5.4 Chronic infection and infected nonunion

1 Introduction 543

2 Classification of osteomyelitis 544
2.1 Classification according to anatomical localization 544
2.2 Classification according to the implant 545

3 Diagnosis of chronic infection and infected nonunion 545
3.1 Clinical and laboratory findings 545
3.2 Bacteriology and histology 545
3.3 Imaging techniques 545
3.4 Condition of the affected limb and of the patient 546

4 Principles of treatment 546
4.1 Debridement 547
4.2 Stabilization 548
  4.2.1 External fixation
  4.2.2 Plates and nails
4.3 Reconstruction of bone 549
  4.3.1 Decortication—autogenous cancellous bone graft
  4.3.2 Open bone grafting according to Papineau
  4.3.3 Callus distraction (Ilizarov)
  4.3.4 Free vascularized bone graft
4.4 Soft-tissue coverage 552
4.5 Antibiotics 552

5 Treatment concepts for typical cases 552
5.1 Hypertrophic infected nonunion 552
5.2 Avital and unstable infected nonunion 552
5.3 Avital infected nonunion with segmental bone defect 553
5.4 Chronic infection 553
  5.4.1 Chronic infection after plate osteosynthesis
  5.4.2 Chronic infection after intramedullary nailing
  5.4.3 Recurrence of osteomyelitis after several years

6 Bibliography 554
5.4 Chronic infection and infected nonunion

1 Introduction

Chronic osteomyelitis is a problem in surgery. The origins of infection can be found in avascular dead bone (sequestrum) that has persisted for longer than 6 weeks. Chronic osteomyelitis begins with either a neglected acute infection or it may slowly develop as the delayed first manifestation of a missed infection (chapter 5.3) [1].

- Devitalized bone fragments within an infected environment become sequestra, which cause persistence of chronic infection.

Granulation tissue develops and is eventually transformed into a layer of dense fibrous tissue. This membrane isolates the infected area and acts as a barrier around the sequestra and devitalized bone. Periosteal new bone formation around the periphery of the infected area produces an involucrum that further walls off the infection (Fig 5.4-1). Chronic infections may also be associated with retained foreign bodies [2].

Fig 5.4-1a–g Development of an infected nonunion and its treatment in a 49-year-old male.

a–b Plate osteosynthesis of an open tibial fracture type 42-A1.2. Several empty drill holes indicate that the surgeon had some problems during surgery.

c Four months later and after plate removal, sequestration of an entire segment of the tibia. The periosteal new bone formation adjacent to the diaphysis indicates the presence of some vital callus.

d Complete sequestration of the necrotic segment after 10 months.

e Thorough debridement, external fixation, and cancellous bone graft as a second step procedure.

f 6 months later, full weight bearing.

g Full consolidation after 2 years.
Complications

Bacteria react to the host’s attempts at eradication by releasing a variety of protective factors. Glycocalyx (slime), a hydrated mucopolysaccharide layer, covers material, such as avascular necrotic bone or metal implants. The glycocalyx protects the bacteria in a sessile state, increases bacterial surface adherence, and isolates them from the effects of antibiotics, antibodies, and immune-directed phagocytosis. This increases their resistance to destruction by a factor of 500 [3], from which stems the difficulty in eliminating implant-related infections. The most common organisms cultured in chronic osteomyelitis are *Staphylococcus aureus* and *Staphylococcus epidermidis*. Both of these species can form a biofilm-protective layer of glycocalyx [3] and can invade osteoblasts, thereby becoming intracellular [2]. As a consequence, chronic osteomyelitis with persistent drainage and sequestra formation is resistant to eradication by long-term antibiotics alone.

- All patients with chronic osteomyelitis must be considered as potential MRSA (methicillin-resistant *Staphylococcus aureus*) carriers who require special isolation.

Surgical intervention is the only effective method to eliminate such infection and promote healing. Most gram-negative bacteria do not have a biofilm-forming capacity, with the notable exception of *Pseudomonas aeruginosa* [4].

### 2 Classification of osteomyelitis

#### 2.1 Classification according to anatomical localization

Chronic osteomyelitis may be classified according to its localization within the bone [5, 6]. This classification (Fig 5.4-2) takes into consideration the importance of bone necrosis and vascularity, hence the more favorable prognosis of medullary infections. This classification helps direct surgical and pharmacological treatment. Four entities are differentiated: type I (medullary), type II (superficial), type III (localized), and type IV (diffuse osteomyelitis).

![Fig 5.4-2](image-url)  
**Anatomical classification of adult osteomyelitis according to Cierny and Mader [5].**  
**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 within an isolated area consisting of cortical sequestra (S) and granulation tissue.  
**Type III** Localized osteomyelitis involving the whole cortex and the adjacent medullary canal. Pin-track infections and plate infections serve as examples.  
**Type IV** Diffuse osteomyelitis as a fully developed disease of the entire bone. It involves both the cortex and the medullary cavity, leading to extensive devitalization of bone.
5.4 Chronic infection and infected nonunion

2.2 Classification according to the implant

Classification according to the implant involved has the advantage of being more specific for chronic postoperative osteomyelitis. We can distinguish between pin-track osteomyelitis, plate osteomyelitis (either superficial or deep), and after intramedullary nailing (chapter 5.3).

3 Diagnosis of chronic infection and infected nonunion

3.1 Clinical and laboratory findings

Chronic discharge, pain, erythema (and rarely edema) are typical clinical findings. Discharge is often intermittent and localized in an area of scar tissue, limiting the possibilities of revision. On the other hand, the surgeon needs to know the extent of the infection, the degree of bone necrosis, the localization of sequestra and the overall condition of the patient and the function of the limb involved. Comorbidities and other factors that affect the outcome must be thoroughly assessed. Laboratory values such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are usually elevated but may be normal. Leukocyte counts are usually normal but may be elevated [2]. If positive, they are helpful in monitoring the treatment plan, but negative findings do not mean that the disease is not present.

3.2 Bacteriology and histology

- The bacteriological analysis should be based on several deep-tissue samples of bone and granulation tissue from different areas affected by the infection.

Swabs taken from either the fistula or the superficial discharge are not adequate and may be misleading in determining the agent as there may be contamination with other bacteria. In implant-associated infections, for maximum diagnostic yield, deep specimens should be obtained from up to five sites around the implant at debridement. More than five neutrophils/high power field suggests infection with specificity of 93–97% [2].

3.3 Imaging techniques (chapter 5.3)

A complete series of x-rays, from the original fracture to the current state, is helpful for the analysis of an infected nonunion.

- Necrotic areas are usually recognized by a lack of new bone formation adjacent to them, while sequestra are very dense and appear completely isolated (Fig 5.4-1) from the surrounding bone.

Today, CT and MRI are the best methods to determine the extent of the disease and the location of sequestra. Consultation with an experienced radiologist is very beneficial in deciding which investigation would be helpful, especially in the presence of metal implants.

- CT scan investigation may be preferred to demonstrate sequestration within periosteal new bone (Fig 5.4-3) [7], while MRI gives more information on soft-tissue involvement [2].

Three-phase skeletal scintigraphy or special scintigraphy with, for example, radioactive indium or labeled antibodies against granulocytes can be helpful [6, 8, 9].
Complications

Fig 5.4-3 CT analysis searching for sequestration in a 31-year-old male. Six years after complex femoral fracture with early infection after ORIF. Sinus producing MRSA (methicillin-resistant Staphylococcus aureus). Part of the sequestrated femoral diaphysis is encapsulated in periosteal new bone formation.

3.4 Condition of the affected limb and of the patient

In order to evaluate the benefits and the risks of any reconstruction, the limb distal to the infected focus must be carefully assessed. The vascularity and the sensibility of the limb and the function of the joints must be tested and correlated with the needs and expectations of the patient. The pros and cons of reconstruction of the limb or amputation, supported by a detailed treatment plan, must be discussed with the patient and relatives. Patient health and medical status (e.g., diabetes mellitus) must be considered. Smoking must cease if there is to be successful therapy of chronic infection. There are physical as well as psychological aspects to be considered. Patients who have been non-weight bearing for many years and are expected to have a prolonged period of reconstruction and rehabilitation may not have the energy or motivation to cooperate.

4 Principles of treatment

- The principles of the management of chronic osteomyelitis and infected nonunions are similar and consist of
  - identification of the infective organism;
  - eradication of infection by surgery combined with antibiotics;
  - creation of a viable and stable soft-tissue environment;
  - reconstruction, alignment, and stabilization of the skeleton.

Every case of osteomyelitis is to be considered individually, since there is no standard procedure that can be routinely applied to every patient.
4.1 Debridement

- All dead tissues, especially dead bone, all implants (except for those providing stability), old suture material, and sinuses have to be resected.

To prevent the creation of additional necrotic bone areas, care must be taken to avoid any stripping of the vascularized periosteum. The resection of necrotic bone, which is in contact with vital bone is the most difficult step. Dead bone does not show any bleeding points; it is very brittle when chiseled off (Fig 5.4-4). In areas of cancellous bone the dead tissue is best removed with a high-speed burr until bleeding is encountered (paprika sign) (Fig 5.4-5). Intramedullary debridement in a diaphysis is best done by gentle intramedullary reaming. Sometimes a second look should be considered.

- In case of instability, it is essential to provide stable fixation in spite of the infection.

**Fig 5.4-5** Cross section of a diaphysis. Debridement of the medullary cavity. Dead, not bleeding bone (green) is curetted or removed with a high-speed burr.

**Fig 5.4-4a–c** Local debridement of an infected nonunion (Video 5.3-1).

a The nonunion is covered with granulation tissue stained with methylene blue.
b After resection of the granulation tissue, the necrotic bone adjacent to the nonunion contrasts distinctly with the vital bone.
c After debridement only vital, bleeding bone is left.
4.2 Stabilization

- Skeletal stability allows
  - fracture healing;
  - functional aftercare;
  - easier wound care;
  - supports the eradication of infection;
  - later reconstructive surgery, if necessary.

Step-by-step or staged procedures may be required depending on the extent of infection, the degree of stability, and the condition of the patient.

4.2.1 External fixation

External fixation is one of the methods of stabilization in infected nonunion. It must follow the general rules of external fixation (chapter 3.3.3). In septic surgery, external fixation may need to remain for up to a year or more. To satisfy this demand, the chosen frame should be constructed more rigidly than with an acute fracture. The risk of pin-track infection is higher than usual but loosening may be reduced by using Schanz screws coated with hydroxyapatite. It may be necessary to replace one or more pins during the course of treatment. There are basically two fixation systems applicable: the Ilizarov ring fixator with thin tensioned wires or a simpler frame built from the tubular system with Schanz screws.

The tubular system (Fig 5.4-6) has the advantage of allowing free access for wound care and eventual plastic reconstructive surgery. Its simplicity allows the system to be adapted to most clinical situations. Monotube systems may sometimes be easier to place but are less versatile.

In the Ilizarov fixator the circular arrangement of rings, together with multiple thin pretensioned wires, which can be placed individually, allows for compression and lengthening, as well as for gradual correction of axial deformities [10].

Tensioned wires are also reported to have fewer pin-related problems.

4.2.2 Plates and nails

- It is essential with infected nonunions to establish the level of stability still provided by the current internal fixation. If the implant is loose or no longer functioning, it has to be removed or preferably replaced by some other form of stable fixation.

Although new internal fixation generally carries a risk of recurrence of infection, it may be considered for long bones after

Fig 5.4-6 Infected nonunion without loss of length in a tibia. Decortication and cancellous bone graft in an infected nonunion.

1 Area debrided from medial aspect will be covered with muscle flap or free vascularized flap.
2 Decortication, from posterior or lateral aspects, of the fibula and the lateral and posterior aspects of the tibia.
3 Placement of autogenous cancellous bone graft. Care must be taken not to injure the anterior tibial artery, veins, and nerve.
4.3  Reconstruction of bone

As a rule, all measures for obtaining bony bridging are much safer if carried out after a complete debridement. In problematic cases, reconstruction of bone defects should be done as a second step (Fig 5.4-7).

- Healing is more reliable if the reconstructive measures are pursued in an area of vital tissue with new healthy skin and soft-tissue cover.

4.3.1  Decortication—autogenous cancellous bone graft

The technique of decortication is described in the chapter on aseptic nonunion (chapter 5.2, Fig 5.2-7). It is performed over a distance of about 2 cm proximal and distal to the involved area (Fig 5.4-7). Cancellous bone is harvested, preferably from the anterior or posterior iliac crest. Dense pieces of cancellous bone are morsellized, which allows for quicker vascularization with minimal risk of sequestration. In the lower leg, a posterolateral or central placement of the graft into a vital bed avoids the infected focus (Fig 5.4-6) [11]. In the humerus or femur the best position of the graft mainly depends on the defect and the soft-tissue envelope.

Fig 5.4-7a–d  Debridement, decortication, and cancellous autograft combined with distraction and secondary compression.

- Infected nonunion with sequestra (1) and periosteal new bone formation (2).
- Debridement, external fixation, and distraction by about 5 mm. In the drawing fixation pins are shown close to the site of nonunion, but in clinical scenario would be placed far from the infection site.
- Decortication leaving the decorticated bone pieces in connection with the adjacent muscles; cancellous autograft inserted.
- 6 weeks later, woven bone interlaces the cancellous bone graft and the decorticated bone lamellae. At this time compression may be applied to accelerate remodeling of the bone graft and callus formation.
If a bone graft has to be applied to an area where the soft tissue is defective, the establishment of a healthy soft-tissue cover (usually a flap) should precede grafting.

In intramedullary infections (chapter 5.3), a large core tube temporarily placed into the reamed medullary canal can be of help in introducing the cancellous bone graft [12].

4.3.2 Open bone grafting according to Papineau [13]
Open bone grafting leaving the graft exposed with no skin cover is a method with a long tradition. It often achieves bony bridging and secondary soft-tissue coverage at the same time. Its main disadvantage is the need for a relatively large amount of bone to fill in a relatively small defect. Its advantage is its high success rate in small metaphyseal defects (70–90%) [1].

4.3.3 Callus distraction (Ilizarov)
Ilizarov has introduced the technique of gradual callus distraction following corticotomy, in order to restore limb length or to bridge a defect (Fig 5.4-8; 5.4-9) [10].

The great advantage of the Ilizarov method is that while callus distraction helps to correct the length, rotation, and axial alignment of the bone, the soft tissues are distracted as well, thereby minimizing the need for additional reconstruction.

After extensive local resection of the necrotic bone followed by external fixation, a transverse corticotomy is performed away from the defect, preferably close to a metaphysis. The corticotomy is performed either a week after the debridement or—in low-grade infections—simultaneously. Distraction is not commenced for 10 days, but during this time the gap is kept at a distance of 1 mm. Thereafter, the newly formed callus is slowly distracted at a rate of 1 mm per day in 4–5 steps, evenly distributed over 24 hours. Partial weight bearing is usually allowed. The progress of the distraction, callus maturation,

Fig 5.4-8a–b  Segmental bone transport using the tubular system.

a  Bone transport system combined with a unilateral external fixator mounted anteriorly on a tibia with distal defect. There is shortening as judged by the overlap of the fibula (1). Resection of the infected nonunion (2) and proximal corticotomy (3). Gradual distraction of 1 mm per day in 4–5 steps.
b  Lengthening (4) compensates both tibial shortening (1) and the resection distance (2). Consolidation of the distraction area and at the docking site (5).
and correction of any deformity are monitored by x-rays. When the planned length is reached, weight bearing is gradually increased. Full weight bearing is usually achieved 4–6 months after closure of the defect. As the docking sites have a tendency to delayed union, decortication and bone grafting of these areas may be required or in some cases internal fixation is needed. Bone transport may be long and cumbersome; it therefore requires a commitment by both the patient and the physician. The patient has to be seen regularly during the distraction period, and physiotherapy should be instituted early to mobilize the adjacent joints. In trauma cases, neurological problems due to overstretching of the nerves are rare. Callus distraction over an intramedullary nail may reduce the period of external fixation but is not without hazards, especially in patients who have had previous infections [14, 15].

4.3.4 Free vascularized bone graft

- Free vascularized bone grafts (from the fibula or the iliac crest) are especially suitable for the bridging of bone defects longer than 10 cm [16, 17].

The advantage is that, after bone integration at the recipient site, they undergo gradual hypertrophy, slowly adapting their size and structure to the local needs. It may, however, take years until full loading is possible, which requires long-term protective measures, especially in the lower extremity. Because of the relatively small diameter of the grafts, they are more suitable for forearm and humerus (Fig 5.4-9). In the tibia, one has to consider double grafting, using the contralateral fibula first and, as a second step, the ipsilateral fibula [18].

![Fig 5.4-9a–e](image) Reconstruction of an infected nonunion using bone transport and a circular frame. The infected nonunion and the segment of affected bone have been radically excised. Proximal corticotomy allows bone transport and regeneration. There is a massive hyperemic response in the bone to this treatment and this is believed to be an important factor in the eradication of infection. Final result after docking at the distal site and consolidation of the regenerated bone. The infection was eradicated and varus deformity corrected.
Because of the big difference in size (bone graft versus defect site) the method is of restricted value in the femur.

### 4.4 Soft-tissue coverage

As a rule, soft-tissue coverage without complete debridement is useless.

If a second look is necessary it is advisable to leave the wound open, with an antiseptic spacer in order to prevent superinfection (chapter 5.3). In unexposed small defects with good granulation tissue covering the bone, split skin grafts may be sufficient. In more complex situations local muscle flaps (e.g., gastrocnemius flap), fasciocutaneous flaps, or free vascularized flaps are needed. Negative pressure treatment (vacuum-assisted closure, VAC) (chapter 4.3) is very useful in other situations of open wounds or local soft-tissue defects [19].

### 4.5 Antibiotics

Antibiotics are always to be considered as being complementary to surgery. Their systemic administration has to follow strict rules in order to achieve a therapeutic concentration in the bone. The special situation of implant-related infections has to be respected. For local concentrations of antibiotics and dead space management, chains of beads impregnated with antibiotics or antibiotically impregnated bone substitutes may be useful. They offer a high concentration of antibiotics—usually gentamicin—at the infection focus for a couple of days. They can also serve as spacers for further bone grafting procedures [20, 21]. After final surgical management of an infection, adjunctive, systemic treatment should continue for 4–6 weeks [1, 6].

### 5 Treatment concepts for typical cases

#### 5.1 Hypertrophic infected nonunion

Hypertrophic infected nonunions have adequate biology or blood supply as evidenced by the excessive callus formation on x-rays.

These nonunions frequently possess only a draining sinus and are relatively asymptomatic. Patients are often able to use the affected part of the body quite well, although instability and infection are major problems. Hypertrophic infected nonunions frequently have an angular and/or rotational deformity due to muscle imbalance or weight bearing. The treatment consists of complete debridement of the infective focus, usually combined with definitive soft-tissue cover because of the limited area of infection. External or internal fixation will correct a deformity and provide stability, while a cancellous autograft may be performed after debridement of the infected focus. Consolidation can be observed within 4–6 months.

#### 5.2 Avital and unstable infected nonunion

Instability and nonviable bone are the classical features of an infected nonunion. There is little or no evidence of healing, the bone looks necrotic, osteopenic, or sclerotic, and often there is associated shortening, joint contracture, limb atrophy, and chronic pain.

The treatment of this more complex condition should occur in stages. Thorough debridement is combined with external or internal fixation. The resulting defect has to be assessed. Some shortening may be acceptable to gain stability, while reconstructions of 2–3 cm are possible with local bone grafting (Fig 5.4-1; 5.4-7). However, a risk of secondary angulation exists in reconstructions based purely on cancellous autograft-
5.4 Chronic infection and infected nonunion

Chronic infection, especially in the lower leg. In small tibial defects the graft is usually placed posterolaterally between fibula and tibia (Fig 5.4-6). In the femur and humerus grafting may be combined with plate fixation once the local situation appears to be safe.

5.3 Avital infected nonunion with segmental bone defect

With segmental bone loss and avital bone ends, severe dystrophy of the bone and the soft tissues occurs due to disuse of the limb. For the treatment any attempt at reconstruction has to be preceded by a thorough debridement. Segmental bone loss exceeding 5–6 cm can usually not be bridged successfully by cancellous bone graft. It is therefore advisable to use the callus distraction method for defects up to 10–20 cm (Fig 5.4-8; 5.4-9). The advantage of callus distraction is the creation of a new bone segment which, once matured, resembles the original bone in shape and strength. The problem of soft-tissue cover can usually be solved at the same time. On the other hand, the procedure may be painful and time-consuming. If the bone loss is situated in the forearm or humerus, vascularized grafts have to be considered (Fig 5.4-10). In the lower extremity and if the defect exceeds 6 cm, vascularized bone grafting competes with the method of callus distraction [20].

5.4 Chronic infection

5.4.1 Chronic infection after plate osteosynthesis

In chronic infection after plate osteosynthesis, plate removal and thorough debridement are advocated once the bone has consolidated. Using CT scanning, a thorough analysis of the bone structures can then be performed. During a secondary revision any remaining necrotic areas should be debrided. Plate fixation, external fixation, or alternatives may be used if the bony bridge is insufficient.

5.4.2 Chronic infection after intramedullary nailing

Intramedullary nailing may lead to bone consolidation even in the presence of infection. However, there may remain an infected area within the medullary cavity, with or without a sinus.
Complications

The best treatment for chronic infection after intramedullary nailing is gentle reaming and flushing of the medullary canal using a cortical venting hole distal to the focus.

As an alternative a long chain of gentamicin beads may be inserted into the medullary canal for 2–3 weeks. Because to a large extent vascularity comes from the periosteum, there is little risk of permanent damage. In infections, years after the removal of the nail, the medullary cavity is often filled with endosteal new bone. Reaming can only then be performed after removal of this bone through a distal cortical window and/or vent.

5.4.3 Recurrence of osteomyelitis after several years

Osteomyelitis can recur even after decades of quiescence. Clinical manifestations are pain, tenderness, swelling, fever, and abscess formation. It may be difficult to see any pathological changes on standard x-rays, but CT scans, scintigraphy, or MRI may demonstrate a sequestrum worthy of removal. Systemic antibiotics are also helpful as an adjunct to definitive surgery.

Bibliography