Surgical antibiotic prophylaxis

Matthew Dryden

Abstract

This review is an overview of the principles of surgical antibiotic prophylaxis. It covers the risk of infection in surgery, the benefits and risks of antibiotic prophylaxis, particularly in the light of the global crisis in antibiotic resistance. The choice of antibiotic agent depends on local epidemiology and surveillance, but an example of a prophylaxis guideline is given. The future of prophylaxis and possibility of novel topical agents such as reactive oxygen is discussed.

Keywords Antibiotic prophylaxis; Antibiotic resistance; Reactive oxygen; Surgery

Introduction

This article is an overview of the principles of antibiotic prophylaxis in surgery. It is not a definitive guide and it is important to refer to local guidelines for the choice of specific agents in surgical procedures. Local recommendations should be based on a knowledge of local circumstances and resistance patterns amongst organisms, which means that the choice of antibiotic can be specifically targeted.

The risk of infection in surgery

Certain factors predispose to infection in surgery. These can be patient based or procedure based. Examples of the former can be extremes of age, immunosuppression, diabetes mellitus, smoking, prolonged hospital stay, coexisting infections at other sites and carriage of resistant organsims such as meticillin-resistant *Staphylococcus aureus* or multidrug-resistant coliforms, poor nutritional status or obesity. Procedural factors include surgical technique, adequate haemostasis, maintenance of body temperature, skin antisepsis, operating theatre ventilation and air changes, the presence of a foreign body, tissue trauma and preoperative shaving. This list is by no means exhaustive.

Scoring systems such as the National Nosocomial Infections Surveillance (NNIS)[1] and the America Society of Anesthesiologists[2] help assess infection risk associated with surgery. In addition the surgical procedure is classified as clean (non-contaminated operative site), clean-contaminated (operations where the bowel, respiratory tract or genitourinary systems with their normal flora are breached but there is little spillage), contaminated (where there is significant spillage or contamination of normal flora) and dirty (where the operative site is infected, pus is present or there is prolonged perforation of the bowel). The risk of infection and the type of antibiotic prophylaxis required varies depending on the underlying state of the patient and the type of procedure. An excellent practical guide to prophylaxis in surgery is the SIGN guidance.[3]

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The benefits of antibiotic prophylaxis in surgery

The use of antibiotics was a milestone in the effort to prevent surgical site infections. The aim of antibiotic prophylaxis in surgery is generally thought to be a reduction in surgical site infection (SSI) and short-term morbidity.[3] For some surgery such as prosthetic joint insertion and cardiac valve replacement, prophylaxis aims to reduce long-term morbidity. In many ways the value of antibiotic prophylaxis in reducing the incidence of SSI is related to the severity and consequence of that SSI or when the patient has a high NNIS risk index. For example, abdominal surgery with opening of the bowel was exceptionally hazardous in the pre-antibiotic era as it inevitably led to peritonitis and a high mortality. It was virtually impossible to prevent contamination of the peritoneum with bowel flora, resulting in inevitable infection. So prophylaxis in this context aims to reduce short-term morbidity and mortality.[4]

Risks of antibiotic prophylaxis

Overuse of antibiotics leads to selection of antibiotic resistance. The volume of antibiotic use is directly proportional to the incidence of resistance. One of the aims of rationalizing antibiotic use in surgical prophylaxis has been to reduce the volume of inappropriate antibiotic use to minimize selection pressure and other adverse effects of antibiotics.[5,6]

Allergy to antibiotics, particularly the penicillins, is often reported. Common presentations of penicillin allergy include whole body rash and in the most extreme cases, anaphylaxis. Many symptoms attributed to allergy to an antibiotic are in fact not allergy. These might include headache, nausea and dizziness. It is worth reviewing reported allergy and noting the symptoms, signs, time course, association with other medicines and outcome. Penicillins are useful prophylactic antibiotics and it is unfortunate if a patient is denied these due to spurious allergy. It is often reported that there is a 10% crossover of allergy between penicillins and cephalosporins. This is based on data collected before the 1980s and may be related to the relative impurity of some antibiotics at that time. In practice it is very rare to have cross sensitivity between penicillins and later-generation cephalosporins.[7]

A report recently published by the Royal College of Anaesthetists[8] suggested antibiotics were the main cause of perioperative anaphylaxis in the UK, being responsible for 46% of cases with identified culprit agents. The incidence of antibiotic anaphylaxis was 4.0 per 100,000 administrations. Teicoplanin (16.4 episodes per 100,000 administrations) and co-amoxiclav (8.7 per 100,000 administrations) had the highest incidences of reactions, and both were notably higher than all other antibiotics. Co-amoxiclav and teicoplanin accounted for 17.3% and 13.5%, respectively, of all cases of perioperative anaphylaxis, 23% and 18% of identified culprits, and together accounted for 89% of antibiotic-induced perioperative anaphylaxis.

Antibiotic-associated diarrhoea is well described, although is less likely to occur with single-dose prophylaxis. There is no

good evidence that probiotics reduce the likelihood of antibiotic-associated diarrhoea.

Clostridium difficile colitis (CDI) has become a major complication of antibiotic use and can even occur after single dose antibiotic prophylaxis. Patients are at greater risk of CDI if they are elderly, have had recent antibiotics, have had recent gastrointestinal surgery, are immunosuppressed, are also receiving proton pump inhibitors or are in a hospital with a CDI outbreak. Broad-spectrum agents such as cephalosporins and fluoroquinolones have a greater risk of CDI and a reduction in the use of some broad spectrum antibiotics has reduced CDI.[9]

Other potential adverse effects of antibiotics can also happen including drug interactions, phlebitis related to intravenous administration and very rarely drug toxicity especially with single-dose prophylaxis approach.

Choice of antibiotic

The choice of antibiotic depends on the likely infecting organism for the procedure that is being carried out. Narrow-spectrum, low-cost antibiotics should generally be used for prophylaxis. An example of a surgical antibiotic prophylaxis guideline is given in Table 1. The guideline states the choice of agent, dose, route of

Example of surgical antibiotic guidelines

HEAD AND NECK SURGERY		
Type of Operation	**1st line***	**2nd line***
DENTAL		
Uncomplicated dental extraction	Antibiotics are not usually recommended	
EAR NOSE & THROAT – ENT		
Ear surgery	Antibiotics are not usually recommended	
Routine nose, sinus and endoscopic sinus surgery	Antibiotics are not usually recommended	
Tonsillectomy Adenoidectomy (by curettage)	Antibiotics are not usually recommended	

LINE INSERTION	
Insertion of central line, PICC or Hickmann line	Antibiotics are not usually recommended

GASTROINTESTINAL SURGERY		
Type of Operation	**1st line***	**2nd line***
UPPER GI		
Oesophageal / gastric/ duodenal / Small intestine surgery	**Gentamicin** IV 160mg –240mg stat **PLUS Metronidazole** IV 500mg stat	*Only when gentamicin is contra-indicated* **Co-amoxiclav** IV 1.2g stat (**OR Ciprofloxacin** IV 400mg stat if penicilin allergic **PLUS Metronidazole** IV 500mg stat)
LOWER GI		
Appendectomy **Colorectal surgery**	**Gentamicin** IV 160mg – 240mg stat **PLUS Metronidazole** IV 500mg stat ***At surgeon's discretion:*** **PLUS Amoxicillin** IV 1g stat	*Only when gentamicin is contra-indicated* **Co-amoxiclav** IV 1.2g stat (**OR Ciprofloxacin** IV 400mg stat if penicillin allergy) **PLUS Metronidazole** IV 500mg stat

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GASTROINTESTINAL SURGERY		
Type of Operation	**1st line***	**2nd line***
Hernia repair (groin) • **Inguinal/femoral with or without mesh** • **Laparoscopic with or without mesh** **Hernia repair (incisional) with or without mesh**	Antibiotics are not usually recommended	
	Patients with a high risk of infection (recurrent hernia, advanced age > 75yrs, immunosuppressive conditions, expected long operating times, use of drains, urinary catheter)	
	Flucloxacillin IV 2g stat **PLUS Gentamicin** IV 160mg–240mg stat	***If MRSA colonized **or Penicillin allergy:*** **Teicoplanin** IV 400mg stat **PLUS Gentamicin** IV 160mg - 240mg stat (**OR Ciprofloxacin** IV 400mg stat if gentamicin is contra-indicated)
	Only when gentamicin is contra-indicated **Co-amoxiclav** IV 1.2g stat	
Open/laparoscopic surgery with mesh (eg gastric band or rectoplexy) **Splenectomy**	Antibiotics are not usually recommended except in high risk patients*	
	High risk patients **Gentamicin** IV 160mg–240mg stat **PLUS Metronidazole** IV 500mg stat	*Only when gentamicin is contra-indicated* **Co-amoxiclav** IV 1.2g stat (**OR Ciprofloxacin** IV 400mg stat if penicillin allergy **PLUS Metronidazole** IV 500mg stat)

HEPATOBILIARY		
Bile duct /Pancreatic / Liver / Gall bladder (open) surgery	**Gentamicin** IV 160mg–240mg stat **PLUS Metronidazole** IV 500mg stat ***At surgeon's discretion:*** **PLUS Amoxicillin** IV 1g stat	*Only when gentamicin is contra-indicated* **Co-amoxiclav** IV 1.2g stat (**OR Ciprofloxacin** IV 400mg stat if penicillin allergy **PLUS Metronidazole** IV 500mg stat)
Gall bladder surgery (laparoscopic)	Antibiotics are not usually recommended except in high risk patients*	
	High risk patients* **Gentamicin** IV 160mg–240mg stat **PLUS Metronidazole** IV 500mg stat	*Only when gentamicin is contra-indicated* **Co-amoxiclav** IV 1.2g stat (**OR Ciprofloxacin** IV 400mg stat if penicillin allergy **PLUS Metronidazole** IV 500mg stat)
***High risk patients** (*intraoperative cholangiogram, bile spillage, conversion to laparotomy, acute cholecystitis, pancreatitis, jaundice, pregnancy, immunosuppression, insertion of prosthetic device)* **If treatment regimens are required,** refer to HHFT Empirical Antimicrobial Prescribing Guidelines for adults		
ENDOSCOPIC PROCEDURES		
Routine gastroscopy or colonoscopy	Antibiotics are not usually recommended.	
Percutaneous endoscopic	**Co-trimoxazole** PO 960mg stat via newly inserted PEG/PEJ (i.e.	**Co-amoxiclav** IV 1.2g stat **prior** to procedure

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administration, alternatives for allergy. Each recommendation is based on the likely contaminating pathogens for each procedure and reflects local sensitivity patterns, epidemiological and surveillance data.

The main groups of organisms to be covered by prophylaxis are Gram-positive organisms (staphylococci and streptococci) that are mostly skin associated, coliforms (*Escherichia coli* and similar organisms) and anaerobes that are mainly gut related. The organisms causing surgical site infection at the time of surgery are generally derived from the patient's own flora. The surgical environment and the protective clothing of the surgical staff as well as appropriate operating theatre air flow should minimize transmission from external sources.

Local sensitivity patterns are important. If there is a high rate of meticillin-resistant *S. aureus* (MRSA), then preoperative screening, clearance of carriage with topical treatment and

gastrostomy (PEG) or jejunostomy (PEJ)	10ml Co-trimoxazole suspension 480mg/5ml)	***If high risk of MRSA*** **Teicoplanin** IV 400mg stat **prior** to procedure
Therapeutic endoscopic procedures – ERCP	Antibiotics are not usually recommended	
	The following patients should receive antibiotic prophylaxis: • patients with biliary disorders, in whom complete biliary drainage will be difficult or impossible to achieve • liver transplant • pancreatic pseudocyst, • neutropenic patients • advanced haematological malignancy	
	Gentamicin IV 160mg - 240mg stat	**Ciprofloxacin** IV 400mg stat 1hour prior / PO 500mg stat 1—2hours prior to procedure

WOMEN'S HEALTH		
Type of Operation	**1st line**	**2nd line**
BREAST SURGERY		
Low-risk / superficial breast procedure (e.g. fibroadenoma excision)	Antibiotics are not usually recommended	
Breast surgery (with or without implant) **Oncoplastic breast surgery and reconstruction**	**Flucloxacillin** IV 2g stat **PLUS Gentamicin** IV 160mg—240mg stat ***If anaerobic cover required:*** **PLUS Metronidazole** IV 500mg stat	***If Penicillin allergy:*** **Clindamycin** IV 1.2g stat **PLUS Gentamicin** IV 160mg—240mg stat (**OR Ciprofloxacin** IV 400mg stat if gentamicin is contra-indicated)
	OR **Co-amoxiclav** IV 1.2g stat **alone**	**3rd line** ***& if MRSA colonised*** **Teicoplanin** IV 400mg stat **PLUS Gentamicin** IV 160mg—240mg stat ***If anaerobic cover required:*** **PLUS Metronidazole** IV 500mg stat
GYNAECOLOGICAL SURGERY		
Abdominal hysterectomy **Vaginal hysterectomy**	**Co-amoxiclav** IV 1.2g stat	**Metronidazole** IV 500mg stat **PLUS Gentamicin** IV 160mg—240mg stat (**OR Ciprofloxacin** IV 400mg stat if gentamicin is contra-indicated)
Uncomplicated Laparoscopy	Antibiotics are not usually recommended	
Intrauterine contraception device (IUCD) insertion	Antibiotics are not usually recommended	

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antibiotics such as glycopeptides which cover MRSA are appropriate. There are increasing concerns with other types of multidrug-resistant (MDR) bacteria. Examples of these are vancomycin-resistant enterococci (VRE) and carbapemase-producing enterobacteriaceae (CPE). These organisms can seriously limit the success of surgery. If local surveillance identifies that these organisms are present, then control measures such as screening, isolation, antibiotic stewardship/control and strict infection control measures will need to be instigated.

Principles of antibiotic use

Consideration of the antibiotic pharmacokinetics should be taken into account. Antibiotics given too early or too late will be ineffective. Intravenous antibiotics are generally administered by the anaesthetist at induction. The aim is to ensure adequate levels of antibiotic at the site of surgery before potential contamination with bacteria. For most types of surgery a single therapeutic dose with a half life long enough to cover the duration of the surgical

Fibroid embolization	**Ciprofloxacin** PO 750mg stat 2hours before procedure **PLUS Metronidazole** PO 400mg stat 2hours before procedure	**Co-amoxiclav** IV 1.2g stat
OBSTETRICS		
Caesarean section	***> 34 weeks gestation*** **Co-amoxiclav** IV 1.2g stat before incision ***≤ 34 weeks gestation*** **Cefuroxime** IV 1.5g stat before incision	***Any gestational age and true penicillin allergy*** **Gentamicin** IV 120mg stat **PLUS Clindamycin** IV 600mg stat
Assisted delivery	Antibiotics are not usually recommended	
Perineal tear: 3rd / 4th degree perineal tear involving the anal sphincter / rectal mucosa **Manual removal of placenta**	**Co-amoxiclav** IV 1.2g stat **FOLLOWED BY** **Co-amoxiclav** PO 375mg – 625mg 8hourly for 5days	**Gentamicin** IV 160mg - 240mg stat **PLUS Metronidazole** IV 500mg stat **FOLLOWED BY** **Clindamycin** PO 300mg – 450mg 6hourly for 5days
	Patients with proven chlamydia or gonorrhoea infection Treat infection	
Induced abortion 2nd trimester	**Azithromycin** PO 1g stat preferably 2 hours prior to procedure **PLUS Metronidazole** PR 1g /PO 800mg stat, preferably 2 hours prior to or at the time of procedure	**Doxycycline** PO 100mg 12hourly for 7 days preferably starting 2 hours prior to the procedure **PLUS Metronidazole** PR 1g / PO 800mg stat, preferably 2 hours prior to or at the time of procedure
	If confirmed negative test for C. trachomatis infection **Metronidazole** PR 1g / PO 800mg stat prior to or at the time of procedure *(no additional antibiotics required)*	
Evacuation of incomplete miscarriage	Antibiotics are not usually recommended	

UROLOGY		
Type of Operation	**1st line**	**2nd line**
Trans-rectal biopsy of prostate	**If no previous antibiotics for urinary conditions / procedures** **Ciprofloxacin** PO 750mg stat 1–2 hours **prior** to procedure **If previous antibiotics given** **Either Co-trimoxazole** PO 960mg stat 2 hours prior to procedure **OR Fosfomycin** PO 3g stat 2–3 hours **prior** to procedure	

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procedure is adequate. Prolonged courses of prophylactic antibiotics increase the risk of adverse effects and do not provide additional protection.[3]

Single-dose prophylaxis should be encouraged whenever possible including in cases of arthroplasty which should not exceed cover for 24 hours.[10] Additional doses of prophylaxis may be considered when surgery exceeds four hours or if there is heavy blood loss.[11]

Antibiotic prophylaxis should usually be administered via the intravenous route. There are some circumstances when oral antibiotics with good bioavailability may be used for prophylaxis. An example of this is the use of fluoroquinolones in transrectal prostate biopsy.[12] The antibiotic has to be given sufficiently early to achieve good tissue levels at the time of the procedure. Recent increases in resistance amongst coliforms to fluoroquinolones has resulted in failures of this prophylaxis.[13] This is an example of how the global crisis in antibiotic resistance can affect successful surgery. The spread of MDR Gram-negative bacteria is a major issue across the globe. Bowel colonization with such resistance organisms in otherwise healthy individuals can seriously compromize the success of routine procedures.

UROLOGY		
Type of Operation	**1st line**	**2nd line**
Percutaneous nephrolithotomy **Transurethral resection of the prostate (TURP) including biopsy** **Shock wave lithotripsy** **Endoscopic ureteric stone fragmentation / removal**	**Gentamicin** IV 160mg – 240mg stat at induction	***Only when gentamicin is contra-indicated (see above)*** **Co-amoxiclav** 1.2g stat (**OR Ciprofloxacin** IV 400mg stat if penicillin allergy)
Cystoscopy	Antibiotics are not usually recommended	
Transurethral resection of bladder tumour (TURBT)	**If high risk of UTI and at surgeon's discretion** **Gentamicin** IV 160mg – 240mg stat **OR** contact microbiology for targeted therapy	***Only when gentamicin is contra-indicated (see above)*** **Co-amoxiclav** 1.2g stat (**OR Ciprofloxacin** IV 400mg stat if penicillin allergy)
Urinary catheter insertion, change or removal	Antibiotics are not usually recommended	
	In exceptional circumstances, antibiotics may be considered • if previous catheter-related bacteraemia • choice of antibiotic will be guided by microbiology results	
ORTHOPAEDIC AND TRAUMA SURGERY		
Type of Operation	**1st line**	**2nd line**
ORTHOPAEDIC & SOFT TISSUE SURGERY		
Arthroplasty **Open surgery for closed fracture** **Hip fracture** **Hand & foot surgery involving bone**	**Flucloxacillin** IV 1–2g stat **PLUS Gentamicin** IV 160mg – 240mg stat ***At surgeon's discretion:*** up to 2 further doses of **Flucloxacillin** IV 1g 6-hourly (*No further Gentamicin required*)	**If MRSA colonized** **Teicoplanin** IV 10mg/kg (max 1500mg) stat **PLUS Gentamicin** IV 160mg - 240mg stat *(No further Teicoplanin or Gentamicin required as both have long half-lives)*
Open fracture, severe trauma, bites	Treat with topical Surgihoney Reactive Oxygen Gel into open area plus coamoxiclav 625mg for 5 days	
Orthopaedic surgery (without implant) **Soft tissue surgery**	Antibiotics are not usually recommended	

* Follow updated local surgical prophylaxis guidance
** Patients known to carry MRSA should ideally have a course of eradication therapy prior to high–risk surgery, e.g. cardiothoracic, neurosurgery, orthopaedic surgery and vascular surgery.

Table 1

Antibiotic prophylaxis – the future

Global spread of antibiotic resistance is a serious concern for the future success of surgery. The potential consequences of antimicrobial resistance are increases in morbidity and mortality, increased use of medical resources, increase in hospital length of stay, closure of units and cancellation for surgery. All these may already be a problem in areas where there is high antibiotic resistance with poor surveillance and antibiotic stewardship programmes.

What strategies may mitigate these consequences? Good surveillance, antimicrobial stewardship and infection prevention measures should be mandatory in all health authorities. Development of rapid diagnostic tests can support the measures above. New classes of antibiotics have not been found. Most antibiotic developments in recent years have been largely within existing classes of agents.

One promising development may be reactive oxygen (RO) treatment.[14] Originally developed from natural honey, RO is highly antimicrobial, active against most bacteria, even MDR strains. The synthetic RO is being developed as a pharmaceutical product for the treatment of complex polymicrobial soft tissue infection. A licensed product, SHRO, has been used in surgical prophylaxis. In an open labelled temporal evaluation, SHRO applied as a single dose into the wound at skin closure reduced the rate of wound infection in Caesarean sections by 60%.[15] SHRO was also effective in eradicating MDR strains from wounds and has been used as prophylaxis in coating prosthetic joints in orthopaedic surgery.[16] Further randomized controlled trials need to be carried out, but prophylaxis with RO is a very promising development. It could reduce selection and colonization with MDR bacteria and preserve systemic antibiotics for serious infection. There are advantages too to topical prophylaxis. The active agent is placed in the tissue where inoculation with the pathogenic microbes occurs. There is avoidance of the adverse effects of systemic antibiotics such as disruption of the microbiome and antibiotic associated diarrhoea. In the case of RO, there is evidence that as well as infection prophylaxis RO may support tissue healing and regeneration. ◆

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