

POWYS ANTIBIOTIC FORMULARY FOR PRIMARY CARE

This policy is based on the Health Protection Agency 'Management of Infection Guidance for Primary Care' and has been adapted for local use to take into account local sensitivity data from our surrounding District General Hospitals.

Advice

Contact details for local microbiology teams

Hospital	Telephone Numbers	Contact	E-mail
Royal Shrewsbury	01743 261161	Dr G Harvey	graham.harvey@sath.nhs.uk
Hereford County	01432 277177	Dr A Johnson Dr V Sivaprakasam	alison.johnson@hhtr.nhs.uk venkat.sivaprakasam@hhtr.nhs.uk
Nevill Hall	01873 732817	Dr N Carbarns	neil.carbarns@wales.nhs.uk
Singleton	01792 715048		
Bronglais	Microbiology service provided by Carmarthan		
Prince Charles			

Unless otherwise stated, these guidelines are intended for adults only. Different antibiotic doses and choices may be needed for children.

Aims

- ☐ to provide a simple, best guess approach to the treatment of common infections
- ☐ to promote the safe, effective and economic use of antibiotics
- ☐ to minimise the emergence of bacterial resistance/*Clostridium difficile* 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. A dose and duration of treatment is usually suggested, but may need modification for age, weight and renal function. In severe or recurrent cases consider a larger dose or longer course
3. Lower threshold for antibiotics in immunocompromised or those with multiple morbidities; consider culture and seek advice.
4. Prescribe an antibiotic only when there is likely to be a clear clinical benefit.
5. Consider a no, or delayed, antibiotic strategy for acute self-limiting upper respiratory tract infections ^{1,A+}
6. Limit prescribing over the telephone to exceptional cases.
7. Use simple generic antibiotics if possible. Avoid broad spectrum antibiotics (eg co-amoxiclav, quinolones and cephalosporins) when narrow spectrum antibiotics remain effective, as they increase risk of *Clostridium difficile*, MRSA and resistant UTIs.
8. Avoid widespread use of topical antibiotics (especially those agents also available as systemic preparations e.g. fusidic acid).
9. In pregnancy AVOID tetracyclines, aminoglycosides, quinolones, *high dose* metronidazole (2g). Short-term use of nitrofurantoin (at term, theoretical risk of neonatal haemolysis) is unlikely to cause problems to the foetus. Trimethoprim also unlikely to cause problems unless poor dietary folate intake or taking another folate antagonist such as an antiepileptic.
10. 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
11. Where a 'best guess' therapy has failed or special circumstances exist, contact the appropriate microbiologist from the table above.

ILLNESS	COMMENTS	DRUG	DOSE	DURATION OF TREATMENT
UPPER RESPIRATORY TRACT INFECTIONS¹				
Influenza¹⁻³ HPA Influenza	Annual vaccination is essential for all those at risk of influenza. For otherwise healthy adults, antivirals are not recommended. Treat 'at risk' patients, ONLY within 48 hours of onset & when influenza is circulating in the community or in a care home where influenza is likely. At risk: • Pregnant • 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 oral capsule bd or if there is resistance to oseltamivir use 5 days zanamivir 10mg (2 inhalations by diskhaler) bd. For prophylaxis see (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) ^{3A-} consider 2 or 3 day delayed or immediate antibiotics ^{1A+} Substantial numbers of patients need to be treated with antibiotics to prevent Quinsy (NNT>4000) ^{4B-} and Otitis Media (NNT 200) ^{2A+}	Phenoxymethylpenicillin ^{5B-}	500mg qds 1g BD ^{6A+} (qds when severe ^{7D})	10 days ^{8A+}
		Penicillin Allergy: Clarithromycin	250-500mg bd	5 days ^{9A+}
Acute Otitis Media (Child doses) CKS	Optimise analgesia and target antibiotics^{2,3B-} Avoid antibiotics as 60% are better in 24 hours without: they only reduce pain at 2 days (NNT15) and do not prevent deafness^{4A+} Consider 2 or 3-day-delayed ^{1A+} or immediate antibiotics for pain relief if: • < 2yrs with bilateral AOM (NNT4) or marked otoscopic signs and ≥3 symptoms⁵⁻⁷⁺ • All ages with otorrhoea (NNT3)^{8A+} More than 4000 patients would need to be treated with antibiotics to prevent Mastoiditis (NNT >4000) ^{9B-}	Amoxicillin ^{10A+} (child doses) Penicillin Allergy: Erythromycin ^{11D}	40mg/kg/day in 3 doses (max. 3g daily) ^{10B-} <2yrs 125mg qds 2-8yrs 250mg qds 8-18yrs 250-500mg qds	5 days ^{13A+} 5 days ^{13A+}
Acute Otitis Externa CKS	First use aural toilet (if available) and analgesia. Cure rates similar at 7 days for topical	First line: Acetic acid 2% (EarCalm)	1 spray tds	7 days

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	acetic acid or antibiotic +/- steroid ^{1A+} If cellulitis or disease extending outside ear canal, start oral antibiotics and refer ^{2A+}	Second Line: Neomycin sulphate with corticosteroid ^{3A-,4D} e.g. Betnesol N or Predsol N	3 drops tds	7 days min to max 14 days ^{1A+}
Acute Rhinosinusitis ^{5C} CKS	Avoid antibiotics as 80% resolve in 14 days without, and they only offer marginal benefit after 7 days NNT15 ^{2,3A+} Use adequate analgesia ^{4B+} Consider 7-day-delayed or immediate antibiotic when purulent nasal discharge NNT8 ^{1,2A+} In persistent infection use an agent with anti-anaerobic activity e.g. co-amoxiclav ^{6B+}	Amoxicillin ^{4A+,7A} Or Doxycycline Or Phenoxymethylpenicillin ^{8B+} <i>For persistent symptoms:</i> Co-amoxiclav ^{6B+}	500mg tds 1g if severe ^{11D} 100mg bd on 1 st day followed by 100mg od or for severe infections 100mg bd 500mg qds 625mg tds	7 days ^{9A+} 7 days 7 days 7 days
LOWER RESPIRATORY TRACT INFECTIONS				
Note: Low doses of penicillins are more likely to select out resistance ¹ . Do not use quinolones (ciprofloxacin, ofloxacin) first line due to poor pneumococcal activity. Reserve all quinolones (including levofloxacin) for proven resistant organisms. Consider the use of oral steroids e.g prednisolone 30 – 40mg od for 5 days and optimising inhaled steroid dose.				
Acute Cough, Bronchitis CKS NICE 69	Antibiotics have little benefit if no co-morbidity ^{1-4A+} Symptom resolution can take 3 weeks. Consider 7 – 14 day delayed antibiotic with symptomatic advice/leaflet ^{1,5A+}	Amoxicillin OR doxycycline	500 mg tds 100mg bd on 1 st day followed by 100mg od or for severe infections 100mg bd	5 days 5 days
Acute exacerbation of COPD NICE 101 GOLD	Treat exacerbations promptly with antibiotics if purulent sputum and increased shortness of breath and/or increased sputum volume ^{1-3B+} Risk factors for antibiotic resistant organisms include co-morbid disease, severe COPD, frequent exacerbations,	Amoxicillin OR doxycycline	500mg tds 100mg bd on 1 st day followed by 100mg od or for severe infections	5 days 5 days

ILLNESS	COMMENTS	DRUG	DOSE	DURATION OF TREATMENT
	antibiotics in last 3 months ² .	Clarithromycin in penicillin allergic and doxycycline contraindicated	100mg bd 500mg bd	5 days
		If resistance risk factors: co-amoxiclav	625mg tds	5 days
Community acquired Pneumonia (treatment in the community ^{2,3}) BTS Guideline 2009	Use CRB65 score to help guide and review ¹ each scores 1: • Confusion (AMT<8) • Respiratory rate >30/min • BP systolic<90 or diastolic≤60 • 65 years of age or over Score 0: suitable for home treatment; 1-2: hospital assessment or admission 3-4 urgent hospital admission If delayed admission or life threatening give immediate IM benzylpenicillin or amoxicillin 1g po ^D . Mycoplasma infection is rare in over 65s ¹	If CRB65=0:Amoxicillin ^{A+} OR clarithromycin ^{A-} OR doxycycline ^D If CRB65=1 & at home Amoxicillin ^{A+} AND clarithromycin ^{A-} OR doxycycline alone	500mg tds 500mg bd 100mg bd on 1 st day followed by 100mg od or for severe infections 100mg bd 500mg tds 500mg bd 100mg bd on 1 st day followed by 100mg od or for severe infections 100mg bd	7 days 7 days 7 days 7 – 10 days 7 – 10 days
MENINGITIS (NICE Fever Guidelines)				
Suspected meningococcal disease HPA	Transfer all patients to hospital immediately. If time before admission give IV benzylpenicillin or cefotaxime ^{1,2B+} unless hypersensitive, i.e. history of difficulty breathing, collapse, loss of consciousness, or rash ^{1B-} (give IM if vein cannot be found)	IV or IM benzylpenicillin Or IV or IM cefotaxime	Adults and children 10 yr and over: 1200 mg Children 1 - 9 yr: 600 mg Children <1 yr: 300 mg Age 12+ years: 1g Child < 12 years: 50mg/kg	
Prevention of secondary case of meningitis:		Only prescribe following advice from a public health doctor 9am – 5pm: ☎ Out of hours: On call ☎		

ILLNESS	COMMENTS	DRUG	DOSE	DURATION OF TREATMENT
URINARY TRACT INFECTIONS				
People > 65 years: do not treat asymptomatic bacteriuria; it is common but is not associated with increased morbidity ^{1B+} 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 ^{3B}				
UTI in men & women (no fever or flank pain) HPA QRG SIGN CKS men CKS women	Women with severe/ ≥ 3 symptoms: treat ^{1,2C} Women with mild/ ≤ 2 symptoms: use dipstick to guide treatment. Nitrite & blood/leucocytes has a 92% positive predictive value ; -ve nitrite, leucocytes, and blood has a 76% negative predictive value ^{3A-} Men: send pre-treatment MSU ^{1,4C} OR if symptoms mild/non-specific, use -ve nitrite and leucocytes to exclude UTI ^{5C}	trimethoprim ^{6B+} or nitrofurantoin ^{7B+8C}	200mg bd 100mg MR bd ^{9C,11B+}	Women 3 days ^{11,12A+} Men 7 days ^{1,4C}
		Second line: perform culture in all treatment failures ^{1B} Amoxicillin resistance is common; only use if susceptible ^{14B+} Community multi-resistant Extended-spectrum Beta-lactamase <i>E. coli</i> are increasing: consider nitrofurantoin (or fosfomycin 3g stat in women ^{15,16B,17A} plus 2nd 3g dose in men 3 days later ¹⁸), on advice of microbiologist		
UTI in pregnancy HPA QRG CKS	Send MSU for culture & sensitivity and start empirical antibiotics ^{1A} Short-term use of nitrofurantoin in pregnancy is unlikely to cause problems to the foetus ^{2C} Avoid trimethoprim if low folate status or on folate antagonist (eg antepileptic or proguanil) ²	First line: nitrofurantoin if susceptible, amoxicillin Second line: trimethoprim Third line: cefalexin ^{4C,5B-}	100mg MR bd 500mg tds 200mg bd (off label) <i>give folic acid if first trimester</i> 500mg bd	All for 7 days ^{6C}
UTI in children HPA QRG CKS	Child <3 months refer urgently for assessment ^{1C} Child ≥ 3 months: use positive nitrite to start antibiotics ^{1A+} Send pre-treatment MSU for all Imaging: only refer if child <6 months or atypical UTI ^{1C}	Lower UTI: trimethoprim ^{1A} or nitrofurantoin ^{1A-} if susceptible, amoxicillin ^{1A} Second line: cefalexin ^{1C} Upper UTI: co-amoxiclav ^{1A} Second line: cefixime ^{2A}	See BNF for dosage	Lower UTI - 3 days ^{1A+} Upper UTI – 7-10 days ^{1A+}

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Acute Pyelonephritis CKS	If admission not needed, send MSU for culture & sensitivities and start antibiotics ^{1C} If no response within 24 hours, admit ^{2C}	ciprofloxacin ^{3A-} or co-amoxiclav ^{4C}	500mg bd 500/125mg tds	7 days ^{3A-} 14 days ^{4C}
Recurrent UTI in women ≥3 UTIs/year	Post-coital prophylaxis ^{1,2B+} or standby antibiotic ^{3B+} Nightly: reduces UTIs but causes adverse effects ^{1A+}	Nitrofurantoin Or trimethoprim	50 – 100mg 100mg	Post coital stat (off label) ^{2B+,3C} , or Prophylaxis od at night ^{1A+}
GASTRO-INTESTINAL TRACT INFECTIONS				
Eradication of <i>Helicobacter pylori</i> NICE HPA ORG CKS Symptomatic relapse	Eradication is beneficial in known DU, GU ^{1A+} or low grade MALToma ^{2B+} For NUD, the NNT is 14 for symptom relief ^{3A+} Consider test and treat in persistent uninvestigated dyspepsia ^{4B+} Do not offer eradication for GORD ^{1C} Do not use clarithromycin or metronidazole if used in the past year for any infection ^{5A+,6A+} DU/GU relapse: retest for H pylori using breath or stool test OR consider endoscopy for culture & susceptibility ^{1C} NUD: Do not retest, offer PPI or H ₂ RA ^{1C, 3A+}	First line ^{1A+} Omeprazole PLUS clarithromycin AND metronidazole (MZ) OR amoxicillin (AM) Second line ^{6A+} Omeprazole PLUS bismuthate (De-nolab®) PLUS 2 unused antibiotics: amoxicillin metronidazole tetracycline ^{8C}	20mg bd 250mg bd with MZ 500mg bd with AM 400mg bd 1g bd 20mg bd 120mg qds 1g bd 400mg tds 500mg qds	All for 7 days ^{1,7A+} Relapse ^{10C} or MALToma ^{1C} 14 days
Acute Diverticulitis CKS	People with mild, uncomplicated diverticulitis can be managed at home with paracetamol, clear fluids, and antibiotics.	Co-amoxiclav Or (if allergic to penicillin) Metronidazole Plus Ciprofloxacin	500/125mg tds 400mg tds 500mg bd	7 days 7 days 7 days
Infectious Diarrhoea CKS	Refer previously healthy children with acute painful or bloody diarrhoea to exclude <i>E coli</i> 0157 infection ^{1C} Antibiotic therapy not indicated unless patient systemically unwell ^{2C} 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 ^{3C}			
<i>Clostridium Difficile</i> DH & HPA	Stop unnecessary antibiotics and/or PPIs ^{1,2B+} 70% respond to MZ in 5 days; 92% in 14days ³ Treat ribotype 027 with vancomycin. Admit if severe: T >38.5; WCC >15, rising creatinine or signs/symptoms of severe colitis ^{1C}	1 st /2 nd episodes Metronidazole (MZ) ^{1A-} 3 rd episode/severe/type 027 oral vancomycin ^{1A-}	400 or 500mg tds 125mg qds	10-14days ^{1C} 10-14 days ^{1C}

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	Severity of Clostridium difficile infection can be defined as: Mild: not associated with an increased white cell count (WCC). It is typically associated with <3 episodes of loose stools (defined as loose enough to take the shape of the container used to sample it) per day. Moderate: associated with an increased WCC (<15 x 10 ⁹ /L) and typically associated with 3–5 loose stools per day. Severe: associated with a WCC >15 x 10 ⁹ /L, or an acutely increased serum creatinine concentration (> 50% increase above baseline), or a temperature higher than 38.5°C, or evidence of severe colitis (abdominal or radiological signs). The number of stools may be a less reliable indicator of severity. Life-threatening: signs and symptoms include hypotension, partial or complete ileus, or toxic megacolon.			
Traveller's Diarrhoea CKS	Only consider standby antibiotics for remote areas or people at high-risk of severe illness with travellers' diarrhoea ^{1,2C} If standby treatment appropriate: ciprofloxacin 500 mg bd for 3 days (private Rx) ^{2C, 3B+} If quinolone resistance high (e.g. south Asia): consider bismuth subsalicylate (Pepto Bismol) 2 tablets qds as prophylaxis ^{2B+} or for 2 days treatment ^{4B+}			
Threadworms 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 ^{1C}	>6 months: mebendazole (off-label if <2yrs) 3-6 mths: piperazine+sennosides < 3mths: 6 wks hygiene ^{1C}	100 mg ^{1C} 2.5ml spoon ^{1C}	Stat Stat, repeat after 2 weeks
GENITAL TRACT INFECTIONS				
STI Screening	People with risk factors should be screened for chlamydia, gonorrhoea, HIV, syphilis. Refer individuals and partners to GUM service. Risk factors: < 25y, no condom use, recent (<12mth)/frequent change of partner, symptomatic partner ^{1,2}			
Chlamydia Trachomatis SIGN BASHH HPA CKS	Opportunistically screen all aged 15-25yrs ¹ Treat partners and refer to GUM clinic ^{2,3} B+ Pregnancy ^{1C} or breastfeeding: azithromycin is the most effective option ⁵ A+;6B- Due to lower cure rate in pregnancy, test for cure 6 weeks after treatment ^{3C}	azithromycin ^{4A+} or doxycycline ^{4A+} <i>Pregnant or breastfeeding:</i> azithromycin ^{5A+} or erythromycin ^{5A+} or amoxicillin ^{5A+}	1g 100mg bd 1g (off label) 500mg qds 500mg tds	Stat ^{4A+} 7 days ^{4A+} Stat ^{5A+} 7 days ^{5A+} 7 days ^{5A+}
Vaginal Candidiasis BASHH HPA CKS	All topical and oral azoles give 75% cure ^{1A+}	clotrimazole ^{1A+} or oral fluconazole ^{1A+}	500 mg pess/ 10% cream 150 mg orally	Stat Stat
	Pregnancy: avoid oral azole ^{2B-} use intravaginal for 7 days ^{3A+,2,4 B-}	clotrimazole ^{3A+} miconazole 2% cream ^{3A+}	100 mg pessary at night 5 g intravaginally bd	6 nights ^{5C} 7 days
Bacterial Vaginosis BASHH HPA CKS	Oral metronidazole (MZ) is as effective as topical treatment ^{1A+} but is cheaper. Less relapse with 7/7 than 2g stat at 4 wks ^{3A+} Pregnant ^{2A+} /breastfeeding: avoid 2g stat ^{3A+,4B-}	oral MZ ^{1,3A+} or MZ 0.75% vag gel ^{1A+}	400 mg bd or 2 g 5 g applicatorful at night	7 days ^{1A+} Stat ^{3A+} 5 nights ^{1A+}

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	Treating partners does not reduce relapse ^{5B+}	or clindamycin 2% crn ^{1A+}	5 g applicatorful at night	7 nights ^{1A+}
Trichomoniasis BASHH HPA CKS	Treat partners and refer to GUM clinic ^{1B+} In pregnancy or breastfeeding: avoid 2g single dose MZ ^{2B-} . Consider clotrimazole for symptom relief (not cure) if MZ declined ^{3B+}	metronidazole (MZ) ^{4A+} clotrimazole ^{3B+}	400 mg bd or 2 g 100 mg pessary at night	5 – 7 days ^{4A+} Stat ^{4A+} 6 nights ^{3B+}
Pelvic Inflammatory Disease RCOG BASHH CKS	Refer woman and contacts to GUM clinic ^{1,2B-} Always culture for gonorrhoea & chlamydia ^{2B+} 28% of gonorrhoea isolates now resistant to quinolones ^{3B+} If gonorrhoea likely (partner has it, severe symptoms, sex abroad) use ceftriaxone regimen or refer to GUM	metronidazole PLUS doxycycline ^{1, 2,4B-} <i>If high risk of Gonorrhoea</i> Ceftriaxone ^{3,5C} PLUS Metronidazole ⁶ PLUS doxycycline ^{1,2,4B+}	400 mg bd 100mg bd 500mg IM 400 mg bd 100mg bd	14 days 14 days stat 14 days 14 days
Acute Prostatitis BASHH CKS	Send MSU for culture and start antibiotics ^{1C} . 4-wk course may prevent chronic prostatitis ^{1C} Quinolones achieve higher prostate levels ²	Ciprofloxacin ^{1C} Or Ofloxacin ^{1C} 2 nd Line Trimethoprim ^{1C}	500mg bd 200mg bd 200mg bd	28 days ^{1C} 28 days ^{1C} 28 days ^{1C}
SKIN INFECTIONS				
Impetigo CKS	For extensive, severe, or bullous impetigo, use oral antibiotics ^{1C} Reserve topical antibiotics for very localised lesions to reduce the risk of resistance ^{1,5C,4B+} Reserve mupirocin for MRSA ^{1C}	Oral flucloxacillin ^{2C} <i>If penicillin allergic:-</i> Oral clarithromycin ^{2C} Topical fusidic acid ^{3A+} MRSA only mupirocin ^{3A+}	500mg qds 250-500mg bd tds tds	7 days 7 days 5 days 5 days
Eczema CKS	If no visible signs of infection, use of antibiotics (alone or with steroids) encourages resistance and does not improve healing ^{1B} In eczema with visible signs of infection, use treatment as in impetigo ^{2C}			
Cellulitis CKS	If patient afebrile and healthy other than cellulitis, use oral flucloxacillin alone ^{1,2C} If river or sea water exposure, discuss with microbiologist. If febrile and ill, admit for IV treatment ^{1C} Stop clindamycin if diarrhoea occurs.	flucloxacillin ^{1,2,3C} <i>If penicillin allergic:</i> clarithromycin ^{1,2,3C} or clindamycin ^{1,2C} facial: co-amoxiclav ^{4C}	500mg qds 500mg bd 300-450mg qds 500/125mg tds	All for 7 days. If slow response continue for a further 7 days ^{1C}
Leg Ulcers HPA QRG	Ulcers always colonized. Antibiotics do not improve healing unless active	Active infection if cellulitis/increased pain/pyrexia/purulent exudate/odour ^{2C}		

ILLNESS	COMMENTS	DRUG	DOSE	DURATION OF TREATMENT
Click link for advice on swabbing CKS	infection ^{1A+} If active infection, send pre-treatment swab ^{3C} Review antibiotics after culture results.	If active infection Flucloxacillin Or clarithromycin	500mg qds 500mg bd	As for cellulitis
MRSA	For MRSA screening and suppression, see HPA MRSA quick reference guide .			
	If active 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.	If active infection, MRSA confirmed by lab results, infection not severe and admission not required ^{1,2B+}		
		If active infection confirmed: Doxycycline alone ^{1B+} OR Clindamycin alone ^{1,2B+}	100mg bd 300 – 450mg qds [if diarrhoea, stop]	Both for 7 days
PVL S aureus HPA ORG	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}			
Bites CKS	Thorough irrigation is important ^{1C}	<i>Prophylaxis or treatment</i> co-amoxiclav	375-625mg tds ^{4C}	All for 7 days ^{4,5,6C}
Human:	Assess risk of tetanus, HIV, hepatitis B&C ^{1C} Antibiotic prophylaxis is advised ^{3B-}	<i>If penicillin allergic:</i> metronidazole PLUS doxycycline (cat/dog/man) OR metronidazole PLUS clarithromycin (human bite) AND review at 24&48hrs ^{7C}	200-400mg tds 100mg bd ^{5C}	
Cat or Dog:	Assess risk of tetanus, rabies ^{2C} Give prophylaxis if ³ cat bite/puncture wound; bite to hand, foot, face, joint, tendon, ligament; immunocompromised/diabetic/asplenic/cirrhotic		200-400mg tds 250-500mg bd ^{6C}	
Scabies CKS	Treat all home & sexual contacts within 24h ^{1C} Treat whole body from ear/chin downwards and under nails. If under 2/elderly, also face/scalp ²	permethrin ^{3A+} <i>If allergy:</i> malathion ^{3C}	5% cream 0.5% aqueous liquid	2 applications 1 week apart ^{1C}
Fungal infection – skin CKS body & groin CKS foot CKS scalp	Terbinafine is fungicidal ¹ , so treatment time shorter than with fungistatic imidazoles. If candida possible, use imidazole ¹ If intractable: send skin scrapings ^{2C} . If infection confirmed, use <u>oral</u> terbinafine/itraconazole ^{3B+}	Topical terbinafine ^{4A+} or topical imidazole ^{4A+} Or (<i>athlete's foot only</i>): topical undecanoate ^{4B+}	bd bd bd	
				1-2 weeks ^{4A+} for 1-2 wks after healing (i.e. 4-6wks) ^{4A+}

ILLNESS	COMMENTS	DRUG	DOSE	DURATION OF TREATMENT
	Scalp: discuss with specialist.	(Mycota [®])		
Fungal infection - fingernail or toenail CKS	Take nail clippings: start therapy only if infection is confirmed by laboratory ^{1C} Terbinafine is more effective than azoles ^{6A+} Liver reactions rare with oral antifungals ^{2A+} If candida or non-dermatophyte infection confirmed, use oral itraconazole ^{3B+ 4C} For children, seek specialist advice ^{3C}	Superficial only amorolfine 5% nail lacquer ^{5B-} <i>First line:</i> terbinafine ^{6A-} <i>Second line:</i> itraconazole ^{6A+}	1-2x/weekly fingers toes 250 mg od fingers toes 200 mg bd fingers toes	6 months 12 months 6 – 12 weeks 3 – 6 months 7 days monthly 2 courses 3 courses
Varicella Zoster/ Chicken pox CKS & Herpes Zoster /Shingles CKS	Pregnant/immunocompromised/neonate: seek urgent specialist advice ^{1B+} Chicken pox: if started <24hr of rash & >14yr or severe pain or dense/oral rash or 2 ^o household case or steroids or smoker consider aciclovir ²⁻⁴ Shingles: treat if >50 yrs ^{5A+} and within 72 hrs of rash ^{6B+} (PHN rare if <50yrs ^{7B-}); or if active ophthalmic ^{8B+} or Ramsey Hunt ^{9C} or eczema.	<i>If indicated:</i> aciclovir ^{3B+,7A+} <i>Second line for shingles if compliance a problem, as ten times cost</i> Valaciclovir ^{10B+}	800mg five times a day 1g tds	7 days ^{3B+} 7 days ^{10B+}
Cold Sores	Cold sores resolve after 7–10 days without treatment. Topical antivirals applied prodromally reduce duration by 12-24hrs ^{1,2,3B+,4}			
EYE INFECTIONS				
Conjunctivitis CKS	Most bacterial conjunctivitis self-limiting. Treat if severe, as most viral or self-limiting. Bacterial conjunctivitis is usually unilateral and also self-limiting; ^{2C} 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 ³	<i>If severe:</i> ^{4,5B+,6B1} chloramphenicol 0.5% drop and 1% ointment <i>Second line:</i> fusidic acid 1% gel	2hrly for 2 days then 4hrly (whilst awake) At night bd	All for 48 hours after resolution

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.

Study design	Recommendation grade
Good recent systematic review of studies	A+
One or more rigorous studies, not combined	A-
One or more prospective studies	B+
One or more retrospective studies	B-
Formal combination of expert opinion	C
Informal opinion, other information	D

Clinical Knowledge Summaries for the NHS 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

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).

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
- advice about using the delayed prescription if symptoms are not starting to settle in accordance with the expected course of the illness or if a significant worsening of symptoms occurs

- advice about re-consulting if there is a significant worsening of symptoms despite using the delayed prescription.
- A delayed prescription with instructions can either be given to the patient or left at an agreed location to be collected at a later date.

Influenza

1. National Institute for Health and Clinical Excellence. Amantadine, oseltamivir and zanamivir for the treatment of influenza (review of NICE technology appraisal guidance 58) <http://www.nice.org.uk/nicemedia/pdf/TA168quickrefguide.pdf> Accessed 05.08.10
2. Oseltamivir resistance in European influenza viruses. Health Protection Agency 2008. http://www.hpa.org.uk/webw/HPAweb&HPAwebPrinterFriendly/HPAweb_C/1204186172107?p=1204186170287 Accessed 05.08.10
3. Turner D, Wailoo A, Nicholson K, Cooper N, Sutton A, Abrams K. Systematic review and economic decision modelling for the prevention and treatment of influenza A and B. Health Technology Assessment 2003;7(35):iii-iv, xi-xiii, 1-170.

Sore Throat

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 Sore Throat: NICE 69 includes 3 trials that use a delayed-antibiotic strategy for treating Acute Sore Throat. Two USA studies used a 2-day-delayed antibiotic and the UK primary care study used a 3-day-delayed antibiotic.**
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 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 MJ. 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. Scharztz 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: The best evidence for a 10 day course of penicillin comes from the early trials using the parenteral 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.**

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, Foggo BA. Antibiotics, sore throats and rheumatic fever. *BJGP* 1985;**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.*

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.*
3. Bertin L, Pons G, d'Athis P, Duhamel JF, Maueilonde C, Lasfargues G, Guillot M, Marsac A, Debregeas B, Olive G. A randomized, doubleblind, multicentre controlled trial of ibuprofen versus acetaminophen and placebo for symptoms of acute otitis media in children. *Fundam Clin Pharmacol* 1996;**10**(4):387-92 **RATIONALE:** *This small RCT is probably the best trial evidence we have specifically for analgesia use in AOM. Both Paracetamol and Ibuprofen showed a non-significant trend towards effective analgesia compared with placebo. Note that all children were also treated with an antibiotic.*
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.pub2. (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-to-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, Appleman CL, Burke P, McCormick DP, Damoiseaux RA, Little P, Le Saux N, 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 be advised that symptoms may persist for up to 7 days, and they should optimise analgesia use.*
6. Hoberman A, Paradise JL, Rockette 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
7. Tähtinen PA, Laine MK, Houvinen P, Jalava J, Ruuskanen O, Ruohola A. A placebo-controlled trial of antimicrobial treatment for acute otitis media. *NEJM*
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 otorrhoea, 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).
10. Takata GI, Chan LS, Shekelle P, et al. Evidence assessment of management of acute otitis media: The role of antibiotics in treatment of uncomplicated acute otitis media. *Pediatrics* 2001;**108**:239-247 RATIONALE: Pooled analyses did not show any difference in efficacy between comparisons of penicillin, ampicillin, amoxicillin (2 or 3 times daily; standard or high dose), amoxicillin-clavulanate, cefaclor, cefixime, ceftriaxone, azithromycin and trimethoprim.
11. Macrolides concentrate intracellularly and so are less active against the extracellular *H influenzae*.
12. Sox CM, Finkelstein JA, Yin R, Kleinman K, Lieu TA. Trends on otitis media treatment failure and relapse. *Pediatrics* 2008;**121**(4):674-9. RATIONALE: High-dose amoxicillin treatment did not reduce the risk of individual infections resulting in adverse outcomes.
13. 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.

Acute Otitis Externa

1. Kaushik V, Malik T, Saeed SR. Interventions for acute otitis externa. *Cochrane Database of Systematic Reviews* 2010, Issue1. 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. 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.
3. 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.'
4. 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; Otopsporin and Predsol-N.

Acute Rhinosinusitis

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 Journal* 2008;**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? *BMJ* 1998;**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 Care* 2000;**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 Pharmacology* 2009;**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.*

Additional reference:

Hansen JG, Hojbjerg 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, Orqvist A, Schabert T, Torres A, van der Jeijden G, Werheijm TJM. Guidelines for the management of adult lower respiratory tract infection. *Eur Respir J* 2005;**26**:1138-80. <http://www.erj.ersjournals.com/contents-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 ($FEV_1 < 50\%$). 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.

Acute 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.
2. Fahey T, Smucny J, Becker L, Glazier R. Antibiotics for acute bronchitis. In: The Cochrane Library, 2006, Issue 4. Chichester, UK: John Wiley & Sons, Ltd http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD000245/pdf_fs.html Accessed 05.08.10. Systematic review of nine studies (4 in primary care). Studies in primary care showed antibiotics reduced symptoms of cough and feeling ill by less than one day in an illness lasting several weeks in total.
3. Chronic cough due to acute bronchitis. *Chest*. 2006;**129**:95S-103S. Clinical guidelines on managing cough associated with acute bronchitis. Large body of evidence including meta-analyses and systematic reviews does not support routine antibiotic use.
4. Wark P. Bronchitis (acute). In: Clinical Evidence. London. BMJ Publishing Group. 2008;**07**:1508-1534 Discusses the evidence to support self care and limiting antibiotic prescriptions. Systematic review of 13 RCTs found that antibiotics only modestly improved outcomes compared with placebo.
5. Francis N et al. Effect of using an interactive booklet about childhood respiratory tract infections in primary care consultations on reconsulting and antibiotic prescribing: a cluster randomised controlled trial. *BMJ*, 2009;**339**:2885 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.

COPD

1. Anthonisen MD, Manfreda J, Warren CPW, Hershfield ES, Harding GKM, Nelson NA. Antibiotic therapy in exacerbations of chronic obstructive pulmonary disease. *Ann Int Med* 1987;**106**:196-204. Describes the cardinal signs of an infective exacerbation of COPD and the evidence for commencing antibiotics. Randomised double blinded cross-over trial showed a significant benefit from using antibiotics. Success rate with antibiotic therapy 68% vs 55% with placebo.
2. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for Diagnosis, Management, and Prevention of COPD. Management of exacerbations. Updated December 2009. Discusses the aetiology, pathophysiology and evidence based therapeutic management of COPD. Antibiotic therapy is stratified according to severity of disease. *S. pneumoniae*, *H. influenzae*, *M. catarrhalis* remain the predominant pathogens in mild disease.
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> 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.

Community-acquired pneumonia

1. BTS guidelines for the management of community-acquired pneumonia in adults. *Thorax* 2009;**64** (Suppl III):III 1-55 Updated guideline on the management of CAP – includes diagnosis, severity assessment, microbiological profile and therapeutic management in both the community and hospital. Assessing severity using CRB65 scores in addition to clinical judgement allows patients to be stratified according to increasing risk of mortality. (score 0, mortality risk 1.2%; score 1. 5.3%; score 2. 12.2%; scores 3-4, up to 33%). Patients with a CRB65 score ≥ 1 are deemed to have moderately severe CAP and should be assessed with a view to hospital admission. Patients with moderately severe CAP should receive antibiotics which also cover atypical organisms.
2. Loeb M. Community-acquired pneumonia. In: Clinical Evidence. London BMJ Publishing Group. 2008;**07**:1503-1516. (Accessed 6th January 2010. While there is no direct information about the benefits of antibiotics in the treatment of CAP in the community, there is consensus they are beneficial. No one regime has shown superiority over another.
3. van der Poll T, Opal S. Pathogenesis, treatment and prevention of pneumococcal pneumonia. *Lancet*. 2009;**374**:1543-1556. Detailed review of pneumococcal pneumonia, the most common cause of CAP. Includes discussion of clinical features, risk factors and rationale for high dose penicillins to overcome resistance..

MENINGITIS

1. NICE. Bacterial meningitis and meningococcal septicaemia. National Collaborating Centre for Women's and Children's health 2009. <http://guidance.nice.org.uk/CG102/Guidance> Accessed 05.08.10. 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, either in primary or secondary care. The NICE guideline development group recommended benzylpenicillin because it is the most frequently used antibiotic in primary care and they found no evidence to recommend an alternative antibiotic. Although the scope of this guideline is for children, it seems reasonable to extrapolate the advice to older age groups.
2. 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> 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

1. Abrutyn E, Mossey J, Berlin JA, Boscia J, Levison M, Pitsakis P, Kaye D. Does asymptomatic bacteriuria predict mortality and does antimicrobial treatment reduce mortality in elderly ambulatory women? *Ann Int Med* 1994;**120**(10):827-33. A cohort study and a controlled trial found that bacteriuria was not an independent risk factor for mortality in elderly women without catheters, and that its treatment did not lower the mortality rate.
2. 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. Asymptomatic bacteriuria is seldom associated with adverse outcomes in people with indwelling catheters. Treatment of bacteriuria causes harms: increased short-term frequency of symptomatic infection, and re-infection with organisms of increased antimicrobial resistance.
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, septal defects, patent ductus, 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.

Uncomplicated 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 05.08.10. 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.
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.
3. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin no. 91: Treatment of urinary tract infections in non-pregnant women. *Obstetrics and Gynecology* 2008;**111**(3):785-794. Diagnosis in women: expert consensus is that it is reasonable to start empirical antibiotics in women with symptoms of UTI without urine culture.
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. Randomised 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. 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%).*
12. Falagas, M.E., Kotsantis, I.K., Vouloumanou, E.K. and Rafailidis, P.I. Antibiotics versus placebo in the treatment of women with uncomplicated cystitis: a meta-analysis of randomized controlled trials. *Journal of Infection* 2009;**58**(2):91-102. *Clinical cure for antibiotics compared with placebo: OR 4.67 (95% CI 2.34 to 9.35; four RCTs, n = 1062).*
13. Milo G, Katchman EA, Paul M, Christiaens T, Baerheim A, Leibovici L. Duration of antibacterial treatment for 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).
14. Newell A, Bunting P, Anson K, Fox E. Multicentre audit of the treatment of uncomplicated urinary tract infection in South Thames. *International Journal of STD & AIDS* 2005;**16**:74-77. *This audit of urine samples taken at presentation found that 43.3% of isolates were resistant to amoxicillin, 22.6% were resistant to trimethoprim, and 10.3% were resistant to nitrofurantoin.*
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.*
17. Falagas ME, Kastoris AC, Kapaskelis AM, Karageorgopoulos DE. Fosfomycin for the treatment of multidrug-resistant, including extended-spectrum beta-lactamase producing, Enterobacteriaceae infections: a systematic review. *Lancet Infect Dis* 2010;**10**:43-50. *Ninety seven per cent of ESBL-producing E coli isolates and 81% of Klebsiella pneumonia ESBL-producing isolates were susceptible to fosfomycin.*

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).

Advice to patient: As there is a delay in obtaining fosfomycin in the community, the patient should be advised to consult GP if symptoms worsen whilst awaiting supply.

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*. 2006 <http://www.sign.ac.uk/guidelines/fulltext/88/index.html> Accessed 05.08.10. *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.*
2. UKTIS. The treatment of infections in pregnancy. *The UK Teratology Information Service*. 2008. (Tel: 0844 892 0909, www.toxbase.org) Accessed 05.08.10. *Amoxicillin and cefalexin: The available data suggest that neither penicillins nor cephalosporins are associated with an increased risk of congenital malformations when used during pregnancy. Nitrofurantoin: significant placental transfer of nitrofurantoin does not occur. Nitrofurantoin has not been associated with an increased risk of congenital malformations. Nitrofurantoin has been associated with haemolysis in people with glucose-6-phosphate*

dyhydrogenase (G6PD) deficiency. However, the risk seems very small because placental transfer is so low. There is only one reported case of haemolytic anaemia in a newborn whose mother was treated at term with nitrofurantoin. Trimethoprim: trimethoprim is a folate antagonist. Folate supplementation during the first trimester reduces the risk of neural tube defects in offspring of pregnant women treated with trimethoprim. In women with normal folate status, who are well nourished, trimethoprim is unlikely to cause folate deficiency. However, it should not be used by women with established folate deficiency or low dietary folate intake, or by women taking other folate antagonists (e.g. antiepileptic drugs or proguanil).

3. Ruxton CHS and Derbyshire E. Women's diet quality in the UK. *Nutrition Bulletin* 2010;**35**:126-137. Data from the National Diet and Nutrition Surveys show that women's dietary intake of iron, vitamin D, calcium and folate remain below recommended levels.
4. The Health Protection Agency and the British Society for Antimicrobial Chemotherapy recommend that cefalexin is reserved for third-line use for the treatment of a UTI in a pregnant woman. Cefalexin has a good safety record in pregnancy. However, because it is a broad-spectrum antibiotic, it increases the risk of *Clostridium difficile*, and there have been recent reports of *C difficile* in pregnant women.
5. Rouphael NG, O'Donnell JA, Bhatnagar J, Lewis F, Polgreen PM, Beekman S, Guarner J, Killgore GE, Koffman B, Campbell J, Zaki SR, McDonald LC *Clostridium difficile*-associated diarrhoea: an emerging threat to pregnant women. *Am J Obs Gynaecol* 2008;**198**:e1-635.e6 In this series of 10 cases, most were associated with antibiotic use. Seven of the women were admitted to intensive care. Three infants were stillborn and 3 women died.
6. 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 7 days of antibiotics should be used to treat urinary tract infections during pregnancy.

Children

1. National collaborating centre for women's and children's health. NICE clinical guideline. *Urinary tract infection in children. Diagnosis, treatment and long-term management*. <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.
2. Hodson EM, Willis NS, Craig JC. Antibiotics for acute pyelonephritis. *Cochrane Database of Systematic Reviews* 2007. <http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD003772/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, ceftibuten 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, Sanfélix J, Gosalbes V, Perrota 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 19 RCTs of poor methodological quality calculated an NNT of 1.85 for nightly prophylaxis for 6–12 months. But adverse effects do occur and 30% of women did not adhere to treatment. Benefit 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.

GASTRO-INTESTINAL TRACT INFECTIONS

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.
2. Malfertheiner P, Megraud F, O'Morain C, Bazzoli F, El-Omar E, Graham D, Hunt R, Rokkas T, Vakil N, Kuiper EJ, The European Helicobacter Study Group (EHSg). Current concepts in the management of *Helicobacter pylori* infection: the Maastricht III Consensus Report. *Gut* 2007;**56**:772-781. MALToma: sixty two percent of patients with low grade gastric MALT lymphoma have complete remission after *H pylori* eradication within 12 months. Second-line treatment: bismuth-based quadruple therapy is a preferred option.
3. Moayyedi P, Soo S, Deeks JJ, Delaney B, Harris A, Innes M, Oakes R, Wilson S, Roalfe 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 resistance to metronidazole. Metronidazole resistance reduced efficacy by 18% while clarithromycin resistance was estimated to reduce efficacy by 35%. Clarithromycin resistance reduced the efficacy of a PPI + clarithromycin + amoxicillin by 66%.
6. Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. *BMJ* 2010;**340**:c2096 Individuals prescribed an antibiotic in primary care for a respiratory or urinary infection develop bacterial resistance to that antibiotic. The effect is greatest in the month immediately after treatment but may persist for up to 12 months.
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.
10. British National Formulary. 58th Edition. 2009. London: BMJ Group and RPS Publishing. Second-line therapy: expert opinion is that a 14-day course of quadruple therapy consisting of a PPI + bismuth + metronidazole + tetracycline can be used for eradication failure.

Infectious diarrhoea

1. The Griffin Report. Report of the Independent Investigation Committee June 2010. Review of the major outbreak of *E. coli* O157 in Surrey, 2009 An evaluation of the outbreak and its management, with a consideration of the regulatory framework and control of risks relating to open farms. 2010 www.griffininvestigation.org.uk Accessed 05.08.10.
2. Farthing M, Feldman R, Finch R, Fox R, Leen C, Mandal B, Moss P, Nathwani D, Nye F, Percival A, Read R, Ritchie L, Todd WT, Wood M. The management of infective gastroenteritis in adults. A consensus statement by the British Society for the Study of Infection. *J Infect* 1996;**33**:143-52. Empirical treatment for patients well enough to be managed in primary care is not recommended because the majority of illnesses seen in the community do not have an identifiable bacterial cause. In addition, an RCT of quinolones as empiric therapy found no benefit in patients whose stool cultures were negative.
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.
4. *E coli* O157 Independent Investigation Committee. Review of the major outbreak of *E coli* O157 in Surrey, 2009. <http://www.griffininvestigation.org.uk/> Accessed 05.08.10. The Griffin report recommends that *E coli* O157 should be suspected in any child presenting with bloody diarrhoea.

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.
3. Belmares J, Gerding DN, Parada JP, Miskevics S, Weaver F, Johnson S. Outcome of metronidazole therapy 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/yellowBookCh4-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 (Pepto-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.
3. de Bruyn, G., Hahn, S. and Borwick, A. Antibiotic treatment for travellers' diarrhoea. The Cochrane Library. Issue 3. 2000 John Wiley & Sons, Ltd. http://mrw.interscience.wiley.com/cochrane/cochrane_search_fs.html?products%3Dall&Query5%3D&Query4%3D&FromYear%3D&Query3%3D&Query2%3D&Query1%3DTravellers%2BDiarrhoea&ToYear%3D&mode%3Dstartsearch&zones5%3Dtables&zones4%3Dabstract&zones3%3Dauthor&zones2%3Darticle%2Dtitle&zones1%3D%2528article%2Dtitle%252Cabstract%252Ckeywords%2529&opt4%3DAND&opt3%3DAND&opt2%3DAND&unitstatus%3Dnone&opt1%3DOR& Accessed 05.08.10. Of 20 RCTs identified, ten RCTs evaluated short-courses of quinolones, three RCTs evaluated stat doses of quinolones, and one RCT evaluated azithromycin for travellers' diarrhoea.
4. Steffen R, Mathewson JJ, Ericsson CD, Du Pont HL, Helminger A, Balm TK, Wolff K, Witassek F. Traveller's diarrhoea in West Africa and Mexico: faecal transport systems and bismuth subsalicylate for self-therapy. *J Infect Dis* 1988;**157**(5):1008-13. A two-day treatment course of bismuth reduced the number of stools by 17% compared with placebo.

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

1. National Chlamydia Screening Programme <http://www.chlamydiaSCREENING.nhs.uk/ps/index.html> Accessed 05.08.10.
2. BASHH and MedFASH. Standards for the management of sexually transmitted infections (STIs). *British Association of Sexual Health and HIV and the Medical Foundation for AIDs and Sexual Health*. 2010. www.medfash.org.uk Accessed 05.08.10.

Chlamydia trachomatis

1. National Chlamydia Screening Programme <http://www.chlamydiaSCREENING.nhs.uk/ps/index.html> Accessed 05.08.10.
2. SIGN. Management of genital *Chlamydia trachomatis* infection: a national clinical guideline. *Scottish Intercollegiate Guidelines Network* 2009. <http://www.sign.ac.uk/guidelines/fulltext/109/index.html> Accessed 05.08.10. *Treatment of partners: the treatment*

of partners prior to resuming sexual intercourse is the strongest predictor for preventing re-infection. Treatment in pregnancy: expert opinion is that azithromycin 1g stat is the first-line treatment for Chlamydia in pregnant women. Although there are fewer safety data than for amoxicillin or erythromycin, the available data are reassuring, it is better tolerated and, because it is a single dose, there are no issues with compliance or early cessation of treatment because of adverse effects.

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.
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*. 2008. (Tel: 0844 892 0909, www.toxbase.org) Accessed 05.08.10. Azithromycin: there are fewer published data on the use of azithromycin during pregnancy and breastfeeding. The limited published data and follow-up data collected by the National Teratology Information Service do not demonstrate an increased risk of congenital malformations following exposure to azithromycin in human pregnancy. Erythromycin: data from more than 7000 pregnancies does not indicate that erythromycin is associated with an increased risk of congenital malformations or any other adverse fetal effects. A recent study has suggested a possible increased risk of cardiovascular malformations and pyloric stenosis; however, causality has not been established and the individual risk, if any, is thought to be low. 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.

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 intravaginal 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).
2. UKTIS. Use of fluconazole in pregnancy. *The UK Teratology Information Service*. 2008. (Tel: 0844 892 0909, www.toxbase.org) Accessed 05.08.10. Data on the outcomes of over 1,700 pregnancies exposed to low-dose fluconazole (150 mg stat) show no increased incidence of spontaneous abortions, malformations, or patterns 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 should be with an imidazole. However, fluconazole (150mg stat) 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).
4. Schaefer C, Peters P, Miller RK. Drugs during pregnancy and lactation: treatment options and risk assessment. Academic Press 2007. Clotrimazole and miconazole are the topical antifungals of choice during pregnancy. There is no evidence of an increased risk of spontaneous abortions or malformations with use of clotrimazole or miconazole during pregnancy.
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 5g 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/clsystrev/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) Accessed 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

1. BASHH. UK National Guideline on the Management of *Trichomonas vaginalis*. *British Association for Sexual Health and HIV*. 2007. <http://www.bashh.org/documents/87/87.pdf> Accessed 05.08.10. Treatment of partners: the recommendation to also treat partners for trichomoniasis, irrespective of the results of investigations is based on two prospective RCTs.
2. UKTIS. Use of metronidazole in pregnancy. *The UK Teratology Information Service*. 2008. (Tel: 0844 892 0909, www.toxbase.org) Accessed 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.
3. Du Bouchet I, Spence MR, Rein MF, Danzig MR, McCormack WM. Multicentre comparison of clotrimazole vaginal tablets, oral metronidazole, and vaginal suppositories containing sulphanilamide, aminacrine hydrochloride, and allantoin in the treatment of symptomatic trichomoniasis. *Sex Transm Dis* 1997;**24**:156-160. In 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/clsystrev/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). 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.

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/servlet/Satellite?c=Page&childpagename=HPAweb%2FPage%2FHPAwebAutoListName&cid=1153999752025&p=1153999752025&pagename=HPAwebWrapper&searchmode=simple&searchterm=grasp> Accessed 05.08.10. *Ciprofloxacin resistance is now endemic in England and Wales, accounting for 28% of all gonorrhoea isolates tested in 2008.*
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 step-wise 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*.

Acute prostatitis

1. BASHH. UK National Guidelines for the Management of Prostatitis. *British Association for Sexual Health and HIV*. 2008. 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 prostatic fluid levels ranged from 3.22 to 4.25 mcg/g).

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 Polymixin are reserved for use in areas where there are rising rates of resistance to fusidic acid. Polymixin (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. www.nice.org.uk 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.

Cellulitis

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. Buccal 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 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](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.
3. Health Protection Agency. Investigation of skin and superficial wound swabs. National Standard Method BSOP 11 Issue 3. http://www.hpa-standardmethods.org.uk/pdf_sops.asp. Accessed 05.08.10. Wound swabs should be taken from clinically infected ulcers before starting antibiotics. Taking swabs after starting antibiotics may affect the swab results. Sensitivity results can help guide the appropriate use of further antibiotics if the infection is not clinically improving on empirical treatment.

MRSA

1. Gould FK, Brindle R, Chadwick PR, Fraise AP, Hill S, Nathwani D, Ridgway GL, Spry MJ, Warren RE on behalf of the MRSA working party of the British Society for Antimicrobial Chemotherapy. Guidelines (2008) for the prophylaxis and treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) infections in the United Kingdom. *J Antimicrob Chemother* 2009;**63**:849-861. The BSAC recommends that, for non-hospitalized patients with cellulitis and confirmed MRSA, doxycycline or clindamycin monotherapy is recommended depending on susceptibility results, unless the infection is severe and/or carries a high risk of bacteraemia or endocarditis.
2. Nathwani D, Morgan M, Masteron RG, Dryden M, Cookson BD, French G, Deirdre Lewis on behalf of the British Society for Antimicrobial Chemotherapy. Guidelines for UK practice for the diagnosis and management of methicillin-resistant *Staphylococcus aureus* (MRSA) infections presenting in the community. *J Antimicrob Chemother* 2008;**61**:976-994. Community-acquired MRSA strains that are erythromycin-resistant are initially susceptible to clindamycin but can potentially develop resistance to clindamycin during therapy. The global reported rates of such inducible resistance vary from 2% to 94%. A double disc diffusion test (D-test) can be used to determine whether clindamycin-susceptible community-acquired MRSA strains harbour inducible resistance. The local laboratory should perform a D-test.

PVL *Staphylococcus aureus*

1. HPA. Guidance on the diagnosis and management of PVL-associated *Staphylococcus aureus* infections (PVL-SA) in England. 2nd Edition. 2008. <http://www.hpa.org.uk/HPA/Topics/InfectiousDiseases/InfectionsAZ/1207208304710> Accessed 05.08.10. *Expert opinion based on review of the literature and experiences of colleagues in the UK, Europe, the USA, and Canada.*

Bites (human or animal)

1. Health Protection Agency. Guidelines for the management of human bite injuries. Guidance for healthcare professionals on dealing with injuries where teeth break the skin. Health Protection Agency North West 2007. www.hpa.org.uk Accessed 05.08.10. *Gives guidance on initial wound assessment, wound care, and assessment of risk of tetanus and blood-borne viruses.*
2. CKS. Bites – human and animal. *Clinical Knowledge Summaries*. 2007. http://www.cks.nhs.uk/bites_human_and_animal Accessed 05.08.10. *Expert opinion is that prophylaxis for animal bites is not required unless bite to the hand, foot, and 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.*

Scabies

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 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.*
2. ABPI Medicines Compendium. Lyclear Dermal Cream. Datapharm Communications Ltd. 2008. <http://www.medicines.org.uk/EMC/medicine/10439/SPC/Lyclear+Dermal+Cream/> Accessed 05.08.10.

- 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> 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

- ABPI Medicines Compendium. Lamisil AT 1% cream. 2009. Datapharm Communications Ltd. <http://www.medicines.org.uk/EMC/searchresults.aspx?term=Lamisil&searchtype=QuickSearch> Accessed 05.08.10. *Terbinafine cream is not licensed for the treatment of Candida infection.*
- HPA and the Association of Medical Microbiologists. Fungal skin & nail infections: diagnosis & laboratory investigation. Quick reference guide for primary care for consultation and local adaptation. 2009 http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1240294785726 Accessed 05.08.10. *The recommendation to send skin scrapings to confirm the diagnosis before starting oral treatment is based on expert opinion and clinical experience.*
- 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/CD003584/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% 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*
- 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. <http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD001434/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 (for 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) Undecanoates: 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

- 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.*
- 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. The risk of having asymptomatic raised liver transaminases was less than 2% for all treatments. The risk of having raised liver transaminases that required treatment discontinuation with continuous treatment ranged from 0.11% (itraconazole 100mg/day) to 1.22% (fluconazole 50mg/day). The risk with pulse treatment ranged from 0.39% (itraconazole 400mg/day) to 0.85% (fluconazole 300-450mg/week).*
- 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.*
- 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.

Chickenpox/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/clsystrev/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 acyclovir 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).
5. Hope-Simpson RE. Postherpetic neuralgia. *Brit J Gen Pract* 1975;**25**:571-75. Study showing that incidence of post-herpetic neuralgia in a general practice population increases with age and is much more common in over 60 year olds.
6. Wood MJ, Shukla S, Fiddian AP, Crooks RJ. Treatment of acute herpes zoster: effect of early (<48 h) versus late (48-72 h) therapy with acyclovir and valaciclovir on prolonged pain. *J Infect Dis* 1998;**127**(Suppl 1):S81-S84. A study of two databases (n = 1076) found no difference in time to complete resolution of zoster-associated pain whether treatment was started within 48 hours or between 48 and 72 hours of the onset of cutaneous herpes zoster. Acyclovir HR 2.2, 95% CI 1.03 to 4.71. Valaciclovir HR 1.40, 95% CI 1.04 to 1.87.
7. Wood MJ, Kay R, Dworkin RH, Soong S-J, Whitley RJ. Oral acyclovir therapy accelerates pain resolution in patients with herpes zoster: A meta-analysis of placebo-controlled trials. *Clin Inf Dis* 1996;**22**:341-7. Meta-analysis of four RCTs (n = 691) found greatest benefit in those aged over 50 years, in whom pain resolved twice as fast with acyclovir compared with placebo. Oral acyclovir also reduced the incidence of post herpetic neuralgia pain.
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 that can occur following herpes zoster involving the trigeminal nerve. Aciclovir, famciclovir, and valaciclovir have all been shown to reduce the complications of ophthalmic shingles in RCTs.
9. Dworkin RH, Johnson JW, Bruer J et al. Recommendations for the management of Herpes Zoster. *Clin Infect Dis* 2007;**44**(Suppl 1):S1-S26. Expert opinion is that treatment of shingles should be considered for non-truncal involvement, people with moderate

or severe pain, or those with moderate or severe rash. Evidence from RCTs supports treatment for all those over 50 years to prevent the incidence of post-herpetic neuralgia.

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 Chemother* 1995;**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.
11. Shen MC, Lin HH, Lee SS, Chen YS, Chiang PC, Liu YC. Double-blind, randomized, acyclovir-controlled, parallel-group trial comparing the safety efficacy of famciclovir and acyclovir in patients with uncomplicated herpes zoster. *J Microbiol Immunol Infect* 2004;**37**:75-81. In this small study (n = 55), famciclovir and acyclovir were comparable in healing of lesions and cessation of acute-phase pain.

Cold sores

1. Sprurance SL, Nett R, Marbury T, Wolff R, Johnson J, Spaulding T. Acyclovir cream for the treatment of herpes labialis: results of two randomized, double-blind, vehicle-controlled, multicentre clinical trials. *Antimicrob Agents Chemother* 2002;**46**:2238-2243. Aciclovir 5% cream reduced the mean duration and pain of an episode by about half a day.
2. Sprurance SL, Rea TL, Thoming C, Tucker R, Saltzman R, Boon R. Penciclovir cream for the treatment of herpes simplex labialis. A randomized, double-blind, multicentre, placebo-controlled trial. *JAMA* 1997;**277**:1374-1379. Penciclovir 1% cream reduced the mean duration of cold sores by 0.7 days.
3. Raborn GW, Martel AY, Lassonde M, Lewis MA, Boon R, Sprurance SL. Effective treatment of herpes simplex labialis with penciclovir cream: combined results of two trials. *J Am Dent Assoc* 2002;**133**:303-309. Penciclovir reduced the mean duration of cold sores by 1 day.
4. Arduino PG and Porter SR. Oral and perioral herpes simplex type 1 (HSV-I) 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.
2. American Academy of Ophthalmology Corneal/External Disease Panel. Preferred Practice Pattern Guidelines. Conjunctivitis. American Academy of Ophthalmology. 2008. Diagnosis: this guideline contains a useful table of signs and symptoms for all causes of conjunctivitis.
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.*