# Antibiotics and prophylaxis

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

## Antimicrobial Agent or Class

<table>
<thead>
<tr>
<th>Antimicrobial Agent or Class</th>
<th>Gram-Positive Pathogens</th>
<th>Gram-Negative Pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin or ampicillin</td>
<td>Streptococcus</td>
<td>Escherichia coli</td>
</tr>
<tr>
<td></td>
<td>Enterococci</td>
<td>Proteus mirabilis</td>
</tr>
<tr>
<td>Amoxicillin with clavulanate</td>
<td>Streptococcus</td>
<td>E. coli</td>
</tr>
<tr>
<td></td>
<td>Enterococci</td>
<td>P. mirabilis</td>
</tr>
<tr>
<td>Ampicillin with sulbactam</td>
<td>Staphylococcus (not MRSA)</td>
<td>P. mirabilis</td>
</tr>
<tr>
<td></td>
<td>Enterococci</td>
<td>Haemophilus influenza, Klebsiella species</td>
</tr>
<tr>
<td>Antistaphylococcal penicillins</td>
<td>Streptococcus</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Staphylococcus (not MRSA)</td>
<td></td>
</tr>
<tr>
<td>Antipseudomonal penicillins</td>
<td>Streptococcus</td>
<td>Most, including Pseudomonas aeruginosa</td>
</tr>
<tr>
<td></td>
<td>Enterococci</td>
<td></td>
</tr>
<tr>
<td>First-generation cephalosporins</td>
<td>Streptococcus</td>
<td>E. coli</td>
</tr>
<tr>
<td></td>
<td>Staphylococcus (not MRSA)</td>
<td>P. mirabilis</td>
</tr>
<tr>
<td>Second-generation cephalosporins (cefaamandole, cefuroxime, cefaclor)</td>
<td>Streptococcus</td>
<td>Klebsiella species</td>
</tr>
<tr>
<td>Second-generation cephalosporins (cefoxitin, cefotetan)</td>
<td>Staphylococcus (not MRSA)</td>
<td>H. influenzae, Klebsiella species</td>
</tr>
<tr>
<td>Third-generation cephalosporins (ceftaxone)</td>
<td>Streptococcus</td>
<td>E. coli, P. mirabilis</td>
</tr>
<tr>
<td>Third-generation cephalosporins (ceftazidine)</td>
<td>Staphylococcus (not MRSA)</td>
<td></td>
</tr>
<tr>
<td>Aztreonam</td>
<td>Streptococcus</td>
<td>Most, including P. aeruginosa</td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td>Staphylococcus (urine)</td>
<td>Most, including P. aeruginosa</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>Streptococcus</td>
<td>Most, including P. aeruginosa</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>Staphylococcus (not MRSA)</td>
<td>Many Enterobacteraceae (not Providencia, Serratia, Acinetobacter)</td>
</tr>
</tbody>
</table>
Antibiotics and prophylaxis

Penicillins
Bacteriocidal by preventing cell wall formation
Active vs. gram +ve and gram -ve
Pneumonoccal, streptococcus, meningococcus
Benzyllpenicillin/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
β-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 (cilastin)
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)
Antibiotics and prophylaxis

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, ofloxacine, 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
Antibiotics and prophylaxis

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/erythromicin
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

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

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
Antibiotics and prophylaxis

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

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clean</td>
<td>Uninfected wound without inflammation or entry into the genital, urinary, or alimentary tract</td>
</tr>
<tr>
<td>Clean Contaminated</td>
<td>Uninfected wound with controlled entry into the genital, urinary, or alimentary tract</td>
</tr>
<tr>
<td>Contaminated</td>
<td>Uninfected wound with major break in sterile technique (gross spillage from gastrointestinal tract or nonpurulent inflammation)</td>
</tr>
<tr>
<td>Dirty Infected</td>
<td>Wound with pre-existing clinical infection or perforated viscera</td>
</tr>
<tr>
<td></td>
<td>Old traumatic wounds with devitalized tissue</td>
</tr>
</tbody>
</table>

Tom Walton January 2011
Table 11.4: recommendations for antibiotic prophylaxis in standard urological surgery

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

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

<table>
<thead>
<tr>
<th>Patient Type</th>
<th>Antimicrobial Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk</td>
<td>Ampicillin, 2 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</td>
</tr>
<tr>
<td>High risk with ampicillin or amoxicillin allergy</td>
<td>Vancomycin, 1 g IV over 1-2 hr, + gentamicin, 1.5 mg/kg (not to exceed 120 mg) 30 min preoperatively</td>
</tr>
<tr>
<td>Moderate risk</td>
<td>Amoxicillin, 2.0 g 1 hr preoperatively</td>
</tr>
<tr>
<td>Moderate risk with ampicillin or amoxicillin allergy</td>
<td>Vancomycin, 1.0 g IV over 1-2 hr, completed ≤ 30 min preoperatively</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Patient Type</th>
<th>Antimicrobial Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total joint inserted &gt; 2 years ago, pins, plates, screws + no host risk factors</td>
<td>Not recommended empirically</td>
</tr>
<tr>
<td>Total joint inserted &lt; 2 years ago or aberrant host factor(s)</td>
<td>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</td>
</tr>
</tbody>
</table>