GUIDANCE ON THE TREATMENT AND MANAGEMENT OF INFECTION IN PRIMARY CARE
(Antimicrobial Prescribing)

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Approved By Area Prescribing Committee
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Review Date April 2015
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Version 4.0 (26th November 2013)
Introduction

This guidance document has been produced in line with the Health Protection Agency and British Infection Association ‘Management of Infection Guidance for Primary Care’ which was first produced in 2000 and reviewed in November 2012.

It is intended for use by those clinicians prescribing antimicrobials for the management of infections in Primary Care in North and North East Lincolnshire. Prescribing data will be used to monitor compliance.
Aims
- To provide a simple, effective, economical and empirical approach to the treatment of common infections.
- To minimise the emergence of bacterial resistance in the community.

Principles of Treatment
1. This guidance is based on the best available evidence but professional judgement should be used and patients should be involved in the decision.
2. It is important to initiate antibiotics as soon as possible in severe infection.
3. A dose and duration of treatment for adults is usually suggested, but may need modification for age, weight and renal function. Children's doses are provided when appropriate and can be accessed through the symbol. In severe or recurrent cases consider a larger dose or longer course. Please refer to BNF for further dosing and interaction information (e.g. interaction between macrolides and statins) if needed and please check for hypersensitivity.
4. Lower threshold for antibiotics in immunocompromised or those with multiple morbidities; consider culture and seek advice.
5. Prescribe an antibiotic only when there is likely to be a clear clinical benefit.
6. Consider a no, or delayed, antibiotic strategy for acute self-limiting upper respiratory tract infections. 1A+
7. Limit prescribing over the telephone to exceptional cases.
8. Use simple generic antibiotics if possible. Avoid broad spectrum antibiotics (e.g. amoxicillin, quinolones and cephalosporins) when narrow spectrum antibiotics remain effective, as they increase risk of Clostridium difficile, MRSA and resistant UTIs. Where broad spectrum antibiotics are recommended as second line treatment, this should be on the basis of a culture and sensitivity result.
9. Avoid widespread use of topical antibiotics (especially those agents also available as systemic preparations, e.g. fusidic acid).
10. In pregnancy take specimens to inform treatment; where possible avoid tetracyclines, aminoglycosides, quinolones, high dose metronidazole (2 g) unless benefit out ways risks. Short-term use of nitrofurantoin (at term, theoretical risk of neonatal haemolysis) is not expected to cause foetal problems. Trimethoprim is also unlikely to cause problems unless poor dietary folate intake or taking another folate antagonist eg antiepileptic.
11. Where a ‘best guess’ therapy has failed or special circumstances exist, microbiological advice can be obtained from the Consultant Microbiologist via the Hospital Switchboard: 01472 874111 or 01724 282282

General information on prescribing recommendations

The information contained within this document is for guidance to assist in the prescribing of antimicrobials. The doses specified are recommended for use in those with normal pharmacokinetic handling of the drug. Dose adjustments may be necessary in children or those of advanced age or with co-morbidities that could affect the pharmacokinetics of the drug (e.g. liver or renal impairment, pregnancy). Certain drug interactions may also have an impact on antimicrobial drug dosing. Please refer to the BNF for children for child doses. Clicking on the symbol will take users to the relevant section within the BNF for children.

Before prescribing, the information contained within these guidelines should be read in conjunction with the most recent British National Formulary (www.bnf.org or www.bnfc.org) or the electronic medicines compendium (www.emc.medicines.org.uk) for contra-indications, cautions, use in pregnancy / breast feeding and other disease states (e.g. renal or hepatic impairment) and drug interactions.
Main Risk Factors for *Clostridium difficile associated diarrhoea (CDAD)*

Risk factors for CDAD are given below. The more of these risk factors a patient has, the higher the risk is likely to be.

- Age >65 years (especially >75 years)*
- Previous CDAD*
- Recent exposure to cephalosporins*, quinolones* or clindamycin*. Other broad-spectrum antibiotics such as co-amoxiclav (Augmentin®) have been less strongly associated with CDAD, but may also be risk factors especially if prolonged / multiple courses.
- Recent prolonged* / multiple* or IV antibiotic exposure (especially if antibiotics listed above)
- Nursing / residential home resident
- NG or PEG tube in-situ
- Prolonged hospital stay anticipated
- Recent hospital stay
- Extensive co-morbidity
- Gastrointestinal surgery
- Severe underlying / inter-current illness
- Low albumin / poor nutritional status
- H₂ antagonist or proton pump inhibitor therapy*
- Immunosuppression

*These are probably the most important, particularly in combination
**ILLNESS** | **COMMENTS** | **DRUG** | **ADULT DOSE** | **DURATION OF TREATMENT**
--- | --- | --- | --- | ---
**UPPER RESPIRATORY TRACT INFECTIONS**

**Influenza**
- **HPA Influenza**
- **UKTIS**

Annual vaccination is essential for all those at risk of influenza. For otherwise healthy adults antivirals not recommended. Treat "at risk" patients, when influenza is circulating in the community and within 48 hours of onset in or a care home where influenza is likely. At risk: pregnant (including up to two weeks post partum), 65 years or over, chronic respiratory disease (including COPD and asthma) significant cardiovascular disease (not hypertension), immunocompromised, diabetes mellitus, chronic neurological, renal or liver disease. Use 5 days treatment with oseltamivir 75 mg bd unless pregnant or if there is resistance to oseltamivir, use 5 days zanamivir 10 mg BD (2 inhalations by diskhaler) and seek advice. For prophylaxis, see NICE. (NICE Influenza). Patients under 13 years see HPA Influenza link.

**Acute Sore Throat**
- **CKS**

Avoid antibiotics as 90% resolve in 7 days without, and pain only reduced by 16 hours 2A+.
   - If Centor score 3 or 4: (Lymphadenopathy; No Cough; Fever; Tonsillar Exudate) 1A- consider 2 or 3-day delayed or immediate antibiotics 1A+ or rapid antigen test.
   - RCT in <18yr olds shows 10d had lower relapse8
   - Antibiotics to prevent Quinsy NNT >4000 3B-
   - Antibiotics to prevent Otitis media NNT 200 3A++

<table>
<thead>
<tr>
<th>Drug</th>
<th>ADULT DOSE</th>
<th>DURATION OF TREATMENT</th>
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</thead>
<tbody>
<tr>
<td>Penicillin Allergy:</td>
<td>500 mg QDS 1G BD</td>
<td>10 days 3A+</td>
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<tr>
<td>Clarithromycin</td>
<td>250-500mg BD</td>
<td>5 days 9A+</td>
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</tbody>
</table>

**Acute Otitis Media**
- **(child doses)**
- **CKS**

Optimise analgesia and target antibiotics 2,3B-
- OM resolves in 60% in 24 h without antibiotics, which only reduce pain at 2 days (NNT15) and does not prevent deafness 4A+.
   - Consider 2 or 3-day delayed 1A+ or immediate antibiotics for pain relief if:
     - <2 years AND bilateral AOM (NNT4) or bulging membrane & ≥ 4 marked symptoms 5-7a
     - All ages with otorhoea NNT3 8a+
   - Abx to prevent Mastoiditis NNT >4000 9B-

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<thead>
<tr>
<th>Drug</th>
<th>ADULT DOSE</th>
<th>DURATION OF TREATMENT</th>
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<tbody>
<tr>
<td>amoxicillin 10a+</td>
<td>1 month – 1 yr 125mg tds 1-5yrs 250mg tds 5-12yrs 500mg tds 12-18yrs 500mg tds</td>
<td>5 days 11a+</td>
</tr>
<tr>
<td>Penicillin Allergy: erythromycin 11D</td>
<td>&lt; 2 yrs 125mg QDS 2-8yrs 250mg QDS 8-18yrs 250-500mg QDS</td>
<td>5 days 11a+</td>
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</tbody>
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**Acute Otitis Externa**
- **CKS**

First use aural toilet (if available) & analgesia
- Cure rates similar at 7 days for topical acetic acid or antibiotic +/- steroid 1A+.
   - If cellulitis or disease extending outside ear canal, start oral antibiotics and refer 2Aa.

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<tr>
<th>Drug</th>
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<th>DURATION OF TREATMENT</th>
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<tbody>
<tr>
<td>First Line: acetic acid 2%</td>
<td>1 spray TDS</td>
<td>7 days</td>
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<tr>
<td>Second Line: neomycin sulphate with corticosteroid 3A-4D</td>
<td>3 drops TDS</td>
<td>7 days min to 14 days max 1A+</td>
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</table>

**Acute Rhinosinusitis**
- **SC**
- **CKS**

Avoid antibiotics as 80% resolve in 14 days without, and they only offer marginal benefit after 7 days NNT15 3A++.
Use adequate analgesia 4B+
   - Consider 7-day delayed or immediate antibiotic when purulent nasal discharge NNT9 1,2A+
   - In persistent infection use an agent with anti-anerobic activity eg. co-amoxiclav 9B+

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<th>Drug</th>
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<th>DURATION OF TREATMENT</th>
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<tbody>
<tr>
<td>amoxicillin 6A+ 7A or doxycycline or phenoxymethylpenicillin 9B+</td>
<td>500mg TDS 1g if severe 1D 200mg stat/100mg OD 500mg QDS</td>
<td>7 days 9A+</td>
</tr>
</tbody>
</table>
For persistent symptoms: co-amoxiclav 9B+ | 625mg TDS | 7 days |

- Please refer to the BNF for children for child doses - Clicking on the symbol ☑ will take users to the relevant section within the BNF for children
<table>
<thead>
<tr>
<th>ILLNESS</th>
<th>COMMENTS</th>
<th>DRUG</th>
<th>ADULT DOSE</th>
<th>DURATION OF TREATMENT</th>
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<tr>
<td><strong>LOWER RESPIRATORY TRACT INFECTIONS</strong></td>
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<tr>
<td><strong>Acute cough, bronchitis</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Antibiotic little benefit if no co-morbidity&lt;sup&gt;1,3A&lt;/sup&gt; Consider 7d delayed antibiotic with advice&lt;sup&gt;1&lt;/sup&gt; Symptom resolution can take 3 weeks. Consider immediate antibiotics if &gt; 80yr and ONE of: hospitalisation in past year, oral steroids, diabetic, congestive heart failure OR &gt; 65yrs with 2 of above</td>
<td>amoxicillin or doxycycline</td>
<td>500 mg TDS</td>
<td>5 days</td>
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<td>200 mg stat/100 mg OD</td>
<td>5 days</td>
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<tr>
<td><strong>Acute exacerbation of COPD</strong>&lt;sup&gt;2,3&lt;/sup&gt;</td>
<td>Treat exacerbations promptly with antibiotics if purulent sputum and increased shortness of breath and/or increased sputum volume&lt;sup&gt;1-3B&lt;/sup&gt;. Risk factors for antibiotic resistant organisms include co-morbid disease, severe COPD, frequent exacerbations, antibiotics in last 3 m&lt;sup&gt;2&lt;/sup&gt;</td>
<td>amoxicillin or doxycycline clarithromycin If resistance: co-amoxiclav</td>
<td>500 mg TDS</td>
<td>5 days&lt;sup&gt;4C&lt;/sup&gt;</td>
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<td>200 mg stat/100 mg OD</td>
<td>5 days&lt;sup&gt;4C&lt;/sup&gt;</td>
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<td>500 mg BD</td>
<td>5 days&lt;sup&gt;4A&lt;/sup&gt;</td>
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<td>625 mg TDS</td>
<td>5 days&lt;sup&gt;4A&lt;/sup&gt;</td>
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<tr>
<td><strong>Community-acquired pneumonia - treatment in the community</strong>&lt;sup&gt;3,5&lt;/sup&gt;</td>
<td>Use CRB65 score to help guide and review:&lt;sup&gt;7&lt;/sup&gt; Each scores 1: Confusion (AMT&lt;8); Respiratory rate &gt;30/min; Age &gt;65; BP systolic &lt;90 or diastolic ≤60; Score 0: suitable for home treatment; Score 1-2: hospital assessment or admission Score 3-4: urgent hospital admission Mycoplasma infection is rare in over 65s&lt;sup&gt;1&lt;/sup&gt;</td>
<td>IF CRB65=0: doxycycline&lt;sup&gt;10&lt;/sup&gt; or amoxicillin&lt;sup&gt;11&lt;/sup&gt; or clarithromycin&lt;sup&gt;12&lt;/sup&gt;</td>
<td>200 mg stat/100 mg OD</td>
<td>7 days</td>
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<td>500 mg TDS</td>
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<td></td>
<td>500 mg BD</td>
<td>7 days</td>
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<td><strong>MENINGITIS (NICE fever guidelines)</strong></td>
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<tr>
<td><strong>Suspected meningococcal disease</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Transfer all patients to hospital immediately. IF time before admission, and non-blanching rash, give IV benzylpenicillin or cefotaxime&lt;sup&gt;13B&lt;/sup&gt; unless definite history of hypersensitivity&lt;sup&gt;13K&lt;/sup&gt;.</td>
<td>IV or IM benzylpenicillin or IV or IM cefotaxime</td>
<td>Age 10+ years: 1200 mg Children 1 - 9 yr: 600 mg Children &lt;1 yr: 300 mg Age 12+ years: 1 gram Child &lt; 12 yrs: 50mg/kg</td>
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<td>(give IM if vein cannot be found)</td>
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</table>

Note: Low doses of penicillins are more likely to select out resistance<sup>6</sup> Do not use quinolone (ciprofloxacin, ofloxacin) first line due to poor pneumococcal activity. Reserve all quinolones (including levofloxacin) for proven resistant organisms.

Prevention of secondary case of meningitis: Only prescribe following advice from Public Health Doctor: 9 am – 5 pm: ☎️ 01904 468900 Out of hours: Contact on-call doctor via hospital switchboard ☎️ 01472 874111 or 01724 282282


Endorsed by:
### URINARY TRACT INFECTIONS - refer to HPA UTI guidance for diagnosis information

<table>
<thead>
<tr>
<th>UTI in adults (no fever or flank pain)</th>
<th>UTI in pregnancy</th>
<th>UTI in Children</th>
<th>Acute pyelonephritis</th>
<th>Recurrent UTI in non-pregnant women ≥ 3 UTIs/year</th>
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<tbody>
<tr>
<td><strong>HPA QRG SIGN CKS, CKS</strong></td>
<td><strong>HPA QRG CKS</strong></td>
<td><strong>HPA QRG CKS</strong></td>
<td><strong>NICE</strong></td>
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<td><strong>Women</strong></td>
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<td>severe/or ≥ 3 symptoms: treat:</td>
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<td>cefixime, nitrofurantoin (reference)</td>
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<tr>
<td>or trimethoprim (reference)</td>
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<tr>
<td>nitrofurantoin<strong>1A</strong>, nitrofurantoin***</td>
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<tr>
<td>100mg m/r BD or 200mg BD</td>
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<td><strong>Women all ages 3 days</strong></td>
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<td><strong>2A+, 3B+</strong></td>
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<tr>
<td><strong>Men</strong></td>
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<tr>
<td>Consider prostatitis &amp; send pre-treatment</td>
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<td><strong>MSU</strong></td>
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<td><strong>1C OR</strong></td>
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<td>if symptoms mild/non-specific, use</td>
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<tr>
<td><em>ve dipstick to exclude UTI</em>* 1C**</td>
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<td><strong>Second line</strong></td>
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<td><strong>perform culture in all treatment failures</strong></td>
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<tr>
<td>Amoxicillin resistance is common; only use susceptible 1B+</td>
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<tr>
<td>Community multi-resistant <em>E. coli</em> are increasing: consider nitrofurantoin (or fosfomycin 5g stat in women13,16B,17A) plus 2nd 3g dose in men 3 days later19, on advice of microbiologist</td>
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<tr>
<td><strong>Acute prostatitis</strong></td>
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<td><strong>BASHH, CKS</strong></td>
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<td>Send MSU for culture and start antibiotics 1C.</td>
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<td>4-wk course may prevent chronic prostatitis 1C</td>
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<td>Quinolones achieve higher prostate levels 1C</td>
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<td>ciprofloxacin 1C or ofloxacin 1C</td>
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<td><strong>2nd line:</strong> trimethoprim 1C</td>
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<td>100mg m/r BD or 200mg BD</td>
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<td><strong>28 days 1C</strong></td>
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<td><strong>28 days 1C</strong></td>
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<tr>
<td><strong>UTI in pregnancy</strong></td>
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<td><strong>HPA QRG CKS</strong></td>
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<tr>
<td>Send MSU for culture and start antibiotics 1A.</td>
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<tr>
<td>Short-term use of nitrofurantoin in pregnancy is unlikely to cause problems to the foetus 3C</td>
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<tr>
<td>Avoid trimethoprim if low folate status 1 or on folate antagonist (eg antiepileptic or proguanil)2</td>
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<tr>
<td><strong>First line:</strong> nitrofurantoin if susceptible, amoxicillin</td>
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<td><strong>Second line:</strong> trimethoprim</td>
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<td><strong>Give folate if 1st trimester</strong></td>
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<td><strong>Third line:</strong> cefalexin 1C, 1C</td>
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<td>100mg m/r BD or 500mg m/r BD</td>
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<td><strong>500mg m/r BD</strong></td>
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<td><strong>200mg BD</strong></td>
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<td><strong>200mg BD</strong></td>
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<td><strong>28 days 1C</strong></td>
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<td><strong>28 days 1C</strong></td>
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<td><strong>28 days 1C</strong></td>
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<tr>
<td><strong>UTI in Children</strong></td>
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<td><strong>HPA QRG CKS</strong></td>
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<tr>
<td>Child &lt;3 mths: refer urgently for assessment1A</td>
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<tr>
<td>Child ≥ 3 mths: use positive nitrite to start antibiotics 1A. Send pre-treatment MSU for all.</td>
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<tr>
<td>Imaging: only refer if child &lt;6 months, recurrent or atypical UTI1C</td>
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<td><strong>Lower UTI:</strong> trimethoprim 1C or nitrofurantoin 1C, 1C</td>
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<tr>
<td><strong>susceptible, amoxicillin 1A</strong> Second line: cefalexin 1C</td>
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<td><strong>3B</strong></td>
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<tr>
<td><strong>Upper UTI:</strong> co-amoxiclav 1C Second line: cefixime</td>
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<tr>
<td><strong>Lower UTI</strong></td>
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<tr>
<td><strong>Post coital stat (off-label)</strong> 2B+, 3C</td>
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<tr>
<td><strong>Upper UTI 7-10 days 1A+</strong></td>
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<tr>
<td><strong>Acute pyelonephritis</strong></td>
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<td><strong>NICE</strong></td>
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<td>If admission not needed, send MSU for culture &amp; sensitivities and start antibiotics 1C</td>
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<tr>
<td>If no response within 24 hours, admit 1C</td>
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<td>ciprofloxacin 1C or co-amoxiclav 1C</td>
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<td>500mg m/r BD or 500/125 mg TDS</td>
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<td><strong>7 days 1C</strong></td>
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<td><strong>14 days 1C</strong></td>
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<tr>
<td><strong>Recurrent UTI in non-pregnant women ≥ 3 UTIs/year</strong></td>
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<tr>
<td>Cranberry products, 3A, 3B+ OR Post-coital 1B+, 3B+</td>
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<tr>
<td>OR stand-by antibiotics 3B+ may reduce recurrence. Nightly: reduces UTIs but adverse effects 1A+</td>
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<tr>
<td>Antibiotics: nitrofurantoin 1A+ or trimethoprim</td>
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<td>50–100 mg or 100 mg</td>
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<tr>
<td><strong>Post coital stat (off-label)</strong> 2B+, 3C</td>
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<tr>
<td><strong>Prophylaxis OD at night</strong> 1A+</td>
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</table>


**People > 65 years: do not treat asymptomatic bacteriuria; it is common but is not associated with increased morbidity** 1C+

**Catheter in situ: antibiotics will not eradicate asymptomatic bacteriuria; only treat if systemically unwell or pyelonephritis likely** 2B+

Do not use prophylactic antibiotics for catheter changes unless history of catheter-change-associated UTI or trauma 1B (NICE & SIGN guidance).
## Gastro-intestinal Tract Infections

### Oral candidiasis

Antifungal agents absorbed from the gastrointestinal tract prevent oral candidiasis in patients receiving treatment for cancer.  

Drugs fully absorbed (fluconazole, and itraconazole) and partially absorbed (miconazole and clotrimazole) are effective compared with placebo or no treatment.  

### Eradication of Helicobacter pylori

**NICE**  
**HPA QRG**  
**CKS**

Eradication is beneficial in known DU, GU $^A$ or low grade MALToma $^B$.  

For NUD, the NNT is 14 for symptom relief $^A$.  

Consider test and treat in persistent uninvestigated dyspepsia $^D$.  

Do not offer eradication for GORD $^E$.  

Do not offer eradication for DU/GU relapse:  

- retest for *H. pylori* using breath or stool test  
- consider endoscopy for culture & susceptibility $^C$.  

**Symptomatic relapse**

NUD: Do not retest, offer PPI or 

**Antibiotic therapy not indicated unless systemically unwell.** $^E$.  

If systemically unwell and campylobacter suspected (e.g. undercooked meat and abdominal pain), consider clarithromycin 250–500 mg BD for 5–7 days if treated early. $^C$.

### Clostridium difficile

**DH & HPA**

Stop unnecessary antibiotics and/or PPIs $^F$.  

70% respond to MTZ in 5days; 92% in 14days $^G$.  

If severe symptoms or signs (below) should treat with oral vancomycin, review progress closely and/or consider hospital referral.  

Admit if severe: T >38.5; WCC >15, rising creatinine or signs/symptoms of severe colitis $^C$.

1$^*/2^*$ episodes metronidazole (MTZ) $^A$  

3$^*$ episode/severe type 027 oral vancomycin $^A$  

400 or 500 mg TDS  

125mg QDS  

10-14 days $^C$  

10-14 days $^C$  

### Traveller’s diarrhoea

**CKS**

Only consider standby antibiotics for remote areas or people at high-risk of severe illness with travellers’ diarrhoea $^I$.  

If standby treatment appropriate give: ciprofloxacin 500 mg twice a day for 3 days (private Rx). $^A$, $^F$.  

If quinolone resistance high (eg south Asia):  

consider bismuth subsalicylate (Pepto Bismol) 2 tablets QDS as prophylaxis $^B$ or for 2 days treatment $^B$.

### Threadworm

**CKS**

Treat all household contacts at the same time PLUS advise hygiene measures for 2 weeks (hand hygiene, pants at night, morning shower) PLUS wash sleepwear, bed linen, dust, and vacuum on day one $^C$.  

- 6 months: mebendazole (off-label if <2yrs)  
- 3-6 mths: piperoxine+senna < 3mths: 6 wks hygiene $^C$.  

100 mg $^C$  

2.5ml spoonful $^C$  

stat, repeat after 2 weeks
### GENITAL TRACT INFECTIONS

Contact UKTIS for information on foetal risks if patient is pregnant.

<table>
<thead>
<tr>
<th>STI screening</th>
<th>Chlamydia trachomatis/urethritis</th>
<th>Trichomoniasis</th>
<th>Pelvic Inflammatory Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>People with risk factors should be screened for chlamydia, gonorrhoea, HIV, syphilis. Refer individual and partners to GUM service. Risk factors: &lt; 25y, no condom use, recent (&lt;12mth)/frequent change of partner, symptomatic partner.</td>
<td>Opportunistically screen all aged 15-25yrs. Treat partners as per local guidance (PMS contract). For GMS practices, refer to GUM service. Pregnancy or breastfeeding: azithromycin is the most effective option. Due to lower cure rate in pregnancy, test for cure 6 weeks after treatment.</td>
<td>All topical and oral azoles give 75% cure. In pregnancy: avoid oral azoles and use intravaginal treatment for 7 days.</td>
<td>Refer woman &amp; contacts to GUM service. Always culture for gonorrhoea &amp; chlamydia. 28% of gonorrhoea isolates now resistant to quinolones. If gonorrhoea likely (partner has it, severe symptoms, sex abroad) use ceftriaxone regimen or refer to GUM.</td>
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<tr>
<td>SIGN, BASHH HPA, CKS</td>
<td>azithromycin or doxycycline.</td>
<td>clotrimazole 1A+</td>
<td>metronidazole PLUS doxycycline 1, 2, 4B+</td>
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<td></td>
<td>Pregnant or breastfeeding: azithromycin or erythromycin or amoxicillin.</td>
<td>oral fluconazole 1A+ or miconazole 2% cream or clotrimazole 1A+</td>
<td>metronidazole PLUS doxycycline 1, 2, 4B+</td>
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<td></td>
<td>1 g, 100 mg BD</td>
<td>500 mg pess or 10% cream or 100 mg pessary at night or 5 mg intravaginally BD</td>
<td>400 mg BD or 1 g or 2 g or 100 mg pessary at night.</td>
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<td>1g (off-label use)</td>
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<td>5 g applicatorful at night or 5 g applicatorful at night</td>
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<td>500 mg QDS</td>
<td></td>
<td>400 mg BD or 2 g or 100 mg pessary at night.</td>
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<td>500 mg TDS</td>
<td></td>
<td>400 mg BD or 2 g or 100 mg pessary at night.</td>
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<tr>
<td></td>
<td>400 mg BD</td>
<td></td>
<td>500 mg IM or 400 mg BD or 100 mg BD.</td>
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<td>100mg BD</td>
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<td>400 mg BD or 100 mg BD.</td>
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<td>stat 1A+</td>
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<td>stat 1A+</td>
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<td>7 days 4A+</td>
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<td>7 days 4A+</td>
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<td></td>
<td>stat 5A+</td>
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<td>14 days 3A+</td>
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<td>14 days 3A+</td>
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<td>stat 4A+</td>
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<td>stat 6A+</td>
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<td>14 days 3A+</td>
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<td>14 days 3A+</td>
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<td>14 days 3A+</td>
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</table>

**Note:**
- **MTZ:** Metronidazole
- **QL:** Quinolones
- **CDD:** Ceftriaxone
- **UNC:** Unconjugated
- **NCP:** Non-conjugated polyethylene glycol

**Dosages:**
- **1A+:** 100mg BD or 2g or 100mg pessary at night.
- **4A+:** 1g (off-label use) or 500mg QDS or 500mg TDS or 400mg BD or 100mg BD. Stat 1A+ or 7 days 4A+ or 14 days 3A+.
- **6A+:** 500mg pess or 10% cream or 5mg intravaginally BD.
- **2A:** 500mg BD or 2g or 100mg pessary at night. Stat 1A+ or 7 days 2A+ or 14 days 2A+.
- **2A+:** 5g applicatorful at night or 5g applicatorful at night.
- **3A+:** 400mg BD or 2g or 100mg pessary at night. Stat 1A+ or 7 days 3A+ or 14 days 3A+.
- **1:** 100mg BD or 2g or 100mg pessary at night. Stat 1A+ or 7 days 1A+ or 14 days 1A+.
- **5:** 400mg BD or 2g or 100mg pessary at night. Stat 1A+ or 7 days 5A+ or 14 days 5A+.
<table>
<thead>
<tr>
<th>ILLNESS</th>
<th>COMMENTS</th>
<th>DRUG</th>
<th>ADULT DOSE</th>
<th>DURATION OF TREATMENT</th>
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</thead>
<tbody>
<tr>
<td><strong>SKIN INFECTIONS</strong></td>
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<tr>
<td>Impetigo CKS</td>
<td>For extensive, severe, or bulbose impetigo, use oral antibiotics 1C</td>
<td>oral flucloxacillin 2C</td>
<td>500 mg QDS</td>
<td>7 days</td>
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<td></td>
<td>Reserve topical antibiotics for very localised lesions to reduce the risk of resistance 1C, 4B+</td>
<td>If penicillin allergic: oral clarithromycin 2C, 4B+</td>
<td>250-500 mg BD</td>
<td>7 days</td>
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<td>topical fusidic acid 3A+</td>
<td>TDS</td>
<td>5 days</td>
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<td></td>
<td><strong>MRSA</strong> only mupirocin 3A+</td>
<td>TDS</td>
<td>5 days</td>
</tr>
<tr>
<td>Eczema CKS</td>
<td>If no visible signs of infection, use of antibiotics (alone or with steroids) encourages resistance and does not improve healing 1C In eczema with visible signs of infection, use treatment as in impetigo 1C</td>
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<tr>
<td>Cellulitis CKS</td>
<td>If patient afebrile and healthy other than</td>
<td>flucloxacinil 1C, 2C</td>
<td>500 mg QDS</td>
<td>All for 7 days.</td>
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<tr>
<td></td>
<td>oral flucloxacinil alone 1C, 2C</td>
<td>If penicillin allergic: clarithromycin 1C, 2C or clindamycin 1C, 2C</td>
<td>500 mg BD</td>
<td>If slow response continue for a further 7 days 2C</td>
</tr>
<tr>
<td></td>
<td>If river or sea water exposure, discuss with</td>
<td>facial: co-aximaclov 4C</td>
<td>300-450 mg QDS</td>
<td></td>
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<tr>
<td></td>
<td>microbiologist. If febrile and ill, admit for IV treatment 1C</td>
<td></td>
<td>500/125 mg TDS</td>
<td></td>
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<tr>
<td></td>
<td><strong>MRSA</strong> confirmed: Use of clindamycin 1C, 3A+</td>
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<tr>
<td></td>
<td>Stop clindamycin if diarrhoea occurs.</td>
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<tr>
<td>Leg ulcer HPA ORG CKS</td>
<td>Ulcers always colonized. Antibiotics do not improve healing unless active infection 1B+</td>
<td>Active infection if cellulitis/increased pain/pyrexia/purulent exudate/odour</td>
<td>500 mg QDS</td>
<td>As for cellulitis</td>
</tr>
<tr>
<td>MRSA</td>
<td>For MRSA screening and suppression, see HPA MRSA quick reference guide. Refer to CPG Infection Control Team 01472 721346</td>
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<td>For active MRSA infection: Use antibiotic sensitivities to guide treatment. If severe infection or no response to monotherapy after 24-48 hours, seek advice from microbiologist on combination therapy.</td>
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<td>If active infection confirmed</td>
<td>100 mg BD</td>
<td>Both for 7 days</td>
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<td><strong>MRSA</strong> confirmed: by lab results, infection not severe and admission not required 1B+;</td>
<td>300-450 mg QDS</td>
<td>If diarrhoee, stop</td>
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<tr>
<td><strong>PVL HPA ORG</strong></td>
<td>Panton-Valentine Leukocidin (PVL) is a toxin produced by 2% of S. aureus. Can rarely cause severe invasive infections in healthy people. Send swabs if recurrent boils/abscesses. At risk: close contact in communities or sport; poor hygiene 1C</td>
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<tr>
<td><strong>Bites (human or animal): CKS</strong></td>
<td>Thorough irrigation is important 1A+ Assess risk of tetanus, HIV, hepatitis B&amp;C 1C</td>
<td>Prophylaxis or treatment: co-aximaclov</td>
<td>375-625 mg TDS 4C</td>
<td>All for 7 days 4A, 5C</td>
</tr>
<tr>
<td>Human:</td>
<td>Antibiotic prophylaxis is advised 1B+ Assess risk of tetanus and rabies 1C Give prophylaxis if 1A: cat bite/puncture wound; bite to hand, foot, face, joint, tendon, ligament; immunocompromised/diabetic/asplenic/ cirrhotic</td>
<td>If penicillin allergic: metronidazole PLUS doxycycline (cat/dog/man) or metronidazole PLUS clarithromycin (human bite) AND review at 24/48hrs 3C</td>
<td>200-400 mg TDS</td>
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<td>Cat or dog:</td>
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<td>100 mg BD</td>
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<td>200-400 mg TDS</td>
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<td>250-500 mg BD 4C</td>
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<tr>
<td>Scabies CKS</td>
<td>Treat all home &amp; sexual contacts within 24h 1A+ Treat whole body from ear/chin downwarad and under nails. If under 2/elderly, also face/scalp 2C</td>
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<tr>
<td>Dermatophyte infection – skin CKS</td>
<td>Terbinafine is fungicidal, so treatment time shorter than with fungstatic imidazoles If candida possible, use imizadole 1C If intra tactile: send skin scrapings 1C If infection confirmed, use oral terbinafine/itraconazole 1B+</td>
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<td>body &amp; groin</td>
<td>Scalp: discuss with specialist</td>
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<tr>
<td></td>
<td>foot</td>
<td>Topical terbinafine 2A+</td>
<td>0.5% aqueous liquid</td>
<td>2 applications</td>
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<td></td>
<td>scalp</td>
<td>or topical imidazole 4A+ or (athlete’s foot only): topical undecanoates (Mycostatin) 4B+</td>
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<td>1 week apart 1C</td>
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<tr>
<td>Dermatophyte infection - nail CKS</td>
<td>Take nail clippings: start therapy only if infection is confirmed by laboratory 1C Terbinafine is more effective than azoles 5A+ Liver reactions rare with oral ter bifurcas 5A+ If candida or non-dermatophyte infection confirmed, use oral itracaconazole 3B+</td>
<td>Superficial only amorfoline 5B</td>
<td>1-2x/weekly fingers</td>
<td>6 months</td>
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<td>for 1-2 wks after healing</td>
<td>5% nail lacquer 5A+</td>
<td>12 months</td>
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<td>(i.e. 4-6wks) 4A+</td>
<td>First line: terbinafine 6A+</td>
<td>6 – 12 weeks</td>
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<td>250 mg OD fingers toes</td>
<td>3 – 6 months</td>
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<td>7 days daily</td>
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<td>2 courses</td>
<td>3 courses</td>
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<td>Varicella zoster/chickenpox CKS</td>
<td>Pregnant/immuno compromised/neonate: seek urgent specialist advice 1B+</td>
<td>If indicated: aciclovir 1B+, 5A+</td>
<td>800 mg five times a day</td>
<td>7 days 1B+</td>
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<tr>
<td>Herpes zoster/shingles CKS</td>
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<tr>
<td>Cold sores</td>
<td>Cold sores resolve after 7-10d without treatment. Topical antivirals applied promodurally reduce duration by 12-24hrs</td>
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<tr>
<td><strong>EYE INFECTIONS</strong></td>
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<td>Conjunctivitis CKS</td>
<td>Treat if severe, as most viral or self-limiting. Bacterial conjunctivitis is usually unilateral and also self-limiting; 1C it is characterised by red eye with mucopurulent, not watery, discharge; 65% resolve on placebo by day five 1A+ Fusidic acid has less Gram-negative activity 1C</td>
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</table>
**ILLNESS** | **COMMENTS** | **DRUG** | **ADULT DOSE** | **DURATION OF TX**
---|---|---|---|---
**DENTAL INFECTIONS - derived from the Scottish Dental Clinical Effectiveness Programme 2011 SDCEP Guidelines**
- This guidance is not designed to be a definitive guide to oral conditions. It is for GPs for the management of acute oral conditions pending being seen by a dentist or dental specialist. GPs should not routinely be involved in dental treatment and, if possible, advice should be sought from the patient’s dentist, who should have an answer-phone message with details of how to access treatment out-of-hours, or NHS Direct on 0845 465 7900

**Mucosal ulceration and inflammation** *(simple gingivitis)*
- Temporary pain and swelling relief can be attained with saline mouthwash
- Use antiseptic mouthwash: clindamycin 240mg TDS; Chlorhexidine 0.12% (Do not use within 30 mins of toothpaste)
- The primary cause for mucosal ulceration or inflammation (aphthous ulcers, oral lichen planus, herpes simplex infection, oral cancer) needs to be evaluated and treated.

**Acute necrotising ulcerative gingivitis**
- Commence metronidazole 400mg TDS and refer to dentist for scaling and oral hygiene
- Use in combination with antiseptic mouthwash if pain limits oral hygiene

**Pericoronitis**
- Refer to dentist for irrigation & debridement
- If persistent swelling or systemic symptoms use metronidazole 500mg TDS
- Use antiseptic mouthwash if pain and trismus limit oral hygiene

**Dental abscess**
- Regular analgesia should be first option until a dentist can be seen for urgent drainage, as repeated courses of antibiotics for abscess are not appropriate
- Anti-infective antibiotics are preferred if there are signs of severe infection, systemic symptoms or high risk of complications
- Severe odontogenic infections; defined as cellulitis plus signs of sepsis, difficulty in swallowing, impending airway obstruction, Ludwig’s angina. Refer urgently for admission to protect airway, achieve surgical drainage and IV antibiotics
- The empirical use of cephalosporins, co-amoxiclav, clarithromycin, and clindamycin do not offer any advantage for most dental patients and should only be used if no response to first line drugs when referral is the preferred option

| If pus drain by incision, tooth extraction or via root canal
- Send pus for microbiology. *True penicillin allergy*: use clarithromycin or clindamycin if severe. *If spreading infection* (lymph node involvement, or systemic signs ie fever or malaise) ADD metronidazole 500mg TDS | Amoxicillin or Phenoxymethylpenicillin
*True penicillin allergy:* Clarithromycin
Severe infection add Metronidazole 500mg TDS or if allergy Clindamycin | 500 mg TDS
500 mg 1g QDS | Up to 5 days review at 3d
5 days
5 days

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- Regular analgesia should be first option until a dentist can be seen for urgent drainage, as repeated courses of antibiotics for abscess are not appropriate
- Anti-infective antibiotics are preferred if there are signs of severe infection, systemic symptoms or high risk of complications
- Severe odontogenic infections; defined as cellulitis plus signs of sepsis, difficulty in swallowing, impending airway obstruction, Ludwig’s angina. Refer urgently for admission to protect airway, achieve surgical drainage and IV antibiotics
- The empirical use of cephalosporins, co-amoxiclav, clarithromycin, and clindamycin do not offer any advantage for most dental patients and should only be used if no response to first line drugs when referral is the preferred option

| If pus drain by incision, tooth extraction or via root canal
- Send pus for microbiology. *True penicillin allergy*: use clarithromycin or clindamycin if severe. *If spreading infection* (lymph node involvement, or systemic signs ie fever or malaise) ADD metronidazole 500mg TDS | Amoxicillin or Phenoxymethylpenicillin
*True penicillin allergy:* Clarithromycin
Severe infection add Metronidazole 500mg TDS or if allergy Clindamycin | 500 mg TDS
500 mg 1g QDS | Up to 5 days review at 3d
5 days
5 days

**Mucosal ulceration and inflammation** *(simple gingivitis)*
- Temporary pain and swelling relief can be attained with saline mouthwash
- Use antiseptic mouthwash: clindamycin 240mg TDS; Chlorhexidine 0.12% (Do not use within 30 mins of toothpaste)
- The primary cause for mucosal ulceration or inflammation (aphthous ulcers, oral lichen planus, herpes simplex infection, oral cancer) needs to be evaluated and treated.

**Acute necrotising ulcerative gingivitis**
- Commence metronidazole 400mg TDS and refer to dentist for scaling and oral hygiene
- Use in combination with antiseptic mouthwash if pain limits oral hygiene

**Pericoronitis**
- Refer to dentist for irrigation & debridement
- If persistent swelling or systemic symptoms use metronidazole 500mg TDS
- Use antiseptic mouthwash if pain and trismus limit oral hygiene

**Dental abscess**
- Regular analgesia should be first option until a dentist can be seen for urgent drainage, as repeated courses of antibiotics for abscess are not appropriate
- Anti-infective antibiotics are preferred if there are signs of severe infection, systemic symptoms or high risk of complications
- Severe odontogenic infections; defined as cellulitis plus signs of sepsis, difficulty in swallowing, impending airway obstruction, Ludwig’s angina. Refer urgently for admission to protect airway, achieve surgical drainage and IV antibiotics
- The empirical use of cephalosporins, co-amoxiclav, clarithromycin, and clindamycin do not offer any advantage for most dental patients and should only be used if no response to first line drugs when referral is the preferred option
The following references were used when developing these guidelines:

This guidance was initially developed in 1999 by practitioners in South Devon, as part of the S&W Devon Joint Formulary Initiative, and Cheltenham & Tewkesbury Prescribing Group and modified by the PHLS South West Antibiotic Guidelines Project Team, PHLS Primary Care Co-ordinators and members of the Clinical Prescribing Sub-group of the Standing Medical Advisory Committee on Antibiotic Resistance. It was further modified following comments from Internet users. The guidance has been updated regularly as significant research papers, systematic reviews and guidance have been published. The Health Protection Agency works closely with the authors of the Clinical Knowledge Summaries.

Grading of guidance recommendations

The strength of each recommendation is qualified by a letter in parenthesis.

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<tr>
<th>Study design</th>
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<tr>
<td>Good recent systematic review of studies</td>
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<td>One or more rigorous studies, not combined</td>
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Clinical Knowledge Summaries for the NHS [www.cks.nhs.uk](http://www.cks.nhs.uk), BNF (No 58), SMAC report - The path of least resistance (1998), SDHCT Medical Directorate guidelines + GU medicine guidelines, Plymouth Management of Infection Guidelines project LRTI and URTI.

UPPER RESPIRATORY TRACT INFECTIONS


A no antibiotic prescribing strategy or a delayed antibiotic prescribing strategy should be negotiated for patients with the following conditions: acute otitis media, acute sore throat, common cold, acute rhinosinusitis, acute cough/acute bronchitis. Depending on patient preference and clinical assessment of severity, patients in the following specific subgroups can also be considered for immediate antibiotics in addition to the reasonable options of a no antibiotic strategy or a delayed prescribing strategy:

- bilateral acute otitis media in children under two years,
- acute otitis media in children with otorrhoea,
- acute sore throat/acute tonsillitis when three or four of the Centor criteria are present.

For all antibiotic prescribing strategies, patients should be given advice about the usual natural history of the illness, including the average total length of the illness (before and after seeing the doctor):

- acute otitis media: 4 days;
- acute sore throat/acute pharyngitis/acute tonsillitis: 1 week;
- common cold: 1½ weeks;
- acute rhinosinusitis: 2½ weeks;
- acute cough/acute bronchitis: 3 weeks.

Advice should also be given about managing symptoms, including fever (particularly analgesics and antipyretics).

When the delayed antibiotic prescribing strategy is adopted, patients should be offered the following:
- reassurance that antibiotics are not needed immediately because they are likely to make little difference to symptoms and may have side effects.
Influenza


Acute Sore Throat


2. Spinks A, Glasziou PP, Del Mar C. Antibiotics for sore throat. Cochrane Database of systematic reviews 2006, Issue 4.Art. No CD000023.DOI:10.1002/14651858.CD000023.pub3. (Review content up to date 24 November 2008). RATIONALE: This meta-analysis includes 27 RCT’s and 2,835 cases of sore throat. Without antibiotics 40% of sore throats resolve in 3 days and 90% in 7 days. Antibiotics do confer a marginal benefit: To resolve one sore throat at 3 days the NNT is 6 and at 7 days the NNT is 21. However, absolute benefits are modest, especially as the Number Needed to Harm for antibiotic use in respiratory infections is about 15.

3. Centor RM, Whitherspoon JM, Dalton HP, Brody CE, Link K. The diagnosis of strep throat in adults in the emergency room. Med Decision Making 1981;1:239-46. RATIONALE: Centor Criteria: History of fever; absence of cough; tender anterior cervical lymphadenopathy and tonsillar exudates. A low Centor score (0-2) has a high negative predictive value (80%) and indicates low chance of Group A Beta Haemolytic Streptococci (GABHS). A Centor score of 3-or-4 suggests the chance of GABHS is 40%. If a patient is unwell with a Centor score of 3-or-4 then the chance of developing Quinsy is 1:60.

4. Peterson I, Johnson AM, Islam A, Duckworth G, Livermore DM, Hayward AC. Protective effect of antibiotics against serious complications of common respiratory tract infections: retrospective cohort study with the UK General Practice Research Database. BMJ 2007;335:982-4. RATIONALE: This UK retrospective cohort study looked at the extent to which antibiotics prevent serious suppurative complications of self-limiting upper respiratory tract infections. To prevent an episode of Quinsy the NNT is of acute sore throat with antibiotics is >4000. This supports the recommendation that in the UK antibiotics should not be used to prevent suppurative complications of acute sore throat. Most patients with Quinsy develop the condition rapidly and don’t present first with an acute sore throat.

5. Kagan, B. Ampicillin Rash. Western Journal of Medicine 1977;126(4):333-335 RATIONALE: Amoxicillin should be avoided in the treatment of acute sore throat due to the high risk of developing a rash, when the Epstein Barr virus is present.

6. Lan AJ, Colford JM, Colford JMJ. The impact of dosing frequency on the efficacy of 10 day penicillin or amoxicillin therapy for streptococcal tonsillopharyngitis: A meta-analysis. Pediatr 2000;105(2):E19. RATIONALE: This meta-analysis provides the evidence that BD dosing with phenoxymethylpenicillin is as effective as QDS in treating GABHS.

7. Expert opinion is that phenoxymethylpenicillin should be dosed QDS for severe infections in order to optimise the therapeutic drug concentrations.

8. Schwartz RH, Wientzen RL Jr, Predreira F, Feroli EJ, Mella GW, Guandolo VL. Penicillin V for group A streptococcal pharyngotonsillitis. A randomized trial of seven vs ten days’ therapy. JAMA 1981 Oct 16;246(16):1790-5 RATIONALE: form. This RCT demonstrates that a 10 day course of oral phenoxymethylpenicillin is better than 7 days for resolution of symptoms and eradication of GABHS. In total, 210 middle-class paediatric patients (children aged 1-18 years) with positive group A streptococcal sore throat were admitted to the study. Of the remaining 191 patients available for analysis, 96 were randomly
9. Altamimi S, Khali A, Khalaiwa KA, Milner R, Pusic MV, Al Othman MA. Short versus standard duration antibiotic therapy for acute streptococcal pharyngitis in children. Cochrane Database of systematic reviews 2009, Issue 1. Art No.: CD004872. DOI: 10/1002/14651858.CD004872.pub2. RATIONALE: This recent meta-analysis shows short-course (including 5 days Clarithromycin) broad-spectrum antibiotics are as efficacious as 10-day-penicillin for sore throat symptom treatment and GABHS eradication. 10-day-phenoxymethylpenicillin remains the treatment of choice. Evidence suggests the use of broader spectrum antibiotics will drive the emergence of bacterial resistance; increase the risk of developing Clostridium difficile Associated Disease; and are associated with more adverse drug reactions. 5-days-clarithromycin should be reserved for those with true penicillin allergy.

Additional references:

Howie JGR, Foggio BA. Antibiotics, sore throats and rheumatic fever. BJGP 1983;35:223-224. RATIONALE: This Scottish retrospective study confirms the low incidence of Rheumatic Fever in the UK, (0.6 per 100,000 children per year). It would take 12 working GP life times to see one case of Rheumatic Fever. The risk of developing Rheumatic Fever was not reduced in this study by treating sore throats with antibiotics. This supports the recommendation that in the UK antibiotics should not be used to prevent non-suppurative complications of acute sore throat.

Taylor JL, Howie JGR. Antibiotics, sore throat and acute nephritis. BJGP 1983;33:783-86. RATIONALE: This study shows that Glomerulonephritis is a rare condition, (2.1 per 100,000 children per year) and that treating acute sore throat with antibiotics doesn’t prevent it occurring.

Maholtra-Kumar S, Lammens C, Coenen S, Van Herck K, Goossens H. Effect of azithromycin and clarithromycin therapy on pharyngeal carriage of macrolide-resistant streptococci in healthy volunteers: a randomised, double-blind, placebo controlled study. Lancet 2007;369:482-490. RATIONALE: This randomised, double blind, placebo controlled study showed both azithromycin and clarithromycin significantly increased the proportion of macrolide-resistant streptococci compared with the placebo at all points studied. Peaking at day 8 in the clarithromycin group (mean increase 50.0%, 95% CI 41.7–58.2; p<0.0001) and at day 4 in the azithromycin group (53.4%, 43.4–63.5; p<0.0001). The proportion of macrolide-resistant streptococci was higher after azithromycin treatment than after clarithromycin use, with the largest difference between the two groups at day 28 (17.4% difference, 9.2–25.6; p<0.0001). Use of clarithromycin, but not of azithromycin, selected for the erm (B) gene, which confers high-level macrolide resistance.


Acute Otitis Media

1. NICE 69: National Institute for Health and Clinical Excellence. Prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care. 2008. (Clinical guideline 69) RATIONALE: Acute Otitis Media: NICE 69 includes 3 trials that use a delayed-antibiotic strategy for treating AOM. Two USA studies used a 2-day-delayed antibiotic and the UK primary care study used a 3-day-delayed antibiotic.

2. Little P, Gould C, Williamson I, Moore M, Warner G, Dunleavy J. Pragmatic randomised controlled trial of two prescribing strategies for childhood acute otitis media. BMJ 2001;322:336-42 RATIONALE: This RCT makes two important observations: that parents tend to underestimate the amount of analgesia they’ve administered and that when recommending a no-antibiotic strategy it is all the more important to optimise analgesia.


4. Sanders S, Glasziou PP, Del Mar C, Rovers MM. Antibiotics for acute otitis media in children. Cochrane Database of Systematic Reviews 2004, Issue 1. Art. No.:CD000219.DOI:10.1002/14651858.CD000219 9pub2. (Content up to date 08.11.08) RATIONALE: Most (66%) of children are better in 24 hours and antibiotics have no effect. 80% of children are better in 2-7 days and antibiotics have a small effect (symptoms reduced by 16 hours), (RR 0.72; 95% CI 0.62 to 0.83). Antibiotics did not reduce tympanometry (deafness), perforation or recurrence. Vomiting, diarrhoea or rash was more common in children taking antibiotics (RR 1.37; 95% CI 1.09 to 1.76) with a Number Needed to Harm of 16.
5. Rovers MM, Glasziou P, Appelman CL, Burke P, McCormick DP, Damoiseaux RA, Little P, Lalloo U, Hoes AW. Predictors of pain and/or fever at 3 to 7 days for children with acute otitis media not treated initially with antibiotics: a meta-analysis of individual patient data. Pediatrics 2007;119(3):579-85 RATIONALE: The risk of prolonged illness was 2 times higher for children <2 years with bilateral AOM than for children with unilateral AOM. For this sub-group parents should believe that symptoms may persist for up to 7 days, and they should optimise analgesia use. The protective immunity against infections with encapsulated bacteria, such as the species that cause AOM, depends on the ability to produce specific antibodies against bacterial capsular polysaccharides, which is inadequate until 2 years of age. The anatomic features of the eustachian tubes and the nasopharynx also differ with age. Consequently, children under 2 years of age seem to be more susceptible to AOM.

6. Hoberman A, Paradise JL, Roockett HE, Shaikh N, Wald ER, Kearney DH, Colborn K, Kurs-Lasky M, Bhatnager S, Haralam MA, Zoffel LM, Jenkins C, Pope MA, Balentine TL, Barbadora KA. Treatment of acute otitis media in children under 2 years of age. NEJM 2011;364:105-115 This study included 291 children 6-23 months with otoscopically confirmed OM and compared co-amoxiclav to placebo. There was no significant difference in initial resolution of symptoms between co-amoxiclav and placebo (p=0.14). Sustained resolution of symptoms, was slightly higher for co-amoxiclav 20% by day 2, 41% by day 4, and 67% by day 7, as compared with 14%, 36%, and 53% with placebo (P = 0.04 for the overall comparison). At day 10-12 clinical results were less favourable in children with bilateral AOM (p=0.002), more bulging tympanic membrane compared to less (p<0.001), higher symptom scores at entry, (p=0.004, score >8 for fever, tugging ears, crying more, irritability, difficulty sleeping, less playful, eating less, where O=no symptoms, 1 a little , 2 A lot).


8. Rovers MM, Glasziou P, Appelman CL, Burke P, McCormick DP, Damoiseaux RA, Gaboury I, Little P, Hoes AW. Antibiotics for acute otitis media: a meta-analysis with individual patient data. Lancet 2006;368:1429-1435 RATIONALE: Note this is sub-analysis of data. In children <2 years old with bilateral AOM, 30% on antibiotics and 55% of controls had pain and/or fever at 3 to 7 days (RD -25%; 95% CI: -36, -14) and the NNT was 4 in children with otorhoea, 24% on antibiotics and 60% of controls had pain and/or fever at 3 to 7 days (RD-36%; 95% CI: -53, -19) and the NNT was 3.

9. Thompson PL, Gilbert RE, Long PF, Saxena S, Sharland M, Wong IC. Effect of antibiotics for otitis media on mastoiditis in children: a retrospective cohort study using the United Kingdom general practice research database. Pediatrics 2009;123(2):424-30 RATIONALE: Antibiotics halved the risk of mastoiditis, but GP’s would have to treat 4831 episodes of AOM to prevent one episode of mastoiditis. Although mastoiditis is a serious illness, most children make an uncomplicated recovery after mastoidectomy or IV antibiotics. (Incidence mastoiditis 0.15 per 1000 child years).


12. Macrolides concentrate intracellularly and so are less active against the extracellular H influenzae.

13. We recommend clarithromycin as it has less side-effects than erythromycin, greater compliance as twice rather than four times daily & generic tablets are similar cost. In children erythromycin may be preferable as clarithromycin syrup is twice the cost. Azithromycin has a greater half life in comparison to clarithromycin and erythromycin and thus provides more opportunity for resistant organisms to develop.


12. Kozyrskyj AL, Hildes Ripstein GF, Longstaffe SE, et al. Short-course antibiotics for acute otitis media. Cochrane Database Syst Rev 2000;(2):CD001095. RATIONALE: This review found that 5 days of antibiotic treatment was as effective as 10 days in otherwise healthy children with uncomplicated AOM.
MANAGEMENT OF INFECTION GUIDANCE FOR PRIMARY CARE

Acute Otitis Externa

1. Kaushik V, Malik T, Saeed SR. Interventions for acute otitis externa. Cochrane Database of Systematic Reviews 2010, Issue 1. Art. No.:CD004740. DOI: 10.1002/14651858.CD004740.pub2. RATIONALE: The best evidence we have to date. Includes 19 low quality RCT's only two of which are from primary care, and therefore probably included more severe or chronic cases. One big downside for primary care is that over half of the trials involved ear cleaning. The meta-analysis demonstrates topical treatments alone are adequate for treating most cases of AOE. Acetic acid was as effective and comparable to antibiotic/steroid for the first 7 days, but inferior after this point. It is important to instruct patients to use drops for at least one week, and to continue for up to 14 days if symptoms persist.

2. Thorp MA, Krunger J, Oliver S et al. The antibacteriological activity of acetic acid and Burow's solution as topical otological preparations. Journal of laryngology and Otology, Vol 112/10 (925-8). Oct 1998. There is little evidence to support the use of one agent over the other. Both have shown a similar efficacy compared to other topical treatments such as antibiotics and corticosteroids, although caution should be taken due to the lack of quality in these studies. Based on the fact that acetic acid is recommended as 1st line treatment for mild otitis externa whilst aluminium is for more resistant cases or extensive swelling, acetic acid's availability compared to aluminium acetate and that an ear wick requires specialist referral for insertion, acetic acid would seem to be a better first-line option. Although there are no trials of acetic acid versus placebo there are trials comparing its use to a topical antibiotic-corticosteroid combination they show equivalence. Only one study was found from a literature search which compared the efficacy between acetic acid and aluminium acetate (also known as Burow's solution). This was a small (n=20) in vitro study which compared activity of one, two and three percent acetic acid with Burow's solution (aluminium acetate 13%) on an agar plate with the following organisms; Pseudomonas aeruginosa, Staphylococcus aureus, Proteus mirabilis and Streptococcus pyogenes. The activity of each agent was ascertained by the size of the zone of inhibition of bacterial growth. Burow's solution showed significantly larger average zones of inhibition than acetic acid (p < 0.001). Both the two and three percent acetic acid as well as the Burow's solution were active against all organisms tested.

3. CKS (2007) Acute otitis externa. Clinical Knowledge Summaries. http://www.cks.nhs.uk/otitis_media_acute/management/scenario_acute_otitis_media_initial_presentation#.386925. Accessed 05.07.11. For acute acid CKS states that: "Acetic acid alone has not been compared with placebo for treating otitis externa in randomized controlled trials (RCTs). One double blind RCT found no statistically significant difference in efficacy between topical acetic acid and a topical antibiotic-corticosteroid combination at day 7. However, an antibiotic-corticosteroid combination was more effective after 14 and 21 days of treatment. A single blind RCT found that a topical acetic acid-antibiotic-corticosteroid combination was more effective than topical acetic acid alone after 14 days. The evidence comparing topical acetic acid-antibiotic-corticosteroid combinations with topical antibiotic-corticosteroid combinations is not of sufficient quality to determine which is more effective."

Whilst for aluminium acetate it states: "Aluminium acetate has not been compared with placebo for the treatment of otitis externa. Two randomized controlled trials (RCTs) found no clinically important difference between topical aluminium acetate and topical antibiotics with or without corticosteroid. However, these results should be interpreted with caution because of the very low methodological quality of the studies."

4. Rosenfeld RM, Brown L, Cannon R, Dolor RJ, Ganiats TG, Hannley M, Kokemueller P, Marcy M, Roland PS, Shiffman RN, Stinnett SS, Witsell DL, Singer M, Wasserman JM. Clinical Practice Guideline: Acute Otitis Externa. Otolaryngology – Head and Neck Surgery 2006;134(Suppl 4):S4-S23 RATIONALE: Up to 40% of patients with AOE receive oral antibiotics unnecessarily. The oral antibiotics in the trials were often inactive against P aeruginosa (incidence 36%) and S aureus (incidence 21%). Topical antibiotics such as neomycin have a broader spectrum of activity. When using topical antibiotics in this situation bacterial resistance is far less of a concern as the high concentration of the drug in the ear canal will generally eradicate all susceptible organisms, plus those with marginal resistance. Malignant Otitis Externa is an aggressive infection that affects the immunocompromised and elderly that requires prompt admission. Facial Nerve paralysis may be an early sign. GPs should refer severe cases, characterised by unremitting pain, cranial nerve deficits, perforated tympanic membrane or history of previous ear surgery.

5. Abelardo E, Pope L, Rajkumar K, Greenwood R, Nunez DA. A double-blind randomised clinical trial of the treatment of otitis externa using topical steroid alone versus topical steroid-antibiotic therapy. European Archives of Oto-rhino-laryngology: 2009;266(1):41-5 RATIONALE: A hospital outpatient RCT showing superiority of topical steroid-antibiotic therapy. The Cochrane Review 2010 also stated that ‘the evidence for steroid-only drops is very limited and as yet not robust enough to allow us to reach a conclusion or provide recommendations.’

6. NEOMYCIN SULPHATE with CORTICOSTEROID is suggested as topical antibiotic + steroid as it contains an antibiotic that is not used orally, Neomycin is active against Pseudomonas and Staphylococci the most common bacterial causes, plus there is the choice of four agents: Betnesol-N; Otomize; Otosporin and Predsol-N.

Produced 2000 – Latest Review November 2012; minor word amendments; recurrent UTI Feb 2013. Amendments 05.04.12: Meningitis 1.11.12: aims; principles of treatment; UTI; Chlamydia trachomatis. Added 1.11.12: Oral Candidiasis; Dental infections; Children doses. Next Review: November 2014
1. NICE 69: National Institute for Health and Clinical Excellence. Prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care. 2008. (Clinical guideline 69). Although there are no specific studies looking at delayed antibiotics for acute rhinosinusitis, NICE 69 recommends the same approach as for the other self-limiting respiratory tract infections. The 7-day delay is recommended as systematic review shows no benefit of antibiotics in rhinosinusitis within the first 7 days.

2. Young J, De Sutter A, Merenstein D, van Essen GA, Kaiser L, Varonen H, Williamson I, Bucher HC. Antibiotics for adults with clinically diagnosed acute rhinosinusitis: a meta-analysis of individual patient data. Lancet. 2008;371:908-914 RATIONALE: This meta-analysis included 2,547 pts from 9 Placebo-controlled trials. This primary care meta-analysis showed that 15 people would have to be given antibiotics before an additional patient was cured. The Odds Ratio of treatment effect for antibiotics relative to placebo was 1.37 (95% CI 1.13 to 1.66). A further sub-group analysis showed that those patients with purulent discharge were more likely to benefit from antibiotics with a NNT of 8. There was no additional benefit of antibiotics for: older patients; more severe symptoms or longer duration of symptoms.

3. Ahovuo-Saloranta A, Borisenko OV, Kovanen N, Varonene H, Rautakorpi UM, Williams Jr JW, Makela M. Antibiotics for acute maxillary sinusitis. Cochrane Database of Systematic Reviews 2008, Issue 2.Art. No.: CD000243. DOI:10.1002/14651858.CD000243.pub2. (Last assessed as up-to-date 28 May 2007) RATIONALE: This is a big clinical review (57 studies), that contained 6 placebo controlled trials.5 of these were in primary care and involved 631 patients. There was a slight statistical difference in favour of antibiotics compared with placebo (RR 0.66; 95%CI 0.65 to 0.84). Note cure/improvement rate was high in placebo group (80%) compared with the treatment group (90%). Antibiotics have a small treatment effect in patients with uncomplicated acute rhinosinusitis, in a primary care setting, for more than seven days.

4. Ah-See KW, Evans AS. Sinusitis and its management. BMJ 2007;334:358-61 RATIONALE: Adequate analgesia is becoming recognised as the first-line management for acute rhinosinusitis. Robust evidence for this is limited, as it is for analgesia use in general. This is partly due to the widespread accepted efficacy and tolerability of analgesics, that such research isn’t deemed necessary. We have to make do with the consensus expert opinion.

5. Thomas M, Yawn B, Price D, Lund V, Mullol J, Fokkens W. EPOS Primary Care Guidelines: European Position Paper on the Primary Care Diagnosis and Management of Rhinosinusitis and Nasal Polyps 2007 – a summary. Primary Care Respiratory Journal2008;17(2):79-89. RATIONALE: This primary care guideline states that: ‘Acute rhinosinusitis is an inflammatory condition that may be diagnosed on the basis of acute symptoms of nasal blockage, obstruction, congestion with or without facial pain or reduced smell; many episodes are self-limiting, but where symptoms persist or increase after 5 days, topical steroids may be considered to reduce the inflammatory reaction.’

6. Bartlett JG, Gorbach SL. Anaerobic infections of the head and neck. Otolaryngol Clin North Am 1976;9:655-78. RATIONALE: Anaerobes are an unusual finding in acute upper respiratory infections such as acute rhinosinusitis and acute otitis media, but are increasingly found in chronic disease. Co-amoxiclav is active against many anaerobes as well as S. pneumoniae and H. influenzae.

7. De Ferranti SD, Lonnidis JPA, Lau J, Anniger WV, Barza M. Are amoxicillin and folate inhibitors as effective as other antibiotics for acute sinusitis? BMJ1998;317:632-7 RATIONALE: On current evidence, no one class of antibacterial is more likely than another to cure patients with sinusitis.

8. Hansen JG, Schmidt H, Grinsted P. Randomised double-blind, placebo controlled trial of penicillin V in the treatment of acute maxillary sinusitis in adults in general practice. Scan J Prim Health Care2000;18:44-47. RATIONALE: This primary care study (133 patients) demonstrates that Penicillin V is more effective than placebo in the treatment of acute maxillary sinusitis, but only where there is pronounced pain.

9. Falagas ME, Karageorgopoulos DE, Grammatikos AP, Matthaiou DK. Effectiveness and safety of short vs. long duration of antibiotic therapy for acute bacterial sinusitis: a meta-analysis of randomised trials. British Journal of Clinical Pharmacology2009;67(2):161-71 RATIONALE: there was no difference in the comparison of short-course (3-7 days) with long-course treatment (6-10 days). The pragmatic interpretation of this meta-analysis is that a 7 day course is optimal.

10. In severe sinusitis a 1g dose may be considered to ensure bactericidal concentrations of amoxicillin in the sinuses. Lower concentrations may encourage the stepwise form of resistance that occurs with pneumococci.

Acute cough, bronchitis

1. NICE Clinical Guideline 69. Respiratory Tract Infections - antibiotic prescribing for self-limiting respiratory tract infections in adults and children in primary care. July 2008. Describes strategies for limiting antibiotic prescribing in self-limiting infections and advises in which circumstances antibiotics should be considered. A no antibiotic or a delayed antibiotic prescribing strategy should be agreed for patients with acute cough/chronic bronchitis. In the 2 RCTs included in the review, the delay was 7-14 days from symptom onset and antibiotic therapy. Patients should be advised that resolution of symptoms can take up to 3 weeks and that antibiotic therapy will make little difference to their symptoms and may result in side effects. Patients should also be advised to seek a clinical review if condition worsens or becomes prolonged. The evidence behind these statements is primarily from the studies referred to below.


5. Francis N et al. Effect of using an interactive booklet about childhood respiratory tract infections in primary care consultations on reconsidering and antibiotic prescribing: a cluster randomised controlled trial. BMJ. 2009;339:b2885 Utilising an information booklet during primary care consultations for children with RTIs significantly decreased antibiotic use (absolute risk reduction 21.3% (95%CI, 13.7-28.9 p<0.001). Reconsultation occurred in 12.9% of children in intervention group and 16.2% in control group (absolute risk reduction 3.3%, no statistical difference). There was no detriment noted to patient satisfaction in the intervention group.

6. Treatment of acute bronchitis available in Clinical Knowledge Summaries website: http://www.cks.library.nhs.uk/search/?&page=1&q=sore%20throat%20acute&site=0 Accessed 05.08.10.

Acute exacerbation of COPD


Hansen JG, Hoijbjerg T, Rosborg J. Symptoms and signs in culture proven acute maxillary sinusitis in general practice population. APMIS 2009;117(10):724-9 RATIONALE: We don’t yet have robust diagnostic criteria for those patients with acute rhinosinusitis that would most benefit from antibiotics. This primary care prospective cohort study of 174 patients shows: Fever >38 degrees; maxillary toothache and raised ESR were associated with S. pneumoniae and H. influenzae positive rhinosinusitis.

LOWER RESPIRATORY TRACT INFECTIONS

1. Woodhead M, Blasi F, Ewig S, Huchon G, Leven M, Ortgvist A, Schabert T, Torres A, can der Jeijden G, Werheij TJM. Guidelines for the management of adult lower respiratory tract infection. Eur Respir J 2005;26:1138-80. http://www.erj.ersjournals.com/content-by-date.0.shtml (Accessed 3rd January 2010). Appendices 1, 2 and 3 give a detailed account of the definitions of LRTI, the microbiological aetiologies of LRTI unspecified, community acquired pneumonia, exacerbations of COPD and bronchiectasis and the pharmacodynamic/pharmacokinetic properties of the antibiotics used to treat them. Strep. Pneumoniae remains the most commonly isolated pathogen in all of the above except in bronchiectasis. The infective agents causing exacerbations of COPD differ according to the severity of the underlying condition suggesting that more broad spectrum antibiotics are indicated in patients with severe COPD (FEV, < 50%). Antibiotic classes are discussed with reference to their mode of action in terms of time dependent or concentration dependent effect, their tissue penetration and whether they exert a post antibiotic effect. Other factors such as bioavailability are also considered.

Additional reference:


3. Chronic obstructive pulmonary disease. Management of COPD in adults in primary and secondary care. NICE Clinical Guideline 12 February 2004. [http://guidance.nice.org.uk/CG101](http://guidance.nice.org.uk/CG101). Accessed 05.08.10. A meta-analysis of nine trials found a small but statistically significant effect favouring antibiotics over placebo in patients with exacerbations of COPD. Effect size 0.22 (95% CI, 0.1 to 0.34). Four studies assessed whether there was a relationship between severity of exacerbation and the effectiveness of antibiotic use. Three of these studies suggest that the worse the COPD severity of exacerbation (lung function impairment (FEV1, PEFR), purulence of sputum) then the greater the degree of benefit from antibiotics.

4. El Moussaoui R, Roede BM, Speelman P, Bresser P, Prins JM, Bossuyt PMM. Short-course antibiotic treatment in acute exacerbations of chronic bronchitis and COPD: a meta-analysis of double-blind studies. *Thorax* 2008;63:415-22. In this meta-analysis they concluded that a short course of antibiotic treatment was as effective as the traditional longer treatment in patients with mild to moderate exacerbations of chronic bronchitis and COPD. The meta-analysis included 21 double-blind randomised clinical trials with 10,698 adults with exacerbation of COPD or chronic bronchitis, no antimicrobial therapy at the time of diagnosis and random assignment to antibiotic treatment for less than or equal to 5 days versus more than 5 days. At early follow-up (<25 days), the summary odds ratio (OR) for clinical cure with short treatment versus conventional treatment was 0.99 (95% CI 0.90 to 1.08). At late follow-up the summary OR was 1.0 (95% CI 0.91 to 1.10). No trials of amoxicillin or doxycycline were included in the meta-analysis; however there is no microbiological reason that a 5 day course of these agents would be inferior to a 5 day course of clarithromycin in acute exacerbations of COPD.

### Community-acquired pneumonia


### Meningitis


2. Saeed, K., 2011. ‘One for all’ concerns regarding NICE antibiotic guidelines on suspected bacterial meningitis! [letter] *Brit J Gen Pract* 2011;61:606-. Expert opinion is that in children or young people with suspected bacterial meningitis or meningococcal septicaemia, transfer to hospital is the priority, and that intravenous benzylpenicillin should be given at the earliest opportunity if a non-blanching rash is present, either in primary or secondary care. The NICE guideline development group recommended benzylpenicillin because they are aiming to cover only meningococcal septicaemia, which causes highest mortality, and it is the most frequently used antibiotic in primary care and they found no evidence to recommend an alternative antibiotic. Following prompt admission evaluation a more definitive choice of antimicrobials can be made. Although the scope of the NICE guideline is for children, it seems reasonable to extrapolate the advice to older age groups.

3. SIGN. Management of invasive meningococcal disease in children and young people. Scottish Intercollegiate Guidelines Network. 2008 [http://www.sign.ac.uk/guidelines/fulltext/102/index.html](http://www.sign.ac.uk/guidelines/fulltext/102/index.html). Accessed 05.08.10. Expert opinion is that parenteral antibiotics (either benzylpenicillin or cefotaxime) should be administered in children as soon as invasive meningococcal disease is suspected, and not delayed pending investigations.

### Urinary Tract Infections

**Notes**


3. NICE. Infection control. Prevention of healthcare-associated infections in primary and community care. The National Collaborating Centre for Nursing and Supportive Care and the Thames Valley University, 2003 http://guidance.nice.org.uk/CG2 Accessed 05.08.10. This guideline originally stated that prophylactic antibiotics were also indicated for people with heart valve lesions, sepal defects, patent ducus, or prosthetic valves. However, NICE state that this recommendation has been superseded by their 2008 guideline on prophylaxis of endocarditis, which states that prophylactic antibiotics are no longer required for people with those conditions requiring a catheter change.

**UTI**

1. SIGN. Management of suspected bacterial urinary tract infection in adults: a national clinical guideline. Scottish Intercollegiate Guidelines Network. 2006 http://www.sign.ac.uk/guidelines/fulltext/88/index.html Accessed 25.07.12. Diagnosis in women: expert consensus is that it is reasonable to start empirical antibiotics in women with symptoms of UTI without urine dipstick or urine culture. Diagnosis in men: a urine sample is recommended because UTI in men is generally regarded as complicated (it results from an anatomic or functional abnormality) and there are no studies on the predictive values of dipstick testing in men. Duration of treatment for men: there is no evidence to guide duration of treatment; expert consensus is that 7 days of antibiotics should be used because men are likely to have a complicating factor. Second line treatment: resistance is increasing to all antibiotics used to treat UTI, if possible antibiotic choice should be based on microbiology results.

2. Lutters M, Vogt-Ferrier NB. Antibiotic duration for treating uncomplicated, symptomatic lower urinary tract infections in elderly women. Cochrane Database of Systematic Reviews. 2002(3):CD001535. In this Cochrane Review Lutters and Vogt-Ferrier examined 4 studies comparing 3 days to 7 days treatment of ciprofloxacin or norfloxacin and 1 study comparing 3 days to 5 days treatment of trimethoprim in uncomplicated UTI in elderly women (age 60 or more). There was no significant difference in persistent UTI, clinical failure or re-infection rates but side-effects were higher in those given 7 days treatment.


4. Little P, Turner S, Rumsby K., Warner G, Moore M, Lowes JA, Smith H, Hawke C, Turner D, Leydon GM, Arscott A, Mullee M. Dipsticks and diagnostic algorithms in urinary tract infection: development and validation, randomised trial, economic analysis, observational cohort and qualitative study. Health Technology Assessment 2009;13(19):1-96. In women with uncomplicated UTI, the negative predictive value when nitrite, leucocytes, and blood are ALL negative was 76%. The positive predictive value for having nitrite and EITHER blood or leucocytes was 92%.

5. Grabe M, Bishop MC, Bjerkland-Johansen TE, Botto H, Cek M, Lobel B, Naber KG, Palou, J, Tenke, P, Wagenlehner F. Guidelines on Urological Infections. European Association of Urology 2009: 1-110. Diagnosis in men: a urine sample is recommended because UTI in men is generally regarded as complicated (it results from an anatomic or functional abnormality) and there are no studies on the predictive values of dipstick testing in men. Duration of treatment for men: there is no evidence to guide duration of treatment; expert consensus is that 7 days of antibiotics should be used because men are likely to have a complicating factor.

6. Although use of dipstick testing has not been well studied in men, it seems reasonable to extrapolate results from studies of dipstick testing in women with suspected UTI to men with only mild symptoms of UTI as contamination is likely to be lower.

7. Gossius G and Vorland L. The treatment of acute dysuria-frequency syndrome in adult women: Double-blind, randomized comparison of three-day vs ten-day trimethoprim therapy. Current Therapeutic Research, Clinical & Experimental 1985;37: 34-42. Two-weeks after completion of treatment, 94% of women using a 3-day course of trimethoprim achieved bacteriological cure compared with 97% of those using a 10-day course of trimethoprim (n = 135).
8. Christiaens TCM, De Meyere M, Verschragen G, Peersman W, Heytens S, De Maeseneer JM. Randomized controlled trial of nitrofurantoin versus placebo in the treatment of uncomplicated urinary tract infection in adult women. Brit J Gen Pract 2002;52:729-34. This small (n = 78) double-blind RCT found that nitrofurantoin 100mg qds for 3 days was more effective than placebo (NNT = 4.4, 95% CI 2.3 to 79).

9. The HPA and the Association of Medical Microbiologists recommend trimethoprim and nitrofurantoin as first-line empirical treatment for uncomplicated UTI in women and men because they are narrow-spectrum antibiotics that cover the most prevalent pathogens. Broad spectrum antibiotics (e.g. co-amoxiclav, pivmecillinam, quinolones and cephalosporins) should be avoided when narrow spectrum antibiotics remain effective, as they increase risk of Clostridium difficile, MRSA and resistant UTIs. The choice of trimethoprim or nitrofurantoin as first line varies by locality and is dependent on resistance rates to the two agents. Resistance to nitrofurantoin is generally lower however nitrofurantoin should not be used if upper UTI suspected or in patients with eGFR less than 60mL/minute/1.73m². Several guidelines recommend that nitrofurantoin should not be used to treat UTI in men. This is on the grounds that it can be difficult to exclude the possibility of prostatitis, and that nitrofurantoin is not present in therapeutic concentrations in prostatic secretions. However, these recommendations refer to UTI with fever or other signs of acute prostatitis, and neither guideline expressed concern that acute prostatitis would be likely in men with symptoms of lower UTI and without fever and other symptoms of prostatitis.

10. MeReC Bulletin. Modified-release preparations. 2000;11(4). Modified- release preparations can be used to reduce dosing frequency. Reduced dosing frequency (e.g from four times a day to twice a day) improves compliance.

11. Spencer RC, Moseley DJ, Greensmith MJ. Nitrofurantoin modified release versus trimethoprim or co-trimoxazole in the treatment of uncomplicated urinary tract infection in general practice. J Antimicrob Chemother 1994;33(Suppl A):121-9. This non-blinded RCT (n = 538) found that nitrofurantoin MR had equivalent clinical cure rates to co-trimoxazole, and trimethoprim. The rate of gastrointestinal adverse effects was similar between groups (7-8%).


13. Milo G, Katchman EA, Paul M, Christiaens T, Baerheim A, Leibovici L. Cure for antibiotics compared with placebo: OR 4.67 (95% CI 2.34 to 9.35; four RCTs, n = 1062).

14. Newell A, Bunting P, Anson K, Fox E. Multicentre audit of the treatment of uncomplicated urinary tract infection in women. Cochrane Database Review. The Cochrane Library 2006, Issue 2. http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD004682/pdf_fs.html Accessed 05.08.10. No difference in outcome between 3 day, 5 day or 10 day antibiotic treatment course for uncomplicated UTI in women (RR 1.06; 95% CI 0.88 to 1.28; 32 trials, n = 9605).

15. DTB. Risks of extended-spectrum beta-lactamases. Drug and Therapeutics Bulletin 2008;46(3):21-24. Extended spectrum beta-lactamases (ESBLs) are able to hydrolyse antibiotics that were designed to resist the action of older beta-lactamases. These organisms may be resistant to most antibiotics commonly used to treat UTI, such as trimethoprim, ciprofloxacin, co-amoxiclav, and all cephalosporins. Most ESBL-producing E coli are sensitive to nitrofurantoin.

16. Naber KG, Schito G, Botto H, Palou J, Mazzei T. Surveillance study in Europe and Brazil on clinical aspects and Antimicrobial Resistance epidemiology in Females with Cystitis (ARESC): implications for empiric therapy, European Urology 2008;54:1164-1175. In all countries, susceptibility rate to E. coli above 90% (p < 0.0001) was found only for fosfomycin, mecillinam, and nitrofurantoin.


Fosfomycin is not available commercially as a licensed product in the UK. Currently the only means of obtaining fosfomycin is to order from a “specials” supplier. There will be a delay in obtaining the product in the community setting and careful consideration needs to be given when prescribing and supplying to patients who may need treatment more urgently.

Brands: These include - MONURIL® (Zambon – Italy; Netherlands) and MONUROL® (Pharmazam – Spain USA, Hong Kong).
Nutritional interactions: Food intake can slow down the absorption of fosfomycin with, as a result, lower concentrations in the urine. Fosfomycin should, therefore, be administered while fasting or 2 or 3 hours before meals.

18. Martindale 30th (The Extra Pharmacopeia) and 36th Editions (The Complete Drug Reference). Concentrations of fosfomycin are maintained in the urine for 2 days. A single dose is therefore sufficient in uncomplicated UTI in women. A second dose is required at 3 days in men to maintain inhibitory concentrations to ESBLs in the urine for the 6-7 days recommended for treatment of UTI in men.

**UTI in pregnancy**

1. SIGN. Management of suspected bacterial urinary tract infection in adults: a national clinical guideline. Scottish Intercollegiate Guidelines Network. 2012 [http://www.sign.ac.uk/guidelines/fulltext/88/index.html](http://www.sign.ac.uk/guidelines/fulltext/88/index.html) SIGN Flow diagram for pregnant women. Accessed 10.09.12. MSU should be performed routinely at the first antenatal visit. If bacteriuria is reported, it should be confirmed with a second MSU. Dipstick testing is not sufficiently sensitive to be used for screening for bacteriuria in pregnant women.


It is important to ensure adequate treatment of maternal infections in pregnancy as failure to treat may lead to adverse maternal and fetal effects as a consequence of uncontrolled infection or fever. When considering treatment with antibacterial agents during pregnancy, the following factors should be considered: the severity of the maternal infection, the effects of any fever present on the pregnancy, the effects of failing to treat the mother, and the potential fetotoxicity of the drugs to be used. Where possible, the results of culture and sensitivity tests should be available before making a treatment choice.

**Penicillins, along with cephalosporins,** may be used in pregnancy if considered clinically appropriate. Exposure to penicillins at any stage of pregnancy would not usually be regarded as medical grounds for termination of pregnancy.

**Penicillins** – may be used at any stage in pregnancy if considered clinically appropriate.

**Cephalosporins** – may be used at any stage in pregnancy if considered clinically appropriate.

**Gentamicin** – limited data; systemic use may be considered if the clinical indication is strong. Topical use is not expected to be associated with an increased risk to the fetus.

**Trimethoprim** – risk of neural tube defects due to folate deficiency; folate supplementation is required if trimethoprim is prescribed in pregnancy.

**Metronidazole** – limited safety data; use may be considered if the clinical indication is strong.

**Quinolones** – limited safety data; use may be considered if the clinical indication is strong. If a quinolone is required, ciprofloxacin is the agent of choice in the class.

**Nitrofurantoin** – limited safety data; rare but severe adverse effects have been reported. Treatment with any antibiotic drug listed in this summary at any stage in pregnancy would not usually be regarded as medical grounds for termination of pregnancy. For advice on specific antibiotics in pregnancy please see the individual monographs.

If you are pregnant and require advice regarding exposure to antibiotics please contact your health care professional who can consult GP if symptoms worsen whilst awaiting supply.

**Accessed 10.09.12.**

Endorsed by:

Children


Amendments 05.04.12: Meningitis 1.11.12: aims; principles of treatment; UTI; Chlamydia trachomatis.

Added 1.11.12: Oral Candidiasis; Dental infections; Children doses. Next Review: November 2014

http://www.nice.org.uk/nicemedia/pdf/CG54fullguideline.pdf Accessed 05.08.10. Diagnosis and referral; expert opinion is that children under the age of 3 months with suspected UTI should be admitted; that imaging during the acute episode is only needed for atypical UTI or for children under the age of 6 months with UTI. Choice of antibiotics for lower UTI: NICE identified 3 RCTs comparing trimethoprim to other antibiotics for UTI in children, and one systematic review comparing short and long course of antibiotics for UTI in children that included studies assessing trimethoprim, nitrofurantoin and amoxicillin. The NICE guideline development group recommend trimethoprim, nitrofurantoin, amoxicillin, or cefalexin for empirical treatment of lower UTI in children. Duration of antibiotics for lower UTI; one systematic review found no difference in efficacy between short courses (2-4 days) and longer courses (7-14 days) of antibiotics in children with lower UTI. Upper UTI; one systematic review combined two studies of co-amoxiclav treatment for 10-14 days compared with IV antibiotic treatment. No difference in efficacy was found.


http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD001209/frame.html Accessed 05.08.10. Twenty three studies (3407 children) were eligible for inclusion. No significant differences were found in persistent kidney damage at six to 12 months (824 children: RR 0.80, 95% CI 0.50 to 1.26) or in duration of fever (808 children: MD 2.05, 95% CI -0.84 to 4.94) between oral antibiotic therapy (10 to 14 days of cefixime, cefixibuten or co-amoxiclav) and IV therapy (3 days) followed by oral therapy (10 days).

Acute pyelonephritis

1. Grabe M, Bishop MC, Bjerkland-Johansen TE, Botto H, Cek M, Lobel B, Naber KG, Palou, J, Tenke, P, Wagenlehner F. Guidelines on Urological Infections. European Association of Urology 2009: 1-110. Expert consensus is that admission should be arranged for more severe cases of acute uncomplicated pyelonephritis (e.g. dehydrated, cannot take oral medication, signs of sepsis).

2. The Health Protection Agency and the Association of Medical Microbiologists recommends that people with acute pyelonephritis are admitted if there is no response to antibiotics within 24 hours. Lack of response to treatment is likely to be due to antibiotic resistance. The complications of acute pyelonephritis can be life-threatening.

3. Talan DA, Stamm WE, Hooton TM, Moran GJ, Burke T, Iravani A, Reuning-Scherer J and Church DA. Comparison of ciprofloxacin (7 days) and trimethoprim-sulfamethoxazole (14 days) for acute uncomplicated pyelonephritis in women. A randomized trial. JAMA 2000;283:1583-90. This randomized double-blind controlled trial found that 7 days of ciprofloxacin 500 mg bd was as effective as 14 days co-trimoxazole. (E coli isolates were 100% susceptible to ciprofloxacin in this study.)

4. The Health Protection Agency and the Association of Medical Microbiologists recommend ciprofloxacin and co-amoxiclav for the empirical treatment of acute pyelonephritis. This is based on the need to cover the broad spectrum of pathogens that cause acute pyelonephritis, and their excellent kidney penetration. Although they are associated with an increased risk of Clostridium difficile, MRSA, and other antibiotic-resistant infections, this has to be balanced against the risk of treatment failure and consequent serious complications in acute pyelonephritis.

Recurrent UTI in non-pregnant women

1. Albert X, Huertas I, Pereiró I, Sanfeliúx J, Gosalves V, Perrotta C. Antibiotics for preventing recurrent urinary tract infection in non-pregnant women. Cochrane Database of Systematic Reviews 2004, Issue 3, http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD001209/frame.html Accessed 05.08.10. Nightly prophylaxis: pooled data from 10 RCTs of poor methodological quality calculated a Relative Risk of having one microbiological recurrence (MR) was 0.21 (95% CI 0.13 to 0.34), favouring antibiotic and the NNT was 1.85. over 6-12 months. But adverse effects do occur and 30% of women did not adhere to treatment. The benefit is lost as soon as prophylaxis stops. Post-coital antibiotics; one study of post-coital ciprofloxacin compared with ciprofloxacin prophylaxis found no significant difference between regimens on the rate of UTIs.

2. Stapleton A, Latham RH, Johnson C, Stamm WE. Postcoital antimicrobial prophylaxis for recurrent urinary tract infection. A randomized, double-blind, placebo-controlled trial. JAMA 1990;264(6):702-706. This small (n = 27) RCT found that the relative risk of symptomatic recurrence was lower with post-coital co-trimoxazole (RR 0.15, 95% CI 0.04 to 0.58). Adverse event rates were low and not significantly different between antibiotic and placebo.

3. Grabe M, Bishop MC, Bjerkland-Johansen TE, Botto H, Cek M, Lobel B, Naber KG, Palou, J, Tenke, P, Wagenlehner F. Guidelines on Urological Infections. European Association of Urology 2009: 1-110. Standby antibiotics; expert opinion, based on one open prospective trial, is that standby antibiotics may be suitable if the rate of recurrences is not too common. Post-coital antibiotics; expert opinion is that the same antibiotics and same doses as for nightly prophylaxis can be used as a stat dose for post-coital prophylaxis of UTI.
4. Cranberry juice has been found to potentially prevent infection by interfering with the attachment of bacteria to urethelial cells. There are many other compounds found in cranberries that have yet to be explored for their potential adherence activity, but A-type proanthocyanidins (PACs) have been shown to potentially inhibit the adherence of P-fimbriated Escherichia coli to the urogenital mucosa. Without adhesion, E.coli cannot infect the mucosal surface of the urinary tract.

There have been two recent systematic reviews examining the evidence for cranberry products for recurrent UTI. A 2012 Cochrane review of 24 studies (4473 participants) found a small trend towards fewer urinary tract infections in people taking cranberry juice or other products compared to placebo or no treatment but this was not significant (Jepson et al., 2012). Chi-Hung et al (Arch Intern Med 2012) examined 10 trials (1494 subjects, 9 community based): cranberry-containing products were significantly more effective in women with recurrent UTIs (RR, 0.53; 95% CI, 0.33-0.83) (I² = 0%), female populations (RR, 0.49; 95% CI, 0.34-0.73) but there was substantial heterogeneity across trials.

Many people in the Cochrane review studies stopped drinking the juice, suggesting it may be difficult to continue long term. Cranberry capsules may be more convenient than juice and high strength capsules may be most effective.

Thus women should be advised about the relative benefits and risks of daily prophylactic antibiotics, versus post-coital antibiotics, versus stand by antibiotics and cranberry products, so they can make an informed decision. Advise patients taking warfarin to avoid taking cranberry products unless the health benefits are considered to outweigh any risks.

Chi-Hung W, Cheng-Chung F, Nai-Chuan C, Shi-Hung Liu S, Ping-Hsun Y, Tao-Yu W, et al. Cranberry-containing products for prevention of Urinary Tract Infections in susceptible populations. Arch Intern Med 2012; 172(13): 988-996. This systematic review with meta-analysis of randomised controlled trials included 1494 subjects in the qualitative analysis in 10 review trials, with all but one of the trials following subjects living in the community. Administration of cranberry-containing products differed significantly in form, daily dosage, PAC content, and dosing frequency. Results: cranberry-containing products seemed to be more effective in women with recurrent UTIs (RR, 0.53; 95% CI, 0.33-0.83) (I² = 0%), female populations (RR, 0.49; 95% CI, 0.34-0.73) (I² = 34%), children (RR, 0.33; 95% CI, 0.16-0.69) (I² = 0%), cranberry juice users (RR, 0.47; 95% CI, 0.30-0.72) (I² = 2%), and people using cranberry-containing products more than twice daily (RR, 0.58; 95% CI, 0.40-0.84) (I² = 18%). The results suggest that cranberry-containing products are associated with protective effect against UTIs. However, this result should be interpreted in the context of substantial heterogeneity across trials.


This review identified 24 studies (4473 participants) comparing cranberry products with control or alternative treatments. There was a small trend towards fewer UTIs in people taking cranberry product compared to placebo or no treatment but this was not a significant finding. Many people in the studies stopped drinking the juice, suggesting it may not be an acceptable intervention. In the long term cranberry products (such as tablets or capsules) were also ineffective (although had the same effect as taking antibiotics), possibly due to lack of potency of the ‘active ingredient’.

However, four of the five studies in women with recurrent UTI (594 participants) which included a placebo group provided data that could be combined in a meta-analysis (Kontikari 2001; Barbosa-Cesnik 2011; Stothers 2002; Sengupta 2011). Results showed a small, non-significant reduction in risk of repeat symptomatic UTI with cranberry treatment compared to placebo or no treatment (RR 0.74, 95%CI 0.42 to 1.31). Two studies in women with recurrent UTI (McMurdo 2009; NAPRUTI Study 2011) and one study in children (Uberos 2010) compared cranberry product with antibiotic prophylaxis. All three studies used either cranberry capsules or syrup, rather than cranberry juice. Analysis of the two studies in women showed that cranberry product compared to antibiotic were equally as effective in reducing the risk of repeat UTI in women (RR 1.31, 95% CI 0.85 to 2.02) The study in children also showed that the cranberry product were equally as effective in reducing the risk of repeat symptomatic UTI compared to antibiotics (RR 0.69, 95% CI 0.32 to 1.31).

*MSU for all men: acute prostatitis is a severe illness. It is important that an MSU is sent for culture and sensitivities to ensure that an appropriate antibiotic is used. Treatment regimens: there are no randomized controlled trials of quinolones or trimethoprim for the treatment of prostatitis. Expert opinion is that, for men with acute prostatitis who are suitable for oral antibiotic treatment, ciprofloxacin 500mg BD for 28 days or ofloxacin 200mg BD for 28 days will provide sufficient levels within the prostate gland. Expert opinion is that trimethoprim 200mg BD for 28 days is a suitable alternative for men who are intolerant or allergic to quinolones. Duration of treatment: the optimum duration of treatment is unknown. Expert opinion is that a 4-week course of antibiotics is required to reduce the risk of developing chronic bacterial prostatitis.*

2. Micromedex. Drugdex drug evaluations. Thompson Healthcare. 2009. *Trimethoprim reaches good concentrations in prostatic tissue (peak prostate concentration was reported to be 2.3 mcg/g 280 minutes after an oral dose compared with serum levels of 2.2mcg/mL at 125 minutes after an oral dose). Ciprofloxacin reaches high concentrations in prostatic fluid, often exceeding serum levels (at 2 to 4 hours following oral administration, prostatic fluid levels ranged from 0.02 to 5.5 mcg/mL compared with serum levels of 1 to 2.5 mcg/mL). Ofloxacin also reaches high concentrations in prostatic fluid (at 1 to 4 hours following oral administration prostate guide levels ranged from 3.22 to 4.25 mcg/g.*

**GASTRO-INTESTINAL TRACT INFECTIONS**

**Oral candidiasis**


**Eradication of Helicobacter pylori**

1. NICE. Dyspepsia: managing dyspepsia in adults in primary care. National Institute for Health and Clinical Excellence. August 2004 www.nice.org.uk/nicemedia/pdf/CG017fullguideline.pdf Accessed 05.08.10. NICE give guidance on when to consider *H pylori* test and treat in primary care. First-line *H pylori* eradication: NICE recommend a twice daily full-dose PPI plus clarithromycin 250mg bd and metronidazole 400mg bd, or a PPI plus clarithromycin 500mg bd plus amoxicillin 1g bd. Second-line *H pylori* eradication: NICE recommend that a regimen is used that does not include the antibiotics given previously. Duration of treatment: although 14-day triple therapy gives almost a 10% higher eradication rate, the absolute benefit of *H pylori* therapy is modest in NUD and undiagnosed dyspepsia and the longer duration of therapy does not appear cost effective. In patients with PUD increasing the course to 14 days also gives a nearly 10% higher eradication rate, but does not appear cost effective. MALToma: expert opinion is that for MALT lymphoma, the increased efficacy of a 14-day regimen will reduce the need for chemotherapy and/or gastric resection.


3. Moayyedi P, Sos S, Deeks JJ, Delaney B, Harris A, Innes M, Oakes R, Wilson S, Roafle A, Bennett C, Forman D. Eradication of *Helicobacter pylori* for non-ulcer dyspepsia. The Cochrane library 2006. Issue 2 http://mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD002096/frame.html Accessed 05.08.10. Pooled data from 17 RCTS (n = 3566) found there was a 10% relative risk reduction in dyspepsia symptoms in people with non-ulcer dyspepsia randomized to receive *H pylori* eradication (95% CI 6% to 14%) compared to placebo. The NNT to cure one case of dyspepsia was 14 (95% CI 10 to 25).

4. Delaney BC, Qume M, Moayyedi P, Logan RFA, Ford AC, Elliott C, McNulty C, Wilson S, Hobbs FDR. Helicobacter pylori test and treat versus proton pump inhibitor in initial management of dyspepsia in primary care: multicentre randomised controlled trial (MRC-CUBE trial). BMJ 2008;336:651-654. At 12 months, there were no significant differences in QALYs, costs, or dyspeptic symptoms between the group assigned to initial *H pylori* test and treat and the group assigned to initial acid suppression (n = 699).

5. Fischbach L and Evans EL. Meta-analysis: the effect of antibiotic resistance status on the efficacy of triple and quadruple first-line therapies for *Helicobacter pylori*. Aliment Pharmacol Ther 2007;26:343-357. Pooled data found that the efficacy of a PPI + clarithromycin + metronidazole was reduced more by resistance to clarithromycin than by

7. Luther J, Higgins PDR, Schoenfield PS, Moayyedi P, Vakil N, Chey WD. Empiric quadruple vs. triple therapy for primary treatment of Helicobacter pylori infection: systematic review and meta-analysis of efficacy and tolerability. Am J Gastroenterol 2010;105:65-73. Pooled data from 9 RCTs (n = 1679) found that eradication rates were comparable between clarithromycin triple therapy (77%) and bismuth-containing quadruple therapy (78%). Most trials of 7-10 days duration.

8. The Health Protection Agency recommends that oxytetracycline is not substituted for tetracycline hydrochloride as part of the quadruple therapy regimen. Oxytetracycline is thought to have different mucus penetration properties to tetracycline hydrochloride. In addition, the treatment studies have been done with tetracycline hydrochloride. If third line treatment is required, clinicians may also consider changing the PPI to rabeprazole, as it has a different metabolism to the other PPIs, which may be metabolised rapidly in some patients, causing treatment failure.

9. Fuccio L, Minardi ME, Zagari RM, Grilli D, Magrini N, Bazzoli F. Meta-analysis: duration of first-line proton-pump inhibitor based triple therapy for Helicobacter pylori eradication. Annals Internal Medicine 2007; 147: 553-562. Pooled data found that extending the course of triple therapy from 7 to 14 days increased eradication rates only by about 5% (no statistically significant difference). The authors concluded that this is unlikely to be a clinically useful difference.


Infectious diarrhoea


3. The Health Protection Agency and Association of Medical Microbiologists recommend that, if campylobacter is strongly suspected as the cause of diarrhoea, consider empirical treatment with clarithromycin. Quinolones are not recommended because there is increasing resistance of campylobacter to quinolones, and broad spectrum antibiotics such as quinolones are not recommended for empirical therapy because they are associated with an increased risk of Clostridium difficile, MRSA, and resistant UTIs.


Clostridium difficile

1. DH and HPA. Clostridium difficile infection: how to deal with the problem. 2009. Department of Health and the Health Protection Agency. www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_093220 Accessed 05.08.10. Metronidazole is recommended for first- or second-episodes of C. difficile infection because it is cheaper than oral vancomycin and there are concerns that overuse of vancomycin will result in the selection of vancomycin-resistant enterococci. Oral vancomycin is preferred for severe C. difficile infection because of relatively high failure rates of metronidazole in recent reports, and a slower clinical response to metronidazole compared with oral vancomycin treatment.

2. Linsky A, Gupta K, Lawler EV, Fonda JR, Hermos JA. Proton pump inhibitors and risk for recurrent Clostridium difficile infection. Arch Intern Med 2010;170:772-778. This cohort study found that PPI use during incident C difficile treatment was associated with a 42% risk of recurrence.
management of infection guidance for primary care

3. Belmares J, Gerdig DN, Parada JP, Miskevics S, Weaver F, Johnson S. Outcome of metronidazole treatment for Clostridium difficile disease and correlation with a scoring system. J Infect 2007;55:495-501. This retrospective review of 102 patients given a 5-day course of metronidazole for clostridium difficile infection found that 70.3% responded by the end of the 5-day course. Twenty-one of the remaining 30 patients eventually responded to metronidazole, but needed longer treatment courses.

Traveller’s diarrhoea

1. Dupont HL. Systematic review: prevention of travellers’ diarrhoea. Aliment Pharmacol Ther 2008;27:741-51. Expert opinion is that people travelling to a high-risk area whose condition could be worsened by a bout of diarrhoea may be considered for standby antibiotics.

2. Centres for Disease Control and Prevention – Travellers’ Health: Yellow Book. http://www.cdc.gov/travel/yellowbook/Ch4-Diarrhea.aspx Accessed 05.08.10. High-risk countries are defined as most of Asia, the Middle-East, Africa, Mexico, Central and Southern America. Expert opinion is that bismuth subsalicylate (Pepito-Bismol) can be used for prophylaxis: one trial found it reduced the incidence of traveller’s diarrhoea from 40% to 14%. However, adverse effects are common and, due to its salicylate content, bismuth subsalicylate has several contraindications.


Threadworm

1. CKS (2007) Threadworm. Clinical Knowledge Summaries. http://www.cks.nhs.uk/search?&page=1&q=threadworm&site=0 Accessed 05.08.10. There is only limited evidence regarding the two products licensed for the treatment of threadworm in the UK. Mebendazole is recommended first line based on expert opinion and its relatively better safety profile compared with piperazine. Piperazine is licensed only from 3 months of age, and although the BNF recommends off-label use of mebendazole for children aged 6 months and over, it does not recommend it for infants under 6 months of age. Expert opinion is that strict hygiene methods for 6 weeks can be used as an alternative treatment in those who cannot take mebendazole or piperazine. This is based on the life cycle of the threadworm (adults survive for about 6 weeks) and the long viability of eggs (up to 2 weeks).

Genital Tract Infections

STI screening


Chlamydia trachomatis


3. BASHH. UK National Guidelines for the Management of Genital Tract Infection with Chlamydia trachomatis. British Association for Sexual Health and HIV. 2006 http://www.bashh.org/documents/61/61.pdf Accessed 05.08.10. Treatment of partners: partners should also be treated for C trachomatis infection. Re-testing: expert opinion is that a test of cure is not routinely recommended, but should be performed in pregnancy, or where non-compliance or re-exposure are suspected. The higher rate of positive tests after treatment during pregnancy is attributed to either less efficacious treatment regimen, non-compliance, or re-infection.


Endorsed by: Royal College of General Practitioners
4. Lau CY, Qureshi AK. Azithromycin versus doxycycline for genital chlamydial infections: a meta-analysis of randomised controlled trials. Sexually transmitted diseases. 2002;29:497-502. Pooled data (12 RCTs, n = 1543) found that microbiological cure was achieved in 97% of people taking azithromycin and 98% of those taking doxycycline, p = 0.296; no significant difference.

5. Brocklehurst P, Rooney G. Interventions for treating genital Chlamydia trachomatis infection in pregnancy. Cochrane Database of Systematic Reviews 1998, Issue 4, http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD000054/frame.html Accessed 05.08.10. Pooled data from four RCTs found that 8% of women taking azithromycin (11/145) failed to achieve microbiological cure compared with 19% of women taking erythromycin (27/145); OR 0.38, 95% CI 0.19 to 0.74. Pooled data from three RCTs found that 9% of women taking amoxicillin (17/199) failed to achieve microbiological cure compared with 15% of women taking erythromycin (28/191); OR 0.54, 95% CI 0.28 to 1.02.

6. UKTIS. The treatment of infections in pregnancy. National Teratology Information Service. 2012. (Tel: 0844 892 0909, www.toxbase.org) Accessed 10.09.12. Azithromycin: There are few published data on the use of azithromycin in human pregnancy however the currently available data do not indicate that the use of azithromycin in pregnancy is associated with an increased risk of malformations. An increased incidence of cardiovascular defects and pyloric stenosis have been suggested for macrolides as a class, although causality has not been established conclusively. Erythromycin: Erythromycin is a broad spectrum macrolide antibiotic. The majority of studies do not support an association between erythromycin exposure and any malformation or any adverse fetal effect, however associations have been made with an increased incidence of cardio vascular defects and pyloric stenosis, although causality has not been conclusively established. Amoxicillin: there is no evidence to suggest that penicillins are associated with an increased risk of malformations or other forms of fetal toxicity in human pregnancy.

7. GRASP Steering Group. GRASP 2008 report: trends in antimicrobial resistant gonorrhoea. Health Protection Agency, 2009. http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/Gonorrhoea/AntimicrobialResistance/ (Accessed 7th July 2010). Ciprofloxacin resistance is now endemic in England and Wales, accounting for 28% of all gonorrhoea isolates tested in 2008. The Health Protection Agency and the Association of Medical Microbiologists had said that, for practical issues of administration in primary care, a stat dose of oral cefixime 400mg could be substituted for IM ceftriaxone. However, resistance to cefalosporins is increasing and treatment failures have been reported with cefixime; therefore, if gonorrhoea is suspected, IM ceftriaxone is the cephalosporin of choice.

8. Ross IDC, Cronjé HS, Paszkowski T, Rakoczi I. Moxifloxacin versus ofloxacin plus metronidazole in uncomplicated pelvic inflammatory disease: results of a multicentre, double blind, randomised trial. Sex Transm Infect 2006;82(6):446-51. This trial in 564 patients with uncomplicated PID in hospitals from 13 countries, compared oral metronidazole 500mg twice daily with either oral ofloxacin 400mg twice daily or moxifloxacin 400mg once daily. Clinical resolution with both regimens was 90% and bacteriological cure was similar. Metronidazole is included in the regimen to improve the coverage for anaerobic bacteria. Anaerobes are of relatively greater importance in patients with severe PID. Ofloxacin and moxifloxacin should be avoided in patients who are at high risk of gonococcal PID because of increasing quinolone resistance in the UK (eg when the patient’s partner has gonorrhoea, in clinically severe disease, following sexual contact abroad). Quinolones should also be avoided as first line empirical treatment for PID in areas where >5% of PID is caused by quinolone resistant Neisseria gonorrhoeae.

9. Ison CA, Mouton JW, Jones K. Which cephalosporin for gonorrhoea? Sex Transm Infect 2004;80:386-88. This study used previously published pharmacokinetic data on cefixime, ceftriaxone and cefuroxime to model the length of time tissue concentrations to these drugs would be above the MIC90 (concentration needed to kill 90% of gonorrhoea isolates). Cefuroxime concentrations are too low. Ceftriaxone attains the optimal concentrations to prevent the development of step-wise mutations and resistance in Neisseria gonorrhoeae.

10. British Association for Sexual Health and HIV.


- 2005 United Kingdom National Guideline for the Management of Pelvic Inflammatory Disease. http://www.bashh.org/documents/118/118.pdf Accessed 07.10.10 Recommended regimens: the recommended regimens for outpatient management are either ofloxacin plus metronidazole for 14 days, or a stat dose of IM ceftriaxone plus metronidazole and doxycycline for 14 days. Ofloxacin should be avoided in women who are at high risk of gono coccal PID, because of increasing quinolone resistance in the UK. Treatment of partners: partners should be screened for gonorrhoea and chlamydia.


This systematic review identified 34 trials of antibiotic treatment for PID. Most studies were small, open-label, and of poor methodological study. One small trial was found that compared oral ofloxacin plus metronidazole with clindamycin plus gentamicin. The cure rate was 15/15 for ofloxacin plus metronidazole plus 17/18 for clindamycin plus gentamicin. The systematic review found one trial of ceftriaxone plus doxycycline, two trials of cefoxitin plus probenecid and doxycycline, and three trials of cefoxitin plus doxycycline compared to other antibiotics. Meta-analysis of these six studies found no difference in cure rates between IM ceftriaxone plus doxycycline and the comparator antibiotics.

12. RCOG. Management of Acute Pelvic Inflammatory Disease. Green Top Guideline No.32. Royal College of Obstetricians & Gynaecologists. 2008. www.rcog.org.uk (Accessed 30th December 2009) Recommended regimens: the recommended regimens are broad spectrum to cover N. gonorrhoea, C. trachomatis, and anaerobes. For outpatient management, either ofloxacin plus metronidazole for 14 days, or a stat dose of IM cefuroxime plus doxycycline and doxycycline for 14 days are recommended. Broad-spectrum treatment is warranted in PID because of the consequences of untreated infection (ectopic pregnancy, infertility, pelvic pain). Cefoxitin has a better evidence base for the treatment of PID than ceftriaxone, but it is not readily available in the UK. Ceftriaxone is therefore recommended. Although the combination of doxycycline and metronidazole (without IM ceftriaxone) has previously been used in the UK to treat PID, there are no clinical trials that adequately assess its effectiveness and its use is not recommended. Replacing intramuscular ceftriaxone with an oral cephalosporin (eg cefixime) is not recommended because there is no clinical trial evidence to support its use, and tissue levels are likely to be lower which might impact on efficacy. Reports of decreasing susceptibility of Neisseria gonorrhoeae to cephalosporins also supports the use of parenteral based regimens at a dose of 500mg ceftriaxone when gonococcal PID is suspected (to maximise tissue levels and overcome low resistance).


Ciprofloxacin resistance is now endemic in England and Wales, accounting for 28% of all gonorrhoea isolates tested in 2008. The Health Protection Agency and the Association of Medical Microbiologists had said that, for practical issues of administration in primary care, a stat dose of oral cefixime 400mg could be substituted for IM ceftriaxone. Resistance to ceftriaxone is increasing and treatment failures have been reported with ceftriaxone; therefore, if gonorrhoea is suspected, IM ceftriaxone is the cephalosporin of choice.

14. Ross JDC, Cronjé HS, Paszkowski T, Rakoczi I. Moxifloxacin versus ofloxacin plus metronidazole in uncomplicated pelvic inflammatory disease: results of a multicentre, double blind, randomised trial. Sex Transm Infect 2006;82(6):446-51. This trial in 564 patients with uncomplicated PID in hospitals from 13 countries, compared oral metronidazole 500mg twice daily with either oral ofloxacin 400mg twice daily or moxifloxacin 400mg once daily. Clinical resolution with both regimens was 90% and bacteriological cure was similar. Metronidazole is included in the regimen to improve the coverage for anaerobic bacteria. Anaerobes are of relatively greater importance in patients with severe PID. Ofloxacin and moxifloxacin should be avoided in patients who are at high risk of gonococcal PID because of increasing quinolone resistance in the UK (eg when the patient’s partner has gonorrhoea, in clinically severe disease, following sexual contact abroad). Quinolones should also be avoided as first line empirical treatment for PID in areas where >5% of PID is caused by quinolone resistant Neisseria gonorrhoeae.

15. Ison CA, Mouton JW, Jones K. Which cephalosporin for gonorrhoea? Sex Transm Infect 2004;80:386-88. This study used previously published pharmacokinetic data on cefixime, ceftriaxone and cefuroxime to model the length of time tissue concentrations to these drugs would be above the MIC90 (concentration needed to kill 90% of gonorrhoea isolates). Cefuroxime concentrations are too low. Ceftriaxone attains the optimal concentrations to prevent the development of step-wise mutations and resistance in Neisseria gonorrhoea.


Vaginal Candidiasis

1. Nurbhai M, Grimshaw J, Watson M, Bond CM, Mollison JA, Ludbrook A. Oral versus intravaginal imidazole and triazole anti-fungal treatment of uncomplicated vulvovaginal candidiasis (thrush). Cochrane Database of Systematic Reviews 2007, Issue 4. http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD002845/frame.html Accessed 05.08.10. No statistically significant differences were observed in clinical cure rates of antifungals administered by the oral or the vaginal route. At short-term follow-up, 74% cure was achieved with oral treatment and 73% cure with intra-vaginal treatment (OR 0.94, 95% CI 0.75 to 1.17).

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flucanazole (150 mg as a single dose) show no increased incidence of spontaneous abortions or malformations and no pattern of defects. However, there may be an increased risk of malformations associated with high dose chronic therapy (>400 mg/day). First-line treatment of candidal infection in pregnancy is with a topical imidazole such as clotrimazole. Flucanazole (150 mg as a single dose) may be a suitable second-line treatment if clotrimazole is ineffective.

3. Young GL, Jewell D. Topical treatment for vaginal candidiasis (thrush) in pregnancy. Cochrane Database of Systematic Reviews 2001, Issue 4. http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD000225/frame.html Accessed 05.08.10. This Cochrane review found that topical imidazole appears more effective than nystatin at treating vaginal candidiasis in pregnancy. In addition, treatment for only four days was less effective than treatment for seven days (OR 11.7, 95% CI 4.21 to 29.15).


5. The Health Protection Agency and the Association of Medical Microbiologists recommend 6 nights treatment with clotrimazole 100mg pessaries during pregnancy because this is the quantity in one original pack of clotrimazole 100 mg pessaries.

Bacterial vaginosis

1. Joesoef MR, Schmid GP, Hillier SL. Bacterial vaginosis: review of treatment options and potential clinical implications for therapy. Clin Infect Dis 1999;28(suppl 1):S57-S65. Pooled data from five RCTs found no significant difference between cumulative cure rates 5-10 days after finishing treatment for metronidazole 400 mg BD for 7 days (86%), intravaginal metronidazole 3g BD for 5 days (81%) or intravaginal clindamycin 5g at night for 7 days (85%).

2. McDonald HM, Brocklehurst P, Gordon A. Antibiotics for treating bacterial vaginosis in pregnancy. Cochrane Database of Systematic Reviews 2007, Issue 1. http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD000262/frame.html Accessed 05.08.10. Pooled data from 10 RCTs indicated that both oral and intravaginal antibiotics are effective at eradicating bacterial vaginosis in pregnant women. Oral antibiotics compared with placebo (seven trials, n = 3244) OR 0.15, 95% CI 0.13 to 0.17. Intravaginal antibiotics compared with placebo (three trials, n = 1113) OR 0.27, 95% CI 0.21 to 0.35.

3. Joesoef MR, Schmid GP. Bacterial vaginosis: review of treatment options and potential clinical implications for therapy. Clin Infect Dis 1995;20(suppl 1):S72-S79. The 2g single dose is less effective than the 7-day course at 4-week follow up. When data from studies that only directly compared the two dose regimens were pooled, the cumulative cure rates 3-4 weeks after completion of treatment were 62% for the single-dose regimen and 82% for the 7-day regimen (p < 0.005).

4. UKTIS. Use of metronidazole in pregnancy. The UK Teratology Information Service. 2008. (Tel: 0844 892 0909, www.toxbase.org) Accesses 05.08.10. The available data (almost exclusively based on oral treatment) does not indicate an increased risk of adverse fetal effects associated with metronidazole use during pregnancy. The manufacturer advises avoidance of the 2g stat regimen during pregnancy.

5. BASHH. National guideline for the management of bacterial vaginosis. British Association for Sexual Health and HIV. 2006. http://www.bashh.org/documents/62/62.pdf Accessed 05.08.10. No reduction in relapse rate was reported from two studies in which male partners of women with BV were treated with metronidazole, tinidazole, or clindamycin.

Trichomoniasis


2. UKTIS. Use of metronidazole in pregnancy. The UK Teratology Information Service. 2008. (Tel: 0844 892 0909, http://www.uktis.org/docs/Metronidazole.pdf) Accessed 10.09.12. Metronidazole was shown to be mutagenic and carcinogenic in some animal studies. However available data, which is almost exclusively based on oral exposure, does not indicate an increased risk of adverse fetal effects associated with metronidazole use in human pregnancy. Where possible, the results of culture and sensitivity tests should be available before making a treatment choice. However if treatment is required before test results become available, then penicillins or cephalosporins may be used if considered clinically appropriate. The manufacturer advises avoidance of the 2g stat regimen during pregnancy.

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this randomized, open-label trial (n = 168) clotrimazole vaginal tablets were not found to effectively eradicate trichomoniasis. However, a reduction in symptoms was reported. The numbers of patients who had positive cultures after treatment were 40/45 (88.9%) in the clotrimazole group, 35/43 (81.4%) in the AVC suppository group, and 9/45 (20%) in the metronidazole group (P < 0.001).

4. Forna F, Gulmezoglu MU. Interventions for treating trichomoniasis in women. Cochrane Database of Systematic Reviews. 2003. Issue 2. http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD000218/frame.html Accessed 05.08.10. Pooled data from two RCTs (n = 294) found an 88% cure rate in women treated with metronidazole 2 g stat compared with a 92% cure rate in women treated with metronidazole for 5 or 7 days. Relative risk of no parasitological cure 1.12, 95% CI 0.58 to 2.16.

Pelvic Inflammatory Disease

1. RCOG. Management of Acute Pelvic Inflammatory Disease. Green Top Guideline No.32. Royal College of Obstetricians & Gynaecologists. 2008. http://www.rcog.org.uk/womens-health/clinical-guidance/acute-pelvic-inflammatory-disease-pid Accessed 05.08.10. Recommended regimens: the recommended regimens are broad spectrum to cover N. gonorrhoea, C. trachomatis, and anaerobes. For outpatient management, either ofloxacin plus metronidazole for 14 days, or a stat dose of IM cefuroxime plus metronidazole and doxycycline for 14 days are recommended. Broad-spectrum treatment is warranted in PID because of the consequences of untreated infection (ectopic pregnancy, infertility, pelvic pain). Ceftaxime has a better evidence base for the treatment of PID than ceftriaxone, but it is not readily available in the UK. Ceftriaxone is therefore recommended. Although the combination of doxycycline and metronidazole (without IM ceftriaxone) has previously been used in the UK to treat PID, there are no clinical trials that adequately assess its effectiveness and its use is not recommended.

2. BASH. UK National Guideline for the management of PID. British Association for Sexual Health and HIV. 2005. http://www.bashh.org/documents/118/118.pdf Accessed 05.08.10. Recommended regimens: the recommended regimens for outpatient management are either ofloxacin plus metronidazole for 14 days, or a stat dose of IM cefuroxime plus metronidazole and doxycycline for 14 days. Ofloxacin should be avoided in women who are at high risk of gonococcal PID, because of increasing quinolone resistance in the UK. Treatment of partners: partners should be screened for gonorrhoea and chlamydia.

3. GRASP Steering Group. GRASP 2008 report: trends in antimicrobial resistant gonorrhoea. Health Protection Agency. 2009. http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/Gonorrhoea/AntimicrobialResistance/ (Accessed 7th July 2010). Ciprofloxacin resistance is now endemic in England and Wales, accounting for 28% of all gonorrhoea isolates tested in 2008. The Health Protection Agency and the Association of Medical Microbiologists had said that, for practical issues of administration in primary care, a stat dose of oral cefixime 400mg could be substituted for IM ceftriaxone. However, resistance to cephalosporins is increasing and treatment failures have been reported with cefixime; therefore, if gonorrhoea is suspected, IM ceftriaxone is the cephalosporin of choice.

4. Meads C, Knight T, Hyde C and Wilson J. The clinical effectiveness and cost-effectiveness of antibiotic regimens for pelvic inflammatory disease. West Midlands Health Technology Assessment group. 2004. www.rep.bham.ac.uk Accessed 05.08.10. This systematic review identified 34 trials of antibiotic treatment for PID. Most studies were small, open-label, and of poor methodological study. One small trial was found that compared oral ofloxacin plus metronidazole with clindamycin plus gentamicin. The cure rate was 15/15 for ofloxacin plus metronidazole plus 17/18 for clindamycin plus gentamicin. The systematic review found one trial of ceftriaxone plus doxycycline was found, two trials of cefoxitin plus probenecid and doxycycline, and three trials of cefoxitin plus doxycycline compared to other antibiotics. Meta-analysis of these six studies found no difference in cure rates between IM cephalosporin plus doxycycline and the comparator antibiotics.

5. Ison CA, Mouton JW, Jones K. Which cephalosporin for gonorrhoea? Sex Transm Infect 2004;80:386-88. This study used previously published pharmacokinetic data on cefixime, ceftriaxone and cefuroxime to model the length of time tissue concentrations to these drugs would be above the MIC90 (concentration needed to kill 90% of gonorrhoea isolates). Cefuroxime concentrations are too low. Ceftriaxone attains the optimal concentrations to prevent the development of stepwise mutations and resistance in Neisseria gonorrhoea.

6. Ross JDC, Cronjé HS, Paszkowski T, Rakoczi I. Moxifloxacin versus ofloxacin plus metronidazole in uncomplicated pelvic inflammatory disease: results of a multicentre, double blind, randomised trial. Sex Transm Infect 2006;82(6):446-51. This trial in 564 patients with uncomplicated PID in hospitals from 13 countries, compared oral metronidazole 500mg twice daily with either oral ofloxacin 400mg twice daily or moxifloxacin 400mg once daily. Clinical resolution with both regimens was 90% and bacteriological cure was similar. Metronidazole is included in the regimen to improve the coverage for anaerobic bacteria. Anaerobes are of relatively greater importance in patients with severe PID. Ofloxacin and moxifloxacin should be avoided in patients who are at high risk of gonococcal PID because of increasing quinolone resistance in the UK (eg when the patient’s partner has gonorrhoea, in clinically severe disease, following sexual contact abroad). Quinolones should also be avoided as first line empirical treatment for PID in areas where >5% of PID is caused by quinolone resistant Neisseria gonorrhoeae.
Impetigo

1. The Health Protection Agency and the Association of Medical Microbiologists recommend that topical antibiotics are reserved only for treatment of very localised lesions because fusidic acid is an antibiotic that is also used systemically. There are concerns that widespread use of topical fusidic acid will lead to increased resistance, rendering systemic fusidic acid (used for severe staphylococcal infections such as osteomyelitis or systemic MRSA) ineffective. If a topical antibiotic is used, a short course (such as 5 days) reduces exposure and the risk of resistance. Since few agents are effective against MRSA, mupirocin should be reserved for such cases.

2. The Health Protection Agency and the Association of Medical Microbiologists recommend flucloxacillin for first-line treatment of impetigo because it is a narrow-spectrum antibiotic that is effective against Gram-positive organisms, including beta-lactamase producing Staphylococcus aureus, and it demonstrates suitable pharmacokinetics, with good diffusion into skin and soft tissues. Clarithromycin is recommended for people with penicillin allergy because it is also active against most staphylococcal and streptococcal species.

3. Koning S, Verhagen AP, van Suijlekom-Smit LWA, Morris AD, Butler C, van der Wouden JC. Interventions for impetigo. Cochrane Database of Systematic Reviews. 2003, Issue 2. http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD003261/frame.html Accessed 05.08.10. Many RCTs identified by this Cochrane review were of poor methodological quality. Pooled data from four RCTs found no difference in cure rates between topical mupirocin and topical fusidic acid (OR 1.22, 95% CI 0.69 to 2.16). Most RCTs that compared topical compared with oral antibiotics used mupirocin. However, mupirocin is reserved for MRSA and should not be used first-line for impetigo. Topical fusidic acid was significantly better than oral erythromycin in one study, but no difference was seen between fusidic acid and oral cefuroxime in a different arm of the same study. Topical bacitracin was significantly worse than oral cefalexin in one small study, but there was no difference between bacitracin and erythromycin or penicillin in two other studies. The results of one non-blinded RCT suggested that topical fusidic acid was more effective than topical hydrogen peroxide, but this did not quite reach statistical significance.

4. The Health Protection Agency and the Association of Medical Microbiologists recommend that topical retapamulin or Polymyxin are reserved for use in areas where there are rising rates of resistance to fusidic acid. Polymyxin (contains bacitracin) has less robust RCT evidence than fusidic acid. Although topical retapamulin has been demonstrated to be non-inferior to topical fusidic acid for the treatment of impetigo in one randomized controlled trial, it is more expensive and there are less safety data available (it is a black triangle drug).

5. Denton M, O’Connell B, Bernard P, Jarlier V, Williams Z, Santerre Henriksen A. The EPISA study: antimicrobial susceptibility of Staphylococcus aureus causing primary or secondary skin and soft tissue infections in the community in France, the UK, and Ireland. J Antimicrob Chemother 2008;61:586-588. Of S. aureus isolates from the UK, only 75.6% were susceptible to fusidic acid. A diagnosis of impetigo was associated with reduced fusidic acid susceptibility.

Eczema

1. Birnie AJ, Bath-Hextall FJ, Ravenscroft JC, Williams HC. Interventions to reduce Staphylococcus aureus in the management of atopic eczema. Cochrane Database of Systematic Reviews. 2008, Issue 3. http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD003871/frame.html Accessed 05.08.10. Most RCTs identified by this Cochrane review were of small, of poor quality and heterogeneous. Oral antibiotics were not associated with benefit in two small trials of people with eczema without visible signs of infection (n = 66). Adding antibiotics to topical steroids reduced the numbers of S aureus in 4 trials (n = 302) but not in a further 9 trials (n = 677).

2. National Collaborating Centre for Women's and Children's Health (2007) Atopic eczema in children: management of atopic eczema in children from birth up to the age of 12 years (full NICE guideline). National Institute for Health and Clinical Excellence. http://guidance.nice.org.uk/CG57 Accessed 05.08.10. In view of the lack of robust trial evidence, the GDG’s view was that flucloxacillin should normally be the first-line treatment for active S aureus and streptococcal infection because it is active against both. Erythromycin or clarithromycin should be used when there is local resistance to flucloxacillin and in children with a penicillin allergy because it is as effective as cephalosporins and less costly. It is the view of the GDG that topical antibiotics, including those combined with topical corticosteroids, should be used to treat localised overt infection only, and for no longer than two weeks.
1. CREST Guidelines on the management of cellulitis in adults. Clinical Resource Efficiency Support Team. 2005. www.crestni.org.uk Accessed 05.08.10. Expert consensus is that people who have no signs of systemic toxicity and no uncontrolled co-morbidities can usually be managed on an outpatient basis with oral antibiotics. Flucloxacillin 500mg QDS (or clarithromycin 500mg BD for those with penicillin allergy) are suitable oral antibiotics because they cover staphylococci and streptococci, the most commonly implicated pathogens. Clindamycin 300mg QDS is also recommended as a further alternative for people with penicillin allergy. Most cases of uncomplicated cellulitis can be treated successfully with 1-2 weeks of treatment.

2. Jones, G.R. Principles and practice of antibiotic therapy for cellulitis. CPD Journal Acute Medicine. 2002;1(2):44-49. Oral agents will be as effective as intravenous agents for cellulitis if they can maintain the free antibiotic level above the MIC of the pathogen for more than 40% of the dose interval. Flucloxacillin 500 mg, clarithromycin 500 mg and clindamycin 300 mg are suitable oral doses.

3. Morris AD. Cellulitis and erysipelas. Clinical Evidence. 2007. London. BMJ Publishing Group. This systematic review found no RCTs of antibiotics compared with placebo of sufficient quality for inclusion. Although 11 RCTs were identified that compared antibiotic treatments, these studies were small and only powered to demonstrate equivalence, not superiority, between antibiotics. Two RCTs using intravenous flucloxacillin were found, but none using oral flucloxacillin. Oral azithromycin was compared with erythromycin, flucloxacillin, and cefalexin in three RCTs. Oral co-amoxiclav was compared with fleroxacin (available in Germany) in one sub-group analysis.

4. Fischer RG and Benjamin DK Jr. Facial cellulitis in childhood: a changing spectrum. Southern Medical Journal. 2002; 95:672-674. Baccal cellulitis is commonly due to Haemophilus influenzae infection, although rates are decreasing following the Hib immunization programme. The Health Protection Agency and the Association of Medical Microbiologists recommends co-amoxiclav for empirical treatment of facial cellulitis because it is a broader spectrum than flucloxacillin and also covers H. influenzae.


Leg ulcer

1. O’Meara S, Al-Khurdi D, Ovington LG. Antibiotics and antiseptics for venous leg ulcers. Cochrane Database of Systematic Reviews. 2010. Issue 1. http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD003557/frame.html Accessed 05.08.10. Most studies identified by this Cochrane review were of poor methodological quality. Use of antibiotics did not promote healing compared to placebo in four trials of people with leg ulcers without visible signs of infection.

2. RCN The nursing management of patients with venous leg ulcers. Recommendations. Royal College of Nursing. 2006 http://www.rcn.org.uk/development/practice/clinicalguidelines/venous_leg_ulcers Accessed 05.08.10. Expert consensus is that swabbing (and so by definition antibiotic therapy) is unnecessary unless there is evidence of clinical infection such as inflammation, redness, or cellulitis; increased pain; purulent exudates; rapid deterioration of the ulcer; pyrexia; or foul odour.


MRSA


PVL


Bites (human or animal)


2. CKS. Bites – human and animal. Clinical Knowledge Summaries. 2007. http://www.cks.nhs.uk/bites_humand_animal Accessed 05.08.10. Expert opinion is that prophylaxis for animal bites is not required unless bite to the hand, foot, face; puncture wounds; all cat bites; wounds requiring surgical debridement; wounds involving joints, tendons, ligaments, or suspected fractures; wounds that have undergone primary closure; wounds to people who are at risk of serious wound infection (e.g. those who are diabetic, cirrhotic, asplenic, immunosuppressed, people with a prosthetic valve or a prosthetic joint).

3. Medeiros I, Saconat H. Antibiotic prophylaxis for mammalian bites. Cochrane Database of Systematic Reviews, 2001 Issue 2. http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD001738/pdf_fs.html Accessed 05.08.10. Human bites: only one trial (n = 48) analyzed human bites, and the infection rate in the antibiotic group (0%) was significantly lower than the infection rate in the control group (47%); OR 0.02, 95% CI 0.00 to 0.33. Dog bites: pooled results from six RCTs (n = 463) found that the infection rate was not reduced after the use of prophylactic antibiotics (4%) compared with the control group (5.5%); OR 0.74, 95% CI 0.30 to 1.8. Cat bites: one small study (n = 11) reported a lower infection rate in the treatment group who received prophylactic antibiotics (0%) compared with the control group (67%).

4. First-line antibiotic. The Health Protection Agency and the Association of Medical Microbiologists recommend co-amoxiclav for treatment or prophylaxis of human or animal bites because it is a broad-spectrum antibiotic that is effective against the most commonly isolated organisms from human bites (alpha- and beta-haemolytic streptococci, S. aureus, S. epidermis, corynebacteria, and E. corrodens) and animal bites (such as Pasteurella [57% of dog bites and 75% of cat bites], streptococci, staphylococci, moraxella, neisseria, and anaerobes).

5. First-line antibiotics in penicillin allergy for animal bites. The Health Protection Agency and the Association of Medical Microbiologists recommend metronidazole PLUS doxycycline for adults with penicillin allergy who require treatment or prophylaxis of an animal bite. Doxycycline has activity against pasturella species (the most common pathogen), staphylococci and streptococci. Metronidazole is included to cover anaerobes. Macrolides are not recommended for animal bites because they do not adequately cover pasturella. Seek specialist advice for children under the age of 12 years (doxycycline contraindicated).

6. First-line antibiotics in penicillin allergy for human bites. The Health Protection Agency and the Association of Medical Microbiologists recommend metronidazole plus either doxycycline or clarithromycin for adults and children with penicillin allergy who require treatment or prophylaxis of a human bite. Both doxycycline and clarithromycin are active against staphylococci and streptococci (the most common pathogens). Metronidazole is included to cover anaerobes. Doxycycline, but not clarithromycin is active against Eikenella species, which is also a common pathogen isolated from human mouths.

7. The Health Protection Agency and the Association of Medical Microbiologists recommend that people with penicillin allergy are reassessed at 24 and 48 hours after starting a course of antibiotic treatment because the recommended regimen covers the majority, but not all, of the likely pathogens from an animal or human bite.
1. HPA. The management of scabies in the community. *Health Protection Agency North West.* 2005. [http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1194947308867](http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1194947308867) Accessed 05.08.10. **Treatment of all contacts:** expert opinion is that the index case and all members of the household and sexual contacts should be treated within 24 hours of one another, even in the absence of symptoms, to reduce the risk of re-infestation. **Two treatments, 7 days apart:** expert opinion is that two treatment sessions are needed to treat scabies effectively.


3. Strong M, Johnstone P. Interventions for treating scabies. *Cochrane Database of Systematic Reviews.* 2007. Issue 3 [http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD000320/frame.html](http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD000320/frame.html) Accessed 05.08.10. **Permethrin:** topical permethrin appeared more effective than oral ivermectin, topical crotamiton, and topical lindane. The greatest body of evidence is for topical permethrin compared with lindane (*n* = 735, five RCTs: RR 0.32, 95% CI 0.13 to 0.75). **Malathion:** no RCTs were found that evaluated the efficacy of malathion for the treatment of scabies. Malathion has only been evaluated in uncontrolled studies.

**Dermatophyte infection – skin**


3. Bell-Syer SEM, Hart R, Crawford F, Torgerson DJ, Tyrrell W, Russel I. Oral treatments for fungal infection of the foot. *Cochrane Database of Systematic Reviews.* 2002. Issue 2 [www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD001434/frame.html](http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD001434/frame.html) Accessed 05.08.10. **Terbinafine:** one RCT (*n* = 41) found that oral terbinafine, 250 mg a day for 6 weeks, was more effective than placebo for treating athlete’s foot. At 8 weeks, 65% of the terbinafine group were cured, compared with none of the placebo group (relative risk [RR] of cure with terbinafine 25, 95% CI 2 to 384). **Itraconazole:** one RCT (*n* = 77) found that oral itraconazole, 400 mg a day for 1 week, was more effective than placebo. At 9 weeks, 55% of the itraconazole group were cured compared with 8% of the placebo group (RR of cure with itraconazole 7.95, 95% CI 2 to 20). **Terbinafine vs itraconazole:** Pooled data from three RCTs (*n* = 222) found no difference in cure rates between oral terbinafine 250 mg a day for 2 weeks (76% cured), and itraconazole 100 mg a day for 4 weeks (71% cured); risk difference 5%, 95% CI –6 to +27.

4. Crawford F and Hollis S. Topical treatments for fungal infections of the skin and nails of the foot. *Cochrane Database of Systematic Reviews.* 2007. Issue 3 [www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD003584/frame.html](http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD003584/frame.html) Accessed 05.08.10. **Terbinafine and imidazoles:** pooled data (8 RCTs; *n* = 962) found little difference between allylamines (e.g. terbinafine for 1-2 weeks) and imidazoles (4-6 weeks) at 2 weeks after baseline. But at 6 weeks after baseline, there was a relative reduction in treatment failure with allylamines compared with imidazoles (RR 0.63, 95% CI 0.42 to 0.94). **Treatment with an imidazole for 4-6 weeks reduced the risk of treatment failure by 60% compared with placebo at 6-weeks (Risk Ratio 0.40, 95% CI 0.35 to 0.46; *n* = 1235).** Treatment with an allylamine for 1-4 weeks reduced the risk of treatment failure by 67% compared with placebo at 6 weeks (Risk Ratio 0.33, 95% CI 0.24 to 0.44; *n* = 1116). **Udendocanoates:** this systematic review identified two RCTs of undecanoates compared with placebo (*n* = 283). There was a 71% relative reduction in the risk of treatment failure at 6 weeks with 4 weeks treatment with undecanoates compared with placebo (Risk Ratio 0.29, 95% CI 0.12 to 0.70).

**Dermatophyte infection – nail**

1. Roberts DT, Taylor WD, Boyle J. Guidelines for treatment of onychomycosis. *Brit J Dermatol* 2003;148:402–410. **Confirmation of diagnosis:** only 50% of cases of nail dystrophy are fungal, and it is not easy to identify these clinically. The length of treatment needed (6-12 months) is too long for a trial of therapy.

2. Chung CH, Young-Xu Y, Kurth T, Orav JE, Chan AK. The safety of oral antifungal treatments for superficial dermatophytosis and onychomycosis: a meta-analysis. *Am J Med* 2007;120:791–798. **Pooled data from about 20,000 participants found that both continuous and pulse therapy with terbinafine, itraconazole, or fluconazole were well tolerated.**
3. CKS. Fungal nail infection (onychomycosis) Clinical Knowledge Summaries 2009. http://www.cks.nhs.uk/fungal_nail_infection Accessed 05.08.10. Non-dermatophyte nail infection; there is limited evidence that both terbinafine and itraconazole are effective. Candidal nail infection; there is evidence that itraconazole is effective for candidal nail infection. There is weak evidence that terbinafine is also effective. Specialist advice for children; this is because fungal nail infection is rare in children, and the preferred treatments are not licensed for use in children.

4. The HPA Mycology Reference Laboratory recommends itraconazole for non-dermatophyte infections because although some of the infecting organisms are not particularly susceptible to this agent in vitro, it does reach high concentrations in nail tissue. It can be given as a pulse therapy regimen rather than continuous treatment.

5. Reinel, D. Topical treatment of onychomycosis with amorolfine 5% nail lacquer: comparative efficacy and tolerability of once and twice weekly use. Dermatology. 1992;184(Suppl 1): 21-24. One RCT (n = 456) without a placebo control found that 46% of those randomized to amorolfine applied once a week for 6 months achieved mycological cure of dermatophyte infection compared with 54% of those who applied topical amorolfine twice a week.

6. Crawford F & Ferrari J. Fungal toenail infections. In Clinical Evidence Concise. London. BMJ Publishing Group. 2006;15:561-63 Terbinafine vs itraconazole: one systematic review pooled data from two randomized controlled trials (n = 501). At 1-year follow-up, the cure rate following 12 weeks of treatment was greater for people with dermatophyte onychomycosis treated with oral terbinafine 250mg once a day (69%) compared with oral itraconazole 200mg daily (48%). Absolute risk reduction 21%, 95% CI 13% to 29%. Pulsed vs continuous itraconazole: four small RCTs were identified that found no statistically significant difference between continuous and pulsed itraconazole for dermatophyte onychomycosis.

Varicella zoster/chicken pox
Herpes zoster/shingles

1. DH. Immunisation against infectious diseases – The Green book. Chapter 34. Varicella. Department of Health 2006. http://www.dh.gov.uk/en/PublicHealth/Healthprotection/Immunisation/Greenbook/DH_4097254 Accessed 05.08.10. Pregnant women are at greater risk of varicella pneumonia, and there is a risk to the fetus of congenital varicella syndrome if exposure occurs during the first 20 weeks of pregnancy, and severe disease in the neonate if varicella is contracted a week before delivery. Neonates and immunocompromised individuals are at greater risk of disseminated or haemorrhagic varicella. Urgent specialist assessment is needed for all neonates, pregnant women, or immunocompromised individuals with varicella to assess the need for varicella immunoglobulin and antiviral treatment.

2. Klassen TP and Hartling L. Aciclovir for treating varicella in otherwise healthy children and adolescents. Cochrane Database of Systematic Reviews. 2005, Issue 4. http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD002980/frame.html Accessed 05.08.10. Pooled data from three studies who enrolled participants within 24 hours of rash onset found that aciclovir was associated with a small reduction in the number of days with fever (-1.1, 95% CI -1.3 to -0.9) and in reducing the maximum number of lesions. Results were less supportive of a reduction in the number of days of itching. There were no differences in complication rates between those treated with aciclovir or placebo.

3. Swingler G. Chicken Pox. In: Clinical Evidence Concise. London. BMJ Publishing Group. 2006;15:267-79. One systematic review was identified that found one RCT (n = 148 adults) which compared early versus late administration of aciclovir 800mg five times a day compared with placebo. It found that aciclovir given within 24 hours of the onset of rash significantly reduced the maximum number of lesions (P < 0.01) and the time to full crusting of lesions (P = 0.001) compared with placebo. It found no significant difference in time to full crusting of lesions if aciclovir was given 24–72 hours after the rash (P > 0.2).

4. The Health Protection Agency recommends that treatment with aciclovir should be considered (if it can be started within 24 hours of the rash) in those with severe chickenpox (including secondary cases) and in those at increased risk of complications (adults and adolescents aged 14 years and over, smokers, people on steroids).


1. Sheik A and Hurwitz B. Antibiotics versus placebo for acute bacterial conjunctivitis. Cochrane Database of Systematic Reviews 2006. Issue 2. [http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD001211/frame.html] Accessed 05.08.10. Meta-analysis of five RCTs (n = 1034) found that antibiotics (one trial each of ocular polymixin plus bacitracin, ciprofloxacin, norfloxacin, fusidic acid, and chloramphenicol) reduce early clinical remission rates (Risk Ratio on days 2 to 5 1.24, 95% CI 1.05 to 1.45). Clinical remission rates compared with placebo are lower if remission is assessed later (Risk Ratio on days 6 to 10 1.11, 95% CI 1.02 to 1.21). However, most cases resolve spontaneously, with clinical remission being achieved in 65% (95% CI 59 to 70%) by days 2 to 5 in those receiving placebo.


4. Arduino PG and Porter SR. Oral and perioral herpes simplex type 1 (HSV-1) infection: review of its management. Oral Dis 2006;12(3):254-70. Prophylaxis with oral antivirals may be of use for those with frequent, severe episodes, predictable triggers e.g. sunlight or for immunocompromised individuals (i.e. at higher risk of complications). Seek specialist advice if long-term prophylaxis is being considered.

EYE INFECTIONS

 Conjunctivitis

1. Sheikh A and Hurwitz B. Antibiotics versus placebo for acute bacterial conjunctivitis. Cochrane Database of Systematic Reviews 2006. Issue 2. [http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD001211/frame.html] Accessed 05.08.10. Meta-analysis of five RCTs (n = 1034) found that antibiotics (one trial each of ocular polymixin plus bacitracin, ciprofloxacin, norfloxacin, fusidic acid, and chloramphenicol) reduce early clinical remission rates (Risk Ratio on days 2 to 5 1.24, 95% CI 1.05 to 1.45). Clinical remission rates compared with placebo are lower if remission is assessed later (Risk Ratio on days 6 to 10 1.11, 95% CI 1.02 to 1.21). However, most cases resolve spontaneously, with clinical remission being achieved in 65% (95% CI 59 to 70%) by days 2 to 5 in those receiving placebo.


8. International Herpes Management Forum. Improving the management of varicella, herpes zoster, and zoster-associated pain. 2002. [www.ihmf.org] Accessed 05.08.10. Antiviral treatment is recommended for ophthalmic shingles to prevent the potentially sight-threatening complications than can occur following herpes zoster involving the trigeminal nerve. Aciclovir, famiclovir, and valaciclovir have all been shown to reduce the complications of ophthalmic shingles in RCTs.


10. Beutner KR, Friedman DJ, Forszpaniak C, Anderson PL, Wood MJ. Valaciclovir compared with acyclovir for improved therapy for herpes zoster in immunocompetent adults. Antimicrob Agents Chemother1995;39:1546-1553. This randomized double-blind controlled trial (n = 1141) in people aged 50 years and over within 72 hours of onset of herpes zoster found that valaciclovir 1g three times a day for 7 or 14 days reduced the time to resolution of pain compared with acyclovir 800mg five times a day for 7 days. Median time to cessation of pain was 38 days for valaciclovir for 7 days compared with 51 days for acyclovir (p = 0.001), and was 44 days for valaciclovir for 14 days.


Cold sores


3. ABPI Medicines Compendium. Summary of product characteristics for Fucithalmic. 1997. Datapharm Communications Ltd. http://www.medicines.org.uk/EMC/searchresults.aspx?term=Fucithalmic&searchtype=QuickSearch Accessed 05.08.10. Fucithalmic is active against a wide range of gram-positive organisms, particularly Staphylococcus aureus. Other species against which Fucithalmic has been shown to have in vitro activity include Streptococcus, Neisseria, Haemophilus, Moraxella and Corynebacteria.

4. Rose PW, Harnden A, Brueggemann AB, Perera R, Sheikh A, Crook D, Mant D. Chloramphenicol treatment for acute infective conjunctivitis in children in primary care: a randomised double-blind placebo-controlled trial. Lancet 2005;366:37-43. This study (n = 326) found that most children presenting with acute infective conjunctivitis in primary care will get better by themselves, and there is no statistically significant difference between using placebo or chloramphenicol. Clinical cure by day 7 occurred in 83% of children given placebo compared with 86% of children given chloramphenicol. Risk difference 3.8%, 95% CI -4.1% to 11.8%.

5. Reitveld RP, ter Riet G, Bindels PJ, Bink D, Sloos JH, van Weert HC. The treatment of acute infectious conjunctivitis with fusidic acid: a randomised controlled trial. Br J Gen Pract 2005;55:924-930. This primary care-based study (n = 163) found no statistically significant difference in clinical cure rates at 7 days in people using fusidic acid (62%) compared with placebo (59%). Adjusted risk difference 5.3%, 95% CI -11% to 18%.

6. Walker S, Daiper CJ, Bowman R, Sweeney G, Seal DV, Kirkness CM. Lack of evidence for systemic toxicity following topical chloramphenicol use. Eye 1998;12:875-879. Despite widespread prescribing of topical chloramphenicol, the incidence of aplastic anaemia in the UK remains low, and epidemiological data do not suggest an association between aplastic anaemia and topical chloramphenicol. Furthermore, a study of chloramphenicol levels in 40 patients found that chloramphenicol failed to accumulate to detectable levels in serum following one and two weeks of topical treatment.

This guidance is based on the Scottish Dental Clinical Effectiveness Programme guide to drug prescribing in dentistry.

To provide evidence for the guidance a literature review using Medline and Cochrane has been conducted, by Dr Joanne Hooker, up to October 2011 searching for Gingivitis; Antibiotics & dental abscess; Mucosal ulceration; Metronidazole; Oral Inflammation; Microbial flora & oral cavity; Oral hygiene; Oral microbial pathogens; Acute necrotising ulcerative gingivitis; Ludwig’s angina; Dental/periodontal abscesses; Mucositis; Odontogenic infection; Antimicrobials & dentistry; Pericoronitis; Periodontal disease; Mouthwash/mouthrinse; Periodontitis; Chlorhexidine; Anti-plaque/anti-gingivitis; Hydrogen peroxide; Antimicrobial susceptibility; Saline solution. The rationale was written by Dr Joanne Hooker under the guidance of Dr Ciomadh McNulty and reviewed by stakeholders. Where only expert opinion was available, the guidance was based on the literature on the main pathogens and their antimicrobial susceptibility profiles in the UK.

**Dosage of antimicrobials recommended in this guidance:**

The Scottish Dental Clinical Effectiveness Programme 2011 recommends doses of 250mg amoxicillin or 200mg metronidazole when antimicrobials are appropriate. We recommend a higher dose of 500mg amoxicillin and 400mg metronidazole. The rationale for this is when antimicrobials are considered appropriate, it is important to have sufficient concentrations at the site of infection. For β-lactams such as amoxicillin this is time-dependent (i.e. the time period above the MIC) and 500mg TDS amoxicillin is more likely to attain this. For metronidazole, the killing effect is dose-dependent and the greater the concentrations above the MIC the better. AUC/MIC > 70 is only attainable against *Bacteroides fragilis* with a 400mg dose.

**Mucosal Ulceration & Inflammation (Simple gingivitis)**

1. An extensive literature search using Medline and Cochrane failed to find any robust clinical evidence on saline mouthwash. The recommendations are, therefore, based on expert opinion from the Scottish Dental Clinical Effectiveness Programme which recommends salt solution (half a teaspoon of salt dissolved in warm water) or compound sodium chloride mouthwash (prescribe 300ml) and dilute with an equal volume of water) as required until symptoms resolve. NB advise patient to spit out mouthwash after rinsing.

2. The Scottish Dental Clinical Effectiveness Programme (2011). Recommends chlorhexidine 0.2% mouthwash or chlorhexidine oromucosal solution, alcohol free 0.2% (300ml); rinse 10ml for one minute twice each day. Spit out mouthwash after use. Leave 30 minute interval between using chlorhexidine mouthrinse and using toothpaste due to staining of teeth and dilution of chlorhexidine. This recommendation is based on the trials outlined below in references 3 – 6.

3. Berchier CE, Slot DE, Van Der Weijden GA. The efficacy of 0.12% chlorhexidine mouthrinse compared with 0.2% on plaque accumulation and periodontal parameters: a systematic review. *J Clin Periodontol*, 2010;37: 829-39. (The Netherlands). This systematic review from the Netherlands aimed to evaluate the effects of 0.12% chlorhexidine versus 0.2% chlorhexidine in the management of gingival inflammation and plaque control. Medline, Pub-med and Cochrane were searched for randomised controlled trials and cohort studies. 409 titles and abstracts identified eight eligible publications. Overall there was no evidence for the benefit of 0.2% over 0.12% in the reduction of gingivitis however there was some evidence in favour of 0.2% regarding the reduction of plaque.

4. Lang NP, Hase JC, Grassi M, Hammerle CHF, Weigel C, Kelty E, Frutig F. Plaque formation and gingivitis after supervised mouthrinsing with 0.2% delmopinol hydrochloride, 0.2% chlorhexidine digluconate and placebo for 6 months. *Oral Diseases*, 1998;4:105-113 (Switzerland). Double-blind, randomised six month clinical trial. This study of 162 patients with gingivitis, based in Switzerland, compared the effects of 0.2% chlorhexidine mouthwash or 0.2% delmopinol mouthwash (which inhibits adhesion of oral micro-organisms to the tooth surface reducing plaque formation) to placebo on plaque formation and gingivitis. Both were more effective than placebo, however, chlorhexidine was statistically significantly more effective (in relation to the clinical outcome parameters measured to quantify gingivitis and plaque formation). The trial also concluded that the long-term use of chlorhexidine was found to be less tolerated by the subjects.

5. Gunsolley JC. A meta-analysis of six-month studies of antiplaque and anti-gingivitis agents. A meta-analysis of the efficacy of anti-gingivitis and anti-plaque agents in sixth-month trials. *J Am Dent Assoc* 2006;137:1649-57. Seven studies, conducted between 1989 and 2005 (including 2258 subjects in total) looked at chlorhexidine 0.12% mouthwash and evaluated its efficacy at reducing gingival inflammation by using the Modified Gingival Index scoring system*. Chlorhexidine had the most consistent results, demonstrating statistical significance in favour of its anti-gingivitis effects (P = 0.13). *The Modified Gingival Index is a statistically sensitive scoring system that allows the non-invasive assessment of subtle signs of the severity and extent of gingival inflammation (Lobene, RR et al).

6. Lobene, RR; Weatherford, T; Ross, NM; Lamm, RA; Menaker, L. A modified gingival index for use in clinical trials. *Clinical Preventative Dentistry*. 1986 Vol 8 No.1 (USA)
Acute necrotising ulcerative gingivitis

1. The mainstay of treatment is local antiseptics and hygiene measures; adjunctive antibiotics are only required in cases of systemic involvement or where there is failure to improve following primary dental management. Metronidazole recommended; amoxicillin is an alternative.

2. Duckworth R, Waterhouse JP, Britton DE, Nuki K, Sheiham A, Winter R, Blake GC. Acute ulcerative gingivitis. A double-blind controlled clinical trial of metronidazole. Br Dent J 1966;21:120:599-602. In this double-blind clinical trial 33 patients with ANUG were treated for 2 days with metronidazole (200mg TDS) and 33 patients with penicillin (250mg QDS). There was no placebo group. There was no difference in the initial response rate but at 12 month follow-up there were significantly more recurrences in the penicillin group compared with placebo (p = 0.004).

3. Wade AB, Blake GC, Miza KB. Effectiveness of metronidazole in treating the acute phase of ulcerative gingivitis. Dent Pract 1966;16:440-444. In this double-blind clinical trial 25 patients with ANUG were treated for 2 days with metronidazole (200mg TDS) and 25 patients used sodiumperborate mouth rinse (one sachet TDS). There was no placebo group. The initial response was significantly better in the metronidazole group but there was no long term follow up. This data supports the use of metronidazole in the treatment of ANUG.

4. Losche WJ, Syed SA, Laughon BE, Stoll J. The bacteriology of acute necrotizing ulcerative gingivitis. J Periodontol 1982;53:223-230. In this small longitudinal study a total of eight patients with ANUG were included. Those systemically ill (n=3) were treated with metronidazole (200mg TDS) and those with local symptoms only received standard periodontal therapy. Those systematically ill had more microbiological findings initially. Metronidazole treatment reduced the number of anaerobes but at a 2-3-month follow-up these had reverted to pre-treatment levels. This study supports the efficacy of metronidazole on anaerobic pathogens in the treatment of ANUG and highlights the efficacy of standard periodontal treatment.

5. Preshaw PM. Antibiotics in the treatment of periodontitis. Dental Update 2004;31:448-456. Informal expert opinion (UK). This review recommends root surface instrumentation, chemical plaque control (chlorhexidine mouthwash) and oral hygiene advice as the gold standard treatment. Metronidazole (400 mg 3 times daily for 3 days) can be added in the acute stages.

6. Kuriyama T; Williams, DW; Yanagisawa, M; Iwahara, K; Shimizu, C; Kakagawa, K; Yamamoto, E; Karasawa, T. Antimicrobial susceptibility of 800 anaerobic isolates from patients with dental/periodontal infection to 13 oral antibiotics. Oral Microbiol Immunol 2007;22:285-288 (Japan & Wales). A clinical study looking at the antimicrobial susceptibility of 800 anaerobic isolates from dental/periodontal infections. Strict anaerobes predominate, P. intermedia (a common pathogen in ANUG) found to be 100% susceptible to metronidazole. This supports the use of metronidazole in this condition. Fusobacterium species has good susceptibility to amoxicillin/clavulanic acid, a wide range of cephalosporins, clindamycin and metronidazole.

7. Dahlen G. Microbiology and treatment of dental abscesses and periodontal-endodontic lesions. Peridontol 2000 2002;28:206-239. (Sweden) Metronidazole is effective against strict anaerobes (the common pathogens seen in ANUG). Four studies demonstrated that Prevotella, Porphyromonas species and Fusobacterium species were 100% susceptible to metronidazole. This study highlighted the benefits of metronidazole in the face of β-lactamase-producing anaerobes and also the penicillin allergic patient.

Pericoronitis

1. Pericoronitis is the inflammation and infection of perimolar soft tissue, often provoked by emerging molar teeth. Formal expert opinion from the Scottish Dental Clinical Effectiveness Programme 2011 indicates that this condition should be managed by referral to a dentist for local surgical treatment primarily with irrigation or incision and debridement of the lesion. Antibiotics can be added where there is systemic involvement or on-going symptoms. The HPA recommends metronidazole 400mg TDS for 3 days. If metronidazole is not tolerated an alternative is amoxicillin 500mg TDS for 3 days (in adults the dose can be doubled in severe infections). See note above references.
2. Ellison SJ. The role of phenoxymethylpenicillin, amoxicillin, metronidazole and clindamycin in the management of acute dentoalveolar abscesses – a review. Br Dent J 2009;206:247-62. Drawing from conclusions derived from this British literature review and literature search of over 5,000 references worldwide using Embase, Medline and Cochrane (search criteria: antibiotics and dental) this review recommends the use of metronidazole 200mg TDS for 3 days as first line treatment in pericoronitis. The HPA, however, recommends 400mg TDS. See note above references.

3. Sixou J-L, Magaud C, Jolivet-Gougeon A, Cormier M, Bonnaure-Mallet M. Evaluation of the mandibular third molar pericoronitis flora and its susceptibility to different antibiotics prescribed in France. J Clin Microbiol 2003;12:5794–5797. This French study looked at the microbial flora isolated from samples taken from 35 patients with pericoronitis and evaluated their susceptibility to amoxicillin, pristinamycin (a macrolide) and metronidazole (alone or in combination with the macrolide spiramycin). Obligate anaerobes were isolated in 91% of cases and resistance to metronidazole was not evident in any species. Amoxicillin was highly active against 91.5% of aerobes and anaerobes isolated and therefore in severe infections amoxicillin can be added to metronidazole.

4. Dahlen G. Microbiology and treatment of dental abscesses and periodontal-endodontic lesions. Peridontol 2000 2002;28:206-239. (Sweden) This informal expert review evaluated 7 studies looking at the microbial findings in pericoronitis and concluded that anaerobic species predominate, sharing a similar microbiological profile to that of a dental abscess.

**Dental Abscess**

There are few randomised controlled trials or systematic reviews looking at outcomes of dental abscess with and without antibiotics. The guidance is mainly based on expert opinion and laboratory susceptibility data of the organisms usually found in the dental conditions described.

1. Matthews DC, Sutherland S, Basrani B. Emergency management of acute apical abscesses in the permanent dentition: a systematic review of the literature. J Can Dent Assoc 2003;69:660. In the management of localized acute apical abscess in the permanent dentition, the abscess should be drained through a pulpectomy or incision and drainage. This analysis indicated that antibiotics are of no additional benefit. In the event of systemic complications (e.g., fever, lymphadenopathy or cellulitis), or for an immunocompromised patient, antibiotics may be prescribed in addition to drainage of the tooth.

2. Dahlen G. Microbiology and treatment of dental abscesses and periodontal-endodontic lesions. Peridontol 2000 2002;28:206-239. This review recommends that definitive surgical treatment to drain the abscess (through incision, extraction or removal of necrotic pulp) by a dentist is the primary management of a dentoalveolar abscess. The use of antibiotic treatment is required only in cases where there is evidence of systemic illness or in the severely immunocompromised and is aimed at limiting spread and preventing serious complications.

3. Ellison SJ. The role of phenoxymethylpenicillin, amoxicillin, metronidazole and clindamycin in the management of acute dentoalveolar abscesses – a review. Br Dent J 2009;206:247-62. This British literature review and literature search of over 5,000 references worldwide using Embase, Medline and Cochrane (search criteria: antibiotics and dental) concluded that there is little evidence-based antibiotic prescribing in the case of dental infections and to help control increasing antimicrobial resistance it is important to only prescribe antimicrobials if indicated. Antimicrobials should be prescribed if systemic sign of acute dental abscess include: pyrexia, trismus, lymphadenopathy, gross facial or ocular oedema, dysphagia, tachycardia or rigors.

4. Kuriyama T, Absi EG, Williams DW, Lewis MAO. An outcome audit of the treatment of acute dentoalveolar infection: impact of penicillin resistance. Br Dent J 2005;198:759-63 (UK). 112 patients with dentoalveolar infection underwent incisional or dental pulp chamber drainage and were assigned to one of six different antibiotic regimes. No significant difference in outcome was found with any regime, and the presence of penicillin-resistant strains did not influence the outcome where surgical management was already established (Student-T analysis for the comparison of clinical improvement scores) questioning the indication for antibiotics at all. However this study did not look at cases where antibiotics were not prescribed where adequate drainage had been achieved, and reinforced that it would be unethical to undertake such a study where systemic signs of infection were evident.

5. Preshaw PM. Antibiotics in the treatment of periodontitis. Dental Update 2004;31:448-56. Informal expert opinion. Scientific research demonstrating the impervious nature of dental biofilms to antibiotics (microorganisms can survive concentrations 500-1000 times greater than required for systemic delivery, Walker 2002) illustrated the rationale for definitive surgical management prior to considering this as an adjunct and Preshaw reinforces that in most cases systemic treatment is not required.

6. Robertson D, Smith AJ. The microbiology of the acute dental abscess. Med Microbiol. 2009;58:155-62. Informal expert opinion, literature review. Despite few well controlled trials, the literature available supports the use of urgent surgical...
management of the dental abscess in combination with antimicrobial agents where there is evidence of cellulitis or sepsis.

7. Scottish Dental Clinical Effectiveness Programme, 2011. Formal expert opinion. The Scottish guidance recommends 250mg amoxicillin. Expert opinion at the HPA and Department of Health Advisory Group on Antimicrobial Resistance & Healthcare Associated Infection it to increase concentrations at the site of infection above the minimum inhibitory concentration needed to eradicate the infecting bacteria, especially for more resistant Bacteroides spp. In severe infection double the dose of amoxicillin (from 500mg – 1g TDS) or in the case of phenoxymethylpenicillin (500mg – 1g QDS).

8. Eick S, Pfister W, Straube E. Antimicrobial susceptibility of anaerobic and capnophilic bacteria isolated from odontogenic abscesses and rapidly progressive periodontitis. Int J Antimicrob Agents 1999;12:41-6. This German study looking at the susceptibility of microbiological samples taken from 140 patients with dentoalveolar disease (periodontitis or odontogenic abscess) showed that the isolates consisted mainly of gram negative anaerobes which were highly susceptible to metronidazole and clindamycin. 6% of the periodontal isolates (plaque) and 22% of the abscess isolates (pus) were resistant to penicillin.

9. Kuriyama T., Absi EG, Williams DW, Lewis MAO. An outcome audit of the treatment of acute dentoalveolar infection: impact of penicillin resistance. Br Dent J 2005;198:759-63 (UK). A clinical study looking at the antimicrobial susceptibility of 800 anaerobic isolates from dentoalveolar infections in Japan. The study concluded that amoxicillin is still advocated as a first-line agent as it exhibits a high level of activity against the majority of organisms responsible for dentoalveolar infections. However, resistance to amoxicillin was seen in β-lactamase producing Prevotella species and therefore in more severe infections these organisms need to be covered. Amoxicillin/clavulanate, clindamycin and metronidazole have excellent activity against Prevotella species and the other anaerobes found in dentoalveolar infections. Susceptibility and resistance profiles of cephalosporins were found to be similar to amoxicillin, and therefore have no advantage over amoxicillin and are associated with greater side effects and the development of resistance.

10. Kulik EM, Lenkeit K, Chenaux S, Meyer J. Antimicrobial susceptibility of periodontopathogenic bacteria. J Antimicrob Chemother 2008;61:1087-1091. A laboratory-based microbiological study in Switzerland (where antibiotic use is among the lowest in Europe) looking at the resistance profiles of three predominant periodontopathogenic bacteria isolated from dental abscesses over a fourteen year period to 2005, concluded that there was limited antibiotic resistance to phenoxymethylpenicillin, amoxicillin/clavulanic acid, clindamycin, tetracycline and metronidazole. The study reiterated the polymicrobial nature of periodontal infections and that while resistance may well be present amongst commensal flora, resistance to individual species implicated in dental abscesses is not currently an issue.

11. Martin MV, Longman LP, Hill JB, Hardy P. Acute dentoalveolar infections: an investigation of the duration of antibiotic therapy. British Dental Journal, 1997;183:135-37. This British study looked at 759 patients with acute dental abscess (and associated systemic features), managed with either abscess drainage or tooth extraction in combination with amoxicillin, clindamycin or erythromycin. The outcome measured the resolution of systemic symptoms (swelling and temperature) after 2-3 days and then at 10days and found 98.6% of cases had resolution of symptoms at the first review (whereupon antibiotics were discontinued), furthermore these patients did not need an additional course of antibiotics at a later stage. This study shows that if drainage has been established antibiotics may not be needed beyond 2-3 days. Clinical review may be difficult so our guidance recommends 5 days duration.

12. Scottish Dental Clinical Effectiveness Programme 2011. Formal expert opinion. Avoid clindamycin, clarithromycin, cephalosporins and amoxicillin/clavulanate as first line agents (no advantage over amoxicillin, phenoxymethylpenicillin, metronidazole or erythromycin). Clindamycin and amoxicillin/clavulanate can be used as second-line agents where infection has not resolved however there is a risk of Clostridium difficile. An alternative diagnosis should be sought if the abscess is not resolving with local measures in combination with first-line antimicrobials.