EXCERPT

Klaus-Dieter Kühn *Editor*

Management of Periprosthetic Joint Infection

A global perspective on diagnosis, treatment options, prevention strategies and their economic impact

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Klaus-Dieter Kühn (Ed.)

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A global perspective on diagnosis, treatment options, prevention strategies and their economic impact

With 196 figures

Springer

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Medical University of Graz

The Roman encyclopaedist Aulus Cornelius Celsus (ca. 25 BC–ca. 50 AD) described the diagnosis and therapy of fistulae caused by infectious disease, followed by the Andalusian physician and surgeon Abulcasis (Abu al-Qasim al-Zahrawi; 936 AD–1013 AD), who had already developed sophisticated surgical instruments to probe and excise these fistulae (see Fig. 1). At a time when electronically downloadable open-access articles are en vogue, the present volume stands in the tradition of good old-fashioned books with the great advantage of giving the readers a concise overview of the different topics. Professor Kühn has successfully managed to motivate a large number of internationally renowned experts in the diagnosis and treatment of periprosthetic joint infection to put their compressed experience, ideas, and recommendations into this volume. I sincerely thank him for this effort and hope you, the reader, gain new ideas from this book that will contribute towards the successful treatment of your patients.

A. Leithner

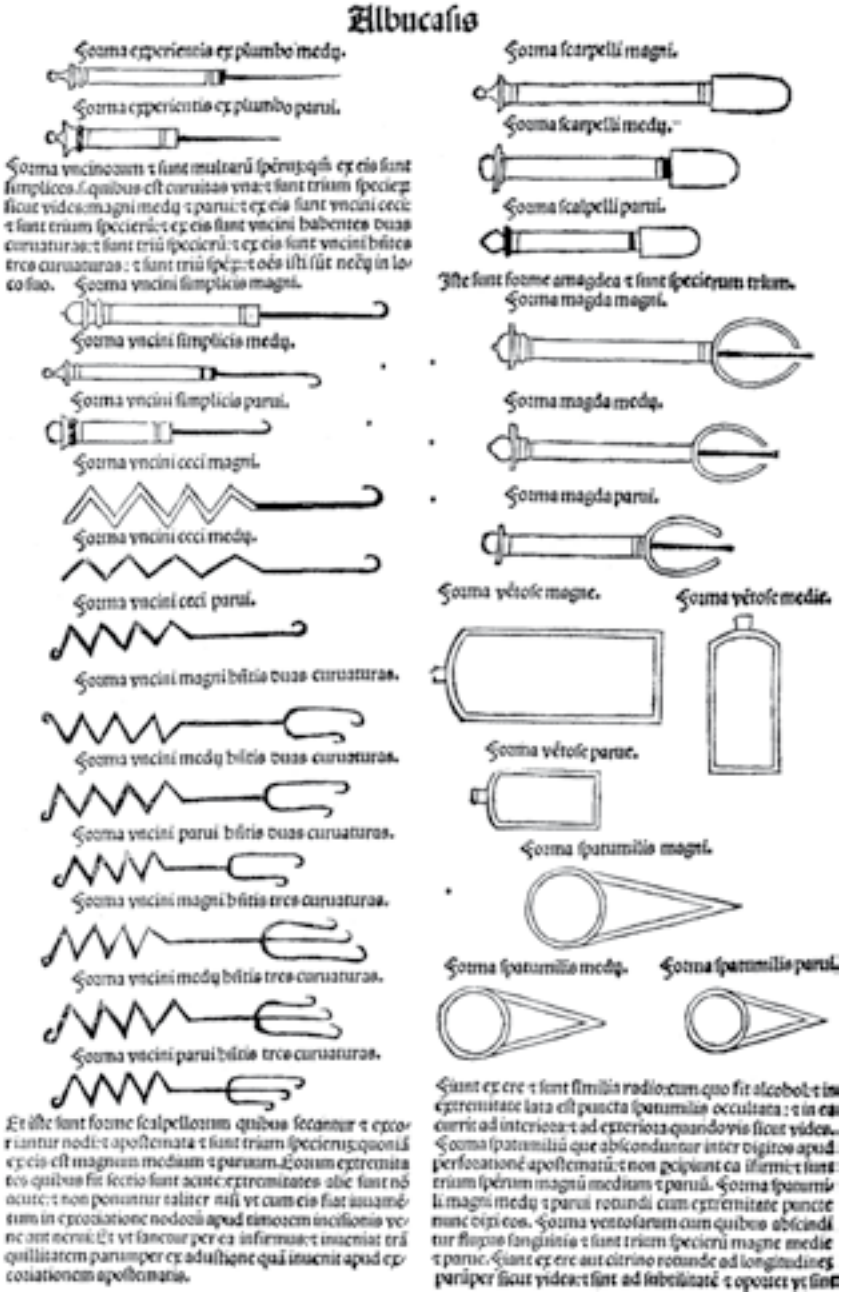

Fig. 1 Surgical instruments; anon, after designs originally drawn by Abulcasis (ca. 1000); Woodcut circa 1500; Chauliac, Guy de, Chirurgia parva. (Wellcome Library, London; https://wellcomeimages.org/indexplus/image/L0002051.html)

Foreword

The editor of this book, Klaus-Dieter Kühn, has succeeded in motivating many well-known experts to present their knowledge in the field of periprosthetic joint infections (PJI). Amongst these authors you will find different specialists – orthopaedic surgeons, infectious disease specialists and microbiologists. The chapters focus on a range of issues related to PJI, including economic factors, clinical aspects, diagnosis, prevention, microbiologic analyses, treatment algorithms, antibiotic-loaded bone cement, spacers and the potential of implants with anti-infective coating.

The strength of this book lies in the generously illustrated chapters that present a great variety of PJI cases. In presenting these cases, the authors explain the basis of their decisions for an adequate treatment. The careful study of this illustrative material allows the reader to choose the most appropriate algorithm for their practice. However, there is not much discussion on the results achieved with these algorithms.

This volume can be recommended to anyone dealing with PJI as a treasure trove of ideas. It is of special interest for orthopaedic surgeons or infectious disease specialists who are confronted with clinical infections. It will be the duty of each individual reader to gather their own clinical experience on the basis of the new ideas presented in this book.

The treatment of musculoskeletal infections has changed a great deal in the past few decades. One of the most important achievements is that treatment of musculoskeletal infections is decided in a team. This should be composed of at least an orthopaedic surgeon and an infectious disease specialist, supported on a case-by-case basis by a microbiologist, a pathologist and a plastic surgeon. In countries that do not have the speciality of infectious diseases, internists should be motivated to acquire special knowledge in this field.

As a young resident in the 1970s, I was shocked by the fate of patients affected by PJI. I often saw them suffering from large open wounds after incomplete removal of the implants and the bone cement. Frequently, they remained handicapped for the rest of their life. Fortunately, step by step, we learnt how to improve this situation. After realizing that debridement means the complete removal of all foreign bodies – including any gentamicin beads left behind – healing of the wounds could be achieved. New ideas such as loading bone cement with gentamicin, re-implantation of a prosthesis after a successful Girdlestone situation and the method of Buchholz, daring to carry out a one-step exchange in PJI, came into the picture.

At the orthopaedic department in Liestal Hospital near Basel we were faced with a growing number of patients who were referred to us with bone infections. Progressively, we learnt about the key elements necessary for a better handling of these cases. A thorough debridement included not only the removal of all foreign bodies, but also an adequate resection of necrotic bone. We tested the quality of debridement by analysing the resected bone in our own laboratory for non-decalcified histology so as to be sure not to resect neither too much nor too little. After debridement we proceeded to immediate closure of all wounds, if necessary with the help of the plastic surgeon instead of allowing for a delay by application of negative pressure dressing. Any imminent leaking of a postoperative wound was prevented by an immediate re-intervention completed with new drainage.

Re-implantation of a total joint after a Girdlestone hip was successfully changed to a two-step replacement with an interval of only 2–3 weeks. Following the idea of Buchholz, in cases of PJI proven by arthrocentesis presenting with uneventful tissues we favoured a one-step exchange. Finally, revision with retention of the prosthesis was chosen for early infections of up to 3 weeks. By introducing this Liestal algorithm the number of recurrences gradually decreased, as proved in the repeated scientific follow-ups of all our cases.

Using the following additional diagnostic measures, the number of PJI without known micro-organisms dropped below 4%: discontinuation of the antibiotic therapy for 2 weeks, harvesting of three to five tissue samples instead of swabs, sonication of the removed foreign bodies and leucocyte count in the synovial fluid.

Feeling that I was not sufficiently trained to manage the antibiotic therapy, I looked for help, which I found with the infectious disease specialist Werner Zimmerli, who worked at the University of Basel. He later changed to Liestal where he became the head of the internal medicine department. To treat early biofilms without exchange of the prosthesis represented a significant challenge. We could achieve much better results treating early staphylococcal infections by adding rifampicin to the conventional antibiotic. This was proven with a randomized study.

A number of micro-organisms were resistant to our two-step exchange with a short interval. Infections by so-called difficult-to-treat bacteria – such as small colony variants of common bacteria, enterococci, rifampicin-resistant staphylococci, fungi and some others – could be treated by another type of two-stage procedure that included a long interval of 8–10 weeks without a spacer. During this period, a curative antibiotic treatment of the infection without foreign material can be achieved.

The main secrets for a successful treatment of PJI are:

- Clear definition of the different elements of the treatment and their application without compromise.
- Rigorous application of an algorithm once it has been selected as a basis for a scientific control
- Collaboration of the orthopaedic surgeon and the infectious disease specialist with access to specialized partners in microbiology, histology and plastic surgery
- Long-term follow-up of all the patients treated, including a scientific analysis of the results in order to prove the quality of the chosen algorithm

To promote better treatment, »Swiss orthopaedics« in 2006 created an expert group on »infections of the musculoskeletal system« comprising a representative number of orthopaedic surgeons and infectious disease specialists. This group edited a pocketbook including an e-book version on the treatment of these infections, which can be ordered for free on www.swissorthopaedics.ch or www.ebjis.org.

If this present book on PJI motivates the reader to do a better job in the therapy of these unfortunate patients by following strict algorithms and practising an interdisciplinary treatment, then it has achieved an important goal.

Peter E. Ochsner
Emeritus Extraordinarius Professor in Orthopaedics at the University of Basel

Preface

Periprosthetic joint infection (PJI) is among the most serious complications in the field of endoprosthetics. The number of PJIs is increasing worldwide and poses a real interdisciplinary challenge for everyone involved. Beside its immense impact on patients and the health-care system, the diagnosis and management of PJI are very difficult, since there is no »gold standard«.

This book provides basic and advanced knowledge of the diverse aspects of periprosthetic joint infections and a comprehensive overview on a global scale, which was possible only because of the close collaboration of international experts. Various issues such as diagnosis, treatment options, prevention strategies and their economic impact are addressed in order to exchange versatile experience and know-how. Furthermore, attention was given to antibiotic-loaded bone cements (ALBC), spacer management and anti-infective implant coatings.

This compilation offers an ample summary to a multidisciplinary audience. Not only for the microbiologist, who is responsible for identifying the causative germs, the infectious disease specialist, who can recommend the appropriate antibiotic therapy, the clinical pharmacist, who is consulted regularly throughout the therapy to discuss the risk of potential drug interactions, or the surgeon, who will proceed with the revision surgery, following defined algorithms, but also for any other interested reader. Moreover, it may also help affected patients to understand the clinical procedure.

This book aims to contribute to a fruitful international debate concerning the ideal management of PJI. In addition, the reader can use this book as a solid platform for comparing their own approach to PJI treatment with the specialists' recommendations.

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Acknowledgements

My sincere thanks to all the authors for agreeing to provide a scientific contribution to this book. Despite having many other obligations, they took the time to share their clinical experience and offer valuable information for the reader. Based on this essential support, it was possible to give a comprehensive overview of the topic of periprosthetic joint infections on a global scale.

Because of the abundant clinical data, it would have been impossible to produce a successful compilation of all the multifaceted contributions without additional scientific support. Thus, I would like to express a special thanks to S. Vogt and C. Berberich for our great scientific discussions, as well as E. Lieb, L. Schell, M. Schulze, J. Schmiedel, O. Vornkahl, D. Müller, and A. Klotz for their support during the review procedure. In particular, I thank A. Roggeman, who was always willing to offer assistance in the international correspondence and networking.

Since the book includes various contributions from many different countries it was often necessary to contact the authors directly. This would have been impossible without S. Buitendag and A. Peyper (SA), M. Zaaijer (B, NL), T. Smith (UK), S. Tye and C. Berberich (AUS), L. Kiontke (UK, AUS, USA), E. Lieb (F), and T. Kluge (USA), whom I want to thank for their commitment.

Furthermore, I would like to thank M. Zimni for the creation of the book cover and other graphics, U. Dächert of Springer for managing the publication of the book, I. Athanassiou for professional editing, and S. Janka for the initial compilation of the submitted contributions.

Special thanks to A. Holl for her competent assistance in creating figures as well as in viewing and editing the contributions all the way to the printing stage.

My thanks to Prof. Dr. A. Leithner, Medical University of Graz, Department of Orthopaedic Surgery, for the opportunity and freedom to create the present book.

Last, but not least, I would like to thank Prof. P. Ochsner for the friendly and professional foreword.

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2 Economic Aspects

2.1 Economic Aspects of Periprosthetic Joint Infections

Tim Hanstein and Ralf Skripitz

Abstract

With the introduction of lump sum reimbursements in the European health-care systems, economic pressure on hospitals arose. Therefore, besides medical aspects, economic aspects also have to be taken into account for each procedure. Total hip replacement (THR) and total knee replacement (TKR) as primary procedures are considered to be cost-covering treatments from the hospital perspective. However, the adverse event of a periprosthetic joint infection (PJI) is usually above average costs, while it is reimbursed with the same amount as an aseptic revision. Published cost data for the treatment of PJI in France, Germany and the UK have been compared with the costs of an aseptic revision and the ensuing reimbursement to check whether PJIs in the knee and hip are cost-covering procedures or not. The studies show an average cost increase for septic revisions of up to 260% compared with aseptic revisions. Especially the increased costs for antibiotics were disproportionately high compared with the total cost increase. Except for one study, all studies have shown that reimbursement for PJI treatment does not cover the hospital's expenses. Compared with aseptic revisions, PJIs are associated with significantly increased treatment costs. However, both treatments are still being reimbursed with the same amount. While the optimization potential is limited, the hospitals should have better reimbursement opportunities so as to focus on the medical aspects of the procedures. A DRG split and a specific code for the treatments performed could bring an end to the unification of septic and aseptic revisions.

2.2 Periprosthetic Joint Infections in the Spectrum of the German Diagnosis-Related Groups System

Sascha Gravius and Hendrik Kohlhof

Abstract

The number of periprosthetic joint infections (PJI) is continuously increasing. Treatment of PJI is associated with an enormous economic impact for the hospital and the corresponding health-care system and the related costs are not fully reflected within the German diagnosis-related groups (G-DRGs). The G-DRG is a medico-economic patient classification system which classifies patients with similar medical conditions incurring similar treatment costs into »diagnosis-related groups« (DRG) with regard to complications and comorbidities. Treatment of PJI requires both surgical and antibiotic therapy. There are various treatment options available – such as debridement, antibiotics and implant retention (DAIR) as well as single-stage, two-stage and three (multiple)-stage prosthesis exchange. All these different procedures are grouped into different DRGs. In this chapter we describe the depiction of costs for treatment of PJI in the G-DRG system according to the specific therapeutic procedures.

3 Clinical Aspects

3.1 Clinical Aspects of Prosthetic Joint Infection

Vincent Moretti and Javad Parvizi

Abstract

Prosthetic joint infection (PJI) is a rare but potentially catastrophic complication after joint replacement. A thorough understanding of the pathomechanism, common clinical presentations, definitional parameters, diagnostic tests, and current antibiotic prophylaxis recommendations for PJI is critical for prevention and recognition of this devastating problem. Bacterial access to the joint space occurs via one of three main pathways: intraoperative introduction at the time of index surgery; contiguous spread of an infection from an adjacent site; and haematogenous seeding from transient bacteraemia or a remote site of infection. Once in contact with the prosthesis, bacteria initiate a complex multi-phase adhesion process that binds them to the implant and they can begin forming a protective biofilm layer. The clinical presentation of PJI is variable. Reported symptoms and physical signs can include joint pain, incisional erythema or drainage, joint swelling or effusion, joint warmth, fever, and a sinus tract at the involved joint. Although there is no official diagnostic definition of PJI, the guidelines recently put forth by the Musculoskeletal Infection Society are the most widely accepted. These guidelines incorporate many of the current laboratory tests that are available to assist physicians in diagnosing PJI, including serum erythrocyte sedimentation rate and C-reactive protein levels; synovial white blood cell count and differential; synovial leukocyte esterase level; synovial fluid or tissue cultures; and histologic analysis of periprosthetic tissue. Many other laboratory tests are also available and still others are under development. Antibiotic prophylaxis is an essential tool for preventing PJI and nearly all guidelines recognize preoperative antibiotics to be a critical part of modern arthroplasty surgery. A solitary systemic intravenous antibiotic, such as cefazolin or cefuroxime, is generally the preoperative antibiotic of choice for lower-limb arthroplasty, although the ideal timing and duration of systemic prophylactic antibiotic use remain controversial.

4 Diagnosis

4.1 Diagnosis of Prosthetic Joint Infections

Lorenzo Drago and Elena De Vecchi

Abstract

The diagnosis of prosthetic joint infections still represents a major challenge for orthopaedists, microbiologists and infectious disease specialists. The main issue is related to the lack of a univocal, worldwide accepted gold standard, so that diagnosis is based on fulfilment of a series of major and minor criteria and requires a multidisciplinary approach that integrates results from microbiological, biochemical, histological analyses with clinical and radiological examination. In this context, cultures are usually considered as the mainstay of diagnosis of prosthetic joint infections. However, culture is limited by a variable sensitivity and by prolonged incubation, which may delay patient management. Moreover, risk of isolating contaminating agents further complicates decision-making, since bacteria commonly residing on skin, such as coagulase-negative staphylococci and propionibacteria, are among the most frequently isolated pathogens in this kind of infection. Diagnosis may be performed on samples collected before or during surgery. In the former, increased levels of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are suggestive of infection when no other causes of alteration are identified, but synovial fluid represents the sample of choice for culture and determination of inflammatory parameters such as leukocyte esterase, CRP and alpha defensin. Intraoperative samples include joint fluid, periprosthetic tissues and prosthetic implants. To improve culture sensitivity it is crucial to remove microorganisms from the biofilm they produce on tissues and implants. For this purpose, homogenization and treatment with dithiothreitol represent an effective and practical approach, being characterized by high sensitivity. Traditional culture requires prolonged incubation, at least 15 days, and therefore alternatives to shorten this time have been proposed. Inoculation of samples into bottles for blood culture has been reported to have high sensitivity and may represent a valid choice. A further improvement might be expected by the use of molecular methods, but contrasting results have been reported and, currently, further investigations are needed. Histological examination is particularly valuable when the possibility of infection is not completely confirmed or excluded after a thorough preoperative evaluation, but it requires skilled personnel with experience in orthopaedic infections. In conclusion, diagnosis of prosthetic joint infection is a complex process which requires a multidisciplinary approach. Clinicians should be informed on the potentiality of the available assays in order to use them appropriately.

4.2 Diagnosis of Pathogens

Frank-Christiaan B.M. Wagenaar, Dean F.M. Pakvis, and Lars Frommelt

Abstract
The number of periprosthetic joint infections (PJIs) continues to rise. This is mainly caused by the ever-increasing worldwide demand for joint arthroplasty but also due to more patients at risk for a PJI. The most common causative pathogens of PJI are *Staphylococcus aureus* and coagulase-negative Staphylococci (CNS, with *Staphylococcus epidermidis* as the most common species). Nevertheless, multidrug resistance is a rising issue in many countries and is particularly created by poor antibiotic policy (both in human and veterinarian medicine) by doctors and governments. Currently, the only definitive proof of PJI is the detection of a causative pathogen. All other available diagnostic modalities remain indirect measures of PJI. Therefore, the current diagnosis of pathogens remains centred around analysis tissue biopsy (cultures) and joint fluid (leukocyte count, polymorphonuclear granulocyte % and several cultures). Optimized practical and laboratory procedures are crucial aspects in PJI diagnostics. Still, a PJI may be present despite negative culture results that can remain a diagnostic and therapeutic challenge.

4.3 Diagnosis of Pathogens Causing Periprosthetic Joint Infections

John Segreti

Abstract
Periprosthetic joint infections (PJI) are an uncommon but serious complication of total joint arthroplasty (TJA). Infection may result in significant morbidity and functional limitation for the patient and is associated with twice the length of hospitalization and excess cost. Establishing the diagnosis of PJI utilizes a combination of synovial fluid analysis, histopathologic examination, intraoperative appearance, and bacterial cultures. New diagnostic methods, such as multiplex polymerase chain reaction (PCR) and mass spectrometry, are under development, but the utility of these highly sensitive diagnostic techniques with unknown specificity should be interpreted with caution. Such methods also fail to determine the antibiotic susceptibility of the identified organisms. Thus traditional microbiology remains the mainstay for identifying organisms causing PJI and determining their antimicrobial susceptibility. Only by knowing the antibiotic susceptibility of the infecting organisms can one reasonably assure administration of appropriate antibiotic therapy. Therefore, attempts need to be made to optimize the yield of traditional cultures.

5 Prevention

5.1 Prophylaxis for Implant-Related Infections: Current State of the Art

Willemijn Boot and H. Charles Vogely

Abstract
Joint replacement is a successful surgical procedure. Unfortunately, some patients will experience a serious complication such as an infection. Many methods for infection prophylaxis are currently being investigated to improve the protection of the implant. Since use of systemic antibiotics has disadvantages such as insufficient local concentrations and toxicity, many researchers are focussing on providing local protection. The most recent developments have occurred in the fields of carriers of antimicrobial agents, coatings for implants, and local infection prophylaxis with antimicrobial agents as alternatives for antibiotics.

5.2 Prophylaxis During Total Hip and Knee Replacement

Jason Chan and Paul Partington

Abstract
Periprosthetic joint infection (PJI) is an infrequent complication of elective joint replacement surgery which can result in disastrous consequences. Multiple factors are involved in causing PJI. Strategies to minimize the risk of PJI require a multidisciplinary team approach. This chapter reviews best evidence-based practice and how it influences practice in our unit at Northumbria Healthcare NHS Foundation Trust (NHFT).

5.3 Strategies for Preventing Infections in Total Hip and Total Knee Arthroplasty

Christopher W. Jones, Ben Clark, and Piers Yates

Abstract
We present a multidisciplinary, evidence-based approach of the strategies for reducing the risk of prosthetic joint infection (PJI) in total hip arthroplasty (THA) and total knee arthroplasty (TKA). There are three key periods: preoperatively, intraoperatively and post-operatively. Proven strategies to decrease the risk of infection in THA and TKA include the preoperative medical optimization of patients, identification and reduction of *Staphylococcus aureus* colonization (MSSA and MRSA), fastidious perioperative skin preparation, selection and timing of prophylactic antibiotic and the avoidance of allogeneic blood transfusions. Intraoperatively the vital importance of achieving and maintaining a sterile field, providing ultra-clean air flow, adopting strict gowning, draping and gloving protocols, and ensuring robust sterilization procedures has long been recognized. Post-operatively, wound care regimens, drain management and inpatient care protocols have all been shown to play important roles.

5.4 Treatment of Bone and Joint Infection: Clinical Practice at the Centre de Référence des Infections Ostéo-Articulaires Complexes (CRIOAc) Lyon, France

Anthony Viste, Florent Valour, Yannick Herry, Frederic Laurent, Vincent Ronin, Isabelle Bobineau, Frédéric Aubrun, Sébastien Lustig, and Tristan Ferry

Abstract

Bone and joint infections (BJI) are very diverse and heterogeneous. Indeed, different parts of the skeleton could be infected by a variety of mechanisms (trauma, following surgery or bacteraemia) and by a variety of pathogens (single or multiple bacteria or fungi that can resist different antimicrobial drugs). Moreover, BJI can be acute or chronic (with the involvement of a variety of microbial persistence mechanisms for the latter) and be associated or not with an implant (osteosynthesis or prosthesis). The French Health Ministry selected nine dedicated university clinics throughout seven geographical regions to act as reference centres, called the Centres de Référence des Infections Ostéo-articulaires complexes (CRIOAc). The CRIOAc Lyon, located in the Auvergne-Rhône-Alpes Region in France (ca. 8 million of inhabitants) has developed over many years an extensive approach to managing complex BJI, by promoting multidisciplinary approaches, prospective cohort studies, and individualized innovative strategies to facilitate patient therapy. In this chapter, we present some examples of complex BJI cases managed at the CRIOAc Lyon.

6 Treatment

6.1 Treatment of PJI: Overview

Tamon Kabata and Hiroyuki Tsuchiya

Abstract
Periprosthetic joint infection (PJI) is a generic term comprising intraoperative bacterial infection during total joint arthroplasty, infection that spreads from a local infected site, haematogenous infection, and recurrent infection after suppurative arthritis; it does not include superficial infection. PJI has a significant impact on the mortality of patients. Thus, appropriate treatment and diagnosis are required. For the revision procedures for PJI, clear evidence has not been established on the indication of one-stage and two-stage revision procedures. Generally, the two-stage revisions are regarded to be the gold standard, and one-stage revisions are usually not recommended when the causative bacteria are multidrug-resistant bacteria or Gram-negative organisms. If the revision surgery is considered not to be beneficial for a patient based on the systemic condition, activities of daily living (ADL) and the prognosis, then resection arthroplasty and amputation may be selected. If the operative procedure itself is considered not to provide any benefit to a patient, suppression therapy using only antibiotics could be one of the treatment options. For a better treatment of PJI, each patient should carefully be evaluated so as to apply an individualized treatment strategy. A stricter systemic management and meticulous operative procedure are also required.

6.2 Treatment of Orthopaedic Septic Revisions at the Medical University of Graz

Florian Amerstorfer and Mathias Glehr

Abstract
Prosthetic joint infection (PJI) is one of the most serious complications of joint replacement and associated with significant morbidity and mortality. Owing to the increasing numbers of total joint arthroplasty procedures in the past few years, the total number of PJI has also been increasing, leading to enormous health-care costs. Depending on the classification of the infection (acute versus late), as well as the health and local status of the patient, surgery with additional antibiotics may be performed to erase the pathogen, which is the main goal in PJI treatment. Debridement and implant retention is one option to treat acute post-operative PJIs if the implants are stable. One- or two-stage-exchange is required if the implants are unstable with or without bone loosening and soft tissue damage. Resection arthroplasty, arthrodesis or amputation are the last options and are only necessary after multiple re-operations due to re-infection with massive bone destruction and soft tissue damage.

6.3 Treatment of Prosthetic Joint Infections

J.G.E. Hendriks, Robin W.T.M. Van Kempen, and L. van Dommelen

Abstract
A prosthetic joint infection (PJI) is difficult to treat because of the biofilm mode of growth on the prosthesis. Reported treatment results have improved over the past few decades, with cure rates up to 95%. Unfortunately, publications are hard to compare, mainly because the extent of debridement is not systematically described and likely differs between clinics. We have established a joint protocol with orthopaedic surgeons and medical microbiologists involving accurate microbiological diagnosis and targeted treatment, debridement and local antiseptic and anbiotic treatment. In this treatment approach we have discerned five PJI treatment scenarios: (1) debridement, antibiotics, irrigation, and retention of prosthesis (DAIR); (2) failure to respond to DAIR; (3) two-stage protocol; (4) inadvertent one-stage protocol; and (5) cases where patients decline an operation or are inoperable. Recently, we have started to prospectively collect our data, which includes data on clinical follow-up as well as patient-reported outcome measures. We will use these data to improve our protocol and to inform patients on the expected outcome of their treatment.

6.4 The University Hospitals of Louvain Experience and Care Pathways for PJIs: How We Do It

Jeroen Neyt

Abstract
Disclaimer: This chapter is aimed at assisting orthopaedic surgeons who might not be treating periprosthetic joint infections (PJIs) on a full-time basis. Neither the author nor the publisher is – with this chapter – providing a medical or other professional service. If medical advice or an expert opinion is required, the services of a competent professional should be sought. The information in this chapter should not be regarded as standard of care.

6.5 Treatment of Prosthetic Joint Infections

Olivier Borens and John McManus

Abstract
Prosthetic joint replacement is one of the most successful surgical procedures of the past century and the number of implanted artificial joints is rapidly growing. While the results of the procedure are generally positive, infections may occur, leading to patient suffering, surgeon frustration, and significant costs to the health-care system. Infection after prosthetic joint replacement is thus a feared complication as healing rates can be low, functional results poor and patient satisfaction abysmal. However, if a patient-adapted treatment of infected total joints is used, an overall success rate of above 90% can be obtained. The patient-adapted treatment concept is based on five strong pillars: teamwork, understanding biofilm, proper diagnostics, proper definition, clear classification and patient-tailored treatment.

6.6 Prosthetic Joint Infection: Treatment

James R. Berstock and Jason C.J. Webb

Abstract
The management of prosthetic joint infection (PJI) remains challenging and requires a bespoke approach based on numerous clinical factors and collaboration within a truly multidisciplinary specialist team. The broad treatment categories include early debridement and implant retention, one- or two-stage exchange arthroplasty, excision arthroplasty, or lifelong antibiotic suppression. In this chapter we discuss our experience treating PJI at the Avon Orthopaedic Centre, a tertiary referral unit for PJI and the lead centre for the INFORM trial, a multicentre randomized controlled trial comparing one- vs two-stage exchange arthroplasty for PJI in the United Kingdom.

6.7 Dutch Protocol for Treatment of PJIs with Illustrative Clinical Cases

René H.M. ten Broeke

Abstract
In this chapter several examples are given of the treatment scenarios for infected total hip and knee prostheses. They all concern patients who have been operated on in the infection unit of the orthopaedic department of Maastricht University Medical Centre, The Netherlands. These scenarios have been identified clinically and the advised treatment options are based on recent literature; they were formulated and recently presented by the Working Group on Orthopaedic Infections, a subgroup of the Dutch Orthopaedic Society (NOV). Although they do not have the status of broadly accepted guidelines, they do provide the orthopaedic society with a format on how to deal with these challenging complications. Despite there still being several recognized controversies in this area, these examples reflect the way PJIs are currently being treated in The Netherlands.

7 Antibiotic-Loaded Bone Cement

7.1 Benefit and Risks of Antibiotic-Loaded Bone Cements

Pablo Sanz-Ruiz, Manuel Villanueva-Martínez, and Christoph Berberich

Abstract
The use of antibiotic-loaded bone cement (ALBC) has proven effective in the treatment and prophylaxis of periprosthetic infections after hip and knee arthroplasty. However, there is concern about its effects on mechanical properties of bone cement, systemic toxicity, antibiotic resistance and added costs upon routine use. In this chapter, we critically address these questions and further describe the mechanisms of action of ALBC, the choice of local antibiotics, the effect on the prophylaxis and treatment of PJI and the different factors that may influence the cost–benefit analysis. Finally, we present our own institutional experience with the implementation of routine ALBC use in all cemented hip and knee arthroplasty procedures comparing infection rates and costs per patient before and after introducing this change in our surgical protocol.

7.2 Therapy Using Antibiotic-Loaded PMMA

Götz von Foerster, Lars Frommelt, and Thorsten Gehrke

Abstract
Use of antibiotic-loaded polymethylmethacrylate (PMMA) bone cement (ALBC) in artificial joint replacement has a long tradition for fixation of total joint replacement (TJR). Buchholz started the clinical use of antibiotic-loaded PMMA for prophylaxis or treatment of periprosthetic joint replacement. The use of PMMA as a drug-delivery device can be non-specific as in prophylaxis or specific if the PJI pathogen is known. Industrial preparations with vancomycin + gentamicin and clindamycin + gentamicin are available for therapy, whereas gentamicin and colistin + erythromycin preparations are dedicated to prophylaxis. Pre-manufactured spacers containing antimicrobial agents are not the subject of this chapter. For specific local antibiotic therapy, knowledge of the pathogen is beneficial for two-stage procedures and is a prerequisite in one-stage exchange procedure. By admixing of suitable antibiotics to PMMA bone cement, specific antimicrobial local therapy is possible in cases where no adequate industrial preparations are available. For reasons of mechanical stability of the bone cement, the amount of antibiotics is limited if PMMA bone cement is used for TJR fixation. Practical hints for hand-mixing are given here and four case reports are presented, showing how ALBC can be used in clinical routine.

7.3 The Role of Antibiotic-Loaded Bone Cement in Periprosthetic Joint Infection

Yuhan Chang

Abstract

Antibiotic-loaded bone cement (ALBC) has been widely used in infection prophylaxis and infection eradication in total joint arthroplasty (TJA). Regarding the dose of antibiotic load, ALBCs can simply be divided into low or high dose for either infection prophylaxis or treatment. Gram-positive pathogens including *Staphylococcus aureus* and coagulase-negative *Staphylococcus* are the most common organisms implicated in the periprosthetic joint infection (PJI). However, Gram-positive bacteria are not the only bacteria found in PJI. Although less commonly associated with PJI, Gram-negative bacteria account for 6–23% of all cases of PJI. In order to eradicate both Gram-positive and Gram-negative pathogens in TJA, an antibiotic with a broad spectrum of antibacterial activity would be a more appropriate choice for polymethyl methacrylate-loaded bone cement. Therefore, the choice of antibiotic for ALBC loading has become a critical issue in PJI prevention and treatment. The efficiency of the release of antibiotics from bone cement is a critical factor that determines the antibacterial activity of ALBC. To increase antibiotic release, soluble fillers such as glycine, xylitol, sucrose, erythritol or liquid-form antibiotics can be added into the bone cement to increase its porosity and consequently increase the penetration of dissolution fluids. Systemic toxicity related to high antibiotic levels eluted from the cement, development of drug-resistant bacteria, allergic reactions to the specific antibiotic used, and the cost are potential concerns of using ALBC.

7.4 PMMA Cements in Revision Surgery

Ashutosh Malhotra, Elke Lieb, Christoph Berberich, and Klaus-Dieter Kühn

Abstract

Surgical debridement of infected and necrotic tissue is the mainstay of therapy for a prosthetic joint infection (PJI). The administration of antibiotics represents an important therapy-supporting measure aiming at reducing the number of infecting bacteria to such low numbers that the immune system is able to eradicate the germs and prevent relapses. Antibiotic-loaded bone cements (ALBCs) in revision surgeries have shown clinical benefit in the treatment of infected joint arthroplasties. The addition of anti-infective agents to the PMMA powder and their release characteristics from the outer surface of the cement matrix allow ALBCs to function as a local drug delivery system (DDS). Given the rising number of commercial ALBCs on the market, it may be difficult for the surgeon to make an appropriate choice with the view towards the most promising clinical long-term results. There are only a few special revision ALBCs currently marketed including Antibiotic Simplex® E+Col (erythromycin + colistin), Copal® G+C (gentamicin + clindamycin), Copal® G+V (gentamicin + vancomycin), Refobacin® Revision (gentamicin + clindamycin) and VancoGenx® (gentamicin + vancomycin). All these ALBCs differ in their physical and chemical properties, which may potentially influence the clinical outcome. Additionally, there are other differences in the quality and quantity of added antibiotics (AB), the antibiotic elution characteristics and the antibiotic influence on the mechanical properties of the cements. Revision PMMA cements are often also used as a spacer because of their particular AB combination and high antibiotic release properties. The possibility of the manual addition of extra (sterile) antibiotics or anti-infective agents to PMMA spacers potentially further increases the efficacy and elution kinetics but may also negatively impact the mechanical stability of the cements.

8 Spacers

8.1 Spacer Management

Manuel Villanueva-Martinez, Pablo Sanz-Ruiz and Christoph Berberich

Abstract
The use of an antibiotic-loaded spacer in the treatment of prosthetic joint infections has become generally accepted practice. The purpose of such spacers is to maintain a certain amount of joint stability and mobility and to provide high intra-articular concentrations of local antibiotics needed to eradicate the infection. The choice of spacer depends on many factors, including the degree of bone loss, the state of the soft tissue, the choice of antibiotics, and the financial and technical restraints. A benefit common to both articulating and non-articulating antibiotic-loaded spacers is that significant higher intra-articular levels of antibiotic can be delivered than with parenteral antibiotics. The only commercial presentations with a synergistic effect are Copal® G+C and Copal® G+V (gentamicin combined with clindamycin or vancomycin). These cements cover a broad spectrum of bacteria and release higher doses of antibiotics at the site of infection. Synergy between aminoglycosides + vancomycin, aminoglycosides + clindamycin and, occasionally, a cephalosporin (ceftazidime, ceftriaxone, cefepime, and cefotaxime, which are available in powder form in most countries) can enable coverage of a broad spectrum of micro-organisms. The synergistic effect helps to inhibit the formation of biofilm and eradicate the infection.

8.2 Articulating Cement Spacers for the Treatment of Hip and Knee Arthroplasty Associated Infections

David Campbell

Abstract
The use of an articulating spacer is a ubiquitous tool for the management of periprosthetic infections. The use of an articulating spacer for hip or knee infections is at least as efficacious as other methods when considering infection resolution. They facilitate delivery of antibiotics to the source of infection, stabilize the skeleton, manage soft tissues and vastly improve the morbidity of patients during the interval period between removal of the infected components and re-implantation of the definitive implant. There are an increasing number of prosthetic options available. The PROSTALAC hip system and subsequent modifications utilizing routine hip components are effective techniques allowing for relatively normal function including the options of long stem fixation where osteotomies are performed. The »Kiwi« technique is a further modification where a primary femoral component is loosely cemented in situ. These implants are sufficiently stable to allow full weight-bearing, and long-term retention of the implant is an occasional option. Monoblock femoral components are popular choices intended for short-term use that are commercially available as a pre-manufactured implant, manufactured by the surgeon utilizing a mould system and a variety of monoblock spacers crafted by the surgical team. Articulating knee spacers include infection-specific implants such as the PROSTALAC system and custom devices, which effectively simulate normal prosthetic function during the interval period. A popular method of re-sterilizing the existing femoral component has been supplanted by the use of a new femoral component articulating against a thin polyethylene because of re-sterilization requirements. A variety of pre-manufactured cement-on-cement articulating devices are available including mould systems that require the surgeon to manufacture the implants with antibiotic-loaded acrylic cement.

8.3 Spacer Management in the Treatment of Late Periprosthetic Infections of the Hip

Bernd Fink

Abstract
In late periprosthetic joint infection, all foreign material has to be removed, and in septic two-stage revision an antibiotic-loaded spacer is an option for filling the joint gap. It preserves the function of the joint, and thus the patient can be mobilized and re-implantation of total hip arthroplasty is technically easier in the second stage. The spacers also have an important role in the local antibiotic therapy of periprosthetic joint infection by releasing antibiotics. One disadvantage of spacers is the wear of cement particles, which have to be removed radically via debridement in the second stage.

8.4 Spacer Management

Kiran Singisetti and Ian Stockley

Abstract
Periprosthetic joint infection (PJI) is a potential serious complication following arthroplasty surgery. It has significant implications for the patient in terms of morbidity but also economic implications for both the patient and the health-care system in general. Whilst new diagnostic and treatment options for PJI evolve, there have been attempts to develop a consensus approach amongst surgeons worldwide to try and standardize the management of PJI (Parvizi and Gehrke 2013). We describe here our approach in managing PJI related to hip and knee arthroplasty. A detailed description of the operative techniques involved is beyond the scope of this chapter; however, as each case is dealt within its own merits, a basic understanding of the management principles involved is important.

9 Coating

9.1 Antibacterial Coating of Implants in Orthopaedics and Trauma

Finding the Right Pathway to a More Effective Surgical Site Infection Prevention

Carlo Luca Romanò, Enrico Gallazzi, Sara Scarponi, Ilaria Morelli and Lorenzo Drago

Abstract
According to current knowledge, the most critical pathogenic event in the development of implant-related infection is probably biofilm formation, which starts immediately after bacterial adhesion on implanted devices, leading to their irreversible colonization. A rationale prevention of biomaterial-associated infections should then specifically focus on both bacterial adhesion and biofilm formation inhibition. Nonetheless, currently available prophylactic measures, although partially effective in reducing surgical site infections, are not based on the pathogenesis of biofilm-related infections and unacceptable high rates of septic complications, especially in high risk patients and procedures are still reported. In the last decades, several studies have investigated the ability of implant surface modifications to mitigate possible adverse events, including implant-related infections. Here we provide a brief overview and a classification of the various technologies under study or already in the market, with particular reference to a novel approach, based on a fast-resorbable hydrogel coating, that may change the paradigm of long-lasting antibacterial implant protection towards a more feasible short-term one, that may minimize the risk of long-term interference with the function of implanted biomaterials and of bacterial resistance induction, while effective protection at an acceptable cost/benefit ratio

9.2 Anti-infective Coating to Prevent Prosthetic Joint Infection

Hiroyuki Tsuchiya and Tamon Kabata

Abstract
Orthopaedic implants with anti-infective coating have attracted attention as an adjunctive measure to reduce the rate of periprosthetic infections. They can be classified into at least three groups: (1) passive surface finishing/modification, (2) active surface finishing/modification, and (3) perioperative antibacterial local carriers or coatings. There have been many ideas for making antibacterial implants and a significant number of fundamental experiments have been reported. However, only a few clinical trial reports have been published about the actual application of this fundamental research. The coating technologies must be proven to be safe in the short and long term, should not interfere with osseointegration or induce bacterial resistance in the long run, and should be easy to implement in clinical practice and at an affordable cost.

9.3 Aspects of Antimicrobial Implant Coating

Andreas Kolb, Susann Klimas, Thomas Kluge and Klaus-Dieter Kühn

Abstract

Periprosthetic joint infection is still a major problem in arthroplasty. During surgery, the surface coating of metallic implants can prevent biofilm formation by influencing the behaviour of the germs for a short period of time. The coating strategy is aimed at securing the implant surface and additionally supporting the human immune system with germ eradication in the bone–implant interface. Therefore, a coated implant surface implant acts as a colonization barrier for germs via the antibiotics incorporated within a polymethyl methacrylate (PMMA) cement matrix. From a regulatory perspective, such anti-infective coated implants are classified as medical devices which are approved as so-called combination products. Registration of such combination products is very challenging particularly because clinical data are required. Nevertheless, a comparison of different coating strategies is not possible because comprehensive experimental models are not yet available. The basis for the evaluation of the safety of the coating is a suitable experimental function model as well as testing of the elution of the antimicrobial substances with a reproducible method.

Management of Periprosthetic Joint Infection

Kühn *Ed.*

Periprosthetic joint infection (PJI) is among the most serious complications in the field of endoprosthetics. The number of PJIs is increasing worldwide and poses a real interdisciplinary challenge for everyone involved. For the patient concerned, it is necessary to promptly work out an adequate therapy solution to fight off the infection. Both the clinical experience of the surgeon and the proper diagnostic processes are prerequisite for the reliable detection and identification of an infection. The microbiologist is responsible for identifying the causative germs by screening the patient's synovial fluid and tissue samples. Based on the findings and subsequent resistance testing, the infectious disease specialist can recommend the appropriate antibiotic therapy. Furthermore, the clinical pharmacist is consulted regularly throughout the therapy to discuss the risk of potential drug interactions. The surgeon will proceed with the revision surgery, following defined algorithms. Adequate radical debridement of infected and necrotic surrounding tissue is the most important step towards a successful cure of the infection. Accompanying the surgery, anti-infective agents are given systemically and locally. While systemic application of anti-infectives mainly reduces the number of haematogenic-spreading planktonic germs, local application immediately forms a colonization barrier and protects the implant from sessile biofilm formation.

Concurrently, antibiotics are actively released from the implant, resulting in local germ reduction. Thus, local agents are embedded in the concept of surgical PJI treatment as a reliable adjuvant measure and they sustainably support the successful outcome. In one-stage procedures, local agents are released from specialized antibiotic-loaded bone cements, while in two- or multi-stage procedures, local agents are released from corresponding temporary spacers (interim prostheses). Even from an economic standpoint, the combination of systemic and local agent application is meaningful. Furthermore, there are some interesting trends towards the coating of metallic implants to protect against biofilm formation on the implant surface.

On the basis of their personal experience, specialists from all over the world present, explain and discuss preventive approaches, appropriate diagnostic strategies for detection, reproducible effective surgical treatments as well as the economic impact of PJI. The reader can use this book as a solid platform for comparing their own approach to PJI treatment with the specialists' recommendations.

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