infection related to pressure ulcer or neuropathic foot, presence of implant, need for soft tissue repair or negative pressure therapy and previous antimicrobial use), clinical outcome after 12 months of treatment (remission of infection was considered the favorable outcome; recurrence of infection, amputation and death were considered unfavorable outcomes; loss of follow-up was analyzed separately) and AE during treatment (impaired renal function; liver abnormalities; nausea; skin rash; neurological abnormalities and other events in general). Quantitative variables were described using summary measures and compared using Student's t or Mann-Whitney tests. Qualitative characteristics were described with absolute and relative frequencies and compared using chi-square or exact tests (Fisher's exact or likelihood ratio test).

Results: Regarding baseline characteristics, proportion of male patients was higher in the group treated with colistin ($p = 0.028$). In the group treated with tigecycline, there was a significant predominance of smokers ($p = 0.021$) and patients with chronic osteomyelitis ($p = 0.036$). Regarding clinical outcomes after 12 months of treatment, there was no difference between groups. Overall incidence of AE was significantly higher among patients treated with colistin ($p=0,047$), as well as renal impairment ($p = 0.003$). Incidence of nausea was higher in patients treated with tigecycline ($p = 0.046$), but there was no difference between groups in relation to altered liver enzymes and other events.

Conclusions: In this retrospective analysis, there was no significant difference between clinical outcomes of patients with CRAB osteomyelitis treated with colistin compared to tigecycline. Although the occurrence of nausea was greater in the group receiving tigecycline, this antimicrobial appeared to have a better safety profile for treatment of osteomyelitis related to XDR *A. baumannii*.

[FP29] EFFICACY AND SAFETY OF INTRAVENOUS FOSFOMYCIN IN PATIENTS WITH PERIPROSTHETIC JOINT INFECTION: PRELIMINARY RESULTS FROM THE PROOF STUDY - A PROSPECTIVE MULTICENTER STUDY.

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Aim: We evaluated the efficacy and safety of treatment regimens in a pathogen and surgery specific mode according to a standardized algorithm for the treatment of periprosthetic joint infection (PJI) based on combinations with 15g/d intravenous fosfomycin followed by oral antibiotics for totally 12 weeks.

Method: Consecutive patients with PJI caused by at least one of the following isolates were prospectively included: staphylococci (MIC ≤32 mg/l), streptococci (MIC ≤128 mg/l), enterococci (MIC ≤128 mg/l), Enterobacteriaceae (MIC ≤32 mg/l) and Pseudomonas spp. (MIC ≤128 mg/l). PJI was defined by the proposed European Bone and Joint Infection Society (EBJIS) criteria. Follow up with clinical (joint function and quality of life scores), laboratory and radiological evaluation at 3, 12 and 24 months after last surgery is performed. Infection outcome was assessed as the proportion of infection-free patients. The probability of infection-free survival was estimated using the Kaplan-Meier survival method.

Results: 50 patients were screened for eligibility, of which 2 were excluded due to intolerance or allergy to fosfomycin, 1 due to isolation of fosfomycin resistant pathogen and 2 patients died due to unrelated cause to infection. The remaining 45 patients were included. Due to persistence of infection, 3 patients underwent prosthesis explantation after initial debridement and retention, 1 patient underwent debridement of Girdlestone-situation; all 4 infections were caused by S. aureus. At 2 patients debridement of hematoma after Girdlestone approach was performed. 41 patients were infection-free (91%) after a median follow-up of 6 month (range, 1 - 14 months). Nausea (n=14) and hypokalemia (n=13) were the most frequent adverse events and resolved after fosfomycin discontinuation; 5 patients had diarrhea and vomiting was observed in 2 patients. Isolated pathogens were staphylococci (n=30), streptococci (n=3), enterococci (n=5) and gram-negative rods (n=2). Cultures were negative in 9 patients and polymicrobial in 2 patients. The infection occurred postoperatively in 31 patients (69%) and hematogenously in 14 (31%). Two-stage exchange was performed in 27 (60%), debridement with retention in 13 (29%) and one-stage exchange in 5 patients (11%).

Conclusions: The applied PJI treatment algorithm including intravenous fosfomycin in the initial postoperative period was associated with infection-free outcome of 91% after a median follow-up of 6 month. The Kaplan-Meier survival method showed the probability of infection-free survival of 88.5% after 1 year. Adverse events occurred in 21 patients (46%) mostly nausea and hypokalemia were reported. Adverse events were mild and resolved completely.

[FP30] LONG-TERM LINEZOLID USE (>28 DAYS) IN PATIENTS WITH ORTHOPEDIC INFECTIONS IS GENERALLY SAFE AND WELL TOLERATED

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Aim: Long term use of antibiotics following surgical debridement are the cornerstone of PJI treatment. Due to increasing resistance of bacteria for many first line antibiotics new options are needed. One such option is linezolid known for its low percentage of resistance against many Gram positive bacteria causing PJI. Success rates up to 86% have been reported. At the same time many adverse events (AE) have been described including anemia, thrombocytopenia, gastrointestinal effects and sometimes neuropathy, e.g. irreversible vision loss [1, 2]. Therefore, linezolid use is advised to be limited to a maximum of 28 days. Literature about the effects of prolonged use is currently lacking and therefore this study will aim to determine the safety of long-term (>28 days) linezolid use in patients with orthopedic infections.

Methods: We performed a retrospective descriptive study on patient records of orthopedic patients who were treated with linezolid between January 2014 and January 2019 for >28 days. Data were collected from medical charts including co-morbidities, pre-existing liver/kidney dysfunctions, diagnosis, treatment, type of prosthesis, pathogens, adverse events associated with linezolid use and follow up laboratory data.

Results: 91 patients treated with linezolid were identified. 46 patients (25 male), mean age 64 (SD 11.49) received long-term linezolid with an average treatment duration of 45.3 (range 29 – 91) days. AE were observed in 32 with gastrointestinal AE's (16 patients) being the most frequent following anemia (7 patients) thrombocytopenia (6 patients), leucopenia (2 patients). One patient reported optic neuritis but no association with linezolid could be confirmed. Linezolid treatment was ended in 7 patients (15.2%) due to AE (predominantly anemia) compared to 14 patients (31.1%) who received short-term treatment (predominantly gastrointestinal AE). Decreased post-surgery hemoglobin levels tended to increase during the first two weeks of linezolid use after which hemoglobin levels showed an average decrease of 0.39 mmol/L between week 2 and week 7 of treatment. Leucocyte and thrombocyte levels showed an average decrease between baseline measures and week 7 of treatment of $2.21*10^9$/L and $89.0*10^9$/L respectively. AE were resolved after a mean 12 days (range 2-30 days)

Conclusions: Long-term linezolid use was not associated with an increase in serious irreversible AE and can therefore be considered generally safe, provided that patients are well monitored considering high drop out in the first weeks mainly due to gastrointestinal AE and anemia during prolonged treatment. These observations help to fill the gap in knowledge about prolonged linezolid use.

[FP31] REAL LIFE EFFICACY AND SAFETY OF DALBAVANCIN MONOTHERAPY AS SALVAGE TREATMENT IN BONE AND JOINT INFECTION

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Aim: bone and joint infection (BJI) in aging population, continues to be associated with significant morbi-mortality. In western Europeans countries, the Gram positive BJI are preponderant. Vancomycin was the "gold standard" and the full treatment requires prolonged antibiotic therapy. Dalbavancin is a semi-synthetic lipoglycopeptideanalog of teicoplanin class of antibiotics with bactericidal activity and a long half-life.The use of dalbavancin in BJI could be an option

Methods: during November 2017 and April 2019, Dalbavancin was used in monotherapy as salvage option in BJI: 1500 mg, 1st (D1) and 8th day (D8), repeated if needed. The clinical and biological follow up was for 6 months if osteomyelitis or BJI without prosthesis and 1 year if prosthesis (PJI).

Results: the demographics of 16 patients are: 75.0% men (n=12), mean age 77.8 years [64-90], 37.5% (n=6) diabetes, 68.8% (n=11) renal failure, 37.5% (n=6) atrial fibrillation, 18.8% (n=3) cardiac bioprosthesis, 31.2% (n=5) lower limb arteriopathy, and one patient with active neoplasia. The BJI characteristic's: 50% (n=8) secondary to health care;5 vertebral osteomyelitis; 12 lower limb BJI : 8 joint infection of witch 6 PJI (4 knee, 2 hip) and 4 foot osteomyelitis; 2 shoulder PJI; 3 patients had 2 or more localisations of BJI.In 68.8% (11/16) BJI, bacteraemia occurred with 68.8% (n=11) of possible or certain infective endocarditis (Duke criteria) and 37.5% (n=6) of deep abscess. The DAIR was of 83.4% (5/6).

Monobacterian biopsy in 75.0% (n=12). Out of 32 micro-organisms, 25 were Dalbavancin susceptible:56.0% (14/25) Staphylococcus aureus (10 methicillin susceptible), 3 Streptococcus, 5 Enterococcus faecalis, 2 Corynebacterium, 1 coagulase negative staphylococcus.

Mean of 1stantibiotherapy: 18.3 days [0-49], with 2 patients who had dalbavancine as only antibiotic. Number of dalbavancine doses: 75% (n=12) patients had 2 injection (D1, D8), 18.8% (n=3), 4 injections D1, D8, D28 and D35 and 1 patient had one dose.

Principal reason of changing by dalbavancine: 50% (8/16) poor tolerance of antibiotics, 12.5% (2/16) poor compliance of patient, 18.8% (3/16) poor efficacy of 1stantibiotherapy, 18.8 %(3/16) only for the patient's comfort.

Clinically success: 75% (12/16) with 5 patients in follow up today. Three patients died and one is cured with teicoplanin and rifampicin.

Three patients presented side effects: one diarrhea, one headache and one transient asthenia. No renal damage was found and no allergy.

Conclusion: This report highlights the potential role of dalbavancin in treating unstable and weak patients who require long-term antimicrobial therapy with fewer antibiotic choices.

[FP32] PREDISPOSING FACTORS FOR MULTIDRUG-RESISTANT GRAM-NEGATIVE PROSTHETIC JOINT INFECTIONS: THE ROLE OF PRIOR USE OF ANTIBIOTICS AND THE NONELECTIVE ARTHROPLASTY DUE HIP FRACTURE.

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Aim: Infection is one of the worst complications following total joint arthroplasty, which is often associated with significant morbidity and increased medical costs. Although Gram–positive bacteria remains the most prevalent causative agents, an increase in prosthetic joint infections (PJI) due to gram-negative bacteria (GNB) has been reported. Additionally, the emergence of multidrug resistant resistance (MDR) in GNB impacts the therapeutic options and may increase the rate of treatment failure and drug toxicity adverse effects due the prescription of harmful and toxics antimicrobial schemes. The purpose of the present study was to describe the predisposing factors associated to PJI caused by MDR-GNB in a specialized orthopedic reference hospital in Brazil from 2014 through 2018.

Method: Retrospective case-control analysis of patients treated for MDR-GNB PJI over a four-year period (2014-2018). Data were collected from medical, surgical and laboratory records. PJI were defined according the criteria of MSIS. MDR was defined as non-susceptibility to at least one agent in three or more antimicrobial categories. Patients with prosthetic infection with at least two positive tissue cultures for MDR-GNB were selected. Univariate and multivariate logistic regression models were used to determine the independent risk factors associated with MDR-GNB PJI. Controls: patients with PJI with at least two positive tissue culture for non MDR- GNB

Results: A total of 104 patients were selected, 59 patients in the MDR-GNB PJI group and 44 in the control. Patients with MDR-GNB PJI were elderly (mean age of 68.36), distribution among sex was similar (49.2% female and 50.8% male) and 72.3% had one or more comorbidities. Most frequently identified comorbidities were diabetes (10.2%), malnutrition (5.5%), hypertension (4.7 %) and obesity (3.9%). Hip replacement accounted for 91.5% of the cases and 59.3% were revision arthroplasty. The mean time between the placement of the prothesis and the onset of PJI signs and symptoms was 438 days. In the univariate regression, the significant risk factors for MDR-GNB PJI were revision arthroplasty, alcoholism, nonelective arthroplasty, prior antimicrobial use, presence of concomitant infection and blood transfusion. However, in the multivariate analysis, prior use of antimicrobials (OR 9.31, CI95% 3.02-28.64) and the nonelective arthroplasty (OR 6.29, CI95% 1.75-22.6) remained as independent risk factors for MDR-GNB PJI

Conclusions: Previous use of antimicrobial and nonelective arthroplasty are important risk factors for PJI by GNB MDR.

[FP33] TREATMENT AND OUTCOMES OF CALCANEAL OSTEOMYELITIS IN ADULTS: A SYSTEMIC REVIEW

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Aim: Calcaneal osteomyelitis is an uncommon and challenging condition. In this systemic review we aim to analyse the concomitant use of bone debridement and soft tissue management for patients diagnosed with calcaneal osteomyelitis

Method: A complete computerised and comprehensive literature search of Pubmed and Cochrane database was undertaken from January 2000 to October 2018. During the review, studies were screened for information about the surgical and antimicrobial treatment, the complications, the reinfection rate and the functional outcome of patients with calcaneal osteomyelitis.

Results: Of the 20 studies included, seven (35%) described bone treatment only, six (30%) soft tissue treatment only, five (25%) soft tissue and bone treatment, and two (10%) focused on prognostic factors and differences in outcomes between diabetic and non-diabetic patients.

In the studies with bone treatment only, infection recurrence ranged from 0 to 35% and the amputation rate from 0 to 29%. If soft tissue coverage was also needed, both the reinfection rate and amputation rate ranged from 0 to 24%. Studies presenting the functional status showed preservation or even improvement of the preoperative ambulatory status

Conclusions: Calcaneal osteomyelitis is difficult to treat. A multidisciplinary approach involving orthopaedic surgeons, plastic surgeons and infectious disease physicians is necessary for treatment success. Based on the localisation and size of the bone and soft tissue defect, decision for surgical treatment should be made.

[FP34] SEASON AS A PREDICTOR FOR THE INCIDENCE OF SURGICAL SITE INFECTIONS AFTER ORTHOPEDIC TRAUMA SURGERY OF THE LOWER LEG, ANKLE AND FOOT

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Aim: Since surgical site infections (SSIs) remain among the most common complications of orthopedic (trauma) surgery, there has been unwavering attention for potential predictors of a SSI. Specifically in surgical fields with a high complication rate, such as foot/ankle surgery, risk factor identification is of great importance. Recently, some studies have suggested environmental factors such as season to be of influence on the number of SSI[1,2]. Specifically patients operated on in the summer are reported to have a higher incidence of SSIs, compared to other seasons[3]time to debridement and antibiotic administration with respect to risk of infection after open fracture. The purpose of this analysis was to determine if either the incidence of post-traumatic infection or causative organism varies with treating institution or the season in which the open fracture occurred. DESIGN Retrospective review. SETTING Seven level-one regional referral trauma centers located in each of the seven climatic regions of the continental United States (Northwest; High Plains; Midwest/Ohio Valley; New England/Mid-Atlantic; Southeast; South; and Southwest[4,2]. The aim of this study is to identify if "seasonality" is a significant predictor for SSI in a cohort of (trauma) surgical foot and ankle procedures.

Method: This retrospective cohort study included all patients undergoing trauma related surgery (fracture fixation, arthrodesis, implant removal and tendon repair) of the lower leg, ankle and foot. Procedures were performed at a single Level 1 Trauma Center in the Netherlands between September 2015 until February 2019. Potential risk factors/ confounders for SSI were identified using univariate analysis (Chi-Square/Mann-Whitney U). Procedures were divided in two groups: 1) performed in summer (June, July or August), 2) not performed in summer (September-May). The number of SSIs was compared between the 2 groups, correcting for confounders, using multivariate regression.

Results: A total of 605 procedures were included, largely fracture fixation (371, 61.2%). Patients were on average 46 y/o and the majority was male (369, 60.9%). The total number of SSIs was 34 (5.6%). Age, American Society of Anesthesiologists (ASA) classification (1-2 or 3-4) and open fractures were identified as possible predicting factors of SSI. No difference in SSIs was found between summer and other seasons, neither in univariate analysis (4 (3.2%) vs 30 (6.3%), p=0.271), nor when corrected for confounders. Moreover, in multivariate analysis only an ASA of >2 and an open fracture remained as independent predictors of SSI.

Conclusions: No seasonality could be identified in the rate of SSI after trauma surgery of the lower leg, ankle and foot in this cohort. A possible explanation for this lack of effect could be the temperate oceanic climate of the Netherlands. Larger temperature and precipitation differences may also influence the incidence of SSIs. However, previous studies suggesting seasonality in SSIs might also be purely based on coincidence, especially when uncorrected for confounders.

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[FP35] BESIDE INFECTION, DO NOT FORGET TO MANAGE PERIPHERAL ARTERIAL DISEASE IN DIABETIC CHARCOT FOOT.

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Aim: Our study aimed to analyze 1) the prevalence of peripheral arterial disease (PAD) and infection in diabetic patients with and without Charcot foot (CF), 2) the characteristics of PAD in these 2 groups, 3) the prognosis of patients with CF and PAD and/or infection.

Method: We retrospectively reviewed the medical and radiological records of 172 hospitalized patients in our diabetic foot unit between 2010 and 2014. These patients were identified using the ICD-9-CM. The CF group and the diabetic foot (DF) group included 56 and 116 patients, respectively. All statistical analyses were performed using SPSS 25.0.01. A p <0.05 was considered as statistically significant.

Results: In the CF group, the prevalence of PAD and infection reached 66.1% and 67.9%, respectively. Diabetic foot ulcers (DFUs) were neuroischemic, infected or both in 69.5%, 80% and 57.7% of cases, respectively. No significant difference was found with the DF group. PAD in the CF group affected the infrapopliteal arteries alone more often (59.4% vs 26.7%, p 0.005) and neuroischemic DFUs needed less often revascularization (34.4% vs 78.7%, p <0.001). Endovascular revascularization was feasible in 77.8% of cases in the CF group, without significant difference with the DF group. Independent predictors of PAD in CF were DFUs (OR 24.5, CI 1.8-334.4, p 0.016) and coronary artery disease (OR 17.1, CI 1.7-167.4, p 0.016). Both patients' survival and limb salvage were not affected by PAD, neuroischemic DFUs and infected neuroischemic DFUs in the CF group.

Conclusions: In agreement with current literature, our study showed that infection is often associated with DFUs[1], both in DF and CF. However, our study demonstrated that beside infection, PAD is associated with CF more often than previously thought[2]. As a consequence, DFUs in CF are most often neuroischemic. However, our study did not show worse outcomes in patients with CF and PAD or neuroischemic DFUs. This probably results from a less severe PAD in CF, a high rate of successful revascularization as well as a low rate of deaths and major amputations in our study. In conclusion, clinicians should no longer consider the CF as a purely neuropathic foot, especially in the presence of a DFU. Moreover, PAD in CF should be evaluated systematically before any surgical procedure as recommended in DF[3].

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[FP36] NEGATIVE-PRESSURE WOUND THERAPY IN FRACTURE-RELATED INFECTION: THE INFLUENCE ON TISSUE CULTURE RESULTS AND OUTCOME. PRELIMINARY RESULTS FROM A SINGLE CENTRE SERIES.

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Aim: Negative-pressure wound therapy (NPWT) is often propagated as treatment option for fracture-related infection (FRI). After surgical debridement and repeated NPWT dressing changes, the wounds are often closed by free flaps. Sometimes even healing by secondary intention seems an alternative. Recently, concerns have been raised on the long term use of NPWT as it could be related to bacterial overgrowth and possible re-infection. The purpose of this study was to conduct a retrospective evaluation of the influence of long-term NPWT on tissue culture results and outcome in FRI patients

Method: Between January 1st, 2015 and December 31st 2018, a total of 852 patients were treated with NPWT for different indications on the Department of Trauma Surgery. Inclusion criteria for this study were patients with a closed fracture, stabilized with osteosynthetic fixation and complicated with a confirmed FRI according to the *FRI consensus definition*. Patients were included when they received at least three NPWT dressing changes in the operating room. Exclusion criteria were patients younger than 18 years, or the absence of cultures results from dressing changes.

Results: During the study period 23 patients met the inclusion criteria. According to the tripartite classification of Willenegger and Roth, one patient had an early, 14 a delayed and 8 patients a late onset FRI. Overall, 139 NPWT dressing applications were performed, with an average amount of six per patient. In 14 patients (61%) and 57 dressing changes (41%), at least 2 tissue cultures showed the same pathogen or at least one, in case of highly virulent organisms (e.g. *S. aureus*) during a single dressing exchange. Coagulase-negative staphylococci were present in 33% of the cases, followed by *Enterococcus* spp. (21%), *S. aureus* (16%), non-fermentative gram negative bacilli (14%) and *Enterobacteriaceae* (7%). Furthermore, 17 exchanges showed polymicrobial growth. Five patients had repeatedly significant growth of the same pathogen despite adequate antimicrobial therapy, within this group one patient was immunocompromised.

Conclusions: In a large amount of patients (61%), a significant number of positive culture results could be acquired, even in the presence of adequate local and systemic antimicrobial therapy. The clinical relevance of these results remains unclear. This said, it seems important to limit the duration of NPWT as prolonged treatment could increase bacterial overgrowth and possible (re-)infection. Therefore, a rapid definitive soft tissue coverage should be encouraged. Future larger prospective clinical trials are required.

[FP37] BONE TRANSPORT AND TIBIO-TALAR ARTHRODESIS FOR DISTAL TIBIA POST-TRAUMATIC INFECTION

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Aim: Post traumatic distal tibia osteomyelitis (DTOM) with an upper ankle joint involvement is a serious complication after primary osteosynthesis and can be a nightmare for the patient and the surgeon as well. Our aim was to identify mayor complications during treatment and to find the way to prevent or treat them.

Method: It is a retrospective analysis of eight patients with DTOM and an upper ankle joint involvement treated in our institution from 2012 to 2018. The average size of a bone defect after a debridement was 9 centimeters (4-15). Patients were treated in two stages. First stage was segmental bone resection, external fixation and soft tissue envelope reconstruction if necessary. At second stage a distraction frame was applied and proximal corticotomy performed. In all but one case a circular frame was used.

Results: We have had one major intra-operative complication, an injury of arteria tibialis posterior during the corticotomy procedure. Except in one patient we did not observe major problems with pin-track infections. Despite bone-grafting in all patients, we observed three nonunions of docking site. We treated them by external fixator in two and retrograde intramedullar nail in one case.

In two patient the distraction callus was weak. We had to bone graft and secure the callus with a plate in one and use a retrograde reamed intramedullar nail in second patient.

We have observed two callus fracture after removal of the frame. A surgery was needed for both because of the deformation. The first patient was treated by new external frame, the second by retrograde reamed intramedullar nail.

Conclusions: Callus distraction is a valuable option to treat a bone defect. The procedure has many possible problems and complications, especially during treatment of defects larger than six centimeters. It is very difficult for patients to tolerate a frame more than one year. We have found the use of an intramedullar tibial nail inserted in a retrograde way as a helpful option not just to shorten the time of external frame, but in combination with reaming also to accelerate the healing of the distraction callus and the upper ankle joint arthrodesis as well.

[FP38] IS THE MANAGEMENT OF OPEN LEG FRACTURES IN A HOSPITAL FACILITY IN IVORY COAST A PROBLEM AND WHY?

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Introduction: The management of patients with open leg fracture in Ivory Coast does not meet the standards of developed countries due to socio-economic conditions, accessibility and organization of care. However, is this care problematic? Is it associated with more post-traumatic infection or mechanical complications and are these correlated with the delay for treatment and the method of treatment?

Material and Methods: This is a single-center prospective study conducted on between January 2018 and May 2018 at Bouaké University Hospital. The observed parameters included factors related to patient, fracture and treatment conditions and were correlated with the rates of complications by multivariate analysis.

Results: Fractures, mostly comminuted (69.8%), occurred following a road accident (93%). The series has 30 Gustilo 1 and 2 fractures and 13 Gustilo 3 fractures. The average delay before surgery was 26.6 ± 8.1 hours. Fracture stabilization required the use of a cast, an external fixator or an unlocked nail in 27, 10 and 6 cases, respectively. Complications developed in 28 patients (65%), including 17 malunions and 22 postoperative infections. 11 infections were controlled but 8 developed chronic osteomyelitis and 3 septic non-unions. Uncomplicated union was observed in only 15 cases and an acceptable functional outcome in only 16 cases. Gustilo Grade 3 fractures were associated with an increased risk of complication (p=0.02). The delay of management was not correlated with the appearance of a complication. In contrast, the use of plaster immobilization was significantly associated with an increased risk of complications and infection (p = 0.001).

Conclusion: The management of open fractures in our conditions is associated with a high rate of complications and a satisfactory result in a small number of patients. More than the delay of management, the immobilization modalities by plaster and the insufficiency of this method of contention are correlated to the complications. The development of a National Health Care system covering the expenses for emergent treatment, including rapid transportation to hospitals and availability of external fixators at a lower cost would most probably contribute to a reduction of complications and infection.

Keywords: Open fractures, developing countries, fixation, operative time

[FP39] VASCULARIZED FIBULA FLAP IN THE MANAGEMENT OF BONE LOSS SECONDARY TO OSTEOMYELITIS IN CHILDREN.

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Aim: Vascularized fibula flap is one of the available options in the management of bone loss that can follow cases of severe haematogenous osteomyelitis. The aim of this study was to evaluate the outcomes of this procedure in a pediatric population in a Sub-saharan setting.

Method: The retrospective study focuses on the procedures done in the period between October 2013 and December 2016. Twenty-eight patients, 18 males and 10 females, were enrolled. The youngest was 2 years old, the oldest 13. The bones involved were tibia (13), femur (7), radius (5) and humerus (3). In 5 cases the fibula was harvested with its proximal epiphysis, whereas in 17 cases the flap was osteocutaneous and osseous in 6 cases. In most cases, operations for eradication of the infection were carried out prior to the graft. The flap was stabilized mainly with external fixators,rarely with Kirschner's wires or mini-plate. No graft augmentation was used

Results: Graft integration was achieved in 24 cases. Three cases of early flap failure required the removal, while in one case complete reabsorption of the flap was noted a few months after the procedure. The follow-up period ranged from a minimum of 2 and half to a maximum of 6 years. Integration of the graft was obtained in a period of 4 months on average. The fibular flap with epiphysis had good functional outcomes with reconstruction of articular end. Early and delayed complications were observed. All grafts underwent a process of remarkable remodeling. No major problems were observed in the donor site, except for a transitory foot drop that resolved spontaneously.

Conclusions: Reconstruction of segmental bone defects secondary to hematogenous osteomyelitis with vascularized fibula flap is a viable option that salvages and restores limb function. It can be safely used even in early childhood. The fibula can be harvested as required by the local conditions. When harvested with a skin island, bone loss and poor soft tissues envelope may be addressed concurrently. The procedure is long and difficult but rewarding. When surgical skills and facilities are available, it can be carried out even in settings located in low resources countries.

[FP40] CHRONIC OSTEOMYELITIS: PROGNOSTIC AND THERAPEUTIC ASPECT IN THE SERVICE OF PEDIATRIC SURGERY CHU GABRIEL TOURÉ

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Objectives: Our objectives were to describe the therapeutic aspects and assess the prognosis of chronic osteomyelitis in children.

Materials and methods: We made a retrospective study from January 2007 to December 2016. The study concerned children from 0 to15 years, treated for chronic osteomyelitis and monitored in the pediatric surgery department of the teaching hospital Gabriel Toure, Bamako (Mali). The other types of bone infections, osteitis and bone tumors were not included in the study. In 10 years we received and treated 215 children with chronic osteomyelitis. This represented 3.56% of all the hospitalizations. The mean age was 8.8 (± 6.67) years with extremes of 28 days and 15 years. The patients were first seen by the traditional healer in 165 (76.7%) cases. The sex ratio was 1.26. The major clinical feature was local swelling associated with pain in 110 cases (51.2%). In 135 cases (62.8%) the staphylococcus aureus was found in direct examination or culture. After a year we performed a functional and morphological assessment according to the method of DIMEGLIO.

Results: Surgical treatment was performed in all patients. The average delay of stay in hospital was 4.95 ± 4.57 weeks, with extremes of 2 and 12 weeks. The means follow-up was 13 months with extremes of 3 and 20 months. Good results were found in 115 patients, fair in 60 (40 in keloid knee valgus to 11 ° in 10, muscular atrophy 10), bad in 40 (shortening member in 25 non-union in 10 valgus to 18 ° in 5) According Dimeglio score. There was no significant association between the time of consultation, prior treatment received, the surgical technique and the occurrence of complications (p> 0.05).

Conclusion: The management of the chronic osteomyelitis is well codified. The functional prognosis is dependent on an early care and sequels can be dramatic in children of school age.

Keywords: Chronic osteomyelitis, Treatment, Prognosis, Children.

[FP41] THE EXAMPLE OF BONES AND JOINTS INFECTIONS IN CAMEROUN SHOWS THE NEED TO CURB THE ANTIBIOTIC RESISTANCE IN DEVELOPING COUNTRIES

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Aim: Bone and joint infections are frequent in African countries and their prevention and treatment remain a great challenge. This study aimed to determine the bacterial ecology and sensitivity of isolates to locally available antibiotics in orthopedic unit of a tertiary care hospital in Cameroun.

Method: During a 12 months period, all the patients presenting with osteomyelitis or septic arthritis irrespective of the mechanism and the location were enrolled in this study. Intraoperative samples (biopsies) were taken and sent for microbiological analysis, and all strains isolated were tested for antibiotic sensitivity according to conventional methods.

Results: on the 52 bacteriological analysis performed, 48 were positive. The most isolated germs were staphylococcus aureus (41.9 % of isolates), pseudomonas aeruginosa (14.5 %), Escherichia coli (14.5 %) and Klebsiella pneumonia (12.9 %). The antibiotic sensitivity pattern revealed worrying resistance rates for common and affordable antibiotics: ampicillin (94 %), amoxicillin + clavulanic acid (63.9 %), ceftazidim (65.5%), ticarcillin + clavulanate (57.4%), gentamycin (49 %), ciprofloxacin (40 %), cefuroxim (40 %), tobramycin (38.5 %). The strains of Staphylococcus aureus showed resistance to penicillin G (83%), oxacillin (25%), lincomycin (27%) and vancomycin (7%). The overall highest sensitivity rates were observed with amikacin (92 %) and imipenem (90.1%), which for many patients were the only effective locally available antibiotics. The daily cost of treatment with those two antibiotics is close to the guaranteed minimum wage in our country.

Conclusions: The alarming rate of multidrug-resistant bacteria makes the long antibiotic treatment of bone infections unaffordable (in a context of lack of social insurance) for most of our patients. We advocate strong national policies for bacteriological surveillance and antibiotic misuse de-escalation to prevent antibiotic resistance.

[FP42] INTRAMEDULLARY OSTEOMYELITIS CIERNY-MADER TYPE 1. LOCALIZED AND DIFFUSE DIAPHYSEAL INFECTION

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Intramedullary osteomyelitis Cierny-Mader type 1. Localized and diffuse diaphyseal infection

Aim: Intramedullary osteomyelitis remains a challenge in the treatment of bone infections, requires organized, sequential and effective management to prevent its spread and subsequent recurrence. Errors are often made in the comprehensive treatment of this type of infection classified as type 1 of Cierny-Mader, where you can perform an insufficient treatment or in some cases perform very extensive and unnecessary bone resections. A rigorous protocol is proposed, by stages to achieve the total eradication of the infection and a surgical tactic that avoids diffusion of the infection or recurrences

Method: In the prospective case series study, 16 patients with type 1 intramedullary infection of Cierny Mader, diagnosed by radiology, TAC or MRI were included.

The microbiological protocol is carried out, with the germ typing and the corresponding antibiogram, at least 3 samples of deep tissues, the biofilm and segments of dead bone are taken. In the surgical tactic, intramedullary sequestrations are resected, the intramedullary canal is cleaned by stages, initially in the most inflammatory focus detected, the medullary canal is accessed through a planned and defined bone window, with round edges to avoid fractures and allowing access To the flexible reamer and cleaning guides, an additional window is made that avoids the blood dissemination of the infection, the septic embolisms or the contamination of the underlying soft tissues. It is defined if it requires stabilization of the bone with internal or external devices, therapies are applied locally to avoid recolonization, using Bioglass or absorbable substitutes with selective antibiotic. The treatment is associated with intravenous antibiotic therapy between 2 and 6 weeks according to the type of germ and if it is multiresistant.

It guarantees skin coverage and protection of structures at risk such as nerves, tendons and exposed bone.

Results: Successful treatment results are obtained, infection eradication in 100% of cases, the healing of osteomyelitis is achieved by applying an integral management of the intramedullary canal Osteomyelitis and a complete protocol is established.

Conclusions: The tactic and surgical technique applied in the integral management of intramedullary bone infection is essential to obtain definitive results in the eradication of bone infection. Care must be taken that the debridement is complete of the intramedullary canal and additionally, segmental or exaggerated resection of viable bone must be avoided, which survives and heals after the integral management of the infection with effective antibiotic therapy.

[FP43] UNEXPECTED OSTEOARTICULAR TUBERCULOSIS: REVIEW OF OUTCOMES FOLLOWING BIOFILM-TARGETED SURGICAL MANAGEMENT

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Aim: Skeletal tuberculosis (TB) accounts for up to one third of cases of extra-pulmonary TB but comprises a minority of osteoarticular infection in areas with low TB incidence. Consequently, unexpected cases may receive surgical management targeted at non-tuberculous orthopaedic infections. This study reviewed treatment and outcomes of non-spinal osteoarticular TB to assess outcomes from modern surgical techniques.

Method: All patients with a diagnosis of non-spinal osteoarticular TB between 2009-2017 from one tertiary referral centre were included. Retrospective review of surgical intervention, antibiotic treatment and outcome was conducted.

Results: Fourteen patients with an average age of 48 (range 20-77) were identified; all were HIV-negative. Articular infections affected 7 patients, including one prosthetic joint infection. Osteomyelitis affecting the carpus, femur, tibia, olecranon and metatarsals was diagnosed in the remaining patients. Only 4 patients had radiological findings consistent with prior pulmonary TB, and only 3 had a history of prior TB or TB exposure. In 2 cases, symptom exacerbation was associated with local steroid injection. Diagnostic biopsy was employed in 5 cases, of whom 4 proceeded to medical management. Diagnosis was made following positive culture in 86% of cases; all TB isolates were fully sensitive.

71% of cases underwent surgical treatment according to best practice for biofilm-forming infection, including excision of osteomyelitis with local antibiotic therapy for three patients, and first-stage excision with spacer implantation for four patients. Quadruple therapy for an average of 8.5 months, range 6-12 months, was administered. Patients were followed up for a mean of 15.2 months. Half of the patients treated with surgery reported ongoing pain at 3 months and 4 patients underwent further surgery for persistent signs of infection (2 for probable persistent TB, 2 for bacterial super-infection).

Conclusions: The role of surgical debridement in management of osteoarticular TB is unclear. In patients with a previous history of TB exposure a pre-operative diagnosis of TB could prevent unnecessary surgery and therefore prevent associated post-operative complications including bacterial super-infection and pain. Pre-op biopsy should therefore be considered in all patients with a history of TB exposure.

[FP44] INFECTION AFTER OSTEOSYNTHESIS: GOOD RESULTS IN BAD BUGS

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Aim: Management of infection after osteosynthesis (IAO) poses a significant challenge in the setting of multidrug resistant organisms (MDRo). We have analysed whether IAO with MDRo has an adverse outcome.

Method: We have retrospectively analysed patients with IAO from January 2001 to November 2016 with a minimum follow up of 12 months after the discontinuation of antibiotics.

Results: 62 patients with a mean age of 49.76 years presenting a mean 135 days after onset of infection. 40 of them had associated comorbidities, commonest being diabetes mellitus. Majority of the patients were on empirical antibiotics prior to presentation.

Deep cultures taken after implant removal in all cases at our institute grew 77 organisms {25 Gram positive (Gm+), 52 Gram negative (Gm-)}, commonest being *pseudomonas aeruginosa* (n=32). 12 patients had a mixed Gm+ and Gm- infections. 41/ 77 organisms cultured were multi-drug resistant (MDR) (Table 1). Infection remission was achieved in 56 patients (90.3%) at a mean follow up of 42.2 months, with 1 persistent infection, 2 amputations and 3 deaths. Union was achieved in 47/51 non unions.

Conclusions: Radical debridement beyond infection with removal of implants, complemented by targeted local and systemic antibiotics along with a good soft tissue cover, surgical stabilization and bone grafting as needed can help achieve good results in spite of MDR organisms.

Table 1: Antibiotic susceptibility pattern

Micro organism	Open fracture	Closed fracture	Total
Gram positive			
Methicillin-sensitive staphylococcus aureus(MSSA)	2	7	9
Methicillin-resistant staphylococcus aureus (MRSA)	3	9	12
Methicillin- resistant CONS	0	1	1
Gram negative			
Fluroquinolones resistant	12	20	32
Aminoglycosides resistant	11	13	24
Pan susceptible	2	11	13
Extended spectrum beta lactamase (ESBL)	7	5	12
Extended spectrum beta lactamase plus (ESBL Plus)	4	9	13
Carbapenem resistant (CR)	4	7	11
Carbapenem resistant plus (CR Plus)	2	0	2
Multidrug resistant (MDR)	5	9	14
Extensively drug resistant (XDR)	4	7	11
Pan drug resistant (PAN DR)	3	0	3

[FP45] DIAGNOSING CHRONIC PERIPROSTHETIC JOINT INFECTION: DEFINITION MATTER

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Aim: Apart from other biomarkers isolated in the synovial fluid, alpha-defensin appears to be a promising diagnostic tool to confirm a periprosthetic joint infection (PJI) in the hip or knee. The purpose of this study was to evaluate the sensitivity and specificity of an alpha defensin lateral flow (ADLF) test compared to usual standard classifications in the diagnostic management of PJI.

Method: This investigation was set up as a multicenter prospective cohort study. Synovial fluid was obtained by means of joint aspiration or intra-operative tissue biopsies. A presumptive PJI diagnosis was made according to criteria outlined by the Musculoskeletal Infection Society (MSIS), the Infectious Diseases Society of America (IDSA) and the European Bone and Joint Infection Society (EBJIS). The intention to treat by the surgeon was logged. Sensibility and specificity for the ADLF test was plotted for each aforementioned diagnostic algorithm. Spearman correlations between all scores were analyzed. Multiple logistic regression was used to determine the contribution of independent variables to the probability of PJI.

Results: Hundred thirty six patients with a painful arthroplasty were assessed for infection and rated by the treating surgeon as potentially infected or not on the basis of clinical and laboratory information. According to the EBJIS criteria sixty-eight patients were deemed infected, fifty according to the IDSA criteria, forty one according to the MSIS criteria and forty according to the ADLF test. However, the sensitivity of ADLF test was 87.8% for MSIS, 70% for IDSA and 55.8% for EBJIS. The specificity of ADLF test was between 94% - 97%. Good correlation was observed between synovial fluid culture and ADLF test (r = 0.73). Low to excellent correlations between the ADLF test and the EBJIS (r = 0.58), IDSA (r = 0.68), and MSIS score (r = 0.84) were observed. The surgeon's intention to treat correlated well with the MSIS score (r = 0.86), and moderately with the EBJIS (r = 0.59).

Conclusions: ADLF test sensibility was variable, but its specificity was excellent. Most of the cases, not retained by MSIS but classified by EBJIS as infected, got a negative microbiological result. Considering an accepted 20% negative microbiological result rate in PJI diagnostic, EBJIS is clearly overestimating the number of infected cases. MSIS score correlates with the surgeon intention to treat and ADLF test.

[FP46] EPIDEMIOLOGY, MICROBIOLOGICAL DIAGNOSIS, AND CLINICAL OUTCOMES IN PROSTHETIC JOINT INFECTION: RESULTS FROM THE PROSPECTIVE BRAZILIAN-IMPLANT COHORT STUDY (BRICS)

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Aim: Over the past three years, roughly 100,000 hip and knee replacements have been performed by the Brazilian Public Healthcare System. Prosthetic joint infection (PJI) is expected to range between 1% to 10% after primary and revisions joint arthroplasties, respectively. So far, there have been no published national PJI data which would be helpful at developing local preventive strategies and guide surgeons and clinicians. We aimed at *describing the* epidemiological, clinical and microbiological PJI results of *a national and collaboration study among infectious diseases specialists and orthopaedic surgeons, including academic, public and private institutions.*

Method: We prospectively enrolled patients with PJI in a national cohort study among 12 hospitals from 6 different States to describe host, pathogens, diagnosis, surgery strategies adopted (according to the standard hospital-based guideline) and outcome after 1- and 2-years follow-up. PJI was defined using the IDSA criteria (Osmon D, et al. Clin Infect Dis. 2013). Patients were enrolled from July 2013 to December 2015.

Results: Overall, 234 patients undergoing hip, knee and shoulder (n=3) arthroplasty were eligible; 35 were excluded: did not fulfil the inclusion criteria (n=14), withdrawal informed consent (n=11) and early lost to follow-up (n=10). A total of 199 were available for analysis. Twenty-two (11%) patients died during the follow-up, most of which (95%) occurred within 1 year of PJI diagnosis. In the one-year (12 patients lost to follow-up) and two-year (18 patients lost to follow-up) post-diagnosis analysis, overall treatment failure occurred in 13.3% (n=22/166), and 17% (n=25/147). Knee and hip rate failure in the 1- and 2-year follow up were 12.2% (n=9/74), 15.4% (n=14/91), and 16.2% (n=11/68), 18.2% (n=14/77), respectively. Debridement with implant retention (DAIR), one-stage exchange, two-stage exchange, and arthrodesis was performed in 44.7%, 25.4%, 22.3%, 7.6% respectively. Failure rates for DAIR, one-stage exchange, two-stage exchange, and arthrodesis after 1- and 2-year follow-up were 24.2% (n=16/66), 4.3% (n=2/46), 9.8% (4/41), 0% (n=0/15), and 28.6% (n=16/56), 4.8% (n=2/42), 15.8% (n=6/38), 0% (n=0/15), respectively. Microbial diagnosis yielded positive culture in 71.7%. *Staphylococcus aureus* (34%), coagulase-negative staphylococci (28%), *Pseudomonas aeruginosa* (17%) were more prevalent. Polymicrobial PJI were diagnosed in 32.8%.

Conclusions: This is so far the largest Brazilian cohort of patients with PJI showing an overall 2-years failure-free survival rate of 83%, in which DAIR is the most frequent and less successful strategy, single-stage exchange seems to be a growing surgical option. Polymicrobial and non-fermenting Gram-negative bacilli and *Enterobacteriacae* is frequent.

[FP47] THE (DE)TERMINATOR PJI TREATMENT FLOWCHART

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Aim: At present, a variety of clinical guidelines[1, 2] for treatment of periprosthetic joint infections (PJI) inevitably lead to a variety in outcomes by differing case management. Ideally a treatment algorithm should incorporate all components contributing to the decision-making process for a patient tailored solution in PJI. We aim to present a comprehensive and reproducible treatment algorithm based on a validated staging system, a thorough understanding of the host, the causative microbiome and implant complexity.

Method: The diagnosis of a PJI was defined according to major and minor criteria following revised International Consensus Symposium algorithm

The validated McPherson staging system[3] was used in our university hospital from January 2015 until January 2019 in referred PJI patients. Standardised preoperative and postoperative survey documents were completed in order to register data from the patient's medical, social and surgical history. The complexity of the infected implant was taken into consideration, including quantity of preceding procedures, residual bone stock, type of fixation, magnitude of prosthetic components and presence or absence of reconstructive options. Further, preoperatively obtained bacteriological information by means of arthrocentesis or tissue/bone biopsies was categorized according to the mono- or polybacterial nature and to the qualification of virulence and difficulties to treat. Social and professional history, financial impediments and patient's functional outcome wishes were included in the joint decision making.

Results: We present our comprehensive PJI treatment algorithm. The 'deTerminators' we included are a validated staging system focused on the host, the amount of unsuccessful prior attempts, the difficult to treat character of the microbiome, the implant complexity, anatomical location and socioeconomic patient derived factors. Furthermore, we call for source control by minimally invasive means or late DAIR in complex case management combined with lifelong suppressive antibiotic therapy[4] with maintenance of quality of life as the main outcome instead of curative intention.

Conclusions: We present a comprehensive treatment algorithm based on an expanded McPherson staging system coupled with bundled clinical, technical, social and psychological data which should assist the surgeon and the patient to make informed choices. We hope that usage and testing of our algorithm in other centers could further demonstrate its usefulness.

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[FP48] MINIMUM FOUR YEARS FOLLOW-UP RESULTS AFTER SINGLE-STAGE REVISION IN THE MANAGEMENT OF CHRONIC PROSTHETIC-JOINT INFECTION AFTER TOTAL HIP ARTHROPLASTY: RETROSPECTIVE ANALYSIS

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Aim: This study aims to describe our department experience with single stage revision (SSR) for chronic prosthetic-joint infection (PJI) after total hip arthroplasty (THA) between 2005 and 2014 and to analyze success rates and morbidity results of patients submitted to SSR for infected THA according to pathogen.

Method: We retrospectively reviewed our 10 years of results (2005-2014) of patients submitted to SSR of the hip combined with IV and oral antibiotic therapy for treatment of chronic PJI (at least 4 weeks of symptoms), with a minimum follow-up of four years (n=26). Patients were characterized for demographic data, comorbidities, identified germ and antibiotic therapy applied (empiric and/or targeted). Outcomes analyzed were re-intervention rate (infection-related or aseptic), success rate (clinical and laboratory assessment), length of stay, morbidity and mortality outcomes.

Results: In this period, 26 single-stage revisions for chronic PJI of the hip were performed. Patients average age was 72 years (range 44-82). Ten patients were women. The average time of follow up was 69 months (range 4 to 12 years). The most commonly isolated bacteria were coagulase-negative Staphylococci (30%), methicillin-resistant Staphylococcus aureus (MRSA) (18%) and methicillin-sensitive Staphylococcus aureus (15%). It wasn't possible to identify the germ in 19% of the patients and other 23% were polymicrobial. Targeted antibiotic therapy was administered to 73% of patients and the most used targeted antibiotics were Vancomycin (53%), Linezolid (32%) and Rifampicin (21%). Mean length of stay was 25 days. In the follow-up period, 9 patients (35%) required a re-intervention for infection relapse. Two patients (8%) needed surgery because of persistent instability. During the follow-up period, the infection-free survival was 65% (33% for MRSA; 82% for coagulase-negative Staphylococci) and the surgery-free survival was 62%. Six patients (23%) died during the follow-up, all due to other medical conditions not related to hip infection.

Conclusions: Our experience suggests that SSR is associated with good outcomes and low re-intervention rate, except in the case of infection due to MRSA. In this last group, the results were significantly poorer, what leads to suggest that a two-stage revision may be a better option. The potential advantages of a SSR include good rates of infection eradication, a decrease in surgical morbidity and mortality as well as a decrease in healthcare and global economic costs. As such, a one-stage aggressive surgical attitude in addition to targeted antibiotherapy seems to be a suitable solution in selected patients.

[FP49] THE USE OF MASSIVE PROTHESES IN THE PERIPROSTHETIC JOINT INFECTIONS. A SERIES OF 58 PATIENTS TREATED IN ONE OR TWO STAGES

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Aims: To evaluate the place of the massive prostheses in the most complex periprosthetic infections cases (PJis).

Method: Between 2011 and 2017, 516 hip and knee revisions for periprosthetic infections had been performed in our hospital by the same senior surgeon. We report a prospective series of 58 patients treated between 2011 and the end of 2017. 26 male and 32 female with on average 69,4 years old (38-86). Infection involved TKA in 39 cases (26 TKA revisions, 11 primary TKA), THA in 18 cases (10 revisions, 7 primary THA), a femoral pseudoarthrosis with posttraumatic gonarthrosis in one case and a septic humeral pseudoarthrosis in one case.

We used one stage procedures in 38 cases (14 hips, 23 knees, 1 shoulder) and 20 two stages surgeries (16 knees and 4 hips). Additional technics used with massive prostheses, all for TKA PJis: 4 massive extensor systemallografts performed two times in a one stage procedure, two local flaps (medial gastronecmienmuscle). Two perioperative hyperbaric procedures used to limit the risks of wound complications.

Results: The average follow-up is 38 months (12-62 months). The rate of sucess to treat the infection at this follow-up is 89,7 %. We report our feedback of the different massive components uses and the qualities/defaults we noted.

The most frequent complication was skin events like wound swelling and delayed cicatrisations in 13 cases. 3 cases of one stages needed a complementary debridement in the three weeks after the surgery with always a good local and infectious evolution.

This series report 5 failures of two stages TKA revisions. In 4 cases, the initial local soft-tissues conditions was compromised.

Conclusions: The use of massive prostheses to treat PJIs is a good option for the complex cases. It can be a good alternative of knee arthrodesis. These components must be used, preferentially for oldest patients, in cases of extreme bone loss or extensed osteitis to secure the bone debridement and the quality of the reconstruction. In our series, the one stage procedure is a validated option even by using complementary technics as bone allografts, extensor system allografts or flaps. The two stages procedure is a secondary option, particularly when softtissues status is compromised before or after the debridement, and mostly for the knees.

[FP50] IS ONE-STAGE REVISION SURGERY FOR INFECTED THA PREFERABLY WHEN USING VANCOMYCIN CONTAINING BONE GRAFT?

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Is one-stage revision surgery for infected THA preferably when using vancomycin containing bone graft?

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Introduction: Periprosthetic joint infection (PJI) represents the costliest complication in Orthopedics. Studies of mixing vancomycin to bone graft at Impaction Bone Grafting (IBG) have shown high local concentration for 3 weeks.

Patients and methods: 55 consecutive revisions PJI, age 68 (SD 10.9), (9 one-stage and 46 two-stage) were retrospectively analyzed. All cases were revised using IBG. Most cases had vancomycin mixed in graft or added locally in joint. All had bone cement containing Gentamycin and Vancomycin. Follow up 2-16 years included clinical Merle d'Aubigne-Postel score, radiology and laboratory tests. We analyzed surgical time, bleeding, hospitalization time, infection eradication and prosthetic survival for one- and two-stage revision procedures. One patient was lost to follow up and 6 died (2 one- and 4 2-stage) before 2 years. Values are mean and SD. Analyses done by students *t*-test.

Results: Preoperatively scores for 1- and 2-stage groups were 11.7 (0.79) and 10.2 (1.27) respectively. Follow up scores were 17.5 (0.38) and 15.9 (0.73) respectively. Total intra-operative blood loss (ml) for one- and two-stage procedures were 1638 (780) and 2764 (828) respectively $p<0.05$. Total surgery time (minutes): 238 (206) and 409 (108) respectively $p<0.05$. Total hospitalization time (days): 13 (6.2) and 34 (13) $p<0.05$. Radiology at follow-up showed no signs of PJI, signs of mechanical loosening in one. There were no persistent or new PJI, no revision for mechanical loosening. Two revision for any reason in the 2-stage and one in the 1-stage group. Five reoperation without component exchange for periprosthetic fracture, all in the 2-stage group.

Conclusion: No mechanical loosening and no persistent or new PJI are favourable results. Blood loss, hospitalization- and surgery-time were substantially increased for the two-stage group. Muscle atrophy, osteoporotic development and decrease general physical condition are all well-known side effects of two-stage procedure. Revision one-stage hip PJI using IBG avoids increased suffering and resources connected to the two-stage procedure. Literatures have not shown eradication of PJI, to be clearly superior after two- compared to one-stage procedures. Reconstitution of bone defects and the possibility of very high local antibiotic concentration are substantial advantages when using IBG.

We recommend a careful one-stage IBG procedure using antibiotic loaded graft for none "difficult to treat" cases.

[FP51] PERFORMANCE OF SYNOVIAL FLUID D-LACTATE TEST FOR ACCURATE DIAGNOSIS OF PERIPROSTHETIC JOINT INFECTION

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Aim: To evaluated the analytical performance of synovial fluid D-lactate test for the diagnosis of PJI.

Method: Consecutive patients undergoing diagnostic joint aspiration of prosthetic joint were prospectively included. PJI was diagnosed according to the proposed European Bone and Joint Infection Society (EBJIS) definition criteria. Synovial fluid was collected for culture, D-lactate measurement (by spectrophotometry, λ = 570 nm) and leukocyte count and differential (by flow cytometry). The receiver operating characteristic (ROC) analysis was performed to assess the diagnostic performance of D-lactate and leukocyte count.

Results: Diagnostic joint aspiration was performed in 224 patients with prosthetic joints. PJI was diagnosed in 87 patients (39%). The optimal D-lactate cut-off value for diagnosing PJI was 1.2 mmol/l. The sensitivity of synovial fluid D-lactate was 97.7%, specificity 83.9%, whereas the sensitivity of synovial fluid leukocyte count was 87.5% with specificity 95.7%. Concentration of SF D-lactate was significantly higher in patients with PJI compared to aseptic loosening of prosthesis (median (range)) 2.33 (0.99-3.36) vs 0.77 (0.01-2.4), $p<0.0001$. We found positive correlation between D-lactate and erythrocytes in synovial fluid sample in the aseptic group ($\rho = 0.339$, $p< 0.01$).

Conclusions: The synovial fluid D-lactate showed a good diagnostic performance for the diagnosis of PJI, which was comparable to the synovial fluid leukocyte count. Currently available (UV)-based method for detection of D-lactate showed low specificity (84%) due to influence of hemoglobin with the similar absorbance wavelengths (λ = 540 nm). More specific high-performance methods such as electro-chemical sensing system or lateral flow immunochromatographic assays should be implemented.

[FP52] THE USE OF PET-CT REDUCE MORTALITY IN PATIENTS WITH IMPLANT RELATED INFECTION ASSOCIATED STAPHYLOCCOCUS AUREUSBACTEREMIA (SAB)

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Aim: *Staphylococcus aureus* bacteremia (SAB) is associated with significant morbidity and mortality, 20-30 % risk of infection in patient with implant related infection (IRI) .18F-FDG PET/CT is helpfull in the management of SAB, leading to detection of more metastatic foci and treatment modification and finally decrease relapses and mortality rate (1). Our objective was to analyze mortality in high risk SAB patients undergoing 18F-FDG PET/CT and to see whether it's use in patients with IRI reduced their mortality.

Method: We performed a retrospective study at a university hospital in Belgium. All cases of high risk adult SAB between January 2014 and June 2017 were reviewed. We collected the clinical characteristics including presence of metastatic foci on 18F-FDG PET/ CT, mortality at 1 year.

Results: A total of 102 patients were included. Twenty-one patient with IRI were identified (20.6%). In 94.1 % (N=96) SAB were due to methicillin-sensitive *staphylococcus aureus* (MSSA). 18F-FDG PET/ CT was performed in 47% (N =48) of patients and a metastatic foci was identified in 45.8% of cases (N=22/48). The detection of metastatic foci lead to surgical intervention in a site other than the site of IRI in 38% versus 14% (P < 0.001) in patients undergoing or not 18F-FDG PET/CT respectively. The overall mortality rate was 31.3 % (32/102). The mortality rate was 16.6% (8 /48) and 41.3 % (24/54) in patients undergoing or not 18F-FDG PET/ CT respectively (P=0.03). For IRI, the overall mortality was 9.3 % versus 15.6% in patients undergoing or not 18F-FDG PET/ CT respectively (P<0.001). There was a significant difference in mortality rate at 30 (P=0.001), 90 days (P=0.01) and one year (P=0.004) between patients undergoing or not 18F-FDG PET/ CT respectively. In bivariate analysis, the overall, 30, 90 days and one year mortality rate was significantly reduced among patient with kidney failure (P< 0.001), diabetic foot infection (P=0.006), age >70 years (P=0.007) and prosthetic joint or plate infection (P< 0.001) in whom the 18F-FDG PET/ CT was performed.

Conclusions: Mortality rate was reduced in high risk SAB patients undergoing 18F-FDG PET/ CT. The use of 18F-FDG PET/CT reduced mortality in patients with PJI by detecting more metastatic site leading to more aggressive treatment.

1. Berrevoets MAH, Kouijzer IJE, Aarntzen EHJG, Janssen MJR, De Geus-Oei LF, Wertheim HFL, et al. ^{18}FDG PET/CT Optimizes Treatment in *Staphylococcus Aureus* Bacteremia and Is Associated-with Reduced Mortality. J Nucl Med. 2017;58(9):1504-1510.

[FP53] CLINICAL EVALUATION OF SYNOVIAL ALPHA DEFENSIN AND SYNOVIAL C-REACTIVE PROTEIN IN THE DIAGNOSIS OF PERIPROSTHETIC JOINT INFECTION

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Aim: Diagnosing periprosthetic joint infection after total joint arthroplasty is often challenging. The alpha defensin test has been recently reported as a promising diagnostic test for periprosthetic joint infection. The goal of this study was to determine the diagnostic accuracy of alpha defensin testing.

Method: One hundred and eighty-three synovial alpha defensin and synovial fluid C-reactive protein (CRP) tests performed in 183 patients undergoing evaluation for periprosthetic joint infection were reviewed. Results were compared with the Musculoskeletal Infection Society (MSIS) criteria for periprosthetic joint infection.

Results: Alpha defensin tests were performed prior to surgical treatment for infection, and 37 of these patients who had these tests were diagnosed by MSIS criteria as having infections. Among this group, the alpha defensin test had a sensitivity of 81.1% (95% confidence interval [CI], 64.8% to 92.0%) and a specificity of 95.9% (95% CI, 91.3% to 98.5%). There were 6 false-positive results, 4 of which were associated with metallosis. There were 7 false negatives, all of which were associated with either draining sinuses (n = 3) or low-virulence organisms (n = 4). A combined analysis of alpha defensin and synovial fluid CRP tests was performed in which a positive result was represented by a positive alpha defensin test and a positive synovial fluid CRP test (n = 28). Among this group, the sensitivity was calculated to be 73.0% (95% CI, 55.9% to 86.2%) and the specificity was calculated to be 99.3% (95% CI, 96.2% to 99.9%). An additional combined analysis was performed where a positive result was represented by a positive alpha defensin test or positive synovial fluid CRP test (n = 64). Among this group, the sensitivity was calculated tobe91.9%(95%CI, 78.1%to98.3%) andthe specificitywas calculated tobe79.5%(95%CI, 72.0%to85.7%).

Conclusions: Alpha defensin in combination with synovial fluid CRP demonstrates very high sensitivity for diagnosing periprosthetic joint infection, but may yield false-positive results in the presence of metallosis or false-negative results in the presence of low-virulence organisms. When both alpha defensin and synovial fluid CRP tests are positive, there is a very high specificity for diagnosing periprosthetic joint infection.

[FP54] SERONEGATIVE HIP AND KNEE PROSTHETIC JOINT INFECTIONS: IS ERYTHROCYTE SEDIMENTATION RATE A HELPFUL ADJUNCT TO C-REACTIVE PROTEIN?

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Aim: C-reactive protein(CRP) and erythrocyte sedimentation rate(ESR) are non-specific markers with variable reported accuracy in the diagnosis of prosthetic joint infection(PJI). They are often used as a part of the initial diagnostics as they are widely available and inexpensive. Given its high false-negative rate, CRP is an insufficient screening tool for PJI especially in low virulence microorganisms. Nevertheless, many advocate ESR offers no added advantage and is useless in this setting. Our goal is to determine if the combined measurement of ESR and CRP offers increased sensitivity for the preliminary screening of PJI over isolated CRP measurement.

Method: We retrospectively evaluated every single- or first-stage for presumed aseptic or known infected revision total hip/knee arthroplasty procedures between 2013-2018. Cases without preoperative CRP and ESR measurement as well those without synovial fluid for differential leukocyte count and/or no multiple cultures including sonication of removed implant obtained during surgery were excluded. Diagnostic accuracy was compared against two different PJI definitions: 2013 International Consensus Meeting and ProImplant Foundation definitions.

Results: A total of 398 revision were performed during the study period. After excluding 293 cases with insufficient information, a total of 105 patients were studied. Naturally, CRP and ESR mean values were significantly higher among PJI cases compared to aseptic cases. Distribution of cases according to PJI definition used, mean values and diagnostic accuracies are expressed in table 1.

ICM 2013 PJI definition				
	N		mean ESR (mm/h)	mean CRP (mg/L)
Infected	52		63.9	60.3
Aseptic	53		21.6	7.0
	Sensitivity	Specificity	Positive Predictive value	Negative Predictive value
CRP (>10mg/L)	86.5%	90.6%	90.0%	88.9%
ESR (>30mm/h)	84.6%	73.6%	78.6%	83.0%
ESR **and** CRP	94.2%	69.8%	75.4%	92.5%
ProImplant Foundation PJI definition				
	n		mean ESR (mm/h)	mean CRP (mg/L)
Infected	62		63.9	51.4
Aseptic	43		21.6	7.6
	Sensitivity	Specificity	Positive Predictive value	Negative Predictive value

CRP (>10mg/L)	73.8%	88.4%	90.0%	70.4%
ESR (>30mm/h)	77.4%	80.5%	85.7%	70.2%
ESR **and** CRP	85.5%	72.1%	81.5%	77.5%

Conclusions: After the inciting insult, CRP raises and drops rapidly and ESR response is slower but also much more enduring. One can only hypothesize that chronic PJI runs perhaps a fluctuating inflammatory course that can sometimes be more accurately picked up by ESR and not CRP measurement. Our results seem to corroborate that ESR measurement is a valid adjunct to isolated CRP measurement in the initial screening of PJI in painful total joint arthroplasties.

[FP55] COMBINED BIOMARKER ANALYSIS IN PJI DIAGNOSIS – A USEFUL TOOL OR NOT TO RECOMMEND?

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Aim: In the diagnosis of prosthetic joint infection (PJI), many biomarkers have shown a sound performance in terms of accuracy, sensitivity and specificity. In this study we aimed to test the frequently used serum biomarkers C-reactive Protein (CRP), Fibrinogen, Leukocytes, Interleukin-6 (IL-6), Interferon alpha (IF-alpha) and Procalcitonin (PCT) regarding these qualities. Following that, the optimal multi-biomarker combination was calculated to further improve the diagnostic performance.

Method: 124 knee or hip revision arthroplasty procedures were prospectively investigated focusing on preoperative serum blood levels of CRP, Fibrinogen, Leukocytes, IL-6, IF-alpha and PCT. The presence of PJI was determined by a blinded researcher. Logistic regression with lasso-regularization was used for the biomarkers and all their ratios. Following cross-validation on a training sample set to get optimal performance estimates, we performed the final model on a test set (25% of all samples).

Results: Out of all evaluated biomarkers, CRP (AUC 0.91, p-value 0.03) and Fibrinogen (AUC 0.93, p-value 0.02) had the best performances. The optimal combination when testing multiple biomarkers in 32 cross-validation runs was calculated including Fibrinogen, CRP, the ratio of Fibrinogen to CRP and the ratio of serum Thrombocytes to CRP (AUC 0.92, accuracy 0.77, specificity 0.92, sensitivity 0.68, cut-off 0.63, p-value 0.04). The probability per sample (test set) is depicted in figure 1.

Conclusions: It was not possible to increase the diagnostic performance by combining multiple biomarkers using sophisticated statistical methods. The calculated Multi-biomarker models did not improve the AUC, accuracy, sensitivity and specificity when compared to single biomarkers.

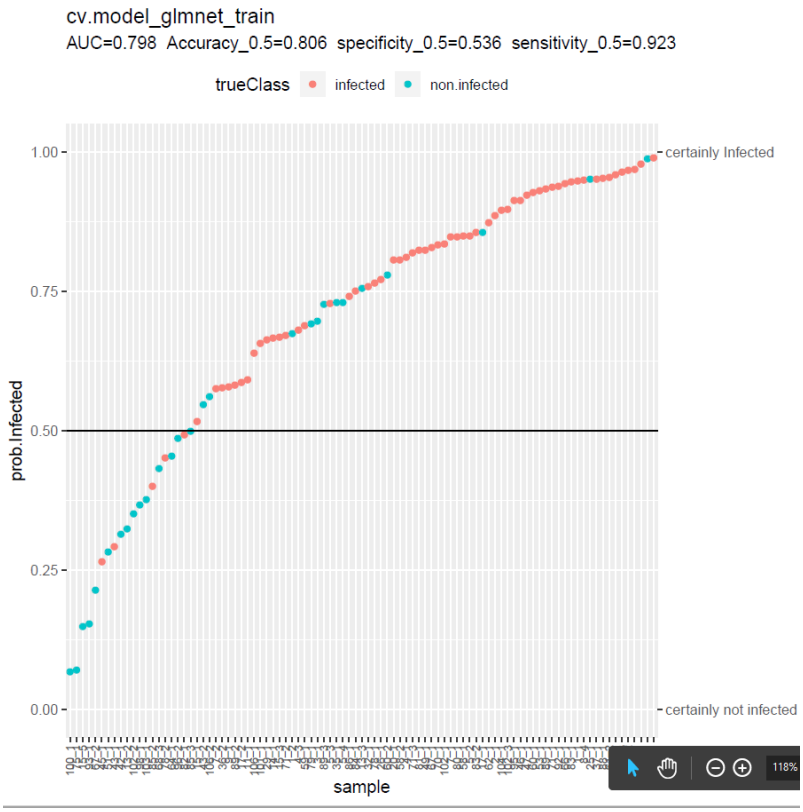

Figure 1. Probability per sample on the final test set.

[FP56] IS A POSITIVE INTRA-OPERATIVE CULTURE ASSOCIATED WITH POOR RESULTS IN PRESUMED ASEPTIC REVISION OF TOTAL HIP AND KNEE ARTHROPLASTIES?

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Aims: The purpose of this study was to evaluate the infection-free outcome of patients underwent revision of total joint arthroplasty (TJA) for presumed aseptic causes, with positive intra-operative cultures.

Patients and Methods: A retrospective cohort study was assembled with 130 patients undergoing revision knee (21 cases) or hip arthroplasty (109 cases) for presumed aseptic causes. For all patients five to seven separate intra-operative cultures were obtained and prosthesis sonication was done. Patients were diagnosed with a previously unsuspected prosthetic joint infection (PJI) if two or more cultures were

positive or a positive prosthesis sonication. Data were reviewed for demographic details, preoperative laboratory results and culture results. The endpoint was infection-free implant survival at 24 months.

Results: Patients with unsuspected PJI was 16 out of 130 (12,3%). Following revision surgery, the rate of infection-free implant survival in patients with an unsuspected PJI was 68,8% (95% confidence intervals (CI) 45,6 to 92) at two years compared with 94,7% (95% CI 90,5 to 98,9) in patients without PJI (p = 0.001).

Conclusion: Around 12% of positive cultures can be expected after TJA aseptic revision surgery; in these cases the rate of infection-free implant survival is lower than in cases without PJI.

[FP57] ANTIBIOTIC TREATMENT AND MICROBIOLOGICAL FINDINGS IN COMPLEX FRACTURE-RELATED INFECTIONS; A SYSTEMATIC LITERATURE REVIEW

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Aim: The aim of this systematic review was to determine all cultured bacteria, antibiotic strategies, and their outcome from literature describing treatment of FRI patients between 1990 and 2018.

Methods: A systematic literature search was performed on treatment and outcome of FRI. All studies in English that described surgical patient series for treatment of FRI were included, using Medline, Embase, Web of Science, Cochrane, and Google Scholar. Publications before 1990 and studies that did not describe FRI patient treatment or did not report original data (*e.g.*, reviews or meta-analyses) were excluded. Study selection and data collection were done by two authors independently. Main collected parameters were preoperative cultures, use of local antibiotics, postoperative antibiotic protocol, cultured microorganisms, and overall outcome of treatment, *i.e.*, eradication of infection and bony union, recurrence, amputations, revisional surgery, and number of complications. Dichotomous data were pooled using Medcalc, and weighted means were calculated for continuous data using Excel.

Results: 2,171 studies were identified. Of these, 110 studies were included, describing 119 patient series, in which 4561 patients (4614 fractures) were treated. The population was predominantly male (76%), and the main location of FRI was the tibia (69%). In 78 (71%) studies, 3,234 microorganisms were cultured, of which Methicillin-sensitive Staphylococcus aureus (MSSA) was found in 1,094 (34%) patients, followed by Coagulase-negative Staphylococci (CNS), 431 (13%), Methicillin-resistant Staphylococcus aureus (MRSA), 283 (9%), and Pseudomonas aeruginosa 276 (9%). Polymicrobial infections were present in 11% of patients. Local antibiotics were used in 63 (53%) patient series, with PMMA being the most frequent carrier (73%). Calcium-based cements were used in nine series (14%). Clear postoperative antibiotic protocols were described in only 39 (35%) studies and differed widely. Bony union and infection eradication were achieved in 92% (CI 90-94) of all patients.Recurrence was seen in 9% (CI 8-11), and amputation was required in 3% (CI 3-4) of patients. The effect of local antibiotics on overall outcome of FRI treatment was unclear.

Conclusions: This systematic literature review clearly shows that standardized antibiotic treatment protocols for FRI patients are lacking and that internationally accepted guidelines are required. The data also confirm that *S. aureus* is the most common microorganism encountered in FRI. Due to the large heterogeneity of used local antibiotics and carriers, a reliable comparison was not feasible. Indications for the use of local antibiotics are unclear, and future prospective studies seem necessary.

[FP58] OUTCOMES IN CULTURE NEGATIVE AND CULTURE POSITIVE OSTEOMYELITIS

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Aim: To evaluate clinical outcomes for patients with osteomyelitis at a major trauma centre limb reconstruction unit.

Method: We prospectively evaluated 137 patients on the limb reconstruction database with long bone osteomyelitis. Data on initial diagnosis, management (bone resection, use of external fixation, dead space and soft tissue management), microbiology and 2-year outcomes were collated. 11 patients' data was incomplete and 9 underwent primary amputations; these were excluded from microbiology data analysis. The patient data was categorised into microbiological culture negative or culture positive groups. Inter-group comparisons were made to evaluate two-year outcomes and percentage failure rate.

Results: Forty percent (55/137) of patients presented with infected non-union, 20% (27/137) infected fractures,19% (26/137) chronic osteomyelitis without implants and 14% (19/137) had infected metalwork. Removal of metalwork, reaming and debridement were the most frequently performed procedures, often in combination. 3% of patients failed treatment and had persistent infected non-union. The most common microorganisms identified in the culture positive group were Staphylococcus aureus (47.6%), Coagulase Negative Staphylococcus species (11.9%) and Enterobacter cloacae (11.9%), however multiple organism growth was more common than single organism growth, 53% and 47% respectively. 8% of culture negative patients had histological evidence of infection on biopsy.

Conclusions: The 2-year failure rate (persistent infective non-union) was higher in the culture negative group (8%) than the culture positive group (1%). The higher failure rate may be secondary to lack of organisms isolated and available sensitivities from deep tissue samples. In 9 cases patient preference led to primary amputation over limb salvage procedures, without further infection. Our work highlights the array of factors contributing to outcome in this patient group. The incidence of micro-organisms commonly encountered in this cohort will provide further evidence to support choice of antibiotic for empirical therapy especially in cases which are culture negative. Finally, there are many challenges in achieving adequate outcomes in patients with long bone infections thus the need for a multidisciplinary team approach in this patient cohort is invaluable. Routine histology testing may be beneficial as this may highlight infective processes in culture negative patents thereby allowing optimization of patient management.

[FP59] MULTI-DRUG (MDR) AND EXTENSIVELY DRUG-RESISTANT (XDR) GRAM NEGATIVE OSTEOSYNTHESIS-ASSOCIATED OSTEOMYELITIS (OAO) OF THE LOWER EXTREMITIES: A MULTI-CENTRE INTERNATIONAL STUDY

Efthymia Giannitsioti[1], Mauro Salles[2], Andreas Mavrogenis[3], Dolors Rodríguez-Pardo[4], Carles Pigrau[4], Alba Ribera[5], Javier Ariza[5], Dolores Del Toro[6], Sophie Nguyen[7], Eric Senneville[7], Eric Bonnet[8], Monica Chan[9], Maria Bruna Pasticci[10], Sabine Petersdorf[11], Alex Soriano[12], , Natividad Benito[13], Nualla O' Connell[14], Antonio Blanco García[15], Gábor Skaliczki[16], Pierre Tattevin[17], Zeliha Kocak Tufan[18], Nikolaos Pantazis[19], Panayiotis D Megaloikonomos[20], Panayiotis Papagelopoulos[21], Antonios Papadopoulos[22]

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Aim: Gram negative bacteria (GNB) are emerging pathogens in chronic post-traumatic osteomyelitis. However, data on multi-drug (MDR) and extensively drug resistant (XDR) GNB are sparse.

Methods: A multi-centre epidemiological study was performed in 10 countries by members of the ESGIAI (ESCMID Study Group on Implant Associated Infections). Osteosynthesis-associated osteomyelitis (OAO) of the lower extremities and MDR/XDR GNB were defined according to international guidelines. Data from 2000 to 2015 on demographics, clinical features, microbiology, surgical treatment and antimicrobial therapy were retrospectively analyzed. Cure was assessed after the end of treatment as the absence of any sign relevant to OAO. Factors associated with cure were evaluated by regression analysis.

Results: A total of 53 infections of OAO of the lower extremities (hip, femur, tibia) were evaluated. Patients were female (n=32, 60.4%), with a mean age (SD) 57(3) years, history of trauma (83%), comorbidities (26.4%). The most frequent GNB were: *E.coli* (n=15), *P.aeruginosa* (n=14), *Klebsiella* spp (n=8), *Enterobacter* spp (n=8) and *Acinetobacter* spp (n=5). *P.aeruginosa* predominated the XDR group than the XDR one (n=6/10 vs n=8/43, p=0.01). Antibiotics were given mostly in combinations (64%) for a median duration of 117 days (SD:31.5). Carbapenems were the most frequently used agents (54.7%), followed by colistin (18.8%) and fluoroquinolones (15%). Surgical treatment included debridement with implant retention (n=22), implant explantation (n=22), new osteosynthesis (n=3), others(n=6). Only failure of the surgical treatment for OAO was associated with lack of cure [OR 8.924 (CI95%: 3.006-26.495), p<0.001] at the end of treatment, for a 12-month follow-up period. Patients' age, gender, comorbidities, history of trauma and surgery, clinical presentation of OAO, type of antimicrobial treatment (use of fluoroquinolones, carbapenems or colistin as monotherapy or in combination) as well as type of surgical intervention (explantation vs implant retention) were not found to significantly influence the patients' outcome. Overall, cure was assessed in 31 patients (58.5%). Death occurred in 7 patients, all older than 60, with failure of surgical treatment (p=0.016). These patients presented with many comorbidities (57%) and without difference in treatment outcome between XDR and MDR infection (p=0.114).

Conclusion. Osteosynthesis-associated infections of the lower extremities caused by MDR/XDR GNB are a severe complication in orthopaedic surgery. The role of surgical treatment is independently associated with outcome regardless of the type of intervention (explantation or implant retention) and the type of antimicrobial treatment.

References

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[FP60] DOES THE BACH CLASSIFICATION OF LONG BONE OSTEOMYELITIS CORRELATE WITH PATIENT REPORTED OUTCOME MEASURES FOLLOWING SURGERY?

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Aim: Bone and joint infections are a serious complication of trauma, surgery and soft tissue infections. However, there are few data presenting patient reported outcome measures for osteomyelitis. A recently proposed method for classification of osteomyelitis, BACH, stratifies patients into 'uncomplicated' and 'complex', based on four key inter-disciplinary components: Bone involvement, Anti-microbial options, soft-tissue Coverage and Host status. We aim to correlate the classification severity with patient reported outcomes following osteomyelitis surgery.

Method: Seventy-one patients with long-bone osteomyelitis, confirmed using a validated composite protocol, were included. Patients received a single-stage procedure at a specialist bone infection unit. Euro-Qol EQ-5D-3L questionnaires and Visual Analogue Scores (VAS) (0-100) were collected prospectively at baseline, 14 days, 6 weeks, 4 months and 1 year post-operatively. The EQ-5D-3L index score, a composite measure of performance of daily activities, was calculated from the 5 domains of the EQ-5D-3L. BACH was applied retrospectively by two independent clinicians blinded to all patient outcomes.

Results: There was significant improvement in VAS (58.2 vs. 78.9, $p<0.01$) and EQ-5D-3L index (0.284 vs. 0.740, $p<0.01$) scores from baseline to 1 year. 'Uncomplicated' osteomyelitis was associated with significantly higher EQ-5D-3L and VAS at 1 year follow-up when compared to 'complex' osteomyelitis (EQ-5D-3L: 0.900 vs. 0.685, $p<0.01$; VAS: 87.1 vs. 73.6, $p<0.05$). Patients with cavitary bone involvement (BACH type B1) reported higher outcome scores at all time points when compared to segmental involvement (B2) or infection involving the joint (B3). Good antimicrobial options gave higher outcome scores compared to patients with multi-drug resistant isolates (A2). Patients who had received microvascular tissue transfer (C2) initially reported lower outcome measures but returned to a similar level to patients who had their wounds closed directly (C1) from 6 weeks. Patients with severe co-morbidity (H2) reported lower outcome scores at all time points compared to those who were fit or with well controlled disease (H1).

Conclusions: Complex cases of osteomyelitis as defined by BACH classification, had poorer patient reported outcomes compared to uncomplicated cases. This was despite being managed in a centre that specialises in bone and joint infection. This study demonstrates that BACH is helpful for assessing case complexity and prognosis in osteomyelitis.

[FP61] THREE YEARS USE OF AN ANTIBIOTIC-LOADED BONE SUBSTITUTE FOR ORTHOPAEDIC INFECTIONS

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Aim: To retrospectively investigate the clinical outcome after surgical, single-stage treatment of orthopaedic infections using antibiotics delivered locally by a calcium sulphate/hydroxyapatite biocomposite[1].

Method: In order to identify the patients, we retrospectively searched several patient associated hospital based databases using free text search with the term "Cerament" between November 2015 and November 2018.

58 cases with confirmed osteomyelitis and in which the bone substitute loaded with Gentamicin and/or Vancomycin had been used were identified and further evaluated.

Results: Mean age was 58.9 years (range: 25-89). 46 (79.3 %) patients had at least 12 months follow up. The remaining 12 patients had a mean follow up time of 10.0 months (range 7-11). Infection was eradicated in 54 patients (93.1 %). In one the patients with recurrent infection repeated surgery with addition of bone substitute loaded with fosfomycin eventually eradicated the infection.

One patient died of causes not related to the infection nor the treatment. Five patients presented transient white wound drainage but no signs of infection. No other side effects were identified.

Conclusions: Local administration of antibiotics and dead space management using a calcium sulphate/hydroxyapatite biocomposite[1] in combination with single-stage surgical debridement, stabilisation and postoperative culture-specific systemic antibiotics resulted in a high amount of eradicated infections and in line with other authors[2].

References:

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[FP62] POLYMICROBIAL INFECTIONS AND MICROBIAL PATTERNS IN SEPTIC NON-UNIONS – A DESCRIPTIVE ANALYSIS OF 42 CASES

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Introduction: Polymicrobial infections are expected to complicate the treatment of bone and joint infections. Septic nonunions often occur after initial open fractures, which prophylactically receive broad-spectrum antibiotics. However, no data that describes frequencies of polymicrobial infections and pathogens evident in course of the treatment of septic nonunions is published. Therefore, this study aims at investigating the frequency and pathogen types in polymicrobial infections.

Methods: Surgically treated Patients with long bone septic nonunion admitted between January 2010 and March 2018 were included in the study. Following parameters were examined: age, gender, American Society of Anesthesiologists (ASA) score, body mass index (BMI), and anatomical location of the infected nonunion. Microbiological culture data, polymerase-chain-reaction results of tissue samples, sonication, and joint fluid of the initial and follow-up revision surgeries were assessed. No exclusion criteria were determined.

Results: The study encompassed 42 patients with a mean age of 53.9 ± 17.7 years (range, 23 – 93). Sixteen (38.1%) patients were female. In 46.3% of the patients open fractures led to septic nonunion. Twenty-six nonunions occurred at the tibia or fibula, 11 were localized at the femur, 2 at the humerus and 3 at the forearm. Only 2 patients were assessed as ASA type 1, while 26 were ASA type 2 and 12 patients ASA type 3. Mean number of performed surgeries was 6 ± 0.67 (range 2 – 21). In 6 patients (14.3%) polymicrobial infection were evident. A change of evidenced pathogens in course of the treatment occurred in 21 patients (50%). In 16 patients (38.1%) previously detected bacteria could be evidenced by microbial testing after further revision surgery. *Staphylococcus aureus* was most often evident (n=34, 30.6%), followed by *Enterococcus* species (n=25, 22.5%) and *Staphylococcus epidermidis* (n=18, 16.2%). Five *Staphylococcus aureus* were resistant to methicillin (MRSA). In patients without polymicrobial infection or further germ detection in course of the treatment 86.4% of the infections were due to Staphylococcus species. Patients with change of detected pathogens and polymicrobial infections suffered from more enterococci infections. Infections due to streptococci and gram-negative bacteria could only be evidenced in patients with polymicrobial infection and pathogen change in course of the treatment.

Conclusion: The observed difference of microbiological patterns in septic nonunion may help to facilitate adjuvant local and systemic antibiotic treatment in septic nonunion patients. Reasons for the observed difference of microbiological patterns and its influence on patient outcome have still to be elucidated.

[FP63] IMPLEMENTING OVIVA: 18 MONTH EXPERIENCE IN A SPECIALIST ORTHOPAEDIC HOSPITAL

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Aim: The OVIVA trial was reported at ECCMID in April 2017, demonstrating that oral antibiotic therapy is non-inferior to IV antibiotic therapy when used in the first 6 weeks of treatment for complex bone and joint infections[1]. At the RNOH we subsequently implemented these findings into clinical practice.

The aim of this study is to describe our experience of implementing OVIVA in a specialist orthopaedic hospital.

Method: We gathered data prospectively for 16 months after the change in practice (May 2017 to September 2018), and retrospectively on all patients receiving treatment for similar time period before the change in practice (December 2016 to April 2017).

Data collected included demographics, treatment and factors influencing treatment decisions.

All reported adverse events were identified from electronic patient notes and categorised according to type, severity and the need to adjust antibiotic therapy. A cost analysis including the costs of drugs, administration and monitoring was performed. Clinical outcomes were assessed at 1 year.

Results: In the pre- implementation group there were a total of 143 patients, of which 77 were male (53.8%). The average age was 60.3 years (15 -89). 43 of 143 (30.1%) patients reported some form of adverse drug reaction. Definite failure of infection treatment at 1 year was 16.1%.

In the post-implementation group there were a total of 170 patients, of which 95 were male (55.9%). The average age was 58.5 years (11 -85). 118 (69.4%) received PO treatment and 52 (30.6%) received IV. Reasons for intravenous treatment included multi-drug resistance, concern regarding adherence, allergies, malabsorption and other. Overall, 65 of 170 (38.2%) patients reported some form of adverse drug reaction, however they were more common in the PO group (41.5%) compared to the IV group (30.8%). Definite failure of infection treatment at 1 year was 18.8% overall, however this was more common in the IV group (30.8%) compared with the oral group (13.6%).

Conclusions:

1. The majority of patients were suitable for oral antibiotic therapy
2. The most common reason for IVs in the post-implementation group was multi-drug resistance
3. Oral antibiotic therapy was less well tolerated compared to IVs.
4. In the post-implementation group the outcomes were worse in the IV group.

References

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Acknowledgements
No funding was received for the production of this work

[FP64] TREATMENT OF PROSTHETIC-JOINT INFECTIONS: THE ROLE OF THE SURGEON

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Aim: There is a constant increase of total joint arthroplasties to improve the quality of life of an aging population. Prosthetic-joint infections are rare, with an incidence of 1-2%, but they represent serious complications in terms of morbidity and mortality. Different therapeutic options exist, but the role of the surgeon's experience has never been investigated. The aim of this retrospective study is to assess the infection eradication success rate depending on the involvement of a septic surgeon.

Method: Patients having a prosthetic-joint infection at Lausanne University Hospital (Switzerland) between 2006 and 2018 were included. The success rate depending on type of surgeon (septic vs non-septic) and type of surgical procedure was analyzed.

Results: 444 patients (61% hips, 37% knees) were identified with a median age of 70 years. The overall success rate was 83% for septic surgeons compared to 61% for non-septic surgeons ($p < 0.05$). The effect of the surgeon was predominant in debridement with retention of the prosthesis where the experience could improve the success rate from 43% (non-septic) to 75% (septic) ($p < 0.05$).

Conclusions: The involvement of a septic surgeon is associated with a significantly higher success rate, suggesting surgical experience is an important factor in treating prosthetic-joint infections.

[FP65] THE FINANCIAL BURDEN OF TREATING OSTEOMYELITIS IN THE UK

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Aims: Infective complications following implant related orthopaedic surgery or fracture related infection are associated with high costs and increased length of stay (LOS). However, the economic burden of disease before, during and after definitive osteomyelitis surgery is not well quantified. The Hospital Episode Statistics (HES) database captures all admissions, outpatient appointments and emergency department attendances at NHS hospitals in England. We identified all patients with a diagnostic code of osteomyelitis and quantified the tariff costs associated with the surgical treatment of osteomyelitis. We also collected all recorded healthcare events related to osteomyelitis for two years preceding the initial osteomyelitis treatment procedure, as well as for two years after the procedure. We compared average osteomyelitis treatment costs in England against a dedicated specialist multidisciplinary bone infection centre.

Methods: We interrogated the HES database for all patients given a diagnostic code of osteomyelitis (M86) between April 2013 and January 2017. We excluded all cases with a diagnosis of osteomyelitis and an index procedure of an amputation for diabetes or arterial disease. Of the remaining 104,622 patients there were 24,408 cases who had their index procedure for osteomyelitis in this time period. Of these we compared a subset of 575 cases treated in a specialist bone infection centre.

Results: Index procedure costs were lower in specialist centres compared to national average (£4100.09 vs. 4835.59) equating to a potential saving of £4.67 million per year if all cases were treated in similar specialist centres. Average LOS for the index procedure was lower in the specialist centre (12.4 days) compared to the national average (17.3 days). Assuming a bed cost of £500 per day, treating all patients in similar specialist centres could save £15.95 million per year. The post procedure costs were lower for specialist centre patients compared to national average, equating to a potential saving of £7.42 million per year. The average post procedural LOS in the national cohort was 2.44 days longer than the specialist centre, equating to an additional 15,508 bed days per year.

Conclusions: Although tariff costs do not reflect true costs this study demonstrates that osteomyelitis is a significant economic burden to the English health service. Treating infection in dedicated specialist multidisciplinary centres requires a lot of resources and costs a lot of money. However, treating infection outside this environment seems to cost more and results in longer inpatient stays and higher associated costs.

[FP66] RISK ASSESSMENT OF RESISTANCE DEVELOPMENT BY ANTIBIOTIC LOADED BONE CEMENT - IS IT A CLINICAL CONCERN?

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Aim: There is an ongoing controversy whether the observed benefit of infection risk reduction by ALBC outweighs the risk of possible antimicrobial resistance development.

Methods: The scientific & clinical literature in PubMed, Medline and Embase has been systematically reviewed with the keywords “antibiotic resistance”, “antibiotic loaded bone cement”, “local antibiotics”, “bacterial colonization” and “joint infection”. In total 28 relevant publications were found with the majority of them reporting laboratory results. Only 7 papers focused on clinical septic situations & patient data

Results:

- Although rare as consequence of the initially high drug concentrations in situ, experimental and clinical studies demonstrated survival of resistant bacteria on ALBC with subsequent bacterial recolonisation of the biomaterial. This was most notable for coagulase-negative staphylococci (CoNS).
- Bacterial survival in presence of ALBC represents a selection process of already pre-existing high level resistant mutants and not antibiotic resistance induction (Fig 1).
- The use of antibiotic combinations with gentamicin in bone cement is associated with a markably lower risk of survival of bacteria resistant to the aminoglycoside (Fig. 2). This is particularly important in patients at high infection risks and in septic revision cases.
- There is no clinical evidence for a widespread increase of clinically important gentamicin resistancies in the orthopaedic ward because of routine use of ALBC.
- On an individual basis, the benefit of a lower infection probability with combined systemic & local antibiotic application should outweigh the risk of selecting a priori resistant bacteria. Each prevented infection case means that a complex and extended antibiotic therapy with risk of resistance development over time has been avoided for a patient.
- In those cases where a priori resistant bacteria have survived the prophylactic exposure to antibiotics in bone cement, they remain in vast majority still susceptible to the clinically important antibiotics used for treatment of prosthetic joint infections.

Conclusions: The benefit of a lower infection probability with ALBC should outweigh the risk of selecting resistant bacteria against the particular antibiotic used in bone cement. A trend towards broad resistance development which may complicate treatment of infection cases was not found.

Fig. 1:

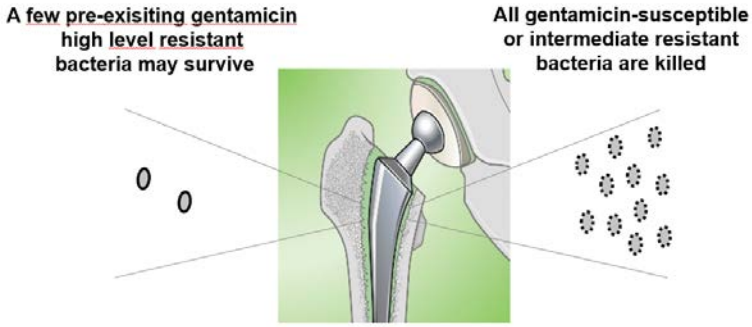
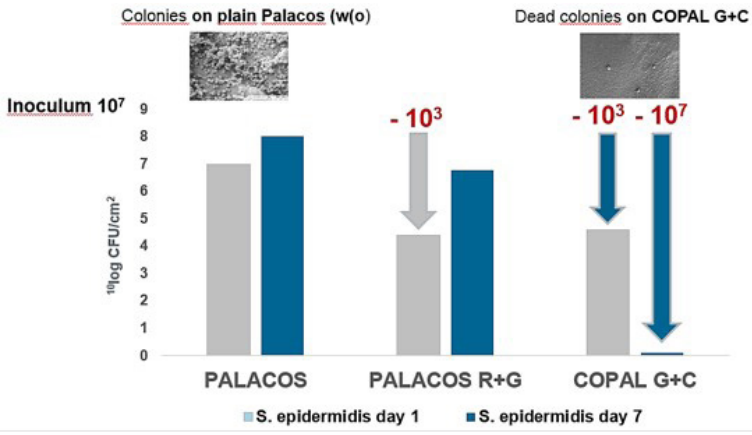

A few pre-exisiting gentamicin high level resistant bacteria may survive
All gentamicin-susceptible or intermediate resistant bacteria are killed

Fig. 2:


Colonies on plain Palacos (w/o)
Dead colonies on COPAL G+C
Inoculum 10⁷
- 10³
- 10³ - 10⁷
log CFU/cm²
PALACOS
PALACOS R+G
COPAL G+C
S. epidermidis day 1
S. epidermidis day 7

[FP67] THE PROSTHESIS PROTECT PROJECT: IMPROVING PATIENT CARE BY IMPLEMENTING A REGIONAL PROSPECTIVE QUALITY REGISTRY FOR PJI

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Aims: Current antibiotic treatment strategies for prosthetic joint infection (PJI) are based mostly on observational retrospective studies. High-quality data from prospective cohorts using identical treatment strategies may improve current clinical practice. We developed a regional network of collaborating hospitals and established a uniform treatment protocol. Data from all patients diagnosed with a PJI are prospectively registered in a an online database. With this quality registry we aim to study the outcome of antibiotic and surgical strategies while adhering to a pre-established treatment protocol.

Methods: A working group of orthopaedic surgeons, infectious disease specialists and microbiologists was established. The working group reached consensus on definition of PJI and a uniform treatment protocol, based on current guidelines and expert-based clinical experience. A website was built to communicate information to colleagues and patients (www.protheseinfectie.nl). In each participating hospital weekly multidisciplinary meetings were started to discuss all PJI cases. All patients are included in an online quality registry and followed for at least two years. We aim to enroll >600 patients with a knee or hip PJI. Research will focus on the duration of antibiotic treatment, antibiotic suppressive therapy and comparison of different oral antibiotic treatment strategies in relation to successful treatment outcomes.

Results: Currently, four regional hospitals are included in the partnership. Multidisciplinary meetings have lowered the threshold to discuss patients, and the adherence to the PJI treatment protocol has improved steadily. Complicated cases are discussed between colleagues from collaborating centers. The collaboration has been perceived as very successful by the participating hospitals. Since 2015, over 300 patients have been included, of whom 52% were male. In 26%, PJI occurred after revision surgery. Staphylococcus aureus was involved in 25% of cases, coagulase-negative Staphylococci in 23%, Streptococci in 13% and Gram-negative micro-organisms in 15%.

Conclusions: In this project, collaboration between different medical specialties through multidisciplinary meetings was the key to the improvement of patient care The regional collaborative project led to the implementation of a uniform treatment protocol for PJI. With this prospective project we aim to improve patient care by providing evidence for optimal antibiotic and surgical strategies for PJI. Ideally, countries should have hospital networks and a uniform method of data collection to make it easy to share data for scientific research.

[FP68] HIGHLY VARIABLE EFFECT OF SONICATION AS A METHOD TO DISLODGE BIOFILM EMBEDDED STAPHYLOCOCCUS EPIDERMIDIS, IN VITRO

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Aim: In cases of prosthetic joint infections the sensitivity of bacterial cultivation of tissue samples is not 100%. In fact, the reported sensitivity based on standardized criteria and rigorous tissue sampling technique probably differs between 86 to 89%. It has been claimed that sonication of explanted prostheses with subsequent culturing of sonication fluid can increase the sensitivity of the test compared to culturing of tissue samples. To what degree bacteria embedded in biofilm is dislodged during the sonication process has to our knowledge not been fully elucidated. We studied the effect of sonication as a method to dislodge biofilm embedded *Staphylococcus epidermidis* in vitro.

Method: 46 steel plates were colonized with biofilm forming *S. epidermidis* ATCC 35984 in TSB with 1% glucose aerobically at 37°C for 24 hours. Plates were cleansed for non-adherent bacteria before microscopy. Biofilm embedded bacteria were stained with LIVE/DEAD ™ BacLight ™ Bacterial Viability Kit for microscopy and visualized under vital conditions using EVOS™ FL Auto 2 Imaging System (epifluorescence) and an inverse confocal laser scanning microscope LSM510 (CLSM). All steel plates were subjected to epifluorescence microscopy before and after sonication. CLSM and SEM were used to confirm the presence of biofilm embedded bacteria after sonication. Pictures from epifluorescence microscopy were processed for image analysis with help of a macro application (Fiji) and the data was expressed as biofilm coverage rate (BCR). The sonication was performed using a BactoSonic® Bandolin sonicator and the applied effect in each glass test tube (40 kHz, 800W) was measured with a Bruel og Kjær 8103 hydrophone. The amount of bacteria in the sonication fluid was quantified by counting the number of colony forming units (CFU).

Three steel plates acted as negative controls.

Results: The BCR was highly variable on the plates after sonication. The biofilm was eradicated from the majority of the plates but a considerable number of plates still had biofilm attached to the surface in a highly variable manner. The amount of bacteria in the sonication fluid correlated poorly with BCR on corresponding plates.

Conclusions: Our conclusion is that the ability of sonication to dislodge biofilm embedded *S. epidermidis* in vitro is not as effective as current opinion might suggest. After sonication biofilm still adhere to a significant number of plates in a highly varying manner. This prompts the need to investigate the effect of sonication on biofilm embedded bacteria formed in vivo.

[FP69] RISK FACTORS FOR CUTIBACTERIUM ACNES SPINAL IMPLANT INFECTION: A CASE-CONTROL STUDY

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Aim: *Cutibacterium acnes* is a significant cause of late-onset spinal implant infection (SII). In addition, usual preoperative prophylactic measures may be insufficient to prevent *C. acnes* operating site colonisation and infection, as demonstrated for prosthetic shoulder surgery. However, little information is available regarding risk factors for SII due to this microorganism. The aims of this study were to determine the characteristics of and risk factors for *C. acnes* SII.

Method: we conducted a retrospective unmatched case-control study including all adult patients treated for mono and polymicrobial *C. acnes* SII during 2010-2015. Controls were randomly selected among patients diagnosed with SII due to other microorganisms during the same period.

Results: Fifty-nine patients with *C. acnes* SII were compared with 59 controls. There was no difference in sex distribution (39% vs 53% men). Patients with *C. acnes* SII were younger (median age 42 *vs*. 65, p< 0.001), thinner (median body mass index (BMI) 21 *vs*. 25 kg/m^2, p< 0.001), and presented a better health status (ASA score≤ 2, 83% *vs.* 65%, p= 0.015; and presence of immunosuppression, 3% *vs.* 27%, p= 0.002). Patients with *C. acnes* SII were more likely to experience delayed/late infections (i.e. diagnosed >3 months post-instrumentation, 66% *vs*. 22%, p< 0.001) and to be instrumented for scoliosis (83% *vs*. 27%, p< 0.001) with an extended osteosynthesis (median number of fused vertebrae 12 *vs.* 5, p< 0.001). However, 20 *C. acnes* SII (34%) developed early (≤3 months) after instrumentation. The clinical presentation was significantly more indolent in the *C. acnes* group (presence of fever, 27% *vs.* 61%, p= 0.001; wound inflammation 39% *vs*. 61%, p< 0.001 and median C-reactive protein level 38 *vs*. 146 mg/L).

Mixed *C. acnes* SII were diagnosed on 24 occasions (41%), 22 of which involving both *C. acnes* and staphylococcal strains.

In the multivariate logistic regression model, factors independently associated with the development of SII involving *C. acnes* were age less than 65 (adjusted odds ratio [aOR] 7.13, 95% CI [2.44–24.4], p= 0.001), BMI< 22kg/m^2 (aOR 3.71 [1.34–10.7], p= 0.012) and a number of fused vertebrae >10 (aOR 3.90 IC 95% [1.51–10.4], p= 0.005).

Conclusions: There were significant differences between SII involving *C. acnes* and those involving other microorganisms. We identified a specific profile of patients at increased risk of developing *C. acnes* SII. These findings could contribute to improve both the prevention and treatment of such infections.

[FP70] IS EXTENDED TROCHANTERIC OSTEOTOMY DURING TWO-STAGE REVISION OF THE HIP A SAFE PROCEDURE?

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Aim: Periprosthetic joint infections (PJI) are a severe complications after hip arthroplasty. The infections rate ranges from 0.7 to 1.3 depending on different reports. The aim of the present study is to evaluate the radiological and clinical outcome of patients that underwent two-stage revision for the treatment of periprosthetic joint infection of the hip when an extended trochanteric osteotomy (ETO) was necessary to remove the femoral stem.

Methods: We retrospectively analyzed data from 84 patients that underwent two-stage revision of the hip between January 2006 and December 2010 at our institution. In forty-nine patients (Group A, 58.3%), the femoral stem was removed without an ETO, while in the remaining thirty-five patients (Group B, 41.7%) an ETO was necessary. In each case a metallic cerclage was used to closure of the flap. The average age for patients in group A was 64.3 years, while the average age in patients in group B was 66.4 years. The mean follow-up was respectively 117 months in group A and 122 months in group B. Eight patients died before the last follow-up, and data from six patients were incomplete. Complications, radiological and clinical outcome were. Mann Whitney U Test and Chi Square Test were used respectively to analyze continues and categorical variables. Cumulative survival of the implants was calculated for reinfection and mechanical complications with Kaplan-Meyer curves.

Results: The mean follow-up was 118 months. The cumulative incidence of reinfection was 4.7% at 1 years and 10.7 at last follow-up. No statistically significant (p-value > 0.05) differences were observed in the two groups neither at 1 year nor at last follow up. The cumulative incidence of mechanical complication was 3.6% at 1 year and 8.3% at last follow-up. No statistically significant differences (p-value > 0.05) were observed in the two groups neither at 1 year nor at last follow up. All the patients had the healing of the ETO at six months (mean 11.4 weeks). The mean Harris Hip Score was 77.5. No statistically significant (p-value > 0.05) differences were observed in the two groups.

Discussion: The results obtained in this retrospective study demonstrates that there is no difference in terms of reinfection-rate, mechanical complications and clinical outcome in patients that underwent two-stage revision with or without an ETO. In presence of a well-fixed femoral stem, performing an ETO could be helpful to expose the femoral canal facilitating the femoral stem's removal avoiding intra-operative femoral fracture.

[FP71] LOCAL BONE ANTIBIOTIC DELIVERY USING POROUS ALUMINA CERAMIC: CLINICAL AND PHARMACOLOGICAL EXPERIENCE

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Aim: Local concentration of antibiotic at the site of infection is a major parameter for its efficiency. However, bone diffusion is poor leading either to their non-use (ex: gentamicin) or the use of high concentration (ex: vancomycin). Local administration could optimize their local concentration combined with lower side effects. We report the clinical experience and pharmacological results of an antibiotic loaded porous alumina used to replace infected bone in 4 patients.

Method: Two patients had a destroyed sternum following mediastinitis; one presented a femoral chronic osteomyelitis due to MRSA and one had an infected ankle arthroplasty. The ceramic was loaded with gentamicin in three cases and vancomycin for the ankle infection. Local dosages thanks to Redon's drain and blood samples were performed. Loading was done to protect the device while implanted in an infected area and was combined with conventional antibiotic therapy.

Results: In comparison to pharmacological parameters: C_{max}/MIC>8 for gentamicin or AUC/MIC>400 for vancomycin, local concentrations were dramatically higher than the one needed (table). Vancomycin concentration was still high after H48. Meanwhile, blood samples didn't find the presence of gentamicin during the 48 hours following implantation. After more than one year of follow-up for all the patients, there is no relapse of infection or signs of device infection, whereas all samples perform during implantations grew with bacteria, meaning that loaded antibiotic played a major role avoiding device colonization in combination with surgical debridement and cleaning.

Conclusions: This mode of administration allows an optimization of the antibiotic delivery, maximizing local concentrations while reducing systemic toxicity. In addition, ceramic mechanical characteristics allow bone replacement (strength >3 times the one of the cancellous bone and osseointegration) and thus enables one-stage surgery instead of two-stage like for the patient with chronic osteomyelitis thanks to a good primary stability.

Area	Antibiotic	Loaded dose (mg)	Local concentration H1 (mg/L)	Comparison to the needed concentration	Local concentration H24 (mg/L)	Comparison to the needed concentration	Detection of antibiotic in blood
Sternum	Gentamicin	320	1500	>175 folds	395	>50 folds	No
Sternum	Gentamicin	160	2100	>260 folds	37	>5 folds	No
Femur	Gentamicin	160	184	>50 folds	13	>4 folds	No
Ankle	Vancomycin	250	NA	NA	548	6 folds	NA

[FP72] KNEE ARTHRODESIS FOR THE SALVAGE OF INFECTED TOTAL KNEE ARTHROPLASTY PREDICTING FAILURE AND THE NEED FOR AMPUTATION

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Aim: Knee arthrodesis (KA) and above knee amputation (AKA) have been used for salvage of failed total knee arthroplasty (TKA) in the setting of periprosthetic joint infection (PJI). The factors that lead to a failed fusion and progression to AKA are not well understood. The purpose of our study was to determine factors associated with failure of a staged fusion for PJI and predictive of progression to AKA.

Method: We retrospectively reviewed a single-surgeon series of failed TKA for PJI treated with two-stage KA between 2000 and 2016 with minimum 2-year follow-up. Patient demographics, comorbidities, surgical history, tissue compromise, and radiographic data were recorded. Outcomes were additional surgery, delayed union, Visual Analog Pain scale (VAS) and Western Ontario and McMaster Activity score (WOMAC). No power analysis was performed for this retrospective study. Medians are reported as data were not normally distributed.

Results: Fifty-one knees underwent fusion with median follow-up of 7 years (interquartile range (IQR) of 2-18 years). Median age was 71 years old (IQR 47 – 98), with a M:F ratio of 23:28. Median BMI was 34.3 kg/m2 (IQR 17.9-61). Infection was eradicated in 47 knees (92.2%); 24 knees (47.0%) required no additional surgery. 41 patients (83.6%) remained ambulatory after knee fusion, with 21% of these patients (10 total) requiring no ambulatory assistive device. Median VAS following arthrodesis was 4.6 (range 0-10). Median WOMAC was 36.2 (range 9-86). Three TKAs (5.9%) underwent AKA for overwhelming infection. Predictors of AKA were chronic kidney disease (OR 4.0, 95% CI 0.6-26.8), peripheral vascular disease (OR 3.5, 95% CI 0.3-44.7), AORI III bone loss (OR 2.6, 95% CI 0.4-35.2), instability (OR 2.2, 95% CI 0.2-15.9), and immunosuppression (OR 1.1, 95% CI 0.1-7.8). Tobacco use (OR 8.6, 95%CI 2.4-31.4), BMI>25 (OR 3.8, 95% CI 0.43-32.5) and instability prior to arthrodesis (OR 2.51, 95% CI 0.77-8.21) were associated with non-union. All other risk factors (gender, diabetes mellitus, chronic kidney disease, peripheral vascular disease, massive bone stock loss, and immunosuppression) were not associated with arthrodesis failure.

Conclusions: Staged KA for PJI in severely compromised hosts provides a functional limb free of infection and rarely results in conversion to AKA. Given our small sample size, ability to establish statistical significance of predictive factors for AKA after PJI was limited, but CKD, peripheral vascular disease, AORI III bone loss, instability, and immunosuppression trended towards significance as predictors of failure of KA after PJI predisposing to AKA.

[FP73] IS COMBINED ANTIBIOTIC THERAPY IN SPACERS SUPERIOR TO MONOTHERAPY WITH AN AMINOGLYCOSIDE? – AN ANALYSIS OF POSITIVE CULTURES DURING THE SECOND STAGE

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Aim: Antibiotic loaded spacers are often used during a two-stage exchange for periprosthetic joint infections (PJI) both for its mechanical properties and as a means for local antibiotic delivery. The main goal of this study is to compare the rate of positive cultures during reimplantation with the use of different antibiotic loaded spacers: aminoglycoside only vs. combined glycopeptide/aminoglycoside vs. combined glycopeptide/carbapenem/aminoglycoside.

Method: We retrospectively evaluated every two-stage exchange procedures for infected hip/knee arthroplasty between 2012-2018. Microbiological findings in the first and second stage were registered as well as the type of spacer and antibiotic(s) used. Cases in whom no cultures were obtained during reimplantation and cases without sufficient data on antibiotic(s) used in cement spacers were excluded.

Results: Fifty-four cases were included (20THA and 34TKA), with an overall rate of positive cultures during reimplantation of 18.5% (10/54). The rate of positive cultures was statistically significant higher among spacers with monotherapy with aminoglycoside compared to spacers with combined antibiotic therapy- 35.7% (5/14) vs. 12.5% (5/40) respectively($p<0.05$). Comparing those with combined glycopeptide/aminoglycoside (2/19) with triple glycopeptide/carbapenem/aminoglycoside therapy (3/21) there was no significant difference. Microorganisms present during the second stage were mostly staphylococci (coagulase-negative in four cases, S.aureus in three), Corynebacterium striatum, Enterococcus faecalis, C.albicans in one case each. In most cases (8/10), the isolated microorganism was the same as the first stage and was resistant to the antibiotic(s) used in the spacer in seven cases. Failure rate with the need for subsequent surgery was significantly higher at 60% (6/10) in cases with positive cultures at reimplantation compared to 4.5% (2/44) for those with negative cultures during reimplantation($p=0.0005$).

Conclusions: It has recently been suggested that adding a glycopeptide to the spacer may be advantageous when compared to spacers with aminoglycoside monotherapy, as it will produce significantly lower rates of positive cultures during reimplantation which have been shown to increase the risk of subsequent failure as is the case in our study. Local unavailability of obtaining powder aminoglycosides has driven us to manually add high doses of vancomycin and meropenem to commercially available low-dose gentamicin cement in many of our spacers and they seem to to perform just as well as commercially available vancomycin/gentamicin combination. Although many other variables not considered in this study may influence the rate of positive cultures during the second stage (quality of initial debridement, systemic antibiotic therapy, etc.), we believe these results portrait a sufficiently accurate picture of clinical results with the use of different spacers.

[FP74] OUTCOME OF TWO STAGE SURGERY: "HONE YOUR WORK CAREFULLY; SPARE NO EFFORT".

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Aim: We wonder what the results of two stage procedures were in terms of morbidity (amputation, dead) and infection recurrence. We also seek to identify risk factors for failure and see if the results of a second two stage surgery were not even worse.

Material and Methods: We retrospectively reviewed 140 prosthetic joint infection (PJI) treated with a two stage procedure. Patient data has been reviewed to determine which factors would be predictive for failure.

Results: From the 140 two stages, 98 patients were infection free at two years. Four died in the following year. 38 patients presented a recurrence within the two years: 2 died and 1 was amputated within one year. Nine were further treated with a second two stage procedure and 26 with debridement and implant retention procedures and antibiotics (DAIR). Six of these last received long terms suppressive antibiotics. In total 27 from the 38 were again diseases free at two years follow up.

The dead and amputation rates are 4,3% and 0,8 % respectively. The rate of success after the first two stage was 80% and after a second two stage procedure 78%. The final rate of PJI cured is 89,3%.

The only difference observed between success and failure after a first two stage procedure was related to microbiology. Polymicrobial infection was 28.6% of the PJI which will fail and only 14,1% in those whose treatment will succeed ($p<0.05$). Looking to the patients that underwent a second two stage surgery, recurrence involved monomicrobial pattern with a microorganism that has developed a resistance to quinolones.

Conclusion: Mortality and amputation in PJI management should be mentioned to patients as significant potential complications. Infection control within a two stage procedure is not as high as reported, unless the final result is considered after secondary procedures. A second two stage procedure was not related with a worse outcome.

Our data confirms the poorer outcome of polymicrobial infection. Recurrence in those patients involves monomicrobial infections with resistant microorganisms. Nevertheless, a second two stage procedure appears acceptable when a DAIR procedure and suppressive antibiotherapy is difficult or impossible due to the microorganism resistance profile.

[FP75] ANTIBIOTIC-LOADED HYDROGEL OUTPERFORMS CLINICAL GOLD STANDARD TREATMENT IN A LARGE ANIMAL MODEL OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS IMPLANT ASSOCIATED OSTEOMYELITIS

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Aim: Implant-associated osteomyelitis is a devastating complication with poor outcomes following treatment, especially when caused by antibiotic-resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA)[1]. A large animal model of a two-stage revision to treat MRSA implant-associated osteomyelitis has been developed to assess novel treatments[2]. A bioresorbable, thermo-responsive hyaluronan hydrogel (THH) loaded with antibiotics has been developed and our aim was to investigate it´s *in vivo* efficacy as a local antibiotic carrier compared to the current standard of care i.e. antibiotic-loaded polymethylmethacrylate (PMMA) bone cement.

Method: 12 female, 2 to 4 year old, Swiss Alpine Sheep were inoculated with MRSA at the time of intramedullary nail insertion in the tibia to develop chronic osteomyelitis. After 8 weeks sheep received a 2-stage revision protocol, with local and systemic antibiotics. Group 1 received the gold standard clinical treatment[3]: systemic vancomycin (2 weeks) followed by rifampicin plus trimethoprim/sulfamethoxazole (4 weeks), and local gentamicin/vancomycin via PMMA. Group 2 received local gentamicin/vancomycin delivered via THH at both revision surgeries and identical systemic therapy to group 1. Sheep were euthanized 2 weeks following completion of antibiotic therapy. At euthanasia, soft tissue, bone, and sonicate fluid from the hardware was collected for quantitative bacteriology.

Results: Sheep tolerated the surgeries and both local and systemic antibiotics well. Gold standard of care successfully treated 3/6 sheep with a total of 10/30 culture-positive samples. All 6 sheep receiving antibiotic-loaded THH were successfully treated with 0/30 culture-positive samples, p=0.0008 gold-standard vs. hydrogel (Fisher`s Exact).

Conclusions: The clinical gold standard treatment was successful in 50% of sheep, consistent with outcomes reported in the literature treating MRSA infection[1]. The antibiotic-loaded THH clearly outperformed the gold standard in this model. Superior efficacy of the THH is likely due to 1) the ability to administer local antibiotics at the both revision surgies due to the bioresorbable nature of the hydrogel, and 2) complete antibiotic release compared to bone cement, which is known to retain antibiotics[4]. Our results highlight the potential of local delivered, biodegradable systems for antibiotics for eradicating implant-related infection caused by antibiotic-resistant pathogens.

References:

[1]Parry 2014
[2]Moriarty 2017
[3]Pro Implant Foundation Guidelines
[4]Nelson 1994

Acknowledgement: Funding provided by AO Trauma.

[FP76] BONE CEMENT WITH MICROENCAPSULATED RIFAMPICIN: A NEW STRATEGY AGAINST PERIPROSTHETIC JOINT INFECTION

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Aim: The demonstration of the in vivo bactericidal efficacy of a new bone cement with rifampicin contained in microcapsules and its intra-articular release profile.

Method: Fifteen New Zealand White rabbits were employed to reproduce periprosthetic infection by intra-articular inoculation of 10^5 CFU/mL of *Staphylococcus aureus* ATCCÒ 29213 using as a target implant a 3D printed stainless steel tibial insert. 7 days after inoculation, the first stage of the two stage exchange was carried out and at this time the animals were divided into two study groups: group C (7 rabbits) that received a spacer with gentamicin and group R (8 rabbits) that received a spacer with gentamicin and rifampicin microcapsules. Response to infection was monitored by clinical (weight and temperature), hematological (leukocyte, lymphocyte and platelet counts) and biochemical (erythrocyte sedimentation rate) analyses at the time of inoculation, at the first stage of exchange, 4 days after first stage and weekly until the fourth week when animals were euthanized. Microbiological counts were performed at the first stage of exchange and at the end of the study.

Results: 14/15 animals (93.3%) developed a PJI 1 week after the inoculation. A statistically significant elevation of the leukocyte and platelet count and a decrease in the percentage of lymphocytes ($p=0.0001$) was found and positive microbiological cultures. Four weeks after the placement of the spacer, no bacterial growth was found in the soft tissue or bone samples of the group with rifampicin microcapsules (group R), being these differences statistically significant with $p=0.01$ and 0.03 respectively. The rifampicin intra-articular release kinetics showed concentrations above the staphylococcal MIC at all time points.

Conclusions: The bone cement with microencapsulated rifampicin is effective in the in vivo treatment of prosthetic joint infection due to biofilm-forming S. aureus.

[FP77] EXTENSIVE DEBRIDEMENT IS FUNDAMENTAL FOR THE SUCCESS OF AN ABSORBABLE GENTAMICIN LOADED BIO-COMPOSITE

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Aim: To study the antimicrobial effect of a gentamicin loaded bio-composite bone void filler in relation to a limited or extensive debridement of osteomyelitis lesions, respectively.

Methods: Nine pigs were inoculated into the right proximal tibial bone with a high virulent gentamicin sensitive strain of *Staphylococcus aureus* (10^4 CFU). Seven days after inoculation, Group A pigs (n=3) were exposed to a limited debridement of the bone lesion, whereas Group B pigs (n=3) were exposed to an extensive debridement. The bone defects of Groups A and B were filled with (2-5 ml) of an absorbable gentamicin (175 mg/10 mL) loaded bio-composite.[1] The animals of Group A and B were euthanized 12 days after revision surgery. Group C animals did not undergo revision surgery and were euthanized seven (n=1) or nineteen (n=2) days post inoculation in order to follow the development of the untreated infection. None of the animals were treated with systemic antimicrobials. All bones were exposed to a post mortem CT scan and rigours pathological examinations. The surrounding bone tissue and the bio-composite were sampled for microbiology.

Results: All animals developed a substantial purulent bone infection in the inoculated leg prior to revision surgery. In the cases of limited debridement, the bone lesions surrounding the bio-composite bone void filler had clearly expanded since revision surgery, and contained extensive amounts of pus, necrotic bone tissue and oedematous fibrotic tissue. In the cases of extensive debridement, the bio-composite bone void filler was surrounded by only a few mm of fibrosis and sclerotic bone tissue *i.e.* the bone lesions were not expanding. However, in one pig the bio-composite bone void filler was communicating with a small purulent osteolytic lesion without a sclerotic border indicating appearance after revision surgery. In all pigs, *S. aureus* bacteria were post mortem cultured from the adjacent bone tissue and the bio-composite surface.

Conclusions: The gentamicin concentrations within the bio-composite could not eradicate the residual infection after debridement. However, extensive debridement and filling of the bone void with gentamicin loaded bio-composite contained the lesion formed by revision surgery, which are important complementing roles as adjuvant to systemic antimicrobial therapy and the immune system in eradication of the infection. The present study emphasizes that extensive debridement is fundamental for successful treatment of bone infections and that antimicrobial loaded bone void fillers or bone substitutes should not be used as an alternative to extensive debridement.

1(CeramentTM½G, BONESUPPORT, Lund Sweden)

[FP78] HIGH-ENERGY FOCUSED EXTRACORPOREAL SHOCKWAVE THERAPY IN ADDITION TO CONVENTIONAL TREATMENT: RESULTS FROM AN IN VIVO RABBIT MODEL OF FRACTURE RELATED INFECTION

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Aim: Focused high energy extracorporeal shockwave therapy (fhESWT) is used to support fracture healing in non-union cases and has been shown to have antibacterial effects. We trialed fhESWT as an adjunct to conventional treatment in a clinically relevant rabbit model of fracture related infection.

Method: A complete humeral osteotomy was performed in 31 rabbits and fixed with a 7-hole-LCP. A fracture-related infection (FRI) was established with *Staphylococcus aureus*. After two weeks, a revision surgery was performed with debridement, irrigation and implant retention. Rabbits then received: no further treatment (controls); shockwaves (at day 2 and 6 after revision, 4'000 Impulses each time with 23kV); systemic antibiotics (rifampin and nafcillin) over one week in weight adjusted dosages; or the combination of antibiotics and shockwaves. Treatments were applied over one week. Blood cultures were taken before and after shockwave sessions. After an additional week without treatment, rabbits were euthanized, and quantitative bacteriology was performed on implants and tissues to determine infection burden. Indicator organs (brain, heart, liver, lungs, kidneys and spleen) were cultured to assess possible bacteraemia due to fhESWT.

Results: All rabbits were infected at revision surgery as determined by bacteriological culture of debrided materials. fhESWT in combination with antibiotic treatment lowered the bacterial burden at euthanasia hundredfold compared to antibiotic treatment alone in all samples (p=0.38). This effect was most prevalent for the implant sample (p=0.08). No significant effect was seen for fhESWT alone compared to untreated controls. No signs of bacteraemia occurred.

Conclusions: The additon of systemic antibiotics had the biggest effect on reduction of bacteria. Although further lowering the bacterial burden in our model the effect of fhESWT as an adjunct was not big enough to be statistically secured in this *in vivo* rabbit model. In certain difficult-to-treat infections the addition of fhESWT might be beneficial. The method appears to be safe in this model of acute FRI as no signs of bacteremia occurred despite the high energy and impulse number. Further investigations are needed to identify the correct indication.

[FP79] ANTIMICROBIAL SILVER-MODIFICATION FOR LOCKING PLATES SHOWS UNEVENTFUL FRACTURE HEALING AND GOOD BIOCOMPATIBILITY – RESULTS OF AN EXPERIMENTAL STUDY IN RABBITS

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Aim: Silver is known for its excellent antimicrobial activity, including activity against multiresistant strains. The aim of the current study was to analyze the biocompatibility and potential influence on the fracture healing process a silver-coating technology for locking plates compared to silver-free locking plates in a rabbit model.

Methods: The implants used in this study were 7-hole titanium locking plates, and plasma electrolytic oxidation (PEO) silver coated equivalents. A total of 24 rabbits were used in this study (12 coated, 12 non-coated). An osteotomy of the midshaft of the humerus was created with an oscillating saw and the humerus stabilized with the 7 hole locking plates with a total of 6 screws. X-rays were taken on day 0, week 2, 4, 6, 8, and 10 for continuous radiographical evaluation of the fracture healing. All animals were euthanized after 10 weeks and further assessment was performed using X-rays, micro-CT, non-destructive four-point bending biomechanical testing and histology. Furthermore, silver concentration was measured in the kidney, liver, spleen and brain.

Results: X-rays showed normal undisturbed healing of the osteotomy in all animals without any differences between the two groups over the entire X-ray analysis over 10 weeks (Figure 1). Callus formation was observed up to week 4 to 5 followed by callus remodeling after 6 weeks indicating physiological fracture healing pattern in both the silver and in the silver free group. Micro CT analysis revealed overall tissue (callus and cortical bone) volume as well as tissue density to be comparable between the two groups. Mechanical testing showed comparable stiffness with an average stiffness relative to contralateral bones of 75.7 ± 16.1% in the silver free control group compared to 69.7 ± 18.5% (p-value: 0.46). Histology showed no remarkable difference in the analysis of the healed osteotomy gap or in the surrounding soft tissue area. Silver content was found to be close to baseline values without differences between the two groups.

Conclusions: This study shows that the presented antimicrobial silver surface modification for locking plates has a good biocompatibility without any negative influence on the fracture healing processes compared to the silver free control group. This allows for further clinical investigation of this silver technology for locking plates in fracture patients with an elevated infection risk, e.g. in patients with open fractures.

[FP80] LOCAL CONCENTRATIONS OF GENTAMICIN OBTAINED BY MICRODIALYSIS AFTER A CONTROLLED APPLICATION OF A GENTACOLL SPONGE IN A PORCINE MODEL

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Aim: Local treatment with gentamicin may be an important tool in the prevention and treatment of surgical site infections in high-risk procedures and patients. The aim of this study was to evaluate the pharmacokinetic profile of gentamicin in bone and surrounding tissue, released from a controlled application of a GentaColl sponge in a porcine model.

Method: In 8 female pigs, a GentaColl sponge of 10x10 cm (1.3 mg gentamicin/cm^2) was placed in a cancellous bone cavity in the proximal tibia. Microdialysis was used for sampling of gentamicin concentrations over 48 hours from the cavity with the implanted GentaColl sponge, cancellous bone parallel to the cavity over and under the epiphyseal plate, cortical bone, the intramedullary canal, subcutaneous tissue, and the joint cavity of the knee. Venous blood samples were obtained as reference.

Results: The main finding was a mean peak drug concentration (95-CI) of gentamicin in the cancellous bone cavity containing the implanted GentaColl sponge of 11,315 (9,049-13,581) **µg/ml**, persisting above 1000 ***µg/ml until approximately 40 hours after application. Moreover, the concentrations were*** low (< 1 ***µg/ml)*** in the surrounding tissues as well as in plasma.

Conclusions: The mean peak gentamicin concentration from the cancellous bone cavity after a controlled application of a GentaColl sponge was high and may be adequate for the prevention of biofilm formation. However, high MIC strains and uncontrolled application of the GentaColl sponge may jeopardize this conclusion.

[FP81] CUTIBACTERIUM AVIDUM PERSISTS IN THE GROIN AREA DESPITE SURGICAL SKIN ANTISEPSIS: A POTENTIAL RISK FACTOR FOR PERIPROSTHETIC JOINT INFECTIONS

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Aim: Periprosthetic joint infections (PJI) are increasing due to our elderly population with the need of a joint prosthesis. These infections are difficult to treat, because bacteria form biofilms within one day on the orthopedic implant surface. Notably, most of the current available antibiotics do not penetrate the biofilm or are not active against the sessile forms of bacteria. Therefore, prevention is key. In the current paradigm, bacteria from the skin surface or dermis - such as *Staphylococcus aureus*, coagulase-negative staphylococci, or *Cutibacterium* sp. – contaminate the periimplant tissue during surgery. *Cutibacterium avidum,* which has increasingly been reported in hip PJIs [1], colonizes the skin in the groin area in 32.3% [2]. We were wondering if standard skin antisepsis before hip arthroplasty is effective to eliminate *C. avidum* colonization in the surgical field.

Method: In a single-center, prospective study, we preoperatively screened all patients undergoing a hip arthroplasty through a direct anterior approach for different skin bacteria in the groin area. Only in patients colonized with *C. avidum,* we intraoperatively searched for persistent bacterial growth during and after triple skin antisepsis with povidone-iodine/alcohol. For that, we collected skin scrapings after first and third antisepsis and biopsies from the dermis at the surgical incision and evaluated bacterial growth and species. In addition, thin sections of the dermis biopsies were submitted to Fluorescence in situ Hybridization (FISH) using pan-bacteria probe EUB338.

Results: From October 2018 until March 2019, 53 patients (47.2% female) were screened. Patients were mainly colonized with coagulase-negative staphylococci (41, 77.4%; 41), *C. avidum* (12, 22.6%), and *Cutibacterium acnes* (8, 15.1%). Intraoperative skin antisepsis of patients colonized with *C. avidum* was ineffective to eliminate any bacteria in 75% (5 out of 7) after the first and 28.6% (2 out of 7) after the third antisepsis. Focusing on *C. avidum*, antisepsis was ineffective in 43% (3 out of 7) and 14% (1 out of 7), respectively. Dermis biopsies were all culture negative, but FISH showed positive ribosome-rich bacteria in 50%.

Conclusions: We show in our ongoing study that the commensal *C. avidum* resists the standard skin antisepsis and bacteria visually persist in the dermis as demonstrated by FISH technique. Standard skin antisepsis is of limited effectiveness, resulting in a risk for intraoperatively acquired PJIs. Thus, new and more effective techniques to improve skin antisepsis are urgently needed.

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[FP82] IODINE IMPREGNATED INCISION DRAPE DOES NOT PREVENT INFECTION IN KNEE ARTHROPLASTY SURGERY – 12 MONTHS FOLLOW-UP IN A COHORT OF 1187 PATIENTS

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Aim: The primary aim of this study was to examine whether the use of iodine impregnated incision drape (IIID) decreased the risk of periprosthetic joint infections (PJIs). The secondary aim was to investigate whether intraoperative contamination could predict postoperative infection.

PJI is a devastating incident for the patients and in a population that is getting older and the incidence of arthroplasty surgery is rising it is vital to keep the infection rate as low as possible. Despite prophylactic measures as pre-operative decontamination, antisepsis and prophylactic antibiotics the infection rate has been constant at 1-2%.

Method: We performed a transregional, prospective, randomized two arm study (IIID vs control group) of 1187 patients undergoing primary knee arthroplasty surgery. A database with patient demographics and surgical observations was established with the purpose of following the patients for ten years. Patients, who developed an infection within the first year of surgery were analyzed for correlation with the intraoperative bacterial findings and the use of IIID.

Results: 970 patients were available for preliminary analysis. 35/970 (3.6%) patients were re-operated during the follow-up period. 14/35 (40%) patients had positive tissue biopsies taken at revision surgery within one year of initial surgery. 15/35 (42%) were deemed infected and received antibiotic treatment. 9/15 patients deemed infected were male. Of the 15 infected patients 2 were contaminated at the primary surgery. Chi square test showed no correlation between contamination and infection (OR 0.87, 95% CI 0.13-6.0, p=0.89). 6 of the 15 infected patients were operated with IIID at the primary surgery. No correlation was found between the use of IIID at primary surgery and subsequent infection (OR 0.67, 95% CI 0.17-2.58, p=0.56.)

Conclusions: We found no effect of the use of IIID and subsequent development of PJI. Nor did we find a correlation between the intraoperative contamination and development of PJI within the first year of follow-up.

Acknowledgements: University of Copenhagen and 3M Health Care (St. Paul, Minnesota) funded the study. 3M did not participate in the design of the study, data collection, data analysis or data interpretation.

[FP83] REDUCED WOUND LEAKAGE AND PROSTHETIC JOINT INFECTIONS IN ARTHROPLASTY WITH MODIFIED WOUND CLOSURE

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Aim: Wound leakage has been shown to increase the risk of prostetic joint infections (PJIs) in primary total hip (THA) and knee arthroplasty (unicondylar and total knee arthroplasty; KA). The aim of this study is to determine whether the addition of a continuous subcuticular bonding stitch to a conventional 3-layer closure method reduces the incidence of prolonged wound leakage and PJIs after THA and KA.

Method: This retrospective cohort study included all patients receiving a THA or KA. Patients in the control group with a 3-layer closure method had surgery between November 1st 2015 and 2016, and were compared to the study group with a 4-layer closure method that had surgery between January 1st 2017 and 2018. The primary outcome was incidence of prolonged wound leakage longer than 72 hours. Differences were evaluated using logistic regression. Incidence of PJIs was the secondary outcome.

Results: A total of 439 THA and 339 KA in the control group and 460 THA and 350 KA in the study group were included. In the control group 11.7% of the patients had a prolonged leaking wound compared to 1.9% in the study group (p<0.001). The modified wound closure method showed a protective effect for obtaining prolonged wound leakage; odds ratios were 0.09 (95%CI 0.04-0.22; p<0.001) for THA and 0.21 (95%CI 0.10-0.43; p<0.001) for KA. PJIs decreased from 1.54% to 0.37% (p=0.019).

Conclusions: The addition of a continuous subcuticular bonding stitch reduces the incidence of prolonged wound leakage and PJIs after THA and KA compared to a conventional 3-layer wound closure method. The large reduction of incidence in wound leakage and PJIs in this study, combined with relatively negligible cost and effort of the modified wound closure method, would advocate for implementing this wound closure method in arthroplasty.

[FP84] UNIVERSAL DECOLONISATION WITH POLYHEXANID PRIOR TO HIP AND KNEE JOINT ARTHROPLASTY. A REGIONAL MULTICENTER TIME SERIES ANALYSIS WITH REGRESSIONAL ANALYSIS.

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Aim: Periprosthetic joint infections (PJI) and surgical site infections (SSI) are one of the most severe complications in joint arthroplasty. Decolonization measures prior to elective orthopedic surgeries have shown to reduce the risk of infection especially in patient identified as carriers of S. aureus. However additional screening measures can be difficult to implement in daily routine.

The objective was to study the influence of universal decolonization with polihaxanid on SSI rates.

Method: Between January 2017 and December 2018 patients scheduled for hip or knee joint arthroplasty in 5 participating orthopedic centers received polyhexanid containing decolonization set consisting of oral, nasal and wipes. Patients were instructed to perform a 5 day decolonization regimen 4 days prior to surgery. SSIs were recorded according to modified CDC criteria for a surveillance period of 90days after surgery.

Results: During the study period, 4437 decolonization sets were distributed to patients. 1869 patients consented to participate in the study and provide detailed feedback on compatibility and compliance. Overall SSI rate was 0.87 per 100 surgeries prior to introduction of the decolonization, while it was 0.97 per 100 surgeries during the period of decolonization and 0.59 per 100 surgeries in those using the decolonization set. SSI rates due to *Staphylococcus aureus* were 0.32 per 100 surgeries, 0.21 per 100 surgeries and 0.05 per 100 surgeries respectively.

In patients receiving an elective hip-joint arthroplasty SSI rate was 0.93 per 100 surgeries prior to introduction, while it was 1.17 per 100 surgeries during the intervention period and 0.96 per 100 surgeries in patients that used the decolonization set. However SSI rates due to *Staphylococcus aureus* were 0.30 per 100 surgeries, 0.14 per 100 surgeries and 0.10 per 100 surgeries respectively.

In patients receiving, an elective knee-joint arthroplasty SSI rate was 0.52 per 100 surgeries prior to introduction, while it was 0.53 per 100 surgeries during the intervention period and 0.12 per 100 surgeries in patients that used the decolonization set. However, SSI rates due to *Staphylococcus aureus* were 0.20 per 100 surgeries, 0.13 per 100 surgeries and 0.00 per 100 surgeries respectively.

In addition to these preliminary results, we will provide and present a further analysis of the study results.

Conclusions: Polyhexanid based universal decolonization measures were safely implemented. Universal decolonization with polyhexanid might have a benefit on S. aureus SSI rates in patients with joint arthroplasty, especially in elective knee arthroplasty. Further evaluations are needed.

[FP85] PREVENTION OF EARLY PERIPROSTHETIC JOINT INFECTIONS IN A UNIVERSITY HOSPITAL

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Aim: The incidence of early periprosthetic joint infection (PJI) after total hip arthroplasty (THA) and total knee arthroplasty (TKA) is between 1 and 2 percent. In our department approximately 700 primary THAs and TKAs are performed annually. In 2015 and 2016 the incidence of early PJIs was nearly 3%. The aim of this study was to see if it was possible to reduce the incidence of infection by employing a bundle of measures by involving staff from all aspects of patient flow and addressing preventing measures in every step of the patients´ course throughout the hospital.

Method: The Arthroplasty surgeon team reviewed the Proceedings of the International Consensus Meeting on Periprosthetic Joint Infection of 2013. Issues where literature had shown a significant effect on prevention of PJI was identified and written in an action plan. An interdisciplinary team with staff from all aspects of patient flow was established. In January 2017 the action plan was presented to the interdisciplinary team. The team discussed in what way the different issues could be solved, and issues that could be addressed without extra costs were implemented immediately. The issues addressed in the meeting were: preoperative risk factors, preoperative skin preparation, perioperative antibiotics, reducing particle amount and reducing traffic in the surgical theatre.

Results: Early PJIs (symptoms within 30 days of index surgery) has been registered in our local quality register since 2011. Every infection is assured in order to apply to international criteria. There were 31 early PJIs among the 1100 primary THAs and TKAs performed before the intervention and 13 early PJIs among the 1100 after. The incidence the last two years before the intervention was 2.7% and the two years after intervention incidence was 1.2% (p=0.009).

Conclusions: In this study we have shown that it is possible to reduce the incidence of early periprosthetic infections after primary THA and TKA in a university hospital. The patients referred to our department are of all categories, from healthy to great comorbidity. By focusing on optimizing the patient, preoperative antibiotics and traffic and behavior in the surgical theatre, we were able to reduce the infection incidence significantly. It is important to address the whole patient course, and introduce bundle of measures, in addition to involving staff from all aspects of the patient flow.

[FP86] THE IMPACT OF UNTOWARD EVENTS DURING PRIMARY OR REVISION TOTAL HIP OR KNEE ARTHROPLASTY SURGERY

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Aim: "There is not a lot of data of the frequency and impact of unwanted events including glove perforation, contamination of the surgical field (drape perforation, laceration, detachment, bone bounced back from an unsterile object), unsterile object in the surgical field (hair, sweat droplet…), defecation, elevated air temperature, and others. Mishaps occur in every surgical theatre. These events should influence the surgical site infection rate but it is not clear to what extent. We wanted to calculate the frequency and measure the impact of these events on the infection and revision rate of the relative patients."

Method: "In our institution, scrub nurses prospectively record untoward events in the theatres. Surgeons register complications before discharge. Stratified failures are recorded since 2002 within a registry. We analysed the respective databases and compared the revision and infection rate in the group with untoward effects with the outcome of all arthroplasty patients within the same time period. Two tailed Z statistical test was used for analysis."

Results: ": Between 1.1.2012 and 31.12.2015 we operated 8130 prosthetic joints: 3994 THR and 3238 TKR including respectively 610 and 288 revisions. During this period we recorded 234 events (2.9 %) including 13 (0.16 %) defecations, 19 (0.2 %) contaminations with hair, 48 (0.6%) draping, gown or field sterility violations, 34 (0,4 %) glove perforations, 19 (0.5 %) occasions with elevated air temperature. In 37 (0,45%) surgeries there was a guest in the theatre. There were 8 (2.8%) infections and 10 (3.5%) revisions in the group with untoward events. The infection rate for all TJR was 0.64% the revision rate for any reason was 2.37%. For all the THR patient of the same study period was 2.1% for any reason and 0.7% for PJI and for the TKR 2.72 and 0.56 respectively. The difference is significant at $p>0.05$ for infection but not significant for revision for any reason."

Conclusions: "In our series, the potentially serious sterility disruptive events in the operative rooms did result in increased infection rate among the involved patients but not an increase in revision rate. There is no data about the rate and the impact of these events besides for perforated surgical gloves with higher reported incidences than in our study influencing infection rate if perioperative antibiotic prophylaxis was not used. Ours is thus the first study to report some numbers about these events."

[BP1] NON-STEROIDAL ANTI-INFLAMMATORY DRUG ADMINISTRATION IMPAIRS ANTIBIOTIC TREATMENT OF ORTHOPEDIC DEVICE-RELATED INFECTION IN A RAT MODEL

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Aim: Non-steroidal anti-inflammatory drugs (NSAIDs) are a cornerstone of perioperative pain management in orthopedic trauma surgery, although concerns persist regarding the potential impact of these drugs on fracture healing. Furthermore, NSAIDs may also exert an influence on host immune defenses, which may also be important in the context of infection treatment. However, this has been very much under-investigated in the clinical and scientific literature. The aim of this study was to determine the impact of NSAIDs on the course of an orthopedic device-related infection (ODRI) and its response to antibiotic therapy in a rat model.

Method: A polyetheretherketone (PEEK) screw was inserted in the proximal tibia of 48 skeletally mature female Wistar rats: 12 control animals received a sterile screw, of which 6 also received NSAID therapy (carprofen, 5 mg/kg s.c. once daily); 36 rats received a *Staphylococcus epidermidis*-inoculated screw, of which 18 received NSAID therapy. Antibiotic therapy was administered from day 7-21 in 9 animals from all groups receiving *S. epidermidis*-inoculated screws (cefazolin: 30 mg/kg; s.c., b.i.d. plus rifampin: 25 mg/kg; s.c., b.i.d.). Bone histomorphometric changes were monitored using longitudinal microCT scanning, performed postoperatively, and at 3, 6, 9, 14, 20 and 28 days (euthanasia). Quantitative bacteriology of the implant, bone and overlying soft tissue was performed to assess infection status of individual animals.

Results: All animals receiving *S. epidermidis*-inoculated screws in the absence of antibiotic therapy were confirmed as infected at euthanasia. Quantitative microbiology showed no significant change in bacterial load in NSAID-treated animals versus control. However, NSAID administration dramatically impaired antibiotic efficacy, with 7/8 animals remaining infected when NSAIDs were co-administered, whilst only 2/9 of control animals were infected when NSAIDs were withheld.

Pronounced osteolysis was observed by day 6-9 in control animals, with reparative processes (periosteal proliferation and mineralization) observed at day 14. NSAID treatment markedly prevented *S. epidermidis*-induced osteolysis, but also reparative processes. Antibiotic treatment did not affect the bone changes.

Conclusions: NSAID administration dramatically affected the response of bone tissue to infection, reducing osteolysis but also impairing reparative processes. Crucially, NSAIDs dramatically reduced antibiotic efficacy. Given these pronounced negative effects, further investigations should be conducted to determine the underlying pathophysiological mechanism and better understand the consequences of the therapeutic use of NSAIDs in human patients with ODRI.

[BP2] EFFICACY OF SB-1 BACTERIOPHAGE IN TREATING AND PREVENTING METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS IN A GALLERIA MELLONELLA MODEL OF IMPLANT-ASSOCIATED INFECTION

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Aim: To investigate the ability of the bacteriophage Sb-1 to treat and prevent implant-associated infections due to methicillin-resistant Staphylococcus aureus (MRSA) in *Galleria mellonella* larvae implanted with a K-wire.

Method: The stability of Sb-1 in *G. mellonella* larvae was investigated by injecting a phage titer of 10^8 PFU and evaluating the presence of Sb-1 in hemolymph at different time points. For infection experiments, sterile stainless-steel K-wires (4 mm, 0.6 mm Ø) were implanted into larvae. Two days after implant, larvae were infected with MRSA ATCC 43300 (1×10^5 CFU) and incubated at 37°C for further 2 days. Implanted-infected larvae were thus treated for 2 days (3×/day) with 10µL of: i) PBS; ii) Sb-1 (10^7 PFU); iii) Daptomycin (4mg/kg), iv) PBS (24h)/Daptomycin(24h); v) Sb-1(24h)/Daptomycin(24h). To evaluate the prophylactic efficacy of Sb-1, an experiment based on phages or vancomycin (10mg/kg) administration, followed by MRSA infection of implanted larvae was performed. Both two days post-infection and post-treatment, K-wires were explanted, and the material was sonicated and plated for MRSA colony counting.

Results: Sb-1 titer resulted stable in hemolymph of *G. mellonella* larvae for 6-8 h post-administration (Figure 1A). Two days post-infection of K-wire implanted larvae, ≈5×10^7 CFU/ml MRSA were found on the material. K-wires from larvae treated with Sb-1 or Daptomycin showed a MRSA CFU/ml reduction of ≈1 log compared to the CFU/ml values of the untreated control. The staggered administration Sb-1/Daptomycin determined higher CFU reduction (≈ 3.5 log) (Figure 1B). Prophylaxis with Sb-1 prevented MRSA infection of 7out of 10 larvae similarly to vancomycin.

Conclusions: *G. mellonella* larvae implanted with K-wires are a suitable model to test antibiofilm formulations *in vivo*. Sb-1 phage is able to prevent implant-associated infection due to MRSA in larvae. Sequential combination of Sb-1 and Daptomycin strongly reduces the MRSA load on implanted K-wires.

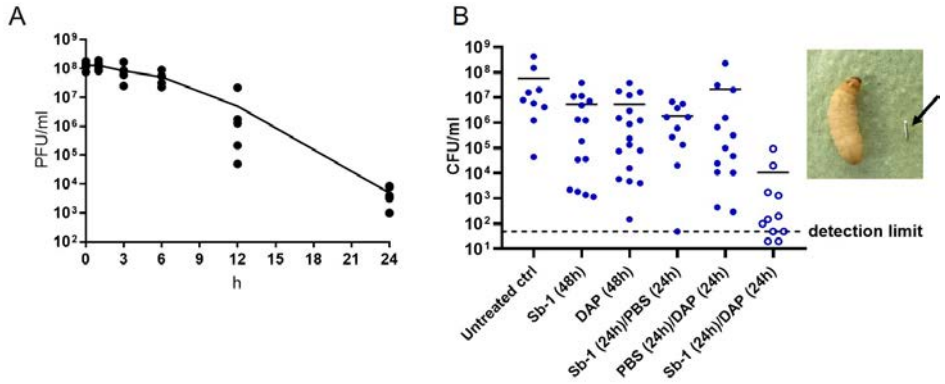

Figure1. A) Stability of Sb-1 in hemolymph of *G. mellonella*. B) CFU/ml number of *S. aureus* from K-wire-implanted larvae treated with different combination of phage and daptomycin (DAP). Black arrow indicates a K-wire.

[BP3] DEVELOPMENT OF A TWO-STAGE ANIMAL MODEL TO EVALUATE NEW THERAPEUTIC STRATEGIES IN THE TREATMENT OF INFECTED NON-UNIONS

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Aim: Treatment of infected and non-infected non-unions remain a major challenge after orthopedic fracture-related surgery. In clinical practice, several revision surgeries are usually required, including a radical debridement and exchange of implants, to control or even eradicate the infection to finally achieve bone healing. However, a clear treatment algorithm in clinical practice may be difficult to follow due to the heterogeneous patient population. Thus, so controlled settings for research purposes is better achieved in standardized animal studies.

So far, there exists no multi-stage animal model that can be realistically transferred to the clinical situation in humans. The importance of such a model is obvious in order to be able to investigate different therapy concepts for infected and non-infected non unions.

Methods: In 20 female Sprague-Dawley rats, a critical size defect by a femur osteotomy with 5 mm width was done. The periosteum at the fracture zone was cauterized proximal and distal to the osteotomy to achieve an hypovascularized situation. After randomization, 10 animals were intramedullary infected with a multisensible Staph. aureus strain (10^3 CFU). After 5 weeks, a second surgery was performed with removing the K-wire, debridement of the osteotomy-gap and re-osteosynthesis with an angle-stable plate. After further 8 weeks all rats were euthanized and underwent biomechanical testing to evaluate bone consolidation or delayed union, respectively. Additional micro-CT analysis, histological, and histomorphometric analysis were done to evaluate bone consolidation or delayed union, respectively, by the score of Lane and Sandhu and to quantify callus formation and the mineralized area of the callus.

Results: 5 weeks after the first surgery a non-union had formed in all septic and aseptic animals. According to the Lane and Sandhu score a significantly higher callus formation was found in the infected group. In all infected animals, the inoculated Staph. aureus strain was detected during the revision surgery.

8 weeks after the second surgery no bone healing could be detected in the µ-CT analysis in both groups and biomechanical testing showed a significant lower maximum torque in both groups as compared to the untreated contralateral femura.

Conclusion: Here we show first results of a new two-stage pseudarthrosis animal model, which reflects a very realistic clinical situation of an infection-related non-union model. Based on this model, various therapeutic strategies in the treatment of infectious and non-infectious pseudarthrosis, such as the use of bone substitutes, can be evaluated in further studies.

[BP4] OPERATING ROOM VENTILATION AND THE RISK OF REVISION DUE TO INFECTION AFTER TOTAL HIP ARTHROPLASTY - ASSESSMENT OF VALIDATED DATA IN THE NORWEGIAN ARTHROPLASTY REGISTER 2005- 2015

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Aim: The aim of this study was to assess the influence of the true operating room (OR) ventilation on the risk of revision due to infection after primary total hip arthroplasty (THA) reported to the Norwegian Arthroplasty Register (NAR).

Method: 40 orthopedic units were included during the period 2005 - 2015. The Unidirectional airflow (UDAF) systems were subdivided into small-area, low-volume, vertical UDAF (lvUDAF) (volume flow rate (VFR) (m^3/hour) <=10,000 and diffuser array size (DAS) (m^2) <=10); large-area, high-volume, vertical UDAF (hvUDAF) (VFR >=10,000 and DAS >=10) and Horizontal UDAF (H-UDAF). The systems were compared to conventional, turbulent ventilation (CV) systems. The association between revision due to infection and OR ventilation was assessed using Cox regression models, with adjustments for sex, age, indication for surgery, ASA-classification, method of fixation, modularity of the components, duration of surgery, in addition to year of primary THA. All included THAs received systemic, antibiotic prophylaxis.

Results: 51,292 primary THAs were eligible for assessment. 575 (1.1%) of these THAs had been revised due to infection. Compared to CV, there was similar risk of revision due to infection after THA performed in ORs with lvUDAF (RR=0.9, 95 % CI: 0.7–1.1) and with H-UDAF (RR=1.3, 95 % CI: 0.9–1.8). The risk of revision due to infection after THA performed in ORs with large-area hvUDAF-systems was lower (RR=0.8, 95% CI: 0.6-0.9, p=0.01) compared to CV.

Conclusions: This study indicates that large-area, high-volume, vertical UDAF systems may be superior to conventional ventilation systems as a prophylactic measure against THA infection. This emphasizes the importance of assessing the big diversity of different ventilation systems when studying effect measures.

[BP5] ANTIMICROBIAL PEPTIDES ERADICATE BACTERIA, INCLUDING PERSISTERS, IN ANTIBIOTIC-TREATED MATURE BIOFILMS

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Aims: Prosthetic joint infection (PJI) remains the most severe complication of arthroplasty. Failure of intensive, long-term antibiotic treatment for PJI often requires removal of the implant. Antibiotic failure is thought to be caused by biofilm and persister formation. Novel anti-biofilm and anti-persister strategies are urgently needed. Here, we investigated the effects of several antimicrobial peptides on the bacteria within antibiotic-treated biofilms in an *in vitro* mature biofilm model on abiotic surfaces (Figure 1).

Methods: On polystyrene, a mature (7 day-old) methicillin-resistant *Staphylococcus aureus* (MRSA) biofilm was developed. Thereafter, bacteria in the biofilm were exposed to rifampicin and ciprofloxacin (both 10x >MIC) for three days. Surviving bacteria in the antibiotic-treated biofilm, presumed to include persisters, were exposed to increasing doses of the antimicrobial peptides SAAP-148, acyldepsipeptide 4 (ADEP4), LL-37 and pexiganan. SAAP-148 was further tested on antibiotic-treated mature biofilms on titanium/aluminium/niobium (TAN) discs and prosthetic joint liners.

Results: Daily exposure of the mature biofilm for seven days with antibiotics resulted in a 4-log reduction of MRSA without elimination of the bacteria. The surviving bacteria within the biofilm were eliminated upon subsequent exposure to SAAP-148 and pexiganan but not with LL-37 ad ADEP4. Antibiotic treatment of mature biofilms on TAN discs followed by SAAP-148 also resulted in eradication of bacteria within the biofilm. SAAP-148 also fully eliminated bacteria within antibiotic-treated mature MRSA biofilms on an ex vivo liner of a prosthetic joint.

Conclusions: A novel mature biofilm model has been developed in which the efficacy of antimicrobial peptides against bacteria, including persisters, residing within a biofilm was investigated. SAAP-148 and pexiganan were highly effective against the bacteria residing in antibiotic-exposed mature MRSA biofilms. This *in vitro* model system will be used to analyze the effects of novel antibiotic strategies and other anti-PJI agents.

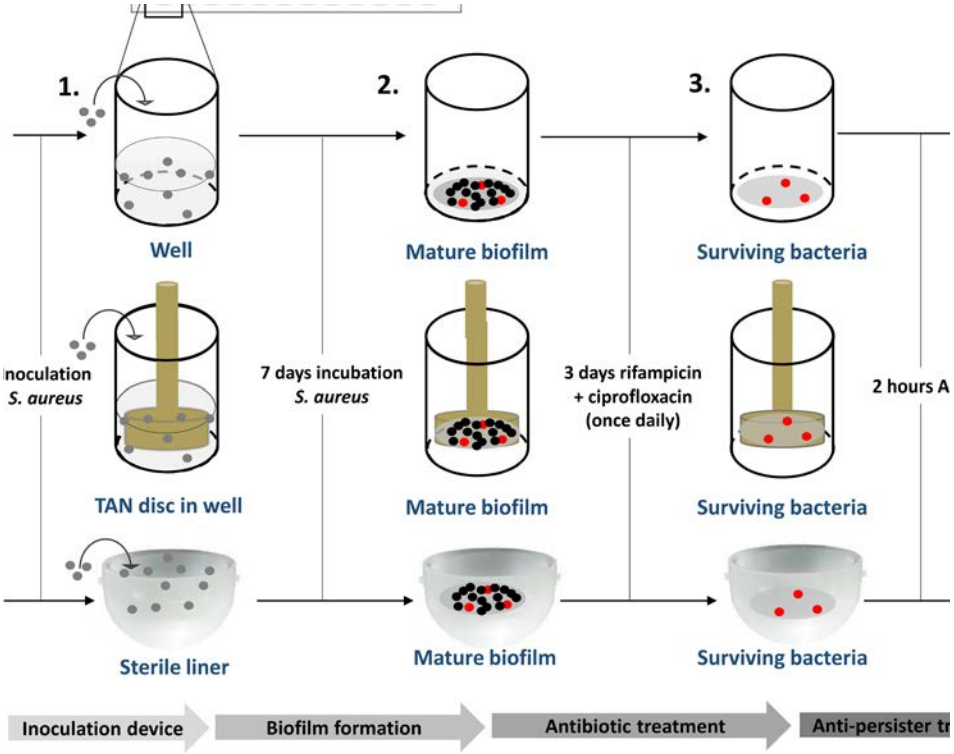

Figure 1. Biofilm model with formation of a mature MRSA biofilm, antibiotic treatment of the biofilm, followed by treatment with antipersister treatment. (AMP:antimicrobial peptide; *S. aureus*: *Staphylococcus aureus*; TAN: Titanium/aluminium/niobium)

[BP6] THE VALUE OF SERUM INFLAMMATORY MARKERS IN THE DIAGNOSIS OF FRACTURE RELATED INFECTIONS

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Background: Preoperative diagnosis of fracture related infections can be challenging, especially when confirmatory criteria such as sinus tract and purulent discharge are absent. Although serum parameters, such as CRP and white blood cell count (WBC), showed poor accuracy in the literature, they are still often used in clinical practice. The European Bone and Joint Infection Society (EBJIS) defined evidence-based criteria for fracture related infection. Elevated serum inflammatory markers were regarded as suggestive criteria only, as the literature was of limited quality. This study assessed the diagnostic value of the serum parameters CRP, WBC and differential cell count in the diagnosis of fracture related infections defined by the EBJIS-criteria for fracture related infections.

Methods: In this retrospective cohort study, 94 patients who underwent surgical treatment for suspected infected non unions after failed fracture fixation were included. Preoperatively, blood samples including serum inflammatory markers were taken. For this study, cut-offs of 5 mg/L for CRP, 10x10^9 cells/L for WBC, and >70% for the percentage of neutrophils were regarded as positive for infection. All patients had intraoperative samples taken for microbiology and histology. Analysis of diagnostic accuracy was based on the receiver-operating characteristic (ROC).

Results: Based on the EBJIS criteria, 40 patients (43%) were diagnosed with a fracture related infection. 11/94 (12%) patients had an elevated serum WBC count, 13/94 (14%) an increased percentage of neutrophils, and 43/82 (52%) an elevated serum CRP. The mean values of CRP concentration, WBC count, and percentage of neutrophils in the infection group were 7.9 mg/L (IQR:6.4 – 9.7), 18.3 G/l (IQR: 3.9 – 24.9), and 63% (IQR: 58 – 67%), respectively. The sensitivity, specificity, and area under the curve of serum WBC count were 20% (95% CI: 10 -35%), 94.4% (84 -99%), and 0.57 (0.50 – 0.64), respectively; of percentage of neutrophils 12.5% (5 – 27%), 85.2% (73 -93%), and 0.49 (0.42 – 0.56); and of serum CRP 67.6% (51 – 90%), 60.0% (45 – 73%), and 0.64 (0.53 – 0.74), respectively. A statistically significant difference between the AUCs of all three serum parameters and AUC of tissue culture as well as AUC of histology was shown (p <0.0001). A simple decision tree approach using only low WBC and CRP may allow identification of aseptic cases.

Conclusion: Based on the standardized and evidence-based EBJIS criteria, the three inflammatory serum markers showed an insufficient accuracy for the diagnosis of fracture related infections. They also correlate poorly with culture or histological diagnosis. Therefore, they should not be used alone as a confirmatory test.

[BP7] GUIDELINE FOR PRECLINICAL STUDIES OF BONE INFECTIONS

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Aim: To conduct a systematic review of non-rodent animal models (rabbit, pig, dog, goat and sheep) of bone infection. In the future, anti-infective technologies aiming to fight bone infections are depending on evaluation in reliable animal models. Therefore, it is highly relevant to evaluate the scientific quality of existing bone infection models.

Method: PubMed and Web of Science were searched systematically. To be included in the systematic review, publications had to deal with bacterial inoculation of non-rodent animals in order to model bone infections in humans. Data was extracted on study design *e.g.* bacterial inoculation dose and infection time, methodological quality and post-mortem evaluation with respect to registration and quantification of pathology and microbiology.

Results: In total, 316 publications were included in the systematic review. A substantial lack of study design information (*e.g.* bacterial identity and infection time) was demonstrated in many of the papers, which hampers reproducibility and continuation of the established work. Furthermore, the methodological study quality was found to be low as definition of infection, randomization, power analysis and blinding were only seldom reported. The use of histology has increased in recent years, but a semi-quantitative scoring of the lesions was often missing, *i.e.* no objective quantification of outcome. Most of the studies focused on whether the inoculated bacteria were present within the bone tissue post mortem or not. However, very often the bacterial burden was not quantified. In many of the models, different antimicrobial interventions were examined, and the lack of quantitative microbiology makes it difficult to estimate and reproduce the effects objectively. Although, antimicrobial effects were described for most interventions, a lack of sterile outcome was observed in many models. Failure to report a sterile outcome reduces the possibility for obtaining valuable knowledge regarding effective antibiotic doses in-vivo. Based on the present review a standard study template guideline for animal models of bone infections was established. The guideline describes details related to the animal, pathogen, animal + pathogen (infected animal) and post mortem analysis that are of crucial importance for validation of results and reproducibility.

Conclusions: Due to a substantial lack of uniformity we miss the opportunity to get maximal knowledge from the preclinical literature. The new guideline will improve reproducibility of future models and translation of findings to the clinical setting. Bone infection organisations/societies and journal editors should encourage compliance with the new guideline.

Reference: *JBJS*, 2019, In press

[BP8] PROSTHETIC JOINT INFECTION (PJI) – IS THIS CORRECTLY RECORDED AS A 'REASON FOR REVISION' ON THE NATIONAL JOINT REGISTRY?

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Aim: Prosthetic joint infection is a serious complication of Total Hip Replacements (THR) and Total Knee Replacement (TKR). Surgeons discussing the risk of a revision procedure becoming necessary, after a THR or TKR for prosthetic joint infection can draw upon the orthopaedic literature and arthroplasty registries. With over 2.35 million records, the National Joint Registry (NJR) in the United Kingdom is the largest arthroplasty registry in the world. It provides a powerful tool to monitor 'Reason for Revision' and influence different surgical strategies. We have investigated the validity of the ´Reason for Revision´ for infections recorded in Consultant Outcome Publications on the NJR.

Methods: Of the 22,046 primary THR and TKR undertaken by 23 surgeons at our hospital, over an eleven-year period, 1.35% (297) were subsequently reported to the NJR as revised where the primary joint replacement was undertaken by one of our 23 surgeons. Review and validation of ´Reason for Revision´ was undertaken using radiological imaging studies, pathology, histology, microbiology and electronic medical records.

Results: Discrepancies in reporting to the NJR were identified for 41 cases (25.6%) for THR and 28 (20.4%) cases for TKR. Revision for infection was under-reported for both THR and TKR by 1.88% and 3.65% respectively. Once validated, 16.86% THR cases were revised for infection. Once validated, 29.9% TKR cases were revised for infection.

Conclusion: If an average of 23% wrong data entry at a highly organised institution is replicated throughout the UK, a formal process to validate primary and revision data submitted to the NJR should be considered. Local scrutiny, review and validation of revision data are all vital to optimise the value of the NJR. Accurate data recorded to the NJR is imperative to provide safe and effective improvements in orthopaedic surgery.

[BP9] THE RISK OF PERIPROSTHETIC JOINT INFECTION DURING BACTEREMIA

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Aim: The risk for developing a periprosthetic joint infection (PJI) as a consequence of bacteremia is not clear, except for *Staphylococcus aureus* bacteremia, and patient-related risk factors for it are not known. The aim of this study was to investigate the risk for developing a PJI during any bacteremia and to find out possible risk factors leading to it.

Method: All patients with a primary knee or hip joint replacement performed between September 2002 and December 2013 in a tertiary care hospital (n=14 378) were retrospectively followed up until December 2014. The mean follow-up time was 6.0 years (range 0–12 years). Positive blood culture results of the patients during the study period were obtained. PJIs during the study period were identified from several data sources. PJIs as a consequence of bacteremia were recorded and confirmed from patient records. Primary PJIs resulting in bacteremia were excluded. Binary logistic regression with univariate analysis was used to study potential risk factors for PJI among those with bacteremia.

Results: Of the study patients, 542 (3.8%) had at least one episode of bacteremia. In total, there were 643 episodes of bacteremia. The incidence rate of bacteremia was 7.4 per 1 000 person-years. Seven percent (47/643) of the bacteremias resulted in a PJI. The risk for PJI was highest for bacteremias caused by *Staphylococcus aureus* (21% of bacteremias led to a PJI) and beta-hemolytic streptococci (21%), but it was low for gram-negative bacteria (1.3%). Patients with two or more bacteremias during the study period had an increased risk for developing a PJI (OR 2.29, 95%CI 1.17–4.50). Bacteremias occurring within a year from previous surgery were associated with the highest risk for developing a PJI. Chronic comorbidities, obesity, gender, joint location, indication for surgery or use of antibiotic-loaded cement did not affect the risk for PJI during bacteremia.

Conclusions: The pathogen causing the bacteremia, number of bacteremias and the timing of bacteremia with respect to previous surgery affect the risk for developing a PJI as a consequence of bacteremia. Thus the type of pathogen, previous history of infections and the timing of bacteremia should be taken into account when evaluating the risk for PJI on a patient with bacteremia. On the other hand, significant patient-related risk factors for PJI during bacteremia could not be identified.

[BP10] THE TERMINAL COMPLEMENT PATHWAY IDENTIFIES PROSTHESIS INFECTION IN PERIPROSTHETIC TISSUE SAMPLES

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Aim: Low-grade infections cannot be easily distinguished from aseptic complications frequently leading to false negative diagnoses and late onset of anti-bacterial therapy. Therefore, there is a great need to establish biomarkers for early detection of low-grade infections.

Method: In this study, we focused on the investigation of anti-α-defensin, anti-C3, anti-C5 and anti-C9 as potential biomarkers for infection in a cohort of hip and knee septic revision cases, taking patient characteristics and comorbidities into account. Here we included 78 patients with septic (35) and aseptic (43) (♀37, ♂42, age 50 – 93 years) revision surgeries of hip and knee. CRP serum levels and leucocyte blood values were evaluated. Patient characteristics, including age, number of prior revision surgeries and comorbidities were recorded. Periprosthetic tissue was stained histologically with Hematoxylin/Eosin and immunhistologically with different antibodies.

Results: The CRP values were significantly increased in the septic cohort, but no changes were observed in leucocyte count. Interestingly, we found a strong increase in the terminal complement system component C9 (septic: 0.1% ± 0.2% aseptic: 0.01% ± 0.05%, p= 0.0004) in the septic periprosthetic tissue. The predictive value of α-defensin staining was not statistically significant (septic: 0.5% ± 0.7% aseptic: 0.1% ± 0.6%, p= 0.09). Analyzing the synovial fluid of aseptic and septic patients, the presence of C9 in the septic group (1.8 ± 0.4) was not significantly higher compared to the aseptic (1.9 ± 0.7) group. The next step was to investigate the specificity C9 detection using different joint related diseases such as chondrocalcinosis (CC), rheumatoid arthritis (RA) and metallosis. The median of C9 staining in the CC group (0 ± 0.0001) was significant lower than the infection group. Similar results have been observed in RA (0.0003 ± 0.2) and the metallosis group (0.0002 ± 0.01).

Conclusions: We found a strong predictive value of anti-C9 staining for tissue infection, suggesting that C9 deposition could be a novel biomarker for the identification of periprosthetic joint infections using tissue biopsies.

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EBJIS 2020

39th Annual Meeting of the European Bone and Joint Infection Society

SAVE THE DATE

10 - 12 September 2020
Ljubljana, Slovenia

Important dates

Abstract Submission Deadline
10 April 2020

Early Registration Deadline
1 July 2020

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Main topics

- Optimising antibiotic treatment of bone & joint infections
- Optimal bone infection sampling and microbiological processing
- Low-grade PJI – what is the best approach?
- Musculoskeletal infections in children
- Infections of arthroscopic implants, osteotomies and tendon reconstructions
- Chronic osteomyelitis with good function. To treat or to live with?
- Spinal infections

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