

## Antibiotics and prophylaxis

<b>Drug or Drug Class</b>	<b>Mechanism of Action</b>	<b>Mechanisms of Drug Resistance</b>
β-Lactams (penicillins, cephalosporins, aztreonam)	Inhibition of bacterial cell wall synthesis	Production of β-lactamase Alteration in binding site of penicillin-binding protein Changes in cell wall porin size (decreased penetration)
Aminoglycosides	Inhibition of ribosomal protein synthesis	Downregulation of drug uptake into bacteria Bacterial production of aminoglycoside-modifying enzymes
Quinolones	Inhibition of bacterial DNA gyrase	Mutation in DNA gyrase-binding site Changes in cell wall porin size (decreased penetration) Active efflux
Nitrofurantoin	Inhibition of several bacterial enzyme systems	Not fully elucidated—develops slowly with prolonged exposure
Trimethoprim-sulfamethoxazole	Antagonism of bacterial folate metabolism	Draws folate from environment (enterococci)
Vancomycin	Inhibition of bacterial cell wall synthesis (at different point than β-lactams)	Enzymatic alteration of peptidoglycan target

<b>Antimicrobial Agent or Class</b>	<b>Gram-Positive Pathogens</b>	<b>Gram-Negative Pathogens</b>
Amoxicillin or ampicillin	<i>Streptococcus</i>	<i>Escherichia coli</i>
	Enterococci	<i>Proteus mirabilis</i>
Amoxicillin with clavulanate	<i>Streptococcus</i>	<i>E. coli</i>
	Enterococci	<i>P. mirabilis</i> <i>Klebsiella</i> species
Ampicillin with sulbactam	<i>Staphylococcus</i> (not MRSA)	<i>P. mirabilis</i>
	Enterococci	<i>Haemophilus influenzae</i> , <i>Klebsiella</i> species
Antistaphylococcal penicillins	<i>Streptococcus</i>	None
	<i>Staphylococcus</i> (not MRSA)	
Antipseudomonal penicillins	<i>Streptococcus</i>	Most, including <i>Pseudomonas aeruginosa</i>
	Enterococci	
First-generation cephalosporins	<i>Streptococcus</i>	<i>E. coli</i>
	<i>Staphylococcus</i> (not MRSA)	<i>P. mirabilis</i> <i>Klebsiella</i> species
Second-generation cephalosporins (cefamandole, cefuroxime, cefaclor)	<i>Streptococcus</i>	<i>E. coli</i> , <i>P. mirabilis</i>
	<i>Staphylococcus</i> (not MRSA)	<i>H. influenzae</i> , <i>Klebsiella</i> species
Second-generation cephalosporins (cefoxitin, cefotetan)	<i>Streptococcus</i>	<i>E. coli</i> , <i>Proteus</i> species (including indole-positive) <i>H. influenzae</i> , <i>Klebsiella</i> species
Third-generation cephalosporins (ceftriaxone)	<i>Streptococcus</i>	Most, excluding <i>P. aeruginosa</i>
	<i>Staphylococcus</i> (not MRSA)	
Third-generation cephalosporins (ceftazidime)	<i>Streptococcus</i>	Most, including <i>P. aeruginosa</i>
Aztreonam	None	Most, including <i>P. aeruginosa</i>
Aminoglycosides	<i>Staphylococcus</i> (urine)	Most, including <i>P. aeruginosa</i>
Fluoroquinolones	<i>Streptococcus</i> †	Most, including <i>P. aeruginosa</i>
Nitrofurantoin	<i>Staphylococcus</i> (not MRSA)	Many Enterobacteriaceae (not <i>Providencia</i> , <i>Serratia</i> , <i>Acinetobacter</i> )

	Enterococci	<i>Klebsiella</i> species
Trimethoprim-sulfamethoxazole	<i>Streptococcus</i>	Most Enterobacteriaceae (not <i>P. aeruginosa</i> )
	<i>Staphylococcus</i>	
Vancomycin	All, including MRSA	None

Penicillins

Bacteriocidal by preventing cell wall formation

Active vs. gram +ve and gram -ve

Pneumococcal, streptococcus, meningococcus

Benzylpenicillin/penicillin V

Flucloxacillin – Staph aureus

Amp/Amoxicillin hydrophilic: E coli, H Influenzae, Salmonella

Co-amoxiclav: amoxicillin + clavulanic acid

Piperacillin/tazobactam: broad spec inc. Pseudomonas

Side effects

Rashes and potentially anaphylaxis, occasionally GI upset

Many people report allergy – need to differentiate between 'true' allergy and side effects

Cephalosporins

Same mode of action as penicillins

Active vs. gram +ve and gram -ve

1st generation: cefradine, cefalexin more g +ve

2nd generation: cefuroxime 50:50

3rd generation: cefotaxime/ceftriaxone more g-ve  
ceftazidime also covers Pseudomonas

Think when converting from IV to oral

Cross allergy with penicillins (10%)

Associated with high risk of C.diff

Carbapenems

$\beta$ -Lactam antibiotic with same mode of action as penicillins

Imipenem/cilastatin (Primaxin), meropenem, ertapenem

Broad spectrum including ESBL producing organisms

Only parenteral route

Caution in epilepsy (cilastatin)

Reduce dose in renal failure

Meropenem preferred for MRSA and pseudomonas infection (more difficult to develop resistance compared with Imipenem)

Ertapenem once daily dosing – suitable for outpatient usage

Cross allergy with penicillins 1-10%

Macrolides

Includes erythromycin, clarithromycin, azithromycin

Bacteriostatic /cidal

Inhibit bacterial protein synthesis

Active vs. gram +ve and gram -ve

Similar range to penicillin; additionally mycoplasma, Legionella

Alternative vs. staph and streps

Many significant interactions including statins, cyclosporin, digoxin, antiepileptics, and warfarin (cytochrome p450 oxidase)

Side effects

Nausea, vomiting, abdominal pain, less commonly rash and urticaria

Caution in patients with predisposition to prolonged QT interval

Tetracyclines

Includes tetracycline, doxycycline

Bacteriostatic - inhibit bacterial protein synthesis (prolonged Rx required)

Active vs. gram +ve, gram -ve and anaerobes, but increasing resistance

Drug of choice for chlamydia (2 weeks Rx)

Poor absorption (chelate with calcium, iron: avoid co-administration with supplements)

Side effects

- GI disturbance
- Teeth discolouration
- Photosensitivity
- (Avoid in children, pregnancy, breast feeding)

### Quinolones

Includes ciprofloxacin, ofloxacin, norfloxacin

Bacteriocidal - inhibits DNA gyrase therefore prevents transcription or replication

Active vs. gram +ve and gram -ve, including pseudomonas aeruginosa, (not Strep. Pneumoniae)

Associated with high risk of C.diff (esp. 027 strain)

Reduced absorption when given with calcium or iron

Well absorbed orally so only IV when not absorbing (IV relatively very expensive)

Side effects

- GI disturbance, headache, rash
- Lowers seizure threshold – caution in epilepsy
- Tendon rupture

Drug interactions

- NSAIDs, theophylline and carbamazepine increase risk of seizures
- Warfarin – INR may increase
- Methotrexate – levels increase, watch for toxicity
- Phenytoin – affects levels and may cause convulsions
- Avoid in children as may cause tendon damage

### Trimethoprim

Bacteriostatic - inhibits dihydrofolate reductase (enzyme required for folate production in bacteria)

Active vs. gram+ve and gram-ve, but increasing resistance

1st line for treatment of UTI – reaches high concentrations in the kidney

Well absorbed when administered orally

May accumulate in renal failure – reduce dose after three days if *initial* GFR < 30ml/min

Side effects

- GI disturbance, rashes, hyperkalaemia, blood disorders
- Reduced tubular secretion of creatinine (GFR normal however)

Drug interactions include

- Warfarin – may increase INR – monitor closely
- Methotrexate – reduces MTX excretion so risk of haematological toxicity
- Phenytoin – both have anti-folate effects and increases phenytoin levels
- Digoxin – may increase digoxin levels

### Nitrofurantoin

Bacteriocidal, unknown mechanism of action

Poor tissue penetration & low blood levels

Poor activity vs. proteus and klebsiella

Concentrates in urine therefore can be used to treat UTIs

Contra-indicated in mild renal impairment (eGFR < 60ml/min) – does not work

Side effects

- GI disturbances, peripheral neuropathy, hypersensitivity, hepatotoxicity
- Risk of hepatic and pulmonary fibrosis and ocular disturbance almost certainly overstated (few isolated cases reports in literature from > 1 million patient years)

### Aminoglycosides

Includes gentamicin, amikacin

Bacteriocidal - inhibit bacterial protein synthesis

Gram-ve mainly, some Gram +ve cocci (staphylococcus)

Synergistic with penicillins as they increase penetration into cell

Highly polar therefore not absorbed orally and do not partition into fat

Dose based on lean body weight – often not performed well (some nomograms use age and height; or ulnar length as surrogate for height)

Side effects

Ototoxicity and nephrotoxicity – monitoring levels is essential

Interactions

Contraindicated in myasthenia gravis – impair neuromuscular transmission

Increased risk of nephrotoxicity when give with ciclosporin

Increased risk of ototoxicity when given with loop diuretics

Glycopeptides

Includes vancomycin and teicoplanin

Bacteriocidal - inhibit cell wall synthesis

Gram+ve organisms (aerobic & anaerobic)

May be used to treat MRSA, Enterococcus

IV route only, exception PO to treat C.difficile

Side effects

Ototoxicity and nephrotoxicity

Levels must be monitored if vancomycin is used (and may be needed for teicoplanin in severe infections)

Vancomycin may cause 'red man syndrome' and hypotension (histamine release) if administered too quickly

Interactions

Increased risk of toxicity when administered with aminoglycosides, loop diuretics or ciclosporin

Nitroimidazoles

Metronidazole

Bacteriocidal - Chemical reduction reaction and inhibits DNA synthesis

Active vs. anaerobes

Diffuses into organism

Alcohol interaction in small proportion of individuals

Rifampicin

Inhibits DNA-dependent RNA polymerase

Always used in combination with other antibiotics

Gram +ve infections, TB, MRSA, C.diff

Use orally as good absorption on empty stomach

Potent liver enzyme inducer so check interactions

Sodium fusidate

Always used in combination with other antibiotics

Good Staph cover

Good penetration to bone & soft tissue

Tablets (fusidate) 500mg tds, syrup (fusidic acid) 750mg tds

Avoid IV route as very irritant & greater risk of liver toxicity

Good prostate penetration

Ciprofloxacin

Doxycycline

Azithromycin/erythromycin

Trimethoprim

**Antibiotic prophylaxis**

'Antimicrobial therapy administered at or around the time of an invasive procedure in order to reduce infective complications'

Remarkably limited evidence base

Definitions controversial:

Is urinary tract surgery clean or clean-contaminated?

Should endpoints be bacteruria or symptomatic UTI/sepsis?

Generally most believe that endoscopic procedures using urethral route 'clean-contaminated' as urethra is colonised; upper tract laparoscopic surgery could be considered 'clean'.

Specific risk factors also influence decision on antibiotic prophylaxis

General risk factors	Special risk factors associated with an increased bacterial load
High age	Long pre-operative hospital stay or recent hospitalization
Deficient nutritional status	History of recurrent genitourinary infections
Impaired immune response	Surgery involving bowel segment
Diabetes mellitus	Colonization with micro-organisms
Smoking	Long-term drainage
Extreme weight	Urinary obstruction
Co-existing infection at a remote site	Urinary stone
Lack of control of risk factors	

Most important:

Indwelling catheter/stent

Previous UTI

Urinary stone disease

Long pre-operative hospital stay

General considerations:

Give oral Abx with good bioavailability 1-2hrs pre-op

Give IV antibiotics at induction

No randomised data regarding duration of prophylaxis

No direct recommendations regarding choice of Abx – depends on local sensitivities

**Specific procedures**

Urethral catheterisation

Risk of infection low – community 1-2%; hospital 5% men; 10% women

Risk of associated UTI ~5% per day

Virtually all patients colonised by 30 days (convenient cut off between short and long-term catheterisation)

More than one organism typical after 30 days

Incidence of bacteraemia 4% for routine catheter changes - therefore not indicated routinely (Polastri 1990)

Urodynamics

Not routine

Consider for patients with risk factors

TRUS and prostate biopsy

Good evidence that Abx reduce fever and UTI (Aron 2000)

At least one day recommended; EAU up to 3 days

- BNF recommends single dose oral cipro and metronidazole or single dose IV gent and metronidazole
- Cystoscopy
  - No evidence
- TURBT
  - Little evidence for benefit
  - Consider in large tumours, prolonged resection time and risk factors
- TURP
  - Majority of evidence supporting prophylactic antibiotics
  - Meta-analysis by Berry 2002 J Urol
    - 32 studies, n=4260
    - Bacteriuria 26% to 9.1% with Abx (65% reduction)
    - Septicaemia 4.4% to 0.7% with Abx (77% reduction)
    - Any duration of therapy was effective – short course (2-5 days until catheter removed) slightly better than single-dose in reducing bacteriuria (68% vs. 57%).
    - NB. All patients with significant bacteriuria (without catheter) should have infection eradicated before TURP
  - BNF recommends single dose oral cipro, IV gent, or IV cefuroxime
- ESWL
  - Overall sepsis seen in ~1% of cases and 3% staghorn calculi
  - Use of prophylactic antibiotics controversial
  - 2 x RCTs showed no benefit for patients without positive UTI or infection stones. Pearle metaanalysis 2007 however showed reduced UTI rate and reduced hospitalisation in patients receiving prophylactic antibiotics at the time of ESWL (all patients negative MSU pre-Rx)
  - Current recommendations for prophylactic antibiotics
    - Infection stones
    - Positive UTI
    - History of recurrent UTI
    - Instrumentation at time of ESWL

**Table 8-13 -- Surgical Wound Classification**

Clean	Uninfected wound without inflammation or entry into the genital, urinary, or alimentary tract
	Primary wound closure closed drainage
Clean Contaminated	Uninfected wound with controlled entry into the genital, urinary, or alimentary tract
	Primary wound closure closed drainage
Contaminated	Uninfected wound with major break in sterile technique (gross spillage from gastrointestinal tract or nonpurulent inflammation)
	Open fresh accidental wounds
Dirty Infected	Wound with preexisting clinical infection or perforated viscera
	Old traumatic wounds with devitalized tissue

Table 11.4: recommendations for antibiotic prophylaxis in standard urological surgery

Procedure	Pathogens (expected)	Prophylaxis	Antibiotics	Remarks
<b>Diagnostic procedures</b>				
Transrectal biopsy of the prostate	Enterobacteriaceae Anaerobes?	All patients	Fluoroquinolones TMP ± SMX Metronidazole?	Short course (<72h)
Cystoscopy Urodynamic examination	Enterobacteriaceae Enterococci Staphylococci	No	Cephalosporin 2 <sup>nd</sup> generation TMP ± SMX	Consider only in risk patients
Ureteroscopy	Enterobacteriaceae Enterococci Staphylococci	No	Cephalosporin 2 <sup>nd</sup> generation TMP ± SMX	Consider in risk patients
<b>Endourological surgery and ESWL</b>				
ESWL	Enterobacteriaceae Enterococci	No	Cephalosporin 2 <sup>nd</sup> or 3 <sup>rd</sup> generation TMP ± SMX Aminopenicillin/BLI*	In patients with stent or nephrostomy tube Consider in risk patients
Ureteroscopy for uncomplicated distal stone	Enterobacteriaceae Enterococci Staphylococci	No	Cephalosporin 2 <sup>nd</sup> or 3 <sup>rd</sup> generation TMP ± SMX Aminopenicillin/BLI Fluoroquinolones	In patients with stent or nephrostomy tube Consider in risk patients
Ureteroscopy of proximal or impacted stone and percutaneous stone extraction	Enterobacteriaceae Enterococci Staphylococci	All patients	Cephalosporin 2 <sup>nd</sup> or 3 <sup>rd</sup> generation TMP ± SMX Aminopenicillin/BLI Fluoroquinolones	Short course Length to be determined Intravenous suggested
TUR of the prostate	Enterobacteriaceae Enterococci	All patients (see Section 10.6.2)	Cephalosporin 2 <sup>nd</sup> or 3 <sup>rd</sup> generation TMP ± SMX Aminopenicillin/BLI	Low-risk patients and small-size prostate require no prophylaxis
TUR of bladder tumour	Enterobacteriaceae Enterococci	No	Cephalosporin 2 <sup>nd</sup> or 3 <sup>rd</sup> generation TMP ± SMX Aminopenicillin/BLI	Consider in risk patients and large necrotic tumours
<b>Open urological surgery</b>				
Clean operations	Skin-related pathogens, e.g. staphylococci Catheter-associated uropathogens	No		Consider in high-risk patients Short post-operative catheter treatment
Clean-contaminated (opening of urinary tract)	Enterobacteriaceae Enterococci Staphylococci	Recommended	Cephalosporin 2 <sup>nd</sup> or 3 <sup>rd</sup> generation TMP + SMX Aminopenicillin/BLI	Single peri-operative course

Clean-contaminated (use of bowel segments)	Enterobacteriaceae Enterococci Anaerobes Skin-related bacteria	All patients	Cephalosporin 2 <sup>nd</sup> or 3 <sup>rd</sup> generation Metronidazole	As for colonic surgery
Implant of prosthetic devices	Skin-related bacteria, e.g. staphylococci	All patients	Cephalosporin 2 <sup>nd</sup> or 3 <sup>rd</sup> generation Penicillin (penicillinase stable)	
Laparoscopic procedures				As for open surgery

### Special situations

#### Risk of endocarditis

NICE guidelines 2008:

At risk patients:

Acquired valvular heart disease (stenosis or regurg)

Valve replacement

Congenital heart disease (including all repairs except ASD, repaired VSD, repaired PDA)

Previous endocarditis

Hypertrophic cardiomyopathy

Antibiotic prophylaxis NOT recommended for patients undergoing genitourinary procedures

For patients undergoing invasive procedures with established GU infection, cover for endocarditis recommended

#### American Heart Association 1997

<b>Patient Type</b>	<b>Antimicrobial Recommendation</b>
High risk	Ampicillin, 2.0 g IM or IV, + gentamicin, 1.5 mg/kg (not to exceed 120 mg) 30 min preoperatively, and ampicillin, 25 mg/kg, or amoxicillin, 25 mg/kg 6 hr postoperatively
High risk with ampicillin or amoxicillin allergy	Vancomycin, 1.0 g over 1-2 hr, + gentamicin, 1.5 mg/kg (not to exceed 120 mg) 30 min preoperatively
Moderate risk	Amoxicillin, 2.0 g 1 hr preoperatively
Moderate risk with ampicillin or amoxicillin allergy	Vancomycin, 1.0 g IV over 1-2 hr, completed ≤ 30 min preoperatively

Vancomycin may be substituted with teicoplanin.

#### Orthopaedic hardware

AUA/AAOS joint statement 2003:

In general, antimicrobial prophylaxis for urologic patients with total joint replacements, pins, plates, or screws is not indicated. Prophylaxis is advised for individuals at higher risk of seeding a prosthetic joint, including those with recently inserted implants (within 2 years) and/or host risk factors

<b>Patient Type</b>	<b>Antimicrobial Recommendation</b>
Total joint inserted > 2 years ago, pins, plates, screws + no host risk factors	Not recommended empirically
Total joint inserted < 2 years ago or aberrant host factor(s)	Oral quinolone or ampicillin, 2 g IV, + gentamicin, 1.5 mg/kg IV, 30-60 min before procedure Substitute vancomycin, 1 g IV, over 1-2 hr before procedure if ampicillin allergy