

# Periprosthetic infection

## Basic division

**Periprosthetic infections** are considered one of the most feared complications in endoprosthetics. We can divide them into four groups. There are several possible classifications, but this is the most effective for clinical practice.

It represents the first group **positive intraoperative culture**. We make the diagnosis from at least two tissue samples taken during the operation. A positive culture does not always have to be an absolute indication for treatment. At least five samples should be taken to avoid contamination. If therapy is necessary, treatment with specific antibiotics for three days to six weeks intravenously or combined orally / intravenously is recommended.

The second group are **acute postoperative infections**, which develops in the first days after surgery, up to a maximum of four weeks after primary implantation. In this case, the source of the infection is most often a surgical wound. The infection is manifested by redness of the joint, heat and the presence of pus in the joint. We determine the diagnosis based on the analysis of a sample aspirated from the wound. A certain advantage of early infection is the easy loosening and replacement of the implant or its parts where the infection can be located. It should be noted that arthroscopic revisions with lavage of infected implants do not lead to a successful treatment of acute infections and therefore need to be replaced.

The third group are **acute blood infection**, when the endoprosthesis is colonized by microorganisms in a hematogenous way. The cause is usually bacteremia with another cause of infection. The sources of infection are the external urinary tract, respiratory tract, gallbladder and teeth, as well as superficial skin lesions, which we should not forget. Therapy is identical to acute postoperative infection if it occurs within 3 weeks after surgery. If it occurs later, we proceed as in late infection.

**Late infections** forms the fourth group, and therefore the last. It occurs later than 4 weeks after surgery and always requires implant replacement. If the infection is diagnosed and treated in time, it is usually not necessary to replace the endoprosthesis. In general, immunocompromised patients are more prone to infection, as is the case with diabetics, rheumatists, asthmatics, etc. In this case, the pathogens tend to be less aggressive. We refer to these as **mitigated infection**. These are often bacteria that naturally colonize the patient's skin.

Infection of the endoprosthesis leads to its gradual **septic release**, when it is absolutely necessary to remove the prosthesis, replace it with an insert, remove the source of the infection with antibiotics and only then operate a new endoprosthesis. Treatment is complicated by the fact that the implant is a foreign material to the body, to which antibiotics have limited penetration. This leads to the gradual colonization of the prosthesis with bacteria and the formation of a polysaccharide biofilm that is almost impermeable to antibiotics. In severe cases, further implantation of the prosthesis is not possible and we proceed to arthrodesis, or we leave the joint free and a fibrous interposition is formed in its place, as is the case with the so-called suspended hip, which allows walking on crutches.

## Agents of infections and related diseases

The most important sources of infection for the patient are his own skin adnexa, then the person of the surgeon and, last but not least, pathogens in the surrounding air. The predominant pathogens are staphylococci, streptococci, gram-negative bacilli and enterococci in descending order (Table 1). In mixed infections, coagulase-negative staphylococci clearly dominate *Staphylococcus epidermidis*, *capitis* and *haemolyticus*, followed *Staphylococcus aureus*. However, even rarer infectious agents can cause surgery.

Originator	Incidence (%)	Presence in the mix. inf. (%)
Coagulase-negative staphylococci	36	41
<i>Staphylococcus aureus</i>	28	27
<i>Propionobacterium</i>	11	5
<i>Enterococcus faecalis</i>	8	5
B streptococci	7	9
<i>Escherichia coli</i>	5	9
<i>Pseudomonas aeruginosa</i>	4	-
MRSA	3	5

[1]

The most at-risk patients are, **diabetics, rheumatists, asthmatics and immunocompromised patients** in general. **Previous surgical procedures** further increase the risk of infection (Tab. 2).

Primary disease	Probability of infection(%)
Primary osteoarthritis, aseptic necrosis	1
Rheumatoid arthritis	2
Two or more previous surgeries, including arthroscopy	3
Revision arthroplasty	4
Immunosuppressed patients	5

[2]

## Diagnostic options

### History

Prolonged healing times of previous wounds, increased use of antibiotics and repeated revision surgeries in the past must be recorded. They can pose a risk of infection as well as poor dental hygiene or the presence of shin ulcers.

### Laboratory tests

Important diagnostic markers are CRP and blood sedimentation, the values of which tend to be increased in 95% of cases of painful endoprostheses. CRP values usually normalize within 2-3 weeks after surgery, in contrast to increased blood sedimentation values, which in some cases may persist for one year after surgery. Leukocyte counts do not have such a diagnostic value, especially in patients with minor infections. However, they are useful parameters for monitoring the extent of infection in cases with generalized symptoms.

### Imaging Methods

X-rays have low sensitivity. Radiological changes are evident only in long-term infections (osteolysis or osteopenia). Osteoblastic changes, osteolysis, the presence of newly formed calcified sites, and periosteal reactions are typical signs of ongoing inflammation. The use of CT has limited possibilities due to artifacts arising from the presence of metal parts of implants.

**Magnetic resonance imaging** is indicated in some cases of soft tissue involvement (some abscesses) during surgery, but it is not suitable for determining whether or not inflammation is present.

**Scintigraphy** offers relatively high sensitivity (> 90%) to demonstrate septic prosthesis release, but low specificity to distinguish aseptic and septic changes. Antigranulocyte scintigraphy has the highest specificity. The relatively good results of PET use have not found application in clinical practice.

### Joint aspirations, microbiological cultures and biomarker analysis

Joint aspiration is the method we choose to detect infection. It is the most accurate method in addition to histological examination of tissue samples. Sources report a sensitivity of 55-100%. A frequent target of criticism is the relatively high proportion of false positive results and false negative detections, which is mainly due to contamination of the sample and the transport medium during collection or incubation time. Absolute sterility is required at collection.

Incubation of the collected cultures must be performed within 14 days of the procedure, as long as the bacterium causing the periprosthetic infection is present in small quantities and organized into biofilm. Only in 73.6% of cases of periprosthetic infection found after 13 days is detectable after 7 days. However, if we adhere to these conditions, we can achieve a success rate of up to 90%.

The number of leukocytes in the synovial fluid aspirate has a high diagnostic weight in patients without inflammatory joint damage of other causality. Here we consider the period up to 6 weeks after the operation to be an early postoperative phase, the infection occurring later to be late. Leukocyte counts vary from joint to joint. For example, for a knee, a cell count greater than 27,800 /  $\mu\text{l}$  has a positive predictive value of 94% and a negative predictive value within the first 6 weeks after surgery. In the late phase, numbers higher than 1,100–3,000 /  $\mu\text{l}$  indicate infection (specificity 98% and sensitivity 99%). In inflammation of the hip, the cell counts are higher than 4200 /  $\mu\text{l}$ . In general, an increase in neutrophils (60-80%) is a sign of ongoing inflammation.

### Sonication, PCR, biomarkers

Ultrasonic sonication of the removed implants dislodges the biofilm very well, which can then be easily used for cultivation. It has been shown that the sample prepared in this way leads to more sensitive detection than tissue samples normally taken. Microorganisms have a greater tendency to cling to the surface of the prosthesis than to move freely in the tissues or fluid we aspire to.

Another possible and at the same time significantly more accurate processing of sonicated material is PCR. We detect specific bacterial DNA using specific primers. The best known is the DNA gene encoding 16S rRNA, which we detect in almost all bacteria.

The last method is the analysis of typical inflammatory biomarkers such as interleukins IL-1 and IL-6. They are a good helper in deciding between septic and aseptic conditions. Its diagnostic value is above the previously mentioned CRP and the value of blood sedimentation.

## Prospects for prevention

Infection prevention is currently a major challenge for the industry. The best infection is one that does not arise. With advances in nanotechnology, new opportunities are emerging to combat this difficult problem. A special nanoarchitectonic surface can effectively prevent the binding of bacteria. These then do not create a commonly formed biofilm that would be difficult to get rid of. The choice of metals with antibacterial activity or their alloys also facilitates the fight against infection. Another relatively ingenious solution is the possibility of fixing the implant by means of cement impregnated with vancomycin, which has proved its worth in practice.

## Links

### Reference

1. Perka a Müller, 2014
2. Perka a Müller, 2014

### Resources

- PERKA, Carsten a Michael MÜLLER. Periprosthetic Infection. In: BENTLEY, George. *European Surgical Orthopaedics and Traumatology: the Efort textbook*. Berlin, Heidelberg: Springer Berlin Heidelberg, 2014, s. 2511. 2014. ISBN 978-3-642-34745-0. DOI: 10.1007/978-3-642-34746-7\_119. Available from: [https://link.springer.com/referenceworkentry/10.1007%2F978-3-642-34746-7\\_119](https://link.springer.com/referenceworkentry/10.1007%2F978-3-642-34746-7_119).
- PILNÝ, Jaroslav. Infekční komplikace totálních endoprotéz. *Ortopedie-traumatologie.cz* [online]. 2011 [cit. 2014-12-08]. Available from: <http://www.ortopedie-traumatologie.cz/Infekcni-komplikace-totalnich-endoprotez>.
- TRAMPUZ, Andrej, Kerry E. PIPER, Melissa J. JACOBSON, Arlen D. HANSEN, Krishnan K. UNNI, Douglas R. OSMON, Jayawant N. MANDREKAR, Franklin R. COCKERILL, James M. STECKELBERG, James F. GREENLEAF a Robin PATEL. Sonication of Removed Hip and Knee Prostheses for Diagnosis of Infection. *New England Journal of Medicine*. 2007-08-16, vol. 357, issue 7, s. 654-663. DOI: 10.1007/s11999-010-1433-2. Available from: <https://www.nejm.org/doi/full/10.1056/NEJMoa061588?cookieSet=1>
- Della Valle C, Parvizi J, Bauer TW, et al. Diagnosis of periprosthetic joint infections of the hip and knee. *J Am Acad Orthop Surg*. 2010;18(12):760-70.
- GHANEM, Elie, Kerry E. PIPER, Melissa J. JACOBSON, Arlen D. HANSEN, Krishnan K. UNNI, Douglas R. OSMON, Jayawant N. MANDREKAR, Franklin R. COCKERILL, James M. STECKELBERG, James F. GREENLEAF a Robin PATEL. Cell Count and Differential of Aspirated Fluid in the Diagnosis of Infection at the Site of Total Knee Arthroplasty. *The Journal of Bone and Joint Surgery (American)*. 2008-08-01, vol. 90, issue 8, s. 1637-. DOI: 10.2106/JBJS.G.00470. Available from: <https://jbjs.org/cgi/doi/10.2106/JBJS.G.00470>
- SCHINSKY, Mark F., Kerry E. PIPER, Melissa J. JACOBSON, Arlen D. HANSEN, Krishnan K. UNNI, Douglas R. OSMON, Jayawant N. MANDREKAR, Franklin R. COCKERILL, James M. STECKELBERG, James F. GREENLEAF a Robin PATEL. Perioperative Testing for Joint Infection in Patients Undergoing Revision Total Hip Arthroplasty. *The Journal of Bone and Joint Surgery (American)*. 2008-09-01, vol. 90, issue 9, s. 1869-. DOI: 10.2106/JBJS.G.01255. Available from: <https://jbjs.org/cgi/doi/10.2106/JBJS.G.01255>
- XU, Yong-Qing, Yue-Liang ZHU, Xin-Yv FAN, Tao JIN, Yang LI, Xiao-Qing HE, Jayawant N. MANDREKAR, Franklin R. COCKERILL, James M. STECKELBERG, James F. GREENLEAF a Robin PATEL. Implant-Related Infection in the Tibia: Surgical Revision Strategy with Vancomycin Cement. *The Scientific World Journal*. 2014, vol. 2014, issue 9, s. 1-6. DOI: 10.1155/2014/124864. Available from: <https://www.hindawi.com/journals/tswj/2014/124864/>
- SKEDROS, John G., Kendra E. KEENAN, Wanda S. UPDIKE, Marquam R. OLIVER, Yang LI, Xiao-Qing HE, Jayawant N. MANDREKAR, Franklin R. COCKERILL, James M. STECKELBERG, James F. GREENLEAF a Robin PATEL. Failed Reverse Total Shoulder Arthroplasty Caused by Recurrent *Candida glabrata* Infection with Prior *Serratia marcescens* Coinfection: Surgical Revision Strategy with Vancomycin Cement. *Case Reports in Infectious Diseases*. 2014, vol. 2014, issue 9, s. 1-9. DOI: 10.1155/2014/142428. Dostupné z: <https://www.hindawi.com/journals/crid/2014/142428/>
- KUIPER, Jesse WP, Kendra E. KEENAN, Wanda S. UPDIKE, Marquam R. OLIVER, Yang LI, Xiao-Qing HE, Jayawant N. MANDREKAR, Franklin R. COCKERILL, James M. STECKELBERG, James F. GREENLEAF a Robin PATEL. Treatment of acute periprosthetic infections with prosthesis retention: Review of current concepts. *World Journal of Orthopedics*. 2014, vol. 5, issue 5, s. 667-. DOI: 10.5312/wjo.v5.i5.667. Available from: <https://www.wjgnet.com/2218-5836/full/v5/i5/667.htm>
- He Chuan, Lu Yong, Jiang Meihua, Feng Jianmin, Wang Yi and Liu Zhihong. Clinical value of optimized magnetic resonance imaging for evaluation of patients with painful hip arthroplasty. *Chin Med J* 2014;127:3876-3880
- GALLO, Jiri, Martin HOLINKA, Calin MOUCHA, Marquam R. OLIVER, Yang LI, Xiao-Qing HE, Jayawant N. MANDREKAR, Franklin R. COCKERILL, James M. STECKELBERG, James F. GREENLEAF a Robin PATEL. Antibacterial Surface Treatment for Orthopaedic Implants: Review of current concepts. *International Journal of Molecular Sciences*. 2014, vol. 15, issue 8, s. 13849-13880. DOI: 10.3390/ijms150813849. Available from: <https://www.mdpi.com/1422-0067/15/8/13849>
- TRAMPUZ, Andrej, Kerry E. PIPER, Melissa J. JACOBSON, Arlen D. HANSEN, Krishnan K. UNNI, Douglas R. OSMON, Jayawant N. MANDREKAR, Franklin R. COCKERILL, James M. STECKELBERG, James F. GREENLEAF a Robin PATEL. Sonication of Removed Hip and Knee Prostheses for Diagnosis of Infection. *New England Journal of Medicine*. 2007-08-16, vol. 357, issue 7, s. 654-663. DOI: 10.1056/NEJMoa061588. Available from: <https://www.nejm.org/doi/full/10.1056/NEJMoa061588?cookieSet=1>

## Source

- ws:Periprotetická infekce