Implant Associated Infection: Victorious Germs or Avoidable Complication?

An interview with Javad Parvizi, MD, PhD, FRCS, and Thorsten Gehrke, MD, PhD

Increasing numbers of implantations are naturally associated with an increasing number of complications. Implant-associated infection is regarded as one of the most challenging complications following total joint replacement surgery. It confronts the surgeon and the patients with serious consequences and is, therefore, widely feared in the orthopaedic surgical community. According to some studies, implant-associated infection constitutes the most common cause of revision total joint replacement during the first 5 years of primary implantation. Although progress has been made in the area of pre- and peri-operative measures, as well as post-operative care in arthroplasty, no significant decrease in the infection rate has been observed over the last two decades. Quality improvements in total joint arthroplasty are apparently not effective in the reduction of infection.

Our major enemy on the infection frontline is the alarming increase in bacterial resistance to antibiotics. We are increasingly confronted with multi-drug resistant pathogens such as the familiar methicillin-resistant Staphylococcus aureus and epidermidis and for some time now the more challenging and more threatening 3MRGN and 4MRGN pathogens. These are multi-drug resistant bacteria known as gram-negative rods that are resistant to 3 or 4 of the known antibiotic groups, which leaves the medical community effectively defenseless against them.

The only thing that still helps in these cases is systematic infection prevention or adequate treatment, which for periprosthetic infections involves radical debridement of all infected soft tissues and bone. The result can be devastating to the patient.

In an effort to gain a more complete understanding of the issues, we sat down with the organizers of the International Consensus Group on Periprosthetic Joint Infection, Professors Javad Parvizi of the Rothman Institute in Philadelphia and Thorsten Gehrke of the Helios Endo-Klinik in Hamburg, Germany, in order to ask some question on this complex subject.

The International Consensus Group on Periprosthetic Joint Infection met in Philadelphia on August 1, 2013. What were the objectives of this newly formed group?

Thorsten Gehrke: Both Dr. Parvizi and I came up with the idea to organize a meeting of this type. It's necessary because right now there are no global standards for prevention, diagnostics and treatment; no scientific evidence is available; and there is great uncertainty worldwide regarding the treatment of periprosthetic infections.
Because it is extremely difficult and ethically problematic to justify conducting evidence-level-1 clinical studies (prospective randomized studies), we decided that if there's no evidence then there should at least be consensus. Using the Delphi method, consensus is achieved if the majority of experts has a single opinion regarding a particular issue based on whatever scientific data and related publications are available.

Javad Parvizi: In order to create this consensus effort, we contacted about 500 experts from roughly 60 countries and formed 15 working groups in order to address various sections of the issue (e.g., definition, prevention, diagnostics, irrigation and debridement, spacers etc.). The working groups reviewed more than 3,500 medical publications leading to more than 24,000 e-mails being exchanged. The groups formulated more than 220 questions. These were presented to the entire group and voted upon as part of the International Consensus Meeting held in Philadelphia in early August 2013.

Different definitions of a prosthesis infection are described in the medical literature. When is the diagnosis of an implant-associated infection considered to be accurate?

Javad Parvizi: As part of the consensus, a majority of 85% of the experts agreed that an implant-associated infection is considered confirmed if the following criteria are met:

- evidence of phenotypically identical organisms in at least two positive periprosthetic cultures or

- a fistula communicating with the joint or
- evidence of at least 3 of the following criteria:
  - increase in the erythrocyte sedimentation rate (ESR) and the C-reactive protein (CRP) in the serum
  - increased number of white blood cells (WBC) in the synovial fluid or
  - positive reaction of leukocyte esterase test strips
  - increased percentage of neutrophils in the synovial fluid (PMN%)
  - positive histological analysis of the periprosthetic tissue
  - a single positive culture.

Infections are often classified as early or late. Current registry data contain evidence indicating that infections can also occur considerably later than once thought. Is this classification still up to date based on what we know now?

Thorsten Gehrke: There are a number of different classifications of periprosthetic infections, each of which consider different criteria. The simplest, most sensible and most conventional classification is actually the classification into early and late infections. An early infection is one which occurs in the first 3 weeks after the implantation of the prosthesis or after the appearance of the first symptoms. All infections that become evident at a later time are called late infections, which means these can develop as hematogenous infections years or even decades later.
There is consensus that the attempt to preserve the prosthesis in early infections appears justified, whereas in the case of all late infections the prosthesis, all foreign bodies, and infectious bony and soft tissues should be removed. Agreement on this was universal.

The clinical finding of a periprosthetic infection is often unspecific. Do you have a tailor-made, standardized algorithm for determining findings at your hospitals?

Javad Parvizi: Every clinic that treats periprosthetic infections should follow a generally recognized standard as well as diagnostic and therapeutic algorithms. In our hospitals the clinical determination of findings is as follows:
First, as a rule the patient presents with pain, the most important clinical symptom of infections. It is particularly suspicious if pain suddenly develops after an interval free of symptoms. A clinical examination is then carried out. If local signs of infection such as redness, swelling, heat or formation of effusion are present in the affected joint, the next step we recommend is to determine the inflammatory parameters in the serum, although as a rule determining the CRP value is sufficient. At the same time we also carry out a puncture of the affected joint in every case of suspected infection. It is necessary to make sure that the puncture is carried out in rooms specifically set up for this purpose or in operating theaters under strictly aseptic conditions. The puncture specimen should then be sent to the closest qualified laboratory as soon as possible; if this is not possible, temporary interim storage in pediatric blood culture bottles is recommended.

Thorsten Gehrke: The puncture specimen should be incubated for at least 14 days to ensure that pathogens that grow slowly are also detected. The patient should be free of antibiotics for at least 10–14 days before the puncture. If the culture is negative despite high-grade clinical and serological suspicion of a periprosthetic infection, we recommend taking open biopsies because these are more accurate. About 98% of all periprosthetic infections can be diagnosed using this algorithm.

Have the strategies for prevention, diagnosis, and treatment of periprosthetic infections changed over the past years, and what is your assessment of the results?

Javad Parvizi: The strategies for prevention, diagnosis and treatment have, in my opinion, clearly undergone positive developments in the last few years. Most hospitals adhere to the algorithms specified by the major professional associations. Because periprosthetic infection has increasingly come under scrutiny as the most serious complication associated with arthroplasty in recent years, centers have been created in most countries for the purpose of treating this complication.
Nevertheless, we are still in the early stages with these strategy measures. The consensus meeting last August was intended to play a part in ensuring that appropriate algorithms are adhered to and treatment principles are implemented, particularly in those countries, which are at a lower level of development. The results of the consensus meeting provide good guidelines for health professionals treating periprosthetic infections.

How should future primary and revision implants in hip and knee arthroplasty be fashioned so that the complex issue of infection can be brought under control? What scientific approaches are there?

Thorsten Gehrke: Implant manufacturers across the board have been working on antibacterial or antiseptic surface treatment of the implant (coatings), for at least two decades. In recent years relatively promising approaches of antibacterial coatings have been developed, which have concentrated increasingly on the use of silver ions as a protection against infection on the implant surface. Silver has the ad-

vantage that there is almost no resistance and the bone in-growth behavior is good despite the proven toxic effect of the silver. Currently, there are only rudimentary evidence-based scientific approaches available, at least for practical application. Nevertheless, there are vast amounts of in-vitro results and theoretical considerations. Meaningful in-vivo data is still rare. Only in recent years have truly promising results in treatment or prevention been shown in cancer patients.

A periprosthetic infection can put a serious strain on the relationship between a doctor and his patient. Can you give your colleagues some advice from your clinical practice on how to deal with affected patients?

Javad Parvizi: The only effective and ultimately also the only correct recommendation is to openly deal with the complication of periprosthetic infection. The patient must be informed as soon as possible about the probability of an infection and undergo appropriate diagnostics. This can only be done in an open and honest dialog with the patient. Recriminations are redundant and irrelevant because of the hygiene standards maintained in most operating theaters around the world. As a rule, periprosthetic infections should be considered a matter of fate. Blame can only be placed on the surgeon or treating physician if there are delays or a wait-and-see approach is taken with the diagnostics and the resulting treatment. To put it in a nutshell, honesty is the best policy. ■

CORRESPONDING AUTHORS:

Javad Parvizi, MD, PhD, FRCS
Department of Orthopaedic Surgery
Jefferson Medical College
Thomas Jefferson University, Philadelphia
Vice Chairman of Research, Rothman Institute
Director, Clinical Research, Rothman Institute
925 Chestnut Street
5th Floor
Philadelphia, PA 19107
USA
Phone: +1 800 321-9999
E-mail: parvj@aol.com

Thorsten Gehrke, MD, PhD
Medical Director
Helios Endo-Klinik
Holstenstraße 2
D-22767 Hamburg
Germany
Phone: +49 40 31 97-1233
Fax: +49 40 31 97-1900
E-mail: thorsten.gehrke@helios-kliniken.de

Javad Parvizi, MD, PhD, studied medicine at the University of Sheffield, UK. He completed his orthopaedic surgical training at the Mayo Clinic in Rochester, Minnesota, USA, which included the achievement of a master's degree in molecular biology. Today, he is Vice Chairman of Research and Director of Clinical Research at the Rothman Institute in Philadelphia, USA. As an orthopaedic surgeon, Javad Parvizi specializes in pelvis, hip, and knee reconstruction with a special interest in hip pain in young adults, and joint preservation procedures, as well as periprosthetic joint infections.

Thorsten Gehrke, MD, PhD, is Medical Director and Head of the Hip Department of the Helios Endo-Klinik in Hamburg, Germany, the only German clinic that is a member of the International Society of Orthopaedic Centers (ISOC). He specializes in hip and knee surgery, in sports medicine as well as in aseptic and septic revision surgeries in the field of arthroplasty. He has an outstanding national and international reputation, particularly in the treatment of infections and single-stage revision procedures.

Thorsten Gehrke is member of several national and international medical societies, such as the American Knee Society and the European Bone and Joint Infection Society. He holds honorary, guest and visiting professorships at universities in Shanghai and Hebei (China), Bogota (Columbia), Chile and Kuwait. He is an associate professor in Buenos Aires (Argentina) and Santiago (Chile). He has published numerous journal articles and book chapters on subjects ranging from anatomy and sports medicine to clinical studies in arthroplasty.

International Consensus Meeting on Periprosthetic Joint Infection

A Brief Summary

by Thorsten Gehrke, MD, PhD, Javad Parvizi, MD, PhD, FRCS

Periprosthetic joint infection (PJI), with all its disastrous implications, continues to pose a challenge for the orthopaedic community. Practicing orthopaedic surgeons have invested great efforts to implement strategies that may minimize surgical site infection (SSI). Although high-level evidence may support some of these practices, many are based on little to no scientific foundation. Thus, there is a remarkable variation in practices across the globe for prevention and management of PJI.

Should one use a laminar flow room for elective arthroplasty? How much and which antibiotic should one add to cement spacers? What metric should one use to decide on the optimal timing for reimplantation? What are the indications and contraindications for irrigation and debridement? How much irrigation and debridement in a joint should be attempted before resection arthroplasty needs to be considered? These are among the many questions that the orthopaedic community faces on a daily basis.

The medical community comprehends the importance of high-level evidence and engages in the generation of such whenever possible. The community also recognizes that some aspects of medicine will never lend themselves to the generation of high-level evidence nor should one attempt to do so. It is with the recognition of the latter that the International Consensus Meeting on Periprosthetic Joint Infection was organized. Delegates from various disciplines, including orthopaedic surgery, infectious disease, musculoskeletal pathology, microbiology, anesthesiology, dermatology, nuclear medicine, rheumatology, musculoskeletal radiology, veterinary surgery, pharmacy, and numerous scientists with an interest in orthopaedic infections travelled to Philadelphia in order to participate in the meeting held on July 31-August 1, 2013. Their goal was to evaluate the available evidence at hand. If no sufficient evidence was found, then the objective was to develop a consensus on current practices for the management of SSI/PJI. This entire process required a great deal of preparatory work over a 10-month period in order to gather all of the supporting information required. Every stone was turned in search of evidence for the questions that were generated by the delegates; over 3,500 related publications were evaluated. The evidence, when available, was assessed. In the case of questions that were not adequately supported in the medical literature, the cumulative wisdom of the more than 400 delegates from 52 countries as well as over 100 different organizations was evaluated and combined in order to present it to the delegates for their consensus vote.

The delegates were engaged every step of the way by communicating through a "specialized website" created for this purpose (**www.ForMD.com**). This website handled over 25,000 communications during the process. The consensus document was developed using the Delphi method under the leadership of Dr. William L. Cats-Baril, a world-renowned expert in consensus document development.

The entire consensus process included as many stakeholders as possible, allowed participation in multiple forums, and provided a comprehensive review of the literature. The topics that were covered included the following: mitigation and education on comorbidities associated with increased SSI/PJI, perioperative skin preparation, perioperative antibiotics, operative environment, blood conservation, prosthesis selection, diagnosis of PJI, wound management, spacers, irrigation and debridement, antibiotic treatment and timing of reimplantation, one-stage versus two-stage exchange arthroplasty, management of fungal or atypical PJI, oral antibiotic therapy, and prevention of late PJI. Every consensus statement underwent extreme scrutiny, especially by those with expertise in a specific area, in order to ensure that implementation of the proposed practices could indeed lead to improvement of patient care.

After analyzing the literature and assembling a preliminary draft of the consensus statement, over 300 delegates attended the face-to-face meeting at Thomas Jefferson University in Philadelphia, Pa., USA. They were involved in active discussions and

voted on the questions / consensus statements. The delegates first met on July 31 in smaller workgroups to discuss and resolve any discrepancies and finalize their particular statements. After revising the consensus statements, the finalized consensus statements were assembled and forwarded to the Audience Response System that evening in order for voting to take place the next day. On August 1, 2013, the delegates gathered into the general assembly hall and voted on the 207 consensus statements that were being presented. The voting process was conducted using electronic keypads, where one could agree with the consensus statement, disagree with the consensus statement, or abstain from voting. The strength of the consensus was judged by the following scale: 1) Simple Majority: No Consensus (50.1-59% agreement), 2) Majority: Weak Consensus (60-65% agreement), 3) Super Majority: Strong Consensus (66-99% agreement) and 4) Unanimous: 100% agreement. Of the 207 statements, there was unanimous vote on only one (controlling OR traffic), 202 statements received super majority (strong consensus), two statements had weak consensus, and only two statements did not achieve any consensus.

The document[1-3] generated is the result of innumerable hours of work by the liaisons, leaders, and delegates dedicated to this initiative. We are certain that the "best practice guide" set forth by this initiative will serve many of our patients for years to come. It is essential to state that the information contained in this document is merely a guide for practicing physicians whose patients have a musculoskeletal infection; it should not be considered as a "standard of care". Clinicians should exercise their wisdom and clinical acumen in making decisions related to each individual patient. In some circumstances this may require implementation of care that differs from what is stated in this document. ■

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Periprosthetic Joint Infection: Could Bearing Surface Play a Role?

by Javad Parvizi MD, PhD, FRCS

Due to its disastrous consequences and rising incidence, periprosthetic joint infection (PJI) has taken center stage in orthopedics to become one of the challenges of the decade.[1] Numerous studies have identified some of the important risk factors for PJI. A recent international consensus meeting held in Philadelphia evaluated the available literature and identified the following as the main host-related issues predisposing a patient to PJI: a history of previous surgery, poorly controlled diabetes mellitus (glucose > 200 mg/L or HbA1C > 7%), malnutrition, morbid obesity (BMI > 40 kg/m2), active liver disease, chronic renal disease, excessive smoking (> one pack per day), excessive alcohol consumption (> 40 units per week), intravenous drug abuse, recent hospitalization, an extended stay in a rehabilitation facility, male gender, the diagnosis of post-traumatic arthritis, inflammatory arthropathy, a prior surgical procedure in the affected joint and severe immunodeficiency.[2-5]

Although the link between numerous host-related and environmental factors and PJI is better understood, the link between the use of different prosthetic biomaterials and PJI has not been clearly defined. PJI is caused by the attachment of infecting organisms to the prosthesis surface and the formation of biofilm, as a result of this one would expect that the "affinity" of organisms to attach themselves to the different biomaterials surfaces would vary. This issue has not been explored to a great degree as there is little clinical data studying the potential influence of different biomaterials on PJI. The international consensus group concluded that, based on the available medical literature, the incidence of PJI does not vary regardless of whether cemented arthroplasty components (without antibiotics) or uncemented arthroplasty components are used, and that the presence of hydroxyapatite on the uncemented surfaces does not seem to influence the incidence of PJI. The same workgroup analyzed the potential link between the type of bearing surface and the subsequent PJI, and 78% of the delegates felt that the available observational data confirmed a higher incidence of PJI following the use of a metal-on-metal bearing surface.

There are a number of potential reasons as to why the incidence of PJI may be higher after the use of a MoM bearing surface. For example, the failure of a MoM bearing surface can result in adverse local tissue reactions (ALTR) and extensive soft tissue destruction, which could then provide a favorable environment for bacterial proliferation.[6] A systematic review conducted by Hosman et al. found that metal particles generated by the MoM bearing surface increased the potential risk of PJI because of the ability of metal particles to modulate the immune system and bacterial growth.[7]

The question that remains is whether other bearing surfaces influence the incidence of PJI as well. We are very interested in this question and have been exploring various databases to search for a possible pattern. The first analysis that we conducted was on the Nationwide Inpatient Sample (NIS) database, which is the largest publicly available, all-payer, inpatient care database in the United States. It contains data collected from approximately 8 million hospital stays each year, which amounts to roughly 20% of all patients treated in US hospitals.[8] Using the ICD-9 codes for defining infection, we found that the incidence of infection was statistically higher in patients with metal-on-polyethylene bearings (1.1%) compared to patients with ceramic-on-polyethylene (0.87%) or ceramic-on-ceramic bearings (0.54%). A similar investigation of the Rothman Institute database revealed a 0.8% incidence of PJI (as defined by Musculoskeletal Infection Society criteria)[9] with metal-on-polyethylene compared to 0.4% with ceramic-on-polyethylene bearings, although the latter difference was not statistically significant. We are aware that our findings have limitations, resulting from the fact that neither the NIS data nor our institutional data were subjected to multivariate analyses. The findings could, for example, be a reflection of the younger age and lower medical comorbidity of patients who receive ceramic bearing surfaces versus those who receive metal-on-polyethylene bearing surfaces. However, the pattern detected is interesting and deserves further exploration. We are therefore evaluating the possibility of conducting a multi-institutional study that can collect granular data and explore the potential link between the type of bearing surface used and subsequent PJI. ■

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Does the Bearing Type Influence the Incidence of Periprosthetic Infections of the Hip?

by Rihard Trebše, MD, PhD[1], Vesna Levašič, MD[1], Ingrid Milošev, PhD[1], Simon Kovač, MD

[1] Valdoltra Orthopedic Hospital, Jadranska cesta 31, SLO-6280 Ankaran, Slovenia

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- periprosthetic infection
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- revision
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Introduction

Each year, orthopaedic implants provide 2.7 million patients worldwide with improved function and freedom from pain. However, infection after joint replacement (PJI) and fixation of bone fractures can lead to high morbidity, increased mortality and substantial costs.[1,2] Due to a growing number of implantations and extending follow-up periods, the incidence of device-associated infections is also likely to increase.[3,4,5] A microbiological cure for chronic device-associated infections is invasive and frequently necessitates the removal of the implant and cement in conjunction with a debridement of all devitalized tissues, which leads to a long-term antimicrobial treatment, resulting in a two-stage revision.[6,7,8,9,10,11,12] Acute PJI may also be treated by less invasive one-stage replacement, debridement and retention; however, this forms of treatment should probably be restricted to centers with dedicated bone infection teams.[13]

Contemporary articulating surfaces in total hip arthroplasty (THA) predominantly consist of a metal part (usually cast cobalt-based Co28Cr6Mo alloys, ASTM F799 and ASTM 1537, ISO 5832) articulating with a plastic polymer (in most cases various types of ultra-high molecular weight polyethylene: MoP), or different types of irradiated polyethylene (MoXPE). Other types of bearings are also widely used, such as ceramic-on-polyethylene (CoP), ceramic-on-irradiated polyethylene (CoXPE), metal-on-metal (MoM) and ceramic-on-ceramic (CoC). New types of bearings have been introduced to increase THA longevity, which prevent the implant loosening usually caused by polyethylene particles-induced osteolysis around one or both of the components.[14]

Although many published studies look at the overall performance of various bearings[15,16], none report exclusively on how the bearing type influences the incidence of THA infection. We found one THA registry[17] that collects information about the failure rate of different bearing systems, but there is no report on the failure mode. The lowest revision rates in this registry are associated with MoM (1.6%: 96 revisions out of 6,119 primaries) and CoC (2.9%: 750 revisions out of 25,918 primaries).

We used very broad criteria to diagnose infections when analyzing our series of MoM THA from the 1990s, and noticed a disturbing infection rate of 4.2%.[18] Since the overall revision rate for infection was approximately 1.5%, we have concluded that the bearing type might have influenced the PJI rate.[19]

Materials and methods

In order to detect potential differences in the incidence of PJI for different bearing combinations, we analyzed the data in the Valdoltra Arthroplasty Registry[20], which was founded in 2002. We used the database to identify all patients fitted with a total hip arthroplasty (THA) between 1.1.2002 to 12.31.2012, and then grouped them according to which bearing had been implanted (Table 1). The rate of revisions due to deep infection for each bearing type was then determined. In the 11-year follow-up period there were 4,770 primary THA in the MoP group, 2,813 in the MoXPE group, 72 in the MoM group, 512 in the CoP group, 376 in the CoXPE group and 1,323 in the CoC group. The number of THA that were revised due to infection was 30 in the MoP group, 29 in the MoXPE group, 0 in the MoM group, 3 in the CoP group, 0 in the CoXPE group and 6 in the CoC group. We calculated the revision rate for infection in each group and compared these rates with the chi-squared test. We excluded the MoM group from the statistical analysis on account of it being too small in comparison to the other groups.

A prosthetic joint infection was diagnosed if at least one of the following criteria was present:

1. growth of the same microorganism in ≥2 cultures of synovial fluid or intraoperative tissue specimens
2. purulence of aspirated fluid or intraoperative tissue (as determined by the surgeon)

3. acute inflammation in the histopathological sample of intraoperative permanent tissue sections (as determined by the pathologist)[13]
4. a fistula communicating with the joint

Statistical analysis

Statistical analysis was performed using version 19 of IBM SPSS. To analyze the differences between the groups, a chi-squared test and a two-tailed t-test were performed. We compared the group with the best revision rate result (CoXPE) to the other 4 groups, setting the significance level at p=0.05.

Results

The infection rate was 0.63% among the 4,770 patients with MoP bearings, 1.63% among the 2,813 patients with MoXPE bearings, 0.00% among the 376 patients with CoXPE bearings and 0.45% among the 1,323 patients with CoC bearings. We excluded the 72 patients with MoM bearings because their numbers were low and the statistics would have been biased. We found statistically significant differences in the infection rates between patients with MoP and CoXPE bearings and between those with MoP and CoC bearings. We did not find any statistical differences between CoXPE and CoC bearings.

Discussion

Periprosthetic tissue is limited in its ability to eradicate infective agents if introduced into the wound during the surgery, especially if a foreign body is present.[21] Adhesion of biomolecules (e.g., proteins) as well as whole organisms, like bacteria or host cells on biomaterial surfaces, is important for the biomaterial's behavior.[22,23,24] It has been proposed that prompt and firm bacterial attachment combined with a poor host cell attachment can lead to implant-related infections (the "race for the surface" hypothesis).[25] An overt infection occurs if the dose and virulence of the organisms overcome the defense mechanisms. Subsequently, biofilm commonly forms, protecting pathogens against phagocytosis, complement and antibiotics[26] with its extracellular polymeric substance.

If PJI develops, clinical presentations depend, as with other types of infections, on the strength of the host's defense mechanism and the virulence of the pathogens. The presence of the foreign material and the propensity of bacteria to develop a protective biofilm on it make PJI different and difficult to eradicate. Two extreme scenarios are expected, with most PJI falling between these two limits. A patient with a strong immune system and an affecting organism of a very low virulence will possibly manifest a state of persistent subclinical infection, meaning that host defense mechanisms have control over biofilm-laden bacteria. A subclinical infection therefore persists but will not manifest itself unless the defense mechanism weakens. Studies that use sensitive diagnostic tools to reveal bacterial presence in presumably aseptic cases support the existence of this extreme scenario.[27,28] In weak hosts, on the other hand, a virulent organism can cause fatal fulminant sepsis. Most PJI fall somewhere in between these two extreme scenarios, depending on the host's defense strength and the pathogen's virulence.

Status/ bearing	MoM	CoXPE	CoC	CoP	MoP	MoXPE
Non-revised	72	376	1,317	509	4,740	2,784
Revised	0	0	6	3	30	29
Total	72	376	1,323	512	4,770	2,813

Table 1: Number of hips implanted with each bearing type within the study period and the number of those revised due to PJI.

Consequently, it can be expected that certain infections will never become clinically evident or may only result in a presumably aseptic loosening sooner or later.[24,29,30] The incidence of this subclinical infection is not known; however, some studies state that the incidence of septic loosening within a range of 5% among the apparently aseptic is not negligible.[28] We may speculate that, in these cases, host defense mechanisms and bacterial virulence factors could stay in balance permanently, for a long time or until a certain interference weakens the local or systemic immune mechanisms. This points to the possibility that natural non-specific mechanisms, such as those involving toll-like-receptors (TLR), and specific mechanisms, such as antigen mediated immunity, may be powerful enough to keep a very low-grade infection under control for an indefinite period, provided there is no disturbance in the balance.

It is important to recognize the possibility of subclinical infections because they may have many real clinical consequences. There are indices pointing in favor of this concept. As has been previously demonstrated, the infection rate following revision surgery depends on the power of the diagnostic tools. Sonication of the explants caused more infections than conventional periprosthetic cultures, further suggesting that more failures are septic than previously suspected.[31] Applying still more sensitive diagnostics, such as PCR technology, seems to result in an even higher number of infection-related revisions.[32]

Systemic disorders, like inflammatory diseases, and therapeutic agents, such as corticosteroids, biologic drugs and chemotherapeutics that induce immunosuppression, are associated with an increased incidence of infection and can cause asymptomatic PJI to become symptomatic.

It is thus possible that the bearing type influences local and, eventually, also systemic, host defenses. We predict that wear particles released from the bearing and their influence on local tissue could represent the mechanism of action. The influence depends on the quantity, size, shape and chemical composition of the particles. Studies have shown[33,34] significantly elevated levels of blood metal ions (cobalt, chrome, titanium, vanadium) and far higher levels are present in the periprosthetic space of some bearings. In-vitro tests have demonstrated the toxic effects that increased levels of metal ions have on lymphocytes and sensitization to metals has also been observed in certain patients.[35]

It has been shown that different particles have different biological activities and subsequently propensities for macrophage activation and osteolysis formation.[36,37] According to some studies, ceramic particles are the most bio-tolerant.[37] On the other hand, the corrosion products of metal particles can induce profound derangements of local tissue,[38] resulting in pseudo-infections or pseudotumors in some patients. The relative bio-tolerance of polyethylene debris stays between that of ceramic and metal.

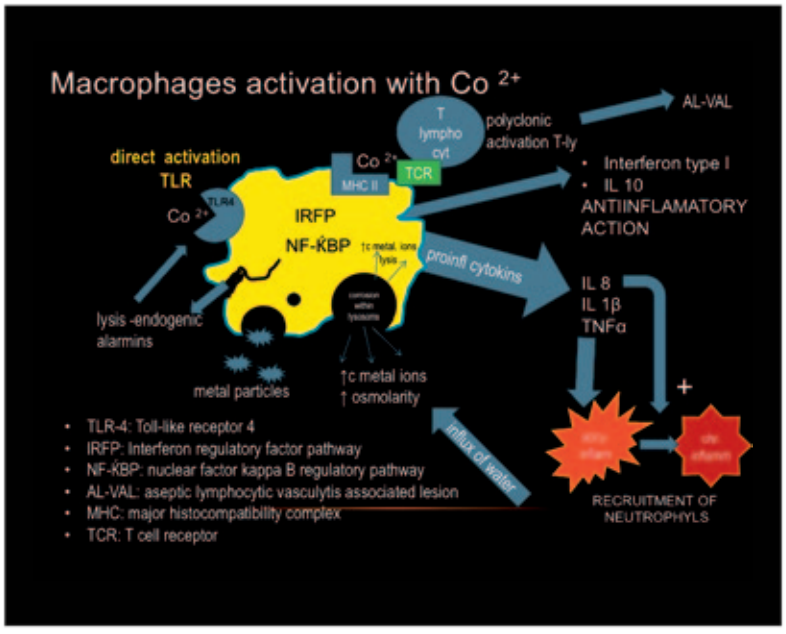

Fig. 1: Complex multiple action of metal particles on macrophages: activation by phagocytosis, direct activation of TLR and the macrophage, polyclonal activation of the T-lymphocyte, rise in tissue osmolality due to intracellular corrosion[42]

Toll-like receptors may also be involved in the pathogenesis of a decreased local immune response to metal ions. A paper by Pajarinnen[39] has shown that foreign body presence in mouse bones down-regulates TLR, particularly in the presence of metal debris. Innate and adaptive immune responses, in which TLR plays an important role, are consequently decreased. Low-grade infections that would otherwise remain permanently under control are prone to actuate in an immunosuppressed milieu.

Metal ions activate antigene presenting cells (APC), which lead to an enhanced expression of the MHC-peptide and costimulatory molecules. The fate of the response, however, depends on which type of T-cell receptor the costimulatory molecules act on.

The whole spectrum of immunological changes in the local and systemic environment caused by the release of particles from the bearings is not known in detail. However, growing evidence demonstrates that important derangements do occur, which alter local and systemic immunologic mechanisms and induce a status of relative immunodeficiency, resulting in higher infection rates.[40,38,41] (Figure 1) The profound influence of metal ions on periprosthetic tissues has been summarized by Konttinen.[38]

It seems that metal ion release influences the incidence of clinically manifested PJI. Articulation is probably the main source of metal ions (particularly in MoM implants), and the importance of taper junctions has also recently been acknowledged. Tapers are prone to crevice corrosion[43], particularly in high torque conditions that occur with larger heads.

Our results indicate that implants with articulations involving a metal component are more prone to becoming infected than those involving ceramic-on-ceramic or ceramic-on-polyethylene bearings, where no metal ion release occurs from the bearing and only minimal release occurs from the taper junction. The presenting results and working hypothesis are in line with the high incidence of infection in our MoM series from the 1990s.[18,44] A direct cause and effect, however, has yet to be proven.

The study has weaknesses. Although all of the surgeons included in the study practice operated on patients in the same hospital, discrete differences in surgical techniques and patient selection were unavoidable. Selection bias may also have influenced the results since the indication for the bearing selection was not always consistent. The homogeneity of the compared groups in terms of age, primary diagnosis and activity level was not checked.

Despite these weaknesses, the results and circumstantial evidence from the literature provide us with enough suspicion to warrant further investigation into the influence of the bearing pair on the incidence of PJI. ■

CORRESPONDING AUTHOR

Rihard Trebše, MD, PhD
Orthopedic Hospital Valdoltra
Jadranska cesta 31
SLO-6280 Ankaran
Slovenia
Phone: +386 5 6696115
Fax: +386 5 6696185
E-mail: rihard.trebse@ob-valdoltra.si

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Rihard Trebše, MD, PhD, is an orthopaedic surgeon and head of the Department for Bone Infections at the Orthopaedic Hospital of Valdoltra, Slovenia. He is President of the Slovenian Orthopaedic Society and acts as a national delegate of Slovenia for the European Hip Society.

Rihard Trebše has performed more than 1.500 THA, more than 350 revision THA, over 1.000 TKA, more than 230 UKA as well as over 210 TSA and treated more than 200 orthopaedic infections.

Rihard Trebše's research is mainly focussed on prosthetic joint infections. He wrote his PhD thesis on the "Treatment of orthopedic device related infection with device retention and defined antibiotic therapy". His ongoing research projects examine, among others, the influence of perioperative antibiotics on intraoperative tissue cultures and the role of endotoxin in the loosening of artificial joints. He is also conducting a study on allergic reactions in metal-on-metal total hip arthroplasty.

Rihard Trebše is member of several professional societies, including the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) as well as the European Study Group for Implant Associated Infections (ESGAI).

He has given numerous talks and published widely both in scientific journals and books. He acts as reviewer for a number of scientific journals, for example, for Acta Orthopaedica, Rheumatology, the Journal of Medical Case Reports and the European Journal of Clinical Microbiology and Infectious Disease.

Contact:
Rihard Trebše, MD, PhD
Orthopedic Hospital Valdoltra
Jadranska cesta 31
SLO-6280 Ankaran
Slovenia
Phone: +386 5 6696115
Fax: +386 5 6696185
E-mail: rihard.trebse@ob-valdoltra.si