Healthcare Improvement Scotland | SAPG Safeguarding antibiotics

Good practice recommendations for redosing antibiotics for surgical prophylaxis in adults

Redosing antibiotics for surgical prophylaxis to maintain antibiotic concentrations during prolonged surgical procedures can significantly reduce the rate of surgical site infections (SSI).[1] These good practice recommendations are based on current good practice in NHS boards in Scotland, published evidence, and information on antibiotic half-lives.

For procedures lasting more than 4 hours, redosing (where indicated) after 4 or 8 hours promotes safe and effective surgical prophylaxis. Decisions around redosing should be made on an individual patient basis taking account of the risks and benefits of repeat dosing. Patients with complex management requirements should be discussed with microbiology colleagues in advance to ensure redosing is safe and appropriate.

These recommendations include redosing advice where there is intraoperative blood loss of 1,500 mL or more.[2] It is not recommended to give a repeat dose of antibiotics after every subsequent 1,500 mL blood loss and specialist advice is needed where blood loss exceeds 3,000 mL.

Drug	**During the procedure**		**If there is blood loss above 1,500 mL** (after giving fluid replacement)	**Drug half-life**
	After 4 hours	**After 8 hours**		
Amoxicillin*	Repeat original dose	Repeat original dose (again)	Repeat original dose	1 hour
Co-amoxiclav* (Amoxicillin + clavulanic acid)	Repeat original dose	Repeat original dose (again)	Repeat original dose	1 hour
Cefuroxime	Repeat original dose	Repeat original dose (again)	Repeat original dose	70 minutes
Clarithromycin	Not required	Repeat original dose	Repeat original dose	3-7 hours
Clindamycin	Repeat original dose	Repeat original dose (again)	Repeat original dose	3 hours
Gentamicin**	Not required	*For patients with creatinine clearance (CrCl) over 60 mL/min* Redosing required when less than or equal to 4 mg/kg dosing only. Give half original dose or alternative antibiotic. For 5 mg/kg dosing, do not redose with gentamicin. As an alternative to gentamicin consider co-amoxiclav 1200 mg or if penicillin allergy give ciprofloxacin 400 mg. Patients undergoing colorectal surgery over 6 hours may require additional antibiotic prophylaxis.[6]	Give half original dose or consider co-amoxiclav 1,200 mg or if penicillin allergy give ciprofloxacin 400 mg	3 hours (if normal renal function)

Drug	During the procedure		If there is blood loss above 1,500 mL (after giving fluid replacement)	Drug half-life
	Over 4 hours	Over 8 hours		
Flucloxacillin	Repeat original dose	Repeat original dose (again)	Repeat original dose	1 hour
Metronidazole	Not required	Repeat original dose	Repeat original dose	8-10 hours
Teicoplanin	Not required	Not required	Give half original dose if 1,500 mL or more blood loss within first hour of operation	100-170 hours

***Amoxicillin and co-amoxiclav** The American Society of Health-System Pharmacists, Infectious Diseases Society of America, Surgical Infection Society, and Society for Healthcare Epidemiology of America recommend redosing ampicillin after 2 hours (note: amoxicillin and ampicillin have similar pharmacokinetic profiles).[3] Consider redosing interval reflecting on local current practice and postoperative infection rates.*

***Gentamicin** Literature suggests redosing of gentamicin is not required when a single dose of 5 mg/kg is used. A lower dose or alternative antibiotic is recommended in patients with reduced renal function (CrCl less than 20 mL/min). A pharmacokinetic evaluation of gentamicin dosing regimens in abdominal surgery found 3 mg/kg was comparable to 5 mg/kg at 6 hours from prophylactic dose; [2] however, longer surgeries, eg over 8 hours, may require redosing if the 3 mg/kg dose is used. Consider redosing with 2.5 mg/kg after 6 hours in patients with CrCl over 50 mL/min undergoing colorectal surgery.[4] Renal toxicity has been observed in patients receiving flucloxacillin and gentamicin for surgical prophylaxis in orthopaedic surgery; therefore, in these instances consider lower doses or alternative antibiotics.*

Summary of Evidence Review

A large cohort study[1] emphasised the importance of redosing in long-duration surgery to prevent the occurrence of SSIs, which are significantly more common in this patient group when redosing is omitted. The National Institute of Health and Care Excellence (NICE)[5] and Stanford Surgical Antimicrobial Prophylaxis Guidelines have been updated since 2018.[6] The NICE guideline restates the 2008 guidance to give a repeat dose of antibiotic prophylaxis when the operation is longer than the half-life of the antibiotic given. United States guidance advises the use of antibiotics that are not commonly recommended in the United Kingdom and recommends redosing after two half-lives; however overall the redosing advice is generally consistent with current Scottish Antimicrobial Prescribing Group guidelines. Canadian guidance (2016) adds that weight-based dosing should be used but does not provide full dosing regimens.[7]

A small study (n=20) conducted in Glasgow investigated prophylactic antibiotic dosage regimens that would maintain plasma concentrations of amoxicillin, metronidazole and gentamicin above the minimum inhibitory concentration (MIC) values for common organisms associated with SSIs in colorectal surgery. The study authors proposed a change to dosing and redosing guidance for patients weighing more than 85 kg or at high risk of infective endocarditis.[4]

A pharmacokinetic evaluation of gentamicin dosing regimens in abdominal surgery found that 3 mg/kg was comparable to 5 mg/kg at 6 hours from prophylactic dose.[2] The article shows reducing levels from 5 hours; therefore, longer surgeries, eg over 8 hours, may require redosing if the 3 mg/kg dose is used.

The table overleaf provides a summary overview of the included evidence sources underpinning these good practice recommendations.

Table: Summary of included evidence sources

Author(s)/year	Study design/ evidence source	Findings and recommendations
Bertschi et al (2019)[1]	Retrospective cohort study (n= 9,045)	Study observed a significant correlation between duration of surgery and SSI incidence (ρ=0.73, p=0.031). Patients (n=593) undergoing surgical procedures of more than 240 minutes duration had the highest SSI rate (16% of cases). 278/593 (47%) of these patients did not receive any redosing. In 45/307 (8%) cases redosing was administered with incorrect timing. Correctly timed redosing was administered to 270/593 (46%) patients. A significantly higher SSI incidence (95% CI 0.37–0.96, p=0.034) was observed in patients who did not receive any redosing.
da Silva Neto et al (2021)[4]	Cohort study (n=20) to identify prophylactic antibiotic dosage regimens that would maintain plasma concentrations of amoxicillin, metronidazole and gentamicin above the MIC values for common organisms associated with SSIs in colorectal surgery	Population pharmacokinetics and pharmacodynamic analyses suggest the following antibiotic doses to maintain a probability of target attainment (PTA) of 90% or more against organisms commonly encountered in colorectal surgery: amoxicillin 1,000 mg preoperatively, with an additional 500 mg intraoperatively at 4 hours in most cases and two hourly if there is a risk of infective endocarditis (IE); metronidazole 500 mg preoperatively, increased to 1,000 mg if the patient's weight is more than 85 kg and redosed at 8 hours; gentamicin 5 mg/kg total body weight (TBW), or adjusted body weight if TBW is greater than ideal body weight, preoperatively, redosed with 2.5 mg/kg intraoperatively at 6 hours. Since the minimum CrCl in the patient group was 50 mL/min, these doses would not apply to patients with lower estimates of CrCl. This study found that the current dosage regimens maintained the desired PTA over the redosing interval for the *S. anginosus* group but not for enterococci (in patients at high risk of IE), the *B. fragilis* group (in patients more than 85 kg), methicillin-susceptible *Staphylococcus aureus*, and *E. coli*. The proposed dosage guidelines offer an improved profile for all three antibiotics and should maintain these PTAs for the likely duration of colorectal surgical procedures.
Heuer et al (2017)[8]	Update on guidance from the Surgical Care Improvement Project and American Society of Health-System Pharmacists	Recommend redosing after two half-lives have passed or in cases of substantial intraoperative blood loss (more than 1,500 mL). Specific drug redosing times given as cefazolin around every four hours. Not necessary in patients with renal insufficiency (CrCl less than 55 mL/min). Clindamycin after 6 hours – no dosing adjustments for patient with decreased hepatic or renal function. Vancomycin – no redosing required because of long half-life.
Infection Prevention and Control Canada (2016)[7]	Perioperative Antibiotic Prophylaxis for the Prevention of SSI	Administer intraoperative redosing if the duration of the procedure exceeds two half-lives of the drug, or there is excessive blood loss. Use weight-based dosing.
National Institute for Health and Care Excellence [NICE] (2020)[5]	Updated guidance	No change from NICE 2008 guidance.
Stanford Antimicrobial Safety	Updated guidance	Recommends weight-based dosing of both cefazolin and vancomycin. Cefazolin should be administered every 4 hours;

Author(s)/year	Study design/ evidence source	Findings and recommendations
and Sustainability Program (2019)[6]		clindamycin every 8 hours; vancomycin does not require redosing given its long half-life. Recommends clinicians consider redosing earlier than specified in the guidance if there is excessive intraoperative blood loss (eg more than 1,500 mL). Aminoglycosides and vancomycin should not be redosed in this setting.
Zelenitsky et al (2016)[2]	Cohort study (n=5,000) to use Monte Carlo simulation with an integrated pharmacokinetic–pharmacodynamic model to evaluate guideline-recommended antimicrobial prophylaxis regimens with anaerobic coverage in abdominal surgery	The findings support avoiding cefoxitin, avoiding clindamycin for anaerobic coverage, selecting 2 g instead of 1 g of cefazolin for patients between 60 and 80 kg, and using 3 mg/kg instead of 5 mg/kg gentamicin.

References

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8. Heuer A, Kossick MA, Riley J, et al. Update on Guidelines for Perioperative Antibiotic Selection and Administration From the Surgical Care Improvement Project (SCIP) and American Society of Health-System Pharmacists. AANA 2017;85(4):293-99. Available online [accessed 16/8/22].

Table of Abbreviations

CrCl	Creatinine Clearance
IE	Infective endocarditis
MIC	Minimum inhibitory concentration
NICE	National Institute for Health and Care Excellence
PTA	Probability of target attainment
SAPG	Scottish Antimicrobial Prescribing Group
SSI	Surgical site infections
TBW	Total body weight