

Systemic and local antibiotics complement one another

Administration of antibiotics can in principle be differentiated into systemic and local administration.

Systemic administration

If an antibiotic is administered intravenously (IV) or orally (PO), this is referred to as systemic administration. The antibiotic is absorbed and distributed via the body's own systems (blood circulation, digestive organs, mucous membranes). The highest concentrations are therefore achieved in the blood and the parenchymal organs or the kidneys. As a result of the limited vascularisation of bone tissue, the concentration of an antibiotic after systemic administration is often relatively low in bone tissue.

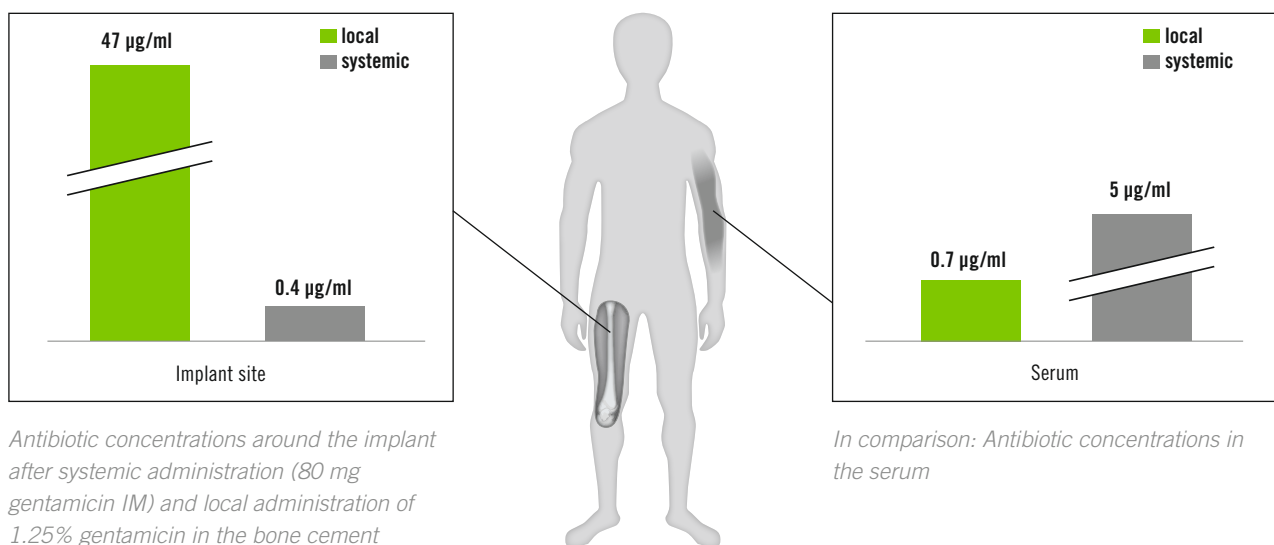
Local administration

Antibiotics are released directly from carrier systems like bone cement or bone substitute material into the bone or the joint compartment. In this way, high antibiotic concentrations are produced exactly where a possible contamination by bacteria has occurred or where an infection has already developed. At the same time, the systemic burden is relatively low with locally administered antibiotics because the active substance remains largely on site.

An optimal combination: The combined administration of systemic and local antibiotics

The systemic and local antibiotic application can optimally supplement one another: two independent antibacterial front lines can be established. This applies particularly if, as in most cases, different antibiotic classes are used systemically and locally. Thus, for example, a cephalosporin (e.g. cefuroxim) is administered systemically and an aminoglycoside (e.g. gentamicin) is used for local prophylaxis.

- Systemic antibiotics lead to a high concentration in the circulation and in the parenchymal organs.
- Local antibiotics lead to a high concentration in the bone and the joint cavities (implant side) with low systemic load.



Literature

- Abdulkarim A et al. Cemented versus uncemented fixation in total hip replacement: a systematic review and meta-analysis of randomized controlled trials. *Orthop Rev (Pavia)* 2013; Mar; 15; 5(1): e8.
- AWMF Leitlinie AK Krankenhaus und Praxishygiene, Stand 2013
- Benito N et al. Etiology of Surgical Site Infections after Primary Total Joint Arthroplasties. *Journal of Orthopaedic Research* 2014; May: 633–637.
- Bert JM, et al. The incidence of tibial component loosening in cemented total knee arthroplasty when the tibial stem is not cemented. Presented at the American Academy of Orthopaedic Surgery Meeting, Orlando 2000.
- Biehl G et al. Experimentelle Untersuchungen über die Wärmeentwicklung im Knochen bei der Polymerisation von Knochenzement. *Arch. Orthop.- Unfall-Chir.* 1974; 78: 62–69.
- Billi F, et al. Techniques for improving the initial strength of the tibial tray-cement interface bond. *Bone Joint J* 2019; 101-B (1 Supple A): 53–58.
- Bökeler U et al. The Influence of a Modified 3rd Generation Cementation Technique and Vacuum Mixing of Bone Cement on the Bone Cement Implantation Syndrome (BCIS) in Geriatric Patients with Cemented Hemiarthroplasty for Femoral Neck Fractures. *Medicina.* 2022; 58(11):1587.
- Breusch [1] S, Malchau H. Optimal Cementing Technique – The Evidence: What is modern cementing technique? In: Breusch S, Malchau H eds. *The Well-Cemented Total Hip Arthroplasty.* Berlin/Heidelberg/New York: Springer Verlag 2005; 147–148.
- Breusch [2] S et al. Der Stand der Zementiertechnik in Deutschland. *Z. Orthop.* 1999; 137: 101–107.
- Breusch [3] J, et al. Lavage technique in total hip arthroplasty: jet lavage produces better cement penetration than syringe lavage in the proximal femur. *J Arthroplasty.* 2000; 15 (7): 921–927.
- Breusch [4] S et al. Zementierte Hüftendoprothetik – Verminderung des Fettembolierisikos mittels gepulster Druckspülung. *Orthopäde* 2000; 29: 578–586.
- Chawda M et al. Comparison of cemented vs uncemented acetabular component positioning using an imageless navigation system. *J Arthroplasty* 2009; Dec; 24(8): 1170–1173.
- Christie J. Medullary lavage reduces embolic phenomena and cardiopulmonary changes during cemented hemiarthroplasty. *J Bone Joint Surg(Br)* 1995; 77: 456–459.
- Darre, E et al. Skin protection against methylmethacrylate. *Acta Orthop. Scand.* 1987; 58: 236–238.
- DeLuise M, Scott CP. Addition of hand-blended generic tobramycin in bone cement: effect on mechanical strength. *Orthopedics* 2004; Dec; 27(12): 1289–1291.
- Dunne NJ, et al. The relationship between porosity and fatigue characteristics. *Biomaterials* 2003; 24 (2): 239–245.
- Donaldson AJ et al. Bone cement implantation syndrome. *Br J Anaesth.* 2009; Jan; 102(1): 12–22.
- Eich G. A microbiology guide. In: Ochsner P: *Infections of the musculoskeletal system, Grandvaux: Swiss orthopaedics in-house-publisher* 2014: 208–231.
- Engesaeter [1] LB et al. Antibiotic prophylaxis in total hip arthroplasty: effects of antibiotic prophylaxis systemically and in bone cement on the revision rate of 22,170 primary hip replacements followed 0–14 years in the Norwegian Arthroplasty Register. *Acta Orthop Scand* 2003; 74(6): 644.
- Engesaeter [2] LB. The Norwegian Hip Register – The Influence of Cement and Antibiotics on the clinical Results of Primary Prostheses. In: Walenkamp G. *Local Antibiotics in Arthroplasty.* Stuttgart/New York: Thieme Verlag 2007.
- Hargrove R et al. Does pulse lavage reduce hip hemiarthroplasty infection rates. *J Hosp Infect.* 2006; 62(4): 446–449.
- Helwig P et al. Tibial cleaning method for cemented total knee arthroplasty: An experimental study *Indian J Orthop.* 2013; 47 (1): 18–22.
- Gehrke T et al. Cemented femoral fixation: A North Atlantic divide. *Seminar in Arthroplasty* 2016; 27:8-10.
- Geier J et al. Allergy diagnostics in suspected implant intolerance: practical approach. A Position Paper of the German Contact Dermatitis Research Group (DKG). *Hautarzt* 2008; 59(7): 594–559
- Griffith R et al. Safety guideline: reducing the risk from cemented arthroplasty for hip fracture 2015. *Anaesthesia* 2015; 70:623-626.
- Guenther D et al: Allergic reactions in arthroplasty: myth or serious problem? *Int Orthoped.* 2016; Feb; 40(2): 239–244.
- Heraeus Medical GmbH [1]. Safety Data Sheet PALACOS® R+G 1x40 INT, Version 4. 0, 18. 07. 2018
- Heraeus Medical GmbH [2]. Instructions for Use PALACOS® R+G, Revision status: 2017–03
- Humez M et al: Registerdaten zur zementierten Endoprothetik. *Orthopädie* 2024;53, 163–175.
- Izakovicova P, Borens O, Trampuz A. Periprosthetic joint infection: current concepts and outlook. *EFORT Open Rev.* 2019; Jul; 4(7): 482–494.
- Jiranek WA, Hanssen AD, Greenwald AS. Antibiotic-loaded bone cement for infection prophylaxis in Total Joint Replacement. *J Bone Joint Surg Am.* 2006; Nov; 88(11): 2487–2500.

- Khanuja HS et al. Revisiting cemented femoral fixation in hip arthroplasty. *The Journal of Bone and Joint Surgery* 2022; 104 (11): 1024-1033.
- Kühn [1] KD. *Bone Cements. Up-to-Date Comparison of Physical and Chemical Properties of Commercial Materials.* Berlin/Heidelberg/New York: Springer Verlag 2000.
- Kühn [2] KD. *Knochenzemente für die Endoprothetik.* Heidelberg: Springer Verlag 2001.
- Kühn [3] KD. *PMMA Cements. Are we aware what we are using?* Heidelberg: Springer Verlag 2014.
- Kühn [4] KD, Höntzsch D. *Augmentation mit PMMA-Zement.* *Unfallchirurg* 2015; 118/9: 737–748.
- Kühn [5] KD, Lieb E, Berberich C. *PMMA Bone Cement: What is the role of local Antibiotics?* *Maitrise Orthopedique* 2016; 243: 1–15.
- Kühn [6] KD, Renz N, Trampuz A. *Lokale Antibiotikatherapie.* *Unfallchirurg* 2017; 120(7): 561–572.
- Kühn [7] KD. *Bone Cements. Up-to-Date Comparison of Physical and Chemical Properties of Commercial Materials.* Berlin/Heidelberg/New York: Springer Verlag 2000.
- Kunutsor SK et al. Debridement, antibiotics and implant retention for periprosthetic joint infections: a systematic review and meta-analysis of treatment outcomes.** *J Infect* 2018;77:479–488.
- Lombardi Jr AV, et al. *Surface-cementation of the tibial component in total knee arthroplasty.* *Proceedings 65th Annual Meeting of the American Academy of Orthopaedic Surgeons, New Orleans, LA 1–4, 1998.*
- Lutz MJ, et al. *The effect of cement gun and cement syringe use on tibial cement mantle in total knee arthroplasty.* *J Arthroplasty* 2009; 24 (3): 461–467.
- Malchau H et al. *Prognosis of Total Hip Replacement – Update and Validation of Results from the Swedish National Hip Arthroplasty Register 1979 – 1998.* *The international journal of risk and safety in medicine* 1996; 8(1): 27–45.
- Malhotra A et al. *PMMA Cements in Revision Surgery.* In: Kühn KD, ed. *Management of Periprosthetic Joint Infection.* Berlin: Springer Verlag 2018; 243–255.
- Maloney WJ, Schmalzried T, Harris WH. *Analysis of long-term cemented total hip arthroplasty retrievals.* *Clin Orthop Relat Res.* 2002; Dec; 405: 70–78.
- Matthews JJ et al. *Combined syringe cement pressurisation and intra-osseous suction: An effective technique in total knee arthroplasty.* *Acta orthopaedica Belgica* 2009; 75(5): 637–41
- Miller MA, et al. *Increased initial cement–bone interlock correlates with reduced total knee arthroplasty micro-motion following in vivo service.* *J Biomech* 2014; 47 (10): 2460–2466.
- Neut D et al. *The effect of mixing on gentamicin release from polymethylmethacrylate bone cements.* *Acta Orthop Scand* 2003; 74(6): 670–676.
- Niki Y et al. *How much sterile saline should be used for efficient lavage during total knee arthroplasty? Effects of pulse lavage irrigation on removal of bone and cement debris.* *Journal of Arthroplasty* 2007; 22(1): 95–99.
- NJR Implant Summary Report: Summary. Report. HP_Cement_Palacos Antibiotic. 17/05/2019. 19:20.
- Olerud F, Olsson C, Flivik G. *Comparison of Refobacin Bone Cement and Palacos with Gentamicin in total hip arthroplasty: an RSA study with two years follow-up.* *Hip int.* 2013; 24(1): 56–62.
- Olsen M et al. *The role of bone cement for the development of intraoperative hypotension and hypoxia and its impact on mortality in hemiarthroplasty for femoral neck fractures.* *Acta Orthopaedica* 2020; 91 (3):293-298.
- Otto-Lambertz et al. *Periprosthetic infection in joint replacement – diagnosis and treatment.* *Dtsch Arztebl Int* 2017; 114(20); 347–353.
- Padmanabhan T, Thomas S. *Methyl methacrylate permeability of dental and industrial gloves.* *The New York state dental journal* 2009; 75(4): 40–42.
- Park SH, et al. *Cement-cement interface strength: influence of time to apposition.* *J Biomed Mater Res* 2001; 58 (6): 741–746.
- Perez-Mañanes R, Vaquero J, Villanueva-Martinez M. *An experimental study of bone cement penetration in total knee arthroplasty depending on cementing technique used.* *Trauma (Spain)* 2012; 23(1): 48–58.
- Rassir R et al. *What Are the Frequency, Related Mortality, and Factors Associated with Bone Cement Implantation Syndrome in Arthroplasty Surgery?* *Clinical orthopaedics and related research* 2021; 479 (4), S. 755–763.
- Refsum AM, et al. *Cementing technique for primary knee arthroplasty: a scoping review.* *Acta Orthop* 2019; 90 (6): 582–589.
- Sanz-Ruiz, P, Villanueva-Martinez M, Berberich C. *Benefit and Risks of Antibiotic-Loaded Bone Cements.* In: Kühn KD, ed. *Management of Periprosthetic Joint Infection.* Berlin: Springer Verlag 2018; 217–228.
- Satalich JR et al. *Cementation in total hip arthroplasty: history, principles, and technique.* *EFORT Open Reviews* 2022; 7(11): 747–757
- Schlegel [1] UJ et al. *Efficacy of vacuum bone cement mixing systems in reducing methylmethacrylate fume exposure: comparison of 7 different mixing devices and handmixing.* *Acta Orthop Scand* 2004; 75: 559–566.
- Schlegel [2] UJ et al. *Pulsed lavage improves fixation strength of cemented tibial components.* *Int Orthop.* 2011; Aug; 35(8): 1165–1169.

- Schönherr et al. Zement in der Hüftendoprothetik – ein Update. OUP 2017; 4: 202–206.
- Seeger JB, et al. The effect of bone lavage on femoral cement penetration and interface temperature during Oxford unicompartmental knee arthroplasty with cement. J Bone Joint Surg Am 2013; 95 (1): 48–53.
- Sellei, RM. Die pulsierende Jet Lavage zur Hochdruckspülung in der zementierten Hüftendoprothetik/The pulsatile jet lavage as high pressure lavage in cemented total hip arthroplasty. Aachen: RWTH Aachen University [Diss.] 2005.
- Sharkey PF, et al. Why are total knee arthroplasties failing today? Clin Orthop Relat Res 2002; 404: 7–13.
- Sigmund IK et al. Mixing Technique of PMMA – Bone Cement Determines the Ideal Insertion Time Point in Cemented Arthroplasty. J Surg. 2018; JSUR-1153.
- Simpson et al. In vitro-Freisetzung von Antibiotika aus SmartSet HV- und Palacos R-Knochenzement. Orthopäde 2005; 34(12): 1255–1262.
- Spierings P. Properties of Bone Cement: Testing and Performance of Bone Cements. In: Breusch S, Malchau H eds. The Well-Cemented Total Hip Arthroplasty. Berlin/Heidelberg/New York: Springer Verlag 2005; 67–78.
- Springer BD et al. Cemented femoral stem fixation: back to the future. JArthroplasty 2023; 38(7): 38–44
- Sprowson AP et al. The use of high-dose dual-impregnated antibiotic-laden cement with hemiarthroplasty for the treatment of a fracture of the hip. Bone Joint J. 2016; 98-B: 1534–1541.
- Steiner O et al. Is benzoyl peroxide detectable under physiological conditions in orthopaedic cement? Int. J. Nano and Biomaterials 2021;10(1): 34-49
- Takahashi E et al. The influence of cement thickness on stem subsidence and cement creep in a collarless polished tapered stem: When are thick cement mantles detrimental? Bone Joint Res. 2017; 6(5): 351–357.
- Thomas [1] P. Allergic reactions to implant materials. Orthopäde 2003; 32: 60–64.
- Thomas [2] P et al. Charakteristika von 200 Patienten mit Verdacht auf Implantatallergie im Vergleich zu 100 beschwerdefreien Endoprothesenträgern. Orthopäde 2013; 8: 607–613.
- Thomsen M et al. Fracture load for periprosthetic femoral fractures in cemented versus uncemented hip stems: an experimental in vitro study. Orthopedics 2008; 31(7): 653.
- Toksvig-Larsen S. Cement interface temperature in hip arthroplasty. Acta Orthop Scand 1991; 62(2): 102–105.
- Trampuz A. Implant-associated biofilm. In: Ochsner P: Infections of the musculoskeletal system, Grandvaux: Swiss orthopaedics in-house publisher, 2014: 208–231.
- Vanlommel J et al. Cementing the tibial component in total knee arthroplasty: which technique is the best? J Arthroplasty 2011; 26(3): 492–496.
- Wahlig H. Kinetics of the liberation of antibiotics from bone cements--results of comparative studies in vitro and in vivo. Chirurgie und Orthopädie 1987; 31: 221–226.**
- Webb JC, Spencer RF. The role of polymethylmethacrylate bone cement in modern orthopaedic surgery. J Bone Joint Surg Br 2007; 89(7): 851–857.
- Wang JS. The benefit of Vacuum Mixing. In: Breusch S, Malchau H, eds. The Well-Cemented Total Hip Arthroplasty, Springer Verlag 2005; 107–112.
- Whitehouse MR, Atwal NS, Pabbruwe M, Blom AW, Bannister GC. Osteonecrosis with the Use of Polymethylmethacrylate Cement for Hip Replacement: Thermal-Induced Damage Evidenced In Vivo by Decreased Osteocyte Viability. Eur Cells Mater 2014; 27: 50–63.
- Wilkinson JM, et al. Effect of mixing technique on the properties of acrylic bone-cement. J Arthroplasty 2000; 15 (5): 663–667.
- Wittmann D et al. Gentamicin allergy as an unexpected 'hidden' cause of complications in knee arthroplasty. Contact Dermatitis 2018; 78(4): 293–294.
- Wouthuyzen-Bakker M et al. Failure After 2-stage Exchange Arthroplasty for Treatment of Periprosthetic Joint Infection: The Role of Antibiotics in the Cement Spacer. In: Clin Infect Dis. 2018; 68(12): 2087–2093
- Zmistowski B, Parvizi J. A quarter of patients treated for PJI dead within 5 years. Orthopedics Today 2013.