### POSTER OVERVIEW

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P1] BONE DEFECT SIZE DEFINES THE CHOICE OF SURGICAL TREATMENT FOR CHRONIC OSTEOMYELITIS OF THE ANKLE JOINT

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¹Vreden Russian Research Institute of Traumatology and Orthopaedics, Saint-Petersburg, Russian Federation

**Aim:** To evaluate surgical treatment options for chronic osteomyelitis of the ankle joint depending on necrosectomy bone defect size.

**Method:** 32 patients with the mean age of 50 years (CI95% 45-54) underwent treatment for chronic osteomyelitis of the ankle joint anatomic type 4, physiologic class B (87%) and A (13%) according to Cierny-Mader classification. 69% (n=22) of them were males.

Haematogenic, post-traumatic and post-operative osteomyelitis was observed in 3% (n=1), 47% (n=15) and 50% (n=16) of cases, respectively. Hepatitis C was diagnosed in 19% (n=6) of patients. Osteomyelitis was recurrent in 72% (n=23) of cases. Patients were divided into three groups depending on necrosectomy bone defect size: I group - 19 patients with defect < 2 cm; II group - 9 patients with 2 ≤ defect ≤ 4 cm; III group - 4 patients with defect>4 cm. Acute shortening of the limb with external fixation, early axial load and the correction of the deformity were performed in all patients of group I and II. In addition, 66.7% of patients in group II had astragalectomy. The Ilizarov method was used in group III. In this group, an antibiotic-laden spacer was installed in two patients due to the intensive tissue destruction triggered by infection. Duration of surgery, intraoperative blood loss, types of pathogens and the rate of infection recurrence were evaluated. The mean follow-up period was 13 months (CI95% 10-16).

**Results:** the highest median duration of surgery (265 min (IQR, 155-319)) and volume of blood loss (550 ml (IQR, 288-775)) were in group III. These values were decreasing in parallel with the defect size. Types of isolated pathogens were similar among patients of all groups. The main pathogen was *S. aureus* (65.6%) including 19% of MRSA. Microbial associations were identified in 10 cases (31.3%) including 3 patients with Acinetobacter spp. In group I infection recurrence occurred in only 1 case (5.3%) in 6 months after surgery while in group II it was observed in 2 cases (22.2%) with evident tissue fluting of the surgical wound bed. In the later 2 cases there was early MRSA and delayed MSSA post-operative infection. There was no infection recurrence in group III.

**Conclusions:** The proper choice of surgical treatment for chronic osteomyelitis of the ankle joint depending on necrosectomy bone defect size demonstrated the high success rate (90.6%). Fluting of the wound bed after acute shortening usually increases the risk of infection recurrence, thus it should be avoided.
LONG-TERM CLINICAL OUTCOME AND SURVIVORSHIP FOLLOWING DEBRIDEMENT, ANTIBIOTICS AND IMPLANT RETENTION (DAIR) IN PRIMARY KNEE PERI-PROSTHETIC JOINT INFECTION – A 15-YEAR EXPERIENCE

Abtin Alvand¹, Floris de Vos¹, George Grammatopoulos¹, Jamie Ferguson¹, Matthew Scarborough¹, Ben Kendrick², Nicholas Bottomley³, Will Jackson³, Roger Gundle³, Adrian Taylor³, Andrew Price³

¹Nuffield Orthopaedic Centre, Oxford University Hospitals, Oxford, United Kingdom

Background: Debridement, Antibiotics and Implant Retention (DAIR) is a treatment option in Peri-prosthetic Joint Infection (PJI) where the prosthesis remains well fixed. Advocates of DAIR argue that this approach can achieve good outcome.

Aim: To establish the 10-year clinical outcome following DAIR in primary knee PJI and identify factors associated with outcome.

Method: This was a retrospective, consecutive case-series of DAIRs performed in our unit, between 1998-2013, for treatment of PJI in primary Total or Unicompartmental Knee Arthroplasty (TKA or UKA). Data recorded included Charlson Comorbidity Index (CCI), interval between index procedure and DAIR [early (<3 months) versus late (>3 months)], interval between onset of symptoms and DAIR [acute (≤3weeks) and chronic (>3weeks)], type of DAIR performed (exchange of polyethylene bearing or not) and organism identified. Outcome measures included complications, mortality, implant survival, and functional outcome (Oxford Knee Score; OKS).

Results: A total of 85 DAIRs (75 TKAs, 10 UKAs) were identified. The mean age was 68 years (32-90) and mean CCI was 1 (0-6). The most common indication for primary surgery was osteoarthritis (83%). Most cases were performed within 3 months from the index procedure (69%). The majority of patients (90%) had a DAIR within 3 weeks of the onset of symptoms. Exchange of polyethylene bearing took place in 59% of cases. Gastrocnemius flap wound coverage was considered necessary in 12% of cases. Staphylococcus aureus was the most common organism (47%), followed by polymicrobial growth (22%) and Streptococci (15%). The 5- and 10-yr all cause mortality was 22% (12-32%) and 30% (18–42%) respectively at a mean follow-up of 6.5 years. 39 patients (46%) had a complication following initial DAIR; this was persistence of PJI in all cases. Although most were treated with a re-DAIR (n=21), 12 required revision and 6 remained on long-term suppressive antibiotics. Of the 21 re-DAIRs, PJI eradication was achieved in 13, whilst 6 required revision, and 3 remained on long-term antibiotics. To date, 17 (19%) knees have been revised; the 10-year implant was 77% (95% CI: 67-87%). Early PJI and bearing exchange were associated with improved PJI eradication (p=0.05). Type of organism did not appear to influence PJI eradication.

Conclusions: This study provides further evidence on the role of DAIR within the knee PJI treatment options. Infection eradication was achieved in 68% of cases; in 23 (25%) a repeat DAIR was required. Polyethylene bearing exchange is of benefit – especially in late PJI.
[P3] CAT AT HOME?

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Aim: Cat-scratch disease (CSD) is a granulomatous inflammation of the lymph nodes, caused by small gram-negative bacteria. The Bartonella species are transmitted by bites or scratches from infected cats, dogs or rabbits (Figure 1). Beside asymptomatic cases, the infection can lead to neurological, ocular or heart diseases or mimic various disorders such as oncological processes. Thus, symptoms can be easily misinterpreted, which may lead to false or delayed diagnosis with inadequate treatment. The aim of this study was to analyze cases of CSD, their management and outcome.

Method: In total four cases of CSD were retrospectively identified. They were primarily transferred to our musculoskeletal oncology outpatient department on suspicion of soft tissue tumors. Their ages were 16, 22, 28 and 37 years at admission (one female, three males). Investigations included serum analysis and histological evaluation from biopsy specimen.

Results: In three cases, soft tissue swelling occurred in the area of the elbow and in one case in the groin area. History revealed swelling and pain without trauma for several weeks. Magnetic resonance imaging had already been performed in all patients, showing soft tissue tumors with an inhomogeneous contrast agent uptake (maximum diameter range from 18 to 36 mm) (Figure 2). Two patients were transmitted to surgery - one incisional and one excisional biopsy were performed. Histology revealed the diagnosis of Bartonella henselea infection (Figure 3). In the other cases, physical examination documented scratches and/or bites seen at the forearm. In these cases the final diagnosis was obtained from serological investigations, showing high antibodies against Bartonella bacteria. Two patients were successfully treated by doxycycline, in the other two cases symptoms disappeared after operation.

Conclusions: The wide spectrum of possible clinical presentation of Bartonella infection may lead to false or delayed diagnosis. MRI with contrast agent is the diagnostic method of choice to characterize soft tissue swelling. However, it cannot differentiate between soft tissue tumors and Bartonella infection. Besides diagnostic imaging, physical examination and the patient’s history display an important part in establishing the correct diagnosis. Thus, when a patient presents with a soft tissue tumor and scratches, one simple question may lead to the right diagnosis: Do you have a cat at home?

Figure 1
Aim: Treatment of chronic osteomyelitis requires primarily an adequate resection of the affected bone segment with subsequent antibiotic medication. Local applied antibiotic with a sustained bioavailability have been reported for efficient prophylactic and therapeutic effects [1]. The resection of an infected bone segment is usually associated with a significant tissue defect which requires complex reconstruction surgery. Recently, we used a novel bio-resorbable bone cement supplemented with Gentamicin *.

Method: A 16 y/o patient with a strong suspicion for chronic osteomyelitis was referred to our outpatient clinic. Diagnosis of chronic osteomyelitis without evidence of bacterial growth was confirmed. A primary sequestrectomy with reconstruction by using a muscle flap was performed.

Five years after primary sequestrectomy patient presented with pain at the right proximal tibia. The SPECT-CT confirmed persistent osteomyelitis at the proximal tibia. Operational intervention revealed non-resorbable suture material from the flap reconstruction five years ago. The reconstruction of the bone defect after thorough going resection was realized by using 30ml antibiotic eluting bone graft substitute* [8] applied in alternating layers with autograft iliac crest spongiosa supported by a plate osteosynthesis.

Results: Microbiological analysis revealed positive growth for Staphylococcus epidermidis and Staphylococcus hominis. White wound secretion presented 10 days after surgery without any signs of inflammation or local infection. Thus, a debridement with tight wound closure was performed which resulted in normal wound healing without further wound secretion.

Conclusions: We provide evidence that the antibiotic eluting bone graft substitute* is safe and suitable defect filler in combination with autologous spongiosa in order to reconstruct lost bone tissue due to chronic osteomyelitis. High local concentration of gentamicin is released from the antibiotic eluting bone graft substitute* [8],[4] which showed a bactericidal in vitro effect [3]. A high volume of Gentamicin* (>20ml) is associated with increased wound secretion beginning 9 to 10 days after application and might require a wound revision but only if the defect is covered by limited amount of subcutaneous tissue.

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*CERAMENT™|G
[PS] CLINICAL EXPERIENCE OF USING HIGH DOSE DAPTOMYCIN (10MG/KG) IN 129 TREATMENT EPISODES FOR BONE AND JOINT INFECTION

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Aim: The aim is to provide an update on our experience with high dose Daptomycin (10mg/kg) for bone and joint infections in the bone infection unit. This unit has been developed since November 2011 by infectious diseases and microbiology staff working within one of the largest tertiary orthopaedic hospitals in the UK.

Method: Retrospective observational study, including all patients who had received long-term Daptomycin from November 2011 to April 2016. Data was collected from electronic databases and patient notes.

Results: In total 129 treatment courses of Daptomycin were received, by 81 patients. The commonest indication was prosthetic joint infection, followed total knee replacements, total hip replacement developed infection more than 3 months after procedure. The most common organism isolated was Staphylococcus epidermidis. Indications for Daptomycin were salvage therapy due to glycopeptide resistance or previous allergy/adverse reactions to other antibiotics.

Preliminary results of 27 treatment courses of Daptomycin were received, by 21 patients. The commonest indication was prosthetic joint infection (n=24 (89%)), of which 57% followed total knee replacements, 24% total hip replacement. 14 (42%) developed infection more than 3 months after procedure. The most common organism isolated was S. epidermidis (81%). 18 (67%) had a previous course of glycopeptides.

Daptomycin was used predominantly as salvage therapy due to resistance or intolerance to previous antibiotics. 10 (37%) were prescribed 6mg/kg, 2 (7%), 8mg/kg, 14 (52%) 10 mg/kg and 1 (4%) 12mg/kg.

Daptomycin caused a creatinine kinase (CK) rise in 4 (15%), 3 were on 6mg/kg doses. 2 were transient rises. Daptomycin was stopped in 4 (15%) cases; 2 (7%) due to uncomplicated high CK, 1 (4%) due to Daptomycin resistant E. faecium, and 1 (4%) because another antimicrobial was deemed more appropriate.

Conclusions: High doses of Daptomycin are known to have better clinical outcomes than standard 4-6mg/kg but there are few reports of routine use of 10mg/kg or higher doses for bone and joint infections. Our data shows that this dose is well tolerated and safe when an active infection service monitors for adverse events. Early outcomes were comparable to published data¹.

Acknowledgements: No external funding received. This work has been undertaken by the authors with support from the hospital’s bone infection unit team including ID/ Microbiologists, OPAT CNS’s and pharmacy.
Aim: The aim of the experiment was to develop a resorbable collagen/hydroxyapatite/vancomycin nanostructured layer with the controlled elution of antibiotics to be used as a bone/implant bioactive interface particularly in the case of prosthetic joint infections or as a preventative procedure regarding primary joint replacement in a potentially infected site.

Method: Nano-structured or micro-structured layers based on collagen (type I, Company I*, Czech Republic) and 0, 5 or 15wt% of hydroxyapatite nanoparticles (avg. 150nm, Company II**, Germany) were prepared employing the lyophilisation or electrospinning of dispersions with or without 10wt% vancomycin hydrochloride (Company III***, France) and subsequently cross-linked by N-(3-dimethylaminopropyl)-N-ethylcarbodiimide hydrochloride/N-hydroxysuccinimide (Company II**, Germany). Pure cross-linked collagen/hydroxyapatite electrospun mats were subsequently impregnated with 10wt% vancomycin. The in vitro release rates of vancomycin and its inactive degradation products were characterized by HPLC. The antimicrobial effects of the layers were determined using agar diffusion testing against four different clinical isolates, namely Staphylococcus aureus, Staphylococcus epidermidis and two Enterococcus faecalis isolates (one acquired from analysis of infected joint replacement).

Results: The maximum concentration of the released active form of vancomycin (700mg/l after 3hours, 150mg/l 21st day) was assessed by means of the vancomycin impregnation of cross-linked electrospun layers. The lowest concentration was determined for those layers electrospun directly from a collagen solution with vancomycin. Agar diffusion tests revealed that the electrospun impregnated layers exhibited the highest activity. Modification using hydroxyapatite exerts no strong effect on vancomycin evolution.

Conclusions: The higher specific surface of nanostructured layers probably plays a negative role in the preparation process due to the higher rate of vancomycin elution to the cross-linking solution. This may be overcome via the subsequent impregnation of the cross-linked layers. Our results suggest that the local application of high-dose vancomycin via drug delivery carriers can provide an effective therapeutic osteomyelitis treatment method that prevents the development of bacterial resistance.

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*VUP Medical  
**Sigma Aldrich  
***Mylan S.A.S
[P7] USEFULNESS OF A MULTIPLEX SEROLOGICAL IMMUNOASSAY TO THE PREOPERATIVE DOCUMENTATION OF PROSTHETIC JOINT INFECTION

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Aim: The preoperative diagnosis of prosthetic joint infection (PJI) is a key step in the management of revision arthroplasty. Chronic infection is a common etiology of implant failure, and preoperative documentation of infection is a major step in the management of patients. A previous study evaluated the performance of a multiplex serological immunoassay* documenting PJIs caused by Staphylococcus sp., Streptococcus agalactiae and Propionibacterium acnes, using the intraoperative microbiological documentation of revision surgeries as an endpoint. We evaluate the performance of the multiplex serological test to aid in the diagnosis of Prosthetic Joint Infections* in comparison to the culture of pre-operative joint aspirations in the management of prosthetic joint infections.

Method: We retrospectively analysed data from a prospective, multicenter, non-interventional study of patients undergoing revision arthroplasty in referral centers for PJIs. PJI was diagnosed when fistula or microbiological criteriae (≥2 positive intraoperative samples or ≥1 obligate pathogen). Patients had preoperative documentation, with the multiplex serological test to aid in the diagnosis of Prosthetic Joint Infections* serological assay and joint aspiration with microbiological culture.

Results: 334 patients with all required assays performed were included for analysis. 60 patients with indetermined results from the multiplex serological test to aid in the diagnosis of Prosthetic Joint Infections* and 61 patients with non-productive aspirations were excluded. 198 patients had positive preoperative cultures whereas only 133 were diagnosed with PJI. Due to low numbers of S. agalactiae and P. acnes PJIs, these parameters were not analysed. The sensitivities of the multiplex serological test to aid in the diagnosis of Prosthetic Joint Infections* and preoperative cultures for staphylococci were not significantly different (70.3% vs 81.1%, p=0.1 respectively), but culture was significantly more specific than serology (81.5% vs 95.4%, p=0.001). When the multiplex serological test to aid in the diagnosis of Prosthetic Joint Infections* was positive, the positive predictive value (PPV) of aspiration culture increased from 90% to 95.9% for staphylococci (90% to 94.4% for S. aureus; 87.5% to 95.7% for S. epidermidis) When the multiplex serological test to aid in the diagnosis of Prosthetic Joint Infections* was negative, the negative predictive value (NPV) of aspiration culture increased from 92.4% to 94.3% for staphylococci (94.3% to 96.2% for S. aureus; 96.1% to 97.4% for S. epidermidis).

Conclusions: The performance of the non-invasive serological assay validates the use of the multiplex serological test to aid in the diagnosis of Prosthetic Joint Infections* for the screening of patients...
prior to aspiration. In cases of positive serological assays, the PPV of microbiological aspiration was enhanced, facilitating the interpretation of \textit{S. epidermidis} aspirate cultures. The assay needs further validation in a general population of revision arthroplasty candidates in order to advocate its use prior to aspiration in a screening process.

*BJI Inoplex*
[P8] TUBERCULOUS SACRO-ILIITIS, ABOUT 5 CASES AND LITERATURE REVIEW

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Aim: The tuberculosis is an endemic pathology in underdeveloped countries. The osteo-articular involvement is rare. Its diagnosis is often made late. The tuberculous sacro-iliitis is an exceptional localization. Through five cases of tuberculous sacro-iliitis, we try to identify the epidemiological, clinical and paraclinical aspects of this entity as well as its evolutive and therapeutic specificities.

Method: We report five cases of tuberculous sacro-iliitis among 5 middle-aged women 42 years, coming from rural area. The pathology has caused a local symptomatology in 3 cases, and has a fortuitous discovery in 2 cases by bone-scintigraphy. Signs of tuberculous impregnation associated to positive Intradermal Tuberculin Test were found in 4 cases. All cases have other tuberculous locations. Pott’s disease was associated in 3 cases. An inflammatory syndrome was found in every case. All the cases were explored by X-Ray completed by CT-Scan or MRI in every case. The diagnostic certainty was obtained by Histology in all cases. The biopsy was guided by CT-Scan in 4 cases. A TB treatment was established for all patients. The mean duration was fifteen months.

Results: The evolution was favorable in every case with restoration of the walking, the regression of the pains, the normalization of the inflammatory biological parameters.

Conclusions: A tuberculous sacro-iliitis must be evoked in front of a sacroiliac symptomatology at every tuberculous patient. The bone-scintigraphy allows the screening of the infra-clinical forms. The CT-scan offers a better analysis of the osseous lesions and their extension in soft tissues. Despite the anamnestic context, clinical and paraclinical suggestion of the tuberculous cause, the isolation of Mycobacterium tuberculosis or its genome by PCR and the histological visualization of a tuberculous granulome remain the only tools to obtain the diagnostic certainty. The treatment is essentially medical based on TB drugs. The surgery keeps some indications. Only the precocity of diagnosis and the good observance of the treatment can guarantee better results.
[P9] VANCOMYCIN ELUTING BONE GRAFT SUBSTITUTE IN A TWO-STAGE INFECTED KNEE REVISION

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**Aim:** The infection of a hinged knee megaprosthesis of a 16-year old HIV-positive female patient with an osteosarcoma in the proximal tibia (Fig.1Ai), subject to a course of chemotherapy (Fig.1Aii), was treated with a two-stage arthrodesis and the co-delivery of an antibiotic-including synthetic bone substitute.

**Method:** In the first stage, after the removal of the knee implant and the resection and thorough debridement of all infected and dead tissue, a metal rod (~35cm) was inserted from the femoral medullary canal into the tibial medullary canal. A Vancomycin eluting bone graft substitute\textsuperscript{1}, consisting of 40% hydroxyapatite and 60% calcium sulphate was injected around the rod and into the cavities in both the femur and tibia (Fig.1B), to provide a high dose of local antibiotic and improve bone stock for the second stage procedure. Two 10mL-products, consisting of 66mg of Vancomycin/mL of product, were used. To preserve leg length and for load-bearing, PMMA was placed around the metal rod and between the femoral and tibial bone ends as a spacer (Fig.1C&D). Four months later, at the second stage, the metal rod was replaced with an uncemented arthrodesis nail (Fig.1E&F).

**Results:** Immediately post-operatively the Vancomycin/bone graft substitute\textsuperscript{1} is clearly visible at the distal femur and proximal tibia (Fig.1E). An x-ray following the second stage procedure four months later shows bone remodeling in all areas where the Vancomycin eluting bone graft substitute\textsuperscript{1} has been injected (Fig.1E&F).

**Conclusions:** A two-stage infected knee revision can be successfully handled with a Vancomycin eluting bone graft substitute\textsuperscript{1} providing a secure treatment of such cases.

**Figure Caption:** Fig.1: Ai,ii:Pre-operative x-rays showing the osteosarcoma & chemotherapy. B,C: insertion of metal rod and injection of Vancomycin/bone graft substitute\textsuperscript{1}. D-E: post-operative x-rays; E,F: clear remodeling in the areas with Vancomycin eluting bone graft substitute\textsuperscript{1}. 

\begin{figure}[h]
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\end{figure}
Aim: Demonstrate the successful use of an antibiotic eluting resorbable bone graft substitute in a forefoot amputated diabetic patient with a new osteomyelitis in the remaining foot as a last possibility to avoid further (major) amputation.

Method: We present the case of a forefoot amputee who had a new osteomyelitis in the stump of the 5th metatarsal bone. The consequence of a surgical excision would have been unavoidable new pressure ulcers on the lateral border of the stump, due to a supination position of the foot, caused by the absence of the short peroneal tendon, which is inserting at the base of the 5th metatarsal bone. Due to the insufficient bone quality and the infection present, a tendon transfer to the 4th metatarsal or a double arthrodesis of the hindfoot was not an option. A major amputation would have been the unavoidable result. We decided to use an antibiotic eluting resorbable bone graft substitute in a salvage procedure hoping to save the stump of the 5th metatarsal bone.

We curetted the bone cavity and filled it with 5cc of an antibiotic eluting resorbable bone graft substitute. The patient received additional iv antibiotics for two weeks and orally for another 4 weeks. We continued the consistent wound treatment and could observe the closure of the ulcer with the previously positive probe-to-bone over the following 4 months.

Results: All signs of infection or inflammation have completely disappeared, the ulcer has healed, and the patient starts ambulating again with his custom-made shoes.

Conclusions: An antibiotic eluting resorbable bone graft substitute can be a useful tool in the context with a salvage procedure in diabetic feet. In this particular case, we are convinced that it was the last reasonable possibility to avoid major amputation.
TREATMENT OF INFECTED NON-UNION WITH ANTIBIOTIC LOADED CALCIUM-SULPHATE – A CASE SERIES REPORT

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Aim: Osteomyelitis (OM) is a heterogeneous pathologic condition of the bone associated with infection and inflammation. It is a complex disease, which requires a multidisciplinary approach and a personalized treatment. The increased number of patients over the last decade, undergoing fracture and reconstructive joint surgery combined with the use of temporary or permanent implants correlates with an increased incidence of OM. We here describe a cohort of patients suffering from infectious nonunions of long bones, which have experienced multiple fracture treatment and revision surgeries.

Method: Given the increased incidence of OM in patients receiving reconstructive surgery with permanent implants, we decided to start a perspective observational study on our cohort. Peripheral blood samples and biopsies of the affected bones are collected at admission. We examined the microbial spectrum and its antibiotic resistance, including Finegoldia magna, Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus mitis, Propionibacterium acnes, Staphylococcus hominis and Staphylococcus capitis. Surgical and antimicrobial treatment was subsequently applied at multiple stages to reach definitive osteogenesis. Following implant removal and sequestrectomy, the bone defect was filled with a combination of autologous bone marrow graft and gentamycin loaded calcium sulphate and hydroxyapatite*. After implant removal and antimicrobial treatment in a multidisciplinary approach with the infectiologists and plastic surgeons the definitive osteosynthesis was performed. Follow-up care was performed by regular monitoring for local and systemic signs of infections.

Results: Biopsies taken at the final stage showed no signs of infection, with no bacterial or fungal growth following at least two weeks in the absence of antibiotic regimen. Combined autologous bone marrow graft with calcium sulphate, hydroxyapatite and gentamicine* was easily applicable and showed full integration on clinical and radiographic follow-up evaluations. Further, no adverse side effect or relapse of infection was observed in our small cohort of patients.

Conclusions: In our study we obtained promising preliminary results, however we need to extend the follow up observation time beyond one year as well as increase the statistical power of our analysis by increasing the number of patients presenting with OM following reconstructive surgery.

* CERAMENT™ G, Bonesupport
[P12] ANTIBIOTIC AND CELL-BASED THERAPY TO PREVENT THE DEVELOPMENT OF S. EPIDERMIDIS-INDUCED NONUNIONS IN RATS

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Aim: Methicillin-resistant S. epidermidis (MRSE) is responsible for biofilm-related infections in orthopedics¹,² and fracture healing delay³. An animal model of MRSE-infected femoral fracture was recently developed⁴. The present study aims to investigate the efficacy of systemically or locally-injected vancomycin or bone marrow-derived mesenchymal stem cells (BMSCs) in preventing the bacterial infection that leads to nonunion development.

Method: Femurs of thirty rats were osteotomized, injected with a clinically-derived MRSE strain and synthesized. Rats were divided into: infected controls (IC); systemically-injected vancomycin (s-VANC); locally vancomycin-enriched hydrogel (l-HYD); systemically-injected BMSCs (s-BMSCs); and locally-injected BMSCs (l-BMSCs). After 6 weeks, the host response to treatments was evaluated through blood (neutrophils, pro-inflammatory cytokines), micro-CT, histological and microbiological analyses.

Results: Immediately after the systemic injection of BMSCs, 50% of the s-BMSCs rats died. After 2 weeks, IC exhibited a significant increase in neutrophil count compared to the basal (p<0.01) and l-HYD values (p<0.05). A higher cytokine trend was measured in IC and l-BMSCs at day 3, and in IC and s-VANC at day 7 compared to the other groups. At day 14, the highest cytokine values were measured in IC and l-HYD, and in l-BMSCs for IL-10. Micro-CT showed a bony bridging >50% in s-VANC, and >75% in l-HYD and l-BMSCs. The IC group confirmed previously published data⁴. A difference of Log(CFU/g)/explant was detected between IC versus s-VANC (p<0.01) and l-HYD (p<0.001) which showed lower values compared to l-BMSCs (p<0.05). Histology demonstrated the presence of woven bone within the fracture site in s-VANC, a more mature bone was found in the l-HYD group. The l-BMSCs group showed a poor bony bridging composed of inflammatory fibrovascular tissue. The IC group showed severe signs of osteomyelitis and nonunion. The gram staining is consistent with microbiological tests.

Conclusions: Our results recommend the synergic use of s-VANC and l-HYD as an effective treatment to prevent biofilm-related nonunion. The bone repair could be enhanced by l-HYD able in stimulating bone-specific cytokines. This study cannot definitely sustain the use of cell therapies for this purpose because of the highly risky BMSCs systemic injection. Hence, the BMSCs immunomodulatory mechanism after local deliver needs to be more deeply investigated before developing cell-based clinical approaches.


Acknowledgements: Italian Ministry of Health funded this study.
Aim: Septic arthritis of the shoulder in children is uncommon. The diagnosis is sometimes difficult to do. The objective of this work is to recognize the clinical particularities of this location and its prognosis

Method: We retrospectively review 23 cases of septic arthritis of shoulder during 6 years from 2010 to 2015.

Were excluded:

- osteomyelitis of the humerus,
- Infection with specific germ and inflammatory arthritis

Results:

Sex ratio was 0.65

The average age at diagnosis was 19.89 months

4 patients have a pathological history (2SCD, 1 was undergoing chemotherapy for neuroblastoma, and one was operated for urethral stenosis.)

Clinically all patients have functional impairment of the upper limb. Fever was present in 56.52%

An inflammatory syndrome was positive in 95.65%

The x-ray showed lacunae in 30.43%.

Identification of the bacteriological agent was able in 78.26% of the joint fluid culture. We notice a predominance of salmonella followed by Sreptocoque.

The average duration of the intravenous antibiotherapy was 15 days. Oral relay was for about 30 days.

At mean of 6.45 months clinical outcomes was satisfactory, the radiological results showed the absence of bone lesion in 56.52%, fragmentation in 13.04% and epiphysal necrosis in 17.39%.

Conclusions: septic arthritis of the shoulder is rare in children, it occurs mostly in fragile patients. Diagnosis may be difficult. The first presentation can be summarized to an impairment of the upper limb.
Aim: To analyse the impact of a standardized protocol, including the use of beads*, for the collection of intraoperative specimens in suspected prosthetic joint infection (PJI).

Method: A new protocol was introduced at our trust in January 2015 for the collection of intraoperative microbiology samples. Six specimens are now taken using clean instruments: five are placed in bottles with beads* and one standard fluid sample is sent.

All patients with total knee or total hip replacements requiring revision or with suspected infection admitted to the Gloucestershire Hospitals NHS foundation trust between August 2014 and July 2015 were identified.

The patient notes were reviewed to confirm the reason for revision surgery, the clinical picture and whether antibiotics were prescribed. Laboratory records were reviewed to identify inflammatory markers, histology results, what type of samples were sent and the results of microscopy and culture.

Growth from the samples was analysed to determine whether the organism was significant by consensus between the surgical team and a consultant microbiologist.

Results: 54 patients were identified and 445 samples were sent. On average 7.9 samples were sent prior to the introduction of the protocol.

On average, 5.25 samples were positive per patient prior to the new protocol and 1.6 were positive when beads* were used.

In patients who were eventually treated with antibiotics, 74% of those with regular samples sent were positive and 78% were positive when the new protocol was introduced. 86% of the bead* samples were positive in these patients.

Previously, 41% of samples were deemed to contain contaminants, which fell to 20% for those adhering to the new protocol.

Conclusions: The use of a standardized protocol has reduced the average number of samples sent intraoperatively and prevented too few samples being taken.

The samples collected directly to bead* containers had improved yield and reduced contamination. This could theoretically be due to minimizing loss of the sample, a more homogenous sample and less handling of the sample.

The cost benefit of this protocol is twofold. Firstly, reducing the average number of samples saves resources both intraoperatively and in the laboratory. Secondly, improving the yield and reducing contamination would enhance appropriate antibiotic prescription.
The use of beads* and a clear standardized protocol for intraoperative sample infection has been effective in our small sample and we would recommend its implementation and further evaluation.

*Ballotini Beads
Aim: *Staphylococcus aureus* is a common cause of implant-associated infections. We investigated the antimicrobial activity of several antibiotics against planktonic and biofilm methicillin-susceptible *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) using isothermal microcalorimetry. This accurate technique enables measurement of growth-related heat production of viable and metabolically active bacteria.

Method: Susceptibility tests to daptomycin, fosfomycin, vancomycin, cotrimoxazole, linezolid and rifampicin were performed versus MRSA ATCC 43300 and MSSA ATCC 29213 strains. Heat flow (µW) and total heat (J) were measured using an isothermal microcalorimeter. The minimal heat inhibitory concentration for planktonic (MHIC\(_p\)) and biofilm (MHIC\(_b\)) were defined as the lowest antimicrobial concentration that inhibited growth-related heat production after 24h and 48h of calorimeter incubation, respectively. For planktonic tests, bacteria (1-5 x 10\(^5\) CFUs/ml) were incubated with different dilutions of antibiotics and placed in the calorimeter. *S. aureus* biofilms were formed on porous glass beads at 37°C in CAMHB. After 24h, beads were incubated in medium containing serial dilutions of antibiotics. After 24h exposure, beads were placed with 3 ml CAMHB in calorimetric ampoules.

Results: MHICs are summarized in Table 1. MHIC\(_p\) ranged from 0.008 to 4 µg/ml for all tested antibiotics against both MRSA and MSSA planktonic bacteria. Against biofilms, most antibiotics lack activity in concentrations up to 1024 µg/ml, except daptomycin and rifampicin, for which MHIC\(_b\) ranged from 64 µg/ml to 256 µg/ml.

Conclusions: All tested antibiotics showed good activity against planktonic bacteria, whereas biofilms were highly resistant. Only daptomycin and rifampicin showed anti-biofilm activity, although at non-physiologically high concentrations. In future studies, combinations of antibiotics should be investigated against biofilms.
Table 1: The MHICₚ and MHICₚₐ (µg/mL) for daptomycin (DAP), fosfomycin (FOS), vancomycin (VAN), cotrimoxazole (SMX-TMP), linezolid (LNZ) and rifampicin (RIF) against MSSA and MRSA determined by microcalorimetry.

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<tr>
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<td>MHICₚₐ</td>
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<td>LNZ</td>
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<td>RIF</td>
<td>0.008</td>
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CASE ORDER HAS AN EFFECT ON PERIPROSTHETIC JOINT INFECTION RISK

Antonia Chen, Michael Kheir, Joshua Greenbaum, Camilo Restrepo, Mitchell Maltenfort, Javad Parvizi

1The Rothman Institute, Philadelphia, United States

Aim: Periprosthetic joint infection (PJI) after total joint arthroplasty (TJA) is a serious complication with multiple causes. A previous study in patients undergoing spine surgery demonstrated that cases performed later in the day were more likely to develop surgical site infection. However, the influence of case order on subsequent PJI after TJA is unknown. Thus, this study aims to determine: 1) if surgical case order is a risk factor for PJI, 2) if TJA patients following an infected case have a higher infection risk, and 3) if terminal cleaning after an infected case is effective in reducing risk of subsequent PJI.

Method: A retrospective, single-institution study was conducted on 31,499 primary or revision TJAs performed from 2000-2014. Surgical case order was determined by the case start time on the day of surgery within the same operating room. PJI was defined using the Musculoskeletal Infection Society criteria. Multiple logistic regression was used to analyze risk factors.

Results: Non-infected cases followed an infected case in the same operating room in 92/31,499 cases (0.29%) and had an increased likelihood of PJI (odds ratio [OR] 3.88, P<0.001). Cases performed after terminal cleaning of a PJI case were not at an increased risk of subsequent PJI (OR 1.35, P=0.110). Case order had an OR of 1.02 (P=0.57) per increment in position; thus, later surgical cases did not have a higher likelihood of infection.

Conclusions: While surgical case order is not an independent risk factor for subsequent PJI, TJA patients that follow an infected case in the same operating room have a higher risk for subsequent infection. Despite improved sterile technique and the use of clean air operating rooms, the risk of contaminating a primary TJA with pathogens from a prior infected case performed in the same room appears to be high. Terminal cleaning appears to be effective in reducing bioburden and infection risk for cases the following day in the same operating room.

References:
Aim: Bone voids may be created during the curettage of skeletal tumors. Calcium phosphate bone void filler (BVF) is commonly used to provide a scaffold for bone healing; however, implantation of foreign material can create a nidus for bacteria. To mitigate the risk of infection, BVF can be impregnated with antibiotics. The purpose of this study was to retrospectively compare the rate of infection between patients who received BVF with and without antibiotics. The authors hypothesized that the rate of infection would be higher in patients who received BVF without antibiotic impregnation.

Method: 63 patients were identified; 17 patients received vancomycin impregnated BVF, and 46 patients received BVF without antibiotics. Criteria for antibiotic impregnation included a void greater than 20 ml or if anatomically there was a higher risk of infection (foot, overlying pannus). Antibiotics were mixed at a ratio of 1 g of vancomycin per 20 ml BVF. The main outcome measure was deep infection requiring reoperation. The rate of infection in the two groups was analyzed using a two-tailed Z score.

Results: BVF was most commonly used in the resection of cystic bone tumors (unicameral bone cyst, aneurysmal bone cyst, n=20), cartilaginous tumors (enchondroma, low grade chondrosarcoma, n=19), fibrous dysplasia (n=7), non-ossifying fibroma (n=5), and giant cell tumor of bone (n=4). Patients received an average of 24.8 ml of BVF (95% CI: 19.5-30.5); the average volume in each group was 21.4 ml in those without antibiotics (95% CI: 16.1-26.7) and 33.2 ml in those with antibiotics (95% CI: 19.8-46.6). There were 3 deep infections that required reoperation; all infections occurred in patients who did not receive antibiotics (3/46, 6.5%). All infections were eradicated following a single irrigation and debridement surgery and systemic antibiotics. There was no statistically significant difference in the rate of infection between patients who received BVF with or without antibiotics (Z score = 1.08, p = 0.28).

Conclusions: A higher rate of infection was observed in patients who received BVF without antibiotics (3/46, 6.5%) versus with antibiotics (0/17, 0%), although this difference was not statistically significant. This study was limited by its retrospective nature and a small heterogeneous sample size. Larger studies are needed to determine whether there is a clinically significant benefit to the antibiotic impregnation of bone void filler in tumor surgery.
Aim: Pyogenic vertebral osteomyelitis (PVOM) is a complex condition requiring input of multiple specialties. There is scarcity of data on coordinating the management process in the literature. Multidisciplinary teams have been reported to bring benefit into outcome of these patients.

Method: We present a care bundle developed in a regional hospital in Czechia with catchment population of 700,000. Our centre provides interdisciplinary care for complex septic conditions in orthopaedics and neurosurgery. Patients are hospitalised (both for conservative as well as perioperative and postoperative care) in the Department of Infectious Diseases (including dedicated high dependency unit) and surgical care is provided by orthopaedic surgeons and/or neurosurgeons as required. This joint interdisciplinary care has been developing over the last 25 years, with annual case load of 20-35 patients with PVOM.

Results: The first task is to verify diagnosis, establish true pathogens, determine the extent of disease and feasibility of surgical intervention. The second step is ongoing management of sepsis. The third step is addressing focal manifestations in spine as well as elsewhere. The last step is determining maintenance antibiotic therapy and rehabilitation strategy.

The scheme of care bundle is described in Figure 1.

Conclusions: PVOM frequently affects older patients with comorbidities. Patients are referred to our centre sometimes after weeks of conservative management in district hospitals, frequently with chronic pain and neurological deficit. Many positive microbiological results are provided upon transfer after many antibiotics had been used. There is increase of other than Staphylococcal aetiology recently, including multidrug resistant Gram-negatives. Besides, PVOM can be only a part of multiple septic manifestations, including endocarditis.

Following the care bundle helps the multidisciplinary team members address all facets of management of the most complex PVOM patients.
## Pyogenic vertebral osteomyelitis care bundle

<table>
<thead>
<tr>
<th>Confirming diagnosis</th>
<th>Systemic infection</th>
<th>Local infection</th>
<th>Maintenance therapy</th>
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<tr>
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<td>- OPAT</td>
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<td>Need combination?</td>
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<td>sepsis, multiple foci?</td>
<td>Management of</td>
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<td>Pus collection: where?</td>
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**Clinical stability**
- Temperature < 37.8°C
- SaO2 > 92%
- BP stable
- Pulse rate < 100/min
- Resp. rate < 25/min
- No confusion
[P19] TOLERABILITY OF DAPTOMYCIN FOR THE TREATMENT OF COMPLEX ORTHOPAEDIC INFECTIONS IN A SPECIALIST ORTHOPAEDIC CENTRE IN THE UNITED KINGDOM

Amy Chue1, Nia Reeves2, Sarah Mimmack2, Pauline Jumaa1

1University Hospital Birmingham and Royal Orthopaedic Hospital, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom
2Royal Orthopaedic Hospital, Birmingham, United Kingdom

Aim: To review the tolerability of daptomycin treatment for complex bone and prosthesis-related infections.

Daptomycin is a cyclic lipopeptide antimicrobial which penetrates soft tissue and bone. It is licensed for use in skin and soft tissue infections and Staphylococcus aureus bacteraemias at doses of 4-6mg/kg. Recently, daptomycin has been used to treat orthopaedic infections at higher doses (8-10mg/kg) with good treatment outcomes, but with higher risks of side effects.

Method: A retrospective review of microbiologically confirmed bone and prosthesis-related infections was performed from 1 April 2011 – 31 January 2016. Data were extracted from the electronic Bone Infection Unit and the pharmacy databases at a specialist orthopaedic hospital. Bone and prosthesis-related infections were defined as infections requiring surgery with microbiologically positive results.

Results: Sixty-one episodes of daptomycin treatment for fifty patients were identified from 1 April 2011 – 31 January 2016. The most frequently infected prostheses treated with daptomycin were total hip replacements (30%), followed by total knee replacements (24%) and femoral endoprosthetic replacements (18%). The commonest surgical indication for daptomycin use was post debridement and washout (DAIR approach) (28%). A range of doses were used (4mg/kg-10mg/kg), with 50% receiving 6mg/kg and 28% receiving 8mg/kg.

Creatinine kinase (CK) levels were available for 55 episodes, and in 44 (80%) episodes were within the normal range. Eleven episodes (20%) had high CK levels (reference range 24 – 170U/L), four occurring with a dose of 6mg/kg, one with 7mg/kg, four with 8mg/kg and two with 10mg/kg. Daptomycin levels were measured in 2/11 cases. One was <20mg/L (6mg/kg) and one was 21.5-29.6mg/L (8mg/kg). Three cases (4.9%) had daptomycin stopped before the end of planned treatment due to high CK levels and symptoms.

Daptomycin levels were measured in 10 cases (16.4%) and were above the recommended pre-dose level of <20mg/L in 9/10 cases. One case stopped daptomycin because of raised CK. All other cases of raised levels were not associated with raised CK and were asymptomatic.

The commonest indication for daptomycin treatment was multidrug resistant Gram positive organisms where linezolid use was unsuitable because of adverse effects or contraindications (n = 18, 36%). The commonest microorganisms requiring treatment with daptomycin were coagulase negative staphylococci (n = 33, 66%), 18 (55%) of which were resistant to teicoplanin. Eleven (22%) were vancomycin-resistant enterococci.
**Conclusions:** Daptomycin was well-tolerated amongst bone infection patients. Daptomycin levels above 20mg/L were not associated with toxicity in the patients where it was measured.
Aim: Periprosthetic joint infection (PJI) complicates between 1-2% of total knee arthroplasties per year and represents the second most common indication for revision arthroplasty of the knee. Silver has been used for its antimicrobial activity in a variety of settings, more recently silver coated prostheses have shown promising results in the prevention and treatment of PJI. This study aims to investigate the clinical outcomes following revision knee arthroplasty using silver coated distal femur endoprosthetic replacements at a single institution.

Method: A retrospective review of consecutive patients undergoing complex revision arthroplasty of the knee in a tertiary referral centre using a silver coated distal femoral endoprosthesis was performed. Data was collected using retrospective analysis of a prospectively collected bone infection database and patient records.

Results: A total of 18 patients treated for PJI of the knee were included in this study with a median follow up of 14 months (range 8 - 41 months). Nine patients (50%) underwent a single stage revision and the remaining patients (50%) had a two-stage revision arthroplasty. The preoperative joint aspiration culture was positive in 13 patients (72%), in which 39% were polymicrobial. A total of 15 microbial species were identified. Coagulase Negative Staphylococci was the most common infecting organism (29%) whilst multi-drug resistant organisms including Vancomycin Resistant Enterococcus, Klebsiella and extended-spectrum beta-lactamase (ESBL)-producing E.coli were present in 62% of cultures. At final follow up, 11 patients (61%) have a CRP value within normal limits (<10 mg/dL). There were no recurrent PJI, with all patients retaining their implants at minimum 8 months follow-up.

Conclusions: Silver coated distal femoral endoprostheses represent an effective option for complex revision arthroplasty. No recurrent early infections were identified despite a high incidence of multi-resistant, polymicrobial PJIs. Whilst these early results are encouraging, further follow up and investigation into the potential bacteriocidal effect of silver when incorporated onto orthopaedic implants, is required.
IN-VIVO AND IN-VITRO EVALUATION OF VANCOMYCIN AND GENTAMICIN ELUTION FROM BONE GRAFT SUBSTITUTES

Thomas Colding-Rasmussen¹, Peter Frederik Horstmann², Hanna Dahlgren³, Eva Liden³, Werner Hettwer², Michael Moerk Petersen²

¹Department of Orthopedics, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark
²Muskuloskeletal Tumor Section, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark
³Bonesupport Ab, Lund, Sweden

Aim: To measure early in-vivo plasma concentrations of Vancomycin and Gentamicin eluted from locally implanted antibiotic-eluting bone graft substitutes¹,² and to evaluate possible in-vitro elution interactions of combined use.

Method: In-vivo plasma concentrations were measured in 5 patients (M/F: 3/2, mean age 67 (52-81) years), who underwent local implantation (Range: 10-20mL) with either a Vancomycin¹- (n=1) or a Gentamicin²-eluting bone graft substitute (n=3) or a combination of both (n=1) between January and May 2016. Blood plasma was collected 1 and 3 hours after implantation and once daily during the first three postoperative days. Samples were analysed using a particle-enhanced turbidimetric inhibition immunoassay (PETINIA).

In-vitro elution profiles of Vancomycin- and Gentamicin-eluting bone graft substitutes¹² (5 mL each) were compared in 4 different scenarios: Each product individually, both products side-by-side, and mixed together. The ratio between product and medium (37°C Ringer solution) was kept the same in all tests. Samples (20% of the medium surrounding the bone substitutes to mimic conditions in a contained bone defect) were collected and replaced on day 1-8, 21, and 28 for analysis.

Results: Mean blood plasma concentration of Vancomycin was 0.3mg/L (Range: 0.0-1.6mg/L) and 0.5mg/L (Range: 0.0-2.1mg/L) for Gentamicin (Fig A & B). The In-vitro release curves of Vancomycin and Gentamicin showed a similar appearance for the different scenarios (Fig C & D). Both the in-vivo and in-vitro curves displayed an initial peak with sustained lower concentrations during the study period.

Conclusions: Local in-vivo implantation of Vancomycin- and Gentamicin-eluting bone graft substitutes¹², results in safe low plasma concentrations in the first three days after surgery when used individually or in combination. Further, when tested in-vitro, combined use does not seem to influence their eluting abilities.

References:
1) CERAMENT™|V – BONESUPPORT AB
2) CERAMENT™|G – BONESUPPORT AB
**Fig. 1.**
A,B) In-vivo Plasma Gentamicin and Vancomycin concentrations
C,D) In vitro Gentamicin and Vancomycin release curves (local concentration)
Aim: Identification of microorganism is essential in establishing appropriate antibiotic treatment for PJI. We wonder what the respective bacterial isolate yield from peroperative tissue biopsies or from the joint fluid is.

Method: Microbiological specimens obtained at the first stage of 181 PJI were retrospectively reviewed. PJI was defined according to the MSIS criteria. 108 synovial fluid samples were immediately divided, when the volume was sufficient, to be inoculated in blood culture vials* and placed in standard sterile transport vials. 864 tissue biopsies were obtained and transferred in standard sterile bacteriological transport vials to the microbiological lab for subcultures. Samples were transferred to the lab where the blood culture vials* were immediately incubated and standard vials subcultured on blood agar dishes. Lecture was done daily for 14 days until positive identification.

Results: 88 blood culture vials* were positive and 20 remained negative. 472 fluid and biopsies cultures were positive and 392 negative. Sensitivity of the blood culture vials* and standard subcultures were 81.5% and 54.6% respectively. Considering the same synovial fluid samples used for the blood culture vials* and subculture, 83 samples were available. Samples were positive with both methods in 59 cases and concordant in every case (identify the same microorganism). The blood culture vials* was positive alone in 10 cases. Subculture identified a microorganism in two cases where the blood culture vials* remained negative. Twelve Cases remained negative with both techniques. Sensitivity of the blood culture vials* and standard culture in this group are 83% and 73% respectively.

Conclusions: The results of our study confirm the increased sensitivity of the blood culture vials* compared to the subculture of the same synovial fluid and even more to the tissue biopsies. These data are consistent with our observation of the superiority of the sensitivity of the blood culture vials* compared to standard culture on preoperative joint aspiration. Using a pediatric bottle* provides the ability to seed lower volumes, better corresponding to the volume found in the joints compared to the volumes needed for an aerobic and anaerobic adult blood culture vial*. As synovial fluid was not available in all cases and biopsies cultures not as effective, it might be of interest to ground biopsies to be able to incubate them in the blood culture vials* bottles. The priority treatment of blood culture bottles, whatever the liquid introduced into the bottle, in our laboratory, avoid lengthy delays of seeding and might partially explain the better yield with this method than with a conventional microbiological technique.

*Pediatric Bactec® vials, Becton Dickinson Diagnostic Instruments, Sparks, Md
Aim: The therapeutic strategy for PJI depends on identifying the causative organism. The identification of the organism can be done preoperatively on the joint fluid obtain by aspiration. We wonder what the most efficient microbiological method in the identification of the infecting microorganism is.

Method: Microbiological data from 67 joint aspirations performed for PJI were retrospectively reviewed. PJI was defined according to the MSIS criteria. Liquid was obtained by joint aspiration under CT-scanner. Liquid was aliquoted in pediatric vials* and standard sterile bacteriological transport vials. Samples were transferred to the lab where the pediatric vials* were immediately incubated and standard vials subcultured on blood agar dishes. Lecture was done daily for 14 days until positive identification.

Results: 67 pediatric vials* and 97 bacteriological transport vials were obtained. 57 pediatric vials* and 53 subcultures of the transport vials were positive. Sensitivity of the pediatric vials* and standard subcultures were 84.8% and 55.8% respectively. The pediatric vials* and subculture were both positive in 35 cases and concordant in every case (identify the same microorganism). The pediatric vials* was positive alone in 21 cases. Subculture identified a microorganism in two cases where the pediatric vials* remained negative. Nine Cases remained negative with both techniques. Results of preoperative cultures were further confirmed at the time of implant removal.

Conclusions: Results confirm the increased sensitivity of the pediatric vials* compared to the subculture of the synovial fluid. Data are consistent with others that have shown the superiority of the sensitivity of the pediatric vials*. Using a pediatric vial* bottle provides the ability to seed lower volumes, better corresponding to the volume found in the joints compared to the volumes needed for an aerobic and anaerobic adult pediatric vial*. Our study does not assess the specificity of the pediatric vials* since it concerns exclusively infected patients. If the method demonstrates great sensitivity, risk of false positive has been measured at 6.2% in blood cultures by Ziegler. He also stressed the importance to incubate the pediatric vial* bottle within less than 12 hours reducing the rate of false negative. The treatment of blood culture bottles, whatever the liquid introduced into the bottle, however, enjoys a priority in our laboratory, avoiding lengthy delays seeding. Is the advantage of the pediatric vials* related to direct seeding and reduced time before incubating? This cannot be answered by this study

*Bactec® (Becton Dickinson Diagnostic Instruments, Sparks, Md)
Anaesthesia for Orthoplastic Surgery in Paraplegic Patients with Pelvic Osteomyelitis: Keep It Simple

Ruth Corrigan¹, Svetlana Galitzine¹, Jyoti Misra¹, Alex Ramsden¹, Martin McNally²

¹Oxford University Hospitals NHS Foundation Trust, Nuffield Orthopaedic Centre, Oxford, United Kingdom

Aim: Pelvic osteomyelitis is a complication of paraplegia. Surgery includes excision of infected soft and bone tissue, and local soft tissue reconstruction. In patients with no sensation below the level of lesion standby anaesthesia (SA) is appropriate for surgery; however, its use can be limited by patients’ anxiety. To our knowledge, this is the first report of use of audio-visual distraction (AVD) to simplify SA in paraplegic patients.

Method: We report a series of three patients who underwent four orthoplastic operations and benefitted from AVD as part of SA. All procedures were done in a lateral ‘sloppy’ position, half way position between a conventional lateral decubitus position and prone position, allowing adequate surgical access and preservation of spontaneous respiration.

Patients’ experience was formally assessed using a standardised questionnaire, as a part of ongoing AVD service evaluation in our institution.

Results:

Case 1: 78 y.o. gentleman with a T10 complete transection, no systemic co-morbidities and MRI suggesting femoral osteomyelitis secondary to a thigh pressure sore. Following Temazepam premedication, he underwent excision of infected bone and soft tissue, and local hamstring advancement for soft tissue closure. SA for a 2hr procedure involved conscious sedation with Midazolam and AVD (a movie on the internet connected tablet using noise reducing headphones).

Case 2: 59 y.o. gentleman with T7/8 complete spinal transection and discharging ischial pressure sore. His comorbidities included controlled atrial fibrillation and diabetes. He underwent a 2hr 30 minutes excision of osteomyelitis and local hamstring advancement under conscious sedation and AVD (games and movie).

Case 3: 51 y.o. gentleman with paraplegia secondary to spina bifida and an infected ischial pressure sore. Comorbidities included asthma and hypertension. His 2hr 40 minutes orthoplastic procedure was performed under SA with conscious sedation and AVD (music). A week later an evacuation of postoperative haematoma was done under sedation using his own iphone for audio distraction.

Postoperatively, the patients completed a standardized questionnaire. All felt comfortable or very comfortable. One patient commented that he was aware of the surgeons ‘hammering the bone’ but was not alarmed by this. All three patients rated their experience as better than their previous general anaesthesia.

Conclusions: This case series extends published literature on use of AVD to include major surgery in paraplegic patients. Patients’ feedback was extremely positive. We advocate AVD to simplify anaesthesia in this complex patient group.

References:

Aim: check the reliability of the alpha defensin test to detect prosthetic infections in joint replacement revisions

Method: from April 2015 till April 2016 we performed the quick alpha defensing test* on synovial liquid aspirated from 22 joint prosthesis with suspected periprosthetic infection. In 14 cases (9 knees and 6 hips) we found a positive test. In 12 cases (9 knees and 3 hips) we did a surgical revision in two stage of the prosthesis and during the joint removal procedure the alpha defensin test was repeated, in 11 cases the test was still positive. In 2 cases of negative test on the aspirated synovial fluid we did a surgical revision of the implant single stage and the intra-operative test was negative.

Results: In 11 cases out of 14 with pre-operative positive test we have found a correlation between the pre-operative results and those intra-operative. Considering that 2 cases positive pre-operative decided not to undergo surgical procedure despite the suspected infection, the correlation between pre and intra-operative test was observed in 91,6% of cases (11 out of 12).

In other two cases of negative pre-operative test we performed the surgical revision (2 hips) anyway and the intra operative test was still negative. In these cases the test negativity helped us in choosing which surgical procedure was to be performed.

Conclusions: In our series (unfortunately not too large) the correspondence between pre and intra operative infection was very high (91,6%) and this fact confirms the predictive validity of the test.

Most important in our experience were the two cases in which, on the strength of the negative test we performed a single stage revision. In those patient the negative test was important to decide the different revision procedure and the patients are still free from peri-prosthetic infection. In our experience the alpha defensin test is a reliable tool to detect prosthetic infection also during surgical procedure.

* Synoviasure®
BONE AND JOINT INFECTIONS DIFFICULT TO DIAGNOSE: INTEREST OF AUTOMATED MULTIPLEX-PCR CURETIS SYSTEM

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¹Nantes University Hospital, Bacteriology and Infection Control, Nantes, France
²Chu Nantes, Service D’Orthopédie, Nantes, France
³Nantes University Hospital, Orthopaedic Unit, Nantes, France
⁴Nantes University Hospital, Bacteriology Department, Nantes, France

**Aim:** Despite numerous efforts to improve the diagnosis of bone and joint infections (BJI), some cases remain difficult to elucidate. Recently, we reported an 89% of positive culture on crushed samples for suspected cases of infection. Therefore, to obtain 100% of bacteriological documentation, new tools should be implemented. The aim of this study was to assess the cartridge system*, a specific multiplex PCR designed for the diagnosis of BJI.

**Method:** Three difficult cases were investigated. The first patient came for a loosening 8 years after a first septic revision of his hip prosthesis. Based on the guidelines, 6 per-operative samples were performed. Blood bottle culture, ARN16S PCR and ITI cartridge were performed.

The second patient had two hip prosthesis. An MSSA bloodstream infection occurred. Under antibiotics, a lavage debridement was performed on the right most painful side and the left side was also punctured. ITI cartridge were performed on 4 samples. The third patient, presenting with a humeral fracture, required two surgical interventions for septic recurrence.

**Results:** First patient: Despite 6 per-operative samples, no bacterium grew at day 14. One blood bottle culture led to *S. capitis* (1/3), 16S PCR sequencing revealed *S. capitis* (2 samples/3) and ITI® cartridges detected methicillin-susceptible *S. capitis* (3/6) and *P. acnes* (2/6). The high clinical suspicion of infection lead us to test these new tools and discuss the results during multidisciplinary meeting.

Second patient: We would like to know which of the two prosthesis was infected. Due to antibiotic, cultures remain sterile despite warm, pain and redness at the right side. Indeed, only the ITI® cartridges performed on the 2 right clinical samples revealed a MSSA. ITI® cartridges performed on 2 left samples were negative.

Third patient: During the first reoperation, *P. acnes* and *P. avidum* were found in culture. Despite an adapted treatment, during the third surgery, *P. avidum* was detected in culture. An ITI® cartridge was performed and the presence of both species was confirmed.

**Conclusions:** This automated multiplex PCR can be useful for difficult to diagnose BJI, especially for low-grade infections, torpid/chronic infections and patients under antibiotic treatment during surgery. Certainly expensive but very easy to perform, this test could be indicated in cases of high suspicion of infection when cultures remain sterile. A further prospective study is needed to assess its impact on the early diagnosis and the most adapted treatment.

* Unyvero i60 ITI®
THE INFLUENCE OF THIRD BODY DAMAGE BY A CALCIUM SULFATE BONE VOID FILLER ON THE WEAR OF TOTAL KNEE REPLACEMENTS

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Aim: Calcium sulfate is increasingly being used for dead space management in infected arthroplasty revision surgery¹. The potential for calcium sulfate to become trapped in the articulating surface and accelerate wear of total knee replacements (TKR) is a concern. The aim of this study was to investigate the influence of third body damage caused by a recrystallised, synthetic calcium sulfate (RCS) on the wear of TKRs.

Method: To simulate third body damage, 5cc of RCS beads were trapped between the articulating surfaces of a TKR in a knee joint simulator and run dry for 60 cycles before adding lubricant to the test and running for 115,000 cycles to represent the 6 weeks the BVFs are in the body prior to their absorption. 3 million cycles of wear simulation was then carried out against these potentially damaged femorals with the wear of the ultra-high-molecular-weight polyethylene (UHMWPE) tibias compared to negative controls (no damage to femorals) and positive controls (femorals scratched with a diamond stylus ) N=6 for all groups.

Results: The wear rate of the RCS group was equivalent (p>0.05) to that of the negative control. The wear of the positive control group was significantly (p<0.05) higher than the negative control showing damage of sufficient magnitude to the femoral component can increase UHMWPE wear.

Conclusions: This study demonstrated a ‘worse case’ methodology for simulating third body damage in TKRs and showed that when RCS beads are used close to articulating surfaces of TKRs, they do not influence wear (Figure 1) and as such may not be detrimental to the longevity of the implant.

This study was sponsored by Biocomposites Ltd. UK.
* Stimulan, Biocomposites Ltd.

Mean wear rate/Million cycles of UHMWPE tibias (n=6)
Aim: The synovial fluid analysis is an important method in diagnosing and managing septic arthritis. To reach a quick diagnosis, preferably faster than the microbiological cultures, could be a great advantage in the therapy. The isoperibolic calorimetry has recently been found useful in the differential diagnosis of septic and non-septic periprosthetic conditions. The aim of this study was to evaluate whether there is a specific pattern in the isotherm proliferation characteristics of the different bacterial strains. The sensitivity of our method was also determined by using synovial fluid samples with different bacterial concentrations.

Method: Authors developed a standardized, experimental model to assess the proliferation characteristics of septic synovial fluid infected by different bacterial strains. Briefly, aseptic human synovial fluid was inoculated with five different human pathogen bacterial strains to reach the $10^5$ CFU/mL concentrations. The infected synovial fluid samples were then processed and thermal characteristics (time of maximal proliferation and calorimetric enthalpy) were monitored by a calorimeter* (used in isotherm mode at T=37°C). In another set of experiments, thermal analyzes were performed using the synovial fluid samples infected by the same bacteria species with different CFU/mL concentrations to test the sensitivity of the method.

Results: The proliferation scans clearly demonstrated specific, representative thermograms in case of each individual bacterial strain. The method was found reliable at the $10^5$ CFU/mL bacterial concentrations. Importantly, the scans also detected characteristic differences of the proliferation parameters in the lower bacterial concentration ranges.

Conclusions: Here we found that the isoperibolic calorimetry is a reliable method in the determination of different bacterial strains from synovial fluid samples. The method can provide data much faster (in approximately 4 hours following sample collection at $10^5$ CFU/mL bacterial concentrations), compared to the microbiological culturing. Therefore, thermoanlyzes of human synovial fluid samples by isoperibolic calorimetry could be a useful tool in the diagnostics of septic arthritis.

* SETARAM Micro DSC-II
KNEE ARTHRITIS IN CHILDREN: WHEN CAN BE SAFELY TREATED WITH NEEDLE JOINT ASPIRATION? A LARGE CHILDREN'S TERTIARY HOSPITAL STUDY

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Aim: Early joint decompression associated to antibiotic therapy is the most important procedure to reduce joint damage in septic knee arthritis in children. Several joint decompression methods have been described such as arthrotomy with open debriding, arthroscopic drainage or needle joint aspiration. The aim of the present study was to determinate which patients with acute septic knee arthritis could be safely treated with needle joint aspiration.

Method: Patients with an acute knee arthritis diagnosed between September 2003 and December 2013 in our children's tertiary hospital were retrospective review. All cases were initially treated with needle joint aspiration. Primary end-point was failure of joint aspiration.

Results: A total of 74 patients were included in the study. Forty-two (56.8%) were male and median age was 1.49 years. Mean delay between onset of symptoms and diagnosis was 3.6 days and in 25 (33.8%) cases patients needed more than one visit to the emergency room. Median CRP (C-reactive protein) value was 36.3 mg/L and was >20 mg/L in 59 (79.7%) cases. A total of 11 (14.9%) patients showed failure of the joint aspiration treatment between 3 and 21 days after initial joint aspiration. The step-wise forward logistic regression model only identified as independent predictor of joint aspiration failure an age >3 years old (OR:5.64; 95%CI: 1.38 to 29.61; p=0.018). Joint aspiration did not fail in any patient younger than 12 months and neither in any patient younger than 3 years old with CRP value below 20 mg/L. Otherwise, treatment failed in 38% of patients older than 3 years and in 16% of patients between 1 and 3 years with a CRP>20mg/L

Conclusions: Septic knee arthritis treated with needle joint aspiration succeed in all patients younger than 1 year and in all patients between 1 and 3 years with a CRP<20mg/L. Alternative treatment such as arthroscopy debridement should be early considered in patients older than 3 years and patients between 1 and 3 years with CRP>20mg/L.
[P30] RELIABILITY OF A NEW MOLECULAR METHOD FOR DIAGNOSIS OF PROSTHETIC JOINT INFECTIONS BEFORE AND AFTER BROTH ENRICHMENT

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Aim: In the diagnosis of prosthetic joint infections (PJIs), rapid identification of the causative agents may be a critical issue. Nucleic acid amplification tests present some potential benefits over traditional microbial cultures, including improved turnaround time. However, use of molecular methods for PJIs diagnosis remains a matter of debate. The implant* and Tissue Infection cartridge (U-ITI) system** is a semi-quantitative DNA test based on the parallel performance of eight multiplex PCR reactions and designed to detect up to 114 genomic targets for identification of microorganisms typically associated with PJIs and antibiotic resistance markers. The aim of this study was to evaluate application of the U-ITI system in comparison with conventional culture for diagnosis of PJIs.

Method: The study was performed on periprosthetic tissues, prosthetic joint implants and synovial fluids from 31 patients with suspected PJIs. Cultures were performed by plating concentrated synovial fluids and dithiothreitol eluates from prostheses and periprosthetic tissues onto solid and liquid media. Cultures were incubated for 15 days and daily checked for growth. Pathogen identification and susceptibility testing were performed using a fully automated microbial identification system***. For molecular analysis, concentrated DTT eluate, concentrated synovial fluid and broth showing bacterial growth were lysed in a sample tube* for a 30-min. Then, samples were transferred into a cartridge**** containing reagents for DNA purification, PCR primers and probes for array hybridization. Results, derived from images processed by the software*, generated complete diagnostic information within 4.5 h.

Results: A total of 33 samples from 31 patients were analyzed: 13 synovial fluids and 20 tissue and prosthetic samples. Data from 3 patients (9.8%) were not considered because grown microorganisms were not included in the panel*. On the whole, the 2 methods gave concordant results in 19/28 patients (67.8%). Interestingly, molecular analysis of broth cultures increased sensitivity of the assay, since in 5 cases results obtained from direct culture were confirmed by analysis* of broth cultures. When only data obtained from molecular analysis of broth cultures were considered, concordance increased up to 94.1%.

Conclusions: Considering that the assay* provides microbial identification and detection of the major resistance determinants in about 4.5 hrs, it may be hypothesized that it could be associated to broth cultures, allowing a faster identification than with traditional biochemical identification methods. Further studies will be necessary for evaluating its performances in other clinical/experimental settings and in a larger population.

*Unyvero

** Curetis, Germany

*** Vitek2 Compact (BioMerieux, France)

****Unyvero i60
[P31] HMPAO LABELED LEUKOCYTE IMAGING AND OSTEOARTICULAR INFECTION

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Aim: Demonstrate the suspected osteoarticular infection HMPAO labeled leukocyte imaging and its correlation with the clinical pathology and the importance of the test in clinical practice.

Method: Report of two clinical cases using HMPAO labeled leukocyte imaging for the diagnosis of osteoarticular infection and its correlation with the clinical pathology and the importance of the imaging exam for the diagnosis of osteoarticular infection.

Results: Case 1: male, 26, consolidated left femoral fracture with internal fixation and persistent osteomyelitis, after 5 years, even after removal of the synthesis material. MRI of femur determined the presence of inflammatory process in place of removed synthesis material, and the HMPAO labeled leukocyte imaging outlined the infection in three specific locations. Debridement of the lesion with chronic inflammatory process was performed, granulation tissue and fibrosis were shown in clinical pathology and cure of osteomyelitis was seen after 6 weeks of sulfamethoxazole/trimethoprim.

Case 2: male, 22, polyarticular pyoarthritis Staphylococcus aureus treated and complicated with bilateral osteonecrosis of the head of the femur. MRI identified necrotic bone in the femoral head (bilateral). Patient underwent treatment for six weeks with oxacillin and sulfamethoxazole/rimethoprim and bilateral total hip arthroplasties which showed a significant improvement. Pathologic anatomy showed chronic inflammation lymphoplasmocytic with medullary tissue necrosis, pseudo-cysts, foreign body granulomas and stromal fibrovascular regeneration and HMPAO labeled leukocyte imaging outline the infection in the right femur head and the absence of infection in the prosthesis left hip.

Conclusions: HMPAO labeled leukocyte imaging helps in anatomical accuracy of the location of osteoarticular infection, even after recent surgery and removal of synthetic material.
Aim: The aim of this study was to test the use of a synovial fluid biomarker, α-defensin, in diagnosing periprosthetic joint infection in knee revision surgery for suspicious arthroplasty infection.

Method: Between March 2014 and January 2016 we enrolled 20 patients undergone to knee arthroplasty revision surgery due to doubtful infection. Cases were categorized as infected or non-infected using Musculoskeletal Infection Society criteria. Synovial fluid was obtained and tested for α-defensin using a commercially available kit*. During surgery frozen section, periprosthetic tissues cultures and sonication of explanted components were performed.

Results: In our series, the α-defensin test had a sensitivity of 88.8% and a specificity of 100% with a positive predictive value of 100% and negative predictive value of 91.6%.

Conclusions: In case of uncertain diagnosis for prosthetic joint infection the α-defensin test seems to be sensitive and specific for predicting or excluding infection and it should be considered in this group of patients.

*Synovasure, Citrano Laboratories, subsidiary of CD Diagnostics, Towson, MD, USA
[P33] COATING OF TITANIUM IMPLANTS WITH GENTAMICIN-TANNIC ACID SHOWED A RAPID ELUTION OF GENTAMICIN AND REDUCED IMPLANT RELATED INFECTION IN A RAT OSTEOMYELITIS MODEL

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Aim: Implant related infection is a feared complication in orthopaedic surgery. One approach to minimize the risk of implant related infection is to establish anti-infective coatings, e.g. PDLLA-gentamicin or chlorhexidine coatings. We used tannic acid to immobilize gentamicin on the surface of titanium implants for prophylaxis of infection. An established rat osteomyelitis model with bilateral placement of titanium alloy implants in the tibiae was employed to analyse the prophylactic effect of gentamicin-tannic acid coatings in vivo.

Method: Plasma chemical oxidation (PCO) was used to produce implants with a porous, calcium and phosphate rich surface (bioactive TiOB). These implants showed improved osseointegration and were used as base material for the gentamicin group (C). 15 rats were randomly assigned to three groups: (A) titanium alloy; phosphate buffered saline (PBS) inoculum (negative control), (B) titanium alloy; S. aureus inoculum (positive control), (C) bioactive TiOB plus gentamicin-tannic acid coating; S. aureus inoculum. Contamination of implants, bacterial load of bone powder and radiographic as well as histological signs of implant-related osteomyelitis were evaluated at four weeks.

Results: In-vitro elution testing of the implants showed rapid and complete elution of gentamicin within 24 hours.

Gentamicin-tannic acid coating prevented implant contamination in 9 of 10 implants. Only one implant showed colonisation of bacteria (swab of entry point and roll-out test positive for S. aureus). The histological and radiographic osteomyelitis scores were significantly reduced in group (C) compared to the positive control (B).

Conclusions: Rapid elution of gentamicin was effective to prevent implant-related infection in an established rat osteomyelitis model in 90% of the implants.
FUNCTIONAL RESULTS AFTER TWO-STAGE REVISION SURGERY OF INFECTED TOTAL KNEE REPLACEMENT – IS THIS A RELEVANT FACTOR IN CHOOSING BETWEEN ONE AND TWO-STAGE SURGERY?

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Aim: Infection after total knee replacement is a devastating complication with significant impact on patient’s quality of life. Despite the recent developments in its treatment, some questions remain controversial.

The surgical strategy for treating chronic infection is one of such controversies. Although the two-stage approach is more frequently used, more and more authors defend performing one-stage procedures. One of the alleged advantages of this option is the better functional outcome that the reduced surgical insult potentially offers.

The aim of this study is to evaluate patient reported functional outcomes after two-stage revision surgery of infected total knee replacement, comparing them with outcomes after one-stage surgery in aseptic failures and primary complex knee replacements.

Method: Knee replacements performed by the same surgeon between September of 2013 and September 2015, using the same revision prosthesis⁴, were included. These comprised patients that underwent complex primary knee replacement, one-stage revision for aseptic loosening and two-stage revision for infection with temporary use of mobile spacers.

Clinical records were analysed and patients were contacted by telephone to answer the Knee injury and Osteoarthritis Outcome Score (KOOS) and a satisfaction scale.

Results: Twenty-three patients were identified and 20 (15 women) included, with medium age of 69 years. Four cases were complex primary replacements, five one-stage revisions and 11 two-stage revisions (with no relapses). No statistically significant differences were found regarding age, gender distribution or follow up time between groups. Patients that underwent both one or two-stage revision surgery had significantly higher body mass index (p<0.05).

In the Symptoms subscale, two-stage procedures patients had a significantly better performance than those undergoing one-stage revision (88.3 vs. 59.2; p<0.05). In the other subscales the same trend was observed, but with no statistical significance (Pain: 82.5 vs. 63.6; Activities of daily living: 73.2 vs. 56.8; Sports and Recreation: 26.4 vs. 25.0; Quality of life: 47.8 vs. 40.2). Two-stage results overlap complex primary replacement functional outcomes.

Moreover, identical results regarding satisfaction were found in all three groups (two stage revision: 4.4, one stage revision: 4.2, primary replacement: 4.3).

Conclusions: In this study a satisfactory functional result for two-stage surgery was found, as these patients performed at least not inferiorly to the one-stage and primary replacement groups.

Although this does not constitute definitive evidence, these results are encouraging and question the
better functional outcome argument for one-stage revision surgery of infected total knee replacement.

* NexGen® LCCK, Zimmer®
[P35] QUANTITATIVE STUDY ON ANTIBIOTIC RELEASE FROM CEMENT IN 3 DIFFERENT FORMULATIONS: PRELIMINARY RESULTS

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Aim: The purpose of this study is to investigate the best preparation method of the powder mixture of cement, solvent and antibiotic in order to obtain the greatest amount of antibiotic in articulation and for the longest possible time.

Method: Three different compounds were packaged in a sterile environment:
1st sample: vancomycin 4GR. + solvent + cement powder 40GR.
2nd sample: vancomycin 4GR. + saline (4ML) + cement powder 40GR. + solvent
3rd sample: vancomycin 4GR. + cement powder 40 GR. + solvent
At time T0 the three samples were placed in sterile tubes, adding to each 5 ml of SPB solution (sterile phosphate buffer) and put in a stove at 37°C for 24 hours.
It was also created a sample of SPB without cement, "T control." The study consists of two times:
1: daily, in which replace the SPB recreating the physiological conditions of the human body
2: to T1, T2, T3, T5, T10, T20, T40, T50, T60.
We proceeded to:
  a) Withdrawal of the cement cylinder with antibiotic and transfer to a new sterile tube to which 5 ml of PBS are added and repositioning in stove at 37 ° C for 24 hours
  b) Qualitative and quantitative assessment of the incubated liquid with cement in the previous 24 hours
  c) Withdrawal of 2,5 ml of the previous liquid for microbiology and its conservation at -80° C
  d) Withdrawal for biochemical analysis with HPLC (High Performance Liquid Chromatography)

Results: From the analysis of the raw data it was shown that at T1 there was a prevalence of antibiotic release from the sample 1 (17702 g / ml), compared to sample 2 (1814 g / ml) and 3 (1501 g / ml). This difference was maintained until the time T20; from T21 the antibiotic release gradually leveled in 3 samples. The elution of the antibiotic remained detectable up to T60. Just a few data emerge from the literature on the cement packaging method in the operating room. Our work shows that the sample preparation is decisive on the quantity of released antibiotic, especially for the first 20 days. Preliminary data in our possession agree with the hypothesis that the antibiotic release is detectable up to 60 days.

Conclusions: It is useful to know the actual kinetics of the antibiotic in articulation. Further studies are necessary to determine the effectiveness of the antibiotic against micro-organisms and how long it acts.
Aim: To evaluate the efficacy of bioglass* in the treatment of patients with chronic osteomyelitis and compare the results with calcium sulphate antibiotic beads in one medical centre.

Method: Retrospective analysis of 16 cases. Inclusion criteria: patients diagnosed clinically and radiographically of osteomyelitis and treated surgically (Group A: cavitary bone defects treated with bioglass and Group B: cavitary bone defects treated with calcium sulphate antibiotic beads) during the period of 2014 and 2015 in one medical centre.

Results: Patients in group A (bioglass treatment): total of 7 patients with mean age: 45 years (29-86), male-to-female ratio 6:1, average length of hospital stay: 22 days and mean follow-up time: 12 months (7-17). Granule size: medium and mean volume: 15cc (5-30). Mean erythrocyte sedimentation rate (ESR) before surgery: 57mm/hr. Mean c-reactive protein (CRP) before surgery: 59 mg/L. Mean ESR in last blood test: 20mm/hr. Mean CRP in last blood test: 7,7mg/L. 2 postoperative complications: seroma formation and delayed wound healing. No recurrences.

Patients in group B (calcium sulphate antibiotic beads treatment): total of 9 patients with mean age: 45 years (16-66), male-to-female ratio 6:3, average length of hospital stay 15 days and mean follow-up time: 10 months (6-14). Mean ESR before surgery: 58mm/hr. Mean CRP before surgery: 52 mg/L. Mean ESR in last blood test: 6mm/hr. Mean CRP in last blood test: 0,1 mg/L. 1 postoperative complication: segmental bone defect nonunion. No recurrences.

Most frequent cause of osteomyelitis in both groups: postsurgical. Most frequent pathogen: S. aureus. Most common osteomyelitis location: tibia.

Conclusions: In the antibiotic era, chronic osteomyelitis remains difficult to treat. Aggressive surgical debridement and pathogen-specific antibiotics is key to eradicate infection. A great advance in treatment is the utilization of synthetic bone substitutes although current evidence is low. In this study, we demonstrate how bioglass and calcium sulphate antibiotic beads are both equally effective treatment options for cavitary bone defects in osteomyelitis. Nevertheless, bioglass has a clear advantage over calcium sulphate because it does not need to be associated with antibiotics due to its unique bacterial growth inhibiting effect.

*BAG-S53P4
Aim: Clinical experience with gentamicin eluting bone graft substitute after septic bone debridement.

Method: We present 5 cases after septic debridement in osteomyelitis. Two patients had bone gaps in the proximal humerus, three patients in the distal tibia. All the patients developed recurrent fistula due to the dead space in the bone. In all cases the cavitary defects were debrided, carefully rinsed and filled with a ceramic bone graft substitute*.

Results: In 4 cases we observed a complete bone remodeling after 12 months. The substance was easy to mix and to handle. One patient had permanent secretion and recurrence of his anaerobic bone infection.

Conclusions: The gentamicin eluting bone graft substitute enlarges the spectrum of bone filling substances for the treatment of the chronic osteomyelitis.

*Cerament G™
STERNOCLAVICULAR HYPEROSTOSIS: A REPORT OF 4 CASES WITH POSITIVE PROPIONEBACTERIUM ACNES BIOPSIES

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Aim: Sternocostoclavicular hyperostosis (SCCH) is a chronic inflammatory disorder which presents with swelling, erythema and pain of the sternoclavicular joint. Although the etiology of SCCH is not clear, it is considered an aseptic condition.

We describe a series of patients with clavicular hyperostosis and bone biopsy positive for Propionebacterium acnes.

Method: Results are based on a retrospective review of patients with hyperostosis and with painful osteoarticular lesions from 2008 to 2016. Patient records, laboratory, clinical, radiographic features and bone biopsies for bacterial growth were evaluated.

Results: The patients were 3 males and 1 female with the median age of 48 years. All had painful lesions of the sternoclavicular joint, one patient with additional lesions in the 1st sternocostal joint. Three of the patients were operated with harvesting of tissue biopsies from the joint, one with CT-guided biopsy. The biopsies were cultured aerobically and anaerobically (for at least 7 days). Culture results showed growth of P. acnes in all together 15 of 15 biopsies. They were all sensitive to penicillin and clindamycin. All of the patients were treated with antibiotics guided by sensitivity tests. One of the patients received hyperbaric oxygen therapy (HTO) in addition to antibiotics.

All of the patients received 3 months of antibiotic treatment, the first two weeks intravenously. Two of the patients are so far symptom free. One of the patients had recurrent symptoms after 4 years of remission. The last patient who had several recurring periods was treated with additional HTO and is now in her second year of remission.

Conclusions: Although sternoclavicular hyperostosis is considered an aseptic inflammation, our findings suggest that an effort should be made to acquire bone biopsies for microbial cultures.
Aim: A 51 year old patient, with chronic polyarthritis, under immunomodulation treatment (Prednisone & Tofacitinib), was scheduled for a bilateral total knee prosthesis; the indication being devastating pain of the articulations. Following the first knee prosthesis, she suffered ulceration of the contralateral fifth metatarsal head region with a communicating fistula to the joint and a positive probe to bone finding.

Method: In a day hospital setting, we performed debridement of soft tissue and resected the fifth metatarso-phalangeal joint. We collected at least 10 histologic and bacteriologic probes. We reamed the medullary canal of the remaining fifth MT and filled it with an antibiotic loaded resorbable bone-graft substitute (Gentamycin). The former space of the MT head was filled with a resorbable Gentamycin sponge. The treatment was completed by closing the wound with single stitches, oral Clyndamycin treatment in accordance to the culture results and a forefoot discharging orthesis.

Results: Histologically we documented inflammatory remodeling of the bone probe, while pre-operative plain radiology and MRI findings were not clearly positive; the laboratory showed elevated CRP and leukocytes. The intra-operative bacteriological probes demonstrated Staph. aureus, sensitive to Gentamycin. Therefore, the Cierny-Mader osteomyelitis classification was grade II.

6 weeks after the operation, having achieved perfect local healing, the patient autonomously suspended the antibiotic treatment and stopped wearing the orthesis.

Immediately after this, she successfully underwent her second total knee prosthesis operation.

10 months after our debridement, the patient shows no signs of recurrence and ambulates with normal shoes.

Conclusions: In selected patients, even in immune-compromised situations, debridement and an antibiotic loaded bone-graft substitute implant is a good alternative treatment of osteomyelitis.

We demonstrated, that even a high risk procedure despite an infectious potential, can be done safely.

The bone substitute injection after debridement can easily be performed in a day-hospital setting; it proved to be an easy and safe procedure in our hands.

We treated 8 patients with 9 osteomyelitis in a similar fashion during the last 12 months at our hospital, with a survival rate of 80% at 11 months without any relapse.

Another advantage of the technique seems to be the documented complete reabsorption of the implant after 6 months with induction of a healthy bone growth.
We believe that the success of this method without complications is related to the local presence of antibiotics in the bone substitute which completes the radical eradication of the infection following the debridement.
[P40] PREDICTING LOWER LIMB PERIPROSTHETIC JOINT INFECTIONS: A REVIEW OF RISK FACTORS AND THEIR CLASSIFICATION AND PJII RISK APP DEVELOPMENT

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Aim: In order to develop an application for smartphone to calculate the relative risk of periprosthetic (PJII) infection, we undertook a systematic review to determine overall predictive factors that increase a patient’s risk of developing a lower limb PJII; to this aim, we further investigated the relative contribution of host-related, provider-related and postoperative risk factors.

Method: We included studies reviewing risk factors of developing either a hip or knee PJII published from January 1998 to December 2015. These were identified through international databases and included if they reported statistical significant calculations. Furthermore, an original algorithm and a PJII Risk App had been developed, to allow to automatically calculate the relative risk in a given patient and to store the data collected from each subject, to further permit, in an iterative process, to refine the value each risk factor and their combination.

Results: Twenty-seven original articles report risk factors relating to hip PJII (n=4, 14.8%), knee (n=3, 11.1%), or both (20, 74.1%). The main risk factors were the presence of a surgical site infection not involving the prosthesis (OR 35.9), preoperative high dose steroids (OR 21.0), BMI > 50 (OR 18.3), tobacco use (OR 12.76), and BMI < 20 (OR 6.00). The total number of host-related risk factors (n=34) largely exceeded those relating to the treatment provider (n=4). The PJII Risk App, released in January 2016, allowed to store, at the time of writing, 160 patients with their respective risk factors.

Conclusions: There is significant variation in the risk factors that places a patient at higher risk of a PJII. Host-related risk factors play the most relevant role, but the majority are non-modifiable, requiring further individualised steps and personalised care to prevent infection. An application for smartphones may allow quick evaluation of the risk in any given patient, which may be useful both for patients and surgeons, while it can serve as a basis for medico-legal evaluation of post-surgical infections. Moreover, the possibility to store data may allow to update and refine the weight of single and combined risk factors.
CALCIUM-BASED, ANTIBIOTIC-LOADED BONE SUBSTITUTE AS AN IMPLANT COATING: A PILOT CLINICAL STUDY

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Aim: Implant-related infections remain a major complication in orthopaedic surgery. The ability of the microorganisms to adhere to the implant and to immediately produce a protective biofilm layer is currently considered a crucial step in implant-related infections pathogenesis. Thus, implant protection with an antibacterial coating may prevent bacterial adhesion and biofilm formation. However, in spite of extensive preclinical research in the field, antibacterial coatings to protect orthopaedic implants in the clinical setting remain particularly few. The aim of this present study is to evaluate the safety of a calcium-based, gentamycin-loaded bone substitute as an antibacterial coating of cementless joint prosthesis.

Method: From March 2013 to October 2014, 15 consecutive patients, scheduled for cementless two-stage revision surgery for periprosthetic infection were included in this prospective observational pilot study. A gentamicin-loaded calcium-based resorbable bone substitute (60% calcium sulphate, 40% hydroxyapatite), was applied at surgery on the stem surface of hip (n=6) or knee (n=9) revision prosthesis. After surgery, all patients underwent clinical, laboratory and radiographic evaluation at 3, 6 and 12 months and yearly thereafter.

Results: At a minimum 12 months follow-up, 14/15 (93.3%) patients showed no recurrence of infection and no signs of radiographic loosening of the stem. No adverse events associated with the use of gentamicin loaded bone substitute were observed. The only patient with recurrence of infection had a severe soft tissue compromise requiring a muscle flap. However, also in this patient no clinical or radiographic signs of stem loosening were observed.

Conclusions: This is the first pilot clinical study on the short-term safety of using a calcium-based, gentamycin-loaded bone substitute as a surface coating on cementless prosthetic implants. Our data, although in a limited case series, demonstrates the safety of this application with promising results in infection prevention. If confirmed by larger studies, these findings may open a new prospective to protect intra-operatively orthopedic implants from bacterial adhesion, through the use of resorbable, osteoconductive, antibiotic carriers.

References:

1. Cerament G, BoneSupport AG,, Lund, Sweden
DIAGNOSTIC AND PROGNOSTIC VALUE OF PRESEPSIN AS MARKER OF POST-OPERATIVE ORTHOPAEDIC JOINT PROSTHESIS INFECTION

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2Department of Biomedical Sciences for Health, University of Milan, Milan, Italy
3Laboratory of Clinical-Chemistry and Microbiology, Irccs Galeazzi Institute, Milano, Italy
4Centre for Reconstructive Surgery and Osteoarticular Infections, Orthopaedic Research Institute Galeazzi, Milano, Italy
5Irccs Policlinico Dan Donato, San Donato Milanese MI, Italy
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Aim: Presepsin, the soluble fraction of CD14, was recently described as a powerful diagnostic tool, able not only to detect sepsis but also to discriminate different grade of sepsis severity. The aim of this project was to investigate of the diagnostic and prognostic value of Presepsin on PIJ, by correlating Presepsin values with other emerging infection marker such as TREM-1(Triggering receptor expressed on myeloid cells 1), CD-163, SuPAR (Soluble Urokinase Plasminogen Activating Receptor), OPN (Osteopontin), and MMP-9 (Metalloproteinase-9) involved in the inflammatory response associated to PJI. The mechanism of action of Presepsin in the inflammatory response was also investigated, in particular evaluating the inflammatory mediators involved such as the cytokines CCL2 and the inflammatory cytokines IL-6.

Method: The population of 100 selected patients undergoing prosthesis revision was enrolled and subdivided into two groups according to the cause of prosthesis implant failure: 48 patients having bacterial infection and 52 patient with no infection, undergoing aseptic loosening of the implant. Blood drawings was be performed from all patients at T0 (before surgery), T1 (48 hours after surgery), T2 (1 week) and at three months after surgery (T3) for plasma +EDTA separation and -80°C storage. In addition, the following parameters was measured: C-Reactive Protein (CRP), IL-6, SuPAR, TREM-1, CCL2, MMP-9, CD-163.

Results: Presepsin has a greater diagnostic value than CRP and IL-6 in the diagnosis of PJI, and therefore it can be considered a better diagnostic marker that could be introduced in the clinic for the detection of PJI. OPN, CCL2 and SuPAR displayed good diagnostic values in PJI, while CD163, TREM-1 and MMP-9 displayed very low diagnostic potential.

Conclusions: Presepsin can be considered an useful tool for the diagnosis and clinical monitoring of prosthetic joint infection, and it can also be supported by a panel of new inflammatory makers involved in monocyte/macrophage mediated inflammatory response such as OPN, CCL2 and SuPAR. This would allow a prompt therapeutic intervention in order to avoid the revision surgery, which has more impact on the patient.

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²Southmead Hospital, Southmead Rd, Bristol, United Kingdom

Aim: To evaluate the antimicrobial activities, antibiotic release and antibiotic resistance of old antibiotic loaded acrylic cement

Method: 49 patients undergoing revision hip arthroplasty for mechanical failure and for which antibiotic loaded cement were used during their primary hip replacement were recruited for this study. The mean interval between the primary hip arthroplasty and the revision surgery was 140 months (11.7 years). From each patient, at least one of three modes of sampling was performed: bone cement retrieval (for assessment of antimicrobial properties) and joint fluid aspirate or urine sample collection (both for antibiotic concentration assays). A bacillus subtilis was used to assess for antimicrobial activity, while urinary and joint aspirate gentamicin concentrations were determined by immunoassay. In addition, gentamicin was tested for resistance using a Coagulase negative staphylococci (CoNS) strain.

Results: 97% of the retrieved cement samples demonstrated significant antimicrobial activity in the Bacillus subtilis bioassay. And although none of the patients had detectable urinary gentamicin at the sensitivity limit of the assay, 96% of the joint aspirates collected had detectable gentamicin at a mean concentration of 0.5mg/L.

At the start of the experiment the CoNS strain was sensitive to gentamicin, however, resistance developed after just four culture cycles and that resistance also occurred against the other aminoglycosides tested alongside gentamicin.

Conclusions: Our study demonstrates that even ALAC as old as 27 years still elutes antibiotics at levels effective enough against certain bacteria. Undesirably, in these aseptic joint failures, the low concentrations of gentamicin measured may promote bacterial resistance if inoculation occurs. Therefore, there exists a Faustian pact with ALAC between prevention of infection and bacterial resistance. Nevertheless, Joint registry figures still report better outcome for infection prevention with the use of ALAC compared to joint replacement using plain cement or uncemented fixation.
Aim: To gather qualitative data from patients on the burden, impact, and costs of post-operative infections.

Method: Adults with post-surgical infections resulting from spinal, knee or hip replacement surgery were recruited by a single clinical site to participate in a focus group or one-on-one interview. A semi-structured discussion guide was used and all sessions were audio-recorded. A systematic qualitative analysis of the transcripts was conducted using a software following a coding dictionary. Participants also completed the PROMIS Physical Functioning (PF) Short Form 10A and the Veterans Rand (VR) 12-Item Health Survey.

Results: One focus group (n=3) and 12 telephone interviews were conducted with 15 adults (spinal: n=4; knee: n=3; hip: n=8); mean age 56.7 years (SD=10.6), 60% male, 87% Caucasian. The average time between diagnosis of infection and enrolment into the study was 8.7 months. Mean scores were: PROMIS PF Short Form 10A 39.3 (SD=12.1), VR-12 Physical Component 36.4 (SD=13.1), and VR-12 Mental Component 43.5 (SD=10.6). Participants reported a range of interrelated burdens and impacts due to post-surgical infections: Personal/Social/Emotional, Financial/Employment, Physical Functioning, Fatigue and Sleep Disturbance and Other (Table 1). Few differences were seen between spinal, knee and hip surgery participants with regards to the impact experienced, though mobility was more severely impacted for hip and knee patients. Recruitment for the study was challenging as a high proportion of potentially eligible participants were unwilling to participate, as they did not wish to revisit the negative impacts associated with their infections.

Conclusions: To our knowledge, this is one of few studies to explore the impact of post-surgical infections directly from patients. This impact is important to measure as post-surgical infections impart a broad and significant impact on patients and their families. Infections impact patient quality of life and place substantial social, economic, emotional, and physical burdens on these patients.

Table 1. Summary of Impacts

<table>
<thead>
<tr>
<th>Domain</th>
<th>Impact Category</th>
<th>Commonly Reported Impacts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Personal/Social/Emotional</td>
<td>Personal Life/Relationships</td>
<td>Relationship with partner (n=6)</td>
</tr>
<tr>
<td></td>
<td>Social</td>
<td>Difficulty visiting friends/going out (friends, Church, etc.) (n=9), Isolation (n=5), No social life (n=4)</td>
</tr>
<tr>
<td></td>
<td>Emotional/ Psychological</td>
<td>Loss of independence (n=7), Fear/anxiety (n=5), Depression (n=4), Sadness (n=3), Adjustment difficulties (n=3)</td>
</tr>
<tr>
<td>Financial/Employment</td>
<td>Financial</td>
<td>Paying additional costs (i.e. copays, physical therapy, transport, modifications to home) (n=9), Financial hardship (n=4), Insurance coverage (no additional payments made) (n=4), Reduced income (self) (n=3)</td>
</tr>
<tr>
<td></td>
<td>Employment</td>
<td>Taking additional time off from work than planned (n=6), No impact on job (i.e. retired or on social security disability) (n=5), Supportive and</td>
</tr>
<tr>
<td>Category</td>
<td>Issues</td>
<td></td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td><strong>Physical Functioning</strong></td>
<td>Walking (e.g. to store, dog) <em>(n=11)</em>, Pain/discomfort/numbness <em>(n=10)</em>, Standing <em>(n=9)</em>, Tiredness/fatigue/ lack of energy <em>(n=7)</em>, Climbing stairs <em>(n=7)</em>, Other symptoms <em>(n=6)</em>, Decline in strength (core, overall body) <em>(n=5)</em>, Muscular issues (tightness, spasms, decline in tone) <em>(n=4)</em>, Get in and out of car <em>(n=4)</em>, Getting out of a chair <em>(n=3)</em>, Not being able to exercise/dance <em>(n=3)</em></td>
<td></td>
</tr>
<tr>
<td><strong>Daily Activities</strong></td>
<td>Showering or bathing <em>(n=9)</em>, Toileting <em>(n=5)</em>, Dressing (shoes off, wearing baggy clothes) <em>(n=4)</em>, Fatigue-related inability to do things <em>(n=4)</em>, Meal/Food preparation <em>(n=4)</em>, Shopping <em>(n=4)</em>, Cleaning clothes <em>(n=3)</em></td>
<td></td>
</tr>
<tr>
<td><strong>Fatigue and Sleep Disturbance</strong></td>
<td>Fatigue or Lack of Energy <em>(n=4)</em>, Lack of energy <em>(n=4)</em></td>
<td></td>
</tr>
<tr>
<td><strong>Sleeping Issues</strong></td>
<td>Difficulty falling asleep <em>(n=5)</em>, Pain and discomfort <em>(n=3)</em>, Renting or buying equipment to aid sleep <em>(n=3)</em></td>
<td></td>
</tr>
</tbody>
</table>

*ATLAS.ti*
[P45] PREDICTING LOWER LIMB PERIPROSTHETIC JOINT INFECTIONS: A REVIEW OF RISK FACTORS AND THEIR CLASSIFICATION

David George¹, Lorenzo Drago¹, Sara Scarponi³, Enrico Gallazzi³, Fares Haddad¹, Carlo Romanò³

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³Centre for Reconstructive Surgery and Osteoarticular Infections, Orthopaedic Research Institute Galeazzi, Milano, Italy

Aim: We undertook a systematic review to determine overall predictive factors that increase a patient’s risk of developing a lower limb PJI, and to assess the relative contribution of host-related and provider-related factors, and determine which postoperative factors are indicators of infection.

Method: We included studies reviewing risk factors of developing either a hip or knee PJI published from January 1998 to November 2015. These were identified through international databases, and included if they reported statistical significant calculations.

Results: Twenty-seven original articles report risk factors relating to hip PJI (n=4, 14.8%), knee (n=3, 11.1%), or both (20, 74.1%). The main risk factors were the presence of a surgical site infection not involving the prosthesis (OR 35.9), preoperative high dose steroids (OR 21.0), BMI > 50 (OR 18.3), tobacco use (OR 12.76), and BMI < 20 (OR 6.00). The total number of host-related risk factors (n=34) largely exceeded those relating to the treatment provider (n=4) [table 1]. The main indicators of a PJI were those relating to the wound, such as a surgical site infection (OR 35.9) and discharge (OR 18.7).

Conclusions: There is significant variation in the factors that places a patient at higher risk of a PJI. Host-related risk factors play the most relevant role, but the majority are non-modifiable, requiring further individualised steps and personalised care to prevent infection.

Table: Classification of risk factors and probability of infection (main factors)
<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Minimum increase</th>
<th>Maximum increase</th>
<th>Statistical parameter</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HOST-RELATED RISK FACTORS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(A) Modifiable</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic steroids</td>
<td>3.3</td>
<td>21.00</td>
<td>OR</td>
<td>10, 16</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>5.4</td>
<td>12.76</td>
<td>OR</td>
<td>18, 27</td>
</tr>
<tr>
<td>Nasal MRSA infection</td>
<td>-</td>
<td>8.24</td>
<td>OR</td>
<td>26</td>
</tr>
<tr>
<td>BMI &lt; 20</td>
<td>-</td>
<td>6.00</td>
<td>OR</td>
<td>16</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>-</td>
<td>5.10</td>
<td>OR</td>
<td>16</td>
</tr>
<tr>
<td>COPD</td>
<td>1.22</td>
<td>4.34</td>
<td>OR</td>
<td>1, 26</td>
</tr>
<tr>
<td>BMI &gt; 40</td>
<td>-</td>
<td>4.13</td>
<td>OR</td>
<td>18</td>
</tr>
<tr>
<td>Pre-operative BM</td>
<td>-</td>
<td>2.25</td>
<td></td>
<td>12</td>
</tr>
<tr>
<td>(B) Non-modifiable</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.4</td>
<td>5.47</td>
<td>OR</td>
<td>10, 21</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>-</td>
<td>5.40</td>
<td>HR</td>
<td>23</td>
</tr>
<tr>
<td>Male</td>
<td>1.89</td>
<td>3.55</td>
<td>HR, OR</td>
<td>15, 26</td>
</tr>
<tr>
<td>Age</td>
<td>-</td>
<td>3.36</td>
<td>OR</td>
<td>21</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>1.18</td>
<td>3.30</td>
<td>OR</td>
<td>1, 10</td>
</tr>
<tr>
<td>Malignancy</td>
<td>-</td>
<td>3.10</td>
<td>OR</td>
<td>2</td>
</tr>
<tr>
<td><strong>PROVIDER-RELATED RISK FACTORS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(A) Modifiable</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quadriceps release (TKR)</td>
<td>-</td>
<td>4.76</td>
<td>HR</td>
<td>15</td>
</tr>
<tr>
<td>Non-same day procedure</td>
<td>-</td>
<td>4.16</td>
<td>OR</td>
<td>18</td>
</tr>
<tr>
<td>Prolonged operation</td>
<td>1.78</td>
<td>3.38</td>
<td>HR</td>
<td>9, 18</td>
</tr>
<tr>
<td>(B) Non-modifiable</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Revision arthroplasty</td>
<td>2.00</td>
<td>4.23</td>
<td>OR</td>
<td>4, 18</td>
</tr>
</tbody>
</table>
APPLICATION OF BIOACTIVE GLASS PROVEN COST-EFFECTIVE IN TREATMENT OF PATIENTS WITH CHRONIC OSTEOMYELITIS

Jan Geurts¹, Tom Van Vugt¹, Chris Arts¹

¹Maastricht University Medical Center, Maastricht, Netherlands

Introduction: Chronic osteomyelitis was traditionally treated with a two-stage surgery with antibiotic-loaded polymethylmethacrylate (PMMA) as local antibacterial therapy. Two-stage surgeries are associated with high morbidity, long hospitalizations and high costs. S53P4 bioactive glass is a biodegradable antibacterial bone graft substitutes that enables a one stage surgery in local treatment of chronic osteomyelitis. Several clinical studies showed good results and low complication rates, but the cost-effectiveness of S53P4 bioactive glass in chronic osteomyelitis treatment was never studied.

Aim: Chronic osteomyelitis is classically treated in a two-stage fashion with intermittent placement of PMMA beads. More recent developments like bioactive glass allow one-stage treatment. Several clinical studies showed good results and low complication rates, but the cost-effectiveness of S53P4 bioactive glass in chronic osteomyelitis treatment was never studied. In this retrospective cohort study we aimed to prove that treatment of patients with S53P4 bioactive glass is cost-effective compared to treatment with antibiotic-loaded PMMA. We hypothesized that, although S53P4 is an expensive biomaterial, this treatment will be cost-effective due to the shortening of hospital stay and the prevention of a second operation.

Methods: We conducted a retrospective cohort study comparing a treatment cohort that received debridement surgery, S53P4 bioactive glass implantation and systemic antibiotics and a control group that received two-stage debridement surgery, antibiotic-loaded PMMA implantation and systemic antibiotics. All patients with chronic osteomyelitis in long-bones, who received one of two treatment algorithms, from 2006 until 2015 were included. All hospital-related costs from start of diagnosis until one year after surgery were clarified and compared. Patient outcomes were eradication of infection based on blood analysis, x-ray imaging and clinical outcomes.

Results: A total of 37 patients are included in this study, based on treatment 16 patients were allocated to the treatment group and 21 to the control group. These groups were not significantly different at baseline. We observed a decrease in hospitalization days of 14 days (p<0.001) and the number of surgeries decreased from 2.33 to 1.25 (p<0.001). Despite the higher material costs versus €2.132,50 to €362,97 (P=0,004), we observed total costs of €18.586,49 in the treatment group versus €27.134,96 in the control group. Eradication of infection is seen in 100% of patients in the treatment group compared to 76% in the control group (p=0,066). The combination of the total costs and the success rates of these two treatments result in an incremental cost-effectiveness ratio (ICER) of €35.618,63/successfully treated patient.

Conclusions: This study shows a cost effectiveness of S53P4 bioactive glass in the treatment of chronic osteomyelitis. The cost-effectiveness ratio shows a substantial cost saving per successfully treated patient. The major part of these costs savings are due to a reduction in hospitalization, number of surgeries and surgery costs.
The Royal London is the largest trauma centre in London. Patients with suspected bone infection following trauma are referred to the tertiary centre and discussed in an MDT setting with the Orthopaedic, Pharmacy and Microbiology team every week. Follow up occurs in an OPAT service and a specialist bone infection clinic. Infected metalwork in lower limbs in trauma patients poses a unique challenge and we assessed our large cohort to evaluate epidemiology and outcomes.

Patients were selected based on positive microbiology identified from intraoperative deep tissue samples of tibia and femur taken at the Royal London from February 2012 to August 2015.

Thirty one patients were identified in total as having infection of the lower limbs. Twenty-six patients (23M: 3F) were identified in having infection of the tibia post open reduction and internal fixation. Six (5M: 1F) had infected femoral metalwork. The age range was 22-85 (average age was 48 years).

*Staphylococcus aureus* was the most common organism, isolated in 13 patients. Nineteen patients had metalwork infected with gram negative organisms. Multi-drug resistant (MDR) organisms (vancomycin resistant enterococcus, Methicillin resistant *S. aureus*, extended spectrum β-lactamases and carbapenemase producing enterobacteriaceae) were identified in seven patients. Four of the seven patients who had MDR organisms isolated had their initial injury abroad and three had eventual amputations of the affected limb.

Ten patients had more than one significant organism isolated (maximum three). These patients required a longer course of antibiotics (average 81 days).

The range of time of insertion of metalwork following fracture to surgical intervention ranged from one month to 24 years. (average 251 months).

Five patients underwent washout or debridement only. One patient had antibiotics alone and the rest underwent removal of metalwork (only one did not have an antibiotic tail). Following surgery the average duration of antibiotics was 50 days (range 2 weeks to 6 months). Twenty-one patients had an extended (> 4 weeks) of antibiotics, and all patients had an initial period of intravenous treatment. There was no difference in outcome in patients who were treated with intravenous or oral antibiotics in the community.

Management of patients with infection following trauma offers a different challenge compared to native bone and positive outcomes require a multidisciplinary approach, and early identification of potentially challenging cases. Outpatient antimicrobial therapy of traumatic lower limb infections require appropriate support to achieve results.
SONICATION OF INFECTED ORTHOPEDIC IMPLANTS DETECTED RARE MISCELLANEOUS BACTERIA: ARE THEY TRUE PATHOGEN?

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1National and Kapodistrian University of Athens, 4th Department of Internal Medicine, Athens, Greece
2National and Kapodistrian University of Athens, Athens, Greece
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4University of Athens, Infectious Diseases Research Laboratory, 1st Department of Internal Medicine, Athens, Greece

Aim: Implant-associated infections are difficult to diagnose because of biofilm formation on the surface of the implant. Sonication of the infected implant has increased susceptibility of routine cultures and subsequently contributed to an adequate antimicrobial treatment of orthopedic device infections*. However, little is known on the significance of rare and non-expected isolates from the sonication fluid. We retrospectively analyzed routine laboratory cultures at our reference centre for orthopedic implant infections.

Method: All removed orthopedic implant with either known or highly suspected infections were submitted to sonication process and conventional cultures. Isolation and identification of all pathogens was performed by a Automated Microbiology System**. Periodical cultures of the sonication equipment was also done in order to assess lack of contaminants during sonication procedure. A cut off value of 50cfu was considered as positive for isolates detected at the sonication fluid. Demographics, treatment and follow-up was recorded for all patients.

Results: A total of 11 miscellaneous isolated was evaluated (Burkholderia cepacia (n=1), Pseudomonas oryzihabitans (n=2), Rhizobium radiobacter (n=1), Comamonas testosteroni (n=1), Chromobacterium riolacecium (n=1), Rhizobacterium ramnosum(n=1), Corynobaeterium spp (n=1), Agrobacterium spp (n=1), Pasterella multocida (n=1), Bacillus cereus (n=1). Patients were old (mean60y), men (n=7), with long-standing hip and knee arthroplasty infection with or without osteosynthesis. Mean duration of infections before surgical removal of the implant was 12 months (6-24). Staphylococci and Gram negative (Klebsiella, E. coli, Pseudomonas aeruginosa) were isolated in previously removed tissues/implants or simultaneously with the rare pathogens. In all cases, antimicrobial treatment was amended following microbiological documentation provided by sonication procedure. Ciprofloxacin was added in 8 cases and cotrimoxazole in one.

Conclusions: In long-standing arthroplasty infections, miscellaneous pathogens may be embedded in the biofilm formation on the implant surface. The exact role of these pathogens is still unclear, however, they should be carefully evaluated and not be considered as contaminants. Further evaluation in more sonication samples should be performed.


** BD automated Phoenix-100 system
[P49] OSTEOMYELITIS WITHIN ECTOPIC OSSIFICATION IN THE LOWER LIMB: A CASE REPORT

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²Nuffield Orthopaedic Centre, Oxford University Hospitals, Oxford, United Kingdom

Aim: Ectopic ossification is a process whereby bone forms in tissues which do not usually ossify. It is known to develop in patients with traumatic brain or spinal cord injuries, neurological disorders, severe burns and to a lesser extent following trauma or surgery to the lower limbs. Complications arising from such bone formation include swelling and reduced range of motion in nearby joints. However infection within such ossification is rare and very few cases have been reported.

We present one such case of osteomyelitis arising from within an area of ectopic ossification in the lower limb.

Method: A 47 year old gentleman with a congenital gigantism of the leg presented to our unit with a chronic discharging sinus over the lateral aspect of the lower limb. He had underwent a soft tissue de-bulking surgical procedures 30 years prior which was complicated by haematoma formation requiring surgical drainage. He subsequently developed a persistent discharging sinus

Examination revealed a firm but non tender lump deep to the old scar and the sinus. On plain radiograph the lump appeared as ectopic calcification within the subcutaneous tissue at the level of mid shaft of the fibula. An MRI of his leg further showed further the sinus tracking to the area of ectopic bone, but with no involvement of the underlying tibia or fibula.

Results: An excision of the sinus and ectopic bone was performed. No tracking into the deeper soft tissues or long bones was found and following thorough debridement the wound was closed primarily. Cultures from the heterotopic ossification and soft tissue sample grew enterobacter cloacae, pseudomonas species and Staphylococcus aureus. He was treated with four weeks of intravenous Amikacin and ciprofloxacin followed by a further 6 weeks of oral antibiotics. At six months follow up the wounds remained healed with no signs of recurrence.

Conclusions: Ectopic formation of bone is occasionally mistaken for osteomyelitis prior to diagnosis, however this is the first reported case of osteomyelitis within ectopic ossification. Treatment required complete excision of the ectopic bone and antibiotic treatment.
TWO STAGE REVISION SURGERY OF INFECTED KNEE ARTHROPLASTY—CONVENTIONAL SPACER VERSUS SPACER WITH SUPERFICIAL VANCOMYCIN COATING

Mathias Glehr¹, Florian Amerstorfer¹, Martina Schober¹, Patrick Sadoghi¹, Gerald Gruber¹, Klaus-Dieter Kühn¹, Andreas Leithner¹

¹Department of Orthopedic Surgery, Medical University of Graz, Graz, Austria

Aim: Two-stage revision surgery with the use of temporary bone cement spacer is the most widely accepted and performed treatment of infected knee replacement arthroplasty. Besides preserving limb length and minimizing soft tissue contractures, temporary cement spacers act as local antibiotic carrier. In order to increase the efficiency of active antibiotic substances, we established a novel surgical technique of superficial vancomycin coating (SVC) of bone cement. The aim of this study was to determine the reinfection rate during spacer implantation period using a conventional cement spacer as well as conventional spacer with additional SVC.

Method: In total 123 two-stage revision surgeries with the use of non-articulation spacers were analyzed retrospectively (Table 1).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Conventional block spacer</th>
<th>Conventional block spacer with additional SVC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>104</td>
<td>19</td>
</tr>
<tr>
<td>Age</td>
<td>68</td>
<td>73</td>
</tr>
<tr>
<td>Range</td>
<td>33-87</td>
<td>51-88</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
<td>56</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>48</td>
</tr>
</tbody>
</table>

Table 1: Epidemiological patient characteristics

For a conventional non-articulating spacer 1g of Vancomycin powder* was mixed to every 40 mg of bone cement**. For the SVC group 2 grams of Vancomycin powder were added superficially to the surface of the bone cement, which was also mixed with 1 g of vancomycin powder to every 40 mg bone cement, and pressed onto manually before curing. In the SVC group, we investigated the concentration of vancomycin in wound fluid and serum samples daily for 5 days or until the drains were removed. Furthermore creatinine levels were documented in this group pre- and post-operative.

Results: In the conventional spacer group the spacer was explanted after a median of 9 weeks (range 2-72). Within this time 19 reinfections (18%) occurred, which made subsequent spacer exchange surgery necessary. In the SVC group, the spacer period was median 9 weeks (range 3-12). Only one reinfection (5%) occurred in a patient with a gram-negative infection. Highest median vancomycin level from the drain was documented on postoperative day 1 with a value of 399,0 μg/mL (range 74,3 – 1650,0), continually decreasing until postoperative day 4. Serum vancomycin levels with a median of <2,0 μg/mL were present (range <2.0 – 5,3) from postoperative day one to five. No serum creatinine increase of 0.5 mg/dL from creatinine baseline value or a ≥50% increase from baseline was detected.
**Conclusions:** Superficial Vancomycin Coating of bone cement in orthopedic revision surgery represents a safe method to increase local vancomycin concentrations that may lead to a reduction of reinfection rate during spacer period.

* Vancomycin-MIP®
**PALACOS® R+G
[PS1] FATE OF Spacer EXCHANGES IN PERIPROSTHETIC JOINT INFECTION

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\textbf{Aim:} It is not uncommon that some surgeons perform an interim spacer exchange, mainly due to the impression that infection still persists and insertion of a “new load” of antibiotics may eradicate it. There is little to no literature reporting outcomes of spacer exchanges. This study aims to report the characteristics and outcomes of PJI patients who underwent spacer exchange during the course of their two-stage exchange arthroplasty.

\textbf{Method:} Our institutional database was used to identify 76 cases (58 knees, 18 hips) who underwent a spacer exchange from 2000-2014 and had one-year minimum follow-up. We matched 3:1 for controls who underwent two-stage exchange without interim spacer exchange in terms of gender, age, joint, body mass index, comorbidities, operative time, length of stay, year of surgery, type of spacer (articulating vs. static), and resistant organisms. A retrospective review was performed to extract relevant information regarding treatment and microbiology and so on. Musculoskeletal Infection Society criteria were used to define PJI\textsuperscript{1}; treatment success was defined using the Delphi criteria.\textsuperscript{2}

\textbf{Results:} The mean age, spacer duration, and follow-up were 65.1, 1.3, and 4.1 years, respectively. 30.3\% of patients were never reimplanted. Patients underwent an average of 2.14 spacer implantations (range:2-4). 18.3\% of patients had an initial articulating spacer. Reasons for first spacer exchange were suspected infection or wound issues (66/76), dislocation (8/76), tibial fracture (1/76), or unknown (1/76). Resistant organisms comprised 45.5\% of persistent infections during first spacer exchange. Complications prior to reimplantation included 10 spacer dislocations, 11 wound-related complications, 5 PJI-related mortalities, 3 arthrodeses, 2 girdlestones, and 5 amputations (several patients had multiple complications).

Complications after reimplantation included 15 reinfections, 2 PJI-related mortalities, and 1 girdlestone. The mean time from initial spacer to death for those not reimplanted was 2.8 years compared with 5.5 years for those reimplanted (P=0.08). 28.9\% (22/76) of our cohort failed after reimplantation compared to 18.0\% (41/228) of matched controls who did not receive a spacer exchange. Kaplan Meier survivorship curves revealed a significantly lower treatment success rate in our cohort compared to matched controls (p=0.035).

\textbf{Conclusions:} Patients requiring an interim spacer exchange during two-stage exchange arthroplasty have a protracted course and poor outcomes with high rates of salvage procedures, reinfections, and mortality. The management of PJI remains imperfect, and this study brings into question the logic behind an interim spacer exchange practice.

Aim: Ertapenem is a therapeutic option in patients with difficult to treat bone and joint infections (BJI). The subcutaneous (SC) route of administration is convenient in ambulatory care setting and has shown favorable pharmacokinetic (PK) profile and tolerance\cite{1,2}. However few PK data supporting the use of ertapenem subcutaneously are available.

Method: This was a retrospective analysis of data collected in patients with BJI who received ertapenem administered as a SC or intravenous (IV) 30-min infusion, from August 2010 to March 2014. An ertapenem plasma concentration profile was determined on at least one occasion in each patient, and typically included trough, peak, and 6h post-dose levels measured by HPLC. Population PK analysis was performed by using the NPAG algorithm implemented in the Pmetrics program \cite{3}. Then, 1000-patient Monte Carlo simulations were performed based on the final model to investigate the influence of ertapenem route of administration (SC or IV), dosage (1g once or twice daily), and renal function on the probability of target attainment (PTA), considering an efficacy target defined as a percentage of time during which ertapemen free plasma concentration remain above the MIC ($f_{T>MIC}$) of 40\%\cite{4}.

Results: Forty-six PK profiles (13 with IV and 33 with SC ertapenem) with a total of 133 concentrations from 31 subjects (21 males and 10 females; mean age, 58 ± 16 years) were available for the analysis. A two-compartment model, with linear SC absorption and linear elimination best fit the data. Creatinine clearance (CCR) was found to significantly influence ertapenem plasma clearance. Both population and individual predictions correlated well with observed concentrations ($R^2 = 0.77$ and 0.95, respectively), with little mean prediction error (-0.40 and -1.94 mg/L, respectively) and root mean squared error (18.1 and 8.3 mg/L, respectively). Simulations showed that twice daily dosing, SC administration and renal impairment were associated with increased $f_{T>MIC}$ and higher PTA. As an example, for a MIC of 1 mg/L, the PTA in patients with CCR of 100 ml/min were 100%, 100%, 91.8%, and 70.1% for the regimens SC/q12, IV/q12, SC/q24, IV/q24, respectively.

Conclusions: The results suggest that 1 g administered twice daily, subcutaneously may optimize ertapenem exposure in patients with BJI.

References:


Acknowledgements: This work was not supported by any fund.
Aim: Prosthetic joint infection (PJI) following total joint arthroplasty (TJA) is a devastating complication and is the leading cause of revision TJA in the United States. Making a diagnosis of PJI can be challenging, given the variety of testing modalities available without standardization among physicians. In 2011, the Musculoskeletal Infection Society extensively evaluated available evidence and developed a new definition for diagnosis of PJI. According to new guidelines, 4/6 of the following criteria must be met: 1) elevated erythrocyte sedimentation rate (ESR) (>30) and C-reactive protein (CRP) (>10), 2) elevated synovial white blood cells (WBCs) (1100-4000), 3) elevated synovial % polymorphonuclear leukocytes (PMNs) (>64%), 4) presence of purulence in affected joint, 5) isolation of a microorganism in 1 culture of periprosthetic tissue/fluid, and 6) >5 neutrophils per high power field (HPF) in 5 HPFs observed. However, infections caused by low virulence organisms may not meet these criteria, which could lead to under-diagnosis of potentially treatable symptomatic PJI.

Method: Six patients came into our office with persistent knee or hip pain, decreased range of motion, and non-erythematous, non-draining joints following TJA. Initial post-operative x-rays revealed technically well-positioned implants. A thorough workup was performed, including imaging, CBC, ESR, CRP, and synovial fluid aspiration with cell count, differential, and cultures. None of the patients met current diagnostic criteria for PJI. Intraoperative cultures were obtained to guide further management.

Results: Lab results from all 6 patients showed inflammatory markers within cutoff limits, and synovial fluid cultures were negative. In all 6 patients, intraoperative cultures from synovial tissue at a later date demonstrated growth of Staphylococcus epidermidis and/or Propriobacterium acnes, confirming a diagnosis of PJI. After discussing risks and benefits of the surgery, four patients opted for a two-stage revision with 6 weeks of IV antibiotics, while the other 2 patients elected to pursue non-operative treatment with physical therapy. On follow-up appointments, 3 of the 4 surgical patients and 1 of the 2 non-operative patients reported significant improvement in pain, functionality, and quality of life.

Conclusions: Although patients may not meet current suggested diagnostic criteria for PJI, there may be an underlying infectious cause of their symptoms. We recommend that surgeons be aware of the possibility of low-virulence infections in patients with persistent joint pain and decreased range of motion following total joint replacement, in the setting of well-positioned implants.
Aim: The growing number of primary hip arthroplasty also leads to more revision surgeries caused by periprothetic infection. This often results in a decay of joint function and quality of life. Aim of this study was to show the subjective and objective outcome after revision surgeries caused by chronic periprothetic infection.

Method: In a retrospective study from 2003 to 2013, all patients with chronic periprothetic hip infection (infection > 6 weeks after arthroplasty) were assessed and the „Lower-Extremity-Functional-Scale“ (LEFS), „Harris-Hip-Score“ (HHS) and „Physical-Health-Composite-Score“ (PCS) of the „Short-Form-12“ as well as bacterial samples and epidemiological data (i.a. age, ASA-classification, occurrence of infection after primary arthroplasty) were analyzed.

Results: In 79% of in total 102 patients with hip revision arthroplasty because of chronic periprothetic infection (66 yr.; ASA: 2,5; occurrence of infection: 70,6 month; follow-up: 4,1 yr.) eradication of the infection could be achieved. Therefore a girdlestone-situation was necessary in 16% and permanent fistula was required for 5%. In 43 patients the first re-implantation was successful (65 yr.; ASA 2,4; occurrence of infection: 53,7 month; follow-up: 5,0 yr.). In 59 patients an infection recurred after the first re-implantation (68 yr.; ASA 2,5; occurrence of infection: 83,4 month; number of re-implantations: 1,3; follow-up: 3,4 yr.) which was combined with a worse outcome (singular vs. repeated re-implantation: girdlestone 11,6% vs. 25,0%; permanent fistula 0% vs. 8,4%; PCS of SF-12: 36,2 vs. 29,6 (p<0,05); LEFS: 38,5 vs. 32,1 (p=0,11); HHS: 59,9 vs. 48,6 (p<0,05)). Positive bacterial cultures harvested during re-implantation (67 yr.; ASA 2,8; occurrence of infection: 64,2 month; number re-implantations: 0,8; follow-up: 4,2 yr.) resulted in a significant worse outcome compared to the bacterial negative group (66 yr.; ASA 2,3; occurrence of infection: 66,4 7; number of re-implantations: 0,7; follow-up: 3,8 yr.). In this bacterial positive group more permanent fistula (4,8% vs. 0%) and girdlestone-situations (3,2% vs. 0%) were necessary and worse life quality scores could be observed (PCS: 26,6 vs. 37,8 (p<0,01); LEFS: 27,3 vs. 43,0 (p<0,05); HHS: 47,5 vs. 62,2 (p<0,05)).

Conclusions: Revision surgeries of a hip arthroplasty because of a chronic infection show a bad outcome which even gets worse with the amount of failed re-implantations and with the existence of positive bacterial samples during re-implantation. Therefore an eradication of infection seems to be one of the most important prognostic factors regarding the outcome and should be an aim in the surgical approach.
Aim: Superficial wound infections do not lead to chronic prosthetic joint infection but the impact of superficial infections on functional outcomes is unknown. The purpose of this study was to determine and compare the functionality and Health related quality of life (HRQoL) of superficial infections treated successfully after primary total knee arthroplasty (TKA).

Method: In a 3000 prospective TKA cohort, 45 superficial infections were compared with a control group of 629 TKA without complications. Functional outcome, health quality and expectations were compared between the study and control groups.

Results: The groups were comparable in terms of demographic values and preoperative scores. The mean follow-up was 74.57 months (SD ± 7.11). No statistical differences were observed in relative to functional outcome (Knee Society Score and range of motion), HRQoL (Short Form-36) and postoperative expectations.

Conclusions: Successfully treated superficial infections following a TKA do not have different clinical outcomes or HRQoL when compared to TKAs without complications in a long term follow up.
[P56] ANTIMICROBIAL SILVER IMPLANT SURFACE FOR CEMENTLESS JOINT REPLACEMENT - HEALTH SAFETY ASPECTS

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Aim: Infections associated with prosthetic joint replacement are a significant cause of morbidity and a significant financial burden to healthcare systems worldwide. These infections are extremely difficult to treat since implants provide an ideal surface for biofilm formation, which significantly decreases antibiotic effectiveness.

To prevent biofilm formation, a company* has developed a surface modification technology[1] that embeds antimicrobial silver ions into titanium and titanium-alloy-based implantable devices. Upon surgical insertion, the ions are released and kill microorganisms attempting to adhere to the device. This technology has already been successfully applied to a tumour replacement system** and its effectiveness has been clinically confirmed [2].

In this study we have investigated whether this technology is toxicologically safe when applied to the Hip stems system***.

Method: For the toxicological safety assessment we followed ISO 10993 standards. Pharmacokinetic analysis was conducted according to ISO 10993-6 using silver-ion-treated Ti-6Al-4V intramedullary pins.

Results: Based on the target dose of 6±4 µg/cm² the total possible silver ion concentration on the hip stem*** was calculated to be 2.88 mg. The cumulative silver concentration in all organs excluding the liver and tibia was less than 2% of the total delivered at all time-points tested. Elimination of silver ions was observed to be predominantly faecal.

Conclusions: The WHO published a human no observed adverse effect level (NOAEL) of 10g of silver. For silver sensitive patients undergoing joint replacement the NOAEL would be 40 mg, far above the hip stem total. Argyria develops at much higher concentrations[3]. The safety of this technology was confirmed in a pharmacokinetics study where test animals showed no adverse reactions. Silver was shown to be processed in the liver and excreted via biliary excretion. These findings are in line with previous studies[3,4].

This study has demonstrated that embedded silver ions are of no health concern for patients. Silver ion levels remain far below published toxicity thresholds even for patients with sensitivities. Because of the usage of silver ions, risks attributed to nanoparticles are not applicable[5].

Acknowledgments: Funded by Zimmer Biomet.

[1] Trade name “Bactisure Ag™” (Zimmer Biomet)
* Accentus Medical PLC
** Stanmore Implants METS tumour replacement system
***Wagner SL Revision® Hip stems (Zimmer GmbH, Winterthur, Switzerland) system
Aim: A total of 1052 adults with musculoskeletal infection were recruited to the OVIVA trial between 2011 and 2015. The trial is currently in follow up and is yet to report the final results, but preliminary analysis of selected baseline data from this multi-centre cohort provides a unique opportunity to describe patient characteristics, to identify associations with co-morbid risk factors, and to highlight variations in medical and surgical management between centres.

Method: The OVIVA study is a randomised, non-inferiority trial across 29 UK centres recruiting adults with bone or joint infection. Patients who require at least 6 weeks of therapy are randomized within the first week of definitive treatment to receive either oral or intra-venous antibiotics. For those randomized to intravenous therapy, adjunctive oral therapy such as rifampicin is permitted at the discretion of the prescribing clinician.

We analysed preliminary baseline data from the seven centres with the highest number of patients.

Results: Data from 894 individual patients contributed to this analysis. There was a consistent male excess across all 7 sites (577 male : 317 female). The median age was 60 (range 18-92, IQR 49-70). Males were significantly younger than females (median age 57 vs. 64 years, respectively, p<0.0001). Overall, 42% of patients had one or more risk factors associated with infection. The most frequent of these were Diabetes Mellitus (20%), smoking (12%) and ischaemic heart disease (8%); the prevalence of these risk factors varied between centres.

Histopathology samples were sent in 60% of cases, with a wide variation between centres (6-86%). Of 495 evaluable samples, 476 (96%) showed histological features consistent with a primary diagnosis of infection. Of 408 patients treated for prosthetic joint infection, 188 (46%) were managed with a 'DAIR' (Debridement and Implant Retention) although the proportion varied between centres (17 to 72% of cases).

Rifampicin was prescribed for 382/894 (43%) patients. Overall, rifampicin use was significantly greater in the DAIR group (p<0.0001), but substantial variation in practice was observed.

Conclusions: For patients in the highest recruiting centres in the OVIVA trial, preliminary data suggest a male excess and a high prevalence of co-morbid risk factors such as diabetes, smoking and vascular disease. We report important differences in practice between centres, which may help in informing the approach to designing future studies.

(The OVIVA trial is funded by the NIHR Health Technology Assessment programme, project number 11/36/29. Trial registration ISRCTN91566927. Research Ethics Committee number 13/SC/0016)
COMPARISON OF BACTERIAL ADHESION TO MONOFILAMENT, BRAIDED, AND BARBED SUTURES IN A CONTAMINATED WOUND MODEL

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\textsuperscript{2}Cellular and Molecular Microbiology Division, Interfaculty Institute of Microbiology and Infection Medicine, University of Tübingen, German Center for Infection Research, Partner Site Tübingen, Tübingen, Germany
\textsuperscript{3}Bg Trauma Centre Tübingen, Tübingen, Germany
\textsuperscript{4}Medical Faculty of the University of Tübingen, Tübingen, Germany

Aim: When surgeons are dealing with an already infected wound, the properties of the suture type are crucial for the success of the operation. A new suture material is now available characterised by barbs projecting from a monofilament base. For these barbed sutures, several advantages have been claimed, such as shortened wound closure time and reduced maximum wound tension due to knotless suturing. It has also been suggested that these sutures would be advantageous microbiologically in comparison not only to polyfilament sutures, but also to monofilament sutures. We retested the microbial characteristics of barbed\textsuperscript{1} sutures in comparison to monofilament\textsuperscript{2} and both normal\textsuperscript{3} and triclosan-coated\textsuperscript{4} braided sutures."

Method: Sutures were contaminated with \textit{Staphylococcus epidermidis}, \textit{Staphylococcus aureus}, \textit{Escherichia coli}, \textit{Enterococcus faecium}, or \textit{Pseudomonas aeruginosa} and then cultivated on colour-change agar. In a second study arm, sutures were incubated with these bacteria to allow biofilm formation, followed by antibiotic treatment, and, thereafter, colour-change agar cultivation. In both study arms, the halo size around the sutures was measured. The sites of bacterial colonisation were analysed by confocal microscopy.

Results: In the first study arm, monofilament and barbed sutures showed good comparable results, whereas large halos were found around the polyfilament sutures. Growth around triclosan-coated polyfilament sutures depended on bacterial triclosan sensitivity. After biofilm formation and antibiotic treatment, halos were significantly smaller on the barbed than on the polyfilament sutures ($P<.001$), but larger on the barbed than on the simple monofilament sutures ($P<.001$). Bacterial growth was localised between the braided filaments and beneath the barbs (see Figure 1).

Conclusions: From a microbiological perspective, barbed sutures can be recommended in aseptic surgery. In a contaminated situation, however, barbed sutures seem to have poorer characteristics than purely monofilament sutures and should be used only after careful consideration by the surgeon.
**Figure 1:** Confocal microscopy images of suture material after cultivation on agar plates (sutures in blue, bacteria in green).

**Acknowledgements:** No conflict of interest.

**References:**

1. Quill (Surgical Specialties Corporation, Braintree, MA, USA).
2. Ethilon II (Ethicon Inc., Somerville, NJ, USA)
3. Vicryl (Ethicon Inc.)
4. Vicryl Plus (Ethicon Inc.)
Aim: This study aimed to identify risk factors for development of periprosthetic joint infection (PJI) in patients undergoing primary hip and knee arthroplasty.

Method: A consecutive series of 9,971 primary arthroplasties (4,302 hip, 5,669 knee) performed between April 2008 and June 2014 at a high volume arthroplasty centre were identified along with full patient demographic, co-morbidity and peri-operative complication data. Mean age = 68.4 years (SD 9.8), mean body mass index (BMI) = 29.9 kg/m² (SD 5.4). The majority of patients were ASA 1 (n=1,106, 11%) or ASA 2 (n=6,750, 68%). All patients were followed up post-operatively by a dedicated surgical site infection (SSI) monitoring team in order to identify patients who developed a PJI within 1 year. A stepwise multivariable logistic regression model was used to identify patient and surgical factors associated with increased risk of infection. Predictors with a p-value of <0.20 in the univariate analysis were included in the multivariate analysis.

Results: One hundred and twelve (113) cases of PJI were identified (63 hip, 50 knee) representing an infection rate of 1.13% (1.46% hips, 0.88% knees). Significantly increased risk of PJI was observed in: hip arthroplasty as compared to knee arthroplasty (odds ratio (OR) 1.58, 95%CI 1.06 to 2.34, p=0.02); increased BMI (BMI > 40kg/m² led to a 10 fold increase (OR 9.58, 95%CI 4.69 - 19.59, p<0.001) in risk of PJI compared to a BMI of 25 to 30kg/m²); male gender (OR 1.89, 95%CI 1.27 - 2.79, p<0.01) and blood transfusion within 30 days of primary surgery (OR 9.08, 95%CI 5.70 - 14.64, p=<0.001). A significantly reduced risk of PJI was observed with diabetes (OR 0.38, 95%CI 0.18 - 0.80, p=0.01).

Conclusions: This study found increased body mass index, male gender and post-operative blood transfusion to be significant patient risk factors for development of PJI. In the future this risk may be reduced pre-operatively by weight loss programs or through targeted strategies such as use of high-dose dual antibiotic cement for patients of high BMI. Further investigation is ongoing, but the lower risk of infection observed in diabetic patients may be confounded by several factors; for example, these patients may be the target of increased primary care health surveillance conferring an improved immune response, or there may be a cohort of undiagnosed diabetics.
USE OF A VANCOMYCIN-ELUTING BONE GRAFT SUBSTITUTE FOR LOCAL ANTIBIOTIC DELIVERY IN ONE-STAGE REVISION OF AN INFECTED TOTAL FEMORAL REPLACEMENT. A CASE REPORT

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Aim: To report our experience with local delivery of Vancomycin with a synthetic bone graft substitute for single stage revision of an infected total femur prosthesis.

Method: A 73 year-old female was admitted to our department with a complex peri-prosthetic fracture of the right distal femur, located between a total knee replacement and a long revision hip prosthesis, implanted 3 and 7 years previously for osteoarthritis/prosthetic loosening respectively. We suspected that the fracture could be pathologic, because only a minor trauma caused the fracture, and the patient 4 years earlier was treated for breast cancer. She was initially treated with a total femur replacement retaining only the old acetabular component. Seven months post-operatively the patient showed signs of peri-prosthetic joint infection with knee pain, joint swelling and elevated C-reactive protein (CRP). A few weeks prior the patient had received a dental implant. Joint fluid aspiration established presence of non-hemolytic streptococcus mitis and intravenous Penicillin G and oral Rifampicin was initiated. All components of the total femoral replacement not anchored to bone were exchanged and after thorough debridement and lavage, 20mL of a Vancomycin-eluting bone graft substitute was placed around the entire length of the femoral component and into the trabecular metal surface of the proximal femur. Initial postoperative treatment with intravenous Cefuroxime and oral Rifampicin was changed at discharge to oral Rifampicin and Penicillin V as intraoperative cultures had shown no bacterial growth. CRP and leukocytes normalized within 3 months and antibiotic treatment was concluded after 4 months.

Results: 15 months postoperatively, the patient remains pain free, mobile with 2 crutches and still without any clinical signs of infection and normal CRP.

Conclusions: Peri-prosthetic infection after insertion of mega-prostheses and especially total femur replacements are challenging, and often leads to chronic infection and life-long antibiotic therapy or amputation. This case report illustrates the application of an antibiotic-eluting bone graft substitute for one-stage revision of an acutely infected mega-prosthesis, where local delivery of high local antibiotic concentrations may have contributed to eradication of residual organisms and prevention of colonization and biofilm formation on the newly inserted mega-prosthesis.

1) CERAMENT™©BONESUPPORT AB
2) Segmental, Zimmer-Biomet
THE CURRENT CLASSIFICATION SYSTEMS OF OSTEOMYELITIS

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Aim: The aim of this systematic review is to identify available classification systems of osteomyelitis that have been presented within the literature. We aim to analyze their usefulness and shortfalls from today’s view in clinical practice.

Method: The MEDLINE, EMBASE, Ovid and the Cochrane databases were searched for classification systems relating to bone and joint infection. Any classification systems found that related to long bone osteomyelitis were included. Classification systems which focused on vertebral osteomyelitis, maxillofacial osteomyelitis or diabetic foot disease were excluded.

Results: From the original search and review of references, 342 articles were retrieved. There were 144 duplicate publications and a further 198 publications did not meet the inclusion criteria and were excluded. 13 therefore met the inclusion criteria and were reviewed in full. A summary of the results are shown in table 1. None of these classification systems are commonly used. The most commonly

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Table 1
cited are the Cierny and Mader and the Waldvogel systems. Although there has been modification in recent years, both of these classification systems are over 30 years old and in parts, outdated. Furthermore, there is a lack of evidence supporting their clinical effectiveness.

Conclusions: On a patient level, none of the classification system include current multidisciplinary treatment modalities in a clinically practical way. Treatment concepts cannot be meaningfully evaluated as study groups may be too heterogeneous. Without stratifying patients according to the extent of their disease, accurate information regarding treatment options and prognosis cannot be given. On an institutional level, the absence of an accepted classification system for long bone osteomyelitis means that remission rates and disease prognosis are not easily comparable between studies or centres. These conclusions indicate that there is a need for new classification system.
[P62] ANTIBIOTIC-LOADED CALCIUM SULFATE BEADS TO PREVENT PROPIONIBACTERIUM ACNES BIOFILM FORMATION IN VITRO

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**Aim:** Owing to its ubiquitous nature as part of the human bacterial skin flora, *Propionibacterium acnes* isolation from clinical specimens is often considered a contaminant. However, an increasing body of literature implicates *P. acnes* in invasive infections, including prosthetic infections (PIs) following joint arthroplasty, with biofilm formation a key virulence factor. The biofilm phenotype permits evasion of the host immune system and confers antibiotic tolerance thus allowing the establishment of chronic infection. The intraoperative use of absorbable beads, such as pharmaceutical grade calcium sulfate (PG-CS), has been reported to show localised, long-term release of high concentration antibiotics at the site of infection. In this study, we investigate their release kinetics and antibiofilm efficacy.

**Method:** *P. acnes* ATCC 11827 was characterised in terms of its biofilm forming capacity and its resistance to vancomycin and tobramycin against planktonic and biofilm bacteria, a broad spectrum antibiotic combination commonly used in bone cements by orthopaedic surgeons in the U.S.A to target MRSA and gram negative PI pathogens. While these antibiotics are not normally prescribed for *P. acnes*, it is likely that it might sometimes be present, even if not diagnosed by clinical culture due to its slow growth. First, agar diffusion assays were used to determine the release and potency of these antibiotics from synthetic PG-CS and poly(methyl methacrylate) (PMMA) beads against *P. acnes* over time. The PG-CS beads were further evaluated for their ability to prevent bacterial colonisation and biofilm formation in the presence of regular bacterial challenges over 14 days using viable cell counts, confocal and scanning electron microscopy.

**Results:** *P. acnes* was shown to form substantial biofilms over 7 days displaying over a 1000 fold increased tolerance to tobramycin and vancomycin compared to the planktonic phenotype. Agar diffusion assays showed antibiotic release from PG-CS beads was maintained for 60 days, corresponding to complete bead absorption. PMMA beads showed antibacterial efficacy for 111 consecutive days. Antibiotic-loaded PG-CS beads killed planktonic cultures of $10^6$ CFU/ml, prevented bacterial colonisation over multiple days and significantly reduced biofilm formation over a period of 14 days.

**Conclusions:** Antibiotic-loaded PG-CS beads have potential to reduce or eliminate *P. acnes* biofilm formation by providing locally high concentrations over extended time periods. Due to the slow growth rate and biofilm forming capacity of *P. acnes*, sustained and localised high concentrations of antibiotics may offer significant benefit to a PI management strategy.
CASE REPORT: BONE RECONSTRUCTION FOLLOWING BONE LOSS OF 18 CM FOLLOWING OPEN FRACTURE OF THE TibIA USING ANTIBIOTIC ELUTING CERAMIC BONE VOID FILLER

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Aim: Bone loss following infection remains to be a surgical challenge, especially in cases of extensive osteomyelitis. Due to the rarity of these cases, management needs to be flexible and individualized approaches need to be implemented.

Method: Here we present a clinical case with osteomyelitis of the tibia following fracture treatment alio loco leading to partial bone loss of about 18 cm.

Results: A 38-year-old patient presented himself to our outpatient clinic following multiple surgical attempts alio loco to sanitize bone infection following 2nd degree open fracture of the tibia about 4 months ago. Treatment of the fracture was conducted alio loco applying internal fixation. Following initial treatment, wound healing was delayed and resulted in deep infection. Soft tissue infection management alio loco included multiple debridements. Upon presentation in our department, our assessment included MRI scanning and showed osteomyelitis of the tibia of about 18 cm. Our treatment plan included infection management, followed by reconstruction management. Infection management included radical bone debridement, antibiotics and soft tissue management. We decided to keep the dorsal corticalis in situ and conduct fenestration of the tibia by resection of more than 60% of the circumference of the long bone. This resulted in a partial bone loss of about 18 cm. Soft tissue debridement induced necessity for free flap transfer. We used antibiotic eluting ceramic bone void filler application to conduct reconstruction of the bone defect. Our technique resulted in stable bone reconstruction 6 months following surgery without sign of reinfection.

Conclusions: Here we present the case of open fracture related osteomyelitis resulting in bone loss of the tibia. The individualized treatment plan included infection management and reconstruction management, using free flap transfer and antibiotic eluting ceramic void filler.
INVESTIGATION OF A POTENTIAL VANCOMYCIN RESISTANT ENTEROCOCCUS OUTBREAK IN OUR ORTHOPAEDIC UNIT

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Aim: Vancomycin Resistant Enterococcus (VRE) is endemic in our hospitals and is associated with hospital acquired infections and outbreaks. Outcomes of deep VRE infections are poor and rates are increasing. Successful treatment of VRE prosthetic joint infections (PJI) is extremely challenging due to a combination of pathogen specific virulence factors, limited antibiotic options and often host factors. Infection prevention and control is therefore paramount in reducing the risk of this nosocomial complication.

Method: We describe the investigation of a potential outbreak of VRE PJI in our unit after an unexpected case was diagnosed in a host without classic risk factors, at the same time as two other patients with VRE infected metal work were being treated.

Results: The microbiology database was interrogated to identify the total number of cultures positive for Enterococcus species from all clinical specimens sent from the orthopaedic wards in the preceding 6 years (2010-2015). A significant increase in the number of cultures from which Enterococcus sp. was isolated, both vancomycin sensitive and resistant, was seen over this time period. Isolates from deep clinical specimens which had been retained were sent for typing. 2 of the patients under investigation were found to have a unique strain, new to our institution but different to other patients with VRE PJI. Tracking of these patients’ movements through the hospital identified a period of 4 days when they were in opposite beds in an open ward. Cross infection during this time was deemed the most likely explanation for the second case. Possible factors in transmission were systematically reviewed and addressed, including acting upon poor results from infection control audits of shared equipment, environment and hand hygiene.

Multidisciplinary review of infection control in the unit, review of general infection risk reduction measures, as well as review of the isolation policy and facilities available on the ward was completed. Education of staff was undertaken and ongoing infection control audits have revealed a sustained improvement in practice. Active surveillance of Enterococcal isolates from orthopaedic specimens is in place.

Conclusions: VRE PJI is challenging to treat and has poor outcomes. Active surveillance of orthopaedic infections enables earlier identification of problems which must be investigated thoroughly in a multi-disciplinary team.
Aim: Fungal prosthetic joint infection is a rare occurrence and challenging to treat. Risk factors for development of such infections include prolonged antibiotic therapy, immunosuppression and multiple surgeries. As patients with increasingly complex co-morbidities undergo arthroplasty, we may see an increase in incidence. There is little consensus in the literature to guide optimal management and practice varies widely; cases must be considered on an individual basis with management tailored accordingly though outcomes are often reported as poor. In contrast to some centres, we routinely culture prosthetic joint specimens specifically for fungi and report the findings of a retrospective review of all cases of fungal PJI over 10 years.

Method: Our microbiology database was interrogated for fungal isolates from all deep tissue, bone and joint fluid samples in orthopaedic arthroplasty patients over a 10 year period (2006-2015). We analysed case notes for diagnostic features, risk factors, surgical and microbiological interventions and outcomes and classed as definite or possible/probable infections based on recognised criteria. Culture results which appeared to represent contamination only rather than true infection were also recorded.

Results: A total of 103 patients were identified with positive fungal cultures from deep orthopaedic specimens over the 10 year period. 88 were rejected with 10 being from non-arthroplasty infections and 78 representing laboratory contamination of enrichment culture broths. 15 cases of fungal PJI were identified, 14 due to yeasts, with the most common species isolated being Candida albicans (6/14) and C.parapsilosis (6/14). Polymicrobial infection with bacteria as well as fungi was common and present in >50%. Management comprised a mixture of curative and suppressive approaches depending on the individual patient characteristics and estimated likelihood of success. Outcomes were worse in those with polymicrobial infections and multiple revisions. There was a high rate of contamination of surgical specimens with mycelia fungi in 2 peaks over the 10 year period which corresponded with known episodes of laboratory contamination.

Conclusions: This series highlights the complexities and difficulties of appropriately diagnosing and managing patients with fungal PJIs. As diagnostics for fungal infection improve, including systemic markers for invasive disease, the accuracy of diagnosis should improve and subsequently so should our understanding of the relative merits of different treatment strategies.
**Aim:** This abstract describes a new EU HORIZON 2020 project (no. 634588). In the last decades, an increasing number of antibiotic resistant bacterial pathogens have become an important problem worldwide. This includes also biofilm-associated pathogens, causing orthopedic prosthetic infections. Therefore, the search for new bioactive agents that will be effective against bacteria in their two stages of life (planktonic and biofilm forming) is of high priority. The overall objective of this project is to search for such bioactive agents from the largest EU microalgae collection.

**Method:** Fifteen partners from 8 different European countries are working together in order to search for antibacterial agents produced by microalgae. For this purpose, 4000 microalgae species will be deeply screened specifically for new antibacterial molecules. Structural elucidation of these molecules will ensure that only new chemical entities will go to further project stages. It is anticipated that that new chemical entities also will show new mechanisms of antibacterial action. The next stage of the project is to test the toxicity level of selected molecules by using the *C. elegans* model. Selected hit molecules will be meticulously and accurately assayed at the cellular and molecular level. These studies will allow us to determine the cellular process affected in biofilm-forming pathogens. Finally, the effect of the most promising molecules (n=3-5) will be tested *in vivo* by using a porcine model for prosthetic and implant associated bone infections. Anti-biofilm molecules will also be incorporated into nanoparticles in order to develop methodologies able to incorporate these compounds into prosthetic devices matrixes, which will again be analyzed in the porcine model.

The project is scheduled for 4 years ending in March 2019. The final budget for the NOMORFILM project is 7.6 million Euros. The project entails trans-disciplinary actions between microbiologist, chemists, doctors, veterinarians, cell biologist, molecular biologist, and experts on nano-biomaterials. Five industrial companies and ten European Universities are involved.

**Results:** At the moment the project is in the initial phase of screening microalgae and analyzing selected hit molecules.

**Conclusions:** We expect to isolate new pharmaceutical molecules with anti-biofilm activities *in vitro* and *in vivo*. These molecules are expected to be used in clinical studies and thereby represent a new family of antimicrobial compounds.

**To know more about the NoMorFilm project:**

**Webssite:** www.nomorfilm.eu

**Facebook:** facebook.com/NoMorFilm/

**Twitter:** #NoMorFilm
ASSOCIATION OF VITAMIN D RECEPTOR GENE TaqI, BsmI, Foki AND ApaI POLYMORPHISMS AND SUSCEPTIBILITY OF EXTREMITY CHRONIC OSTEOMYELITIS IN CHINESE POPULATION

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Aim: Previous studies have indicated that vitamin D receptor (VDR) TaqI, BsmI, Foki and ApaI gene polymorphisms are associated with the risk of several inflammatory diseases. However, potential association of the VDR gene polymorphisms with susceptibility to extremity chronic osteomyelitis remains unclear. The present study aimed to investigate link between VDR gene polymorphisms and the risk of extremity chronic osteomyelitis in Chinese population.

Method: A total of 233 patients with extremity chronic osteomyelitis and 200 healthy controls were genotyped for the 4 single-nucleotide polymorphisms (SNPs) (TaqI, BsmI, Foki and ApaI) in VDR gene using the SNaPshot genotyping method.

Results: The frequencies of mutant allele C in rs731236 (P = 0.044, OR = 1.830, 95% CI 1.009 - 3.319) and rs2228570 (P = 0.041, OR = 1.336, 95 % CI 1.012 - 1.764) were significantly higher in patients than those in healthy controls. In addition, outcomes of the logistic regression analysis adjusted by gender and age revealed that significant links were found between rs731236 (P = 0.05, OR = 1.887, 95% CI 1.001 - 3.558), rs2228570 (P = 0.042, OR = 1.594, 95 % CI 1.016 – 2.500) and the risk of developing chronic osteomyelitis by dominant genetic model. However, no significant associations were found between BsmI (rs1544410) or ApaI (rs7975232) gene polymorphisms and the susceptibility to the disease.

Conclusions: To our knowledge, we reported for the first time that VDR gene TaqI (rs731236) and Foki (rs2228570) polymorphisms may contribute to the increased risk of chronic osteomyelitis in Chinese population.
Aim: The making of a NINJA: to report a local initiative to set up a regional prosthetic joint infection (PJI) network in the Northern Netherlands. (NINJA: Northern Infection Network Joint Arthroplasty).

Method: In the Northern part of the Netherlands there are 22 hospitals performing joint arthroplasty. The insurance companies and the health care inspection are continuously pushing hospitals to focus on certain areas and they do not make contracts any more with some of our regional hospitals for infection care. The University hospital alone cannot handle the increasing amount of patients with PJI given the complexity and the associated costs. A managed clinical network (MCN) was designed and installed consisting of various levels of experience and collaboration in patient care and clinical research.

Level A is every general hospital, treating their own early PJI with a DAIR, in case of persistent infection and indication for total revision patients are sent to level B or C. Level B: 4 hospitals doing septic revisions, Level C is a university hospital for ASA 3-4 patients with PJI or PJI with multi-resistant microbes or fungus PJI.

Results: The first experience is satisfactory. Local clinicians have a low threshold to ask for advice or refer to level B or C expertise.

Conclusions: A regional MCN for PJI creates a win-win situation for all participants: patients, doctors, insurance companies, health care inspection and hospital management.
Aim: To report on the initiative of development of common European guidelines for imaging in diagnosis PJI.

Method: Via the Oxford guidelines 2011 according to PICO method 25 statements have been developed concerning imaging in the diagnosis of PJI and a systematic review has been done by the European Association of Nuclear Medicine, European Society of Radiology, EBJIS and endorsed by the European Society of Clinical Microbiology and Infectious Diseases.

Results: Based on the systematic review, advise will be provided including a flowchart for imaging in diagnosis of PJI.

Conclusions: The systematic review is ongoing, aim of this abstract is to report this initiative and share the present status of this project.
Aim: Periprosthetic joint infection is one of the major causes of morbidity following total knee arthroplasty (TKA). Although its incidence is less than 1%, it has significant clinical, psychological, and financial impacts. Two-stage protocols have traditionally been considered the ‘gold standard’, with one-stage revision for infection still in its relative infancy, performed at select centres with appropriate expertise and resources. Although there is no clear evidence in the literature which is definitively associated with better outcomes, single-stage procedures are advantageous in terms of overall hospital stay, cost, and patient satisfaction. The objective of this study was to determine whether the results of one-stage revision for infected TKA were comparable or better than the published rates for two-stage procedures.

Method: We reviewed 80 consecutive patients (41 males, 39 females; mean age, 72 years) who underwent one-stage revision TKA for infection at our institution between 2008 and 2014. All procedures were performed by the senior author, with a defined débridement protocol and immediate single-stage exchange (as opposed to a 2-in-1 protocol). Reconstruction and fixation was by a predominantly uncemented method. The infective organism(s) were identified in 65 patients (81.25%), with antibiotics targeted post-operatively as per culture and sensitivity profiles where available, and with microbiology advice in all cases.

Results: 73 patients (91.25%) were infection free at most recent follow-up. 7 recurrences (8.75%) were noted, and 4 of these cases eventually underwent limb salvage with knee arthrodesis. No amputations were performed and no patients were lost to follow-up.

Conclusions: One-stage revision for infected TKA, performed according to a specific protocol in a tertiary centre with multidisciplinary input, is equivalent to the best outcomes reported for two-stage revisions. If further studies support these findings, it is our opinion that it will become the treatment strategy of choice for similar centres and high volume revision arthroplasty surgeons.
Aim: We present a highly drug resistant case of Viridans group Streptococcus (VGS) causing periprosthetic joint infection. A 60-year old female underwent routine gamma nailing of the right hip after sustaining a right intertrochanteric femur fracture. One month post-operatively, the patient presented with increasing pain in the right hip and acutely elevated C-reactive protein. Right hip aspirate yielded a positive culture for two strains of multi-drug resistant VGS identified as S. mitis.

Method: Whole genome sequencing (WGS) of pure culture isolates was performed on the Sequencing System* at the National Microbiology Lab (Winnipeg, Manitoba). Organism identification was confirmed by 16S polymerase chain reaction (PCR) and whole genome sequencing (WGS). Susceptibility was done several times using broth microdilution methods. All interpretations are based on the Clinical & Laboratory Standards Institute (CLSI) M100-S26 document. Bioinformatic analyses of the genomic sequences, including detection of carbapenemases and analysis of penicillin-binding proteins (PBPs), was used to investigate the mechanism of resistance.

Results: Susceptibility by broth microdilution revealed both isolates to be resistant to penicillin (minimum inhibitory concentration, MIC 4 ug/mL), ceftriaxone (>2), cefotaxime (4), and cefepime (4). Both strains exhibited non-susceptibility to cefuroxime (>4), ertapenem (2), meropenem (2), and imipenem (0.5). One strain was also non-susceptible to daptomycin (2). All susceptibilities were verified several times with no contamination of purity plates. Both strains maintained susceptibility to non-beta lactam agents such as vancomycin, clindamycin, linezolid, and levofloxacin. The patient was treated with an extended course of clindamycin due to its high oral bioavailability and osteoarticular penetration. At almost one year post debridement and treatment, the patient has been successful in retaining the joint. No proteins with homology to β-lactamases or carbapenemases were present in the genome sequence of the isolates. The sequences of the β-lactam target proteins PBP2x and PBP2b were similar to those from strains with high β-lactam MICs (penicillin and cephalosporin MIC, no data for carbapenems). In particular, PBP2x from our isolates contained 16 amino acid variations that were associated with reduced β-lactam susceptibility.

Conclusions: This case illustrates the potential for VGS organisms to be multidrug resistant highlighting the importance of traditional susceptibility testing (as opposed to presumed susceptibility to beta-lactams as in beta haemolytic Streptococci or molecular detection of known resistance genes) of isolates from sterile sites. The prevalence of carbapenem resistant VGS is not widely published as carbapenems are not frequently tested against these organisms.

* Illumina MiSeq platform
A PROSPECTIVE COMPARATIVE STUDY OF PIN SITE INFECTION IN PEDIATRIC SUPRACONDYLAR HUMERAL FRACTURES. DAILY PIN CARE VS. NO PIN CARE

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**Aim:** Pin site infection is a critical issue for patients’ safety in skeletal fixation using percutaneous pins or wires. Closed reduction and percutaneous Kirschner wires fixation are the mainstay of treatment in pediatric supracondylar humeral fractures. Little information is available in the literature about the optimal regimen of pin site care in children.

**Method:** We performed a prospective comparative study of 61 children with supracondylar humeral fractures between June 2011 and March 2013 after approval by the institutional review board. They were allocated into two groups of different postoperative pin site care methods by the emergency department arrival date and received fracture fixation within 24 hours. Postoperatively, 30 children underwent pin site cleaning every day whereas the other 31 patients did not have the pin sites cleaned until the pins removal 4–6 weeks later.

**Results:** Demographic data were not significantly different between the two groups. The infection rate was significantly higher in patients who underwent daily pin site care (90.3% vs. 53.3%, p=0.001). Of the 144 pin sites, infection occurred at 42 (57.5%) pin sites in the daily care group and at 19 (26.8%) pin sites in the non-care group. The number of telephone consultations for postoperative care was significantly higher in the daily care group (1.0 call/case vs. 0.27 call/case, p=0.007).

**Conclusions:** Daily pin site care was associated with a higher infection rate and greater stress in postoperative care that required more telephone consultations. The study results could not support daily pin site care. Careful observation of pin sites was recommended in the treatment of pediatric supracondylar humeral fractures.
SYNOVIAL FLUID D-LACTATE MEASUREMENT FOR EARLY DIAGNOSIS OF PROSTHETIC-JOINT INFECTION

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The diagnosis of Prosthetic-Joint Infection (PJI) is extremely difficult due to presentation and preoperative tests are not always obvious and precise, while correct and timely diagnosis is crucial. In this way, it is relevant to test and evaluate of analytical performance characteristics and diagnostic capabilities of the new diagnostic test for PJI. The test is based on the measurement of synovial fluid D-lactate, produced by the microbial enzymes.¹,²,³

Aim: To assess analytical performance characteristics and diagnostic capabilities of the method to determine D-lactate levels in the synovial fluid for the early diagnosis of Prosthetic-Joint Infection (PJI). ⁴

Method: Forty patients undergoing removal of a total knee or hip prosthesis at the Federal Center of Traumatology, Orthopedics and Endoprosthesis Replacement, Barnaul, Russia, were included in the study. Twenty had aseptic failure and twenty had PJI. The diagnosis of PJI was evaluated in accordance with the following criteria of infection.⁵

Results:

Table 1. Characteristics of the patients

<table>
<thead>
<tr>
<th>Test</th>
<th>Patients with PJI (n=20)</th>
<th>Patients with Aseptic Failure (n=20)</th>
<th>Value p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr - mean ± SD</td>
<td>61,1±10,8</td>
<td>55,75±12,38</td>
<td></td>
</tr>
<tr>
<td>Male, n (%) - %</td>
<td>6 (30)</td>
<td>9 (45)</td>
<td></td>
</tr>
<tr>
<td>Site of arthroplasty</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Knee (n=15) (%)</td>
<td>6 (30)</td>
<td>9 (45)</td>
<td></td>
</tr>
<tr>
<td>- Hip (n=25) (%)</td>
<td>14 (70)</td>
<td>11 (55)</td>
<td></td>
</tr>
<tr>
<td>Synovial fluid: nucleated cells count/µl - mean ± SD</td>
<td>217,5 ± 190,84</td>
<td>66850 ± 45026,2</td>
<td>p&lt;0,001</td>
</tr>
<tr>
<td>differential, neutrophils% - mean ± SD</td>
<td>2,25 ± 5,35</td>
<td>94,3 ± 3,81</td>
<td>p&lt;0,001</td>
</tr>
<tr>
<td>Blood leukocyte count - mean ± SD</td>
<td>5,94 ± 1,22</td>
<td>8,77 ± 3,06</td>
<td>p&lt;0,001</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate - mean ± SD</td>
<td>12,1 ± 8,3</td>
<td>48,11 ± 33,76</td>
<td>p&lt;0,001</td>
</tr>
<tr>
<td>Serum C-reactive protein: - mean ± SD</td>
<td>3,11 ± 1,62</td>
<td>48,78 ± 54,80</td>
<td>p&lt;0,001</td>
</tr>
<tr>
<td>Synovial fluid D-lactate - mean ± SD</td>
<td>0,42 ± 0,38</td>
<td>2,50 ± 0,68</td>
<td>p&lt;0,001</td>
</tr>
</tbody>
</table>
ROC analysis showed that the analytical sensitivity and specificity of the method at the separation threshold = 1.05 mmol/L comprised 92.6% and 96.8%, respectively (with their optimal ratio). Specificity of the method was 100% at the threshold concentration of D-lactate = 1.59 mmol/L, which is achieved at the cost of reducing the sensitivity to 74.1%. Thus, the use of threshold concentration of D-lactate = 1.05 mmol/L achieves the optimal correlation of sensitivity and specificity with their satisfactory high values.

**Conclusions:** Thus, the studies have demonstrated high analytical performance characteristics and diagnostic capabilities of the method to determine D-lactate levels in the synovial fluid for the early diagnosis of PJI. We suppose that the optimal value of the threshold concentration of D-lactate in synovial fluid is between 1.05 and 1.59 mmol/L (the first value can be used for screening analysis, the second - to confirm the diagnosis of PJI).

MUSCULOSKELETAL INFECTIONS DUE TO NON-TUBERCULOUS MYCOBACTERIA – CASE SERIES FROM A TERTIARY REFERRAL CENTRE

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Aim: The diagnosis and management of musculoskeletal infections due to non-tuberculous mycobacteria (NTM) is challenging. We describe the experience of culture positive cases that were managed at the Oxford Bone Infection Unit.

Method: We retrospectively identified from the laboratory information management system all cases with tissue or bone specimens from which NTM were cultured between 01/01/1994 and 31/12/2012. Further clinical information was then obtained by reviewing paper and electronic patient records.

Results: We identified 43 cases with at least one positive culture for NTM. In 8 of these cases NTM were considered to be contaminants. Clinical information was unavailable for a further 4 patients. A total of 31 patients were therefore included in the analysis, including 3 patients with >1 culture.

Median age was 54 years (range 18-91); 17 (63%) were male, 5 (19)% were born outside the UK. Median time from onset of symptoms to diagnosis was 4 months (range 0.25 to 48 months). 22% patients were treated with multiple courses of conventional antimicrobials before referral to our department.

Sites of infection included the upper limbs (25), lower limbs (10) and spine (1). 4 patients had multifocal disease. Ten (32%) were soft tissue infections, 9 (29%) tenosynovitis, 7 (22%) native joint infections, and 5 (16%) osteomyelitis.

Histopathology was performed in 14 (45%) cases and showed granulomas and acid fast bacilli in 11 and 3 cases, respectively. Species distribution was as follows: M. marinum 12 (39%), M. chelonae 6 (19%), M. avium intracellulare complex 5 (16%), M. kansasii 5 (15%), M. malmonsae 2 (6%), M. fortuitum 1 (3%). Sensitivities were available in 27 (87%) cases.

A history of domestic fish exposure was elicited in 92% M. marinum cases. 12 patients (44%) were immunosuppressed including 10 on steroid treatment. 17 (54%) patients had surgery, including excision biopsy, tenosynovectomy or debridement. Antimicrobial therapy duration varied according to species and ranged from 1-24 months (median 4.5 months). Two patients relapsed following treatment.

Conclusions: Prompt diagnosis and appropriate management of NTM musculoskeletal infections requires careful clinical assessment and multi-disciplinary input. Current treatment guidelines are informed by limited data from extra-pulmonary infections and therefore draw on experience treating pulmonary disease. Further studies are needed to establish standard case definitions and treatment guidelines for patients with musculoskeletal NTM infections.
[P75] FIRST REPORT OF ISOLATION ESBL-PRODUCING PROVIDENCIA RETTGERI FROM A MULTIGERMAL CONTAMINATED OPEN FRACTURE

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²Kages, Department of Trauma Surgery, Graz, Austria

Aim: The aim is to report about our experiences.

Method: Case report

A young and healthy man had a motorcycle trip through Pakistan. In the outback he had an awful accident and suffered an open distal femur fracture and a proximal tibia fracture at his left limb.

To reach the nearest hospital he was cared by a swine transporter. When the patient reached the hospital he decided, after first aid, to leave and reverse to Austria.

Results: We found ESBL-producing Providencia rettgeri, Acinetobacter baumanii, ESBL-producing Proteus mirabilis and Alcaligenes faecalis, Enterococcus faecium, Enterococcus galinarum, Klebsiella Pneumoniae, Leuconostoc sp., and two different species of Pseudomonas aeruginosa with different resistances.

Conclusions: After a quite intense multimodal treatment with repeated surgeries and high dose antibiotic medication we could save the limb.
EFFECT OF SONICATION ON THE ELUTION OF ANTIBIOTICS FROM POLYMETHYL METHACRYLATE (PMMA)

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Aim: In the setting of prosthetic joint infections treated with two-stage procedure, spacers are generally sonicated after removal to look for persistent infection. We hypothesize that the sonication process may cause an increased elution of antibiotics, leading to elevated concentrations in the sonication fluid inhibiting bacterial growth. We aimed to evaluate in vitro the influence of sonication on the elution of antibiotics from polymethyl methacrylate (PMMA) over time and to determine whether these concentrations are above the minimum inhibitory concentration (MIC) for microorganisms relevant in prosthetic joint infections.

Method: PMMA blocks impregnated with vancomycin, fosfomycin, gentamicin or daptomycin were incubated in phosphate-buffered saline (PBS) at 37°C for up to 6 weeks. PBS was changed once a week in order to mimic human conditions. Concentrations were determined from samples of each antibiotic every week, and after 5 minutes of sonication at 2, 4 and 6 weeks.

Results: A burst release was observed during the first week for fosfomycin, gentamicin and daptomycin with concentrations 13-30 times higher the MIC for most bacteria. Concentrations of gentamicin and daptomycin remained above the MIC after 6 weeks, while fosfomycin became undetectable at 6 weeks. Release of vancomycin was stable over the 6 weeks with concentrations twice above the MIC. With sonication process, there was a trend toward an increase in the elution of antibiotics as shown in Figure 1.

Conclusions: The effect of sonication could play a role in clinical results, especially for daptomycin and gentamicin for which the MIC is close to the concentration of antibiotics at 4 and 6 weeks. We assume that elution of antibiotics from PMMA along with the effect of sonication could inhibit bacterial growth from spacers, resulting in false negative results in the setting of two-stage exchange procedures for prosthetic joint infections.

Acknowledgements: Source of funding: Heraeus Medical
Figure 1. Antibiotic release in PBS at 37°C during 6 weeks. Mean and standard deviation of triplicate experiments. * indicates statistical significance (p < 0.05).
DIAGNOSIS OF INFECTION IN FRACTURE NON-UNION: A PRELIMINARY EVALUATION OF HISTOLOGY, MICROBIOLOGY AND CLINICAL FEATURES

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Aim: Infection is a significant cause of non-union, but diagnosis can be difficult. Radiological investigations do not help to differentiate the two. We investigated histology in establishing the diagnosis of infection.

Method: 53 patients with established non unions were studied. Infected non-union was present when there was an active sinus, intraoperative purulence or when microbiological cultures were positive. Aseptic non-union was diagnosed when there were no active sinuses, no risk factors, and no positive cultures. Patients with previous open fractures or other clinical risk factors for infection (not draining sinus) but with negative cultures were regarded as having possible infected non-union. Histological specimens taken at open surgery for the non-union were examined by a specialist osteoarticular pathologist and defined as positive when features were in keeping with active infection (acute inflammatory infiltrate, positive Gram stain), and negative when features were not in keeping with active infection. The accuracy of histology was then determined in the three groups.

Results: Infected non-union was diagnosed as above in 24 patients. 8 patients had no features of infection. 21 patients had possible infection. Histology confirmed the presence of infection in 17 of 24 infected non-unions. It confirmed the absence of infection in all 8 aseptic non-unions, with no false positives. This gave a sensitivity of 70.8% (95% CI, 48.6-86.6% ) and specificity of 100% (95% CI, 59.8 – 100%). The predictive value of a positive test was 100% and of a negative test was 53.3 %. In the 21 patients with clinical risk factors for infection but negative microbiological cultures, histology suggested an infected non-union in only 2 cases.

<table>
<thead>
<tr>
<th>Infected Non-union</th>
<th>Positive</th>
<th>Possible</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histology positive</td>
<td>17</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Histology negative</td>
<td>7</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>24</td>
<td>21</td>
<td>8</td>
</tr>
</tbody>
</table>

Conclusions: In our series, histology was highly specific. Histology conclusively established the diagnosis of infection in definite infected non-unions. It may be useful when clinical diagnosis is inconclusive and microbiological cultures are negative.
Aim: The combination of calcium sulfate (CS) with antibiotics is increasingly being used in periprosthetic joint infection, trauma and lower extremity osteomyelitis1-3. The approved indication of CS as a medical device is to fill bony voids or defects and may be used at an infected site. The addition and release of antibiotics is ancillary to its function as a void filler. It is important to understand the effect the antibiotic has on the physical properties of CS. Any added antibiotic that may reduce the compressive strength may lead to faster absorption and as a result, a more rapid release of the drug. Investigations have already been carried out on the changes to setting time of CS but the effect the antibiotics may have on compressive strength have not yet been documented.

Method: A commercially available recrystallised calcium sulfate* (RCS) was mixed (unloaded) as a control and with 1g vancomycin or 240mg gentamicin, tobramycin (liquid) and a vancomycin/gentamicin (VG) liquid combination per 20g RCS powder. Where a liquid antibiotic was used, the aqueous mixing solution was discarded and the liquid antibiotic used as the hydrating agent. For each of the tested variants formed into 3mm diameter beads, 7cc was then loaded into a steel test chamber and compressed to 500N with a static materials mechanical testing machine. The compressive strain was calculated at 5, 15, 30 and 60 minutes from the start of mixing. Each variant was tested in triplicate and the results averaged.

Results: All increase in strength from 5-60 minutes. Compressive strain was not significantly different for antibiotic combinations tested compared to control, except VG loaded beads were significantly weaker at the 15 minute time point compared to control (P 0.0309). However, at 5, 30 and 60 minutes there was no significant difference identified.

Conclusions: Addition of the antibiotics tested does not significantly affect the compressive strength of RCS beads. The mechanical integrity of RCS is not compromised allowing predictable absorption and elution. Addition of the two antibiotics VG does not compromise strength. Investigations into other antibiotics is warranted.

References:
3. Gauland C.J. Advances in Skin & Wound Care Issue: Volume 24(11), November 2011, pp 515-523

*Stimulan Rapid Cure, Biocomposites Ltd.
Aim: Antibiotic-loaded bone cement (ALBC) is widely used in orthopaedic surgery for both prevention and treatment of infection. Little is known about the effect of antibiotic and bone cement brands on the elution profile and mechanical strength of ALBC.

Method: Standardized specimens consisting one of four brands of bone cement and one of three brands of vancomycin were fashioned, producing 12 combinations of ALBC. Two dosages of vancomycin in 40g bone cement were used to represent the high (4g vancomycin) and low (1g vancomycin) dose groups. The ALBC are immersed in phosphate buffer solution at 37°C and the surrounding fluid was exchanged completely at fixed time points. Concentrations of vancomycin in the fluid were measured using fluorescence polarization immunoassay for up to 336 hours. The ultimate compression strength was tested in axial compression using material testing machine.

Results: Lyo-Vancin in bone cement* and Sterile Vancomycin in bone cement* resulted in the highest cumulative elution in high and low dose groups, respectively. Vanco in bone cement** resulted in the lowest elution in both groups. Vancomycin elution from Lyo-Vancin in bone cement* (31,015 ± 6,317.54 ug) was 452% greater than that of Vanco in bone cement** (5,615 ± 314.65 ug) in the high-dose group, and Sterile Vancomycin in bone cement* (2315 ± 489.66 ug) was 65% greater than it was in the Vanco-bone cement combination (1,246 ± 160 ug) in the low-dose group. The mechanical strength was not significantly compromised in all groups with low dose vancomycin. However, with the addition of high dose vancomycin, there was a mixed amount of reduction in the ultimate compression strength after cement aging, ranging from 2.5% (Vanco in bone cement**) to 34% (Sterile vancomycin in bone cement***).

Conclusions: The selection of brands of vancomycin and bone cement has an important impact on the release efficacy and mechanical strength of ALBC.

*PALACOS
**Simplex P
***Osteobond
Aim: There is a high unmet medical need for novel therapeutic options against bone and joint infections, medical devices infections and endocarditis. These infections are chronic and hard to treat mostly because the offending bacteria are in a ‘persister’ state, a specific metabolic state where they are resistant to high concentrations of antibiotics but are not genetically resistant.

Method: We aimed to identify small molecules specifically killing staphylococci persisters (Staphylococcus aureus, Staphylococcus epidermidis), which would be used in combination with standard antibiotics to cure the hard-to-treat infections where staphylococci are the most frequent culprit. A high throughput phenotypic screening has successfully identified such compounds. The results of the activities conducted to determine the mode of action of these compounds is described here.

Results: The impact of compounds on macromolecules synthesis was assessed. Syntheses of DNA, RNA, proteins and peptidoglycan were affected, suggesting that compounds have a central mechanism of action. Mutants resistant to the anti-persister activity of the compounds were selected. Next generation DNA sequencing was used to map the genetic loci responsible for resistance and the role of one locus was confirmed. Transcriptomic, proteomic, metabolomic and phenotypic microarray profiles of wild-type treated bacteria and of untreated resistant bacteria was assessed.

Conclusions: We found compounds able to eradicate staphylococcal persisters through a new mechanism of action altering bacterial metabolism
STAPHYLOCOCCUS LUGDUNENSIS: AN IMPORTANT CAUSE OF DEVICE-RELATED ORTHOPAEDIC INFECTION

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Aim: As a result of improved molecular diagnostics, Staphylococcus lugdunensis is increasingly identified in bone and joint infection. It shares phenotypic characteristics with Staphylococcus aureus, making it a potentially significant pathogen. We set out to investigate the contribution of Staphylococcus lugdunensis to orthopaedic infections, to describe the in vitro susceptibilities of these isolates, to characterise the patient group, to document the management approach, and to review preliminary outcome data.

Method: We studied patients admitted under elective and trauma orthopaedics teams in a large UK tertiary referral centre for complex orthopaedic infection. In the investigation of device-related infection we routinely take ≥5 independent intra-operative samples using separate sets of instruments. Recently, we have moved to molecular identification of staphylococci using mass spectrometry (Maldi-ToF) and automated susceptibility testing (Phoenix, BD). We interrogated electronic microbiology records for a 24-month period (April 2014 – March 2016) to identify Staphylococcus lugdunensis isolates from orthopaedic samples taken in the context of prosthetic material. Clinical data were extracted from the Electronic Patient Record (EPR).

Results: We identified 68 Staphylococcus lugdunensis isolates from 20 unique patients; 12M:8F; median age 64 years (range 35-89). Susceptibility data were reported for 66/68 isolates. Among these, there was no resistance to glycopeptides, daptomycin, oxacillin, rifampicin, clindamycin or linezolid.

The infected devices were prosthetic joints (n=10), fracture fixation metalware (n=8), and spinal fixation metalware (n=2). Of 9/20 patients treated with intra-venous antibiotics, 5 received a glycopeptide and 4 received ceftriaxone, for a median of 6 weeks. The commonest oral regimen was ciprofloxacin + rifampicin (n=8). The median total antibiotic duration was 12 weeks.

Surgical management strategies included removal of metalware or joint revision (n=12), or debridement and retention of metalware (n=4). The remaining four patients were managed conservatively with a biopsy followed by antibiotic therapy. At follow-up (median 125 days post-surgery), 15 patients had no reported clinical evidence of recurrent/recrudescent infection, one patient had persistent non-union and a decision was made to continue antibiotics. There were no follow-up data for three cases managed conservatively, and one case still awaits follow-up.

Conclusions: These data demonstrate a small but important contribution of Staphylococcus lugdunensis to prosthetic infections in the orthopaedic setting. There is currently equipoise over the optimum surgical approach and the choice, route and duration of antibiotic therapy. This preliminary study can be used to inform future efforts to enhance our understanding of this organism and to standardize treatment.
TUBERCULOUS OSTEOMYELITIS IN CHILDREN AND ADOLESCENTS. A FIVE YEARS CLINICAL STUDY

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Aim: Tuberculous osteomyelitis of the long bones in paediatric age group is not uncommon in countries where tuberculosis is endemic. In order to estimate its prevalence and to evaluate if there was any diagnostic, laboratory and radiographic clue at presentation, routine laboratory tests and radiographs were associated with an intraoperative biopsy for all the patients admitted from 2009 to 2014 with a diagnosis of generic osteomyelitis.

Method: In the period under review 1040 patients were admitted with a diagnosis of generic haematogenous osteomyelitis and enrolled in the study. The average age at presentation was 9.7 years; the youngest patient was 18 months old and the oldest 16 years. Radiographs of the involved segments and laboratory tests (CBC and ESR) were routinely obtained. Surgery was performed in all of them; biopsy specimen consisted of pyogenic membranes and bone chips harvested from the sequestra and medullary canal. Nine months long medical therapy (rifampicin, isoniazid, pyrazinamide and ethambutol) was instituted.

Results: Out of 1040, 89 patients, 51 males and 38 females, were diagnosed with tuberculous osteomyelitis. Seventeen patients had multiple sites involvement. In total 108 bones were involved. Tibia (46) and femur (28) were followed by humerus (18), fibula (6), radius (3), clavicle (2), metatarsals (2), heel (1), iliac bone (1) and phalanges(1). Clinical signs were quite aspecific, with swelling, local tenderness, pus discharging sinuses, exposed sequestra. Radiographic findings were variable and laboratory tests were aspecific. There was a moderate anaemia in all the patients and the ESR was raised in 44 patients; it was above 100 mm/hr in seven patients with multiple sites involvement. HIV test proved negative in 50 kids. The index case was not found for any of the patients. Diagnostic delay varied from 3 months to 5 years; it was 11 months on average. Histology was the clue for the diagnosis. All children were cured with surgery and medical treatment. Permanent sequelae included fused joints, limb length discrepancy, angular deformity.

Conclusions: Tuberculous osteomyelitis is uncommon but not rare in children, even in small ones. This study has shown a prevalence of 8.5%. This should alert the clinician managing osteomyelitis. Since there are no diriment clues offered by clinical history, laboratory tests or radiographic findings, intraoperative biopsy is mandatory in areas where tuberculosis is endemic.
Aim: The purpose of this report was to describe the frequency, clinical picture, diagnostics and outcome of infection with *Mycobacterium tuberculosis* among the patients with infective spondylodiscitis in Slovenia.

Method: Case records of patients with infective spondylodiscitis treated at the Department of Infectious Diseases, University Medical Centre Ljubljana, in years 1991 to 2015 were reviewed searching for patients in whom infection with *M. tuberculosis* was confirmed. The following data were recorded: age, sex, underlying diseases, epidemiological and clinical features, diagnostic examinations, and clinical course and outcome of the disease. The data were analysed using a statistical programme*.

Results: During the study period 5 (2%) out of 250 patients with spondylodiscitis, in whom infection with *M. tuberculosis* was confirmed, were analysed for the present report. There were three females and two males, aged median 58 (49-83) years. At the first presentation clinical findings such as back pain (lasting weeks or months), low grade fever, night sweats, weight loss, and lower extremity weakness were found. One of them had paraparesis of the legs. MRI was performed in all patients showed involvement of thoracic (1 patient), thoracolumbal (1 patient), and lumbar region (3 patients) with disc destruction and epidural abscess creating pressure on the spinal cord in 2 of them. In two patients spinal tuberculosis resembled neoplastic lesions on MRI. Active concomitant pulmonary infection with *M. tuberculosis* was also found in two of them. The diagnosis was established by culture and positive PCR *M. tuberculosis* complex in 3 patients, and by histology in the other 2 patients. The samples were obtained by biopsy. All of them received tuberculosis therapy, and surgical intervention was performed in 2 patients. The outcome of the disease was not favourable in all patients (one immunocompromised patient died).

Conclusions: Results of our study indicate that infection with *M. tuberculosis* in Slovenian patients with spondylodiscitis is rare. The diagnosis must be confirmed by histology and/or microbiological methods. The greatest challenge in diagnosis is to consider infection with *M. tuberculosis* especially in elderly when there is no evidence of active pulmonary disease, and diagnosis may be overlooked. Diagnosis and intervention at early stage avoids unnecessary delay in the treatment thereby reducing morbidity and possible complications.

* EpiInfo 6
Aim: The number of joint replacement surgeries performed has been increasing steadily. Prosthetic joint infection remains one of the most challenging complications of joint arthroplasty, both for diagnosis and treatment. There is no golden standard for the diagnostic work-up for prosthetic joint infection. Since the past few years synovial biomarkers are proposed to improve diagnostic accuracy of prosthetic joint infection. The objective of this review was to summarize the evidence on the accuracy of synovial biomarkers (C-reactive protein, interleukin-6, leukocyte esterase and alpha-defensin) for the diagnosis of prosthetic joint infection.

Method: We conducted a systematic review by searching electronic databases (Pubmed, Cochrane Library and Scopus) for articles published from 1996 to 2016. We included the studies with the highest level of evidence, according to the Oxford 2011 levels of evidence.

Results: We included 24 eligible studies that comprised 2647 revision arthroplasties. All four biomarkers showed high diagnostic value. Alpha-defensin had sensitivity (SE) 95.5%-100% and specificity (SP) 95%-100% (five studies), leukocyte esterase had SE 66%-100% and SP 77%-100% (five studies), CRP had SE 70%-97.3% and SP 78.6-100% (eight studies) and interleukin-6 had SE 62.5%-97% and SP 85.7%-100% (six studies).

Conclusions: The synovial biomarkers alpha-defensin, leukocyte esterase, CRP and interleukin-6 showed high diagnostic value in this systematic review. However, using these synovial biomarkers for diagnostic testing is expensive and not yet available in every hospital. Although these results are very promising, the articles in this review show a lot of variation in thresholds for the biomarkers. Based on these articles, we have made propositions for useful thresholds, but more research is needed to establish the accuracy of these thresholds before these biomarkers can be included in the work-up for diagnosing prosthetic joint infection.
INVESTIGATION OF THE ABILITY TO BE INTERNALIZED IN OSTEOBLASTS AS A PATHOPHYSIOLOGICAL MECHANISM INVOLVED IN STAPHYLOCOCCUS NON-AUREUS BONE AND JOINT INFECTION

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Aim: Implicated in more than 60% of bone and joint infections (BJIs), Staphylococci have a particular tropism for osteoarticular tissue and lead to difficult-to-treat clinical infections. To date, Staphylococcus aureus internalization in non-professional phagocytic cells (NPPCs) is a well-explored virulence mechanism involved in BJI chronicity. Conversely, the pathophysiological pathways associated with Staphylococcus non-aureus (SNA) BJIs have scarcely been studied despite their high prevalence.

Method: In this study, sixteen reference strains from 16 different SNA species were compared in terms of (i) adhesion to human fibronectin, a major protein of the extracellular matrix, based on adhesion microplate assays and (ii) internalization ability, intracellular persistence (by plate counting) and cytotoxicity (by quantifying lactate dehydrogenase (LDH)), based on an in vitro infection model using human osteoblasts. The atypic results concerning internalization obtained with S.pseudintermedius reference strain led us to also extend these experiments to 17 clinical isolates of S.pseudintermedius. The involvement of the subunit β₁ integrin in the invasion process of S.pseudintermedius in osteoblasts was evaluated by the use of murine osteoblasts (OB-β₁⁻/⁻ and OB-β₁⁺/⁺) with functional and deficient subunit β₁ respectively.

Results: Compared to S. aureus (100%), only two species were able to adhere significantly to human fibronectin: S. delphini (80±7.78%) and S. pseudintermedius (104±13.72%, p<0.05). S. pseudintermedius was also associated with high (even superior to S. aureus) internalization ability, intracellular persistence and cytotoxicity. These findings were confirmed using a panel of 17 different S. pseudintermedius isolates. Additionally, S. pseudintermedius internalization by osteoblasts was completely abolished in β₁ integrin-deficient murine osteoblasts. These results suggest the involvement of β₁ integrin in the invasion process, although this mechanism was previously restricted to S. aureus.

Conclusions: In summary, our results suggest that internalization into NPPCs is not a classical pathophysiological mechanism of SNA BJIs. S. pseudintermedius appears to be an exception, and its ability to invade and subsequently induce cytotoxicity in NPPCs could explain its severe and necrotic forms of infection, notably in dogs, which exhibit a high prevalence of S. pseudintermedius infection.
SONICATION—VALUABLE DIAGNOSTIC METHOD OR OVERDIAGNOSIS

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Aim: Total joint replacement is everyday operation in orthopaedic surgery with an average postoperative infection from 0.5% to 3%. In diagnosing periprosthetic infection, of paramount importance is isolation of pathogen microorganisms. Sonication and sonication fluid cultures was introduced in our clinical practice in 2014. With this study, we wanted to compare the results of microbiological cultures of tissue and sonication fluid in diagnosing periprosthetic infection.

Method: During the 2015 altogether were operated and treated 30 patients because of suspected periprosthetic infection with two-stage (short-interval) procedure. In all patients tissue samples were taken for microbiological analysis, and the metal parts of prosthesis were sent to sonication.

Results: Out of the 30 patients treated in 28 patients was isolated microorganism and confirmed the diagnosis of periprosthetic infection. In 77% of patients were positive tissue cultures, while sonication fluid culture was positive in 90% of patients. In 7 cases where the tissue cultures and sonication fluid cultures were positive, there was a different or additional microorganism cultured using sonication (Figure 1).

Figure 1 Tissue and sonication fluid cultures in patients treated for periprosthetic joint infection

Conclusions: Sonication has become an indispensable diagnostic tool in the diagnosis of periprosthetic infection. Sonication enabled the detection of microorganism and in cases where suspected mechanical loosening and thus affect the further therapeutic procedure and treatment of the patients.
Aim: This study aims to identify both the incidence and possible factors that may lead to the development of peri-implant infection in orthopedic surgeries.

Method: Retrospective Cohort Study.

Results: A total of 416 patients were included in the study. All of which were surgeries requiring the use of internal fixation. Of the 416 cases that were included, 28 (6.7%) developed peri-implant infection. 15 (53%) of the patients used a nail and locking screws, 5 (17%) patients used plates and screws, 2 (7%) used pins and wires, 1 (3%) knee prosthesis and 1 (3%) hip prosthesis. 28 (100%) of the patients who developed peri-implant infection presented clinically with local warmth, erythema and tenderness. 26 (95%) presented with discharge, and 19 (70%) presented with a draining sinus. All of the patients demonstrated elevated ESR and CRP levels initially at presentation., implants in 16 (57%) of the patients underwent removal, 30% of which were converted to external fixators due to lack of signs healing clinically and radiographically (p=0.034). The rest of the patients had their implants retained. Infection rate overall was 6.7%.

Conclusions: Based on the data gathered in this study, surgery in the tibia and intramedullary nails were independent risk factors of peri-implant infection. Results of the multivariate logistic regression analysis thus showed that surgery in the tibia are four times more likely to have an infection.
CHARACTERIZATION OF STAPHYLOCOCCUS AUREUS ISOLATES FROM IMPLANT-ASSOCIATED BONE INFECTIONS

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Aim: S. aureus is frequently found in implant-associated bone infections, causing inflammation of bone and bone marrow. The aim of the study was to investigate antimicrobial resistance and virulence characteristics of S. aureus clinical strains that have been isolated from implant-associated bone infections.

Methods: We have collected several S. aureus strains from patients suffering from implant-associated bone infections in Department of Trauma Surgery of University hospital of Giessen. These strains were confirmed by MALDI-TOF and anti-microbial resistance was determined using agar diffusion method. The presence or absence of α-hemolysin and Panton-Valentine leucocidin (PVL) encoding genes was confirmed by PCR. Additionally, these strains were tested in the alternative insect infection model G. mellonella for virulence phenotype, biofilm formation abilities on polystyrene coated 96-well plate and invasion assay in SAOS-2 osteoblast like cell line. For further investigations, we selected high and low virulence strains for whole genomic analysis and quantitative analysis of biofilm associated genes (spa, agrA, hld, sarA, arcA, cap5ABCFG and spoVG) and virulence related genes (fbnA, ebpS, map, scn, hla, psmA1-3, and clfA) during infection of G.mellonella.

Results: The majority of the clinical S. aureus strains isolated from bone infections were sensitive to methicillin. These strains were α-hemolysin-positive and PVL-negative. The virulence phenotypic analysis of clinical strains in insect infection model G. mellonella showed various levels of larvicidal properties (high, intermediate and low virulence phenotypes). All of these strains showed good correlation between their virulence, biofilm formation and osteoblast invasion properties. Comparative genomic analysis and selected gene expression analysis between high and low virulent strains revealed major genetic factors of S. aureus that are related to severe infections in patients.

Conclusions: The examination of the virulence properties of the miscellaneous S. aureus isolates revealed clear heterogeneity. It enabled the classification into different virulence profiles comprising high, intermediate, and low levels. These pathogenicity levels could be correlated with the clinical outcome of the implant-associated infections and allowed an evidence-based treatment of the patients including assessment of the disease progress and antibiotic treatment.
Aim: To investigate if Staphylococcus epidermidis isolates from prosthetic joint infections (PJIs) differ in their ability to evoke an innate immune response compared to S. epidermidis isolates from the normal skin flora.

Method: The fluorescent labelled inhibitor of caspase-1 (FLICA) was used to detect active caspase-1 in human peripheral leukocytes. Caspase-1 is important in the regulation of the inflammatory response to bacteria by its function as a protease involved in the processing of pro-IL-1β to active secreted IL-1β. Ten PJI isolates- and ten commensals of S. epidermidis were incubated with washed human whole blood from three healthy individuals and FLICA for 0.5h, 2h and 6h. Leukocytes were labelled with antibodies so that neutrophils and monocytes could be distinguished. Active caspase-1 in individual cells was determined by flow cytometry detecting FLICA fluorescence.

Results: There was a lower proportion of FLICA-positive neutrophils (defined by unstimulated controls) after incubation with S. epidermidis isolates from PJIs, compared to after incubation with commensal S. epidermidis. This difference was statistically significant after 2h of incubation (17.3% [median] FLICA-positive neutrophils after incubation with PJI isolates vs 24.5% for commensal isolates). The proportion of FLICA-positive neutrophils varied between isolates of S. epidermidis in both groups, and between individuals.

Conclusions: In this pilot study, S. epidermidis isolated from PJIs evoked less innate immune response compared to isolates from the normal skin flora. This might suggest that the predominance of nosocomial sequence types, such as ST2, in PJIs in part is due to bacteria being able to more efficiently evade host inflammasome activation.
[P90] ROLE OF 16S PCR TESTING IN BONE AND JOINT INFECTIONS

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**Aim:** To perform a retrospective analysis of microbiological samples from patients with bone or joint infections between April 2015 and April 2016, comparing culture and 16S PCR results.

**Method:** Patients were identified using the Outpatient Parenteral Antimicrobial Therapy (OPAT) service database of a tertiary referral hospital. All patients with bone or joint infections between 1.4.15-31.3.16 were identified and records were used to identify what microbiological investigations had occurred.

The standard procedure for processing bone, tissue and joint fluid samples at this hospital is as follows: A standard set includes 1 sample of fluid for routine culture, 4 broth samples containing beads for enrichment and 1 tissue sample for histology. The four tissue samples taken in theatre should be transferred immediately by the surgical team under sterile conditions into the broth. The broth samples are vortexed and incubated for 5 days while examining daily for turbidity. The broth is sub-cultured on to standard plates if cloudy; otherwise a terminal subculture is performed at day 5. The pus sample will have microscopy performed and then subbed on to standard media for 5 days incubation. 16S PCR is only performed if requested by the clinicians.

**Results:** 98 patients were identified from the OPAT database of which cultures were negative in 30. Thirteen samples were tested with 16S PCR.

In 9/13 samples, the negative culture result was in concordance with a negative 16 SPCR result. In five patients culture was sent after the commencement of antibiotics. One patient grew *Streptococcus oralis* in his blood cultures and 12 days later (whilst on antibiotics) had negative joint fluid cultures but positive 16SPCR for *Streptococcus tingurinus*. One patient, who had received Ciprofloxacin and Meropenem, had negative cultures but positive PCR with *Pseudomonas species*. One patient, who had not received antibiotics but only had 1 sample for standard culture (no broth samples) was positive with *Streptococcus dysgalactiae* by 16SPCR. Finally one patient had a negative 16 SPCR but the culture was positive with *Prevotella species* (scanty growth) in 1 of 7 samples only. This was felt to be a probable contaminant.

**Conclusions:** There was generally good correlation between results of cultures (using routine culture techniques and broth) and 16 SPCR in patients with bone and joint infections. 16S PCR has a role in patients that have already received antibiotics at the time of culture or in patients without available broth samples, with strong clinical suspicion of infection.
Aim: Describe a case-series of spondylodiscitis admitted in our hospital from 2005 to 2015; describe radiological and clinical evolution of patients who underwent early surgical stabilization (no matter etiology).

Methods: All patient affected by spondylodiscitis (either bacterial or tubercular) from 2005 to 2015 were described. Demographic, laboratory and imaging data were anonymously recorded.

Results: Fifty-one patients were enrolled. Twenty-seven (52.9%) had diagnosis of bacterial spondylodiscitis, 21 (41.1%) had Pott’s disease (11 with microbial confirmation); 3 (5.9%) patients received both treatment, antibacterial and anti tubercular. Thirty patients (58.8%) underwent vertebral biopsy; of these, 17/30 (56.7%) didn’t reach a microbial diagnosis. Globally 29 patients (56.9%) had etiological diagnosis (either vertebral biopsy, needle aspiration from abscess or blood culture in patients with endocarditis and/or sepsis combined). Eleven patients (21.6%) underwent surgical spinal stabilization and decompression (100% minimally invasive posterior approach), 3 bacterial and 8 tubercular infections. Indication for surgery were: instability/deformity (even mild grade), worsening pain, even without neurologic deficit. Mean duration of antibiotic treatment before surgery was 8.2 weeks (4-35); mean follow-up period was 24 months (12-60). None had infection relapse during follow-up period. All patients were considered cured when they reached normalization of inflammation index and had evidence of new bone at imaging. Three patients accepted surgery for removal of orthopedic devices, others refused it because not suffering from intolerance (pain/discomfort).

Conclusions: Early minimally invasive approach allows healing durable with no risk of over-system infections, prevents impaired nerve and vertebral collapse and leads to early weight bearing (Fig.1).
Figure 1: first evaluation (1); one year after surgery (2)

Aim: Comparison of the quality of care focus on differences in yearly postoperative infection rates. Comorbidity is used to control for differences in case-mix. Several comorbidity indices have proven to predict postoperative outcome after total hip and knee arthroplasty (THA and TKA). As far as we are aware these comorbidity indices have not yet been used to predict postoperative infections after THA and TKA. The aim of this cohort study was to find which comorbidity index is best suited for this purpose, using data collected as part of our standard care procedures. We included the following three indices, the functional comorbidity index (FCI), the Charlson comorbidity index (CCI) and the American Society of Anaesthesiologists score (ASA).

Method: All patients who underwent a primary THA or TKA at one of our hospitals in 2014 were included in this cohort study. Medical records were reviewed for complications, ASA score and in order to full out the FCI and CCI. Prosthetic joint infection was defined according to the national PREZIES guideline up to 90 days postoperative.

Results: A total of 1233 patients were included whereof 739 THA and 494 TKA. Aside from the average BMI, which was significantly higher in the TKA group (<0.001), the demographics of the patient groups were comparable. The order of the scores on the indices were similar but the TKA group scored slightly higher on the index with functionality as outcome, the FCI. The THA group scored overall slightly higher on the CCI and ASA. In the TKA group 2.43% developed an infection related complication, compared to 0.68% in the THA group. All analyses for the relation between the scores on the indices and developing a post-operative infection related complication were not significant for both the THA and TKA group.

Conclusions: We were unable to predict postoperative infection in our yearly cohort of 1233 THA and TKA using the FCI, CCI nor ASA index. Power analyses, using the parameters of our cohort, show that the cohort size for making reliable comparisons using the FCI, CCI or ASA indices should be at least 13.032, 15.641 and 43.436 patients respectively. This suggests that yearly comparisons of quality of care solely based on postoperative infection rates are severely flawed. Since routinely used data cannot be relied upon to correct for case-mix and as such are, by itself, not meaningful when predicting better or worse outcome.
Aim: The sonication method has been used for diagnosis of these infections with difficult isolates using conventional microbiological methods. The objective was to analyze and to compare the results of the cultures of the sonication and the cultures using the microbiological conventional methods.

Method: We have analyzed retrospectively data of 48 patients that underwent orthopedic implant withdrawal for septic or aseptic reasons. An analysis of the main variables recorded was conducted: CPR and ESR preoperative and postoperative, joint fluid biochemistry, etc. We also compare the performance of the cultures obtained by classic microbiological methods with the ones obtain by sonication method.

Results: 32 women and 16 men were included. The implants analyzed came from 1 shoulder, 14 hips, 32 knees and 1 foot. 20 patients were diagnosed as septic revisions and 28 as aseptic revisions. When we analyzed the group of patients who received previous antibiotic (13) we found two subgroups, a) positive preoperative cultures (10 patients) and b) negative preoperative cultures (3 patients) In the subgroup a only 5 patients had positive intraoperative cultures (conventional cultures and sonication for the same microorganism). The other 5 patients resulted in negative intraoperative conventional cultures and sonication. In the subgroup b, we found 2 cases where the traditional cultures and the sonication were positive for the same microorganism and 1 case with negative traditional cultures during the intervention and positive sonication. There were 7 patients that did not receive previous antibiotics. 6 of them developed, conventional and sonication cultures positive for the same microorganism. Only one patient had negative traditional intraoperative cultures and sonication positive. All the patients diagnosed as aseptic revisions or implant retrieval demonstrated negative cultures.

Conclusions: The main problem with implants related infection is the diagnosis problems, with high rates of negative cultures. This situation is increased when the patient receive antibiotics prior to surgery. Sonication appears in the literature as a useful diagnostic method. In our series, when the patient received antibiotics, the rate of negative cultures was 46%, and the sonication only was useful for diagnosis in one case (16%) When the patient didn’t received antibiotics, the culture-negative rate was lower (15%) and the sonication helped us to confirm the infection in the patient with conventional negative culture. Although the study has limitations, the sonication had a limited collaboration in the diagnosis, especially in the group of patients with previous antibiotic treatment.
DETERMINATION OF ALPHA-DEFENSIN BY HPLC METHOD IN THE DIAGNOSIS OF INFECTIOUS COMPLICATIONS OF JOINT REPLACEMENT AND SUPPURATIVE ARTHRITIS

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Aim: Our department has developed a method to detect alpha-defensin by high-performance liquid chromatography. Advantage is the accurate quantification and monitoring levels of alpha-defensin. Although the alpha-defensin test* were able to immediately identify the presence of infection, but the problem is the high cost of the test and does not quantify the results. Aim of setting out the "cut off" concentration and concentration of the "gray zone" of alpha-defensin.

Method: Patients were elected as clearly ill so clearly health. On the basis of inflammatory markers, clinical course and outcome cultivation of joint effusion, we have determined whether it is a non-infectious, infectious, rheumatoid and reactive arthritis or infectious complications of joint replacement. Sampling articular punction was performed in a standard manner, puncture sterile safeguards. 1 ml of aspirate was administered via pipette into the test tube with 4 ml of stabilizer. Tubes with synovial effusion and a stabilizer were further processed in the laboratories and measured concentrations of alpha-defensin by HPLC. Results concentrations of alpha-defensin were statistically analyzed.

Results: In 157 patients was measured concentrations of alpha-defensin by HPLC method from joint effusion. On the basis of other tests and clinical course we determined the concentration of alpha-defensin particularly for arthritis and infectious complications of total endoprosthesis. "Cut-off" concentration for infection vs arthrosis, rheumatoid arthritis and reactive arthritis is 97.75 mg/l (sensitivity 0.97, specificity 0.87), Concentration of “gray zone” is of 62.75 to 108.5 mg / l. For infectious complications TEP is a "cut-off" of 38 mg / L (sensitivity: 0.94, specificity: 1).

Conclusions: Based on our results, we carried out to confirm that determine levels of alpha-defensin by HPLC method is very useful additional marker of inflammation in the affected joint. For infections of joint replacements, the situation is simpler, but in the case of diagnosing infectious arthritis must be using an alpha defensin cautious. High levels of alpha-defensin in the articular aspirate may also be in rheumatic, reactive arthritis and also in poorly diagnosable chlamydia arthritis. Use of HPLC is highly beneficial not only from the price aspects, but also because of the possibility of determining the exact concentration, on the basis of which we can adhere to a particular therapeutic procedure and you have the opportunity to assess monitoring the accuracy of treatment.

Acknowledgements: This study was supported by Internal grants Nos 9777 (Advanced therapies) and 6010 of the Motol University Hospital.

*Syovasure
Aim: Evaluate the effectiveness of the treatment of infected Tibial nonunion by bone transport using the Ilizarov external fixator.

Method: From 2007 to 2015, 100 patients (90 males and 10 females) were treated in the orthopaedic department of Al Azhar University Hospital, Damietta, Egypt, with a mean of age 37 years. The average length of the bone defects after radical debridement was 7 cm (range 3-13 cm). The mean follow-up after removal of the apparatus was 25.91 months (18-46 months). 10 patients were lost to follow-up.

Results: All the patients achieved bone union and no recurrence of infection was observed. The mean external fixation index was 1.38 months/cm (range 1.15-1.58 months/cm). According to Association for the Study and Application of the Method of Ilizarov (ASAMI) classification, bone results were excellent in 65, good in 15, fair in 5 and poor in 5; functional results were excellent in 40, good in 40, fair in 10 and no poor.

Conclusions: Our study and the current evidence suggested that Ilizarov methods in the treatment of infected Tibial nonunion acquired satisfied effects in bone and functional results. Radical debridement is the key step to control bone infection.
Aim: Calcaneal osteomyelitis with heel ulcers remains a challenge. Systemic antibiotic therapy alone is usually insufficient in its treatment. Radical surgical excision eradicates infection but leads to a compromised heel. A surgical technique for calcaneal osteomyelitis delivering local high concentration antibiotic with a resorbable calcium based carrier is presented.

Method: We present a prospective series of 2 cases with calcaneal osteomyelitis and chronic heel ulceration where we performed partial calcaneal resection and introduced high concentration local antibiotic with Calcium Sulphate/Hydroxyapatite biocomposite (Cerament G) (10 cc / Gentamycin 175mg) introduced by pressure injection into 3.5 mm drill holes creating a series of antibiotic loaded silos.

Results: Deep wound swabs in our cases grew pseudomonas aeruginosa, staphylococcus aureus, haemolytic streptococcus, proteus vulgaris, corynbacterium ulcerans and striatum. Sensitivity testing indicated susceptibility to ciprofloxacin, gentamycin, merepenem, tigecycline, ceftazidime, trimethoprim, daptomycin and linezolid. Neither case demonstrated systemic antibiotic toxicity. Both c reactive protein and white cell count levels improved significantly (pre op mean 128 mg/l, 8.85 x10^9 post op at 2 weeks mean 13mg/l, 6.7 x 10^9). Successful vacuum assisted closure was achieved in both cases with ulcer healing. Infection control was achieved in both cases. Additional surgical procedures were not required.

Conclusions: This silo technique for osteomyelitis is a novel, safe and effective technique in treating calcaneal osteomyelitis. The technique enables removal of dead bone and part retention of infected bone and a more conservative but mechanically superior calcaneal resection. Sustained antibiotic delivery from the silos provides prolonged local infection control. The technique also lends itself to situations where accurate delineation of infected bone can be difficult.
THE USE OF CALCIUM SULPHATE BIO COMPOSITE WITH ANTIBIOTICS FOR INFECTED LOWER LIMB METALWORK

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Aim: We describe a case series using calcium sulphate bio composite with antibiotics (a radio-opaque, injectable, osteoconductive bone-like material*/a synthetic biocompatible bone graft material**) in treating infected metalwork in the lower limb.

Method: 8 patients aged 22-74 (7 males, 1 female) presented with clinical evidence of infected limb metal work from previous orthopaedic surgery. Metal work removal with application of either cerement in 5 cases (10-20ml including 175mg- 350mg gentamycin) or a synthetic biocompatible bone graft material** in 3 cases (10-20ml including either 1g vancomycin or clindamycin 1.2g or 100mg tigecycline) into the site was performed. Supplemental systemic antibiotic therapy (oral/intravenous) was instituted based on intraoperative tissue culture and sensitivity.

Results: 4 patients had infected ankle metalwork, 2 patients infected distal tibial metalwork and 2 had infected external fixators. Metal work was removed in all cases. The mean pre operative CRP was 15.8mg/l (range 1-56mg/l). The mean postoperative CRP at 1 month was 20.5mg/l (range 2-98mg/l). The mean pre op WCC was 7.9 x10⁹ (range 4.7-10.5 x10⁹). Mean post op WCC at 1 month was 7.1 x10⁹ (range 5.0-9.2 x10⁹). The organisms cultured included enterobacter, staphylococcus aureus, staphylococcus epidermidis, staphylococcus cohnii, stenotrophomonas, acinetobacter, group B streptococcus, enterococcus and escherichia coli. No additional procedures were required in any case. All surgical wounds went on to heal uneventfully. Infection control and union was achieved both clinically and radiologically in all cases.

Conclusions: Our results support the use of a calcium sulphate bio composite with antibiotic as an adjuvant for effective local infection control in cases with implant related bone sepsis. The technique is well tolerated with no systemic or local side effects. We believe that implant removal, debridement and local antibiotic delivery can minimise the need for prolonged systemic antibiotic therapy in such cases.

* Cerament
** Stimulan
[P98] CALCIUM SULPHATE/HYDROXYAPATITE BIO COMPOSITE WITH GENTAMYCIN AS AN AMPUTATION STUMP SEAL FOR PATIENTS WITH ADVANCED OSTEOMYELITIS

Hasan Mohammad1, Tonko Tabain1, Anand Pillai1

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Aim: Preservation of optimum stump length in below knee amputation is important for prosthesis fitting and function. In cases with tibial osteomyelitis with diffuse marrow involvement this can be difficult to achieve. We describe two cases of advanced distal osteomyelitis for which amputations were conducted with the use of Calcium Sulphate/Hydroxyapatite bio composite with Gentamycin* in the amputation stump.

Method: Two male patients aged 56 and 81 years old presented with advanced infection in the foot post trauma, wound breakdown and multiple bony and soft tissue procedures with subsequent infective spread to the tibia. The lower limbs were deemed unsalvageable and below knee amputation was conducted. Calcium sulphate/hydroxyapatite bio composite with Gentamycin* (10ml, 175mg Gentamycin) was inserted into the amputation stump intraoperatively as a distal medullary plug. The stump flaps was closed over the medullary plug in routine fashion.

Results: In both cases the stump wounds healed uneventfully. C reactive protein and white cell count levels were as follows; pre op means <1 mg/l, 25.3 x10⁹ and post op at 2 weeks means 32.5mg/l, 10.85 x 10⁹. There was no excessive wound leakage or prolonged discharge. There were no clinical or radiological signs of infection at the stump ends at 6 months follow up. Both patients went on to prosthetic fitting and rehabilitation with out any further problems.

Conclusions: Our results indicate that the use of an injectable antibiotic containing void filler with the ability to remodel helps to maintain adequate and optimum stump length in patients undergoing below knee amputation for osteomyelitis. The technique also helps to control the immediate postoperative bleeding by acting as a haemostatic plug and enhances wound healing. We believe this technique has a role in other areas of amputation surgery for infective pathology.

*Cerament G
SONICATION OF EXPLANTED SPINAL IMPLANTS A NOVEL TECHNIQUE FOR THE DIAGNOSIS OF SPINAL INFECTION

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Aim: Infection of metalwork is a recognized and significant complication of instrumented spinal procedures. Identification of the causal microbial pathogen is of paramount importance to successful treatment. Standard cultures of tissue samples and explanted metalwork fail to identify the causative pathogen in some cases making treatment of this serious conditions even more challenging. The aim of this study is to outline the use of sonication fluid cultures derived from explanted spinal implants in order to identify the causative microorganism in the absence of positive tissue cultures.

Method: A retrospective analysis of four patients who developed late infection after surgery for correction of spinal deformity. 3 patients (1 M: 2F) underwent surgery for correction of adult scoliotic deformity and 1 patient for correction of Scheuermann’s kyphosis. All patients underwent wound washout and removal of infected metalwork. Explanted pedicle screws were sonicated and fluid cultures were examined. In addition tissue specimens (>5) were collected and cultured according to standard practice. All patients completed a course of prolonged antibiotic treatment on the basis of sonication cultures with subsequent reinstrumentation.

Results: In all four cases routine tissue and explanted implant culture alone or even PCR did not yield any pathogen. Sonication fluid cultures, however, yielded *Staphylococcus aureus* and *Escherichia coli* in one case, *Corynebacterium propinquum* in one patient *Corynebacterium tuberculostearicum* in the third patient, *Staphylococcus aureus*, *Propionibacterium acnes* and *Candida Albicans* in the fourth patient. In all four cases the infection was successfully treated with antibiotics and antifungals in one case. There were no signs of deep wound infection after the reinstrumentation up to the latest follow up.

Conclusions: In cases where standard tissue and explanted implant cultures fail to yield a result, sonication of explanted metalwork and culture of sonicated fluid may be a useful tool to ascertain the identification of the causative microorganism and the patient to receive the appropriate treatment.
DAPTOMYCIN INTRA-ARTICULAR AS RESCUE TREATMENT IN PATIENTS WITH A CHRONIC PJI DUE TO GRAM POSITIVE COCCI

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4Department of Microbiology, Hospital Clinic, University of Barcelona., Barcelona, Spain

Aim: Suppressive antibiotic therapy (SAT) is an alternative for patients with a prosthetic joint infection (PJI) in which the surgical treatment cannot be performed. However in some cases the SAT fails, side effects occur or microorganisms are resistant to all oral antibiotics. Since daptomycin retains antimicrobial activity against both stationary-phase and bacteria in the multiplication phase, its local infusion could be an alternative option in these infections due to Gram positive cocci. The aim of this study was to evaluate the safety and efficacy of daptomycin when administered intra-articular in patients with a PJI in which SAT has failed or was not possible to do.

Method: We identified all patients with a PJI caused by Gram positive cocci treated with intra-articular daptomycin in our institution. We retrospectively reviewed the main variables potentially associated with outcome. Arthrocentesis was performed obtaining as much synovial fluid as possible. Them, the same amount of fluid drained of a solution of daptomycin 2 mg/ml diluted in lactated Ringer’s solution was injected. This procedure was performed daily during five to seven days.

Results: 8 patients were identified with a mean age of 76.4 years and 25% were males. All of them had a total knee arthroplasty and only 2 (25%) were a primary prosthesis. All patients had chronic PJI and the microorganisms isolated were: 3 (37.5%) methicillin-susceptible Staphylococcus aureus, 3 (37.5%) S. epidermidis, 1 (12.5%) E. faecalis and 1 (12.5%) Corynebacterium striatum. Microbiological eradication at the end of the local therapy was achieved in 6 patients (75%) and 5 (62.5%) were asymptomatic after at least 10 months of follow-up (except 1 patient with only 9 weeks of follow up). Microorganisms involved in therapeutic failure were E. faecalis and S. epidermidis (absence of microbiological eradication after treatment) and S. aureus (relapse after weeks without symptoms).

Conclusions: The injection of daptomycin intra-articular could be an option as rescue treatment in those patients with a chronic PJI due to Gram positive cocci in which surgical treatment cannot be performed and SAT has failed or is not well tolerated. More studies are necessary in this field.
[P101] RAPID PRE-OPERATIVE DIAGNOSIS OF PERIPROSTHETIC JOINT INFECTION WITH MICROCALORIMETRY OF JOINT ASPIRATES

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2Charité - Universitätsmedizin Berlin, Centrum für Muskuloskeletale Chirurgie, Klinik für Orthopädie, Berlin, Germany

Aim: To assess the diagnostic accuracy and time-to-positivity of microcalorimetry of pre-operative joint aspirate in comparison to standard pre- and intra-operative diagnostic methods for detection of periprosthetic joint infection (PJI) of the hip and knee.

Method: Pre-operative joint aspirates were prospectively obtained in patients with suspected PJI of the hip or knee from October 2014 to April 2015 in our facility. Diagnosis of PJI was established when at least one of following criteria applied: intra-operative macroscopic purulence/sinus tract, acute inflammation in intraoperative tissue, growth in joint aspirates or intra-operative tissue, >2000 leukocytes/µl or >80% granulocytes in synovial fluid. Culture (incubation 14 days) and microcalorimetry (incubation 5 days) was obtained for joint aspirates. Detection time for calorimetry was established at 10 µW of heat increase. Sensitivity, specificity, accuracy of each test and the time to positivity for microcalorimetry was determined. Significancy of sensitivity and specificity was analyzed with McNemar’s test.

Results: 108 patients were included; 58 had knee and 50 hip prosthesis. The median age (range) was 70 (36-87) years; 40(36%) were males. 46(43%) patients were diagnosed with PJI with following microorganisms: Staphylococcus epidermidis (n=8), Staphylococcus aureus (n=1), other staphylococci (n=5), streptococci (n=7), E. coli (n=3), enterococci (n=3) and others (n=5). Diagnostic results are shown in Table 1. The median time until positivity of microcalorimetry was 6 hours (range 2 – 55 hours). No significant differences of sensitivity and specificity between joint aspirate culture and microcalorimetry were found (p=0.41 and p=0.16, respectively).

Conclusions: Non-culture diagnostic methods (e.g. leukocyte count/differential, tissue histology) were superior to culture methods but cannot identify the infecting microorganism. Among culture-based methods, the sensitivity of microcalorimetry was comparable to that of joint aspirate culture (39% vs. 43%, respectively), while microcalorimetry provided considerably faster results (6 hours vs. 48 hours, respectively). Microcalorimetry of joint aspirate allowed rapid diagnosis of PJI.

<table>
<thead>
<tr>
<th>Diagnostic test</th>
<th>PJI (n = 46)</th>
<th>Aseptic failure (n = 62)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive preoperative joint aspirate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukocyte count or differential</td>
<td>28/34</td>
<td>2/39</td>
<td>82%</td>
<td>95%</td>
<td>89%</td>
</tr>
<tr>
<td>Cytological analysis</td>
<td>26/44</td>
<td>9/58</td>
<td>59%</td>
<td>85%</td>
<td>74%</td>
</tr>
<tr>
<td>Joint aspirate culture</td>
<td>20/46</td>
<td>2/62</td>
<td>43%</td>
<td>97%</td>
<td>74%</td>
</tr>
<tr>
<td>Microcalorimetry</td>
<td>18/46</td>
<td>0/62</td>
<td>39%</td>
<td>100%</td>
<td>74%</td>
</tr>
<tr>
<td>Diagnostic Test</td>
<td>Positive</td>
<td>Negative</td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>Accuracy</td>
</tr>
<tr>
<td>---------------------------</td>
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<td>----------</td>
<td>-------------</td>
<td>-------------</td>
<td>----------</td>
</tr>
<tr>
<td>Tissue histology</td>
<td>20/27</td>
<td>0/24</td>
<td>74%</td>
<td>100%</td>
<td>86%</td>
</tr>
<tr>
<td>Tissue culture</td>
<td>15/33</td>
<td>4/30</td>
<td>46%</td>
<td>87%</td>
<td>65%</td>
</tr>
<tr>
<td>Sonication fluid culture</td>
<td>11/18</td>
<td>1/11</td>
<td>61%</td>
<td>91%</td>
<td>72%</td>
</tr>
</tbody>
</table>

Table 1. Comparison of diagnostic tests for PJI.
**[P102] THE ROLE OF MICROCALORIMETRY AND PCR OF JOINT ASPIRATE FOR EARLY DIAGNOSIS OF SEPTIC ARTHRITIS**

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\(^2\)Charité - Universitätsmedizin Berlin, Centrum für Muskuloskeletale Chirurgie, Klinik für Orthopädie, Berlin, Germany

**Aim:** To evaluate microcalorimetry and multiplex PCR of pre-operative joint aspirate of the hip and knee for early detection of septic arthritis in comparison to current pre- and intra-operative diagnostic standards.

**Method:** Pre-operative joint aspirates were prospectively obtained for patients with suspected arthritis of the hip or knee from October 2014 to September 2015 in our facility. Joint aspirates were analyzed with culture, multiplex PCR and microcalorimetry. Septic arthritis was diagnosed if the joint aspirate culture was positive or the following criteria: typical local inflammatory signs and symptoms, abnormal aspirate fluid leukocyte count (>20,000 leukocytes/µl) or differential (>90% granulocytes) and exclusion of other potential causes of arthritis (i.e. rheumatoid pathology). Sensitivity and specificity of each test were determined and significance was evaluated with McNemar’s Chi squared test.

**Results:** 55 patients were prospectively included (48 knees; 7 hips). The median age (range) was 60 (20 - 85) years; 29 (53%) were males. 27 (49%) patients were diagnosed with septic arthritics and 28 (51%) with aseptic pathology (Table 1). No significant differences (p<0.05) were found between sensitivity of joint aspirate cultures, multiplex PCR and microcalorimetry. Compared to joint aspirate culture PCR failed to detect S. aureus (n=2), streptococci (n=1) and gram-negative rod (n=1). The processing time for PCR was 5 hours, median detection time (range) for microcalorimetry was 9 hours (2.3 – 64 hours) and for cultures 48 hours (1 - 14 days).

**Conclusions:** The sensitivity of microcalorimetry and multiplex PCR were similar to joint aspirate culture, while specificity of calorimetry (96%) and PCR (82%) was high. PCR and calorimetry provided rapid results (within 5 hours and median of 9 hours, respectively), while PCR delivered antimicrobial susceptibility also from non-viable bacteria. With improved sensitivity, microcalorimetry and multiplex PCR may replace cultures of joint aspirates and enable a rapid pre-operative diagnosis of septic arthritis.

<table>
<thead>
<tr>
<th>Diagnostic test</th>
<th>Aseptic joint (n = 28)</th>
<th>Septic arthritis (n = 27)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte count or differential</td>
<td>0/23</td>
<td>18/21</td>
<td>86%</td>
<td>100%</td>
<td>93%</td>
</tr>
<tr>
<td>Cytological analysis</td>
<td>9/26</td>
<td>24/25</td>
<td>96%</td>
<td>65%</td>
<td>80%</td>
</tr>
<tr>
<td>Joint aspirate culture</td>
<td>0/27</td>
<td>9/27</td>
<td>33%</td>
<td>100%</td>
<td>67%</td>
</tr>
<tr>
<td>Microcalorimetry</td>
<td>1/28</td>
<td>10/27</td>
<td>37%</td>
<td>96%</td>
<td>67%</td>
</tr>
<tr>
<td>Test</td>
<td>Positive intraoperative test</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>-------------------</td>
<td>------------------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiplex PCR</td>
<td>5/28 6/27 22% 82% 53%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tissue histology</td>
<td>0/7 10/14 71% 100% 82%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tissue culture</td>
<td>0/12 15/21 71% 100% 81%</td>
<td></td>
<td></td>
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</tbody>
</table>

Table 1. Comparison of diagnostic tests for detection of septic arthritis.
[P103] MICRONAS AS BIOMARKERS FOR EARLY DETECTION OF BACTERIAL PERIPROSTHETIC JOINT INFECTIONS

Evanthia Mourmoura¹, Konstantinos N. Malizos², Sokratis Varitimidis², Nikolaos Stephanou², Ioanna Papatheanasiou¹, Eleni Ntoumou¹, Lydia Anastasopoulou², Aspasia Tsezou¹

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Aim: MicroRNAs (miRNAs) are small non-coding RNA molecules that have been associated with various pathological conditions such as autoimmune diseases and inflammatory responses in bacterial infections. The role of microRNAs in pathogen-host interaction has recently attracted attention, as extracellular microRNAs that exist in the blood can be rapidly quantified in a clinical setting. The aim of the present study was to identify differentially expressed circulating serum microRNAs in patients with and without periprosthetic joint infections that could constitute novel non-invasive biomarkers for early detection of bacterial joint infections.

Method: Total RNA was extracted from serum of 20 patients with periprosthetic joint infections as well as from 6 individuals who had an arthroplasty without infection after 5 years. We evaluated, using real-time PCR, the expression levels of miRNAs associated with inflammation, as miR-16, miR-21, miR-125-5p, miR-19a, miR-19b, miR-223 and miR-365. The expression of selected microRNAs was subsequently validated in synovium from 6 patients with periprosthetic joint infections and 3 healthy controls. Moreover, bioinformatics analysis, using miRNA target prediction databases and network analysis programs revealed the microRNAs' biological functions.

Results: We found that serum expression levels of miR-16, miR-21, miR-125-5p, miR-19a and miR-19b were significantly increased in patients with periprosthetic joint infections compared to healthy controls; however no differences were observed regarding circulating levels of miR-223 and miR-365 between the two groups. Among the differentially expressed miRNAs, miR-16, miR-21 and miR-19a exhibited the largest increase in the patients’ group. The above miRNAs also showed significantly increased expression in the synovium of patients with periprosthetic joint infections in comparison with controls. Additionally, bioinformatics analysis revealed that the above microRNAs were related with biological processes of inflammation and immune response, both involved in pathogenesis of infectious diseases.

Conclusions: Our findings provide novel evidence that inflammation-related circulating microRNAs, miR-16, miR-21 and miR-19a could be used as potential diagnostic and prognostic biomarkers for early detection of bacterial periprosthetic joint infections, while modulation of these miRNAs could possibly represent novel therapeutic targets.

References:

Acknowledgement The work was financed by the Research Committee of University of Thessaly, Faculty of Medicine, Larissa, Greece
COMPARISON OF BACTERIAL RESULTS FROM CONVENTIONAL CULTURES OF THE PERIPROSTHETIC MEMBRANE AND THE NEO-SYNOVIIUM DURING HIP AND KNEE REVISION ARTHROPLASTY

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Aim: Bacterial identification is essential for the correct management of a loosened infected arthroplasty. The current guidelines of the Musculoskeletal Infection Society do not provide objective data regarding the best solid tissue sample for identifying microorganisms. The objective of this study was to compare the yields of periprosthetic membrane and neo-synovium samples.

Method: We performed a prospective study of all hip and knee revisions from September 2014 to December 2015. As soon as the arthrotomy was performed, four periprosthetic samples from different sites were sent to the laboratory for culturing: two samples of synovial fluid and two samples of the neo-synovium. After removing the implants, two samples of the periprosthetic membrane were obtained.

Results: Of a total of 167 revision surgeries (76 hip and 91 knee), 19 presented positive postoperative cultures and were considered as septic revisions; 15 had the same diagnosis using either the neo-synovium or the membrane as solid tissue sample. In three cases the infection could have been diagnosed only by considering both the membrane and the neo-synovium, and in four other cases only one type of solid tissue would have correctly diagnosed the infection.

Conclusions: The yields of periprosthetic membrane and the neo-synovium in diagnosing PJI do not differ significantly. We recommend obtaining samples from the synovial fluid and from both the membrane and the neo-synovium as solid samples for conventional culturing.
Aim: Prosthetic joint infections are rare but severe infections, leading to limb-threatening conditions. In some cases, arthodesis is proposed after failure of prosthetic knee infections management.

The aim of the present study is to describe clinical and microbiological characteristics, and outcome of patients who underwent knee arthodesis with intramedullary nail, following failure of the management of total knee prosthesis (TKP) infection.

Method: Medical charts of patients followed in our centre between January 2013 and December 2015 were reviewed. All patients who underwent knee fusion by intramedullary nail were analysed.

Results: Ten patients underwent knee arthodesis for failed prosthetic joint infection during the study period (6 patients with 2-stage and 4 patients with 1-stage procedure), with a mean age of 69.6 ± 11.9 years, and a M/F sex ratio of 0.42. Three patients had an immunosuppressed status (2 with diabetes mellitus, and 1 with chronic corticosteroid therapy). The patients underwent a mean of 2.8 ± 1.6 revision surgeries (range 1-5) before knee arthodesis, and a flap for soft tissue coverage was performed in 2 patients. Mean curative antibiotic duration was 65.6 ± 41.7 days.

Gram negative bacilli were the most predominant pathogens (60% of patients, 4/6 were fluoroquinolone-resistant), followed by Staphylococcus spp. (50% of patients, with identification of methicillin-susceptible S. aureus in 2 cases, and methicillin-resistant coagulase-negative staphylococci in 3 cases); 2 patients had fungal infection (Candida albicans and C. parapsilosis). Six patients had polymicrobial infection, and 8 patients had a pathogen different from those identified during previous prosthetic knee infection management.

Six patients experienced failure during follow-up (3 relapses due to the same micro-organism, and 3 superinfections with another micro-organism), with a mean delay from implantation to failure of 339 days (range 16-1062). Failure rate tended to be higher for 1-stage than for 2-stage procedures (75% vs 50%; p=0.57). Four patients were in remission with a mean follow-up of 320 days (range 55 - 949).

Conclusions: In our study patients had mainly polymicrobial infections, with a predominance of Gram negative bacilli, and failed in a large proportion of cases (60%).

In most cases, the pathogens identified during arthrodesis implantation were highly resistant and differed from those previously detected during previous surgical interventions on the TKP. A 2-stage procedure may ensure a better remission rate in these patients.
Aims: Spontaneous and surgical spinal infections can be devastating to patients and pose a significant socioeconomic burden to society.

The aim of this study is to characterise the microbiology of all patients with spondylodiscitis in an urban tertiary referral centre, to examine the patterns of antimicrobial resistance in this complex population and to compare on the microbial spectrum published to date.

The infectious disease and microbiology team identified 69 cases of spontaneous or surgical spinal infections from 2010 to 2015. The surgical history and microbiological data for each case was then collected by review of each individual medical record.

Methods: All cases were diagnosed using clinical examination, biochemical markers alongside radiographical findings and microbiological specimens. Surgical information and microbiological data was gathered by direct observation of medical records.

Results: Of 69 cases, monomicrobial infections accounted for 71% whilst 7% were polymicrobial. The most commonly isolated pathogen was *Staphylococcus aureus* found in 31% of positive cultures, followed by *Escherichia coli* in 13%. Other commonly isolated organisms were *Pseudomonas aeruginosa* (11%), TB (7%) and *staphylococcus epidermis* (7%). Many of the organisms isolated demonstrated multidrug resistance. The spectrum and increased incidence of gram-negative organisms stands in contrast to previously published data.

Conclusion: These findings may now aide in guiding the choice of empiric antibiotics whilst awaiting culture results and developing strategies for antimicrobial prophylaxis in spinal surgical procedures.
Aim: Melioidosis is a saprophytic infectious disease caused by Gram-negative soil and surface water-dwelling bacillus *Burkholderia pseudomallei.* Musculoskeletal melioidosis is a well-recognized manifestation of the disease. Human infection occurs, when the organism gains entry through broken skin, by inhalation, and perhaps ingestion.

Method: We report three cases of musculoskeletal melioidosis that presented to our department from 2011 to 2013.

Results:

<table>
<thead>
<tr>
<th>Age/Sex</th>
<th>Site Description</th>
<th>Duration of Symptoms</th>
<th>Management</th>
<th>Antibiotics</th>
<th>Outcome</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>43/Male</td>
<td>Osteomyelitis left femur with thigh abscess <em>(k/c/o Diabetes Mellitus)</em></td>
<td>3 months</td>
<td>Debridement, Negative pressure wound therapy, Skin grafting</td>
<td>Ceftazidime X 2 weeks, Trimethoprim Sulfamethoxazole X 6 months</td>
<td>Complete wound healing. No recurrence</td>
<td>30 months</td>
</tr>
<tr>
<td>63/ Male</td>
<td>Osteomyelitis right tibia <em>(k/c/o Diabetes Mellitus)</em></td>
<td>8 years h/o Osteosynthesis for open fracture with local flap</td>
<td>Debridement, Saucerization and Local rotation flap</td>
<td>Ceftazidime X 2 weeks, Trimethoprim Sulfamethoxazole X 3 months</td>
<td>Complete wound healing. No recurrence</td>
<td>12 months</td>
</tr>
<tr>
<td>48/Female</td>
<td>Multiple abscesses over right shoulder, right hand, elbow, right leg and foot <em>(k/c/o Diabetes Mellitus)</em></td>
<td>2 months</td>
<td>Incision and drainage</td>
<td>Ceftazidime</td>
<td>Expired due to septicaemia</td>
<td></td>
</tr>
</tbody>
</table>
Conclusions: Clinically it mimics other pyogenic infections, Gram-negative sepsis, tuberculosis and has been referred to as the “remarkable imitator” and the “mimicker of maladies”. Diabetes and alcoholism are risk factors. The need for diagnosing this entity is due to the fact that the septicemic form has a mortality rate that exceeds 90%. Laboratories sometimes misidentify it as Pseudomonas species, the difference being that Burkholderia is resistant to Aminoglycosides and Colistin. This should be kept in mind, especially when there is history of travelling to endemic areas. They respond to only specific set of antibiotics i.e. intravenous ceftazidime and combination of Trimethoprim and Sulfamethoxazole.

References:

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Aim: Septic arthritis is a medical emergency that requires prompt diagnosis and treatment to avoid joint morbidity and mortality. *Staphylococcus aureus* was the most commonly cultured organism in septic arthritis, followed by *Streptococci* spp.1

Group B Streptococcus (GBS) is the classical causative organism of neonatal meningitis and pneumonia and post-partum morbidity in mothers. However, there has been a spike in incidence of non-obstetric related GBS infections in Singapore in 2015, which was in line with recent trends in international literature.1,2

Hence, the objective of this study was to identify any corresponding rise in the incidence of GBS septic arthritis in our population. We also sought to evaluate the demographic, initial presentation and clinical outcomes of patients with GBS and non-GBS septic arthritis.

Method: We conducted a retrospective single-center review of 83 patients surgically treated by the National University Hospital orthopaedic department with an operative diagnosis of septic arthritis between 1/1/11 and 31/12/15.

Results: In the study period, 83 cases of septic arthritis were treated. *Staphylococcus aureus* remained the most common cause of septic arthritis with 26 (31.3%) cases. 21 (25.3%) cases were due to *Streptococcus agalactiae*, of which 15 (71.4%) of them occurred between 2014 and 2015.

Group B Streptococcus patients had significantly less (p=0.01) patients with 2 or more co-morbidities (8/21 (38.1%) vs 43/62 (69.4%)), and were significantly more likely (p<0.01) to present with polyarticular involvement (10/21 (47.6%) vs 3/62 (4.8%)). The knee 15 (71.5%) and shoulder 6 (28.6%) were the most common sites of infection in these patients and there was a significant association between elbow septic arthritis and Group B Streptococcal patients (p=0.05).

There was a significantly higher rate (p=0.02) of positive blood cultures in Group B streptococcus patients compared to other patients ((17/21 (81.0%) vs. 26/62 (41.9%)). These patients had a shorter mean hospital stay (21 days vs 25 days) and lower rates of amputation (0% vs 4.83%), and a significantly lower rate of death (p<0.05).

Conclusions: GBS is an increasingly common cause of septic arthritis. These patients tend to have less co-morbidities and often present with polyarthritis and bacteraemia. However they have better outcomes, with shorter hospital stays, and lower rates of amputation and death.

References:
Aim: The role of anaerobic infections in orthopaedics seems to be underestimated. Anaerobes are the integral part of human mucous membranes microflora and under some conditions may become the cause of serious bone and joint infection. The immunodeficient zone around the orthopaedic implant provides the favourable environment for anaerobe growth. The most common anaerobic pathogen in orthopedics is *Bacteroides fragilis*. Some anaerobes have the ability to produce biofilm that reduces the bioavailability of antibiotics. The aim of the study was to examine the influence of an orthopaedic surgeon and other medical personnel on the final results of the diagnosis and treatment of anaerobe infection.

Method: The standard procedure of microbiology sample collection, storage and transportation in the orthopaedic department was analyzed. The potential habits or routines that may influence the diagnosis were studied. The standard time of hospital stay for the selected procedures was compared with an average time required for the culture results and the adjustment of empiric antibiotic protocol.

Results: One of the problems with diagnosis is related to slow growth requiring a long lasting culture and the polymicrobial and endogenous nature of the infections as an aerobic infection facilitates the growth of anaerobic bacteria. Another issue is proper sample collection. Inadequate technique of skin preparation, acquisition, prolonged time of transportation, incorrect temperature, air bubbles within the sample may result in false positive or false negative results. Besides, in most laboratories identification and susceptibility tests for anaerobes are not routinely performed. The first choice drugs in anaerobic bone and joint infections are: metronidazole, carbapenems, clindamycin. A traditional treatment option are penicillines, however, due to beta-lactamase production, the treatment requires combination of penicillin with beta-lactamase inhibitors. Moreover, the increasing rate of clindamycin and amoxicillin/clavulanic acid resistance has been observed within recent years.

Conclusions: Anaerobe isolation is difficult due to their fastidiousness and their involvement may be easily overlooked. The treatment of anaerobic infections is often delayed and unsuccessful. The habits and routines of the personnel and standards of sample handling may influence the final diagnosis and outcome of therapy.
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**Aim:**
The use of ALAC spacers is a golden standard of the treatment of periprosthetic joint infections (PJI). The recommended time from the implantation to explantation of the spacer varies among the orthopaedic centers. The sharp decrease of serum concentration of antibiotic after implantation and the possibility of bacterial growth on the spacer surface suggest that prolonged retention of a spacer is not desirable. The aim of the study was to compare the in vitro action of spacer fragments retrieved at various time points against S. epidermidis.

**Method:**
54 fragments of 14 custom made ALAC spacers with 5% wancomycin explanted from 14 patients during the second stage of PJI treatment. The fragments were harvested from non weight bearing outer surfaces of the spacer and cut to the diameter of about 11mm. The time from the implantation to explantation of the spacer was from 2 months to 91 months. The fragments were incubated in the presence of S. epidermidis on culture media Mueller-Hinton (MH)*. The inhibition zone was measured. 11mm custom made ALAC discs with 5% vancomycin made perioperatively were used as a control (day 0).

**Results:**
The mean inhibition zone around control discs (day 0) was 25mm. All the retrieved fragments presented with antibacterial activity. We have observed a steady decline of the inhibition zone. At 8 months it was 80% of the control. Two spacers retrieved after 3 and 7 years have shown the inhibition zone close to 80%.

**Conclusions:**
The time related decrease of inhibition zone of 5% vancomycin ALAC spacer tested in vitro is much slower than we expected. The elution of vancomycin from ALAC spacer at 8 months was sufficient to provide 80% of the baseline inhibitory effect. The distinct inhibition of S. epidermidis growth was still present at much longer time, however the limited group of patients restrains from drawing more explicit conclusions. We believe that the accidental prolonged spacer retention may be less dangerous as previously thought, as the bactericidal action on the tissue-spacer interface may still be adequate.

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Rhabdomyolysis in a Patient with Spondylodiscitis Treated with Daptomycin

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Aim: Rhabdomyolysis is a known but very rare adverse effect of daptomycin therapy. We report the case of an 86-year old women with spondylodiscitis due to S. aureus and S. capitis who developed severe rhabdomyolysis under daptomycin therapy.

Method: Retrospective evaluation of the case and review of the literature.

Results: An 86-year old women presented with back pain at the clinic for orthopedic surgery in our institution. Computed tomography revealed a pathologic fracture of a vertebral body due to spondylodiscitis. During surgery for stabilization four biopsies were taken intraoperatively and sent for histopathological examination and microbiological culture. All four samples grew Staphylococcus capitis and two samples grew Staphylococcus aureus in addition. After consultation of the antibiotic stewardship team which also comprises a clinical microbiologist an intravenous antibiotic therapy with daptomycin and rifampicin was started according to antibiotic susceptibility testing. After two weeks of therapy the patient developed nausea, vomiting and abdominal pain. She suffered from several underlying diseases including impaired renal function, history of myocardial infarction, atrial fibrillation and history of breast cancer. Her regular medication contained coumarin-derived anticoagulation and statins. The electrocardiogram did not show any signs of acute myocardial infarction. Laboratory results showed tenfold elevated liver transaminases, a tenfold increased troponin T and a 40-fold elevated creatinine kinase. Retrospective analyses revealed the troponin T was increased due to impaired renal function and remained constant at the same high level. The antibiotic stewardship team was consulted again. Rhabdomyolysis due to daptomycin was suspected and the therapy with daptomycin and rifampicin was stopped. Within a few days creatinine kinase and liver transaminase decreased to normal values. Antibiotic therapy was changed to vancomycin, the patient was dialyzed intermittently and recovered. A study including more than 50 patients with co-medication of daptomycin and statins did not find any evidence of muscle injury¹. Nevertheless, single cases with rhabdomyolysis under daptomycin haven been reported².

Conclusions:

1. Rhabdomyolysis is a rare but severe adverse effect of daptomycin therapy
2. The co-medication with a statin seems to be an additional risk for rhabdomyolysis in some patients
3. In patients with impaired renal failure and / or with co-medications that can cause rhabdomyolysis regular control of creatinine kinase levels are necessary
4. An interdisciplinary approach is mandatory in patients with complex disease and history

References:

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IMPLEMENTING AN ORTHOPAEDIC PUNCTURE PROTOCOL TO DIAGNOSE A PROSTHETIC JOINT INFECTION

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Aim: To determine the diagnostic yield of orthopaedic prosthetic joint biopsies in the diagnosis of PJI. Introduction: Since 2012 we introduced a new work-up schedule for diagnosing and treating prosthetic joint infections (PJI). Recent literature and the consensus meeting in Philadelphia advocate the importance of diagnose before treating PJI. The last step in our algorithm for differentiation for PJI versus aseptic loosening, and “easy” versus “difficult to treat”, is a prosthetic joint aspiration with fine needle biopsy. In order to differentiate between an aseptic versus a septic revision, and a one-stage versus a two-stage revision the accuracy of biopsy is of significant importance. Therefore we analyzed our biopsy data.

Method: Patients with a clinical suspicion of a PJI (based on the Zimmerli criteria) and/or patients with loosening of the prosthesis underwent periprosthetic biopsies taken by the orthopaedic surgeon in the operating room (period 2013-2016). Culture yield was compared with prospective data from patients undergoing a biopsy at the radiology department ultrasound guided (period 2012-2013). During revision surgery, multiple periprosthetic biopsies were taken when prosthesis was extracted. The diagnosis PJI was made based on diagnostic criteria described in current guidelines. Patients with a sinus tract were excluded from biopsy in this prospective cohort, since our treatment choice in these patients would be a 2-stage revision. From 78 patients biopsies were taken (in 2 patients twice), 15 ultrasound guided by the radiology department (2012-2013), and 65 on the OR by orthopaedics (2013-2016).

Results: 52 patients underwent a prosthetic revision operation (hip n=44, knee n=7, elbow n=1) from which tissue samples for culture (1-7 per biopsy) and histology (1-2 per biopsy) could be compared with previously taken, radiologic (Median=1) and orthopaedic (Median=4) biopsy samples. In 42 (78%) biopsies the results matched the results of revision operation samples. Compared with the results of the revision surgery, 18 cultures were true positive (with the same micro-organism) and 24 cultures were true negative, excluding a PJI. In three (5,7%) biopsies a micro-organism was found and considered a contamination, while of minimally 5 deep tissue samples during revision procedure remained negative as did histology. Overall four (7,7%) of radiology biopsies, and one (1,9%) on OR taken biopsy (9,6%) was false negative, while multiple deep tissue samples cultured micro-organisms.

Conclusions: In our opinion taking multiple tissue samples in a sterile environment will contribute to the diagnosis of a PJI (histology and cultures), and identification of responsible micro-organism (cultures).
SONICATION CULTURE IMPROVES THE MICROBIOLOGICAL DIAGNOSIS OF MODULAR MEGAPROSTHESSES

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Aim: Modular megaprostheses are known for high infection rates followed by high rates of revisions. Microbial biofilms growing adherently on prosthetic surfaces may inhibit the detection of the pathogens causing prosthetic joint infections. We investigated if sonification culture (SC) improves the microbiological diagnosis of periprosthetic infections of megaprostheses in patients with or without preoperative antibiotic therapy compared to conventional tissue culture (TC) and which pathogens were detected on the surface of megaprostheses with either SC or TC and do the findings help to identify low-grade infections?

Method: Included were 31 patients with modular megaprostheses, whose implant had been explanted due to suspected joint infection or revision surgery between 2008 and 2014. SCs of the explanted modular megaprostheses were cultured according to the protocol by Trampuz et al. The diagnosis of infection was evaluated according to the definition of the Musculoskeletal Infection Society (MSIS).

Results: The sensitivity of SC was 91,3% compared to 52,2% for TC and the specificity was 100% for SC and TC (p=0.004). Under preoperative antibiotic therapy the sensitivity of SC was 83,3% while the sensitivity of TC was 50%. Without preoperative antibiotic therapy the sensitivity of SC was 100% compared to 54,5% for TC. In nine cases SCs detected microorganisms, while TC was negative. Detected bacteria were S. epidermidis in four, Micrococcus species in one, Finegoldia magna in one, Brevibacterium casei in one, Pseudomonas fluorescens in one and Enterococcus faecium in one. Polymicrobial infection was detected in four patients.

Conclusions: SC is a reliable method for dislodging pathogens from the surface of orthopedic implants. The SC of modular megaprostheses showed significantly higher pathogen detection than the periprosthetic TC, especially for low virulence pathogens.
Introduction: Dead space management after eradication of bone infection is a major concern. Antibiotic containing biphasic materials provide an alternative substitute to bone-grafting. Aim: To compare a biomaterial (calcium sulphate+ hydroxyapatite+ gentamicin) with frozen allograft and untreated empty control for dead space management in a non-infected tibial defect rat model.

Methods: A 3 mm x 4 mm defect (metaphyseal) was created in the proximal tibia of Sprague-Dawley rats of 6-weeks age. The animals were allocated into 3 groups, based on the material used for dead space management: 1. Empty control (n=9); 2. Allograft (n=10); 3. Biomaterial (n=10). After sacrifice at 8-weeks, the defect region was evaluated with X-ray, Micro-CT, and DEXA. Statistics: ANOVA with Games-Howell post hoc test.

Results:
1. X-ray: Visual inspection showed an increased density in the biomaterial group.
2. Micro-CT: Mean Mineralized Volume per Defect Volume (MV/DV) was 1.7% (CI:1.1-2.3%) in group 1, 8.9% (CI:6.6-13.1%) in group 2, and 24.9% (CI:12.3-37.5%) in group 3. MV/DV was higher in group 3 compared to group 1 (p=0.006) and group 2 (p=0.047).
3. DEXA: Mean Mineral Content (MC) was 34.4mg (CI:31.7-37.1mg) in group 1, 34.4mg (CI:31.3-37.1mg) in group 2, and 42.96mg (CI:38.6-47.3mg) in group 3. Group 3 showed a significantly higher MC compared to group 1 (p=0.004) and group 2 (p=0.004).

Discussion: In this animal model, we have seen increased mineral volume in a tibial defect after dead space management with a gentamycin eluting biomaterial compared to frozen allograft. Provided this increase in mineral volume corresponds to an equally improved regenerative potential, it could be useful in a clinical setting thus reducing the need of bone grafting. Furthermore the local release of antibiotics may prevent infection recurrence and act in synergy with systemic antibiotic treatment.

References:
Fig.1: Results after dead space management of a tibial defect in a rat model. Micro-CT: Mean Mineralized Volume per Defect Volume (MV/DV) +/- SEM. DEXA: Mean Mineral Content (MC) +/- SEM.
KNEE ARTHRODESIS WITH A LONG INTRAMEDULLARY NAIL AS LIMB SALVAGE FOR COMPLEX PERIPROSTHETIC INFECTIONS

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Aim: Periprosthetic infection following total knee arthroplasty (TKA) is a devastating complication, which is not always satisfactorily resolved by revision surgery. Arthrodesis is a salvage alternative to above-knee amputation or permanent resection arthroplasty. Fixation options include internal compression plating, external fixation, and intramedullary nails. The objective of this study was to evaluate the outcomes of arthrodesis with a long intramedullary nail as a salvage procedure for complex infected primary or revision TKA, or infected non-union of previous failed knee arthrodesis.

Method: We retrospectively reviewed twelve consecutive cases (9 males, 3 females; mean age, 67 years), performed at our institution between 2003 and 2014. In all cases, recurrent infections, significant bone or soft tissue loss, poor bone quality, or other co-morbidities meant that revision arthroplasty was not practical. The mean follow up was 48.5 months (range, 9 – 120 months) and all procedures were performed by a senior orthopaedic surgeon. No patients were lost to follow up. Desired outcomes were the ability to mobilize without pain, solid radiographic fusion, and the eradication of infection.

Results: Eleven patients (92%) demonstrated stable fusion and ten patients (83%) were ambulatory without pain at most recent follow up. Eight patients achieved union at an average of 12 months; three required repeat procedures, achieving union at an average of 9 months. Ten patients (83%) remained without infection at latest review. There was a significant difference (P < 0.01) between the numbers of previous operations amongst the eight patients who initially achieved union (mean, 3.25) and three who subsequently required repeat procedures (mean, 8.33).

Conclusions: In contrast to similar studies, our preference was for a single-stage exchange where possible, although comparable ambulatory and fusion rates were observed. Numerous previous attempts at revision arthroplasty, co-morbidities, and infections with highly resistant organisms may hinder the efficacy of arthrodesis as a definitive salvage procedure. We emphasize the importance of a thorough debridement protocol during the initial removal of infected prosthetic material. Although technically challenging, arthrodesis with a long intramedullary nail can alleviate pain and allow early mobilisation, offering an acceptable limb salvage procedure for carefully selected patients with complex periprosthetic infections.
Aim: The test specifically designed and validated for the diagnosis of Periprosthetic Joint Infection* is a new test for periprosthetic joint infection. This lateral flow assay measures the level of alpha defensin in synovial fluid and provides a Yes/No read out of whether levels are raised above a previously defined cut off for PJI. Our aim is to evaluate the performance of the test specifically designed and validated for the diagnosis of Periprosthetic Joint Infection* in patients with suspected PJI.

Method: All patients undergoing investigation for suspected PJI were evaluated using this novel test prior to commencing treatment. The definition of infection used for the purposes of this evaluation is based on the Public Health England modified CDC definition as used for mandatory reporting of surgical site infection in England and Wales.

Results: 44 tests were performed in 36 joints (19 hips, 15 knees, 1 ankle and 1 shoulder) Repeat tests were performed in cases of suspected contamination on microbiological culture, when the test kit failed and in some cases a repeat test was performed at a pre-operative aspiration and then subsequently at the time of revision. There were 31 negative and 11 positive tests. In 2 cases the test was deemed to have failed because of the absence of a control line. All patients diagnosed with bacterial infection were correctly identified by the test specifically designed and validated for the diagnosis of Periprosthetic Joint Infection* (6 S. Epi, 1 S. Salivarus, 1 corynebacterium). 1 patient was confirmed to have a deep Candidal infection in whom the test specifically designed and validated for the diagnosis of Periprosthetic Joint Infection* was negative. All patients who failed to meet the infection criteria had negative tests* including 3 contaminants (2 P acnes and 1 S epi).

Conclusions: The test specifically designed and validated for the diagnosis of Periprosthetic Joint Infection* represents a useful adjunct to current diagnostic testing in suspected PJI and shows a high accuracy in detecting bacterial infection in this series. The test specifically designed and validated for the diagnosis of Periprosthetic Joint Infection* is particularly useful in cases of uncertainty for example where a suspected contaminant has been grown.

*Synovasure
Aim: The objective of this study was to statistically evaluate our diagnostic findings and compare them to recent publications. Furthermore we wanted to evaluate the algorithm of diagnosis before performing revision surgery and if necessary change or reform our algorithm. Because of the large number of patients general considerations and advises about diagnostics of unclear implant failure should be made.

Method: The retrospective single center study took place in the Auguste-Viktoria-Klinikum Berlin (AVK) in the period of 2010 to 2014 and includes 205 patients with an unclear endoprostheses failure. In order to finally clear up the cause of failure we acquired laboratory, histopathological and microbiological findings by performing an open or percutaneous surgery.

Results: The 205 patients had an average age of 68.9 and the majority were female (61.0 %). We performed 308 operations on the knee (53.7 %), hip (43.3 %) and shoulder (2.9 %). The most frequent proven periprosthetic membrane in the histopathological examination was type I (25.7 %) and type II (22.4 %). The microbiological examination could only detect an infection by a specific pathogen in 19.5 percent of cases. The main germs were coagulase-negative staphylococci (46.0 %), followed by streptococci (13.0 %) and *staphylococcus aureus* (12.0 %). In our study there was a periprosthetic joint infection (PJI) in 29.2 % of the cases. The highest sensitivity (88.9 %) and specificity (99.5 %) accomplishes the histopathological examination for detecting PJI. Microbiological examination accomplishes a lower sensitivity (54.4 %) and an almost equal specificity (95.0 %). There was a statistically significant correlation between the appearance of a PJI and the clinical findings of microbiology and histopathology (p <0.001). The AUC for the serum C-reactive protein (CRP) was 0.79 and for the serum white blood cell (WBC) count 0.57.

Conclusions: The high clinical value of the histopathological examination at clarification of unclear endoprostheses failure could be confirmed in our study. Percutaneous surgery yielded the same histopathological results as open surgery and should always be considered before performing open revision surgery. Our study confirms that serum WBC count has only a minor role for detecting PJI. Optimal threshold for CRP was 13 mg/l. This result affirms other studies that propose a slightly higher threshold than 5 or 10 mg/l. Microbiological examination should combine different procedures such as biopsy, joint aspiration and sonication if possible.
Aim: To compare value of different samples culture for microbiological diagnosis of prosthetic joint infection.

Method: We performed a prospective study on 487 prosthetic joint revisions (170 knee, 317 hip) in our institute during 2012-2014 years. Inclusion criteria were availability preoperative aspirate, removed prosthesis parts and multiple intraoperative tissue samples for microbiological investigation. Direct inoculation joint aspiration fluid into the blood culture bottles was used for preoperative culture. Sonication method was performed as described Trampus (2007).

Results: Aseptic loosening was diagnosed in 349 cases and PJI in 138 cases (67 clinical sign). Among PJI patients 5(4%) were culture-negative. Preoperative aspirate (PA) culture was less sensitive than Intraoperative culture (IOC). Multiple tissue samples (TS) and Prosthetic components (PC) sonication had close diagnostic value.

<table>
<thead>
<tr>
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<th>Sensitivity</th>
<th>Specificity</th>
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<tr>
<td>Preoperative aspirate</td>
<td>78,98</td>
<td>98,56</td>
</tr>
<tr>
<td>Tissue samples</td>
<td>91,3</td>
<td>85,95</td>
</tr>
<tr>
<td>Prosthetic components</td>
<td>87,68</td>
<td>93,41</td>
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All three methods were compared based on detected microorganisms: in 76 cases (55%) was concordance in microorganism detected in all 3 types of sample. PA were less informative then IOC: 23 patients (17%) were culture negative preoperatively, 17 (12%) had partly-matched results, 3 cases (2%) were considered as contamination (Fig.1) Accuracy AP for detection causative microorganism was 83% (90 out of 109).

Fig.1 Compare preoperative culture with IOC results Fig.2 Matching tissue samples and PC cultures results
TS and PC culture were concordant in 93 patients (67%), in 22 patients (16%) only TS were informative for microbiological diagnosis, in 14 cases (10%) only PC sonication culture were informative (Fig.2).

**Conclusions:** PA culture results had not enough accuracy for detection causative microorganism, and should not be base for antibiotic treatment. Combination TS and PC sonication culture could be recommended to improve microbiological diagnosis in PJI.
Aim: There is a high unmet medical need for novel therapeutic options against bone and joint infections, medical devices infections and endocarditis. These infections are chronic and hard to treat mostly because the offending bacteria are in a ‘persister’ state, a specific metabolic state where they are resistant to high concentrations of antibiotics but are not genetically resistant. We aimed to identify small molecules specifically killing staphylococci persisters (Staphylococcus aureus, Staphylococcus epidermidis), which would be used in combination with standard antibiotics to cure the hard-to-treat infections where staphylococci are the most frequent culprits.

Method: We set up two models with high number of persisters: established biofilms on abiotic surfaces and stationary phase of planktonic growth. We performed a high throughput screening on mature S. aureus or S. epidermidis biofilms. We used the experimental conditions where resistance to antibiotic treatments is maximal.

Results: We retained 3 chemical series for their activity on staphylococci persisters, bacterial selectivity and potential for oral administration. Their activity was confirmed in a mouse subcutaneous-implanted catheter model and improved in combination with conventional antibiotics.

Conclusions: Persister bacteria, although tolerant to high concentrations of antibiotics, are sensitive to our molecules. Their activities are improved in combination with antibiotics.
Aim: *Staphylococcus epidermidis* is a common pathogen in prosthetic joint infections (PJI). Few studies have focused on the treatment and the results of treatment in PJI due to *S. epidermidis* in general, and in particular PJI due to methicillin resistant *S. epidermidis* (MRSE). In a retrospective study we compared the results of treatment of PJI due to *S. epidermidis* and *S. aureus*.

Method: In the period 2007 - 2012 we identified 202 patients operated for PJI. The following definitions were applied: 1) PJI: Growth of the same microorganism in at least two biopsies/joint fluid. 2) Successful treatment: Patients with a well fixed prosthesis with no signs of infection two years after completed treatment. 3) Failures: Patients with a chronic fistula, permanent resection arthroplasty, amputation, arthrodesis, lifelong antibiotic treatment. We excluded patients with a causative microbe other than *S. epidermidis* and *S. aureus* and patients with a polymicrobial infection. We also excluded patients who died during the follow up period of two years.

Results: 64 patients had an acute or chronic infection of hip and knee prosthesis. 32 patients had an infection due to *S. epidermidis*, of which all were MRSE. 32 patients had a PJI due to *S. aureus* (all MSSA). MRSE were cultured in 10 acute cases and 22 chronic cases, and *S. aureus* in 22 acute cases and 10 chronic cases (p= 0,006, chi square test). In patients with an acute postoperative infection the failure rate was 1/10 in cases due to MRSE and 6/22 in cases due to *S. aureus*. In patients with a chronic infection the failure rate was 3/22 in cases due to MRSE and 3/10 in cases due to *S. aureus*. The number of operations related to the PJI was 3(1-7) in cases due to MRSE and 3 (1-9) in cases due to *S. aureus*. The time needed (median) for successful treatment was 5(2-46) months in cases due to MRSE and 6(2-26) months in cases due to *S. aureus*.

Conclusions: According to the present study all *S. epidermidis* identified in a PJI were MRSE. MRSE were more common in chronic infections compared to *S. aureus*. The results of treatment of PJI due to MRSE compared to the results of treatment of patients with a PJI due to *S. aureus* are similar.

Acknowledgements: The research is part of the internal quality control and no funding was received as the hospital is public financed.
Aim: Given the epidemiological and treatment changes that have occurred in the infectious diseases we decided to evaluate the changes of Osteomyelitis (OM) through 5 decades in our unit.

Method: A retrospective study of 71 records (1972-1976), 74 records (1997-2005) and 71 records (2010-2015) with diagnosis of OM treated in our unit, was carried out.

Results: Chronic presentation has declined dramatically (from 89% in the seventies to 6% today). The age group > 10 years, adolescence, went from being the least frequent (28%) in the 70’s to be the most important today. The genre has always been dominated by males with a ratio of approximately 3:1. The time between the onset of symptoms and the first consultation has decreased. The consultation motive initially was distributed between pain, increased volume and fever, today is pain the main symptom (75%). The history of trauma has remained constant (35%). Comorbidity has increased over the years from 9% to 17% (obesity). The most frequent location has always been tibia, with a progressive decrease of femur and humerus, and a progressive increase of the calcaneus (4% to 21%). The leukocytosis was always mild with an average of 11,300 mm3. PCR is used since the 90s and has meant an advance on suspicion being raised in most cases (ᵡ 71 mg /l). The ESR has always been an important marker of infectious compromise later and has remained on average 60 mmH. The support tests varied from the X-ray (most important was the clinic) in the seventies to bone scintigraphy today. Over the years the Oxacillin has been and remains the antibiotic of choice to start therapy until ATB susceptibility testing. Intravenous treatment time decreased from 12 days to 7 days. Surgical treatment has varied from 92% to 36% today, and techniques are less sophisticated. Taking culture has taken root in our colleagues (73%) and positivity arrives today to 53%. The SAMS is still the main germ involved (89% to 74%), but others have appeared. The total treatment time decreased from 34 to 25 days.

Conclusions: Undoubtedly the OM has changed in many ways, and for the better, offering unimagined results 40 years ago; and they go accompanied with the technological, pharmacological and knowledge advances. However, clinical suspicion remains essential in making the diagnosis and improving the results of the OM.
Aim: We present the case of a 57 years old male with chronic osteomyelitis of the tibia and a large sinus tract after an open fracture. The fracture was initially treated with open reduction and internal fixation. Three revision surgeries were performed. Four months postoperative after a failed broken implant a re-plating was necessary. The second revision with conversion to an intramedullary nail was performed 2 years after trauma because of a non-union. Due to infection with persistent pain the third revision with removal of the nail and placement of an Ilizarov ring fixator with Gentamicin-chain insertion was done 4 years after trauma. Eighteen years after the initial trauma the patient presented with a poorly controlled diabetes (HbA1c 8.4 %), smoked (40py) and was off antibiotics for the last four months. Previous performed wound swabs had shown colonization with *Proteus mirabilis* and *Pseudomonas aeruginosa*. Preoperative workup (X-rays, MRI, PET-CT, MR angiography, needle angiography) confirmed a single osteomyelitis lesion, without joint involvement and normal perfusion.

Method: After general health optimization with improving the diabetic control (HbA1C 6.8 %) and smoking cessation a fourth revision surgery was performed 20 years after initial trauma. In this surgery the defect was debrided and filled with gentamycin loaded cement. To cover the soft tissue defect a musculocutaneous suralis flap was performed. In the intraoperative microbiological workup *Proteus mirabilis* was detected. The patient was treated with Ceftriaxon for the first 14 days and then with Ciprofloxacin for a total of 6 weeks postoperative. The histological workup demonstrated no malignant transformation. After 3 days of bedrest the patient was allowed to partial weight bear.

Results: At the six week follow up the wounds were healed and dry, the patient was fully weight bearing without any pain and inflammatory markers were normal. X-ray was according to the time without abnormalities.

Conclusions: One-stage debridement and augmentation with antibiotic loaded cement seems to be a viable treatment option even for long-standing chronic osteomyelitis. We believe that preoperative general health optimization is mandatory and may lead to better outcomes with fewer complications.
Aim: Implant-associated infections constitute devastating complications in orthopedic surgery, which frequently can only be overcome by revision surgery, and in the worst case may lead to amputation. Most device-related infections are thought to be caused by perioperative inoculation. Systemic antibiotic prophylaxis is therefore routinely used and has been proven to be effective to a certain degree. Yet, device-related infections still occur with methicillin-resistant strains being particularly threatening. Pathogenesis of implant-associated infections start with bacterial colonization of the implant surface and the bacteria switching from the planktonic state to a sessile form. In the early phase of this process bacteria compete with the patient’s body cells. Coatings are hence an attractive approach to complement systemic antibiotic-based prophylaxis by protecting the implant from bacterial colonization.

Method: aap Implantate AG has developed a silver-based antimicrobial coating for the novel antibacterial trauma system*. By silver ion release in the early postoperative phase the antibacterial coating* is intended to prevent bacterial colonization of the implant. Silver has several advantages as an antimicrobial agent. It is highly effective against a broad spectrum of potential pathogens including methicillin-resistant bacteria such as MRSA and MRSE. Moreover, silver shows high efficacy during the time span of highest risk and a low toxicity to human cells. Silver ions have the capacity to migrate into biofilms and reach bacteria not only in an early but also in an advanced state of biofilm formation. As prokaryotes are more sensitive to the toxic effects of silver than eukaryotes silver-based coatings can create a competitive advantage for bone tissue in the colonization of the device. Once a colonization of body cells, e.g. surrounding fibroblasts, has taken place biofilm formation becomes less likely.

Results: The antibacterial coating* has proven effective against various bacteria including MRSA in experimental tests (in vivo and in vitro). Moreover, the product shows excellent biocompatibility.

Conclusions: The antibacterial trauma system* represents a promising means to reduce implant-associated infections.

*LOQTEQ®
Aim: Hypothermia, a body temperature of <36°C, has been shown to increase cardiac mortality, the incidence of postoperative infections, and the length of hospitalization following general surgery. However, studies assessing the incidence of hypothermia during primary total hip and total knee arthroplasty (THA and TKA) and its correlation with prosthetic joint infections (PJI) have not been demonstrated.

Method: In this prospective observational study, incidence of hypothermia and its correlation with prosthetic joint infections in a large cohort of patients undergoing elective unilateral total knee or hip replacement was measured. We included 2600 patients, all operated between 2011 and 2014; 1127 undergoing TKA and 1473 undergoing THA.

Results: The overall incidence of hypothermia was 11.7%. The infection percentage was 1.0% in hypothermic patients versus 1.9% in normothermic patients (p=0.27). A linear regression analysis showed a significant decrease in incidence of hypothermia among the years 2011-2014 (P<0.05). Incidence of hypothermia was 18.4% in 2011 versus 8.4% in 2014 (P<0.05).

Conclusions: In conclusion, more than 10% of our patients was exposed to hypothermia. However, we did not find a correlation with hypothermia and PJI. We found a 10% decrease incidence of hypothermia over the years without any change in protocol. The reduction of hypothermia could be explained by a higher awareness among surgical staff.

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Aim: Osteomyelitis in children is usually acute, and haematogenous in origin. Outcomes are excellent despite a lack of evidence from systematic reviews to guide the choice and duration of antibiotic therapy. S. aureus has historically been described as the most common cause although a microbiological diagnosis is not obtained in between 20-50% of cases. Recent studies have demonstrated an increase in reported cases due to fastidious organisms such as K. kingae, as a result of improved microbiological identification strategies. We evaluated a cohort of 35 cases from a tertiary referral centre for a broad range of characteristics, including clinical presentation, microbiological and radiological investigation, management and outcomes.

Method: A case note review of 35 cases of osteomyelitis presenting between 2012 and 2015 to the Orthopaedic department of a large teaching hospital.

Results: In keeping with the literature, 50% of cases occurred in the under-5s (range 3 months – 15 years) and there was a male preponderance (1.4:1). All but one presented with pain at the site of infection and in most cases the C-reactive protein was raised (84%), but relatively few had a documented temperature (33%) or raised white cell count (14%). Plain radiography was normal in 56%, and the most sensitive radiological modality was MRI which was diagnostic in 24/26 cases. 19 required surgery and a further 3 had radiologically guided aspiration of a subperiosteal collection. A microbiological diagnosis was obtained in 69%, and S. aureus was the predominant cause (17 cases). Empiric treatment was with Flucloxacillin in a majority of cases (87%). Most (63%) were treated for 6 weeks in total (range 14 days to 3 months), with a single antimicrobial agent (66%) and a median of 10 days of therapy intravenously. Median time to normalisation of inflammatory markers was 11 days and median length of inpatient stay 12 days. Follow up was for a median of 7 months with no recorded relapses.

Conclusions: Our cohort differed from the literature in presentation with lower rates of fever but higher rates of localising symptoms. There was also an increased rate of positive microbiological testing perhaps reflecting a high rate of sampling prior to antibiotic therapy. This cohort predates use of techniques such as 16S-PCR analysis which may have yielded more diagnoses of fastidious organisms such as K. kingae, in particular for a subset of our patients (n=4) who had normal inflammatory markers and more indolent presentations.
PAEDIATRIC SEPTIC ARTHRITIS IN A TEACHING HOSPITAL COHORT: CLINICAL AND MICROBIOLOGICAL CHARACTERISTICS, MANAGEMENT AND OUTCOMES

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Aim: The clinical presentation of paediatric septic arthritis varies according to the age of the child, site of infection and infecting pathogen. Prompt diagnosis and timely intervention are key to successful outcomes. Newer diagnostics have led to increased isolation of more fastidious pathogens such as K. kingae. There has also been a recent trend to use a shorter course of intravenous antibiotics before switching to oral therapy. We interrogated our paediatric osteoarticular infection database for consecutive cases of septic arthritis presenting between 2012-2015, with respect to presentation, diagnosis, management and outcomes.

Method: A case note review was undertaken of 12 cases of septic arthritis presenting between 2012-2015 to the orthopaedic department of a large teaching hospital.

Results: Cases ranged in age from 9 months-13 years with 67% presenting between 2 months-2 years. All cases were lower limb with >50% involving the hip. There was a left sided preponderance.

All patients had systemic symptoms and localising signs starting 1 day-2 weeks prior to presentation. 50% had a fever of >38°C on admission. All patients had raised total white cells, with a median CRP 41 (11-366).

Diagnostic aspirates were taken in all patients with 50% yielding positive cultures. 17% were placed in blood culture bottles. 17% samples were taken before antibiotics, and 25% afterwards with the precise timing of the reminder being unknown. 62.5% from those aged 2 months to 2 years were culture negative whereas all samples taken in >2 year olds were culture positive (S.aureus, N.meningitidis and Candida). In the younger age group, pathogens isolated were S.aureus, group A streptococcus and coagulase-negative-staphylococcus.

Antibiotic therapy varied. Of the culture negative cases, 60% had broad spectrum antibiotics followed by MSSA targeted therapy. Total duration of therapy varied from 21-56 days, with intravenous therapy given for an average 31 days. All cases underwent surgical intervention with a washout +/-debridement.

Outcomes were good with only 2 cases having documented late complications: avascular necrosis in one and psychological trauma in another.

Conclusions: The high rate of culture negativity in the 2 month-2 year cohort warrants further investigation. New diagnostics locally will enable molecular testing of paediatric joint aspirates and may help further define this group. The duration of antibiotic therapy is relatively long compared to some cohorts, and will be reviewed. A clinical, diagnostic and management pathway has been developed to standardise and optimise management of these children.
Aim: Current techniques for diagnosis of prosthetic joint infections (PJI) can be of low sensitivity, with prior antimicrobial therapy or infection by fastidious organisms particularly influencing culture results. Fast, accurate and reliable diagnosis of PJI is necessary to inform treatment choices, particularly in consideration of antibiotic resistant organisms. Next-generation sequencing (NGS) has demonstrated potential as a tool for diagnosis of bacterial, viral and parasitic infections directly from clinical samples. We assess the ability of NGS to detect bacterial infections in prosthetic joints directly from clinical samples compared to standard microbiology culture diagnosis.

Method: Samples were sonication fluids or peri-prosthetic tissues. Samples were received and processed by the microbiology laboratory using standard procedures, before storage of sonication fluids at -20°C prior to processing for NGS. Whole human cells and tissue debris were removed by filtering, then bacterial cells were mechanically lysed before DNA extraction. After purification, DNA was sequenced on a sequencer* using a protocol**. Metagenomic classification was performed by k-mer matching of trimmed sequencing reads using KRAKEN and a custom database containing all human, bacterial and viral RefSeq genomes.

Results: 81 sonication fluids from a total of 71 patients were received and processed by standard microbiology techniques and for NGS. 51 samples were culture positive (50/51 samples sonication fluid and tissue culture positive, 1/51 sonication fluid culture positive, tissue culture negative) and 30 were culture negative (18/30 samples culture negative in both sonication fluid and tissue, 12/30 sonication fluid culture negative, tissue culture positive). The sequence results identified over 90% of DNA extracted as human; this was removed from further analysis. Of the culture positives 38/51 (76%) were concordant, with the majority species identified agreeing with culture results. Discrepant NGS results included only one species identified from a mixed infection, and additional species identified that were not observed in culture. Due to the sensitivity of NGS, low levels of background reads were detected in culture negative samples that were not deemed to be clinically significant.

Conclusions: We demonstrate as a proof of principle that NGS can provide informative diagnostic information in the case of PJI. Further depletion of human DNA will lead to improved genomic information on the cause of infection, strengthening the case for NGS as a diagnostic tool.

This study was supported by the Oxford NIHR Biomedical Research Centre.

*Illumina MiSeq sequencer
**Nextera XT
ADAPTATION OF THE CAPACITY TO FORM BIOFILM IN STAPHYLOCOCCUS AUREUS ISOLATES DURING THE COURSE OF HUMAN CHRONIC BONE AND JOINT INFECTIONS

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Aim: Prosthetic joint infection (PJI) is associated with high rates of chronicity and relapse (10-20% of cases). One of the major bacterial mechanisms is the formation of biofilm, within which bacteria are protected from antimicrobials and host immune response. The present study aimed to determine and compare the ability to form biofilm of 3 pairs of isolates collected in 3 different patients during the initial and recurrent BJI episodes.

Method: Three couples (C1, C2 and C3) of methicillin-susceptible S. aureus (MSSA) strains collected from patients with persisting or relapse of BJI were tested. The capacity to form biofilm of the initial and recurrent isolates were compared using crystal violet assay containing i) Brain Hearth Infusion supplemented with 1% glucose (BHIg), ii) a pool of human serum supplemented with 1% glucose (SERg). The lecture was performed i) after 24h for BHIg, ii) after 7, 14, 21 and 28 days for SERg. Biofilm formation on a glass slide in a dynamic BHIg fluid was evaluated by plate count after 24h. The early kinetics (0, 2, 4, 6 and 24 hours) of biofilm formation in BHI was assessed using a scanner specially adapted to read microplates*. Finally, a new bacterial susceptibility test**, allowing the determination of the biofilm Minimal Inhibitory Concentration (bMIC) preventing biofilm, using a scanner specially adapted to read microplates*, was performed.

Results: For the C2 pairs, the recurrent isolate revealed a higher capacity to form biofilm in BHIg using crystal violet assay than the initial isolate (C2 p<0.001; C1-C3 NS). Regarding formation in SERg, C1 recurrent isolate was able to form a high biofilm from day 5 in contrast to initial isolate for which biofilm was not formed even after day 30 (no difference for C2 and C3). Biofilm formed in dynamic fluid was significantly higher for the C2 and C3 recurrent isolates than for the initial isolates (p<0.01). If no difference, in the early kinetics of biofilm formation, was observed using a scanner specially adapted to read microplates*, the new bacterial susceptibility test**, revealed that the bMIC for fosfomycin in the C1 recurrent isolate was lower than for the C1 initial strain (16µg/mL Vs. 128µg/mL).

Conclusions: Although the expression of biofilm formation differed from one couple to another, depending of the experimental conditions, the enhanced capacity of biofilm formation affect the recurrent strains compared to initial stain in each patient. These findings suggest that S. aureus PJI chronicization is associated with an in vivo bacterial adaptation/selection regarding biofilm formation.

*Biofilm Ring Test™
**Antibiofilmogram®
Aim: Hidden deep implant-related infection is believed to be linked to pedicle screw loosening after spine surgery. Low-grade bacterial infection can be hard to diagnose and may be undetected by conventional culture based methods. Next generation sequencing (NGS) could help to uncover hidden bacterial infections as a possible cause for implant loosening. This case report describes the use of NGS in the diagnostic work-up of a patient with pedicle screw loosening after spine surgery.

Method: A 60 y/o male had to undergo revision spine surgery for pedicle screw loosening and adjacent segment disease 3 years after primary surgery performed because of osteochondrosis L3-S1 and spinal canal stenosis. In addition, the patient had left and right knee prostheses, and suffered from arterial hypertension and hyperuricemia. At revision surgery, samples from pedicle screw canals were collected for microbiological diagnosis. The removed screws were sonicated, and sonication fluids were cultured and sent for molecular analysis. For culturing Schaedler agar, thioglycollate medium and bouillon bottles under aerobic and anaerobic conditions were used. Upon growth in bouillon differentiation on Schaedler agar followed. Isolates were identified by MALDI-TOF.

For the molecular detection, DNA was extracted using a kit for human DNA removal*. The V1-3 region of 16S rRNA gene was PCR-amplified with bacterial primers 27F and 534R (30 cycles) and paired-end sequenced on a DNA sequencer**. Paired-end reads were trimmed (trimmomatic v.0.32) and merged (FLASH v.1.2.11). The reads were screened for potential PhiX contamination***, clustered into operational taxonomic units (sequence identity ≥ 97%) using a sequence analysis tool****, and subsequently classified using the RDP classifier with the MiDAS database (v.1.20).

Results: Clinically there were no signs of local or general infection. Serum parameters were normal (C-reactive protein 0.7 mg/L, WBC 6.2 Gpt/L) at revision surgery. No other infectious foci were noticed. Histology showed no signs of infection. Routine microbial culturing was negative. However, long-term cultures detected Propionibacterium acnes. Molecular analysis revealed presence of Corynebacterium species. The patient received oral clindamycine 600 mg 3 times/day for 6 weeks; 10 months later he had no problems from the lumbar spine. Follow-up CT scan showed no recurrence of pedicle screw loosening.

Conclusions: Molecular analysis using NGS may be useful to detect hidden low-grade infection especially in the setting of pedicle screw loosening after spine surgery. It could be a crucial additional method in combination with routine clinical microbiology to improve our understanding of implant loosening.

* MolYsis complete5 (Molzym, Germany)
** Miseq DNA sequencer (v3 chemistry, 2×300 bp)
***USEARCH v.7.0.1090
[P130] HIGH ACTIVITY OF BACTERIOPHAGES AGAINST PLANKTONIC AND BIOFILM ESCHERICHIA COLI BY MICROCALORIMETRY

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**Aim:** Despite the introduction of new antibiotics, resistant microorganisms remain an unresolved challenge pushing the medical community to investigate new and alternative ways to fight infections, particularly those associated with implants. The aim of this study was to systematically explore and characterize rapidly bactericidal (lytic) bacteriophages against *E. coli* in planktonic and biofilm forms using a highly sensitive assay measuring growth-related heat production (microcalorimetry).

**Method:** T3 phage was tested against *E. coli* TG-1. Microcalorimetry was performed using an isothermal calorimeter (TAM III, TA Instruments) at 37°C in sealed glass ampoules containing BHI. *E. coli* (5x10⁶ and 5x10⁷ cfu/ml) were exposed to different concentration of bacteriophage (MOI = multiplicity of infection, given by the ration of N° of bacteria / N° of phages). A positive control, without the presence of phages is also used. Heat flow (µW) and total heat (J) were measured for 24 hours.

**Results:** Figure 1 shows high activity of bacteriophages against planktonic (Fig. A) and biofilm (Fig. B) *E. coli*. Bacteria are exposed to bacteriophages in different concentrations. Bacteriophages largely inhibit the growth of bacteria independent of the initial inoculum used. T3 was able to inhibit the growth of both, planktonic and bacteria *E. coli* at different MOI. Bacteriophage also shown a dose dependent activity against planktonic and biofilm *E. coli*.

**Conclusions:** Bacteriophages largely inhibited the growth of planktonic and biofilm bacteria independent of the initial inoculum. In view of increasing antimicrobial resistance, phages represent a promising alternative or complementary approach to antibiotics. This findings need to be studied and confirmed in-vivo using a foreign-body infection model.
Figure 1. Bacteriophage T3 against *E. coli* TG1 by microcalorimetry
SWABS FOR PJIS DIAGNOSIS: STILL USED, STILL UNNECESSARY

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Aim: Diagnosis of prosthetic joint infections (PJIs) presents some drawbacks, including sample collection and transport and risk of microbial contamination (1, 2). Although swabs are not recommended for PJIs diagnosis, to date many orthopedic surgeons still use them. Aims of this study were: a) evaluation of sensitivity of a new device for sample collection, transport and treatment* (a closed and sterile chemical debonding biofilm system) in comparison with flocked swabs; b) demonstration of reliability of the system to find bacteria on removed prosthetic implants* in detecting pathogens from pooled samples to decrease number of swabs from single patient (usually 4-8).

Method: two groups of 30 patients each undergoing surgery for suspected PJIs were enrolled in the study; one was used for comparison of sensitivity of the system to find bacteria on removed prosthetic implants* with flocked swabs, while the reliability of the device was evaluated in the other group by analyzing pooled samples in comparison with single swabs. After collection of periprosthetic tissues and implants into the system to find bacteria on removed prosthetic implants*, dithiothreitol solution (DTT) was released into the device, which was shaken for 15 min. DTT was aspirated, transferred into sterile plastic tubes and centrifuged. The pellet and the swabs were then plated onto agar plates and inoculated into broth. Plates and broths were incubated for 48 hrs and 15 days and daily checked for microbial growth. DTT-treated samples and swabs were considered positive if at least one colony grew on agar plates or if growth was observed during broth enrichment. The same microorganism isolated from at least 2 swabs was considered suggestive for infection.

Results: The system to find bacteria on removed prosthetic implants* demonstrated a higher sensitivity if compared to swabs (77% vs 46%, respectively) allowing to obtain 35% of positive results vs 20% of positivity with swabs. In the second group, we observed a 71% concordance between the system to find bacteria on removed prosthetic implants* pooled samples and single swabs (42% positive and 29% negative results). In addition, the system to find bacteria on removed prosthetic implants* was able to detect pathogen in 20% of cases where swabs were negative, in 9% of patients microbial growth was observed in at least 2 swabs collected from superficial infected wounds and not with the system to find bacteria on removed prosthetic implants* for which this kind of samples was not collected.

Conclusions: these preliminary results highlight the stronger ability of the system to find bacteria on removed prosthetic implants* in identifying microorganisms involved in PJIs compared to swabs. In order to decrease the number of samples needed for PJIs diagnosis, this study demonstrated also that culture of pooled samples with the system to find bacteria on removed prosthetic implants* is more reliable than separate analysis of different swabs.

*MicroDTTect (4 i srl, Italy)
Aim: Pyogenic spinal infection (PSI) is still a low incidence disease. It is often associated with a high comorbidity. When treating PSI operative treatment is often the only alternative due to extensive damage caused by the disease. In some cases conservative treatment, adapted to the patient’s needs and individual risk of an operation, can be considered. We searched for parameters that might help to objectify this mainly clinical decision.

Method: We performed a monocentral retrospective analyses of 36 Patients treated over two years. Three groups were formed; patients with primarily operative treatment (due to osseous destruction)[p.o.] ; patients treated conservatively (antibiotic treatment and partly interventional drainage of paravertebral abscesses)[p.c.] and patients with primarily conservative treatment who developed an operative indication[conv.]. Following factors were surveilled: Age; comorbidity; mortality; existence of paravertebral abscess; inflammatory blood parameters (C-reactive protein [CRP] and white blood cell count [WBC] upon admission and discharge); Microbial growth in obtained blood cultures and biopsies.

Results: The average patient’s age was 69.3 years. Comorbidity score (Charlson index) was 2 in the p.o. group; 1.88 in the p.c. group and 3.4. in the conv. group. Mortality across the groups was 5.7%. Paravertebral abscess formation was found in 37.5% of the p.c. group same as in the conv. group, in the p.o group in 12.5%. Average CRP upon admission was 60mg/l in the p.c. group, 117mg/l in the p.o. group and 150mg/l in the conv. group. On discharge the p.c. group showed an average CRP of 29.1mg/l, the p.o. an average of 36 mg/l and the conv. group an average of 55mg/l. The p.c. group and the p.o. group showed no elevated WBC in average both on admission and discharge. Only the conv. group showed borderline elevated WBC on admission (10.8Gpt/l) with a normal value on discharge. Microbial cultures of bioptic material showed growth of *Staphylococcus aureus* in 4 out of 11 samples. One out of the 11 samples showed growth of *E.coli*. 5 out of 36 patients showed *Staphylococcus aureus* in obtained blood cultures, Streptococci and *Staphylococcus haemolyticus* in one each.

Conclusions: Several well reported facts about PSI were represented in our analysis, such as WBC being a poor predictor of severity and *Staphylococcus aureus* being the main bacteria behind this disease. So far only CRP levels upon admission show promise to be of substantial help in deciding who to operate and who to treat conservatively.
THE MICROBIOLOGY PROFILE OF PROSTHETIC JOINT INFECTIONS IN TAIWAN

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Aim: Little information is available regarding the microbiology profile of prosthetic joint infection (PJI) in Taiwan. We aim to (1) analyse the microbiology profile of hip and knee PJI in Taiwan and (2) compare the microbiological difference between hip and knee PJI.

Method: We performed a retrospective study of all PJI cases at our institute, a tertiary care referral centre over 9 years, during January 2006 to December 2014.

Results: There were 159 and 135 cases identified in hip and knee PJI respectively. The first-time infection episodes were included. 63% of causative pathogens were monomicrobial, 10% polymicrobial and 27% negative-culture. The distribution of causative pathogen type was as the following: 48% were aerobic Gram-positive, 3.4% anaerobic, 8.5% Gram-negative, 2.4% fungal, and 1.7% mycobacterial. The most common causative pathogen was S. aureus (78 episodes, 27%), following by coagulase-negative staphylococci (CoNS, 42 episodes, 14%) and streptococci species (13 episodes, 4.4%). Methicillin-resistant S. aureus (MRSA) and methicillin-resistant CoNS (MR-CoNS) were isolated in 31 episodes (10.5%) and 32 episodes (10.9%) respectively. 40% of S. aureus and 76% of CoNS were methicillin-resistant. Methicillin-resistant staphylococci accounted for 21% of all PJI. Anaerobic pathogens, including Propionibacterium species and Peptostreptococcus species were more likely to occur in hip prosthesis (10 vs. 0 episodes; p = 0.002). Fungal PJI were mainly candida species (5 episodes, 1.7%). Mycobacterium mainly cause PJI in knee (0 vs. 5 episodes, p = 0.02). Enteric Gram-negative bacilli (GNB), including E. coli, K. pneumonia, E. cloacae and Serratia marcescens, etc., were isolated in 17 episodes (5.8%) among monomicrobial PJI and 9 episodes (3%) among polymicrobial PJI. Enteric GNB were more likely to involve in hip prosthesis as well (20 vs. 6 episodes; p = 0.014). Polymicrobial pathogens were isolated more frequently from the hip joint than from the knee joint (22 vs. 6 episodes, p = 0.006).

Conclusions: The high prevalence of methicillin-resistant staphylococci including MRSA and MR-CoNS in PJI may warrant the need of perioperative antimicrobial prophylaxis and empiric antibiotic therapy that covers these organisms. Due to higher incidence of anaerobic, enteric GNB and polymicrobial pathogens in hip PJI compared with knee PJI, this may indicate a different prevention and treatment strategy in hip PJI. Since the relatively high incidence of fungal and mycobacterial PJI in Taiwan compared with the previous literature, obtaining periprosthetic intraoperative samples including fungal and mycobacterial culture routinely should be attempted.
[P134] ERYSIPELOTHRIX RHUSIOPATHIAE OSTEOMYELITIS OF THE FOOT

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**Aim:** Erysipelothrix rhusiopathiae is an unusual cause of osteomyelitis. The bacterium usually causes a skin infection in humans known as erysipeloid, which is considered to be an occupational disease in animal workers. We report a rare case of osteomyelitis of the forefoot due to *Erysipelothrix rhusiopathiae*.

**Method:** A 69-year-old female patient was admitted to the Orthopaedic Department of our hospital with an ulcer of the fifth metatarsophalangeal joint of the right foot and a painless dislocation of the joint. She had a history of neuropathic foot disease. She reported that she had had the ulcer for more than 6 weeks and she also reported a habit of walking barefoot on the beach. She was afebrile and with no other constitutional symptoms. Laboratory investigation showed an elevated white blood cell count, erythrocyte sedimentation rate at 80 mm, and C-reactive protein level at 37 mg/dL (normal value <0.5 mg/dL). All other blood tests had results within normal ranges. MRI and Tc⁹⁹m bone scanning revealed osteomyelitis of the fifth metatarsal and fifth toe. A fifth ray amputation was performed and bone and tissues were taken intraoperatively for culture. After 48 hours small α-haemolytic colonies grew on blood agar plates that were incubated in 5-10% CO₂ and anaerobically. The Gram-positive bacterium was identified as *Erysipelothrix rhusiopathiae*. Susceptibility testing results showed that the pathogen was susceptible to penicillin, ampicillin, imipenem, cefuroxime, ceftriaxone, clindamycin, ciprofloxacin and linezolid, but resistant to vancomycin, teicoplanin, trimethoprim–sulfamethoxazole and tetracycline.

**Results:** The infection was treated with fifth ray amputation and intravenous antibiotic administration of ciprofloxacin (600mg twice daily) and clindamycin (600mg thrice daily) for 3 weeks, followed by oral ciprofloxacin of 500mg twice daily for ten more weeks. The patient had an uneventful recovery. After 9 months there is no evidence of relapse.

**Conclusions:** *Erysipelothrix rhusiopathiae* is rarely found in routine cultures and its small colonies can remain undetected. Correct identification of the pathogen and subsequent appropriate and effective treatment leads to the eradication of the infection.
Nasal colonization with \textit{Staphylococcus aureus} is an established risk factor for developing staphylococcal surgical site infections in the short term. It is not known, however, if patients with (community-acquired) \textit{S. aureus} soft tissue infections have a higher risk for future “orthopaedic” infections in the long term.

Method: We conducted an epidemiological survey of adult patients hospitalized for combined surgical and medical treatment of skin and soft tissue due to \textit{S. aureus} in the only public hospital in Geneva. By reviewing nursing and medical files from the emergency department and hospital wards of our tertiary center, we assessed any other infections they developed (excluding recurrences) after or before the index one.

Results: Among 802 index episodes of skin and soft tissue infections, 553 (69\%) were caused by \textit{S. aureus}, of which 23 were due to healthcare-associated and 15 due to community-acquired methicillin-resistant \textit{S. aureus}. The patients’ median age was 50 years and 204 (25\%) were immune-compromised. The time span between the patient’s first and last consultation (for any reason) in our center was 21.2 years (interquartile range, 10–29 years). In follow-up after the initial infection, 63 patients developed other nosocomial or community-acquired infections. Future infection was more common in those who had had a skin or soft tissue infection due to \textit{S. aureus} compared to a non-staphylococcal infection. Of these, patients with a \textit{S. aureus} (compared to non-\textit{S. aureus}) soft tissue infection had a higher rate of future orthopaedic infections due to \textit{S. aureus} (55/553 vs. 8/249; Pearson-$\chi^2$-test; $p<0.01$). This association was not present for the 372 cases of bursitis: 10/10 vs. 301/362; ($p=0.16$) of which (84\% in total) were due to \textit{S. aureus}.

Conclusions: Adult patients previously hospitalised for moderate to severe skin and soft tissue infections (except for septic bursitis) due to \textit{S. aureus}, compared to non-staphylococcal infections, may be at higher risk of other “orthopaedic” infections, in particular infections due to \textit{S. aureus}.
Very Early Results of the Bone Graft Eluting Gentamicin* and the Bone Graft Eluting Vancomycin** in Septic and Contaminated Indications at Limb Surgery

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Oulu University Hospital, Oulu, Finland

Aim: Open fractures are contaminated and sometimes comminuted, when there’s a risk of bone loss after the debridement. Dead space has shown to be a risk of deep infection. In traditional two-stage operation PMMA + antibiotic beans or a spacer are used as a void-filler, which had to be removed in a second operation of autologous bone transplantation. New bone void filling materials give an option of a single stage operation without late bone transplant.

We analyzed retrospectively the very early results of our operations with antibiotic resorbable cement from the patient’s clinical history recordings.

Method: Between years 2014-2015 we applied the bone graft eluting gentamicin* (CG) or the bone graft eluting vancomycin** (CV) as a void-filler in 18 cases (10 male and 8 female) of various septic or contaminated bone defects in lower (17) or upper (1) limb. CG and CV are synthetic bioceramic bone substitutes, which contain gentamycin (CG) or vancomycin (CV) antibiotics mixed in biphasic powder (calcium sulphate 60% and hydroxyapatite 40%).

After a mean of 4.1 (1-15) initial operations we applied CG or CV to treatment area. The case was estimated healed when the enclosed systemic antibiotic treatment and clinical controls were carried out and the patient didn’t have symptoms of a persisting disease. Result is failure if re-infection occurs and intermediate, if the result is something else.

Results: The mean postoperative follow up at was 5.0 (0.6-14.3) months. 56% (N=10/18) of the patients healed. Four cases (22%) were unsuccessful and cement was removed in mean 5.5 (0.5-14.0) mth. In four (22%) cases the role of the bone void filler*** was uncertain.

Adjuvant systemic antibiotic treatment withstood postoperatively a mean 21.8 (0-75) days in healed cases.

Conclusions: The reason for our modest results may be that we used this new material in multiple indications. It takes a long time to heal in deep complex injuries and we do not know the final result for all with a short follow up. Most difficult cases in our series are around the ankle joint. Perfect debridement and a good soft tissue cover of the affected focus should be performed after the application of the cement.

* Cerament G™ (Bonesupport AB, Lund, Sweden)
** Cerament V™ (Bonesupport AB, Lund, Sweden)
*** CERAMENT™ (Bonesupport AB, Lund, Sweden)
Aim: In the treatment of chronic osteomyelitis often a two stage approach is used. In the first stage, after excision of avital and infected bone, non-resorbable antibiotic carriers (e.g. PMMA-beads, Gentamicin-collagen or PMMA-spacers) are implanted. During the second stage, the bone defect is reconstructed with allo- or autograft. To reduce the number of surgeries and hospital stay, a one-stage procedure with debridement and reconstruction at the same time would be promising. Such a one-stage approach is feasible with the use of allograft plus a resorbable, antibiotic eluting and osteoconductive bone graft substitute.

Method: We report a case of a 45 year old male presenting with discomfort of the proximal tibia for about 13 years. During this time episodes of redness of the skin, swelling of soft tissue and pain alternated with symptom-free episodes. Radiographs of the proximal tibia showed sclerosis of the bone, but no osteolysis or sequestrum. Differential diagnosis included chronic osteomyelitis and bone tumors, so biopsies were taken. Microbiology was negative, but histology showed signs of chronic bone infection. PCR for microorganisms remained negative. In a multi-disciplinary team (MDT) meeting with the bone tumor unit the decision for excision of the affected bone and bone void filling was taken.

Results: On 26th October 2015 surgery was performed. Via an anterior-lateral approach a cortical window was prepared and altered bone completely excised. The cancellous bone appeared avascular and sclerotic. The amount of affected bone was larger than suspected on the radiographs, so a bone defect of approx. 10 x 3 x 4 cm was created. This void was filled with allograft and a bone graft eluting gentamicin* in a layer-by-layer technique. For structural support a locking plate was placed to allow immediate full weight bearing. Histology showed signs of chronic osteomyelitis. Microbiologic analyses found Propionibacterium after 14 days of culture. Wound healing was without any problems. Systemic antibiotic therapy was stared with Meropenem and Fenoximetylenicillin i.v. and then changed to Penicillin p.o for a further 14 days in view of the microbiology results. Follow-up radiographs at four months show good integration of the bone graft. No recurrence of osteomyelitis has been observed so far.

Conclusions: The combination of allograft and an antibiotic eluting bone graft substitute in a layer-by-layer technique can be helpful to fill bone voids after debridement to protect bone healing and bone remodelling. The outcome is encouraging but further evaluation of the method is necessary.

*Cerament G™ (Bonesupport AB, Lund, Sweden)
Introduction: Open wounds and bone defects of extremities often result from war injuries. The Masquelet procedure allows the reconstruction of even segmental bone defects. Bacterial multi drug resistance has been frequently reported given these circumstances, however, with little detailed information on multi drug resistance and surgery success. To gain more insight, our aim was to study 1) the type and frequency of bacterial multi drug resistance using hygienic swab testing and tissue from open wounds from war wounded and 2) the effect on the reconstruction of segmental bone defects according to Masquelet.

Methods: The retrospective data analysis was based on detection of bacteria via MacConkey-Agar and PCR from hygienic swab testing and open wounds in 91 war-wounded patients admitted to hospital between 2012 and 2015. They originated from Syria (10 patients), Lybia (63), Ukraine (13) and Iraq (5). The Masquelet procedure was performed in 15 segmental bone defects. Surgery success was evaluated by cure of infection and wound/bone healing.

Results: In total, bacterial multi drug resistance using hygienic swab testing was detected in 41 out of 91 patients (45%). The three most commonly found organisms were Escherichia coli, Klebsiella pneumoniae, and Staphylococcus aureus. Bacterial multi drug resistance was highest for 3MRGN (17/41), followed by 4 MRGN (9/41) and MRSA (8/37). In addition, bacterial multi drug resistance in tissue of open wounds was detected in 45 out of 50 wounds. Here, the three most commonly found organisms were Acinetobacter baumanii, Pseudomonas aeruginosa, Enterococcus faecalis; bacterial multi drug resistance was highest for 4MRGN (13/21), followed by 3MRGN (6/21) and ESBL (2/21). 3MRGN and 4MRGN bacteria were detected in two thirds of the segmental bone defects, however, without negative effect on the surgery success.

Conclusions: Bacterial multi drug resistance was detected in nearly 50% of war-wounded patients from Syria, Libya, Ukraine and Iraq. However, no correlation was observed between type of bacteria derived from hygienic swab testing and open wounds in the same patient. The common and serious observation of bacterial multiresistance requires the implementation of hygienic care standards and education of medical and nursing staff, it supports Antibiotic Stewardship programs and the need for therapeutic drug monitoring of antibiotics.
Aim: In developing countries osteomyelitis is very common, due to a high level of open fractures, which often result in infection and the prevalence of sickle cell disease, which has been shown to result in osteomyelitis in 30% of the subjects. Scarce data is available on the economic burden for the local health system and the patients however. For our research, we examined the cost of treating osteomyelitis in a developing country, and if such a country meets the requirements to implement the next generation osteomyelitis therapies such as bioactive glass.

Method: Research was performed at an orthopaedic hospital in Ghana between February 2016 and March 2016. Subjects who were diagnosed with osteomyelitis and treated with sequestrectomy between January 2013 and March 2016 were included. Different financial costs related to the treatment of osteomyelitis were collected and calculated. Total prices calculated in Ghanaian cedi (GHS) were converted to Euro with the exchange rate on April 19th 2016, being 4,3412 GHS to 1 Eur.

Results:

Table 1. Average costs involved in treatment of osteomyelitis

<table>
<thead>
<tr>
<th>Cost parameters (GHS)</th>
<th>Consultation</th>
<th>Radiography</th>
<th>Sequestrectomy</th>
<th>FBC</th>
<th>Cultures</th>
<th>Antibiotic treatment</th>
<th>Hospital stay</th>
<th>Total cost (GHS)</th>
<th>Total cost (Euro)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total group (n = 23)</td>
<td>25</td>
<td>179</td>
<td>1200</td>
<td>15</td>
<td>25</td>
<td>33,6</td>
<td>1223,3</td>
<td>3313,6</td>
<td>763,3</td>
</tr>
</tbody>
</table>

* FBC = full blood count

Conclusions: With only a gross domestic product (GDP) of 1276 Euro per person in Ghana and an average cost of 763,3 Euro for the treatment of osteomyelitis, being diagnosed with osteomyelitis is a burden for the patient and their family. Latest generation therapies such as bioactive glass could reduce these costs, however, currently, the medical setting in Ghana nor its health care system (reimbursement) allow for implementing these new therapies.

1. W Ebong, Annals of Rheumatic Diseases, 1986; 45, 911-915
Aim: The aim of this study was to compare infection clearance rates, radiographic and functional outcomes after two-stage revision of total hip arthroplasty with (1) gentamicin-loaded bone cement spacer or (2) Girdlestone resection arthroplasty as the first stage of treatment.

Method: We retrospectively reviewed data of 48 patients (20 females, 28 males) with implanted spacers and 53 patients (21 females, 32 males) treated with resection arthroplasty at tertiary care university hospital in the years 2008-2012. Minimum follow-up was three years (range, 3-7 years). Treatment choice was at the operating surgeon’s discretion.

Results: In the spacer group, mean age at the time of first stage was 62 years (range 24-79 years), time from primary replacement 14 months, and the time from the first to the second stage of the revision 7 months. At latest, minimum 3-year follow-up, two were still ambulating with a spacer in situ, and five were re-revised with another spacer before the reimplantation of the THA.

In the resection arthroplasty group, mean age at the time of first stage was 64 years (range, 37-87 years), time from primary replacement 13 months, and the time from the first to the second stage of revision – 10 months. At the latest follow-up, four patients were ambulating with resection arthroplasty, one did not clear his infection and one died of unrelated causes.

Conclusions: The cure ratio appeared to be the same within both groups (Fisher exact test, p=0.08). Patients with spacers achieved better functional results, used less supports for ambulation and had less leg length discrepancy after the second stage of revision. In the light of those results, we cannot recommend for the use of resection arthroplasty in the treatment of the infected THR.
Aim: This case report describes an 84 year old Caucasian lady from the UK, with known chronic lymphocytic leukaemia and type II diabetes mellitus. She developed multi-focal bone and soft tissue infection with *Nocardia nova*, six months after sustaining an elbow laceration during a fall whilst gardening.

Method: A chronic wound with a sinus developed over the medial aspect of the right elbow. Ultrasound showed a complex subcutaneous collection. Microbiological specimens obtained at the time of drainage grew *Nocardia nova* and a subsequent MRI scan demonstrated distal humeral osteomyelitis. CT imaging showed no evidence of cerebral or pulmonary nocardia, but did reveal widespread lymphadenopathy commiserate with her known CLL, and an additional complex collection in the right axilla. Biopsy of this was consistent with an abscess although no organisms were cultured or detected on 16S PCR testing. Photographs and imaging will be shown and discussed, together with the microbiological results and sensitivities, in the context of a discussion about which antimicrobial agents were chosen to treat her infection, and for how long.

Results: Three months of intravenous antibiotics, including nurse-administered therapy at home, followed by consolidation with oral antibiotics has so far yielded excellent clinical and functional results.

Conclusions: Deep-seated or osteo-articular nocardia infections are difficult to treat, and in the context of underlying immunosuppression, require long courses of antibiotic therapies. Comorbidities, concomitant medication and the resistance pattern of the nocardia, can make antibiotic choices difficult. Outpatient parenteral antimicrobial therapy (OPAT) programmes enable stable patients to undertake part of their intravenous treatment at home.
Introduction: For late prosthetic joint infections (PJI), complete removal of the infected prosthesis is necessary to cure the infection. Unfortunately, because of severe comorbidities, a subgroup of patients is not able to undergo a revision surgery. Most of these patients are treated with long-term antibiotic therapy to suppress the infection as long as possible.

Aim: To determine the outcome of PJI in patients treated with long-term antibiotic suppressive therapy.

Method: We retrospectively collected data (period 2007-2014) from patients with a PJI who were on antibiotic suppressive therapy, and treated and followed at the University Medical Center Groningen. Suppressive therapy was defined as antibiotic treatment that was started after 3 months of the ‘regular’ antibiotic treatment. Treatment was considered to be failed, when the patient still experienced joint pain, when surgical intervention was needed to control the infection and/or when death occurred due to the infection.

Results: We included 21 patients with a median age of 67 years (range 21-88) and with a median follow-up of 21 months (range 3-81). Coagulase negative staphylococci (CNS) (n=6), S. aureus (n=6) and polymicrobial flora (n=5) were mostly found as causative pathogens. Most patients with CNS and S. aureus were treated with minocycline (67%) and clindamycin (83%) respectively as suppressive antibiotic therapy. Nine patients reported gastro-intestinal side effects that led to a switch of antibiotic treatment or a dose adjustment. Overall, treatment was successful in 67% of patients. Failure was due to persistent joint pain (n=1), surgical intervention because of an uncontrolled infection (n=3), and death due the infection (n=3). Patients who failed on suppressive therapy did not have a longer follow-up in comparison to patients whose treatment was successful (median follow up 15 months versus 27 months, respectively). We observed a treatment success of 90% in patients with a ‘standard’ prosthesis (n=11). This success was 50% in patients with a tumor-prosthesis (n=10). Also, treatment was successful in 83% of patients with a CNS as causative microorganism for the infection. No difference was observed between prosthetic knee and hip infections.

Conclusions: Although removal of the implant remains first choice in patients with late PJI, long-term antibiotic suppressive therapy is a reasonable alternative treatment option, with treatment failure in less then one third of patients, for patients with a PJI who are no candidate for revision surgery. We observed the highest treatment success in patients with a ‘standard’ prosthesis and a PJI caused by CNS.
CIERNY-MADER TYPE IV CHRONIC OSTEOMYELITIS: THE RESULTS OF PATIENTS TREATED WITH AGGRESSIVE DEBRIDEMENT AND INDUCED MEMBRANE TECHNIQUE

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Aim: The purpose of this study was to assess the result and related factors of Cierny-Mader Type IV chronic osteomyelitis treated with stage methods of aggressive debridement and induced membrane technique.

Method: From January 2012 to January 2014, 38 consecutive adult patients of Cierny-Mader Type IV chronic osteomyelitis were treated by this stage method in our clinical center with a minimum of 2-years follow-up. The clinical and imaging results were retrospectively analyzed.

Results: Of 38 patients, two were lost to follow-up evaluation. Five patients had a second debridement and eight needed a local flap transfer to cover the wound in the first stage. Patients formed a mean of 5.5 cm (range: 2-10.9) segmental bone defect; Sixteen patients had autograft and twenty had autograft mixed allograft in the second stage. The mean follow-up time was 29.5 months (range: 24-45). Bone union was achieved in all patients. Clinical eradication of osteomyelitis was achieved in 35 (98%) patients, 35 (97%) patients were able to walk independently, and 31 patients (86%) returned to work. Patients returned to a mean of 82% (46.3%-100%) lower extremity function. Bone union time was not dependent on the length of bone defect, but associated with the infection site (p = 0.005) and age (p = 0.005).

Conclusions: C-M Type IV chronic osteomyelitis is a refractory osteomyelitis with extensive bone lesion and compromised soft tissue. The stage method of aggressive debridement and induced membrane technique in treating diffuse chronic osteomyelitis take into account both infection control, and the repairing of bone defect and compromised soft tissue. The treatment result was satisfied.
[P144] DETECTION OF PERIPROSTHETIC JOINT INFECTIONS IN PRESUMED ASEPTIC PATIENTS

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Aim: The HypOrth project (New approaches in the development of Hypoallergenic implant material in Orthopaedics: Steps to personalised medicine) aims to investigate adverse immune reactions to implant materials. For this project, it is of utmost importance to exclude patients with periprosthetic joint infections (PJIs). The aim of this study was to rule out PJIs in included patients using prolonged culture and next generation sequencing (NGS) based molecular analysis.

Method: This study was approved with IRB approval No 150/12. Prior to surgery, the revision patients were examined and underwent joint fluid aspiration under sterile conditions. Only patients with negative joint aspirates after 14 days culturing were included. No antibiotics were administered prior to surgery and during surgery. Up to six tissue samples were collected for culture and one sample for pathological investigation. Joint fluid and one tissue biopsy were sampled for molecular analysis. The removed prostheses were sonicated and sonication fluid was used for molecular analysis. Prophylactic antibiotics (1.5g Cephalosporine, 2nd generation) were administrated after sampling. All tissue samples were cultured for 14 days. Final microbiological diagnosis was based on tissue cultures and pathological results.

For the molecular detection, DNA was extracted using a kit for human DNA removal*. The V1-3 region of 16S rRNA gene was PCR amplified with bacterial primers 27F and 534R (30 cycles) and paired-end sequenced on a DNA sequencer**. The paired-end reads were trimmed using trimmomatic (v. 0.32) and then merged using FLASH (v. 1.2.11). The reads were screened for potential PhiX contamination using USEARCH (v. 7.0.1090), clustered into operational taxonomic units (sequence identity ≥ 97%) using USEARCH, and subsequently classified using the RDP classifier with the MiDAS database (v. 1.20).

Results: Out of 70 included patients five patients were considered infected: One solely by culture (Staphylococcus aureus), one solely by NGS (Staphylococcus sp.) and three with concordant data by both methods (no. 1: S. epidermidis by both methods; no. 2: Staphylococcus capitis by culture, S. epidermidis by NGS; no. 3: S. epidermidis and Enterococcus faecalis by culture, E. faecalis by NGS).

Conclusions: These five patients will become part of a separate infection group in the analysis of immune reaction of patients with prosthetic joints. The data emphasize the importance of thorough microbiological analysis and illustrates the value of both culture and NGS - both from a clinical point of view and for research purposes.

*MolYsis complete 5 (Molzym, Germany)
** Miseq DNA sequencer (v3 chemistry, 2 × 300 bp)
EVALUATION REGARDING LONG-TERM OUTCOME OF A SPECIAL TREATMENT ALGORITHM FOR IMPLANT ASSOCIATED INFECTIONS OF THE ANKLE

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\textsuperscript{1}Bg Trauma Center Tübingen, Tübingen, Germany

Aim: Ankle fractures are frequently occurring injuries. Despite the relatively simple operative technique patients often suffer from postoperative complications. Little is known about postoperative treatment of implant associated infections of the ankle. Therefore this study shows and evaluates a treatment algorithm in long- and short-term outcome compared to infection free patients.

Method: Data from patients of over 20 years of a level 1 trauma center and university hospital was retrospectively analyzed including age, gender, comorbidities, smoking status, fracture classification, the number of revisions, the length of in-patient stay due to fracture and infection and the results of microbiological specimen with the length of antibiotic treatment. Moreover, present long-term outcome was evaluated by the AOFAS hindfoot score, the ankle osteoarthritis score and the SF-36 score compared to a match paired infection free patient’s cohort.

Results: 44 patients could be retrospectively evaluated (51% male, 49% women, mean age 46 ± 17 years). Most of the cases were Weber B fractures (38%) following an in-patient stay from 51 ± 4.3 days after primary treatment and 77 ± 10.0 days after secondary treatment in our hospital. Microbiological specimen showed in 77\% \textit{Staphylococcus aureus} with following antibiotic treatment for 13.9 ± 3.1 days in mean. Common comorbidities/risk factors were cardiovascular disease (28\%), smoking (15\%) and diabetes (18\%). Cure of infection and osseous consolidation could be stated in 100\%.

Patients with implant associated infection had significantly more risk factors than the match paired infection free patients (1.1 ± 0.1 / 0.33 ± 0.1 per patient). The match paired group showed significantly better long-term outcome in mean regarding ankle osteoarthritis score (2.0 ± 1.2 / 13.9 ± 4.7) and AOFAS hindfoot score (96.7 ± 1.9 / 87.3 ± 3.4). We could also state better outcome in patients who initially underwent our standardized treatment algorithm with generally fair outcome in both groups regarding the SF-36 score.

Conclusions: Immediate revision surgery with radical debridement, microbiological specimen, antibiotic therapy and insertion of a permanent drainage until osseous consolidation is reached with following removal of the implant in patients with implant associated infections after ankle fracture and ORIF leads to cure of infection and fair long term outcome in all cases. Special care must be taken of risk factors like diabetes and smoking.