



## Dwuetapowa endoprotezoplastyka rewizyjna w leczeniu zakażeń okołoprotezowych.

### Czy spacer może stanowić źródło reinfekcji?

Two-Stage Revision Arthroplasty in the Management of  
Periprosthetic Joint Infections.

Can Spacer Be a Source of Reinfection?

Przemysław Bereza | Damian Kusz

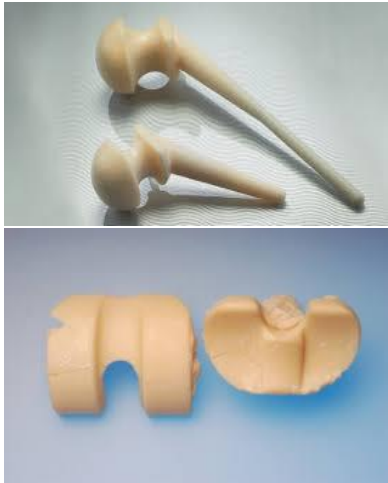
Katedra i Klinika Ortopedii i Traumatologii Narządu Ruchu

Śląski Uniwersytet Medyczny w Katowicach



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## Spacer



## Occurrence of PJIs:

- **0.4 - 2.5%** - after THA
- **1- 2%** - after TKA
- **3.2–7 %** - after **revision arthroplasties**

## TWO-STAGE REVISION ARTHROPLASTY:

- the preferred method of treating PJI
- the best strategy for infected-joint arthroplasty treatment

## Indications to two-stage revision arthroplasty:

- patients with systemic manifestations of infection (sepsis)
- obvious infection but no organism has been identified
- preoperative cultures results difficult to treat, antibiotic-resistance
- presence of a sinus tract
- inadequate and non-viable soft tissue coverage





## Spacer



### Pre-formed spacers:

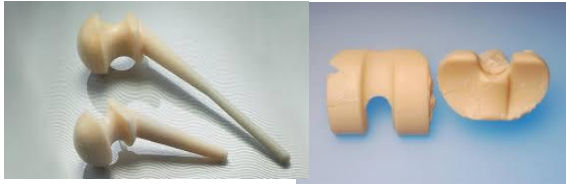
- implantable devices indicated to temporarily replace a prosthesis in a septic revision procedure
- allow local antibiotic administration
- maintenance of joint space and mobilisation
- maintenance of patient mobility between stages
- facilitate of definitive re-implant surgery
- standardized mechanical performance
- reduction of functional recovery time after the two stage procedure



# Microbiologic effectiveness of spacer

- allow local antibiotic administration with minimal risk of systemic toxicity
- minimize a risk of bacterial resistance to antibiotics, with the higher concentration of antibiotic in site of infection than the Minimal Inhibitory Concentration (MIC)
- **continuous presence of antibiotic in a temporary implant, which stops / reduces the growth and colonization of spacer**





## Spacer



- Recent studies reported **14.5 to 29 %** positive sonicate cultures of the removed spacers.

(Sorli L. et al. JBJS 2012; Marin M et al. JClinMicrobiol.2012; Mariconda.et al. BMC MscDis.2013)

- The incidence of reinfection after two-stage exchange arthroplasty has been estimated at **10–31 %**.

(Kurd MF et al. Clin Orthop Res.2010; Kubista et al. Int.Orthop. 2012)

We investigated bacterial species in supposedly healed PJI patients during second-stage exchange arthroplasties.

This study was designed to detect and/or isolate bacteria presented on the surfaces of the prefabricated antibiotic-loaded spacers during the second stage revision surgery.

Bereza et al. *BMC Musculoskeletal Disorders* (2016) 17:138  
DOI 10.1186/s12891-016-0991-1

BMC Musculoskeletal  
Disorders

RESEARCH ARTICLE

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## Comparison of cultures and 16S rRNA sequencing for identification of bacteria in two-stage revision arthroplasties: preliminary report

Przemysław Bereza<sup>1\*</sup>, Alicja Ekiel<sup>2</sup>, Aleksandra A  
Piotr Wojciechowski<sup>1</sup>, Aleksander L. Sieron<sup>3</sup> and

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ORIGINAL PAPER

**Identification of silent prosthetic joint infection: report of a prospective controlled study**

Przemysław L. Bereza · Alicja Ekiel · Aleksandra Auguściak-Duma ·  
Małgorzata Aptekorz · Iwona Wilk · Damian J. Kusz ·  
Piotr Wojciechowski · Gayane Martirosian

**Identification of Asymptomatic Prosthetic Joint Infection: Microbiologic and Operative Treatment Outcomes**

Przemysław L. Bereza<sup>1</sup>, Alicja Ekiel<sup>2</sup>, Aleksandra Auguściak-Duma<sup>3</sup>, Małgorzata Aptekorz<sup>2</sup>,  
Iwona Wilk<sup>2</sup>, Piotr Wojciechowski<sup>1</sup>, Damian J. Kusz<sup>1</sup>, and Gayane Martirosian<sup>2,4</sup>

Our clinical interest to perform this study was to find the answer to following questions:

- if the supposedly healed PJI should be considered as aseptic without the fear for reimplantation
- if failures could be predictable in some cases?





## Characteristic of studied patients

- 13 patients (7 women and 6 men)  
attending the Department of Orthopaedic and Traumatology, Medical University of Silesia, School of Medicine in Katowice, Poland  
awaiting second-stage revision arthroplasty of hip or knee, primary qualified as PJI, or highly suspected as PJI, based on the established criteria
- Age: 50–84 years (mean age 69.2)
- Operated joints: 4 hips and 9 knees
- **The average period between the 1<sup>st</sup> and 2<sup>nd</sup> stage of revision arthroplasty: 153.1 days (approximately 5 months)**
- Minimum follow-up: 2 years (mean, 32 months; range, 25–36 months)

## Material and methods:

- ◆ Laboratory markers (serum indicator of infection: WBC, ESR, CRP)
- ◆ Preoperative culture of synovial fluid from joint aspiration
- ◆ Intraoperative tissue cultures
- ◆ **Sonification of removed spacer**
- ◆ Molecular techniques: 16S rRNA sequencing
- ◆ Histopathological analysis

# Study

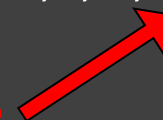
**Table 1** Clinical details of patients

Patient	Affected joint	CRP before 2 <sup>nd</sup> stage	Time between 1 <sup>st</sup> and 2 <sup>nd</sup> stage (days)	Treatment	Culture result - 1 <sup>st</sup> stage			Culture results - 2 <sup>nd</sup> stage			Molecular identification Bacteria identified by 16S rRNA gene sequencing	Followup (mean, 32 months; range, 25–36 months)
					Intraop. specimen	Preop. samples (joint fluid)	Intraop. specimen	Sonicate	Intraop. specimen	Sonicate		
1	H	<5	263									
2	H	<5										
3	K	<5										
4	K	<5										
5	H	6,4										
6	K	<5										
7	K	6										
8	K	<5										
9	K	<5										
10	K	<5										
11	K	27,1										longed therapy joint
12	H	<5										
13	K	<5	18									prolonged antibiotic therapy (prolonged wound healing)

## C-reactive protein:

- was significantly elevated in 1 of 13 cases (patient nr 11) - the failure after 2-years observation
- in remaining 2 cases CRP level was minimally elevated - without failures in follow up
- In the group with no elevated CRP level (10 patients) - 4 culture-positive cases (patients 4, 8, 9, 13)

failure



H hip, K knee



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# Study

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						Preop. samples (joint fluid)	Intraop. specimen	Sonicate		
1	H	<5	263	Restoration Stryker	negative	negative	negative	negative	<i>Geobacillus stearothermophilus</i> , <i>G. vulcani</i>	healed
						negative	negative	negative	<i>Lactobacillus jensenii</i> , <i>L. acidophilus</i> , <i>L. formicilis</i>	death
						negative	negative	negative	<i>Pseudomonas aeruginosa</i> , <i>P. resinovorans</i>	healed
						negative	negative	<i>Ralstonia pickettii</i>	<i>Novosphingobium nitrogenifigens</i> , <i>N. hassiacum</i> , <i>Bradyrhizobium japonicum</i> , <i>B. liaoningense</i> ,	healed
5	H	6,4	145	Restoration Stryker	negative	negative	negative	negative	<i>Klebsiella pneumoniae</i>	healed
6	K	<5	170	Scorpio TS Stryker	negative	negative	negative	negative	<i>Klebsiella pneumoniae</i>	healed
7	K	6	184	Scorpio TS Stryker	<i>Micrococcus</i> sp.	negative	negative	negative	<i>S. lugdunensis</i> , <i>S. hominis</i>	healed
8	K	<5	88	Scorpio TS Stryker	<i>Streptococcus viridans</i>	negative	<i>S. epidermidis</i>	negative	<i>Corynebacterium ureiceleivorans</i> , <i>C. mucifaciens</i>	healed
9	K	<5	150	Scorpio TS Stryker	<i>E.coli</i>	negative	negative	<i>Ralstonia pickettii</i>	<i>Rubrobacter xylanophilus</i> , <i>Clostridium saccharoperbutylacetonicum</i>	healed
10	K	<5	150	Scorpio TS Stryker	<i>Enterococcus faecalis</i>	negative	negative	negative	<i>Tuberibacillus calidus</i> , <i>Bacillus algicola</i>	healed
11	K	27,1	140	Scorpio TS Stryker	<i>Acinetobacter baumani</i> <i>Enterobacter cloacae</i>	negative	negative	negative	negative	failure: prolonged antibiotic therapy (recurrent joint effusion)
12	H	<5	135	Restoration Stryker	<i>Enterococcus faecium</i>	negative	negative	negative	<i>Brevibacterium ravenburgense</i> , <i>B. paucivorans</i>	healed
13	K	<5	180	Arthrodesis ChM plate	<i>Staphylococcus aureus</i>	negative	<i>S. epidermidis</i>	<i>S. epidermidis</i>	<i>Acinetobacter johnsonii</i> , <i>A. parvus</i>	failure: prolonged antibiotic therapy (prolonged wound healing)

The negative joint fluid culture results before 2nd stage revision in all cases.

H hip, K knee



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# Study

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					Intraop. specimen	Preop. samples (joint fluid)	Intraop. specimen	Sonicate		
1	H	<5	263	Restoration Stryker	negative	negative	negative	negative	<i>Geobacillus stearothermophilus</i> , <i>G. vulcani</i>	healed
2						negative	negative	negative	<i>Lactobacillus jensenii</i> , <i>L. acidophilus</i> , <i>L. formicilis</i>	death
						negative	negative	negative	<i>Pseudomonas aeruginosa</i> , <i>P. resinovorans</i>	healed
						negative		<i>Ralstonia pickettii</i>	<i>Novosphingobium nitrogenifigens</i> , <i>N. hassiacum</i> , <i>Bradyrhizobium japonicum</i> , <i>B. liaoningense</i> ,	healed
						negative	negative	negative	<i>Klebsiella pneumoniae</i>	healed
						negative	negative	negative	<i>Klebsiella pneumoniae</i>	healed
						negative	negative	negative	<i>S. lugdunensis</i> , <i>S. hominis</i>	healed
						<i>S. epidermidis</i>	negative	negative	<i>Corynebacterium ureiceleivorans</i> , <i>C. mucifaciens</i>	healed
						negative		<i>Ralstonia pickettii</i>	<i>Rubrobacter xylanophilus</i> , <i>Clostridium saccharoperbutylacetonicum</i>	healed
						negative	negative	negative	<i>Tuberibacillus calidus</i> , <i>Bacillus algicola</i>	healed
						negative	negative	negative	negative	failure: prolonged antibiotic therapy (recurrent joint effusion)
						negative	negative	negative	<i>Brevibacterium ravenburgense</i> , <i>B. paucivorans</i>	healed
13	K	<5	180	Arthrodesis Chm plate	<i>Staphylococcus aureus</i>	negative		<i>S. epidermidis</i>	<i>S. epidermidis</i> , <i>Acinetobacter johnsonii</i> , <i>A. parvus</i>	failure: prolonged antibiotic therapy (prolonged wound healing)

The presence of microorganisms on the surface of prefabricated spacers:

- in 15 % of patients in intraoperative specimens
- in 23 % cases after sonication

H hip, K knee



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The presence of bacterial DNA was confirmed with molecular testing in **92 %** of patients with negative synovial fluid cultures.

Sequencing of 16S rRNA revealed 2 or more different opportunistic bacteria:

- *S. epidermidis*
- *Klebsiella pneumoniae*
- *Acinetobacter spp.*
- *Pseudomonas spp.*
- *Lactobacillus spp.*

most of them belongs to human or environmental microflora with low virulence.



Molecular identification Bacteria identified by 16S rRNA gene sequencing	Followup (mean, 32 months; range, 25–36 months)
<i>Geobacillus stearothermophilus</i> , <i>G. vulcani</i>	healed
<i>Lactobacillus jensenii</i> , <i>L. acidophilus</i> , <i>L. formicilis</i>	death
<i>Pseudomonas aeruginosa</i> , <i>P. resinovorans</i>	healed
<i>Novosphingobium nitrogenifigens</i> , <i>N. hassiacum</i> , <i>Bradyrhizobium japonicum</i> , <i>B. liaoningense</i> ,	healed
<i>Klebsiella pneumoniae</i>	healed
<i>Klebsiella pneumoniae</i>	healed
<i>S. lugdunensis</i> , <i>S. hominis</i>	healed
<i>Corynebacterium ureicelerivorans</i> , <i>C. mucifaciens</i>	healed
<i>Rubrobacter xylanophilus</i> , <i>Clostridium saccharoperbutylacetonicum</i>	healed
<i>Tuberibacillus calidus</i> , <i>Bacillus algicola</i>	healed
negative	failure: prolonged antibiotic therapy (recurrent joint effusion)
<i>Brevibacterium ravenburgense</i> , <i>B. paucivorans</i>	healed
<i>S. epidermidis</i> , <i>Acinetobacter johnsonii</i> , <i>A. parvus</i>	failure: prolonged antibiotic therapy (prolonged wound healing)

## Follow-up

In 10 patients no failures were noted: lack of any clinical features of infection, radiological findings of implants loosening, increasing laboratory markers, and prolonged antibiotic therapy. The clinical examination revealed good outcomes.

Failure at final follow-up was recorded in 2 (16.6 %) patients

Identification Bacteria	Followup (mean, 32 months; range, 25–36 months)
<i>thermoophilus</i> ,	healed
<i>W, L. calis</i>	death
<i>pinosa</i> ,	healed
<i>nitrogenifigens, rhizobium ingense</i> ,	healed
<i>iae</i>	healed
<i>iae</i>	healed
<i>ominis</i>	healed
<i>eicelerivoxans</i> ,	healed
<i>ophilus, Clostridium tetanicum</i>	healed
<i>s, Bacillus algicola</i>	healed
<i>anspurgense</i> ,	healed
<i>ansonij, A. parvus</i>	failure: prolonged antibiotic therapy (recurrent joint effusion)
	failure: prolonged antibiotic therapy (prolonged wound healing)

failure: prolonged antibiotic therapy (recurrent joint effusion)

failure: prolonged antibiotic therapy (prolonged wound healing)



## Follow-up: failure: PATIENT NR 11

(persistent elevated concentration of CRP before 2nd stage)

- periodic effusion without persistent pain
- the presence of MSSE in 1/3 arthrocentesis in the early postoperative period
- minimal radiolucency under the tibial component - not assessed as implant loosening

Targeted antimicrobial therapy was administered.

For these reasons this case was assessed as a failure.

Pat	Pre op	Post op	Molecular identification Bacteria	Followup (mean, months; range, 36 months)
	negative	negative		
	negative	negative		
				healed
				healed
			<i>stridium</i>	healed
			<i>algicola</i>	healed
				healed
				failure: prolonged antibiotic therapy (recurrent joint effusion)
				healed
			<i>rus</i>	failure: prolonged antibiotic therapy (prolonged wound healing)



## Follow-up: failure: PATIENT NR 13

Infection with *S. epidermidis*

- medical history of the patient (knee joint infection many years ago, clinical signs of infection after primary knee joint arthroplasty)

- the growth of *S. aureus* from intraoperative tissue samples taken during the 1<sup>st</sup> stage revision surgery.

Patient	Culture results - 2 <sup>nd</sup> stage	Molecular identification Bacteria	Followup (mean, 32 months; range, 25-36 months)
			healed
			death
			healed
			healed
			healed
			healed
			healed
			healed
			healed
	negative	negative	failure: prolonged antibiotic therapy (recurrent joint effusion)
	negative	<i>Brevibacterium ravenburgense</i> , <i>B. paucivorans</i>	healed
	<i>S. epidermidis</i>	<i>Acinetobacter johnsonii</i> , <i>A. parvus</i>	failure: prolonged antibiotic therapy (prolonged wound healing)

## Follow-up: failure: PATIENT NR 13

Finally underwent **arthrodesis** of the knee joint (general medical condition and the high risk of reinfection)

Prolonged wound healing, the positive culture results from intraoperative specimens and sonicate fluid (*S.epidermidis*) were the reason for long-term antibiotic therapy in this case.

Patient	Culture results - 2 <sup>nd</sup> stage	Molecular identification Bacteria	Followup (mean, 32 months; range, 25-36 months)
			healed
			death
			healed
			ens, healed
			healed
			healed
			healed
			ns, healed
			tridium healed
			algicola healed
			failure: prolonged antibiotic therapy (recurrent joint effusion)
	negative	negative	healed
	<i>S. epidermidis</i>	<i>S. epidermidis</i> <i>Acinetobacter johnsonii</i> , <i>A. parvus</i>	failure: prolonged antibiotic therapy (prolonged wound healing)

**Follow-up: failure:  
PATIENT NR 13**

Followed by recommendation  
of some authors :  
removal of prosthesis or  
arthrodesis can be performed  
in cases of serious  
comorbidity or unacceptable  
by the patient repeated  
surgery or which seem  
deemed unsafe.

Patid	ure results - 2 <sup>nd</sup> stage	Molecular identification Bacteria	Followup (mean, 32 months; range, 25-36 months)
amp d)			healed
			death
			healed
			ns, healed
			healed
			healed
			healed
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			tridium healed
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			failure: prolonged antibiotic therapy (recurrent joint effusion)
	negative	<i>Brevibacterium ravenburgense</i> , <i>B. paucivorans</i>	healed
	<i>S. epidermidis</i>	<i>S. epidermidis</i> <i>Acinetobacter johnsonii</i> , <i>A. parvus</i>	failure: prolonged antibiotic therapy (prolonged wound healing)

## 1.

The lack of clinical signs of infection, negative culture results of pre- and intraoperative samples do not exclude existence of bacteria on the surfaces of preformed antibiotic-loaded spacers used in two-stage exchange arthroplasties.

## 2.

The positive results of sonication and molecular tests should be interpreted as real pathogenicity factors in the light of the clinical, microbiological and histopathological data, especially for patients with immunodeficiency.

## 3.

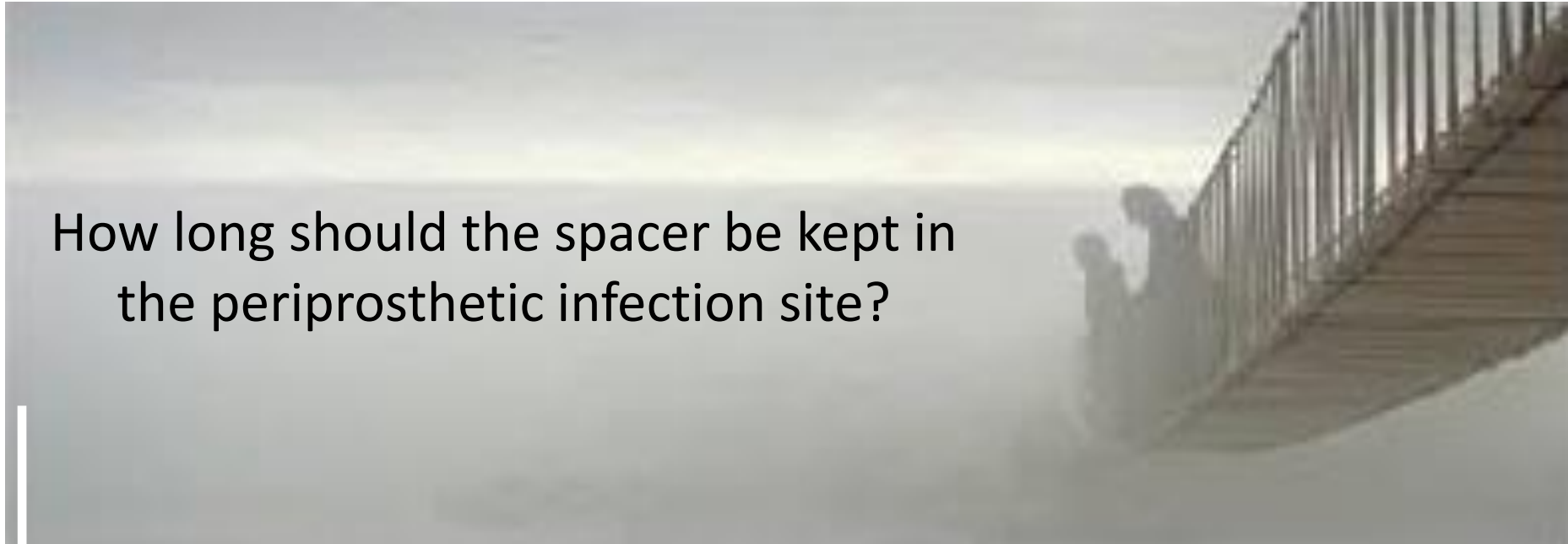
More attention should be paid to reimplantation of spacers in patients without clinical symptoms of infection with prolonged elevated level of CRP and in cases of prior infectious process of operated joint.

4.

Period between stages...

# Conclusion

How long should the spacer be kept in the periprosthetic infection site?



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How long should the spacer be kept in the periprosthetic infection site?

Prolonged period between two stages of revision arthroplasty could be the reason for colonization of spacer surfaces with new microorganisms, especially dangerous for patients with immunodeficiency.

## IDSA GUIDELINES



# Diagnosis and Management of Prosthetic Joint Infection: Clinical Practice Guidelines by the Infectious Diseases Society of America<sup>a</sup>

Douglas R. Osmon,<sup>1</sup> Elie F. Berbari,<sup>1</sup> Anthony R. Berendt,<sup>2</sup> Daniel Lew,<sup>3</sup> Werner Zimmerli,<sup>4</sup> James M. Steckelberg,<sup>1</sup> Nalini Rao,<sup>5,6</sup> Arlen Hanssen,<sup>7</sup> and Walter R. Wilson<sup>1</sup>

<sup>1</sup>Division of Infectious Diseases, Mayo Clinic College of Medicine, Rochester, Minnesota; <sup>2</sup>Bone Infection Unit, Nuffield Orthopaedic Centre, Oxford University Hospitals NHS Trust, United Kingdom; <sup>3</sup>Division of Infectious Diseases, Department of Internal Medicine, University of Geneva Hospitals, <sup>4</sup>Basel University Medical Clinic, Liestal, Switzerland; <sup>5</sup>Division of Infectious Diseases, Department of Medicine, and <sup>6</sup>Department of Orthopaedic Surgery, University of Pittsburgh School of Medicine, Pennsylvania, and <sup>7</sup>Department of Orthopedics, Mayo Clinic College of Medicine, Rochester, Minnesota

ly qualify for this procedure. In earlier cohort studies, early reimplantation within 3 weeks after resection resulted in a higher failure rate [110]. Cohort studies from Europe revealed a favorable outcome with **reimplantation within 2–6 weeks** while systemic antimicrobials are still being administered in selected situations when the infection is not due to MRSA, enterococci, multidrug-resistant gram-negative organisms [2]. **Delayed reimplantation after 4–6 weeks of intravenous antimicrobial therapy and an antibiotic-free period of 2–8 weeks** has been highly successful. This strategy is used frequently in the United States [13, 104, 106, 120]. The use of an articulating

Rand JA, Bryan RS. Reimplantation for the salvage of an infected total knee arthroplasty. *J Bone Joint Surg Am* 1983; 65:1081–6.

Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. *N Engl J Med* 2004; 351:1645–54.

Segawa H, Tsukayama DT, Kyle RF, Becker DA, Gustilo RB. Infection after total knee arthroplasty. A retrospective study of the treatment of eighty-one infections. *J Bone Joint Surg Am* 1999; 81:1434–45.

Brandt CM, Duffy MC, Berbari EF, Hanssen AD, Steckelberg JM, Osmon DR. *Staphylococcus aureus* prosthetic joint infection treated with prosthesis removal and delayed reimplantation arthroplasty. *Mayo Clin Proc* 1999; 74:553–8.

Hanssen AD, Rand JA, Osmon DR. Treatment of the infected total knee arthroplasty with insertion of another prosthesis. The effect of antibiotic-impregnated bone cement. *Clin Orthop Relat Res* 1994; 44–55.

Westrich GH, Walcott-Sapp S, Bornstein LJ, Bostrom MP, Windsor RE, Brause BD. Modern treatment of infected total knee arthroplasty with a 2-stage reimplantation protocol. *J Arthroplasty* 2010; 25:1015–21, 1021.e1–2.



## 4.

Taking into consideration our results and observations of other authors, **the shortening of time interval between stages to 6–14 weeks is beneficial.**

Bertazzoni Minelli E, Benini A, Magnan B, Bartolozzi P. Release of gentamicin and vancomycin from temporary human hip spacers in two-stage revision of infected arthroplasty. *J Antimicrob Chemother.* 2004;53:329–34.

Fink B, Vogt S, Reinsch M, Büchner H. Sufficient release of antibiotic by a spacer 6 weeks after implantation in two-stage revision of infected hip prostheses. *Clin Orthop Relat Res.* 2011;469:3141–7.



# Is there a place for one-stage arthroplasty?

## INDICATION:

- when effective antibiotics are available but not in patients with systemic manifestations of infection (sepsis).

## RELATIVE CONTRAINDICATIONS:

- lack of identification of an organism preoperatively
- the presence of a sinus tract
- severe soft tissue involvement that may lead to the need for flap coverage



*Thank you for attention!*

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