Infections of the musculoskeletal system
Basic principles, prevention, diagnosis and treatment

1st electronic edition in English 2016

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In a fast growing discipline such as orthopaedic surgery, continuous specialisation is a given situation and is essential to maintain expertise. However, the narrowing area of specialisation that results entails the risk of losing the general overview, which can only be compensated by specialists joining forces. Such networking does not always come naturally and can be difficult since it depends on the communication skills of human beings.

It is therefore with great pleasure and respect that the board of the Swiss Society of Orthopaedics and Traumatology (swiss orthopaedics) presents here the result of an exceptional joint effort by the Swiss Society of Infectious Diseases and swiss orthopaedics. They have united in a common task to provide a summary of the basic principles, diagnosis, prevention and treatment of infections of the musculoskeletal system.

Special thanks go to Peter Ochsner and Werner Zimmerli, both honorary members of swiss orthopaedics, who developed a sophisticated approach for periprosthetic joint infections in Switzerland and acted as catalysts for this code of practice.

Infections of the musculoskeletal system, especially when associated with an implant such as a joint prosthesis, are still a serious complication that can entail long-term treatment. Infection is often associated with loss of the implant and success for a particular patient is sometimes uncertain. Infections present a serious challenge to the confidence a patient has in his or her doctor because the path to success is not wholly predictable for either party. As complications are fortunately rather rare, knowledge of the diagnostic steps involved and the therapy required is limited. This compendium is intended to help infectious disease specialists and orthopaedic surgeons determine the correct treatment for patients with infections of the musculoskeletal system, particularly for implant-associated infections. The manual emphasises the importance of pooling the specific knowledge and experience of infectious disease specialists and orthopaedic surgeons to increase the success rate of treatments and thus the well-being of the patient.

The German edition of this handbook sold out quickly and we hope that the English version will follow suit. It would be an even greater success if it inspires doctors specialising in infections to join forces to make ongoing improvements and updates to the textbook.

Bern, June 2014

Bernhard Christen
President of swiss orthopaedics
Infections of the musculoskeletal system occur either spontaneously (e.g., arthritis of the native joint, spondylodiscitis, etc.) or as a postoperative complication (e.g., implant-associated infection). Orthopaedic surgeons rarely deal with infections on a routine basis. If these infections develop as nosocomial complications, affected patients often feel threatened and anxious. A frank discussion and a thorough explanation of the diagnostic and therapeutic measures can restore the patient’s trust in the treating doctors. Close collaboration between orthopaedic surgeons and infectious disease specialists is critical in bone infection and patients should experience this collaboration at their bedsides.

This book intends to provide recommendations for the procedures to follow in individual situations. They are aimed primarily at those orthopaedic surgeons and infectious disease specialists who do not regularly treat these sorts of patients. They explain both the diagnostic steps as well as the rational therapies. An additional objective is to introduce the orthopaedic surgeon to the approach of the infectious disease specialist and vice versa.

The ‘Infections of the musculoskeletal system’ expert group was commissioned by Swiss orthopaedics to produce a book to promote greater understanding of these diseases among orthopaedic surgeons. Approximately half of the expert group is composed of orthopaedic surgeons and the other half of infectious diseases specialists from Swiss orthopaedics and the Swiss Society for Infectious Diseases, respectively.

Drafting this publication was considerably more difficult than originally thought. Our aim was to select the most important ones. Concise presentation took priority over exhaustive treatment of the issues. Brand names were omitted as a matter of principle. The present English edition is based on the second revised and extended German edition.

This booklet would not have been possible without the active support of our sponsor. We would like to thank Heraeus Medical GmbH for the creative design of the text and for printing the guidelines.

On behalf of the expert group,  
Frenkendorf and Lausanne,  
September 2014  
Peter E. Ochsner and Olivier Borens
The appreciation that musculoskeletal infection involves interplay between the patient physiology and the pathological infection in the bone provides an ideal condition for multi-disciplinary working between surgeons, physicians and laboratory scientists. This book is an excellent example of that essential team-working. Swiss orthopaedics and the Swiss Society for Infectious Diseases are to be congratulated in overcoming the difficulties of communication between different professional groups in producing these helpful, concise and evidence-based guidelines.

Our understanding of bone and joint infections has changed dramatically in the last 30 years. But also, the disease is changing with a reduction in haematogenous osteomyelitis, both acute and chronic and a move towards more implant-related and contiguous focus infection. The rise of resistant strains of bacteria, the problems of small colony variants and intra-cellular persistence of micro-organisms present new challenges for treatment.

It is a pleasure to read a textbook which emphasizes clinical assessment, good sampling techniques, accurate diagnosis and general principles of treatment alongside the more usual descriptions of surgery and antimicrobial therapy. The group of experts and guest authors draws together a wealth of experience, scientific knowledge and published work which gives real authority to the contents of each section.

The organisation of infection services in Switzerland and other parts of Europe has been very influential in promoting modern management of infection. The production of this new edition of the book in English should help to disseminate this knowledge more widely. The format of a small book will allow it to be carried into many clinical settings.

In the past, there has been a rather negative view of the treatment of musculoskeletal infection, particularly among those who see chronic infection rarely. This book makes clear what is possible in the prevention, diagnosis and treatment today and should encourage clinicians to engage with bone infection patients and specialists to achieve the best outcome.

Oxford, September 2014

Martin McNally
Translation Editor
An interdisciplinary work of this nature would be hardly feasible without the energetic support of many people. We would like to thank our many advisers and assistants for their help.

The expert group consulted many of our colleagues for this project. In addition to the many who we have not named, these colleagues included the following (by chapter):

- **Chapter 2**: Prof. Dr med. Andreas Widmer, Universitätsspital, Basel (statements regarding prevention)
- **Chapter 4**: Dr med. Martin Clauss, Liestal (critical review of the text), Prof. Dr med. Uli Exner, Zurich (use of silver-coated tumour prostheses), Dr med. Lars Frommelt, Microbiologist, HELIOS ENDO-Klinik, Hamburg (addition of antibiotics to cement), PD Dr med. Andreas Krieg, Universitätskinderklinik beider Basel (use of silver-coated tumour prostheses), Dr pharm. Anke Leumann, Bahnhofapotheke, Lörrach (addition of antibiotics to cement), Heraeus Medical GmbH Wehrheim (antibiotics in PMMA cement), Dr med. Peter Wahl, Hôpital cantonal, Fribourg (critical review of the text, use of calcium sulphate)
- **Chapter 6**: Dr med. Steffen Bergelt, Aarau (suggestions concerning histology and the corresponding illustrations), Dr Sigrid Pranghofer and Dr. Martin Altwegg, Labor Bioanalytica, Lucerne (review of the microbiology sections and PCR), Dr med. Michael Wissmeyer, HCUGE, Geneva (review of and additions to nuclear medicine diagnostics), Dr Michaela Schneiderbauer, University of Miami (suggestions for the 2nd edition), Prof. Dr. Daniel Kalbermatten, Universitätsspital Basel (Fig. 6-3)
- **Chapter 9**: Prof. Dr med. André Gächter, Mörschwil (illustrations and additions), Dr Michaela Schneiderbauer, University of Miami (critique of revised edition)
- **Chapter 12**: Prof. Dr med. Dirk J. Schäfer, Universitätsspital, Basel (relative importance of various plastic and reconstructive techniques; he also performed all of the free graft procedures shown as examples in the figures.)
- **Chapter 13**: Dr med. Thomas Böni, orthopädische Universitätsklinik Balgrist, Zurich (many additions)
- **Chapter 15**: Dr Sigrid Pranghofer, Lucerne (critical review of the text, preparation of all the illustrations in the chapter),
- **Chapter 17**: Dr Stefano Giulieri, CHUV, Lausanne (chapter additions)
- **Chapter 19**: Dr Sigrid Pranghofer, Lucerne and PD Dr Seife Hailemariam, Institut für Histologie und zytologische Diagnostik, Aarau (joint implementation of the proposed form in clinical use)

We would also like to express our special thanks to Heraeus Medical GmbH, Wehrheim (Germany) for their friendly support with the design and technical realisation of the project.

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Table of contents

Fundamentals

1 Implant-associated biofilm
Andrej Trampuz

1.1 Definition 21
1.2 Biofilm development and maturation 22
1.3 Implant/biofilm interactions 22
1.4 Development of variants of microorganisms 24
1.5 Pathogenesis of implant-associated infections 24
1.6 References 25

2 Prevention of perioperative infections
Markus Vogt, Ilker Uçkay, Paul Bodler

2.1 General 27
2.2 Preoperative measures 27
2.3 Intraoperative measures 28
2.4 Postoperative measures 29
2.5 Perioperative management of patients with infections/colonisation with multi-resistant bacteria 30
2.6 Antibiotic prophylaxis in orthopaedic surgery 31
2.6.1 Fundamentals of perioperative antibiotic prophylaxis 31
2.6.2 Practical approach 31
2.6.3 Procedures with no evidence of the efficacy of antibiotic prophylaxis 33
2.6.4 When is the prevention of possible haematogenous prosthetic joint infections recommended? 34
2.7 References 36

3 Systemic antibiotic therapy
Werner Zimmerli

3.1 Basics of antimicrobial treatment 39
3.2 Definitions concerning the use of antibiotics 43
3.3 Procedures in the case of therapeutic failure 43
3.4 Antibiotics 44
3.5 References 48
4  Local treatment with antiseptics and antibiotics

4.1 Objectives of local therapy
4.2 Fundamentals
4.3 Antiseptics and their main indications
   4.3.1 The most important antiseptics for use with open wounds and for coating implants
   4.3.2 Antiseptic barrier for slow-healing and non-healing wounds
4.4 Antibiotics and their main carriers
   4.4.1 Antibiotics
   4.4.2 Carriers of antibiotics
   4.4.3 PMMA bone cement with antibiotics
   4.4.4 Collagen sponges with antibiotics
   4.4.5 Calcium sulphate with antibiotics
   4.4.6 Coated implants
4.5 References

5  Negative-pressure wound therapy

5.1 Fundamentals
5.2 Therapeutic principles
5.3 Indications and contraindications
5.4 Negative-pressure dressing, antiseptic drape or plastic surgery
5.5 Don'ts
5.6 References

6  Diagnosis of infections of the musculoskeletal system

6.1 Blood tests
   6.1.1 White blood cells, differential blood count
   6.1.2 C-reactive protein (CRP)
   6.1.3 Erythrocyte sedimentation rate (ESR)
   6.1.4 Procalcitonin
   6.1.5 Interleukin 6 (IL-6)
### Special infections

#### 7 Periprosthetic joint infection

*Peter E. Ochsner, Werner Zimmerli, Hubert Nötzli*

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.1</td>
<td>Fundamentals</td>
</tr>
<tr>
<td>7.1.1</td>
<td>Preliminary remarks</td>
</tr>
<tr>
<td>7.1.2</td>
<td>Aetiology</td>
</tr>
<tr>
<td>7.1.3</td>
<td>Localisation</td>
</tr>
<tr>
<td>7.1.4</td>
<td>Incidence</td>
</tr>
<tr>
<td>7.1.5</td>
<td>Risk factors</td>
</tr>
<tr>
<td>7.1.6</td>
<td>Classification</td>
</tr>
<tr>
<td>7.2</td>
<td>Clinical symptoms and diagnostic procedures</td>
</tr>
<tr>
<td>7.2.1</td>
<td>Medical history and findings</td>
</tr>
<tr>
<td>7.2.2</td>
<td>Laboratory tests</td>
</tr>
<tr>
<td>7.2.3</td>
<td>Imaging</td>
</tr>
<tr>
<td>7.3</td>
<td>Treatment algorithm</td>
</tr>
<tr>
<td>7.4</td>
<td>Surgical treatment</td>
</tr>
<tr>
<td>7.4.1</td>
<td>Cornerstones of surgical treatment</td>
</tr>
<tr>
<td>7.4.2</td>
<td>Specific techniques in surgical treatment</td>
</tr>
<tr>
<td>7.5</td>
<td>Antibiotic therapy</td>
</tr>
<tr>
<td>7.6</td>
<td>Expected clinical results</td>
</tr>
<tr>
<td>7.7</td>
<td>Don’ts</td>
</tr>
<tr>
<td>7.8</td>
<td>References</td>
</tr>
</tbody>
</table>

#### 8 Infected osteosynthesis, infected nonunion and chronic osteomyelitis

*Peter Ochsner, Werner Zimmerli*

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.1</td>
<td>Fundamentals</td>
</tr>
<tr>
<td>8.1.1</td>
<td>Aetiology</td>
</tr>
<tr>
<td>8.1.2</td>
<td>Incidence</td>
</tr>
<tr>
<td>8.1.3</td>
<td>Classification options for estimating the severity of post-traumatic infections and/or the spread of bone necrosis</td>
</tr>
<tr>
<td>8.2</td>
<td>Bone development around the fracture</td>
</tr>
<tr>
<td>8.3</td>
<td>Confirmation of infection</td>
</tr>
<tr>
<td>8.4</td>
<td>Post-traumatic arthritis</td>
</tr>
<tr>
<td>Section</td>
<td>Title</td>
</tr>
<tr>
<td>---------</td>
<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td>8.5</td>
<td>Antibiotic therapy</td>
</tr>
<tr>
<td>8.5.1</td>
<td>Indications</td>
</tr>
<tr>
<td>8.5.2</td>
<td>Duration of therapy, problems</td>
</tr>
<tr>
<td>8.6</td>
<td>Early first presentation – infected osteosynthesis</td>
</tr>
<tr>
<td>8.6.1</td>
<td>Clinical symptoms and diagnostic procedures</td>
</tr>
<tr>
<td>8.6.2</td>
<td>Indications for active treatment</td>
</tr>
<tr>
<td>8.6.3</td>
<td>Surgical treatment</td>
</tr>
<tr>
<td>8.6.4</td>
<td>Prognosis and complications</td>
</tr>
<tr>
<td>8.7</td>
<td>Delayed first presentation – infected nonunion</td>
</tr>
<tr>
<td>8.7.1</td>
<td>Clinical symptoms and diagnostic procedures</td>
</tr>
<tr>
<td>8.7.2</td>
<td>Treatment indications</td>
</tr>
<tr>
<td>8.7.3</td>
<td>Surgical treatment</td>
</tr>
<tr>
<td>8.7.4</td>
<td>Specific treatment options</td>
</tr>
<tr>
<td>8.7.5</td>
<td>Prognosis and complications</td>
</tr>
<tr>
<td>8.8</td>
<td>Late first presentation – chronic post-traumatic osteomyelitis</td>
</tr>
<tr>
<td>8.8.1</td>
<td>Clinical symptoms and diagnostic procedures</td>
</tr>
<tr>
<td>8.8.2</td>
<td>Treatment indications</td>
</tr>
<tr>
<td>8.8.3</td>
<td>Surgical treatment</td>
</tr>
<tr>
<td>8.8.4</td>
<td>Specific treatment options</td>
</tr>
<tr>
<td>8.8.5</td>
<td>Prognosis and complications</td>
</tr>
<tr>
<td>8.9</td>
<td>Differential diagnosis: Chronic haematogenous osteomyelitis in adults</td>
</tr>
<tr>
<td>8.9.1</td>
<td>Clinical symptoms and diagnostic procedures</td>
</tr>
<tr>
<td>8.9.2</td>
<td>Treatment indications</td>
</tr>
<tr>
<td>8.9.3</td>
<td>Surgical treatment</td>
</tr>
<tr>
<td>8.9.4</td>
<td>Prognosis, complications</td>
</tr>
<tr>
<td>8.10</td>
<td>Don`ts</td>
</tr>
<tr>
<td>8.11</td>
<td>References</td>
</tr>
</tbody>
</table>
9 Infectious arthritis

Werner Zimmerli, Olivier Borens

9.1 Background
9.1.1 Aetiology
9.1.2 Incidence
9.1.3 Risk factors
9.1.4 Affected joints

9.2 Clinical symptoms and diagnostic procedures
9.2.1 Medical history
9.2.2 Clinical findings
9.2.3 Laboratory tests
9.2.4 Imaging
9.2.5 Differential diagnosis

9.3 Therapeutic principles
9.3.1 Arthrocentesis
9.3.2 Arthroscopy
9.3.3 Arthrotomy
9.3.4 Synovectomy
9.3.5 Antibiotic treatment
9.3.6 General information about physiotherapy

9.4 Don'ts
9.5 References

10 Spondylodiscitis

Ivan Broger, Stefan Seiler

10.1 Fundamentals
10.1.1 Definition
10.1.2 Pathogenesis
10.1.3 Epidemiology

10.2 Clinical symptoms and diagnostic procedures
10.2.1 Clinical findings
10.2.2 Laboratory tests
10.2.3 Radiological diagnostics / Imaging techniques
10.2.4 Microbiology

10.3 Therapeutic principles
10.3.1 Conservative treatment – antibiotics and rest
10.3.2 Surgical treatment – surgery plus antibiotics

10.4 Prognosis and complications
10.5 Don’ts
10.6 References
## 11 Soft tissue infections

*Domizio Suvà, Olivier Borens, Ilker Uçkay*

11.1 General aspects
- 11.1.1 Classification
- 11.1.2 Laboratory tests, microbiology and histology

11.2 Some important Infections
- 11.2.1 Furunculosis and localised skin abscesses
- 11.2.2 Erysipelas
- 11.2.3 Cellulitis
- 11.2.4 Septic bursitis
- 11.2.5 Necrotising fasciitis (NF)

11.3 References

## 12 Open wounds

*Stefan Seiler*

12.1 Fundamentals
- 12.1.1 Aetiology
- 12.1.2 Wound types

12.2 Diagnostics and clinical findings
- 12.2.1 Medical history
- 12.2.2 Clinical assessment
- 12.2.3 Laboratory tests
- 12.2.4 Microbiology
- 12.2.5 Radiological diagnostics / Imaging techniques
- 12.2.6 Prerequisites for wound healing

12.3 Therapy
- 12.3.1 Treatment of acute wounds (soft tissue defect, grade II/III open fracture)
- 12.3.2 Treatment of subacute and chronic wounds
- 12.3.3 Systemic measures

12.4 Don’ts

12.5 References
## 13 Diabetic foot

*Olivier Borens*

13.1 Fundamentals  
13.1.1 Incidence  
13.1.2 Pathogenesis  
13.1.3 Classification

13.2 Clinical findings

13.3 Diagnostics

13.4 Therapeutic principles  
13.4.1 Treatment steps in the case of open diabetic foot wounds  
13.4.2 Preventive measures

13.5 Prognosis and complications

13.6 References

## 14 Osteomyelitis and infectious arthritis in children and adolescents

*Fritz Hefti*

14.1 Classification

14.2 Acute haematogenous osteomyelitis  
14.2.1 Aetiology and pathology  
14.2.2 Incidence and localisation  
14.2.3 Clinical findings and diagnostics  
14.2.4 Therapy  
14.2.5 Follow-up examinations and prognosis

14.3 Special forms of acute osteomyelitis  
14.3.1 Acute multifocal haematogenous osteomyelitis  
14.3.2 Neonatal osteomyelitis

14.4 (Primary) chronic osteomyelitis  
14.4.1 Aetiology  
14.4.2 Clinical findings and diagnostics  
14.4.3 Therapy  
14.4.4 Postoperative treatment  
14.4.5 Follow-up examinations, post-infection deformities  
14.4.6 Growth disturbance
14.5 Special forms of chronic osteomyelitis
   14.5.1 Garré’s sclerosing osteomyelitis
   14.5.2 Chronic recurrent multifocal osteomyelitis (CRMO)
   14.5.3 Specific osteomyelitis (tuberculosis)
   14.5.4 BCG osteomyelitis
   14.5.5 Exogenous osteomyelitis

14.6 Infectious (purulent) arthritis
   14.6.1 Aetiology and localisation
   14.6.2 Growth disturbance
   14.6.3 Clinical findings
   14.6.4 Diagnosis and treatment
   14.6.5 Post-infectious deformities

14.7 Don’ts

14.8 References

---

**Appendix**

15 A microbiology guide

*Gerhard Eich*

15.1 Introduction

15.2 Fundamentals
   15.2.1 Virulence and pathogenicity
   15.2.2 Endogenous and exogenous infections
   15.2.3 Bacterial lifeforms
   15.2.4 Diagnosis
   15.2.5 Resistance testing

15.3 Specific bacteria
   15.3.1 Gram-positive bacteria
   15.3.2 Gram-negative bacteria
   15.3.3 Anaerobic bacteria
   15.3.4 Other microorganisms

15.4 Fungi

15.5 Nomenclature and notation guidelines for microorganisms

15.6 References
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definitions</td>
<td>225</td>
</tr>
<tr>
<td>Paul Bodler</td>
<td></td>
</tr>
<tr>
<td>17 Common errors in the treatment of infections of the musculoskeletal system</td>
<td>232</td>
</tr>
<tr>
<td>Ilker Uçkay, Markus Vogt</td>
<td></td>
</tr>
<tr>
<td>17.1 Diagnostics</td>
<td>232</td>
</tr>
<tr>
<td>17.2 Antibiotic therapy</td>
<td>233</td>
</tr>
<tr>
<td>17.3 Miscellaneous</td>
<td>235</td>
</tr>
<tr>
<td>18 Infection therapy passport</td>
<td>237</td>
</tr>
<tr>
<td>Thomas Maurer</td>
<td></td>
</tr>
<tr>
<td>18.1 Purpose of the infection therapy passport</td>
<td>237</td>
</tr>
<tr>
<td>18.2 Use of the infection therapy passport</td>
<td>237</td>
</tr>
<tr>
<td>19 Documentation of samples collected for bacteriology and histology</td>
<td>241</td>
</tr>
<tr>
<td>Peter E. Ochsner</td>
<td></td>
</tr>
<tr>
<td>19.1 Background</td>
<td>241</td>
</tr>
<tr>
<td>19.2 Purpose of using a specific form</td>
<td>241</td>
</tr>
<tr>
<td>19.3 Design of the form</td>
<td>241</td>
</tr>
<tr>
<td>Index of terms</td>
<td>244</td>
</tr>
<tr>
<td>Index of figures</td>
<td>261</td>
</tr>
</tbody>
</table>
A biofilm is an efficient strategy used by microorganisms to improve survival in unfavourable conditions, e.g., lack of nutrients, and to maintain and propagate the colony (microbial population). Biofilms have developed as the result of evolution and adaptation by microorganisms to their habitat. More than 80% of all microorganisms exist in nature as a biofilm. With the rise in the use of implants, the medical profession is increasingly confronted with microorganisms that persist within the body in biofilms, responding to the antibodies and immune cells of the body’s defences and developing resistance to antibiotics.

1.1 Definition

Bacteria can exist as 2 different life forms (Fig. 1-1):
- Planktonic (free-floating) form, metabolically active, rapid replication
- Biofilm, less metabolically active, stationary growth phase

Due to their slow replication, bacteria in biofilms are up to 1000 times more resistant to antibiotics. Only a few antibiotics are able to kill off bacteria in biofilms with reasonable certainty, provided that the biofilm has had less than 3 weeks to develop. Rifampicin is able to eliminate staphylococci and streptococci, while quinolones are able to eliminate Gram-negative rods. These antibiotics play an important role in curative treatment of implant-associated infections.

Fig. 1-1: Planktonic and biofilm-associated forms of bacteria
Microorganisms form a matrix of polymerised exopolysaccharide (EPS) in which the individual bacteria are embedded. A mature biofilm comprises up to 25–30% bacteria and 70–75% amorphous matrix.

Biofilms can develop over weeks and years into complex three-dimensional structures with water canals (primitive circulation mechanisms) that communicate with each other using chemical messengers known as quorum-sensing molecules. The ultrastructure of the biofilm adapts to the given conditions, whereby adhesion, accumulation and dispersal processes are genetically regulated.

1.2 Biofilm development and maturation

Following adhesion, the microorganisms propagate on the surface (proliferation) and form a multilayered structure (early biofilm). The next step involves the development of a stable cell matrix (mature biofilm), followed by dispersal of individual microorganisms from the surface (Fig. 1-2). The dispersed bacteria adopt their planktonic form in which they return to a metabolically active state and divide rapidly.

1.3 Implant/biofilm interactions

The first step in an implant-associated infection requires adhesion of microorganisms to the foreign body material (Fig. 1-3). Physical and chemical mechanisms are responsible for the interaction between the microorganisms and the implant surface during colonisation prior to contact with the host’s blood and plasma.
Immediately following contact with the blood or plasma, the surface characteristics of the implant material undergo a drastic change with initial absorption of albumin. The composition of deposited host molecules (e.g., fibronectin, fibrinogen, vitronectin, von Willebrand factor) and cellular elements (e.g., thrombocytes, fibroblasts and activated endothelial cells) becomes increasingly complex over time, resulting in a change to the surface that promotes the adhesion of microorganisms.

Antimicrobial coatings, e.g., with silver, or modification of the implant surface, e.g., by using a nanostructure, can reduce adhesion of the bacteria, thus minimising the risk of an implant-associated infection.

![Diagram of Biofilm on the Surface of an Implant](Image)

**Fig. 1-3: Biofilm on the surface of an implant.** Free-floating planktonic bacteria are killed by antibiotics and antibodies while adherent bacteria that are protected within the extracellular matrix in the biofilm survive. Following contact with foreign bodies, granulocytes/phagocytes are degranulated and lose their phagocytic function.
1.4 Development of variants of microorganisms

Atypical variants of microorganisms, so-called ‘small colony variants’ (SCV) can develop near the implant. These are subpopulations of staphylococci and other bacterial species, e.g., *Pseudomonas aeruginosa* or *Escherichia coli*, that are characterised by reduced division rates, atypical cell morphology, reduced pigment formation and reduced metabolic activity. The SCV phenotype is associated with increased biofilm formation allowing an increase in persistent infections in the presence of foreign materials with elevated resistance to antibiotics. SCVs belong to the ‘difficult-to-treat’ bacteria. In cases of confirmed SCV, two-stage prosthesis replacement is usually required in order to cure the infection (see Chapter 15.2.3, Fig. 7-3).

1.5 Pathogenesis of implant-associated infections

An implant can become infected in three different ways (Fig. 1-4):

- Intraoperatively by direct colonisation of the foreign material through the surgical wound or the air
- By haematogenous or lymphogenous transmission of the pathogen from a different focus of infection, e.g. from an urinary tract infection, skin infection or pneumonia
- By colonisation as a result of direct contact with a neighbouring infected site, e.g. osteomyelitis, or diffusion through neighbouring tissues from outside the body, e.g. in the case of an infected wound or haematoma or a diabetic ulcer.

![Fig. 1-4: Frequency of perioperative and haematogenous prosthesis infections after primary implantation](image)
Classification of an infection as exogenous or haematogenous is not always straightforward. However, impaired wound healing, infective foci that are remotely located and specific microorganisms often enable correct classification. Most infections occur intraoperatively or due to postoperative impaired wound healing. This confirms the efficacy of preventive measures such as perioperative antibiotic prophylaxis. It has been found that these measures result in a significant reduction not only of early infections but also of delayed infections.

### 1.6 References

**Further reading**

Additional articles


2 Prevention of perioperative infections

2.1 General

Perioperative infections are among the most feared and most frequent complications following orthopaedic procedures. Very often, they result in prolonged hospital stays and high costs.

Perioperative infections are primarily triggered by the patient’s skin flora and may also be caused by bacteria present in the surrounding ambient air. Many such infections are preventable. Perioperative infections occur pre-, peri- or postoperatively.

The recommendations for the prevention of perioperative infections in Chapters 2.2–2.4 are classified below based on the quality of the underlying studies:

- Group A based on level I studies
- Group B based on level II and III studies
- Group C based on level IV and V studies

The most important measure for the reduction of perioperative infections is preoperative antibiotic prophylaxis. This is discussed in detail in Chapter 2.6.

2.2 Preoperative measures

A  If the patient has a systemic or local bacterial infection, then this infection should be treated and any elective surgery should be postponed. In contrast, antibiotic treatment is not indicated for an asymptomatic colonisation of the urinary tract by bacteria or Candida spp., i.e., an asymptomatic urinary tract infection, does not warrant delay of an elective operation.

- Blood glucose levels should be kept under optimal control in patients with diabetes.

B  Patients should be made aware that they are at higher risk of developing a perioperative infection if they smoke.

- Showering with an antiseptic prior to surgery reduces the microbial colony density of the skin flora. This measure, however, is unable to achieve a significant reduction in the infection rate. At the very least, patients should shower on the day before surgery and on the day of surgery using medical soap. A new preoperative preventive approach is to screen patients (with subsequent preoperative decolonisation of the surface of the body and nostrils) for the presence of S. aureus (regardless of whether methicillin susceptible or MRSA). However the duration and mode of decolonisation is not currently evidence based. In practice, many health care facilities, especially in European countries outside
Switzerland, perform preemptive decolonisation with chlorhexidine and/or intranasal mupirocin for 3–7 days for at-risk patients with verified *S. aureus* colonisation.

- Prior to the first operation the surgical team should wash their hands to ensure that they are macroscopically clean.
- The surgical team should disinfect their hands with an alcoholic disinfectant with a residual effect, e.g., chlorhexidine, for 2–5 minutes in accordance with a fixed routine. Fingernails must be kept short. No artificial nails or jewellery are permitted to be worn.
- Hands must be disinfected again prior to any subsequent operation.
- Suitable thermal insulation should be applied in order to prevent the patient from developing hypothermia prior to surgery.
- The contaminated surface of the patient’s skin must first be washed and then mechanically cleaned.
- Alcohol-based agents (70 %) combined with chlorhexidine and/or iodine are currently recommended worldwide for disinfection of the operating field.
- Contamination by skin flora can be reduced by using iodine-impregnated incise drapes. However, this is unlikely to reduce the infection rate. The same is true for incise drapes without iodine impregnation, which are occasionally used but whose benefit has not yet been established.
- Hair should only be removed if it is within the surgical field. Electric clippers with a disposable head should be used. Hair removal should be performed immediately prior to surgery wherever possible.
- All persons working within the operating room should be vaccinated against hepatitis B.
- Employees should report if they have contracted a communicable disease. Guidelines should be in place concerning the required actions and conduct in cases of illness.
- Preoperative hospital stays should be kept as short as possible.

### 2.3 Intraoperative measures

A  The patient should be well supplied with oxygen and not be hypothermic.

B  The operating room should be maintained at a positive pressure above that of adjoining rooms. Operating rooms where joint replacement surgery is performed should probably be equipped with a laminar airflow system. However, there is no hard scientific evidence for this recommendation. Laminar airflow enables a reduction in the microbial count within the operating room but does not reduce the incidence of postoperative clinical infections.
The doors of the operating room should remain closed and be opened as seldom as possible.
The surgical team must wear masks (type II face mask) that cover the mouth and nose and caps that completely cover the hair. Personnel within the sterile area must wear sterile overcoats and gloves.
Sterile surgical overcoats must be water repellent.
Surgical clothing that has become soiled must be changed. It remains a topic of debate whether surgical clothing and sterile draping must be changed for revision procedures due to infection after complete debridement and possible prosthesis explantation and prior to the introduction of the new prosthesis and/or osteosynthesis material.
The surgeon should change gloves prior to insertion of the definitive prosthesis even though there is no hard evidence for this recommendation.
The surgeon can reduce the risk of infection by means of adequate haemostasis and by carefully handling the soft tissue, resecting non-vital tissue and avoiding dead space.
Drains should be diverted through a separate incision located at a distance from the actual wound. Closed drainage systems should be used.

C Only those personnel whose presence is essential should be in the operating room.
Surgery times should be kept as short as possible. ‘A good surgeon operates slowly and finishes quickly.’

2.4 Postoperative measures

A The use of occlusive dressings may reduce the risk of infection.

B Dressings should not be changed any earlier than 24 hours following surgery.
Hands should be disinfected before and after changing a dressing.
Drains should be removed as soon as possible but this decision should also be based on fluid production in the case of revisions due to infection.

C Dressings should be changed using clean technique (with gloves!).
Patients and their relatives and friends should be instructed in how to treat the wound properly and recognise the symptoms of a wound infection.
2.5 Perioperative management of patients with infections/colonisation with multi-resistant bacteria

The current literature provides no consensus or scientific evidence concerning the additional measures that are necessary in these situations. Isolation measures in these cases are handled very differently in Switzerland and elsewhere. The isolation requirements outside the operating room are less strict compared with the sterility requirements applied to typical patients within the operating room. The requirements are stricter concerning removal of the surgical clothing (cap, mask, apron, gloves) within the operating room at the end of an operation and cleaning operating rooms between operations. Placing patients with multi-resistant bacteria at the end of the surgery schedule does not result in a verifiable minimization of risk. On the other hand, the isolation measures prescribed by the department must continue to remain in effect when patients are removed from the operating room. It is therefore recommended, wherever clinically possible, to transfer these patients directly to their rooms without keeping them in a recovery room. The Infection Control Officer must be free to increase isolation measures if the need arises.

Special measures must be imposed in the case of the following bacterial groups:

- Methicillin-resistant *S. aureus* (MRSA): Outpatient screening of patients from endemic MRSA areas is advisable prior to hospitalisation. Perioperative antibiotic prophylaxis with vancomycin.
- ESBL carriers (Gram-negative microbes, such as *Escherichia coli* or *Klebsiella*): They populate the genitourinary and rectal areas. As a result, expanding the standard prophylaxis beyond this region during orthopaedic procedures is not necessary.
- Aerogenically transmissible pathogens, such as untreated, open tuberculosis: Move the operation to the end of the schedule and use ultrafiltration surgical masks and negative pressure in the operating room, wherever possible.
2.6 Antibiotic prophylaxis in orthopaedic surgery

2.6.1 Fundamentals of perioperative antibiotic prophylaxis

Perioperative antibiotic prophylaxis performed correctly reduces the rate of postoperative infections and has become widely established for defined orthopaedic procedures as a result. Effective and optimally applied antibiotic prophylaxis, however, is no substitute for good surgical technique with as little trauma as possible and competent postoperative management.

2.6.2 Practical approach

Number of antibiotic doses administered

The administration of a single dose of antibiotics (single shot) is sufficient for operations lasting up to 3 hours. A longer antibiotic regimen distributed over multiple doses does not provide any added benefit but does risk the development of resistance.

Additional prophylaxis should be administered when operations last longer than 3 hours, when blood loss is more than 2000 mL or in situations which require infusion volumes greater than 2000 mL. This ensures adequate antibiotic levels in the tissue during wound closure. Another dose should be administered as soon as the first of the above named parameters has been reached.

Evidence

The efficacy of antibiotic prophylaxis in orthopaedic surgery has been proven. In a randomised study of 2137 patients undergoing hip replacement, the infection rate was 3.3% with placebo (35/1067) and 0.9% with cefazolin (10/1070). Further studies and meta-analyses have confirmed the efficacy of antibiotic prophylaxis during orthopaedic procedures.

Time of antibiotic administration

Antibiotic prophylaxis is intended to ensure that bactericidal concentrations are maintained within the tissue from the time of incision to wound closure. A new prospective observational study of 3836 surgical procedures and a prophylactic dose of 1.5 g cefuroxime IV confirmed that prophylaxis administration 30–59 minutes prior to incision resulted in wound infection rates that were significantly lower than administration during the final 30 minutes (Tab. 2-1).
A prospective study of 2847 patients investigated wound infection rates in relation to the time of prophylactic antibiotics administration. While the wound infection rate was low with prophylaxis administration within 2 hours prior to incision (0.6 %), the rates were significantly higher with earlier (2.4 %) or later (3.3 %) administration.

**Our recommendation:** Based on clinical studies, the infection rate is lowest when the time of antibiotics administration coincides with anaesthetic induction (30–59 minutes prior to incision).

**Operations with tourniquets**
Up to now, antibiotic prophylaxis has usually been administered 30–60 minutes prior to application of the tourniquet for operations using tourniquets (e.g., knee arthroplasty). In a recently published, large-scale, randomised, double-blind and placebo-controlled study of patients undergoing knee arthroplasty, 442 patients received conventional prophylaxis with 1.5 g cefuroxim 10–30 minutes prior to application of the tourniquet and 466 patients received the same dose 10 minutes prior to removal of the tourniquet. The wound infection rate at 3 months was 3.4 % in the conventional group and 1.9 % in the experimental group (p = 0.21). Even after one year there was no significant difference between infection rates (3.6 % vs. 2.6 %, respectively).

**Our recommendation:** If an intraoperative microbiological diagnosis (sample collection) is planned, then antibiotics should be administered 10 minutes prior to removal of the tourniquet (Tab. 2-1).

### Tab. 2-1: Start of antibiotic prophylaxis

<table>
<thead>
<tr>
<th>Indication</th>
<th>Antibiotic and administration *</th>
</tr>
</thead>
<tbody>
<tr>
<td>All operations involving osteosynthesis and prosthetic joints</td>
<td>1.5 g cefuroxime, 1 g cefazolin or 2 g cefamandole with anaesthetic induction If tourniquet is planned: 30–60 minutes prior to application of the tourniquet</td>
</tr>
<tr>
<td>Grade 1 and 2 open fractures</td>
<td>Immediately upon admission to hospital, then next dose prior to surgery if surgery is delayed by more than 3 hours. Prophylaxis duration 24 hours</td>
</tr>
<tr>
<td>Grade 3 open fractures</td>
<td>Preemptive/early empirical antibiotic therapy starting at the scene of the accident or in the emergency room for 3 days (e.g., amoxicillin/ clavulanic acid IV 3 x 2.2 g)</td>
</tr>
<tr>
<td>Planned microbiological diagnosis</td>
<td>Prophylaxis immediately following sample collection, 10 minutes prior to release in the case of a tourniquet</td>
</tr>
</tbody>
</table>

* Administration as short infusion 30–60 minutes prior to incision. An additional dose of the particular antibiotic should be administered intraoperatively in the case of procedures lasting longer than 3 hours.
If an existing infection is suspected (microbes still unknown) and sample collection is planned, then prophylaxis should be administered in such exceptional cases immediately following intraoperative sample collection in order to maximize the chances of identifying the microbes (even though microbe identification is often still possible in practice following a single prophylaxis administration).

**Antibiotic selection**

Cephalosporins have proven to be an effective prophylaxis in orthopaedic surgery. With their spectrum of activity against potential pathogens (staphylococci, streptococci and Gram-negative bacteria), first-generation (cefazolin) or second-generation (cefuroxime, cefamandole) cephalosporins have become well established in bone surgery. Vancomycin should be used in the case of severe cephalosporin allergy, skin colonisation with methicillin-resistant *S. aureus* (MRSA) or a high hospital rate of MRSA infections. It is advisable to consult an infectious disease specialist. Broad-spectrum antibiotics (ceftriaxone, imipenem, piperacillin/tazobactam) are not superior to the cephalosporins currently in use for perioperative prophylaxis. They are used as second-line antibiotics and thus should not be used for prophylaxis. In the case of more prolonged antibiotic therapy it may be necessary to screen for methicillin-resistant coagulase-negative staphylococci.

*Our recommendation:* A single-dose prophylaxis of 1 g vancomycin with an infusion duration of 60 minutes should be considered prior to another implantation of orthopaedic material in the case of patients with previous antibiotic therapy lasting longer than 2 weeks or in the case of known MRSA carriers. In these special situations some clinics administer an additional antibiotic with a Gram-negative spectrum of action as a single-shot infusion in order to prevent potential ‘wound infections with Gram-negative pathogens’. An experienced infectious disease specialist should be consulted concerning antibiotic type and dosage. However, this approach is not supported by any studies.

### 2.6.3 Procedures with no evidence of the efficacy of antibiotic prophylaxis

Prophylaxis is not recommended for the following orthopaedic surgery procedures:
- Arthroscopic procedures without introduction of foreign material
- Spinal procedures without implants
- Arthrotomy
- Amputations, if not infection-induced
- Removal of osteosynthesis material
2.6.4 When is the prevention of possible haematogenous prosthetic joint infections recommended?

While intra- or perioperatively acquired exogenous prosthetic joint infections mainly appear within the first 2 years, patients with artificial joints face a life-long risk of haematogenous infection following surgery. An article on pathogenesis reported 27 (43%) haematogenous infections out of 63 prosthetic hip infections. Of these, three-quarters were late infections. Unlike those patients without implants, patients with an implant acquire a granulocyte defect and are therefore much more susceptible to significantly lower concentrations of bacteria in the blood necessary to induce foreign body infections. However, studies in animal models with repeated artificially induced bacteraemia found that concentrations of at least 1000 staphylococci/mL blood are necessary in order to induce a foreign body infection.

Dental treatments
A distinction must be drawn between common dental treatments and treatment of dental infections.

Common dental treatments
Paediatric studies have found that following tooth extractions low-concentration bacteremia (1–28 bacteria/mL blood) can occur over several minutes. While the bacteria that appear following tooth extractions include up to one third viridans streptococci, these bacteria are found in only 2% of established haematogenous prosthetic joint infections – in other words, very rarely. This contradicts the hypothesis that dental procedures play a significant role in the pathogenesis of haematogenous prosthetic joint infections. The American Dental Association and the American Academy of Orthopedic Surgeons issued joint guidelines in 2003 in which they stated that there is no scientific evidence that haematogenous prosthetic joint infections could be prevented with antibiotic prophylaxis. However, prophylaxis may be considered for specific high-risk patients, e.g., immunosuppressed patients or patients with a recently implanted prosthetic joint. Unfortunately, this recommendation is not based on evidence.

A recent prospective case-control study at the Mayo Clinic involving 339 patients with prosthetic hip and knee infections and an equal number of prosthetic joint patients without infections was able to clearly demonstrate for the first time that dental procedures are not a risk factor for prosthetic joint infections and that antibiotic prophylaxis had no impact on the potential to develop a prosthetic joint infection. The risk of infection was significantly higher with diabetes mellitus (odds ratio [OR] 1.8; 95% CI 1.2–2.8), following a revision operation (OR 2.4, 1.6–3.5), in immunosuppressed patients (OR 2.2; 1.6–3), for surgery lasting longer than 4 hours
(OR 2.7, 1.5–5), for postoperatively exudative wounds (OR 18.7; 7.4–47) and in the case of infections of non-neighboring organs (OR 2.2; 1.5–3.25). Antibiotic prophylaxis had no significant effect in the case of dental procedures with low (OR 0.8; 0.5–1.2) and higher risk of bacteremia (OR 0.7; 0.5–1.1). While the results of this case-control study are not as significant as the results of a randomised study, the extremely high number of patients required for a randomised study makes it difficult to conduct such a study.

*Our recommendation:* No prophylaxis in the case of standard dental treatments.

**Infections in the oral/dental area**
There is a real risk of haematogenous spread in these situations. We recommend performing any potential dental procedures prior to implant surgery and avoiding dental procedures within the first year following implant surgery, wherever possible. Infections of the oral cavity, e.g., dental granuloma or severe periodontitis, require antibiotic therapy and no prophylaxis.

**Acute skin infections**
These are the most important cause of haematogenous prosthetic joint infections. Among 67 patients with late prosthetic joint infections, 46% had skin infections and two thirds of these infections were caused by *S. aureus*. Odontogenic causes were suspected in only 3 patients in whom the isolated pathogens were typical oral bacteria. *S. aureus* bacteremia poses the highest risk to the development of implant-associated infection. Of the 44 prosthetic joint patients with *S. aureus* bacteremia, 34% developed a haematogenous prosthetic joint infection.

In summary, rapid and suitable treatment of any infection is much more important than antibiotic prophylaxis. Skin infections are dangerous and patients must be told to seek medical attention immediately. In addition, patients must be examined for potential prosthetic joint infections during and after any infection but especially in the case of *S. aureus* bacteremia.

**Our recommendation in summary**
- Good oral hygiene and dental procedures before or after implant surgery
- No prophylaxis necessary by the dentist; in the case of a tooth abscess therapy is required, not prophylaxis
- The most important causes of haematogenous prosthetic joint infection include acute skin infections, pneumonia and symptomatic urinary tract infections. As for all other forms of sepsis, these infections should be identified and treated early.
2.7 References

Further reading

- Tanner J, Swarbrook S, Stuart J. Surgical hand antisepsis to reduce surgical site infection. Cochrane Database Syst Rev 2008: CD004288
- WHO Guidelines for safe surgery. World Health Organization 2009

Additional articles

- Borens O, Yusuf E, Trampuz A. Surgical Site Infections (SSIs): Risk Factors and Prevention Strategies. European Instructional Lectures. EFORT II Book 2013


Giulieri SG, Graber P, Ochsner PE et al. Management of infection associated with total hip arthroplasty according to a treatment algorithm. Infection 2004; 32: 222–8


3 Systemic antibiotic therapy

3.1 Basics of antimicrobial treatment

In order to make optimal use of antimicrobial therapy, many aspects must be taken into account, including the spectrum of activity, local resistance patterns (epidemiology), special features of the patient (age, underlying diseases, renal insufficiency, etc.), pharmacokinetics, toxicity, mode of elimination of the drugs, clinical studies involving the infection to be treated and economic aspects.

Diagnosis of pathogens
Antimicrobial therapy must be based on adequate diagnostics in order to prevent the misuse of antibiotics. Appropriate methods include:
- Microscopic identification (e.g. gonococci in the synovial fluid specimen)
- Microbiological (culture) pathogen identification (e.g. in blood, biopsy material, sonication fluid, synovial fluid specimen)
- Antigen identification (e.g. pneumococcal antigen in urine)
- Nucleic acid identification (e.g. *Borrelia burgdorferi* in the synovial fluid)
- Antibody identification (e.g. *Mycoplasma pneumoniae* in serum)

Microbiological cultures including susceptibility testing are especially important in the treatment of life-threatening infections, or if multi-resistant bacteria are suspected. Diagnostic work-up is also crucial in patients with infections requiring long-term therapy such as vertebral osteomyelitis, septic arthritis or implant-associated infections. In patients with high risk for relapse (e.g. conservatively treated epidural abscesses), knowledge of the infecting agent allows choice of the most appropriate antibiotic for long-term therapy, considering pharmacokinetics (bioavailability) and susceptibility.

Susceptibility testing
Susceptibility testing is intended to provide predictive evidence concerning the efficacy of antibiotics in the patient. Proof of susceptibility, however, is no guarantee of efficacy *in vivo*. Other criteria, such as pharmacokinetics, specific compartment, growth phase of the bacteria, pH at the target location and bacterial density, also play a significant role. Due to the fact that implant-associated pathogens are adherent and not growing (for biofilm bacteria, see Chapter 1), it is especially difficult to predict efficacy in the case of these infections based on susceptibility testing.

Susceptibility testing involves exposing the isolated pathogens to various concentrations of antimicrobial substances under standardised conditions. If the pathogen grows beyond a defined concentration, it is considered to be resistant to the sub-
stance in question. This breakpoint concentration is called the minimum inhibitory concentration (MIC). The MIC can be determined directly using the dilution method. Simpler methods include indirect determination with the disc diffusion test or the Epsilometer test (E-test). For details, see Chapter 15.2.5.

**Implant-associated pathogens**

The different pathogens exhibit a variety of characteristics. Any dissimilarity between the susceptibility of a bacterium in routine in-vitro testing and its susceptibility in vivo, in the body of the patient may be due to specific characteristics of the pathogen. Tab. 3-1 summarizes several characteristics that are important for therapy.

**Tab. 3-1: Characteristics of the pathogen**

<table>
<thead>
<tr>
<th>Characteristic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracellular location, e.g. Legionella, Mycobacteriae, Chlamydiae</td>
</tr>
<tr>
<td>High bacterial density (abscess)</td>
</tr>
<tr>
<td>Emergence of resistance during ongoing therapy</td>
</tr>
<tr>
<td>Multi-resistance</td>
</tr>
<tr>
<td>Biofilm, e.g. adherence to surface of implant</td>
</tr>
<tr>
<td>Slow-growing or non-growing bacteria, e.g. in the case of implant-associated infections</td>
</tr>
</tbody>
</table>

Bacterial density in abscesses is higher than in the test tube during standard susceptibility testing *in vitro* (>10⁶ CFU/mL vs. 10⁵ CFU/mL). Due to the fact that certain antibiotics, e.g. betalactams, are much less effective against high numbers of bacteria (inoculum effect), this situation must be taken into account when selecting a therapy. This is the reason why the focus of infection must be eradicated using careful debridement prior to antibiotic treatment in the case of implant-associated infections (see Chapter 4.4.1). The risk of therapeutic failure and emergence of resistance is high without surgical treatment. The impact of the inoculum effect is especially unfavourable, if the pathogen becomes resistant during exposure to the antibiotic, which is typically the case with rifampicin. The risk of a mutation depends on the number of microorganisms present at the start of therapy.

In some types of infection, bacteria are not planktonic (i.e. in suspension) but rather adherent to surfaces. This is especially observed in chronic osteomyelitis or implant-associated infection. The killing of these adherent bacteria cannot be predicted using routine susceptibility testing. Antibiotics that target the cell wall are particularly ineffective, due to the slower growth rate of adherent bacteria, during which cell wall synthesis is turned down. This must be taken into consideration when selecting antimicrobial therapy.
Occurrence of resistance
Resistance usually appears by selection when there is widespread use of antimicrobial agents in a population. This explains the epidemiologic differences between geographic areas. However, resistant pathogens may also be selected in an individual patient in the case of antibiotic therapy of an open wound (fistula, secretion). Certain pathogens may even become resistant to the antibiotic administered during therapy (emergence of resistance). In the case of *Pseudomonas aeruginosa*, this risk is high for all antibiotics (cephalosporins, antipseudomonal penicillins, carbapenems and quinolones). In case of staphylococci, it has been only observed when using fluoroquinolones, rifampicin and fusidic acid. As a result, these substances should only be administered in combination against staphylococci. The risk for emergence of resistance is especially high in the case of rifampicin. According to a Swiss multi-centre study, risk factors for the development of resistance include multiple previous surgical procedures at the site of infection, starting treatment with a high initial bacterial load (e.g., inadequate surgical debridement!), intravenous treatment of too short duration (< 2 weeks) and inadequate rifampicin therapy (e.g., monotherapy or combination with oral antibiotic with poor bioavailability).

Patient factors
Many specific features of the patient have an impact on antibiotic selection. Tab. 3-2 summarises the most important patient features.

**Tab. 3-2: Patient factors that determine antimicrobial therapy**

<table>
<thead>
<tr>
<th>Age (pharmacokinetics, toxicity)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underlying diseases (kidney disease, liver disease)</td>
</tr>
<tr>
<td>Recent surgery (deep wound infection)</td>
</tr>
<tr>
<td>Recent hospitalisation (colonisation with resistant pathogen)</td>
</tr>
<tr>
<td>Recent infection (e.g. relapse of an abscess or endocarditis)</td>
</tr>
<tr>
<td>Travel (epidemiology of potential pathogens, resistance situation of the pathogens)</td>
</tr>
<tr>
<td>Immunocompromised host (neutropenia, transplant surgery, lymphoma, etc.)</td>
</tr>
<tr>
<td>Implanted foreign body (biofilm infection)</td>
</tr>
<tr>
<td>Site of infection (compartments with barriers for antimicrobial substances)</td>
</tr>
</tbody>
</table>
Based on the above, it follows that the selection of antibiotics to treat many infectious diseases cannot be based solely on the results of susceptibility testing. In addition to susceptibility testing, the results of clinical studies are especially necessary for selecting the correct drug in the case of staphylococcal sepsis, osteomyelitis, arthritis or implant infections. If these infections are not treated in accordance with the recommendations derived from clinical studies, then there is an increased risk of therapeutic failure or recurrence. Recurrences are especially common following inadequate therapy of an implant-associated infection.

**Mode of application**

In addition to the status of the patient (inability to swallow, impaired gastrointestinal motility), the pharmacokinetic properties of the drug are especially crucial when deciding whether a therapy should be administered intravenously or orally. Parenteral antimicrobials are usually significantly more expensive than oral drugs. As a result, oral drugs should be used, wherever possible, for economic reasons. However, this is not possible for some indications and antimicrobials. For example, the serum concentrations achieved with oral beta-lactam antibiotics are approximately ten times lower than the serum concentrations that can be achieved with parenteral substances. In special cases, the entire antibiotic therapy must be parenterally administered. Outpatient parenteral therapy requires the implantation of a catheter (e.g., Port-A-Cath). Conversely, fluoroquinolones may also be administered orally in the case of severe infections, provided that the patient does not experience vomiting. Rifampicin, fusidic acid, linezolid or trimethoprim/sulphamethoxazole also have excellent bioavailability.

Osteomyelitis or native joint arthritis may be treated orally for the entire duration of therapy, if antibiotics with good bioavailability are used, that are appropriate for the pathogen based on its susceptibility. Examples include staphylococci that are susceptible to fluoroquinolones and rifampicin or fluoroquinolone-susceptible Gram-negative rods. These treatment regimens have been tested in clinical studies.

Conversely, implant-associated arthritis is routinely treated intravenously during the first 2 weeks. This is based on a controlled study. However, there are no clinical trials comparing different types of application or different durations of therapy. Nevertheless, there are convincing arguments for initial IV therapy. Enteral absorption is often impaired during the perioperative phase. Bacterial density tends to be high initially at the focus of infection. Therefore, at this time there is extra risk for emergence of resistance to antibiotics such as rifampicin and fluoroquinolones. In fact, shortened initial intravenous therapy or the lack of such therapy represents a significant risk factor for the emergence of rifampicin resistance, as shown by a recent Swiss multi-centre study.
Patient support during prolonged antibiotic therapy
Infections of the musculoskeletal system, often require prolonged antibiotic therapy which continues long after the patient has left hospital. Periodic CRP checks are necessary to monitor the course of treatment. Other lab work is also necessary, depending on the type of antibiotic being administered. The Infection Therapy Passport makes it significantly easier to support patients during such treatments in collaboration with their general practitioners (see Chapter 18).

3.2 Definitions concerning the use of antibiotics

- **Prophylaxis**: The antibiotic reaches the wound before the pathogen. Example: Surgical prophylaxis, usually single-dose.
- **Pre-emptive therapy**: The antibiotic reaches the wound after the pathogen, but before the wound has become infected. Example: Antibiotic administration following open fracture, usually for approx. 3–5 days.
- **Empirical therapy**: Antibiotic administration without knowledge of the individual microbiology. Example: Antibiotic therapy based on epidemiological considerations, a procedure which is also called “educated guess”.
- **Targeted therapy**: Antibiotic administration based on a defined microorganism with proven susceptibility.

3.3 Procedures in the case of therapeutic failure

If an antibiotic therapy does not achieve the desired effect, then the problem must be re-evaluated. Special attention must be paid to the accuracy of the clinical diagnosis. If so, then it must be determined whether the typical pathogens of the diagnosed infection are susceptible to the administered antibiotic. Some pathogens may become resistant during the course of the therapy. However, this is the exception and is observed mainly with *Pseudomonas aeruginosa*. More commonly, a superinfection with resistant bacteria or fungi is due to selection for these pathogens.

A therapy may also fail for pharmacokinetic reasons. Thus, for example, it is not correct to treat a *S. aureus* sepsis with oral flucloxacillin/cloxacillin, because the achievable serum concentrations are totally insufficient. Interactions between phagocytes, bacteria and antimicrobial drugs may also explain therapeutic failure. This mechanism affects fluoroquinolones which have reduced effectiveness in acidic environments and aminoglycosides which are inactivated in pus. This must be taken into consideration when selecting antibiotics for conservative therapy of abscesses, which are always a domain of surgical therapy. The systematic evaluation of the potential causes of therapeutic failure mentioned above can optimise the chance of
a secondary response. This procedure is ultimately important from an epidemiological standpoint because empiric switches usually involve choosing very broad-spectrum antibiotics, which induce a high selection pressure for multiresistant microorganisms.

3.4 Antibiotics

Mode of action
Tab. 3-3 presents the modes of action of the various antibiotic classes.

<table>
<thead>
<tr>
<th>Antibiotic class</th>
<th>Site of action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beta-lactam antibiotics</strong></td>
<td>Proper development of the cell wall is impaired through binding to the penicillin-binding proteins, resulting in death of the bacteria</td>
</tr>
<tr>
<td>Penicillin</td>
<td></td>
</tr>
<tr>
<td>Penicillinase-resistant penicillins</td>
<td></td>
</tr>
<tr>
<td>Aminopenicillins</td>
<td></td>
</tr>
<tr>
<td>Ureidopenicillins</td>
<td></td>
</tr>
<tr>
<td>First- to fifth-generation cephalosporins</td>
<td></td>
</tr>
<tr>
<td>Carbapenems</td>
<td></td>
</tr>
<tr>
<td>Glycopeptides</td>
<td></td>
</tr>
<tr>
<td>Vancomycin</td>
<td></td>
</tr>
<tr>
<td>Teicoplanin</td>
<td></td>
</tr>
<tr>
<td>Lipopeptide</td>
<td></td>
</tr>
<tr>
<td>Daptomycin</td>
<td></td>
</tr>
<tr>
<td>Rifamycins</td>
<td></td>
</tr>
<tr>
<td>Rifampicin, rifabutin</td>
<td></td>
</tr>
<tr>
<td>Macrolides</td>
<td></td>
</tr>
<tr>
<td>Erythromycin, clarithromycin, azithromycin</td>
<td></td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td></td>
</tr>
<tr>
<td>Gentamicin, amikacin, netilmicin, tobramycin</td>
<td></td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td></td>
</tr>
<tr>
<td>Norfloxacin, ciprofloxacin, ofloxacin, levofloxacin, moxifloxacin</td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td></td>
</tr>
</tbody>
</table>

Tab. 3-3: Mechanism of action of antibiotics
Tab. 3-3: Mechanism of action of antibiotics (continued)

<table>
<thead>
<tr>
<th>Antibiotic class</th>
<th>Site of action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tetracyclines</strong></td>
<td>Inhibition of bacterial protein synthesis through binding to ribosomal 30S subunit</td>
</tr>
<tr>
<td>Doxycycline, minocycline (second generation)</td>
<td></td>
</tr>
<tr>
<td>Tigecycline (third generation)</td>
<td></td>
</tr>
<tr>
<td><strong>Fusidanes</strong></td>
<td>Inhibition of protein synthesis</td>
</tr>
<tr>
<td>Fusidic acid</td>
<td></td>
</tr>
</tbody>
</table>

**Spectrum of the individual antibiotics**

The most important substances and their antimicrobial spectrum are summarized below. Exact guidelines concerning selection of the substance, dosage and application can be found in Tab. 7-1 and 9-2. For more information, especially concerning adverse events, please refer to the corresponding reference books.

**Penicillin and aminopenicillins**
- Penicillin V (oral), penicillin G (IV), amoxicillin (oral, IV).
- Spectrum of susceptible bacteria: Beta-lactamase-negative staphylococci, haemolytic and viridans streptococci, pneumococci, meningococci, anaerobic oral flora, among others

**Aminopenicillin with betalactamase inhibitor**
- Amoxicillin/clavulanic acid, ampicillin/sulbactam
- Spectrum: Staphylococci (except for methicillin-resistant *S. aureus* [MRSA], methicillin-resistant *Staphylococcus epidermidis* [MRSE]), *Haemophilus spp.*, anaerobes, *Escherichia coli*, *Klebsiella spp.*, *Proteus spp.*

**Penicillinase-resistant penicillins**
- Flucloxacillin, cloxacillin, nafcillin
- Spectrum: *S. aureus* and coagulase-negative staphylococci (not including MRSA, MRSE)

**Ureidopenicillins**
- Piperacillin/tazobactam
- Spectrum: *Pseudomonas aeruginosa* and other Gram-negative rods, staphylococci (except for MRSA, MRSE), other Gram-positive cocci and anaerobes
Carbapenems
- Carbapenems: Imipenem, meropenem, ertapenem
- Spectrum: Very broad spectrum, especially against Enterobacteriaceae, S. aureus and anaerobes

Cephalosporins

Tab. 3-4: Cephalosporin generations and spectrum of action

<table>
<thead>
<tr>
<th>Generation</th>
<th>Parenteral, e.g.</th>
<th>Oral, e.g.</th>
<th>Spectrum</th>
</tr>
</thead>
<tbody>
<tr>
<td>First</td>
<td>Cefazolin</td>
<td>Cefadroxil</td>
<td>Gram-positive except for enterococci</td>
</tr>
<tr>
<td>Second</td>
<td>Cefamandole, Cefuroxim</td>
<td>Cefuroxim axetil</td>
<td>Proteus spp., Escherichia coli, staphylococci (alternative), Haemophilus influenzae</td>
</tr>
<tr>
<td>Third</td>
<td>Ceftriaxone, Ceftazidime</td>
<td>Cefpodoxime proxetil, cefixime</td>
<td>Ceftriaxone: more broadly effective against Gram-negative bacteria; ceftazidime: less effective against streptococci, effective against Pseudomonas aeruginosa</td>
</tr>
<tr>
<td>Fourth</td>
<td>Cefepime</td>
<td>–</td>
<td>Similar to the third generation but spectrum even broader, especially against Gram-negative bacteria with extended-spectrum beta-lactamase production. Also effective against Pseudomonas aeruginosa</td>
</tr>
<tr>
<td>Fifth</td>
<td>Ceftobiprole, Ceftaroline</td>
<td>–</td>
<td>Similar to the third generation but also more effective against penicillin-resistant pneumococci and effective against methicillin-resistant staphylococci (MRSA, MRSE)</td>
</tr>
</tbody>
</table>

Macrolides
- Erythromycin, roxithromycin, clarithromycin, azithromycin
- Spectrum: Moraxella catarrhalis, Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella pneumophila, Gram-positive anaerobes, Bordetella pertussis, Corynebacterium diphteriae, Campylobacter jejuni

Rifamycins
- Rifampicin, rifabutin
- Spectrum: Staphylococci, streptococci, Propionibacterium spp., mycobacteria
- Please note: Must always be combined, also effective against biofilm bacteria, thus especially important for implant-associated infections
Aminoglycosides
- Amikacin, gentamicin, netilmicin, tobramycin
- Spectrum: Gram-negative bacteria (including *Pseudomonas spp*.), staphylococci. Synergism with penicillin G against streptococci and enterococci and with antipseudomonal beta-lactam against *Pseudomonas aeruginosa*

Glycopeptides
- Vancomycin, teicoplanin
- Spectrum: Exclusively effective against Gram-positive, methicillin-resistant staphylococci, enterococci, Corynebacteria (prosthetic joint infection), streptococci, *Clostridium difficile*

Cyclic lipopeptide
- Daptomycin
- Spectrum: Exclusively effective against Gram-positive staphylococci, including methicillin-resistant glycopeptide-resistant enterococci and streptococci, *Clostridium perfringens*

Fluoroquinolones
- Ciprofloxacin (IV, PO), levofloxacin (IV, PO), moxifloxacin (IV, PO)
- Spectrum:
  - Ciprofloxacin: *Enterobacteriaceae* (*E. coli*, *Proteus spp.*, *Klebsiella spp.*, *Salmonella spp.*, *Shigella spp.*), *Haemophilus spp.*, *Pseudomonas aeruginosa*
    (unique oral antipseudomonal medication)
  - Levofloxacin and moxifloxacin: Staphylococci (in combination with rifampicin), *Enterobacteriaceae*, pneumococci (also penicillin-resistant), streptococci, *Haemophilus spp.*, *Chlamydiaceae*, *Mycoplasma*, *Legionella*

Trimthoprim/sulphamethoxazole
- Spectrum: Staphylococci, Gram-negative rods

Clindamycin
- Spectrum: Streptococci, staphylococci, anaerobes, among others

Metronidazole
- Spectrum: Anaerobes, amoebas, *Clostridium difficile*

Tetracyclins
- Doxycyclin, minocyclin
- Spectrum: Broad but bacteriostatic only. Effective in combination with rifampicin against staphylococci
Oxazolidinones

- Linezolid
- Spectrum: *Enterococcus faecium* (including vancomycin-resistant bacteria), methicillin-resistant *S. aureus* (MRSA), penicillin-resistant pneumococci

Fusidic acid

- Spectrum: *S. aureus*, coagulase-negative staphylococci, Gram-positive anaerobes
- Please note: Because of the risk of emergence of resistance, it should be given in combination, e.g. with rifampicin

### 3.5 References

**Further reading**


**Additional articles**

4.1 Objectives of local therapy

Antiseptics
- Wound infections should be prevented during wound healing.
- Superinfections should be prevented in chronic open wounds.

Antibiotics
- For localised infections, particularly high concentrations of antibiotics should be temporarily reached after debridement.
- High antibiotic levels can be achieved for a short period using local therapy, despite inadequate local circulation and avoiding potentially toxic side effects with systemic application.

Antiseptics and antibiotics
- Foreign body surfaces (e.g., bone cement, [tumour] prosthesis) should be protected against biofilm formation.

4.2 Fundamentals

Local antiseptics and antibiotics must be considered – like systemic antibiotics – as an adjuvant therapy in the treatment of acute and chronic infections of the musculoskeletal system. Their use always follows surgical procedures. Their indications are partly specific, partly complementary. They can provide an opportunity to circumvent or minimise potential problems associated with kidney and liver disease, or toxic side effects (e.g., in the inner ear) of systemic antibiotics by their local use.

Locally applied antibiotics may achieve local tissue concentrations that are up to 1000 times higher than parenteral therapy with no systemic side effects.

In the 1970s, Buchholz began to add empirical antibiotics to bone cement [polymethyl methacrylate, PMMA]. The incidence of long-term infection following implantation of primary and revision implants was compared in the Norwegian Arthroplasty Register. Adding gentamicin to cemented implants resulted in an infection rate similar to non-cemented implantation and significantly lower than the infection rate for implants that were cemented without the addition of gentamicin.

Unfortunately, there is a lack of good clinical studies for nearly all of the other applications discussed in this chapter.
4.3 Antiseptics and their main indications

4.3.1 The most important antiseptics for use with open wounds and for coating implants

While disinfecting the hands and the operating field with solutions containing alcohol is safest (see Chapter 2.2), adjuvant treatment of wounds mainly involves aqueous solutions, ointments or gels. The following active substance groups are predominant:

Polyhexanide
(0.02–0.04% with a surface tension-reducing additive) This substance was studied in Switzerland by Kallenberger, Good and Willenegger, who introduced it in 1979. It acts on the superficial layer of bacteria in the wound. The application of polyhexanide damages the uppermost cell layer of the body tissue but the active macromolecules do not penetrate deeply and are barely absorbed. This encourages the formation of granulation tissue. Local proteins and/or blood do not deactivate the substance. Use in joints cannot be approved because of potential destruction of the superficial germinative cells. The substance is effective even with increasing dilution provided exposure is sufficiently prolonged. No resistances are known, with the exception of acid-resistant rods. Polyhexanide is also available in tubes as a gel.

Aqueous povidone-iodine solution or wound ointment
(11 mg iodine as povidone-iodine/mL). These iodine compounds have proven to be effective disinfectants for decades. They are applied to wounds as aqueous solutions or fatty ointments. With long-term use on wounds, the highly reactive iodine – which is the disinfectant – is successively deactivated and becomes less effective in the presence of protein and/or blood. Considerable quantities of iodine may be absorbed if the compound is applied over large surfaces.

Aqueous chlorhexidine solution
Aqueous chlorhexidine solution (5 mg/mL) is a proven antiseptic with few known resistances that is well tolerated by wounds and mucosa. It may slow the formation of granulation tissue in wounds.

Silver nitrate
Silver nitrate is applied in the form of sticks. It is extremely aggressive and burns when it comes into contact with moisture, e.g., excessive granulation tissue (classic treatment with ‘lunar caustic’). Silver coatings are recommended for tumour pros-
theses, which are associated with an especially high risk of periprosthetic infection. There is little documented evidence of its efficacy to date, but it definitely lasts longer than coatings with gentamicin (see Chapter 4.4.6).

4.3.2 Antiseptic barrier for slow-healing and non-healing wounds

With unimpaired wound healing, a surgical wound will dry within days and be sealed against bacteria. If it remains moist or re-opens, then immediate revision is indicated. A superinfection must be prevented until the wound heals. Placement of an antiseptic drape with an additional antiseptic, e.g., polyhexanide, is advisable in the case of more extensive wounds. A moist dressing, which is changed every 12–24 hours, is placed over the large, disinfected wound site (Fig. 4-1a/b).

Alternatively, an antiseptic in gel form may also be considered; this form of antiseptic simplifies wound care particularly in outpatient treatment situations. If clean granulation tissue has formed on the surface, then a split-thickness skin graft can be applied to speed healing. In the case of small wounds, surface application of an antiseptic followed by placement of an absorbent sterile compress may suffice.
4.4 Antibiotics and their main carriers

4.4.1 Antibiotics

Numerous criteria must be considered when selecting antibiotics for local application, including:

Pathogen spectrum
As for antibiotics used for systemic application, the same rule applies here: the spectrum of action should be broad for unknown bacteria and specific for known bacteria. However, the antibiotics available for local application are often limited (see Chapter 3.4).

Resistance to temporarily high temperature
Antibiotics intended for the impregnation in PMMA cement must be able to withstand PMMA polymerisation temperatures of up to 90 °C without any loss of action (see Chapter 4.4.3).

Stability of the antibiotics
Antibiotics must maintain long-term stability as a chemical substance:

- in aqueous solution
- at body temperature (37–38 °C)

Aminoglycosides (e.g., gentamicin) have been shown to remain unchanged over very long periods. In contrast, beta-lactams, such as penicillins and cephalosporins, degrade and/or lose their effect in aqueous environments in as little as a few hours. The long-term stability of carbapenems, including meropenem and imipenem, is not precisely known.

Cell toxicity with respect to the body’s cells
Osteoblast cultures were studied by continuous exposure to antibiotic concentrations of 10–5000 μg/mL over 10–14 days. Vancomycin, amikacin, tobramycin, trimethoprim, daptomycin, meropenem and imipenem demonstrated low levels of toxicity even at concentrations of over 100 μg/mL. In contrast, quinolones, rifampin, colistimethate sodium and gentamicin were considerably more toxic. In clinical use, high tissue concentrations can usually be expected only for 1–2 days, making the clinical significance of these studies unclear (Fig. 4-2).
Elution characteristics
Knowing the elution characteristics is important for all antibiotic-impregnated carriers:

- How much of the antibiotic is released by the carrier within a given time period (initial days, weeks, months)?
- The elution characteristics depend on the various carrier substances and the local environment as well as the antibiotics in use and their solubility in water. The extent of antibiotic release into the environment is expressed in μg/mL of surrounding fluid (Fig. 4-2).
- Intramedullary nails coated with gentamicin release the antibiotic within the first few hours.
- Antibiotic release from collagen sponges occurs mainly on the first day and then decreases very rapidly.
- With PMMA cement, the release of therapeutically effective antibiotic concentrations is limited to a few days (Fig. 4-2).
- It may be possible to extend this therapeutic period somewhat for calcium sulphate.
- The above illustrates that the therapeutic effect of all of these applications is short, while a protective effect may last for somewhat longer.

*Fig. 4-2: Antibiotic release from PMMA beads. Daily measurement in collected drain fluid. Large spread of the values. Highly water-soluble gentamicin is released more rapidly over several days, while the release of vancomycin is more linear. The carrier and the antibiotic are important for a specific elution curve (Anagnostakos et al. 2009).*
Potential antibiotics for individual admixture
Available as a sterile powder and suitable for admixture with PMMA, calcium sulphate and mixed products:
- Vancomycin (glycopeptide) is released over a relatively long period (Fig. 4-2) with low cytotoxicity.
- Clindamycin (lincosamide group)
- Erythromycin (macrolide)
- Colistimethate sodium (polymyxin group) tends to be cytotoxic.
- Carbapenems have a broad spectrum of action. Meropenem is sufficiently hydrolytically stable. However, nothing is known about its long-term stability. Imipenem is not recommended for impregnation due to its chemical structure and the associated stability issues.

Only available in selected countries in sterile, aqueous form, only suitable for admixture with calcium sulphate, hydroxylapatite and/or mixed products:
- Aminoglycosides: gentamicin, tobramycin, amikacin
- Linezolid (synthetic antibiotic)

Special problems
Rifampicin is not suitable for mixing with PMMA because it increases the curing time of the PMMA cement by up to 24 hours. Quinolones are temperature-stable but cytotoxic at high concentrations. They impair the hardening of calcium sulphate.

Important notice: Antibiotics should be mixed only in powder form into the PMMA-cement in order to have an adequate quality of cement
For mode of action and spectrum of action, see Chapter 3.4.

4.4.2 Carriers of antibiotics
There are numerous conceivable carriers. Those of practical significance include the following:
- Polymethylmethacrylate, PMMA
- Collagen sponges
- Calcium sulphate (plaster cast) as well as other osteoconductive mineral substances and composite products
- Implants

There are many premixed, ready-to-use products for which the manufacturer is responsible for the mixture (antibiotic cements, gentamicin cement beads, gentamicin collagen sponges, preformed spacers impregnated with antibiotics) and
mixtures for which the surgeon is responsible for preparation and application. For elution characteristics, see Chapter 4.4.1.

4.4.3 PMMA bone cement with antibiotics

PMMA bone cement is the only approved agent for the fixation of prosthetic implants to the skeleton, unless an uncremented fixation mechanism is selected. PMMA is inexpensive, easily malleable and has defined mechanical properties. The polymerisation temperature in vitro may reach up to 90°C. The maximum temperature in vivo is often much lower, between 40°C and 50°C, depending on layer thickness and ambient temperature in particular. The elution characteristics are known (Fig. 4-2). Therapeutically effective antibiotic release is concentrated within the first few days. The entire quantity of released antibiotic depends on surface area and porosity. Small beads release more antibiotic relative to weight than large cement fragments. Some of the antibiotic remains in the cement structure as elution is never complete. The extent to which protection against the formation of biofilm by sensitive bacteria persists after longer periods is not completely understood. If the added antibiotics stop working or if resistant bacteria appear, then biofilm formation is to be expected, which may result in reinfection.

The most extensive experience with the impregnation of PMMA cement involves gentamicin and tobramycin, while experience with clindamycin, vancomycin, colistin and erythromycin is less extensive.

Available preprepared combinations (a selection)
PMMA cements with predefined amounts of added antibiotics

- Standard cements: 40 g with 1 g gentamicin or 1 g tobramycin
- Revision cements: 40 g with 1 g gentamicin and 1 g clindamycin or 0.5 g gentamicin and 2 g vancomycin or 0.5 g erythromycin and 3 million IU colistimethate sodium
- Beads with 4.5 mg gentamicin per bead

Preparation of individual combinations
The following questions must be answered prior to the preparation of individual combinations:
- What is the precise objective of a special combination?
- Is there a preprepared mixture available with the desired spectrum of action?
- Are the intended antibiotics able to withstand PMMA cement polymerization temperatures (approx. 90°C) and remain unchanged?
Practical preparation sequence

1. Definition of the intended use of the bone cement
   - Definitive fixation of a prosthetic joint, production of a longer-term indwelling spacer: High mechanical stability of the cement. The polymer powder and the antibiotics to be added must be meticulously mixed in order to achieve the most homogeneous mixture possible. The total quantity of added antibiotics must not exceed 10 % of the polymer powder. In other words, no more than 4 g antibiotics are permitted to be added to 40 g polymer powder. The total quantity of antibiotics added by the manufacturer and by the surgeon must be calculated here.
   - All other applications: If need be, the quantity of added antibiotics may be a little higher than 10 %. While the need for homogeneous distribution remains a topic of debate, most experts agree that it is advisable.

2. Antibiotic selection
   The antibiotics listed above include only those antibiotics that are available as sterile powders. Rifampin causes major delays of up to 24 h in the hardening of PMMA cement and must not be used.

3. Sequence for adding the antibiotics
   Fig. 4-3

---

**Fig. 4-3: Mixing additional antibiotics into bone cement**

1. Set-up
   - A mortar and pestle and the polymer powder are prepared on a sterile table. The antibiotics to be added are kept ready.

2. Preparation of granular antibiotics
   - Granular/lyophilised antibiotics are poured into the sterile mortar from outside by a second person and ground into a fine powder.
3. Stepwise addition of polymer powder

The same quantity of polymer powder (grey) is added to the antibiotic powder (white) and mixed with the pestle to a uniform consistency.

Double the quantity of powder in the vessel by adding the total amount again of polymer powder and mix again. Repeat this procedure until all of the polymer powder has been added.

4. Blending the cement

Pour liquid monomer into a mixing vessel, acid antibiotic/cement mixture.

Blend as usual. Cement is ready to use after approx. 1 minute. The mixture can be mixed using a vacuum mixing system (starting at step 4 a).

Fig. 4-3: Mixing additional antibiotics into bone cement (continued)
Forms of application for antibiotic-impregnated PMMA cement

Cementing of primary and revision implants
Studies based on the Norwegian Arthroplasty Register provide solid evidence that the use of gentamicin-impregnated cement results in long-term reduction of the infections to be expected.

Cementing of revision implants with infections (one- or two-stage)
The use of antibiotic-impregnated cements is based on the above recommendations. There are currently no studies that provide clear evidence concerning the use of cements with multiple antibiotics added. Long-term defence against biofilm formation on the surface of the cement is expected, particularly the formation of biofilm involving bacteria that are sensitive to the added antibiotics. The long-term stability of the added antibiotics is important (see above). This protection is only relative because the entire implant is not coated with the cement.

Preparation of spacers
To provide a bridging structure following the removal of infected implants and also in exceptional cases following prolonged debridement involving an infected nonunion or segmental infected bone defect.

Objective
The objective of a spacer depends on the underlying treatment algorithm. The antimicrobial spectrum of the added antibiotics should be as broad as possible for unknown pathogens and as specific as possible for known pathogens. We categorically recommend short-term use of spacers (2–8 weeks). The use of exposed metal surfaces, such as metal balls, in hips involves the risk of new biofilm formation. Spacers should provide a certain level of stability and function (hip and/or knee flexion). Hip spacers should be designed with sufficient offset and rotational stability to prevent the risk of dislocation.

Available procedures
- Industrially preformed spacers: These are available in different sizes and contain a defined quantity of antibiotics. However, they often do not provide an exact fit, making it necessary to adapt the bone stock or add additional cement.
- Commercially available moulds for preparation of spacers in the operating room: The cement and antibiotics to be added can be freely selected. Otherwise, these spacers suffer the same problems encountered with industrially preformed spacers.
- Hand-moulded spacers: The surgeon prepares these spacers based on his or her experience. These spacers are the most reliable and tend to be the most
functional. Hemispherical moulds in various sizes are required to mould the round head component on a hip spacer (Fig. 4-4, 7-5). Moulds made of PMMA without antibiotics and formed on the basis of a removed implant are well suited for the production of a knee spacer (Fig. 4-5). The removed implant is then available for sonication.

Fig. 4-4: Preparation of an individual hip spacer: a) The removed implant is used as the basis for the mould. The planned shape of the spacer is drawn on sterile paper. The inclusion of sufficient offset and a sloping distal support surface for the spacer on the sloping osteotomy stabilise rotation and reduce the risk of dislocation. The head is formed into a round shape using a mould greased with watersoluble jelly as used for intraoperative ultrasound examinations. b) The spacer is centrally reinforced, e.g., with a long, 3-mm Kirschner wire. With transfemoral approach the distal part of the diaphysis is secured with a cerclage wire.
Local treatment with antiseptics and antibiotics

Fig. 4-5: a) Following removal of the implant with long osteotomy of the tibial tuberosity, it is greased with watersoluble jelly as used for intraoperative ultrasound examinations and used to produce a mould made of PMMA cement. A small sheet of film is placed on each of the debrided condyles and fresh cement is applied. The mould is then used to shape the surface of the cement. The back of the spacer takes on the shape of the surface of the bone. The spacers click into place on the femur and tibia. b) Spacers in correct position. Two Kirschner wires are usually sufficient to provisionally secure the tuberosity of the tibia.
Coating implants with PMMA cement with individual antibiotic admixture

In infected diaphyseal fracture, removal of the intramedullary nail and reaming may leave the bone unstable. This can be managed by inserting a new intramedullary nail coated with antibiotic-impregnated cement. High levels of local antibiotic are achieved at the fracture site, simultaneously promoting healing of the fracture (Fig. 4-6).

Fig. 4-6: Use of a ‘nail’ coated with antibiotic cement to replace an infected intramedullary nail.

a) Preoperative infected nail with incomplete osseous bridging.
b) A silicone or PE tube of the desired diameter and an extra-long 3-mm Kirschner wire are placed at the ready.
c) The tube is filled with the intended antibiotic cement; the Kirschner wire is inserted and clipped.
d) Use the proximal curve determined by Herzog for application in the tibia. Remove the PE tube.
e) Postoperative situation with the ‘cement nail’.
PMMA beads impregnated with antibiotics
Due to their larger surface area, beads release considerably more antibiotic than fixed cement (Fig. 4-2). Beads are well suited for filling osteomyelitis cavities, open medullary canals and other bone defects. The beads should be removed after about one week or removal may become difficult and the beads may also develop into biofilm carriers of resistant bacteria. Commercially prepared beads have better elution curves than custom-prepared beads and are resistant to breakage.

4.4.4 Collagen sponges with antibiotics
Collagen sponges are only available impregnated with gentamicin. They have a local haemostatic effect. They are easy to mould but absorb blood quickly and lose volume. They are poorly suited for filling bone cavities. They mostly dissolve within 7–14 days. Elution is very high during the first 2 days and then decreases very rapidly. The insertion of multiple sponges involves the risk of systemic side effects (nephrotoxicity). Cytotoxicity is probably limited due to the rapid drop in antibiotic levels. Their efficacy is controversial. A randomised study on their use as a prophylactic agent for heart procedures with transsternal approach was unable to demonstrate any positive effects.

4.4.5 Calcium sulphate with antibiotics
Calcium sulphate is available as a sterile powder. It is ultra-purified or synthetically manufactured and hardens to form a plaster when mixed with water or aqueous antibiotic solutions. Maximum temperatures do not exceed 40 °C during setting. Plaster dissolves in about 3–6 weeks in soft tissue environments and 6–12 weeks in bone environments. Plaster may contribute to an acidic pH in the environment with unknown impacts on wound healing and efficacy of the added antibiotics.

Production of antibiotic-impregnated plaster of Paris pellets
Both powdered and aqueously dissolved antibiotics can be added to calcium sulphate. If aqueous antibiotics are used, then the quantity of water to be added must be correspondingly reduced. The quantity of antibiotic that can be added is then often low. The freshly mixed paste is pressed into silicone mats with holes. The hole size can be between 3 and 6 mm. Depending on the added antibiotic, the plaster may take between 5 minutes and several hours to harden, whereby the latter case is not clinically practical.
Application
The beads can be introduced into soft tissue and bone cavities. Unlike in the case of PMMA, calcium sulphate releases its entire antibiotic content during the degradation/dissolution process. The elution curves differ depending on the antibiotic and the carrier substance. It is not necessary to remove the beads because they spontaneously dissolve.

Variations
- Preformed beads consisting of half hydroxylapatite and half calcium sulphate that bind to antibiotics dissolved in liquid are commercially produced.
- Preformed calcium sulphate, calcium carbonate, glycerol tripalmitate beads – each loaded with 2.5 mg gentamicin – are available. These take longer to dissolve and are intended to promote osteoconduction. However, this is contentious and is not well demonstrated in clinical studies.

4.4.6 Coated implants

Tibial intramedullary nails coated with covalently bonded gentamicin are available. However, this protective coating dissolves in less than one day. The protective effect against infection has not been proven in a randomised study.

4.5 References

Further reading
- Kühn KD. PMMA Cements. Springer Berlin, Heidelberg 2014
Local treatment with antiseptics and antibiotics


Additional articles

5 Negative-pressure wound therapy

5.1 Fundamentals

Negative-pressure wound therapy is a non-invasive method which promotes wound healing. It involves the controlled application of negative (sub-atmospheric) pressure to the local wound environment using a vacuum pump. The wound is filled with a special foam to distribute the suction evenly across the bed of the wound and which is sealed to the skin using an adhesive plastic drape. A tube is then connected to a vacuum pump and inserted into an opening on the drape to remove excess fluid from the wound bed.

In a prospective, randomised trial comparing this method with conventional anti-septic drape (see Chapter 4.3.2), there was a time-dependent reduction in the wound surface area and a significant reduction in Gram-negative bacteria with the negative pressure. Unfortunately, there was also a significant increase in Staphylococcus aureus observed. For open fractures treated using vacuum-assisted closure therapy or anti-septic drape, the complication rate was lower after vacuum-assisted closure therapy. It should be remembered, however, that definitive plastic wound closure should occur by day 7 at the latest. For chronic wounds, the sponges were examined with sonication following an average application period of 3 days. Large numbers of bacteria, often with polymicrobial colonisation, were found in 97% of cases with an upward trend in patients undergoing longer negative-pressure wound therapy.

The procedure has been further developed in order to prevent superinfections:

- Addition of silver to the sponges to reduce local bacterial counts
- Alternating instillation and aspiration of antiseptics in the wound environment
- When treating prosthetic infections, some authors suture the skin over the deeply inserted sponges.

Despite these innovations, the considerable risk of high bacterial counts limits the indication, as described in 5.3.

Costs include the rental costs for the suction pump, the sponges, the wound treatment set, operating room costs and the inpatient and/or outpatient treatment costs.

5.2 Therapeutic principles

Surgical debridement is the mandatory basis of the therapy. If direct wound closure is possible – whether because the wound is small in size or the wound bed conditions are favourable – then this is preferable to any other treatment method. If it is not possible to directly cover the wound using a plastic/reconstructive procedure due to poor condition of the wound bed, then applying a temporary vacuum dress-
Negative-pressure wound therapy may be considered. Once the dressing has been applied, it must be left in place for 3–5 days. It is then changed in the operating room, during which time follow-up debridement may be performed. Once normal granulation tissue has formed and the wound has contracted to an adequate size, a reconstructive procedure may be performed to enable the wound to fully heal.

If a vacuum dressing is left on too long, there is a risk of the foam material becoming incorporated into the granulation tissue during healing. This chapter does not provide a detailed description of how to apply, maintain, change and remove a vacuum dressing because orthopaedic indications tend to be rare.

### 5.3 Indications and contraindications

**Indications**

- Acute wounds: soft tissue defects due to trauma-induced wounds with no direct contact with the bone or joint (see Chapter 12), second degree burns, recent plastic tissue reconstructions and skin transplants

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**Fig. 5-1: Compartment syndrome, foot fasciotomy primary incision:**

*Fig. 5-1: Compartment syndrome, foot fasciotomy primary incision: a) after 1 week, b) vacuum dressing for 10 days, c) direct suture, d) mesh-graft on remaining wound surface area*
- Open fractures: as a short-term immediate measure (less than 7 days)
- Sub-acute wounds: compartment wounds, surgical dehiscence, abdominal wounds (Fig. 5-1)
- Chronic wounds: pressure ulcers and diabetes-related wounds
- Special indications: post abscess treatment or soft tissue debridement with large wound site

**Contraindications** (see Chapter 5.1 Fundamentals)
- All wounds not pretreated with debridement, including
  - untreated osteomyelitis
  - non-debrided necroses and/or eschar formation
- Prosthetic joint infection and infected osteosynthesis (Fig. 5-2)
- Fistulas connecting to foreign bodies
- Malignant tumours
- Exposed, sutured, pre-irradiated blood vessels in the wound bed
- Severe coagulopathy; local tendency to bleed

For foreign bodies directly contacting the surface via the overlying wound, there is a considerable risk of secondary superinfection with resistant bacteria. The risk is especially high if negative bacterial selection occurs as a result of simultaneous antibiotic therapy (Fig. 5-2).

![Fig. 5-2: Infection, total knee arthroplasty, condition after 3 months of negative-pressure wound therapy, multi-resistant bacteria present.](image)
5.4  **Negative-pressure dressing, antiseptic drape or plastic surgery (see chapter 4.3.2, chapter 12.3)**

The following points must be considered when deciding whether to apply negative-pressure wound therapy:

- Time following development of the wound: recent open fracture or chronic venous leg ulcer
- Wound assessment: size, wound characteristics (simple soft tissue wound or connection to implants, bones or joints)
- Local options: affiliation with a plastic surgeon, in-house experience

For severe wounds, transferring the patient to a specialist centre must always be considered.

5.5  **Don’ts**

Never apply a vacuum dressing

- Without prior debridement
- If there is open connection between an endoprosthesis and the skin defect to be covered (risk of a superinfection)
- To open fractures after the first 7 days from injury. Plastic surgery closure should be achieved by 7 days at the latest.

5.6  **References**

Further reading

- Fleischmann W, Lang E, Russ M. Infektbehandlung durch Vakuumversiegelung. Unfallchirurg 1997; 100: 301–4

Additional articles

This chapter describes the technical options for diagnosing infections of the musculoskeletal system. The focus is on diagnosing periprosthetic joint infections (PJI) as well as the early stages of post-traumatic infection. This chapter does not deal with the important aspects of recording medical histories and clinical diagnostics. These details are provided in the individual sections for the medical conditions.

6.1 Blood tests

With any blood test it must be remembered that an infection may be present even if the values are normal! Additional diagnostic tools must be used.

6.1.1 White blood cells, differential blood count

Determining the white blood cell count (normal range 4–10 x 10⁶/L) is part of a routine examination. An elevated white blood cell count can have a number of causes. A supplementary differential blood count is also important.

Bacterial infections are one of the possible causes of a high neutrophil count with left shift. In the case of infectious arthritis, the white blood cell count sensitivity is only 75% while the specificity is 55% (n=156).

6.1.2 C-reactive protein (CRP)

CRP is an acute-phase protein. The normal level depends on the method used and is usually 0.5 mg/dL or 5 mg/L. The CRP level is independent of age, sex, blood loss and anaesthesia. It makes sense to determine a preoperative value. The extent of the surgical procedure, the administration of steroids or other immunosuppressants and/or postoperative haematoma influence the CRP level. It increases within 6–24 hours in response to inflammatory processes and has a half life of approximately one day. As a result, the CRP level is an important postoperative clinical parameter. It usually peaks on postoperative day 2–3 and then continues to fall steadily over a postoperative course free of complications. A persistently elevated CRP level or a postoperative increase may indicate an infection at the site of the operation. The sensitivity and specificity values reported in the case of periprosthetic hip and knee joint infections are: sensitivity 91–96%, specificity 74–92% (n=105–296).
6.1.3 Erythrocyte sedimentation rate (ESR)

The ESR (normal range: women = 6–20 mm/h; men = 3–15 mm/h) is a non-specific haematology test whose diagnostic specificity is usually low. It is worth noting that significant deviations have been reported, depending on the publication. While a diagnostic sensitivity of 75% and a specificity of only 11% are reported for infectious arthritis (n=107), better results have been published for periprosthetic hip and knee infections (sensitivity 82–93%, specificity 66–85%, n=105–296). A number of authors have reported an increase in sensitivity using ESR together with CRP for the diagnosis of PJI. In many countries, ESR is considered obsolete for diagnosing an infection.

6.1.4 Procalcitonin

Procalcitonin is a good parameter for distinguishing between bacterial and viral respiratory infections. The place of procalcitonin in the diagnosis of bacterial and nonbacterial joint infections is under debate. A recent study cast doubt on its value in the diagnosis of periprosthetic infections.

6.1.5 Interleukin 6 (IL-6)

The cytokine interleukin 6 may be considered a useful parameter because it returns to baseline levels as early as 3 days postoperatively during normal healing processes. This enables more rapid detection of postoperative infections. IL-6 has also achieved high specificity as a diagnostic marker in some studies. The authors recommend combining IL-6 and CRP. Because the costs of determining IL-6 levels in the lab are considerably higher than CRP, it is too expensive for routine clinical use.

A recent study compared the diagnostic value of CRP, procalcitonin and interleukin-6 in prosthetic joint infections. Despite the valuable information provided by the latter, CRP remains the most important test.

6.2 Arthrocentesis

Native joints

In cases of suspected joint infection, an arthrocentesis should be done as soon as possible for diagnosis. Because the cell count alone does not provide sufficient evidence of an infection in the case of a native joint, it is necessary to wait for the bacteriology results. This usually takes too long. Therefore, if there is a strong
suspicion of a native joint infection, it is recommended to combine diagnostics and treatment, e.g., using arthroscopic lavage. This approach should be performed without delay. The objective is to protect the cartilage against bacterial destruction through rapid, early intervention.

Prosthetic joints

- Newly suspected infection: The joint should be punctured as soon as possible because timely diagnosis enables the option of simpler treatment and implant retention (see also Chapter 2.1). The decision to intervene and then initiate empirical antibiotic therapy is based on the number of white blood cells and/or granulocytes found in the puncture specimen.
- Chronic symptoms: In cases of suspected low-grade infection with no signs of systemic infection, the antibiotic regimen should be discontinued for at least two weeks prior to the arthrocentesis.

6.2.1 Technique of arthrocentesis

An arthrocentesis must be performed under the most sterile conditions possible. Be aware that the risk of infection of a prosthetic joint is more than 100,000 times higher compared to a native joint. There are a number of recommendations regarding the technique:

- From an orthopaedic and infectious-disease standpoint, effective disinfection (alcohol-based agent), sterile draping and the wearing of sterile gloves and a face mask are recommended.
- Important: aspiration through skin lesions (infections, psoriasis) must be avoided!
- Arthrocentesis of prosthetic joints should never be performed in the office or patient examination room but rather in a separate room and preferably in the operating theatre where the risk of infection is significantly lower.
- Sample containers (plain tube, EDTA tube, blood culture vial, aerobic and anaerobic) are placed at the ready (Fig. 6-1).
- Apply local anaesthetic to the subcutaneous level only (local anaesthetic in the joint distorts the cell count and causes false-negative bacteriology results due to its bacteriostatic effect). A subsequent stab incision avoids the biopsy needle to cut a skin cylinder eventually later pushed in the joint with the risk of contaminating/infecting the joint.
- The puncture volume obtained is then dispensed according to the following priorities. In the case of small puncture specimens it is not possible to fill all of the tubes:
  1. EDTA tube, 1 mL (must be inverted several times immediately following transfer of the synovial fluid to be completely mixed with the EDTA to prevent coagulation, otherwise an automated cell count will not be possible).
2. First the aerobic and then the anaerobic blood culture vial (at least 1 mL each, preferably 2–5 mL each, following disinfection of the rubber stopper). The use of blood culture vials enables automated processing and increases sensitivity. The literature reports sensitivities (50–93%) and specificities (82–97%) that vary depending on the method used.

3. Plain tube (0.5–1 mL) for Gram stain test
- An additional synovial fluid specimen should be aspirated into a no-additive tube for polymerase chain reaction (PCR) testing. An infectious disease specialist should be consulted as to whether this is indicated.
  - Specific PCR: e.g. *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Borrelia burgdorferi*
  - Eubacterial PCR: e.g. if the presence of difficult to culture small colony variants of microorganisms is suspected (see Chapters 1.4 and 15.2.3) as well as for samples of material from patients who have received prior antibiotic treatment
- Rapid transport (see also Chapter 6.4)
- In the case of hip joints, always add an arthrogram (see also Chapter 6.2.5)

---

Fig. 6-1: Materials for joint puncture

a) Local anaesthesia with a long infiltration needle, cutaneous and subcutaneous application only. Local anaesthetic in the joint may interfere with bacterial growth!

b) No. 11 blade for stab incision: avoids the risk of a skin cylinder being cut by the needle and pushed into the joint.

c) Long biopsy needle and 10-mL or 20-mL syringe for the hip joint, diameter 1.5–2.0.

d) EDTA tube (white blood cell count and differentiation, crystals, protein, glucose, PCR) at least 1 mL, invert 5x to prevent coagulation.

e) Blood culture vials, aerobic and anaerobic. Following disinfection of the stopper, first insert at least 1 mL, preferably up to 5 mL, into the aerobic vial then without air into the anaerobic vial.

f) No-additive tube for bacteriology (Gram stain test, mycobacteria, fungi) at least 1 mL.
Punctio sicca
- the impossibility to aspirate fluid does not exclude the possibility of an infection. In case of periarticular abscess formation there may be a sort of a valve system not allowing the fluid to reach the the needle. you may inject some Ringer fluid and try to aspirate some liquid for culture thereafter. A quantification of the white cell count is then nomore possible.

6.2.2 Cell count, differentiation, Gram stain test

Cell count
Synovial cell counts provide reliable results for the diagnosis of infection, particularly in patients with prosthetic joints. In the case of periprosthetic knee and hip joint infections, there are defined thresholds for the leucocyte counts and granulocyte fraction in the puncture specimen. These counts can be distorted in patients with inflammatory rheumatic diseases and neutropenia.
- Total knee arthroplasty: An infection is present with a cell count > 1.7 x 10^3/µL (sensitivity 94%, specificity 88%) or with granulocyte ratio > 65% (sensitivity 97%, specificity 98%).
- Total hip arthroplasty: An infection is present with a cell count > 4.2 x 10^3/µL (sensitivity 84%, specificity 93%) or with granulocyte ratio > 80% (sensitivity 84%, specificity 82%).
- Native joints: In contrast to prosthetic joints, there are no precisely defined thresholds for native joints. An infection is considered likely with a cell count > 50 x 10^3/µL (sensitivity 62%, specificity 92%) or with a neutrophil granulocyte level > 90% (sensitivity 73%, specificity 79%) (see also Chapter 9.2.3).

Cell count determinations are useful in verifying a suspected infection. Even if the cause is not yet known, therapeutic measures can be initiated immediately. During the first 8 weeks after total joint replacement the white cell count in the synovial fluid is not reliable.

Crystals
Crystal analysis provides information about crystal-induced synovitis but it does not rule out an infection.

Viscosity
A highly viscous puncture specimen decreases the likelihood for infection.
**Gram stain test**
The Gram stain test is only useful for a rapid diagnosis if it is positive. Its low sensitivity of $< 26\%$ (specificity $> 97\%$) shows that this is seldom the case. *A punctio sicca* (‘dry tap’ in which no fluid is aspirated) can never rule out an infection. For example, hip joint pressure due to periarticular fistulous tract can be reduced to such an extent that no material can be aspirated. Joint lavage with sterile fluid and subsequent aspiration have proven successful in such cases. However, the quantitative cell count determined using this technique can no longer be used to establish the diagnosis.

6.2.3  Microbiological results

The interpretation of cultures is easy, when the growth is early and the synovial cell count is typical for a periprosthetic infection. If contamination is suspected arthrocentesis may be repeated to clarify the situation with a second culture.

6.2.4  Testing the synovial fluid with biomarkers

Five different biomarkers seem to support the diagnosis of periprosthetic joint infections: α-defensin, ELA2, BPI, NGAL, and lactoferrin. There is some indication, that the determination of alpha-defensin in the synovial fluid can be helpful in the diagnosis of periprosthetic infection. Up to date the evidence is still relatively low. We therefore advocate an intraoperative application of the test only, if a preoperative arthrocentesis does not allow to harvest enough synovial fluid for a leucocyte count (see Chapter 6.2.2).
6.2.5 Contrast-enhanced arthrography

Imaging using contrast agent administered once the puncture is complete via the in situ needle is especially useful in the case of prosthetic hip joints. It reveals protrusions from the joint cavity, abscess cavities, and fistulous tracts, even if no external fistula is visible (Fig. 6-2). These signs are often criteria for two-stage revision. Improved resolution through digital subtraction technique is possible.

![Contrast-enhanced arthrography](image)

*Fig. 6-2: Contrast-enhanced arthrography. In the image on the left the contrast agent extends into the subcutaneous tissue in two fistulous tracts; in the image on the right there is an intraosseous abscess cavity.*

6.3 Imaging diagnostics

If radiology is used to diagnose infection, the pathophysiology of the infection must be understood in addition to imaging. In pathophysiological terms, we distinguish between:

- Acute infection: vasodilatation, increased neutrophil and monocyte penetration, exudation and migration
- Chronic infection: proliferation of lymphocytes and macrophages in the tissue, vascularisation, scarring

**Methods of imaging diagnostics**

- Conventional x-ray examination
- Computed tomography (CT)
- Magnetic resonance imaging (MRI)
- Scintigraphy
- Single-photon emission computed tomography (SPECT/CT)
- Positron emission tomography (PET)
- PET/CT

6.3.1 Conventional x-ray

Conventional x-ray scans only show the bone remodelling in the case of osteomyelitis and prosthesis-associated infections (Fig. 6-3). However, osteolysis and loosening are also often associated with aseptic processes. This reduces the specificity of these radiological signs. Serial x-rays over a certain period can measure changes to the cortical bone and migration of a prosthesis, for example (Fig. 8-3). Rapidly progressive and/or irregular periprosthetic osteolysis suggests an infection (see cover image).

Exposures: AP and lateral views and possibly additional oblique views can greatly increase the predictive value (Fig. 8-7).
### What should you look for?
- Bones: density, sclerosis, sequestra, osteolysis
- looseness of prothestic joint or internal fixation device
- Surrounding tissue reaction

*Tab. 6-1: Role of conventional x-ray for the diagnosis of infections*

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Drawbacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>– Good imaging of the bone structure</td>
<td>– Visible changes often less specific for infections</td>
</tr>
<tr>
<td>– Development of changes can be detected by comparing with previous X-rays</td>
<td>– Poor imaging of soft tissue</td>
</tr>
<tr>
<td>– Fewer metallic artefacts</td>
<td>– Sequestra, fistulas, abscesses only partially detectable, improved detection by contrast filling of the fistula</td>
</tr>
</tbody>
</table>

Indication: Quick overview examination, simplest monitoring of progression by comparing to all earlier x-rays

#### 6.3.2 Computed tomography with contrast agent

(Contrast agent: $10^{-3}$ mol/kg body weight)

Computed tomography (CT) with contrast agent enables the diagnosis of joint effusion, fistulas, soft tissue abscesses, sequestra (Fig. 6-4), bone erosion and periprosthestic rarefaction of the bone. Metallic artefacts have a major negative impact on image quality. Artefacts can be reduced by using special techniques which enable detection of prothestic loosening and signs of soft tissue infection.
Fig. 6-4: Osteomyelitis 2 years after internal fixation, 1 year following plate removal. Numerous sequestra could only be localised using CT. Arrow: 1 peripheral sequestrum, 2 central sequestra quite deeply embedded in the newly formed bone (see also Fig. 8-12).

Tab. 6-2: Role of CT scan for the diagnosis of infections

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Drawbacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>– Short examination time</td>
<td>– Relatively poor imaging of soft tissue</td>
</tr>
<tr>
<td>– Good imaging of the bone structure</td>
<td>– Metal artefacts</td>
</tr>
<tr>
<td>– Best imaging of sequestra</td>
<td>– Radiation exposure</td>
</tr>
<tr>
<td>– Reconstructions possible in all planes</td>
<td></td>
</tr>
<tr>
<td>– No claustrophobia (unlike with MRI)</td>
<td></td>
</tr>
</tbody>
</table>

Indication: Preoperative search for sequestra and necrosis in the bones combined with filling of fistulas, distribution of fistula system, air bubbles
6.3.3 Magnetic resonance imaging

(Contrast agent: $10^{-5}$ mol/kg body weight)
Magnetic resonance imaging (MRI) can be performed on patients with and without non-ferromagnetic implants. MRI can resolve soft tissue changes better than CT or conventional x-rays. It also visualizes anatomic details more precisely than scintigraphy. The method is especially important in the spinal region (Fig. 10-1, 10-2). As with CT scans, the main disadvantage of MRI involves imaging interferences close to metallic implants.

Functional magnetic resonance imaging in the case of infections
There have been experimental studies conducted using iron nanoparticles which accumulate in macrophages during inflammation. This enables acute and chronic infections to be very easily distinguished and imaged.

This method cannot be used in humans at this stage because the iron nanoparticles are too toxic at the concentrations administered.

Tab. 6-3: Role MRI for the diagnosis of infections

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Drawbacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>– Shows acute inflammations with high sensitivity and specificity</td>
<td>– Specificity is reduced with chronic infections (only 60% with chronic postoperative osteomyelitis)</td>
</tr>
<tr>
<td>– Shows complications such as abscesses and fistulas</td>
<td>– Bone oedema is overestimated</td>
</tr>
<tr>
<td></td>
<td>– Susceptibility artefacts*</td>
</tr>
</tbody>
</table>

*Susceptibility artefacts: No differentiation between chronic inflammation and scarred repair.

Differentiation tips: The bone repair process should be completed approximately 1 year after surgery; if not, then the presence of a chronic infection is likely. Do not disregard scarring (medullary cavity).

6.3.4 Contrast-enhanced arthrography

See Chapter 6.2.5 and Fig. 6-2

6.3.5 Sonography

Ultrasound examinations can be used to locate a joint effusion or for controlled puncture and drainage of such an effusion. Sonography is especially useful in the case of prosthetic hip joint-associated infections where effusions often cannot be diagnosed clinically.
6.3.6 Nuclear imaging

Using molecular imaging, scintigraphic scans show the physiological processes that precede radiologically visible, anatomical changes. The concentrations of radioactive substances that are required are much lower than the concentrations required for MRI and CT (concentration of radiopharmaceuticals: $10^{-9}$ to $10^{-12}$ mol/kg). Another benefit is that a general, functional diagnosis of the bone metabolism can be established in addition to the principle issue in question. Drawbacks include the limited spatial resolution associated with conventional systems and the relatively long time required for the scanning procedure. We will limit ourselves to the following:

- Bone scintigraphy with $^{99m}$Technetium phosphonate (with or without SPECT/CT)
- $^{99m}$Tc antigranulocyte scintigraphy and $^{99m}$Tc-HMPAO leukocyte scintigraphy (with or without SPECT/CT)
- $^{18}$F-fluorodeoxyglucose positron-emission tomography/computed tomography (FDG-PET/CT)

**Bone scintigraphy**

$^{99m}$Technetium ($^{99m}$Tc)-labelled phosphonates are used in bone scintigraphy. The substance is distributed via the circulatory system following injection. This enables zones that are well supplied with blood (zones of infection) to be imaged immediately following injection during the tissue perfusion and blood-pool phase. The substance then accumulates in the bones within approximately 3–4 hours (late phase). Sites of increased bone metabolism, e.g., inflammations and infections, are especially well imaged (increased uptake), which makes the scan very sensitive.

Due to its poor specificity, bone scintigraphy with $^{99m}$Tc does not usually provide enough information when used as the sole imaging technique to confirm diagnosis of an implant-associated joint infection. Depending on the type of prosthesis, increased accumulation is a normal physiological process during the first (1–2) postoperative years and corresponds to remodelling in peri-prosthetic bones. In addition, bone scintigraphy is often unable to distinguish aseptic loosening from a prosthesis-associated infection. As a result, bone scintigraphy can be combined with inflammation scintigraphy.

**$^{99m}$Tc-antigranulocyte scintigraphy and $^{99m}$Tc-HMPAO leukocyte scintigraphy**

$^{99m}$Tc-labelled monoclonal antigranulocyte antibodies have an accuracy of 81% in the diagnosis of a prosthesis-associated infection (Fig. 6-5). This technique is widespread in Europe. There are physiological accumulations in the liver, spleen and colon. Antigranulocyte scintigraphy does not work on the axial skeleton because the promyelocytes in the blood-forming bone marrow are also labelled. Ectopic blood-forming bone marrow also accumulates antibodies. It is potentially difficult
to distinguish between a low-grade infection and aseptic inflammation. Follow-up examinations may trigger immune reactions (in 4% of cases formation of human anti-mouse antibodies [HAMA]). For the very complex method involving labelled autologous leukocytes, the values for sensitivity, specificity and accuracy are 94%, 83% and 89%, respectively.

Fig. 6-5: Persistent fistula despite 3 months of negative-pressure wound therapy following total knee arthroplasty and early revision due to staphylococcal infection. Antigranulocyte scintigraphy with massive periprosthetic accumulation. Tuberosity of the tibia has not healed following osteotomy. Rifampicin-resistant coagulase-negative staphylococci identified upon explantation.

**Single-photon emission computed tomography (SPECT/CT)**
In the case of SPECT/CT, the scintigraphic methods described above are carried out using a next-generation hybrid device; this involves coupling the gamma camera used in nuclear medicine with CT to produce and then merge anatomical and functional scans using the same device. The highly active sites detected using the scintigraphic method are integrated into the CT. This makes localization of scintigraphically active sites easier, thus increasing the specificity of the scans. It also means additional scans are often unnecessary.

**18F-fluorodeoxyglucose positron-emission tomography/computed tomography (FDG-PET/CT or PET/CT)**
- Colour imaging of regional glucose metabolism. Phagocytes consume approximately 50 times more glucose than the surrounding environment, meaning that accumulation of phagocytes during an infection is accompanied by significantly increased glucose uptake in the scintigram.
- High sensitivity, satisfactory local resolution
- 3D data
- Relatively quick scanning procedure (2 hours)
- Normal: major accumulation in the brain, individually variable levels in the heart, liver and gastrointestinal tract
- PET implements an approach using specific radioactively labelled molecules to image cell and organ functions. By comparison, MRI uses a different approach based on the imaging of protons and Brownian motion and cannot always be applied due to certain contraindications (e.g., pacemaker, toxicity of the contrast agents, etc.).
- Therapy monitoring possible
- Diagnosis of spondylodiscitis possible (unlike antigranulocyte scintigraphy)
- Indications: can possibly be used to establish status following internal fixation (depending on the time since the procedure), abdominal infections, vascular implants, autoimmune diseases, fever of unclear origin in neutropenic patients.
- Administrative problem: health insurance funds are not yet required to cover this procedure in outpatient settings. Health insurances must be consulted.

In combination with computed tomography (FDG-PET/CT) the diagnostic value is significantly improved:
- Excellent local resolution of CT combined with functional PET scan
- High sensitivity and specificity for chronic inflammations
- Can also be performed with metal implants
- Difficult to differentiate tumour/inflammation. In such cases, however, FDG-PET can identify the ideal site of a possible biopsy. Depending on the region of the body/organ, tumour-specific PET tracers (e.g., amino acids/oligopeptides, choline) can be used for further differentiation.
- Administrative issues:
  - Availability: Complex nuclear imaging with PET scanning is not universally available across Europe, but is increasingly used in University-based hospitals and some private institutions.
  - Cost effectiveness: Simple nuclear imaging is not expensive and is covered in most public and insurance-based systems. Combined scanning (particularly with FDG) may require specific funding arrangements.

The role of FDG-PET in differentiating between an infection and aseptic loosening of a prosthetic hip joint is still considered controversial because of the lack of standardised interpretation criteria. While Love et al. reported a poor specificity of just 9% compared to a high sensitivity of 100%, Stumpe et al. of the Zurich group reported a high specificity of 83% with a low sensitivity of 28%. Obviously, more studies are needed before the procedure can be routinely used in the diagnosis of implant-associated infections.
6.3.7 Summary of imaging diagnostics for infections of the musculoskeletal system

- A conventional x-ray is usually sufficient as the first imaging procedure (issue: signs of loosening, radiolucent lines, etc.)
- In the case of suspected low-grade infections or complex situations, further imaging (MRI, scintigraphy with SPECT/CT, etc.) must be considered.
- Extremities: Antigranulocyte scintigraphy possible, ideally combined with SPECT/CT
- CT in the case of osteomyelitis in order to plan a procedure to investigate sequestrum formation
- FDG-PET/CT is a modern, highly sensitive option for chronic infections. Limitations: reduced availability, costly, currently not everywhere covered by health insurance funds in outpatient settings, depending on localisation, reliable differentiation between tumour/inflammation not possible

6.4 Biopsies

6.4.1 Discontinuation of antimicrobial therapy – Pretreatment before diagnostic sampling

Prior to collecting microbiological samples, any antibiotic regimen should be discontinued for 2 weeks, provided the progression of the disease allows this. Prophylactic antibiotics should not be administered until after the samples have been collected. If samples are collected with the use of a tourniquet (constriction of blood flow), then prophylactic and/or therapeutic antibiotics should be introduced into the blood stream at the full dosage just immediately prior to removal of the tourniquet.

6.4.2 Biopsy technique

Sample type
Swabs should not be used. Biofilm bacteria cannot be extracted from biofilms using swabs. Swabs may contain contaminating microbes. Their sensitivity is significantly less than that of tissue samples. Foreign bodies such as plates, screws, prosthetic joints can be sonicated. Pus ensures rapid diagnosis of acute infections. It is recommended, in some centres, to use separate instruments for each sample. We think, that contamination is better ruled out by the parallel analysis of each tissue biopsy by bacteriology and histology.
Technical procedure
A large piece is collected from each region to be tested and divided into 2 pieces for bacteriology and histology with each edge being approximately 0.5 cm long (Fig. 6-6). Contamination of the collected samples is prevented by immediately transferring them to transport containers.

Fig. 6-6: Two samples each from the same region are taken for bacteriology and histology (left), both assigned the same number. Larger numbers of samples are collected if a difficult to diagnose low-grade infection is expected.

Sample collection site
Samples should always be collected from a zone in which the tissue structure is visibly inflamed (e.g., abnormally soft, degraded). Tissue in the vicinity of sequestra is informative. If an implant-associated infection is suspected, then the samples must be collected from the immediate vicinity of the foreign body. In these cases, infection tends to be localised around the implant, while more remote regions will not be affected in low-grade infections. Samples collected directly from the skin or superficially from a fistula canal are unsuitable because these samples are often contaminated with skin microbes and lead to false results.

It is important to precisely document the collection site so that the region in which the microbes are growing can be isolated. Microbiology and histology samples must be assigned the same number so that the bacteriology results can be compared with the corresponding histology results. Intraoperative biopsies have a sensitivity of 65–94% and a specificity of 69–87%.

Number of samples
A minimum of 3 tissue samples must be collected. One study found that sensitivity was 50% with 2–3 samples and 72.7% with more than 5 samples. More samples reduce the risk of an incorrect assessment due to contamination. Bacterial growth in
one of 2 samples does not indicate whether infection or contamination is involved. Contamination can be assumed if there is growth in 1 of 7 samples. Simultaneously collecting tissue for bacteriology and histology enables more reliable differentiation between contamination and infection.

**Documentation of samples**

A standard form that is acceptable to both the microbiology and histology labs and that ensures uniform collection of patient data and identification of samples is suitable for documenting the various samples (see also Chapter 19).

Note: The more acute and obvious the infection is, the fewer the samples required (at least 3). If a low-grade infection is suspected, then a large number of samples (at least 6) should be collected for bacteriology and histology.

**Tab. 6-4: Summary of bacteriology sample processing**

<table>
<thead>
<tr>
<th></th>
<th>Joint puncture specimen</th>
<th>Biopsies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Volume</strong></td>
<td>Approx. 1–20 mL (see also Chapter 6.2 Arthrocentesis)</td>
<td>Approx. 0.5 x 0.5 x 0.5 cm per biopsy</td>
</tr>
<tr>
<td><strong>Number</strong></td>
<td>1</td>
<td>At least 3; if low-grade infection is suspected, at least 6</td>
</tr>
<tr>
<td><strong>Transport container</strong></td>
<td>Sterile container with no additives (Gram stain test) EDTA tube (automated cell count and one aerobic and one anaerobic blood culture vial, see also Chapter 6.2 Arthrocentesis)</td>
<td>Sterile container with no additives For longer shipping times, it is recommended to consult the lab to determine if a special transport container should be used.</td>
</tr>
<tr>
<td><strong>Lab form</strong></td>
<td>Precise description of the material, collection date and time, and note as to whether periprosthetic joint infection is suspected (see Chapter 19)</td>
<td></td>
</tr>
<tr>
<td><strong>Gram stain test</strong></td>
<td>Low sensitivity</td>
<td>Not recommended due to very low sensitivity</td>
</tr>
<tr>
<td><strong>Culture</strong></td>
<td>Aerobic and anaerobic cultures are performed. The cultures are prepared using non-selective media such as sheep blood agar and chocolate agar. Liquid media must also be used to detect growth. The incubation period must be of sufficient length (10–14 days) so that slow-growing microbes (Propionibacterium spp. or SCV) can also be detected.</td>
<td></td>
</tr>
<tr>
<td><strong>PCR</strong></td>
<td>Eubacterial (broad-range) PCR has low sensitivity. Its routine use is not recommended for all patients. An additional biopsy is sent to the lab as a reserve. This is used for PCR if bacteriology remains negative.</td>
<td></td>
</tr>
</tbody>
</table>
6.4.3 Transport to the lab

Samples should be received by the laboratory as soon as possible, optimally within 4 hours of collection. Samples sent by post must always be sent by express post. The lab should be notified by phone about the samples to ensure they are processed immediately. If samples cannot be sent immediately, for instance, if samples are collected at night, then they should be stored at room temperature.

6.4.4 Bacteriological tests

If an implant-associated infection is suspected, then extended incubation of the biopsies in fluid enrichment broth for 10 days will improve the sensitivity of pathogen detection in the samples. This period is followed by subcultivation on solid media with resistance testing. The extended incubation period of 10–14 days is important because otherwise slow-growing microbes will not be detected, e.g., Propionibacterium spp. (Table 6-4). The detection of “small colony variants” (SCV) asks for special experience to recognise the extremely tiny colonies.

6.4.5 Polymerase chain reaction (PCR) for the molecular detection of bacteria

Principle

Eubacterial PCR: (EUB-PCR; synonym: broad-spectrum PCR) uses primers that bind to conserved regions of the bacterial 16S rDNA. This allows the DNA of virtually all bacteria to be amplified. In the case of a positive result, the pathogen responsible is identified using sequencing and comparison with a database. This method is suitable for detecting monobacterial infections in test materials that are normally sterile independent of culture conditions as well as to identify isolated material. New information technology tools also sometimes enable interpretation of mixed sequences.

For technical reasons, the sensitivity is lower than that of specific PCR tests. The latter are therefore preferable if the presence of a specific pathogen is suspected. A negative result does not rule out a bacterial infection. Specificity is generally high. However, it must be ensured that contamination does not occur as a result of skin flora (regardless of sufficient levels of disinfection because even organisms that have been killed can be detected). Where possible, liquid transport media should not be used either as even sterile solutions often contain bacterial DNA.
Specific PCR: uses primers and probes to detect a defined pathogen. This only makes sense if the presence of a particular pathogen is suspected. There are very few indications in this regard in orthopaedics.

**Indication**

These procedures are also suited to detecting dead bacteria, which is why they are used primarily in microbiological cultures that show negative results, as well as following prior antibiotic therapy. Up to now, resistance has only been apparent in isolated cases (e.g., resistance in the case of Staphylococcus aureus, MRSA, vancomycin-resistant enterococci (VRE), mycobacteria and rifampicin).

The microbiological laboratory must be notified in advance that molecular diagnostics (PCR) are required for negative cultures.

**Current practical approach**

- **Arthrocentesis:** A no-additive tube is recommended for molecular diagnostics.
- **Tissue samples:** When biopsies are submitted, the microbiological laboratory must be notified that molecular diagnostics are required for negative cultures. This means that the tissue samples submitted must be processed in a specific fashion. They are finely crushed using a mortar and pestle and divided into two parts. One part is used for the cultures. The other part is stored so that this material can be used for broad-spectrum PCR in the case of a negative culture. Due to the costs involved, the laboratory will not automatically initiate the use of molecular diagnostics if this has not been ordered.

**Future approach**

Automated multiplex PCR testing is being introduced, which will also take implant-associated pathogens into consideration. The testing also enables inferences to be made regarding resistance to certain antibiotics.

### 6.4.6 Histological tests (Fig. 6-7)

A single positive tissue sample is already evidence of an infection, even without positive bacteriology results. It is critically important for the reliability of the diagnosis that the tissue for the test is collected from the region in which an infection is suspected. In the case of suspected implant-associated infections, samples must always be collected in the immediate vicinity of the implant (membranes surrounding the implant or prosthesis, joint neocapsule). The histology results can also be helpful for distinguishing between infection and contamination. If, for example, coagulase-negative staphylococci are found in only one sample and positive histology is present we conclude that there is an infection (see also Chapter 6.4.2).
Neutrophil granulocytes are indicators of bacterial infections. They are found in greater numbers in the case of acute infections (Fig. 6-7 a). Bacteria are more rarely found. In the case of low-grade infections in connection with implants, a search for granulocytes must be performed (Fig. 6-7 c). The granulocytes are counted in at least 10 high-power fields (400x magnification) and must exceed a total of 20–25 (Morawietz et al. 2009). Neutrophil granulocytes can be specifically imaged using immunohistochemical staining (CD15) (Fig. 6-7 d). This makes detection of granulocytes considerably easier, enabling a meaningful diagnosis even if the number of neutrophil granulocytes is low. Typical accumulations of granulocytes are not found in the case of all infections. Granulocyte accumulation is not present in every type of implant-associated infection. As an example, tissue granulocytes may be very scarce in Propionibacterium acnes infection.

Fig. 6-7: High-grade infection (top):

a) Synovial membrane with numerous granulocytes, high-grade infection, foreign body giant cells;
b) Large numbers of granulocytes with simultaneous presence of giant cells with phagocytised material.

Low-grade infection (below):

c) Isolated granulocytes (arrow),
d) Granulocytes much more visible with immunohistochemical staining (CD15)
Prosthetic loosening is often simultaneously present in the case of delayed or late infections. The analysis of periprosthetic membranes is often complicated due to the presence of foreign body reactions to wear particles. Four types of periprosthetic membranes (Plural) have been defined (Morawietz et al. 2006), including:

- Type I: Wear particle induced type = with signs of wear only
- Type II: Infectious type = with signs of infection only
- Type III: Combined type = simultaneous signs of wear and infection (Fig. 6-7 b)
- Type IV: Indeterminate type = does not fulfil criteria for type I or type II

6.5 Testing of explanted foreign bodies using sonication

Sonication is used to identify the bacteria in the biofilm on explanted implants and prosthetic joints. The procedure involves first vortexing the implants in a liquid bath. The ultrasonic waves generate a rapid change in pressure on the surface of the implant which dislodges the biofilm (Fig. 6-8). Vortexing is repeated and the liquid is then used to diagnose bacterial infection with conventional culture.

In a study of 79 patients with periprosthetic joint infection and 252 patients with aseptic failure it was found that sonication was significantly more sensitive than tissue biopsy (tissue biopsy 60.8%, sonication 78.5%) with almost identical specificity (tissue biopsy 99.2%, sonication 98.8%).

![Diagram of the sonication workflow](https://www.example.com/sonication_diagram.png)

**Fig. 6-8: Diagram of the sonication work flow. Ultrasonic penetration takes place through alternating phases of compression (C) and rarefaction (R).**
In patients whose antibiotic therapy was discontinued less than 14 days prior to surgery, sonication fluid culture was significantly more sensitive than conventional bacteriology.

The pathogen is also identified more quickly with sonication fluid culture than conventional bacteriology, making it possible to switch more rapidly to a suitable postoperative antibiotic if resistance has developed. Sonication is not targeted for identifying mycobacteria or fungi; special cultures should still be used.

**Explantation and shipment**

In order to prevent inadvertent contamination, implants must be shipped in sterile, stable containers. Laboratories usually provide their own transport containers that have been evaluated for sonication (Fig. 6-9).

Because gloves represent the highest risk for microbial contamination and sonication is very sensitive, the implant should only be handled with suitable instruments or fresh gloves and placed directly into the special transport container.

![Fig. 6-9: Example of a sterile transport container](image)

When explanting a prosthesis that has been anchored with antibiotic cement, it is recommended to remove the cement from the prosthesis and ship the prosthetic parts without cement. Newly fractured cement may release antibiotics that are still active and this could have a negative impact on the identification of microbes. For shipment, see also Chapter 6.4.3.
6.6  References

Further reading

- Morawietz L, Tiddens O, Mueller M et al. Twenty-three neutrophil granulocytes in 10 high-power fields is the best histopathological threshold to differentiate between aseptic and septic endoprosthesis loosening. Histopathology 54; 2009: 847–53

Additional articles


Levine BR, Evans BG. Use of blood culture vial specimens in intraoperative detection of infection. Clin Orthop Relat Res 2001; 382: 222–31


Ochs BG, Kommerell M, Geiss HK et al. [Improving microbiological diagnostics in septic orthopaedic surgery. Comparative study of patients receiving systemic antibiotic therapy]. Orthopäde 2005; 34: 345–51


- Worthington T, Dunlop D, Casey A et al. Serum procalcitonin, interleukin - 6, soluble intercellular adhesin molecule - 1 and IgG to shortchain exocellular lipoteicholic acid as predictors of infection in total joint prosthetic revision. BJBS 2010; 67: 71–6
7 Periprosthetic joint infection

7.1 Fundamentals

7.1.1 Preliminary remarks

Periprosthetic joint infections present in a variety of ways. How the infection manifests and how it develops depends, amongst other things, on the pathogens involved, the joint affected (soft tissue cover, mechanics, load), the patient’s concomitant medical conditions and the pathogenesis of the infection (exogenous, haematogenous with or without concomitant sepsis). Given the considerable differences in terms of requirements, a number of different approaches to treatment are needed in order to achieve an optimum treatment outcome. The aim of these recommendations is to provide assistance in selecting reliable, evidence-based approaches which allow optimum results to be achieved without undue effort.

7.1.2 Aetiology

The presence of foreign materials increases the pathogenicity of bacteria. Implant related infections develop in the presence of even a very small number of bacteria (e.g. 100 \( S.\ aureus \) bacteria). These can develop exogenously, intraoperatively, perioperatively or haematogenously at any time, even decades after implant placement.

The most common pathogens are coagulase-negative staphylococci (30–43 %), \( S.\ aureus \) (12–23 %), mixed flora (10–11 %), streptococci (9–10 %), Gram-negative rods (3–6 %), enterococci (3–7 %) and anaerobes (2–4 %). This level of microbial diversity indicates that microbiological identification of the bacteria using resistance testing is essential. Empirical therapy without reliable prior identification of the bacteria must be avoided.

7.1.3 Localisation

Bacteria adhere to the implant where they form a biofilm and trigger infection in the periprosthetic tissue (see Chapter 1). The infection is also found directly in the tissue adjacent to the implant. Samples for bacteriology and histology must therefore be collected from the periprosthetic area (see Chapter 6.4).
Due to the epiphyseal/metaphyseal fixation of most prosthetic joints, the blood supply to the bone generally remains good. Sequestration only occurs in exceptional cases. When performing debridement, full retention of the bone is thus generally justified. Bone necrosis is an unusual occurrence (Fig. 7-1). It is associated, for example, with periprosthetic fractures of the shaft or fixation of prosthetic joints in allografts.

**Fig. 7-1:** ♀, 60 years old. Infection with associated fistula, following total hip replacement surgery for stiff hip dysplasia. Recurrence of fistula 4 months after implant removal. Fistula filled with contrast agent and methylene blue. Following soft tissue debridement, the methylene blue still stains parts of the greater trochanter, which are resected. The histological analysis indicated necrotic bone, which only occasionally occurs in prosthetic joint infections.
7.1.4 Incidence

The risk of postoperative prosthetic joint infection following hip or knee arthroplasty is 0.5–2 % over an observation period of 2 years. For prosthetic shoulders and elbows, the risk is considerably higher at approximately 3-4 %. After the first 2 years, the risk of a haematogenous infection is 2.3 infections per 1000 prosthetic joint years.

7.1.5 Risk factors

Comorbidities (rheumatoid arthritis, psoriasis, joint infiltration with steroids, systemic steroid therapy, malignant neoplasm, diabetes mellitus, early infectious arthritis or revision arthroplasty), a high NNIS score (National Nosocomial Infection Surveillance) and postoperative factors (superficial wound infection, hematoma, moist wound, dehiscence, pressure ulcer) increase the risk of periprosthetic infection.

7.1.6 Classification

Early infection (0–3 months; Fig. 7-2a)
Early infections are usually triggered by virulent pathogens such as *S. aureus*.

Delayed infection (3–24 months) = low grade
Delayed infections are generally acquired intraoperatively and involve low-virulence pathogens such as coagulase-negative staphylococci or *Propionibacterium acnes*.

Late infection (> 24 months; Fig. 7-2b)
Late infections are almost always of haematogenous origin, most frequently as a result of bacteremic infections of the skin (*S. aureus*), the respiratory tract (pneumococci), the intestine (*Salmonella spp.*) or the urinary tract (*Escherichia coli*).

Early infections are occasionally referred to as surface or deep. This classification is dangerous as it can be misleading, resulting in superficial revision surgery outside the deep fascia. It has been shown that failure to explore the tissues down to the implant has a very high risk of persistent infection. Acute, minimally symptomatic,
subacute or chronic infections can occur. If acute infections persist for > 3-4 weeks, this has a crucial impact on possible treatment options (Fig. 7-3). For this reason, infections can be alternatively classified as follows:

- Acute haematogenous infection (infection lasting < 3 weeks following normal postoperative progress)
- Early post-interventional infection (within a month of an invasive procedure such as implant placement, arthroscopy, etc.)
- Chronic infection (symptoms > 3 weeks after the early postoperative period)

### 7.2 Clinical symptoms and diagnostic procedures

#### 7.2.1 Medical history and findings

Symptoms and findings depend on the type of infection.

**Early infection**

Acute pain in the wound area, reddening, swelling and excess heat, possibly fever. The possibility of early infection should be considered (Fig. 7-2 a) for wounds that exude for a protracted postoperative period, if there is renewed secondary secretion or if the wound temporarily dries out (beware: generally after discharge from hospital) or with an extensive haematoma combined with signs of infection indicated by laboratory results (persistent or secondary increase in CRP). If the symptoms are not correctly recognised or if active surgical intervention does not take place within 4 weeks, fistulas generally develop and the infection can then only be cured by replacing the implant.

**Delayed infection**

Fistulas, deep latent abscesses (Fig. 7-2 b) but also non-specific symptoms such as persistent postoperative pain following an initial period without any discomfort. Occasionally sub-febrile temperatures.

**Late infection**

The symptoms of haematogenous infection are similar to those of early infection. In addition, symptoms and findings consistent with primary infection may also be present (cough and fever with pneumonia or erythema with a skin infection). Responding quickly when acute symptoms commence generally allows the prosthetic joint to be retained. The greatest risk with regard to haematogenous periprosthetic infection is septicaemia associated with Staphylococcus aureus.
7.2.2 Laboratory tests

See Chapter 6.1
- C-reactive protein (CRP)
- Blood count (thrombocytes, leukocytes, haemoglobin)
- Liver function values (AS, AT, ALAT, alkaline phosphatase) as a basis for antibiotic therapy
- Creatinine, possibly cystatin C in paraplegics (or measurement of creatinine clearance in 24-hour urine sample)

Neither CRP nor a differential blood count of leukocytes enable a periprosthetic infection to be detected or excluded. Procalcitonin is not very sensitive to localised infections, including periprosthetic infection. Empirical use of antibiotics where infection is suspected is not indicated unless the patient is systemically unwell. This compromises the sensitivity of molecular diagnostics in revision surgery with resistance testing, which must provide the basis for therapy. Fistula swabs are often misleading, as they do not enable reliable diagnosis of the pathogen due to a lack of correlation with the pathogen identified intraoperatively (irrelevant skin bacteria as a result of contamination).

Arthrocentesis
This is a key form of analysis (see Chapter 6.2). It should, however, always be carried out in consultation with the surgeon as it involves a greater risk of infection than aspiration of the native joint. The cell count in the synovial fluid is only diagnostically reliable once a period of 2 months has passed since surgery. In the case of prosthetic knee joints, an implant-related infection can be assumed with a white blood cell count > 1700/µL and/or a granulocyte percentage of > 65% with a good level of sensitivity (94% and 97%) and specificity (88% and 98%). For prosthetic hip...
joints, the thresholds are higher at 4200/µL leukocytes and/or a granulocyte percentage > 80%. At these thresholds, the sensitivity is 84% / 84% with a specificity of 93% / 82%. These values are considerably lower than the thresholds in patients with inflammatory arthropathy or with arthritis in a natural joint (see Chapters 6.2 and 9.2.3). The Gram stain test of the synovial fluid shows poor sensitivity of less than 26%. At 45–100%, the sensitivity of the culture is highly variable. It is particularly low if antibiotics have been previously administered.

The diagnostic value of cultures based on tissue collected arthroscopically or intraoperatively is significantly higher. In contrast, intraoperative swabs should be strictly avoided because biopsies have a much higher level of sensitivity.

In certain situations, special requirements must be communicated to the laboratory. For example, if long-term therapy against staphylococci has not been successful, the patient must be actively tested for small colony variants. The diagnostic laboratory should also be warned of the potential for slow-growing pathogens or those that are difficult to culture (e.g., Brucella, Granulicatella or mycobacteria). Eubacterial PCR (see Chapter 6.4) is an alternative for negative microbiological cultures.

**Sonication (see Chapter 6.5)**
Cultures of the medium in which the implants (prosthetic joints, screws, etc.) have been pre-treated by sonication offer the highest sensitivity, particularly when preceded by antibiotic therapy.

When dealing with laboratories, it is worth using a special form for implant-related infections that is suitable for microbiological and histological analyses and sonication (see Chapter 19).

### 7.2.3 Imaging

- Conventional x-ray examination (Fig. 6-3)
- Request specific analysis (see Chapter 6.3) if there are any uncertainties. If need be, antigranulocyte scintigraphy (Fig. 6-5) can help, possibly in combination with SPECT/CT.
7.3 Treatment algorithm

Primary objectives of treatment
- Elimination of the infection
- An implant that functions correctly without any pain

These objectives can best be achieved if infection is recognised at an early stage and consistent treatment principles are respected.

Five different types of intervention are possible as a rule
- Surgical debridement with retention of the implant
- One-stage implant replacement
- Two-stage implant replacement with a spacer and a short interval or without a spacer and with a long interval
- Explantation of the implant (hip, shoulder) or arthrodesis (knee, upper ankle joint, shoulder, elbow) without reimplantation
- Suppressive long-term therapy with antibiotics and no surgical intervention

There are clearly-defined criteria for each of these types of intervention. In contrast, both antibiotic therapy alone and surgical revision without adequate antibiotic therapy are inappropriate. Therapy must be jointly planned by an orthopaedic surgeon and an experienced infectious disease physician. The suggestion presented here (Fig. 7-3) corresponds to the authors’ validated procedure. To date, it has been tested for the hip, knee, elbow and shoulder, in some cases on numerous occasions. If the intervention and antibiotic therapy are correctly selected, a success rate of at least 80–90% can be expected.

Further development of this algorithm can be expected, although changes must be reviewed scientifically before they are introduced.
If all of the following criteria are met, the implant can be retained:

Duration of symptoms ≤ 3 weeks
+ Stable implant
+ No fistulas and no severe soft tissue damage*
+ Susceptibility to antibiotics and effective against adherent pathogens

Debridement with retention of the implant

If the above conditions are not all met, the implant must be removed:

Soft tissue* intact or only minor damaged

One-stage replacement

Damaged soft tissue or fistulas*

Two-stage replacement with a short interval (2–4 weeks), spacer

Microorganisms that are resistant or difficult to treat**

Two-stage replacement with a long interval (at least 8 weeks), no spacer

Anaesthesia involves a high risk, poor general condition, patient is confined to their bed

Suppressive long-term therapy with antibiotics

Prolonged medical history with various unsuccessful attempts at therapy, soft tissue is severely damaged

Explantation of the implant (hip, shoulder) or arthrodesis (knee, upper ankle joint)

Damaged bone and severely damaged soft tissue around the knee joint, sepsis cannot be controlled

Amputation

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* Damage to soft tissue is limited if after the revision uncomplicated healing can be expected, no fistulas or abscesses. During the period immediately following surgery, a weeping wound with fresh haematomas is consistent with one-stage revision surgery (Fig. 7-2).

** Microbes that are considered difficult to treat include enterococci, small-colony staphylococci variants, quinolone-resistant Pseudomonas aeruginosa as well as all types of multi-resistant microorganisms or fungi. Meticillin-resistant S. aureus are a problem primarily associated with hospital hygiene in cases where there is no additional multi-resistance, e.g., against rifampin.

Fig. 7-3: The algorithm for surgical treatment principles in infections associated with prosthetic joints
7.4 Surgical treatment

Surgical treatment requires experience, as the so-called ‘standard case’ more often than not is an exception. This is particularly true when evaluating preoperative clinical findings and postoperative progress with its associated pitfalls. Surgical measures are classified into those that are essentially the same across all 5 types of intervention and those that are typical for particular treatment approaches.

7.4.1 Cornerstones of surgical treatment

Approach
The selected approach must be large enough to ensure good visibility. Particularly in the hip area, following minimally-invasive approaches, it is sensible to select a new approach that also enables transfemoral approaches or trochanteric osteotomies. It is crucial that aggressive debridement and complete explantation even of a fixed implant can be done without risking additional bone or soft tissue damage. Knee approaches also usually require widening and are often supplemented using a tuberosity osteotomy.

Debridement
Debridement equates to cleaning up the site of infection. Its primary objective is to reduce the bacterial count at the site of infection to optimise the conditions for antibiotic therapy (see Chapter 3.1). Radical excision of the periprosthetic tissue is mandatory. In the case of a fistula, it is useful to fill the tract with a mixture comprising one part methylene blue and one equal part x-ray contrast agent (Fig. 7-1). This allows the use of an image intensifier to estimate the extent of the fistula prior to revision surgery, and complete wound excision can then be achieved using the dye. Extensive joint capsule protrusions and fistulas also require resection (see Fig. 6-2). In prosthetic joint infections, necrotic bone only requires resection in exceptional cases (Fig. 7-1). Lavage of the wound bed, perhaps with the addition of antiseptic, e.g., polyhexanide, appears useful. The benefits of using jet lavage are disputed as bacteria may be forced deeper into the tissue.

For infectious synovitis, open synovectomy is clearly preferable to arthroscopy, also for the knee joint. Tissue samples must be collected from the periprosthetic area (see Chapter 6.4). The less likely an infection is, the greater the number of samples that must be collected – a pair of samples from each site with one each for histology and bacteriology. Do not take swabs. They show very poor sensitivity due to the small amount of material obtained and the potentially antibacterial effect of the swab itself.
Drainage
Thorough drainage of the surgical site is essential. The drains should have a large diameter and be evenly distributed across the surgical site so that the lumens are not immediately sealed by coagulate. Often, large quantities of exudate are drained over the course of several days as there is considerable soft tissue oedema, particularly with acute infections. Nevertheless, drains should be removed as soon as possible when an implant is present, by about day 4.

Skin suture
Following tight fascial suture closure, the subcutaneous area is reduced by suturing. Assuming that sufficient tissue reserves are available, scars should be excised and the healthy skin precisely co-apted prior to skin suturing. In the event of excessive tension or defects, see ‘Restoration of soft tissue’ below.

Follow-up revisions
Following the removal of the Redon drainage set after revision surgery, secondary fluid accumulation may occur. Regular, careful checks of the scar area are mandatory. If there is a risk that the wound could reopen, immediate revision surgery with renewed drainage must be recommended. The fluid that accumulates in deep areas is generally sterile. However, if the wound opens prior to revision surgery, there is a risk of exogenous superinfection.

The alternative option is a second look procedure. This is routinely scheduled 3–5 days after surgery in order to facilitate postoperative lavage of the haematoma. Insertion of sponge for negative-pressure therapy in the subfascial plane has been described but with little documented evidence (see Chapter 5).

The steps described above apply for all revision procedures.
7.4.2 Specific techniques in surgical treatment

Debridement without explantation of the implant
The procedure must be carried out within 3 weeks of the symptoms of infection occurring (Fig. 7-2a). Prior arthrocentesis is advisable as this allows any resistant bacteria that may be present to be identified. The measures correspond to those described above. Most experts recommend that mobile prosthetic parts be replaced. Our own investigations do not support this view. The explanted parts can be analysed using sonication. Particularly for the knee, thorough debridement of the popliteal fossa is only successful if the inlay is removed, even if only temporarily. Follow-up treatment is functional.

One-stage implant replacement
Prior arthrocentesis is advisable. Specific surgical steps:

- Implant explantation: loose implants must always be removed prior to infection revision procedures. If the infection persists for longer than 3 weeks, securely fixed implants should also be removed. Cementless implants must be handled in the same way as cemented implants. All foreign bodies in the implant area – including small residual amounts of cement and screw tips that have broken off – must be completely removed.

- Implant reimplantation: in our experience, the implant may be selected based on the local bone stock. It is equally possible to use cemented or cementless models. Due to the low recurrence rates, it was not possible in our follow-up examinations to make any inferences as to whether certain implants are more likely to result in a recurrence. Other schools of thought recommend cemented implants, which require special revision cements to protect the periprosthetic area. Alternatively, high concentrations of specially selected antibiotics can be mixed with the cement. For information on antibiotics suitable for this purpose as well as the mixing technique to be used, see Chapter 4.4.3 and Fig. 4-3. For the knee, the use of a hinged prosthesis is advisable in situations where synovitic swelling has resulted in significant loosening of the ligaments. Correct reconstruction of the extensor mechanism is crucial to success. There is little documented evidence regarding the value of silver-coated tumour implants (see Chapter 4.4.6). Follow-up treatment corresponds to that of revision surgery that is not associated with infection.
Two-stage implant replacement with a spacer and a short interval

This variant is particularly suited to difficult soft-tissue situations but not for problematic bacteria (Fig. 7-2b, 7-4).

Fig. 7-4: ♀ 67 years of age: protracted infection, left hip, with posterior luxation and fistulas. S. aureus. Two-stage replacement with a short interval.

- Spacers: these should ideally be adapted to the existing defect so that no bone must be sacrificed to anchor the spacer and secure fixation. For this reason we recommend custom made spacers (see Chapter 4.4.3). In the hip and shoulder area, hemispheres shaped using shell moulds can be used, in combination with a stem that is reinforced in the centre using metal (Fig. 4-4, 7-5). In the knee, spacers can be created using the original implant as the basis for the shell moulds (Fig. 4-5). Spacers should intentionally maintain length, reduce the risk of dislocation and, at the very least, facilitate mobility when not bearing weight. They allow for greater patient comfort during the intervening period between removal and reimplantation of the implant. The placement period is calculated based on the algorithm.

Fig. 7-5: Spacer preparation. a) In combination with an angled plate, the head is moulded in an appropriately-sized shell. b) The plate acts as a central reinforcement. High viscosity cement is modelled and the formed spacer is pressed into the cleaned medullary cavity. c) Prior to reimplantation, the spacer can generally be tapped out in one piece.
Others favour leaving the spacer for 3 months with replacement only after a period of 4 weeks without antibiotics. As a result, the wear resistance of the articular components is very important. Monitoring of the infection is performed by measuring the CRP level. The sensitivity of aspiration – even after a period without antibiotics – is uncertain.

- Restoration with soft tissue defects: this is often particularly important in the knee area and ankle joint. The most reliable results can be achieved if soft tissue cover is achieved when the implant is removed or within 2 weeks. Free flaps may be complex, but they do not damage the soft tissue surrounding the implant (Fig. 7-6). In the knee, gastrocnemius muscle flaps often present a useful alternative (Fig. 7-7). Smokers must abstain completely from nicotine while treatment is in progress.

- Reimplantation: apart from the necessary prior removal of the spacer, the reimplantation of a prosthetic joint corresponds to the one-stage procedure.
- Follow-up treatment: using a spacer, joint mobility may be encouraged within the limits of acceptable discomfort. Weight-bearing is not increased if the interval until reimplantation is short. Following reimplantation, functional follow-up treatment must be arranged, similar to that of standard revision surgery.
Two-stage implant replacement without a spacer and with a long interval
This method of treatment requires an extended plastic splint for the hip when lying down, or in the case of the knee, a unilateral external fixator (Fig. 7-7). The interval of at least 8 weeks allows 6 weeks of curative antibiotic therapy, even in the case of bacteria that are difficult to treat, followed by a break of 2 weeks without any antibiotics.

Once the implant has been removed, follow-up treatment must be adapted to the selected method. Limited bed rest with hip extension. Mobilisation with rolling movement with an external fixator over the knee.

On reimplantation, broad spectrum antibiotics are administered for prophylactic purposes (see Chapter 2.6.2) so that the original antibiotic therapy can be resumed until the results from the samples collected intraoperatively are obtained.

Explantation of the implant (hip, shoulder) without reimplantation or arthrodesis (knee, upper ankle joint, shoulder, elbow)

Explantation of the implant only (Girdlestone hip): when the implant is removed, the muscles extending up to the proximal femur should be protected as far as possible. If a supracondylar Steinmann pin traction was previously carried out for 4–6 weeks in combination with bed rest, the only measures required are an extended plastic cast during the night with mobilisation during the day.
Knee arthrodesis: arthrodesis with an external fixator (Fig. 7-8) is the most reliable approach from an infectious disease perspective but it is difficult, particularly where large bone defects are present.

Fig. 7-8: 55 years of age: Clinical condition after 2 knee replacements and problems with the extensor mechanism (revised several times). Arthrodesis performed with a three-dimensional external fixator, stable consolidation at 7 months with 4 cm shortening.

It is not unusual for remaining pseudarthrosis to require subsequent repair with an extended interlocking nail or plate osteosynthesis. The use of what is known as an arthrodesis nail with a spacer effect following curative antibiotic therapy is suggested, however, it is associated with a risk of recurrent infection particularly with bacteria that are difficult to treat.
Suppressive long-term therapy with antibiotics and without surgical intervention
This should be restricted to individual patients for whom the risk of surgical treat-
ment cannot be justified and for whom no tangible benefit would be derived. The
daily application of a fistula pouch (stoma bag) is often necessary.

7.5 Antibiotic therapy

Prior to commencing any antibiotic therapy, the bacteria responsible and their
levels of resistance must be verified. Antibiotic therapy is clearly defined for pro-
thetic joint infection with staphylococci. Numerous studies have shown that com-
binations with rifampicin are particularly effective as this medication actively com-
bats staphylococci in the adherence or stationary growth phase. Rifampicin must
always be administered in combined form, ideally together with quinolones (cipro-
floxacin, levofloxacin) or with fusidic acid in the event of resistance to quinolones.
There are insufficient data available regarding other combinations such as with co-
trimoxazole, clindamycin, minocycline or linezolid. The usual choice of antibiotics
based on the spectrum of pathogens is summarised in Tab. 7-1.

Tab. 7-1: Antibiotic therapy of infections* associated with prosthetic joints

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Antibiotic</th>
<th>Dose</th>
<th>Application</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Staphylococcus aureus or coagulase-negative staphylococci</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methicillin-susceptible</td>
<td>Flucloxacillin¹ + rifampicin</td>
<td>2 g every 6 hours</td>
<td>IV PO/IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>450 mg every 12 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td>For 2 weeks, followed by</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ciprofloxacin</td>
<td>750 mg every 12 hours</td>
<td>PO</td>
</tr>
<tr>
<td></td>
<td>or levofloxacin</td>
<td>500 mg every 12 hours</td>
<td>PO</td>
</tr>
<tr>
<td></td>
<td>Both + rifampicin</td>
<td>450 mg every 12 hours</td>
<td>PO</td>
</tr>
<tr>
<td>Methicillin-resistant</td>
<td>Vancomycin + rifampicin</td>
<td>1 g every 12 hours</td>
<td>IV PO/IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>450 mg every 12 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td>For 2 weeks, followed by</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ciprofloxacin² or levofloxacin² or teicoplanin</td>
<td>750 mg every 12 hours</td>
<td>PO</td>
</tr>
<tr>
<td></td>
<td>or fusidic acid</td>
<td>500 mg every 12 hours</td>
<td>PO</td>
</tr>
<tr>
<td></td>
<td>or co-trimoxazole</td>
<td>400 mg every 24 hours</td>
<td>IV/IM</td>
</tr>
<tr>
<td></td>
<td>or minocycline</td>
<td>500 mg every 8 hours</td>
<td>PO</td>
</tr>
<tr>
<td></td>
<td>All + rifampicin</td>
<td>1 forte table every 8 hours</td>
<td>PO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>100 mg every 12 hours</td>
<td>PO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>450 mg every 12 hours</td>
<td>PO</td>
</tr>
</tbody>
</table>
Tab. 7-1: Antibiotic therapy of infections* associated with prosthetic joints (continuation)

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Antibiotic</th>
<th>Dose</th>
<th>Application</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Streptococcus spp.</em> (except <em>Streptococcus agalactiae</em>)</td>
<td>Penicillin G or ceftiraxone</td>
<td>5 million units every 6 hours 2 g every 24 hours</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>For 4 weeks, followed by</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Amoxicillin</td>
<td>750–1000 mg every 8 hours</td>
<td>PO</td>
</tr>
<tr>
<td><em>Enterococcus spp.</em> (penicillin-susceptible) and <em>Streptococcus agalactiae</em></td>
<td>Penicillin G or amoxicillin + aminoglycoside</td>
<td>5 million units every 6 hours 2 g every 4–6 hours</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>For 2 to 4 weeks, followed by</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Amoxicillin</td>
<td>750–1000 mg every 8 hours</td>
<td>PO</td>
</tr>
<tr>
<td><em>Enterobacteriaceae</em></td>
<td>Ciprofloxacin</td>
<td>750 mg every 12 hours</td>
<td>PO</td>
</tr>
<tr>
<td><em>Non-fermenters</em> (e.g., <em>Pseudomonas aeruginosa</em>)</td>
<td>Ceftazidime or cefepime + aminoglycoside</td>
<td>2 g every 6 hours</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>For 2 to 4 weeks, followed by</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ciprofloxacin</td>
<td>750 mg every 12 hours</td>
<td>PO</td>
</tr>
<tr>
<td><em>Anaerobes</em> (e.g., <em>Propionibacterium acnes</em>)³</td>
<td>Clindamycin</td>
<td>600 mg every 6–8 hours</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>For 2 to 4 weeks, followed by</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Clindamycin</td>
<td>300 mg every 6 hours</td>
<td>PO</td>
</tr>
<tr>
<td><em>Co-infection</em> (without methicillin-resistant staphylococci)</td>
<td>Amoxicillin/clavulanic acid Carbapenem</td>
<td>2.2 g every 8 hours Depending on the preparation</td>
<td>IV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>For 2 to 4 weeks, followed by</td>
<td></td>
</tr>
</tbody>
</table>

Note: resistance testing should be carried out for each pathogen prior to beginning therapy. The dose is specified for adults with normal kidney and liver function. PO = oral; IV = intravenous; IM = intramuscular.

* The total duration of antibiotic therapy in patients in the case of implant retention, one-stage replacement or two-stage replacement with a short interval (2–3 weeks): 3 months for hip, shoulder and elbow implants and 6 months for knee implants. This therapy duration has not yet been verified in any controlled comparative study, which is why IDSA Guidelines have retained these recommendations. However, observational studies have also described shorter therapy regimens as effective.

1 In patients with a hypersensitivity reaction (exanthem), cefazolin can be administered (2 g every 8 hours, IV). In patients with an anaphylactic reaction, beta-lactams must be substituted by vancomycin (1 g every 12 hours, IV).

2 Methicillin-resistant *Staphylococcus aureus* should not be treated using quinolones as these could develop resistance during therapy.

³ Alternatively, penicillin G or ceftriaxone can be administered to combat Gram-positive anaerobes such as *Propionibacterium acnes*, and metronidazole (500 mg every 8 hours, IV or PO) can be administered to combat Gram-negative anaerobes such as *Bacteroides spp.*
For periprosthetic joint infection, the principle is that all pathogens must be eliminated as the body’s own immune system cannot eliminate persistent pathogens. We recommend a duration of therapy of 3 months for hip implants and 6 months for knee implants. Using an infection therapy passport (see chapter 18) makes it significantly easier to support outpatient therapy of this kind over a longer period of time. This passport also specifies all the necessary laboratory tests for the various antibiotics.

7.6 Expected clinical results

One-stage replacement generally results in better functional outcomes than two-stage replacement. In the knee, the best results are achieved following debridement and implant retention. However, the appropriate therapeutic approach must be selected based on the algorithm.

7.7 Don’ts

- No antibiotic therapy without a microbiological diagnosis
- No intraoperative swabs; instead, biopsies for cultures and histology
- No exclusively oral therapy with substances with poor bioavailability (penicillins, cephalosporins)
- No monotherapy using rifampicin
- Only begin using rifampicin once the wound has dried (risk of introducing resistant strains of staphylococcus)
- No monotherapy using quinolones to combat staphylococci
7.8 References

Further reading


Additional articles

8  Infected osteosynthesis, infected nonunion and chronic osteomyelitis

Peter Ochsner, Werner Zimmerli

8.1 Fundamentals

8.1.1 Aetiology

Most infections following osteosynthesis are exogenous (= acquired pre-, intra- or postoperatively); haematogenous infections are rare. Entry points include open wounds, surgical incisions and postoperative wounds with impaired healing. Specific risk factors include open fractures, severe soft tissue injuries and complex fractures with extensive devascularisation of the bone and soft tissues (Fig. 8-1).

<table>
<thead>
<tr>
<th>Infection presentation</th>
<th>Early (Within 2 weeks)</th>
<th>Delayed (3–10 weeks)</th>
<th>Late (&gt; 10 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haematogenous (rare)</td>
<td>Catheter infections,</td>
<td>S. aureus septicemia, skin and soft tissue infections, urogenital infections, Salmonella Enterocolitis</td>
<td></td>
</tr>
<tr>
<td>Timeline</td>
<td>Day 1</td>
<td>1/2 week</td>
<td>3/4 week</td>
</tr>
</tbody>
</table>

Fig. 8-1: Connections between time of occurrence, cause and manifestation of post-traumatic infections
Bacteriology is multi-faceted. With closed fractures, infections tend to be monomicrobial, while with open fractures the infections are often polymicrobial. Particularly common microorganisms include *Staphylococcus aureus*, coagulase-negative staphylococci, streptococci and Gram-negative bacteria. Anaerobes, enterococci and others are rare.

**Acute infections following osteosynthesis** (Chapter 8.6)
These infections occur due to colonisation of local soft tissues within the wound or surgical area. If not treated properly, bacteria become established in necrotic osseous areas and in biofilms on implants (see Chapter 1). They often develop acutely and present soon after osteosynthesis. They must be differentiated from haematomas and impaired wound healing which are often precursors to infection. The decision concerning timely revision is based on skill, instinct and experience. In this case, it is better to perform one too many revisions than to miss the right moment.

**Infected nonunion** (Chapter 8.7)
The onset of infected nonunion is often gradual with few obvious clinical symptoms. Bacteria penetrate the region of the fracture and colonise areas of bone necrosis in the fracture zone. Here, for example, they can escape cellular defences by taking refuge in osteocyte cavities (see Chapter 8.2). Antibiotic regimens that are too short or involve dosages that are too low without prior debridement may be able to temporarily suppress the infection but union of the fracture will usually be delayed and the infection will persist.

**Chronic post-traumatic osteomyelitis** (Chapter 8.8)
This occurs when bacteria persist in the remaining necrotic bone or in the biofilm on any foreign materials remaining in the body. A stable bridge is established over the earlier fracture zone. The focus of the osteomyelitis with sequestered fragments of dead bone is often surrounded by a massive periosteal involucrum. Fistulas caused by sequestrated bone fragments may reopen even decades later. This cycle often involves fistulas that close temporarily, resulting in retention pain, followed by a reopening of the fistulas. Chronic haematogenous osteomyelitis must be considered as a differential diagnosis (Chapter 8.9).
8.1.2 Incidence

An acute infection or infected nonunion is to be expected in about 2–4% of all osteosynthesis procedures. In the case of open fractures, particularly Gustilo 3B injuries (see Chapter 16), the incidence is considerably higher and may be over 30%. Conversely, chronic osteomyelitis is rare but is often very persistent.

8.1.3 Classification options for estimating the severity of post-traumatic infections and/or the spread of bone necrosis

The appearance of post-traumatic infections varies widely. In contrast to periprosthetic joint infections, it is difficult to establish a readily comprehensible algorithm. It is necessary to develop an individual picture of each infection for which the following factors are particularly important: age of the patient, extent of the trauma, time of initial manifestation, localisation and type of osteosynthesis.

Age of the patient
Severe, direct traumas mainly affect young men, 15 to 35 years of age, and are much rarer in women. Soft tissue atrophy, osteoporosis and frailty associated with advanced age have a negative impact on the prognosis.

Extent of the trauma
Clinicians rely mainly on fracture classification, soft tissue assessment and the accident history to evaluate the degree of severity.

- Fracture classification: the Müller AO classification system is organised on the basis of fracture severity. Type C fractures are particularly serious, especially those fractures in subgroup 3.3.
- Soft tissue evaluation: the Gustilo open fracture classification system is very important here (see Chapter 16). Grade 3B fractures have a particularly poor prognosis. Although severe soft tissue injuries are important for the prognosis, they are difficult to classify. Major soft tissue defects, exposed areas of bone and fistulas present at the start of treatment have a negative impact on the prognosis.
- Accident history: reconstructing the exact sequence of events that led to the accident provides essential clues as to the severity of the trauma. Motorcycle accidents and falls from great heights are especially serious. Indirect traumas are less significant than improper treatment.
Time of initial presentation of the infection
Point at which clinical signs of infection (erythema, pain, fistulas, leukocytosis, persistently elevated C-reactive protein [CRP]) first appear:
- Early = up to 2 weeks after surgery: with early detection, in cases with stable fixation, these infections can usually be healed using debridement accompanied by targeted antibiotic therapy and possibly measures involving the soft tissues but with no need for any complex measures.
- Delayed = 3–10 weeks after surgery: symptoms often appear gradually in such cases. These infections impair bone healing, typically resulting in infected non-union. Treatment can be extremely demanding and time-consuming.
- Late = more than 10 weeks after surgery: fracture bridging is usually well underway prior to manifestation of the infection. Treatment can be standardised and is often successful.

Localisation of the infection
The site of the infection often determines the success or failure of treatment. Thick surrounding soft tissues – even if they are more severely damaged – are easier to repair than thin surrounding soft tissues. Reconstruction processes are faster in spongious bone than in cortical bone. The prognosis is particularly poor if joints are involved.
- Superficial – deep
  - Superficial infections with limited soft tissue cover (e.g., malleolar fractures, distal radius fractures, elbow fractures): clinically, these can be detected early. Laboratory infection parameters are usually only slightly elevated and are sometimes even normal. They are significantly elevated only in acute infections.
  - Infections occurring in bones with good soft tissue cover e.g., femur and humerus fractures): these are often accompanied by diffuse pain. They are often diagnosed late based on a fistula that splits open, elevated infection parameters (CRP, leukocytosis) or an imaging procedure.
- Diaphyseal – epi/metaphyseal
  - Diaphyseal infections affect the cortical bone. Large areas of necrotic bone must be expected with comminuted fractures. This often leads to time-consuming treatments. The joints are only rarely involved.
  - Epi/metaphyseal infections almost always affect the joints as well (especially in the case of major traumas). Although the joints are soon differentiated from the osseous focus of infection due to the rapid healing of spongious bone along the joint, intra-articular malalignment is virtually impossible to correct following the onset of an infection.
Type of osteosynthesis and associated bone necrosis

Each osteosynthesis results in a special pattern of necrotic bone based on interactions with the fractured bone. An extended bone necrosis makes it difficult to treat the infection. The necroses associated with both the fracture and osteosynthesis must be estimated to identify all the necrotic bone. Each fixation method involves a typical risk of necrosis:

- **External fixation (Fig. 8-2a):** An external fixator is primarily used for severe trauma, e.g., grade 3 open fracture. When applied at a suitable distance from the fracture, it preserves the fracture zone and soft tissues. Blunt drill bits and high drill speeds may overheat the bone, while using Schanz screws with a diameter greater than the drill hole may result in local bone cracks. The resulting local bone necrosis may allow bacteria to penetrate the bone along the Schanz screws, potentially causing local infections. Drill hole osteomyelitis results, which could potentially spread to the fracture zone. This may also compromise any conversion to internal osteosynthesis. However, external fixation leaves the periosteum virtually undamaged.

**Fig. 8-2:** Impact of various osteosynthesis techniques, including a) external fixation, b) plate and c) reamed interlocking nail with closed reduction, on bone necrosis and ongoing bone development. For details, see text.
Plate osteosynthesis (Fig. 8-2b): with plate osteosynthesis, the following measures may cause bone necrosis in addition to the initial trauma: stripping the periosteum from the bone prior to plate application, large contact surface in the case of plates without undercuts or incorrect or repeated drilling of screw holes. Plates with fixed-angle locking screws achieve stability of the fracture without compressing the plate onto the bone, which may reduce the extent of bone necrosis induced by the plate. There is only limited documented evidence as to whether minimal access plating through small percutaneous incisions causes less soft tissue or bone damage. Plates prevent periosteal new bone formation in the area covered by the plate, which is especially important for osseous bridging in the case of infected non-union.

In summary, a plate will cause periosteal and bone damage to varying degrees. A plate fixed to the bone makes periosteal bone formation impossible. If an infection occurs, then it can be restricted to the vicinity of the plate if the soft tissue and bone environment are alive (infected plate). Small, adjacent bone necroses may lead to microsequestra under the plate. If more extensive bone necroses are also involved, then this is called a plate osteomyelitis.

Reamed interlocking nail with closed reduction (Fig. 8-2c): The narrow central areas of the medullary cavity are expanded using the intramedullary reamer following insertion of a wire guide. This destroys the intramedullary vessels. Local endosteal devascularisation is influenced by the local damage to the intramedullar vessels by the reamer and the overheating of the cortical bone by blunt intramedullary reamer heads. In exceptional situations extremely severe heat necrosis can involve the whole thickness of the cortex.

On the other hand, drilling forms bone debris that mixes with haematoma in the fracture region and has an osteoinductive effect similar to an autologous spongioplasty. To preserve the residual adhesion of the bone fragments to the periosteum in the case of a comminuted fracture (Fig. 8-2c), the intramedullary reamer can be stopped anterior to the fracture zone and passed over this area to then continue reaming the distal main fragment. Recent studies have shown that the benefits of any resulting bone debris in the restoration of the fractured bone outweigh the risk of infection associated with local devascularisation due to drilling.

If an infection develops, it will spread along the entire intramedullary nail and interlocking screws (intramedullary nail osteomyelitis). The infection becomes established on the metal and in the areas of bone necrosis. Fistulas may
form at the level of the fracture but also at the entry points of the nails and interlocking screws. Small sequestra may demarcate at the surface of the cortical bone around the nails, particularly with central intramedullary zones that have been reamed.

**Combined classification according to Cierny and Mader**

This classification is mainly used in the anglo-american literature. It differentiates four anatomic types of osteomyelitis:

- **Type I**: Medullary osteomyelitis. Infection within the medullary cavity, usually without involvement of the epiphyseal area.
- **Type II**: Superficial osteomyelitis involving the outer cortical area, the subcutaneous tissue and the skin. The infection resides in an isolated area.
- **Type III**: Localized osteomyelitis involving the whole cortical thickness and the adjacent medullary canal
- **Type IV**: Diffuse osteomyelitis as a fully developed disease of an entire segment of bone. It involves both the cortex and the medullary cavity, leading to extensive devitalisation.

Classification is difficult due to the lack of a clear delineation between types; as a result, this system has not become firmly established in the German-speaking countries.

### 8.2 Bone development around the fracture in the case of infections

The following main causes must be considered when estimating total bone necrosis:

- Accident
- Previous surgical and conservative treatments
- Implants used (Fig. 2 a-c)
Infected osteosynthesis, infected nonunion and chronic osteomyelitis

Fig. 8-3: ♂ patient, 25 years of age: a) incomplete wedge fracture with direct trauma, plate osteosynthesis. At b) 3 weeks, c) 2½ months, d) 4 months, successive demarcation of the wedge fragment and widening of the fracture gap but dorsolateral bridging callus, e) following removal of the metal and the visible sequestrum, residual bone bleeding but irregular bone structure, external fixation, successive bone remodeling, f) situation at 5 years without any further measures
Examining all available x-rays in chronological order provides the most useful information in order to estimate bone necrosis. Taken together, they enable functional processes to be identified. Over time, periosteal reactions, the fusion of bone fragments, local bone hypertrophy but also sequestrations can be observed or at least surmised. In diagnosis of an infection, three-phase scintigraphy of the skeleton, possibly in connection with SPECT/CT, and computed tomography supplement the suspected diagnosis (see Chapter 6-3), particularly in cases of infected non-union and chronic osteomyelitis.

- Periosteal bone formation requires a living periosteum and provides evidence of the vitality of the underlying bone. Under infectious conditions, newly formed bone is for the most part not susceptible to infection. There are some exceptions (Fig. 8-8). New periosteal bone may centralise sequestra (Fig. 6-4).
- The lack of a periosteal reaction over a prolonged period is indicative of necrotic bone.
- If particular bone fragments or segments lose bone density, then this is evidence of bone remodelling and thus viability. If bone segments appear more dense than the surrounding bone over time, then this is evidence of bone necrosis.
- If two adjacent bone fragments fuse together, then at least one of these fragments must be vital. Following fusion, the ongoing remodelling process will cross the fragment margin, potentially revitalising dead fragments.
- The formation of irregular edges with fine corners on the surface of the bone is indicative of osteoclast activity in a region with bone necrosis. If small or large bone fragments separate from other fragments during this process, then these are called sequestra.
- The bone remodelling processes originating from vital areas of bone combine at some point with those involving the formation of sequestra from dead areas of bone. At this point, any local sequestra are successively surrounded by new periosteal bone formation.
- Temporary administration of antibiotics may inhibit local infection activity and impede sequestrations, thus fostering revitalisation without being able to heal the infection.
- Under unstable fracture conditions, infections cause massive delays in bone healing or make it impossible for the bone to heal at all.
8.3 Confirmation of infection

Meeting at least one of the following criteria provides proof of infection:
- Abscess with pus discharge following incision
- Presence of a fistula
- Microbiological detection of the same pathogen in at least two samples (tissue samples, sonication fluid)
- Histological preparations containing a total of more than 20–25 granulocytes in 10 fields of view at 400 x magnification (Morawietz et al. 2009).

Abscesses and fistulas are expressions of a deep infection. They originate from bacteria that have become established in necrotic osseous areas and in biofilms on implants. Microbiological detection of infection can only succeed if strict rules are observed (see Chapter 6.4). Fistula swabs often detect contaminating microbes and should therefore not be used as a basis for treatment. Histological tests become much more important if bacteriological results are negative or if it is necessary to distinguish between contaminants and pathogenic bacteria. To obtain meaningful information in precisely these situations, using a special form for coordinated histological and microbiological testing of tissue and sonication of foreign materials is advisable (see Chapter 19).

8.4 Post-traumatic arthritis

There is a risk of post-traumatic arthritis in cases of
- direct joint injury or
- spread of an infection from an infected osteosynthesis into the joint during the first weeks following fracture treatment.

Timely detection and treatment of joint infections is crucial for positive long-term outcomes. As a result, clinicians must actively examine patients for any joint involvement and start appropriate treatment immediately. Chapter 9 describes the procedure for large joints. For small joints, (repeated) aspiration and simultaneous antibiotic treatment of the septic arthritis are generally sufficient. A few weeks following fracture osteosynthesis there is no risk of arthritis developing because by then the joint region will once again be completely separated from the adjacent and infected bone structure.
The long-term prognosis will depend on timely and effective infection treatment and reconstruction of the joints during osteosynthesis. Inappropriate measures not infrequently lead to subsequent post-infection osteoarthritis, requiring arthrodesis (ankle joint, wrist joint). The insertion of prosthetic joints is associated with a considerably elevated risk of infection (knee, hip).

8.5 Antibiotic therapy

8.5.1 Indications

Antibiotics are used to supplement surgical treatment in the following situations:

- With early infections and stable implants, following debridement as a curative therapy, provided that the pathogens are susceptible to antibiotics effective against adherent bacteria (biofilm). This is the case with rifampicin-susceptible staphylococci or quinolone-susceptible Gram-negative rods.
- With infections lasting more than 3 weeks, if the implants are stable and the fracture is showing signs of bridging after the debridement. In such situations, antibiotics are administered as a suppressive therapy until consolidation. Once consolidation has been achieved, the metal is removed, debridement is repeated and antibiotic therapy is continued for several weeks for curative purposes.
- With debridement, metal removal and sometimes with stabilisation using an external fixator as a curative therapy.

It is essential that an empirical therapy is not administered without first collecting microbiological tissue samples.

8.5.2 Duration of therapy, problems

Curative therapy typically lasts 6 weeks for post-traumatic infections. A longer period is probably advisable in cases of osteomyelitis that have persisted for decades. Suppressive therapy is continued until the fracture consolidates and the osteosynthesis material is removed. If implants are involved, then the therapy is administered parenterally for 2 weeks. Osteomyelitis without implants may be treated orally for the entire duration of therapy provided appropriate antibiotics with good bioavailability are available for the pathogen, based on resistance testing (see Chapter 3.3).
The clinical presentation of acute infections following osteosynthesis has changed thanks to the systematic use of antibiotic prophylaxis. Infections that can be detected within the first few days have become rarer, while infections with delayed presentation and less clear infection symptoms have become more common. As a result, delayed detection of slowly developing infections or the use of empirical antibiotic therapy prior to confirmation of the diagnosis have unfortunately become more common. Because patients are generally discharged early from hospital, the role of rehabilitation specialists and general practitioners is critical for early detection of infections.

8.6 Early first presentation – infected osteosynthesis

8.6.1 Clinical symptoms and diagnostic procedures

Medical history and clinical findings (Fig. 8-4, 8-5)
Pain after a few days, sudden discharge of pus or gradually increasing swelling with newly exuding wound. Impaired wound healing, haematoma, erythema, swelling, excess heat (Fig. 8-4).

Important: always examine patients for post-traumatic arthritis in the case of intra-articular fractures (see Chapter 8.4).

![Fig. 8-4: Various images of early first presentation: a) acute infection at 6 days, b) elbow infection at 10 days, c) infection at 14 days](image)

Laboratory tests
Elevated white blood cell count and/or left shift. CRP remains elevated in the follow-up examination or increases again secondarily.
Imaging
X-ray: is the osteosynthesis stable? Is the involved joint reconstructed anatomically? Additional imaging within the first two weeks is of less importance than the interpretation of the clinical symptoms by an experienced clinician. Changes in the lab values (CRP, white blood cells) are to be observed.

8.6.2 Indications for active treatment

- Acute inflammation in the surgical field with differential diagnosis of postoperative haematoma
- Suspected infectious arthritis with status post osteosynthesis of a joint fracture
- Wound with impaired healing combined with elevated inflammatory markers

Fig. 8-5: 66 years of age: a) lateral tibial plateau fracture, b) aligned and supported by osteosynthesis, c) acute infection 18 days, before and after surgical revision with debridement and drainage for three days, lavage with antiseptic, amoxicillin/clavulanic acid, then flucloxacin IV, later ciprofloxacin and rifampicin PO for a total of 6 weeks, d) situation after 4 months before metal removal, e) symptom-free after 1 year.
8.6.3 Surgical treatment (see Chapter 7.4.1)

Debridement (Fig. 8-5)
Debridement is intended to remove haematoma, collect tissue for microbiological and histological diagnostics (see Chapter 6.4) and verify that the osteosynthesis device is stable and seated correctly. Start with empirical or targeted antibiotic therapy following diagnostic tissue collection. This is followed by extensive drainage and wound closure provided this can be done without introducing tension into the soft tissues. If closure is not possible, application of an antiseptic drape (see Chapter 4.3.2) or a negative-pressure dressing (see Chapter 5.3), is immediately followed by planning of closure together with a plastic surgeon within 8 days.

Bone transplants
These should usually be avoided in early infections (see Chapter 8.7.3).

Plastic defect closure
Where indicated, this can be performed following surgical management of arthritis or osteomyelitis and initiation of appropriate antibiotic therapy based on potential resistances. In addition, the soft tissue status must allow for defect closure. These cases mainly involve the use of split-thickness skin grafts (mesh grafts), local rotation flaps (e.g., gastrocnemius muscle flaps) (see Chapter 8–12) or wing flaps. More elaborate procedures are rarely necessary, except in cases of open fractures.

8.6.4 Prognosis and complications

Prognosis
The earlier the detection, the sooner the surgical debridement, the better the skin closure and the more targeted the antibiotic therapy, then the more favourable the prognosis for rapid healing of the infection and prevention of infectious arthritis.

Complications
Undetected infectious arthritis with secondary arthrodesis, occurrence of difficult-to-treat bacteria, sequestration of large, necrotic bone fragments, transition to infected non-union and chronic osteomyelitis follow inconsistent therapeutic attempts using surgery and antibiotics.
8.7 Delayed first presentation – infected nonunion

8.7.1 Clinical symptoms and diagnostic procedures

Medical history and clinical findings
Difficulty walking and load-dependent pain are predominant. The latter is absent if the periosteum surrounding the non-union experienced massive destruction due to the severity of the trauma. This is of decisive clinical significance for subsequent treatment because the patient will be unable to comply with load limitations and will thus require special assistance. Spontaneous discharge of small sequestra may be observed in some cases.

Functional status assessment of the lower leg
This is important in view of what are often very elaborate reconstruction efforts, sometimes lasting more than one year. It involves deciding between a reconstruction attempt and amputation. The following factors favour preservation:
- Foot: intact plantar sensitivity, no or correctable pes equinus, pain-free ankle joint with above-average mobility or fixed at right angle
- Knee: above-average mobility, no severe or painful osteoarthritis, no or correctable malposition (axis or rotation)
Other regions of the body to be reconstructed must be similarly assessed from a functional standpoint.

Clinical findings
Limping or use of crutches, impaired mobility, occasionally intermittent fistulas but also complete fistula systems (Fig. 8-6 b,c).

Fig. 8-6: Various clinical symptoms of infected pseudarthrosis: a) scar zone without fistulas, b) intermittent fistula, c) purulent fistula system.
**Laboratory tests**
Infection parameters (white blood cells, CRP) are often normal or only moderately abnormal.

**Imaging (see Chapter 6.3)**
- Standard x-rays: these are the most important basis for a diagnosis. In addition to follow-up examinations (Fig. 8-3), recent images in 4 views (anterior-posterior, lateral and obliques) are especially informative (Fig. 8-7). These 4 views are also suitable for monitoring postoperative progress. The condition of the non-union is of particular interest: the extent of an existing bone defect, periosteal reaction, residual foreign bodies (metal, cement beads), sequestra in the bone and soft tissues (Fig. 8-3, 8-7), etc.
- Computed tomography, possibly with contrast sinogram: this is the most sensitive examination method for sequestra. Extensive experience is needed to differentiate between bone irregularities following complicated bone healing and areas of infected bone necrosis and sequestra.
- Three-phase and antigranulocyte scintigraphy: help to assess bone viability and localise infection. Supplemental SPECT/CT provides better anatomic resolution.
- MRI: clearly reveals the zone of inflammation based on the oedema but does not reveal sequestra; plays a subordinate role in therapeutic decision-making.
- Fistulography: particularly useful in the operating room. The fistulae are injected with a mixture of methylene blue and x-ray contrast agent. This enables the fistulae to be traced with the image intensifier and intraoperative imaging using the blue trace up to the bone but not inside the bone itself (Fig. 7-1, 8-11).
8.7.2 Treatment indications

- Incomplete bone consolidation, usually with loose or partially broken osteosynthesis material
- Sequestrum formation
- Fistulation
- Chronic infectious arthritis
- Bone defect
- Soft tissue defect
8.7.3 Surgical treatment

Debridement and sample collection
In a supplement to Chapter 8.6.3, the following are important:
- Resection of the fistulae and abscess membranes after staining (Fig. 7-1, 8-11)
- Complete metal removal, including broken screw parts, drill bits, remaining cement beads, etc.
- Removal of all sequestra
- Resection of necrotic bone that is characterised by the absence of bleeding points and major splintering when struck with a chisel. Ensure bone debridement is complete by releasing the tourniquet at the end
- In difficult situations, extensive segmental resection in preparation for segment transport (see ‘Bone grafting measures’, Fig. 8-8)

Stabilisation
Options include:
- Immediate stabilisation with external fixation
- A two-stage procedure with temporary immobilisation (orthosis) in the interim. The interim period provides time for additional clarification and curative antibiotic treatment in the absence of foreign material with difficult-to-treat bacteria.
- A locking intramedullary nail during the second stage as an example of tubular bone reconstruction that enables early full mobilisation (Fig. 8-9)

Bone grafting measures
The goal should always be full-length reconstruction. Depending on the extent of the defects, options include:
- Autologous cancellous bone grafting (preferably from the posterior iliac crest on the same side) with defects with no or only limited loss of length. As an alternative or complementary measure bone mill, harvested by intramedullary reaming of the femur, can be used. If there is a segmental defect, it is advantageous to distract the defect zone somewhat initially so that it can be compressed again after 6–8 weeks. It can be assumed that the graft will begin to stabilise the defect zone at 1½–2 months (Fig. 8-3). Reconstruction around a central intramedullary nail (Fig. 8-9), silicone tube or cement nail (Fig. 4-6) reduces bone graft volume and supports long-bone repair.
- Segment transport using an Ilizarov fixator for defects with length losses ranging from about 4 cm to more than 15 cm. The method usually heals skin defects and scar zones simultaneously because the segment transport procedure stretches healthy skin, too (Fig. 8-8).
Fig. 8-8: ♂ 52 years of age: a) 4½ years after healing, spontaneously reactivated infected non-union. Soft tissue defect in scar zone, originating from a ‘cross-leg’ flap, b) block resection 8 cm in length, proximal corticotomy, c) distraction in initial phase, large soft tissue defect, d) following completion of the distraction, soft tissue defect closed without plastic surgery, e) due to docking problems, decortication and plate osteosynthesis, situation at 10 months. Above the arrow: consolidated distraction section
- Procedure: Extensive resection of the affected bone segment to ensure that the adjoining osteotomies are vital, metadiaphyseal corticotomy without severing the medullary vessels, if possible, distraction of the corticotomy site by about 1 mm, wait 10 days before starting daily distraction of about 1 mm in 4–6 stages. Weekly check-ups during transport. Following completion of transport, increasing weight bearing with a fixator. As a rule of thumb, to calculate the time required for the distraction zone to consolidate: 10 days (waiting period) + distraction time (1 mm/day) + 5 months consolidation period (± 2 months). The docking site for the transport segment must be monitored separately. As soon as the distraction is complete, it must be considered whether additional measures, such as decortication, spongioplasty or osteosynthesis, should be done at the same time as the distraction to ensure consolidation.

- Free, vascularised bone grafts with/without simultaneous shift of muscle and skin areas: the active bridging of the defect starts with the contact to living bone with adequate stability immediately following transplantation of vital bone material. It is also possible to preserve all vital bone areas in the defect zone and to adapt the bone transplant precisely to the defect (Fig. 8-9). It is often necessary to simultaneously reconstruct the soft tissues, often with a free muscle or skin flap. In order to ensure healing, it is usually advisable to supplement the bone graft with autologous cancellous bone grafting.

- Bone allografts: bone allografts are not suitable for defect filling. Allogeneic cancellous bone is not very osteoinductive. Cortical allografts are useful for bridging tumour defects but are susceptible to infection and not suitable for applications involving infections.

- Bone morphogenic protein (BMP 2 and 7): while the osteoinductivity of BMP has been proven, success in clinical applications has been disappointing when its high price is considered. BMP-2 was used in a randomised, multi-centre study for fresh grade two and three, open fractures (as per Gustilo classification, see Chapter 16). An effect, although statistically weak, was detected for grade 3b fractures. A second study compared the use of BMP 2 with reamed intramedullary nailing and found no significant difference. BMP 7 was similarly used in cases of – uninfected – tibial non-union. Its use was comparable to autologous cancellous grafts with astonishingly low healing rates in both groups of only 81 % and 85 %, respectively.

- Bone replacement materials: the positive effects of all other bone replacement materials in clinical use are significantly less well documented.
Fig. 8-9: Male 47 years of age: infected non-union with enterococci. Two-stage procedure with difficult-to-treat bacteria. Preparatory debridement, metal removal, curative antibiotic therapy for 6 weeks, discontinuation of antibiotics for 2 weeks. a) Preoperative scar zone and defect, b) decortication, interlocking nail, lateral autologous cancellous graft, the free scapula bone flap will bridge the visible open gap, c) postoperative following free scapular flap with bone fragment inserted medially into bone defect and fixated d) after 7 months securely bridged, full weight bearing for past 3 months, scar zone on pretibial skin fully restored.
8.7.4 Specific treatment options

Early and delayed infection after intramedullary nailing
If during the course of fracture healing, a trend towards bridging is observed along with simultaneous, progressive infection, e.g., fistula formation, then it is advisable to

- perform local debridement with collection of tissue samples,
- initiate empirical, suppressive antibiotic therapy following tissue collection, adjust therapy following receipt of the bacteriological results and continue treatment until adequate bridging has been achieved, and
- remove the nail and ream, the intramedullary cavity to a diameter about 2 mm wider than the diameter of the removed nail (see Chapter 8.8.3), irrigate and - depending on stability – apply external fixation, insert an intramedullary nail coated with antibiotic cement (see Fig. 4-6) or use an adapted orthosis.

8.7.5 Prognosis and complications

Prognosis
Targeted procedures performed by sufficiently experienced teams of orthopaedic surgeons, infectious disease specialists and plastic surgeons are nearly always successful in the stable reconstruction of an extensive, infected defect non-union over a correspondingly prolonged period, sometimes up to a year. The functional outcome of the lower extremity depends on the status of the foot and knee (see 8.7.1).

Complications
Each treatment method has its own rate of complications. Because multiple methods are often combined, these rates add up. Typical scenarios include:

- Recurrent infection in a defect zone
- Failure of a free flap
- Problems with osseous union of the transported segment in the case of distraction osteogenesis
- Fatigue fractures following defect reconstruction using cancellous grafts alone (Fig. 8-7).
- Pes equinus often develops as a result of inadequate functional support.
8.8 Late first presentation –
chronic post-traumatic osteomyelitis

8.8.1 Clinical symptoms and diagnostic procedures

Medical history and clinical findings

- Development without interruption from a post-traumatic infection or secondary presentation following an asymptomatic interval lasting months to decades
- Start of a new episode characterised by a gradual or sudden recurrence of erythema. Alternating fistula occurrence and closure accompanied by retention pain.
- May be accompanied by pain and fever. Patients are mainly affected by:
  - pungent pus odour – a change in microbes may alter this,
  - inability to bathe in public pools
  - inability to work due to pus discharge in occupations involving food, e.g., hospitality, bakery, butcher’s shop, etc., and
  - reduced physical capabilities.
- Very rarely a fistula carcinoma develops, usually only with fistulas that have been present for decades. These tend to be only locally aggressive and rarely metastasize.

Fig. 8-10: 18 years after fracture, osteomyelitis with distal abscess (arrows)
Laboratory tests
Infection parameters (white blood cells, CRP) are often normal or only moderately abnormal.

Imaging (see Chapters 6.3, 8.7.1)
- Standard x-rays: monitoring of progress. The appropriate images are often missing. Recent images in 4 views (anterior-posterior, lateral and obliques, see Fig. 8-7) provide an important overview. Periosteal bone formation, residual foreign bodies (metal, cement beads, mobile sequestra in the soft tissues or bone, etc.) are of particular interest. Search for distal abscess (Fig. 8-10).
- Computed tomography, possibly with contrast agent in fistula: this is the most sensitive examination method to detect sequestra. It is essential to look for isolated bone fragments (which are sometimes very small) in the often bulky bone mass, which is often very dense, (Fig. 6-4). Examination for zones of massive endosteal bone formation within the medullary cavity, sometimes accompanied by a distal intra-osseous abscess cavity, which may form fistulas toward the surface in some cases.
- Three-phase and antigranulocyte scintigraphy: help to assess the localisation of infection. Supplemental SPECT/CT may provide more precise information.
- MRI: reveals the oedema associated with the zone of inflammation.
- Fistulography: particularly useful in the operating room. (see Chapter 8.7.1, Fig. 7-1)

8.8.2 Treatment indications
- Chronic fistula
- Chronic pain
- Lack of consolidation
- Chronic infectious arthritis
- Soft tissue defect

8.8.3 Surgical treatment
Localised debridement
With chronic osteomyelitis, local revision is performed if the findings are localised. Soft tissue revision follows the fistula tract. The size of the bone fenestration is determined on the basis of the CT findings. Round holes are drilled at each end of the fenestration to prevent subsequent fatigue fractures as far as possible (Fig. 8-11). The endosteal bone formation in the intramedullary cavity and any sequestra it con-
tains that are causing the fistula are extensively removed using bent chisels and bone burrs, while preserving adequate stability. Metal parts, retained cement beads and other foreign bodies are removed. Several tissue samples are collected for microbiological and histological analysis.

Intramedullary reaming
Particularly suitable for the treatment of centralised regions of necrotic bone. These lesions occur mainly in association with (reamed) intramedullary nail procedures. However, other sequestra, e.g., following plate osteosynthesis (Fig. 6-4), also become centralised primarily due to periosteal bone regeneration (involucrum) and are accessible using this approach (see Chapter 8.2). Thanks to ample blood flow, mainly from the periosteum, bone necrosis is not expected to recur.

- Peripheral sequestra are removed (Fig. 6-4, 8-12a).
- The diaphysis is reamed along its entire length in order to eliminate the central sequestrum zones (Fig. 8-2c). Approaches include the classic access approaches for intramedullary nailing of the femur and tibia.
- If the intramedullary cavity is completely filled with bone in some places, then the bone is opened proximally and distally. A bone fenestration with rounded ends is created in the zone filled with endosteal bone and the bone is locally evacuated. This enables the guide wire to pass this area (Fig. 8-11, 8-12d).

Fig. 8-11: Bone fenestration with osteomyelitis focus. a) Tracing of the blue-stained fistula up to the bone, b) creation of a round drill hole at both ends of the planned fenestration with a diameter of 10–12 mm and connection with two saw cuts; removal of the fenestration with narrow chisel. The interior of the medullary cavity can be evacuated via this fenestration using a bent chisel and bone burr.
- A lateral venting hole is created distally (Fig. 8-12d). The bone is then reamed to the greatest extent possible while still ensuring that the periosteal thickening will maintain bone stability. Reaming diameters of up to 18 mm are not uncommon in the femur. Reamers with good heat dissipation and freshly sharpened bits must be used to prevent overheating of the cortex. The drilling debris is able to escape through the venting hole during drilling.
- Finally, the area is irrigated to thoroughly remove the drilling debris. If a removable, local antibiotic carrier (e.g., beads made of gentamicin-impregnated bone cement) is inserted, then it should not be left in place for longer than 5–7 days. An overflow drainage without suction is inserted to prevent unnecessary blood loss.
- The extremity is usually fully weight bearing. Immediate stabilisation with external fixation is only necessary in exceptional cases.

**Bone grafting measures**
Usually with autologous cancellous grafts; only rarely necessary.

**Plastic defect closure**
In some cases, plastic defect closure of a scar zone or fistula area (Fig. 8-12).

### 8.8.4 Specific treatment options

**Revision of metaphyseal intramedullary cavities with pedicled muscle flaps (especially tibial plateau)**
The classic method of covering lesions with local muscle rotation flaps to improve vascularisation is rarely used nowadays. Blood flow to the bone is usually highly elevated in regions of chronic osteomyelitis. Bone scintigraphy can supply appropriate evidence. With large-volume defects in the tibial plateau, the weight-bearing capacity of the structure may be restored by thickening cortical elements but central defects with poor anterior soft tissue cover often remain. In such cases, a periosseous gastrocnemius muscle flap can be advanced forward via a posterior incision following rigorous debridement in such a way as to also ensure anterior soft tissue restoration.
Fig. 8-12:  54 years of age: see the same case in Fig. 6-4. a) Soft tissue defect in scar zone with visible sequestra, to be removed, b) medial gastrocnemius muscle flap for defect coverage, c) muscle flap with split-thickness skin graft, gentamicin-impregnated beads in the reamed intramedullary cavity, removed after 7 days, d) 10 months after extensive intramedullary reaming with additional bone fenestration to evacuate hypertrophic bone and small sequestra and venting hole in the distal tibia for removal of the drilling debris.
8.8.5 Prognosis and complications

- With clearly identifiable causes and rigorous procedures (e.g., localised removal of sequestra, intramedullary reaming, even for extensive disease), the prospects for healing are around 80–90 %, over the long term.
- A relapse cannot be ruled out, even after a dormancy period of more than 10 years.
- Fistula carcinomas are very rare.

8.9 Differential diagnosis: Chronic haematogenous osteomyelitis in adults (see Chapter 14)

Haematogenous osteomyelitis of the extremities is mainly an illness that affects children and adolescents (see Chapter 14). In acute or primarily chronic cases, it is initially localised in the metaphysis (Fig. 8-13). If it persists, then it migrates successively toward the diaphysis, which becomes enlarged, in some cases hugely so.

Residual traces of chronic osteomyelitis in adults are very rare nowadays in countries with good medical care and occur almost exclusively in elderly patients who had infections during adolescence in the era before antibiotics and in immigrants from developing countries.

Cases of osteomyelitis following severe accidents during childhood or adolescence may simulate chronic haematogenous osteomyelitis.

New cases of haematogenous osteomyelitis in adults typically affect the spine (see Chapter 10) and rarely the long bones, e.g., with brucellosis or tuberculosis. The risk is elevated with prolonged steroid therapy or immunosuppression.

8.9.1 Clinical symptoms and diagnostic procedures

Medical history and clinical findings
Adult patients with chronic haematogenous osteomyelitis are usually aware of their suppurating illness during adolescence, which often involved prolonged hospital stays and surgical procedures. After years without any symptoms, patients consult their doctors concerning painful swelling or fistulae that have reopened. Others experience intermittent swelling and/or severe load-independent pain without fistulae or any actual signs of infection from adolescence onwards. There is no accident history. Scars from earlier fistula tracts, differences in length, axis deviations of the affected area of the skeleton are often noticeable during examinations.
Fig. 8-13: ♀ 8 years of age: acute haematogenous osteomyelitis with no evidence of bacteria: a) pre- and postoperatively following curettage and drainage, b) after 2 and c) 7 years the metaphyseal focus migrates successively toward the diaphysis with massive shaft thickening, d) after 28 years the patient has suffered severe, chronic pain without fistulae for many years. Compare with the unaffected femur. e) fenestration and extensive evacuation, more extended revision after 2 years, no culture of bacteria, significant pain reduction even later 12 years.
Laboratory tests
Often normal or somewhat elevated CRP values provide little information. In painful, non-fistulating forms bacteriological tests are often negative.

Imaging
The examination methods correspond to those used for chronic post-traumatic osteomyelitis (see Chapter 8.8.1). There is a lack of history for earlier accidents. The changes are in the metadiaphysis (Fig. 8-13).

8.9.2 Treatment indications
- Chronic fistulae
- Chronic pain

8.9.3 Surgical treatment
In principle, the same treatment options are available as for chronic post-traumatic osteomyelitis. Targeted antibiotic treatment is often not possible if there are no detectable pathogens. Nonetheless, histological tests indicate inflammation/infection.

Localised debridement
If there is a fistula and sequestra can be detected, then proceed as described under 8.7.3. These cases usually also involve treatable bacteria.

Intramedullary reaming
The entire bone area to be treated is infected. The bone is infiltrated with cystic changes up to the surface in some places (Fig. 8-12). There is no cortex reinforced with periosteal bone regeneration. The metaphyso-diaphyseal location with massive bone thickening makes it impossible to perform a classic intramedullary reaming procedure, which would mainly expand the unaffected diaphysis proximally to the affected zone (Fig. 8-13). As a result, any revision must begin with an extensive fenestration of the bone. The affected bone can only be removed up to a point that ensures that structural strength is maintained. Radical segment resection is risky; it would place the vitality of the only remaining epiphysis at risk and make the reconstruction of the defect extremely complicated.
8.9.4 Prognosis, complications

The prognosis is favourable with an active fistula and localisable sequestra but unreliable for attempted reconstruction involving extensive findings with chronic pain. Complications, such as fistula carcinomas, are rare.

8.10 Don’ts

- Empirical antibiotic therapy alone for a wound with impaired healing following osteosynthesis
- Delay surgical treatment of a verified infection, unless it is performed as part of a targeted plan with temporary suppressive antibiotic therapy and definitive healing following successful bridging
- Exclusively surgical and topical treatment of an early infection in the joint region with incipient arthritis with antiseptics but without antibiotics
- Exclusively antibiotic therapy without surgical revision
- Leave large, isolated bone fragments/sequestra in an infected environment in the hope of reintegration

8.11 References

Further reading

Additional articles

- Gustilo RB, Gruninger RP, Davis T. Classification of type III (severe) open fractures relative to treatment and results. Orthopaedics 1987; 10: 1781–8
- Morawietz L, Tiddens O, Mueller M et al. Twenty-three neutrophil granulocytes in 10 high-power fields is the best histopathological threshold to differentiate between aseptic and septic endoprosthesis loosening. Histopathology 54; 2009: 847–53
9 Infectious arthritis

Werner Zimmerli, Olivier Borens

9.1 Background

9.1.1 Aetiology

Acute infectious arthritis develops either by haematogenous seeding or direct inoculation as a result of an injection into the joint, surgical interventions or open-joint injury. The most common pathogen in patients without any predisposition, with rheumatoid arthritis, intravenous drug use or diabetes mellitus is *Staphylococcus aureus*. Coagulase-negative staphylococci are typically only found in the native joint following arthroscopy. In patients with intravenous drug use, group A streptococci (septic phlebitis), *Pseudomonas aeruginosa* (tap water in a used syringe) and *Candida* spp. are also to be expected. Fungal arthritis can also become rapidly fatal. The most common pathogen in small children under the age of 2 is *Kingella kingae*. Cat or dog bites typically result in an infection with *Pasteurella multocida* or *Capnocytophaga* spp., rat bites lead to *Streptobacillus moniliformis* infections, and a bite from a human results in infections (e.g., arthritis of finger joints following a ‘fist-to-mouth’ injury) caused by pathogens in oral flora (HACEK group: *Haemophilus* spp., *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens* and *Kingella kingae*). Following gynaecological interventions (curettage or childbirth) or with humoral immune deficiency, the patient should be explicitly tested for *Mycoplasma hominis*. If the patient’s medical history indicates promiscuity and unprotected sex, gonococcal arthritis must be considered with polyarticular arthritis and macular exanthem. If the arthritis is unclear and the patient’s medical history includes the consumption of unpasteurised milk products in a Mediterranean country, the patient must be tested for brucellosis (specifically request the culture in the laboratory and serology). If the patient’s medical history indicates oligoarthritis in combination with diarrhoea or mesenteric lymphadenitis, the patient must be tested for *Tropheryma whippelii*.

9.1.2 Incidence

2–10 cases/year/100,000 population, 5–10 cases per 10,000 patients hospitalised in an acute care facility. The risk of iatrogenic infectious arthritis is reported as 1:22,000. This risk is considerably higher following arthroscopic procedures, namely 1:250 to 1:1000.
9.1.3 Risk factors

Pre-existing arthropathy, systemic comorbidity, immunosuppression and conditions associated with an increased risk of bacteraemia (intravenous drug use, endocarditis and other systemic infections, *S. aureus* colonisation). A steroid injection further increases the risk. If steroids are administered during arthroscopy, the risk is 27.4 greater than if no steroids are administered.

9.1.4 Affected joints

90 % monoarthritis, 10 % oligoarthritis. Most common sites: Knee (45–55 %) and hip joint (15–25 %), shoulder, elbow, ankle or wrist combined 5–10 %, other joints, e.g., the sacroiliac joint (particularly in women following gynaecological procedures) < 5 %.

9.2 Clinical symptoms and diagnostic procedures

9.2.1 Medical history

- Joint pain (pain when at rest, becomes more acute when bearing weight)
- Impaired joint function
- Sudden swelling, erythema, excess heat, possible fever (does not occur in 50 % of cases, probably due to the use of analgesics or antibiotics)

9.2.2 Clinical findings

- Pain on palpation and movement, erythema, excess heat, effusion (these signs are frequently not present for the hip joint; often there is only pain that is felt when the joint moves and with axial compression)
- Fever, however seldom > 39 °C. About one third are sub-febrile
- Monoarticular (generally) versus oligoarticular (typical of gonococcal arthritis)
- Possibly accompanied by exanthem (typical of meningococcal and gonococcal arthritis)
9.2.3 Laboratory tests

- White blood cell count, differential blood count and CRP (but all blood tests are non-specific)
- Collection of 2–3 anaerobic and aerobic blood cultures
  - Arthrocentesis prior to administration of antibiotics
  - Crystals (beware: evidence of pyrophosphate crystals does not rule out bacterial arthritis)
  - White blood cell count (> 50 x 10^3/μL: sensitivity 62%, specificity 92%), granulocyte percentage (> 90%: sensitivity 73%, specificity 79%)
  - Bacterial culture (Gram staining positive in only 50% of cases). In the case of prior antibiotic therapy, inoculation into blood culture vials is more sensitive.

9.2.4 Imaging

- Conventional x-ray: evidence of pre-existing arthropathy (e.g., rheumatoid arthritis, osteoarthritis, osteomyelitis, spondyloarthritis, chondrocalcinosis)
- Ultrasound: for targeted needle aspiration
- Bone scintigraphy is positive within 10 days; only useful for demonstrating unilateral sacroiliitis due to lack of specificity.
- Computed tomography (CT) is sensitive for detecting erosions, joint effusion and soft tissue infections
- Magnetic resonance imaging (MRI) is more sensitive than other modalities, however, it is only required for sternoclavicular arthritis, sacroiliitis, symphysitis or possibly postoperatively (e.g., following anterior cruciate ligament surgery).

9.2.5 Differential diagnosis

- Crystal arthropathy (gout, chondrocalcinosis): cannot be distinguished from infectious arthritis, analyse synovial fluid specimen for crystals. However, the presence of crystals does not rule out bacterial arthritis.
- Reactive arthritis (following diarrhoea, dysuria with infection due to *Chlamydia spp.*)
- Rheumatoid arthritis
- Differential diagnosis of haemarthrosis: haemophilia, haemodialysis, trauma
- Osteonecrosis (glucocorticoid therapy)
- Rarely: sarcoidosis (arthritis of the ankle joint), post-streptococcal pharyngitis, Still's disease (pharyngitis, rash, arthralgia)
If bacterial arthritis is suspected, the patient should be managed accordingly, until the diagnosis is definitely excluded.

9.3 Therapeutic principles

Both to confirm the diagnosis and to remove synovia which contains nocive enzymes damaging the cartilage, arthrocentesis must be carried out as soon as infectious arthritis is considered a possibility. Early and aggressive therapy to relieve the joint provides the best results. The following is generally applicable:

- Arthroscopy, or arthrotomy in serious cases, are the methods of choice.
- For large joints, repeated aspiration alone does not enable a precise initial diagnosis, such as that possible with arthroscopy.
- Closed suction drainage systems and distension irrigation systems pose a risk of superinfection.

9.3.1 Arthrocentesis

When infectious arthritis is suspected, arthrocentesis must be carried out. Aspiration allows the pathogen to be identified (Gram staining and microbiology) while also directly reducing necrotic material and granulocytes, thus lessening the damage to the cartilage. Aspiration is a provisional measure, which for large joints (knee, hip, shoulder and elbow) should be rapidly followed by surgical lavage of the joint, generally via arthroscopy. In smaller joints, repeated aspiration and rarely insertion of a drain is indicated.

9.3.2 Arthroscopy

This is the method of choice for infectious arthritis in a large joint at stages 1 and 2 as defined by Gächter (Tab. 9-1 and Fig. 9-1).

- When? As early as possible, if a bacterial infection is suspected in a large joint.
- How often? This depends on both the initial situation and the local and general clinical response to surgical and antibiotic treatment. The general approach is to repeat arthroscopy every 2–3 days. Where interim aspiration is performed, final arthroscopy may be useful for the purposes of final evaluation.
- Which irrigation solution? Ringer’s solution or NaCl (true to the motto: ‘Dilution is the solution to pollution’)
- Note: do not use antiseptics such as chlorhexidine or polyhexanide due to the risk of chondrolysis and destruction of the joint!
Where implants or prostheses are located in the knee area and also following ACL surgery in particular (with infection often beginning in the drill channel), an open procedure is preferable.

9.3.3 Arthrotomy

This is the method of choice, if arthroscopy is not technically feasible (see also above), or if it is no longer viable because the situation is already very advanced (stage 4 as defined by Gächter).

9.3.4 Synovectomy

For stages 1 and 2 as defined by Gächter (Tab. 9-1 and Fig. 9-1), synovectomy should not be carried out as this reduces the diffusion of antibiotics into the joint facilitated by the strong perfusion in the synovial membrane. For stage 3, arthroscopic shaving may also be considered, while an arthrotomy is preferable if the synovial membrane is thick. For stage 4, an open synovectomy is recommended.

Tab. 9-1: Staging of infectious arthritis as defined by Gächter

<table>
<thead>
<tr>
<th>Stage</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Synovitis, cloudy fluid, possible petechiae, no radiological changes</td>
</tr>
<tr>
<td>2</td>
<td>Highly inflammatory synovitis, clumps of fibrin, pus, no radiological changes</td>
</tr>
<tr>
<td>3</td>
<td>Thickening of the synovial membrane (possibly several centimetres), adhesion with pouch formation, no radiological changes visible</td>
</tr>
<tr>
<td>4</td>
<td>Pannus formation, proliferation of aggressive synovitis on and later beneath the cartilage (subchondral erosions), radiological changes visible</td>
</tr>
</tbody>
</table>
9.3.5 Antibiotic treatment

**Systemic Therapy**
Following arthrocentesis, therapy is initially empirical and is then continued on the basis of susceptibility testing.

- Empirical therapy: no visible pathogen in the Gram stain test: an antibiotic that is very effective against staphylococci and streptococci, e.g., cefazolin 3–4 x 2 g/day or cefuroxime 3–4 x 1.5 g/day IV Gram-positive cocci: amoxicillin/clavulanic acid (3 x 2.2 g/day IV). Gram-negative cocci: ceftriaxone (1 x 2 g/day IV). Gram-negative rods: cefepime (2–3 x 2 g/day IV).
- Targeted antibiotic therapy: in accordance with Tab. 9-2

*Fig. 9-1: Arthroscopic images of stages 1–3. Stage 4 (open) with revised synovectomy (for details see Tab. 9-1)*
Tab. 9-2: Targeted antibiotic therapy in bacterial arthritis

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Antibiotic</th>
<th>Daily dose</th>
<th>Application</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Staphylococcus aureus</strong> or coagulase-negative staphylococci</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methicillin-susceptible</td>
<td>Flucloxacillin1 or ciprofloxacin or levofloxacin</td>
<td>4 x 2 g 2 x 750 mg 1 x 750 mg 2 x 300 mg</td>
<td>IV PO PO PO</td>
</tr>
<tr>
<td></td>
<td>PO drugs + rifampicin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methicillin-resistant</td>
<td>Vancomycin or teicoplanin or co-trimoxazole or ciprofloxacin or levofloxacin2 or fusidic acid or minocycline</td>
<td>2 x 1 g 1 x 400 mg 2–3 x 1 forte tablet 2 x 750 mg 1 x 750 mg 3 x 500 mg 2 x 100 mg 2 x 300 mg</td>
<td>IV IV/IM PO PO PO PO PO PO</td>
</tr>
<tr>
<td></td>
<td>PO drugs + rifampicin</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Streptococcus spp.</strong></td>
<td>Penicillin G or ceftriaxone</td>
<td>4 x 5 million units 1 x 2 g</td>
<td>IV IV</td>
</tr>
<tr>
<td><strong>Enterobacteriaceae, gonococci, meningococci</strong> (quinolone-susceptible)</td>
<td>Ciprofloxacin</td>
<td>2 x 750 mg</td>
<td>PO</td>
</tr>
<tr>
<td><strong>Non-fermenters</strong> (e.g., Pseudomonas aeruginosa)</td>
<td>For 2 weeks: Ceftazidine or cefepime + aminoglycosides</td>
<td>3 x 2 g 3 x 2 g According to substance</td>
<td>IV IV PO</td>
</tr>
<tr>
<td></td>
<td>Followed by 2–4 weeks: Ciprofloxacin</td>
<td>2 x 750 mg</td>
<td></td>
</tr>
</tbody>
</table>

Note: For targeted long-term therapy, resistance testing must be done. The duration of therapy is 3–6 weeks in total depending on the pathogen, response to therapy and possible accompanying osteomyelitis. The specified dose corresponds to the adult dose with normal kidney and liver function. PO (oral); IV (intravenous); IM (intramuscular); forte tablets: trimethoprim 160 mg, sulfamethoxazole 800 mg.

1 In patients with a delayed hypersensitivity reaction to penicillin, cefazolin (3 x 2 g IV) can be administered. In patients with an immediate hypersensitivity reaction, beta-lactams must be substituted by vancomycin (2 x 1 g IV).

2 Methicillin-resistant Staphylococcus aureus is generally resistant to quinolones. Exceptions are community-acquired MRSA.
Local Therapy
The intra-articular administration of antibiotics is contraindicated as chemical synovitis may be triggered and because parenteral antibiotics and antibiotics with high oral bioavailability (e.g. fluoroquinolones) reach the joints effectively due to the good blood flow in the synovial membrane.

9.3.6 General information about physiotherapy
Physiotherapy of the infected joint is important and necessary in order to ensure that the cartilage is supplied with nutrients through diffusion. For the knee and hip, a passive motion brace is useful. The joint should not initially bear any weight (bed rest or relief through 2 crutches) and be placed in a functionally favourable position (not fully extended). Passive range-of-motion and isometric exercises to build up strength accelerate rehabilitation and reduce the risk of subsequent joint stiffness.

9.4 Don’ts
- Administration of antibiotics prior to performing arthrocentesis and collecting blood cultures
- Antibiotics without local treatment (aspiration, arthroscopy, possible arthrotomy)
- Antibiotic injection into the joint. Diffusion via the synovial membrane is sufficiently effective.
- Injection of antiseptic into the joint. Risk of destroying the regenerative cartilage cells
- Needle-aspiration drainage (risk of superinfection)
- Immobilisation using a fixator or plaster splint rather than non-forced physiotherapy
- Switching to oral therapy after a few days, if no antibiotic with good bioavailability is available.
- Full weight-bearing in the acute phase
9.5 References

Further references


Additional articles

10 Spondylodiscitis

10.1 Fundamentals

10.1.1 Definition

- Spondylitis: osteomyelitis of the vertebrae
- Discitis: infection in the intervertebral disc space
- Spondylodiscitis: infection in the intervertebral disc space and osteomyelitis of the vertebrae (Fig. 10-1 and 10-2)
- Epidural abscess: expansion of the infection into the epidural space (Fig. 10-2)
- Paravertebral abscess: expansion to surrounding soft tissue/muscle structures (e.g. psoas abscess) (Fig. 10-2)

10.1.2 Pathogenesis

- Haematogenous: skin, genitourinary system, respiratory tract, gastrointestinal tract, endocarditis, dentogenic
- Exogenous (rare): postoperative (approx. 1% following discectomy), post-interventional (infiltrations, punctures), post-traumatic
- Adults: intervertebral disc is avascular. Haematogenous spread of the pathogens via terminal arterioles/venous plexus near the vertebral end plates (spondylitis), then via the end plates into the intervertebral disc space (spondylodiscitis)
- Children: intervertebral disc is still vascularised, usually resulting directly in discitis via haematogenous spread.

10.1.3 Epidemiology

- Incidence: 2–7% of all osteomyelitis cases. 0.2–2/100,000/year, especially from the fifth decade onwards
- Males: Females = 2–3: 1 (reason unclear). Lumbar spine (approx. 50%) > Thoracic spine > Cervical spine. Diagnosis often delayed
- Risk factors: age, immunosuppression, diabetes mellitus, obesity, IV. drug abuse, malignant tumours, chronic steroid medication, renal failure, bacteri-aemia/fungaemia (particularly endocarditis, intravascular implants), previous spinal surgery
10.2 Clinical symptoms and diagnostic procedures

10.2.1 Clinical findings

- Medical history: often not characteristic. Either acute fulminant development of symptoms with localised pain and high fever or gradual insidious onset. 98% of patients report back pain (constant pain or night-time pain). Local tenderness, myalgia, hypokinesia with adaptive posture, 60–70% patients have a fever. Depending on the region, pain radiating into the arms, thorax/abdomen or lower extremities
- Findings: tenderness or pain on percussion; compression pain (pain on heel strike), adaptive posture. Possible neurological deficits
- Search for the origin of the infection: recent past infections, dental treatments, medically invasive procedures such as punctures, infiltrations or catheter examinations
- Children: often accompanied by limping, refusal to walk/stand, potential abdominal pain (especially with an infection process in the thoracic spine)

10.2.2 Laboratory tests

- C-reactive protein (CRP)
- Leukocytes (elevated in only 2/3 of cases)

10.2.3 Radiological diagnostics / Imaging techniques

- Conventional x-rays: only of limited value in the initial stages. Abnormalities cannot be detected near the superior and inferior vertebral end plates until 2–8 weeks have elapsed. Important for follow-up, after 6/12 weeks.
- MRI with gadolinium: imaging method of choice with highest sensitivity and specificity. However, abscess expansion often appears too extensive (Fig. 10-1, 10-2). However, MRI is not suitable for follow-up (with the exception of epidural abscess) due to delayed normalisation of the MRI findings.
- $^{99m}$Tc scintigraphy: sensitivity 87–98%, specificity 91–100% (with high prevalence). Positive after approx. 48 h.
Fig. 10-1: ♂ 81 years of age: MRI with spondylodiscitis (L5/S1) adjacent to severe osteochondrosis (L4/L5)

Fig. 10-2: ♂ 66 years of age: Spondylodiscitis with breach into surrounding area with epidural (white arrow) and paravertebral abscess (black arrows)
10.2.4 Microbiology

- No antibiotics prior to microbiological diagnostics. At least 48-hour break if already administered. 1–2 weeks would be preferable but this is usually inadvisable with acute symptoms.
- Blood cultures: positive in 50% at most
- CT-guided needle biopsy: positive result in up to 70% at most (depending on examiner). If negative: transpedicular or open biopsy
- Biopsy: transpedicular biopsy by spine surgeon (e.g. Magerl biopsy cannula) provides significantly more tissue for the culture/histology than CT-guided biopsy. Highly dependent on the examiner.
- In the case of a negative biopsy:
  - perform broad-band PCR from biopsy material
  - consider tuberculosis, brucellosis (expanded diagnostics) or pathogens that cannot be cultivated [e.g. request *Tropheryma whipplei*, polymerase chain reaction (PCR)].
  - differential diagnosis: activated osteochondrosis

10.3 Therapeutic principles

Principle: do not initiate antibiotic therapy until the bacteriological results are available unless the severity of the situation makes it necessary to administer empirical therapy.

10.3.1 Conservative treatment – antibiotics and rest

**Indication**

- No or only limited vertebral destruction
- No significant abscess

**Antibiotic therapy**

For uncomplicated acute spondylodiscitis: 6 weeks IV/PO based on microbial findings in consultation with infectious disease specialist. Components that prolong therapy: Implants, psoas/epidural abscess

- Initial empirical IV therapy with amoxicillin/clavulanic acid
- Treatment adapted to the results of the bacterial culture results in consultation with infectious disease specialist
- Tuberculosis: at least 12 months
Rest
Using brace (depending on severity of pain)

Regular follow-ups
- Laboratory tests: weekly CRP, other follow-ups depending on antibiotic
- Conventional x-rays every 6 weeks

10.3.2 Surgical treatment – surgery plus antibiotics (see above)

Indications
- Relevant neurological deficits
- Epidural abscess
- Formation of a large, paraspinal abscess
- No response to conservative therapy
- Persistent, severe pain
- Progressive vertebral destruction/instability
- Progressive deformity

Operations
- Posterior epidural abscess: decompression/laminectomy. Drainage. If posterior elements also affected: fusion
- Destruction/anterior abscess: radical debridement of infected soft tissue and bone tissue, defect filling with bone graft (only limited size possible, risk of partial absorption) or titanium mesh cage.
- Cage filling with autologous bone from iliac crest mixed with gentamicin fleece strips. Possible ventral stabilisation system. Additional dorsal stabilisation using pedicle screw system. Additionally stabilise one segment in the case of poor bone quality.

Surgical approaches
- Craniocervical: transoral
- Cervical spine: anterolateral
- Upper thoracic spine: costotransversectomy
- Middle thoracic spine: transthoracic
- Thoracolumbar junction/upper lumbar spine: transdiaphragmal/retroperitoneal
- Lower lumbar spine: retroperitoneal or transperitoneal
10.4 Prognosis and complications

Outcome usually favourable with adapted treatment. According to recent studies, the implantation of metallic implants into the infected region following radical debridement is widely accepted with high healing rates and few recrudescent infection situations.

10.5 Don’ts

- Do not treat without positive biopsy/blood cultures or broad-range PCR
- Do not rely on negative gram stain test
- Do not continue conservative treatment with severe destruction, malposition or extensive abscess

10.6 References

Further reading


Additional articles

11 Software infections

11.1 General aspects

The diagnosis of soft tissue infections is essentially based on the clinical picture. The recognition of a clinical entity may be difficult in presence of atypical symptoms. In the majority of cases a non-surgical treatment is chosen to begin with unless an abscess formation or a rapidly progressing situation is observed, which asks for immediate surgical intervention. The therapeutic decision is never simple and asks for a multidisciplinary approach. To wait and see what happens can result in a catastrophe for the patient (e.g. necrotizing fasciitis). On the other hand there are situations in which a surgical intervention is not indicated as for instance in the presence of redness of the lower extremity caused by chronic ischaemia (see Chapter 13). There are also rare autoimmune entities, such as pyoderma gangrenosum, which can mimic the appearance of ulcerating infections and for which surgery can worsen the ulceration.

The objective of this short summary of the most frequent soft tissue infections is to clarify when surgical intervention is necessary or when antibiotic treatment alone may be sufficient.

11.1.1 Classification

Soft tissue infections may be classified according to:

- The anatomic localisation:
  - Skin (Erysipelas)
  - Subcutaneous tissue (cellulitis, necrotising fasciitis)
  - Muscles (myositis with streptococci, myonecrosis in gas gangrene)
- The causative microbes:
  - Beta-haemolytic streptococci, *Staphylococcus aureus*, possibly *Clostridium perfringens* (classical gas gangrene)
- The urgency of treatment (Tab. 11-1)
- The extent of the infection: focal (abscess) or diffuse infection.
<table>
<thead>
<tr>
<th>Classification</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slowly progressive infections</td>
<td>- Impetigo&lt;br&gt;- Folliculitis&lt;br&gt;- Single furunculosis (except for drainage) (see 11.2.1)&lt;br&gt;- Erysipelas (see 11.2.2)&lt;br&gt;- Cellulitis (see 11.2.3)&lt;br&gt;- Pyoderma gangrenosum (primary sterile chronic ulcerating skin affection of unclear aetiology exacerbated by surgical interventions (Koebner phenomenon), NB: disinfection with solutions containing iodine exacerbates the affection)</td>
</tr>
<tr>
<td>Infections needing surgical intervention</td>
<td>- Carbuncle&lt;br&gt;- Phlegmon&lt;br&gt;- Advanced infectious bursitis (see 11.2.4)&lt;br&gt;- Abscess</td>
</tr>
<tr>
<td>Severe, life-threatening soft tissue infections with rapid progression</td>
<td>- Necrotising fasciitis (see 11.2.5)&lt;br&gt;- Myonecrosis&lt;br&gt;- Toxic shock syndrome associated with abscesses</td>
</tr>
</tbody>
</table>

### 11.1.2 Laboratory tests, microbiology and histology

**Laboratory tests**

Blood biochemistry only confirms inflammation. The values are not diagnostic on admission but may be helpful for monitoring during the follow-up period.

**Microbiology**

Almost every pathogen, e.g., *S. pyogenes*, can cause all presentations of the clinical picture. Blood cultures and tissue biopsies, apart from abscesses and material harvested during revision, should be sent for analysis, prior to starting empiric broad-spectrum antibiotic treatment. The growth of microorganisms *per se* from superficial or deep necrotic swabs is not evidence of infection, since ischaemia, necrosis, allergy etc. may equally disrupt the skin barrier with subsequent bacterial colonisation.
**Histology and radiology**

May help to confirm clinical suspicion, particularly of necrotising fasciitis and pyoderma gangrenosum. CT scan and MRI are helpful in the identification of abscesses or to confirm fasciitis, guiding the surgeon towards appropriate debridement.

### 11.2 Some important Infections

#### 11.2.1 Furunculosis and localised skin abscesses

**Aetiology**

Spontaneous localised skin abscesses without adjacent skin and soft tissue infection are due to *S. aureus*, unless proven otherwise. Postoperative fluid collections or abscesses in patients with substance abuse disorders can be due to almost every possible pathogen.

**Treatment**

Every abscess must be incised and drained. A single abscess without an accompanying infection of the underlying soft tissue does not always require additional antibiotic therapy after surgical management. For recurrent furunculosis, total-body staphylococcal decolonisation is often warranted.

#### 11.2.2 Erysipelas

**General aspects**

The most severe form of superficial skin infection involving the epidermis and dermis, leading to bacteraemia in 2% of cases. Causative bacteria are group A beta-haemolytic streptococci (80%) and *S. aureus*.

**Diagnosis**

Prominent lymphatic blockage results in a painful bright red patch with a raised sharp border, which clearly demarcates infection from surrounding skin. Predisposing conditions include interdigital mycoses, foot abrasions, chronic ulcers, lymphoedema, venous stasis and diabetes.
Therapy
(Amino)penicillins, cephalosporins or amoxicillin/clavulanic acid are the drugs of choice for a routine duration of 7–10 days. Usually there is no need to continue antibiotics until the disappearance of all signs of redness. In the absence of verified microorganisms, empiric therapy with broad spectrum antibiotics is the rule, especially for patients pretreated with antibiotics or those in intensive care. Cases not adequately treated by cephalosporins or amoxicillin/clavulanic acid are rare. With poor response to treatment, surgeons and doctors should search for abscesses which may require drainage. Community-acquired MRSA among patients returning from tropical countries, the Mediterranean region or North America can pose difficulties for treatment.

11.2.3 Cellulitis

General aspects
Acute spreading infection affecting the dermis and hypodermis but not the muscle fasciae. Differentiation from more aggressive pathologies is somewhat difficult (see below).

Diagnosis
Pain, redness and mild swelling. Initially, the symptoms are non-specific and difficult to differentiate from other soft tissue infections, including necrotising fasciitis, since the borders of the infection are not well defined.

Microbiology
The most common causes are beta-haemolytic streptococci, but other Gram-positive and negative organisms can be found. Differentiation between cellulitis and erysipelas is sometimes difficult.

Therapy
Antibiotic therapie combined with or without surgery. The decision to operate is linked to the presence of collections of fluid visualized by imaging or of necroses needing debridement.
11.2.4 Septic bursitis

**Fig. 11-1 Acute septic bursitis**

**Aetiology**
Blunt trauma or a wound close to a bursa (pre- and infrapatellar area, olecranon, greater trochanter).

**Diagnosis**
Pain and tenderness over the elbow, the patella or the greater trochanter, while the adjacent joint itself is pain-free and has an almost full range of motion.

**Microbiology**
*Staphylococcus aureus* (>90%), *Streptococcus pyogenes*.

**Differential diagnosis**
Rheumatologic disease such as gout.

**Therapy**
(Fig. 11-1) Operative revision with bursectomy and immediate wound closure or delayed after 2–4 days. Empiric antibiotic therapy with cephalosporins or amoxicillin/clavulanic acid. Begin with an IV therapy and switch to oral therapy early after closure of the wound. The usual length of antibiotic therapy is 7 days.
11.2.5 Necrotising fasciitis (NF)

General aspects
This is the most feared soft tissue infection. Patients with a suppressed immune system appear to be particularly at risk but NF can affect even healthy young patients. The term fasciitis is somewhat confusing and refers to the involvement of the superficial fascia located between the dermis and hypodermis and not to infection of muscle fascia. In untreated cases, there is a rapid spread to surrounding tissues, bacteraemia, multi-organ failure and death. Muscle fascia can be involved, thus leading to fasciomyositis, or rarely to gas gangrene in cases of muscle infection due to Clostridium perfringens or Clostridium septicum. Involvement of genitalia is known as Fournier’s gangrene.

Diagnosis
Clinically, necrotising fasciitis begins with signs comparable to cellulitis or erysipelas that fails to improve with antibiotics and quickly spreads by way of bacterial enzymes and toxins that cause necrosis of the surrounding tissue. There is often a discrepancy between the character of the visible injury or redness and the intensity of pain. Systemic signs of sepsis, including hypotension, fever and acidosis, may become apparent.

Fig. 11-2 Necrotising fasciitis. Note the 'typical' dishwater pus.
Microbiology
The microbiology can be mixed but the classical hallmark of community-acquired NF is *Streptococcus pyogenes*.

Surgical treatment
NF is a surgical emergency and an experienced surgical team should be involved as early as possible. The surgeon may note a lack of resistance of the normally adherent subcutaneous tissues to blunt finger dissection, lack of bleeding from the deep soft tissues or ‘dishwater pus’ (Fig. 11-2). All involved tissues that can easily be elevated from the fascia with gentle pressure or a dissecting finger should be removed. It is extremely difficult to decide about the extent of debridement. Patient survival is correlated with the delay between the onset of the symptoms and the first debridement. A planned second-look at 12–24 hour intervals is customary and should be performed earlier if the general condition of the patient worsens. In extreme cases amputation may be life-saving.

Antibiotic treatment
Initial empirical antibiotic therapy includes carbapenem or other broad-spectrum antibiotics (plus vancomycin in many cases). This choice of broad-spectrum antibiotics is due rather to a fear of a potentially lethal evolution than being actually supported by microbiological data. Indeed, beta-haemolytic streptococci and *Clostridium perfringens* are susceptible to penicillin. *Staphylococcus aureus* is usually susceptible to first-and second-generation cephalosporins or amoxicillin/clavulanic acid. Hence, even in polymicrobial infection, these most damaging pathogens are still largely covered by cephalosporins or amoxicillin/clavulanic acid. The duration of antibiotic therapy for patients with septic shock depends on the presence of secondary haematogenous seeding and patient evolution. There is a lack of any convincing evidence regarding the ideal duration of antibiotic therapy, which varies between 7 and 14 days.

Association with clindamycin
Clindamycin 900 mg three times a day (over 3 to 5 days) is often added to the empiric antibiotics in severe cases. This combination is analogous to recommendations for the treatment of toxic shock syndrome in which clindamycin neutralises the toxin production of the streptococci or staphylococci. The rationale for its use in NF, without toxic syndrome, is based less on evidence but corresponds to widespread practice in Switzerland.
Intravenous immunoglobulins
Their use as supportive therapy is debatable. They are administered as single doses of 2 g/kg or a three-day course beginning with 1 g/kg the first day followed by 0.5 g/kg the two other days. The rationale for this choice is cited as activation of complement, promotion of antibody-dependent cytotoxicity, reduction of interleukin-6 and TNF-alpha production and inhibition of superantigens.

Hyperbaric oxygen
The rationale for its use is based upon experience with anaerobic gas gangrene. There are no reported randomised trials or case-control studies, but a positive outcome has been published in individual cases. It is costly, labour-intensive and only accessible in a few centres. Hyperbaric oxygen therapy never should delay surgical intervention.

Prognosis
The mortality rate is around 20–30%, but lower incidences of 10% have been reported. It depends essentially on the rapidity and adequacy of surgical debridement and the underlying comorbidities of the patient.

11.3 References

Further reading

Additional articles

12.1 Fundamentals

12.1.1 Aetiology

- Potential aetiologies for open wounds include injuries, such as lacerations, cuts and stab wounds, foreign body perforations or open fractures.
- A wound may remain open following surgery due to impaired healing or infection.
- In addition, circulatory disorders (chronic venous insufficiency, peripheral arterial occlusive disease) or skin disorders may lead to open wounds or ulcers.

12.1.2 Wound types

- Acute wound (soft tissue defects, open fractures)
- Subacute wound (compartment wounds, secondary wound dehiscence following surgical procedures)
- Chronic wounds (pressure ulcer, diabetic wounds)

12.2 Diagnostics and clinical findings

12.2.1 Medical history

Important medical history questions include:
- How long has the wound existed?
- How did the wound occur? Injury mechanism?
- Is there an underlying disease?

12.2.2 Clinical assessment

- Wound assessment: localisation, size, depth, signs of inflammation or infection and degree of wound contamination
- Wound bed: granulation tissue present? Are there any exposed structures (e.g. tendons, vessels)? Is there an abscess?
- Wound margin: healthy skin, scarred zone, width of both
- General assessment parameters: body temperature (fever?), pulse, blood pressure
- Circulatory situation? Neurological deficits?

12.2.3 Laboratory tests

- White blood cell count
- C-reactive protein (CRP)
- Coagulation parameters
- Albumin
- If antibiotics are being administered: creatinine, liver function tests, depending on the antibiotic

12.2.4 Microbiology

- Aspiration if there is fluctuation
- Tissue biopsy in case of revisions
- Blood cultures if there is fever

12.2.5 Radiological diagnostics / Imaging techniques

- Is there a fracture?
- Is there a foreign body?
- Are there signs of osteomyelitis?

12.2.6 Prerequisites for wound healing

- The patient should be healthy: systemic measures (see Chapter 12.3.3).
- The wound should be clean and free of infection: local measures (see Chapters 12.3.1 and 12.3.2).
12.3 Therapy

It is advisable to follow a simple algorithm when treating open wounds (Fig. 12-1).

<table>
<thead>
<tr>
<th>Condition of the patient</th>
<th>Stable, healthy</th>
<th>Unstable, concomitant problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local measures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic measures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Condition of the wound</td>
<td>Clean/acute</td>
<td>Contaminated/infected/chronic</td>
</tr>
<tr>
<td>Wound closure, possibly with plastic surgery</td>
<td>Debridement/drainage/lavage</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative-pressure wound therapy? (see Chapter 5)</td>
</tr>
<tr>
<td>Healing</td>
<td>Primary wound healing</td>
<td>Secondary wound healing</td>
</tr>
</tbody>
</table>

*Fig. 12-1: Treatment algorithm for the treatment of open wounds.*

12.3.1 Treatment of acute wounds (soft tissue defect, grade II/III open fracture)

**Evaluation**

It is essential to provide skin closure for soft tissue defects, grade II open fractures and extended skin defects by plastic surgery in grade III open fracture by the day 7 at the latest. If the admitting hospital cannot achieve this, the patient should be immediately transferred to an appropriate specialist centre.

**Sequence**

1. Debridement: radical cleansing of the wound, removal of foreign bodies and traumatised, non-viable tissue
2. Fracture stabilisation: external or internal, depending on the degree of severity
3. Primary wound closure: due to the risk of superinfection with nosocomial pathogens, this is the top priority for open fractures and must be achieved as soon as possible. For short-term wound care, temporary negative-pressure wound therapy may be used until optimal treatment conditions are in place,
i.e. by a plastic reconstructive surgeon. Scientific evidence confirms that closure within the first 3 days and by day 7 at the latest is considered optimal with or without plastic surgery.

- Immediate wound closure in the case of small defects, lack of soft-tissue tension (beware: wound oedema)

- Free graft in the case of larger defects (Fig. 8-9) Lateral upper arm flaps may also be transplanted with potential connection of a sensitive nerve branch (Fig. 7-6).

- Vascularised local muscle and skin flaps are used less often these days in acute situations because they result in – additional – iatrogenic damage in the traumatised region at the donor site. They are used more frequently in the case of chronic defects (Fig. 7-7 and 8-12).

- Allowing granulation tissue to form on the wound in the fracture region with subsequent split-skin graft is associated with a significantly higher risk of infection (Fig. 5-1).

Fig. 12-2: ♂ patient, 26 years of age. Grade II open fracture bridged with an external fixateur (a), the open wound (b) before debridement and local rotation flap. Primary healing. Clinical appearance at 16 months (c) fracture healed with external fixation alone.
12.3.2 Treatment of subacute and chronic wounds

Debridement, drainage, lavage

With the aim of removing foreign bodies and non-viable tissue, reducing bacteria and collecting bacteriology and histology samples

- Wound debridement: radical debridement of necrotic tissue is the key to successful secondary wound healing. This measure transforms a chronic, slow-healing wound into an acute wound with improved healing.
- Abscess drainage: *Ubi pus, ibi evacua* (Where there is pus, drain it).
- Lavage: There is no consensus on the type of rinsing solution (saline alone or saline with additives/antiseptics) or the lavage technique to be used. A meta-analysis was unable to find a statistically significant difference between isotonic saline solution, distilled water or boiled water in terms of the number of infections and wound healing. High-pressure pulsatile lavage (HPPL) tends to have unfavourable outcomes. It results in more tissue damage and drives contaminants and bacteria more deeply into the tissue. More bacteria are also retained than with lavage using a 10- to 100-mL syringe with splash guard.

Measures for the treatment of clean/cleansed wounds

- Surgical wound closure using the same procedure as for fresh wounds (see Chapter 12.3.1)
- For local conditions which remain unfavourable:
  - If there is communication between implants and infected fractures, clean both (see Chapters 7, 8).
  - Local measures such as hydrocolloid dressing and hyperbaric oxygen therapy to encourage the formation of granulation tissue
  - Antiseptic coverage: covering the wound with a local antimicrobial agent or an occlusive dressing promotes a moist wound environment. This speeds wound healing and reduces pain and the risk of a superinfection (see Chapter 4.3.2 and Fig. 4.-1).
  - Negative-pressure wound therapy to reduce the size of the wound site, provided that there is no communication with a fracture zone, osteomyelitis or foreign material such as osteosynthesis or implants (see Chapter 5, Fig. 5-1).
  - Improvement of arterial blood supply
12.3.3 Systemic measures

- In all cases, stabilise physiologic parameters
- Tetanus prophylaxis
- Antibiotic therapy with corresponding lab parameters (only after samples have been collected, if possible)

12.4 Don’ts

Do not apply vacuum pumps to grade III open fractures if there is no possibility of definitive soft tissue treatment in the admitting hospital and no guarantee of definitive wound closure within 7 days at the latest.

12.5 References

Further reading


Additional articles

13.1 Fundamentals

As a result of peripheral neuropathy, foot injuries are common among diabetics and often lead to ulcers. When healing does not occur, approx. 10–15% of patients will need an amputation. Diabetic ulcers are often due to multiple factors (diabetes mellitus, peripheral arterial occlusive disease, neuropathy). The amputation risk can be reduced by 50% with proper patient education, diabetes management, correct shoe wear and reduction of additional cardiovascular risk factors.

Fig. 13-1: Pathogenesis of diabetic foot
13.1.1 Incidence

Approx. 15% of diabetics develop an ulcer (Malum perforans) on the foot.

13.1.2 Pathogenesis

Numerous problems associated with diabetic feet are largely multi-factorial (Fig. 13-1).

13.1.3 Classification

The Wagner grading system is the most useful system for the classification of diabetic foot lesions into stages 0–5 (Fig. 13-2, 13-3). The presence of ischaemia and infection play an especially important role. As a result, Armstrong added the designations of A (= ischaemic) and B (= infected) to Wagner’s grading system. For example, stage 3 AB is a lesion extending to the joint capsule without osteomyelitis with simultaneous presence of infection and ischaemia.

Fig. 13-2: Wagner’s grading system for the classification of diabetic foot
Stage 0: At-risk foot, intact skin
Stage 1: Superficial ulcer of skin or subcutaneous tissue
Stage 2: Ulcers extend into tendon, bone, or capsule (no abscess, no osteomyelitis)
Stage 3: Deep ulcer with abscess/osteomyelitis or infectious arthritis
Stage 4: Gangrene of toes or forefoot (foot-preserving procedure possible)
Stage 5: Midfoot or hindfoot gangrene (normally requires amputation), life-threatening sepsis possible!
13.2 Clinical findings

- The foot must be thoroughly examined for minor skin lesions. These often involve merely fissures or small ulcers between the toes or in the folds of the foot.
- Non-healing ulcers on the foot involving little or no pain.
- The foot often exhibits pre-existing deformities and functional impairment.
- Swelling, erythema and warmth are indicative of an infection.
- Chronic ulcers often involve osteomyelitis despite the lack of signs of inflammation.
- Any erythema extending > 2 cm around a chronic ulcer is indicative of a limb-threatening infection.
- A thick, swollen, red toe (“sausage toe”) is indicative of osteomyelitis.
- Secretions and foul odour are unfavourable signs.
- May involve fever, some patients may report chills.
13.3 Diagnostics

Infectious disease laboratory tests
C-reactive protein (CRP), leukocytosis, possibly erythrocyte sedimentation rate (ESR).

Blood glucose
Imbalances often accompany an infection.
“Probe to bone”: According to Shone, if there is no contact between the probe and the bone when examining an ulcer, then the likelihood that there is no underlying osteomyelitis is 85%!

Contribution of impaired vascularity
Most cases involve a combined micro- and macroangiopathy. If there is no palpable pulse, then vascular clarification must always be performed: Plethysmograph, Doppler imaging, transcutaneous oxygen measurement (PtCO₂).

Microbiological diagnostics
Three deep tissue biopsies for bacteriology and bone histology in the case of deep ulcers. No swabs or superficial biopsies should be taken! Primarily Gram-positive organisms will appear in fresh cases of malum perforans. Gram-negative bacteria (mixed infection with an average of 4–5 different pathogens, including anaerobes!) are common among patients with antibiotic pretreatment and/or chronic wounds.

Imaging techniques (see also Chapter 6.3)
- Conventional x-ray examination (Fig. 13-4) (Osteolysis? Air bubbles? Joint destruction? Deformity?). Osteolytic changes will show at 2 weeks at the earliest.
- MRI is the most reliable technique for the detection of osteomyelitis. It has a sensitivity of 86% and specificity of 92%, but poses the risk of overestimating the findings due to soft tissue oedema. Abscesses requiring surgical intervention are readily detectable. Please note: Magnetic resonance imaging is not among the primary diagnostic tools.
- Computed tomography (CT), as needed, for the clarification of bone destruction/sequestra in preparation for surgery
- Single-photon emission computed tomography/CT (SPECT/CT): Non-specific and thus unsuitable for diagnosing infections
- Early differentiation between osteomyelitis and Charcot stage 1 is often difficult, especially in the case of ulcers, making a biopsy necessary.
13.4 Therapeutic principles

13.4.1 Treatment steps in the case of open diabetic foot wounds

The following situations can be treated conservatively (on a trial basis):
- Diffuse, more minor infections (cellulitis, phlegmon without abscess)
- Localised acute osteomyelitis
- Occlusive treatment of infected ulcers is contraindicated!

Antibiotic therapy alone has a failure rate of approx. 30% and may result in the formation of resistances, allergies, kidney failure, Clostridium difficile diarrhoea and pseudomembanous colitis.

Fig. 13-4: X-ray of a diabetic foot with multiple pathologies in the upper ankle joint, Lisfranc joint, metatarsal V, and metatarsophalangeal articulations.
The following situations should receive surgical treatment:
- Infections that threaten the extremity, abscess formation, gas formation
- Sequestra, necrosis

Especially unfavourable factors for both therapeutic approaches include:
- Poor circulation
- Renal insufficiency requiring dialysis
- Immunosuppression

It is important to discuss the details of these often difficult and protracted treatments with patients prior to starting them.

**Conservative therapy**
- Local treatment of non-infected ulcers: Debridement, removal of calluses/rhagades
- Pressure relief: Total contact cast (Fig. 13-5), or a special orthosis for diabetics, an orthopaedic shoe with insoles. Total contact casts are the gold standard for taking pressure off non-infected ulcers. These casts are highly effective even in patients with doubtful compliance because patients are unable to remove them. Open ulcers are able to heal because of the even weight distribution along the entire foot in the cast.

*Fig. 13-5: Total contact cast and foot following removal of the cast with healed ulcer.*

**Antibiotic therapy**
- Antibiotic therapy is not indicated in the case of a colonised malum perforans without osteomyelitis due to the risk of the development of resistance. Empirical oral outpatient therapy may be administered in the case of a local infection (cellulitis).
- Targeted inpatient i.v. antibiotic therapy is recommended in the case of deep ulcers following biopsy. The duration of hospitalisation and treatment is based on outcome.
- Empirical i.v. therapy:
  - Amoxicillin with clavulanic acid i.v. (4 x 1.2 g i.v. to 3 x 2.2 g i. v./d)
  - In the case of penicillin allergy: Clindamycin
- Chronic, severe infection: Mixed infection: Gram-positive cocci, Gram-negative rods (*Pseudomonas*) and anaerobes
  - Piperacillin with tazobactam
  - Carbapenem, if life-threatening
  - Cefepime (+ clindamycin or metronidazole in the case of anaerobes)
  - Oral follow-on treatment: Clindamycin and ciprofloxacin
  - Specific therapy based on pathogen spectrum and/or antibiogram
  - An infectious therapy passport (see also Chapter 18) accompanying prolonged antibiotic therapy facilitates documentation and follow-ups.

Important: Charcot foot (Fig. 13-6) is primarily a non-infectious disease.

![Charcot foot](image)

*Fig. 13-6: Charcot foot. Condition after amputation of first ray and second toe, plantar flexion of hind foot with ulcer below navicular bone following destruction of Lisfranc joint.*
Surgical treatment

Important: Vascular status must be determined prior to each surgical procedure. If there are no palpable foot pulses, then angiological investigation must be performed.

- Deep debridement
- Bone resection, e.g. plantar tubercle in the case of plantarly protruding navicular bone (Fig. 13-5)
- Position correction
- Internal amputations of distal metatarsal bones with retention of toes favourable for rays 2–4
- Amputation, e.g. of the fifth ray, transmetatarsal, Pirogov’s, Syme’s, Boyd’s

There is a broad, ongoing debate concerning the most suitable surgical methods; as a result, we have not covered them here in detail.

13.4.2 Preventive measures

- Patient self-examination is very important: Patients should inspect their feet each day, e.g. using a mirror to examine the sole of the foot in the case of impaired sensitivity. If self-examination is not possible, e.g. due to poor vision, then arrange examinations by relatives/friends or medical personnel.
- Best possible blood glucose control
- Identify risk factors: Impaired circulation, somatosensory disorders, skin thinning, foot deformities. Podiatric medical pedicure (not covered as a standard benefit by all health insurance funds!)
- Adapted footwear (orthopaedic shoes with insoles)

13.5 Prognosis and complications

The risk of a relapse can be reduced by 30% with proper patient management and guidance, including behavioural training, optimal diabetes control, and regular examinations (by the patient, relatives/friends, general practitioner, podiatrist).
13.6 References

Further reading


Additional articles

- Kuehn BM. Prompt response, multidisciplinary care key to reducing diabetic foot amputation. JAMA 2012; 308: 19–20
- Sanverdi SE, Ergen BF, Oznur A. Current challenges in imaging of the diabetic foot. Diabet Foot Ankle 2012; 3: 10.3402 Epub, free article
- Schwegler B, Stumpe KD, Weishaupt D et al. Unsuspected osteomyelitis is frequent in persistent diabetic foot ulcer and better diagnosed by MRI than by 18F-FDG PET or 99mTc-MOAB. J Intern Med 2008; 263: 99–106
14 Osteomyelitis and infectious arthritis in children and adolescents

Fritz Hefti

14.1 Classification

A feature peculiar to children and adolescents is the occurrence of spontaneous haematogenous osteomyelitis where there is no implant and no external cause. As well as acute and primarily chronic forms, there are also a number of special forms. Acute osteomyelitis develops over a period of less than 2 weeks and is accompanied by signs of infection (fever, laboratory parameters). Chronic osteomyelitis develops much more slowly and is not necessarily preceded by an acute phase. General signs of infection may not be present.

Classification

- Acute osteomyelitis
  - haematogenous osteomyelitis
  - acute, unifocal osteomyelitis
  - special forms:
    - acute multifocal osteomyelitis
    - neonatal osteomyelitis
    - spondylodiscitis
- Chronic osteomyelitis
  - primary chronic osteomyelitis
  - special forms:
    - Garre’s sclerosing osteomyelitis
    - multifocal chronic recurrent osteomyelitis (CRMO)
    - specific osteomyelitis (tuberculosis, BCG)
  - exogenous (secondary) osteomyelitis
    - post-traumatic
    - postoperative
- Infectious arthritis

14.2 Acute haematogenous osteomyelitis

14.2.1 Aetiology and pathology

- Very typical in children and adolescents.
- Bacteria generally enter the metaphysis of the long bones as a result of bacteraemia. Due to the specific vascular anatomy with spiral arterioles it is particularly easy for bacterial colonies to develop in the metaphysis. Phagocytes
associated with the vascular tissue are absent around these vessels. This encourages bacterial damage to the endothelium with secondary thrombosis, resulting in necrosis of the otherwise exceptionally well-vascularised metaphyses.

- The source of infection generally remains unknown (nasal and oral cavity, skin, respiratory tract, gastrointestinal tract, urogenital system, etc.).
- The site of infection generally remains restricted locally and leads to metaphyseal osteolysis. If the process is not halted through therapy, this results in:
  - Subperiosteal abscess: bacteria may multiply significantly in the transition zone between arterioles and venous sinusoids. The local inflammatory process increases the permeability of the blood vessels, leading to purulence in the subperiosteal area. Subsequently a perforation through the metaphyseal cortex may occur. Expansion of the subperiosteal abscess cuts off the underlying bone from the blood supply and causes avascular necrosis. This results in the formation of a sequestrum. As the elevated periosteum is generally vital, it forms new bone in which the sequestrum may become encapsulated (known as an involucrum).
  - Infectious arthritis: In areas where there is direct contact between the metaphysis and the joint capsule, a subperiosteal abscess can penetrate the adjacent joint, triggering secondary septic arthritis. This can typically occur both in the hip and the knee. In infants and small children up to the age of 3, joint infections frequently occur (in about one-third of cases) as there are more blood vessels crossing the epiphyseal plates in this age group than in older children.

### 14.2.2 Incidence and localisation

The incidence varies considerably and appears to be decreasing in industrialised nations. About 3 new infections per 100,000 children are detected each year. Acute haematogenous osteomyelitis can be located at any site in any bone, however, it is observed most frequently in the metaphyses of long bones. Sites of predilection also include the pelvis and spine.

### 14.2.3 Clinical findings and diagnostics

Although the clinical findings can be quite variable (particularly in very young children), the symptoms are nevertheless typical in most cases. Generally, however, the child feels unwell. Children over the age of 1 year tend to exhibit systemic sepsis as well as a high fever, which may not be present in children younger than 1 year or
in older children and adolescents. Localising the pain may be difficult. A history of stomach or back pain or more vague or uncharacteristic symptoms in older children can be misleading. The range of motion of the adjacent joint is generally limited. If the affected bone has little surrounding soft tissue, painful swelling and reddening is often evident.

**Laboratory diagnostics**
The differential blood count (non-specific), C-reactive protein (CRP) levels and erythrocyte sedimentation rate (ESR) are generally strongly elevated.

**Imaging diagnostics**
- Ultrasound: direct examination to identify any subperiosteal abscesses and joint effusion.
- Scintigraphy: only of diagnostic relevance if local aspiration (joint, abscess) and blood cultures are negative. As osteomyelitis is typically localised in the metaphysis, interpretation can sometimes be difficult due to physiological accumulation of tracer around the epiphyseal plate. Prior to surgical treatment, the scintigram should indicate if there are other sites of infection that require treatment.
- MRI: compared to x-ray imaging, this is a more sensitive means of diagnosis (Fig. 14-1).
- X-ray imaging: used for long-term follow-up. The osteolytic site of infection in itself is not an accurate indicator of the therapy to be selected.

**Microbiology**
This varies, with typical pathogens depending on the patient’s age:
- Infants under 2 months old: *Staphylococcus aureus*, *Streptococcus agalactiae*, Gram-negative Enterobacteriaceae as well as *Candida albicans*
- Children under 3 years: *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus pneumoniae*, recently also *Kingella kingae* and *Haemophilus influenzae*.
- Older children: primarily *Staphylococcus aureus*, *Streptococcus pyogenes*.
- Currently there are increasing numbers of methicillin-resistant staphylococci (MSRA).

Before starting antibiotic therapy, the priority is to identify the microbes that have triggered the condition. 3 blood cultures (regardless of variations in febrile temperature) taken at intervals of 30 minutes result in bacterial diagnosis in more than 50% of cases. If a subperiosteal abscess or joint effusion (hip) are present, aspiration from the painful area, possibly also with ultrasound guidance is mandatory. Samples should be tested for aerobes and anaerobes.
14.2.4 Therapy

Antibiotics as an exclusive therapy following early diagnosis

These are only effective in the early stages prior to abscess formation. Systemic antibiotics cannot eliminate bacteria either in necrotic bone or with encapsulated purulence. Parenteral non-specific therapy should start after collecting blood cultures.

Depending on age, different antibiotics are used empirically to begin with:

- Infants below the age of 2 months: cephalosporins from the cefuroxime group or a beta-lactamase-resistant penicillin in conjunction with clindamycin.
- Small children up to the age of 5 years: beta-lactamase-resistant penicillin as well as cephalosporins from the cefuroxime group.

Dosage must be as high as possible. Infants up to the age of 1 are treated for sepsis right from the beginning, i.e., with high-dose antibiotics, generally aminopenicillins/aminoglycoside or with a 3rd generation cephalosporin. Therapy is adjusted as soon as the microbes or their resistance are known. CRP analysis on day 2. If there is a

Fig. 14-1: Acute osteomyelitis of the distal femoral metaphysis in an 11-year-old girl. On the conventional x-ray image, osteolysis is apparent close to the epiphyseal plate on the lateral side; fluid accumulation in this area is clearly visible on the MRI. Together with the clinical findings (fever, elevated CRP and ESR), the diagnosis of acute osteomyelitis is evident. No abscesses or sequestra are present, with the result that exclusive antibiotic treatment can be carried out with no surgical intervention.
clear improvement in the inflammatory parameters (fever, pain, CRP), conservative treatment is continued. If antibiotic treatment is commenced appropriately in the early stages, the likelihood of recovery without surgery is more than 90%.

**Combined surgical and antibiotic therapy in disease progression**

If clinical findings and CPR levels have not clearly improved by day 5 following the beginning of treatment or if a subperiosteal abscess and/or septic arthritis are present, surgery must be carried out. The difficulty is that without abscesses or joint effusion, there are no prospective parameters to identify cases which are becoming chronic. Monitoring the progression is a crucial factor. Under no circumstances should an attempt be made to substitute surgery with longer-term administration of antibiotics alone.

Appropriate surgery has been performed if:

- the bone abscess is fully debrided
- all necrotic material (sequestra) is thoroughly removed. This material must be analysed bacteriologically for aerobic and anaerobic microbes, in addition to histological analysis
- extensive intraoperative lavage is carried out (no closed irrigation, no gentamicin-impregnated beads). If there is no further necrosis present, acute osteomyelitis will heal
- it is followed by appropriate antibiotic therapy.

**Combined therapy in the chronic stage**

If the condition has already entered the chronic stage prior to the beginning of therapy, the inflammatory parameters may have spontaneously normalised both in terms of clinical and laboratory findings (CRP and ESR).

A combination of appropriate surgery as well as parenteral administration of antibiotics over a period of 6 weeks may inactivate the situation to such an extent that the risk of recurrence is minimised, at least for the coming years.

**Postoperative treatment**

Immobilisation is generally more likely to be counterproductive; with severe pain, wearing a plaster splint for a few days may provide adequate pain relief. As a rule, treatment is functional and may include the use of a continuous passive motion unit. The child is also mobilised where possible (even if a drip is in use). If the legs are affected, use crutches to ensure they are not bearing weight. Weight bearing can be increased as the pain subsides.
Duration of therapy and end of treatment
Most of the more recent studies support the principle of short-term antibiotic therapy.

- Antibiotics as an exclusive therapy in early treatment: if the administration is started in a timely fashion, osteomyelitis will heal once the inflammatory parameters (fever, pain, CRP) have normalised. This is generally the case 5 to a maximum of 14 days after the beginning of treatment. This defines the end of treatment for acute haematogenous osteomyelitis. Additional enteral administration of antibiotics is not required. The patient is discharged and may return home. CRP levels are checked again 1 week later.
- Disease progression with surgical debridement: continue parenteral antibiotic therapy until CRP levels normalise.
- Chronic stage: parenteral therapy for a period of 6 weeks.

14.2.5 Follow-up examinations and prognosis
If CRP levels are normal and the patient does not have any symptoms and is not suffering from unexplained attacks of fever, clinical follow-ups can be done at intervals of 3 months and later every 6 months for up to two years with the aim of detecting any recurrence or growth disorders. After 6 months the osteolytic site of bone infection should be filled spontaneously. If necessary a further follow-up can be scheduled after 6 months.

- Mortality: this has dropped to practically 0% in industrialised nations.
- Residual traces: now seldom, even in osteomyelitis that has become chronic (damage to the epiphyseal plate with growth disorders, pseudarthrosis and formation of sequestra). A chronic-stage condition, however, that includes the formation of sequestra, which spread along the entire diaphysis as well as the surrounding joint, is a serious complication. This will often produce local complications (instability, risk of fracture, destruction of the joint) and the probability that complete recovery is unlikely to be achieved (see Chapter 8.9, Fig. 8-13).

An induced growth disturbance is to be expected after any infection of the growing skeleton. The sequelae depend on the age of the patient, similar to posttraumatic growth disturbances. In most cases, the result is overgrowth of the limb that is not always necessarily of clinical significance (and if it is, then only with regard to the lower extremities). If premature, partial or total closure of the epiphyseal plate occurs following chronic progression of the condition, treatment of the deformity will depend on the age of the patient as well as his symptoms and must be treated accordingly.
14.3. Special forms of acute osteomyelitis

14.3.1 Acute multifocal haematogenous osteomyelitis

Pathogenesis and diagnostics
Fortunately very rare. Haematogenous dissemination from an acute site of infection simultaneously to several bones, not to be confused with chronic recurrent multifocal osteomyelitis (CRMO), see Chapter 14.5.2. Pathogens are generally staphylococci. A temporary impairment of the immune system is assumed to be an aetiological factor, however, it has not yet been possible to prove actual immunodeficiency. Primary symptoms include pain in various parts of the body as well as the signs of general sepsis (fever, fatigue, cardiovascular instability, elevated inflammatory parameters). Both small children and adolescents may be affected. Skeletal scintigraphy makes it easier to locate the sites of inflammation. MRI is used to identify abscesses.

Therapy
Administration of antibiotics in high doses, surgical debridement of sites of infection abscesses and/or necrosis. Appropriate treatment at a very early stage is the only way to ensure adequate healing of this form of osteomyelitis.

14.3.2 Neonatal osteomyelitis

Pathogenesis
The clinical findings in neonates are fundamentally different to those of older children. This is due to the particular circulation in the metaphyseal/epiphyseal area where a significantly greater number of blood vessels cross the epiphyseal plate. Other factors are the distinctive spectrum of pathogens and the immune system, which is in an immature stage of development.

Diagnosis
This is hampered by the lack of verbal communication. Fever and increased ESR levels are often not present, which can result in incorrect interpretation. Look for indirect signs: limited mobility of the affected extremity with compensatory movements (pseudoparalysis), hypersensitivity to touch, extended position, poor general condition. Swelling and reddening generally already signify the presence of purulence within the joint. In neonates, extensive destruction, penetration of purulence into the joint and definitive damage to the epiphyseal plate and the joint cartilage can
quickly occur. In neonates, the spectrum of pathogens is much more varied than in older children (see chapter 14.6, Fig 14-4. Fig. 14-5). The long-term sequelae can be very severe, if there is damage to the epiphyseal plate or to the joint.

14.3.3 Spondylodiscitis

The diagnosis of septic spondylitis or spondylodiscitis is often delayed. Symptoms in the abdominal area may be mistaken for appendicitis. Hip and thigh pain or difficulty to walk may also be predominant. Localised tenderness or pain on percussion as well as an extended spinal position are indicative of the condition.

14.4 (Primary) chronic osteomyelitis

Associated terms

- Brodie’s abscess: metaphyseal intraosseous abscess formation with no preceding acute stage
- Lymphoplasmacellular osteomyelitis: classical primary chronic osteomyelitis

14.4.1 Aetiology

Bacteria spread via the circulatory system into the metaphyses. Initial local limitation of the inflammation, often with encapsulation of the site of inflammation but without abscess formation and generalised symptoms of illness. The relationship between the immunological response and the pathogenicity of the microbes appears to be different to the acute forms. Bacteria are only found in around 30% of cases – evidently due to the low level of virulence. The spectrum corresponds approximately to that of acute haematogenous osteomyelitis. The illness is determined by immunological factors that have not yet been fully clarified. Recovery is possible without long-term sequelae, however, the condition may occasionally become chronic with the development of multifocal metastatic inflammations.

14.4.2 Clinical findings and diagnostics

Variable, unspecific clinical findings. Often, a ‘pseudo-’ or minor trauma initially draws attention to underlying pain that was already present. Symptoms gradually become more pronounced over a period of weeks or months. The patient ultimately
either recovers spontaneously or symptoms continue to worsen (albeit not dra-matically). There is usually no generalised response from the body, meaning that there are no typical inflammatory parameters. If primary diagnostics using conventional x-ray imaging fail to indicate the presence of an osteolytic site of infection despite increasing non-specific pain and/or localised swelling, a symptomatic treatment using immobilisation and administration of anti-inflammatory medication is started. If symptoms worsen despite continuing this therapy over a period of up to 2 weeks, detailed imaging-based diagnostics are indicated (see below). Diagnosis is often too late. The sites of predilection are the ankle and knee area.

**Laboratory diagnostics**
Generally normal. No general signs of inflammation.

**Imaging diagnostics**
X-ray imaging and MRI play an important diagnostic role, however, they are often difficult to interpret and it is not uncommon that they are initially negative. A typical finding is an osteolytic, metaphyseal site of infection (Fig. 14-2).

Fig. 14-2: Primary chronic osteomyelitis of the proximal tibia (Brodie’s abscess) in a 14-year-old boy. In the native images, extensive osteolysis is visible in the epiphyseal/metaphyseal area with a sclerotic margin. The MRI shows an accumulation of fluid that crosses the growth line.
Biopsy
Indicated in osteolytic sites of infection. A tumour is also possible as a differential diagnosis. Collection of several tissue samples for bacteriology (aerobes and anaerobes) and histology. Histology is often unspecific with just a few inflammatory cells. If there is no bacterial growth, proceed with broad-spectrum PCR. Calorimetry may also be a useful addition.

14.4.3 Therapy
Careful debridement (curettage) of the site of infection as thoroughly as possible. Multiple sample collection. The material intended for histology must not be fixed in formaldehyde because biochemical analysis (PCR) and other forms of analysis (e.g., tumour typing) may be necessary. No irrigation-drainage, no antibiotics prior to identification of the bacteria. Local antiseptic lavage at most, provided that no joints are affected. If a germ can be isolated, targeted post-primary antibiotic therapy is carried out intravenously for 5 days at a high dosage. An optimum duration cannot be defined as the inflammatory parameters are initially normal as a rule and cannot be used as clinical parameters.

Suspected tumour: due to the risk of contamination, do not combine the biopsy with curative therapy!

Note: In acute haematogenous osteomyelitis, antibiotic treatment may be supplemented by surgery. In primary chronic osteomyelitis, surgery may be followed by antibiotic treatment.

14.4.4 Postoperative treatment
Functional treatment, possibly with the use of a continuous passive motion unit. When localised in the lower extremity, relief with crutches depending on the severity of the defect. If the necrosis was not removed in its entirety during primary surgery, if the bone defect develops a bacterial superinfection or if local signs of irritation or abscess formation develop as the condition progresses, secondary radical resection is carried out. Vascularised muscle flaps may be considered for very large defects.
14.4.5 Follow-up examinations, post-infection deformities

The objective of clinical and radiological follow-up every 6–8 weeks is to ensure that no superinfections are overlooked and to monitor the spontaneous in-filling of the bone defect. There should be gradual increase in weight bearing. Further radiological follow-up after 6 and 12 months. We do not consider scintigraphic follow-up to be necessary as the regeneration process can take a long time, and accordingly, increased uptake levels are seen for another 6–12 months. This should not be mistaken for a recurrence. If there is a clinical suspicion of a recurrence, antigranulocyte scintigraphy is indicated. If a large bone defect does not spontaneously decrease in size within three months, spongioplasty may be required.

Long-term follow-up after 2 years is aimed at identifying clinical deformities:
- Difference in leg length
- Diaphyseal deformations with inactive infection sites (e.g., outgrowth of the bone)
- Overgrowth disturbances with increased length
- Direct partial or complete epiphyseal closure (rare)

14.4.6 Growth disturbance

The growth prognosis depends on the type of osteomyelitis. Growth stimulation is much more common than growth impairment.

14.5 Special forms of chronic osteomyelitis

14.5.1 Garré’s sclerosing osteomyelitis

In German-speaking countries, the diagnosis of “primary chronic osteomyelitis” is morphologically associated with a plasmacellular, albuminous or sclerosing non-pyogenic osteomyelitis. Garré did not consider his chronic sclerosing osteomyelitis to be a separate condition, but a ‘specific form and a sequela of acute infectious osteomyelitis’. As early as 1893, he discussed low bacterial virulence and the immune status of an organism as a prerequisite for this development. Today, the concept of
Garré's sclerosing osteomyelitis is often incorrectly considered to be a separate condition rather than as a particular form of progression.

Clinical findings
Onset is gradual. Non-specific, variable symptoms with a tendency to progress. They are particularly prone to localisation in the long bones, however, there are exceptions. Local hyperthermia is typical but not mandatory.

Microbiology
Evidence of bacteria is rare although bacteria are assumed to be the trigger. A possible reason for this is the low virulence of the responsible bacteria.

Histology
The diagnosis is substantiated by intralesional biopsies. Histology detects sclerosis of the medullary cavity but only very few inflammatory cells.

X-ray image
Expansion of the cortical bone, irregular structure, sclerosis of the medullary cavity (Fig. 14-3). The periosteum appears to be elevated.

Fig. 14-3: Garré's sclerosing osteomyelitis of the right ilium of a 15-year-old boy; x-ray and CT scan. The entire ilium is affected including the acetabular area, and the bone shows both significant sclerosis as well as irregularly distributed lytic components.
Therapy
There is no standard procedure. In some cases, fenestration and exposure of the medullary cavity (if possible with a biopsy) are sufficient in order to initiate regression. In other cases, recovery does not occur until after full resection of the sclerotic bone segments. It is important that periosteal and medullary revascularisation remain possible. This is achieved for example by reaming the medullary cavity or via extensive longitudinal fenestration.

14.5.2 Chronic recurrent multifocal osteomyelitis (CRMO)

In this disorder, multiple inflammatory sites of infection develop, although no pathogens can be identified. Any bone can be affected. The metaphyses of the long bones are more likely to be affected, however, the vertebrae (vertebra plana), the sternal end of the clavicle, the sacroiliac joint or the mandible may also be involved. This condition is also known as SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis and osteomyelitis). The question is now being discussed as to whether this is actually a rheumatic or autoimmune disorder rather than a type of osteomyelitis.

Clinical findings
Local pain without intrinsic general symptoms. Symptoms may abate intermittently and then recur at the same or other locations. Days, months or sometimes even years can pass between these episodes. Occasionally, changes also occur in the skin such as palmoplantar pustulosis, psoriasis, or acne, in conjunction with or also following the onset of bone pain.

Laboratory tests
Moderate increase in ESR is possible.

Therapy
Non-steroidal analgesics and possibly bisphosphonates. We do not recommend administering antibiotics.

Prognosis
The prognosis is good.
14.5.3 Specific osteomyelitis (tuberculosis)

Bone infection with *Mycobacterium tuberculosis* is rare in Europe today. Although tuberculosis primarily affects the lungs, bones and joints are common locations for post-primary tuberculous infection sites. Typical presentations are:

- Finger and/or the metacarpal bones in children under 5 years: cystic expansion of the bone, known as spina ventosa (tuberculous dactylitis)
- Spine: collapse and fusion of the vertebrae causing a severe Gibbus deformity, abscess along the psoas muscle down to the inguinal ligament.
- Joint tuberculosis: typically monoarticular in the large joints, with pain, swelling, effusion, contracture and, ultimately, destruction of the joint.

Laboratory tests
Laboratory results are not characteristic.

Biopsy
Essential for diagnosis, tuberculous granulomas with Langhans giant cells, epithelioid cells, also possibly with acid-resistant rod-shaped bacteria.

Microbiology
Direct bacteriological analysis does not lead to identification of the microbe. If the direct preparation is negative, it is necessary to wait for the results of the cultures. Newer procedures can reduce the waiting time until a definitive diagnosis is made and resistance testing is finalised, down to 2 or 3 weeks. PCR can be helpful.

Therapy
Antibiotics, generally as a combination of rifampicin and isoniazid for 9–12 months. Tuberculous spondylitis always requires surgical treatment with debridement of the affected vertebra and, if necessary, strut grafting with autologous bone.

14.5.4 BCG osteomyelitis

Occasionally, chronic osteomyelitis may be triggered as a result of a BCG vaccine with weakened tuberculosis pathogens. The metaphyseal infection sites develop close to the vaccine area within 4 years of vaccination. Local pain occurs without general signs of infection. The x-ray image may mimic a tumour. Histological analysis identifies tuberculosis granulomas. The infection site generally recovers without further incident following curettage.
14.5.5 Exogenous osteomyelitis

These infections, which also occur in children and adolescents, are caused by severe open injuries, penetrating, soiled or inadequately treated skin wounds, purulent bursitis or surgical procedures. In terms of diagnostics and treatment, there are no significant differences compared to adults (see Chapter 8).

14.6 Infectious (purulent) arthritis

Infectious arthritis is discussed in detail in Chapter 9. The principles of diagnosis and therapy are broadly the same in children and adolescents as in adults. Only some particular features will be discussed here.

14.6.1 Aetiology and localisation

Unlike adults, infectious arthritis in children almost always occurs as a result of haematogenous dissemination, either directly into the synovial fluid or via the metaphysis into the joint. Osteomyelitis sites close to a joint can also initially cause effusion (primarily without microbes) and subsequently provoke secondary infection of the joint as a result of penetration or perforation (see Chapter 14.2.1). Up to the age of approximately 3 years, the epiphyses are supplied by blood vessels that cross the epiphyseal plate. Later, the epiphysis and metaphysis are supplied separately by a largely independent vascular system. Until the age of three, metaphyseal infections can more easily enter the joint via the transepiphyseal vessels than in older children.

The distribution of pathogens roughly corresponds to that of osteomyelitis, with the same correlation with age. Staphylococcus aureus bacteria are present in almost 50% of cases, less common are coagulase-negative streptococci, Streptococcus pneumoniae, salmonella, Haemophilus influenzae and group B streptococci. The hips (50%), knee and ankle joint are predominantly affected. However, theoretically any joint can be affected.

14.6.2 Growth disturbance

Any infection that becomes established in the joint with a duration of more than 4 days causes irreversible direct or indirect damage to the cartilage. The damage is caused primarily by leukocytes rather than the bacteria.
A certain amount of joint remodelling and restoration of the cartilage is possible using hyaline and fibrous cartilage substitute, however, this can never be exactly predicted. The residual mobility once the acute phase has abated plays a crucial role in regeneration. Scarring can occur, which, particularly in the hip joint, can result in increasing subluxation and secondary dislocation (Fig. 14-4).

![Fig. 14-4: Hip joint of a 15-year-old girl, following pyogenic septic arthritis as an infant. Subluxation of both hip joints and severe damage to all joint components.](image)

The epiphyseal plates may also become damaged, generally on one side, which causes severe axis deviation (Fig. 14-5). Depending on age, complete plate damage can result in severe shortening of the leg.

14.6.3 Clinical findings

Diagnosis in infants is particularly challenging. The child no longer spontaneously moves the affected extremity and resists attempts at movement by the parents. There is often no fever. However, the child seems unwell, and appears to be suffering from sepsis.
In older children, fever is an obvious primary symptom in around 85–90% of cases, in addition to joint effusion. The predominant symptom is a spontaneous onset, painful limitation of range of motion of the affected joint. Spontaneous limping is seen when a lower extremity is affected. Medical history can become distorted, for example, if the onset of illness coincides with real or apparent trauma. Symptoms always worsen.

Fig. 14-5: Right knee of a 4-year-old girl, following septic arthritis of the knee as an infant and severe axis deviation as a result of damage of the lateral growth plate.
14.6.4 Diagnosis and treatment

Emergency aspiration in all febrile patients with joint effusion. Diagnosis is made on the basis of the effusion for the knee, clinical symptoms as a rule for the ankle joint and elbow and ultrasound for the hips and other joints if in doubt. As part of the preparations for aspiration of joint effusion under general anaesthesia, the following laboratory tests are carried out: 3 blood cultures at 30-minute intervals, ESR, CRP, differential blood count. X-ray imaging to exclude an osteolytic site of infection in the adjacent bones. Aspiration is the first-line therapy and also supports diagnosis. If the synovial fluid specimen is clear, it is necessary to wait for the bacteriology results. If it is cloudy or perhaps even purulent, arthroscopic lavage is immediately carried out under the same anaesthesia and antibiotic therapy is initiated (see Chapter 9).

14.6.5 Post-infectious deformities

Post-infectious deformities generally present complex and difficult treatment challenges. Extensive joint destruction is often a tragedy for a child. In children, stiff joints should not be accepted too soon, even when associated with serious contractures. In many cases, with aggressive, consistent and long-term mobilisation and physiotherapy, it is possible to restore function to a child’s severely damaged joints, thanks to their enormous potential for remodelling. This requires repeated manipulation under anaesthesia, intensive postoperative physiotherapy with epidural pain relief as well as subsequent long-term physiotherapy.

14.7 Don’ts

- Start with antibiotic therapy prior to identification of the microbe (several attempts must be made if necessary)
- Immobilisation for long periods
- Omission of surgical exploration if there is an abscess or sequestrum with acute osteomyelitis
- Antibiotic treatment of the primary chronic osteomyelitis without previous surgical debridement
- Omission of joint lavage if infectious arthritis is present
14.8 References

Further reading


Additional articles

15.1 Introduction

In order to make the best possible use of bacteriological findings, they must be interpreted within the clinical context. Is the bacterium that has been detected an infectious agent or a contaminant? Where did the microorganism originate? Is it endogenous (is it necessary to search for a focus?) or was it introduced into the body during a procedure? What problems are associated with the therapy? What are the most effective antibiotics? What is the risk of resistance emerging? What complications can be expected? Should negative bacteriological findings be relied on or could it be that the method selected was unable to detect the relevant microorganisms?

This chapter is intended to assist clinicians with limited microbiological experience in dealing with these issues. It is not possible to systematically describe bacteriology in this context. This chapter will first explain some basic characteristics of microorganisms that are relevant for clinical understanding. The second part presents the most important bacteria from a clinical perspective with respect to infections of the musculoskeletal system.

15.2 Fundamentals

15.2.1 Virulence and pathogenicity

Very few of the vast number of microorganisms are capable of causing infections in humans. These microbes possess characteristics (virulence factors) which enable them to reproduce and spread within the host tissues. These characteristics include, for example, the ability to attach themselves to the host tissue (adherence) or to create a suitable milieu through the action of toxins. Reproduction of the microorganisms usually damages the host tissue (pathogenicity). There may also be damage to the host as a result of major local or systemic immune reactions triggered by the microbes. Virulent bacteria usually multiply rapidly and trigger a major inflammatory response, causing an acute infection.

Conversely, there are microorganisms with no or only a few virulence factors. If they are detected, they are often classified as part of the normal flora or considered to be contaminants. Examples include coagulase-negative staphylococci and
propionibacteria, which form part of the normal skin flora. However, there is no clear-cut boundary between pathogenic and non-pathogenic microorganisms. Typical pathogens, such as pneumococci, meningococci or *Staphylococcus aureus*, are often detected in sample materials such as mucosa without these results necessarily indicating the presence of a disease. Under the right conditions, non-pathogenic bacteria can trigger infections. In these situations they often take advantage of a deficiency in the immune system. The presence of a foreign body may induce such a local immunodeficiency, enabling otherwise non-pathogenic coagulase-negative staphylococci or propionibacteria to cause an infection. However, these infections usually do not trigger a systemic inflammatory response but rather a minor, localised response (low-grade infection). With foreign body-associated infections these responses are limited to the immediately adjacent zone.

### 15.2.2 Endogenous and exogenous infections

Bacteria originating from their usual physiological sites (e.g., streptococci from the oropharynx) or from another focus of infection (e.g., enterobacteria associated with a urinary tract infection) can cause a metastatic focus by haematogenous spread. This is referred to as an *endogenous* infection. Arthritis, spondylodiscitis and prosthetic joint infections may be endogenous. These usually involve virulent bacteria, resulting in acute infections. Exogenous infections are caused by microorganisms from outside the body introduced during a procedure (surgery, aspiration, etc.). This may involve virulent bacteria which result in acute or sub-acute infections or less virulent bacteria which lead to low-grade infections. This is illustrated for prosthetic joint infections (see Chapter 7): the wound may become contaminated with virulent or less virulent bacteria during surgery. The former situation may lead to an acute infection that will manifest within the first 3 months following surgery; the latter case usually results in a low-grade infection with symptoms possibly taking up to 2 years to develop. Conversely, haematogenous infections may also develop years later and are caused by virulent bacteria usually with an acute course (see Chapter 7.1.6).
15.2.3 Bacterial lifeforms

Bacteria may take on two fundamentally different lifeforms: as free-floating (planktonic) bacteria in a liquid (or in a host tissue), where they rapidly multiply and are metabolically active, or as adherent bacteria attached to a surface in the form of a biofilm. This major difference between these two forms has critical effects on the diagnosis and treatment of infections. For example, ultrasonic treatment (sonication) of explanted foreign bodies improves the detection of bacteria in biofilm (see Chapter 6.5). Many antibiotics are also less effective against bacteria in biofilms because these bacteria are less metabolically active than planktonic bacteria (see Chapter 1).

An additional form of bacteria is small colony variants (SCV) (Fig. 15-1). These are subpopulations that differ from bacteria with normal phenotypes in that they form smaller colony sizes on agar plates, among other characteristics. The smaller size of these colonies is due to their slower growth rate caused by an acquired metabolic defect. They are difficult to detect in laboratory tests (extended incubation is necessary for growth, subject to overgrowth by other microorganisms, have atypical appearance of the colonies). It is also difficult to treat infections caused by SCV bacteria because SCVs are inherently resistant to various antibiotics and may persist inside cells. They are able to subsequently convert back into normal, virulent phenotypes, giving a high risk of recurrent infection. SCVs are known for numerous bacteria (including staphylococci, Salmonella spp., Escherichia coli, Pseudomonas aeruginosa) and have been detected in many clinical situations (including abscesses, respiratory tract infections, osteomyelitis). SCVs of S. aureus have been intensively studied. They play an especially important role in osteomyelitis and foreign body infections. SCVs develop as a result of prolonged, continuous exposure to aminoglycosides, for example, following implantation of gentamicin-impregnated beads during

Fig. 15-1: Small colony variant (SCV) of Staphylococcus aureus. The sparse colonies are considerably smaller than ‘normal’ colonies. They are characterised by inhibited and atypical growth and their shape is irregular. They usually lack the typical beta haemolysis. (see Fig. 15-4a)
osteomyelitis debridement. Prosthetic joint infections caused by \textit{S. aureus} SCVs are considered difficult to treat. It is necessary to completely remove all foreign material in order to cure the infection (see Chapter 7.3: two-stage revision with long interval).

15.2.4 Diagnosis

Culture and resistance testing are the gold standard for diagnosing and treatment of a bacterial infection. It is rarely difficult to detect virulent bacteria, provided the patient has not received antibiotic treatment or a current antibiotic regimen has been discontinued for a period of 2 weeks prior to testing. These bacteria generally grow in normal culture media within 24–48 hours. Other bacteria grow more slowly, however, and so can only be detected if the bacteriological samples are incubated for a prolonged period. This applies particularly to propionibacteria and certain anaerobes but also to small colony variants of \textit{S. aureus}. It is also important for the yield of bacteriological tests to ensure that suitable samples are collected (multiple tissue biopsies, no swabs) and that these samples are quickly processed in the laboratory. In particular, anaerobes and delicate microorganisms such as \textit{Haemophilus spp.} and \textit{Neisseria spp.} may die with excessive transport times. If patients have received antibiotics prior to sample collection or if it is suspected that the bacteria may be difficult to culture, then pathogen detection using eubacterial PCR or sonication may be successful (see Chapters 6.4, 6.5). If a mycobacterial infection is suspected, the laboratory must be explicitly requested to use an appropriate culture. Specific PCRs are available for other pathogens (e.g., \textit{Borrelia spp.} in synovial fluid, \textit{Chlamydia spp.}, gonococci, mycobacteria) or pathogen detection may be successful with serological methods (e.g., with \textit{Brucella spp.}).

15.2.5 Resistance testing

Conventional antibiograms provide results in qualitative terms (e.g., susceptible, intermediate or resistant). Until recently, the agar diffusion test (Kirby-Bauer method) was the most widespread method in use. This involves uniformly applying the bacteria to be tested on an agar plate that is then loaded with wafers, each containing a defined quantity of an antibiotic. Following an incubation period of 16–20 hours, the zone of inhibition around the wafers is measured and used to calculate the sensitivity
or resistance (Fig. 15-2). In recent years, this test method has been partly replaced by automated systems which use the microdilution method. Bacterial growth is measured in wells containing different concentrations of antibiotics.

In select cases, for example, invasive infections with pneumococci or viridans streptococci, quantitative determination of the *minimum inhibitory concentration* (MIC) is advisable (with results given in mg/L). An Epsilometer test is currently the most common method used for this purpose (Fig. 15-3).

Resistance testing provides an important foundation for selecting antibiotics but does not guarantee therapeutic success. It must be kept in mind that growth conditions in standardised lab tests diverge greatly from the growth conditions within the tissue (see Chapter 3.1). A certain level of experience is also required to interpret antibiograms. Not all antibiotics that are indicated by their sensitivity are equally effective. The results of clinical trials and published treatment guidelines should also be considered when selecting antibiotics. For example, infections with *S. aureus* should not be treated with ceftriaxone because it is significantly less effective than flucloxacillin, which is typically used against staphylococci. Other antibiotics, such as rifampicin or quinolones for staphylococcus infections, must be combined to prevent the emergence of resistance during treatment.

![Fig. 15-2: Agar diffusion test (Kirby-Bauer method) to determine the susceptibility of bacteria to antibiotics. The greater the zone of inhibition, the more effective the antibiotic.](image-url)
Antibiograms that are missing information are a source of constant questions. These gaps are due to a number of reasons:

- The sensitivity to certain antibiotics may be deduced from the test results for a different antibiotic. For example, enterococci that are susceptible to ampicillin are always susceptible to amoxicillin and amoxicillin/clavulanic acid, even if this is not explicitly stated.
- The use of some antibiotics is never advisable with certain pathogens, which is why no resistance testing is performed for the following: *P. aeruginosa* is always resistant to amoxicillin/clavulanic acid and infections with enterococci should never be treated with cotrimoxazole or clindamycin.
- The zone of inhibition and MIC are interpreted in Europe on the basis of the guidelines of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) and classified as susceptible, intermediate or resistant. If these categories are not defined for certain bacteria, no interpretation can be made. In such situations, however, the laboratory can determine the MIC for the selected antibiotic and provide it without any interpretation. Clinicians must then decide for themselves which is the best antibiotic to be used.

![Fig. 15-3: Determining the minimum inhibitory concentration (MIC) using the Epsilometer test (MIEC oxide). The antibiotic is applied with a gradient from one end of the test strip to the other. The MIC can be read off at the point where the ellipsoid zone of inhibition touches the test strip (at 2 mg/L in the example shown).](image)
15.3 Specific bacteria

One of the fundamental classifications of bacteria involves their behaviour during Gram staining. Differences in the staining response are due to the fact that, in addition to the cytoplasmic membrane, Gram-positive bacteria are surrounded by a thick cellular wall composed of peptidoglycans. Gram-negative bacteria have only a thin cellular wall with an additional outer lipid membrane.

15.3.1 Gram-positive bacteria

Staphylococci (Fig. 15-4)

Morphology: Gram-positive cocci, grow in clusters
Habitat: Skin and mucosa
Classification: Based on the coagulase reaction staphylococci are classified as coagulase-positive or coagulase-negative. S. aureus is the sole coagulase-positive staphylococcus among the clinically relevant staphylococci.

Fig. 15-4: Two typical cultures on a sheep blood agar plate:
a) Staphylococcus aureus: characteristic phenotype with pigmentation and β-haemolysis, Gram-positive cocci in clusters, b) Staphylococcus epidermidis: typical coagulase-negative staphylococci with no pigment or haemolysis.
Technique: sample material is distributed using a loop in the upper left portion of the agar plate. After the loop has been annealed, it is dragged across the previously inoculated field, including the upper right field of the culture medium. The loop is then annealed again and the same procedure is repeated for the lower right field. Abundant growth on both plates compared to Fig. 15-1.
S. aureus is an important pathogen and causes a wide range of disorders from harmless skin infections to life-threatening sepsis and endocarditis. In cases of bacteraemia, secondary foci of infection are also especially common on implants. All other staphylococci are subsumed under the term 'coagulase-negative staphylococci'. These are mostly non-pathogenic and are thus often considered to be contaminants upon detection. However, they are able to adhere to foreign bodies and cause infections in such situations. S. lugdunensis differs from other coagulase-negative staphylococci because it possesses many of the virulence factors of S. aureus. It also causes invasive infections without the presence of a foreign body.

Therapy: Beta-lactam antibiotics are the most important group of antibiotics for treating staphylococcus infections. Vancomycin or daptomycin are used in the presence of methicillin resistance. All staphylococci form biofilms on foreign bodies. Rifampicin alone is capable of eradicating staphylococci in biofilms, but must be used in combination with another active antibiotic to prevent the emergence of resistance. It should not be started until the surgical wound is dry. In foreign body-related-infections with rifampicin-resistant staphylococci, curative treatment is only possible once all of the foreign material has been removed.

Streptococci (Fig. 15-5)

Morphology: Gram-positive cocci, arranged in chains

Habitat: Normal flora of the gastrointestinal tract and mucosa

Classification: Streptococci are classified into α-Streptococci, which cause green haemolysis on sheep blood agar plates, and are further differentiated into those that trigger β-haemolysis and those that do not trigger haemolysis. β-haemolysis streptococci are then classified based on the Lancefield grouping method (A–G). Group A streptococci (S. pyogenes) are mainly pathogens that cause pharyngitis and soft tissue infections. Bacteriemia with group B streptococci (S. agalactiae) or viridans streptococci (with or without endocarditis) may result in metastatic infections of the musculoskeletal system (arthritis, spondylodiscitis).
Therapy: All streptococci are fundamentally susceptible to penicillin; however, there has been an increase in the detection of streptococci with reduced susceptibility to penicillin (increased minimum inhibitory concentration, MIC). The efficacy of penicillin can be improved by combining it with an aminoglycoside.

### Enterococci

**Morphology:** Gram-positive cocci, arranged in chains

**Habitat:** Normal flora of the gastrointestinal tract

**Classification:** Among the various enterococci, *E. faecalis* and *E. faecium* are especially clinically significant.

**Therapy:** Enterococci are resistant to most antibiotics and have a high tolerance for the remaining available antibiotics. Essentially, only penicillins, imipenem, glycopeptides (vancomycin) and daptomycin are effective. Among the penicillins, amoxicillin has the lowest MIC. The efficacy of penicillins and glycopeptides may
be increased by combining them with an aminoglycoside (bactericidal combination). *E. faecium* is also usually resistant to penicillins. In addition, enterococci may also be resistant to vancomycin, which greatly limits the therapeutic options. If they cause implant-associated infections, then they must be considered as “difficult to treat” (see Fig. 7-3).

**Abiotrophia and Granulicatella**

**Morphology:** Gram-positive coci, arranged in chains  
**Habitat:** Normal oral flora  
**Characteristics:** Bacteria of these two genera used to be called ‘nutritionally deficient streptococci’ because their growth depends on the presence of pyridoxal (vitamin B6). They are difficult to culture.  
**Therapy:** Reduced susceptibility to penicillin is relatively common and resistance testing requires special methods due to the special culture conditions of these bacteria. Severe infections should be treated with a combination of penicillin and an aminoglycoside.

**Corynebacterium**

**Morphology:** Gram-positive rods with club-shaped ends  
**Habitat:** Sometimes among normal skin and oral flora, sometimes originating from the environment  
**Characteristics:** *C. diphtheriae* and *C. ulcerans* are the pathogens that cause diphtheria, starting with infections of the pharynx or skin. The remaining *Corynebacteria spp.* are considered non-pathogenic but may cause infections involving intravascular catheters. *Corynebacteria spp.* are also rarely involved in implant infections. It is important to verify the presence of the bacteria in multiple biopsy samples to rule out contamination.  
**Therapy:** The susceptibility of *Corynebacteria spp.* to various antibiotics is unable to be empirically predicted; therapy must be based on the particular resistance testing.
**Bacillus (Fig. 15-6)**

**Morphology:** Gram-positive, spore-forming rods  
**Habitat:** Widespread throughout the environment  
**Characteristics:** *Bacillus spp.* may sometimes be detected in open wounds but usually have no clinical significance. The most commonly detected Bacillus species is *B. cereus*, which may also cause gastroenteritis through contaminated food. *B. anthracis* is the pathogen that causes anthrax.

**Therapy:** Contamination must be ruled out. Antibiotic therapy is based on resistance testing.

![Image](https://via.placeholder.com/150)

*Fig. 15-6: Bacillus cereus exhibits haemolytic growth in blood agar and is resistant to penicillin. Gram positive rods. The empty spaces in the rods are spores (arrows).*

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**15.3.2 Gram-negative bacteria**

**Enterobacteria (Fig. 15-7)**

**Morphology:** Gram-negative rods  
**Habitat:** Enterobacteria belong to the normal gut flora but may also be found as environmental microbes. They may colonise open wounds and cause nosocomial infections.

**Classification:** The Enterobacteriaceae family encompasses many genera; the most clinically significant include: *Escherichia coli*, *Klebsiella spp.*, *Proteus spp.*, *Enterobacter spp.*, *Citrobacter spp.*, *Serratia spp.*, *Morganella spp.* and *Salmonella spp.*

**Therapy:** In the past enterobacteria exhibited varying levels of susceptibility to amoxicillin/clavulanic acid and second- generation cephalosporins but they are generally susceptible to third- and fourth-
generation cephalosporins and carbapenems. However, resistance against those broad-spectrum antibiotics emerged due to the appearance of various novel beta-lactamases:

- **ampC beta-lactamases**: Certain enterobacteria (*E. cloacae, C. freundii, Serratia marcescens* and *Morganella morganii*) possess the gene for a beta-lactamase that can inactivate third-generation cephalosporins. This gene is usually not expressed and the bacteria test susceptible to these antibiotics. However, mutations may result in a constant production of these beta-lactamases and the bacteria develop resistances to third-generation cephalosporins.

- **ESBLs (extended-spectrum beta-lactamases)** are beta-lactamases that stem from conventional beta-lactamases common among enterobacteria but which may also inactivate third- and fourth-generation cephalosporins due to mutations. They are found particularly with *E. coli, Klebsiella pneumonia* and *Klebsiella oxytoca* but may also occur with other enterobacteria. Carbapenems remain effective against enterobacteria that have ESBLs.
- **Carbapenemases** are beta-lactamases that can inactivate carbapenems as well as cephalosporins, rendering the entire group of beta-lactam antibiotics ineffective and often making treatment very difficult.

- Enterobacteria also form biofilms on foreign bodies. In-vitro experiments have found that quinolones are most effective against enterobacteria in biofilms. The most effective quinolone against Gram-negative bacteria is ciprofloxacin. Curative treatment of foreign body infections with ciprofloxacin-resistant enterobacteria is only possible once all of the foreign material has been removed.

**Pseudomonas aeruginosa** (Fig. 15-8)

**Morphology:** Gram-negative rods

**Habitat:** Environmental microbe in moist milieus can sometimes be detected in the gastrointestinal tract. They colonise open wounds and the airways of mechanically ventilated patients and may cause nosocomial infections.

**Therapy:** *Pseudomonas aeruginosa* is naturally resistant to many antibiotics and is also difficult to treat with the remaining available antibiotics because it forms a thick biofilm. It is considered a difficult-to-treat microbe for foreign body infections and requires removal of the foreign material. Quinolones are the only antibiotics that can be orally administered, with ciprofloxacin being the most effective.
15.3.3 Anaerobic bacteria

Propionibacteria (Fig. 15-9)

Morbidity: Gram-positive, branched, non-spore-forming rods

Habitat: Normal skin flora (especially in areas with high numbers of sweat glands) and mucosa. *P. acnes* is far and away the most common propionibacterium detected in clinical samples.

Characteristics: Propionibacteria are usually considered to be contaminants (particularly in blood cultures). However, they may also cause endocarditis (especially in the presence of artificial heart valves) and are often the cause of infected prosthetic shoulder implants. Propionibacteria grow slowly and samples must be incubated for a suitably long period (2 weeks minimum). They tend to be susceptible to amoxicillin, rifampicin, levofloxacin and clindamycin, among others. However, resistance may emerge and resistance testing should be performed.

*Fig. 15-9: Propionibacterium acnes:* round, spherical colonies, branching Gram-positive rods.
Clostridia
Morphology: Gram-positive, spore-forming rods
Habitat: Various species of Clostridium belong to the normal intestinal flora, while others are environmental microbes.
Characteristics: The pathogenicity of clostridia is based on the effect of produced toxins. Known disorders include tetanus, botulism and Clostridium difficile colitis. Toxins are also responsible for the fulminant progression of gas gangrene caused by *C. perfringens*, *C. septicum* and related clostridia. With infections of the musculoskeletal system, clostridia from open wounds may be detected, for example, with open bone fractures. Most clostridia are penicillin sensitive while *C. difficile* colitis is treated with oral Vancomycin.

Peptostreptococci and Finegoldia
Morphology: Gram-positive cocci
Habitat: Normal flora of the gastrointestinal tract, oropharynx and skin.
Characteristics: Peptostreptococci and Finegoldia have occasionally been detected as contaminants but also as infectious agents in various compartments of the body. The most common infectious agent affecting the musculoskeletal system is *Finegoldia magna*. They are difficult to detect because they grow slowly.

15.3.4 Other microorganisms

Mycobacteria
Morphology: Acid-fast rods
Classification: Mycobacteria of the tuberculosis complex (predominantly *M. tuberculosis* and *M. bovis*) are obligate pathogens and primarily cause pulmonary tuberculosis; however, extrapulmonary manifestations are well described. The spine is most commonly affected (Pott's disease) part the musculoskeletal system. Treatment is with 3 or 4 drug regimens over a 6-12 month period. Atypical mycobacteria include environmental microbes that are often considered to be contaminants in clinical samples but, individual species may cause infections, particularly in the lungs and soft tissue. Immunosuppressed patients are especially affected. Infections of the musculoskeletal system have been described but are very rare. Removal is required with foreign body infections.
15.4 Fungi

Classification: Clinically significant fungi can be subdivided into yeast fungi (e.g., *Candida spp.*) and mould fungi (e.g., *Aspergillus spp.*).

Characteristics: Infections of the musculoskeletal system are rare but occur mainly following implantation of a foreign body. The most commonly detected pathogen is *Candida spp.*, but mould fungi may also cause infections. All foreign body-associated fungal infections are considered difficult to treat and require the removal of the foreign material.

15.5 Nomenclature and notation guidelines for microorganisms

Bacteria are designated with a binomial Latin name written in italics, consisting of the name of the genus (higher-order classification) followed by the name of the species, e.g., *Staphylococcus aureus* or *Staphylococcus epidermidis*. The abbreviation ‘sp.’ is used when the actual species names are not specified, e.g., *Staphylococcus sp.* indicates any one bacterium species within the Staphylococcus genus. The abbreviation ‘spp.’ (e.g. *Staphylococcus spp.*) indicates all of the species belonging to a genus. If bacteria are designated using the English name or a descriptive name, then normal script is used (staphylococci, enterococci).

15.6 References

Further reading

Additional articles

Antibiotic therapy
We differentiate between prophylactic (preventive) pre-emptive, empirical and targeted therapy. Precise definition (see Chapter 3.2).

Antiseptic coverage
Coverage of a wound with a moist dressing that includes an antiseptic to be changed each day with the objective of preventing a superinfection until the wound has healed or the wound is closed by means of plastic surgery (see Chapter 4.3.2, Fig. 4-1).

Arthritis, infectious
Staging as defined by Gächter: There are 4 stages based on the degree of severity (for a precise definition, see Tab. 9-1 and Fig. 9-1).

Bacteria, difficult-to-treat
In terms of implant-associated infections, bacteria are considered difficult to treat if there are no antibiotics available that can reliably eliminate the resting bacteria bound within the biofilm. In other words, the likelihood of healing is not high unless curative antibiotic therapy is administered following removal of the implant (see Chapters 7.3 and 7.4). Difficult-to-treat bacteria include:
- rifampicin-resistant staphylococci,
- enterococci,
- small-colony variants (SCV) primarily of staphylococci (Fig.14-1) but also of Salmonella spp, Escherichia coli, Pseudomonas aeruginosa (see Chapter 1.4, 15.2.3)
- enterobacteria and Pseudomonas aeruginosa that are resistant to quinolones (see Chapter 15.3.2),
- fungi (see Chapter 15.4)
Infections with unknown pathogens that have been clearly detected in histological tests are also difficult to treat.

Biofilm
Microorganisms adhering to the surface of implants and which are embedded in a glycoprotein matrix. Bacteria and fungi in biofilm are metabolically inactive and thus less susceptible to most antibiotics (see Chapter 1).
Brodie’s abscess
Late stage of a healing or primary chronic osteomyelitis. This is characterised by a central inflammatory focus that is differentiated from a broad, sclerotic bone margin and is usually localised in the metaphysis, frequently in the tibia. It mainly affects adolescents and young adults with an above-average immune status (see Chapter 14.4).

Charcot foot
Neuroarthropathy that may occur as part of a neuropathy, especially with diabetic foot syndrome. Polyneuropathy results in increased demineralisation in the bones of the foot. No longer protected by pain due to the neuropathy, the foot is overloaded, leading to destruction of the bone and skin ulceration. Clinical and radiological findings may simulate an acute infection (see Chapter 13, Fig. 13-5).

Coagulase reaction
Method for differentiating staphylococci: *Staphylococcus aureus*, which forms a clot when mixed with fibrinogen-containing plasma, is coagulase-positive. Nearly all other pathogenic staphylococci, e.g., *Staphylococcus epidermidis*, are coagulase-negative (see Chapter 15.3.1).

Debridement
Debridement means ‘to lay open’. In orthopaedic surgery, it also means to remove infected or dead tissue. It is used to reduce the bacterial count at the site of infection as far as possible and optimise the conditions for antibiotic therapy (see Chapter 3.1). The critical steps may include:

- Removal and replacement of the implants in cases of haematogenous infections lasting longer than 3 weeks or if an exogenous infection is first debrided more than 1 month after surgery
- Removal of the tissue surrounding the implant and necrotic bone (see Fig. 7-1, Fig. 8-3)
- Excision of often extensive joint capsule protrusions and fistulas containing detritus (see Chapter 6.2)
- Adequate wound drainage to prevent postoperative haematoma
- Open synovectomy with joint infections (stages 3 and 4) (see Chapter 9.3.4)
- Tissue samples must be harvested from periprosthetic area or “implant bed” (see Chapter 6.4)
Diabetic foot
Development of bone changes and wounds with poor healing tendency of the foot due to multiple factors (circulatory disorder and neuropathy) associated with diabetes mellitus (see Chapter 13)

Diagnosis of infection
Meeting at least one of the following criteria provides confirmation of the diagnosis of infection:
- Abscess with pus discharge, possibly following incision
- Presence of a fistula/sinus
- Microbiological identification of the same pathogen in at least two samples (tissue samples, sonication of foreign bodies)
- Histological testing of periprosthetic tissue/implant bed: total of more than 20–25 granulocytes in 10 fields of view at 400 x magnification (Morawietz et al. 2009).

Gram staining
Christian Gram developed a staining technique in which bacteria surrounded by a thick cellular wall composed of peptidoglycans turn blue (Gram-positive bacteria) and those with only a thin cellular wall with an additional outer lipid membrane turn red (Gram-negative bacteria) (see Chapter 15.3).

Healing in periprosthetic infections
Healing in periprosthetic infections is defined as meeting the following criteria:
- No history or clinical signs of infection symptoms
- Normalisation of C-reactive protein (CRP) < 10 mg/L and/or erythrocyte sedimentation rate < 20 mm/h
- No radiological signs of infection > 24 months after the first infected revision

Healing is considered likely to occur in relapse-free patients between 12 and 24 months.

A persistent infection (or relapse) occurs with recrudescent infection with the same microorganisms and is not time dependent.

A new infection is defined as occurrence of an infection with different microorganisms.
**Infection classification** (see Chapter 7.1.6, Chapter 8.1.3)

*Tab. 16-1: Infection classification*

<table>
<thead>
<tr>
<th>Infection classification based on time of initial manifestation after surgery</th>
<th>Osteosynthesis</th>
<th>Early infection</th>
<th>≤ 2 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Delayed infection</td>
<td>2–10 weeks</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Late infection</td>
<td>≥ 10 weeks</td>
<td></td>
</tr>
<tr>
<td>Joint replacement</td>
<td>Early infection</td>
<td>≤ 3 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Delayed infection</td>
<td>3–24 months</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Late infection</td>
<td>≥ 24 months</td>
<td></td>
</tr>
</tbody>
</table>

| Infection classification based on pathogenesis | Exogenous | Inoculation from outside (perioperative) usually manifesting within the first 2 years |
|---|---|
| | Haematogenous | Inoculation via the blood stream at any time |

**Inoculum effect**

Bacterial density is higher in abscesses than in standardised resistance testing (> $10^6$ CFU/mL vs. $10^5$ CFU/mL). The inoculum effect refers to the decreasing efficacy of certain antibiotics, e.g., beta-lactam antibiotics, with increasing microbial counts, which must be taken into account during therapy. This is the reason why with implant-associated infections the focus of infection must be eradicated using careful debridement prior to antibiotic treatment (see Chapter 3.1).

**Low-grade infection**

With implant-associated infections, low-virulence, otherwise non-pathogenic bacteria such as *Staphylococcus epidermidis* take advantage of the fact that the body’s defences against infection are weakened due to a locally acquired granulocyte defect in the immediate vicinity of the implant. These bacteria can also establish themselves in a biofilm on the surface of the implant. This leads to an exogenous infection with delayed manifestation that is restricted to the immediate vicinity of the foreign body.
**Minimum inhibitory concentration (MIC) and pharmacodynamics**

The minimum inhibitory concentration (MIC) corresponds to the antibiotic level at which bacteria are inhibited. The relationship between the antibiotic level and the MIC can be used to estimate how long the antibiotic level will remain above the MIC between dosages. In the case of all beta-lactams (penicillins and cephalosporins), it is beneficial to maintain the antibiotic level above the MIC at the focus of infection for as long as possible. For severe infections (e.g., endocarditis or periprosthetic infection), it is therefore advisable to determine the MIC (see Chapter 15.2.5, Fig. 15-3).

**MRSA**

Methicillin-resistant *Staphylococcus aureus*: Although it is no longer currently used in clinical applications, methicillin is an indicator of resistance to flucloxacillin, amoxicillin/clavulanic acid and cephalosporins.

**MRSE**

Methicillin-resistant *Staphylococcus epidermidis* (see MRSA).

**Open fracture**

*Tab. 16-2: Gustilo-Anderson open fracture classification*

<table>
<thead>
<tr>
<th>Grade</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Clean wound, wound &lt; 1 cm in length, simple fracture</td>
</tr>
<tr>
<td>2</td>
<td>Wound &gt; 1 cm in length without extensive soft-tissue damage</td>
</tr>
<tr>
<td>3a</td>
<td>Open fracture with adequate periosteal cover of the fractured bone despite extended soft tissue damage, caused by high-energy trauma</td>
</tr>
<tr>
<td>3b</td>
<td>Open fracture with extensive soft-tissue loss, periosteal stripping and bone exposure</td>
</tr>
<tr>
<td>3c</td>
<td>Any open fracture associated with an arterial injury requiring repair</td>
</tr>
</tbody>
</table>
**Osteomyelitis**
Infection of the cortical bone and bone marrow. Osteomyelitis is classified as acute or chronic, depending on progression. An aetiological distinction is drawn between exogenous and haematogenous osteomyelitis. Exogenous infections may spread from a wound, e.g., a pressure ulcer, or penetrate the bone via an open fracture, a surgical access site or a post-operative wound with impaired healing.

**PCR**
The polymerase chain reaction (PCR) is a method used to identify bacterial DNA. With PCR bacteria can be detected even if they have already been killed. This means that eubacterial PCR can occasionally identify bacteria that cannot be cultivated. It is considerably more difficult to interpret the PCR with polymicrobial findings. In addition, molecular biological analysis only enables the identification of isolated resistances (e.g., MRSA or rifampicin resistance). Presently the method is constantly undergoing further development (see Chapter 6.4).

**Sensitivity of a diagnostic test**
Likelihood of a test detecting a true positive value with a positive test result.

\[
P(\text{positive result} | \text{true positive}) = \frac{\text{Number of true positives}}{\text{Number of true positives} + \text{number of false negatives}}
\]

**Sepsis**
Acute systemic inflammatory response that forms an organism’s reaction to an infection. Often life-threatening, high risk of haematogenous spread to endoprosthetic implants, especially with *S. aureus*.

**Sequestrum**
Infected, necrotic bone fragment that no longer has a stable connection to vital bone (see Chapter 8.2).

**Single-shot**
Single antibiotic dosage administered as a prophylaxis prior to surgical procedures (see Chapter 2.5.2).
SIRS
Systemic Inflammatory Response Syndrome. This is referred to as sepsis if it is caused by an infection. In addition to a detected or presumed focus of infection, at least two of the following criteria must be met in order to confirm a diagnosis of sepsis:
1. Body temperature $> 38 \, ^\circ \text{C}$ or $< 36 \, ^\circ \text{C}$
2. Heart rate $> 90$ beats/min (tachycardia)
3. Tachypnoea: Breathing rate $> 20$ breaths/min or hyperventilation with \(\text{pCO}_2 < 32 \, \text{mmHg}\)
4. Leukocytosis ($> 12,000/\mu\text{L}$) or leukopaenia ($< 4000/\mu\text{L}$) or left shift (i.e., $> 10\%$ immature leukocytes in the differential blood count

Small colony variants (SCV)
Bacterial populations (usually \textit{Staphylococcus aureus}) that form small colonies due to their slow growth. These occur during prolonged exposure to antibiotics and cause chronic and recurrent infections. They are highly resistant to antibiotics not showing a reliable in-vitro / in-vivo correlation (see Chapters 1.4 and 15.2.3, Fig. 15-1).

Sonication
Procedure for detecting bacterial colonies fixed in the biofilm on removed implants. The biofilm is removed from foreign bodies using ultrasound. The bacteria are released and can then be cultivated in the appropriate media (see Chapter 6.5).

Specificity of a diagnostic test
Likelihood of a test to detect a true negative value with a negative test result.

\[
P(\text{positive result} | \text{true negative}) = \frac{\text{Number of true negatives}}{\text{Number of true negatives} + \text{number of false positives}}
\]

Spondylitis
Bacterial or abacterial inflammation of one or more vertebrae (see Chapter 10.1).

Spondylodiscitis
Bacterial or abacterial inflammation of one or more intervertebral disc spaces and the adjacent vertebrae. It is virtually always attributable to spondylitis in adults (see Chapter 10.1).

Tissue sampling
Samples of tissue (bone, soft tissue, implant components) harvested by sterile means from regions around the infective focus.
17 Common errors in the treatment of infections of the musculoskeletal system

Ilker Uçkay, Markus Vogt

17.1 Diagnostics

Superficial wound swabs
Just like intact skin, every wound or ulcer is always colonised with a variety of bacteria and fungi. Thus, superficial microbiological swabbing for therapy monitoring, or prior to antibiotic therapy is not only expensive, but is also useless. This is due to the polymicrobial nature of colonisation and frequent antibiotic resistance among skin commensals. Clinicians are often misled into adjusting their therapies to cover all germs, which results in an unnecessary broadening of the antibiotic spectrum. The correlation is poor between the microorganisms in a wound swab and the underlying pathogen (see Chapter 6.4). In contrast, cultures from biopsies, arthrocentesis, implants or abscesses are the correct means of ensuring an accurate microbiological diagnosis.

Insufficient number of tissue samples
For optimal differentiation between ‘real’ pathogens and mere contaminants, multiple tissue samples must be collected. Experts and literature recommend at least 3 deep tissue samples or 5–6 samples in case of suspected low-grade infections (see Chapter 6.4).

Microbiological sampling without discontinuing antibiotic therapy
One single antibiotic dose can be sufficient to prevent bacterial growth. If there is time, all antibiotics should be discontinued prior to sample collection. Experts recommend a two-week window, especially when reimplantation of an implant is planned (two-stage revision).

Short microbiological culture times in implant-related infections
Unlike most pathogens, skin commensals such as propionibacteria or staphylococcal small-colony variants (SCV) are slow-growing. Microbiology lab technicians should be instructed to incubate samples (including sonication) for at least 10–14 days rather than for 5–7 days (especially when the patient is currently on antibiotic therapy).

Starting antibiotic therapy prior to confirmed infection
Orthopaedic infections are seldom immediately life-threatening. There is sufficient time to confirm an adequate diagnosis with identification of microbes. A correct microbiological diagnosis of the underlying pathogens and its susceptibility pattern cannot be emphasized enough.
Even in rare cases of sepsis or other life-threatening conditions, blood cultures and, wherever possible, aspiration of the clinically affected joints should be performed prior to the start of antibiotic therapy.

17.2 Antibiotic therapy

Excessively long perioperative prophylaxis
Extending the perioperative antibiotic prophylaxis by more than one day cannot be justified, even in the case of errors in aseptic technique during surgery. Such an approach is not more effective in preventing infections than the timely administration of a single dose (see Chapter 2.5.2).

However, open Gustilo Grade 3 fractures require a pre-emptive therapy for three days aiming to eradicate the bacteria that have contaminated the wound during the accident (see Chapter 3.2).

Overestimating skin colonisation with MRSA
Even though a patient’s skin may be colonised with methicillin-resistant *S. aureus* (MRSA), this is no proof that MRSA is always responsible for the underlying infection. Moreover, following a surgical debridement, an initial empiric therapy with amoxicillin/clavulanic acid or a first- or second-generation cephalosporin is usually sufficient until the microbiology results become available (usually within about 2 days). Provided that surgical debridement has been performed, an initially wrong antibiotic choice does not lead to a worse outcome after a 6-week’s course of targeted antibiotic therapy.

Underdosing of antibiotics in osteoarticular infections
Not every antibiotic is equally effective regarding bone or synovial penetration. Usual doses are defined for intravenous therapy and bloodstream infections. While intravenous therapy is not a problem with standard dosing (Tab. 7-1, 9-2), oral therapy must be selected based on oral bioavailability and ability to penetrate bone. For oral therapy, suitable antibiotics include quinolones (ciprofloxacin, levofloxacin), clindamycin, rifampicin as well as co-trimoxazole, fusidic acid and linezolid. In contrast, beta-lactam antibiotics such as penicillin, its derivatives or cephalosporins have a significantly poorer oral bioavailability for bone and synovial penetration compared to IV therapy (see Chapter 3.1).
Excessively long administration for curative purposes
Current expert recommendations with respect to the duration of antibiotic administration are conservative and rather on the safe side. These recommendations may also seem excessive in favourable cases. Consequently, it is probably futile to further extend these recommended durations on an individual basis, in as much as this prolongation is likely associated with increased side effects and possible development of resistant endogenous flora and increased costs. No study shows a benefit when prolonging beyond these international recommendations. Exceptions should always be discussed with an infectious disease specialist with experience in orthopaedic infections.

Likewise, a persistent elevated serum CRP value (without clinical problems) at the end of scheduled therapy is no reason for prolonging the antibiotic regimen. Persistently elevated CRP values might have multiple causes that may require active work-up.

Clindamycin with simultaneous macrolide resistance
Clindamycin is chemically related to macrolide antibiotics (e.g., erythromycin, see Tab. 3-3). Sometimes in daily practice, the same microorganism might appear susceptible to clindamycin and yet resistant to erythromycin in routine testing. This supposed susceptibility to clindamycin \textit{in vitro} may be misleading because ‘inducible clindamycin resistance’, with therapeutic failure, may occur with continuation of clindamycin.

Options here include either foregoing administration of clindamycin or formal ruling out of inducible clindamycin resistance. This usually requires an additional test, the ‘D test’.

Monotherapy with rifampicin or fusidic acid
Rifampicin and fusidic acid are potent antibiotics effective against staphylococci. Rifampicin is well established for treating implant-associated infections with staphylococci. However, both drugs should not be administered alone because of a rapid (within 48 hours in the case of rifampicin) or gradual (fusidic acid) emergence of resistance. The combinations of quinolones with rifampicin or fusidic acid with rifampicin for quinolone-resistant staphylococci are useful options.

Rifampicin for suppressive therapy, implant-free osteomyelitis, and Gram-negative bacteria
In the case of suppressive therapy and osteomyelitis without implants, rifampicin provides no benefit but can result in cumulative side effects and development of resistance among staphylococci. Although subject of emerging in vitro studies, Gram-negative bacteria do not need rifampicin for their treatment \textit{in vivo}. 

234
Rifampicin interaction with many simultaneously administered medications
Rifampicin is a potent inducer of the hepatic cytochrome system, which is essential for the catabolism of many drugs. The efficacy of anticoagulants (phenprocoumon, acenocoumarol), oral contraceptives, malaria prophylaxis, methadone, ciclosporin, calcium antagonists, anti-epileptic agents and many other medications may be reduced. Active evaluation for interactions and serum level testing of key drugs (if available) are required when administering rifampicin.

Rifampicin with open wounds
If rifampicin is applied on open or weeping wounds, there may be a risk of rifampicin-resistance selection. As a result, rifampicin should not be used for severely weeping wounds (Fig. 6-5, 7-6).

Change in antibiotic therapy because of growth in bacteria with resistance during ongoing therapy
It is common to select and grow skin commensals resistant to the administered antibiotic when performing microbiological tissue samples during ongoing or recently discontinued antibiotic therapy. Classic examples include the presence of coagulase-negative staphylococci on agar plates of samples performed during treatment with amoxicillin/clavulanic acid or cephalosporins. The clinical course alone is decisive. As long as this is satisfactory, antibiotic therapy should not be adapted.

17.3 Miscellaneous

Interdisciplinary discussion between orthopaedic surgeons, infectious disease specialists and other specialists
The ideal time for an interdisciplinary discussion is prior to the start of therapy, in order to enable joint setting of the diagnostic objectives as well as the modalities of a combined surgical and medical treatment.

Curative approach without surgical treatment
Curative treatment of chronic osteomyelitis and implant-associated infections without at least one concomitant surgical debridement is unrealistic. The likelihood of long-term remission is less than 10%. So-called ‘suppressive antibiotic therapy’ is only palliative and rarely administered for multi-morbid and elderly patients; and very often equally requires initial surgery. Combinations with rifampicin are unnecessary for this palliative approach (see above).
Negative-pressure (vacuum) wound therapy wounds with exposed implants
Negative-pressure wound therapy in wounds with lasting several weeks without surgical treatment of the foci of infection involving implants as described above is highly likely to result in superinfections. Direct plastic closure following deep surgical debridement is always preferable.
18 Infection therapy passport

18.1 Purpose of the infection therapy passport

Patients with implant-associated infections usually require combined antibiotic therapy over the course of several months. Experience has shown that during follow-up treatment, important details regarding duration and dosage as well as the results of laboratory tests go missing. Moreover, it is important to engage the patient in the precise plan for treatment by providing a written record of the agreed therapy. This therapy must be defined in terms of duration, medication and dosage. A further benefit is that in the event of an emergency, all important information regarding the infection is immediately accessible.

The infection therapy passport contains all the important details regarding the spectrum of pathogens, the antibiotics used and their corresponding dosage, the therapy start and end date as well as the recommended infection monitoring tests (Fig. 18-1, 18-2). Depending on the side effects, recommendations are given regarding periodic testing of liver and kidney function, for example. The name and contact details of the doctor responsible for the treatment are also provided in the event of queries.

18.2 Use of the infection therapy passport

The infection therapy passport is completed in full and its use explained to the patients, shortly before they are discharged from inpatient care. Patients must always take this document to all appointments with their general practitioner and the doctor handling the case in the hospital. Routine laboratory tests are generally carried out by the general practitioner (GP). The results are entered directly into the infection therapy passport, which is then returned to the patient. The information can be communicated to the doctor handling the case in the hospital by bringing the passport to appointments or by faxing the centre page (Fig. 18-2, 18-3). Ensuring that the passport is carefully updated saves time-consuming questions regarding the main points of treatment. Should unexpected events occur, such as an increase in CRP, new side-effects, etc., the GP can communicate directly with the contact person indicated on the passport.

Now in its fourth edition, the infection therapy passport is even better adapted to practical requirements. It is currently available in English, German, French and Italian. Information on where to obtain the passport is provided in the passport itself as well as on the inside cover of this book.
# Infection Therapy Passport

For follow-up of orthopaedic antibiotic treatment for infections.
To be brought to all consultations by the patient!

<table>
<thead>
<tr>
<th>Name</th>
<th>DOB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>/ /</td>
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</tbody>
</table>

Diagnosis

Antibiotic allergy

**Information for the doctor**

Your patient underwent surgical treatment of a bone or joint infection and was started on antibiotics. To check the progress of treatment, we rely on thorough documentation of the chemical laboratory parameters and so kindly ask you to arrange for regular laboratory tests and to enter the results in the following pages. We are happy to answer your questions at any time. Should clinical signs or lab results suggest that the antibiotic treatment needs to be modified, we can of course arrange to discuss the matter on an interdisciplinary level (with specialists in orthopaedics and infectious diseases) and issue therapeutic recommendations. As background information, please fax page 2 and 3 of this passport to the doctor responsible for treatment (see below).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Measurement Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP, WBC</td>
<td>measured every _____ weeks</td>
</tr>
<tr>
<td>Hepatic values (ASAT, ALAT, AP)</td>
<td>measured every _____ weeks</td>
</tr>
<tr>
<td>Creatine kinase</td>
<td>measured every _____ weeks</td>
</tr>
<tr>
<td>Renal values (creatinine, urea)</td>
<td>measured every _____ weeks</td>
</tr>
<tr>
<td>INR (in pistol on anticoagulation)</td>
<td>measured every _____ weeks</td>
</tr>
<tr>
<td>Other</td>
<td>measured every _____ weeks</td>
</tr>
<tr>
<td>Clostridium antigen test</td>
<td>only in the event of diarrhoea during antibiotic treatment (&gt; 3 evacuations of liquid stool/day)</td>
</tr>
</tbody>
</table>

**For the treating doctor**

<table>
<thead>
<tr>
<th>Stamp</th>
<th>Name</th>
<th>Telephone</th>
<th>Fax</th>
<th>Email</th>
</tr>
</thead>
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</tbody>
</table>

Published by Swiss orthopaedics and the Swiss Society for Infectious Diseases expert group “Infections of the musculoskeletal system”.

It was developed by Prof. Peter E. Ochsner and Prof. Werner Zimmerli at the Cantonal Hospital of Liestal, Switzerland.

---

*Fig. 18-1: Infection therapy passport, page 1 – General information*
### Diagnostics

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Documented proof</th>
<th>Material for microbiology</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td></td>
<td>a–b–c–d–e–f–g–h</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td></td>
<td>a–b–c–d–e–f–g–h</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td></td>
<td>a–b–c–d–e–f–g–h</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td></td>
<td>a–b–c–d–e–f–g–h</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td></td>
<td>a–b–c–d–e–f–g–h</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td></td>
<td>a–b–c–d–e–f–g–h</td>
<td></td>
</tr>
</tbody>
</table>

a) synovia  b) tissue specimen  c) exudate/abscess  d) haematoma  e) blood culture  f) implant broth culture  g) implant sonication fluid  h) other:

### Intravenous therapy

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose</th>
<th>from – to</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

### Oral therapy

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose</th>
<th>from – to</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

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Fig. 18-2: Infection therapy passport, page 2 – Information on the spectrum of pathogens, antibiotic therapy
Infection Therapy Passport
For follow-up of orthopaedic antibiotic treatment for infections.
To be brought to all consultations by the patient!

Name
DOB
Diagnosis
Antibiotic allergy

Information for the doctor
Your patient underwent surgical treatment of a bone or joint infection and was started on antibiotics.

To check the progress of treatment, we rely on thorough documentation of the chemical laboratory parameters and so kindly ask you to arrange for regular laboratory tests and to enter the results in the following pages. We are happy to answer your questions at any time. Should clinical signs or lab results suggest that the antibiotic treatment needs to be modified, we can of course arrange to discuss the matter on an interdisciplinary level (with specialists in orthopaedics and infectious diseases) and issue therapeutic recommendations. As background information, please fax page 2 and 3 of this passport to the doctor responsible for treatment (see below).

- CRP, WBC measured every weeks
- Hepatic values (ASAT, ALAT, AP) measured every weeks
- When using rifampicin, quinolone, fusidic acid, daptomycin
- Creatine kinase measured every weeks
  
  When using daptomycin
- Renal values (creatine, urea) measured every weeks
- INR (in patients on anticoagulation) measured every weeks

Monitor closely when using rifampicin, caution when discontinuing rifampicin

- Other measured every weeks
- Clostridium antigen test only in the event of diarrhoea during antibiotic treatment (>3 evacuations of liquid stool/day)

For the treating doctor

Stamp
Name
Telephone
Fax
Email

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This Infection Therapy Passport can be obtained free of charge in English, German, French and Italian from: Heraeus Medical GmbH, Philipp-Reis-Str. 8/13, D-61273 Wehrheim, contact.medical@heraeus.com

Layout and printing: Heraeus Medical GmbH

Fig. 18-3: Infection therapy passport, pages 3 and 4 – Laboratory test results
19.1 Background

In the diagnosis of implant-associated infections, it is recommended that sonication and histology are also carried out in addition to conventional bacteriology. This is particularly important for what are referred to as ‘low-grade’ infections. In this respect, it is often crucial that the bacteriology and histology results of the same sample are compared (see Chapter 6.4).

19.2 Purpose of using a specific form

The targeted evaluation of the samples by the laboratories requires a minimum of information regarding the medical history and clinical findings for each case. Where possible, this information should only be recorded once and in more detail than usual.

A comparative analysis of bacteriology and histology of the same sample is only possible if samples collected from the same site are immediately noted and numbered in the same way (see Chapter 6.4).

Every laboratory, almost without exception, requires its own request form to be completed when it receives an order to carry out an analysis. For microbiological samples, it is customary to complete a separate form for each sample. As large numbers of tissue samples are often collected, particularly for low-grade infections, this results in repetitive, routine work that can lead to the forms being filled in carelessly.

19.3 Design of the form

In collaboration with a number of orthopaedic specialists, infectious disease specialists and microbiological and histological laboratories, we have developed a joint evaluation form that has been successfully tested in practice (Fig. 19-1, 19-2). Despite initial scepticism, the form has now been accepted by all parties. The form includes the following:

- Questions about the patient’s details for all samples that must be answered in greater detail than is usual
- Tissue samples are numbered (1, 2, 3, etc.) and each sample is divided into two equal parts (keeping the same number) with one part placed in a container for bacteriology and the other for histology
- Foreign bodies and fluids intended for bacteriological analysis are labelled alphabetically (A, B, C, etc.)
The material intended for sonication, all of which was collected during surgery and packed inside a sterile container specially designed for this purpose, is noted.

Fig. 19-1: Front of the form ‘Coordinated bacteriological and histological analysis of implant-related infections’.
Collected on  
Date ___________ Exact time ______________

1. Tissue for bacteriology and histology
For each number, one tissue sample each for histology and bacteriology from the same site in the two corresponding containers. Number using Arabic numerals.

<table>
<thead>
<tr>
<th>No.</th>
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<th>Superficial</th>
<th>Deep</th>
<th>Peri-prosthetic</th>
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Important: Perform molecular diagnostics (PCR) for negative cultures: O Yes O No

2. Fluids/foreign bodies for conventional bacteriology
Number each sample, each in a separate bacteriology container, using letters.

<table>
<thead>
<tr>
<th>No.</th>
<th>What?</th>
<th>Source?</th>
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<tr>
<td>A</td>
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<tr>
<td>C</td>
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<tr>
<td>E</td>
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</table>

3. Implant (parts) and other foreign bodies for sonication
All the objects listed below are placed into a sterile container supplied by the laboratory on the operating table. Important: Do not include fragments of bone cement.

Once the form has been completed, copy it and provide each laboratory with a copy. A copy should also be added to medical records.

Fig. 19-2: Back of the form ‘Coordinated bacteriological and histological analysis of implant-related infections’.
Abiotrophia 217
abscess 80, 124, 165, 180, 192, 194, 232
Brodie’s abscess 195
deep abscess 98
drainage 177
epidural abscess 157
paravertebral abscess 157
skin abscess 166
subperiosteal abscess 189, 190
accident history 117
acne 200
Actinobacillus
actinomycetemcomitans 147
adherence 208
adjuvant therapy 49
agar diffusion test
(Kirby-Bauer method) 212
algorithm for prosthetic joint infections 102
aminoglycoside 44, 47, 54, 111, 153, 216f
aminopenicillins 44f
amoxicillin/clavulanic acid 45, 111, 152,
213, 218, 221, 233
in infectious arthritis 152
in the case of diabetic foot 185
with unknown pathogens 233
ampicillin 213
amputation
amputation risk 179
internal amputation 186
anaerobic 95
antibiogram 211f
antibiotic
antibiotic classes 44
antibiotics window 232
beta-lactam antibiotics 44, 215
bioavailability 233
carriers of antibiotics 54
calcium sulphate 62
collagen sponges 62
plaster of Paris pellets 62
PMMA bone cement 55
cell toxicity 52
discontinuation of antibiotic regimen 84, 211
dose of antibiotics 31
elution characteristics 53
indications 225D
mechanism of action of antibiotics 44
mode of action 44
penetration into the bone 213, 233
resistance to temporarily high temperature 52
spectrum of the individual antibiotics 45
stability 52
switch in medication 235
underdosing 233
use of antibiotics 43D
antibiotic prophylaxis 31f
antibiotic selection 33
cephalosporins 33f
evidence 31
excessively long 233
haemotogenous prosthetic joint infections 34
microbiological diagnosis 32
MRSA 33
number of antibiotic doses administered 31
open fractures 32
osteosynthesis 32, 126
antibiotic prophylaxis f
prosthetic joints 32
  time of antibiotic administration 31
tourniquets 32
vancomycin 33
antibiotic therapy 39, 110f, 125, 184, 201
duration of therapy 125
empirical therapy 43, 125, 152, 232f
indications 125
in implant-associated arthritis 42
in infectious arthritis 152
patient factors 41
patient support 43
pre-emptive therapy 43
problems 125
suppressive therapy 110, 136
systemic therapy 39f
targeted therapy 43
therapeutic failure 43
without verified diagnosis 232f
antigranulocyte scintigraphy 81, 130, 138
antimicrobial coating 23
antisepctic 49f, 197
antisepctic coverage 177, 225D
antisepctic drape 51, 65, 68, 128D
arthritis
aminoglycoside 153f
amoxicillin/clavulanic acid 152
arthrocentesis 150
arthroscopy 150
arthrotomy 151
aspiration 205
brucellosis 147
cefazolin 152
cefepime 152f
ceftazidime 153
ceftiraxone 152f
cefuroxime 152
chronic infectious arthritis 131, 138
clinical findings 148
closed suction drainage 150
arthrosis f
coadminstration 153
  diagnosis 148f
distension irrigation system 150
  flucloxacillin 153
gonococcal arthritis 147f
imaging 149
incidence 147
infectious arthritis 147D, 150, 188f,
  202D, 225
infectious (purulent) arthritis 202
laboratory 149
levofloxacin 153
localisations 148
minocycline 153
pathogen 147
physiotherapy 154
post-traumatic arthritis 124
prognosis 202
pyogenic septic arthritis 203
reactive arthritis 149
rheumatoid arthritis 97
rifampicin 153
risk factors 148
shaving 151
staging 151D
synovectomy 151
targeted antibiotic therapy 152
teicoplanin 153
therapy principles 150
vancomycin 153
arthrocentesis 71
  cell count 74
    for hip joint prosthetic infection 74
    for knee joint prosthetic infection 74
  cells 74
  contrast-enhanced arthrography 76
  crystals 74
  EDTA tube 72
  for contrast-enhanced arthrography 76
  for native joints 71, 74
  for prosthetic joints 72
arthrocentesis f
  gram stain test 74
  plain tube 73
  punctio sicca 74
  technique 72
  total hip arthroplasty 74
  total knee arthroplasty 74
  viscosity 74

arthrodesis 102, 109
arthrography 73, 76
arthroscopy 103, 150
arthrotomy 150f
Aspergillus spp. 223
azithromycin 44, 46

B
Bacillus 218
  Bacillus anthracis 218
  Bacillus cereus 218
  Bacillus spp. 218

bacteria 35, 87, 116, 210f, 215f
  adherent 210
  anaerobic 116, 214, 218, 221
  apathogenic 209
  bacteriæmia 35, 215f
  bacterial lifeforms 210
  biofilm 210
  planctonic 210
  bacteriological tests 87, 211
  bacteriology 116
  biofilm 210
  difficult to treat 217, 225
  type of bacteria 202
Bacteroides spp. 111
biofilm 21f, 210, 215, 220, 225D

biopsy
  collection 84, 103, 241
  discontinuation of antimicrobial therapy 84
  documentation 86, 241f
  intraoperative measures 28
  microbiological samples 84
  number of samples 85, 232
  sample collection 32, 85
  sample type 84
  technique 84f
tissue samples 84, 132, 211
  transport 87, 211

blood
  blood culture 149, 233
  blood tests 70
  differential blood count 70

bone
  ability to penetrate the bone 233
  bone debris 120
  bone defect 131
  bone fenestration 139, 143
  bone grafts 132, 134, 140
  bone morphogenetic protein (BMP 2 and 7) 134
  bone necrosis 119, 121, 139
  bone replacement 134
  bone resection 186
  bone scintigraphy 81
  bone transplant 128

bone allografts 134

Borrelia
  Borrelia burgdorferi 39
  Borrelia spp. 211

Brodie abscess 195, 226D

Brucella spp. 211

brucellosis 147

BSG (ESR) 71

D = Reference with the definition of a term
<table>
<thead>
<tr>
<th>Term</th>
<th>Page(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>bursectomy</td>
<td>168</td>
</tr>
<tr>
<td>bursitis</td>
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<tr>
<td>advanced infectious bursitis</td>
<td>165</td>
</tr>
<tr>
<td>septic bursitis</td>
<td>168</td>
</tr>
<tr>
<td>calcium sulphate</td>
<td>53f, 62</td>
</tr>
<tr>
<td>calculation of duration of consolidation</td>
<td>134</td>
</tr>
<tr>
<td><em>Candida</em> spp.</td>
<td>147, 223</td>
</tr>
<tr>
<td><em>Capnocytophaga</em> spp.</td>
<td>147</td>
</tr>
<tr>
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<td>44ff, 54, 111, 185, 219</td>
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<td>165</td>
</tr>
<tr>
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<td>46</td>
</tr>
<tr>
<td>cefamandole</td>
<td>32, 46</td>
</tr>
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<td>32, 46, 111, 152</td>
</tr>
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<td>46, 111, 152f</td>
</tr>
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<td>46</td>
</tr>
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</tr>
<tr>
<td>ceftazidime</td>
<td>111, 153</td>
</tr>
<tr>
<td>ceftriaxone</td>
<td>46, 111, 152f</td>
</tr>
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<td>32f, 46, 152</td>
</tr>
<tr>
<td>cell count</td>
<td>74</td>
</tr>
<tr>
<td>cellulitis</td>
<td>164ff</td>
</tr>
<tr>
<td>cephalosporins</td>
<td>46, 218</td>
</tr>
<tr>
<td>first-to-fifth-generation</td>
<td>44</td>
</tr>
<tr>
<td>with unknown pathogens</td>
<td>233</td>
</tr>
<tr>
<td>charcot foot</td>
<td>185, 226D</td>
</tr>
<tr>
<td>chills</td>
<td>181</td>
</tr>
<tr>
<td>chlorhexidine</td>
<td>28, 50</td>
</tr>
<tr>
<td>chronic pain</td>
<td>138, 144</td>
</tr>
<tr>
<td>ciprofloxacin</td>
<td>44, 47, 110, 220f, 233</td>
</tr>
<tr>
<td>gram-negative pathogens</td>
<td>220</td>
</tr>
<tr>
<td>in infectious arthritis</td>
<td>153</td>
</tr>
<tr>
<td>in the case of diabetic foot</td>
<td>185</td>
</tr>
<tr>
<td>Citrobacter</td>
<td></td>
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<tr>
<td><em>Citrobacter freundii</em></td>
<td>219</td>
</tr>
<tr>
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<td>218</td>
</tr>
<tr>
<td>clarithromycin</td>
<td>44, 46</td>
</tr>
<tr>
<td>classification</td>
<td></td>
</tr>
<tr>
<td>infection classification</td>
<td>228D</td>
</tr>
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<td>117</td>
</tr>
<tr>
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<td></td>
</tr>
<tr>
<td>(Cierny-Mader)</td>
<td>120, 188</td>
</tr>
<tr>
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<td>44, 47, 54, 111, 170, 221f, 233</td>
</tr>
<tr>
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<td>185</td>
</tr>
<tr>
<td>resistance</td>
<td>234</td>
</tr>
<tr>
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<td>234</td>
</tr>
<tr>
<td>clostridia</td>
<td>222</td>
</tr>
<tr>
<td><em>Clostridium</em></td>
<td></td>
</tr>
<tr>
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<td>222</td>
</tr>
<tr>
<td><em>Clostridium perfringens</em></td>
<td>164, 169, 222</td>
</tr>
<tr>
<td><em>Clostridium</em> septicum</td>
<td>169, 222</td>
</tr>
<tr>
<td>coagulase reaction</td>
<td>214, 226D</td>
</tr>
<tr>
<td>coci, gram-positive</td>
<td>215</td>
</tr>
<tr>
<td>coinfection</td>
<td>111</td>
</tr>
<tr>
<td>colistimethate sodium</td>
<td>54</td>
</tr>
<tr>
<td>collagen sponges</td>
<td>53, 62</td>
</tr>
<tr>
<td>computed tomography</td>
<td>78, 123, 130, 138, 182</td>
</tr>
<tr>
<td>consolidation, incomplete</td>
<td>131, 138</td>
</tr>
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<td>contamination</td>
<td>208</td>
</tr>
<tr>
<td>contracture</td>
<td>205</td>
</tr>
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<td>76, 80</td>
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<tr>
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Index of terms

<table>
<thead>
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<td>co-trimoxazole</td>
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<td>70, 190, 234</td>
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<td>190</td>
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<td>86</td>
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<td>21, 125</td>
</tr>
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<td>cuts</td>
<td>173</td>
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<tr>
<td>cyclic lipopeptide</td>
<td>47, 74</td>
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**diabetic foot**
- carbapenems
- cefepime
- clindamycin
- conservative therapy
- diagnostics
- foot care/pedicure
- maxipime
- metronidazole
- orthopaedic shoes
- patient education
- piperacillin/tazobactam
- pressure ulcer
- self-examination
- surgical treatment
- therapy
- total contact cast
- ulcer
- unfavourable factors
- Wagner grading system

**diabetic wound**

**diagnosis**
- bacterial infections
- diagnosis of pathogens
- errors
- infections of the musculoskeletal system

**discitis**

**disinfectant**

**doppler imaging**

**doxycycline**

**drains**

**drug use**

D = Reference with the definition of a term
### E

| **early infection** | 97 |
| **deep** | 97 |
| **surface** | 97 |
| **empirical therapy** | 43 |
| **endocarditis** | 148, 215, 221 |
| **enterobacteria** | 111, 153, 209, 218 |
| **antibiotic susceptibility** | 218 |
| **biofilm** | 220 |
| **Enterobacter spp.** | 218 |
| **enterococci** | 95, 213, 216 |
| **antibiotic resistance** | 216 |
| **daptomycin** | 216 |
| **glycopeptides** | 216 |
| **imipenem** | 216 |
| **penicillin** | 216 |
| **Enterococcus** | 111 |
| **Enterococcus cloacae** | 219 |
| **Enterococcus faecalis** | 216 |
| **Enterococcus spp.** | 111 |
| **epsilometer test** | 212 |
| **eradication** | 233 |
| **erysipelas** | 164ff |
| **erythrocyte sedimentation rate (ESR)** | 71 |
| **erythromycin** | 44, 54, 234 |
| **Escherichia coli** | 210, 218f |
| **extended-spectrum beta-lactamase (ESBL)** | 219 |
| **external fixation** | 108f, 119, 132 |

### F

| **fasciomyositis** | 169 |
| **fatigue fracture** | 131 |
| **FDG-PE** | s. positron emission tomography |
| **Finegoldia** | 222 |
| **Finegoldia magna** | 222 |
| **first manifestation** | 118, 126, 129, 137 |
| **fistula** | 76f, 78, 102, 116, 120, 124 |
| **chronic fistula** | 138, 144 |
| **filling of the fistula** | 78f, 96 |
| **fistula carcinoma** | 137, 142 |
| **fistulation** | 131 |
| **fistulography** | 130, 138 |
| **fluclouxacillin** | 45, 212 |
| **in infectious arthritis** | 153 |
| **in S. aureus** | 212 |
| **fluoroquinolones** | 44, 47 |
| **foliculitis** | 165 |
| **follow-up revisions** | 104 |
| **foreign body infections** | 77, 82, 209 |
| **Fournier's gangrene** | 169 |
| **fracture** | 117 |
| **fracture classification** | s. open fracture |
| **fracture, open** | 175 |
| **fracture stabilisation** | 175 |
| **free flaps** | 107, 176 |
| **bone graft, vascularised** | 134 |
| **gastrocnemius muscle flap** | 107f, 128, 140f |
| **scapular flaps** | 135 |
| **upper arm flaps** | 107 |
| **fungi** | 223 |
| **furunculosis** | 166 |
| **fusidanes** | 45 |
Index of terms

fusidic acid 110, 233f
combination with rifampicin 234
in infectious arthritis 153
resistance 234

G

gas gangrene 164
gentamicin 44, 47, 53
gentamicin-impregnated beads 141
girdlestone hip 108
glycopeptide 44, 47, 54
gonococci 39, 147f, 153
gout 168
gram staining 75, 86, 214, 227D
Granulicatella 217
Granulicatella adiacens 108
granulocyte percentage 99
growth disturbance 202
growth prognosis 139, 198

H

HACEK group 147
haemarthrosis 149
haematoma 97, 116
Haemophilus 190, 202
Haemophilus influenzae 190, 202
Haemophilus spp. 147, 211
hair removal 28
heat necrosis 120
hepatitis B 28

hinged prosthesis 105
hip spacer s. spacer
histological test 88
hydraulic mobilisation 205
hyperbaric
hyperbaric oxygen 171
hyperostosis 200

identification of microbes 232
IL-6 s. interleukin
imaging 76, 130, 138, 144
imipenem 46, 216
immune
immune response 208
immunodeficiency, local 209
immunohistochemical staining 89
immunosuppression 34, 148
immunoglobulins 171

impetigo 165
implant
coated implants 63
implant-associated infection 39, 209, 217, 241
implant explantation 102, 105, 108
implant reimplantation 105
implant replacement
one-stage 105
two-stage 102, 106, 108
implant retention 98, 111
incidence 117

D = Reference with the definition of a term
incise drapes 28
induced growth disorder 193
infected pseudarthrosis 116f, 120, 129 stabilisation 132 surgical treatment 132 two-stage procedure 132 infection 188, 234 acute infection 97 after intramedullary nailing 136 diaphyseal infection 118 endogenous infection 209 epi/metaphyseal infection 118 exogenous infection 209 haematogenous infection 34, 98, 209 high-grade infection 89 implant-associated infection 102, 209, 217, 241 infection classification 228D infection rate 27f infectious agent 208 in the oral/dental area 35 localisation of the infection 118 perioperative infection prophylaxis intraoperative measures 28 postoperative measures 29 preoperative measures 27 perioperative infections 27 proof of infection 124D superficial infection 118 infections of the musculoskeletal system antigranulocyte scintigraphy 81 arthrocentesis 71 bacteriological test 87 biopsy 84 computed tomography (CT) 78 diagnosis 70 imaging 76 imaging diagnostics 76 joint puncture 71 lab 70 leukocytes 70

infections of the musculoskeletal system f magnetic resonance imaging (MRI) 80 MRI 80 nuclear medicine imaging 81 PET 82 PET/CT 82 physiotherapy 205 positron-emission tomography 82 scintigraphy 81 sonography 80 SPECT/CT 82 treatment errors 232 x-ray 77 infection therapy passport 112, 237 inflammation scintigraphy 81 inoculum effect 40 interleukin-6 (IL-6) 71 interlocking nail 109, 120 intramedullary drilling 120f intramedullary reaming 136f, 141, 144 ream diameter 140 venting hole 140 J joint destruction 182 joint effusion 190 K Kingella kingae 147, 190 Klebsiella Klebsiella oxytoca 219 Klebsiella pneumonia 219 Klebsiella spp. 218 knee arthrodesis 109
<table>
<thead>
<tr>
<th>Term</th>
<th>Page(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>knee spacer s. spacer</td>
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<tr>
<td>Koebner phenomenon</td>
<td>165</td>
</tr>
<tr>
<td>L</td>
<td></td>
</tr>
<tr>
<td>lab</td>
<td>77, 82</td>
</tr>
<tr>
<td>laboratory tests</td>
<td>144</td>
</tr>
<tr>
<td>lacerations</td>
<td>173</td>
</tr>
<tr>
<td>laminar airflow</td>
<td>28</td>
</tr>
<tr>
<td>late infection</td>
<td>34, 98</td>
</tr>
<tr>
<td>lavage</td>
<td>177</td>
</tr>
<tr>
<td>leukocytes</td>
<td>70</td>
</tr>
<tr>
<td>infections of the musculoskeletal system</td>
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<tr>
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<td>81</td>
</tr>
<tr>
<td>levofloxacin</td>
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</tr>
<tr>
<td>linezolid</td>
<td>48, 54, 233</td>
</tr>
<tr>
<td>lipopeptide</td>
<td>44</td>
</tr>
<tr>
<td>local immunodeficiency s. implant-associated infection</td>
<td></td>
</tr>
<tr>
<td>local treatment</td>
<td>49</td>
</tr>
<tr>
<td>antibiotics</td>
<td>49</td>
</tr>
<tr>
<td>antiseptics</td>
<td>49</td>
</tr>
<tr>
<td>low-grade infection</td>
<td>86, 89, 209, 228D, 241</td>
</tr>
<tr>
<td>lunar caustic</td>
<td>50</td>
</tr>
<tr>
<td>malignant neoplasm</td>
<td>97</td>
</tr>
<tr>
<td>malum perforans</td>
<td>180, 182, 184</td>
</tr>
<tr>
<td>meningococci</td>
<td>209</td>
</tr>
<tr>
<td>meropenem</td>
<td>46, 54</td>
</tr>
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<td>mesh graft</td>
<td>128</td>
</tr>
<tr>
<td>metaphysis</td>
<td>202</td>
</tr>
<tr>
<td>meticillin-resistant Staphylococcus aureus s. MRSA</td>
<td></td>
</tr>
<tr>
<td>metronidazole</td>
<td>47, 185</td>
</tr>
<tr>
<td>MIC</td>
<td>40, 212fD, 216, 229</td>
</tr>
<tr>
<td>microangiopathy</td>
<td>182</td>
</tr>
<tr>
<td>microbiology</td>
<td>208, 232</td>
</tr>
<tr>
<td>culture times</td>
<td>232</td>
</tr>
<tr>
<td>number of tissue samples</td>
<td>232</td>
</tr>
<tr>
<td>on antibiotic therapy</td>
<td>232</td>
</tr>
<tr>
<td>samples s. biopsy</td>
<td></td>
</tr>
<tr>
<td>microorganisms</td>
<td>208</td>
</tr>
<tr>
<td>minocycline</td>
<td>47, 110, 153</td>
</tr>
<tr>
<td>mobilisation under anaesthetic</td>
<td>205</td>
</tr>
<tr>
<td>mode of application</td>
<td>42</td>
</tr>
<tr>
<td>moist dressing</td>
<td>51</td>
</tr>
<tr>
<td>Morganella</td>
<td></td>
</tr>
<tr>
<td>Morganella morganii</td>
<td>219</td>
</tr>
<tr>
<td>Morganella spp.</td>
<td>218</td>
</tr>
<tr>
<td>moxifloxacin</td>
<td>44, 47, 233</td>
</tr>
<tr>
<td>MRI</td>
<td>130, 138, 182, 190</td>
</tr>
<tr>
<td>MRSA</td>
<td>30, 111, 153, 167, 229D, 233</td>
</tr>
<tr>
<td>MRSE</td>
<td>229D</td>
</tr>
<tr>
<td>Müller AO classification</td>
<td>117</td>
</tr>
</tbody>
</table>

D = Reference with the definition of a term
### Muscle and Skin Flaps
- **Pedicled**
- **Rotation Flaps**
- **Vascularised, Local**

#### Mycobacterium
- *Mycobacterium bovis*
- *Mycobacterium tuberculosis*

#### Mycoplasma
- *Mycoplasma hominis*
- *Mycoplasma pneumoniae*

#### Myonecrosis

#### Myositis

#### Open Fracture
- **Grade I**
- **Grade II**
- **Grade III**
  - Gustilo open fracture classification

#### Operating Field

#### Oral Hygiene

#### Osteolysis

#### Osteomyelitis
- **Acute Haematogenous Osteomyelitis**
- **Acute Multifocal Haematogenous Osteomyelitis**
- **Acute Osteomyelitis**
- **Acute, Unifocal Osteomyelitis**
- **BCG Osteomyelitis**
- **Blunt Hole Osteomyelitis**
- **Bone Fenestration**
- **Chronic Haematogenous Osteomyelitis**
- **Chronic Osteomyelitis**
- **Chronic Post-Traumatic Osteomyelitis**
- **Chronic Recurrent Multifocal Osteomyelitis (CRMO)**
- **Cierny-Mader Classification**
- **Diffuse Osteomyelitis**
- **Exogenous Osteomyelitis**
- **Garré's Osteomyelitis**
- **Garré's Sclerosing Osteomyelitis**
- **Growth Disturbance**
- **Haematogenous Osteomyelitis**
  - in Adults
  - in Children
- **Infected Plate Osteomyelitis**
- **Intramedullary Nail Osteomyelitis**
- **Local Osteomyelitis**
- **Lymphoplasmacellular Osteomyelitis**
- **Medullary Osteomyelitis**
- **MRI**

#### Native Joints

#### Necrotising Fasciitis

#### Negative Pressure
- **Negative Pressure System**
- **Wound Therapy**
- **Contraindications**
- **Indications**

#### Neisseria

#### Netilmicin

#### Neuropathy

#### No-Additive Tube

#### Norfloxacin

#### Nuclear Imaging

#### Occlusive Dressings

#### Ofloxacin
osteomyelitis f
multifocal chronic recurrent osteomyelitis (CRMO) 188
multifocal haematogenous osteomyelitis 194
multifocal osteomyelitis 200
neonatal osteomyelitis 188, 194
plasmacellular osteomyelitis 195
primary chronic osteomyelitis 188, 195
prognosis 136, 143, 144
scintigram 190
sclerosing osteomyelitis, Garré 198
specific osteomyelitis (tuberculosis) 188, 201
superficial osteomyelitis 120
x-ray 190

osteosynthesis
acute infection 116
bone necrosis 119
empirical antibiotic therapy 128
infection 126
plate osteosynthesis 109, 120
surgical treatment 128

oxazolidinones 48

oxygen
hyperbaric 177
measurement, transcutaneous (PtcO₂) 182

P

Pasteurella multocida 147

pathogen
pathogen detection identification 211
PCR 211
sonication 211
pathogen spectrum 52

patient factors 41
patient support 43
PCR (polymerase chain reaction) 73, 87f, 197, 201, 211, 230
penicillin 44f, 216f
penicillin allergy 153
Penicillin G 111, 153

Peptostreptococci 222
periodontitis 35
perioperative infection prophylaxis 27
intraoperative measures 28
postoperative measures 29
preoperative measures 27
periosteal bone regeneration 120, 123, 139
peripheral artery occlusive disease 179
periprosthetic membranes, analysis 900
PET/CT 82
phlegmon 165
physical therapy 205
physiotherapy
in infection 205
in infectious arthritis 154
piperacillin/tazobactam 45, 185
plain tube 73
plaster splint 192
plastic defect closure 128, 140
plastic surgery 68
plethysmograph 182
PMMA beads impregnated with antibiotics 62
PMMA bone cement 49, 55, 58
polymerisation temperatures 52

D = Reference with the definition of a term
PMMA bone cement with antibiotics 55f
available preprepared combinations 55
clindamycin 55
coating implants with PMMA cement 61
colistin 55
erthyromycin 55
forms of application 58
gentamicin 55
preparation of individual combinations 55
primary implants 58
revision implants 58
spacers 58
vancomycin 55

pneumococci 209, 212
pneumonia 35
polyhexanide 50
polymerase chain reaction (PCR) 87
polymethylmethacrylat s. PMMA bone cement
position correction 186
positron emission tomography 82
Pott's disease 222
povidone-iodine solution 50
preemptive therapy 43, 233
prevention, measures 186
probe to bone 182
procalcitonin 71
prophylaxis 43
intraoperative measures 28
postoperative measures 29
preoperative measures 27
propionibacteria 87, 209, 211, 221, 232
antibiotic susceptibility 221

Propionibacterium
Propionibacterium acnaes 111, 221
Propionibacterium spp. 89
prosthetic joint infection 95
aetiology 95
algorithm 101
antibiotic prophylaxis 34
antibiotic therapy 110
classification 97
clinical findings 98
dental treatments 34
diagnostics 98
early infection 98
haematogenous prosthetic joint infections 34
imaging 100
incidence 97
laboratory tests 99
localisation 95
prevention 34
risk factors 34, 97
second look surgery 104
skin infections 35
surgical treatment 103f
therapy 101
therapy algorithm 101f
urinary tract infections 35
with arthrocentesis 99

Proteus spp. 218
pseudarthrosis 109
pseudomembranous colitis 183
Pseudomonas aeruginosa 45, 111, 147, 153, 210, 213, 220
antibiotic resistance 220
biofilm 220
pseudoparalysis 194
psoriasis 97
pulse lavage 177
**punctio sicca** 75
pustulosis 200
pyoderma gangrenosum 164ff

**Q**
quinolones 111, 212, 220f, 233f
combination with rifampicin 234
Enterobacteria, biofilm 220
monotherapy 112
*Pseudomonas aeruginosa* 220
quorum-sensing molecules 22

**R**
resection of necrotic bone 132
resistance testing 75, 211
revision arthroplasty 97
revision cements 105
rhagades 181
rheumatologic disease 168
rifabutin 44, 46
rifampicin 44, 47, 54, 110, 112, 212, 215, 221, 233f
combination with quinolones 234
contraindications 234
cytochrome system 235
in infectious arthritis 153
interactions 235
loss of effect 225
monotherapy 112
resistance 234
staphylococci 215, 234
with open wounds 235

**S**
salmonella 202
*Salmonella spp.* 87, 202, 210, 218
sample collection s. biopsy
SAPHO syndrome 200
sausage toe 181
Schanz screws 119
scintigram 190
SCV s. small colony variants
segment transport using
Ilizarov fixator 132
corticotomy 134
docking site 134
sensitivity 231D
sepsis 230D, 233
sequestra 191
sequestrum 78f, 123, 138, 192, 230D
microsequestrum 120
sequestrum formation 131
sequestrum zones 79, 139
*Serratia*
*Serratia marcescens* 219
*Serratia spp.* 218
shaving 151
silver nitrate 50
single furunculosis 165

D = Reference with the definition of a term
single-photon emission computed tomography 82
single-shot 230D
SIRS 231D
skin infections 35
small colony variants (SCV) 24, 87f, 210f, 231fD
aminoglycoside exposure 210
E. coli 210
foreign body infections 210
osteomyelitis 210
prosthetic joint infection 211
Pseudomonas aeruginosa 210
S. aureus 210
staphylococci 210
therapy 210
smoking 107
soft tissue 74
damaged 102
soft tissue assessment 117
soft tissue defects 107, 131, 138
soft tissue oedema 104
somatosensory disorders 179
sonication 90f, 100f, 210, 231D
sonography 80
spacer 58, 106
commercially available moulds for the preparation of spacers 107
hand-moulded spacers 58
industrially preformed spacers 58
specificity 231D
SPECT/CT 82, 130, 138
spina ventosa 201
spine 222
split-skin 176
split-skin graft 80, 128, 141
split-thickness skin graft 80, 128, 141
spondylodiscitis 157, 188, 195, 209, 215, 231D
microbiology 160
surgery 161	
tab wounds 173
therapy 160
spongioplasty 120, 134
S. pyogenes 165
standard x-rays s. x-ray
staphylococci 210, 212, 214, 234
beta-lactams 215
biofilm 215
coaugulate-negative staphylococci 214
coaugulate-positive staphylococci 214
coaugulate reaction 214
meticillin resistance 215
Staphylococcus aureus 95, 110, 116, 147, 153, 208, 214
bacteriaemia 35
colonisation 148
S. aureus 166
S. aureus colonisation 76
sepsis 43, 98
Staphylococcus lugdunensis 215
steroids, steroid therapy 97, 148
Streptobacillus moniliformis 147
streptococci 95, 116, 209, 215
beta-haemolytic streptococci 164, 167
group A 215
group A beta-haemolytic streptococci 166
group B 215
non-haemolytic 215
susceptibility to penicillin 216
viridans 212
Index of terms

**Streptococcus** 202
  *Streptococcus agalactiae* 111, 190, 215
  *Streptococcus pneumoniae* 202
  *Streptococcus pyogenes* 168, 170
  *Streptococcus spp.* 111, 153

*studies in animal models* 76
*superinfection* 49, 51, 65, 67
*suppressive therapy* 102, 110, 125
*surgery times* 29
*surgical treatment* 128, 138, 144
*susceptibility testing* 39
*swabs* 84, 99, 103, 211, 232
*synovectomy* 103, 151
*synovitis* 200

**T**

*targeted therapy* 43
*technical procedure* 85
*teicoplanin* 44, 47, 110
*tetanus prophylaxis* 178
*tetracyclines* 45, 47
*thermal insulation* 28
*three-phase scintigraphy* 123, 130, 138
*tissue samples* s. biopsy
*tobramycin* 44, 47, 55

*tooth*
  *dental granuloma* 35
  *dental procedures* 35
  *dental treatments* 34
  *implant surgery* 35
  *tooth abscess* 35
  *tooth extractions* 34

*toxic shock syndrome* 165
*toxic syndrome* 170
*toxins* 208
*Tropheryma whipplei* 147
*tuberculosis* 201
*two-stage procedure* 132

**U**

*ulcer* 173, 181
*ureidopenicillins* 44, 45
*urinary tract infections* 35

**V**

*vacuum* 65
  negative-pressure dressing 128
  negative-pressure wound therapy 177, 236
*vancocycin* 30, 44, 47, 52f, 110f, 215, 216
  in infectious arthritis 153
  with meticillin resistance 215
*vertebra plana* 200
*vessels, endomedullary* 120
*virulence* 208
*viscosity* 74

D = Reference with the definition of a term
W

white blood cells 70
wing flap 128
wound 29
  acute wound 173, 175
  chronic wound 173
  compartment wound 173
  dehiscence wound 97
  impaired wound healing 116
  non-healing wounds 51
  open wound 173
  subacute wound 173
  treatment 29, 177
  wound closure 175
  wound dehiscence 173
  wound infection rates 31

X

x-ray 77, 123
  in osteomyelitis 190
  standard x-rays 138
  x-ray imaging 182

Z

zone of inhibition 211
All of the drawings and graphics have been created and/or modified for each section by the respective authors. The figures and tables in each section were also created by the respective authors with the exception of the following figures:

- Dr. Steffen Bergelt, Laboratory for Histology and Cytological Diagnostics, Aarau: Fig. 6-7
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This book is the result of a collaborative effort between Swiss orthopaedics and the Swiss Society for Infectious Diseases. Representatives of these two organizations authored this publication being members of the expert group „Infections of the musculoskeletal system“.

This book is aimed at orthopaedists, infectious disease specialists, and trauma surgeons whose daily routine does not include these kinds of infections. The basic principles, prevention, diagnosis, and treatment of infections are intended to be presented in a concise form, along with topics including biofilm, microbiology, definitions, and common errors.

This book is intended

- to provide professionals with in-depth insight into the field
- a readily accessible guide with important information applicable to concrete cases

Another special objective is to encourage greater cooperation between infectious disease specialists and orthopaedists/trauma surgeons together with microbiologists, pathologists, and plastic surgeons, as necessary, in the handling of these difficult infections.