Continuing Medical Education

Perioperative Antibiotic Prophylaxis

Indications and Modalities for the Prevention of Postoperative Wound Infection

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Summary

Background: Postoperative surgical site infections (SSI) account for almost 25% of all nosocomial infections in Germany and are a source of increased morbidity and mortality.

Method: This review is based on pertinent publications retrieved by a selective search in PubMed and on national and international guidelines.

Results: The individual risk factors for SSI must be assessed before any surgical procedure. A body-mass index above 30 kg/m2 is associated with an unadjusted risk ratio of 1.35 [1.28; 1.41] for SSI, which rises to 3.29 [2.99; 3.62] if the patient is also immunosuppressed. The risk of SSI is also significantly higher with certain types of procedure. Perioperative antibiotic prophylaxis (PAP) is clearly indicated for operations that carry a high risk of SSI (e.g., colorectal surgery) and for those that involve the implantation of alloplastic material (e.g., hip endoprostheses). PAP can usually be administered with basic antibiotics such as cefazoline. The basic principles of PAP are that it should be given by the anesthesia team in the interval from 60 minutes preoperatively up to shortly before the incision, and that its administration should only be for a short period of time, usually as a single shot. Continuing PAP onward into the postoperative period leads to increased toxicity, bacterial superinfections, and antibiotic resistance.

Conclusion: The evidence shows that perioperative antibiotic prophylaxis is a component of a bundle of measures that can help prevent SSI. Strict indications and adherence to the basic principles of PAP are essential for therapeutic success.

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Postoperative surgical site infections (SSIs) are serious and often preventable complications that increase patient morbidity and mortality and constitute a major financial burden for the health-care system (1, 2). The evidence shows that perioperative antibiotic prophylaxis (PAP) is one of many easily implementable measures that can lower the rate of SSI. This article focuses on intravenous perioperative antibiotic prophylaxis for surgical procedures. Special aspects of peri-interventional antibiotic prophylaxis, e.g., in the context of endoscopic interventions, are addressed in the German S3 guideline on perioperative and periinterventional antibiotic prophylaxis, now in preparation. For more information on oral antibiotic prophylaxis, e.g., before gastrointestinal procedures, the reader is referred to the S3 guideline on the perioperative management of gastrointestinal tumors (POMGAT), which was published in November 2023 (3).

Learning objectives

This article should enable the reader to:

- know the epidemiology and risk factors of SSI and the measures that can be taken to prevent it,
- evaluate the indications for perioperative antibiotic prophylaxis, know the more commonly used drugs, and be acquainted with certain special situations, and

Background
Post-operative wound infections are among the more common nosocomial infections. They cause considerable medical and economic damage.

Perioperative antibiotic prophylaxis
Perioperative antibiotic prophylaxis is one of many easily implemented, evidence-based measures that can lower the SSI rate.

Box

Selected risk factors for postoperative wound infection

Patient-related

- age > 65 years
- prior radiotherapy
- prior skin infection
- diabetes mellitus
- smoking
- obesity (BMI > 30 kg/m2)
- hypoalbuminemia
- nasal colonization with S. aureus
- immunosuppression
- other preoperative infections

Patient-independent

- surgical experience
- long duration of procedure (> 3 hours)
- perioperative blood transfusion
- breach in aseptic technique
- room air technology other than class 1a
- noise (e.g., conversation) in the operating room
- excessive movement of persons through the operating room

- know the modalities and indicators for the correct implementation of intravenous PAP.

Epidemiology

The findings of the 2016 national point-prevalence survey on nosocomial infection and antibiotic use in German acute-care hospitals were published in the Deutsches Ärzteblatt in 2017. The prevalence of nosocomial infection was 4.6%. SSI accounted for ca. 22% of the total; every year, approximately 1% of persons undergoing surgery as inpatients (nearly 200,000 patients) sustain an SSI (1). If only surgical interventions are considered, SSIs are found to account for more than 40% of nosocomial infections. The survey also revealed that more than 50 % of PAP was accounted for by perioperative "prophylaxis" that was given for a prolonged period without any underlying scientific evidence. If antibiotics were not used in this way, total antibiotic use in the inpatient sector would be 10–20% lower. In another study, data were analyzed from almost 5 million patients who were treated in 79 German hospitals from 2010 to 2016 (2). An SSI was documented in 10,807 of 221,113 patients (4.9%).

Some types of surgery (e.g., colorectal surgery (8.4%) versus hip replacement (4.3%), $p < 0.001$) were found to be associated with a significantly higher SSI rate (the quotient of SSIs to the total number of operations). Further factors associated with a higher SSI rate (without adjustment) were obesity (defined as BMI > 30 kg/m2) and immunosuppression (relative risk [RR], 1.35 [1.28; 1.41] and 3.29 [2.99; 3.62], respectively).

SSI was associated with higher mortality (9.3% vs. 4.5%, $p < 0.001$), longer hospital stays (28 vs. 12 days, $p < 0.001$), and higher cost per case (19,008 versus 9,040 euros, $p < 0.001$). The mean underfunding per case was 1,534 euros. The psychological consequences for patients, some of whom must live with an open wound for a long time and endure social isolation and emotional trauma, are an intangible burden that has yet to be adequately studied.

SSI rates range from under 1% (e.g., for hip arthroplasty) to over 15% (e.g., for open pancreatic surgery), depending on the type of procedure and the patient's risk factors. Moreover, many postoperative wound infections only arise after discharge from the hospital. In a meta-analysis, 141,347 pooled wound infections that occurred after 1,432,293 operations were evaluated: 84,984 (60.1%) of them arose after discharge (4).

Definition and risk factors

In the 1970s, the U.S. Centers for Disease Control and Prevention (CDC) introduced definitions of three classes of SSI that are still in use in nearly all surveillance systems and publications worldwide. These three classes are (5):

- superficial SSI (cutis, subcutis; A1),
- deep SSI (muscle, fascia; A2), and
- wound infections in internal organs or body cavities (A3).

The causes of postoperative wound infection are multiple and complex, involving both patient-related and pre-, intra- and postoperative surgical factors. A comprehensive presentation of risk factors for SSI is found in (6) and (7); see also the *Box* accompanying this article. The list makes it clear that SSI prevention is a multidisciplinary task that extends beyond the operation itself and certainly is not restricted to the administration of antibiotics.

The evidence-based prevention of wound infection

To prevent postoperative wound infection, patient management should be protocol-defined, in accordance with evidence-based measures and recommendations. The WHO recommendations on the prevention of postoperative wound infection, published in 2016 (5), were intended as a concise summary of a wide range of measures. The German Commission for Hospital Hygiene and Infection

Prevalence

The prevalence of nosocomial infection in a survey was 4.6%. SSI accounted for ca. 22% of the total; every year, approximately 1% of persons undergoing surgery as inpatients (nearly 200,000 patients) sustain an SSI.

The CDC classification of wound infection

- superficial SSI (cutis, subcutis; A1),
- deep SSI (muscle, fascia; A2), and
- wound infections in internal organs or body cavities (A3).

Table 1

A selection of evidence-based measures for the prevention of postoperative wound infection

Measure (reference)	Number of RCTs	SSI rate without measure (no. of pt.)	SSI rate with measure (no. of pt.)	RR [95% CI]	p value	Approximate change of SSI rate
Shaving (10)	n = 7	2.1 % (19/887)	4.2 % (34/819)	1.82 [1.02; 3.14]	0.03	+80 %
Nasal decolonization and washing with chlorhexidine*1 (11)	n = 5	2 % (253/12 790)	0.8 % (152/19 940)	0.41 [0.30; 0.50]	< 0.001	–60 %
Normothermia (12)	n = 3	13 % (37/290)	4.7 % (14/299)	0.36 [0.20; 0.66]	0.008	–65 %
Normoglycemia (13)	n = 15	16 % (392/2 488)	9.4 % (231/2 464)	0.59 [0.50; 0.68]	< 0.001	–40 %
Skin disinfection with alcohol and chlorhexidine (14)	n = 20	4.8 % (725/15 263)	2 % (425/13 743)	0.65 [0.55; 0.77]	< 0.001	–35 %
Use of negative-pressure systems*2 (15)	n = 28	14 % (315/2 205)	8.8 % (194/2 193)	0.61 [0.49; 0.76]	< 0.001	–40 %
Use of triclosan-coated suture material (16)	n = 25	9.7 % (581/5 949)	6.9 % (420/6 008)	0.73 [0.65; 0.82]	0.005	–30 %

*1 Effect statistically significant only for high-risk procedures (cardiac surgery, orthopedic surgery).
*2 Effect statistically insignificant for visceral surgical, gynecological, and urological procedures.
CI, confidence interval; pt., patients; RCT, randomized and controlled trial; RR, risk reduction; SSI, surgical site infection

Prevention (KRINKO) has also published recommendations for the prevention of postoperative wound infection (8). *Table 1* contains a listing of individual measures for the prevention of SSI that are supported by evidence of the highest level, according to a recent review (9) of meta-analyses, systematic reviews and Cochrane reviews that appeared after the WHO recommendations were published in 2016 (10–15), as well as a further meta-analysis (16).

Perioperative antibiotic prophylaxis (PAP)

Perioperative antibiotic prophylaxis consists of the short-term, usually single-shot administration of an antibiotic to prevent wound infections caused by bacteria that are either already present at the surgical site or enter it during the operation. In view of the very wide variety of surgical procedures that can be performed, the indications for antibiotic prophylaxis and the specific drugs to be used cannot be presented here with specific reference to each type of procedure. For information of this type, the reader is referred to the American guideline (17). The fundamental considerations are explained in what follows; these should be individually adapted to the operation in question, and to the risk profile of the patient.

Indication

According to a common classification that has been in use for decades (5), surgical interventions are classified as:

- clean (the incision is not exposed to inflammation, there is no opening of the respiratory, gastrointestinal or urogenital tract, and the operation is performed under aseptic conditions; SSI rates generally < 1%);
- clean-contaminated (opening of the respiratory, gastrointestinal, or urogenital tract, with no more than a small amount of leakage of contaminated fluid; SSI rates of 1% to ca. 10%);
- contaminated (the incision is exposed to acute inflammation but not purulent secretion, or there is visible contamination of the wound, or opening of the respiratory, gastrointestinal or urogenital tract, or leakage of significant amounts of contaminated fluid, or open injuries treated within four hours; SSI rates above 10% and up to 40 %);
- dirty (presence of pus, or surgery for hollow organ perforation, or open injuries not treated for more than 4 hours; SSI rates above 40%).

PAP is generally indicated for clean-contaminated or contaminated operations because of their high SSI rates (17). Antibiotic administration in dirty procedures, where an infection is already present during surgery, should be regarded as antibiotic therapy, rather than prophylaxis. Clean procedures in which no alloplastic material is implanted and without patient-related risk factors generally do not require PAP (17). PAP may be justified for a clean procedure in the presence of multiple patient-related risk factors. The same applies to clean procedures in which alloplastic material is implanted, because an SSI, if it arises, may necessitate removal of the implant, with very serious consequences for the patient. For emergency procedures

The evidence-based prevention of wound infection
To prevent postoperative wound infection, patient management should be protocol-defined, in accordance with evidence-based measures and recommendations.

The indication for general antibiotic prophylaxis
Clean procedures in which no alloplastic material is implanted and without patient-related risk factors generally do not require PAP.

Table 2

Proposed indications for perioperative antibiotic prophylaxis depending on the procedure category

Category of procedure	Average SSI rate	Indication for PAP	Illustrative type of operation	Antibiotic (example)
clean, no implant	< 1 %	only with multiple risk factors	thyroidectomy	cefazolin if indicated
clean, with implant, open surgery	1–10 %	yes	total hip replacement	cefazolin
clean, with implant, minimally invasive	1–2 %	only with multiple risk factors	laparoscopic hernia repair	cefazolin if indicated
(clean-) contaminated, open surgery	10–40 %	yes	open colorectal resection	cefuroxime and metronidazole
(clean-) contaminated, minimally invasive	2–10 %	yes	laparoscopic colorectal resection	cefuroxime and metronidazole
(clean-) contaminated, with implant	5–10 %	yes	femorocrural bypass for infected diabetic foot	cefazolin
(clean-) contaminated, mucosal, no implant	< 1 %	only with multiple risk factors	hemorrhoidectomy	cefuroxime and metronidazole if indicated

PAP, perioperative antibiotic prophylaxis; SSI, surgical site infection

and reoperations, PAP is generally indicated. *Table 3* contains suggested indications for PAP with examples based on international recommendations (5–9). These must be adapted to the individual type of operation and are not meant to apply unchanged to all surgical procedures.

The choice of antibiotic

For each type of surgical procedure, there are typical pathogens that can cause an SSI *(Table 3)*. The physician taking the patient's history should pay special attention to potential antibiotic allergies, despite the rarity of IgE-mediated penicillin allergy (which is present in only ca. 2% of patients who state that they are allergic to penicillin) and of cross-reactivity to cephalosporins (< 5%) (18). In general, basic drugs should be used if possible. For example, cefazolin, a first-generation cephalosporin, is recommended for prophylaxis before surgical procedures in which SSIs are likely to be caused by Gram-positive pathogens that normally reside in the skin (e.g., *Staphylococcus aureus, Streptococcus spp.*). In operations where SSIs are likely to be caused by *Enterobacterales* or anaerobes (e.g., colorectal surgery), a combination of a second-generation cephalosporin (e.g., cefuroxime) with metronidazole is recommended. Drugs with a cumbersome mode of administration (e.g., slow infusion over two hours) and/or poor tissue penetration (e.g., vancomycin) should be avoided if possible. Similarly, very broad-spectrum antibiotics such as meropenem are appropriate for the empirical treatment of severe infection but should not be used routinely for PAP. Some exceptions are listed below under "targeted prophylaxis."

The following factors should enter into the choice of the antibiotic:

- medical history (including allergies)
- type of surgical procedure
- expected or preoperatively detected pathogen spectrum
- local resistance situation
- recommendations of local guidelines
- pharmacokinetics (in particular, tissue penetration)
- potential adverse effects and toxicity

Antibiotics that can be recommended for specific procedures are listed in (17).

PAP in special situations

PAP in patients over age 65

Patients over age 65 with and SSI have a threefold higher mortality than those under age 65 (12.6% vs. 4.4%) SSI (19). In a review, special features were identified (19), including nasal screening and decolonization for *Staphylococcus aureus* with mupirocin and chlorhexidine before cardiac and orthopedic/trauma surgical procedures, creatinine clearance measurement before major operations lasting more than three hours, the avoidance of fluoroquinolones and aminoglycosides for PAP, and very strict adherence to the principle of terminating PAP when the procedure is over (93% of patients who die of a *Clostridioides difficile* infection are over age 65).

The implantation of alloplastic material

Antibiotic prophylaxis is indicated as a pragmatic measure in clean procedures involving the implantation of alloplastic material, e.g., hip replacement surgery.

Minimally invasive, clean procedures

In minimally invasive, clean procedures, PAP may be dispensed with, as the rate of SSI is very low.

Adaptation of PAP in morbidly obese patients

Unfortunately, there are no RCTs on the topic of PAP in morbid obesity. Edmiston et al (20) gave patients 2 g of cefazolin before Roux-en-Y bypass surgery and determined serum and tissue concentrations as a function of BMI. The percentage of patients with therapeutic tissue concentrations above the minimum inhibitory concentration (MIC) was only 48.1% among patients whose BMI was between 40 and 50 kg/m^2, and even lower in more severely obese patients: 28.6% for BMI 50–60 kg/m^2, and 10.2% for BMI > 60 kg/m^2. This implies that the dose of PAP should be higher in patients with higher BMI, although the optimal doses remain unclear. Chopra et al. (21) recommend 2 g of cefazolin for patients with BMI 30–50 kg/m^2 and 3 g of cefazolin for those whose BMI exceeds 50 kg/m^2. Data of a high evidence level are unavailable (22).

Targeted prophylaxis in pancreatic surgery

Targeted prophylaxis is defined as specifically adapted PAP for patients with a known pathogen spectrum that has been determined by culture before surgery, e.g., of specimens taken during endoscopic retrograde cholangiopancreatography for bile drainage in patients with common bile duct stenosis. Multiple studies have been carried out to compare targeted PAP with standard PAP with respect to SSI rates and pathogens cultured from infected surgical wounds after pancreatic surgery. Seven of them (four prospective observational studies, two retrospective studies, one RCT) with a total of 849 patients who had undergone pancreaticoduodenectomy were included in a meta-analysis (23). *Enterokokkus spp.* was the most commonly detected pathogen. The SSI rate was significantly lower after targeted PAP than after standard PAP (21.1 % vs. 41.9 %; RR 0.55, [0.37; 0.81]). This effect was even more pronounced when only studies were considered in which there were comparable numbers of patients who had undergone preoperative biliary drainage (RR 0.45, [0.35; 0.59]). If cholangiitis is found intraoperatively, antibiotics are indicated, but this, by definition, is treatment, rather than prophylaxis. In a recently published RCT, a lower SSI rate was found when piperacillin/tazobactam was used generally in pancreatic surgery, compared to a reference group treated with cefoxitin (24). The primary endpoint, SSI at 30 days, was reached by fewer patients in the former than in the latter group (19.8% vs. 32.8%; –13.0 percentage points [-19.1%; –6.9%]; $p < 0.001$).

Targeted prophylaxis for multidrug-resistant Gram-negative pathogens

Multidrug-resistant Gram-negative (MRGN) bacteria are an increasing problem in Germany and around the world. For a long time, only limited data were available on the effects of MRGN-adapted PAP on ESBL-producing *Enterobacterales* that are detectable preoperatively by rectal screening. The WHO and KRINKO recommendations therefore contain no clear information on this point. Recently, however, a prospective, non-randomized before-and-after study (25) compared 247 patients with documented colonization by ESBL-producing *Enterobacterales* who received cephalosporin-based PAP with 221 who received ertapenem-based PAP: the overall SSI rates differed significantly, with 22.7 % in the cefuroxime/metronidazole group vs. 15.8 % in the ertapenem group (absolute risk difference –7.7 %, [-13.6 %; –0.8 %]), as did the rates of SSI due to ESBL (6.5% vs. 0.9%, absolute risk difference –5.6%, [-8.9 %; –2.3 %]). The NNT (number needed to treat) for the prevention of wound infection by ertapenem was 13. A European guideline (26) recommends preoperative rectal screening for 3MRGN *Enterobacterales* before colorectal and transplant surgery, with the adjustment of PAP to include ertapenem (or the like) if these are detected.

Table 3

Selected typical procedure-specific pathogens of postoperative wound infection

Operation	Commonly detected pathogens causing SSI
orthopedic/trauma surgery	*S. aureus (30%), coagulase-negative staphylococci (15%), enterococci (10%)*
endocrine and abdominal wall surgery	*S. aureus (60%), enterococci (20%)*
cardiac and vascular surgery	*S. aureus (25%), coagulase-negative staphylococci (20%), enterococci (10%)*
gastroduodenal procedures	enterococci (30 %), Enterobacterales (30 %)
hepatobiliary surgery	*Enterobacterales (40%), enterococci (30%)*
colorectal surgery, intra-abdominal urological surgery	*Enterobacterales (60%), enterococci (20%), anaerobes (10%)*
thoracic surgery	*Enterobacterales (30%), Pseudomonas (30%), S. aureus (20%)*

SSI, surgical site infection

Modalities of PAP

The recommendations for specific measures (modalities) to be taken in the implementation of PAP are based on a systematic review that was commissioned by, and created with the aid of, the European Center for Disease Prevention and Control (ECDC). Five evidence-based modalities were identified, each of which can be monitored with indicators in audits or other types of surveillance (27). These measures include the following:

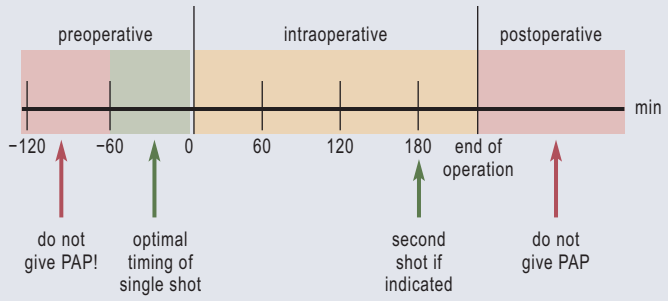
High BMI and obesity

Giving a higher dose of PAP to patients with a high BMI is recommended, although the advantage has not been unambiguously demonstrated in clinical studies.

Targeted prophylaxis

Targeted prophylaxis is defined as specifically adapted PAP for patients with a known pathogen spectrum that has been determined by culture before surgery.

Figure



Timeline for the proper implementation of perioperative antibiotic prophylaxis (PAP). (modified from [38])
PAP, perioperative antibiotic prophylaxis

- regular analysis (at least once per year) of wound infection data by an antimicrobial stewardship team
- administration of PAP by the anesthesiologist
- correct timing of PAP (60 minutes to shortly before the incision)
- single-shot principle; second administration in the event of prolonged surgery or marked blood loss
- termination of PAP at the end of the operation

This combination of modalities was recommended as a five-point plan by the German Society for General and Visceral Surgery (DGAV) (28). The evidence for each of them will be presented below.

Antimicrobial stewardship teams

40 studies were considered, of which 24 were non-controlled before-and-after (NCBA) studies, 12 were observational cohort studies, 2 were CBA studies, and 2 were interrupted time series (ITS) studies (27).

These studies involved a total of over 600,000 patients. The overall evidence revealed that the formation of an interdisciplinary antibiotic stewardship team that met regularly and applied appropriate protocols significantly improved adherence to the proper administration of PAP and significantly lowered the SSI rate (r = –0.20, p = 0.004).

Administration of PAP by the anesthesiologist

In an uncontrolled before-and-after study (29), the responsibility for administering PAP was transferred to the anesthesia department. Adherence to correct timing of PAP rose from 11% to 91%, and the rate of SSI in cardiac surgery fell from 3.8 % to 1.4 %. In another study with a very similar design (30), adherence to correct timing rose from 72% to 92% (p < 0.001), and the SSI rate fell from 3.5% to 1.5% (p = 0.001).

The timing of intravenous PAP

In a meta-analysis (31), the following evidence-based conclusions were drawn from the published literature (14 observational studies on a total of approximately 53,000 patients):

- PAP administered after the incision is associated with a significantly increased rate of SSI (OR 1.89; [1.05; 3.40]).
- PAP given more than two hours before surgery is also associated with an increased SSI rate (OR 5.26; [3.29; 8.39]).

In a further study (32), multivariate logistic regression analysis revealed no differences in the frequency of SSI depending on whether the antibiotic was administered 60 minutes before, 30 minutes before, or just before the incision. In a recently published cohort study (33), however, the administration of cefuroxime as PAP 10–25 minutes before the incision was associated with a significantly lower SSI rate than its administration 30–55 minutes before the incision (adjusted odds ratio [aOR] 0.89; [0.82; 0.97]; p = 0.009).

The single-shot principle and the repeated administration of PAP in longer procedures

In its recommendations for the prevention of wound infection, published in 2016 (5), the WHO stated just as clearly as the ECDC had done a few years earlier (27) that PAP should be administered as a single shot for all procedures lasting less than three hours. A second intraoperative dose is recommended in case of major blood loss (> 2 L) or procedures whose duration exceeds the half-life of the antibiotic (rule of thumb: three hours). In a retrospective cohort study (34) with a total of 4078 patients, 180 (4.4%) developed a wound infection; the non-administration of a second intraoperative antibiotic dose in procedures that were over three hours long more than quadrupled the risk of wound infection (RR 4.61; [1.33; 15.91]).

Consequences of prolonged PAP

Prolonged PAP can lead to the development of resistance, *Clostridioides difficile* infection, and direct antibiotic toxicity (e.g., renal damage). A pertinent retrospective analysis (35) involved data from nearly 80,000 patients who had undergone different types of surgery: elective orthopedic surgery, cardiac surgery, vascular surgery, and colorectal surgery. The adjusted odds ratio (aOR) for reversible or irreversible renal damage rose with each additional day of PAP (cardiac procedures: 24 to 48 hr: (aOR) 1.03; [0.95; 1.12]; 48 to 72 hr: aOR, 1.22; [1.08; 1.39]; 72 hr: aOR 1.82; [1.54; 2.16]; noncardiac procedures: 24 to 48 hr: aOR 1.31; [1.21; 1.42]; 48 to 72 hr: aOR 1.72; [1.47; 2.01]; 72 hr: aOR 1.79; [1.27; 2.53]). The unadjusted number needed to harm

Modalities of PAP

- administration of PAP by the anesthesiologist
- correct timing of PAP (60 minutes to shortly before incision)
- single-shot principle; second administration in the event of prolonged surgery or marked blood loss
- termination of PAP at the end of the operation

The timing of intravenous PAP

- PAP administered after the incision is associated with a significantly increased rate of SSI.
- PAP given more than two hours before surgery is also associated with an increased SSI rate.

Table 4

Synopsis of important publications on SSI prevention and perioperative antibiotic prophylaxis

Reference	Study design	Study topic	Findings	Comments
Eckmann, 2022 (2)	retrospective cross-sectional study, propensity-score matching	medical and economic harm of SSI in Germany	BMI > 30 mg/m2, immunosuppression, type of surgical procedure, increased mortality and prolonged hospital stay are associated with the development of an SSI	the first study to show the medical and economic damage caused by SSI
Seidelman, 2023 (9)	systematic review	evidence-based measures for the prevention of SSI	significant reduction in SSI rate by not shaving the skin, performing screening and nasal decolonization with mupirocin, and washing with chlorhexidine during orthopaedic and cardiac surgery, perioperative maintenance of normothermia and normoglycaemia, skin disinfection with chlorhexidine-containing disinfectants and use of negative-pressure systems in primary wound closure	an excellent review of existing level 1 evidence on the prevention of SSI
Righi, 2023 (26)	European guideline	PAP in the setting og colonization with MRGN	rectal screening in high-risk populations and adjustment of PAP in the event of preoperative detection of third-generation cephalosporin-resistant Enterobacterales is advisable before colorectal surgery and liver transplantation; no recommendation in the event of preoperative detection of carbapenem-resistant Enterobacterales, owing to a lack of evidence	the only existing guideline worldwide on PAP in the setting of colonization by MRGN
Zweigner, 2013 (27)	systematic review	evidence-based modalities of PAP	formation of an antimicrobial stewardship team, administration of PAP by anesthesiologist, administration of PAP 60 minutes before to just before incision, repeated administration if the operation is more than 3 hours long or blood loss exceeds 1 L, discontinuation of PAP at the end of surgery, indicators to improve the quality of PAP	pragmatic aids to the concrete implementation of PAP with measurable parameters
Branch-Elliman, 2019 (35)	multicenter retrospective cohort study	medical harm due to postoperativel continued PAP	continuing PAP postoperatively does not lower the SSI rate and is associated with significantly increased nephrotoxicity and *Clostridioides difficile* infections	clear documentation of the considerable harm done by continuing PAP postoperatively
de Jonge, 2020 (37)	systematic review	effect of postoperatively continued PAP on SSI rate	continuing PAP postoperatively does not lower the SSI rate	a thorough review of the literature, with clearly stated conclusions

MRGN, multiresistant Gram-negative pathogens; PAP, perioperative antibiotic prophylaxis; SSI, surgical site infection

(NNH) was 9 (24 to 48 hr of PAP), 6 (48 to 72 hr of PAP) and 4 (72 and more hours of PAP). Data on the harm caused by each additional day of antibiotic administration, with respect to adverse effects, bacterial superinfection, and the development of resistance, are presented in (36). 35 systematic reviews of 71 RCTs were included. Of a total of 23,174 patients, 20,345 were evaluated with respect to adverse effects (which arose in 19%), 5776 with respect to superinfection (which arose in 4.8%), and 2330 with respect to antibiotic resistance (which developed in 10.6%). Each day of antibiotic therapy was associated with a significant rise in adverse effects by 4% (OR 1.04; [1.03; 1.07]) and in severe adverse effects by 9% (OR 1.09; [1.00; 1.19]). The values for superinfection and the development of resistance were not significantly increased.

The postoperative continuation of PAP

The putative value of postoperative antibiotic prophylaxis to lessen SSI was studied in a meta-analysis of RCTs (37). The included trials covered a wide range of procedures (gastrointestinal, cardiac, thoracic, gynecological, orthopedic, maxillofacial). There were 52 RCTs, with a total of 19,273 patients, in which the continuation of PAP after surgery (varying from a single postoperative dose to five days after surgery) was compared with PAP that was terminated as soon as the procedure ended. 24 of these RCTs met so-called best practice standards, i.e., PAP was given within 60 minutes before the incision, and a repeated dose was given intraoperatively if this was indicated on the basis of the half-life of the antibiotic and the duration of the procedure. The high-quality trials did not reveal any lowering of the SSI rate with postoperatively continued

PAP for long operations

A second intraoperative dose is recommended in case of major blood loss (> 2 L) or procedures whose duration exceeds the half-life of the antibiotic (rule of thumb: three hours). The postoperative continuation of PAP does not lower the SSI rate.

Prolonged PAP

The postoperative continuation of PAP can harm patients through toxicity, bacterial superinfection, and the development of resistance.

PAP (RR 1.04, [0.85; 1.27]). The heterogeneity of the studies was low (I2 < 0.1%). The Figure depicts the timing of PAP during an operation (modified from [38]). Key publications on PAP with the most important findings are summarized in Table 4.

Overview

The prevention of SSI is a multidisciplinary task that should include evidence-based bundles of measures. PAP that is administered properly for correct indications significantly lowers the risk of wound infection after many types of surgical procedure. On the other hand, improperly administered antibiotic prophylaxis, and especially prophylaxis that is continued after surgery, can have major deleterious effects without lowering the SSI rate any further; these include bacterial superinfection, acute toxicity, the development of resistance, and increased cost to the health-care system.

Conflict of interest statement

CE is head of the working group on general and visceral surgical infection of the German Society for General and Visceral Surgery and received an honorarium for a podcast from Infectopharm.

AB is a co-opted member of the Executive Committee of the BDA (Professional Association of German Anesthesiologists) for the area of intensive care medicine.

MP received an honorarium for a podcast from Infectopharm.

JR and SJSA declare that no conflict of interest exists.

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Questions on this article

CME credit for this unit can be obtained via cme.aerzteblatt.de until 4 April 2025.

Only one answer is possible per question. Please select the answer that is most appropriate.

Question 1

In 2016, the prevalence of nosocomial infections and antibiotic use was determined in a survey of German hospitals. What was the approximate prevalence of nosocomial infections in this survey?

a) 1%
b) 2%
c) 5%
d) 10%
e) 25%

Question 2

In most surveillance systems, postoperative wound infections (surgical site infections, SSI) are classified according to the depth of the infection. Which of the following distinctions is made in the most commonly used classification?

a) superficial vs. hematogenous dissemination
b) superficial vs. deep vs. involving the internal organs or body cavities
c) with vs. without fascial involvement
d) superficial vs. other
e) deep vs. other

Question 3

Which of the following statements about risk factors for postoperative wound infection is true?

a) The wound infection rate is independent of the duration of the procedure.
b) The wound infection rate is independent of the patient's age.
c) The wound infection rate is independent of prior radiotherapy.
d) The wound infection rate is higher in diabetic patients.
e) The wound infection rate is independent of the patient's weight.

Question 4

Aside from perioperative antibiotic prophylaxis, there are other evidence-based measures for preventing postoperative wound infection. Which of the following is among them?

a) irrigation of the wound with povidone-iodine solution at the end of the operation
b) using antiseptic-coated surgical drapes
c) normothermia
d) hypoglycemia
e) sterile skin disinfection with solutions that contain soap

Question 5

Which of the following statements about procedure-specific wound infection rates and the indication for perioperative antibiotic prophylaxis is true?

a) Clean-contaminated open colorectal resection has an average SSI rate of 10–40%.
b) Thyroidectomy has a wound infection rate of ca. 10%.
c) Shoulder arthroscopy has a wound infection rate of ca. 10%.
d) Perioperative antibiotic prophylaxis should not be given for pancreatic surgery.
e) Perioperative antibiotic prophylaxis should not be given for oncological resection of lung carcinoma.

Question 6

A left hemicolectomy for colon carcinoma is indicated. Preoperative rectal screening reveals no evidence of resistant Gram-positive or Gram-negative pathogens. What perioperative antibiotic prophylaxis is advisable?

a) vancomycin
c) tigecycline
d) cefuroxime and metronidazole
e) meropenem

Question 7

Which of the following statements about targeted PAP in pancreatic surgery is correct?

a) Enterococci are rarely (< 1%) detected in SSI.
b) Targeted PAP has no effect on the SSI rate.
c) A meta-analysis documented the lowering of the SSI rate by targeted PAP.
d) Meropenem does not cover enterococci and is thus particularly suitable for targeted PAP.
e) Intraoperatively diagnosed cholangiitis i*s not an indication fo*r antibiotic treatment.

Question 8

Which of the following statements about preoperatively detected colonization with multidrug-resistant Gram-negative pathogens is correct?

a) The rate of multidrug-resistant Gram-negative pathogens is not increasing worldwide.
b) The rate of multidrug-resistant Gram-negative pathogens is not increasing in Germany.
c) SSI due to ESBL-producing enterobacteria are significantly more common when PAP is performed with cephalosporins rather than ertapenem.
d) Preoperative rectal screening for 3MRGN Enterobacterales is not recommended before colorectal and transplant surgery.
e) It is not recommended that PAP should be adjusted when 3MRGN Enterobacterales are detected before colorectal and transplant surgery.

Question no. 9

Which of the following is an evidence-based modality of perioperative antibiotic prophylaxis that can lower the wound infection rate?

a) meeting of the antimicrobial stewardship team once every 5 years
b) administration of prophylaxis by the hospital hygiene specialist
c) administration of prophylaxis from ca. 60 minutes before the incision until just before it
d) not repeating antibiotic administration if the operation lasts longer than 3 hours
e) continuing prophylaxis for 5 days after surgery

Question no. 10

What is a possible consequence of the postoperative continuation of perioperative antibiotic prophylaxis?

a) It reduces the wound infection rate.
b) It reduces the development of resistance.
c) It does not lead to increased toxicity.
d) It can promote bacterial superinfection.
e) It lowers costs.