Established in 1871

Swiss Medical Weekly

Formerly: Schweizerische Medizinische Wochenschrift

An open access, online journal • www.smw.ch

Review article: Medical guidelines | Published 28 September 2022 | doi:10.4414/SMW.2022.w30230
Cite this as: Swiss Med Wkly. 2022;152:w30230

Swiss recommendations on perioperative antimicrobial prophylaxis in children

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Summary

Infection following surgical procedures leads to significant morbidity and mortality in all age groups. Sterile techniques, antibiotic prophylaxis and improved postoperative wound care have contributed to the decline of surgical site infections since the early days of surgery. Recommendations on the use of perioperative antimicrobial prophylaxis exist for adults, but are rare for the paediatric population. Here, we provide a standardised approach to the effective use of antimicrobial agents for the prevention of surgical site infections in children contributing to a targeted and rational perioperative use of antibiotics in Switzerland.

Introduction

The following recommendations were endorsed by the Swiss Society for Infectious Diseases (SSI), the Swiss Paediatric Surgery Society (SPSS), the Paediatric Expert Group of the Swiss Society for Orthopaedics and Traumatology (Swiss Orthopaedics) and the Swiss Society for Paediatric Gastroenterology, Hepatology and Nutrition (SSPGHN).

Surgical site infection (SSI) is a relatively common complication of surgery with significant associated morbidity, mortality and cost [1]. Among surgical patients, SSIs account for 38% of nosocomial infections and occur in 2–5% of the more than 30 million patients undergoing surgical procedures each year [2]. SSI rates have declined dramatically since the early days of surgery due to ubiquitous use of sterile technique, antibiotic prophylaxis and improved postoperative wound care [1]. The efficacy of perioperative antimicrobial prophylaxis could be clearly shown for a large number of procedures in adults [3]. For example, multiple studies have found that antimicrobial prophylaxis in cardiac procedures lowers the occurrence of postoperative SSI up to five-fold [4]. A systematic review of 45 studies including 9576 patients undergoing appendectomy also showed that the use of perioperative antibiotics is superior to placebo for preventing wound infection and intra-abdominal abscess [5]. Another example is a randomised, double-blind, placebo-controlled study of patients in Spain undergoing thoracic surgery comparing a single dose of cefazolin as perioperative antibiotic prophylaxis. The study was stopped early due to the significant difference in SSI rates between groups (1.5% with cefazolin versus 14% with placebo, $p < 0.01$) [6].

The ideal perioperative antimicrobial prophylaxis aims at the prevention of postoperative SSIs, has no side effects and leads to minimal negative consequences for the microbial flora of the patient or the hospital. In order to achieve these goals the chosen antimicrobial agent should be effective against the pathogens considered most likely to contaminate the surgical site and has to be administered at the right time and at the right dose in order to ensure adequate serum and tissue concentrations during the time of potential contamination. At the same time, the duration of ideal perioperative antimicrobial prophylaxis should be as short as possible to minimise side effects and reduce the development of resistance.

These recommendations are intended to provide a standardised approach to the effective use of antimicrobial agents for the prevention of SSIs and should contribute to a rational and targeted prescription of antibiotics. All recommendations are limited to perioperative antimicrobial prophylaxis. Compliance with hygiene measures and optimal surgical techniques are factors that can positively influence the occurrence of SSI [7, 8]. These factors are not discussed here.

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Methods

Unless stated otherwise, all recommendations are based on the *Clinical practice guidelines for antimicrobial prophylaxis in surgery* jointly published 2013 by the American Society of Health-System Pharmacists (ASHP), the Infectious Diseases Society of America (IDSA), the Surgical Infection Society (SIS) and the Society for Healthcare Epidemiology of America (SHEA) [3]. Additional literature was identified by searches of Medline, Embase and the Cochrane Database of Systematic Reviews and included in these recommendations if relevant. The last search was performed on 22 May 2022. Dose recommendations in table 1 were derived from the Swiss Database for Dosing Medicinal Products in Paediatrics (SwissPedDose, https://db.swisspeddose.ch/) and have been developed in a standardised harmonisation process throughout Switzerland [9].

Evidence of perioperative antimicrobial prophylaxis in children

In most cases the data in paediatric patients are limited and paediatric recommendations on perioperative antimicrobial prophylaxis are extrapolated from adult recommendations Therefore the evidence described here is based, unless otherwise stated, on expert opinion (evidence level C). Additionally, if the original recommendation for adults was already based on evidence level C, this will be stated in a corresponding foot note.

General recommendations

Choice and correct administration of perioperative antimicrobial prophylaxis are under the responsibility of the operating surgeon and should be reviewed before skin incision during the time out procedure as a part of the World Health Organization (WHO) recommended practices to ensure the safety of surgical patients [10]. As with any general recommendation, it is ultimately the responsibility of the supervising physician in the individual clinical situation to adapt the recommendations if necessary.

Indication

Type, location and duration of the planned surgical procedure have an impact on the risk of developing postoperative infections. Additionally, the microbial contamination of the surgical area, the presence of prosthetic implants (e.g., pacemaker, osteosynthesis material) as well as the patient's immune competence are of particular importance. To determine whether perioperative antimicrobial prophylaxis is indicated, the contamination level of the surgical intervention must be distinguished between clean, clean-contaminated and contaminated surgical procedures. This distinction is based on the higher rate of postoperative SSI after clean-contaminated and contaminated procedures compared to clean procedures.

A perioperative antimicrobial prophylaxis is indicated in surgical procedures associated with a high rate of postoperative infection (i.e., clean-contaminated or contaminated procedures), and in certain clean procedures where severe consequences of potential infection have to be expected (e.g., prosthetic implants, cardiac surgery, neurosurgery), even if infection is unlikely. In addition, antimicrobial prophylaxis may be justified for any procedure if the patient has an underlying medical condition associated with a high risk of SSI including the presence of immunosuppression or immunodeficiency. The use of antimicrobial agents for contaminated procedures or established infections such as bowel perforation or abscess drainage is classified as treatment of presumed infection and not as prophylaxis.

The indication and implementation of endocarditis prophylaxis for children with an appropriate risk applies regardless of these recommendations in accordance with the recommendations of the Swiss Society for Paediatric Cardiology (SSCP) [11].

Choice of the antimicrobial agent

For an effective surgical antimicrobial prophylaxis, the chosen agent should be active against the pathogens most likely to cause SSIs. The predominant organisms causing SSIs after clean procedures belong to the skin flora, including *Staphylococcus aureus* and coagulase-negative staphylococci (e.g., *Staphylococcus epidermidis*). In clean-contaminated procedures, including abdominal procedures and heart, kidney, and liver transplantations, the predominant organisms include Gram-negative rods and enterococci in addition to organisms of the skin flora. In general, only well-tolerated and cost-effective antimicrobial agents should be used for surgical prophylaxis. In these guidelines, antimicrobial agents with the narrowest spectrum of activity required for efficacy in preventing infection are recommended. Antibiotics belonging to the WHO WATCH or RESERVE group [12], such as third and fourth generation cephalosporins, carbapenems and glycopeptides, should only be used for perioperative antimicrobial prophylaxis in exceptional cases (e.g. colonisation with methicillin-resistant *S. aureus* [MRSA]).

Timing, dose and duration of the perioperative antimicrobial prophylaxis

Successful perioperative antimicrobial prophylaxis requires the presence of the antimicrobial drug at the surgical site at the time when contamination occurs. To obtain effective serum and tissue concentrations of the antimicrobial agent at the time and during the duration of the intervention, and thus during the possible contamination of the surgical area, the antimicrobial or the combination of antimicrobials must be administrated within 60 minutes before surgical incision, or in the case of surgery using tourniquets, within 60 minutes before the tourniquet is applied. The administered dose for surgical prophylaxis corresponds to the usual therapeutic single dose for children and it is generally administered intravenously. A single preoperative dose is sufficient in most cases. If the duration of the procedure exceeds two half-lives of the antimicrobial agent used, a second dose should be administered. Also, in the case of large blood loss (>25 ml blood/kg body weight), an additional dose is to be given. If antimicrobial prophylaxis is, exceptionally, continued, this administration should be strictly limited to a maximum of 24 hours [13], regardless of the continued presence of drains, central intravascular catheters or other invasive devices.

Special situations

Colonisation with multiresistant pathogens

The decision on the adjustment of the perioperative antimicrobial prophylaxis in patients with a previous infection or colonisation with multiresistant organisms depends on the planned intervention and on the proximity of the probable reservoirs to the incision and to the surgical site. General recommendations for these cases are difficult and of limited value, therefore the optimal individual perioperative antimicrobial prophylaxis should be elaborated by seeking expert advice from a paediatric infectious diseases specialist. Especially in patients who are colonised with multi-resistant Gram-negative bacteria, there is not enough evidence to support a generally customised perioperative antimicrobial prophylaxis and the decision must be made individually. On the contrary, in the case of colonisation with MRSA the addition of an effective antimicrobial agent should be considered for all patients who undergo one of the procedures listed below. Ideally, MRSA carriers should be decolonised before high-risk interventions such as cardiac surgery [14, 15].

Serious drug-induced reaction or allergy to beta-lactam antimicrobials

In patients with a history of clear or suspected IgE-mediated reaction (e.g., urticaria, anaphylaxis or bronchospasm) or of a serious drug-induced reaction (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis, DRESS [drug rash with eosinophilia and systemic symptoms]) after the use of penicillins or other beta-lactam antibiotics, the alternative antimicrobial agent for surgical prophylaxis should be prescribed as defined below. All other patients should receive the first choice perioperative antimicrobial prophylaxis. The opinion of an allergist can be sought in unclear situations if time allows.

Children receiving antimicrobial treatment for concomitant bacterial infection

In general, elective surgical procedures should be postponed in the case of a concomitant bacterial infection outside the surgical site. In all other cases (i.e., the surgery cannot be postponed or the infection is related to the surgical procedure), the same principles described above for the choice of the antimicrobial agent apply. If the agent used therapeutically is appropriate for surgical prophylaxis, administering an extra dose within 60 minutes before incision is sufficient. Otherwise, the antimicrobial prophylaxis recommended for the planned procedure should be used.

Procedure-specific recommendations

Procedures not mentioned in the specific recommendations do not require a perioperative antimicrobial prophylaxis.

Conclusions

Despite the important lack of evidence to guide recommendations on surgical antimicrobial prophylaxis in paediatric patients, a standardised approach to the use of perioperative antibiotics in children should be aimed for, to reduce the risk of SSI and avoid antibiotic overuse in this population. At the same time randomised trials are needed to increase the level of evidence and further optimise antibiotic use in the vulnerable paediatric population.

Acknowledgments
Swiss Society for Infectious Diseases (SSI): Nicolas Müller

Table 1:
Recommended doses and redosing intervals for commonly used antimicrobials for surgical prophylaxis in children.

Antimicrobial	Recommended dose [a,b]	Maximum single dose [b]	Recommended redosing interval in children with normal renal function [a, c]
Amikacin	15 mg/kg	1500 mg	NA
Amoxicillin	50 mg/kg	2000 mg	2 h
Amoxicillin/clavulanic acid	50 mg/kg[d]	2000 mg[d]	2 h
Cefazolin	30 mg/kg	2000 mg	4 h
Cefuroxime	50 mg/kg	1500 mg	4 h
Clindamycin	10 mg/kg	900 mg	6 h
Gentamicin	7.5 mg/kg	NA	NA
Metronidazole	15 mg/kg	500 mg	NA
Trimethoprim/sulfamethoxazole[e]	3 mg/kg[f]	160 mg[f]	NA

[a] Recommended dose for children 1 month to 18 years. For newborns and preterm infants dose may differ, but also in this case the recommended dose for surgical prophylaxis corresponds to the usual therapeutic dosage (single dose).

[b] No adaptation needed in children with renal dysfunction if given as a single dose, but if applicable, redosing interval should be modified according to glomerular filtration rate.

[c] Redosing in the operating room is recommended at an interval of approximately two times the half-life of the agent in patients with normal renal function. Recommended redosing intervals marked as "not applicable" (NA) are based on typical case length; for unusually long procedures, redosing may be considered.

[d] Based on the amoxicillin component.

[e] Not recommended in newborns <1 month of age.

[f] Based on trimethoprim component.

Table 2:
Perioperative antimicrobial prophylaxis in neonates under 72 hours of age.

Procedure	Most likely pathogens	Recommended agents
All major surgical procedures, excluding esophageal atresia and laparotomy	Group B streptococci, enterococci, enterobacterales	Amoxicillin + gentamicin or amikacin
Laparatomy, oesophageal atresia	Same as above with the addition of intestinal anaerobic bacteria	Amoxicillin + gentamicin or amikacin + metronidazole

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Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest was disclosed.

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Table 3:
Cardiac and thoracic surgery.

Procedure	Most likely pathogens	Recommended agents	Alternative agents for patients with beta-lactam allergy
Thoracotomy including cardiac procedures,[a] pacemaker implantation and interventional heart catheterisation with prosthetic material[b]	*S. aureus*, *S. epidermidis*	Cefazolin	Clindamycin
Oesophageal surgery involving entry into lumen	*S. aureus*, streptococci, oral anaerobic bacteria	Amoxicillin/clavulanic acid	Clindamycin + gentamicin or amikacin
Video-assisted thoracoscopic surgery (VATS)[c]	*S. aureus*, *S. epidermidis*	Cefazolin	Clindamycin

[a] Duration of the antimicrobial prophylaxis for procedures involving heart-lung machine: total of 24 hours with postoperative administration every 8 hours.

[b] Heart catheterisation without implantation of prosthetic material does not require an antimicrobial prophylaxis.

[c] Evidence level C in adults.

Table 4:
Gastrointestinal and urological surgery.

Procedure		Most likely pathogens	Recommended agents	Alternative agents for patients with beta-lactam allergy
Laparatomy/laparoscopy involving entry into lumen[a]	Gastric procedures incl. PEG tube placement, J-tube placement, small intestine without obstruction,[b] biliary tract[c, d]	*S. aureus, S. epidermidis*, streptococci, enterobacterales	Cefazolin or cefuroxime	Clindamycin + gentamicin or amikacin
	Small intestine with obstruction,[b] colorectal procedures incl. appendectomy	Same as above with the addition of intestinal anaerobic bacteria	Cefuroxime + metronidazole	Clindamycin + gentamicin or amikacin
Hernia repair		*S. aureus, S. epidermidis*, streptococci	Cefazolin or cefuroxime	Clindamycin
Urological procedures[e]	Lower tract instrumentation incl. MCUG/MUS,[g] cystoscopy und posterior urethral valves resection	Enterobacterales	Trimethoprim/sulfamethoxazole[f]	
	Urological procedures with or without entry into urinary tract	Enterobacterales, *S. aureus*, *S. epidermidis*	Cefuroxime	Clindamycin + gentamicin or amikacin
	Urological procedures with colonic interposition / neobladder	Same as above with the addition of intestinal anaerobic bacteria	Cefuroxime + metronidazole	Clindamycin + gentamicin or amikacin

[a] Laparoscopic procedures without lumen entry require a perioperative antimicrobial prophylaxis only in case of concurrent risk factors: diabetes mellitus, immunosuppression, treatment with PPI.

[b] Evidence level C in adults.

[c] Uncomplicated laparoscopic cholecystectomy requires a perioperative antimicrobial prophylaxis only in case of concurrent risk factors: immunosuppression, diabetes mellitus, jaundice, acute cholecystitis, history of gallstones less than 30 days prior procedure, emergency procedure or switch to open procedure.

[d] Based on the current evidence no perioperative antimicrobial prophylaxis is recommended for endoscopic retrograde cholangiopancreatography (ERCP) [16, 17].

[e] Continuing presence of urinary catheters (eg. bladder catheter, double-J catheter) does not represent an indication for prolonged antimicrobial prophylaxis after procedure.

[f] If there is an existing antibiotic prophylaxis in vesicoureteral reflux this will be continued (one dose within 60 minutes before procedure) for the procedure.

[g] MCUG: micturating cystourethrogram; MUS: micturating ultrasonography.

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Table 5:
Neurosurgery, head and neck and orthopaedic surgery.

Procedure		Most likely pathogens	Recommended agents	Alternative agents for patients with beta-lactam allergy
Neurosurgery	Elective craniotomy	*S. aureus*, *S. epidermidis*	Cefazolin	Clindamycin
	Cerebrospinal fluid-shunting procedures incl. implantation of intrathecal pumps[b]	*S. aureus*, *S. epidermidis*	Cefazolin + vancomycin i.th.[a]	Clindamycin + vancomycin i.th.[a]
Head and neck surgery	Tonsillectomy, adenoidectomy, tympanostomy tubes and endoscopic sinus surgery	NA[c]	None	NA[c]
	Craniofacial procedures with opening of the mucosa[b]	*S. aureus*, streptococci, oral anaerobic bacteria	Amoxicillin/clavulanic acid	Clindamycin
Orthopaedic surgery	Clean operations involving hand, knee (incl. arthroscopy), or foot and not involving implantation of prosthetic material	NA[c]	None	NA[c]
	Spinal procedures with and without prosthetic material	*S. aureus*, *S. epidermidis*	Cefazolin	Clindamycin
	Other orthopaedic procedures with implantation of prosthetic material[b]	*S. aureus*, *S. epidermidis*	Cefazolin	Clindamycin
	Open fracture type I and II(other than distal phalanx[d])	*S. aureus*, *S. epidermidis*, *Clostridium* sp.	Cefazolin	Clindamycin
	Open fracture type III (other than distal phalanx[d])	Same as above with the addition of Gram-negative bacteria	Cefazolin or cefuroxime + gentamicin or amikacin[d]	Clindamycin + gentamicin or amikacin
Plastic and reconstructive surgery	Clean with risk factors[f] or clean-contaminated[g] plastic and reconstructive surgery	*S. aureus*, *S. epidermidis*	Cefazolin or cefuroxime	Clindamycin

[a] Vancomycin 10mg i.th. 1x during the procedure (not used in every hospital).

[b] Evidence level C in adults.

[c] NA: not applicable.

[d] Open fracture of the distal phalanx do not require antimicrobial prophylaxis.

[e] Duration of the antimicrobial prophylaxis: total of 72 hours or no longer than 24 hours after soft tissue coverage has been achieved with postoperative administration every 8 hours (cefazolin or cefuroxim) respectively every 24 hours (gentamicin or amikacin) [18].

f Risk factors: prolonged procedure (>2 hours), complicated anatomy of the involved area [19].

[g] Clean-contaminated procedures: post-traumatic surgery, procedures involving opening of the mucosal or lumen entry [19].

Table 6:
Transplantation surgery.

Procedure	Most likely pathogens	Recommended agents	Alternative agents for patients with beta-lactam allergy
Heart and lung transplantation	*S. aureus*, *S. epidermidis*	Cefazolin or cefuroxime	Clindamycin
Kidney transplantation	*S. aureus*, *S. epidermidis*, enterobacterales	Cefazolin or cefuroxime	Clindamycin + gentamicin or amikacin
Liver transplantation	S. aureus, S. epidermidis, enterobacterales, enterococci	Amoxicillin/clavulanic acid	Clindamycin + gentamicin or amikacin