PROGRAMME AND ABSTRACTS

# EBJIS 2021

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

7 - 9 October 2021 · Ljubljana, Slovenia

www.ebjis2021.org

European Bone & Joint Infection Society
EB JIS


# **EBJIS** 2021

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

# Index

# EBJIS Membership

*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*

## Member benefits

- You will receive a discount from the Annual EBJIS Meeting registration fee which is similar to the annual membership fee (130 euros).
- Become an EBJIS Fellow: members are eligible to apply for the fully-funded annual Travelling Fellowship program www.ebjis.org/fellowship Three Travelling Fellowships are awarded every year.
- As a member of EBJIS you are eligible to receive reduced article processing charges when publishing an open-access article in The Journal of Bone and Joint Infection (JBJI). admini-strator.copernicus.org/authentication
- Access all EBJIS Newsletters and all the re-cent news related to Bone and Joint Infection.
- Access the EBJIS Annual General Assembly with voting rights on key decisions.
- Access the EBJIS community that encourages discussion and collaboration between the EBJIS Members on clinical cases.
- The Executive Committee support Members who organise scientific 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 many coun-tries around the world, to facilitate contacts with interested colleagues and to encourage Bone and Joint Infection centres.

**Annual membership fee: € 130**

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

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

# Welcome

**Dear colleagues and friends,**

It is a great honour to host and organise the 39th Annual Meeting of the European Bone and Joint Infection Society, which will take place in Ljubljana, Slovenia on 7-9 October 2021. Although the COVID-19 pandemic has severely affected our work and our lives, we are happy that the face-to-face meeting will be held at the GR – Ljubljana Convention and Exhibition Centre, conveniently located close to the city centre, a few minutes' walk from the Ljubljana central station. For the participants that will not be able to come to Ljubljana, all the programme will also be available online.

Ljubljana, the capital of Slovenia, a university city with 285.000 inhabitants, lies halfway between Vienna and Venice at the crossroads of different cultures, geographical regions, and historical developments. It is a very friendly and green city, located within a convenient two-hour flight from almost all major European airports. Although most hotels are within walking distance from the conference venue, Ljubljana offers congress participants free-of-charge use of public transport.

The conference will bring together experts, practitioners and companies involved in the treatment of bone and joint infections. Professionals attending the conference will benefit from high-level scientific presentations, knowledge sharing and networking opportunities. We believe that despite the COVID-19 pandemic we have prepared an interesting programme that includes keynote lectures, free paper sessions, industry symposia and posters.

We look forward to welcoming you to Ljubljana.

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

**Marko Pokorn**
Local chair

**Rihard Trebše**
President of EBJIS

# Organisation

**EBJIS Executive Committee**

| | |
|---|---|
| President | Rihard Trebše |
| Vice President | Alex Soriano |
| Past President | Martin McNally |
| Secretary General | Charles Vogely |
| Treasurer | Martin Clauss |
| Members | Marjan Wouthuyzen-Bakker |
| | Ricardo Sousa |
| Country delegates Chair | Christof Wagner |

**Local Organising Committee**

| | |
|---|---|
| Chair | Marko Pokorn |
| Members | Rihard Trebše |
| | Drago Dolinar |
| | Petra Bogovič |
| | Lea Papst |
| | Samo Jeverica |
| | Rene Mihalič |
| | Boštjan Sluga |

# General information

**Conference website**
www.ebjis2021.org

**Conference venue**
GR - Ljubljana Exhibition
& Convention Center
Dunajska Cesta 18
1000 Ljubljana, Slovenia

**Badges**
The conference name badges must be always worn 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 7 October, farewell lunch on Saturday 9 October and certificate of attendance.

**CME credits**
The conference has been accredited 15 European CME credits (ECMEC) by the European Accreditation Council for Continuing Medical Education (EACCME). 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**
The cloak room is in the foyer next to the registration desk and will be available during the scheduled programme.

**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 minutes 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 to secure that no copyright issues will arise.

**Speakers' Preview room (Apel room, 1st floor)**

Opening hours:

| | |
|---|---|
| Thursday 7 October | 7:00 - 17:00 |
| Friday 8 October | 7:45 - 17:00 |
| Saturday 9 October | 8:00 - 12:00 |

**WIFI**
Free access to the WIFI at the conference venue is provided.
Username: GR
Password: 11110000

**COVID-information**
It is mandatory to always wear a face mask indoors, please bring this on your own. The conference venue provides hand sanitizers and ensures extra cleaning of surfaces. The Recovered / Vaccinated /Tested (RVT)-rule is mandatory and you must show documentation for this when you enter the conference venue. A negative PCR test is valid for 72 hours and a negative rapid antigen test is valid for 48 hours.

# Social events

**Welcome Reception**
Date 7 October 2021
Time 17:30 - 19:30
Place Exhibition area at the conference venue

The reception is included in the registration fee.

**EBJIS Gala Dinner**
Date 8 October 2021
Time 20:00 - 23:00
Place Grand Hotel Union,
Miklošičeva cesta 1
1000 Ljubljana

The gala dinner will take place at the beautiful Grand Hotel Union.

NB: The dinner is not included in the registration fee.

**Conference Secretariat**
CAP Partner
Nordre Fasanvej 113, 2
DK-2000 Frederiksberg
Denmark
Tel.: +45 70 20 03 05
ebjisconference@cap-partner.eu
www.cap-partner.eu

**EBJIS Secretariat**
ZA La Pièce 2
1180 Rolle
Switzerland
+41 21 822 09 20
info@ebjis.org
www.ebjis.org

**Social media**

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

Find EBJIS on LinkedIn
Search for "EBJIS Non Profit Organization"

Find EBJIS on Twitter
Search for “@EBJIS_

# Programme overview

## Thursday 7 October 2021

| | Room: Marmorna Hall, ground floor | |
|---|---|---|
| 07:00 | **Registration at the foyer** | |
| 08:30-08:50 | **Welcome & Opening Ceremony** | **Marko Pokorn & Rihard Trebše** |
| 08:50-09:50 | **Key session 1: Perceptions in Managing Orthopaedic Infections** | **Chairs: Marko Pokorn & Rihard Trebše** |
| 08:50-09:05 | Risk and medical decision making | Hansjorg Neth |
| 09:05-09:20 | How can we investigate bone and joint infections? | Martin McNally |
| 09:20-09:35 | Antibiotic stewardship in Orthopaedics | Bojana Beović |
| 09:35-10:35 | **Key session 2: Optimising Antibiotic Treatment of Bone & Joint Infections** | **Chairs: Lea Papst & Marjan Wouthuyzen-Bakker** |
| 09:35-09:50 | Optimizing PJI treatment – Management adaptation according to the pathogen, patient and surgeon | Andrej Trampuž |
| 09:50-10:00 | Intravenous or oral antibiotics in PJI | Matthew Scarborough |
| 10:00-10:10 | Interactions between antibiotics and other drugs | Nataša Faganeli |
| 10:10-10:20 | Pharmacokinetics of antibiotics in osteoarticular infections | Francoise van Bambeke* |
| 10:20-10:35 | Discussion | |
| 10:35-11:15 | ***Refreshment break*** | ***Posters & Exhibition*** |
| 11:15-12:40 | **Free Papers A (10 x 6 min. + 2 min.)** | **Chairs: Rene Mihalič & Marko Pokorn** |
| 12:40-14:00 | ***Industry Symposium A (12:50-13:50)*** | ***Lunch & Exhibition*** |
| 14:00-15:00 | **Key session 3: Optimal Bone Infection Sampling and Microbiological Processing** | **Chairs: Petra Bogovič & Alex Soriano** |
| 14:00-14:15 | The use of histology in the diagnosis of bone and joint infections | Irene Sigmund |
| 14:15-14:30 | Is innoculation in blood culture bottles for joint aspirates really the best option | Samo Jeverica |
| 14:30-14:45 | Optimizing the processing of microbiological samples in orthopaedics | Bridget Atkins |
| 14:45-15:00 | Discussion | |
| 15:00-15:50 | **Free Papers C (5 x 6 min. + 2 min.)** | **Chairs: Samo Jeverica & Marko Pokorn** |
| 15:50-16:20 | ***Refreshment break*** | ***Posters & Exhibition*** |
| 16:20-17:20 | **Key Session 4: Low-Grade PJI – according to the EBJIS definition** | **Chairs: Ricardo Sousa & Marjan Wouthuyzen-Bakker** |
| 16:20-16:35 | How to define a low-grade PJI | Alex Soriano |
| 16:35-16:50 | Is *Cutibacterium acnes* really a pathogen? | Yvonne Achtermann |
| 16:50-17:05 | Surgical approach to a low-grade PJI | Martin Clauss |
| 17:05-17:20 | Discussion | |
| 17:30-19:30 | **Welcome Reception - conference venue** | |

*Online presentation

| | Room: Urška, 2nd floor | |
|---|---|---|
| 11:15-12:40 | **Free Papers B**<br>**(10 x 6 min. + 2 min.)** | **Chairs:**<br>**Boštjan Sluga &**<br>**Lea Papst** |
| 12:40-14:00 | ***Industry Symposium B (12:50-13:50)*** | |
| 14:00-15:00 | | |
| 14:00-14:15 | | |
| 14:15-14:30 | | |
| 14:30-14:45 | | |
| 14:45-15:00 | | |
| 15:00-15:50 | **Free Papers D**<br>**(5 x 6 min. + 2 min.)** | **Chairs:**<br>**Lea Papst &**<br>**Drago Dolinar** |
| 15:50-16:20 | | |
| 16:20-17:20 | **Key session 5:**<br>**Musculoskeletal Infections in Children** | **Chairs:**<br>**Marko Pokorn &**<br>**Markus Pääkkönen** |
| 16:20-16:35 | Diagnostic approaches in children with OAI | Jesús Saavedra-Lozano |
| 16:35-16:50 | The role of the orthopaedic surgeon in paediatric osteoarticular infections | Markus Pääkkönen |
| 16:50-17:05 | Shortening the duration of antimicrobial treatment in paediatric OAI – Where is the limit? | Saul Faust* |
| 17:05-17:20 | Discussion | |

*Online presentation

# Programme overview

## Friday 8 October 2021

| | Room: Marmorna Hall, ground floor | |
|---|---|---|
| 07:45 | **Registration at the foyer** | |
| 08:30-09:30 | **Key Session 6:<br>Uncommon Infections** | **Chairs:<br>Klaus Kirketerp Møller<br>& Rene Mihalič** |
| 08:30-08:45 | Small orthopedic implant associated infection | Volker Alt |
| 08:45-09:00 | Infection after ACL reconstruction | Daniel Pérez-Prieto |
| 09:00-09:15 | Infection of the hands (bites mycobateria) | Nicholas Riley* |
| 09:15-09:30 | Discussion | |
| 09:30-10:30 | **Key Session 7:<br>Non-Operative Management of Chronic Infections** | **Chairs:<br>Olivier Borens &<br>Ferdinando Da Rin de<br>Lorenzo** |
| 09:30-09:45 | Living with a leaking hole in the limb | Mathias Glehr |
| 09:45-10:00 | Conservative management of chronic infections: Experience with subcutaneous antimicrobial suppressive treatment and bacteriophages | Tristan Ferry |
| 10:00-10:15 | PJI sinus tract : do we need antibiotics or not? | Marjan Wouthuyzen-Bakker |
| 10:15-10:30 | Discussion | |
| 10:30-11:00 | ***Refreshment break*** | ***Posters & Exhibition*** |
| 11:00-12:30 | **Free Papers E<br>(10 x 6 min. + 2 min.)** | **Chairs:<br>Rihard Trebše &<br>Lea Papst** |
| 12:30-13:45 | ***Industry Symposium C (12:35-13:35 )*** | ***Lunch & Exhibition*** |
| 13:45-14:45 | **Key Session 8:<br>Spinal Infections** | **Chairs:<br>Martin Clauss &<br>Drago Dolinar** |
| 13:45-14:00 | Vertebral osteomyelitis | Werner Zimmerli |
| 14:00-14:15 | Spinal tuberculosis | Jaime Esteban |
| 14:15-14:30 | Infection after spinal instrumentation | F.C. Öner* |
| 14:30-14:45 | Discussion | |
| 14:45-15:45 | **Free Papers G<br>(7 x 6 min. + 2 min.)** | **Chairs:<br>Rihard Trebše &<br>Samo Jeverica** |
| 15:45-16:15 | ***Refreshment break*** | ***Posters & Exhibition*** |
| 16:15-17:15 | **Free Papers I<br>(7 x 6 min. + 2 min.)** | **Chairs:<br>Drago Dolinar &<br>Lea Papst** |
| 17:30-18:45 | | |
| 20:00-23:00 | **EBJIS Gala Dinner - Grand Hotel Union** | |

*Online presentation

# Friday 8 October 2021

| | Room: Urška, 2nd floor | |
|---|---|---|
| 07:45 | | |
| 08:30-09:30 | | |
| 08:30-08:45 | | |
| 08:45-09:00 | | |
| 09:00-09:15 | | |
| 09:15-09:30 | | |
| 09:30-10:30 | | |
| 09:30-09:45 | | |
| 09:45-10:00 | | |
| 10:00-10:15 | | |
| 10:15-10:30 | | |
| 10:30-11:00 | | |
| 11:00-12:30 | **Free Papers F**<br>**(10 x 6 min. + 2 min.)** | **Chairs:**<br>**Petra Bogovič &**<br>**Samo Jeverica** |
| 12:30-13:45 | | |
| 13:45-14:45 | **Key Session 9:**<br>**Septic Arthritis in Native Joints** | **Chairs:**<br>**Charles Vogely &**<br>**Christof Wagner** |
| 13:45-14:00 | What we know and still don't know about Kingella kingae<br>(13:45-14:05) | Pablo Yagupsky* |
| 14:00-14:15 | Septic arthritis in native joints – Guideline<br>(14:05-14:25) | Christen Ravn &<br>Jeroen Neyt |
| 14:15-14:30 | | |
| 14:30-14:45 | Discussion (14:25-14:45) | |
| 14:45-15:45 | **Free Papers H**<br>**(7 x 6 min. + 2 min.)** | **Chairs:**<br>**Petra Bogovič &**<br>**Rene Mihalič** |
| 15:45-16:15 | | |
| 16:15-17:15 | **Free Papers J**<br>**(7 x 6 min. + 2 min.)** | **Chairs:**<br>**Marko Pokorn &**<br>**Rene Mihalič** |
| 17:30-18:45 | **General Assembly (for EBJIS members, by invitation only)** | |

*Online presentation

# Programme overview

## Saturday 9 October 2021

| | Room: Marmorna Hall, ground floor | |
|---|---|---|
| 08:00 | **Registration at the foyer** | |
| 08:30-09:00 | **Travelling Fellowship Report** | |
| 09:00-10:00 | **Key Session 10: Fracture-Related Infections** | **Chairs: Andrej Trampuz & Boštjan Sluga** |
| 09:00-09:15 | Algorithm on treatment | Mario Morgenstern |
| 09:15-09:25 | Managing Early infection (cases) | Jamie Ferguson |
| 09:25-09:35 | Prevention and treatment of pin infections during external fixation | Martin McNally |
| 09:35-09:45 | Slovenian experience of managing fracture-related infections | Boštjan Sluga |
| 09:45-10:00 | Discussion | |
| 10:00-10:30 | ***Refreshment break*** | ***Posters & Exhibition*** |
| 10:30-12:00 | **Best Papers (10 x 6 min. + 2 min.)** | **Chairs: Irene Sigmund & Martin Clauss** |
| 12:00-12:15 | **Best JBJI Paper** | **Parham Sendi*** |
| 12:15-12:45 | **Honorary lecture: The Future of Infection Prevention** | **Antonia Chen*** |
| 12:45-13:00 | **Closing Remarks & Prizes** | |
| 13:00-14:00 | **Farewell lunch** | ***Posters & Exhibition*** |

*Online presentation

# Programme

**EBJIS** 2021

# Thursday 7 October 2021

| | | Room: Marmorna Hall, ground floor | |
|---|---|---|---|
| 07:00 | | **Registration at the foyer** | |
| 08:30-08:50 | | **Welcome & Opening Ceremony** | **Marko Pokorn & Rihard Trebše** |
| 08:50-09:50 | | **Key session 1: Perceptions in Managing Orthopaedic Infections** | **Chairs: Marko Pokorn & Rihard Trebše** |
| 08:50-09:05 | | Risk and medical decision making | Hansjorg Neth |
| 09:05-09:20 | | How can we investigate bone and joint infections? | Martin McNally |
| 09:20-09:35 | | Antibiotic stewardship in Orthopaedics | Bojana Beović |
| 09:35-10:35 | | **Key session 2: Optimising Antibiotic Treatment of Bone & Joint Infections** | **Chairs: Lea Papst & Marjan Wouthuyzen-Bakker** |
| 09:35-09:50 | | Optimizing PJI treatment – Management adaptation according to the pathogen, patient and surgeon | Andrej Trampuž |
| 09:50-10:00 | | Intravenous or oral antibiotics in PJI | Matthew Scarborough |
| 10:00-10:10 | | Interactions between antibiotics and other drugs | Nataša Faganeli |
| 10:10-10:20 | | Pharmacokinetics of antibiotics in osteoarticular infections | Francoise van Bambeke* |
| 10:20-10:35 | | Discussion | |
| 10:35-11:15 | | ***Refreshment break*** | ***Posters & Exhibition*** |
| 11:15-12:40 | | **Free Papers A (10 x 6 min. + 2 min.)** | **Chairs: Rene Mihalič & Marko Pokorn** |
| 11:15-11:23 | FP A 01 | Outcome Of Streptococcal Prosthetic-Joint Infections | Arnaud Fischbacher |
| 11:23-11:31 | FP A 02 | The Influence Of The Duration Of The Spacer Interval On The Clinical Outcome During Two-Stage Prosthesis Exchange In Septic Hip And Knee Revision Arthroplasty | Jan Pützler |
| 11:31-11:39 | FP A 03 | No Reduction Of Periprosthetic Joint Infection Rates After A National Infection-Control Initiative: An Incidence Study Of 45 438 Primary Total Knee Arthroplasties. | Olof Thompson |
| 11:39-11:47 | FP A 04 | Multicenter Retrospective Observational Study Of Gram-Negative Prosthetic-Joint Infections | Matteo Carlo Ferrari |
| 11:47-11:55 | FP A 05 | Double-Dose Cefuroxime Concentrations In Bone, Synovial Fluid Of The Knee Joint And Subcutaneous Adipose Tissue–A Randomised Porcine Microdialysis Study | Andrea René Jørgensen |
| 11:55-12:03 | FP A 06 | Rifampicin Restores The Metabolic And Bone-Formation Activities Of Osteoblasts After Intracellular Staphylococcus Aureus Infection | Mannala Gopala |
| 12:03-12:11 | FP A 07 | Healing Prognostic Factors After Dair Treatment Of Late Acute Total Knee Arthroplasty Infection | Gloria Pedemonte |
| 12:11-12:19 | FP A 08 | Microbiological Results And Clinical Outcome Of Two-Stage Revisions With Repeat First Stage Procedures In The Treatment Of Periprosthetic Hip And Knee Joint Infections | Bernhard J.H. Frank |
| 12:19-12:27 | FP A 09 | Periprosthetic Joint Infections Are Hard To Capture. A Comparison Between The National Dutch Arthroplasty Registry And A Detailed Regional Periprosthetic Registry. | Jon Goosen* |
| 12:27-12:35 | FP A 10 | Safety Of Tedizolid As Suppressive Antimicrobial Therapy For Patients With Complex Implant-Associated Bone And Joint Infection Due To Multidrug-Resistant Grampositive Pathogens: Results From The Tedisat Cohort Study | Truong-Thanh Pham* |
| 12:35-12:40 | | Discussion | |

*Online presentation

**Room: Urška, 2nd floor**

| 11:15-12:40 | | Free Papers B<br>(10 x 6 min. + 2 min.) | Chairs:<br>Boštjan Sluga &<br>Lea Papst |
|---|---|---|---|
| **11:15-11:23** | FP B 01 | The Characteristics Of Early Fracture-Related Infections In A Large Retrospective Multicenter Cohort Study | Michelle Buijs |
| **11:23-11:31** | FP B 02 | Is The Use Of Guideline-Based Systemic Antibiotics In Fracture Related Infection Correlated With A Favourable Clinical Outcome? | Bridget Atkins |
| **11:31-11:39** | FP B 03 | Can Necrotic Bone Be Objectively Identified In Chronic Fracture Related Infections? — First Clinical Experience With An Intraoperative Fluorescence Imaging Technique | Markus Rupp |
| **11:39-11:47** | FP B 04 | Antibiotic Prescribing For Open Fractures: A Quality Improvement Project To Enhance Boast 4 Attainment | Anja Imsirovic |
| **11:47-11:55** | FP B 05 | What Affects Outcome After Treatment Of Fracture-Related Infection? | Martin McNally |
| **11:55-12:03** | FP B 06 | Management Of Soft-Tissue Reconstruction In Fracture-Related Infection: Orthoplastic Long-Term Outcome And Risk Factor Analysis | Rik Osinga |
| **12:03-12:11** | FP B 07 | High Incidence Of *Enterobacter Cloacae* In Acute Infections Post Osteosynthesis Of Ankle Fractures. Multicenter Study. | Ana Ortega Columbrans |
| **12:11-12:19** | FP B 08 | Are *Cutibacterium acnes* Present At The End Of Primary Shoulder Prosthetic Surgeries Responsible For Total Shoulder Arthroplasty Infection? Prospective Study. | Albert Alier* |
| **12:19-12:27** | FP B 09 | Calprotectin Lateral Flow Test as a rule out test for periprosthetic joint infection | Alison Klika* |
| **12:27-12:35** | FP B 10 | Hiv Infection And Fracture-Related Infections: A Systematic Review And Meta-Analysis | Len Marais* |
| **12:35-12:40** | | Discussion | |

*Online presentation

# Thursday 7 October 2021

| | | Room: Marmorna Hall, ground floor | |
|---|---|---|---|
| 12:40-14:00 | | *Industry Symposium A (12:50-13:50)* | *Lunch & Exhibition* |
| 14:00-15:00 | | **Key session 3: Optimal Bone Infection Sampling and Microbiological Processing** | **Chairs: Petra Bogovič & Alex Soriano** |
| 14:00-14:15 | | The use of histology in the diagnosis of bone and joint infections | Irene Sigmund |
| 14:15-14:30 | | Is innoculation in blood culture bottles for joint aspirates really the best option | Samo Jeverica |
| 14:30-14:45 | | Optimizing the processing of microbiological samples in orthopaedics | Bridget Atkins |
| 14:45-15:00 | | Discussion | |
| 15:00-15:50 | | **Free Papers C (5 x 6 min. + 2 min.)** | **Chairs: Samo Jeverica & Marko Pokorn** |
| 15:00-15:08 | FP C 01 | What Is The Role Of Open Tissue Biopsy In Uncertain Cases Of Low-Grade Infections In Total Knee Arthroplasty? | Jan Pützler |
| 15:08-15:16 | FP C 02 | Metagenomic Nanopore Sequencing For The Diagnosis Of Prosthetic Joint Infections: Can We Do More Than Detect Species From Sonication Fluids? | Teresa Street |
| 15:16-15:24 | FP C 03 | Dithiotreitol And Next Generation Sequencing Show Similar Diagnostic Security As Periprosthetic Tissue Cultures To Diagnose Pji | Ann-Kathrin Meinshausen |
| 15:24-15:32 | FP C 04 | Evaluation Of An Automated Multiplex PCR Joint Infection Panel For The Detection/Identification Of Pathogens In 201 Synovial Fluid Specimens In A Monocentric Study | Frederic Laurent |
| 15:32-15:40 | FP C 05 | Synovial Fluid Testing For The Diagnosis Of Prosthetic Joint Infection According To The New EBJIS Definition – Can Simple And Inexpensive Biomarkers Convey Added Information? | Sara Elisa Diniz |
| 15:40-15:50 | | Discussion | |
| 15:50-16:20 | | *Refreshment break* | *Posters & Exhibition* |
| 16:20-17:20 | | **Key Session 4: Low-Grade PJI – according to the EBJIS definition** | **Chairs: Ricardo Sousa & Marjan Wouthuyzen-Bakker** |
| 16:20-16:35 | | How to define a low-grade PJI | Alex Soriano |
| 16:35-16:50 | | Is *Cutibacterium acnes* really a pathogen? | Yvonne Achtermann |
| 16:50-17:05 | | Surgical approach to a low-grade PJI | Martin Clauss |
| 17:05-17:20 | | Discussion | |
| 17:30-19:30 | | **Welcome Reception - conference venue** | |

*Online presentation

| | | Room: Urška, 2nd floor | |
|---|---|---|---|
| 12:40-14:00 | | *Industry Symposium B (12:50-13:50)* | |
| 14:00-15:00 | | | |
| 14:00-14:15 | | | |
| 14:15-14:30 | | | |
| 14:30-14:45 | | | |
| 14:45-15:00 | | | |
| 15:00-15:50 | | **Free Papers D (5 x 6 min. + 2 min.)** | **Chairs: Lea Papst & Drago Dolinar** |
| 15:00-15:08 | FP D 01 | Microbiological Findings Matter- Determining The Best Possible Antibiotic Treatment For Early, Delayed And Late Fracture-Related Infections | Nike Walter |
| 15:08-15:16 | FP D 02 | Vertebral Osteomyelitis Is Characterized By Increased Rank/Opg And Rankl/Opg Expression Ratios In Vertebral Bodies And Intervertebral Discs. | Siegmund Lang |
| 15:16-15:24 | FP D 03 | Dalbavancin In The Treatment Of Periprosthetic Joint Infections Of The Hip And Knee | Sebastian Simon |
| 15:24-15:32 | FP D 04 | Evaluation of resistance selection by gentamicin and vancomycin loaded calcium sulphate/hydroxyapatite bone graft substitute on bacterial strains responsible for prosthetic joint infection | Elena Di Vecchi |
| 15:32-15:40 | FP D 05 | Photothermaa Eradicates Bacterial Biofilm In A Rabbit Model Of Periprosthetic Joint Infection | Anabelle Visperas* |
| 15:40-15:50 | | Discussion | |
| 15:50-16:20 | | | |
| 16:20-17:20 | | **Key session 5: Musculoskeletal Infections in Children** | **Chairs: Marko Pokorn & Markus Pääkkönen** |
| 16:20-16:35 | | Diagnostic approaches in children with OAI | Jesús Saavedra-Lozano |
| 16:35-16:50 | | The role of the orthopaedic surgeon in paediatric osteoarticular infections | Markus Pääkkönen |
| 16:50-17:05 | | Shortening the duration of antimicrobial treatment in paediatric OAI – Where is the limit? | Saul Faust* |
| 17:05-17:20 | | Discussion | |
| 17:30-19:30 | | | |

*Online presentation

| | | Room: Marmorna Hall, ground floor | |
|---|---|---|---|
| 07:45 | | **Registration at the foyer** | |
| 08:30-09:30 | | **Key Session 6: Uncommon Infections** | **Chairs: Klaus Kirketerp Møller & Rene Mihalič** |
| 08:30-08:45 | | Small orthopedic implant associated infection | Volker Alt |
| 08:45-09:00 | | Infection after ACL reconstruction | Daniel Pérez-Prieto |
| 09:00-09:15 | | Infection of the hands (bites mycobateria) | Nicholas Riley* |
| 09:15-09:30 | | Discussion | |
| 09:30-10:30 | | **Key Session 7: Non-Operative Management of Chronic Infections** | **Chairs: Olivier Borens & Ferdinando Da Rin de Lorenzo** |
| 09:30-09:45 | | Living with a leaking hole in the limb | Mathias Glehr |
| 09:45-10:00 | | Conservative management of chronic infections: Experience with subcutaneous antimicrobial suppressive treatment and bacteriophages | Tristan Ferry |
| 10:00-10:15 | | PJI sinus tract : do we need antibiotics or not? | Marjan Wouthuyzen-Bakker |
| 10:15-10:30 | | Discussion | |
| 10:30-11:00 | | ***Refreshment break*** | ***Posters & Exhibition*** |
| 11:00-12:30 | | **Free Papers E (10 x 6 min. + 2 min.)** | **Chairs: Rihard Trebše & Lea Papst** |
| 11:00-11:08 | FP E 01 | The European Bone And Joint Infection Society Prosthetic Joint Infection Definition Is More Sensitive And Performs Better In Ruling Out Infection Preoperatively Than Previous Definitions | Ana Ribau |
| 11:08-11:16 | FP E 02 | Predictive Modeling With Next Generation Sequencing: A Validated Multi-Institutional Adjunct For Diagnosis Of Periprosthetic Joint Infection | Karan Goswami |
| 11:16-11:24 | FP E 03 | What Are The Optimal Cut-Off Values For Synovial Fluid Leukocyte Count And Differential In The Detection Of Prosthetic Hip Infection? | Rene Mihalic |
| 11:24-11:32 | FP E 04 | Role Of Serum D-Dimer And Fibrinogen Values In The Diagnosis Of Peri-Prosthetic Knee Infection: Results Of A Prospective Multicenter Study. | Nicola Logoluso |
| 11:32-11:40 | FP E 05 | Reinfection Or Persistence Of Periprosthetic Joint Infection? Next Generation Sequencing Reveals New Findings | Karan Goswami |
| 11:40-11:48 | FP E 06 | Performance Of Routinely Available Serum Parameters In Diagnosing Periprosthetic Joint Infections | Irene Katharina Sigmund |
| 11:48-11:56 | FP E 07 | Synovial Fluid Viscosity Measurement; An Important Diagnostic Procedure In Prosthetic Joint Infections Diagnostics | Samo Roskar |
| 11:56-12:04 | FP E 08 | Is Joint Aspiration To Rule Out Prosthetic Joint Infection Required Before Every Revision Joint Arthroplasty? Validation Of Institutional Criteria Using The New European Bone And Joint Infection Society Definition | André Vinha |
| 12:04-12:12 | FP E 09 | Serum D-Dimer Can Predict Failure Following Reimplantation | Karan Goswami |
| 12:12-12:20 | FP E 10 | The Calprotectin Lateral Flow Test For The Diagnosis Of Prosthetic Joint Infections When The Recommended Algorithms Do Not Apply | Igor Lazic* |
| 12:20-12:30 | | Discussion | |

*Online presentation

| | | Room: Urška, 2nd floor | |
|---|---|---|---|
| 07:45 | | | |
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| 10:30-11:00 | | | |
| **11:00-12:30** | | **Free Papers F (10 x 6 min. + 2 min.)** | **Chairs: Petra Bogovič & Samo Jeverica** |
| **11:00-11:08** | FP F 01 | Influence Of Ceftriaxone On Human Bone Cell Viability And Mineralization Potential - An Vitro Study | Peter Wahl |
| **11:08-11:16** | FP F 02 | Vancomycin Bone And Tissue Concentrations Following Tibial Intraosseous Administration – Evaluated In A Porcine Model | Josephine Olsen Kipp |
| **11:16-11:24** | FP F 03 | Inflammatory Bowel Diseases Increase The Risk Of Periprosthetic Joint Infection | Emanuele Chisari |
| **11:24-11:32** | FP F 04 | Periprosthetic Fungal Infections – An Analysis Of 29 Cases From A Single Center | Christoph Theil |
| **11:32-11:40** | FP F 05 | Liposomal Amphotericin B Local Antifungal Therapy: Five Years Of Clinical Use | Maria Dudareva |
| **11:40-11:48** | FP F 06 | The Influence Of Unsuspected Intraoperative Positive Cultures In Aseptic Total Hip Revision Surgery | Jan Pützler |
| **11:48-11:56** | FP F 07 | Synovial Commercial Antibody Testing Does Not Provide Vantage Compared To Traditional Culture In The Microbial Identification Of Periprosthetic Joint Infection | Emanuele Chisari |
| **11:56-12:04** | FP F 08 | Demonstration Of Local Acute Phase Response During Osteomyelitis | Louise Kruse Jensen |
| **12:04-12:12** | FP F 09 | Squamous Cell Carcinoma Complicating Chronic Osteomyelitis: A Systematic Review And Case Series | Martin McNally |
| **12:12-12:20** | FP F 10 | Plasma-Cell Infiltration On Histopathological Samples Of Chronic Bone And Joint Infections Due To *Cutibacterium acnes*: A Series Of 25 Cases | Alexis Trecourt* |
| **12:20-12:30** | | Discussion | |

*Online presentation

| | | Room: Marmorna Hall, ground floor | |
|---|---|---|---|
| 12:30-13:45 | | *Industry Symposium C (12:35-13:35 )* | *Lunch & Exhibition* |
| 13:45-14:45 | | **Key Session 8: Spinal Infections** | **Chairs: Martin Clauss & Drago Dolinar** |
| 13:45-14:00 | | Vertebral osteomyelitis | Werner Zimmerli |
| 14:00-14:15 | | Spinal tuberculosis | Jaime Esteban |
| 14:15-14:30 | | Infection after spinal instrumentation | F.C. Öner* |
| 14:30-14:45 | | Discussion | |
| 14:45-15:45 | | **Free Papers G (7 x 6 min. + 2 min.)** | **Chairs: Rihard Trebše & Samo Jeverica** |
| 14:45-14:53 | FP G 01 | A High Prevalence Of *Cutibacterium Acnes* Infections In Scoliosis Revision Surgery,A Diagnostic And Therapeutic Dilemma | Marjan Wouthuyzen-Bakker |
| 14:53-15:01 | FP G 02 | Antimicrobial Susceptibility Of Isolated Pathogens From Pyogenic Spondylodiscitis: A Comparison Of Community-Acquired And Healthcare-Associated Infections. | Siegmund Lang |
| 15:01-15:09 | FP G 03 | Effects Of Rifampicin On Moxifloxacin Concentrations In Porcine Cervical Spine: A Randomized Microdialysis Study | Mats Bue |
| 15:09-15:17 | FP G 04 | Orthoplastics In Periprosthetic Joint Infection Of The Knee: Treatment Concept For Composite Soft-Tissue Defect With Extensor Apparatus Deficiency | Rik Osinga |
| 15:17-15:25 | FP G 05 | Uniplanar Versus Biplanar Monolateral External Fixator Knee Arthrodesis After End-Stage Failed Infected Total Knee Arthroplasty: A Comparative Study | Maria Jurado Ruiz |
| 15:25-15:33 | FP G 06 | Vacuum Assisted Closure (Vac)-Instill Spacer In Septic Two-Stage Revision Total Knee Arthroplasty – A Pilot Study | Mathias Glehr |
| 15:33-15:41 | FP G 07 | Management Of Chronic Femoral And Tibial Osteomyelitis: A Systematic Scoping Review | Aiman Aslam* |
| 15:41-15:45 | | Discussion | |
| 15:45-16:15 | | *Refreshment break* | *Posters & Exhibition* |
| 16:15-17:15 | | **Free Papers I (7 x 6 min. + 2 min.)** | **Chairs: Drago Dolinar & Lea Papst** |
| 16:15-16:23 | FP I 01 | Should All Patients Diagnosed With A Culture Negative Periprosthetic Joint Infection Be Treated With Antibiotics? A Multicenter Observational Study | Marjan Wouthuyzen-Bakker |
| 16:23-16:31 | FP I 02 | DAIR After Revision Arthroplasty: Success Rate Comparable To DAIR After Primary Arthroplasty But Antimicrobial Mismatch Is A Risk Factor For Failure | Karin Veerman |
| 16:31-16:39 | FP I 03 | Early Periprosthetic Joint Infection After Revision Arthroplasty: New Ingredients To Select Empirical Treatment | Karin Veerman |
| 16:39-16:47 | FP I 04 | Long-Term Patient-Related Quality Of Life After Knee Periprosthetic Joint Infection | Nike Walter |
| 16:47-16:55 | FP I 05 | Predisposing Factors For Failure In PJI: are Gram-Negative Multidrug Resistant Bacterial Infections Increasing The Rate Of Failure? | Salles Mauro Salles* |

*Online presentation

| | | Room: Urška, 2nd floor | |
|---|---|---|---|
| **12:30-13:45** | | | |
| **13:45-14:45** | | **Key Session 9:**<br>**Septic Arthritis in Native Joints** | **Chairs:**<br>**Charles Vogely &**<br>**Christof Wagner** |
| **13:45-14:00** | | What we know and still don't know about Kingella kingae<br>(13:45-14:05) | Pablo Yagupsky* |
| **14:00-14:15** | | Septic arthritis in native joints – Guideline<br>(14:05-14:25) | Christen Ravn &<br>Jeroen Neyt |
| **14:15-14:30** | | | |
| **14:30-14:45** | | Discussion (14:25-14:45) | |
| **14:45-15:45** | | **Free Papers H**<br>**(7 x 6 min. + 2 min.)** | **Chairs:**<br>**Petra Bogovič &**<br>**Rene Mihalič** |
| **14:45-14:53** | FP H 01 | Assessing Pre-Referral Microbiology In Osteomyelitis: What Does It Tell Us? | Andrew Hotchen |
| **14:53-15:01** | FP H 02 | The Value Of Neutrophil-Lymphocyte Ratio, Platelet-Lymphocyte Ratio, Monocyte-Lymphocyte Ratio And Platelet Count-Mean Platelet Volume Ratio In The Diagnosis Of Septic Arthritis | Bedri Karaismailoglu |
| **15:01-15:09** | FP H 03 | Chronic And Acute Periprosthetic Joint Infections Could Be The Result Of Damage To The Integrity Of The Gut Epithelial Barrier | Emanuele Chisari |
| **15:09-15:17** | FP H 04 | Organism Profile Causing Periprosthetic Joint Infection: The List Is Growing | Santiago Restrepo |
| **15:17-15:25** | FP H 05 | Timing Of Antimicrobial Prophylaxis And Tourniquet Inflation -<br>A Randomized Controlled Microdialysis Study | Pelle Hanberg |
| **15:25-15:33** | FP H 06 | Laminar Air Flow Does Not Have A Protective Effect On The Rate Of Periprosthetic Joint Infection After Primary Total Joint Arthroplasty | Karan Goswami |
| **15:33-15:41** | FP H 07 | Does Early Antibiotic Administration Affect Culture Yields And Clinical Outcomes In Septic Arthritis Patients? | Antonia Chen* |
| **15:41-15:45** | | Discussion | |
| **15:45-16:15** | | | |
| **16:15-17:15** | | **Free Papers J**<br>**(7 x 6 min. + 2 min.)** | **Chairs:**<br>**Marko Pokorn &**<br>**Rene Mihalič** |
| **16:15-16:23** | FP J 01 | Does Local Implantation Of Gentamicin Impair Renal Function In Patients Undergoing Surgery For Chronic Osteomyelitis And Fracture-Related Infection? | Martin McNally |
| **16:23-16:31** | FP J 02 | Perioperative Myocardial Injury And Mortality After Revision Surgery For Major Musculoskeletal Infection | Mario Morgenstern |
| **16:31-16:39** | FP J 03 | Efficacy Of Various Surgical Irrigation Solutions Against Established Biofilm: A Comparative In Vitro Investigation | Karan Goswami |
| **16:39-16:47** | FP J 04 | Extraspinal Osteoarticular Tuberculosis, About 40 Cases | Mohamed Ben Jemaa |
| **16:47-16:55** | FP J 05 | Analysis Of Biofilm Formation In Anterior Cruciate Ligament Plasties. Comparative In Vitro Study | Daniel Perez-Prieto |

*Online presentation

| | | Room: Marmorna Hall, ground floor | |
|---|---|---|---|
| **16:55-17:03** | FP I 06 | International Organism Profile Of Periprosthetic Total Hip And Knee Infections | Alison Klika* |
| **17:03-17:11** | FP I 07 | Symptom Duration Is Associated With Failure Of Periprosthetic Joint Infection Treated With Dair | Hongyi Shao* |
| **17:11-17:15** | | Discussion | |
| **17:30-18:45** | | | |
| **20:00-23:00** | | **EBJIS Gala Dinner - Grand Hotel Union** | |

*Online presentation

| | | Room: Urška, 2nd floor | |
|---|---|---|---|
| **16:55-17:03** | FP J 06 | Validation And Relevance Of In Vivo Biofilm Model Galleria Mellonella To Study Implant-Associated Bacterial Biofilms | Gopala Mannala |
| **17:03-17:11** | FP J 07 | A Novel Activated-Zinc Antiseptic Solution Effective Against *Staphylococcus Aureus* And *Pseudomonas Aeruginosa* In A Pig Model | Derek Hill* |
| **17:11-17:15** | | Discussion | |
| **17:30-18:45** | | **General Assembly (for EBJIS members, by invitation only)** | |

*Online presentation

# Saturday 9 October 2021

| | | Room: Marmorna Hall, ground floor | |
|---|---|---|---|
| 08:00 | | **Registration at the foyer** | |
| 08:30-09:00 | | **Travelling Fellowship Report** | |
| 09:00-10:00 | | **Key Session 10:<br>Fracture-Related Infections** | **Chairs:<br>Andrej Trampuz &<br>Boštjan Sluga** |
| 09:00-09:15 | | Algorithm on treatment | Mario Morgenstern |
| 09:15-09:25 | | Managing Early infection (cases) | Jamie Ferguson |
| 09:25-09:35 | | Prevention and treatment of pin infections during external fixation | Martin McNally |
| 09:35-09:45 | | Slovenian experience of managing fracture-related infections | Boštjan Sluga |
| 09:45-10:00 | | Discussion | |
| 10:00-10:30 | | ***Refreshment break*** | ***Posters & Exhibition*** |
| 10:30-12:00 | | **Best Papers<br>(10 x 6 min. + 2 min.)** | **Chairs:<br>Irene Sigmund &<br>Martin Clauss** |
| 10:30-10:38 | BP01 | In Patients With Bone And Joint Infection, Six And Twelve Weeks Of Antimicrobial Therapy Seems To Have A Similar Impact On The Gut Microbiota And No Particular Antibiotic Seems To Impact Its Recovery | Tristan Ferry |
| 10:38-10:46 | BP02 | Bone And Joint Infections: Synergistic Antibiofilm Effect Of Exebacase And Antibiotics Against *Staphylococcus epidermidis* Strains | Frederic Laurent |
| 10:46-10:54 | BP03 | Quality of Life in patients with chronic osteomyelitis referred to a tertiary bone infection centre | Andrew Hotchen |
| 10:54-11:02 | BP04 | If, When, And How To Use Rifampin In Acute Staphylococcal Periprosthetic Joint Infections, A Multicentre Observational Study | Marjan Wouthuyzen-Bakker |
| 11:02-11:10 | BP05 | Is The European Bone And Joint Infection Society Definition Of Prosthetic Joint Infection Meaningful In Our Clinical Practice?<br>- A Multicentric Validation Study | Ricardo Sousa |
| 11:10-11:18 | BP06 | Comparison Of A High-Virulent Versus A Low-Virulent *Staphylococcus aureus* Strain In A Murine Fracture-Related Infection Model. | Susanne Bärtl |
| 11:18-11:26 | BP07 | The Joint-Specific BACH Classification: A Predictor Of Outcome In Prosthetic Joint Infection. | Andrew Hotchen |
| 11:26-11:34 | BP08 | Shotgun Metatranscriptomics For Pji Diagnosis: A Novel Prospective Investigation | Karan Goswami |
| 11:34-11:42 | BP09 | Development Of Phage Therapy To Treat Staphylococci Bone And Joint Infections In France: Isolation And Characterization Of Seventeen Novel Anti-Staphylococcus Bacteriophages | Camille Kolenda |
| 11:42-11:50 | BP10 | Microbiological And Ultrastructural Evaluation Of The 191219 S. Aureus Bacteriophage Activity Against Planktonic, Intracellular And Biofilm Infection With *Staphylococcus aureus* | Gopala Mannala |
| 11:50-12:00 | | Discussion | |
| 12:00-12:15 | | **Best JBJI Paper** | **Parham Sendi*** |
| 12:15-12:45 | | **Honorary lecture: The Future of Infection Prevention** | **Antonia Chen*** |
| 12:45-13:00 | | **Closing Remarks & Prizes** | |
| 13:00-14:00 | | **Farewell lunch** | ***Posters & Exhibition*** |

*Online presentation

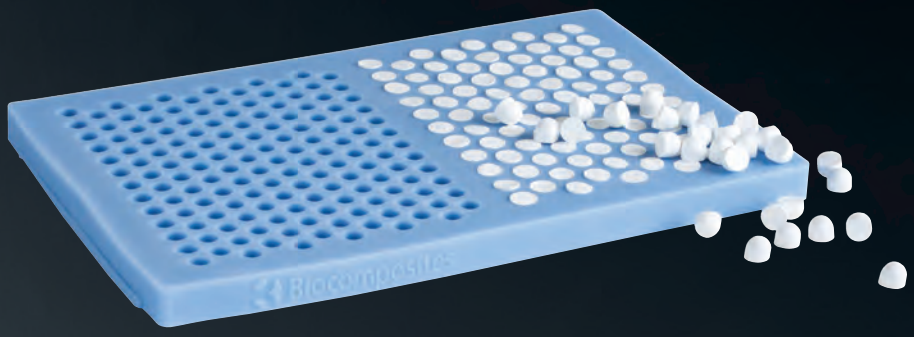
# Industry symposia

# STIMULAN®

POWER TO TRANSFORM OUTCOMES™

## Perfect partner for carrying antibiotics

- ✓ The only calcium matrix approved for use in bone and soft tissue
- ✓ Approved for mixing with vancomycin, gentamicin and tobramycin
- ✓ Can be placed directly into infected and non-infected sites




Discover more by downloading
Biocomposites Companion

Download on the App Store

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For indications, contraindications, warnings and precautions see Instructions for Use. Concurrent use of locally administered antibiotics may affect setting time, absorption characteristics and/or bone formation. It is the surgeon/healthcare professional's responsibility to give due consideration to the details in the medicinal product marketing authorisation in deciding whether it is appropriate for the patient under his/her care. The relevant Summary of Product Characteristics (SmPC) must be consulted. The type and dose of medicinal substance should also be assessed according to the individual patient's clinical circumstance. This brochure may include the use of STIMULAN or techniques that go beyond the current clearance/approval granted by the relevant regulatory authority. Please contact your local representative for further information.



Patents granted: GB2367552, EP 1204599 B1, US 6780391, EP 2594231 B1, US 88883063, CN ZL201210466117.X, GB2496710, EP 3058899 B1, US 10390954
Patents pending: GB1502655.2, US 15/040075, CN 201610089710.5, GB1704688.9, EP 18275044.8, US 15/933936, CN 108619579A



Biocomposites®

# Industry Symposia A

Biocomposites®

**Thursday, October 7, 12:50 - 13:50**
Room: Marmorna Hall, ground floor

**The role of STIMULAN® as a local antibiotic carrier in complex infected bone and soft tissue cases**

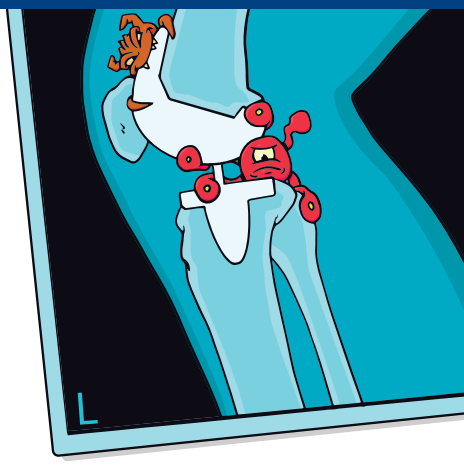
**Agenda**
- Understanding the enemy – Resistance and Persistence
- Clinical challenges in resolving implant-related infections
- The importance of local antibiotic carriers
- The relevance of antibiograms and breakpoints in the context of local antibiotic carriers
- Antibiotic resistance: are we fighting a futile battle against a more patient and powerful enemy?

**Speaker**
PD Dr. med. Andrej Trampuz
Head of Infectiology and Septic Surgery at Charité – Universitätsmedizin Berlin

PIONEERING DIAGNOSTICS

BIOMÉRIEUX

# BioFire® Joint Infection Panel*




## 1 Test. 39 Targets. ~1 Hour.

***Investigational use only. Not intended for use in diagnostic procedures. Not available for sale. Under review by the FDA, panel menu subject to change.**

## BioFire Joint Infection Panel Targets

### GRAM-POSITIVE BACTERIA

*Anaerococcus prevotii/vaginalis*
*Clostridium perfringens*
*Cutibacterium avidum/granulosum*
*Enterococcus faecalis*
*Enterococcus faecium*
*Finegoldia magna*
*Parvimonas micra*
*Peptoniphilus*
*Peptostreptococcus anaerobius*
*Staphylococcus aureus*
*Staphylococcus lugdunensis*
*Streptococcus* spp.
- *Streptococcus agalactiae*
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*

### GRAM-NEGATIVE BACTERIA

*Bacteroides fragilis*
*Citrobacter*
*Enterobacter cloacae* complex
*Escherichia coli*
*Haemophilus influenzae*
*Kingella kingae*
*Klebsiella pneumoniae* group
*Morganella morganii*
*Neisseria gonorrhoeae*
*Proteus* spp.
*Pseudomonas aeruginosa*
*Salmonella* spp.
*Serratia marcescens*

### YEAST

*Candida* spp.
- *Candida albicans*

### ANTIMICROBIAL RESISTANCE GENES

**Carbapenemases**
IMP
KPC
NDM
OXA-48-like
VIM

**ESBL**
CTX-M

**Methicillin Resistance**
*mecA/C* and MREJ

**Vancomycin Resistance**
*vanA/B*

### Fast Turnaround Time

- Uses multiplex PCR to deliver results in about an hour
- Requires only 0.2mL of synovial fluid
- Simultaneous detection and identification of bacteria, fungi, and antimicrobial resistance genes

### Proposed Broad Menu

- Detects the majority of pathogens causing joint infections
- Detects 8 antimicrobial resistance markers, helping guide targeted therapy
- Detects fastidious organisms and difficult-to-grow anaerobes[1]

BIOFIRE®

**VISIT US AT BOOTH #17**

1. Kensinger B, et al. Evaluation of the BioFire® Bone and Joint Infection (BJI) Panel for the detection of microorganisms and resistance markers in synovial fluid specimens [abstract]. ECCMID 2020; Paris, France.

BFR0001-5058-01

# Industry Symposia B


**Thursday, October 7, 12:50–13:50**
Room: Urška, 2nd floor

**Syndromic Testing for the Diagnosis of Septic Arthritis and Prosthetic Joint Infections: the BioFire® Joint Infection Panel***

**Agenda**
- Welcome Remarks
- A Preview of the BioFire® Joint Infection (JI) Panel*
- How Can Rapid Syndromic Testing Help in the Diagnosis of Joint Infections?
- Questions and Answers"

**Speakers**

Dr. Marjan Wouthuyzen-Bakker
Internist-infectiologist - University Medical Center Groningen (Groningen - The Netherlands)

Prof. Frédéric Laurent
Medical Microbiologist - Hôspital de La Croix Rousse (Lyon - France)

Dr. Sébastien Spinali
Vice President EME Medical Affairs - bioMérieux (Lyon - France)

Dr. Bart Kensinger
Associate Director Clinical Affairs - BioFire Diagnostics, a bioMérieux Company (Salt Lake City (UT) - USA)

Dr. Jaime Esteban
Associate Physician of the Department of Clinical Microbiology - Fundación Jiménez Diaz (Madrid - Spain)

*Investigational use only. Not intended for diagnostic procedure. Not available for sale. Under review by the FDA, panel menu subject to change

# Welcome to our Symposium

BONESUPPORT™

Friday the 8th October 2021
12:35 - 13:35
Room: Marmorna Hall

European Bone & Joint Infection Society EBJIS

## Improving the patient experience of bone infection - Get it right the first time

This symposium will be presented as a discussion of varied infection cases, discussed with an expert multidisciplinary team

- Welcome and introduction to the Oxford experience - Prof. McNally
- Case presentation - Dr. Olsen
- Case presentation - Dr. Spranger
- Case presentation - Mr. Ferguson
- Panel discussion and questions from the audience - All
- Summary and take home messages - Prof. McNally

Panel:
**Prof. Martin McNally,** Lead Consultant in Limb Reconstruction Surgery, Oxford Bone Infection Unit in the Nuffield Orthopaedic Centre, Oxford University Hospitals, UK
**Dr. Rik Osinga,** Specialist in Plastic, Reconstructive and Aesthetic Surgery at Universitätsspital Basel
**Dr. Marjan Wouthuyzen-Bakker,** Infectious Disease Specialist, Department of Medical Microbiology and Infection Prevention, University of Groningen

Case presenters:
**Dr. Claes Olsen,** MD Specialist, Department of Orthopaedic Surgery, Sahlgrenska University Hospital, Gothenburg
**Dr. med. Nikolai Spranger,** Managing Senior Consultant, Department of Orthopaedic and Trauma Surgery, BG Unfallkrankenhaus Berlin
**Mr. Jamie Ferguson,** Consultant in Limb Reconstruction Surgery and Trauma, Oxford Bone Infection Unit and Oxford Trauma Unit, Oxford University Hospitals, UK

# Industry Symposia C


**Friday, 8 October, 12:35-13:35**
Room: Marmorna Hall, ground floor

**Improving the patient experience of bone infection - Get it right the first time**

**Agenda**
- Welcome and introduction to the Oxford experience
- Case presentations
- Panel discussions and questions from the audience
- Summary and take home messages

**Speakers:**

**Panel**

Prof. Martin McNally
Lead Consultant in Limb Reconstruction Surgery, Oxford Bone Infection Unit in the Nuffield Orthopaedic Centre, Oxford University Hospitals, UK

Dr. Rik Osinga
Specialist in Plastic, Reconstructive and Aesthetic Surgery at Universitätsspital Basel

Dr. Marjan Wouthuyzen-Bakker
Infectious Disease Specialist, Department of Medical Microbiology and Infection Prevention, University of Groningen

**Case presenters**

Dr. Claes Olsen
MD Specialist, Department of Orthopaedic Surgery, Sahlgrenska University Hospital, Gothenburg

Dr. med. Nikolai Spranger
Managing Senior Consultant, Department of Orthopaedic and Trauma Surgery, BG Unfallkrankenhaus Berlin

Mr. Jamie Ferguson
Consultant in Limb Reconstruction Surgery and Trauma, Oxford Bone Infection Unit and Oxford Trauma Unit, Oxford University Hospitals, UK

Heraeus

Medical

IMPROVE THE CHANCES

# REDUCE RISK FOR INFECTION

## COPAL® G+C

**Reduction of infection risk* using dual antibiotic-loaded bone cement in high risk patients**

↓ 34% in primary hip & knee arthroplasty

↓ 69% in fractured neck of femur

↓ 57% in aseptic revision TKA

* as reported in study results

www.heraeus-medical.com

10699

# Exhibitor directory

**EBJIS** 2021

# Platinum Partners

| Company | Contact details | Company description |
|---|---|---|
| Biocomposites | **Biocomposites Ltd**<br>www.biocomposites.com<br>Booth 4 | At Biocomposites, we are distinct in that our team of specialists is singularly focused on the development of innovative calcium compounds for surgical use. With over 30 years' experience and an unrivalled dedication to quality, the products we research, engineer and manufacture are at the forefront of calcium technology. 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**<br>www.bonesupport.com<br>Booth 3 | 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®\|G with gentamicin, and CERAMENT® V with vancomycin. |
| Heraeus | **Heraeus Medical GmbH**<br>www.heraeus.com<br>Booth 13 | 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 |
|---|---|---|
|  | **Biomérieux**<br>www.biomerieux.com<br>Booth 17 | A world leader in the field of in vitro diagnostics for over 50 years, bioMérieux provides fast & robust technologies that support clinicians in making informed decisions from actionable results. Our future BioFire® Joint Infection Panel will detect multiple bacteria, fungi, and antimicrobial resistance genes directly from a single patient sample with results available in about 1 hour. |
|  | **InfectoPharm**<br>www.infectopharm.com<br>Booth 15 | InfectoPharm is a family-owned company located in Germany. With IV FOSFOMYCIN (product names Fomicyt®, InfectoFos® and Fosfomycin InfectoPharm), InfectoPharm offers a therapeutic option to fight severe infections in a broad indication spectrum. It is an antibiotic of it´s own class with unique product characteristics: unique mode of action, a tissue penetration champion, capable of penetrating tissue with poor accessibility with high bactericidal levels with broad spectrum against Gram positive and - negative pathogens including MDR bacteria. |
|  | **Lyfstone AS**<br>www.lyfstone.com<br>Booth 2 | Lyfstone AS provides the orthopaedic health care professionals with a point-of-care test for ruling out Prosthetic Joint Infection (PJI) by measuring the levels of Calprotectin in synovial fluid. Rapidly ruling out infection creates the opportunity for same-day diagnostics for evidence-based decisions and patient flow. Lyfstone® Calprotectin for synovial fluid is a quantitative, accurate, cost-saving and efficient tool providing results within 15 minutes. The test is a diagnostic aid for screening of suspected PJI patients. |

## Silver Partner

| Company | Contact details | Company description |
|---|---|---|
| ECTB | **EUROPEAN CELL AND TISSUE BANK**<br>www.ectb.eu<br>Booth 14 | EUROPEAN CELL AND TISSUE BANK, a non-profit association, based in Austria. In compliance with the EU directives, we procure, store, processes and distribute tissue, and offer with OSmycin™, a human bone allograft, impregnated with antibiotics (Vancomycin or Tobramycin). OSmycin™ for simultaneously preventing infection and biofilm while reconstructing of bone defects. |

## Bronze Partners

| Company | Contact details | Company description |
|---|---|---|
| bonalive | **Bonalive Biomaterials Ltd**<br>www.bonalive.com<br>Booth 8 | 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 |
| G21 STRENGTH FOR LIFE | **G21**<br>www.g21.it<br>Booth 10 | G21 is a leading developer and manufacturer of bone cements and acrylic resins with long experience in orthopedics, orthopaedic oncology and minimal invasive spine surgery.<br>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. |
| Johnson & Johnson | **Johnson & Johnson**<br>www.jnjmedicaldevices.com<br>Booth 6 | For over 130 years, Johnson & Johnson has maintained a tradition of quality and innovation with manufacturing products in medical devices industry, pharmaceuticals and consumer packaged goods. |
| RESORBA BIOSURGICALS | **Resorba**<br>www.resorba.com<br>Booth 5 | RESORBA's core competencies lie in the manufacturing and distribution of collagen products for all surgical disciplines for more than 89 years. |
| TECRES | **Tecres**<br>www.tecres.it<br>Booth 9 | TECRES has got nearly forty 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. |

# Exhibitors

| Company | Contact details |
|---|---|
| curasan Regenerative Medicine | **Curasan**<br>www.curasan.de<br>Booth 12 |
| NuVasive Specialized Orthopedics | **NuVasive Specialized Orthopedics, Inc.**<br>www.nuvasive.com<br>Booth 11 |
| OSARTIS | **Osartis**<br>www.osartis.de<br>Booth 16 |

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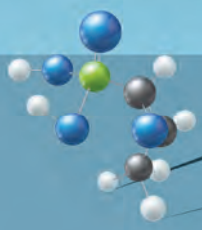

IV Fosfomycin1 is indicated for treatment of the following infections, recently endorsed by the European Medicines Agency (EMA):

- Bone and joint infections
- HAP, including VAP[2]
- Bacterial meningitis
- Complicated urinary tract infections
- Complicated intra-abdominal infections
- Infective endocarditis
- Complicated skin and soft tissue infections
- Bacteraemia[3]

**Name and active ingredients:** Fomicyt 40 mg/ml powder for solution for infusion. One ml of reconstituted solution contains 40 mg fosfomycin. 2 g presentation: Each bottle with 2.69 g of powder contains 2.64 g disodium fosfomycin, corresponding to 2 g fosfomycin and 0.64 g sodium, for reconstitution in 50 ml of solvent. Fomicyt 4 g presentation: Each bottle with 5.38 g of powder contains 5.28 g disodium fosfomycin, corresponding to 4 g fosfomycin and 1.28 g sodium, for reconstitution in 100 ml of solvent. Fomicyt 8 g presentation: Each bottle with 10.76 g of powder contains 10.56 g disodium fosfomycin, corresponding to 8 g fosfomycin and 2.56 g sodium, for reconstitution in 200 ml of solvent **Indications:** Treatment of the following infections in all age groups when it is considered inappropriate to use antibacterial agents that are commonly recommended for their initial treatment: complicated urinary tract infections, infective endocarditis, bone and joint infections, hospital-acquired pneumonia, including ventilator-associated pneumonia, complicated skin and soft tissue infections, bacterial meningitis, complicated intra-abdominal infections, bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above. Consideration should be given to official guidance on the appropriate use of antibacterial agents. **Dosage and administration:** Adults and adolescents 12 years, > 40 kg and with normal renal function (creatinine clearance > 80 ml/min): complicated urinary tract infection 12–24 g in 2–3 divided doses, bone and joint infections 12–24 g in 2–3 divided doses, infective endocarditis 12-24 g in 2–3 divided doses, hospital-acquired pneumonia including ventilator-associated pneumonia 12–24 g in 2–3 divided doses; complicated skin and soft tissue infections 12–24 g in 2–3 divided doses; bacterial meningitis 16–24 g in 3–4 divided doses; complicated intra-abdominal infections 12–24 g in 2–3 divided doses; bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above 12–24 g in 2–3 divided doses. Individual doses must not exceed 8 g. Dose reductions in patients with renal impairment are required (please refer to the SmPC for further information). Paediatric population: for neonates, infants and children <12 years of age (<40 kg) the dosage should be based on age and body weight (please refer to the SmPC for further information). Method of administration: intravenous infusion only. The solvent must be water for injections, 5% or 10% glucose infusion. The duration of infusion should be at least 15 minutes for the 2 g pack size, at least 30 minutes for the 4 g pack size and at least 60 minutes for the 8 g pack size. Please refer to the SmPC for further information. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. **Special warnings and precautions:** It is recommended that fosfomycin is administered as part of a combination antibacterial drug regimen to reduce the risk of selecting for resistance. It is recommended that fosfomycin is selected to treat the listed indications only when it is considered inappropriate to use antibacterial agents that are commonly recommended for their initial treatment. Serious and occasionally fatal hypersensitivity reactions, including anaphylaxis and anaphylactic shock, may occur during fosfomycin treatment. If such reactions occur, treatment with fosfomycin must be discontinued immediately and adequate emergency measures must be initiated.. Antibacterial agent-associated colitis and pseudo-membranous colitis have been reported. It is important to consider this diagnosis in patients presenting with diarrhoea during or subsequent to administration of Fomicyt. Sodium and potassium levels should be monitored regularly in patients receiving fosfomycin, in particular during prolonged treatment. Given the high content of sodium (0.32 grams) per gram of fosfomycin, the risk of hypernatraemia and fluid overload should be assessed before starting treatment, especially in patients with a history of congestive heart failure or underlying comorbidities such as nephrotic syndrome, liver cirrhosis, hypertension, pulmonary oedema or hypoalbuminemia as well as in neonates under sodium restriction. A low-sodium diet is recommended during treatment. An increase in the infusion length and/or a reduction to the individual dose (with more frequent administration) could also be considered. Fosfomycin may decrease potassium levels in serum or plasma, therefore potassium supplementation should be always considered. In patients receiving fosfomycin intravenously haematological reactions including neutropenia or agranulocytosis have occurred. Please refer to the SmPC for further information. **Interactions:** Numerous cases of increased oral anticoagulant activity have been reported in patients receiving antibiotic therapy. The severity of the infection or inflammation, patient age and general state of health appear to be risk factors. Under these circumstances, it is difficult to determine to what extent the infection itself or its treatment play a role in the INR imbalance. However, certain classes of antibiotics are more involved, particularly: fluoroquinolones, macrolides, cyclins, cotrimoxazole, and certain cephalosporins. **Undesirable effects (see SmPC for full details):** Common: dygeusia, hypernatraemia, hypokalemia, erythematous eruption, injection site phlebitis. Uncommon: headache, nausea, vomiting, diarrhea, blood alkaline phosphatase increased (transient), transaminases increased (ALAT, ASAT), gamma-GT increased, rash, asthenia. Very rare: anaphylactic reactions including anaphylatic shock and hypersensitivity, Unknown frequency: agranulocytosis (transient), leucopenia, thrombocytopenia, neutropenia, antibiotic-associated colitis, hepatitis, pruritus, urticaria, angioedema. Please refer to the SmPC for further information. **Pack size:** 30/50/100 ml clear glass bottle with rubber stopper and pull off cap containing 2 g, 4 g, or 8 g. **Date of preparation:** October 2020

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2 Hospital acquired pneumonia, including ventilator associated pneumonia
3 Bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above

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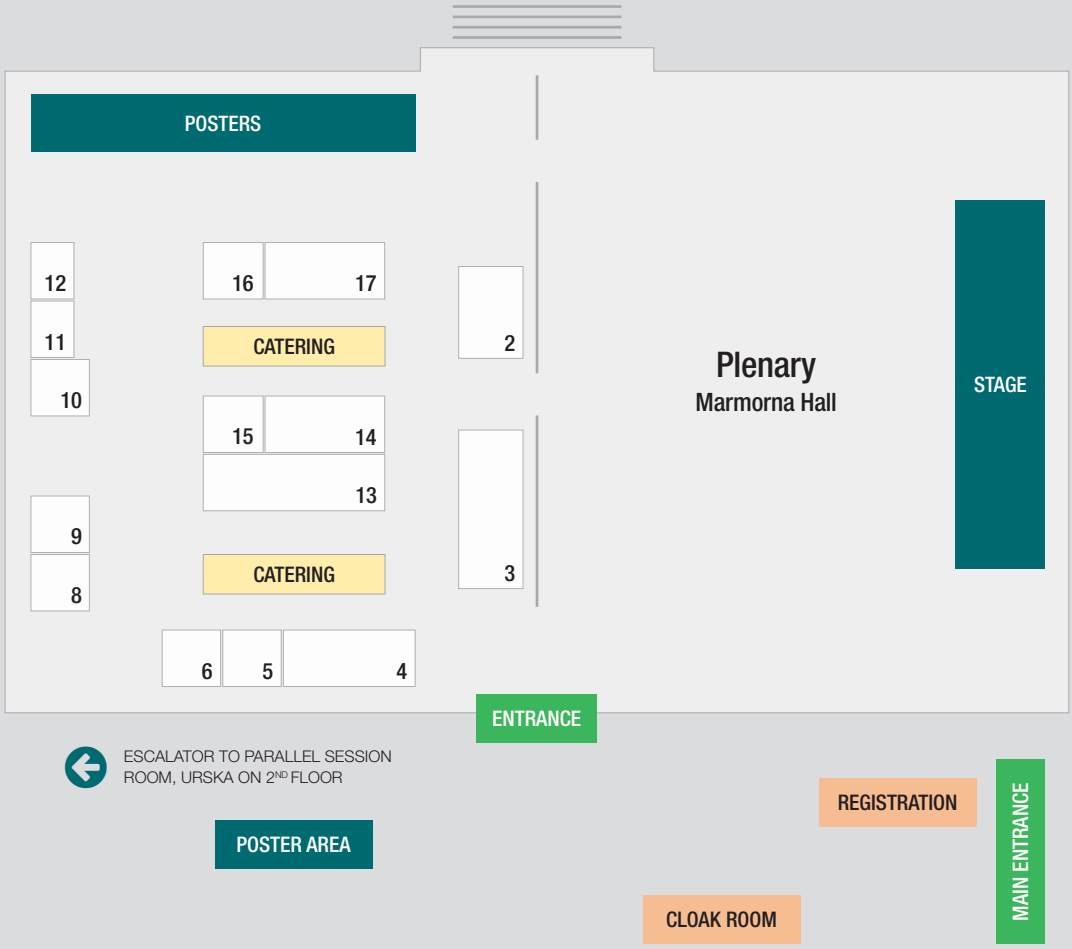
# Floor plan




## Exhibitors

| | | | | | |
|---|---|---|---|---|---|
| 2 | LYFSTONE | 8 | bonalive | 13 | Heraeus |
| 3 | BONESUPPORT | 9 | TECRES | 14 | ECTB |
| 4 | Biocomposites | 10 | G21 | 15 | InfectoPharm Wissen wirkt. |
| 5 | RESORBA | 11 | NuVasive Specialized Orthopedics | 16 | OSARTIS |
| 6 | Johnson & Johnson | 12 | curasan | 17 | bioMérieux |

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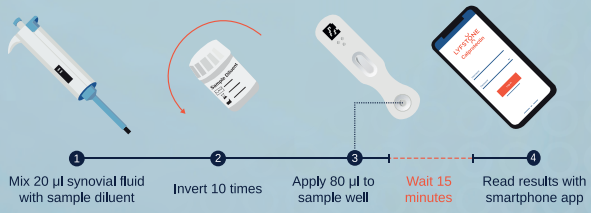
## LYFSTONE: A NEW ADVANCEMENT IN DIAGNOSING PJI

In a prosthetic joint, the first priority is to reliably rule out infection. The Lyfstone test measures the amount of calprotectin in synovial fluid. Elevated levels of calprotectin are proven indicators of both acute and chronic periprosthetic joint infection.

## FAST AND EASY

To assess the risk of periprosthetic joint infection, a small amount of synovial fluid is subtracted from the patient's joints.

The Lyfstone test requires only 20 µl and generates results in 15 minutes. The easy sample work-up allows implementation at any stage of care, from consulting to pre-op to per-op.

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In a prospective clinical study of 123 patients at a leading US Hospital system using the MSIS-13 criteria as comparator, the Lyfstone Calprotectin test showed excellent sensitivity (98.1%) and specificity (95.7%). The calprotectin test outperformed blood-based PJI diagnostic tests such as CRP and ESR, confirming its diagnostic utility.

**Source:** Diagnostic Utility of a Novel Point-of-Care Test of Calprotectin for Periprosthetic Joint Infection after Total Knee Arthroplasty: A Prospective Cohort Study. https://clinicaltrials.gov/ct2/show/NCT03694925

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# Oral abstracts

**EBJIS** 2021

## [FP A 01] OUTCOME OF STREPTOCOCCAL PROSTHETIC-JOINT INFECTIONS

Arnaud Fischbacher[1], Sylvain Steinmetz[1], Loïc Lhopitallier[2], Noémie Boillat-Blanco[2], Olivier Borens[1]

*[1]CHUV, Service d'Orthopédie et de Traumatologie, Switzerland*
*[2]CHUV, Service des maladies infectieuses, Switzerland*

**Aim:** Streptococci cause around 10% of prosthetic-joint infections (PJI). The reported treatment success being poor, antimicrobial recommendations vary regarding its duration and the use of long-term suppression. We aimed to assess the treatment success rate of streptococci PJI without antimicrobial suppression over the last thirteen years.

**Method:** We included patients with streptococcal PJI at Lausanne University Hospital (Switzerland) between 2006 and 2019 in a retrospective cohort. We compared the treatment success rate according to streptococci species and type of surgical procedure.

**Results:** In our cohort we have 635 PJI out of which 69 (11%) were caused by streptococci (***S. agalactiae*** 32%, viridans group 23%, ***S. dysgalactiae*** 17%, ***S. pyogenes*** 8%, ***S. anginosus*** 8%, ***S. bovis*** 5%, ***S. pneumoniae*** 5%). Sixty percent had a hip infection, 40% a knee infection and the median age was 70 years. Two-step exchange was performed in 55%, débridement and retention (DAIR) in 42% and one-step exchange in 3% of the patients. The overall treatment success rate was 80%. The median time to failure was 8 months (CI 0.5-43 months). The success rate was better for two-step exchange compared to DAIR (90% versus 64%, ***p***=0.01). Infections caused by S***treptococcus dysgalactiae*** were associated with a higher failure rate (two-step success rate 67%, DAIR 25%, ***p***=0.009).

**Conclusions:** The treatment success of streptococcal PJI does not seem to be worse arguing against the systematic use of long-term antimicrobial suppression. However, our results suggest that surgical management with two-step exchange and long-term antimicrobial suppression might be useful in selected patients' groups such as those with S***treptococcus dysgalactiae*** PJI.

## [FP A 02] THE INFLUENCE OF THE DURATION OF THE SPACER INTERVAL ON THE CLINICAL OUTCOME DURING TWO-STAGE PROSTHESIS EXCHANGE IN SEPTIC HIP AND KNEE REVISION ARTHROPLASTY

Jan Puetzler[1], Burkhard Moellenbeck[1], Georg Gosheger[1], Tom Schmidt-Braekliing[1], Jan Schwarze[1], Thomas Ackmann[1], Christoph Theil[1]

*[1]Münster University Hospital, Department for General Orthopaedics and Tumororthopaedics, Münster, Germany*

**Aim:** Due to medical and organizational factors, it occurs in everyday practice that spacers are left in place longer than originally planned during a two-stage prosthesis exchange in the case of prosthetic joint infections. Patients are severely restricted in their mobility and, after initial antibiotic administration, the spacer itself only acts as a foreign body. The aim of this study is to analyze whether the duration of the spacer in situ has an influence on the long-term success of treatment and mortality.

**Method:** We retrospectively studied all 204 two-stage prosthesis replacements of the hip and knee from 2012 to 2016 with a minimum follow-up of two years at an arthroplasty center with 3 main surgeons. The duration of the spacer interval was divided into two groups. Patients re-planted within ten weeks (as is standard in multiple algorithms) after systemic antibiotic treatment were assigned to the 'Regular Spacer Interval (< 70 days)' group. If the spacer interval was longer, they were assigned to the 'Long Spacer Interval (≥ 70 days)' group.

**Results:** Patients were on average 67.69 years old (SD 12.3). The mean duration of the spacer-interval was 100.9 days (range: 423.0; SD, 60.0). In 62 patients replantation could be performed within 70 days after replantation, in 142 patients this took longer (max. 438 days). In 26 patients, the spacer had to be changed at least once during this period (11 patients in the hip group, and 15 patients in the knee group). In the remaining cases, other medical or organizational reasons delayed replantation. There was no statistically significant influence of the duration of the inserted spacer on the reinfection rate (n=204, r= 0.034, P=0.21). There was also no influence on mortality (n=204, r=0.13, p=0.23). An overview of the results is depicted in fig. 1

**Conclusions:** The timely replantation of a knee or hip prosthesis seems to be reasonable in general because the patients are strongly limited in their mobility and daily activities by the spacer. However, there does not seem to be a negative influence on infection eradication and survival due to a long spacer interval.

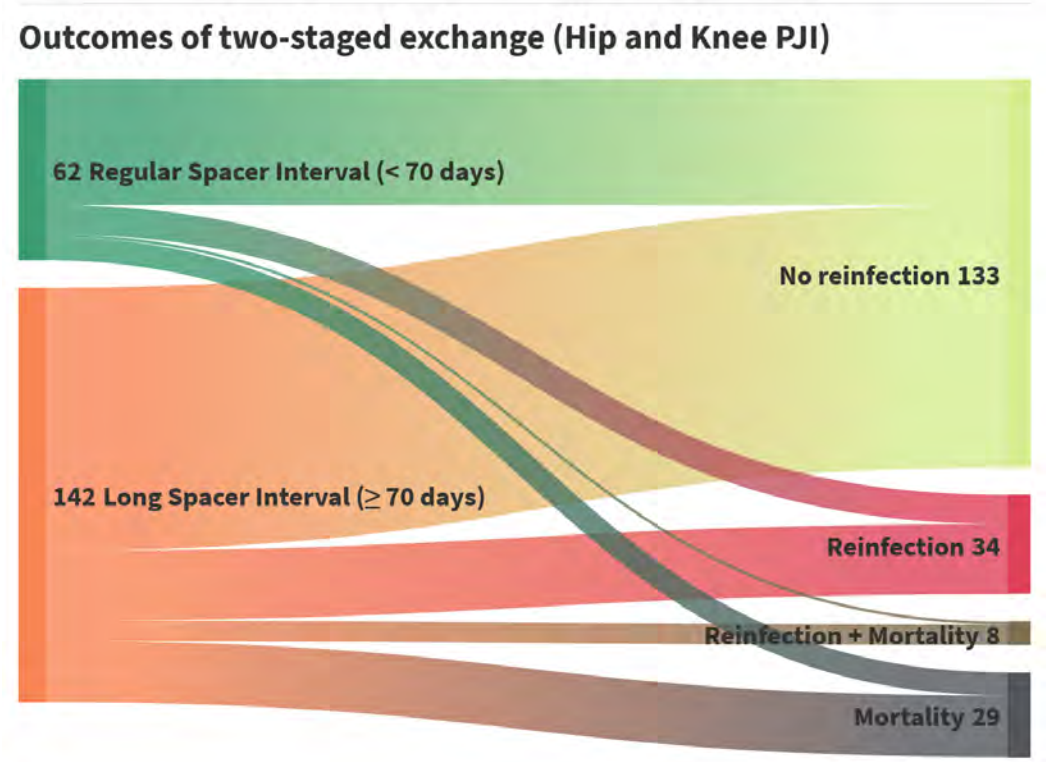


**Figure 1 Overview of the distribution of patients with a spacer interval of < 70 days and patients with a longer interval of ≥ 70 days to the main outcomes: reinfection rate and mortality**

## [FP A 03] NO REDUCTION OF PERIPROSTHETIC JOINT INFECTION RATES AFTER A NATIONAL INFECTION-CONTROL INITIATIVE: AN INCIDENCE STUDY OF 45 438 PRIMARY TOTAL KNEE ARTHROPLASTIES.

Olof Thompson[1], Anna Stefánsdóttir[2], Annette W-Dahl[2], Otto Robertsson[2], Max Gordon[3], Viktor Lindgren[3]

*[1]Lund University, Department of Infection Medicine*
*[2]Lund University, Department of Orthopedics, Sweden*
*[3]Karolinska Institute, Division of Orthopedics, Sweden*

**Aim:** Strenuous efforts to minimize postoperative infection rates have been made, including the Swedish nation-wide initiative Prosthesis Related Infections Shall be Stopped (PRISS). The aim of this study was to calculate the incidence rate of periprosthetic joint infections (PJI) following primary total knee arthroplasty (TKA) before and after PRISS.

**Method:** All 45,438 primary TKAs registered in the Swedish knee arthroplasty register (SKAR) during 2007-2008 and 2012-2013 were included. Matched data on antibiotic prescriptions were obtained from the Swedish Prescribed Drug Register (SPDR). All patients with ≥28 days of continuous antibiotic treatment within 2 years of primary surgery had their medical charts reviewed to identify cases of PJI.

**Results:** 644 PJIs were identified, equaling a 2-year cumulative incidence rate of 1.42% (95% CI: 1.31-1.53). The incidence rate was 1.41% before PRISS and 1.43% after. Diagnosis was made within 30 days of primary TKA in 52%, and within 90 days in 73% of the cases. 603 cases were reoperated. Debridement with exchange of the insert was performed in 32.1% and 62.5% of cases before and after PRISS respectively.

**Conclusions:** No reduction in cumulative PJI incidence was seen after the PRISS initiative.

## [FP A 04] MULTICENTER RETROSPECTIVE OBSERVATIONAL STUDY OF GRAM-NEGATIVE PROSTHETIC-JOINT INFECTIONS

Matteo Carlo Ferrari[1], Arnaud Fischbacher[2], Maddalena Casana[1], Berta Gasol[3], Daniel Pérez-Prieto[3], Olivier Borens[2]

*[1]Humanitas Research Hospital, Rozzano, Italy*
*[2]Lausanne University Hospital, Lausanne, Switzerland*
*[3]Hospital del Mar, Barcelona, Spain*

**Aim:** We aimed to assess the incidence and the outcome of Gram-negative prosthetic-joint infections (PJI) in 3 international tertiary hospital.

**Method:** We included patients with Gram-negative PJI at Humanitas Clinical and Research Hospital (Milan, Italy), Centre Hospitalier Universitaire Vaudois (Lausanne, Switzerland) and Hospital Parc de Salut Mar (Barcelona, Spain) between 2014 and 2018 in a retrospective cohort. We described the treatment's success rate according to Gram-negative species and type of surgical procedure.

**Results:** In the present cohort we have 780 PJI out of which 71 (9.1%) were caused by Gram-negative bacteria (polymicrobial infection 30%, ***Escherichia coli*** 25%, ***Pseudomonas aeruginosa*** 20%, ***Proteus*** spp. 4%, ***Klebsiella*** spp. 3%, ***Morganella morganii*** 3%, ***Enterobacter*** 3%, others 12%). Gram-negative PJI were more common in females (60%) than males (40%). Sixty percent had a hip infection, 40% a knee infection, the median age was 74 years and the median ASA score was 3. It was a chronic infection in 60% of the cases and an acute one in 40%. Two-step exchange was performed in 55%, débridement and retention (DAIR) in 30%, one-step exchange in 11% and implant removal without replacement in 4% of the patients. The overall treatment success rate was 89%. The success rate was better for two-step exchange (95%) compared to DAIR (81%) and one-step exchange (87%) (***p***=0.068). The median antibiotic duration was 68 days and ciprofloxacin was used in 70% of the cured patients versus in 88% of the failures (***p***=0.388). Infections caused by ***Escherichia coli*** were associated with a lower success rate (83%) especially compared to ***Pseudomonas aeruginosa*** (93%) and polymicrobial infections (90%) (***p***=0.358). Finally, the success rate was better in knee PJI compared to hip PJI (97% versus 83%, ***p***=0.121) and in females compared to males (93% versus 82%, ***p***=0.121).

**Conclusions:** The treatment's success of Gram-negative PJI is comparable to reported rates for all bacteria. However, our results suggest that surgical management with two-step exchange might be useful in selected patients' groups such as those with ***Escherichia coli*** PJI. Moreover, ciprofloxacin use seems not to improve cure rate.

## [FP A 05] DOUBLE-DOSE CEFUROXIME CONCENTRATIONS IN BONE, SYNOVIAL FLUID OF THE KNEE JOINT AND SUBCUTANEOUS ADIPOSE TISSUE–A RANDOMISED PORCINE MICRODIALYSIS STUDY

Andrea René Jørgensen[1], Pelle Hanberg[1,2], Mats Bue[1,3,4], Maja Brøgger Thomassen[1], Nis Jørgensen[5], Maiken Stilling[1,3,4]

[1]*Aarhus University Hospital , Aarhus Microdialysis Group, Orthopaedic Research Unit, Aarhus N, Denmark*
[2]*Horsens Regional Hospital , Orthopaedic Surgery , Horsens , Denmark*
[3]*Aarhus University, Clinical medicine , Aarhus N, Denmark*
[4]*Aarhus University Hospital , Orthopaedic Surgery , Aarhus N, Denmark*
[5]*Aarhus University Hospital , Infectious Diseases, Aarhus N, Denmark*

**Aim:** This study evaluated target tissue concentrations of double dose cefuroxime administered intravenously as either one 15 min infusion of 3,000 mg (Group 1) or two single 15 min infusions of 1,500 mg administered 4 h apart (Group 2).

**Method:** Sixteen pigs were randomised into two groups of eight. Cortical and cancellous bone, synovial fluid of the knee joint and subcutaneous adipose tissue concentrations were measured based on sampling via microdialysis. Plasma samples were collected as a reference. Comparison of the groups was based on time with concentrations above relevant minimal inhibitory concentrations (*f*T>MIC) of 4 µg/mL.

**Results:** The mean time *f*T>MIC (4 µg/mL) across compartments was longer for Group 2 (280–394 min) than for Group 1 (207–253 min) ($p<0.01$). Cortical bone showed a tendency towards longer *f*T>MIC (4 µg/mL) in Group 2 (280 min) than in Group 1 (207 min) ($p=0.053$). Within 50 min after administration, the mean concentration of 4 µg/mL was reached in all compartments for both groups. The mean concentrations decreased below 4 µg/mL after approximately 4 h (Group 1) and 3 h (Group 2) from initiation of administration (time zero).

**Conclusions:** During an 8 h interval, double-dose cefuroxime administered as 2 × 1,500 mg with a 4 h interval provides longer time above MIC breakpoint for ***Staphylococcus aureus*** (4 µg/mL) than a single bolus of 3,000 mg cefuroxime. To maintain sufficient tissue concentrations during longer surgeries, re-administration of cefuroxime (1,500 mg) should be considered 3 h after the first administration.

## [FP A 06] RIFAMPICIN RESTORES THE METABOLIC AND BONE-FORMATION ACTIVITIES OF OSTEOBLASTS AFTER INTRACELLULAR STAPHYLOCOCCUS AUREUS INFECTION

Francisca Alagboso[1], Gopala Mannala[1], Sara Steinmann[1], Denitsa Docheva[1], Markus Rupp[1], Christoph Brochhausen[2], Volker Alt[1]

*[1]Laboratory for Experimental Trauma Surgery, Department of Trauma Surgery, University Regensburg Medical Centre, Regensburg, Germany*
*[2]Institute of Pathology, University Regensburg, Regensburg, Germany*

**Aim:** Bone regeneration following the treatment of ***Staphylococcal*** bone infection or osteomyelitis is challenging due to the ability of ***Staphylococcus aureus*** to invade and persist within bone cells, which could possibly lead to antimicrobial tolerance and incessant bone destruction.
Here, we investigated the influence of ***Staphylococcal*** bone infection on osteoblasts metabolism and function, with the underlying goal of determining whether ***Staphylococcus aureus***-infected osteoblasts retain their ability to produce extracellular mineralized organic matrix after antibiotic treatment.

**Method:** Using our ***in vitro*** infection model, human osteoblasts-like Saos-2 cells were infected with high-grade ***Staphylococcus aureus*** EDCC 5055 strain, and then treated with 8 µg/ml rifampicin and osteogenic stimulators up to 21-days.

**Results:** Immunofluorescence and transmission electron microscopic (TEM) imaging demonstrated the presence of intracellular bacteria within the infected osteoblasts as early as 2 hours post-infection. TEM micrographs revealed intact intracellular bacteria with dividing septa indicative of active replication. The infected osteoblasts showed significant amounts of intracellular bacteria colonies and alteration in metabolic activity compared to the uninfected osteoblasts ($p \leq 0.001$). Treatment of ***S. aureus***-infected osteoblasts with a single dose of 8 µg/ml rifampicin sufficiently restored the metabolic activity comparative to the uninfected groups. Alizarin red staining and quantification of the rifampicin-treated infected osteoblasts revealed significantly lower amount of mineralized extracellular matrix after 7-days osteogenesis ($p<0.05$). Interestingly, prolonged osteogenic stimulation and rifampicin-treatment up to 21 days improved the extracellular matrix mineralization level comparable to the rifampicin-treated uninfected group. However, the untreated (native) osteoblasts showed significantly more quantity of mineral deposits ($p \leq 0.001$). Ultrastructural analysis of the rifampicin-treated infected osteoblasts at 21-days osteogenesis revealed active osteoblasts and newly differentiated osteocytes, with densely distributed calcium crystal deposits within the extracellular organic matrix. Moreover, residual colony of dead bacteria bodies and empty vacuoles of the fully degraded bacteria embedded within the mineralized extracellular matrix. Gene expression level of prominent bone formation markers, namely ***RUNX2***, ***COL1A1***, ***ALPL***, ***BMP-2***, ***SPARC***, ***BGLAP***, ***OPG/RANKL*** showed no significant difference between the infected and uninfected osteoblast at 21-days of osteogenesis.

**Conclusions:** ***Staphylococcus aureus*** bone infection can drastically impair osteoblasts metabolism and function. However, treatment with potent intracellular penetrating antibiotics, namely rifampicin restored the metabolic and bone formation activity of surviving osteoblasts. Delay in early osteogenesis caused by the bacterial infection was significantly improved over time after successful intracellular bacteria eradication.

## [FP A 07] HEALING PROGNOSTIC FACTORS AFTER DAIR TREATMENT OF LATE ACUTE TOTAL KNEE ARTHROPLASTY INFECTION

Gloria Pedemonte[1], Fernando Collado Sáenz[1], Ester Garcia Oltra[1], Francisco Aliaga Orduña[1], Jose Antonio Hernandez Hermoso[1]

[1]*Hospital Universitari Germans Trias i Pujol, Orthopaedic surgery, Badalona, Spain*

**Aim:** Debridement, antibiotic and implant retention (DAIR) is an accepted treatment of early and late acute Total Knee Arthroplasty (TKA) infections. DAIR failure may adversely affect the outcome of a subsequent two-stage exchange arthroplasty. Controversy exist on risk factors that can affect DAIR's results.
The aim of the study is to review presurgical, intrasurgical and postsurgical variables that could affect DAIR's result.

**Method:** A retrospective study of 27 DAIRs performed between 2015-2019 to treat late acute TKA infections was carried out. Patients were divided into two groups depending on DAIR's outcome [Healing (H) vs non-healing group (NH)] according on the Delphi-based multidisciplinary consensus criteria on success after treatment of periprosthetic joint infection.
We reviewed presurgical variables, including epidemiological variables (Age, Sex, comorbidities, ASA, Charlson, BMI, alcohol dependency), prosthesis variables (prosthesis type, primary cause of operation, primary TKA surgery center), infection variables (concomitant infection, previous antibiotic treatment, c-reactive protein, synovial WBC count, synovial % PMN, pathogen), KLIC score and CRIME 80 score. Surgical variables such as surgery duration and type of surgery (elective vs urgent). Post-surgical variables like antibiotic treatment duration and destination at discharge.
Normal distribution was assessed by Shapiro-Wilk test. Mann Whitney U test was used to compare the two independent sample variables. Chi-squared test was used for qualitative variables. P-value was established at 0.05 and statistical power at 80%.

**Results:** Infection Healing was achieved in 63% of patients. In presurgical variables, alcohol dependency, hypertension, liver disease, previous surgery performed in another institution were more frequent in NH group ($p < 0.05$). KLIC score value equal or greater than 4 had a higher risk of surgical failure ($p < 0.05$).
Regarding surgical variables, the healing group had more negative cultures than de non-healing one ($p<0.05$). Regarding post-surgical variables, long term antibiotic treatment (six months) achieved more healing after DAIR ($p<0.05$).

**Conclusions:** Alcohol dependency, hypertension, liver disease and KLIC score values equal or greater than 4, may increases the risk of DAIR failure. Finally, we observed that the long-term antibiotic treatment (6 months) favors healing after DAIR.

## [FP A 08] MICROBIOLOGICAL RESULTS AND CLINICAL OUTCOME OF TWO-STAGE REVISIONS WITH REPEAT FIRST STAGE PROCEDURES IN THE TREATMENT OF PERIPROSTHETIC HIP AND KNEE JOINT INFECTIONS

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*[2]Orthopaedic Hospital Vienna-Speising, 2nd Department, Vienna, Austria*
*[3]Sigmund Freud University-Vienna, School of Medicine, Vienna, Austria*
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**Aim:** Little is known about microbiological spectrum and resistance patterns as well as the clinical outcome in patients who undergo a repeat first stage procedure as part of a 2-stage revision arthroplasty for the treatment of periprosthetic hip and knee joint infections.

**Methods:** Between 2011 and 2019, a total of 327 2-stage revision arthroplasties were performed on 312 patients with PJI of the knee and hip at our institution. We performed a retrospective analysis of all patients, who underwent a repeat first stage procedure regarding re-revision rate, host factors, culture negative and positive stages, monomicrobial and polymicrobial infections as well as microbiological spectrum and antimicrobial resistance patterns.

**Results:** Overall, 52/312 (16.7%) patients (27 knee/25 hip) underwent a repeat first stage procedure. There were 35/52 (67.3%) culture positive first, 17/52 (32.7%) culture positive repeat first and 12/52 (23.1%) culture positive second stage procedures. In 13/52 (25%) patients a re-revision surgery was necessary at a median follow-up of 46.8 months (range, 12.2 to 93.3 months). High re-revision rates (10/12 [83.3%]) were found in patients with culture positive second stage and low re-revision rates (3/40 [7.5%]; $p<0.01$) were found in patients with culture negative second stage. The microbiological spectrum changed in 9/11 (81.8%) patients between culture positive first and repeat first stage, in 3/4 (75%) patients between culture positive repeat first and second stage and in 5/6 (83.3%) between culture positive second stage and subsequent re-revision surgery. Moreover, the antimicrobial resistance pattern changed in 6/9 (66.7%) of persistent microorganisms.

**Conclusion:** Microbiological results during first, repeat first and second stage procedures significantly impacted the re-revision rates and changes in microbiological spectrum and resistance patterns between stages are common. However, if eradication of the microorganism at second stage can be accomplished, low re-revision rates can be achieved, even in patients who require a repeat first stage procedure.

## [FP A 09] PERIPROSTHETIC JOINT INFECTIONS ARE HARD TO CAPTURE. A COMPARISON BETWEEN THE NATIONAL DUTCH ARTHROPLASTY REGISTRY AND A DETAILED REGIONAL PERIPROSTHETIC REGISTRY.

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*[3]Orthopedisch Centrum Máxima, Eindhoven, Netherlands*
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**Aim:** National Joint Replacement Registries, which are important sources for periprosthetic joint infection (PJI) data, report an average PJI incidence ranging from 0.5 to 2.0%.[1,2] Unfortunately, national registries including the Dutch Arthroplasty Register (LROI), are not specifically designed to register PJI. In the Netherlands, the LROI is a nationwide population-based registry with an overall completeness of more than 95%.[3] To ensure usability and reliability of PJI data from the LROI, it is important to evaluate the quality and completeness of these data. From 2013 onwards, eight hospitals in the South-East of the Netherlands, collected their PJI data in a detailed regional infection cohort (RIC)[1], specifically designed for this purpose. This study aimed to determine the accuracy and completeness of PJI registration (hip and knee arthroplasty) in the LROI, by comparing the LROI with the RIC.

**Method:** All patients registered with an acute PJI in the RIC between 2014–2018 were selected for the study and were matched with the LROI. According to the Workgroup of American Musculoskeletal Infections Society (MSIS), an acute PJI was defined as at least two phenotypically identical pathogens, isolated in cultures from at least two separate tissues, obtained from the affected peri-prosthetic tissue during the DAIR treatment (debridement, antibiotics, irrigation and retention). Only PJI occurring within 90 days after primary hip or knee arthroplasty were included.[1,4] The LROI data and completeness was based on the entered procedures and documented reason for revision infection, which was not specially based on the MSIS criteria. After checks on missing and incorrectly data, the completeness of registration in the LROI was calculated by comparing the number of registrations in the LROI with data from the RIC (gold standard).

**Results:** Of the 639 primary total hip and knee arthroplasty with a suspected PJI registered in the RIC between 2014-2018, 352 cases met the definition of acute PJI. The overall incidence was 1%.
When compared with the LROI, 164 of these cases were also registered in the LROI as PJI revision, resulting in a 53% underestimation of PJI for the LROI.

**Conclusions:** LROI data on acute PJI shows a significant underestimation, which is comparable to scarce other literature sources. To ensure reliability and usability of national PJI data, a specifically part of the LROI has to be designed for registering PJI similar to the regional cohort.

**References**

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[3]Steenbergen et al. Acta Orthopaedica.2015; 86(4):498-505.
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## [FP A 10] SAFETY OF TEDIZOLID AS SUPPRESSIVE ANTIMICROBIAL THERAPY FOR PATIENTS WITH COMPLEX IMPLANT-ASSOCIATED BONE AND JOINT INFECTION DUE TO MULTIDRUG-RESISTANT GRAMPOSITIVE PATHOGENS: RESULTS FROM THE TEDISAT COHORT STUDY

Tristan Ferry[1], Anne Conrad[1], Eric Senneville[2], Sandrine Roux[1], celine dupieux-chabert[1], Aurélien Dinh[3], Sebastien Lustig[1], Sylvain Goutelle[1], Thomas Briot[1], Truong-Thanh Pham[4], Florent Valour[1]

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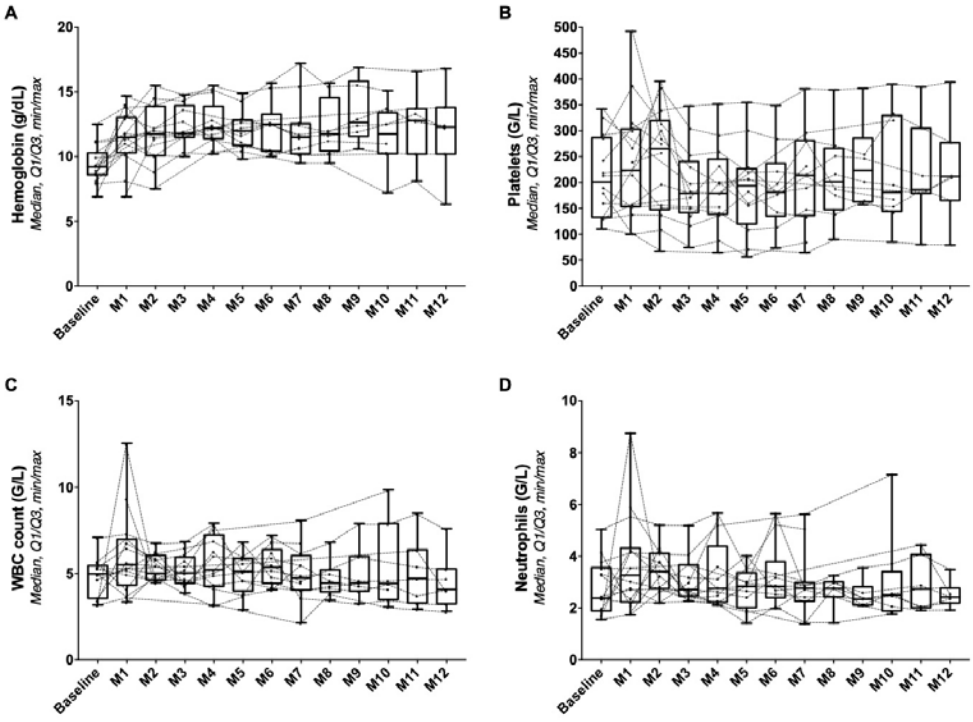
[3]*AP-HP*
[4]*HUG*

**Aim:** Tedizolid is an oxazolidinone antibiotic that: (i) is recommended at the dose of 200 once daily in patients with skin and soft tissue infection; (ii) seems to have a better long-term hematological and neurological safety profile in comparison with linezolid; (iii) remains active on multidrug-resistant (MDR) Gram-positive pathogens. Consequently, it might represent an option as suppressive antimicrobial treatment (SAT) in patients with complex implant-associated bone and joint infection (BJI) due to MDR Gram-positive pathogens.

**Method:** We performed a cohort study (2017-2020) to evaluate the long-term safety of tedizolid (200mg qd) as SAT in patients with implant-associated BJI. In all cases, the use of tedizolid was validated as the last oral treatment option during multidisciplinar meetings in a reference center for the management of BJI. Serious adverse events, any reason for discontinuation, and standard biological data, were prospectively collected.

**Results:** Seventeen patients (13 males; median age 73 years) received tedizolid as SAT for late complex prosthetic-joint infections (n=16) or osteosynthesis (n=1). Pathogens were MDR coagulase negative staphylococci (16 patients), Corynebacterium striatrum (2 patients), Enterococcus faecium (1 patient) and/or S. aureus (1 patient). Tedizolid was always started after a primary treatment (median duration of intravenous 47 days; followed by linezolid in 12 patients including 9 who experienced linezolid-induced serious adverse event) that followed a surgery, mainly debridement and implant retention (13 patients). Median duration of tedizolid was 6 months (min, 1 month; max, 31 months). The only reason for discontinuation was a failure of the conservative strategy that occurred in four patients (17%) during the follow-up. No patients developed a serious adverse event, or a discontinuation of tedizolid due to an adverse event. Anemia was observed in two patients, who had already other known cause of anemia (chronic leukemia and oesophageal varices); stable thrombopenia was observed in a cirrhotic patient (80 G/L, stable during the treatment course of 12 months); and a transient mild neutropenia (1.4 G/L) was observed in another patient (Figure). No neurological adverse event was observed.

**Conclusions:** Tedizolid seems to be a safe option as SAT in patients with complex implantassociated BJI due MDR Gram-positive pathogens.


A
Hemoglobin (g/dL)
Median, Q1/Q3, min/max
B
Platelets (G/L)
Median, Q1/Q3, min/max
C
WBC count (G/L)
Median, Q1/Q3, min/max
D
Neutrophils (G/L)
Median, Q1/Q3, min/max
Baseline
M1
M2
M3
M4
M5
M6
M7
M8
M9
M10
M11
M12

## [FP B 01] THE CHARACTERISTICS OF EARLY FRACTURE-RELATED INFECTIONS IN A LARGE RETROSPECTIVE MULTICENTER COHORT STUDY

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**Aim:** Early fracture-related infections (FRIs) are a common entity in hospitals that treat trauma patients. It is important to be aware of the course of this condition, not only for quality auditing and logistic reasons, but also to counsel patients about the expected course of their disease. The aim of this study was to describe the recurrence rate and need for secondary procedures in early FRI patients.

**Method:** This retrospective multicenter cohort study was conducted in two level 1 trauma centres. All patients between January 1st 2015 to July 1st 2020 with confirmed FRI[1] with an onset of <6 weeks after initial fracture fixation were included. Recorded data included patient demographics, fracture characteristics, trauma mechanism, clinical, radiological and laboratory findings, surgical procedure, microbiology, antimicrobial therapy and follow-up. Univariate and multivariate regressions were performed to assess possible predictors of recurrent FRI.

**Results:** 202 patients were included in this study. The cohort consisted of a majority of men (68,8%) with a mean age of 51,19 years. 95,0% had at least two phenotypically identical cultures, 53,0% confirmatory clinical signs and 47,5% confirmatory operative signs. Staphylococcus aureus, Staphylococcus epidermidis and Corynebacterium species were the most commonly found bacteria. 85 patients (42,1%) needed 1 operation to control their initial infection, 117 patients (57,9%) underwent multiple operations to treat the initial episode of FRI, with an average re-operation rate of 2.2 per patient. 31 patients (15,3%) had a recurrent FRI with an average total number of re-operations of 2.8. The mean follow-up was 12,58 months. Local antimicrobial treatment (ρ=0.011, OR 3,68(1,35-10,02)), Injury Severity Score (ISS) (ρ=0.035, OR 0,50(0,26-0,95)) and open fractures (ρ=0.043, OR 0,42(0,18-0,97)) remained significant as predictors of recurrent FRI after a multivariate analysis.

**Conclusions:** After an early FRI, in 42,1% of all patients the initial FRI is controlled with one re-operation. The majority of patients (57,9%) require multiple operations to control their initial infection with an average of 2.2 procedures per patient. The overall recurrence rate is 15,3% for which on average another 2.8 procedures were required. These results can be used to counsel the early FRI patient and give them an educated opinion in regard to their individualized prognosis.

**References:**

Metsemakers WJ. Fracture-related infection: A consensus on definition from an international expert group. Injury. 2018 Mar;49(3):505-510.

**Acknowledgements:** The authors received no financial support to conduct this research. Special thanks are in order for anyone that has been involved in completing the used database.

## [FP B 02] IS THE USE OF GUIDELINE-BASED SYSTEMIC ANTIBIOTICS IN FRACTURE RELATED INFECTION CORRELATED WITH A FAVOURABLE CLINICAL OUTCOME?

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*[2]University Medical Center Groningen, Trauma Surgery, Netherlands*
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**Aim:** This study investigated the effect of the choice of antibiotic regime on outcome of patients treated for fracture-related infection (FRI) at 3 centres, in the UK and the Netherlands between 2015 and 2019.

**Method:** All patients with FRI, confirmed by the FRI Consensus Definition[1] and treated surgically, were included. Data were collected on patient characteristics, microbial cultures, antibiograms, empiric and definitive systemic antibiotic regimes and local antibiotic use. All patients were followed up for at least one year. The primary outcome was eradication of infection. The chosen antibiotic regimes were compared to the recent guidelines from the FRI Consensus Group[2], to assess the correlation with outcome.

**Results:** 433 FRIs were treated in patients with mean age 49.7 years (range 14-84). Patients were followed up for a mean of 26 months (range 12-72). A microbiological diagnosis was obtained in 353 patients (18.5% culture negative rate), with 46% monomicrobial and 35.5% polymicrobial. ***Staph aureus*** was present in 51.3% of monomicrobial and 55.2% of polymicrobial infections. Negative cultures were much less likely in FRI within 10 weeks of injury (p=0.00001). Treatment failure with recurrent infection occurred in 13.6% of patients. Failure was more likely in culture positive cases (Polymicrobial; p=0.016, monomicrobial 0.039).
Definitive antibiotic regimes were fully compliant with the FRI Guideline in 107 cases (24.7%). In 294 cases (68%) antibiotic regimes outside the guidelines were used. Non-compliance was often due to differences in recommended dosing or overtreatment with extra antimicrobials. 32 cases (7.4%) could not be assessed against the FRI Guidelines as the organisms or regimes were not represented in the guide.
Failure rate with FRI Guideline compliant regimes was 12.1% and with non-compliant, 13.2% (p=0.87). Failure in unclassifiable cases was 21.9%. The use of local antibiotics reduced the recurrence rate from 18.3% without local antibiotics to 10.3% with local antibiotics (p=0.022).

**Conclusions:** This study demonstrated that there can be considerable variability in the choice of antimicrobial regimes in FRI. Some deviations from the FRI Guideline did not result in poorer outcomes. These smaller differences in antimicrobial choice may not be major determinants of outcome.

1 **McNally M, et al.** *EFORT Open Rev* 2020; 5: 614-619.
2 **Depypere M, et al.** *J Orthop Trauma* 2020; 34: 30-41.

## [FP B 03] CAN NECROTIC BONE BE OBJECTIVELY IDENTIFIED IN CHRONIC FRACTURE RELATED INFECTIONS? — FIRST CLINICAL EXPERIENCE WITH AN INTRAOPERATIVE FLUORESCENCE IMAGING TECHNIQUE

Markus Rupp[1], Leopold Henssler[1], Christoph Brochhausen[2], Jozef Zustin[3], Sebastian Geis[4], Christian Pfeifer[1], Volker Alt[1], Maximilian Kerschbaum[1]

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*[3]Pathology Regensburg*
*[4]University Medical Center Regensburg, Plastic, Hand and Reconstructive Surgery, Germany*

**Aim:** Adequate debridement of necrotic bone is of paramount importance for eradication of infection in chronic osteomyelitis. Currently, no tools are available to detect the exact amount of necrotic bone in order to optimize surgical resection. The aim of the present study was to evaluate the feasibility of an intraoperative illumination method (VELscope®) and the correlation between intraoperative and pathohistological findings in surgically treated chronic fracture related infection patients.

**Method:** Ten consecutive patients with chronic fracture related infections of the lower extremity were included into this prospectively performed case series. All patients had to be treated surgically for fracture related infections requiring bony debridement. An intraoperative illumination method (VELscope®) was used to intraoperatively differentiate between viable and necrotic bone. Tissue samples from the identified viable and necrotic bone areas were histopathologically examined and compared to intraoperative findings.

**Results:** In all included patients, the intraoperative illumination was deemed helpful to differentiate between necrotic and viable bone tissues during bony debridement. The histopathological examination of the samples showed good correlation of the intraoperative illumination findings with histopathological signs of necrosis for areas deemed dead and histopathological signs of intact bone for areas deemed vital during illumination.

**Conclusions:** The fluorescence-assisted, intraoperative detection of necrotic and viable bone using the VELscope® is an easy-to-use procedure that can help surgeons to optimize intraoperative bone resection in chronic fracture related infections by unmasking viable from necrotic bone tissue. This may help to improve resection techniques and eventually treatment outcome in patients in the future.

## [FP B 04] ANTIBIOTIC PRESCRIBING FOR OPEN FRACTURES: A QUALITY IMPROVEMENT PROJECT TO ENHANCE BOAST 4 ATTAINMENT

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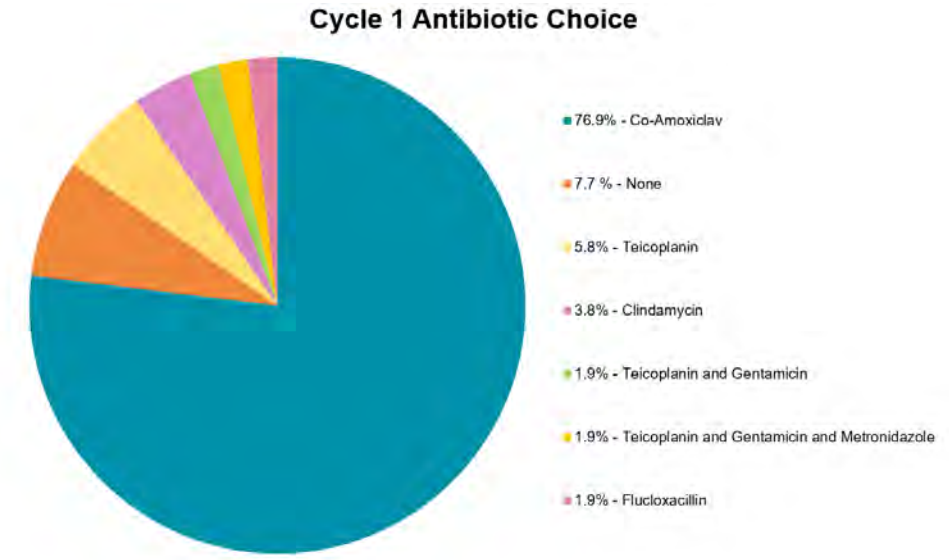
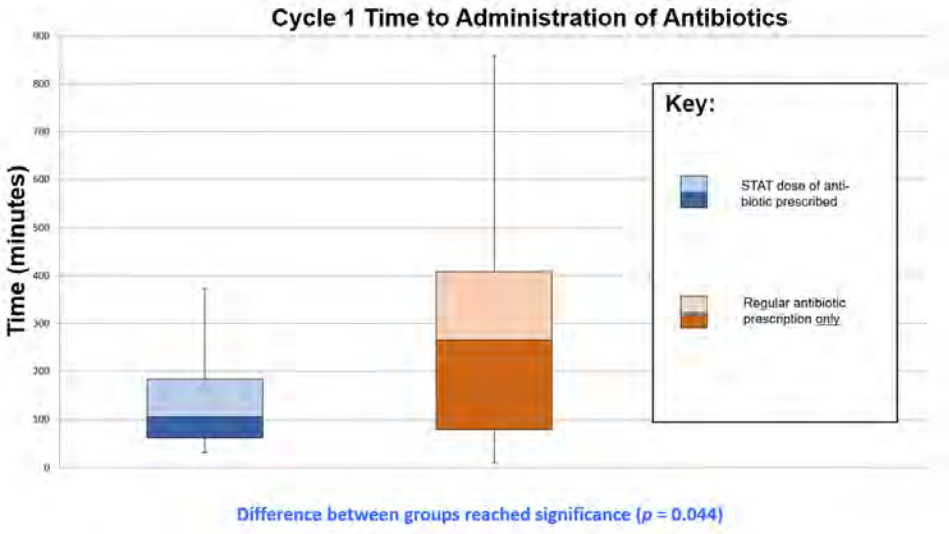
**Aim:** The primary aim of this quality improvement project was to assess compliance with BOAST 4 guidelines for the delivery of antibiotic prophylaxis in patients presenting to a major trauma centre with open limb fracture, and evaluate the impact of implemented changes on attainment of these guidelines. Secondary aims were to assess adherence to local guidelines for the type of antibiotic prescribed.

**Method:** A multi-cycle audit and quality improvement project was carried out for all patients presenting to Brighton and Sussex University Hospitals NHS Trust (BSUH) with open limb fractures from 1st September 2018 to 31st January 2019, and 1st November 2019 to 31st March 2020. Patients were identified through retrospective screening of electronic operation records (Bluespier) by authors, and paper records were subsequently reviewed for data pertaining to antibiotic prescriptions. Following the initial audit cycle, targeted teaching was carried out for orthopaedic trainees, new posters were placed in key clinical areas to highlight local guidelines, and alterations to the trauma clerking proforma were implemented, to include BOAST 4 guidelines.

**Results:** In cycle 1, a total of 52 patients received surgical treatment for open limb fractures, of which 48 (92.3%) were prescribed antibiotics prior to definitive management, with a mean time to administration of 271 minutes. Of these, 41 (78.8%) received prescriptions according to BSUH guidelines. The use of STAT prescriptions was found to significantly reduce the mean time to administration from 298 minutes to 144 minutes ($p = 0.044$). In cycle 2, a total of 29 patients received surgical treatment for open limb fractures, of which all 100% were prescribed antibiotics prior to definitive management, with a reduced mean time to administration (233 minutes). Of these, 26 (89.7%) received prescriptions according to BSUH guidelines, and a significantly greater proportion ($p = 0.0003$) received initial STAT 'once-only' prescriptions (51.7% vs. 15.4%).

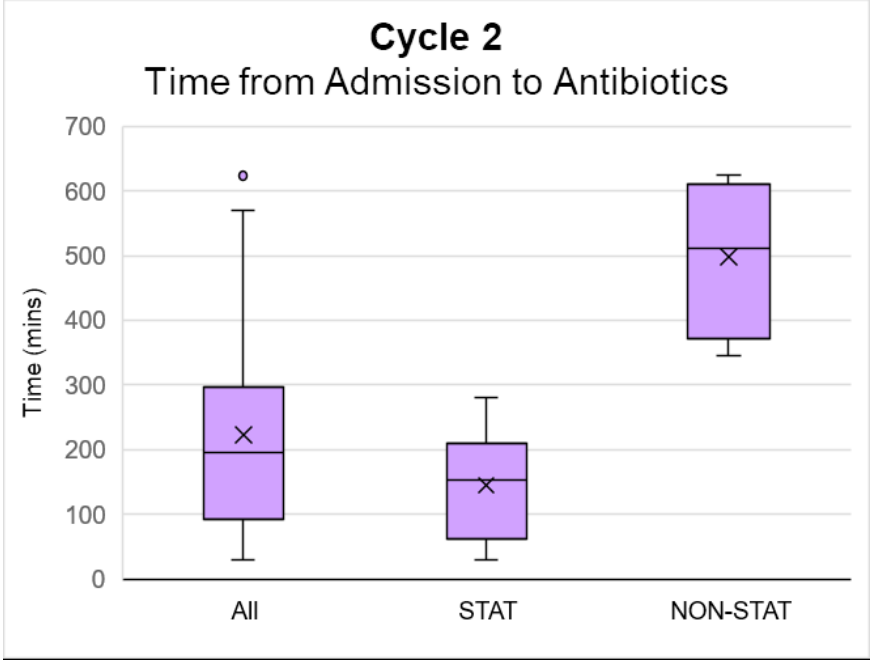
**Conclusions:** This quality improvement project has demonstrated the successful implementation of targeted changes to improve the attainment of BOAST 4 guidelines. Following a multi-cycle audit, all patients now receive antibiotic prophylaxis, with a higher proportion receiving antibiotics according to local BSUH guidelines. Furthermore, the use of STAT 'once-only' prescriptions, which was shown to be beneficial during the first audit cycle, has now significantly increased following intervention.

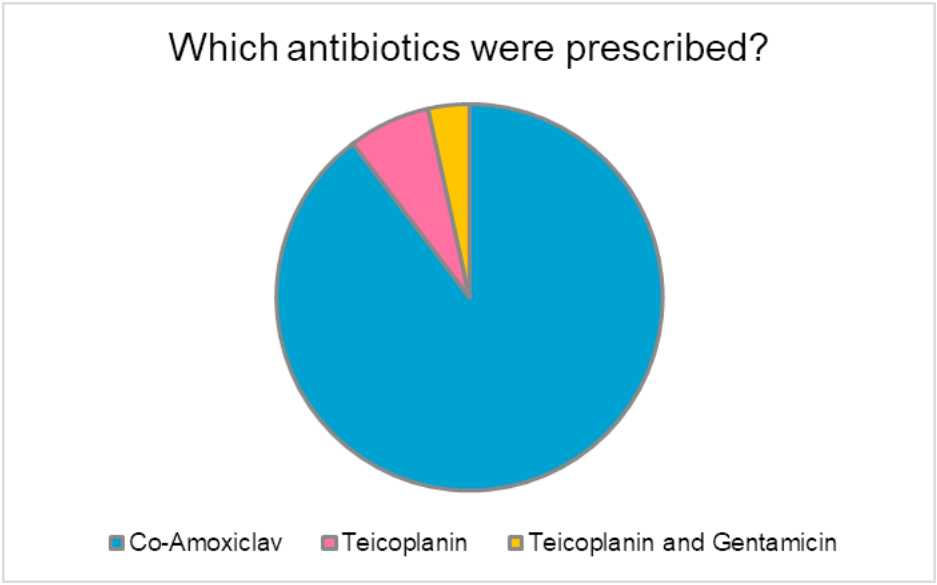



Difference between groups reached significance ($p = 0.044$)

- ✓ First antibiotic dose to be prescribed STAT on admission
- ✓ Handover to A&E staff to ensure timely administration
- ✓ Informative posters in clinical areas to act as prompts
- ✓ Targeted teaching for junior orthopaedic trainees on induction
- ✓ Alterations to trauma clerking proforma




Which antibiotics were prescribed?
Co-Amoxiclav
Teicoplanin
Teicoplanin and Gentamicin

## [FP B 05] WHAT AFFECTS OUTCOME AFTER TREATMENT OF FRACTURE-RELATED INFECTION?

Martin McNally[1], Ruth Corrigan[1], Jonathan Sliepen[2], Falco Hietbrink[3], Frank IJpma[2], Marjan Wouthuyzen-Bakker[4], Rob Rentenaar[3], Bridget Atkins[1], Geertje Govaert[3]

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**Aim:** This study investigated the management and clinical outcomes of patients treated for confirmed fracture-related infection (FRI) at 3 centres, in the UK and the Netherlands between 2015 and 2019.

**Method:** All patients with FRI, confirmed by the FRI Consensus Definition[1] and treated surgically, were included. Data were collected on patient characteristics, time from injury to FRI surgery, soft tissue reconstruction, type of stabilization and use of local antibiotics. All patients were followed up for at least one year. The rates of eradication of infection and union were assessed. The associations between treatment methods, time from injury and outcomes were determined.

**Results:** 433 FRIs were treated in patients with mean age 49.7 years (range 14-84). FRI affected the tibia in 226(52.2%), femur in 94(21.7%), pelvis in 26(6%), humerus in 20(4.6%) and foot bones in 19(4.4%). Patients were followed up for a mean of 26 months (range 12-72). Overall, eradication of infection was successful in 86.4% of cases and 86% of unhealed infected fractures were healed at final review. 3.3% required amputation.
Successful outcome was not dependent on age, or time from injury (recurrence rate 16.5% in FRI treated at 1-10 weeks after injury; 13.1% at 11-52 weeks; 12.1% at >52 weeks: p=0.52).
Method of stabilization had a major affect on outcome. Debridement and retention of a stable infected implant (DAIR) had a failure rate of 22.3%, implant exchange (to new internal fixation) 16.7%, conversion to external fixation 7.4%. DAIR was significantly worse than conversion to external fixation (p=0.01). There was no effect of the time from injury on the outcome of DAIR or any other fixation method.
The use of a free flap in the tibia improved the success rate from 80.4% to 92.1% (p=0.044). Outcome was adversely affected by use of a split skin graft alone in soft tissue reconstruction (44% failure)(p=0.006). The use of local antibiotics reduced the recurrence rate from 18.3% to 10.3% (p=0.022).

**Conclusions:** This study is the first to consider outcome for all FRIs, at all time points, with all treatment modalities. Treatment was mostly successful but may be improved with better directed use of free flaps, local antibiotics and limitation of DAIR. The results suggest that the division of FRIs into categories based on time from injury, may not be helpful with modern treatment.

1 **McNally M, et al.** *EFORT Open Rev* 2020; 5: 614-619.

## [FP B 06] MANAGEMENT OF SOFT-TISSUE RECONSTRUCTION IN FRACTURE-RELATED INFECTION: ORTHOPLASTIC LONG-TERM OUTCOME AND RISK FACTOR ANALYSIS

Seraina Ladina Carina Müller[1;2], Mario Morgenstern[1;3], Richard Kühl[1;4], Thaddäus Muri[1;3], Daniel Kalbermatten[2], Martin Clauss[1;3], Dirk Schaefer[1;2], Parham Sendi[1;3;4;5], Rik Osinga[1;2]

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*[2]University Hospital Basel, Department of Plastic, Reconstructive, Aesthetic and Hand Surgery, Basel, Switzerland*
*[3]University Hospital Basel, Department of Orthopaedic and Trauma Surgery, Basel, Switzerland*
*[4]University Hospital Basel, Infectious Diseases and Hospital Epidemiology, Basel, Switzerland*
*[5]University of Bern, Institute for Infectious Diseases, Bern, Switzerland*

**Aim:** Fracture-related infection (FRI) is a severe post-traumatic complication which can be accompanied with a soft-tissue defect or an avital soft-tissue envelope. In these cases, a thoroughly planned orthoplastic approach is imperative since a vital soft-tissue envelope is mandatory to achieve fracture union and infection eradication. The aim of our study was to analyse plastic surgical aspects in the management of FRIs, including the type and outcome of soft-tissue reconstruction (STR), and to investigate the long-term outcome of FRI after STR.

**Method:** Patients with a lower leg FRI requiring STR that were treated from 2010 to 2018 at our center were included in this retrospective analysis. STR involved the use of local, pedicled and free flaps. The primary outcome was the success rate of STR, and the secondary outcome was long-term fracture consolidation and cure of infection.

**Results:** Overall, 145 patients with lower leg FRI were identified, of whom 58 (40%) received STR. Muscle flaps were applied in 38, fascio-cutaneous flaps in 19 and a composite osteo-cutaneous flap in one case. All patients underwent successful STR (primary STR in 51/58 patients, 7/58 patients needed secondary STR). A high Charlson Comorbidity Index Score was a significant risk factor for flap failure (p=0.011). Patients with free-flap STR developed significantly more severe complications and needed more surgical interventions (Clavien-Dindo ≥IIIa; p=0.001). Out of the 43 patients that completed long-term follow-up (mean 24 months), fracture consolidation was achieved in 32 and infection eradication in 31. Polymicrobial infection was a significant risk factor for fracture non-union (p=0.002). American Society of Anesthesiologists (ASA) classification of 3 or higher (p=0.040) was a risk factor for persistence or recurrence of infection.

**Conclusions:** In our population, 58/145 patients with FRI required STR. STR was successful in all patients eventually, in 7/58 patients secondary STR was necessary. Therefore, STR should be sought even if primary STR fails. Despite successful STR, the long-term composite outcome showed a high rate of failed fracture consolidation and failed eradication of infection, which was independent of primary STR failure.

## [FP B 07] HIGH INCIDENCE OF ENTEROBACTER CLOACAE IN ACUTE INFECTIONS POST OSTEOSYNTHESIS OF ANKLE FRACTURES. MULTICENTER STUDY.

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**Aim:** The purpose of this study is to analyze the demographic and microbiological variables of acute ankle infections posterior to ankle osteosynthesis and to determine the different characteristics of patients with***E. cloacae*** infection.

**Method:** A multicenter retrospective observational study (4 national hospitals) of acute post osteosynthesis infections of ankle fracture operated between 2015 and 2018 was implemented. The demographic and microbiological variables relating to the surgical intervention and the antibiotic treatment performed were collected. A descriptive assessment of all the variables and a univariate comparison between patients with ***E. cloacae*** infection and patients with alternative microorganism infections were performed. The SPSS v25 program for Windows was the choice for statistical analysis.

**Results:** 71 Patients with an average age of 57 years were included, the majority being males (55%). 31% of patients were diabetic, 27% had vascular pathology, and 18.3% had a BMI greater than 35. Trimalleolar fracture was the most common in our study being 52%. 26.8% were open fractures. The microorganisms isolated were: 25% ***S. aureus***, 22.5% ***E. cloacae*** and 22.5% polymicrobial. Accounting for polymicrobial infections, the presence of ***E. cloacae*** rises to 32%. In the univariate analysis, only significant differences were found in age (patients with ***E. cloacae*** infection were older) and the use of VAC therapy.

**Conclusions:** In our series, higher percentages of ***E. cloacae*** infection wereobserved than those described in the literature.There are statistically significant differences in the variables of age and need for VAC therapy. The high incidence of ***E. cloacae*** infections suggests the vital importance of adapting antibiotic prophylaxis, ensuring the coverage of this microorganism.

## [FP B 08] ARE CUTIBACTERIUM ACNES PRESENT AT THE END OF PRIMARY SHOULDER PROSTHETIC SURGERIES RESPONSIBLE FOR TOTAL SHOULDER ARTHROPLASTY INFECTION? PROSPECTIVE STUDY.

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**Aim:** *Cutibacterium acnes* (*C. acnes*) is the most cultured organism implicated in periprosthetic shoulder infections. Nevertheless, the clinical significance of its persistence on the skin surface and in the deep layers during shoulder arthroplasty surgery remains still unknown.The purpose of this study was to know if the ***C. acnes*** isolate present in deep tissues at the end of a primary shoulder arthroplasty could be responsible for shoulder arthroplasty infection.

**Method:** Prospective study including 156 patients undergoing primary shoulder arthroplasty. In all the patients included 5 to 12 tissue samples were obtained and were specifically cultured to detect ***C. acnes*** presence. DNA was extracted from the ***C. acnes*** colonies selected with the QIAsymphony DSP Virus/Pathogen Midi Kit (Qiagen, Hilden, Germany). Libraries were prepared using Nextera XT kit (Illumina) and sequenced in an Illumina MiSeq sequencer. Sequencing files were pre-processed using The Microbial Genome Atlas pipeline. Samples that failed on QC analysis were discarded for further analysis. Isolate nucleotide distances were calculated using Genome-based distance matrix calculator from the enveomics collection. Comparative genomic analysis was performed between intra- and inter-patients' isolates. Data analysis was performed using R 3.6.3.

**Results:** For twenty-seven out of 156 patients (17.31%), ***C. acnes*** was present at the end of the primary surgery. Two of these patients (both male) developed a ***C. acnes*** periprosthetic shoulder infection after 6 and 4 months from the primary surgery. DNA from the ***C. acnes*** responsible for the periprosthetic infection was further analysed by whole genome sequencing (WGS). Average Nucleotide Identity (ANI) value was assessed, measuring the nucleotide-level genomic similarity between genome pairs. We found a clear ANI clustering in two major groups which corresponded, mainly, to the associated phylotype (97%-98% ANI). Moreover, when analysing both isolates that developed a periprosthetic shoulder infection, we found that all the revision-surgery isolates clustered nearer to their corresponding primary-surgery isolates (99.4% of similarity) than to the other independent bacterial isolates, supporting the causal relationship between the initial and the delayed infection.

**Conclusions:** *C. acnes* present at the end of the primary surgery can be the cause of early- or delayed-periprosthetic joint infections in shoulder arthroplasty, revealing the potential route of infection. Therefore, efforts must be made in terms of antibiotic prophylaxis and skin preparation to limit infections of total shoulder arthroplasties.

## [FP B 09] CALPROTECTIN LATERAL FLOW TEST AS A RULE OUT TEST FOR PERIPROSTHETIC JOINT INFECTION

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**Aim:** Several options to standardize the definition of periprosthetic joint infection (PJI) have been created including the 2013 Musculoskeletal Infection Society (MSIS), 2018 Intentional Consensus Meeting (ICM), and the 2019 proposed European Bone and Joint Infection Society (EBJIS) criteria. Synovial fluid biomarkers have been investigated in an effort to simplify and improve the diagnosis of PJI. The aim of this study was to test the sensitivity, specificity, positive, and negative predicted values (PPV and NPV, respectively) of a calprotectin point of care (POC) test for diagnosing PJI in revision total knee arthroplasty (TKA) patients comparing different sets of criteria (2013 MSIS, 2018 ICM, and 2019 EBJIS criteria) used to define patients as with or without infection.

**Method:** From October 2018 to January 2020 and under IRB approval 123 intraoperative samples of synovial fluid were prospectively collected at two academic hospitals in the same institution from revision TKA patients. All patients underwent standard clinical and laboratory evaluation for PJI at our institution, allowing for categorization using the 3 criteria. Patients were adjudicated by 2 blinded and independent reviewers for the 3 sets of criteria. The 3 criteria agreed 91.8% of the time. Four likely cases by the 2019 proposed EBJIS were considered unlikely and 1 inconclusive case by the 2018 ICM was considered not infected for the purposes of analysis. Calprotectin POC testing followed manufacturer's instructions using a threshold of >50 mg/L to indicate PJI. Sensitivities, specificities, PPV, NPV, and areas under the curve (AUC) were calculated for the 3 sets of criteria.

**Results:** Using 2013 MSIS criteria the calprotectin POC test demonstrated a sensitivity, specificity, PPV, NPV AUC of 98.1%, 95.7%, 94.5%, 98.5%, and 0.969, respectively. Using 2018 ICM the POC test demonstrated a sensitivity, specificity, PPV, NPV and (AUC) of 98.2%, 98.5%, 98.2%, 98.5%, and 0.984, respectively. Using the 2019 proposed EBJIS criteria the POC test demonstrated a sensitivity, specificity, PPV, NPV and area under the curve (AUC) of 93.2%, 100.0%, 100.0%, 94.2%, and 0.966, respectively.

**Conclusions:** The calprotectin lateral flow POC test has an excellent sensitivity and specificity regardless of the set of criteria used to define PJI. These results are promising and suggest that the calprotectin lateral flow test may be used as a rule out test in a cost conscious health care model or when conventional diagnostic tools may not be available. Further investigations of the calprotectin PCO test must be completed to validate these results.

## [FP B 10] HIV INFECTION AND FRACTURE-RELATED INFECTIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Aim:** To conduct a systematic review and meta-analysis comparing the development of early and late fracture-related infections (FRI) following closed and open fractures in HIV-positive and HIV-negative patients.

**Method:** A systematic literature search was conducted using MEDLINE through the OVID interface, ProQuest, Web of Science, The Cochrane Library and Scopus. Only studies involving HIV-positive who underwent operative fixation (internal or external) of open or closed fractures, with a HIV-negative control group, were considered eligible. Following eligibility assessment, studies were included with the main outcome of interest being the development of either early or late fracture-related infection at the site of surgery in patients with open and closed fractures.

**Results:** Eleven studies were included (n = 2634). The studies' follow-up periods were between one and 39 months with an average of 11 months. Three studies were conducted before the introduction of ARV (anti-retroviral) therapy (1994) and two did not involve any patients on ARV's. Across the entire group, for both open and closed fractures, the risk of a fracture-related infection was greater in HIV-positive patients (Odds ratio (OR) = 1.61; 95% CI = 0.93-2.79, p = 0.04). When looking at closed fractures treated operatively, an OR = 4.59 was found in HIV-positive patients in terms of the risk of fracture-related infection (95% CI = 0.30-68.99, p < 0.001). Open fractures showed similar results with an OR of 3.48 in HIV-positive patients (95% CI = 0.55 – 21.99, p < 0.001). Studies performed prior to the widespread introduction of anti-retroviral therapy and/or did not have any patients on antiretroviral therapy showed a greater infection risk in patients living with HIV infection with OR 3.53 (95% CI = 1.85 – 6.74, p = 0.36). However, studies performed in the era after the introduction of antiretroviral therapy showed no increase of infection risk for HIV-positive patients with an OR = 0.91 (95% CI = 0.58 – 1.43, p = 0.76).

**Conclusions:** The assumption that HIV infection increases the risk for fracture-related infection remains unsubstantiated. The introduction of anti-retroviral therapy may have confounded the issue and we noted an apparent decrease in the risk in later studies. More data is required from well-designed larger studies to inform future analysis.

## [FP C 01] WHAT IS THE ROLE OF OPEN TISSUE BIOPSY IN UNCERTAIN CASES OF LOW-GRADE INFECTIONS IN TOTAL KNEE ARTHROPLASTY?

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**Aim:** Diagnosis and isolation of a causative organism is imperative for successful treatment of periprosthetic joint infections (PJI). While there are several diagnostic algorithms using microbiology, serum and synovial markers, the preoperative diagnosis of a low-grade infection remains a challenge, particularly in patients with unsuccessful aspiration. An incisional biopsy may be used in these cases as additional diagnostic tool. In this retrospective study we evaluated microbiological findings, sensitivity and specificity of open synovial biopsies in cases of inconclusive preoperative diagnostics.

**Methods:** In a retrospective databank analysis (2010-2018), we identified 80 TKAs that underwent an open biopsy because of inconclusive results after applying the CDC Criteria (2010) or the MSIS (2011-2018) for PJI. Infection makers in the serum (C-reactive protein [CRP], leucocytes count and interleukin-6 [IL-6]) and in the synovial aspirate (leucocyte count, percentage of neutrophiles) prior to the biopsy were analyzed. All biopsies were performed by suprapatellar mini-arthrotomy. If a subsequent revision surgery was performed, the isolated organisms in the open biopsy were compared to the results in the revision surgery and sensitivity and specificity were calculated. Serum markers were checked for correlation with a positive result in the open biopsy using Cramer-V and Chi²-Test.

**Results:** A positive result in the open biopsy occurred in 32 cases (40%) while 48 cases (60%) showed no growth of microorganisms. A preoperative elevated serum CRP (≥1mg/dl) showed a significant correlation for a positive biopsy (p=0.04). The odds ratio for a positive biopsy was 2.57 (95% CI 1.02-6.46) with elevated serum CRP. A revision surgery of the TKA with additional tissue sampling was performed in 27 (84%) cases with a positive biopsy and in 32 (67%) cases with a negative biopsy. The intraoperative tissue samples from the revision surgery showed microbial growth in only 52% of cases that were believed to be culture positive from the biopsy results, while positive cultures occurred in 41% of the cases with an initially negative biopsy. Patients with ≥ two cultures of the same microorganism in the biopsy presented a positive result in 73% of their revision surgeries.
The open biopsy showed a sensitivity of 48% with a specificity of 62% in our collective, if revision surgery was performed.

**Conclusion:** Open biopsy may be considered with inconclusive preoperative serum and synovial fluid diagnostics for PJI, but sensitivity and specificity were rather low in this special collective. Further studies with bigger collectives should be performed to determine potential markers with a higher sensitivity.

## [FP C 02] METAGENOMIC NANOPORE SEQUENCING FOR THE DIAGNOSIS OF PROSTHETIC JOINT INFECTIONS: CAN WE DO MORE THAN DETECT SPECIES FROM SONICATION FLUIDS?

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**Aim:** Metagenomic nanopore sequencing is demonstrating potential as a tool for diagnosis of infections directly from clinical samples. We have previously shown nanopore sequencing can be used to determine the causative bacterial species in prosthetic joint infections (PJI). However, to make predictions regarding antimicrobial resistance, human DNA contamination must be reduced so a greater proportion of sequence data corresponds to the microbial portion of the DNA extract. Here, we utilise selective DNA extraction from sonication fluid samples to begin to make predictions regarding antimicrobial resistance in PJI.

**Method:** We investigated host cell DNA depletion with 5% saponin selective human cell lysis followed by nuclease digestion. Subsequently, bacterial cells were mechanically lysed before DNA extraction. Sequencing libraries from samples treated with and without saponin were prepared with a Rapid PCR Barcoding Kit[1] and sequenced in multiplexes of 2-8 samples/flowcell on a GridION. Sequencing reads were analysed using the CRuMPIT pipeline and thresholds to indicate presence of a specific bacterial genus/species were investigated. Antimicrobial resistance determinants were detected using previously published sequences specifically for ***Staphylococcus aureus***, as an example organism frequently causing PJI.

**Results:** 247 DNA extracts from 113 individual patient sonication fluids plus controls were subjected to metagenomic sequencing, comprising 55 monomicrobial (10 of which were culture-positive at <50 CFU/ml), 2 polymicrobial and 58 culture-negative samples. 5% saponin depleted human DNA contamination, reducing the number of human sequenced bases to a median 12% from 98% in comparison to 5µm filtration without saponin. In 11 samples 5% saponin depleted human bases by <12% in comparison to 5µm filtration, which may be indicative of incomplete depletion. Bacteria observed in sonication fluid culture were identified to species-level in 49/65 (75%) cases, and to genus-level in 51/65 (78%). Specificity of sequencing was 103/114 (90%). Sequencing made a completely successful prediction of antimicrobial susceptibility in 8/19 ***S. aureus*** culture-positive samples treated with 5% saponin, and a partial prediction in 5/19 for the 8 antibiotics investigated. Without 5% saponin treatment sequencing could only detect a limited number of AMR determinants in 3/19 samples. Sequencing correctly predicted 13/15 (87%) resistance phenotypes where sufficient sequence data was available.

**Conclusions:** Nanopore metagenomic sequencing can provide species identification in PJI. Additionally, depletion of human DNA improves depth of coverage and allows detection of antimicrobial resistance determinants, demonstrating as a proof of principle that nanopore sequencing could potentially provide a complete diagnostic tool in PJI.

[1]Oxford Nanopore Technologies

## [FP C 03] DITHIOTREITOL AND NEXT GENERATION SEQUENCING SHOW SIMILAR DIAGNOSTIC SECURITY AS PERIPROSTHETIC TISSUE CULTURES TO DIAGNOSE PJI

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**Aim**: The need for a revision surgery caused by periprosthetic joint infection (PJI) is a common phenomenon in orthopaedic surgery. PJI caused by biofilm forming bacteria is often difficult to diagnose. For this reason, the use of sonication of the septic explant or the use of dithiothreitol (DTT) to break up the biofilm to improve the diagnosis security by microbiological cultures has been proposed. DTT breaks up bacterial biofilms by reducing disulfide bonds between proteins and polysaccharides in the extracellular matrix of the biofilm, thereby liberating the imbedded bacteria. The aim of this study was to compare the diagnosis results of DTT-containing microDT-Tect devise[1] with the results from routine PJI diagnostic.

**Method**: A total of 101 patients of hip and knee revision surgeries were included in this study (39 aseptic, 29 septic and 33 spacer revision). Pre-surgery CRP serum levels and leucocyte blood values were recorded. Patient characteristics, such as age, comorbidities and implantation time of the prosthesis were included. We compared the microbiological diagnostic from tissue biopsies with the results of bacteria cultures from DTT-solution as well as DNA from DTT samples for next-generation sequencing (NGS).

**Results**: In the septic cohort, we found a concordance of 72% between the standard microbiology diagnostic with bacteria cultivated from DTT solution. In the aseptic and spacer cohort, the similarity was about 94%. However, the comparison between routine microbiological diagnostic and NGS in the septic cohort was less effective. While in the aseptic cohort, the concordance between NGS results from the DTT solution and routine diagnostic was similar to the bacteria cultivated from DTT solution. In a next step, we compared the identified microorganisms with the different techniques. Especially microorganisms from the Staphylococcus genus were detected efficiently with all tested methods. The other organisms, such as Streptococcus spp., Enterococcus spp. and Propionibacterium spp. were less concordant, although only few cases were detected in our cohort.

**Conclusion**: Our data indicate that the standard microbiological diagnostic works very accurate. The use of the microDTTect device did not improve the results but gave comparable results. NGS was not superior to the standard microbiological diagnostic.

## [FP C 04] EVALUATION OF AN AUTOMATED MULTIPLEX PCR JOINT INFECTION PANEL FOR THE DETECTION/IDENTIFICATION OF PATHOGENS IN 201 SYNOVIAL FLUID SPECIMENS IN A MONOCENTRIC STUDY

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**Aim:** Bone and Joint Infections (BJIs) present with non-specific symptoms and can be caused by a wide variety of bacteria and fungi, including many anaerobes and microorganisms that can be challenging to culture or identify by traditional microbiological methods. Clinicians currently rely primarily on culture to identify the pathogen(s) responsible for infection. The BioFire® FilmArray® Bone and Joint Infection (BJI) Panel (BioFire Diagnostics, Salt Lake City, UT) was designed to detect 15 gram-positive (seven anaerobes), 14 gram-negative bacteria (one anaerobe), two yeast, and eight antimicrobial resistance (AMR) genes from synovial fluid specimens in an hour. The objective of this study was to evaluate the performance of an Investigational Use Only (IUO) version of the BioFire BJI Panel (BBJIP) compared to conventional used as reference methods.

**Method:** In a monocentric study, leftover synovial fluid specimens were collected in a single institution including 4 hospitals and tested using conventional bacterial culture (Standard of Care (SoC)) according to routine procedures following French national recommendations. Specimen has been placed in a refrigerator (4°C) as soon as possible after collection and stored for less than or equal to 7 days before enrollment. Performance of the IUO version of the BBJIP was determined by comparison to SoC for species identification.

**Results:** To date, 201 specimens have been collected and tested using BBJIP. A total of 39 pathogens were obtained in culture. Compared to SoC culture, the overall PPA was 89.7% (35 TP, 4 FN (SA, 1; Strepto Spp, 2; P. micra, 1) and the overall NPA was 99.7% with 16 FP for a total of 5374 bacterial targets screened. Two complementary molecular tests using home-made PCR are underway to definitively conclude about the FN et FP for BBJIP observed in the preset study.

**Conclusions:** The BioFire BJI Panel appears as a promising, sensitive, specific, and robust test for rapid detection of 31 microorganisms (including anaerobes) and eight AMR genes in synovial fluid specimens. The number of pathogens and resistance markers included in the BioFire BJI Panel, together with a reduced time-to-result and increased diagnostic yield compared to culture, is expected to aid in the management of BJIs.

## [FP C 05] SYNOVIAL FLUID TESTING FOR THE DIAGNOSIS OF PROSTHETIC JOINT INFECTION ACCORDING TO THE NEW EBJIS DEFINITION – CAN SIMPLE AND INEXPENSIVE BIOMARKERS CONVEY ADDED INFORMATION?

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**Aim:** Our goal is to assess diagnostic accuracy of synovial fluid testing in diagnosing prosthetic joint infection(PJI) as defined by the European Bone and Joint Infection Society(EBJIS). In addition to differential leukocyte count, simples and inexpensive biomarkers such as synovial fluid C-reactive protein(CRP), adenosine deaminase(ADA) and alpha-2-macrogloblulin(A2M) were also investigated and its possible role in increasing accuracy assessed.

**Method:** Between January/2013 and December/2019 total hip or knee arthroplasty revision cases (regardless of preoperative diagnosis) were prospectively included provided enough synovial fluid for biomarker analysis was collected and at least four tissue samples, as well as the implant for sonication, were gathered for microbiological study. Definitive diagnosis was classified according to the new EBJIS PJI definition. Using receiver operating characteristic curves, we determined cutoff values as well as diagnostic accuracy for each marker.

**Results:** Out of 364 revision arthroplasties performed, 102 fully respected inclusion criteria. There were 58 unlikely, 8 likely and 36 confirmed infections. Synovial fluid total leukocyte count, proportion of polymorphonuclear neutrophils(PMN), CRP, ADA and A2M were significantly different between groups. Area under the curve was 0.94 for total leucocyte count, 0.91 for proportion of PMN, 0.90 for CRP, 0.82 for ADA and 0.76 for A2M. Sensitivity, specificity and predictive values for statistically optimal but also selected rule-in and rule-out cutoffs values are shown in Table 1. Interpreting a raised level of CRP(>2.7mg/L) or ADA(>60U/L) together with high leukocyte count(>1470 cells/µL) or proportion of PMN(>62.5%) significantly increases specificity and positive predictive value for affirming PJI.

**Conclusions:** Differential leukocyte count cutoffs proposed by the EBJIS PJI definition are shown to perform well in ruling out (<1,500 cells/µL) and ruling in (>3,000 cells/µL) PJI. Adding simple and inexpensive biomarkers such synovial CRP or ADA is helpful in interpreting inconclusive results.

Table 1. Statistically optimal and selected rule-in and rule-out cutoffs diagnostic performance

| | Proposed cutoff(s) | Sensitivity | Specificity | Positive Predictive Value | Negative Predictive Value |
|---|---|---|---|---|---|
| Total leukocyte count *(cells/µL)* | ***1,470**** | *91.7%* | *92.4%* | *88.7%* | *94.5%* |
| | ***2,645*** | *77.8%* | *98.5%* | *97.1%* | *87.3%* |
| | ***3,280*** | *77.8%* | *100%* | *100%* | *87.4%* |
| Proportion of PMN *(%)* | ***62.5**** | *88.9%* | *83.9%* | *78.1%* | *92.1%* |
| | ***64.4*** | *86.1%* | *88.7%* | *83.2%* | *90.8%* |
| | ***79.5*** | *75.0%* | *98.4%* | *96.8%* | *85.9%* |
| C-reactive protein *(mg/L)* | ***1.2*** | *90.6%* | *82.5%* | *77.0%* | *93.1%* |
| | ***2.7**** | *84.4%* | *92.1%* | *87.4%* | *90.1%* |
| | ***8.1*** | *71.9%* | *95.2%* | *90.7%* | *83.9%* |
| Adenosine Deaminase *(U/L)* | ***40*** | *90.6%* | *64.5%* | *62.3%* | *91.4%* |
| | ***60**** | *71.9%* | *80.6%* | *70.6%* | *81.6%* |
| | ***85*** | *50.0%* | *90.3%* | *76.9%* | *73.6%* |
| α-2-macroglobulin *(mg/L)* | ***420**** | *82.1%* | *74.6%* | *67.7%* | *86.6%* |
| | ***985*** | *39.3%* | *93.2%* | *78.9%* | *70.3%* |
| Leukocyte count > *1,470* **and** PMN> 62.5% | | *85.3%* (68.9-95.0) | *96.7%* (88.6-99.6) | *93.4%* (78.3-98.2) | *92.3%* (84.3-96.4) |
| Leukocyte count > *1,470* **and** CRP > 2.7 mg/L | | *77.4%* (58.9-90.4) | *98.3%* (90.9-100.0) | *96.1%* (78.0-99.4) | *88.9%* (80.6-93.9) |
| Leukocyte count > *1,470* **and** ADA > 60 U/L | | *64.5%* (45.4-80.8) | *96.7%* (88.6-99.6) | *91.5%* (72.8-97.7) | *83.3%* (75.6-89.0) |
| PMN> 62.5% **and** CRP > 2.7 mg/L | | *83.3%* (65.3-94.4) | *98.3%* (90.8-100.0) | *96.4%* (79.0-99.5) | *93.0%* (85.5-97.4) |
| PMN> 62.5% **and** ADA > 60 U/L | | *66.7%* (47.2-82.7) | *98.2%* (90.4-100.0) | *95.3%* (74.2-99.3) | *84.4%* (76.5-90.0) |

* optimal ROC curve proposed values; PMN – polymorphonuclear neutrophils; CRP – C-reactive protein; ADA - Adenosine Deaminase

## [FP D 01] MICROBIOLOGICAL FINDINGS MATTER- DETERMINING THE BEST POSSIBLE ANTIBIOTIC TREATMENT FOR EARLY, DELAYED AND LATE FRACTURE-RELATED INFECTIONS

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**Aim:** Fracture-related infection (FRI) is a challenging complication. This study aims to investigate *(1) microbial patterns in fracture-related infection (FRI), (2) the comparison of isolated pathogens in FRI patients with early, delayed and late onset of infection and (3) antibiotic susceptibility profiles to identify effective empiric antibiotic therapy for FRI.*

**Method:** Patients treated for FRI from 2013 to 2020 were grouped into early (*< 2 weeks)*, delayed (2- 10 weeks) and late (> 10 weeks) onset of infection. Pathogens detected during treatment were evaluated for pathogens. Antibiotic susceptibility profiles were examined with respect to broadly used antibiotics and antibiotic combinations.

**Results:** In total 117 patients (early n=19, delated n=60, late n=38) were included in the study. Infection was polymicrobial in 10 cases (8.6%) and culture-negative in 11 cases (9.4%). ***Staphylococcus aureus*** was the most frequently detected pathogen (40.5%), followed by ***Staphylococcus epidermidis*** (17.2%) and gram-negative bacteria (16.4%). Pathogen distribution did not differ statistically significant between the groups. Highest effectiveness could be achieved by the combination of *meropenem + vancomycin (95.7%) and gentamycin + vancomycin (94.0%). More than 90% of all patients would have also been covered by co-amoxiclav + glycopeptide (93.2%), ciprofloxacin + glycopeptide and piperacillin/tazobactam + glycopeptide (92.3% each) as well as ceftriaxone + glycopeptide (91.5%). Comparing the p*redicted efficacy of empiric antimicrobial regimens between the subgroups only revealed a statistically significant difference regarding the combination ***ciprofloxacin*** with a glycopeptide (F= 3.304, p=.04), for which more patients with an early onset of infection would have been susceptible.

**Conclusions:** Microbiological pattern for the causative microorganism between early, delayed and late FRI are comparable. Empiric therapy combinations such as *meropenem + vancomycin, gentamycin +vancomycin or co-amoxiclav + glycopeptide are effective antibiotic strategies.* To bypass unwanted side effects of systemic antibiotics and reduce the risk of antimicrobial resistance, the administration of local antibiotic carriers should be implemented in clinical practice.

## [FP D 02] VERTEBRAL OSTEOMYELITIS IS CHARACTERIZED BY INCREASED RANK/OPG AND RANKL/OPG EXPRESSION RATIOS IN VERTEBRAL BODIES AND INTERVERTEBRAL DISCS.

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**Aim:** Vertebral osteomyelitis (VO) is an infection of the spine mostly caused by bacterial pathogens. The pathogenesis leading to destruction of intervertebral discs (IVD) and adjacent vertebral bodies (VB) is poorly described. We aimed to investigate the connection between infection, bone- and disc-metabolism in VO patients.

**Method:** Fourteen patients with VO (infection group) and 14 patients with incomplete burst fractures of the spine (fracture group as controls) were included prospectively. Demographic data, treatment details, laboratory infection markers, and patient-reported outcome were assessed. Tissue biopsies from affected IVDs and adjacent VBs were analyzed for mRNA-expression levels of 18 target genes including chemokines, adipokines and genes involved in bone-metabolism by RT-qPCR.

**Results:** The Receptor activator of NF-κB/Osteoprotegerin (RANK/OPG) expression ratio was elevated in VB and IVD of the infection group ($p<0.001$ and $p=0.028$, respectively). The RANK-ligand (RANKL)/OPG expression ratio was elevated in VB of the infection group ($p<0.01$). Expression of the chemokines IL8 and CCL20 was significantly higher in VB samples of the infection group ($p<0.05$). The expression of leptin was higher in IVD tissue, the mRNA expression of omentin and resistin was lower in in VBs of the infection group (each $p<0.05$). OPG mRNA expression was significantly lower in infected VB and in IVD tissue compared to the fracture group (both $p<0.05$).

**Conclusions:** We identified similar expression patterns of pro-inflammatory cytokines and the RANK/RANKL/OPG axis in VBs and IVDs of patients with VO. This finding suggests that common immuno-metabolic pathways are involved in mechanisms leading to tissue degradation in VBs and IVDs during VO.

## [FP D 03] DALBAVANCIN IN THE TREATMENT OF PERIPROSTHETIC JOINT INFECTIONS OF THE HIP AND KNEE

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**Aim:** Dalbavancin is a novel second-generation lipoglycopeptide antibiotic with strong activity against many gram-positive bacteria and a prolonged half-life of 6-11 days. This allows a once a week intravenous application and therefore an outpatient intravenous therapy. Currently, only little is known about the use of Dalbavancin in Periprosthetic joint infection (PJI).
The aim of this study was to prospectively evaluate the use of Dalbavancin in the treatment of PJI of the hip and knee at a single institute. Therefore, we analyzed 90 consecutive patients with a minimum follow up of 1 year.

**Method:** Between 02/2017 and 02/2020 a total of 89 (45 male/44 female) patients with PJI of the hip 56/89 (62.9%) and knee 33/89 (37.1%) who received at least one dosage of Dalbavancin were included. The mean patient age was 71.0±9.9 years. The average BMI was 29.8±5.6 kg/m$^2$. There were 50/89 (56.2%) patients with PJI after primary and 39/89 (43.8%) patients with PJI after revision arthroplasty. All patients fulfilled MSIS criteria and had a positive microbiological result. The most common pathogens were Staphylococcus epidermidis 41/89 (46.1%), Enterococcus faecalis 11/89 (12.4%), Cutibacterium species 11/89 (12.4%) and Staphylococcus aureus 5/89 (5.6%). In 81/89 (91.0%) there was a mon infection and in 8/89 (9.0%) there was a polymicrobiel infection. In 29/89 (32.6%) patients we observed an early acute infection, in 5/89 (5.6%) a late acute infection and in 58/89(65.2%) a chronic infection. The mean follow up period was 64.72±23.3 months.

**Results:** Patients received 2.4±1.2 dosages (1500mg or 1000mg) of Dalbavancin with a median treatment period of 7 days (6; 111 days). No severe side effects were observed during the follow up period. Nausea was reported in 4/89 (4.5%) patients, diarrhea in 3/89 (3.4%) patients and absence of appetite in 1/89 (1.1%) patients during Dalbavancin treatment. At the time of latest follow-up no signs of infection were found in 70/89 (78.7%) patients. In 6/89 (6.7%) patients no 2$^{nd}$ stage was performed, due to poor general condition. In 11/89(12.4%) patients a re-revision due to persistent PJI was performed. Out of those patients 9/11 (81.8%) had an infected revision Total joint arthroplasty.

**Conclusions:** Our study results indicate that Dalbavancin is a promising treatment option for patients with PJIs after knee and hip arthroplasty which allows outpatient intravenous therapy. Further studies with longer follow-up period and a comparison with standard of care antibiotic therapy are needed.

## [FP D 04] EVALUATION OF RESISTANCE SELECTION BY GENTAMICIN AND VANCOMYCIN LOADED CALCIUM SULPHATE/HYDROXYAPATITE BONE GRAFT SUBSTITUTE ON BACTERIAL STRAINS RESPONSIBLE FOR PROSTHETIC JOINT INFECTION

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**Aim:** Bone and implant-associated infections caused by microorganisms that grow in biofilm are difficult to treat because of persistence and recurrence. Systemic administration of antibiotics is often inefficient because the poor vascularization of the site of infection. This issue has led to the development of biomaterials capable to locally deliver high doses of therapeutic agents to the injured bone with minimal systemic effects. In this context, calcium sulphate/hydroxyapatite (CS/HA) bone graft substitutes are widely used being safe, osteoconductive and resorbable biomaterials that can be easily enriched with consistent amounts of antibiotics. In this in vitro study, the capability of the eluted antibiotics to select the tested bacterial strains for antibiotic resistance was evaluated to confirm the safe use of the product.

**Method:** S. aureus, S. epidermidis and P. aeruginosa isolated in our Institute from bone and joint infection with different resistance phenotypes were used. 6 x 2.5 mm CS/HA discs were generated by pouring the antibiotic loaded formulations in a mold and were used as a modified disk diffusion test. The resistance selection was evaluated by subculturing cells growing on the edge of the zone of inhibition (ZOI) for seven days. Minimum inhibitory concentrations (MICs) of gentamicin and vancomycin were determined by broth microdilution method before and after the selection of resistance assay. In addition, MICs were assessed after seven day passage on antibiotic free agar plates to evaluate if eventual decrease of antibiotic susceptibility was stable or only transient.

**Results:** Commonly, no adaptation in presence of both CS/HA formulations was observed by analysing ZOI on agar medium. The kinetic of decrease of the ZOI was similar between the strains, with the exception of gentamicin resistant staphylococci in presence of gentamicin loaded CS/HA, which was faster with respect to the susceptible strains.

**Conclusions:** The present study shows that elution of gentamicin and vancomycin from CS/HA bone graft substitutes did not induce a decrease in susceptibility to these antibiotics in an in vitro setting, suggesting the safe use of the product.

## [FP D 05] PHOTOTHERMAA ERADICATES BACTERIAL BIOFILM IN A RABBIT MODEL OF PERIPROSTHETIC JOINT INFECTION

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**Aim:** Periprosthetic joint infection (PJI) is a devastating complication of total joint arthroplasty. While research has focused on developing better tests for disease diagnosis, treatment options have stayed relatively constant over the years with high failure rates ranging from 30%-50% and are due in part to the protective biofilm produced by some bacterial species. Current treatment options are compromised by the presence of biofilm, emphasizing the need for novel treatment strategies to be developed. Our group has developed a novel treatment (PhotothermAA) which has demonstrated ***in vitro*** its ability to target bacterial biofilm. The purpose of this study was to test this PhotothermAA technology ***in vivo*** in a rabbit model of PJI for its efficacy in eradicating biofilm.

**Method:** Four New Zealand white rabbits were implanted with a titanium tibial implant to mimic a total knee arthroplasty, and inoculated with $5x10^6$ CFU of ***Xen36*** (bioluminescent ***Staphylococcus aureus***). After two weeks, rabbits underwent an I&D procedure and treated with control hydrogel (n=2) or PhotothermAA (n=2) for two hours. After incubation, gel was heat activated with a laser for ten minutes, washed out, and closed. Rabbits were sacrificed two weeks after treatment for scanning electron microscopy (SEM) biofilm analysis of implant.

**Results:** All rabbits underwent surgery and treatment without any major complications. SEM images showed that I&D alone was not enough to eradicate bacterial biofilm. Treatment with PhotothermAA completely eradicated biofilm on the head of the implant, the area in direct contact with the PhotothermAA gel and laser treatment (Figure 1). Interestingly, areas not directly in contact with the treatment saw a reduction in bacterial biofilm but effects decreased with distance, suggesting direct contact is not required for treatment effect.

**Conclusions:** PhotothermAA is able to eradicate bacterial biofilm ***in vivo***. This has the potential to become a new treatment strategy for PJI.

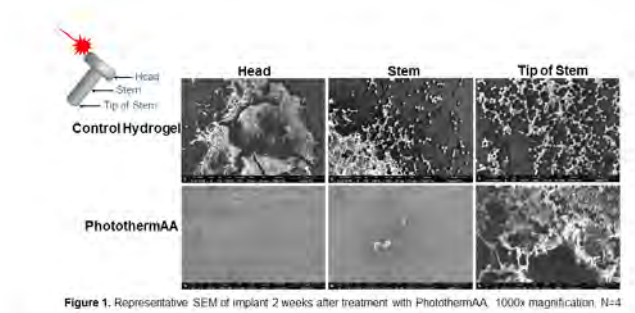


**Figure 1.** Representative SEM of implant 2 weeks after treatment with PhotothermAA. 1000x magnification. N=4

## [FP E 01] THE EUROPEAN BONE AND JOINT INFECTION SOCIETY PROSTHETIC JOINT INFECTION DEFINITION IS MORE SENSITIVE AND PERFORMS BETTER IN RULING OUT INFECTION PREOPERATIVELY THAN PREVIOUS DEFINITIONS

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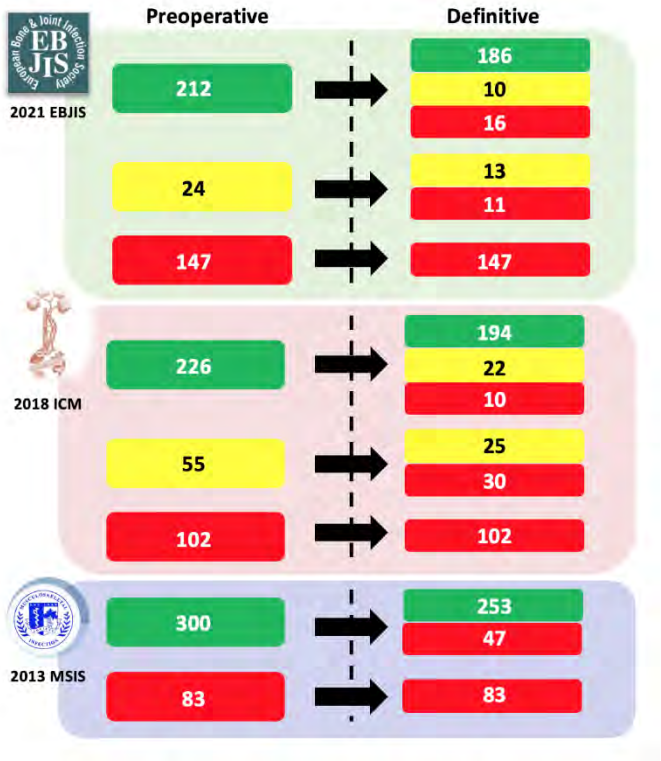
**Aim:** Accurate diagnosis is key in correctly managing prosthetic joint infection (PJI). Our aim is to compare the preoperative performance of three PJI definitions comparing it to definitive postoperative classification.

**Method:** This is a multicenter retrospective study of patients who have undergone total hip or knee revision surgery in four different European institutions. For this specific study, cases with no preoperative synovial fluid differential leukocyte count and less than four intraoperative microbiology samples were excluded.
Cases were classified using the 2021 EBJIS, the 2018 International Consensus Meeting(ICM) and the 2013 Musculoskeletal Infection Society(MSIS) PJI definitions. Preoperative classification was based on clinical features, inflammatory markers and synovial fluid leukocyte count and microbiology results.

**Results:** Preoperative and definitive PJI classification status of the 384 patients included are presented in figure 1.
EBJIS definition showed the highest agreement between preoperative and definitive classification (k=0.86, CI95% 0.81-0.90, p<0.001) compared to ICM 2018 (k=0.80, CI95% 0.75-0.84, p<0.001) or MSIS 2013 (k=0.70, CI95% 0.62-0.77, p<0.001).
Compared to its respective definitive classification: EBJIS preoperative ***unlikely*** result shows 86.8%(95%CI 81.3%-91.2%) sensitivity and 87.7%(95%CI 83.3%-91.1%) negative predictive value(NPV); ICM 2018 preoperative ***not infected*** result shows 83.5%(95%CI 77.4%-88.5%) sensitivity and 86.2%(95%CI 81.9%-88.6%) NPV and; MSIS 2013 preoperative ***not infected*** result shows 63.9%(95%CI 55.0%-72.1%) sensitivity and 84.3%(95%CI 81.1%-87.1%) NPV. Around half of the preoperative EBJIS ***likely*** (45.8%) and ICM 2018 ***inconclusive*** (54.5%) turn out to be infected postoperatively.
If we consider the more sensitive definition(EBJIS) as the gold standard: ICM 2018 preoperative ***not infected*** result shows 75.1%(95%CI 68.5%-81.0%) sensitivity and 78.3%(95%CI 73.9%-82.2%) NPV and; MSIS 2013 preoperative ***not infected*** result shows 42.1%(95% CI 35.2%-49.4%) sensitivity and 62.0% (59.2%-64.8) NPV.

**Conclusions:** The EBJIS 2021 definition is not only the most sensitive definition as it was shown to be the most effective in preoperatively ruling out PJI when there is a negative result.


Preoperative
Definitive
2021 EBJIS
212
186
10
16
24
13
11
147
147
2018 ICM
226
194
22
10
55
25
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102
102
2013 MSIS
300
253
47
83
83

## [FP E 02] PREDICTIVE MODELING WITH NEXT GENERATION SEQUENCING: A VALIDATED MULTI-INSTITUTIONAL ADJUNCT FOR DIAGNOSIS OF PERIPROSTHETIC JOINT INFECTION

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**Aim:** The clinical relevance of microbial DNA detected via next-generation sequencing (NGS) remains unknown. This multicenter study was conceived to: 1) identify species on NGS that may predict periprosthetic joint infection (PJI), then 2) build a predictive model for PJI in a developmental cohort, and 3)validate predictive utility of the model in a separate multi-institutional cohort.

**Method:** Fifteen institutions prospectively collected samples from 194 revision TKA and 184 revision THA between 2017-2019. Synovial fluid, tissue and swabs were obtained intraoperatively and sent to MicrogenDx (Lubbock,TX) for NGS analysis. Reimplantations were excluded. Patients were classified per the 2018 ICM definition of PJI. DNA analysis of community similarities (ANCOM) was used to identify 17 bacterial species of 294 (W-value>50) for differentiating infected vs. noninfected cases. Logistic regression with LASSO selection and random-forest algorithms were then used to build a model for predicting PJI. ICM classification was the response variable (gold-standard) and species identified through ANCOM were predictors. Patients were randomly allocated 1:1 into training and validation sets. Using the training set, a model for PJI diagnosis was generated. The entire model-building procedure and validation was iterated 1000 times.

**Results:** The model's assignment accuracy was 75.9%. There was high accuracy in true-negative and false-negative classification using this model, which has previously been a criticism of NGS. Specificity was 97.1%, PPV 75.0% and NPV 76.2%. On comparison of abundance between ICM-positive and ICM-negative patients, ***Staphylococcus aureus*** was the strongest contributor (F=0.99) to model predictive power. In contrast, ***Cutibacterium acnes*** was less predictive (F=0.309) and abundant across infected and noninfected revisions.

**Discussion:** This is the first study to utilize predictive algorithms on a large multicenter dataset to transform analytic NGS data into a clinically relevant diagnostic model. Our collaborative findings suggest NGS may be an independent adjunct for PJI diagnosis, while also facilitating pathogen identification. Future work applying machine-learning will improve accuracy and utility of NGS.

## [FP E 03] WHAT ARE THE OPTIMAL CUT-OFF VALUES FOR SYNOVIAL FLUID LEUKOCYTE COUNT AND DIFFERENTIAL IN THE DETECTION OF PROSTHETIC HIP INFECTION?

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**Aim:** The cut-off values for synovial fluid leukocyte count and neutrophils differential (%PMN) for differentiating aseptic from septic failure in total knee arthroplasties were already defined in the past. Our goal was to determine the cut-off values for synovial fluid leukocyte count and %PMN in failed total hip arthroplasties (THA).

**Method:** Patients undergoing revision THA were prospectively included. In perioperative assessment phase, synovial fluid leukocyte count and %PMN were determined. During the surgery, at least 4 intraoperative samples for microbiological and one for histopathological analysis were obtained. Infection was defined as presence of sinus tract, inflammation in histopathological samples, and ≥2 tissue and/or synovial fluid samples growing the same microorganism. Exclusion criteria were systemic inflammatory diseases, revision surgery performed less than 3 months from index surgery and insufficient tissue sampling.

**Results:** During the study period (between June 2006 and June 2011) 227 revision THAs were performed by the senior author. 31 patients were excluded. 196 patients (mean age, 69 years; 68% females) with THA failure were included. Aseptic failure was diagnosed in 150 patients (76,5%) and THA infection was diagnosed in 46 patients (23,5%). Synovial fluid leukocyte counts were significantly higher in the infected group (median, $5.50x10^6$ leukocytes/ml range, 0.05 to $143.9x10^6$ leukocytes/mL) than in the aseptic group (median, $0.23x10^6$ cells/ml; range, 0 to $21.3x10^6$ leukocytes/ml, P<0,0001). The %PMN was also significantly higher in the infected group (median, 83%; range, 6% to 97%) than in the aseptic group (median, 27,5%; range, 0% to 94%, P<0,0001). A synovial fluid leukocyte count of > $1.54x10^6$ leukocytes/ml, had a sensitivity of 63%, specificity of 95%, positive and negative predictive values of 78% and 89%, respectively. A synovial fluid %PMN of > 64%, had a sensitivity of 65%, specificity of 93%, positive and negative predictive values of 73% and 90%, respectively.

**Conclusion**: The synovial fluid leukocyte count of > $1.54x10^6$ leukocytes/ml and %PMN of > 64% are useful and reliable tests for excluding THA infection, having a negative predictive value of around 90%. This tests and calculated cut-off values are highly recommended in the diagnostic process of failed THAs.

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## [FP E 04] ROLE OF SERUM D-DIMER AND FIBRINOGEN VALUES IN THE DIAGNOSIS OF PERI-PROSTHETIC KNEE INFECTION: RESULTS OF A PROSPECTIVE MULTICENTER STUDY.

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**Aim:** Despite the availability of numerous tests, the diagnosis of periprosthetic infection (PJI) continues to be complex. Although several studies have suggested that coagulation-related markers, such as D-dimer and fibrinogen, may be promising tools in the diagnosis of prosthetic infections, their role is still controversial. The aim of this study is to evaluate the diagnostic accuracy of serum D-dimer and fibrinogen in patients with painful total knee replacement.

**Method:** 83 patients with painful total knee replacement and suspected peri-prosthetic infection were included. All patients underwent pre-operative blood tests to evaluate inflammation indices (ESR and CRP) and serum D-Dimer and Fibrinogen levels. The diagnostic performance of the tests was assessed using the ICM definition as the gold standard. The diagnostic accuracy of the D-dimer and fibrinogen was measured by assessing sensitivity, specificity and by calculating the area under the ROC curve.

**Results:** The definition of prosthetic infection based on the ICM criteria has made it possible to classify 40 peri-prosthetic infections and 43 aseptic failures. The mean value of fibrinogen, D-Dimer, VES and PCR observed in patients with prosthetic infection was significantly higher than in patients with aseptic failure [fibrinogen 468 mg / dl vs 331 mg / dl, p <0.001; D-Dimero 2177 ng/mL vs. 875 ng / mL, p <0.005], ESR 49 mm / hr vs 24 mm/h, p <0.001; PCR 25.5 mg /L vs 8.9 mg/L, p <0.001]. The optimal threshold value of the fibrinogen indicative of the presence of infection was 418 mg/dl, with a sensitivity of 72% and a specificity of 88%. The serum concentration of d-dimer greater than 945 ng / ml showed a sensitivity of 72.5% and a specificity of 76.7%.

**Conclusions:** Although in this multicenter prospective study we found that serum D-dimer may have significantly higher statistical values in PJI than aseptic failures, its diagnostic power appears however limited when compared with other markers including plasma fibrinogen. Fibrinogen is regularly analyzed before surgery, the evaluation of this marker does not involve additional costs. The diagnostic accuracy appears to be similar to that of classic markers such as the level of PCR and VES. Plasma D-dimer may have a limited value in the diagnosis of PJI unlike plasma fibrinogen which has shown moderate sensitivity and excellent specificity. However in our limited series of cases, both tests cannot be used alone in the diagnosis of infection, but could contribute to the diagnosis if contextualized to ves and pcr.

## [FP E 05] REINFECTION OR PERSISTENCE OF PERIPROSTHETIC JOINT INFECTION? NEXT GENERATION SEQUENCING REVEALS NEW FINDINGS

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**Aim:** Surgical management of PJI remains challenging with patients failing treatment despite the best efforts. An important question is whether these later failures reflect reinfection or the persistence of infection. Proponents of reinfection believe hosts are vulnerable to developing infection and new organisms emerge. The alternative hypothesis is that later failure is a result of an organism that was present in the joint but was not picked up by initial culture or was not a pathogen initially but became so under antibiotic pressure. This multicenter study explores the above dilemma. Utilizing next-generation sequencing (NGS), we hypothesize that failures after two-stage exchange arthroplasty can be caused by an organism that was present at the time of initial surgery but not isolated by culture.

**Method:** This prospective study involving 15 institutions collected samples from 635 revision total hip(n=310) and knee(n=325) arthroplasties. Synovial fluid, tissue and swabs were obtained intraoperatively for NGS analysis. Patients were classified per 2018 Consensus definition of PJI. Treatment failure was defined as reoperation for infection that yielded positive cultures, during minimum 1-year follow-up. Concordance of the infecting pathogen cultured at failure with NGS analysis at initial revision was determined.

**Results:** Among the total cohort, 203 revisions were considered infected and 432 were aseptic (based on ICM-criteria). Of the infected cases, 157 were NGS-positive and 46 NGS-negative. Twenty-nine ICM-positive patients (29/157;18.5%) failed by reoperation with an organism confirmed on culture. In 23 of these (23/29;79.3%), the organism at failure was present on NGS at initial revision. The remaining 6 cases detected discordant organisms between initial NGS and culture at failure. Of the 432 ICM-negative patients, NGS identified microbes in 48.1% (208/432) of “aseptic” revisions, and 17 of these failed. Thirteen of the 17 failures (76.5%) were due to an organism previously detected by NGS at initial revision.

**Conclusion:** Our collaborative findings suggest that most failures (79.3%) by infection recurrence could be attributed to an organism previously detected by NGS at index revision surgery.

## [FP E 06] PERFORMANCE OF ROUTINELY AVAILABLE SERUM PARAMETERS IN DIAGNOSING PERIPROSTHETIC JOINT INFECTIONS

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**Aim:** Although established serum inflammatory biomarkers, such as serum C-reactive protein (CRP) and serum white blood cell count (WBC), showed low accuracies in the literature, they are still commonly used in diagnosing periprosthetic joint infections (PJI). For a sufficient preoperative diagnosis novel more accurate serum parameters are needed. The aim of our study was to evaluate the performances of the established and novel routinely available serum parameters in diagnosing periprosthetic joint infections when using the proposed European Bone and Joint Infection Society (pEBJIS) criteria.

**Method:** In this retrospective study, 177 patients with an indicated revision surgery after a total joint replacement were included from 2015 to 2019. The easily accessible and routinely available serum parameters CRP, WBC, the percentage of neutrophils (%N), the neutrophils to lymphocytes ratio (NLR), fibrinogen and the platelet count to mean platelet volume ratio (PC/mPV) were evaluated preoperatively. The performances were examined via receiver operating characteristic (ROC) curve analysis (AUC). The curves were compared using the z-test. Seventy-five cases (42%) showed a PJI based on the pEBJIS-criteria.

**Results:** The sensitivities of serum CRP (cut-off: ≥10mg/L), WBC (≥10x10^9 cells/L) , %N (≥69.3%), NLR( ≥ 3.82), fibrinogen (≥ 457 mg/dL) , and PC/mPV (≥ 29.4) were calculated with 68% (95% CI: 57-78), 36% (26 – 47), 66% (54 – 76), 63% (51 – 73), 69% (57 – 78), and 43% (32 – 54), respectively. Specificities were 87% (79 – 93), 89% (81 – 94), 67% (57 76), 73% (63 – 81), 89% (80 – 93), and 81% (72 – 88), respectively. Serum CRP and fibrinogen showed better performances than the other evaluated serum parameters ($p$<0.0001). The median serum CRP (17.6 mg/L) in patients with PJI caused by a low virulence microorganism was lower compared with infections caused by high virulence organisms (49.2 mg/L; $p$=0.044). Synovial fluid leucocyte count and histology showed better accuracies than serum CRP, serum WBC, %N, NLR, serum fibrinogen, and PC/mPV ($p$<0.0001).

**Conclusions:** Although serum CRP and fibrinogen showed the best performances among the evaluated serum inflammatory markers, their results should be interpreted with caution in clinical practice. Serum parameters may remain normal in chronic infections or may be elevated in patients with other inflammatory conditions. In addition, they also correlated poorly with synovial fluid leukocyte count and histology. Therefore, serum parameters are still insufficient to confirm or exclude a periprosthetic joint infection. Hence, they can only be recommended as suggestive criteria in diagnosing PJI.

## [FP E 07] SYNOVIAL FLUID VISCOSITY MEASUREMENT; AN IMPORTANT DIAGNOSTIC PROCEDURE IN PROSTHETIC JOINT INFECTIONS DIAGNOSTICS

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**Aim:** Prosthetic joint infection (PJI) presents the second most common complication of total joint arthroplasty (TJA). Accumulating evidence suggests that up to 20% of aseptic failures are low-grade PJI. However, there is still no single test to reliably diagnose all PJI. In his thesis, Mazzucco emphasized the viscosity differences between normal, osteoarthritic, and rheumatic synovial fluid. Similarly, a recent study by Fu et al. reported significantly lower viscosity in patients with PJI compared to the aseptic failure cohort. The primary aim of our study was to determine whether synovial fluid viscosity is a more reliable diagnostic criterion for PJI compared to the synovial fluid cell count with differential and serum C-reactive protein (CRP) levels.

**Method:** We prospectively analyzed the viscosity of synovial fluid samples obtained during TJA of hip and knee joint revision procedures. We sampled 2.5-5 mL of synovial fluid for viscosity measurement. The samples were centrifuged (4 min at 7000 rpm) and the resulting supernatant was immediately transferred into the Ostwald viscometer. Viscosity was derived from the time required for a given volume of synovial fluid to pass the viscometer at 20 °C. The synovial fluid samples were also analysed for their cell count with differential and serum CRP was measured. The definite diagnosis of PJI was established on basis of EBJIS criteria. For the viscosity, the threshold for detecting PJI was set at 65 seconds.

**Results:** Between December 2020 and March 2021, we analyzed 12 knee and 11 hip TJA revision samples. These included 14 septic and 9 aseptic synovial fluid samples. The average viscometer time in the PJI group was 31s (range 20-48s) compared to 247s (range 68-616s) in the group of aseptic revision procedures. The specificity and sensitivity of our viscosity measurements were 100%. The sensitivity and specificity of cell count was 100% and 85.7%, for the synovial fluid differential they were 100% and 85.7%, and for the CRP they were 88.9% and 71.4%, respectively.

**Conclusions:** Our study is the first to report a significant difference in synovial fluid viscosity between the PJI and the aseptic cohort. It points towards the diagnostic superiority of viscosity measurements over conventional synovial fluid cell count, synovial fluid differential, and serum CRP levels. Albeit currently limited by small sample size, the study remains ongoing.

## [FP E 08] IS JOINT ASPIRATION TO RULE OUT PROSTHETIC JOINT INFECTION REQUIRED BEFORE EVERY REVISION JOINT ARTHROPLASTY? VALIDATION OF INSTITUTIONAL CRITERIA USING THE NEW EUROPEAN BONE AND JOINT INFECTION SOCIETY DEFINITION

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**Aim:** Synovial fluid investigation is the best alternative to diagnose prosthetic joint infection (PJI) before adequate microbiological/histology sampling during revision surgery. Although accurate preoperative diagnosis is certainly recommended, puncturing every patient before revision arthroplasty raises concerns about safety and feasibility issues especially in difficult to access joint (e.g., hip), that often require OR time and fluoroscopy/ultrasound guidance.
Currently there is no clear guidelines regarding optimal indications to perform preoperative joint aspiration to diagnose PJI before revision surgery. The main goal of this study is to determine the accuracy of our institutional criteria using the new European Bone and Joint Infection Society (EBJIS) PJI definition.

**Method:** We retrospectively evaluated every single- or first-stage for presumed aseptic or known infected revision total hip/knee arthroplasty procedures between 2013-2020. Preoperative clinical and laboratory features were systematically scrutinized. Cases with insufficient information for accurate final PJI diagnosis (i.e., no perioperative synovial fluid examination or no multiple cultures including sonication of removed implant) were excluded.
Preoperative joint aspiration is recommended in our institution if any of the following criteria are met: 1) elevated CRP and/or ESR; 2) early failure (<2 years) or repeat failure; 3) high clinical suspicion/risk factors are present. Performance of such criteria were compared against final postoperative EBJIS definition PJI diagnosis.

**Results:** A total of 364 revision THAs or TKAs were performed during the study period. After excluding 258 cases with insufficient information, a total of 106 patients were ultimately included. 38 (35,8 %) were classified as confirmed infections, 10 (9.4 %) as likely infected and 58 (54.7%) as infection unlikely.
Of those, 37 confirmed infection cases, 9 likely infected cases and 32 infection unlikely cases did have indication for preoperative synovial fluid collection before revision surgery.
Institutional criteria showed 95.8 % Sensitivity, 44.83 % Specificity, 92.9 % Negative Predictive Value (NPV) and 59 % Positive Predictive Value (PPV).

**Conclusions:** Sensitivity and NPV of the aforementioned institutional criteria are very high even with the use of the more sensitive EBJIS PJI definition. As such they seem to be a valid alternative in selecting patients that should be punctured before revision arthroplasty. They identify the vast majority of infected patients while saving a significant number of patients from unnecessary procedures.

## [FP E 09] SERUM D-DIMER CAN PREDICT FAILURE FOLLOWING REIMPLANTATION

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**Aim:** D-dimer is a widely available serum test that detects fibrinolytic activities that occur during infection. Prior studies have explored its utility for diagnosis of chronic periprosthetic joint infections (PJI), but not explored its prognostic value for prediction of subsequent treatment failure. The purpose of this study was to: (1) assess the ability of serum D-dimer and other standard-of-care serum biomarkers to predict failure following reimplantation, and (2) establish a new cutoff value for serum D-dimer for prognostic use prior to reimplantation.

**Method:** This prospective study enrolled 92 patients undergoing reimplantation between April 2015 and March 2019 who had previously undergone total hip/knee resection arthroplasty with placement of an antibiotic spacer for treatment of chronic PJI. Serum D-dimer level, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) levels were measured preoperatively for all patients. Failure following implantation was defined per the Delphi consensus criteria. Optimal cutoffs for D-dimer, ESR, and CRP were calculated based on ROC curves and compared in their association with failure following reimplantation criteria at minimum 1-year follow-up.

**Results:** 15/92(16.3%) patients failed reimplantation surgery at mean followup of 2.9 years (range 1.0-4.8). Optimal thresholds for D-Dimer, ESR and CRP were determined to be 1300ng/mL, 30mm/hr, and 1mg/L, respectively. The failure rate in patient with positive D-dimer was significantly higher at 32.0%(8/25) compared to those with negative D-dimer 10.6%(7/66); p=0.024. In comparison, 17.8%(8/45) of patients with ESR above threshold failed, compared to 13.89%(5/41) below (p=0.555) and 16.0%(4/25) of patients with CRP above threshold failed, compared to 16.1%(10/62) below (p=1.000).

**Conclusions:** Patients with elevated D-Dimer appear to be at higher risk of failure after reimplantation surgery. This serum marker may be used to generate an additional data point in patients undergoing reimplantation surgery, especially in circumstances when optimal timing of reimplantation cannot be determined based on clinical circumstances.

## [FP E 10] THE CALPROTECTIN LATERAL FLOW TEST FOR THE DIAGNOSIS OF PROSTHETIC JOINT INFECTIONS WHEN THE RECOMMENDED ALGORITHMS DO NOT APPLY

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**Aim:** The diagnosis of prosthetic joint infection (PJI) is challenging and relies on a combination of parameters. However, the currently recommended diagnostic algorithms have not been validated for patients with recent surgery, dislocation or other events associated with a local inflammatory response. As a result, these algorithms are not safely applicable offhand in such conditions. Calprotectin is a leukocyte protein that has been shown to be a reliable biomarker of PJI. The purpose of this study was to evaluate the use of calprotectin to rule out PJI within 3 months after surgery or dislocation.

**Method:** We included patients who underwent arthroplasty revision surgery at our institution within 3 months after any event causing inflammation. Calprotectin was measured using a lateral-flow assay. European Bone and Joint Infection Society (EBJIS) criteria were used as gold standard. The diagnostic accuracy of calprotectin was calculated.

**Results:** Twenty-two patients (14 females, 8 males) with a mean age of 65.1 ± 12.3 years with 13 total hip (THA) and 9 total knee arthroplasties (TKA) were included. There were 4 instances of possible early-onset acute infection, 4 dislocations, 2 patella tendon ruptures, 1 local tissue reaction to the sutures, 4 cases of early loosening, 2 component breakages and 1 avulsion of a polyethylene patella button.
Using the EBJIS criteria, PJI was confirmed postoperatively in 12 cases. With a cut-off at 50mg/L, the calprotectin lateral flow test was positive in 10 cases. This results in a sensitivity of the calprotectin test of 0.75, a specificity of 0.9, positive and negative predictive values of 0.9 and 0.75, respectively, and a positive and negative likelihood ratio of 7.5 and 0.28, respectively.

**Conclusions:** Aggravating the difficulties of ruling out PJI prior to revision surgery, local inflammation can be caused by some conditions in which the widely accepted PJI definition criteria cannot be applied. Nevertheless, an accurate diagnosis of PJI is just as crucial in these situations as it is in planned revision surgery. This study suggests that calprotectin is a promising diagnostic parameter for ruling out PJI in such cases. The calprotectin lateral-flow assay is readily applicable at the beginning of the procedure, yielding results that can assist in the decision whether to perform septic revision or aseptic partial or component exchange within 15 minutes, and with an overall accuracy of 81.8%.

## [FP F 01] INFLUENCE OF CEFTRIAXONE ON HUMAN BONE CELL VIABILITY AND MINERALIZATION POTENTIAL - AN VITRO STUDY

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**Aim:** Implant-associated infection usually require prolonged treatment or even removal of the implant. Local application of antibiotics is used commonly in orthopaedic and trauma surgery, as it allows reaching higher concentration in the affected compartment, while at the same time reducing systematic side effects. Ceftriaxone release from calcium sulphate has a particularly interesting, near-constant release profile in vitro, making it an interesting drug for clinical application. Purpose of the present study was to investigate the potential cytotoxicity of different ceftriaxone concentrations and their influence on osteogenic differentiation of human pre-osteoblasts.

**Method:** Human pre-osteoblasts were cultured up to 28 days in different ceftriaxone concentrations, ranging between 0 mg/L and 50'000 mg/L. Cytotoxicity was determined quantitatively by measuring lactate dehydrogenase release, metabolic activity and cell proliferation. Gene expression analysis of bone-specific markers as well as mineralization and protein expression of collagen-I (Col-I) were investigated to assess osteogenic differentiation.

**Results:** Cytotoxic effects on human pre-osteoblasts could be shown above 15'000 mg/L after 1 and 2 days, whereas subtoxic effects could be observed at concentrations at 500 mg/L after 10 days. Cell proliferation showed no clear alteration up to 1000 mg/L, though a notable decline at 1500 mg/L could be seen after 10 days. Gene and protein expression of Col-I showed a concentration-dependent decrease at day 10 and 14, but also mineralization levels of human pre-osteoblasts presented a similar trend at day 28. Interestingly, the degree of mineralization was already impaired at concentrations above 250 mg/L.

**Conclusions:** These findings provided extensive insights into the influence of different ceftriaxone concentrations on viability, proliferation, gene and protein expression but also mineralization of human bone pre-osteoblasts. While short-term cytotoxicity is observed only at very high concentrations, metabolism may be impaired at much lower concentrations when exposure is prolonged. Release of ceftriaxone expected from calcium sulphate however remains below thresholds of impaired bone mineralization, even after 4 weeks of exposure. This study demonstrates the importance of properly selecting and monitoring antibiotic concentrations during clinical application.

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## [FP F 02] VANCOMYCIN BONE AND TISSUE CONCENTRATIONS FOLLOWING TIBIAL INTRAOSSEOUS ADMINISTRATION – EVALUATED IN A PORCINE MODEL

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**Background:** Systemically administered vancomycin may provide insufficient target-site concentrations. Intraosseous vancomycin administration has the potential to overcome this concern by providing high target-site concentrations.

**Aim:** To evaluate the local bone and tissue concentrations following tibial intraosseous vancomycin administration in a porcine model.

**Method:** Eight female pigs were assigned to receive 500 mg diluted vancomycin (50 mg/mL) through an intraosseous cannula into the proximal tibial cancellous bone. Microdialysis was applied for sampling of vancomycin concentrations in tibial cancellous bone adjacent to the intraosseous cannula, in cortical bone, in the intramedullary canal of the diaphysis, in the synovial fluid of the knee joint, and in the subcutaneous tissue. Plasma samples were obtained. Samples were collected for 12 hours.

**Results:** High vancomycin concentrations were found in the tibial cancellous bone with a mean peak drug concentration of 1,236 (range 28-5,295) µg/mL, which remained high throughout the sampling period with a mean end concentration of 278 (range 2.7-1,362.7) µg/mL after 690 min. The mean (standard derivation (SD)) peak drug concentration in plasma was 19 (2) µg/mL, which was obtained immediately after administration. For the intramedullary canal, in the synovial fluid of the knee joint, and subcutaneous tissue, comparable mean peak drug concentration and mean time to peak drug concentration were found in the range of 7.5-8.2 µg/mL and 45-70 min, respectively.

**Conclusions:** Tibial intraosseous administration of vancomycin provided high mean concentrations in tibial cancellous bone throughout a 12-hour period, but with an immediate and high systemic absorption. The concentrations in cancellous bone had an unpredictable and wide range of peak concentration. Low mean concentrations were found in all the remaining compartments. Our findings suggest that intraosseous vancomycin administration in proximal tibial cancellous bone only is relevant as treatment in cases requiring high local concentrations nearby the intraosseous cannula.

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## [FP F 03] INFLAMMATORY BOWEL DISEASES INCREASE THE RISK OF PERIPROSTHETIC JOINT INFECTION

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**Aim:** A large body of evidence is emerging to implicate that dysregulation of the gut microbiome (dysbiosis) increases the risk of surgical site infections. Gut dysbiosis is known to occur in patients with inflammatory bowel disease (IBD), allowing for translocation of bacteria across the inflamed and highly permeable intestinal mucosal wall. The null hypothesis was that IBD was not associated with increased risk of periprosthetic joint infection (PJI) after primary total hip and knee arthroplasty. Our aim was to investigate whether a prior diagnosis of IBD was associated with an higher risk of PJI following primary total hip and knee arthroplasty.

**Method:** A matched cohort study was designed. Primary endpoint was the occurrence of PJI at 2-year. Secondary endpoints were aseptic revisions, as well as discharge to rehab facility, complications up to 30 days, and readmission up to 90 days after TJA. ICD-9 and -10 codes were used to identify patients with IBD and the control cohort. A chart review was performed to confirm diagnosis of IBD. Using our institutional database, 154 patients with IBD were identified and matched (3 to 1) for age, sex, body mass index (BMI), year of surgery, and joint affected with 462 individuals without IBD undergoing TJA.

**Results:** The cumulative incidence of PJI was 4.55% among patients with IBD versus 1.32% among the control cohort (p=0.024). When bivariate logistic regression was performed, a diagnosis of IBD was found to be an independent risk factor for PJI (OR 3.56 95% C.I. 1.17 - 11.23; p=0.024) and aseptic revisions (OR 3.47, 95% C.I. 1.30 - 3.47; p=0.012). The rate of postoperative complications was also higher in patients with IBD.

**Conclusions:** Based on the findings of this study, it appears that patients with IBD are at higher risk for failure due to PJI or aseptic loosening after TJA. The exact reason for this finding is not known but could be related to the bacterial translocation from the inflamed intestinal mucosa, the dysregulated inflammatory status of these patients, malnutrition, and potentially other factors. Some of the so-called aseptic failures maybe also as a result of infection that may have escaped detection and/or recognition.

## [FP F 04] PERIPROSTHETIC FUNGAL INFECTIONS – AN ANALYSIS OF 29 CASES FROM A SINGLE CENTER

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**Aims**: Periprosthetic fungal infections are rare and account for 1-2% of all periprosthetic joint infections(PJI). This study aims at presenting treatment details, clinical and microbiological results in a large single centre cohort.

**Methods**: We retrospectively identified 29 patients (9 total knee replacements (TKA) and 20 total hip replacements(THA) treated for a fungal infection between 2007 and 2019. Microbiological findings, patient demographics and complications were analysed. Statistical analysis was performed using descriptive statistics; non-parametric analysis were performed using the Mann-Whitney U-Test. Infection-free survival was determined using Kaplan-Meier analysis and differences in survival were analysed using the log-rank test. The p value was set at $p<0.05$ with 95% confidence intervals (95% CI) provided.

**Results**: 28% (8/29) suffered from reinfection. The reinfection-free survival probability was 65% (95% CI 45-85) after a median follow- up period of 28 months (IQR 6 – 39). With the numbers we had, we were not able to detect a difference between THA and TKA re-infections (p=0.517). Four patients underwent amputation, 3 patients had a definitive girdlestone hip and eight patients died after a median of 5 months after first-stage surgery (IQR 1-7).
All patients treated had positive synovial fluid or tissue cultures for ***Candida species.*** In 22 /29 patients ***C. albicans***, in 3 patients ***C. parapsilosis***, in 2 patients ***C. glabrata*** and in 1 patient each ***C. famata, C. dubliniensis*** and ***C. gulliermondii***. Polymicrobial bacterial infection was found in 86% of patients with ***staphylococci*** in 20 patients, ***E. coli*** in 2 patients, ***vancomycin-resistant enterococci***, ***pseudomonas, acinetobacter*** and ***achromobacter*** species in 1 patient each.
When investigating risk factors for reinfection, with the numbers we had we were not able to find a significant difference for patients with polymicrobial infection (p=0.974), azole-resistant ***Candida*** (***p***=0.491), tobacco users (p=0.175), or diabetics (p=0.54). Furthermore, median age (73 vs. 72, p=0.756) and Charlson comorbidity score (6 (interquartile range(IQR) 4-8) vs. 8 (IQR 5-10), p=0.184) were not different between the groups while on the other hand there was a trend for a higher body mass index in patients with reinfection (34 (IQR 31-38) vs. 28 (IQR 25-33), p=0.075).

**Conclusions**: Fungal PJI is associated with poor reinfection free survival , frequent revisions and high mortality. All infections were caused by ***Candida spp.*** in which azole-resistance most be considered when planning treatment. While polymicrobial infection complicated treatment there was no difference in survival. A higher BMI and comorbidity score might be associated with higher risk for reinfections.

## [FP F 05] LIPOSOMAL AMPHOTERICIN B LOCAL ANTIFUNGAL THERAPY: FIVE YEARS OF CLINICAL USE

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**Aim:** Fungal orthopaedic infections most commonly affect people with complex surgical histories and existing comorbidities. Recurrence and re-infection rates are high, even with optimal surgical and systemic antifungal treatment. AmBisome liposomal amphotericin B has been suggested for local antifungal therapy, as an adjunctive treatment for fungal osteoarticular infections. Few case series have examined its clinical use when combined with polymethylmethacrylate orthopaedic cement, or with absorbable local antibiotic carriers.
We aimed to evaluate the clinical use of local antifungal therapy with AmBisome liposomal amphotericin B, including tolerated doses, serious adverse events, and treatment outcomes.

**Method:** A retrospective cohort of all patients treated with local antifungal therapy with AmBisome liposomal amphotericin B between January 2016 and January 2021 in an orthopaedic tertiary referral hospital was identified using pharmacy records.
Renal function, serious adverse events during treatment, surgical outcomes including spacer fracture and infection recurrence, were identified from electronic clinical records. The project was approved by the Institutional Review Board (clinical audit 6871).

**Results:** 11 operations involving local antifungal therapy with AmBisome liposomal amphotericin B, for 10 patients, were identified. 9 patients were infected with Candida species and one patient with Aspergillus. Follow-up duration ranged from 14 months to 41 months.
Eight first stage arthroplasty revisions, 2 second stage arthroplasty revisions, and one debridement and removal of metalwork for fracture-related infection were performed. Locally implanted doses of AmBisome liposomal amphotericin B ranged from 100mg to 3600mg (50-400mg per 40g mix of polymethacrylate orthopaedic cement). Six patients received AmBisome liposomal amphotericin B in absorbable antibiotic carriers containing calcium sulphate. This was noted to delay carrier setting.
No patients experienced serious adverse events related to toxicity from local antifungal therapy with AmBisome liposomal amphotericin B. There were no spacer fractures. Overall treatment success was 55% at final follow-up, although there were no recurrent fungal infections identified in patients experiencing treatment failure.

**Conclusions:** Local antifungal therapy with liposomal amphotericin B, when combined with surgery and systemic therapy, appears to be a safe and well tolerated intervention in the management of complex fungal osteoarticular infections.

## [FP F 06] THE INFLUENCE OF UNSUSPECTED INTRAOPERATIVE POSITIVE CULTURES IN ASEPTIC TOTAL HIP REVISION SURGERY

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**Aim:** Periprosthetic joint infection (PJI) is a devastating complication in revision total hip arthroplasty (THA). As preoperative diagnosis can be difficult, some patients who undergo planned aseptic revision surgery might have positive intraoperative cultures and later be classified as infected. In this retrospective study we analyzed the influence of intraoperative positive cultures and possible underlying risk factors in patients undergoing planned aseptic THA revision.

**Method:** We retrospectively analyzed 276 cases of aseptic THA revision surgery between 2010 and 2017 who had a minimum follow-up period of 24 months. All patients underwent preoperative serum and synovial diagnostics according to the Center of Disease Control (CDC) (2010) or Musculoskeletal Infection Society (MSIS) Criteria (2011-2017) for PJI and were classified as aseptic prior to surgery. In all cases intraoperative tissue samples were taken and reviewed. Primary endpoint was defined as any complication leading to revision surgery. Secondary endpoint was explantation due to PJI or death. Revision free survival (RFS) and infection free survival (IFS) for intraoperative negative and positive cultures was calculated via Kaplan Meyer Method. Patients' medical history was analyzed for possible risk factors for positive cultures.

**Results:** In 96 (34.78%) cases positive cultures were found. 67 (24.28%) had a single positive culture and 29 (10.51%) had ≥ two positive cultures. Coagulase negative staphylococci were found in 57.69% of the positive cultures. While the revision free survivorship was not different in patients with single positive cultures compared to patients with negative cultures (72.86 (95%CI 60.08-85.64) vs 83.01 months (95%CI 75.42-90.60) p=0.201), patients with ≥ two positive cultures had a reduced mean RFS (38.46 (95%CI 20.16-50.76) vs. 83.01 months (95%CI 75.42-90.60) p<0.02). 22 (7.97%) patients underwent explantation of the THA due to PJI. The IFS was reduced if ≥ two cultures were positive compared to culture negative patients (56.48 (95%CI 46.20-66.75) vs 110.78 months (95%CI 106.78-114.77) p=0.001). Risk for explantation due to PJI increased if ≥ two cultures were positive (Odds Ratio (OR) 3.19 (95%CI 1.36-7.52). A BMI ≥ 30 was associated with the risk of ≥ two positive cultures (OR 2.85 (95%CI 1.40-5.78).

**Conclusions:** Occurrence of two or more positive cultures in aseptic revision THA has devastating influence on the revision free survival and infection free survival. As the risk for ≥ two positive cultures increases almost 3-fold in patients with a BMI ≥ 30, extended preoperative diagnostics in obese patients should be considered to detect possible low grade PJI before revision surgery.

## [FP F 07] SYNOVIAL COMMERCIAL ANTIBODY TESTING DOES NOT PROVIDE VANTAGE COMPARED TO TRADITIONAL CULTURE IN THE MICROBIAL IDENTIFICATION OF PERIPROSTHETIC JOINT INFECTION

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**Aim:** Microbial identification in the setting of periprosthetic joint infections (PJI) is crucial to tailor the best combination of surgical and medical treatment. Given the high cost, low sensitivity and slow results associated with traditional cultures, s synovial fluid antibody assay was developed. We asked whether antibody testing may be used as a proxy to traditional culture in the setting of PJI.

**Method:** A retrospective study of patients who underwent revision total hip (THA) and knee (TKA) arthroplasty between January 2019 and January 2020 was performed. All patients were aspirated prior to revision surgery and antibody testing was performed. All patients had samples harvested for culture as per standard of care. Results of the two tests and their concordance when an organism was identified were compared. A frequency table was used and a McNemar test was used to compare the two methods.

**Results:** 419 patients were included in this study. Antibody testing had a sensitivity and specificity of 21.9% and 92.5%, respectively, compared to traditional cultures. There were 78.1% of false negative and 7.5% of false positives (McNemar test $p<0.001$). Of the 12 patients who had positive results in both tests, 5 (41.7%) had discordant pathogens identified in each test.

**Conclusions:** Synovial fluid antibody testing performed poorly when used as a substitute for cultures and may not be a clinically adequate surrogate despite lower cost and faster results. Not only was there a low sensitivity, but also a high rate of discordant organisms between the two tests when both were positive.

## [FP F 08] DEMONSTRATION OF LOCAL ACUTE PHASE RESPONSE DURING OSTEOMYELITIS

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**Aim:** The liver is the major source of acute phase proteins (APPs) and serum concentrations of several APPs are widely used as markers of inflammation and infection. The aim of the present study was to explore if a local extra hepatic osseous acute phase response occurs during osteomyelitis.

**Method:** The systemic (liver tissue and serum) and local (bone tissue) expression of several APPs during osteomyelitis was investigated with qPCR and ELISA in a porcine model of implant associated osteomyelitis (IAO) at 5, 10 and 15 days after inoculation with ***S. aureus*** or saline, respectively. Additionally, samples were also collected from normal heathy pigs and pigs with spontaneous, chronic, haematogenous osteomyelitis. Afterwards, immunohistochemistry towards different upregulated APPs was performed on the porcine osteomyelitis lesions and on bone biopsies from human patients with chronic osteomyelitis.

**Results:** All infected porcine bone lesions (apart from Day 5 in the IAO model) were made up by necrosis, pus, and various degree of fibrotic encapsulation. A local, highly significant upregulation of Serum Amyloid A (SAA, up to 4000-fold upregulation), Complement component C3 (C3), and Inter-Alpha-Trypsin Inhibitor Heavy Chain 4 (ITIH4) were present in infected pigs compared to sterile controls. For the experimental IAO animals, the upregulation of C3 and ITIH4 increased over time, *i.e.* the highest expression was seen on day 15 after bacterial inoculation. In the liver, only C-reactive protein (CRP) and ITIH4 (not SAA or C3) were slightly upregulated in infected pigs. Serum concentrations of CRP, SAA and haptoglobin were only upregulated at day 5 in IAO infected animals. Immunohistochemically, comparable numbers of APP positive cells (leucocytes and bone cells) were found in human and porcine bone samples with chronic osteomyelitis

**Conclusions:** This is to our knowledge the first description of local APP up-regulation during chronic bone infection. Only small changes in the expression of APPs were found in the liver and serum samples. Thus, the presence of an osseous upregulation of APPs appears to be part of a predominantly local response that will be difficult to measure systemically. The importance of a local immune response in bone infections seems logical as the blood supply is severely impaired during osteomyelitis. There is a real need for supportive diagnostic bone infection criteria which should be based on a comprehensive understanding of the local inflammatory response. As seen from the present study, staining for SAA or C3 could potentially improve the diagnostic performance of histopathology.

## [FP F 09] SQUAMOUS CELL CARCINOMA COMPLICATING CHRONIC OSTEOMYELITIS: A SYSTEMATIC REVIEW AND CASE SERIES

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**Aim:** Squamous cell carcinoma (SCC) is a rare but often devastating complication of chronic osteomyelitis. Optimum diagnosis and management are not well established. This paper aimed to develop a definitive, evidence based approach to its diagnosis and management.

**Method:** A systematic review of relevant published studies available in English from 1999-present was conducted. Strict inclusion criteria ensured that the diagnoses of osteomyelitis and SCC were explicit and valid. Additional cases from our institution were included using the same eligibility criteria. Data regarding patient demographics, osteomyelitis diagnosis, SCC diagnosis and its management and patient outcomes were collected. Statistical significance was assessed by Fisher's exact test.

**Results:** Nineteen publications involving 98 patients plus eight patients managed locally were included. Eighty percent of patients were male, diagnosed with SCC at an average age of 59 years old (24-82 years), 31 years after their osteomyelitis diagnosis (3-67 years). Multiple bones were affected: tibia or fibula (59%), femur (17%), pelvis and sacrum (8%), bones of the foot and ankle (8%) and upper limbs (6%). Malignant transformation was associated predominantly with sinus (82%), ulceration (61%) and discharge (41%). SCC was diagnosed by biopsy (77%) or incidentally (23%) following definitive management for osteomyelitis. Twenty-two percent of patients had a staging CT scan. Seventy-six percent of patients underwent amputation, 16% underwent limb-sparing wide local excision and the remaining patients were palliated.
Incidental diagnosis of SCC was associated with poorer outcomes in terms of death or disease recurrence (one year, $p$=0.052, five years $p$=0.021, Fisher's exact test) as was metastatic disease at SCC diagnosis (one year, $p$=0.006, five years, $p$=0.032, Fisher's exact test) and pelvic or sacral disease (one year $p$<0.001, five years $p$=0.002, Fisher's exact test).
All patients who were not actively treated died within one year of SCC diagnosis. Data was suggestive that more patients who underwent amputation (versus wide local excision) were disease free at one and five years but this was not statistically significant (one year, $p$=0.058, five years, $p$= 0.152, Fisher's exact test).

**Conclusions:** SCC should be suspected in all cases of chronic osteomyelitis with skin changes, particularly where changes exceed 3 years duration and involve the pelvis. Multiple biopsies for histology should be taken in all suspected cases, as well as routinely during surgical excision of osteomyelitis when chronic skin changes are present. Once SCC is identified, staging CT scan should be performed to guide management. Amputation, where possible, should be considered.

## [FP F 10] PLASMA-CELL INFILTRATION ON HISTOPATHOLOGICAL SAMPLES OF CHRONIC BONE AND JOINT INFECTIONS DUE TO CUTIBACTERIUM ACNES: A SERIES OF 25 CASES

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**Aim:** The aim of this study was to confirm that Mirra's criterion (≥ 5 Polymorphonuclears (PMNs) per field in 5 high power fields (HPFs)) is not adequate for diagnosis of chronic bone and joint infections (BJIs) due to ***Cutibacterium acnes*** (***C. acnes***). The second objective was to determine if plasma-cell infiltration, that is a classical marker of chronic inflammation, could be useful for the diagnosis of chronic BJIs due to ***C. acnes***.

**Methods:** We retrospectively selected 25 patients from 2009 to 2013 with chronic BJIs due to ***C. acnes***. In addition of Mirra's criterion, the number of plasma-cells (≥5 plasma-cells/5 HPFs, defined as "CRIOAc Lyon's criterion") was implemented in the histopathological analysis. Patients were defined as infected, if at least one of the two criteria were present.

**Results:** According to Mirra's and CRIOAc Lyon's histopathological criteria, positive histology was observed in respectively 12 (48%) and 16 (64%) cases. In 1 case the samples were not analyzable. Considering the 12 cases with negative Mirra's criterion, high plasma-cell infiltration (≥5 plasma-cells/5 HPFs; Figure 1) was observed in 6 cases (50%), and low plasma-cells infiltration (2-5 plasma-cells/5 HPFs) was observed in 5 other cases (42%).

**Conclusions:** Mirra's criterion is not an adequate criterion to defining chronic BJIs [1, 2]. In our study, more cases of chronic BJIs due to ***C. acnes*** have been diagnosed using CRIOAc Lyon's criterion than Mirra's criterion. Adding CRIOAc Lyon's criterion might restore some histopathological diagnosis of chronic BJIs due to ***C. acnes,*** when a clinical chronic BJI is suspected.

**References:**

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[2] Bori G, et al. Biomed Res Int. 2018; 1412701.

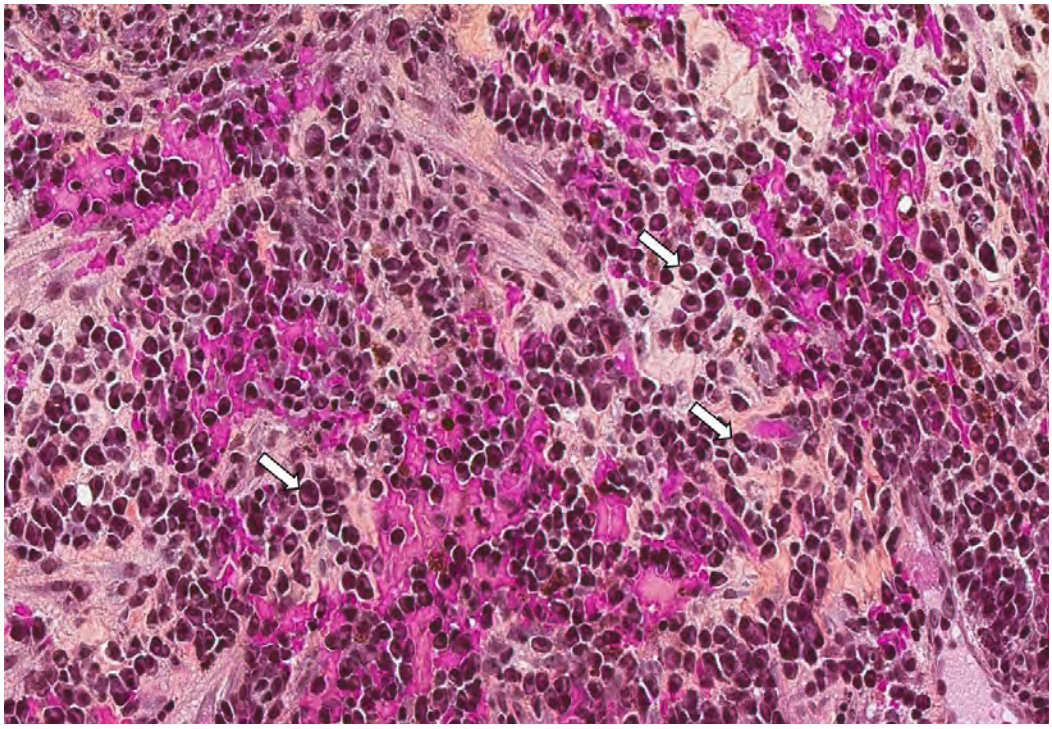

**Figure 1:** Plasma-cell infiltration into synovial tissue (Hematoxylin-Eosin-Safran; x200 magnification). The white arrows indicate plasma-cells: they consist of an eccentric nucleus surrounded by an abundant cytoplasm.

## [FP G 01] A HIGH PREVALENCE OF CUTIBACTERIUM ACNES INFECTIONS IN SCOLIOSIS REVISION SURGERY,A DIAGNOSTIC AND THERAPEUTIC DILEMMA

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**Aim:** Low-grade infections are difficult to diagnose. As the presence of a chronic infection requires extensive surgical debridement and antibiotic treatment, it is important to diagnose a SII prior to surgery, especially when the hardware is revised. We investigated whether serum inflammatory markers or nuclear imaging can accurately diagnose a chronic spinal instrumentation infection (SII) prior to surgery.

**Method:** All patients who underwent revision spinal surgery after a scoliosis correction between 2017 and 2019 were retrospectively evaluated. The diagnostic accuracy of serum C-reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR), $^{18}$F-fluorodeoxyglucose positron emission tomography combined with computed tomography (FDG-PET/CT) and Technetium-99m-methylene diphosphonate (99mTc-MDP) 3-phase bone scintigraphy (TPBS) to diagnose infection were studied. Patients with an acute infection or inadequate culture sampling were excluded. SII was diagnosed if ≥ 2 of the same microorganism(s) were isolated from intra-operative tissue cultures.

**Results:** 31 patients were included. The indication for hardware extraction was pseudoarthrosis in the majority of patients (n = 15). 22 patients (71%) were diagnosed with SII. In all infected cases, ***Cutibacterium acnes*** was isolated, including 5 cases with a polymicrobial infection. Sensitivity, specificity, PPV and NPV was: 4.5%, 100%, 100% and 30.0% for CRP >10.0 mg/L, 5.5%, 100%, 100% and 29% for ESR > 30 mm/h; 56%, 80%, 83% and 50% for FDG-PET/CT and 50%, 100%, 100% and 20% for TPBS, respectively.

**Conclusions:** The prevalence of SII in patients undergoing revision spinal surgery is high, with ***Cutibacterium acnes*** as the main pathogen. No diagnostic tests could be identified that could accurately diagnose or exclude SII prior to surgery. Future studies should aim to find more sensitive diagnostic modalities to detect low-grade inflammation.

## [FP G 02] ANTIMICROBIAL SUSCEPTIBILITY OF ISOLATED PATHOGENS FROM PYOGENIC SPONDYLODISCITIS: A COMPARISON OF COMMUNITY-ACQUIRED AND HEALTHCARE-ASSOCIATED INFECTIONS.

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**Aim:** Empiric antibiotic therapy for suspected pyogenic spondylodiscitis (SD) should be initiated immediately with severely ill patients and may also be necessary for culture-negative SD. The aim of this study was to infer an appropriate empiric antibiotic regimen by analyzing the antimicrobial susceptibility of isolated pathogens from microbiologically proven pyogenic spondylodiscitis.

**Method:** We performed a retrospective review of adult patients with clinically proven SD treated at our level 1 trauma center between 2013 and 2020. Demographic data, radiologic findings, and treatment modalities were evaluated. The appropriateness of empiric antibiotic regimens was assessed based on the antibiograms of the isolated pathogens. Anamneses were used to distinguish between community-acquired (CA) and healthcare-associated (HA) pathogens, which included cases that had a hospital stay or invasive intervention in the past 6 months.

**Results:** A total of 155 patients (male: N=88; female: N=67; mean age 66.1 ± 12.4 years) with SD were identified. In n= 74 (47.7%) cases, the infections were associated with the healthcare system (HA). N=34 (21.9%) patients suffered from sepsis. The lumbar spine was involved in 47.1% of the cases, the thoracic spine in 37.3%, and the cervical spine in 7.8%. In 7.8% of the cases, SD occurred in multiple spinal segments. N=96 (62.0%) patients were treated surgically. The mean hospital stay was 36.4 ± 36.3 days. Antibiograms of n=45 patients (HA: N=22; CA: N=23) could be retrospectively evaluated: The most frequently identified pathogens were ***Staphylococcus aureus*** (46.7%), ***Coagulase-negative Staphylococci*** (17.8%), ***Enterobacteriaceae*** (15.6%) and ***Streptococcus*** species (15.6%). Overall, 82.2% (HA: 68.2%; CA: 95.5%) of the isolated pathogens were sensitive to piperacillin/tazobactam, 77.8% (HA: 81.8%; CA: 72.2%) to vancomycin, 64.4% (HA: 68.2%; CA: 59.1%) to clindamycin, and 55.6% (HA: 36.4%; CA: 72.7%) to ceftriaxone. To a combination of vancomycin plus meropenem 97.8% of pathogens were sensitive (HA: 95.5%; CA: 100.0%), to vancomycin plus ciprofloxacin 91.1% (HA: 86.4%; CA: 95.7%), and to vancomycin plus cefotaxime 93.3% (HA: 90.9%; CA: 95.7%). In 14 cases, empiric antibiosis was adjusted based on the results of the antibiogram.

**Conclusions:** Antibiotic resistance of CA SD pathogens differed significantly from HA SD. The identification of the pathogen and the analysis of its susceptibility guides the antibiotic therapy. Vancomycin in combination with a carbapenem, broad-spectrum cephalosporin, or fluoroquinolone may be appropriate for empiric treatment of HA SD.

## [FP G 03] EFFECTS OF RIFAMPICIN ON MOXIFLOXACIN CONCENTRATIONS IN PORCINE CERVICAL SPINE: A RANDOMIZED MICRODIALYSIS STUDY

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**Aim:** Pyogenic spondylodiscitis remains a therapeutic challenge, as demonstrated by divergent treatment guidelines. The combination of moxifloxacin and rifampicin may be an attractive treatment option for cases caused by staphylococci; however, previous studies have reported a reduction in plasma concentrations of moxifloxacin when co-administered with rifampicin. The magnitude of this reduction in spinal tissues is not known. We aimed to investigate the interaction of rifampicin on moxifloxacin tissue concentrations in vertebral cancellous bone, intervertebral disc and subcutaneous adipose tissue in steady-state conditions using microdialysis in a porcine model.

**Method:** Twenty female pigs were randomized into two groups of ten pigs: Group A received moxifloxacin 400 mg orally once daily for three days preoperatively. Group B received moxifloxacin 400 mg orally for three days preoperatively combined with rifampicin 450 mg twice daily for seven days preoperatively. Measurements were obtained from plasma, vertebral cancellous bone, intervertebral disc and subcutaneous adipose tissue for 24 h. Microdialysis was applied for sampling in solid tissues.

**Results:** Co-administration of moxifloxacin and rifampicin demonstrated a reduction of free moxifloxacin concentrations in spinal tissues. The peak drug concentration ($C_{max}$) and the area under the concentration-time curve ($AUC_{0-24}$) in all tissue compartments decreased in the range of 66–79% and 65–76%, respectively.

**Conclusions:** Using microdialysis, we demonstrated a significant reduction of moxifloxacin $C_{max}$ and $AUC_{0-24}$ in the spinal tissues when co-administered with rifampicin. Further studies are warranted to understand the clinical implications of this finding for the treatment of pyogenic spondylodiscitis.

## [FP G 04] ORTHOPLASTICS IN PERIPROSTHETIC JOINT INFECTION OF THE KNEE: TREATMENT CONCEPT FOR COMPOSITE SOFT-TISSUE DEFECT WITH EXTENSOR APPARATUS DEFICIENCY

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**Aim:** Reconstruction of composite soft-tissue defects with extensor apparatus deficiency in patients with periprosthetic joint infection (PJI) of the knee is challenging. We present a single-centre multidisciplinary orthoplastic treatment concept based on a retrospective outcome analysis over 20 years.

**Method:** One-hundred sixty-seven patients had PJI after total knee arthroplasty. Plastic surgical reconstruction of a concomitant perigenicular soft-tissue defect was indicated in 49 patients. Of these, seven presented with extensor apparatus deficiency.

**Results:** One patient underwent primary arthrodesis and six patients underwent autologous reconstruction of the extensor apparatus. The principle to reconstruct missing tissue 'like with like' was thereby favoured: Two patients with a wide soft-tissue defect received a free anterolateral thigh flap with fascia lata; one patient with a smaller soft-tissue defect received a free sensate, extended lateral arm flap with triceps tendon; and three patients received a pedicled medial sural artery perforator gastrocnemius flap, of which one with Achilles tendon. Despite good functional results 1 year later, long-term follow-up revealed that two patients had to undergo knee arthrodesis because of recurrent infection and one patient was lost to follow-up. In parts, results have been published under doi: 10.7150/jbji.47018.

**Conclusions:** A treatment concept and its rationale, based on a single-centre experience, is presented. It differentiates between various types of soft-tissue defects and shows reconstructive options following the concept to reconstruct 'like with like'. Despite good results 1 year postoperatively, PJI of the knee with extensor apparatus deficiency remains a dreaded combination with a poor long-term outcome.

## [FP G 05] UNIPLANAR VERSUS BIPLANAR MONOLATERAL EXTERNAL FIXATOR KNEE ARTHRODESIS AFTER END-STAGE FAILED INFECTED TOTAL KNEE ARTHROPLASTY: A COMPARATIVE STUDY

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**Aim:** External fixator knee arthrodesis is a salvage procedure mainly used in cases of end-stage infected total knee replacement (iTKR). A stable fixation combined with bone-ends compression is basic to achieve knee fusion in such a scenario, but providing enough stability can be challenging in the presence of severe bone loss after multiple previous procedures. Compared with monoplanar configuration, a biplanar frame achieves improved coronal stiffness, while providing the advantages of good access to the wound and allowance of early ambulation. Our primary hypothesis stated that a biplanar frame would achieve higher and quicker fusion rate than a monolateral configuration.

**Method:** We conducted a retrospective cohort study examining patients managed with biplanar external fixator knee fusion due to non-revisable iTKR between 2014 and 2018. We compared this group of patients with a historical cohort-control patient who had been previously published by our unit in 2013, since we switched from a monoplanar to a biplanar configuration for the management of this kind of complex end-stage iTKR. Primary end-points were fusion rate, time to achieve bone fusion and infection eradication rate. Limb-length discrepancy, pain level, patient satisfaction, and health-related quality of life were also evaluated.

**Results:** A total of 29 cases were finally included; 8 patients were managed with a bilateral external fixator and 21 patients were managed with a monoplanar external fixator. In the biplanar configuration group, infection was eradicated in 100% of the patients, and fusion was achieved in all cases after 5.24 months on average. In comparison, in the monolateral configuration group, infection was eradicated in 18 (86%) out of 21, whereas fusion was achieved in 17 (81%) of the patients after a mean of 10.3 months (range, 4-16). Such difference was statistically significant ($p<0.05$). In both groups, postoperative pain was mild (VAS score 2,25 and 3,4, respectively) and patients expressed a high degree of satisfaction once fusion was achieved.

**Conclusions:** External fixation knee fusion is a useful limb-salvage procedure in end-stage cases of knee PJI. According to our data, the use of a biplanar configuration allows us to reduce in half (10.3 vs 5.2 months, $p<0.05$) the time needed to achieve the solid bone fusion in such a complex scenario. In this cohort of previously multi-operated patients, the satisfaction is high and the level of pain is low if a solid bone fusion free of infection is achieved.

## [FP G 06] VACUUM ASSISTED CLOSURE (VAC)-INSTILL SPACER IN SEPTIC TWO-STAGE REVISION TOTAL KNEE ARTHROPLASTY – A PILOT STUDY

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**Aim:** To improve the challenging treatment of periprosthetic joint infections (PJI), researchers are constantly developing new handling methods and strategies. In patients with PJI after total knee arthroplasty (TKA) and severe local or systemic comorbidities, a two-stage exchange using a temporary antibiotic loaded PMMA-spacer is considered gold standard. This method has undisputed advantages, however, the increased risk of biofilm formation on the spacer surface, bone defects and soft tissue contractions after a six-week spacer interval are severe limitations. Our hypothesis is that a vacuum sealed foam in combination with constant instillation of an antiseptic fluid can address these drawbacks due to a significantly reduced spacer interval.

**Method:** A pilot study was conducted in five PJI cases after TKA with severe comorbidities and/or multiple previous operations to evaluate the feasibility and safety of the proposed method. In the first step, surgical treatment included the explantation of the prosthesis, debridement and the implantation of the VeraFlo-Dressing foam. The foam is connected to the VAC-Instill-Device via an inflow and an outflow tube. The surgical site is sealed airtight with the VAC-film. During the next 5 days, an antiseptic fluid (Lavasorb® or Taurolidine®) is instilled in a 30-minute interval using the VAC-Instill-Device. The limb is immobilized (no flexion in the knee joint, no weight bearing) for five days. Following that, the second operation is performed in which the VAC-VeraFlo™-Therapy System is explanted and the revision TKA is implanted after debridement of the joint.

**Results:** No serious adverse event occurred during the VAC-Instill spacer treatment. The TKA revision was performed after a mean of 5.4 ± 1.9 days. Mean patient age was 71±6 years with a mean of 6 previous PJI surgeries. Host classification according to McPherson was I/B/3, III/B/3 and III/C/3 in three cases. Out of the five cases included, four were successfully treated and remained infect free to date (mean 14.2 ± 12 months; germs: methicillin-resistant s. aureus, e. coli, staph. lugdunensis and one culture neg.). One case with candida infection of a total femur prosthesis had to be treated with an enucleation of the hip due to rising inflammation parameters and signs of sepsis 7 days after VAC-Instill implantation.

**Conclusions:** The presented data on the VAC-Instill spacer method in septic two-stage revision TKA show promising results regarding feasibility and safety. A prospective randomized controlled examination is in progress to evaluate the possible advantages over a two-stage approach using a standard PMMA spacer.

## [FP G 07] MANAGEMENT OF CHRONIC FEMORAL AND TIBIAL OSTEOMYELITIS: A SYSTEMATIC SCOPING REVIEW

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**Aim:** Chronic osteomyelitis reflects a progressive inflammatory process of destruction and necrosis affecting bone architecture. It presents a challenge to manage, requiring multi-stage multidisciplinary interventions, and the literature reports a wide variety of treatment strategies. This systematic scoping review aims to map and summarise existing literature on treatment of chronic osteomyelitis of the femur and tibia and investigates the full range of treatments reported in order to enhance the reader's understanding of how to manage this complex condition.

**Method:** A comprehensive computer-based search was conducted in PubMed, EMBASE, MEDLINE, Emcare and CINAHL, between 1946 and June 2020, for articles reporting treatment of chronic tibial/femoral osteomyelitis. Two reviewers independently performed a two-stage title/abstract and full-text screening, followed by data collection. Studies were included if they described any treatment strategy including at least one surgical intervention. Key information extracted included causative pathogens, treatment protocol and outcome i.e. both success rate, defined as remission achieved following initial treatment with no recurrence during follow-up, and recurrence rate.

**Results:** A total of 1223 articles were identified and 52 articles (2999 patients) ultimately included. Although a wide variety of treatment protocols are reported, all revolve around three key principles: removal of infected tissue, dead space management and antibiotic therapy. Variations are evident when considering use of extensive versus more conservative debridement techniques, and delivery and regime of antibiotic therapy, e.g. whether to use one of, or both systemic and local delivery. The majority (75.45%) of patients presented with stage III or IV disease according to the Cierny-Mader classification and staphylococcus aureus was the most commonly isolated organism. Although there is heterogeneity across studies in reporting outcomes, with only 34 studies reporting success rate as defined in this review, 28 (82.4%) reported a success rate of at least 80%.

**Conclusions:** It is difficult to identify the optimal treatment strategy when reporting of outcomes is not standardised across studies, even in the context of similar techniques being used. Success rates across studies may also vary depending on patient demographics, comorbidities, severity, type and number of causative pathogens and follow-up length. It is now essential to identify specific patient and treatment related factors that may affect clinical outcomes. Given the current dominance of case series in the literature, there is a need for randomised controlled trials to yield further information that could aid future efficient management.

## [FP H 01] ASSESSING PRE-REFERRAL MICROBIOLOGY IN OSTEOMYELITIS: WHAT DOES IT TELL US?

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**Aim:** To compare pre-referral microbiology and previous bone excision in long bone osteomyelitis with intra-operative microbiology from a specialist centre.

**Method:** A prospective observational cohort study of patients referred to a single tertiary centre who met the following criteria: (i) aged ≥18 years, (ii) received surgery for long bone osteomyelitis and (iii) met diagnostic criteria for long bone osteomyelitis. Patient demographics, referral microbiology and previous surgical history were collected at the time of initial clinic appointment. During surgery, a minimum of 5 intra-operative deep tissue samples were sent for microbiology. Antimicrobial options were classified from the results of susceptibility testing using the BACH classification of long bone osteomyelitis as either Ax (unknown or culture negative), A1 (good options available) or A2 (limited options available). The cultures and susceptibility of pre-referral microbiology were compared to the new intra-operative sampling results. In addition, an association between previous osteomyelitis excision and antimicrobial options were investigated.

**Results:** 79 patients met inclusion criteria during the study period. From these, 39 (49.4%) patients had information available at referral regarding microbiology obtained from either sinus swab (n=16), bone biopsy (n=11), previous osteomyelitis excision sampling (n=7), aspiration (n=4) or blood culture (n=1). From these 39 patients, microbiology information at referral fully matched microbiology samples taken at operation in 8 cases (20.5%). Fifteen of the 39 patients (38.5%) had a different species isolated at surgery compared to referral microbiology. The remaining 16 patients (41.0%) had a culture-negative osteomyelitis on surgical sampling. Based on the microbiology obtained in our centre, 35 patients were classified as A1 (44.3%), 15 as A2 (18.9%) and 29 as culture negative, Ax (36.7%). Patients who had received previous excision of osteomyelitis before referral (n=32, 40.5%) had an increased odds ratio (OR) of having microbiology with limited antimicrobial options compared to those undergoing primary osteomyelitis excision (OR: 3.8, 95% CI 1.2 – 11.2, P=0.023, Fisher's exact test).

**Conclusions:** Patients are frequently referred with limited microbiological information. Pre-referral microbiology in long bone osteomyelitis correlated with intra-operative samples taken at our centre in less than one quarter of cases. Pre-referral microbiology data should be used with caution for planning treatment in osteomyelitis. Previous surgery for osteomyelitis was associated with microbiology culture with limited antimicrobial treatment options.

## [FP H 02] THE VALUE OF NEUTROPHIL-LYMPHOCYTE RATIO, PLATELET-LYMPHOCYTE RATIO, MONOCYTE-LYMPHOCYTE RATIO AND PLATELET COUNT-MEAN PLATELET VOLUME RATIO IN THE DIAGNOSIS OF SEPTIC ARTHRITIS

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**Aim:** The diagnosis of septic arthritis mostly relies on clinical examination, several blood parameters including white blood cell count, C-reactive protein, sedimentation and the analysis of the joint aspiration. However, the diagnosis can be difficult when the symptoms are vague and the information obtained from laboratory might be insufficient for definitive diagnosis. This study aimed to evaluate several ratios obtained from routine blood tests for a possible use in the diagnosis of septic arthritis.

**Method:** The adult patients who were operated in our clinic due to septic arthritis between 2014-2020 were identified and retrospectively evaluated. The patients with any blood disorders or missing file information were excluded. A total of 36 patients were found to be eligible for inclusion. The control group included 40 patients without any sign of infection who underwent total knee arthroplasty due to knee osteoarthritis. Preoperative blood tests of each patients were examined. In addition to CRP and sedimentation values, neutrophil-lymphocyte, monocyte-lymphocyte, platelet-lymphocyte and platelet count-mean platelet volume were calculated and receiving operating characteristics (ROC) curve analysis was made to determine the sensitivity, specificity and area under curve (AUC) values of these parameters.

**Results:** The distribution of affected joint in septic arthritis group was as follow; 22 knees, 6 hips, 4 shoulders, 2 elbows, 1 wrist and 1 ankle. The cultures of joint aspiration yielded positive result in 19 patients while the cultures were negative in 17 patients. All of the analyzed parameters were significantly different between the groups ($p<0.001$). ROC curve analysis results are given in detail, in Table 1 and Figure 1. The AUC value was 97.3 when only CRP and sedimentation values were used but increased to 98.6 when neutrophile/ lymphocyte ratio was added and increased to 100 when all analyzed parameters were included.

**Table 1.** The sensitivity, specificity and area under curve values.

| Parameter | Sensitivity (%) | Specificity (%) | Cut-off value | Area under curve |
|---|---|---|---|---|
| **NEUT/LYMP** | 94.1 | 80 | 2.3 | 91.8 |
| **PLAT/ LYMP** | 79 | 65 | 135 | 79.8 |
| **MON/ LYMP** | 76.5 | 82.5 | 0.3 | 88.9 |
| **PLAT/MPV** | 62 | 87.5 | 40 | 73.5 |
| **CRP (mg/L)** | 97 | 85 | 10 | 98.6 |
| **ESR (mm/hour)** | 97 | 90 | 35 | 97.7 |

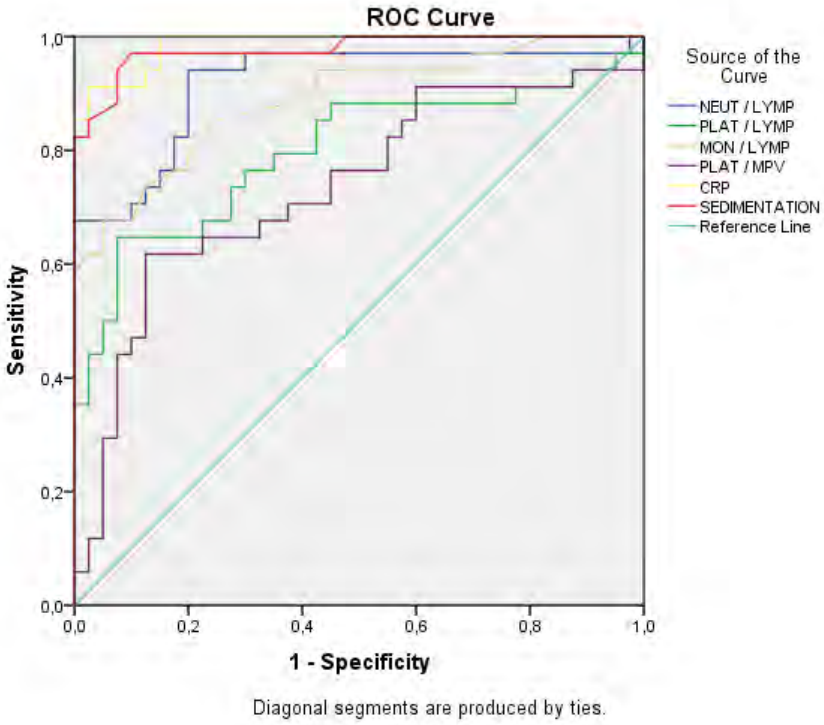


**Figure 1.** ROC curve analysis of the parameters.

**Conclusions:** The analyzed parameters were found to increase the overall sensitivity and specificity when used together with acute phase reactants. However, when evaluated separately, CRP and sedimentation were still found as the most valuable parameters in the diagnosis of septic arthritis. In the diagnosis of septic arthritis, 35 mm/hr cut-off value for sedimentation and 10 mg/L cut-off value for CRP were found more sensitive and specific compared to standard laboratory cut-off values of 20 mm/hr and 5 mg/L.

## [FP H 03] CHRONIC AND ACUTE PERIPROSTHETIC JOINT INFECTIONS COULD BE THE RESULT OF DAMAGE TO THE INTEGRITY OF THE GUT EPITHELIAL BARRIER

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**Aim:** A growing number of recent investigations on the human genome, gut microbiome, and proteomics suggests that the loss of mucosal barrier function, particularly in the gastrointestinal tract, may substantially affect antigen trafficking, ultimately influencing the close bidirectional interaction between the gut microbiome and the immune system. This cross-talk is highly influential in shaping the host immune system function and ultimately shifting genetic predisposition to clinical outcome. Therefore, we hypothesized that a similar interaction could affect the occurrence of acute and chronic periprosthetic joint infections (PJI).

**Method:** Multiple biomarkers of gut barrier disruption were tested in parallel in plasma samples collected as part of a prospective cohort study of patients undergoing revision arthroplasty for aseptic or PJI (As defined by the 2018 ICM criteria). All blood samples were collected before any antibiotic was administered. Samples were tested for Zonulin, soluble CD14 (sCD14), and lipopolysaccharide (LPS) using commercially available enzyme-linked immunosorbent assays. Statistical analysis consisted of descriptive statistics and ANOVA.

**Results:** A total of 96 patients were consented and included in the study. 32 were classified as PJI (23 chronic and 9 acute), and 64 as aseptic. Both Zonulin and LPS were found to be increased in the acute PJI group 8.448 ± 7.726 ng/mL and 4.106 ± 4.260 u/mL, compared to chronic PJI ($p<0.001$) and aseptic revisions ($p=0.025$). sCD14 was found to be increased in both chronic (0.463 ± 0.168 ug/mL) and acute PJI (0.463 ± 0.389 ug/mL) compared to aseptic revisions ($p<0.001$).

**Conclusions:** This prospective ongoing study reveals a possible link between gut permeability and the 'gut-immune-joint axis' in PJI. If this association continues to be born out with larger cohort recruitment, it would have a massive implication in managing patients with PJI. In addition to the administration of antimicrobials, patients with PJI and other orthopedic infections may require gastrointestinal modulators such as pro and prebiotics.

## [FP H 04] ORGANISM PROFILE CAUSING PERIPROSTHETIC JOINT INFECTION: THE LIST IS GROWING

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**Aim:** It is traditionally stated that around 80% of all periprosthetic joint infections (PJI) are caused by well-known gram positive organisms such as ***Staphylococcus aureus***. With the advances in diagnostic modalities and improved abilities to isolate infective organisms, we believe the organism profile causing PJI has changed over time and includes numerous other organisms that were either not recognized as pathogens and/or considered as contaminants.

**Method:** We retrospectively reviewed the medical records of 1,363 patients with confirmed PJI (559 THA and 804 TKA) who received treatment at our institution between 2000 and 2019. Pertinent data related to demographics, microbiological findings, and outcome of treatment were collected. Organisms were differentiated using culture or confirmed by Matrix-Assisted Laser Desorption Ionization-time of flight (MALDI-tof) mass spectrometry. Statistical analysis included logistic regressions.

**Results:** There was a total of 26 different species of organisms that resulted in PJI in our cohort. The rate of PJI caused by slow growing organisms, that are catalase negative, such as ***Streptococcal viridans*** (OR 1.244; 95% CI 1.036-1.494), ***Streptococcus agalactiae*** (OR 1.513; 95% CI 1.207-1.898), and ***Staphylococcus epidermidis*** (OR 1.321; 95% CI 1.191-1.466) has been increasing over time. In contrast, the incidence of PJI caused by coagulase-negative Staphylococcus (OR 0.954; 95% CI 0.927-0.981); resistant species (OR 0.962, 95% CI 0.931-0.995), and Gram-positive species (OR 0.94, 95% CI 0.914-0.966) decreased over time. Notably, there was a higher prevalence of Streptococcal PJI (OR 0.551, 95% CI 0.374-0.812) and culture-negative PJI (OR 0.652, 95% CI 0.478-0.890) seen in knees versus hips.
The rate of culture negative PJI also increased from 20% in 2000 to 28% in 2019. In the latter years of the study, very unusual list of organisms causing PJI were also identified.

**Conclusions:** This study reveals that the list of organism causing PJI has expanded in recent years. The study also find that some the slow growing organisms that were previously believed to be "contaminants" can and do cause PJI in a considerable number of patients. The number of culture negative cases of PJI has also increased at our institution over the years. There are a number of explanations for the latter finding, perhaps with the most important reason being liberal use of antibiotics that interferes with isolation of the infective organism.

## [FP H 06] LAMINAR AIR FLOW DOES NOT HAVE A PROTECTIVE EFFECT ON THE RATE OF PERIPROSTHETIC JOINT INFECTION AFTER PRIMARY TOTAL JOINT ARTHROPLASTY

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**Aim:** Whether laminar airflow (LAF) in the operating room (OR) is effective for decreasing periprosthetic joint infection (PJI) following total joint arthroplasty (TJA) remains a clinically significant yet controversial issue. This study investigated the association between operating room ventilation systems and the risk of PJI in TJA patients.

**Method:** We performed a retrospective observational study on consecutive patients undergoing primary total knee arthroplasty (TKA) and total hip arthroplasty (THA) from January 2013-September 2017 in two surgical facilities within a single institution, with a minimum 1-year follow-up. All procedures were performed by five board-certified arthroplasty surgeons. The operating rooms at the facilities were equipped with LAF and turbulent ventilation systems, respectively. Patient characteristics were extracted from clinical records. PJI was defined according to Musculoskeletal Infection Society criteria within 1-year of the index arthroplasty. A multivariate logistic regression model was performed to explore the association between LAF and risk of 1-year PJI, and then a sensitivity analysis using propensity score matching (PSM) was performed to further validate the findings.

**Results:** A total of 6,972 patients (2,797 TKA, 4,175 THA) were included. The incidence of PJI within 1 year for patients from the facility without laminar flow was similar at 0·4% to that of patients from the facility with laminar flow at 0·5%. In the multivariate logistic regression analysis, after all confounding factors were taken into account, the use of LAF was not significantly associated with reduction of the risk of PJI. After propensity score matching, there was no significant difference in the incidence of PJI within 1 year for patients between the two sites.

**Conclusions:** The use of LAF in the operating room was not associated with a reduced incidence of PJI following primary TJA. With an appropriate perioperative protocol for infection prevention, LAF does not seem to play a protective role in PJI prevention.

## [FP H 07] DOES EARLY ANTIBIOTIC ADMINISTRATION AFFECT CULTURE YIELDS AND CLINICAL OUTCOMES IN SEPTIC ARTHRITIS PATIENTS?

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**Aim:** Septic arthritis is a painful infection of articular joints that is typically treated by irrigation & debridement along with antibiotic therapy. There is debate amongst the medical community whether antibiotic administration should be delayed until fluid cultures have been taken to improve culture yield. However, delaying antibiotics can also have negative consequences, including joint destruction and sepsis. Therefore, the purposes of this study were to determine: 1) whether delayed antibiotic treatment affects culture yield and prognosis and 2) if the culture yield of patients treated for septic arthritis differs for hip, knee, and shoulder based on timing of antibiotic administration.

**Method:** A retrospective analysis was conducted on 111 patients with septic arthritis of the hip, knee, or shoulder admitted from 3/2016 to 11/2018. In patients with multiple septic joints, each joint was analyzed individually (n=122). Diagnosis was determined by the treatment of irrigation & debridement and/or a positive culture. Patients without all intervention times recorded or with periprosthetic joint infection were excluded. Demographics, laboratory tests, culture results, and intervention times were obtained through chart review. Patients were grouped based on antibiotic therapy timing: >24 hours prior to arthrocentesis (Group 1), between 24 hours and 1 hour prior (Group 2), and 1 hour prior to post-arthrocentesis (Group 3). Analysis was conducted using chi-squared tests.

**Results:** The mean age of each group were similar: Group 1 (n=38) 55.7 years, Group 2 (n=20) 57.2 years, and Group 3 (n=64) 54.8 years. No difference was observed in culture sensitivity between groups (p=0.825) with 71.1% (27/38) positive cultures in Group 1, 75% (15/20) in Group 2, and 76.6% (49/64) in Group 3. Similarly, frequency of related readmissions within 90 days (p=0.863) did not significantly vary: 26.3% (10/38) in Group 1, 20% (4/20) in Group 2, and 25% (16/64) in Group 3. Additionally, there were no significant differences in culture sensitivity in the knee (p=0.618; Groups: 87.5%, 75%, 70.6%), shoulder (p=0.517; Groups: 77.8%, 66.7%, 90%), and hip (p=0.362; Groups: 61.9%, 80%, 80%).

**Conclusions:** Culture sensitivities and rates of readmission were similar for all patients regardless of antibiotic administration timing. These results suggest that antibiotic administration should not be delayed in septic arthritis to improve culture yield. However, the data does not suggest that early antibiotic administration will result in better clinical outcomes by lowering readmission rates. Further research is needed to better determine the clinical benefits that early administration of antibiotics may have on patient outcomes.

## [FP I 01] SHOULD ALL PATIENTS DIAGNOSED WITH A CULTURE NEGATIVE PERIPROSTHETIC JOINT INFECTION BE TREATED WITH ANTIBIOTICS? A MULTICENTER OBSERVATIONAL STUDY

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*[5]Institute of Medical Laboratory Diagnostics, HELIOS University Clinic Wuppertal, Germany*
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*[9]University Hospital of Lausanne, Lausanne, Switzerland*
*[10]University of Medicine and Pharmacy of Craiova, Department of Microbiology, Craiova, Romania*
*[11]Ganga hospital, Department of Orthopaedics, Tamilnadu, India*

***Aim:*** To analyze the prevalence of culture negative periprosthetic joint infections (PJI) when adequate culture techniques are applied, and to evaluate the outcome of patients who were treated with antibiotics for a culture negative PJI versus those in whom treatment was withheld.

***Method:*** A multicenter observational study in which acute and chronic PJIs diagnosed between 2013 and 2018 were analyzed. Culture negative PJIs were diagnosed according to the MSIS, ICM and EBJIS definitions.

***Results:*** Out of the 1553 acute PJIs, none were culture negative. Out of the 1556 chronic PJIs, 70 were culture negative (4.7%) and included for further analysis. A total of 36 were treated with antibiotics (51%). After two years of follow-up, no infections occurred in patients in whom antibiotic treatment was withheld, but prosthesis extraction by any cause was observed more often in the no antibiotic group compared to the antibiotic group (32.4% versus 8.3%, P 0.012), especially in the absence of metallosis. Antibiotic treatment was the only independent predictor of prosthesis retention in the multivariate analysis (95% CI 0.15, 0.03 – 0.70).

***Conclusions:*** When adequate culture techniques are applied, the incidence of culture negative PJIs is low. If diagnosed, antibiotic treatment should be administered.

## [FP I 02] DAIR AFTER REVISION ARTHROPLASTY: SUCCESS RATE COMPARABLE TO DAIR AFTER PRIMARY ARTHROPLASTY BUT ANTIMICROBIAL MISMATCH IS A RISK FACTOR FOR FAILURE

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***Aim:*** Success rate of debridement, antimicrobial and implant retention (DAIR) in high suspicion of early PJI after primary arthroplasty is 70-80%. No studies have been performed focusing on outcome of DAIR after revision arthroplasty of the hip (THA) or knee (TKA). The aim of this study is to investigate the outcome of DAIR in suspected early PJI after revision THA or TKA and to identify risk factors for failure.

***Method:*** In this retrospective study, we identified early DAIRs after revision THA or TKA performed between January 2012 and August 2019. All patients received empirical antibiotics directly after the DAIR procedure. Antimicrobial treatment was adjusted to the tissue culture results. Success was defined as: 1) implant retention; 2) no repeated revision arthroplasty or supervised neglect after treatment; 3) no persistent or recurrent PJI after treatment and no administration of suppressive antimicrobial therapy; 4) survival of the patient. Infection free success was defined as: 1) no persistent or recurrent PJI after treatment; 2) no administration of suppressive antimicrobial therapy.

**Results:** The overall success rate after one year of 100 cases with early DAIR after revision THA or TKA was 79% and infection free success rate was 85%. In PJI cases, empirical antimicrobial mismatch with causative micro-organisms was associated with lower success rate (70%) than non-mismatch (95%) (p=0.02). No patients from the non-PJI group failed after one year versus 13 failures within the PJI group. A consecutive DAIR within 90 days after the first DAIR was warranted in 24 cases. Only 4 of 20 PJI cases failed despite the consecutive DAIR.

**Conclusions:** In high suspicion of early PJI after revision arthroplasty, DAIR is a good treatment option with comparable outcome with DAIR after primary arthroplasty. A consecutive DAIR should not be avoided when infection control fails within 90 days after the first DAIR to prevent explantation of the prosthesis. Antimicrobial mismatch is associated with failure and should be avoided.

## [FP I 03] EARLY PERIPROSTHETIC JOINT INFECTION AFTER REVISION ARTHROPLASTY: NEW INGREDIENTS TO SELECT EMPIRICAL TREATMENT

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**Aim:** Periprosthetic joint infection (PJI) is a feared complication of total joint arthroplasty of hip (THA) or knee (TKA). Debridement, antibiotic treatment and implant retention (DAIR) is an effective treatment of early PJI. In the Netherlands, cefazolin resistance in early PJI after primary arthroplasty is low. Little is known about causative micro-organisms and resistance patterns in PJI after revision arthroplasty. No recommendations for empirical treatment are described in the current guidelines. The aim of this study is to describe the characteristics of PJI after revision arthroplasty and to evaluate whether the used empirical treatment regimens are adequate, based on microbiology data.

**Method:** In this retrospective study we included patients with early PJI after aseptic revision of THA or TKA, treated with DAIR between 2012 and 2020. Success rate was defined as implant retention and no persistent or recurrent infection during one year follow-up.

**Results:** We identified 96 patients with PJI. PJI was most frequently caused by ***Staphylococcus spp.*** (n=73), Gram-negative bacilli (n=31) or ***Enterococcus spp.*** (n=13). Polymicrobial infection was diagnosed in 38 PJIs. Mismatches were present in 72 (75%) of the PJIs (95% CI: 0.66-0.84). Table 1 shows the number of mismatches per empirical treatment regimen. Figure 1 shows the responsible micro-organisms for the mismatches. Success rate of PJI treatment was significant reduced for patients with mismatching compared to matching empirical therapy: 62% vs. 95% respectively (OR: 0.09, 95% CI: 0.01-0.68, p=0.004). If vancomycin would have been the empirical treatment, mismatches would have been reduced to 31 (32%) (95% CI: 0.23-0.42). With vancomycin-ciprofloxacin combination therapy the mismatches would have been reduced to 1% (95% CI: -0.01-0.03).

**Conclusions:** There is a high number of mismatches in empirical treatment in early PJI after revision arthroplasty, which have significant influence on the outcome. Based on our data cefazolin should not be recommended as empirical treatment for this specific group. Our data shows that review of local data is necessary to improve treatment strategies, that eventually might improve outcome. Besides changing Gram-positive coverage, a prospective study is needed to assess the benefits of broader spectrum empiric antimicrobial treatment taken into account toxicity and other side effects such as antimicrobial resistance.

## [FP I 04] LONG-TERM PATIENT-RELATED QUALITY OF LIFE AFTER KNEE PERIPROSTHETIC JOINT INFECTION

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**Aim:** We aimed to evaluate the impact of knee periprosthetic joint infection (PJI) by assessing the patients' long-term quality of life and explicitly their psychological wellbeing after successful treatment.

**Method:** Thirty-six patients with achieved eradication of infection after knee PJI were included. Quality of life was evaluated with the EQ-5D and SF-36 outcome instruments as well as with an ICD-10 based symptom rating (ISR) and compared to normative data.

**Results:** At a follow-up of 4.9± 3.5 years the mean SF-36 score was 24.82± 10.0 regarding the physical health component and 46.16± 13.3 regarding the mental health component compared to German normative values of 48.36± 9.4 ($p$< .001) and 50.87± 8.8 ($p$= .003). The mean EQ-5D index reached 0.55± 0.33 with an EQ-5D VAS rating of 52.14± 19.9 compared to reference scores of 0.891 ($p$< .001) and 68.6± 1.1 ($p$< .001). Mean scores of the ISR revealed psychological symptom burden on the depression scale.

**Conclusions:** PJI patients still suffer from significant lower quality of life compared to normative data even years after surgically successful treatment. Future clinical studies should focus on patient-related outcome measures. Newly emerging treatment strategies, prevention methods and interdisciplinary approaches should be implemented to improve the quality of life of PJI patients.

## [FP I 05] PREDISPOSING FACTORS FOR FAILURE IN PJI: ARE GRAM-NEGATIVE MULTI-DRUG RESISTANT BACTERIAL INFECTIONS INCREASE THE RATE OF FAILURE?

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**Aim:** Infection is one of the worst complications following total joint arthroplasty, which is often associated with significant morbidity. Currently, due to the global burden of multidrug-resistant Gram-negative bacteria (MDR-GNB) infections, few multicentre studies have described a microbiological shift from Gram-positive cocci (GPC) towards MDR-GNB PJI (prosthetic joint infection). Additionally, the emergence of MDR-GNB impacts the therapeutic options and may increase the rate of PJI treatment failure. The purpose of the present study was to describe the predisposing factors associated to failure of treatment in an orthopaedic reference hospital in Brazil from 2014 through 2019.

**Method:** Retrospective case-control analysis of patients treated for MDR-GNB PJI over a five-year period. Data were collected from medical, surgical and laboratory records. PJI were defined according the current MSIS criteria. MDR was defined as non-susceptibility to at least one agent in three or more antimicrobial categories. Patients with PJI with at least two positive tissue cultures for MDR-GNB were selected. The control group was patient with PJI caused by multisensitive organism (GNB or GPC). Absence of signs and symptoms of infection during the follow-up period was defined as cure. Definition of failure: death, need for another course of antibiotic, or the need for another surgical procedure to control the infectious site (relapse).

**Results:** A total of 104 patients were selected, 59 patients in the MDR-GNB PJI group and 44 in the control group. Two outcomes were compared: cure or failure. The overall 1-year survival rate was 65.3% with the median survival time being 207.08 days. In the MDR-BGN infection group the 1-year survival rate was 59.3% and the average time of survival was 141.14 days. In contrast, in the Control group the 1-year survival rate was 73.8% with an average survival time of 230.29 days (p = 0.023). HR: 2.447, IC 1.099-5.448. The independent variables in the multivariate analysis associated to treatment failure were MDR-BGN infection (p = 0.023) HR 2,447 IC 1,099 –5,448, revision surgery (p = 0.042) HR 2,027 IC: 2,027-4,061, presence of comorbidities (p = 0.048) HR 2,508 IC: 0,972- 6,469 and previous antimicrobial use in the last 3 months (p = 0.022). HR 2,132 IC: 1,096-4,149**.**

**Conclusions:** GNB-MDR PJI increases approximately 2.5 times the chance of unfavourable outcome such as death and infectious relapse compared to infections with other multisensitive microorganism.

## [FP I 06] INTERNATIONAL ORGANISM PROFILE OF PERIPROSTHETIC TOTAL HIP AND KNEE INFECTIONS

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**Aim:** It is unclear if the prevalence of resistance organisms causing (PJI) in total hip/knee arthroplasty is different among North/South American and European countries. Therefore, we sought to compare causative organisms, rates of resistant organisms, and polymicrobial infections in hospitals in North/South America, and Europe.

**Method:** We performed a retrospective study of 654 periprosthetic hip (n=361) and knee (n=293) infections (January 2006-October 2019) identified at two facilities in the United States (US) (n=159), and single institutions located in Argentina (n=99), Uruguay (n=130), United Kingdom (UK) (n=103), Germany (n=59), and Russia (n=104). The analyses were performed for the entire cohort, knees, and hips. Alpha was set at 0.05.

**Results:** Overall, the most frequent organisms identified were Staphylococcus aureus (24.8%) and Staphylococcus epidermidis (21.7%). The incidence of organisms resistant to at least one antibiotic was 58%. In this regard, there was a significant difference between hips (62.3%) and knees (52.6%) (p=0.014). The rates of resistant organisms among countries were significantly different: 37.7% (US), 66.7% (Argentina), 71.5% (Uruguay), 40.8% (UK), 62.7% (Germany), and 77.9% (Russia) (p<0.001). The overall incidence of polymicrobial infections was 9.3% and the rates across nations were: 9.4% in the US, 11.1% (Argentina), 4.6% (Uruguay), 4.9% (UK), 11.9% (Germany), and 16.3% (Russia) (p=0.026).
In an exclusive analysis of the hips, the incidence of resistant organisms was 62.3% while polymicrobial infections accounted for 10.5% of all cultures. The rates of resistant organisms in each country were: 42.9% in the US, 59.2% (Argentina), 78.5% (Uruguay), 41.3% (UK), 63.9% (Germany), and 80.0% in Russia (p<0.001). The incidences of polymicrobial infections were: 9.1% in the US, 6.1% (Argentina), 6.5% (Uruguay), 6.5% (UK), 16.7% (Germany), and 21.7% in Russia (p=0.024).
Regarding the knees, the incidence of resistant organisms was 52.6% while the frequency of polymicrobial infections was 7.8%. The rates of resistant organisms in each country were: 32.9% in the US, 74% (Argentina), 54.1% (Uruguay), 40.4% (UK), 60.9% (Germany), and 75% in Russia (p<0.001). The frequencies of polymicrobial infections were: 9.8% in the US, 16% (Argentina), 0% (Uruguay), 3.5% (UK), 4.3% (Germany), and 9.1% in Russia (p=0.072).

**Conclusions:** Staphylococcus aureus and epidermidis accounted for almost 50% of all infections. The US and the UK had the lowest incidence of resistant organisms while Germany and Russia had the highest. The UK and Uruguay had the lowest rates of polymicrobial infections. These differences between countries and continents may affect comparative studies that evaluate treatments for PJI.

## [FP I 07] SYMPTOM DURATION IS ASSOCIATED WITH FAILURE OF PERIPROSTHETIC JOINT INFECTION TREATED WITH DAIR

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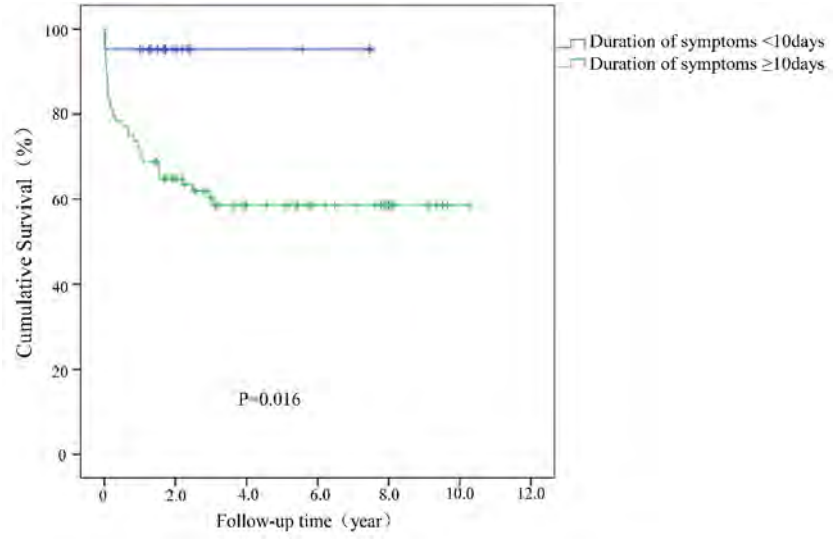
**Aim:** The purpose of this study is to report the overall infection control rate and prognostic factors associated with acute, hematogenous and chronic PJIs treated with DAIR.

**Methods:** All DAIR procedures performed at 2 institutions from 2009 to 2018 (n=104) were reviewed and numerous data were recorded, including demographics, preoperative laboratory tests, Charleston Comorbidity Index, surgical information and organism culture results. Treatment success was defined according to the criteria reported by Diaz-Ledezma. A multivariable analysis was utilized to identify prognostic factors associated with treatment and a Kaplan-Meier survival analysis was used to depict infection control rate as a function of time.

**Results:** The overall treatment success rate in the current cohort of patients was 67.3% at a median 38.6 (23.5-90.7) months follow-up. Patients with a duration of infectious symptoms greater than 10 days were more likely to fail (P=0.035, odds ratio 8.492, 95% confidence interval 1.159-62.212). There was no difference among acute, hematogenous and chronic infections in terms of failure rate even when time was considered (p=0.161).

**Conclusion:** With careful patient selection, DAIR is a reasonable treatment option for PJI and its use in the setting of chronic infection does not appear to be a contraindication. Performing the DAIR procedure within 10 days of the presentation of symptoms had higher rates of treatment success.

Figure 1: Kaplan-Meier (KM) survival analysis for cases with symptom duration greater or less than 10 days.



## [FP J 01] DOES LOCAL IMPLANTATION OF GENTAMICIN IMPAIR RENAL FUNCTION IN PATIENTS UNDERGOING SURGERY FOR CHRONIC OSTEOMYELITIS AND FRACTURE-RELATED INFECTION?

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**Aim**: Chronic bone infections and infected fractures are often treated with excision of the dead bone and implantation of biomaterials which elute antibiotics. Gentamicin has been a preferred drug for local delivery, but this could induce renal dysfunction due to systemic toxicity. This is a particular concern in patients with pre-existing chronic renal disease treated with new antibiotic carriers which achieve very high peak levels of gentamicin in the first few days after surgery[1].

**Method**: 163 patients (109 males; average age 51.6 years) with Cierny-Mader Type 3 or 4 chronic osteomyelitis had a single-stage operation with excision of the dead bone, filling of the osseous defect with a calcium sulphate-hydroxyapatite carrier, containing gentamicin and immediate soft tissue closure[2]. No patient was given systemic gentamicin or other renal toxic antibiotics.
Mean carrier volume was 10.9mls (range 1-30mls) and mean gentamicin dosing was 190.75mg (maximum 525mg). Seven patients had pre-existing renal disease (4 diabetic nephropathy, 1 nephrotic syndrome, 1 renal transplant and 1 previous acute kidney injury).
Serum creatinine levels were collected pre-operatively and during the first seven days post-operatively. Glomerular filtration rate (GFR) was calculated using the CKD-epi creatinine equation. Renal function was defined using the Chronic Kidney Disease (CKD) Staging system.

**Results**: 155 cases had adequate data to allow calculation of pre- and post-operative GFR. Pre-operative CKD staging demonstrated 118 Class I (normal renal function), 30 Class II, 3 Class IIIa, 3 Class IIIb, and 1 Class V disease. Mean pre-operative GFR (99.7ml/min/1.73m$^2$, SD 21.0) was no different to post-operative GFR (103.2ml/min/1.73m$^2$, SD 21.3), p= 0.0861.
Four cases had a >10% decline in GFR below normal, with only one case dropping a CKD stage, from I (normal) to II (mildly decreased).
Only 1/7 cases with pre-existing renal disease had a GFR drop of >10% (from 11ml/min/1.73m$^2$ to 8ml/min/1.73m$^2$).
70/155 (45.2%) had a temporary GFR drop post-operatively, with the biggest drop occurring a mean 3.06 days following surgery (SD 2.1).
No patient had clinical signs of new acute renal impairment post-operatively.

**Conclusions**: Renal function is not significantly affected by local implantation of gentamicin up to 525mg. The presence of pre-existing renal disease is not a contraindication to local gentamicin therapy.

1. Stravinskas et al. *Bone Joint Res* 2016; 5: 427-435.
2. Ferguson et al. *J Bone Joint Infect* 2019; 4(2): 76-84.

## [FP J 02] PERIOPERATIVE MYOCARDIAL INJURY AND MORTALITY AFTER REVISION SURGERY FOR MAJOR MUSCULOSKELETAL INFECTION

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**Aim:** Prosthetic joint infections (PJI) and fracture related infections (FRI) are the most challenging complications in orthopaedic surgery. An interdisciplinary approach is mandatory not only to correctly diagnose and treat major musculoskeletal infections but also to address the comorbidities and impairments these patients are not rarely suffering from. Since, little data exists on cardiac complications following PJI and FRI revision surgery, this study aimed to investigate the risk of perioperative myocardial injury (PMI) and mortality.

**Method:** We prospectively included consecutive patients at high cardiovascular risk (defined as expected postoperative hospital stay of >24 hours PLUS age >45 years with pre-existing coronary, peripheral or cerebrovascular artery disease OR age >65 years) undergoing major orthopaedic surgery between 2014 and 2016. All patients received a systematic screening to reliably detect PMI, using serial measurements of high-sensitivity cardiac troponin T (hs-cTnT). All-cause mortality was assessed at 30 days and one year. Multivariable logistic regression models were applied to compare incidence of PMI and mortality between patients undergoing septic revision surgery (for PJI/FRI) and patients receiving aseptic major bone and joint surgery.

**Results:** In total 911 consecutive patients, with an overall PMI rate of 15.4% (n=140) were included. The PMI incidence in patients undergoing septic revision surgery was significantly higher compared to aseptic orthopaedic surgeries (29.2% vs 14.3%, p=0.001), also after multivariable adjustment (odds ratio 2.1, p=0.02). Mortality was higher at one year (16.9% vs. 8.3%, p=0.037) and numerically at 30 days (6.2% vs. 2.4%, p=0.085) in patients undergoing septic revision surgery. Virulence of the disease-causing pathogen showed no significant relationship with PMI incidence or mortality.

**Conclusions:** Patients undergoing revision surgery for PJI or FRI were at a distinct higher risk of PMI and death compared to matched non-septic patients. In major bone and joint infections screening for PMI and treatment in specialized multidisciplinary units should be considered.

## [FP J 03] EFFICACY OF VARIOUS SURGICAL IRRIGATION SOLUTIONS AGAINST ESTABLISHED BIOFILM: A COMPARATIVE IN VITRO INVESTIGATION

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**Aim:** The efficacy of various irrigation solutions in removing microbial contamination of a surgical wound, and reducing the rate of subsequent surgical site infection (SSI), has been demonstrated extensively. However, it is not known if irrigation solutions have any activity against established biofilm. This issue is pertinent as successful management of patients with periprosthetic joint infection (PJI) includes the ability to remove biofilm established on the surface of implants and necrotic tissues. The purpose of this study was to evaluate the efficacy of various irrigation solutions in eradicating established biofilm, as opposed to planktonic bacteria, in a validated *in vitro* model.

**Method:** Established biofilms of ***Staphylococcus aureus*** and ***Escherichia coli*** were exposed to different irrigation solutions that included Polymyxin 500,000U/L plus bacitracin 50,000U/L, Vancomycin 1g/L, Gentamicin 80mg/L, Normal saline 0.9%, off-the-shelf Betadine 0.3%, Chlorhexidine 0.05%, Benzalkonium 1.3g/L, Sodium hypochlorite 0.125%, and Povidone-iodine 0.5%. Each experiment was conducted in a 96-well microtiter plate with a peg lid and standardized per the MBEC assay manufacturer's protocol. Following 2 minutes of solution exposure to the irrigation solution, residual biofilms were recovered by sonication. Outcome measures for antibiofilm efficacy were residual colony forming units (CFU) and optical density (690nm). Experiments were conducted in 24 replicates and the observations recorded by two blinded observers. Statistical analysis involved t-tests with Bonferonni adjustment.

**Results:** Povidone-iodine 0.5%, Betadine 0.3%, Benzalkonium 1.3g/L, and Sodium hypochlorite 0.125% were significantly more efficacious against ***S.aureus*** biofilm versus all other solutions ($p<0.001$). Against ***E.coli*** biofilm, Povidone-iodine-0.5%, Benzalkonium-1.3g/L and Sodium hypochlorite-0.125% were also most effective compared to other irrigation solutions ($p<0.001$). Polymyxin-bacitracin, Gentamicin, Vancomycin, and Saline solutions had minimal activity against both ***E.coli*** and ***S.aureus*** biofilms ($p<0.001$). Similar trends were observed using both experimental endpoints (CFU and Turbidity) and both investigators (interrater reliability; $r=0.99$).

**Conclusion:** This *in vitro* study observed that topical antibiotic solutions do not have any activity against established biofilms. Irrigations solutions containing adequate amount of povidone-iodine, betadine, sodium hypochlorite, and benzalkonium appear to have activity against established biofilm by gram positive and gram negative organisms. The use of these irrigation solutions may need to be considered in patients with established PJI.

## [FP J 04] EXTRASPINAL OSTEOARTICULAR TUBERCULOSIS, ABOUT 40 CASES

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**Aim:** Extraspinal osteoarticular tuberculosis (TOA-ER) is a rare form of extra-pulmonary tuberculosis. It remains a topical problem not only in underdeveloped countries but also in developed countries due to cases of immune deficiency.
Through a study of 40 cases, we specify the current diagnostic aspects of TOA-ER and detail their therapeutic and evolutionary modalities.

**Method:** The mean age of our patients was 40 years with a clear predominance of females observed (SR = 0.66). 76.31% of the cases were from a rural setting. The impairment was single-focal in 72.5%. Associated tuberculosis location was found in 59% of cases. Pain and swelling were the main clinical symptoms. Signs of tuberculous impregnation were found in less than half of the cases. The IDR was positive in 67%. All patients underwent an appropriate radiological exploration consisting of a standard x-ray (30 cases), CT (21 cases) and MRI (23 cases). technetium-99m bone scintigraphy, performed in 15 cases, detected 5 infra-clinical osteoarticular locations. 77.5% of patients had formal pathological and / or bacteriological confirmation of the diagnosis. All patients had adequate anti-tuberculosis chemotherapy with a mean duration of 18 months. 67% of patients had a surgical debridement procedure.

**Results:** After a mean follow-up of 5 years, the outcome was favourable in 75.2% of cases. A microbiological cure at the cost of serious functional sequelae was noted in 12.8% of cases. The outcome was unfavourable with relapse observed in 4.8% of cases and death in 7.2% of cases.

**Conclusions:** Extraspinal osteoarticular tuberculosis is a fairly common condition in our country. Its insidious clinical course is the cause of diagnostic and therapeutic delay. Its treatment is mainly medical. The surgery keeps some indications. Good therapeutic adherence and early diagnosis are the best guarantees of good therapeutic results.

## [FP J 05] ANALYSIS OF BIOFILM FORMATION IN ANTERIOR CRUCIATE LIGAMENT PLASTIES. COMPARATIVE IN VITRO STUDY.

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**Aim:** Quadrupled hamstring anterior cruciate ligament plasties (4xHp) have been described as having a higher risk of infection than bone patellar tendon bone plasties (BPTBp). There are 2 theories that might explain this phenomenon. One is the presence of sutures in a 4xHp that could act as a foreign body, The other is the more complex preparation of a 4xHp that might lead to higher contamination rates during the process. The objective of the present study was to evaluate the formation of biofilm in these plasties and to compare it between a 4xHp and a BPTBp. The hypothesis was that the presence of sutures in 4xHp would increase the amount of biofilm present in them in comparison to BPTBp.

**Method:** A descriptive in vitro study was conducted. One 4xHp and one BPTBp were prepared. They were subsequently divided into 8 fragments. Three of them were reserved for negative control, and the rest were contaminated with a strain of S. Epidermidis (ATCC 35984) $10^{-5}$. Finally, a quantitative analysis was carried out by means of microcalorimetry and sonication with plating. Additionally, a qualitative analysis was carried out by means of electron microscopy.

**Results:** In isothermal microcalorimetry, both contaminated plasties showed the same growth dynamics with a population peak (200uW) at 8h. No significant differences were found between the bacterial growth profiles of 4xHp and BPTBp.
The product of sonication was plated and the number of colony forming units per milliliter (CFU/ml) was counted at 24 hours. No significant differences were detected between the 4xHp (mean +/- sem = $3,5x10^7$ +/- 3450000) and the BPTBp ($4,6 x10^7$ +/- 1,455e+7). With a p value of 0.6667, there were no differences of significance (Mann-Whitney test).
In the samples analyzed with electron microscopy, no specific biofilm growth pattern was identified upon comparing BPTBp with 4xHp.

**Conclusions:** There were no significant differences at either the quantitative or qualitative level when comparing bacterial growth in BPTBp and 4xHp. Therefore, the presence of sutures in 4xHp cannot be established as a predisposing factor to higher infection rates. These findings may be justified in the sense that the plasties themselves already behave like foreign bodies. Therefore, the presence of sutures does not increase the possibility of biofilm forming on their surface.

## [FP J 06] VALIDATION AND RELEVANCE OF IN VIVO BIOFILM MODEL GALLERIA MELLONELLA TO STUDY IMPLANT-ASSOCIATED BACTERIAL BIOFILMS

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**Aim:** *In vivo* biofilm models play major role to study biofilm development, morphology, and regulatory molecules involve in biofilm. Due to ethical restrictions, the use mammalian models are replaced with other alternative models in basic research. Recently, we have developed insect infection model ***G. mellonella*** larvae to study implant associated biofilm infections. This model organism is easy to handle, cheap and ethical restriction free and could be used for the high through put screening of antimicrobial compounds to treat biofilm. To promote the use of this model in basic research we aimed to validate this based on the typical biofilm features such as less susceptible to the antibiotics, complexity of the biofilm structure and gene expression profile of biofilms.

**Method:** *G. mellonella* larvae are maintained at 30oC on artificial diet in an incubator. Titanium and Stainless steel K-wires were cut into small pieces with size of 4mm. After sterilization with 100% alcohol, these K-wires were pre-incubated in ***S. aureus*** bacterial suspension ($5X10^6$ CFU/ml) for 30 min, washed in PBS and implanted inside the larva after with help of scalpel. The larvae were incubated at 37°C for two day for the survival analysis. To analyze the less susceptibility of the biofilms towards antibiotics, the larvae were treated with gentamicin and compared survival with planktonic infection in G***. mellonella***. To reveal the complex structure of biofilm, the implants were removed and processed for the MALDI analysis. Whole genome-based transcriptome of biofilm was performed to explore the changes in transcriptional landscapes.

**Results:** The results are very promising to validate the use of ***G. mellonella*** as ***in vivo*** model to study the biofilm formation on implanted materials. The gentamicin treatment could rescue the larvae from the planktonic infection, but not from the biofilm infection on the implants. Further, the MALDI analysis could reveal the complex structure and components of S***. aureus*** biofilm formed on the implant inside the larvae. Finally, the transcriptomic analysis revealed the gene expression changes that can be compared to normal biofilm expression profile.

**Conclusions:** Further, comparison of the these results with other in vivo models such as rat and mouse as well as acute and chronic clinical samples from patients with implant-associated bone infections could validate and relevant use of this model to study ***S. aureus*** biofilm infections.

## [FP J 07] A NOVEL ACTIVATED-ZINC ANTISEPTIC SOLUTION EFFECTIVE AGAINST STAPHYLOCOCCUS AUREUS AND PSEUDOMONAS AERUGINOSA IN A PIG MODEL

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**Aim:** Identifying the optimal agent for irrigation for periprosthetic joint infection remains challenging as there is limited data. The ideal solution should have minimal cytotoxicity while maintaining bactericidal activity. We developed a novel activated-zinc solution containing zinc-chloride ($ZnCl_2$) and sodium-chlorite ($NaClO_2$). The purpose of this study was 1.) to investigate the antimicrobial efficacy of 2 concentrations ("CZ1", "CZ2") against ***Staphylococcus aureus*** and ***Pseudomonas aeruginosa*** and 2.) to evaluate untoward effects of the solution on local wound tissue 24 hours after solution exposure in pig wound models.

**Method:** The study was conducted and reported in accordance to ARRIVE guidelines. We created twenty-four 1.5cm wounds on the back of a Yorkshire-cross pig. Wounds were inoculated with standardized ***Pseudomonas*** and ***S. aureus***. 8 wounds were designated as controls (inoculum without treatment), 8 treated with CZ1, and 8 with CZ2. Punch biopsies were taken 1 hour after treatment and bacteria quantified. Wound necrosis/neutrophil infiltrate was measured 24-hours post-exposure.

**Results:** After 1-hour, the control, CZ1 and CZ2 wounds had total bacteria of 5.7, 2.8 and 3.5 logCFU/g, respectively (p=0.017). The control, CZ1 and CZ2 wounds had ***S. aureus*** of 5.3, 2.3 and 1.6 logCFU/g, respectively (p=0.009). The control, CZ1 and CZ2 wounds had ***Pseudomonas*** of 5.5, 0.3 and 0.0 logCFU/g, respectively (p=0.000). After 24 hours of exposure to CZ1 and CZ2, there was no statistically significant increased necrosis (p=0.12, p=0.31, respectively). CZ1 had increased, moderate neutrophil infiltrate (p=0.04) when compared to controls, however CZ2 was not significant (p=0.12).

**Conclusions:** Our novel solution demonstrated 99.5-99.9% reduction in total bacteria, 99.9-99.98 % reduction in ***S. aureus,*** and 100% eradication of ***Pseudomonas*** 1-hour after exposure, without significantly increased necrosis and no-to-minimally-increased neutrophil infiltrate. This novel solution may provide another significant tool in the arsenal to treat and/or prevent PJI and other wound infections.

## [BP01] IN PATIENTS WITH BONE AND JOINT INFECTION, SIX AND TWELVE WEEKS OF ANTIMICROBIAL THERAPY SEEMS TO HAVE A SIMILAR IMPACT ON THE GUT MICROBIOTA AND NO PARTICULAR ANTIBIOTIC SEEMS TO IMPACT ITS RECOVERY

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**Aim:** Bone and joint infections (BJI) need frequently prolonged antibiotic treatment at high dosage for a total of 6 or 12 weeks depending the type of infection. Impact of such prolonged antibiotic exposure on the gut microbiota has never been assessed.

Method: We performed a national multicentric prospective study of patients with BJI to monitor the gut microbiota dynamic all along antimicrobial treatment. Clinical data and stool collection were performed at the baseline visit (B) within 24h before starting antibiotics, at the end of the treatment (EOT) and 2 weeks after antibiotic withdrawal during a follow-up visit (FU). Microbiota composition was determined by shotgun metagenomic sequencing. Biological markers of gut permeability and inflammation were monitored at each time point.

**Results:** Sixty-two patients were enrolled: 27 native BJI, 14 osteosynthesis-related BJI and 21 prosthetic joint infections (PJI). At EOT there was a significant loss of alpha-diversity that recovered at FU in patients with native BJI and PJI but not in patients with osteosynthesis-related BJI ($p<0.05$, Wilcoxon test). At EOT, we observed an increase of Proteobacteria and Bacteroidetes that partially recovered at FU. Principal Component Analysis (PCoA) of the Bray Curtis distance, showed a significant change of the gut microbiota at the end of treatment compared to baseline ($p<0.01$, PERMANOVA) that only partially recover at FU. The taxonomic analysis showed that microbiota composition at FU does not differ significantly at the genus level when comparing patients treated for 6 weeks to patients treated for 12 weeks. No particular antibiotic (especially fluoroquinolones) was associated with a lower Shannon index or distinct dynamic of recovery at the end of treatment. PCoA analysis of the Bray Curtis distance shows that patients with elevated plasma level of CRP (≥5mg/L) at EOT had a distinct gut microbial composition compared to others.

**Conclusions:** In patients with BJI, antibiotics altered the gut microbiota diversity and composition with only partial recovery 2 weeks after antibiotic withdrawal, independently on the duration of the therapy and on the type of the antibiotic used. Elevated CRP at EOT might reflect persistent alteration of the gut microbiota. Assessment of long-term impact after the end of treatment is on-going.

## [BP02] BONE AND JOINT INFECTIONS : SYNERGISTIC ANTIBIOFILM EFFECT OF EXEBACASE AND ANTIBIOTICS AGAINST STAPHYLOCOCCUS EPIDERMIDIS STRAINS

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**Aim:** *Staphylococcus epidermidis* (*S. epidermidis*) is one of the main pathogens responsible for bone and joint infections especially those involving prosthetic materials (PJI). Although less virulent than ***S. aureus***, ***S. epidermidis*** is involved in chronic infections notably due to its ability to form biofilm. Moreover, it is frequently multiresistant to antibiotics. In this context, the development of additional or alternative antibacterial therapies targeting the biofilm is a priority.

**Method:** The aim of this study was to evaluate in vitro the activity of phage lysin exebacase (CF-301) against biofilms formed by 19 ***S. epidermidis*** clinical strains responsible for PJI. We determined the remaining viable bacteria inside the biofilm (counting after serial dilution and plating) and the biomass (bacteria and extracellular matrix, using crystal violet staining) after 24h of exposition to exebacase at different concentrations, alone (0.05; 0.5; 5; 50 and 150 mg/L) or in combination (5, 50 and 150 mg/L) with antibiotics commonly used to treat multi-resistant ***S. epidermidis*** PJI (rifampin (1 mg/L), vancomycin (10mg/L) and daptomycin (10mg/L)). In this study, synergy was defined as a significantly higher effect of the association in comparison to the sum of the effect of each molecule.

**Results:** Exebacase showed a dose-dependent reduction of biomass, ranging from 11 % at 0.5 mg/L to 66 % at 150 mg/L. Exebacase showed a significant bactericidal activity at 50 and 150 mg/l, with a mean decrease of the inoculum of 0.94 and 1.7 log, respectively. In addition, synergistic effects were observed in association with i) rifampin (1 mg/L) showing a mean decrease up to 84% of the biomass and 3.5 log CFU at 150 mg/L of exebacase, ii) vancomycin (10 mg/L) showing a mean decrease up to 81% of the biomass and 2.82 log CFU at 150 mg/L of exebacase, iii) and daptomycin (10 mg/L) showing a mean decrease up to 85% of the biomass and 3.1 log CFU at 150 mg/L of exebacase.

**Conclusions:** Exebacase showed, in vitro, synergistic activity with antibiotics against ***S. epidermidis*** biofilms. It is a promising adjuvant therapy to rifampin, vancomycin and daptomycin in the context of PJI. Further studies are needed, in vitro to understand the mechanism of action on ***S. epidermidis*** biofilm and the heterogeneity of strain behavior and in vivo to confirm the present data.

## [BP03] QUALITY OF LIFE IN PATIENTS WITH CHRONIC OSTEOMYELITIS REFERRED TO A TERTIARY BONE INFECTION CENTRE

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**Aim:** To investigate self-reported quality of life (QoL) in patients with osteomyelitis referred to a specialist centre in the UK and investigate the relationship between QoL and BACH classification.

**Method:** All patients newly referred to a specialist bone infection clinic at a single tertiary centre within the UK between January 2019 and February 2020 were prospectively included. Diagnosis of osteomyelitis was made according to the presence of clinical and radiological criteria for ≥6 months. An EQ-5D-5L questionnaire and visual analogue score (VAS) were completed during the initial clinic appointment. Long-bone osteomyelitis was classified by the attending orthopaedic surgeon using the BACH classification system as either uncomplicated, complex or with limited options available.1 Patients managed non-operatively were subclassified into those who were (i) unfit to receive an operation or (ii) fit and well with stable disease. EQ-5D index scores were compared to a published UK value set of 41 chronic health conditions within the UK.2

**Results:** 201 patients were referred during the study period, with 159 (79.1%) patients diagnosed with long-bone osteomyelitis and 16 (8.0%) with osteomyelitis of the pelvic bones. Patients with pelvic osteomyelitis reported lower EQ-5D index scores compared to long-bone osteomyelitis (EQ-5D: 0.097 vs. 0.435, $p<0.001$) but similar VAS (60.2 vs. 54.6, $p=0.37$). Long-bone and pelvic osteomyelitis gave the 40th and 41st lowest EQ-5D scores respectively when compared to 41 other chronic health conditions including stroke, chronic obstructive pulmonary disease, kidney disease, liver disease and malignancy. Patients classified as having uncomplicated long-bone osteomyelitis reported significantly higher QoL compared to those classified as complex osteomyelitis (EQ-5D: 0.527 vs. 0.401, $p<0.05$; VAS: 66.9 vs. 58.4, $p<0.05$). Patients who were not fit for surgery due to co-morbidity reported similar QoL scores compared to those patients with complex osteomyelitis (EQ-5D: 0.293, $p=0.07$; VAS: 46.6, $p=0.06$). Patients with stable disease who did not require surgery, gave significantly better QoL scores when compared to the other classifications of osteomyelitis (EQ-5D: 0.746, $p<0.01$; VAS: 81.9, $p<0.01$).

**Conclusions:** Patient reported QoL in osteomyelitis correlates with disease complexity as classified according to the BACH classification system. Patients with pelvic and long-bone osteomyelitis rate their QoL lower than patients with other chronic diseases.

**Reference:**

(1)Hotchen ***et al.,*** Bone Joint Res 2019; 8:459-468
(2)Ara and Brazier, Value in Health 2011;14;4:539-545

## [BP04] IF, WHEN, AND HOW TO USE RIFAMPIN IN ACUTE STAPHYLOCOCCAL PERI-PROSTHETIC JOINT INFECTIONS, A MULTICENTRE OBSERVATIONAL STUDY

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**Aim:** Rifampin is considered as the antibiotic corner stone in the treatment of acute staphylococcal periprosthetic joint infections (PJI). However, if, when, and how to use rifampin has been questioned. We evaluated the outcome of patients treated with and without rifampin, and analyzed the influence of timing, dose and co-antibiotic.

**Method:** Acute staphylococcal PJIs treated with surgical debridement between 1999 and 2017, and a minimal follow-up of 1 year were evaluated. Treatment failure was defined as the need for any further surgical procedure related to infection, PJI-related death or the need for suppressive antimicrobial treatment.

**Results:** A total of 669 patients were analyzed. Treatment failure was 32.2% (131/407) in patients treated with rifampin and 54.2% (142/262) in whom rifampin was withheld ($P < 0.001$). The most prominent effect of rifampin was observed in knees (treatment failure 28.6% versus 63.9%, respectively, $P < 0.001$). The use of rifampin was an independent predictor of treatment success in the multi-variate analysis (OR 0.30, 95% CI 0.20 – 0.45). In the rifampin group, the use of a co-antibiotic other than a fluoroquinolone (OR 7.73, 95% CI 4.26 – 14.0) and the start of rifampin within 5 days after surgical debridement (OR 1.88, 95% CI 1.05 – 3.35) were predictors of treatment failure. Clindamycin demonstrated similar efficacy as co-antibiotic. The dosing of rifampin had no effect on outcome.

**Conclusions:** Our data supports the use of rifampin in acute staphylococcal PJIs treated with surgical debridement, particularly in knees. Immediate start of rifampin after surgical debridement should probably be discouraged.

## [BP05] IS THE EUROPEAN BONE AND JOINT INFECTION SOCIETY DEFINITION OF PROSTHETIC JOINT INFECTION MEANINGFUL IN OUR CLINICAL PRACTICE? - A MULTI-CENTRIC VALIDATION STUDY

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**Aim:** There have been many attempts to define the criteria by which prosthetic joint infection(PJI) is diagnosed. Our aim is to validate the 2021 European Bone and Joint Infection Society(EBJIS) definition of PJI.

**Method:** This is a multicenter retrospective study of patients who have undergone total hip or knee revision surgery in four different European institutions between 2013-2018. Cases with less than four intraoperative microbiology samples; no preoperative/intraoperative synovial fluid differential leukocyte count or intraoperative histology were excluded. Minimum follow-up of at least two years after revision surgery if no subsequent infection and/or the need for implant removal was also required. All cases were classified using the 2021 EBJIS, the 2018 International Consensus Meeting(ICM) and the 2013 Musculoskeletal Infection Society(MSIS) PJI definitions.

**Results:** Definitive PJI classification according to the different definitions of the 507 patients included are presented in table 1.
The EBJIS definition classifies 40.4%(205/507) of the cases as confirmed infections compared to 33.9%($p=0.038$) and 29.4%($p<0.001$) in 2018 ICM and 2013 MSIS classifications respectively. Compared to 2018 ICM classification it also offers significantly less undetermined cases – 5.0% vs. 11.4%($p<0.001$).
Free from infection Kaplan-Meyer survival curve shows significantly better outcome for EBJIS unlikely compared to confirmed subgroup($p=0.031$). EBJIS likely subgroup survival is not significantly different from unlikely($p=0.529$) or confirmed($p=0.717$) cohorts.
Among the MSIS not infected cohort the newly classified EBJIS confirmed/likely cases present higher subsequent infection rate (albeit not statistically significant) when compared to EBJIS infection unlikely cases - 16.0%(13/81) vs. 10.1%(28/277). This subsequent PJI rate is similar to the MSIS infected cohort. A similar trend is not obvious within ICM 2018 not infected subgroup.

**Conclusions:** The EBJIS 2021 definition is shown to be the most sensitive definition while also offering a smaller number of undetermined cases. Newly diagnosed infections seem to have a similar prognosis as “classically” infected cases.

**Table 1. Final Diagnosis Classification According to Different Definitions and Subsequent Outcome**

| Classification | Revision Treated as infected? | N | mean follow-up | Subsequent Infection | Subsequent Implant Removal |
|---|---|---|---|---|---|
| **EBJIS 2021** | | | | | |
| **Infection Unlikely** | **overall** | **277 (54.6%)** | **39 (±14) months** | **28 (10.1%)** | **30 (10.8%)** |
| | treated | 21 (7.6%) | 40±16) months | 7 (33.3%) | 1 (4.8%) |
| | not treated | 256 (92.4%) | (39±13) months | 21 (8.2%) | 29 (11.3%) |
| **Infection Likely** | **overall** | **25 (5.0%)** | **47 (±18) months** | **4 (16.0%)** | **7 (28.0%)** |
| | treated | 15(60.0%) | (46±16) months | 3 (20.0%) | 4 (26.7%) |
| | not treated | 10 (40.0%) | (37±13) months | 1 (10.0%) | 3 (30.0%) |
| **Infection Confirmed** | **overall** | **205 (40.4%)** | **37 (±15) months** | **34 (16.6%)** | **24 (11.7%)** |
| | treated | 169 (82.4%) | 37 (±15) months | 33 (19.5%) | 20 (11.8%) |
| | not treated | 36 (17.6%) | 47 (±22) months | 1 (2.8%) | 4 (11.1%) |
| **ICM 2018** | | | | | |
| **Not Infected** | **overall** | **277 (54.6%)** | **37 (±15) months** | **22 (7.9%)** | **35 (12.6%)** |
| | treated | 22 (7.9%) | 38(±16) months | 3 (13.6%) | 3 (13.6%) |
| | not treated | 255 (92.1%) | 39 (±14) months | 19 (7.4%) | 32 (12.5%) |
| **Inconclusive** | **overall** | **58 (11.4%)** | **42 (±17) months** | **13 (22.4%)** | **8 (13.8%)** |
| | treated | 29 (50%) | 43 (±18) months | 9 (31.0%) | 5 (17.2%) |
| | not treated | 29 (50%) | 42 (±16) months | 4 (13.8%) | 3 (10.3%) |
| **Infected** | **overall** | **172 (33.9%)** | **39 (±14) months** | **31 (18.0%)** | **18 (10.5%)** |
| | treated | 154 (89.5%) | 38 (±16) months | 31 (20.1%) | 17 (11.0%) |
| | not treated | 18 (10.5%) | 35 (±13) months | 0 (0%) | 1 (5.6%) |
| **MSIS 2013** | | | | | |
| **Not Infected** | **overall** | **358 (70.6%)** | **39 (±14) months** | **41 (11.4%)** | **46 (12.8%)** |
| | treated | 70 (19.6%) | 39 (±16) months | 18 (25.7%) | 11 (15.7%) |
| | not treated | 288 (80.4%) | 39(±14) months | 23 (8.0%) | 35 (12.2%) |
| **Infected** | **overall** | **149 (29.4%)** | **38 (±15) months** | **25 (16.8%)** | **15 (10.1%)** |
| | treated | 135 (90.6%) | 38 (±16) months | 25 (18.5%) | 14 (10.4%) |
| | not treated | 14 (9.4%) | 35(±10) months | 0 (0%) | 1 (7.1%) |

## [BP06] COMPARISON OF A HIGH-VIRULENT VERSUS A LOW-VIRULENT STAPHYLOCOCCUS AUREUS STRAIN IN A MURINE FRACTURE-RELATED INFECTION MODEL.

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**Aim:** Staphylococcus aureus is the leading pathogen in fracture-related infection (FRI). Virulence factors vary between different strains, which may have a decisive influence on the course of infection. Previous in vitro experiments, in vivo testing in wax moth larvae, and genomic analysis of S. aureus isolates from FRI identified a low- and high-virulent strain. These findings correlated with the acute course of FRI induced by the high-virulent pathogen, whereas the low-virulent strain caused a chronic FRI in its human host. However, the role of bacterial virulence in FRI is not completely understood. Therefore, the present study aimed to compare the identified high- and low-virulent S. aureus isolates in a murine FRI model.

**Method:** Skeletally mature C57Bl/6N mice received a femoral osteotomy stabilized by titanium lokking plates. FRI was established by inoculation of either high-virulent S. aureus EDCC 5458 or low-virulent S. aureus EDCC 5464 in the fracture gap. Mice were euthanized 4 and 14 days after surgery, respectively. Severity and progression of infection were assessed in terms of clinical presentation, quantitative bacteriology, semiquantitative histopathologic evaluation, and serum cytokine profile.
Results:
Quantitative bacteriological results 4 days after surgery revealed a higher bacterial load in soft tissue samples in high-virulent infected animals ($p = 0.026$). Mice infected with the high-virulent strain also displayed higher rates of organ dissemination (24/36 organs in high-virulent, versus 5/36 organs in low-virulent infected animals; $p < 0.0001$).
In the histopathological assessment, bacterial agglomerations at the fracture ends were present to a greater extent in the high-virulent cohort and barely detectable in low-virulent infected mice. In both cohorts, no bone healing was observed after 4 days. On day 14, bone healing at the fracture site was visible in low-virulent infected animals, whereas callus formation was observed in only one animal from the high-virulent infected cohort. Furthermore, osteonecrosis and osteolysis were increased in high-virulent infected animals. Regarding serum cytokines, innate immune markers were elevated in both groups at day 4. By day 14, a more pronounced proinflammatory response indicated by increased serum cytokine levels of IFN-γ, IL-1β, and IL-6 was observed in high-virulent infected animals.

**Conclusions:** The present study demonstrated distinct bacteriological and histopathological differences between two different virulent S. aureus strains previously shown to have different courses in human patients. While host physiology is often considered to have a major impact on the course of FRI, this study highlights the critical influence of the invading pathogen and its virulence characteristics.

## [BP07] THE JOINT-SPECIFIC BACH CLASSIFICATION: A PREDICTOR OF OUTCOME IN PROSTHETIC JOINT INFECTION.

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**Aim:** This study assesses the ability of the JS-BACH classification of bone infection to predict clinical and patient-reported outcomes in prosthetic joint infection (PJI).

**Method:** Patients who received surgery for suspected PJI at two specialist bone infection centres within the UK between 2010 and 2015 were classified using the JS-BACH classification into either 'uncomplicated', 'complex' or 'limited options'. All patients were classified by two clinicians blinded to outcome, with any discrepancies adjudicated by a third reviewer. At the most recent follow-up, patients were assessed for (i) any episode of recurrence since the index operation and (ii) the status of the joint. A Cox proportional-hazard model assessed significant predictors of recurrence following the index procedure. Patient-reported outcomes included the EuroQol EQ-5D-3L index score and the EQ-visual analogue score (VAS) at 0, 14, 42, 120 and 365 days following the index operation.

**Results:** 220 patients met the inclusion criteria during the study period which included PJI of the knee (n=111), hip (n=102), shoulder (n=4) and elbow (n=3). The median time to final follow-up was 4.7 years (inter-quartile range 2.7 – 6.7 years). Controlling for type of index procedure and site of infection, Cox proportional-hazards ratio of recurrence when being classified as complex versus uncomplicated was 25.2 (95% CI 3.45 – 183.7, p<0.001) and having limited options verses uncomplicated was 59.0 (95% CI 7.93 – 439.1, p<0.001). None of the patients who were classified as 'uncomplicated' PJI (0/52) had received either amputation, joint fusion, excision arthroplasty, chronic suppressive anti-biotics, had died from sepsis secondary to PJI or were awaiting treatment for an active infection at final follow-up. This compared to 21.3% (27/127) of patients classified as 'complex' PJI and 65.9% (27/41) of patients classified as 'limited options'. Compared to the age-matched population, patients with 'uncomplicated' PJI reported similar EQ-index scores (age-matched population: 0.782, 'uncomplicated': 0.730, SD 0.326) and EQ-VAS (age-matched: 77.9, 'uncomplicated' PJI: 79.4, SD 20.9). This was significantly higher when compared to patients classified as 'complex' (EQ-index: 0.515 SD 0.323, p<0.012; EQ-VAS: 68.4 SD 19.4, p=0.042) and 'limited options' (EQ-index: 0.333 SD 0.383, p<0.001; EQ-VAS: 60.2, SD 23.1, p=0.005, ANOVA with Tukey post-hoc comparison).

**Conclusions:** We have demonstrated that the JS-BACH classification for bone and joint infection is a significant predictor of clinical outcome and quality of life following surgery for PJI. This will allow clinicians to offer prognostic information to patients and guide the timing of referral for specialist management in PJI.

## [BP08] SHOTGUN METATRANSCRIPTOMICS FOR PJI DIAGNOSIS: A NOVEL PROSPECTIVE INVESTIGATION

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**Aim:** While metagenomic (microbial DNA) sequencing technologies can detect the presence of microbes in a clinical sample, it is unknown whether this signal represents dead or live organisms. Metatranscriptomics (sequencing of RNA) offers the potential to detect transcriptionally "active" organisms within a microbial community, and map expressed genes to functional pathways of interest (e.g. antibiotic resistance). We used this approach to evaluate the utility of metatrancriptomics to diagnose PJI and predict antibiotic resistance.

**Method:** In this prospective study, samples were collected from 20 patients undergoing revision TJA (10 aseptic and 10 infected) and 10 primary TJA. Synovial fluid and peripheral blood samples were obtained at the time of surgery, as well as negative field controls (skin swabs, air swabs, sterile water). All samples were shipped to the laboratory for metatranscriptomic analysis. Following microbial RNA extraction and host analyte subtraction, metatranscriptomic sequencing was performed. Bioinformatic analyses were implemented prior to mapping against curated microbial sequence databases– to generate taxonomic expression profiles. Principle Coordinates Analysis (PCoA) and Partial Least Squares-Discriminant Analysis were utilized to ordinate metatranscriptomic profiles, using the 2018 definition of PJI as the gold-standard.

**Results:** After RNA metatranscriptomic analysis, blinded PCoA modeling revealed accurate and distinct clustering of samples into 3 separate cohorts (infected, aseptic and primary joints) – based on their active transcriptomic profile, both in synovial fluid and blood (synovial anosim p=0.001; blood anosim p=0.034). Differential metatranscriptomic signatures for infected versus noninfected cohorts enabled us to train machine learning algorithms to 84.9% predictive accuracy for infection. Multiple antibiotic resistance genes were expressed, with high concordance to conventional antibiotic sensitivity data.

**Conclusions:** Our findings highlight the potential of metatranscriptomics for infection diagnosis. To our knowledge, this is the first report of RNA sequencing in the orthopaedic literature. Further work in larger patient cohorts will better inform deep learning approaches to improve accuracy, predictive power and clinical utility of this technology.

## [BP09] DEVELOPMENT OF PHAGE THERAPY TO TREAT STAPHYLOCOCCI BONE AND JOINT INFECTIONS IN FRANCE: ISOLATION AND CHARACTERIZATION OF SEVENTEEN NOVEL ANTI-STAPHYLOCOCCUS BACTERIOPHAGES

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**Aim:** Bacteriophages, viruses specific of bacteria, are receiving substantial attention as alternative antibacterial agents to treat bacteria frequently multi-resistant to antibiotics and/or able to form biofilms, such as staphylococci. The latter are responsible for very difficult to treat bone and joint infections (BJIs). In this context, our consortium aims to develop a production of therapeutic phages in accordance with the will of ANSM (French National Agency for the Safety of Medicines and Health Products) to encourage the development of a national academic platform for phage therapy. We report the isolation and characterization of new anti-Staphylococcus phages as well as the evaluation of their activity on a collection of clinical strains of S. aureus (SA) and coagulase-negative staphylococci (CNS) in order to assess their therapeutic potential.

**Method:** Seventeen phages were isolated from wastewater samples. Their identification was obtained by Illumina whole genome sequencing. To evaluate their spectrum of activity, 30 genetically characterized SA strains representative of the main genetic backgrounds as well as 32 strains belonging to 7 CNS species responsible for BJIs were included. The spot test technique, based on the determination of the Efficiency Of Plating ratio, was used (EOP, ratio between the phage titer obtained on a tested strain/titer on a reference strain, close to 1 if high sensitivity to the phage).

**Results:** All isolated phages belonged to the Myoviridae family: 14/17 and 3/17 to the Kayvirus and Silviavirus genera respectively. Silviavirus phages were more active on SA strains (EOP>0.001 for 73-90% of strains) than Kayvirus phages (EOP>0.001 for 13-70% of strains, except for V1SA21: 80%). In total, 83% of strains were susceptible to the phage with the broadest spectrum in each genus, their combination representing a promising opportunity to prevent the emergence of resistance. Kayvirus phages had polyvalent activity on several CNS species (maximum 47% of tested strains), mainly S. lugdunensis, S. capitis and S. caprae, whereas Silviavirus phages were only active on 6-12% of the tested strains.

**Conclusions:** We report the characterization of a large collection of novel phages with complementary spectra against a collection of SA and CNS strains. Further work is currently focused on i) the isolation of anti-S. epidermidis phages, bacterial species against which the present collection of phages was insufficiently active, while it is a major pathogen in this context, ii) the development of production and purification protocols in order to meet the requirements of ANSM for human use.

## [BP10] MICROBIOLOGICAL AND ULTRASTRUCTURAL EVALUATION OF THE 191219 S. AUREUS BACTERIOPHAGE ACTIVITY AGAINST PLANKTONIC, INTRACELLULAR AND BIOFILM INFECTION WITH STAPHYLOCOCCUS AUREUS

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**Aim:** Here, we are aimed to evaluate bacteriophage (191219) to treat ***S. aureus*** implant-associated bone infections by means of testing against ***S. aureus*** during its planktonic, biofilm and intracellular growth phases and finally assessing antimicrobial effect on ***in vivo*** biofilm formed on metal K-wire in an alternative insect model ***Galleria mellonella***.

**Method:** The bacteriophages (191219) were provided from D&D Pharma GmbH. These bacteriophages were tested against ***S. aureus*** EDCC 5055 (MSSA) and ***S. aureus*** DSM 21979 (MRSA) strains. To assess the activity of bacteriophages against planktonic growth phase, bacteriophages and ***S. aureus*** EDCC 5055($1X10^7$ CFU/ml) were co-cultured in LB media as multiplicity of infection (MOI) of 10, 1, 0.1, and 0.01 for 24 hours at 37°C and finally plated out on the LB agar plates to estimate the bacterial growth. The antimicrobial activity of bacteriophages on biofilms in vitro was measured by analyzing the incubating the several fold dilutions of bacteriophages in LB media with biofilms formed on 96-well plate. The eradication of biofilm was analyzed with crystal violet as well as CFU analysis methods. Later, the effect of bacteriophages on intracellular growth of ***S. aureus*** in side osteoblast was tested by treating the ***S. aureus*** infected osteoblasts at 2h, 4h and 24h time points of post treatment. In addition, we have analyzed synergistic effect with gentamicin and rifampicin antibiotics to clear intracellular ***S. aureus***. Finally, experiments are performed to prove the effect of bacteriophages to clear ***in vivo*** biofilm using alternative insect model ***G. mellonella*** as well as to detect the presence of bacteriophages inside the osteoblasts through transmission electron microscopy (TEM) analysis.

**Results:** Our results demonstrate the ***in vitro*** efficacy of bacteriophages against planktonic ***S. aureu***s. Transmission electron microscopy (TEM) experiments revealed severe infection of bacteria by bacteriophages. Bacteriophages also eradicated in a dose-dependent manner in vitro ***S. aureus*** biofilm formation and were active against intracellular ***S. aureus*** in an osteoblastic cell line. TEM analysis visualized the effect of the bacteriophages on ***S. aureus*** inside the osteoblasts with the destruction of the intracellular bacteria and formation of new bacteriophages. For the Galleria infection model, single administration of phages failed to show improvement in survival rates, but exhibited some synergistic effects with gentamicin or rifampicin, which was not statistically significant.

**Conclusions:** In summary, bacteriophages could be a potential adjuvant treatment strategy for patients with implant-associated biofilm infections. Further preclinical and clinical trials are required to establish adequate treatment protocols.

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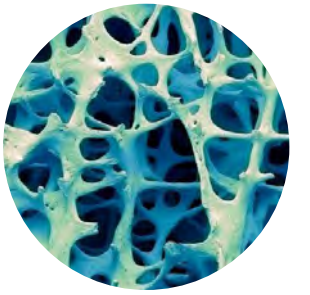

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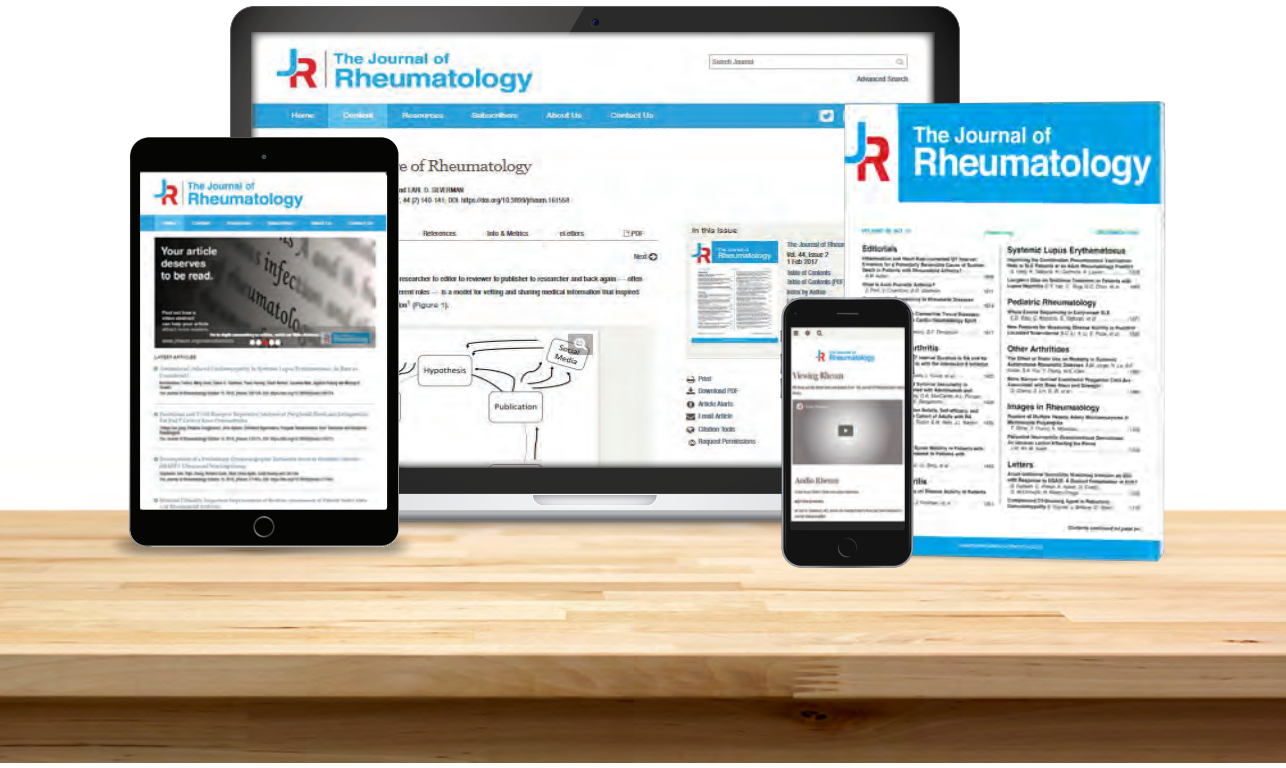


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